

Visible Light Promoted Functionalisation of Carbon-Carbon Sigma Bonds

Jeremy Nugent, Carlos Arroniz, Bethany Shire, Alistair J. Sterling, Helena D. Pickford, Marie L. J. Wong, Steven J. Mansfield, Dimitri F. J. Caputo, Benjamin Owen, James J. Mousseau, Fernanda Duarte, Edward Anderson

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The use of visible light to activate transition metal catalysts towards redox processes has transformed the way organic molecules can be constructed. Promotion of an electron to an excited state enables the generation of organic radicals through electron transfer to or from the metal complex, with the resulting radicals primed for reactions such as addition to carbon-carbon pi bonds. Despite advances in photoredox catalysis which have led to the discovery of numerous such methods for bond construction, this mild approach to the generation of free radicals has not been applied to the functionalisation of carbon-carbon sigma bonds. Here we report the first such use of photoredox catalysis to promote the addition of organic halides to the caged carbocycle [1.1.1]propellane; the products of this process are bicyclo[1.1.1]pentanes (BCPs), motifs that are of high importance as bioisosteres in the pharmaceutical industry, and in materials applications. The methodology shows broad substrate scope and functional group tolerance, and is applicable to both sp^2 and sp^3 carbon-halogen bonds, while the use of substrates containing alkene acceptors enables the single-step construction of polycyclic bicyclopentane products through cyclisation cascades. Finally, the potential to accelerate drug discovery is demonstrated through examples of late-stage bicyclopentylation to access natural product- and drug-like molecules.

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Visible light promoted functionalisation of carbon–carbon sigma bonds

Jeremy Nugent,[#] Carlos Arroniz,[#] Bethany R. Shire, Alistair J. Sterling, Helena D. Pickford, Marie L. J. Wong, Steven J. Mansfield, Dimitri F. J. Caputo, Benjamin Owen, James J. Mousseau, Fernanda Duarte and Edward A. Anderson**

Abstract

The use of visible light to activate transition metal catalysts towards redox processes has transformed the way organic molecules can be constructed.¹ Promotion of an electron to an excited state enables the generation of organic radicals through electron transfer to or from the metal complex, with the resulting radicals primed for reactions such as addition to carbon–carbon pi bonds.^{2,3} Despite advances in photoredox catalysis which have led to the discovery of numerous such methods for bond construction, this mild approach to the generation of free radicals has not been applied to the functionalisation of carbon–carbon sigma bonds. Here we report the first such use of photoredox catalysis to promote the addition of organic halides to the caged carbocycle [1.1.1]propellane; the products of this process are bicyclo[1.1.1]pentanes (BCPs), motifs that are of high importance as bioisosteres in the pharmaceutical industry,^{4,5} and in materials applications.⁶ The methodology shows broad substrate scope and functional group tolerance, and is applicable to both sp^2 and sp^3 carbon–halogen bonds, while the use of substrates containing alkene acceptors enables the single-step construction of polycyclic bicyclopentane products through cyclisation cascades. Finally, the potential to accelerate drug discovery is demonstrated through examples of late-stage bicyclopentylation to access natural product- and drug-like molecules.

Main Text

The visible light activation of photocatalysts towards redox chemistry has become a fundamental tactic in contemporary organic synthesis.¹⁻³ Through metal-to-ligand charge transfer, excited state metal complexes can effect single electron transfer (SET) to activate organic molecules in a mild

and functional group tolerant manner. Among the many transformations possible using photoredox catalysis,^{2,3} the activation of carbon-halogen bonds offers an appealing entry to carbon-centred radicals, enabling processes such as additions to acceptor carbon-carbon pi bonds. The resultant radical species can be quenched reductively by hydrogen atom abstraction, or oxidatively by a radical-polar crossover pathway in which the photocatalyst is reduced, and the ensuing organic cation is captured by a counterion.⁷⁻¹¹ We questioned whether other types of acceptor functionality, specifically strained carbon-carbon sigma bonds, could serve as alkene surrogates in this photoredox atom transfer radical addition (ATRA) chemistry (Fig. 1a); despite the breadth of the field, no examples of such reactivity are known.

To test this hypothesis, we selected [1.1.1]propellane (**1**, tricyclo[1.1.1.0^{1,3}]pentane or 'TCP', Fig. 1a), the central carbon-carbon bond of which releases ~30 kcal mol⁻¹ of strain energy on conversion to bicyclo[1.1.1]pentane (BCP) products (**2**).¹² BCPs are the subject of intense interest in medicinal chemistry as useful surrogates for arene,^{5,13,14} *tert*-butyl¹⁵ and acetylene groups,¹⁶ imparting three-dimensionality and improved pharmacokinetic properties while maintaining substituent geometry compared to their parent motifs, and allowing the exploration of new regions of chemical space (Fig. 1b).⁴ The ring-opening of TCP has been widely used as a route to BCPs,^{6,17-19} however the synthesis of carbon-substituted variants typically requires harsh reaction conditions such as heating with organometallic reagents,^{16,20} or high-pressure mercury lamp irradiation.²¹ In previous work, we described the triethylborane-initiated ATRA of alkyl halides with TCP,²² chemistry that proceeds under mild reaction conditions, but where only relatively activated alkyl iodides gave consistently high yields. We recognised that photoredox catalysis could permit activation of a much wider range of substrates, enabling the synthesis of BCP-containing compounds that has not been possible to date. The BCP halide products are poised for further functionalisation,^{16,21-24} enabling applications in pharmaceutical and agrochemical research. Here we describe the realisation of photoredox-catalysed atom transfer radical addition of organic halides with TCP, including applications to drug-

like molecules, which represent the first examples of photoredox catalysis in carbon–carbon sigma bond activation. We also report the development of cascade ATRA processes, which are without precedent in either strain-relief or photoredox chemistry.

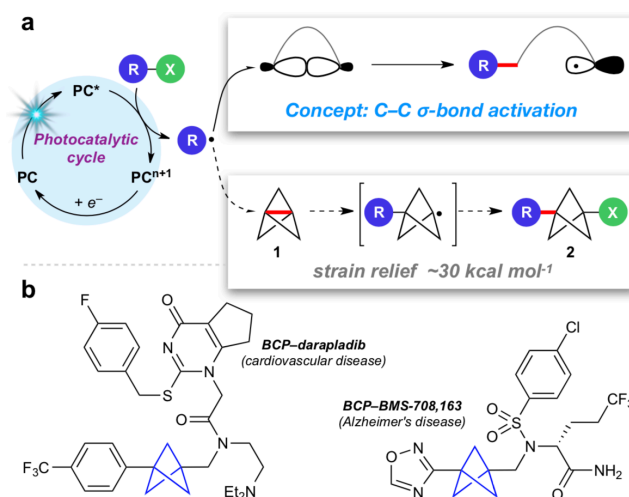


Fig. 1. **a**, Photoredox-catalysed carbon–carbon sigma bond functionalisation. **b**, Examples of bicyclo[1.1.1]pentane (BCP) drug analogues.

Benzyl iodide, a challenging substrate in our previous work,²² was selected as a test substrate (Fig. 2a). A range of photocatalysts were found to be effective in this transformation (see the Supplementary Information for full details), from which *fac*-Ir(ppy)₃ (2.5 mol%) under blue LED irradiation emerged as a suitable and readily available catalyst, with only trace product seen in the absence of catalyst or light. Pivalonitrile proved a superior solvent,²⁵ with low yields observed in more polar media. Two equivalents of TCP gave optimal conversion; incomplete conversion was observed below this loading, and lower yields due to the formation of 'staffane' oligomers when above. This optimised combination delivered bicyclopentane **3** in 87% yield.

These conditions enabled the installation of the BCP motif in a wide variety of substrates, with excellent functional group tolerance (Fig. 2b). Benzylic and heterobenzylic iodides delivered ATRA products in good yields (**3–19**, 51–93%), as did iodides or bromides adjacent to electron-

withdrawing groups (**20–37**, 44–99%). The high yield of aldehyde **23** (72%) underlines the mild nature of the reaction conditions compared with the use of triethylborane (38%).²² Unactivated primary and secondary alkyl iodides also afforded BCPs in excellent yields (**38–46**, 68–99%); notable examples include amines **44** and **45**, a substrate class that is unreactive under

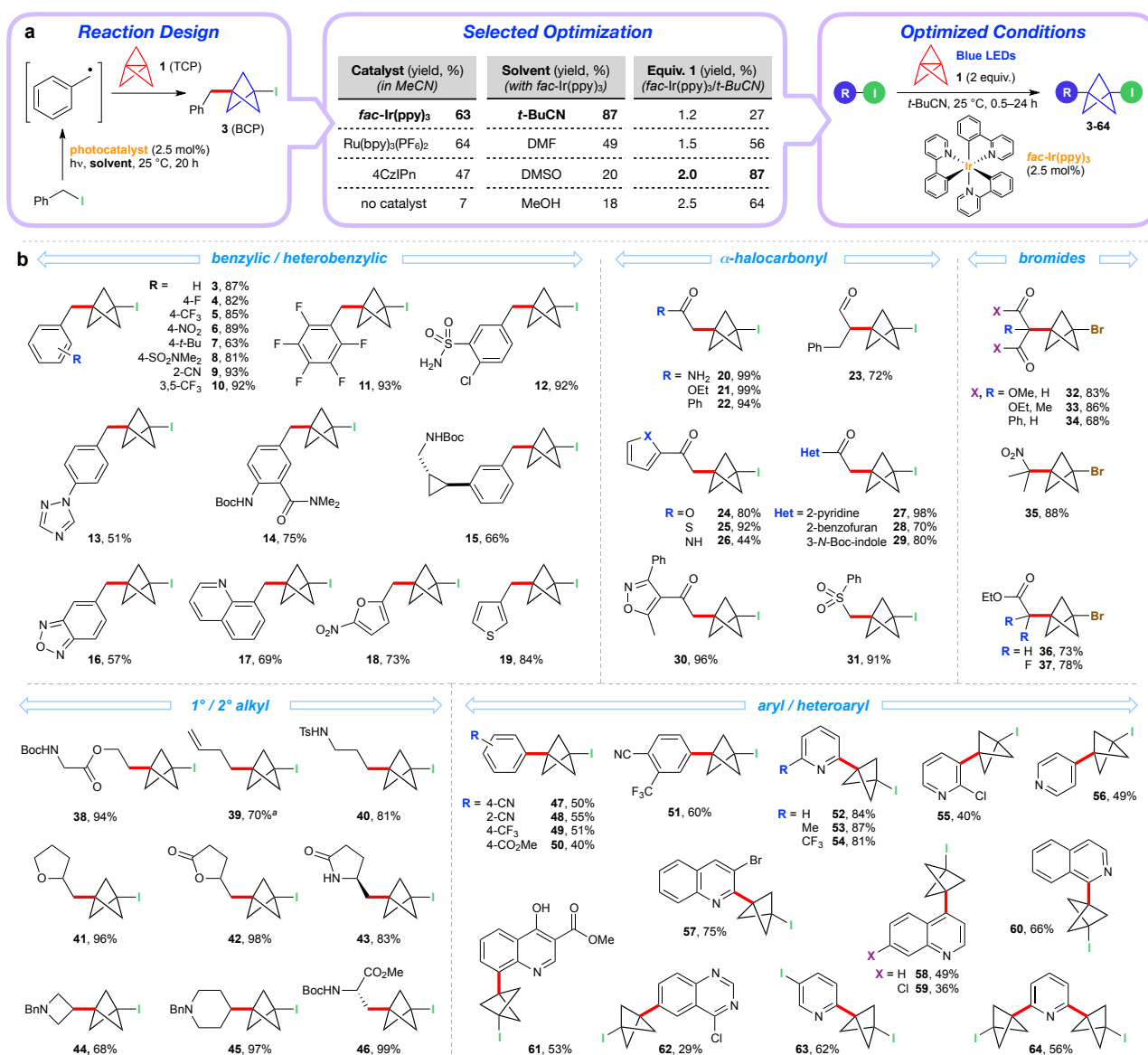


Fig. 2. Visible light-mediated photoredox ATRA of alkyl and (hetero)aryl iodides with tricyclo[1.1.1.0^{1,3}]pentane (TCP, **1**) to prepare C-substituted BCPs. **a**, Optimisation using benzyl iodide identifies *fac*-Ir(ppy)₃ in t-BuCN as a suitable reaction system. **b**, Substrate scope encompassing (hetero)benzylic, electron-deficient, alkyl and (hetero)aryl substrates. See the Supplementary Information for specific reaction times. ^a From cyclopropylmethyl iodide.

triethylborane initiation, and the near-quantitative yield of the BCP-phenylalanine analogue **46** on both 0.15 mmol (99%) and 1.5 mmol (85%, 1 mol% Ir(ppy)₃) scale.

A limitation of previous radical-based approaches to carbon-substituted BCPs has been the poor reactivity of aryl or heteroaryl iodides. This photoredox-promoted ATRA also uniquely accommodated these challenging substrates, delivering valuable (hetero)arylated BCPs **47–64** in moderate to high yields (29–87%). The flexibility of this chemistry is illustrated by the functionalisation of three different positions on the pyridine ring (**52–56**), as well as application to quinoline, isoquinoline and pyrimidine heteroaromatics. Particularly notable are the selective mono-ATRA reaction of 2,5-diiodopyridine (**63**, 62%), and the double bicyclopentylation of 2,6-diiodopyridine (**64**, 56%).

Reactions that form one or more rings in the course of the atom transfer process can occur when the substrate contains acceptor motifs such as alkenes. We questioned whether photoredox-generated radicals could undergo such cyclisation processes prior to interception by TCP – a tandem atom transfer radical cyclisation (ATRC) / bicyclopentylation reaction that would access densely functionalised bicyclopentanes in a single step. Most photoredox-promoted cyclisations proceed in a reductive fashion,²⁶⁻²⁸ and of the few photoredox ATRCs known,^{10,25,29} no two-component processes have been reported. Challenges to this transformation include premature capture of the initially formed radical by TCP pre-cyclisation, or iodine atom abstraction post-cyclisation instead of reaction with TCP, or interruption of the cascade by a catalyst quenching process.

Fig. 3a shows the results of this investigation. Under equivalent conditions, tetrahydrofuran, pyrrolidine and cyclopentane BCPs were formed in excellent yields (**65–73**, 60–98%), with no products of direct addition of the initially formed radical to TCP observed. In many cases, these reactions were accompanied by installation of a stereocentre, which proceeded with selectivities up

to 11:1.³⁰ Bicyclic products could be accessed from cyclic iodides, such as fused heterocycles **74–76** (68–77%) which were formed as single isomers at the new stereocentres. Unusual BCP spirocycles **77–79** were prepared by cyclisation of the indicated precursors (67–79%), and finally a polycyclisation to the angular triquinane **80** was achieved in 72% yield (9:1 dr), where two C–C bonds are forged prior to radical capture by TCP. Notably, such highly functionalised BCP-containing compounds are currently inaccessible by other means.

The potential of this bicyclopentylation to operate in settings relevant to medicinal chemistry research was demonstrated through late-stage diversification of various biomolecules and drug-like compounds (Fig. 3b). An exceptional tolerance of functional groups was observed, with BCP derivatives isolated in excellent yields. Serine-derived iodides were efficiently transformed to BCP dipeptides (**81** and **82**), the latter being a phenylalanine analogue of aspartame. BCP nucleoside **83** was derived in two steps from cyclouridine, without the need for any protecting groups. High facial selectivity was observed in this process, and in the C-glycosylation in glucose derivative **84**. BCP steroids **85** and **86** were obtained from corticosterone and epiandrosterone respectively, with **86** being formed as a single diastereomer due to pyramidalisation of the intermediate radical. Most pleasing were the successful functionalisations of iodides derived from pharmaceuticals and agrochemicals (**87–92**), including metronidazole (antibiotic and antiprotozoal agent), penicillin G (antibiotic), pretilachlor (pesticide), indomethacin (NSAID) and telmisartan (angiotensin II receptor antagonist).

Further transformations of the iodo-BCP products were briefly explored (Fig. 3c). Reduction of the C–I bond in **88** delivered the BCP penicillin G analogue **93**, while lithiation of piperidine adduct **45** followed by cross-coupling¹⁶ afforded the bis-heterocycle-substituted BCP **94**. Lithiation of **49** and electrophilic trapping with CO₂ gave acid **95**, the two step synthesis of which compares favourably with the seven step approach reported in work towards a darapladib analogue.¹³ Finally, the

potential of the iodo-BCP framework to serve as a precursor to other useful functionalities was demonstrated by the Ag(I)-promoted iodide abstraction / rearrangement / cyclisation to spirocyclic cyclobutane-pyrrolidine **96**.

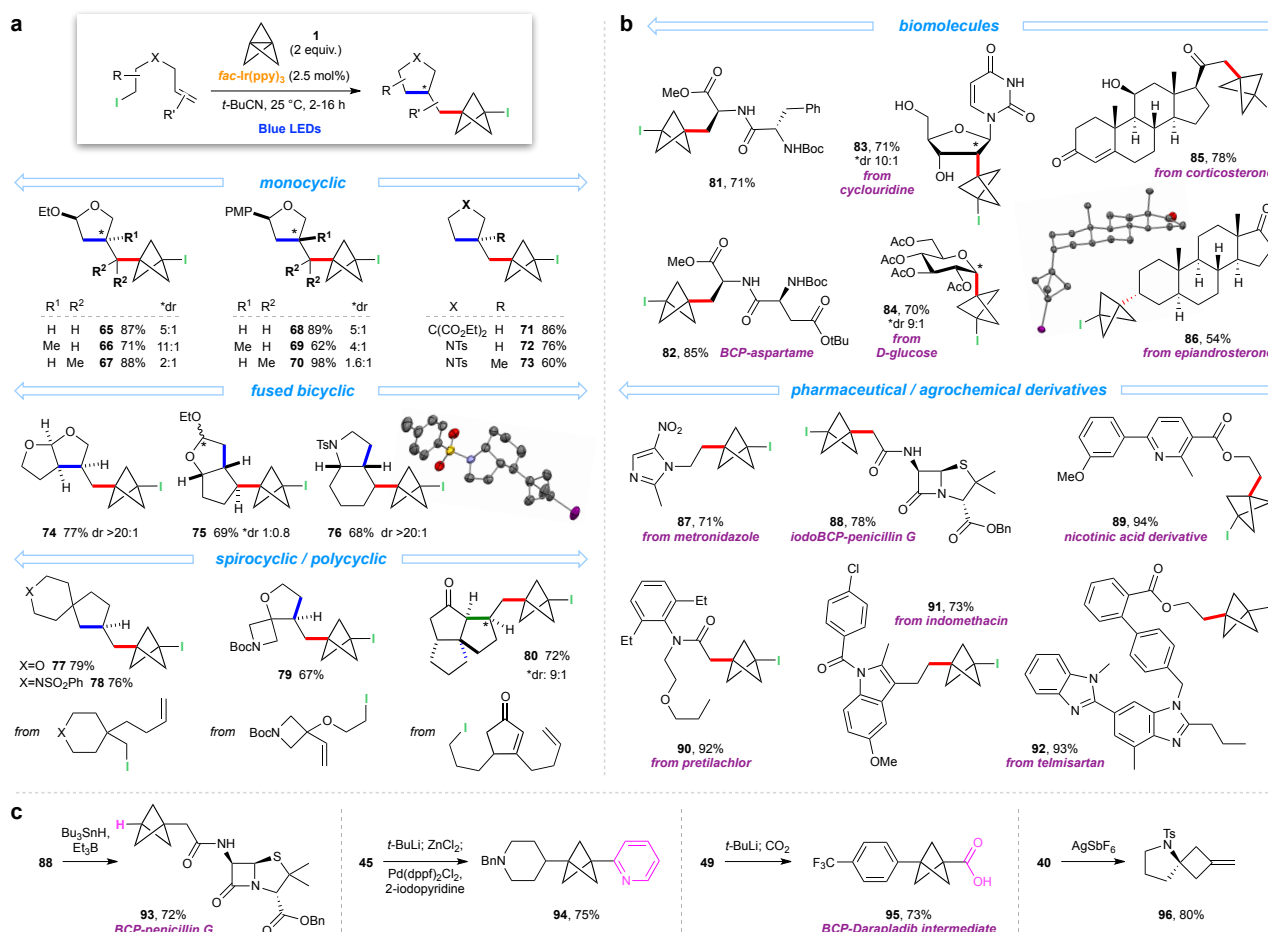


Fig. 3. a, Atom transfer radical cyclisation reactions to form mono, bi- and polycyclic BCP products. Blue and green bonds show the initial cyclisation process, red bonds show the capture of the cyclised radicals by TCP. **b**, Bicyclopentylations of peptides, sugars, nucleosides, steroids, pharmaceuticals and agrochemicals proceed in excellent yields via iodination / ATRA sequences. **c**, Further product transformations.

The mechanism of this strain-release ATRA is proposed to commence with outer-sphere SET from the excited state Ir(III) complex **A** to the halide substrate (Fig. 4a, $E^\circ(\text{Ir}^{4+}/\text{Ir}^{3+*}) = -1.73 \text{ V vs SCE}$). This results in reductive cleavage of the carbon-halogen bond to give radical **B**, which effects

strain-relief ring opening of TCP to give bicyclopentyl radical **C** (Fig. 4b). This intermediate can either undergo propagation (Path **a**) to form the product BCP **D** and regenerate the chain carrier **B**, or it can effect oxidative quenching of the Ir(IV) complex to regenerate the Ir(III) catalyst (Path **b**, $E^\circ(\text{Ir}^{4+}/\text{Ir}^{3+}) = +0.77 \text{ V vs SCE}$) and form bicyclopentyl cation **E**. DFT calculations using the example substrate 4-iodopyridine (Fig. 4b) show strain-relieving addition of pyridyl radical **B** to TCP ($\Delta G = -26.4 \text{ kcal mol}^{-1}$), followed by rate-limiting propagation (TS2, $\Delta G^\ddagger = 11.8 \text{ kcal mol}^{-1}$) via iodine atom abstraction from iodopyridine to complete the ATRA process (**56**). This pathway is in competition with polar crossover via oxidation of BCP radical **C**, which is predicted to result in

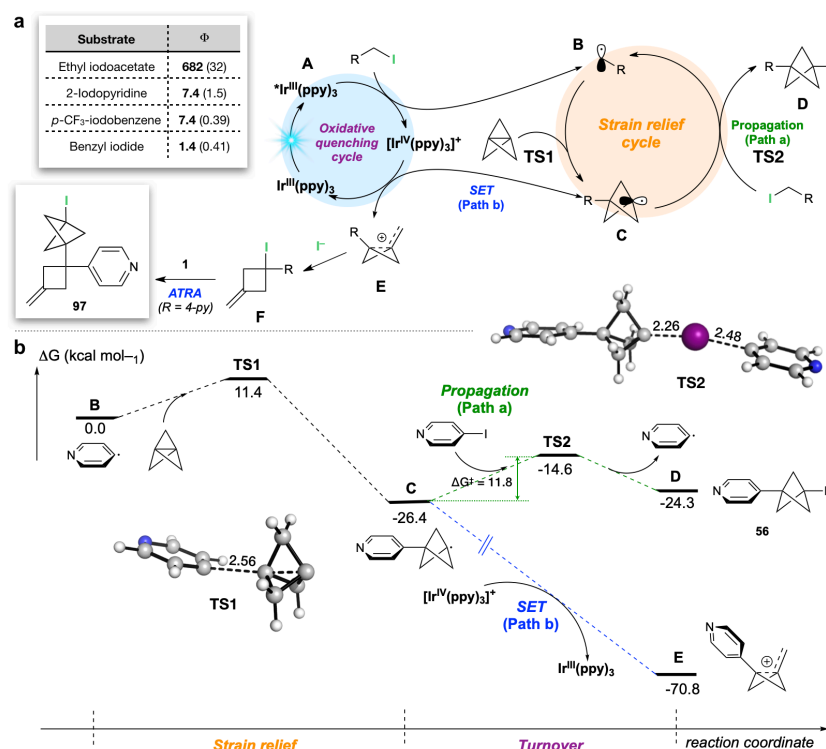


Fig. 4. a, The proposed reaction pathway for the ATRA balances propagation (Path **a**) with oxidative quenching (Path **b**), as illustrated by quantum yield measurements. **b**, Free energy profile calculated at the SMD(MeCN)-RI-B2PLYP-D3BJ/def2-QZVPP//SMD(MeCN)-RI-B2PLYP/def2-TZVP level of theory for 4-iodopyridine shows that the regeneration of Ir(III) via SET by BCP radical **C** can enable turnover of the catalytic cycle. The isolation of **97** supports this mechanistic hypothesis. Bond lengths are reported in Å.

substantial strain-relief ($E_{\text{cell}} = +1.92$ V, $\Delta G = -44.4$ kcal mol⁻¹, see Supplementary Information for a detailed discussion of redox calculations). The resultant non-classical bicyclopentyl cation **E** can then be intercepted by iodide, affording cyclobutyl iodide **F**, a rearrangement that is analogous to the cationic pathway for formation of **96** (Fig. 3c). Direct experimental support for this proposed sequence of events was found in the observation of small amounts of cyclobutyl BCP iodide **97**, which presumably arises from a further ATRA reaction of the cyclobutyl iodide **F** (R = pyridine).

Measurement of quantum yields for a selection of substrates provided further mechanistic insight (Fig. 4a). For ethyl iodoacetate, a quantum yield of 682 indicates a predominant propagation pathway to product **21**. However, values of 7.4 for 2-iodopyridine and *p*-CF₃-iodobenzene, and 1.4 for benzyl iodide, reveal inefficient propagation and significant catalyst turnover, consistent with these substrates being poorly reactive (or unreactive) under triethylborane-initiated ATRA.

In conclusion, we have established a new class of photoredox reactivity through the activation of carbon–carbon sigma bonds by photocatalyst-generated radicals, which enables the bicyclopentylation of *sp*² and *sp*³ carbon–halogen bonds under mild reaction conditions. We also demonstrate the first examples of cascade atom-transfer radical cyclisation reactions, where TCP acts as an efficient intermolecular trap following ring-forming processes. Together with the late-stage derivatisation of biologically-relevant compounds and broad functional group tolerance, this chemistry generates bicyclopentanes that are not accessible by other routes. Given the interest in these motifs as building blocks in medicinal chemistry, agrochemistry, and materials research, this chemistry has the potential for widespread applications.

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Author Contributions

#These authors contributed equally to this work.

E.A.A., C.A., J.J.M. and J.N. conceived the work. E.A.A., J.N., C.A., J.J.M., B.R.S., A.J.S., H.D.P. and M.L.J.W. designed the experiments and analysed the data. J.N., C.A., B.R.S., H.D.P., A.J.S., M.L.J.W. and J.J.M. performed the experiments. D.F.J.C. and B.O. prepared a selection of substrates. A.J.S. and F.D. designed and performed the DFT calculations. S.J.M. solved the crystal structures. E.A.A., J.N. and A.J.S. wrote and edited the manuscript. M.L.J.W., H.D.P., B.R.S., C.A., F.D. and J.J.M. assisted in editing the manuscript.

Competing Interests

The authors declare no competing interests.

Methods

General Procedure for the visible light-promoted atom transfer radical addition of halides to tricyclo[1.1.1.0^{1,3}]pentane.

To a screw-capped vial equipped with a stirrer bar was added *fac*-Ir(ppy)₃ (2.5 mg, 0.025 equiv.), the specified halide (0.15 mmol, 1.0 equiv.), *t*-BuCN (1.5 mL) and tricyclo[1.1.1.0^{1,3}]pentane (2.0 equiv., 0.5–0.7 M solution in Et₂O). The vial was sealed with a PTFE septum cap and placed under argon, and the solution was degassed *via* three freeze-pump-thaw cycles (vacuum was only applied while the reaction mixture was frozen due to TCP volatility). The stirred mixture was irradiated with blue LEDs for the indicated time. The reaction mixture was concentrated, and the residue was purified by column chromatography.

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Visible light promoted functionalisation of carbon–carbon sigma bonds

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1. General Experimental Considerations

NMR Spectroscopy: ^1H , ^{13}C and ^{19}F NMR spectra were recorded on Bruker AV400 or Bruker AVII500 spectrometers using TOPSPIN software, with the deuterated solvent acting as the internal deuterium lock. ^1H NMR spectra were recorded at 400 or 500 MHz, ^{13}C NMR spectra were recorded at 101 or 126 MHz with ^1H decoupling, and ^{19}F NMR spectra were recorded at 376 or 470 MHz. Assignments were determined either on the basis of unambiguous chemical shift / coupling patterns, or from 2D COSY, HMBC, HSQC and / or NOESY experiments. Peak multiplicities are defined as: s = singlet, d = doublet, t = triplet, q = quartet, quin. = quintet, m = multiplet, br. = broad, app. = apparent; coupling constants (J) are reported to the nearest 0.1 Hz.

Infrared Spectroscopy: Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer with the sample being prepared as a thin film on a diamond ATR module. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm^{-1}).

High Resolution Mass Spectrometry: Mass Spectrometry: Low resolution mass spectra were recorded on a Micromass LCT Premier Open Access using electrospray ionisation (ESI). Accurate mass (HRMS) data was determined under conditions of ESI, EI and CI on a Bruker MicroTOF. High resolution values are calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Melting Points: Melting points were obtained using a Griffin melting point apparatus and are uncorrected.

Polarimetry: Optical rotations were recorded on a Perkin Elmer 241 or 341 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). $[\alpha]_{\text{D}}$ are reported in units of $10^{-1} \text{ deg dm}^2 \text{ g}^{-1}$. Concentrations (c) are reported in g/100 mL. Temperatures are reported in $^{\circ}\text{C}$.

Reagents, solvents and techniques: All reagents were used directly as supplied. Solvents were either used as commercially supplied, or as purified by standard techniques. Anhydrous Et_2O , CH_2Cl_2 and toluene were obtained from solvent dispenser units having been passed through an activated alumina column under argon. Unless otherwise stated, non-aqueous reactions were performed using flame-dried glassware under an argon atmosphere.

Reactions were monitored by thin layer chromatography on pre-coated aluminium-backed plates (Merck Kieselgel 60 with fluorescent indicator UV254). Spots were visualised by quenching of UV fluorescence or by staining with potassium permanganate or vanillin, and

retention factors are reported with the solvent system in parentheses. Flash column chromatography was performed on silica gel obtained from Merck (Silica gel Si 60, 0.040-0.063 mm) under a positive pressure of nitrogen, using the stated solvent system.

2. General Procedures

General Procedure 1: Visible light-promoted atom-transfer radical addition of halides to tricyclo[1.1.1.0^{1,3}]pentane.

To a screw-capped vial equipped with a stirrer bar was added *fac*-Ir(ppy)₃ (2.5 mg, 4.0 μmol, 0.025 equiv.), the specified halide (0.15 mmol, 1.0 equiv.), *t*-BuCN (1.5 mL) and tricyclo[1.1.1.0^{1,3}]pentane (2.0 equiv., 0.5–0.7 M solution in Et₂O). The vial was sealed and placed under argon, and the solution was degassed *via* three freeze-pump-thaw cycles (vacuum was only applied while the reaction mixture was frozen due to TCP volatility). The stirred mixture was irradiated with blue LEDs (see Section 4 for experimental setup) for the indicated time. The reaction mixture was concentrated, and the residue was purified by column chromatography.

General Procedure 2: Iodination via Appel reaction.

To a solution of triphenylphosphine (1.5 equiv.) and imidazole (1.5 equiv.) in CH₂Cl₂ at 0 °C was added iodine (1.5 equiv.). The reaction mixture was stirred at 0 °C for 0.5 h. The specified alcohol (1.0 equiv.) was added and the reaction was warmed to room temperature and stirred for 16 h. The reaction was quenched with MeOH (0.2 mL), diluted with water, and the aqueous phase was extracted with CH₂Cl₂. The combined organics were washed with Na₂S₂O₃ (10% aq.) and brine, dried (MgSO₄) and concentrated *in vacuo*. The residue was purified by column chromatography.

General Procedure 3: Iodination via Appel reaction – inverse addition.

To a solution of the specified alcohol (1.0 equiv.) in CH₂Cl₂ at room temperature was added triphenylphosphine (1.3 equiv.) and imidazole (1.5 equiv.). The resulting mixture was cooled to 0 °C and iodine (1.2 equiv.) was added portionwise. The reaction mixture was then left to stir overnight at room temperature, after which, the reaction mixture was poured into water. The phases were separated and the aqueous phase was extracted with Et₂O. The combined organic extracts were dried (Na₂SO₄), filtered and concentrated *in vacuo*. The residue was purified by column chromatography.

General Procedure 4: Iodination via Finkelstein reaction.

See individual procedures for equivalents and concentration.

To a solution of the specified alkyl halide or mesylate (1.0 equiv.) in acetone was added sodium iodide (1.5-5.0 equiv.). The resulting mixture was maintained at the indicated temperature until complete as judged by ^1H NMR spectrum of a reaction aliquot. The mixture was concentrated *in vacuo*, then water and CH_2Cl_2 were added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were washed with $\text{Na}_2\text{S}_2\text{O}_3$ (10% aq.) and brine, dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by column chromatography.

General Procedure 5: Iodination via Iodoetherification reaction.

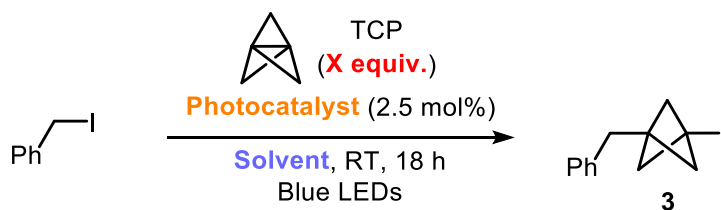
See individual procedures for equivalents and concentration.

A solution of the specified alcohol and alkene in CH_2Cl_2 was cooled to 0 °C and treated with *N*-iodosuccinimide. The resulting mixture was stirred at room temperature for 16 h, then quenched by treatment with $\text{Na}_2\text{S}_2\text{O}_3$ (10% aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 , dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by column chromatography.

General procedure 6: Copper oxide mediated iodination.

To a solution of the specified methyl ketone (1.0 equiv.) in methanol were added CuO (1.0 equiv.) and iodine (1.0 equiv.). The reaction mixture was stirred for 5 min, then refluxed for 2-3 h, and then concentrated *in vacuo*. The residue was taken up in EtOAc, filtered, and the organic filtrate was washed with $\text{Na}_2\text{S}_2\text{O}_3$ (10% aq.), dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by column chromatography.

3. Optimisation Studies



	Photocatalyst	Solvent	TCP equiv.	3 (%) ^a	3 : SM ^b
Catalyst	Ir[(dF(CF ₃)ppy) ₂ (5',5'-d(CF ₃)bpy)] PF ₆	MeCN	2.0	73%	-
	<i>fac</i> -Ir(ppy) ₃	MeCN	2.0	63%	-
	Ir[(3,4'-dMeppy) ₂ (dtbbpy)] PF ₆	MeCN	2.0	60%	-
	Ir[(dF(CF ₃)ppy) ₂ (bpy)] PF ₆	MeCN	2.0	65%	-
	Ir(4'-Fppy) ₃	MeCN	2.0	61%	-
	Ir(2',4'-Fppy) ₃	MeCN	2.0	62%	1.00 : 0.14
	Ru(bpy) ₃ (PF ₆) ₂	MeCN	2.0	64%	-
	Ru(d(Me)bpy) ₂ (PF ₆) ₂	MeCN	2.0	46%	1.00 : 0.40
	[Ir(ppy) ₂ (bpy)]PF ₆	MeCN	2.0	59%	-
	Ir(4'-CF ₃ ppy) ₃	MeCN	2.0	37%	-
	4CzIPz (5 mol%)	MeCN	2.0	47%	-
	Rhodamine B (5 mol%), Green LEDs	MeCN	2.0	0% ^c	1.00 : 1.03
	<i>p</i> -Anisaldehyde (20 mol%), White LEDs	MeCN	2.0	31% ^c	1.00 : 0.93
	None	MeCN	2.0	7% ^c	1.00 : 9.94
	<i>fac</i> -Ir(ppy) ₃ , Dark	MeCN	2.0	0%	-
Solvent	<i>fac</i> -Ir(ppy) ₃	DMF	2.0	49% ^c	-
	<i>fac</i> -Ir(ppy) ₃	MeOH	2.0	18% ^c	1.00 : 2.58
	<i>fac</i> -Ir(ppy) ₃	DMSO	2.0	20% ^c	-
	<i>fac</i>-Ir(ppy)₃	<i>t</i>-BuCN	2.0	87%	-
	Ir[(dF(CF ₃)ppy) ₂ (5',5'-d(CF ₃)bpy)] PF ₆	<i>t</i> -BuCN	2.0	66%	-
TCP	<i>fac</i> -Ir(ppy) ₃	<i>t</i> -BuCN	1.2	27%	1.00 : 0.77
	<i>fac</i> -Ir(ppy) ₃	<i>t</i> -BuCN	1.5	56%	1.00 : 0.14
	<i>fac</i> -Ir(ppy) ₃	<i>t</i> -BuCN	2.5	64%	-

Table 1: Reaction optimisation. ^a Isolated yield unless stated otherwise; ^b Ratio of product to starting material, calculated from integration of ¹H NMR spectra of the crude reaction mixture; ^c Yield calculated from integration of ¹H NMR spectra of the crude reaction mixture using mesitylene as an internal standard.

4. Photochemical Equipment and Setup

Two Blue LED lamps were used for this work:

- a) Tingkam® Waterproof 5M 5050 SMD RGB Led Strips, fixed to the inside of a crystallisation dish (left).
- b) Evoluchem™ 455 nm 18W LED, placed in an Evoluchem™ PhotoRedOx box (right).

For most substrates, full conversion was achieved using the LED strips (set up **a**). For substrates that did not reach completion over 20 h, more powerful set up **b** was required (PhotoRedOx box). For example, **S58** gave only 20% conversion to product **87** using set up **a** (using 2.0 equiv. of TCP) but conversion increased to 71% under set up **b**, under otherwise identical conditions. Using this set up, 3.0 equiv. of TCP was required for full conversion.



Left: Set up **a**: Tingkam® Waterproof 5M 5050 SMD RGB LED Strips fixed to the inside of a crystallisation dish.

Right: Set up **b**: Evoluchem™ 455 nm 18W LED placed in an Evoluchem™ PhotoRedOx box.

5. Experimental Procedures

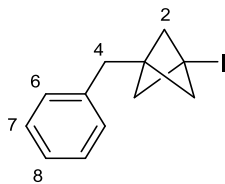
Tricyclo[1.1.1.0^{1,3}]pentane (TCP), 1



To a flame-dried round-bottom flask equipped with a stirrer bar was added 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane (5.0 g, 16.9 mmol, 1.0 equiv.). The reaction vessel was evacuated and back-filled with argon three times, and then anhydrous Et₂O (10 mL) was added. The reaction vessel was cooled to −45 °C (dry ice / isopropanol bath). Phenyllithium (17.8 mL, 1.9 M in Bu₂O, 33.7 mmol, 2.0 equiv.) was added dropwise over 15 min at −45 °C, and the resulting mixture was stirred for 15 min at −45 °C. The cooling bath was replaced with an ice bath, and the reaction mixture was warmed to 0 °C, and then stirred at this temperature for 2 h. The mixture was then distilled at room temperature (10 mbar) using a rotary evaporator, the receiving flask of which was immersed in a dry ice / acetone bath. The TCP-containing distillate (10 mL, TCP concentration 0.91 M in Et₂O, 54%) was transferred to a flame-dried septum-sealed bottle under an inert atmosphere, and stored at −20 °C. The yield was determined by ¹H NMR spectroscopy with 1,2-dichloroethane as an internal standard. The concentration of the TCP solution ranged between 0.51 M and 1.10 M, with yields of 45-61%.

a. Synthesis of BCP Analogues

1-Benzyl-3-iodobicyclo[1.1.1]pentane, **3**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), (iodomethyl)benzene (33 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane) afforded **3** (37 mg, 0.13 mmol, 87%) as a pale yellow solid.

R_f = 0.48 (pentane)

m.p. = 45-47 °C

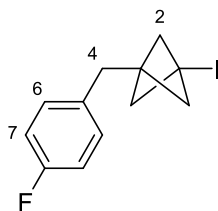
¹H NMR (400 MHz, CDCl₃) δ 7.29-7.17 (3H, m, ArH), 7.06-7.00 (2H, m, ArH), 2.78 (2H, s, H₄), 2.13 (6H, s, H₂).

¹³C NMR (101 MHz, CDCl₃) δ 138.3, 128.9, 128.5, 126.4, 60.4, 48.4, 39.3, 8.5.

HRMS (EI⁺) Found [M-I]⁺ = 157.1017; C₁₂H₁₃ requires 157.1012.

IR (film) ν_{max}/cm⁻¹ 2910, 1181, 842, 745.

1-(4-Fluorobenzyl)-3-iodobicyclo[1.1.1]pentane, **4**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S1** (35 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane) afforded **4** (37 mg, 0.12 mmol, 82%) as a pale yellow solid.

R_f = 0.44 (pentane)

m.p. = 43-45 °C

¹H NMR (400 MHz, CDCl₃) δ 7.03-6.94 (4H, m, H₆, H₇), 2.78 (2H, s, H₄), 2.14 (6H, s, H₂).

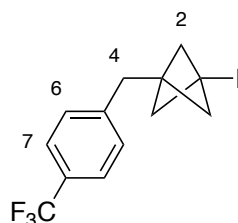
¹³C NMR (101 MHz, CDCl₃) δ 161.7 (d, *J* = 244.3 Hz), 134.0 (d, *J* = 3.2 Hz), 130.2 (d, *J* = 7.9 Hz), 115.4 (d, *J* = 21.3 Hz), 60.3, 48.3 (d, *J* = 1.6 Hz), 38.5, 8.2.

^{19}F NMR (376 MHz, CDCl_3) δ -116.9.

HRMS (EI^+) Found $[\text{M}-\text{I}]^+ = 175.0910$; $\text{C}_{12}\text{H}_{12}\text{F}$ requires 175.0918.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2990, 1509, 1172, 841.

1-Iodo-3-(4-(trifluoromethyl)benzyl)bicyclo[1.1.1]pentane, **5**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), 1-(iodomethyl)-4-(trifluoromethyl)benzene¹ (43 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane) afforded **5** (45 mg, 0.13 mmol, 85%) as white solid.

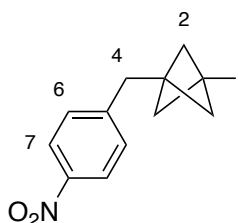
R_f = 0.48 (pentane)

^1H NMR (400 MHz, CDCl_3) δ 7.55 (2H, d, J = 8.0 Hz, H7), 7.17 (2H, d, J = 8.0 Hz, H6), 2.87 (2H, s, H4), 2.16 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl_3) δ 142.4, 129.2, 129.0 (q, J = 33.3 Hz), 125.5 (q, J = 3.8 Hz), 124.4 (q, J = 271.8 Hz), 60.3, 47.9, 39.1, 7.6.

Spectroscopic data in agreement with that reported previously.¹

1-Iodo-3-(4-nitrobenzyl)bicyclo[1.1.1]pentane, **6**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), 1-(iodomethyl)-4-nitrobenzene¹ (40 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 95:5) afforded **6** (44 mg, 0.13 mmol, 89%) as a white solid.

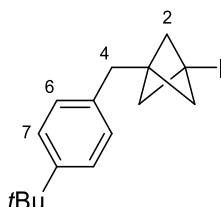
R_f = 0.25 (pentane / Et_2O , 95:5)

¹H NMR (400 MHz, CDCl₃) δ 8.20-8.12 (2H, m, H7), 7.24-7.20 (2H, m, H6), 2.92 (2H, s, H4), 2.16 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 146.9, 145.9, 129.7, 123.9, 60.2, 47.5, 39.2, 7.0.

Spectroscopic data in agreement with that reported previously.¹

1-(4-(*tert*-Butyl)benzyl)-3-iodobicyclo[1.1.1]pentane, 7



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S2** (41 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂ pentane) afforded **7** (32 mg, 0.01 mmol, 63%) as a pale yellow solid.

R_f = 0.31 (pentane)

m.p. = 76-78 °C

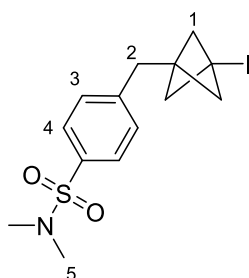
¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (2H, m, ArH), 6.99 (2H, d, *J* = 8.0 Hz, ArH), 2.78 (2H, s, H4), 2.17 (6H, s, H2), 1.31 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 149.2, 135.2, 128.5, 125.4, 60.5, 48.5, 38.7, 34.5, 31.5, 8.8.

HRMS (EI⁺) Found [M-I]⁺ = 213.1645; C₁₆H₂₁ requires 213.1638.

IR (film) ν_{max}/cm⁻¹ 2990, 1182, 843.

4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-*N,N*-dimethylbenzenesulfonamide, 8



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S3** (49 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 3:2) afforded **8** (48 mg, 0.12 mmol, 81%) as a yellow solid.

R_f = 0.40 (pentane / Et₂O, 1:1),

m.p. = 118-119 °C

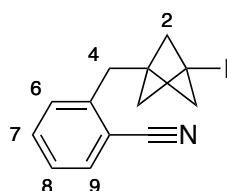
¹H NMR (500 MHz, CDCl₃) δ 7.75-7.68 (2H, m, H4), 7.25-7.21 (2H, m, H3), 2.89 (2H, s, H2), 2.71 (6H, s, H5), 2.16 (6H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 143.6, 133.8, 129.5, 128.2, 60.3, 47.7, 39.2, 38.1, 7.3.

HRMS (ESI⁺) Found [M+H]⁺ = 392.0176; C₁₄H₁₉O₂NIS requires 392.0176.

IR (film) ν_{\max} /cm⁻¹ 2913, 1342, 1163, 953, 840.

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)benzonitrile, **9**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-(iodomethyl)benzonitrile¹ (37 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→1:1) afforded **9** (43 mg, 0.14 mmol, 93%) as a white solid.

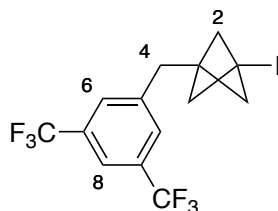
R_f = 0.37 (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 7.62 (1H, d, *J* = 7.7 Hz, H9), 7.52 (1H, td, *J* = 7.7, 1.4 Hz, H7), 7.33 (1H, td, *J* = 7.7, 1.4 Hz, H8), 7.19 (1H, d, *J* = 7.7 Hz, H6), 3.07 (2H, s, H4), 2.19 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 142.2, 133.1, 133.0, 130.1, 127.2, 118.0, 112.6, 60.4, 47.7, 37.7, 7.0.

Spectroscopic data in agreement with that reported previously.¹

1-(3,5-Bis(trifluoromethyl)benzyl)-3-iodobicyclo[1.1.1]pentane, **10**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 3,5-bis(trifluoromethyl)benzyl iodide¹ (53 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification

by column chromatography (SiO₂, pentane) afforded **10** (58 mg, 0.14 mmol, 92%) as a pale yellow solid.

R_f = 0.30 (pentane)

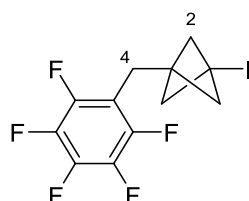
¹H NMR (400 MHz, CDCl₃) δ 7.77-7.74 (1H, m, H8), 7.53-7.49 (2H, m, H6), 2.96 (2H, s, H4), 2.17 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 140.8, 132.0 (q, *J* = 33.2 Hz), 128.9 (q, *J* = 4.1 Hz), 123.4 (d, *J* = 272.7 Hz), 120.7 (m), 60.1, 47.5, 38.9, 6.7.

¹⁹F NMR (376 MHz, CDCl₃) δ -62.9.

Spectroscopic data in agreement with that reported previously.¹

1-Iodo-3-((perfluorophenyl)methyl)bicyclo[1.1.1]pentane, **11**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S4** (46 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane) afforded **11** (52 mg, 0.14 mmol, 93%) as a pale yellow solid.

R_f = 0.48 (pentane)

m.p. = 49-51 °C

¹H NMR (400 MHz, CDCl₃) δ 2.95 (2H, s, H4), 2.19 (6H, s, H2).

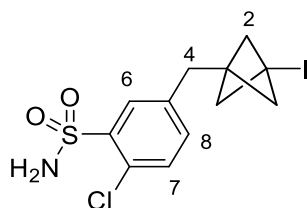
¹³C NMR (101 MHz, CDCl₃) δ 146.4-146.1 (m), 144.5-143.4 (m), 142.1-140.7 (m), 140.3-137.9 (m), 137.4-135.8 (m), 112.1-110.6 (m), 60.3, 49.9, 46.0, 25.8, 5.5.

¹⁹F NMR (376 MHz, CDCl₃) δ -144.22 (dd, *J* = 22.5, 8.6 Hz), -156.28 (t, *J* = 20.8 Hz), -162.05 (td, *J* = 22.1, 8.5 Hz).

HRMS (EI⁺) Found [M-I]⁺ = 247.0537; C₁₂H₈F₅ requires 247.0541.

IR (film) ν_{max}/cm⁻¹ 2994, 1520, 1502, 1180, 976, 850.

2-Chloro-5-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)benzenesulfonamide, **12**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S5** (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, CH₂Cl₂ / MeOH, 95:5) afforded **12** (55 mg, 0.14 mmol, 92%) as a pale yellow solid.

R_f = 0.58 (CH₂Cl₂ / MeOH, 9:1)

m.p. = 115-117 °C (decomp.)

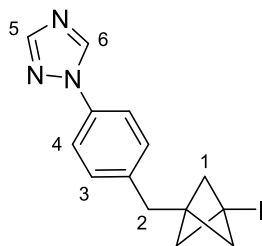
¹H NMR (400 MHz, CD₃OD) δ 7.81 (1H, d, *J* = 2.2 Hz, H6), 7.51 (1H, d, *J* = 8.1 Hz, H7), 7.31 (1H, dd, *J* = 8.1, 2.2 Hz, H8), 2.91 (2H, s, H4), 2.15 (6H, s, H2).

¹³C NMR (101 MHz, CD₃OD) δ 141.9, 139.4, 134.8, 132.7, 130.6, 130.3, 61.2, 48.9, 38.8, 8.2.

HRMS (ESI⁺) Found [M+Na]⁺ = 419.9294; C₁₂H₁₃ClINO₂SNa requires 419.9292.

IR (film) ν_{max}/cm⁻¹ 3287, 3251, 1464, 1328, 1167.

1-(4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl)-1*H*-1,2,4-triazole, **13**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S6** (43 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:3) afforded **13** (27 mg, 0.076 mmol, 51%) as a pale yellow solid.

R_f = 0.10 (pentane / Et₂O, 1:1)

m.p. = 142-144 °C

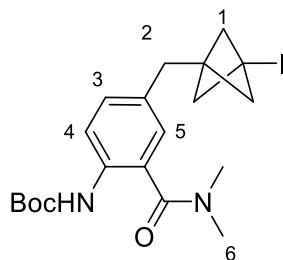
¹H NMR (500 MHz, CDCl₃) δ 8.53 (1H, s, H6), 8.10 (1H, s, H5), 7.63-7.57 (2H, m, H4), 7.22-7.18 (2H, m, H3), 2.87 (2H, s, H2), 2.17 (6H, s, H1).

^{13}C NMR (126 MHz, CDCl_3) δ 152.8, 140.9, 138.7, 135.6, 130.2, 120.4, 60.3, 48.1, 38.8, 7.7.

HRMS (ESI^+) Found $[\text{M}+\text{H}]^+ = 352.0306$; $\text{C}_{14}\text{H}_{15}\text{N}_3\text{I}$ requires 352.0305.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2917, 2874, 2849, 1521, 1276, 1173.

***tert*-Butyl (2-(dimethylcarbamoyl)-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl) carbamate, 14**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), **S7** (61 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 1:1) afforded **14** (54 mg, 0.11 mmol, 75%) as a yellow solid.

$R_f = 0.24$ (pentane / Et_2O , 1:1)

m.p. = 144-145 $^\circ\text{C}$

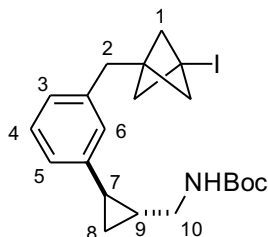
^1H NMR (500 MHz, CDCl_3) δ 8.06 (1H, d, $J = 8.5$ Hz, H4), 7.91 (1H, br. s, NH), 7.06 (1H, dd, $J = 8.5, 2.3$ Hz, H3), 6.87 (1H, d, $J = 2.1$ Hz, H5), 3.06 (6H, m, H6), 2.75 (2H, s, H2), 2.13 (6H, s, H1), 1.50 (9H, s, *t*-Bu).

^{13}C NMR (126 MHz, CDCl_3) δ 170.4, 153.1, 135.9, 131.8, 131.1, 127.8, 123.9, 121.2, 80.6, 60.3, 48.3, 38.5, 35.5, 28.5, 8.1.

HRMS (ESI^+) Found $[\text{M}+\text{H}]^+ = 471.1141$; $\text{C}_{20}\text{H}_{28}\text{O}_3\text{N}_2\text{I}$ requires 471.1139.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2914, 1727, 1631, 1519, 1391, 1169.

tert*-Butyl ((2-(3-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl)cyclopropyl)methyl)-carbamate, **15*



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S8** (58 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **15** (45 mg, 0.01 mmol, 66%) as an orange oil.

R_f = 0.24 (pentane / Et₂O, 4:1)

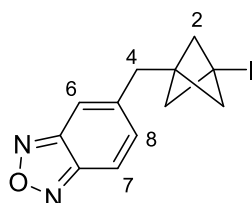
¹H NMR (500 MHz, CDCl₃) δ 7.16 (1H, t, *J* = 7.6 Hz, ArH), 6.88 (1H, dt, *J* = 7.7, 1.5 Hz, ArH), 6.84 (1H, dt, *J* = 7.4, 1.4 Hz, ArH), 6.72 (1H, t, *J* = 1.9 Hz, ArH), 4.67 (1H, s, NH), 3.24-3.06 (2H, m, H10), 2.75 (2H, s, H2), 2.15 (6H, s, H1), 1.77 (1H, q, *J* = 6.4 Hz, H9), 1.45 (9H, s, *t*-Bu), 1.27-1.24 (1H, m, H7), 0.91-0.87 (2H, m, H8).

¹³C NMR (126 MHz, CDCl₃) δ 156.0, 142.9, 138.4, 128.5, 126.4, 126.2, 123.8, 79.4, 60.5, 48.3, 44.9, 39.2, 28.6, 23.3, 22.0, 14.6, 8.4.

HRMS (ESI⁺) Found [M+Na]⁺ = 476.1058; C₂₁H₂₈O₂NINa requires 476.1057.

IR (film) ν_{max} /cm⁻¹ 2975, 1713, 1171, 839.

5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)benzo[*c*][1,2,5]oxadiazole, **16**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S9** (39 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **16** (28 mg, 0.09 mmol, 57%) as a white solid.

R_f = 0.52 (pentane / Et₂O, 9:1)

m.p. = 113-115 °C

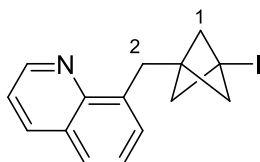
¹H NMR (400 MHz, CDCl₃) δ 7.78 (1H, dd, *J* = 9.2, 1.1 Hz, H7), 7.53-7.42 (1H, m, H6), 7.14 (1H, dd, *J* = 9.2, 1.4 Hz, H8), 2.93 (2H, s, H4), 2.22 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl_3) δ 149.5, 148.5, 142.4, 134.1, 116.6, 114.3, 60.3, 47.2, 39.6, 6.7.

HRMS (CI^+) Found $[\text{M}+\text{H}]^+ = 326.9989$; $\text{C}_{12}\text{H}_{12}\text{IN}_2\text{O}$ requires 326.9989.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2973, 1169, 1007, 841.

8-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)quinoline, **17**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S10** (40 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 4:1) afforded **17** (35 mg, 0.10 mmol, 69%) as a pale yellow oil.

$R_f = 0.45$ (pentane / Et_2O , 4:1)

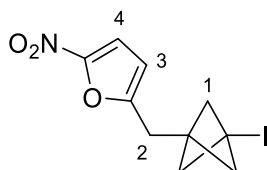
^1H NMR (500 MHz, CDCl_3) δ 8.89 (1H, dd, $J = 4.1, 1.8$ Hz, ArH), 8.13 (1H, dd, $J = 8.3, 1.8$ Hz, ArH), 7.70 (1H, dd, $J = 7.5, 2.1$ Hz, ArH), 7.48-7.42 (2H, m, ArH), 7.39 (1H, dd, $J = 8.3, 4.1$ Hz, ArH), 3.54 (2H, s, H2), 2.13 (6H, s, H1).

^{13}C NMR (126 MHz, CDCl_3) δ 149.5, 146.9, 137.5, 136.4, 129.8, 128.6, 126.7, 126.4, 121.1, 61.1, 48.5, 34.1, 8.5.

HRMS ($\text{ESI}^+/\text{EI}^+/\text{CI}^+$) Found $[\text{M}+\text{H}]^+ = 336.0244$; $\text{C}_{15}\text{H}_{15}\text{NI}$ requires 336.0244.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2990, 2912, 2875, 1499, 1171, 839, 799.

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-5-nitrofuran, **18**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S11** (38 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 4:1) afforded **18** (35 mg, 0.11 mmol, 73%) as an orange oil.

$R_f = 0.21$ (pentane / Et_2O , 4:1)

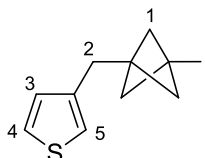
^1H NMR (500 MHz, CDCl_3) δ 7.25 (1H, d, $J = 3.6$ Hz, H4), 6.28 (1H, dt, $J = 3.6, 0.7$ Hz, H3), 2.98 (2H, s, H2), 2.29 (6H, s, H1).

^{13}C NMR (126 MHz, CDCl_3) δ 156.6, 151.8, 112.8, 110.3, 60.7, 45.1, 31.8, 5.6.

HRMS (EI^+) Found $[\text{M}-\text{I}]^+ = 192.0652$; $\text{C}_{10}\text{H}_{10}\text{O}_3\text{N}$ requires 192.0655.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2993, 1528, 1494, 1390, 1354, 1236, 1176.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)thiophene, **19**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), **S12** (34 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 9:1) afforded **19** (37 mg, 0.13 mmol, 84%) as a pale yellow oil.

$R_f = 0.21$ (pentane)

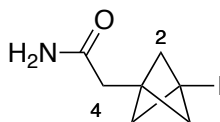
^1H NMR (500 MHz, CDCl_3) δ 7.25 (1H, dd, $J = 4.9, 3.0$ Hz, H4), 6.91 (1H, dd, $J = 3.0, 1.3$ Hz, H5), 6.83 (1H, dd, $J = 4.9, 1.3$ Hz, H3), 2.86 (2H, s, H2), 2.18 (6H, s, H1).

^{13}C NMR (126 MHz, CDCl_3) δ 138.6, 128.4, 125.7, 121.4, 60.6, 48.0, 33.6, 8.1.

HRMS (EI^+) Found $[\text{M}-\text{I}]^+ = 163.0580$; $\text{C}_{10}\text{H}_{11}\text{S}$ requires 163.0576.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2915, 2875, 2849, 1171, 981, 841.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)acetamide, **20**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), 2-iodoacetamide (28 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , EtOAc) afforded **20** (37 mg, 0.149 mmol, 99%) as a white solid.

Scale-up reaction using 0.25 mol% catalyst loading.

fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.0025 equiv.), 2-iodoacetamide (277 mg, 1.5 mmol, 1.0 equiv.) and TCP (3.3 mL, 0.9 M in Et_2O , 3.0 mmol, 2.0 equiv.) in *t*-BuCN (15 mL) were submitted to **General Procedure 1** at room temperature for 30 min. Purification by column chromatography (SiO_2 , EtOAc) afforded **20** (362 mg, 1.44 mmol, 96%) as a white solid.

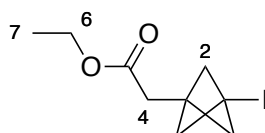
$R_f = 0.19$ (EtOAc)

¹H NMR (400 MHz, CDCl₃) δ 5.64 (1H, br. s, NH), 5.35 (1H, br. s, NH), 2.44 (2H, s, H4), 2.33 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 171.7, 61.0, 44.2, 39.2, 5.9.

Spectroscopic data in agreement with that reported previously.¹

Ethyl 2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetate, **21**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), ethyl iodoacetate (32 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **21** (42 mg, 0.149 mmol, 99%) as a yellow oil.

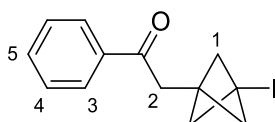
R_f = 0.18 (pentane / Et₂O, 95:5)

¹H NMR (400 MHz, CDCl₃) δ 4.12 (2H, q, *J* = 7.1 Hz, H6), 2.53 (2H, s, H4), 2.31 (6H, s, H2), 1.25 (3H, t, *J* = 7.1 Hz, H7).

¹³C NMR (101 MHz, CDCl₃) δ 170.4, 61.1, 60.7, 43.8, 37.5, 14.4, 6.2.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-phenylethan-1-one, **22**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-iodo-1-phenylethan-1-one¹ (37 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **22** (44 mg, 0.14 mmol, 94%) as a pale yellow solid.

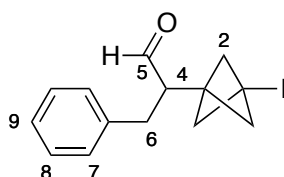
R_f = 0.29 (pentane / Et₂O, 97:3).

¹H NMR (400 MHz, CDCl₃) δ 7.91-7.84 (2H, m, H3), 7.61-7.54 (1H, m, H5), 7.49-7.43 (2H, m, H4), 3.20 (2H, s, H2), 2.34 (6H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 197.3, 136.8, 133.5, 128.8, 128.3, 61.4, 44.1, 40.8, 6.6.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-3-phenylpropanal, **23**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-iodo-3-phenylpropanal¹ (39 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **23** (35 mg, 0.11 mmol, 72%) as a colourless oil.

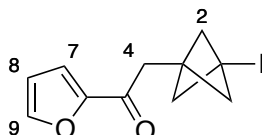
*R*_f = 0.32 (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 9.62 (1H, d, *J* = 2.3 Hz, H5), 7.31-7.27 (2H, m, H8), 7.24-7.18 (1H, m, H9), 7.16-7.12 (2H, m, H7), 3.02 (1H, dd, *J* = 13.9, 8.5 Hz, H6), 2.93 (1H, ddd, *J* = 8.5, 6.0, 2.3 Hz, H4), 2.71 (1H, dd, *J* = 13.9, 6.0 Hz, H6), 2.30 (3H, dd, *J* = 9.4, 1.9 Hz, H2), 2.25 (3H, dd, *J* = 9.4, 1.9 Hz, H2).

¹³C NMR (101 MHz, CDCl₃) δ 201.2, 138.2, 128.8, 128.8, 126.8, 59.8, 54.6, 46.5, 33.0, 6.4.

Spectroscopic data in agreement with that reported previously.¹

1-(Furan-2-yl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethan-1-one, **24**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 1-(furan-2-yl)-2-iodoethan-1-one¹ (35 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5→90:10) afforded **24** (36 mg, 0.12 mmol, 80%) as a white solid.

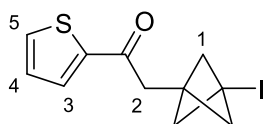
*R*_f = 0.32 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 7.58 (1H, dd, *J* = 1.7, 0.8 Hz, H9), 7.16 (1H, dd, *J* = 3.5, 0.8 Hz, H7), 6.54 (1H, dd, *J* = 3.5, 1.7 Hz, H8), 3.04 (2H, s, H4), 2.32 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 186.1, 152.6, 146.8, 117.6, 112.6, 61.3, 44.0, 41.0, 6.3.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(thiophen-2-yl)ethan-1-one, **25**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-iodo-1-(thiophen-2-yl)ethan-1-one¹ (38 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **25** (44 mg, 0.14 mmol, 92%) as a pale yellow solid.

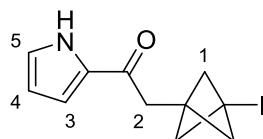
*R*_f = 0.45 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 7.66 (1H, dd, *J* = 4.9, 1.1 Hz, H5), 7.62 (1H, dd, *J* = 3.8, 1.1 Hz, H3), 7.13 (1H, dd, *J* = 4.9, 3.8 Hz, H4), 3.12 (2H, s, H2), 2.34 (6H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 189.9, 144.2, 134.4, 132.4, 128.4, 61.3, 44.1, 41.9, 6.2.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(1*H*-pyrrol-2-yl)ethan-1-one, **26**



fac-Ir(ppy)₃ (0.98 mg, 1.5 μmol, 0.025 equiv.), 2-iodo-1-(1*H*-pyrrol-2-yl)ethan-1-one¹ (14 mg, 0.060 mmol, 1.0 equiv.) and TCP (0.15 mL, 0.8 M in Et₂O, 0.12 mmol, 2.0 equiv.) in *t*-BuCN (0.6 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **26** (7.9 mg, 0.03 mmol, 44%) as a pale yellow solid.

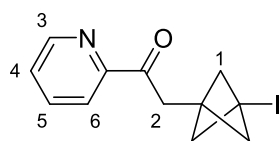
*R*_f = 0.17 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 9.53 (1H, br. s, NH), 7.11-7.01 (1H, m, H5), 6.87-6.78 (1H, m, H3), 6.28 (1H, dt, *J* = 3.8, 2.5 Hz, H4), 2.97 (2H, s, H2), 2.31 (6H, s, H1).

¹³C NMR (100 MHz, CDCl₃) δ 187.1, 131.9, 125.5, 117.2, 111.0, 61.4, 44.5, 40.7, 6.5.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(pyridin-2-yl)ethan-1-one, **27**



fac-Ir(ppy)₃ (0.93 mg, 1.4 μmol, 0.025 equiv.), **S13** (14 mg, 0.057 mmol, 1.0 equiv.) and TCP (0.14 mL, 0.8 M in Et₂O, 0.11 mmol, 2.0 equiv.) in *t*-BuCN (0.6 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **27** (18 mg, 0.056 mmol, 98%) as a pale yellow oil.

R_f = 0.36 (pentane / Et₂O, 7:3)

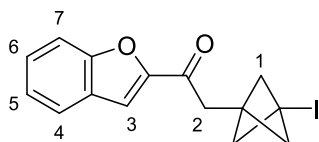
¹H NMR (500 MHz, CDCl₃) δ 8.65 (1H, ddd, *J* = 4.8, 1.8, 1.1 Hz, H3), 8.01 (1H, dt, *J* = 7.7, 1.1 Hz, H6), 7.84 (1H, td, *J* = 7.7, 1.8 Hz, H5), 7.47 (1H, ddd, *J* = 7.7, 4.8, 1.1 Hz, H4), 3.47 (2H, s, H2), 2.34 (6H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 199.1, 153.2, 149.1, 137.2, 127.5, 121.9, 61.5, 44.2, 39.7, 7.1.

HRMS (ESI⁺) Found [M+H]⁺ = 314.0036; C₁₂H₁₃ONI requires 314.0036.

IR (film) ν_{max} /cm⁻¹ 2972, 2915, 2877, 1698, 1176.

1-(Benzofuran-2-yl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethan-1-one, **28**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 1-(benzofuran-2-yl)-2-iodoethan-1-one¹ (43 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **28** (37 mg, 0.11 mmol, 70%) as a pale yellow solid.

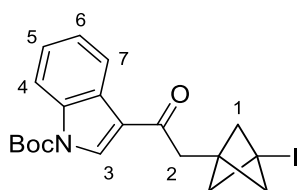
R_f = 0.55 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 7.72 (1H, dt, *J* = 8.0, 1.0 Hz, H4), 7.57 (1H, dd, *J* = 8.4, 1.0 Hz, H7), 7.52-7.45 (2H, m, H3, H6), 7.33 (1H, ddd, *J* = 8.0, 7.1, 1.0 Hz, H5), 3.19 (2H, s, H2), 2.37 (6H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 188.1, 155.8, 152.4, 128.7, 127.1, 124.2, 123.5, 113.3, 112.6, 61.3, 43.9, 41.4, 6.2.

Spectroscopic data in agreement with that reported previously.¹

tert*-Butyl 2-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetyl)-1*H*-indole-1-carboxylate, **29*



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), *tert*-butyl 3-(2-iodoacetyl)-1*H*-indole-1-carboxylate¹ (58 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **29** (54 mg, 0.12 mmol, 80%) as a white solid.

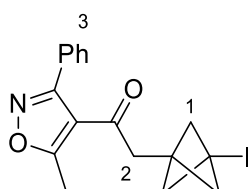
R_f = 0.55 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 8.38-8.33 (1H, m, H7), 8.15 (1H, s, H3), 8.12-8.07 (1H, m, H4), 7.42-7.32 (2H, m, H5, H6), 3.10 (2H, s, H2), 2.37 (6H, s, H1), 1.72 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 193.1, 149.2, 135.7, 132.3, 127.5, 125.8, 124.7, 122.8, 120.3, 115.1, 85.8, 61.4, 44.4, 28.3, 6.5.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(5-methyl-3-phenylisoxazol-4-yl)ethan-1-one, **30**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S14** (49 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **30** (57 mg, 0.14 mmol, 96%) as a pale yellow oil.

R_f = 0.45 (pentane / Et₂O, 7:3)

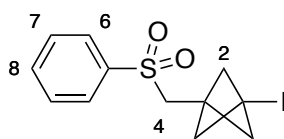
¹H NMR (500 MHz, CDCl₃) δ 7.54-7.44 (5H, m, PhH), 2.67 (3H, s, H3), 2.55 (2H, s, H2), 2.17 (6H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 193.4, 174.9, 161.6, 130.5, 129.2, 129.1, 128.8, 117.2, 61.2, 44.1, 43.6, 13.6, 6.2.

HRMS (ESI⁺) Found [M+H]⁺ = 394.0299; C₁₇H₁₇O₂NI requires 394.0299.

IR (film) ν_{max} /cm⁻¹ 1672, 1568, 1413, 1307, 699.

1-Iodo-3-((phenylsulfonyl)methyl)bicyclo[1.1.1]pentane, **31**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), ((iodomethyl)sulfonyl)benzene¹ (42 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→0:1) afforded **31** (48 mg, 0.14 mmol, 91%) as a white solid.

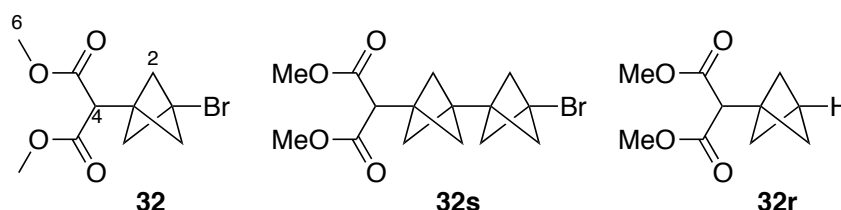
R_f = 0.16 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 7.91-7.85 (2H, m, H6), 7.70-7.64 (1H, m, H8), 7.60-7.55 (2H, m, H7), 3.34 (2H, s, H4), 2.32 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 139.8, 134.1, 129.6, 127.9, 61.3, 57.2, 40.6, 5.0.

Spectroscopic data in agreement with that reported previously.¹

Dimethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)malonate, **32**



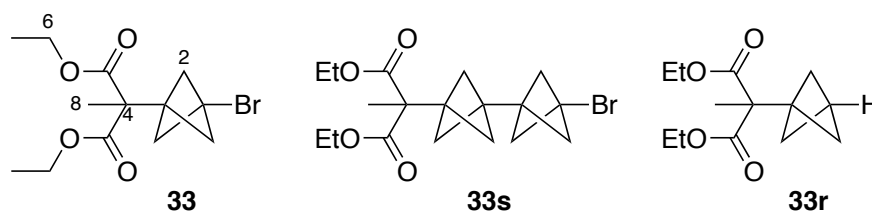
fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), dimethyl 2-bromo-2-methylmalonate (20 μL, 0.15 mmol, 1.0 equiv.) and TCP (0.36 mL, 0.63 M in Et₂O, 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **32**, **32s** and **32r** (38 mg, 1:0.06:0.05 ratio of **32:32s:32r** isolated as an inseparable mixture, 83% yield of **32** as determined by ¹H NMR spectroscopy) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 3.74 (6H, s, H6), 3.64 (1H, s, H4), 2.32 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 167.4, 58.5, 52.8, 52.4, 38.1, 35.9.

Spectroscopic data in agreement with that reported previously.¹

Diethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)-2-methylmalonate, **33**



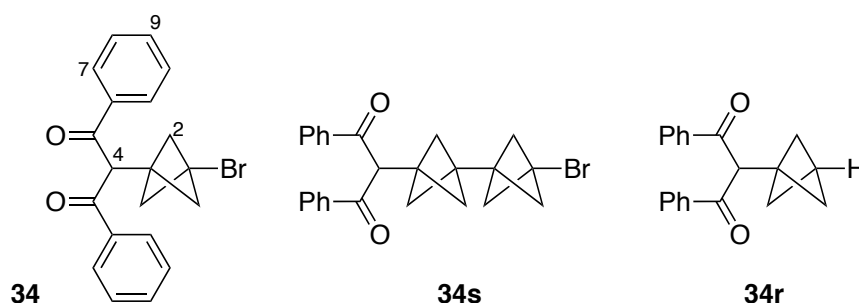
fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), diethyl 2-bromo-2-methylmalonate (29 μL, 0.15 mmol, 1.0 equiv.) and TCP (0.36 mL, 0.6 M in Et₂O, 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **33**, **33s** and **33r** (45 mg, 1:0.06:0.03 ratio of **33**:**33s**:**33r** isolated as an inseparable mixture, 86% yield of **33** as determined by ¹H NMR spectroscopy) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 4.18 (4H, m, H₆), 2.27 (6H, s, H₂), 1.38 (3H, s, H₈), 1.25 (6H, t, *J* = 7.1 Hz, H₇).

¹³C NMR (101 MHz, CDCl₃) δ 170.2, 61.6, 57.4, 54.2, 43.0, 36.4, 18.9, 14.3.

Spectroscopic data in agreement with that reported previously.¹

2-(3-Bromobicyclo[1.1.1]pentan-1-yl)-1,3-diphenylpropane-1,3-dione, **34**



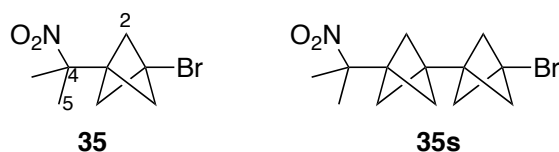
fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-bromo-1,3-diphenylpropane-1,3-dione (46 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.31 mL, 0.6 M in Et₂O, 0.20 mmol, 1.3 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 95:5) afforded **34**, **34s** and **34r** (40 mg, 1:0.04:0.02 ratio of **34**:**34s**:**34r** isolated as an inseparable mixture, 68% yield of **34** as determined by ¹H NMR spectroscopy) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.91-7.87 (4H, m, ArH), 7.58 (2H, ddt, *J* = 7.9, 6.9, 1.3 Hz, H₉), 7.49-7.42 (4H, m, ArH), 5.52 (1H, s, H₄), 2.36 (6H, s, H₂).

¹³C NMR (101 MHz, CDCl₃) δ 193.7, 136.1, 134.0, 129.2, 128.6, 59.3, 56.3, 39.1, 36.5.

Spectroscopic data in agreement with that reported previously.¹

1-Bromo-3-(2-nitropropan-2-yl)bicyclo[1.1.1]pentane, **35**



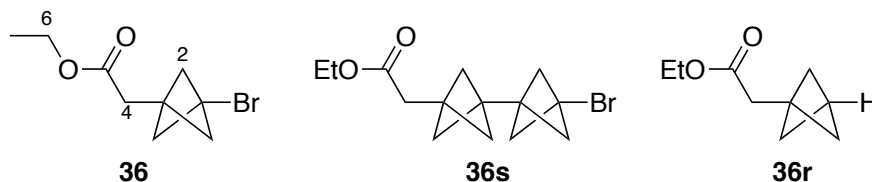
fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-bromo-2-nitropropane (16 μL, 0.15 mmol, 1.0 equiv.) and TCP (0.36 mL, 0.6 M in Et₂O, 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **35** and **35s** (34 mg, 1:0.08 ratio of **35**:**35s** isolated as an inseparable mixture, 88% yield of **35**, as determined by ¹H NMR spectroscopy), as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 2.22 (6H, s, H₂), 1.56 (6H, s, H₅).

¹³C NMR (101 MHz, CDCl₃) δ 86.7, 56.4, 46.0, 34.8, 23.4.

Spectroscopic data in agreement with that reported previously.¹

Ethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)acetate, **36**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), ethyl 2-bromoacetate (17 μL, 0.15 mmol, 1.0 equiv.) and TCP (0.26 mL, 0.6 M in Et₂O, 0.23 mmol, 1.1 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→95:5) afforded **36**, **36s** and **36r** (29 mg, 1:0.13:0.04 ratio of **36**:**36s**:**36r** isolated as an inseparable mixture, 73% yield of **36** as determined by ¹H NMR spectroscopy) as a colourless oil.

R_f = 0.36 (pentane / Et₂O, 9:1)

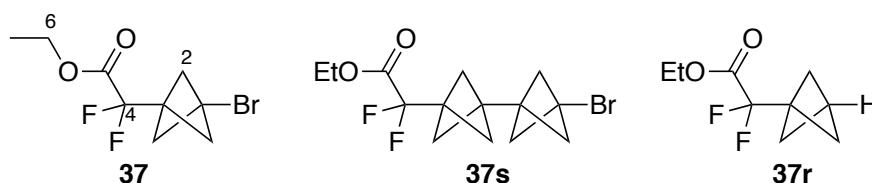
¹H NMR (400 MHz, CDCl₃) δ 4.13 (2H, q, *J* = 7.2 Hz, H₆), 2.57 (2H, s, H₄), 2.24 (6H, s, H₂), 1.26 (3H, t, *J* = 7.2 Hz, H₇).

¹³C NMR (101 MHz, CDCl₃) δ 170.6, 60.7, 59.2, 37.3, 36.5, 36.2, 14.4.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max}/cm⁻¹ 2979, 2917, 1736, 1182, 860.

Ethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)-2,2-difluoroacetate, **37**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), ethyl 2-bromo-2,2-difluoroacetate (19 μL, 0.15 mmol, 1.0 equiv.) and TCP (0.26 mL, 0.6 M in Et₂O, 0.23 mmol, 1.1 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→98:2) afforded **37**, **37s** and **37r** (36 mg, 1:0.15:0.04 ratio of **37**:**37s**:**37r** isolated as an inseparable mixture, 78% yield of **37** as determined by ¹H NMR spectroscopy) as a colourless oil.

R_f = 0.41 (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 4.34 (2H, q, *J* = 7.1 Hz, H₆), 2.38 (6H, s, H₂), 1.36 (3H, t, *J* = 7.1 Hz, H₇).

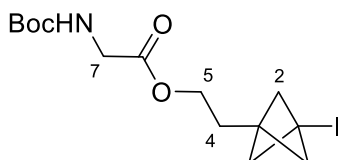
¹³C NMR (101 MHz, CDCl₃) δ 163.0 (t, *J* = 63.3 Hz), 111.7 (t, *J* = 251.7 Hz), 63.6, 56.9 (t, *J* = 2.9 Hz), 40.6, 35.5 (t, *J* = 2.3 Hz), 14.5.

¹⁹F NMR (376 MHz, CDCl₃) δ -108.67.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max} /cm⁻¹ 2984, 1766, 1303, 1201, 1159, 1072, 876.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl (*tert*-butoxycarbonyl)glycinate, **38**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S16** (49 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:1) afforded **38** (56 mg, 0.14 mmol, 94%) as a pale yellow oil.

R_f = 0.23 (pentane / Et₂O, 2:1)

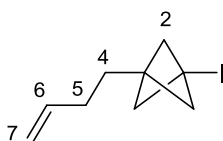
¹H NMR (400 MHz, CDCl₃) δ 4.99 (1H, br. s, NH), 4.11 (2H, t, *J* = 6.4 Hz, H₅), 3.87 (2H, d, *J* = 5.7 Hz, H₇), 2.23 (6H, s, H₂), 1.87 (2H, t, *J* = 6.4 Hz, H₄), 1.44 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 170.3, 155.8, 80.2, 63.0, 60.8, 45.8, 42.5, 30.9, 28.4, 6.5.

HRMS (ESI⁺) Found [M+Na]⁺ = 418.04813; C₁₄H₂₂O₄Na requires 418.04857.

IR (film) ν_{max} /cm⁻¹ 2979, 1700, 1163, 837.

1-(But-3-en-1-yl)-3-iodobicyclo[1.1.1]pentane, **39**



fac-Ir(ppy) (2.5 mg, 4 μ mol, 0.025 equiv.), (iodomethyl)cyclopropane¹ (27 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane) afforded **39** (26 mg, 0.11 mmol, 70%) as a colourless oil.

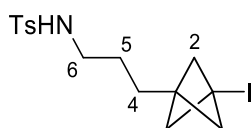
R_f = 0.62 (pentane)

¹H NMR (400 MHz, CDCl₃) δ 5.76 (1H, ddt, J = 16.8, 10.2, 6.5 Hz, H6), 5.06-4.91 (2H, m, H7), 2.20 (6H, s, H2), 2.06-1.95 (2H, m, H5), 1.65-1.58 (2H, m, H4).

¹³C NMR (101 MHz, CDCl₃) δ 138.1, 115.0, 60.7, 48.4, 31.3, 31.1, 7.9.

Spectroscopic data in agreement with that reported previously.¹

N-(3-(3-Iodobicyclo[1.1.1]pentan-1-yl)propyl)-4-methylbenzenesulfonamide, **40**



fac-Ir(ppy)₃ (2.5 mg, 4 μ mol, 0.025 equiv.), **S18** (51 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **40** (49 mg, 0.12 mmol, 81%) as a yellow solid.

R_f = 0.49 (pentane / EtOAc, 7:3)

m.p. = 89-91°C

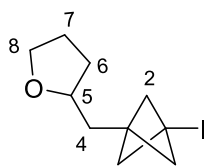
¹H NMR (400 MHz, CDCl₃) δ 7.73 (2H, d, J = 8.2 Hz, ArH), 7.31 (2H, d, J = 8.2 Hz, ArH), 4.71 (1H, t, J = 6.4 Hz, NH), 2.88 (2H, dt, J = 6.4 Hz, H6), 2.43 (3H, s, ArMe), 2.11 (6H, s, H2), 1.59-1.45 (2H, m, H4), 1.43-1.33 (2H, m, H5).

¹³C NMR (101 MHz, CDCl₃) δ 143.6, 137.0, 129.9, 127.2, 60.4, 47.8, 42.9, 29.1, 27.1, 21.7, 7.3.

HRMS (ESI⁺) Found $[M+Na]^+$ = 428.0153; C₁₅H₂₀INO₂SNa requires 428.0152.

IR (film) ν_{max}/cm^{-1} 3281, 2913, 2362, 1446, 1325, 1160, 833.

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)tetrahydrofuran, **41**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S19** (32 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **41** (40 mg, 0.14 mmol, 96%) as a pale yellow oil.

R_f = 0.30 (pentane / Et₂O, 9:1)

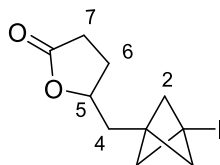
¹H NMR (400 MHz, CDCl₃) δ 3.86-3.76 (1H, m, H8), 3.77-3.69 (1H, m, H5), 3.71-3.60 (1H, m, H8), 2.25 (6H, s, H2), 2.01-1.91 (1H, m, H7), 1.89-1.77 (3H, m, H7, H6, H4), 1.64 (1H, dd, *J* = 14.1, 5.9 Hz, H4), 1.44-1.32 (1H, m, H6).

¹³C NMR (101 MHz, CDCl₃) δ 77.4, 67.7, 61.4, 46.5, 38.0, 31.8, 25.7, 7.9.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max} /cm⁻¹ 2969, 1171, 1064, 835.

5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)dihydrofuran-2(3*H*)-one, **42**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S20** (34 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **42** (43 mg, 0.15 mmol, 98%) as a pale yellow solid.

R_f = 0.18 (pentane / Et₂O, 1:1)

m.p. = 55-57 °C

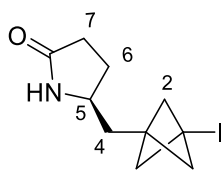
¹H NMR (400 MHz, CDCl₃) δ 4.43 (1H, tdd, *J* = 8.3, 6.6, 4.7 Hz, H5), 2.55-2.48 (2H, m, H7), 2.37-2.30 (1H, m, H6), 2.29 (6H, s, H2), 1.96 (1H, dd, *J* = 14.6, 8.3 Hz, H4), 1.87-1.75 (2H, m, H4, H6).

¹³C NMR (101 MHz, CDCl₃) δ 176.8, 78.8, 61.1, 45.5, 38.1, 28.6, 28.3, 6.6.

HRMS (EI⁺) Found [M-I]⁺ = 165.0906; C₁₀H₁₃O₂ requires 165.0910.

IR (film) ν_{max} /cm⁻¹ 2913, 1770, 1166, 836.

(S)-5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)pyrrolidin-2-one, 43



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S21** (34 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, EtOAc) afforded **43** (37 mg, 0.12 mmol, 83%) as a white foam.

R_f = 0.21 (EtOAc)

¹H NMR (400 MHz, CDCl₃) δ 6.06 (1H, s, NH), 3.62 (1H, quin., *J* = 6.6 Hz, H5), 2.36-2.21 (9H, m, H2, H6, H7), 1.85-1.62 (3H, m, H4, H6).

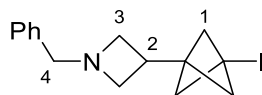
¹³C NMR (101 MHz, CDCl₃) δ 178.0, 61.0, 52.7, 46.1, 39.2, 30.0, 27.7, 6.2.

HRMS (ESI⁺) Found [M+H]⁺ = 292.0193; C₁₀H₁₄INO requires 292.0193.

IR (film) ν_{max}/cm⁻¹ 3186, 2911, 1695, 1176, 830.

[α]_D²⁵ = 11.8° (c = 0.4, CHCl₃)

1-Benzyl-3-(3-iodobicyclo[1.1.1]pentan-1-yl)azetidine, 44



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S22** (41 mg, 0.15 mmol, 1.0 equiv.), and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **44** (35 mg, 0.10 mmol, 68%) as a yellow oil.

R_f = 0.14 (pentane / Et₂O, 1:1)

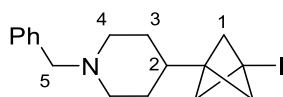
¹H NMR (500 MHz, CDCl₃) δ 7.32-7.21 (5H, m, PhH), 3.53 (2H, s, H4), 3.31 (2H, t, *J* = 7.6 Hz, H3), 2.81 (2H, td, *J* = 6.7, 1.4 Hz, H3), 2.62 (1H, quin., *J* = 7.2 Hz, H2), 2.21 (6H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 138.0, 128.6, 128.5, 127.2, 63.6, 59.2, 57.1, 49.3, 32.2, 8.0.

HRMS (ESI⁺) Found [M+H]⁺ = 340.0556; C₁₅H₁₉NI requires 340.0557.

IR (film) ν_{max}/cm⁻¹ 2919, 2877, 2851, 2820, 1181.

1-Benzyl-4-(3-iodobicyclo[1.1.1]pentan-1-yl)piperidine, **45**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S23** (45 mg, 0.15 mmol, 1.0 equiv.), and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **45** (53 mg, 0.15 mmol, 97%) as a yellow oil.

*R*_f = 0.24 (pentane / Et₂O, 4:1)

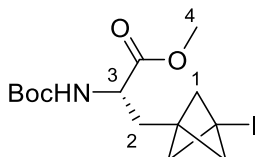
¹H NMR (500 MHz, CDCl₃) δ 7.33-7.22 (5H, m, PhH), 3.47 (2H, s, H5), 2.88 (2H, dt, *J* = 11.9, 3.3 Hz, H4), 2.16 (6H, s, H1), 1.87 (2H, td, *J* = 11.9, 2.5 Hz, H4), 1.54-1.49 (2H, m, H3), 1.44-1.40 (1H, m, H2), 1.25-1.21 (2H, m, H3).

¹³C NMR (126 MHz, CDCl₃) δ 138.5, 129.3, 128.3, 127.1, 63.6, 58.8, 53.5, 51.8, 37.7, 29.1, 8.6.

HRMS (ESI⁺) Found [M+H]⁺ = 368.0867; C₁₇H₂₃NI requires 368.0870.

IR (film) ν_{max}/cm⁻¹ 2914, 2799, 2759, 1175, 975.

N-Boc-β-(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, **46**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), Boc-β-iodo-Ala-OMe¹ (49 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 24 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **46** (58 mg, 0.15 mmol, 99%) as a pale yellow solid.

Scale-up reaction using 1.0 mol% catalyst loading

fac-Ir(ppy)₃ (9.8 mg, 15 μmol, 0.01 equiv.), Boc-β-iodo-Ala-OMe¹ (494 mg, 1.5 mmol, 1.0 equiv.) and TCP (3.3 mL, 0.9 M in Et₂O, 3.0 mmol, 2.0 equiv.) in *t*-BuCN (15 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **46** (505 mg, 1.3 mmol, 85%) as a pale yellow solid.

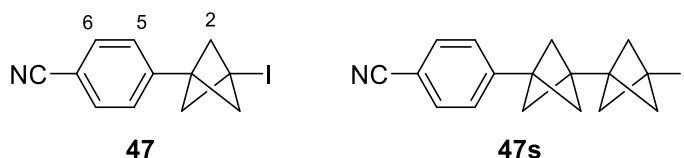
*R*_f = 0.17 (pentane / Et₂O, 4:1)

¹H NMR (400 MHz, CDCl₃) δ 4.97 (1H, d, *J* = 8.3 Hz, NH), 4.34-4.25 (1H, m, H3), 3.74 (3H, s, H4), 2.29-2.20 (6H, m, H1), 2.13 (1H, dd, *J* = 14.6, 4.1 Hz, H2), 1.87 (1H, dd, *J* = 14.6, 7.6 Hz, H2), 1.45 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 172.8, 155.1, 80.3, 61.0, 52.6, 52.0, 45.5, 34.5, 28.5, 6.4.

Spectroscopic data in agreement with that reported previously.¹

4-(3-Iodobicyclo[1.1.1]pentan-1-yl)benzonitrile, **47**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 4-iodobenzonitrile (34 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 97:3) afforded **47** and **47s** (26 mg, 1:0.12 ratio of **47**:**47s** isolated as an inseparable mixture, 50% yield of **47**, as determined by ¹H NMR spectroscopy), as a white solid.

R_f = 0.20 (pentane)

m.p. = 107-109 °C

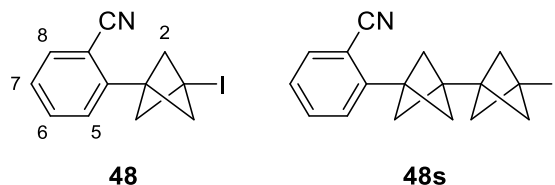
¹H NMR (400 MHz, CDCl₃) δ 7.61-7.57 (2H, m, H6), 7.24-7.20 (2H, m, H5), 2.61 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 143.5, 132.4, 127.0, 118.8, 111.1, 61.8, 50.2, 5.6.

HRMS (EI⁺) Found [M+Na]⁺ = 317.9750; C₁₂H₁₀NINa requires 317.9750.

IR (film) ν_{max}/cm⁻¹ 2360, 2341, 1275, 750, 668, 612.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)benzonitrile, **48**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-iodobenzonitrile (34 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 97:3) afforded **48** and **48s** (26 mg, 1:0.06

ratio of **48:48s** isolated as an inseparable mixture, 55% yield of **48**, as determined by ^1H NMR spectroscopy), as a colourless oil.

R_f = 0.47 (pentane / EtOAc, 9:1)

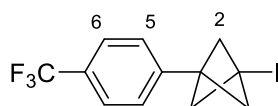
^1H NMR (400 MHz, CDCl_3) δ 7.60 (1H, ddd, J = 7.7, 1.4, 0.6 Hz, H8), 7.52 (1H, td, J = 7.7, 1.4 Hz, H6), 7.34 (1H, td, J = 7.7, 1.2 Hz, H7), 7.18 (1H, ddd, J = 7.7, 1.2, 0.6 Hz, H5), 2.81 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl_3) δ 141.4, 133.7, 132.9, 128.1, 127.8, 118.3, 110.6, 61.5, 49.6, 5.8.

HRMS (ESI $^+$) Found $[\text{M}+\text{Na}]^+ = 317.9751$; $\text{C}_{12}\text{H}_{10}\text{NINa}$ requires 317.9750.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2980, 2225, 1596, 1483, 1444, 1382, 1198, 1190, 1116, 1068, 954, 846, 778, 757.

1-Iodo-3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.1]pentane, **49**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), 1-iodo-4-(trifluoromethyl)benzene (22 μL , 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane) afforded **49** (26 mg, 0.08 mmol, 51%) as a white solid.

R_f = 0.50 (pentane)

m.p. = 148-150 $^\circ\text{C}$

^1H NMR (400 MHz, CDCl_3) δ 7.59-7.54 (2H, m, H6), 7.24 (2H, m, H5), 2.62 (6H, s, H2).

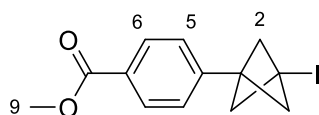
^{13}C NMR (101 MHz, CDCl_3) δ 142.2, 129.4 (q, J = 32.5 Hz), 126.6, 125.5 (q, J = 3.8 Hz), 124.2 (q, J = 271.8 Hz) 61.9, 50.1, 6.1.

^{19}F NMR (376 MHz, CDCl_3) δ -62.5.

HRMS (ESI $^+$, CI $^+$, EI $^+$): Not found.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2918, 2360, 1616, 1327, 1195, 1157, 1114, 1060, 843.

Methyl 4-(3-iodobicyclo[1.1.1]pentan-1-yl)benzoate, **50**



50

fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), methyl 4-iodobenzoate (40 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **50** (20 mg, 0.06 mmol, 40%) as a colourless foam.

R_f = 0.43 (pentane / Et₂O, 9:1)

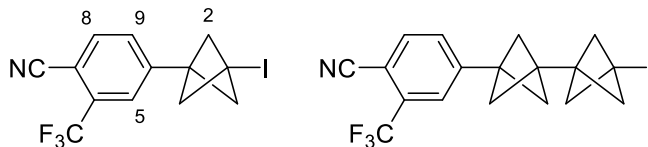
¹H NMR (400 MHz, CDCl₃) δ 7.99-7.95 (2H, m, H6), 7.20-7.16 (2H, m, H5), 3.90 (3H, s, H9), 2.62 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 166.9, 143.3, 129.9, 129.0, 126.2, 61.9, 52.3, 50.3, 6.5.

HRMS (APCI⁺) Found [M+H]⁺ = 329.0030; C₁₃H₁₄O₂I requires 329.0033.

IR (film) ν_{max}/cm⁻¹ 2914, 1719, 1609, 1438, 1406, 1281, 1193, 1110, 1070, 839, 745, 699.

4-(3-Iodobicyclo[1.1.1]pentan-1-yl)-2-(trifluoromethyl)benzonitrile, **51**



51

51s

fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 4-iodo-2-(trifluoromethyl)benzonitrile (45 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **51** and **51s** (35 mg, 1:0.04 ratio of **51**:**51s** isolated as an inseparable mixture, 60% yield of **51**, as determined by ¹H NMR spectroscopy), as a white solid.

R_f = 0.18 (pentane / Et₂O, 9:1)

m.p. = 107-109 °C

¹H NMR (400 MHz, CDCl₃) δ 7.78 (1H, dt, *J* = 8.0, 0.7 Hz, H8), 7.52-7.48 (1H, m, H5), 7.42 (1H, ddd, *J* = 8.0, 1.8, 0.7 Hz, H9), 2.65 (6H, s, H2).

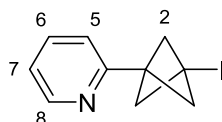
^{13}C NMR (101 MHz, CDCl_3) δ 144.0, 135.0, 133.2 (q, J = 32.8 Hz), 130.0, 124.6 (q, J = 4.6 Hz), 122.3 (q, J = 274.2 Hz), 115.5, 108.7, 61.6, 49.7, 4.7.

^{19}F NMR (376 MHz, CDCl_3) δ -62.2.

HRMS (ESI^+) Found $[\text{M}+\text{Na}]^+ = 385.9625$; $\text{C}_{13}\text{H}_9\text{NF}_3\text{INa}$ requires 385.9624.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2917, 2231, 1614, 1425, 1338, 1296, 1177, 1135, 1078, 1054, 851, 671.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)pyridine, **52**



52

fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), 2-iodopyridine (16 μL , 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / EtOAc, 7:3) afforded **52** (34 mg, 0.13 mmol, 84%) as a pale yellow foam.

R_f = 0.50 (pentane / EtOAc, 7:3)

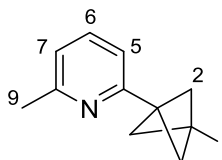
^1H NMR (400 MHz, CDCl_3) δ 8.53 (1H, ddd, J = 4.9, 1.9, 1.0 Hz, H8), 7.63 (1H, td, J = 7.7, 1.9 Hz, H6), 7.16 (1H, ddd, J = 7.7, 4.9, 1.2 Hz, H7), 7.10 (1H, dt, J = 7.7, 1.2 Hz, H5), 2.68 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl_3) δ 157.0, 149.6, 136.7, 122.3, 120.8, 61.6, 51.2, 7.4.

HRMS (EI^+) Found $[\text{M}+\text{H}]^+ = 271.9928$; $\text{C}_{10}\text{H}_{11}\text{NI}$ requires 271.9931.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2919, 1588, 1567, 1471, 1432, 1192, 1091, 844, 795, 747.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-6-methylpyridine, **53**



fac-Ir(ppy)₃ (2.5 mg, 4.0 μmol , 0.025 equiv.), 2-iodo-6-methylpyridine (33 mg, 0.15 mmol, 1.0 equiv.), TCP (0.25 mL, 0.9 M in Et_2O , 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 95:5) afforded **53** (37 mg, 0.13 mmol, 87%) as a colourless oil.

R_f = 0.44 (pentane / Et₂O, 9:1)

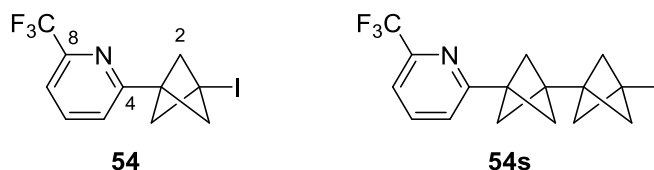
¹H NMR (400 MHz, CDCl₃) δ 7.49 (1H, t, J = 7.7 Hz, H6), 7.00 (1H, d, J = 7.7 Hz, H7), 6.88 (1H, d, J = 7.7 Hz, H5), 2.67 (6H, s, H2), 2.52 (3H, s, H9).

¹³C NMR (100 MHz, CDCl₃) δ 158.4, 156.5, 136.6, 121.8, 117.7, 61.8, 51.3, 24.8, 7.9.

HRMS (ESI⁺) Found $[M+H]^+$ = 286.0086; C₁₁H₁₃NI requires 286.0087.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2922, 1576, 1548, 1115, 773.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-6-(trifluoromethyl)pyridine, **54**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-iodo-6-(trifluoromethyl)pyridine (40 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.45 mL, 0.67 M in Et₂O, 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→95:5) afforded **54** and **54s** (43 mg, 1:0.03 ratio of **54**:**54s** isolated as an inseparable mixture, 81% yield of **54**, as determined by ¹H NMR spectroscopy), as a white solid.

R_f = 0.46 (pentane / Et₂O, 85:15)

m.p. = 56 °C

¹H NMR (400 MHz, CDCl₃) δ 7.79 (1H, td, J = 7.8, 0.7 Hz, H6), 7.54 (1H, dd, J = 7.8, 1.0 Hz, H7), 7.28 (1H, d, J = 7.8 Hz, H5), 2.70 (6H, s, H2).

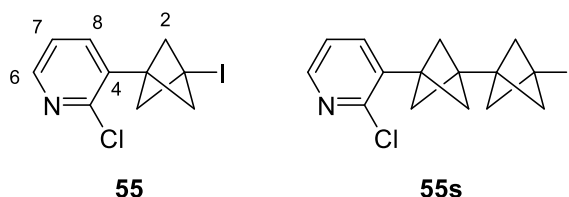
¹³C NMR (101 MHz, CDCl₃) δ 157.7, 148.2 (q, J = 34.3 Hz), 137.8, 123.4, 121.5 (q, J = 274.2 Hz), 118.8 (q, J = 2.8 Hz), 61.7, 50.9, 6.8.

¹⁹F NMR (376 MHz, CDCl₃) δ -68.0.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2921, 1599, 1511, 1355, 1199, 1142, 1094, 852.

3-Chloro-2-(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, **55**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2-chloro-3-iodopyridine (36 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.45 mL, 0.67 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1→4:1) gave **55** and **55s** (20 mg, 1:0.05 ratio of **55**:**55s**, isolated as an inseparable mixture, 40% yield of **55** as determined by ¹H NMR spectroscopy) as a clear oil.

R_f = 0.42 (pentane / Et₂O, 4:1)

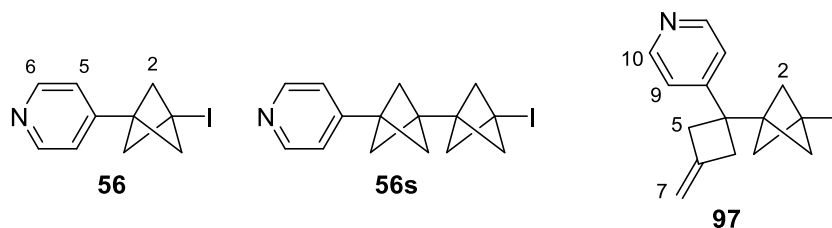
¹H NMR (500 MHz, CDCl₃) δ 8.28 (1H, dd, *J* = 4.8, 2.0 Hz, H6), 7.40 (1H, dd, *J* = 7.5, 2.0 Hz, H8), 7.19 (1H, dd, *J* = 7.5, 4.8 Hz, H7), 2.75 (6H, s, H2)

¹³C NMR (126 MHz, CDCl₃) δ 150.2, 148.4, 137.9, 132.2, 122.6, 61.1, 49.1, 6.5.

HRMS (ESI⁺) Found [M+H]⁺ = 305.9541; C₁₀H₁₀NCII requires 305.9543.

IR (film) ν_{max}/cm⁻¹ 2971, 2915, 1559, 1397, 1191, 843.

4-(3-Iodobicyclo[1.1.1]pentan-1-yl)pyridine, **56** and 4-(1-(3-iodobicyclo[1.1.1]pentan-1-yl)-3-methylenecyclobutyl)pyridine, **97**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 4-iodopyridine (31 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 85:15) afforded **56** and **56s** (26 mg, 1:0.04 ratio of **56**:**56s** isolated as an inseparable mixture, 49% yield of **56**, as determined by ¹H NMR spectroscopy), as a white solid and **97** (4-6% isolated yield) as a white solid.

Data for **56**

R_f = 0.14 (pentane / EtOAc, 7:3)

m.p. = 126-128 °C

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.51-8.44 (2H, m, H6), 7.00-6.95 (2H, m, H5), 2.55 (6H, s, H2).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 149.9, 146.8, 121.3, 61.5, 51.6, 5.8.

HRMS (EI^+) Found $[\text{M}+\text{H}]^+ = 271.9931$; $\text{C}_{10}\text{H}_{11}\text{NI}$ requires 271.9931.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2990, 2911, 2871, 1597, 1551, 1443, 1409, 1200, 1088, 829, 673.

Data for **97**

R_f = 0.33 (pentane / EtOAc, 3:2)

m.p. = 101-103 °C

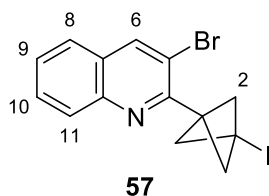
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.54 (2H, d, $J = 4.3$ Hz, H10), 7.02-6.90 (2H, m, H9), 4.86 (2H, app. quin. $J = 2.4$ Hz, H7), 2.97-2.93 (4H, m, H5), 2.10 (6H, s, H2).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 154.0, 149.8, 141.9, 121.5, 108.0, 57.3, 53.6, 43.3, 40.0, 7.5.

HRMS (ESI^+) Found $[\text{M}+\text{H}]^+ = 338.0397$; $\text{C}_{15}\text{H}_{17}\text{NI}$ requires 338.0400.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2989, 2876, 1681, 1597, 1189, 840.

3-Bromo-2-(3-iodobicyclo[1.1.1]pentan-1-yl)quinolone, **57**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), 3-bromo-2-iodoquinoline (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / EtOAc, 95:5) afforded **57** (45 mg, 0.11 mmol, 75%) as a white solid.

R_f = 0.45 (pentane / Et_2O , 95:5)

m.p. = 87-89 °C

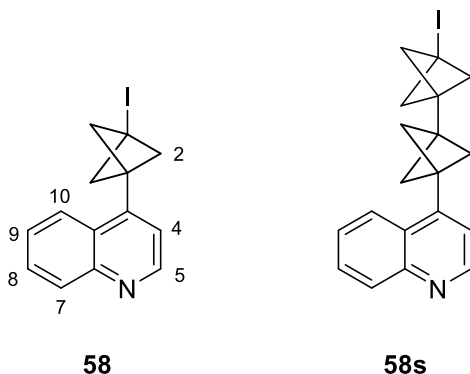
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.29 (1H, d, $J = 1.0$ Hz, H6), 8.02 (1H, ddd, $J = 8.6, 1.9, 1.0$ Hz, H11), 7.73-7.67 (2H, m, H8, H10), 7.56-7.50 (1H, m, H9), 2.95 (6H, s, H2).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 153.5, 146.3, 139.8, 130.1, 129.5, 128.4, 127.6, 126.5, 116.3, 62.0, 53.3, 8.6.

HRMS (EI⁺) Found [M+H]⁺ = 399.9189; C₁₄H₁₂NBrI requires 399.9192.

IR (film) ν_{max} /cm⁻¹ 3004, 1580, 1485, 1403, 1300, 1190, 1146, 987, 864, 836, 749.

3-Chloro-2-(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, 58



fac-Ir(ppy)₃ (7 mg, 0.011 mmol, 0.025 equiv.), 4-iodoquinoline (109 mg, 0.43 mmol, 1.0 equiv.) and TCP (1.0 mL, 0.9 M in Et₂O, 0.86 mmol, 2.0 equiv.) in *t*-BuCN (2.9 mL) were submitted to **General Procedure 1** at room temperature for 18 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1→4:1) gave **58** and **58s** (72 mg, 1:0.05 ratio of **58:58s** isolated as an inseparable mixture, 49% yield of **58**, as determined by ¹H NMR spectroscopy), as a clear oil.

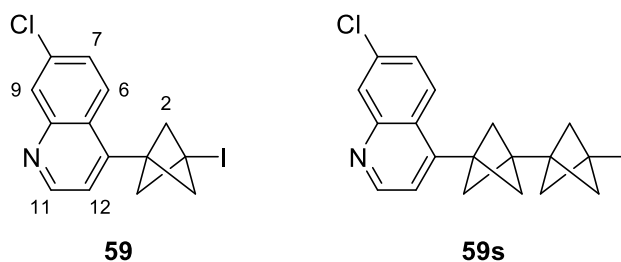
¹H NMR (500 MHz, CDCl₃) δ 8.83 (1H, d, *J* = 4.4 Hz, H5), 8.17-8.09 (2H, m, H7, H10), 7.72 (1H, ddd, *J* = 8.4, 6.9, 1.4 Hz, ArH), 7.57 (1H, ddd, *J* = 8.4, 6.9, 1.4 Hz, ArH), 7.06 (1H, d, *J* = 4.4 Hz, H4), 2.90 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 150.2, 148.7, 143.2, 130.6, 129.4, 127.0, 126.7, 124.5, 120.3, 62.6, 50.4, 6.4.

HRMS (ESI⁺) Found [M+H]⁺ = 322.0079; C₁₄H₁₃NI requires 322.0087.

IR (film) ν_{max} /cm⁻¹ 2993, 2913, 1584, 1508, 1205, 845.

7-Chloro-4-(3-iodobicyclo[1.1.1]pentan-1-yl)quinolone, **59**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 7-chloro-4-iodoquinoline (43 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 9:1) afforded **59** and **59s** (22 mg, 1:0.11 ratio of **59:59s** isolated as an inseparable mixture, 36% yield of **59**, as determined by ¹H NMR spectroscopy), as a white solid.

R_f = 0.34 (pentane / EtOAc, 4:1)

m.p. = 123-125 °C

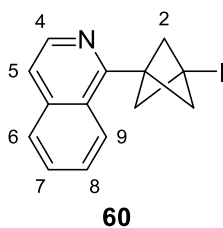
¹H NMR (400 MHz, CDCl₃) δ 8.82 (1H, d, *J* = 4.4 Hz, H11), 8.11 (1H, d, *J* = 2.2 Hz, H9), 8.07 (1H, d, *J* = 9.0 Hz, H6), 7.51 (1H, dd, *J* = 9.0, 2.2 Hz, H7), 7.05 (1H, d, *J* = 4.4 Hz, H12), 2.88 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 151.3, 149.2, 143.3, 135.2, 129.5, 127.7, 125.8, 125.3, 120.4, 62.5, 53.0, 6.1.

HRMS (ESI⁺) Found [M+H]⁺ = 355.9709; C₁₄H₁₂NCII requires 355.9698.

IR (film) ν_{max}/cm⁻¹ 2992, 2915, 2359, 1605, 1583, 1498, 1419, 1206, 1145, 1073, 872, 640.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)isoquinoline, **60**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 1-iodoisoquinoline (38 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 9:1) afforded **60** (32 mg, 0.10 mmol, 66%) as a white solid.

R_f = 0.33 (pentane / EtOAc, 9:1)

m.p. = 123-125 °C

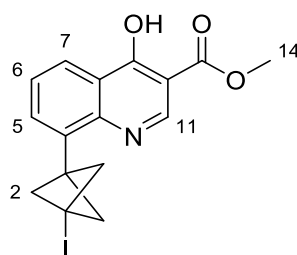
¹H NMR (400 MHz, CDCl₃) δ 8.44 (1H, d, *J* = 5.7 Hz, H4), 8.28 (1H, dt, *J* = 8.4, 1.1 Hz, ArH), 7.83 (1H, dt, *J* = 8.4, 1.1 Hz, ArH), 7.68 (1H, ddd, *J* = 8.4, 6.8, 1.1 Hz, ArH), 7.62-7.55 (2H, m, ArH), 2.98 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 155.7, 142.0, 136.6, 130.1, 127.7, 127.3, 127.0, 125.5, 120.7, 63.1, 52.3, 8.3.

HRMS (APCI⁺) Found [M+H]⁺ = 329.0030; C₁₃H₁₄O₂I requires 329.0033.

IR (film) ν_{max}/cm⁻¹ 2998, 2919, 2362, 1583, 1392, 1194, 1171, 847, 823, 741, 666.

Methyl 4-hydroxy-8-(3-iodobicyclo[1.1.1]pentan-1-yl)quinoline-3-carboxylate, 61



61

fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), methyl 4-hydroxy-8-iodoquinoline-3-carboxylate (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 4:1) afforded **61** (32 mg, 0.08 mmol, 53%) as a white solid.

R_f = 0.50 (pentane / EtOAc, 7:3)

m.p. = 96-98 °C (decomp.)

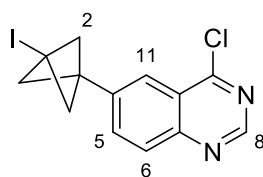
¹H NMR (400 MHz, CDCl₃) δ 11.66 (1H, s, OH), 9.20 (1H, d, *J* = 0.9 Hz, H11), 8.34 (1H, dt, *J* = 8.4, 1.2 Hz, H7), 7.69 (1H, dd, *J* = 8.4, 7.2 Hz, H6), 7.41 (1H, dd, *J* = 7.2, 1.2 Hz, H5), 4.10 (3H, s, H14), 2.87 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 171.0, 156.8, 140.8, 135.4, 130.3, 130.1, 129.8, 128.4, 122.9, 120.7, 63.1, 53.2, 50.5, 6.4.

HRMS (ESI⁺) Found [M+H]⁺ = 396.0091; C₁₆H₁₅O₃NI requires 396.0091.

IR (film) ν_{max}/cm⁻¹ 2923, 1661, 1578, 1458, 1386, 1352, 1273, 1212, 1195, 1161, 844, 796, 627.

4-Chloro-6-(3-iodobicyclo[1.1.1]pentan-1-yl)quinazoline, **62**



62

fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 4-chloro-6-iodoquinazoline (44 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 95:5) afforded **62** (16 mg, 0.04 mmol, 29%) as a pale yellow oil.

R_f = 0.15 (pentane / EtOAc, 95:5)

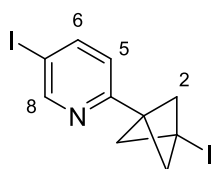
¹H NMR (400 MHz, CDCl₃) δ 9.03 (1H, s, H8), 8.03 (1H, d, *J* = 8.6 Hz, H6), 7.92 (1H, dd, *J* = 1.9, 0.6 Hz, H11), 7.76 (1H, dd, *J* = 8.6, 1.9 Hz, H5), 2.73 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 162.3, 153.8, 150.4, 139.8, 133.5, 129.3, 124.0, 122.5, 61.9, 50.3, 5.6.

HRMS (EI⁺) Found [M+H]⁺ = 356.9651; C₁₃H₁₁N₂ClI requires 356.9650.

IR (film) ν_{max}/cm⁻¹ 2360, 2342, 1564, 1193, 846.

5-Iodo-2-(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, **63**



63

fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2,5-diiodopyridine (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 98:2) afforded **63** (37 mg, 0.09 mmol, 62%) as a white solid.

R_f = 0.40 (pentane / Et₂O, 95:5)

m.p. = 123-125 °C (decomp).

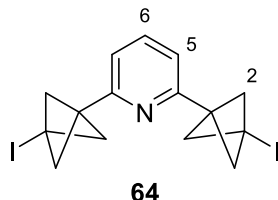
¹H NMR (400 MHz, CDCl₃) δ 8.72 (1H, dd, *J* = 2.2, 0.8 Hz, H8), 7.93 (1H, dd, *J* = 8.2, 2.2 Hz, H6), 6.90 (1H, dd, *J* = 8.2, 0.8 Hz, H5), 2.65 (6H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 155.9, 155.6, 144.8, 122.7, 91.6, 61.5, 50.7, 6.8.

HRMS (ESI⁺) Found [M+H]⁺ = 397.8900; C₁₀H₁₀NI₂ requires 397.8897.

IR (film) ν_{max} /cm⁻¹ 2920, 2359, 2340, 1567, 1508, 1460, 1359, 1193, 1069, 999, 833, 668.

2,6-Bis(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, **64**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), 2,6-diiodopyridine (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.66 mL, 0.9 M in Et₂O, 0.30 mmol, 4.0 equiv.) in *t*-BuCN (1.0 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **64** (39 mg, 0.08 mmol, 56%) as a white solid.

R_f = 0.42 (pentane / Et₂O, 95:5).

m.p. = 84-86 °C (decomp.)

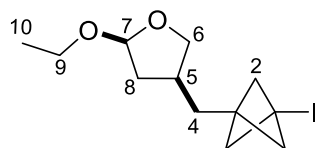
¹H NMR (400 MHz, CDCl₃) 7.53 (1H, t, *J* = 7.7 Hz, H6), 6.93 (2H, d, *J* = 7.7 Hz, H5), 2.63 (12H, s, H2).

¹³C NMR (101 MHz, CDCl₃) δ 156.7, 136.7, 118.8, 61.7, 51.3, 7.9.

HRMS (ESI⁺) Found [M+H]⁺ = 463.9367; C₁₅H₁₆NI₂ requires 463.9367.

IR (film) ν_{max} /cm⁻¹ 3000, 2916, 2360, 2341, 1587, 1565, 1455, 1196, 843, 667.

2-Ethoxy-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)tetrahydrofuran, **65**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S24** (38 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **65** (42 mg, 0.13 mmol, 87%, 5:1 *cis:trans*) as a colourless oil.

*Stereochemistry tentatively assigned by analogy to literature precedent.*²⁻⁴

cis diastereoisomer:

R_f = 0.36 (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 5.10 (1H, dd, *J* = 5.6, 2.6 Hz, H7), 3.94 (1H, t, *J* = 7.9 Hz, H6), 3.78-3.63 (1H, m, H9), 3.47-3.36 (2H, m, H6, H9), 2.29-1.99 (8H, m, H2, H5, H8), 1.69 (2H, d, *J* = 7.2 Hz, H4), 1.50-1.38 (1H, m, H8), 1.18 (3H, t, *J* = 7.1 Hz, H10).

¹³C NMR (101 MHz, CDCl₃) δ 104.1, 71.5, 63.1, 61.0, 48.0, 39.3, 36.5, 35.9, 15.4, 7.5.

trans diastereoisomer:

R_f = 0.36 (pentane / Et₂O, 9:1)

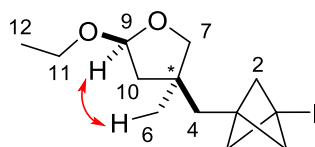
¹H NMR (400 MHz, CDCl₃) δ 5.08 (1H, d, *J* = 5.6 Hz, H7), 4.04 (1H, t, *J* = 8.0 Hz, H6), 3.78-3.63 (1H, m, H9), 3.47-3.36 (2H, m, H6, H9), 2.43-2.34 (1H, m, H8), 2.29-1.99 (7H, m, H2, H5), 1.69 (2H, d, *J* = 7.2 Hz, H4), 1.61 (1H, dd, *J* = 7.2, 4.2 Hz, H8), 1.18 (3H, t, *J* = 7.1 Hz, H10).

¹³C NMR (101 MHz, CDCl₃) δ 103.7, 72.3, 62.8, 61.0, 47.9, 39.6, 36.8, 35.2, 15.3, 7.4.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max}/cm⁻¹ 2972, 2909, 2361, 1444, 1175, 987, 834.

2-Ethoxy-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)-4-methyltetrahydrofuran, **66**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S25** (41 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **66** (41 mg, 0.11 mmol, 71%, 11:1 *cis:trans*) as a colourless oil.

Cis isomer assigned through the above indicated nOes.

cis diastereoisomer:

R_f = 0.30 (pentane / Et₂O, 95:5)

¹H NMR (400 MHz, CDCl₃) δ 5.14 (1H, dd, *J* = 5.8, 3.2 Hz, H9), 3.79-3.67 (1H, m, H11), 3.60-3.54 (1H, m, H7), 3.51-3.38 (2H, m, H7, H11), 2.28 (6H, s, H2), 1.88 (1H, dd, *J* = 13.4, 5.8 Hz, H10), 1.81-1.68 (2H, m, H4), 1.62 (1H, dd, *J* = 13.4, 3.2 Hz, H10), 1.18 (3H, t, *J* = 7.1 Hz, H12), 1.06 (3H, s, H6).

¹³C NMR (101 MHz, CDCl₃) δ 104.6, 77.6, 63.4, 62.4, 47.3, 46.4, 42.7, 41.6, 25.3, 15.4, 7.1.

trans diastereoisomer:

R_f = 0.30 (pentane / Et₂O, 95:5)

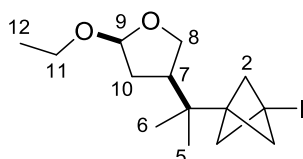
¹H NMR (400 MHz, CDCl₃) δ 5.09 (1H, dd, *J* = 5.7, 2.2 Hz, H₉), 3.79-3.67 (1H, m, H₁₁), 3.60-3.54 (1H, m, H₇), 3.51-3.38 (2H, m, H₇, H₁₁), 2.28 (6H, s, H₂), 1.88 (1H, m, H₁₀), 1.81-1.68 (2H, m, H₄), 1.62 (1H, m, H₁₀), 1.18 (H₃, m, H₁₂), 1.06 (3H, s, H₆).

¹³C NMR (101 MHz, CDCl₃) δ 104.7, 77.6, 63.1, 62.4, 47.1, 46.1, 42.0, 41.6, 24.5, 15.4, 7.1.

HRMS (ESI⁺) Found [2M+H]⁺ = 673.1210; C₂₆H₄₃I₂O₄ requires 673.1251.

IR (film) ν_{max}/cm⁻¹ 2963, 2925, 2360, 1730, 1455.

2-Ethoxy-4-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)propan-2-yl)tetrahydrofuran, **67**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S26** (43 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 17:3) afforded **67** (46 mg, 0.13 mmol, 88%, 2:1 *cis:trans*) as a colourless oil.

*Stereochemistry tentatively assigned by analogy to literature precedent.*²⁻⁴

cis diastereoisomer:

R_f = 0.29 (pentane / Et₂O, 17:3)

¹H NMR (400 MHz, CDCl₃) δ 5.11-5.05 (1H, m, H₉), 3.78 (1H, t, *J* = 8.0 Hz, H₈), 3.74-3.64 (1H, m, H₁₁), 3.54 (1H, dd, *J* = 10.1, 8.0 Hz, H₈), 3.47-3.37 (1H, m, H₁₁), 2.23-2.01 (8H, m, H₂, H₇, H₁₀), 1.61-1.53 (1H, m, H₁₀), 1.18 (3H, t, *J* = 7.1 Hz, H₁₂), 0.83 (3H, s, H₅), 0.81 (3H, s, H₆).

¹³C NMR (101 MHz, CDCl₃) δ 104.0, 67.3, 62.9, 58.3, 56.7, 45.9, 35.8, 35.0, 22.1, 21.5, 15.4, 8.2.

trans diastereoisomer:

R_f = 0.29 (pentane / Et₂O, 17:3)

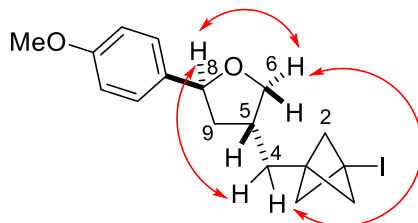
¹H NMR (400 MHz, CDCl₃) δ 5.11-5.05 (1H, m, H₉), 3.89 (1H, t, *J* = 8.7 Hz, H₈), 3.74-3.64 (1H, m, H₁₁), 3.59 (1H, dd, *J* = 8.7, 7.2 Hz, H₈), 3.47-3.37 (1H, m, H₁₁), 2.48-2.36 (1H, m, H₁₀), 2.17 (6H, s, H₂), 1.83 (1H, dd, *J* = 12.8, 8.1 Hz, H₁₀), 1.65 (1H, ddd, *J* = 12.8, 10.4, 5.1 Hz, H₇), 1.18 (3H, t, *J* = 7.1 Hz, H₁₂), 0.80 (3H, s, H₅), 0.77 (3H, s, H₆).

¹³C NMR (101 MHz, CDCl₃) δ 103.8, 68.1, 62.6, 58.3, 56.5, 44.1, 36.3, 34.9, 22.4, 20.6, 15.4, 8.1.

HRMS (Cl^+) $[\text{M}+\text{H}]^+ = 358.0807$; $\text{C}_{14}\text{H}_{24}\text{IO}_2$ requires 351.0815.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2967, 2913, 1192, 1115, 1065, 1045, 838.

4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-2-(4-methoxyphenyl)tetrahydrofuran, 68



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), **S27** (48 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.50 mL, 0.9 M in Et₂O, 0.45 mmol, 3.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 8:2) afforded **68** (51 mg, 0.13 mmol, 89%, 5:1 *trans*:*cis*) as a pale yellow oil.

Trans isomer assigned through the above indicated *nOes*.

trans diastereoisomer:

$R_f = 0.15$ (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 7.25-7.20 (2H, m, ArH), 6.93-6.82 (2H, m, ArH), 4.88 (1H, t, $J = 6.9$ Hz, H8), 4.20 (1H, dd, $J = 8.5, 7.2$ Hz, H6), 3.80 (3H, s, OMe), 3.40 (1H, dd, $J = 8.5, 7.5$ Hz, H6), 2.42-2.24 (1H, m, H5), 2.22 (6H, s, H2), 2.00 (1H, ddd, $J = 12.5, 8.4, 6.4$ Hz, H9), 1.88 (1H, ddd, $J = 12.5, 7.5, 6.9$ Hz, H9), 1.68 (2H, d, $J = 7.2$ Hz, H4).

¹³C NMR (101 MHz, CDCl₃) δ 159.0, 135.3, 127.0, 113.9, 79.8, 74.0, 61.1, 55.4, 47.9, 41.0, 37.2, 36.1, 7.3.

cis diastereoisomer:

$R_f = 0.15$ (pentane / Et₂O, 9:1)

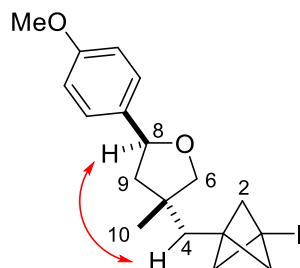
¹H NMR (400 MHz, CDCl₃) δ 7.24-7.19 (2H, m, ArH), 6.90-6.83 (2H, m, ArH), 4.80 (1H, dd, $J = 9.9, 5.5$ Hz, H8), 4.05 (1H, t, $J = 8.2$ Hz, H6), 3.80 (3H, s, OMe), 3.58 (1H, dd, $J = 8.2, 7.3$ Hz, H6), 2.43-2.17 (7H, m, H2, H5), 2.06-1.95 (1H, m, H9), 1.95-1.83 (1H, m, H9), 1.74-1.64 (2H, m, H4).

¹³C NMR (101 MHz, CDCl₃) δ 159.0, 134.7, 127.1, 113.9, 81.1, 73.6, 61.1, 55.4, 47.9, 42.2, 38.6, 36.4, 7.3.

HRMS (Cl^+) Found $[\text{M}+\text{H}]^+ = 385.0658$; $\text{C}_{17}\text{H}_{22}\text{IO}_2$ requires 385.0659.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2966, 2910, 2360, 1513, 1246, 1173, 831.

4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-2-(4-methoxyphenyl)-4-methyltetrahydrofuran, 69



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S28** (50 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 8:2) afforded **69** (37 mg, 0.09 mmol, 62%, 4:1 *trans*:*cis*) as a colourless oil.

Trans isomer assigned through the above indicated *nOes*.

trans diastereoisomer:

R_f = 0.10 (pentane / Et₂O, 9:1)

¹H NMR (400 MHz, CDCl₃) δ 7.32-7.25 (2H, m, ArH), 6.95-6.87 (2H, m, ArH), 4.89 (1H, dd, *J* = 8.7, 7.4 Hz, H8), 3.84 (3H, s, OMe), 3.72 (1H, d, *J* = 8.4 Hz, H6), 3.62 (1H, d, *J* = 8.4 Hz, H6), 2.36 (6H, s, H2), 2.19 (1H, dd, *J* = 12.7, 7.4 Hz, H9), 1.82 (2H, s, H4), 1.68-1.58 (1H, m, H9), 1.19 (3H, s, H10).

¹³C NMR (101 MHz, CDCl₃) δ 159.0, 135.1, 127.0, 113.9, 80.6, 79.7, 62.5, 55.4, 48.2, 47.1, 43.6, 41.4, 25.2, 7.0.

cis diastereoisomer:

R_f = 0.10 (pentane / Et₂O, 9:1)

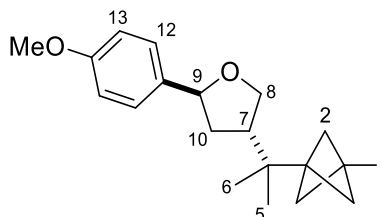
¹H NMR (400 MHz, CDCl₃) δ 7.32-7.25 (2H, m, ArH), 6.95-6.87 (2H, m, ArH), 4.98 (1H, dd, *J* = 9.9, 6.2 Hz, H8), 3.84 (3H, s, OMe), 3.77 (1H, d, *J* = 8.2 Hz, H6), 3.65 (1H, d, *J* = 8.2 Hz, H6), 2.32 (6H, s, H2), 2.08 (1H, dd, *J* = 12.3, 6.2 Hz, H9), 1.78 (2H, s, H4), 1.69-1.63 (1H, m, H9), 1.24 (3H, s, H10).

¹³C NMR (101 MHz, CDCl₃) δ 159.0, 135.2, 126.9, 113.9, 80.2, 80.0, 62.4, 55.4, 48.8, 47.2, 43.8, 42.5, 24.2, 7.0

HRMS (CI⁺) Found [M+H]⁺ = 399.0811; C₁₈H₂₄IO₂ requires 399.0816.

IR (film) ν_{max}/cm⁻¹ 2360, 1603, 1511, 1245.

4-(2-(3-Iodobicyclo[1.1.1]pentan-1-yl)propan-2-yl)-2-(4-methoxyphenyl)tetrahydrofuran, **70**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S29** (52 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **70** (61 mg, 0.15 mmol, 98%, 1.6:1 *trans*:*cis*) as a colourless oil.

Stereochemistry tentatively assigned by analogy to literature precedent.^{5,6}

trans diastereoisomer:

R_f = 0.22 (pentane / Et₂O, 95:5)

¹H NMR (400 MHz, CDCl₃) δ 7.26-7.20 (2H, m, ArH), 6.90-6.84 (2H, m, ArH), 4.81 (1H, dd, *J* = 8.0, 5.8 Hz, H₉), 4.07 (1H, t, *J* = 8.8 Hz, H₈), 3.80 (3H, s, OMe), 3.56 (1H, t, *J* = 8.8 Hz, H₈), 2.31-2.24 (1H, m, H₇), 2.17 (6H, s, H₂), 2.06 (1H, app. dt, *J* = 12.6, 8.0 Hz, H₁₀), 1.82 (1H, ddd, *J* = 12.6, 9.5, 5.8 Hz, H₁₀), 0.86 (3H, s, H₅), 0.83 (3H, s, H₆).

¹³C NMR (101 MHz, CDCl₃) δ 158.9, 135.3, 126.9, 113.9, 80.4, 69.8, 58.3, 56.5, 55.4, 46.0, 37.9, 36.2, 21.7, 21.7, 8.1.

cis diastereoisomer:

R_f = 0.22 (pentane / Et₂O, 95:5)

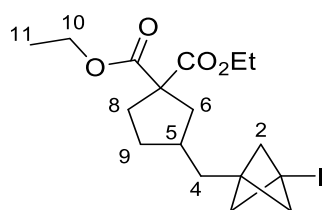
¹H NMR (400 MHz, CDCl₃) δ 7.26-7.20 (2H, m, ArH), 6.90-6.84 (2H, m, ArH), 4.73 (1H, dd, *J* = 10.4, 5.2 Hz, H₉), 3.90 (1H, t, *J* = 8.9 Hz, H₈), 3.80 (1H, t, *J* = 8.9 Hz, H₈), 3.80 (3H, s, OMe), 2.42-2.31 (1H, m, H₇), 2.23-2.13 (7H, m, H₂, H₁₀), 1.59-1.50 (1H, m, H₁₀), 0.84 (3H, s, H₅), 0.84 (3H, s, H₆).

¹³C NMR (101 MHz, CDCl₃) δ 159.1, 134.4, 127.1, 113.9, 81.2, 69.4, 59.6, 58.3, 56.6, 47.6, 36.4, 36.3, 22.3, 21.0, 8.1.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max}/cm⁻¹ 2964, 2875, 1613, 1513, 1246, 1191, 1081, 1035, 831.

Diethyl 3-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)cyclopentane-1,1-dicarboxylate, **71**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S31** (53 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **71** (54 mg, 0.13 mmol, 86%) as a colourless oil.

R_f = 0.51 (pentane / Et₂O, 9:1)

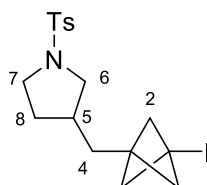
¹H NMR (400 MHz, CDCl₃) δ 4.17 (2H, q, *J* = 7.1 Hz, H10), 4.16 (2H, q, *J* = 7.1 Hz, H10), 2.47-2.38 (1H, m), 2.30-2.23 (1H, m), 2.21 (6H, s, H2), 2.18-2.07 (1H, m), 1.98-1.82 (2H, m), 1.66 (1H, dd, *J* = 13.3, 9.5 Hz), 1.61-1.55 (2H, m), 1.24 (3H, t, *J* = 7.1 Hz, H11), 1.23 (3H, t, *J* = 7.1 Hz, H11).

¹³C NMR (101 MHz, CDCl₃) δ 172.7, 172.6, 61.5, 61.5, 61.3, 60.1, 48.1, 40.9, 37.9, 37.9, 33.8, 32.4, 14.2, 14.2, 7.8.

HRMS (ESI⁺) Found [M+H]⁺ = 421.0878; C₁₇H₂₆IO₄ requires 421.0876.

IR (film) ν_{max}/cm⁻¹ 2981, 2910, 1727, 1250, 1174.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-1-tosylpyrrolidine, **72**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S34** (55 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **72** (49 mg, 0.11 mmol, 76%) as a white solid.

R_f = 0.34 (pentane / Et₂O, 7:3)

m.p. = 93 °C (decomp.)

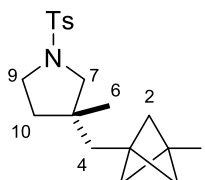
¹H NMR (400 MHz, CDCl₃) δ 7.73-7.67 (2H, m, ArH), 7.36-7.31 (2H, m, ArH), 3.40 (1H, dd, *J* = 9.8, 7.7 Hz, H6), 3.31 (1H, ddd, *J* = 9.7, 8.4, 3.4 Hz, H7), 3.21-3.10 (1H, m, H7), 2.72 (1H, dd, *J* = 9.8, 7.7 Hz, H6), 2.44 (3H, s, Me), 2.16 (6H, s, H2), 2.03-1.88 (2H, m, H8, H5), 1.54-1.41 (2H, m, H4), 1.35 (1H, td, *J* = 8.4, 3.4 Hz, H8).

^{13}C NMR (101 MHz, CDCl_3) δ 143.6, 133.8, 129.8, 127.6, 60.9, 53.1, 47.4, 47.4, 36.9, 35.8, 31.8, 21.7, 6.8.

HRMS (ESI $^+$) Found $[M+H]^+ = 432.0488$; $\text{C}_{17}\text{H}_{23}\text{O}_2\text{NIS}$ requires 432.0489.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2996, 1514, 1247, 1172, 1032, 828, 814, 659.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-3-methyl-1-tosylpyrrolidine, **73**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S36** (57 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 95:5) afforded **73** (40 mg, 0.09 mmol, 60%) as a white solid.

$R_f = 0.30$ (pentane / Et_2O , 4:1)

m.p. = 102-104 $^{\circ}\text{C}$

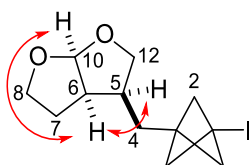
^1H NMR (400 MHz, CDCl_3) δ 7.69 (2H, d, $J = 8.3$ Hz, ArH), 7.32 (2H, d, $J = 8.3$ Hz, ArH), 3.35-3.20 (2H, m, H9), 2.96 (1H, d, $J = 9.6$ Hz, H7), 2.91 (1H, d, $J = 9.6$ Hz, H7), 2.43 (3H, s, ArMe), 2.21 (6H, s, H2), 1.64-1.48 (4H, m, H4, H10), 0.87 (3H, s, H6).

^{13}C NMR (101 MHz, CDCl_3) δ 143.6, 134.1, 129.8, 127.6, 62.3, 59.1, 46.7, 46.5, 42.1, 41.7, 38.1, 23.6, 21.7, 6.5.

HRMS (ESI $^+$) Found $[M+H]^+ = 446.0637$; $\text{C}_{18}\text{H}_{25}\text{INO}_2\text{S}$ requires 446.0645.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2964, 2910, 1334, 1154.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)hexahydrofuro[2,3-*b*]furan, **74**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S37** (38 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 99:1) afforded **74** (37 mg, 0.12 mmol, 77%) as a pale yellow oil.

Stereochemistry assigned through the above indicated nOes.

$R_f = 0.82$ (pentane / Et₂O, 98:2)

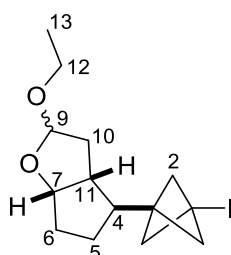
¹H NMR (400 MHz, CDCl₃) δ 5.71 (1H, d, $J = 5.0$ Hz, H10), 3.92 (1H, dd, $J = 8.5, 7.3$ Hz, H12), 3.84 (2H, m, H8), 3.36 (1H, dd, $J = 11.3, 8.5$ Hz, H12), 2.84-2.75 (1H, m, H6), 2.33-2.19 (7H, m, H2, H5), 1.84-1.76 (2H, m, H7), 1.70 (1H, dd, $J = 14.4, 7.6$ Hz, H4), 1.65-1.59 (1H, m, H4).

¹³C NMR (101 MHz, CDCl₃) δ 109.7, 72.4, 69.1, 61.0, 47.5, 45.7, 40.3, 30.4, 25.3, 6.5.

HRMS (ESI⁺) Found [2M+Na]⁺ = 663.0437; C₂₄H₃₄I₂O₄Na requires 663.0444.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2969, 1175, 1010, 831.

2-Ethoxy-4-(3-iodobicyclo[1.1.1]pentan-1-yl)hexahydro-2H-cyclopenta[b]furan, **75**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol , 0.025 equiv.), **S38** (42 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 99:1) afforded **75** (36 mg, 0.10 mmol, 69%, 1:0.8 dr, diastereomeric at the acetal carbon) as a pale yellow oil.

*Stereochemistry assigned through literature analogy.*⁷⁻⁹

major diastereoisomer:

$R_f = 0.75$ (pentane / Et₂O, 98:2)

¹H NMR (400 MHz, CDCl₃) δ 5.09 (1H, d, $J = 5.3$ Hz, H9), 4.60 (1H, td, $J = 6.5, 4.0$ Hz, H7), 3.74-3.64 (2H, m, H12), 2.22-2.13 (8H, m, H2, H4, H7), 2.12-1.58 (5H, m, H5, H6, H10), 1.46-1.21 (1H, m, H5), 1.20-1.14 (3H, m, H13).

¹³C NMR (101 MHz, CDCl₃) δ 105.6, 86.7, 62.7, 59.2, 50.8, 47.7, 45.3, 39.0, 34.3, 29.2, 15.3, 8.5.

minor diastereoisomer:

$R_f = 0.75$ (pentane / Et₂O, 98:2)

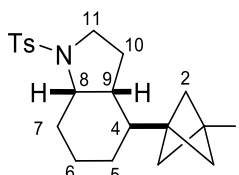
¹H NMR (400 MHz, CDCl₃) δ 5.16-5.13 (1H, m, H9), 4.56-4.51 (1H, m, H7), 3.44-3.33 (2H, m, H12), 2.48-2.41 (1H, m, H11), 2.21-2.15 (6H, m, H2), 2.12-1.58 (6H, m, H4, H5, H6, H10), 1.44-1.22 (1H, m, H5), 1.20-1.14 (3H, m, H13).

^{13}C NMR (101 MHz, CDCl_3) δ 105.3, 84.0, 62.6, 59.5, 50.7, 48.5, 45.2, 39.9, 31.8, 28.6, 15.4, 7.9.

HRMS (ESI^+) Found $[\text{2M}+\text{Na}]^+ = 719.1074$; $\text{C}_{28}\text{H}_{42}\text{I}_2\text{O}_4\text{Na}$ requires 719.1070.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2969, 1443, 1175, 832.

4-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-tosyloctahydro-1H-indole, **76**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S40** (61 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 7:3) afforded **76** (48 mg, 0.10 mmol, 68%) as a white solid.

Stereochemistry assigned via X-ray crystal structure.

$R_f = 0.28$ (pentane / Et_2O , 7:3)

m.p. = 92 $^\circ\text{C}$ (decomp.).

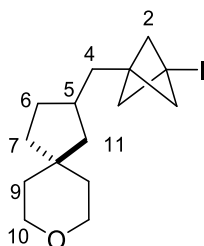
^1H NMR (400 MHz, CDCl_3) δ 7.70 (2H, d, $J = 8.0$ Hz, ArH), 7.33 (2H, d, $J = 8.0$ Hz, ArH), 3.51-3.35 (2H, m, H11, H8), 3.26 (1H, ddd, $J = 10.7, 8.2, 5.5$ Hz, H11), 2.44 (3H, s, Me), 2.20-2.09 (6H, m, H2), 2.05-1.93 (1H, m, H7), 1.70-1.38 (8H, m, H4, H5, H6, H7, H9, H10), 1.13-1.01 (1H, m, H5).

^{13}C NMR (101 MHz, CDCl_3) δ 143.5, 134.5, 129.7, 127.6, 59.7, 59.1, 51.8, 47.4, 40.7, 37.7, 28.6, 28.4, 26.1, 21.6, 19.4, 7.2.

HRMS (ESI^+) Found $[\text{M}+\text{H}]^+ = 472.0802$; $\text{C}_{20}\text{H}_{27}\text{O}_2\text{NIS}$ requires 472.0802.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2928, 2870, 1343, 1176, 1161, 1093, 833, 712.

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-8-oxaspiro[4.5]decane, **77**



fac-Ir(ppy) $_3$ (2.5 mg, 4 μmol , 0.025 equiv.), **S43** (42 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et_2O , 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to

General Procedure 1 at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **77** (41 mg, 0.12 mmol, 79%) as a colourless oil.

R_f = 0.12 (pentane / Et₂O, 9:1)

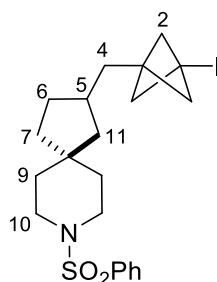
¹H NMR (400 MHz, CDCl₃) δ 3.67-3.57 (4H, m, H10), 2.20 (6H, s, H2), 1.94-1.72 (3H, m, H5, H7, H11), 1.59-1.40 (8H, m, H4, H7, H9), 1.23-1.10 (m, 1H, H6), 0.93 (1H, dd, J = 12.7, 9.4 Hz, H11).

¹³C NMR (101 MHz, CDCl₃) δ 65.8, 65.5, 61.3, 48.4, 46.0, 40.2, 39.5, 39.1, 38.5, 37.7, 36.8, 31.6, 8.2.

HRMS (ESI⁺) Found $[M+H]^+$ = 347.0866; C₁₅H₂₄IO requires 347.0866.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2927, 2849, 2360, 1437, 1173, 7301.

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-8-(phenylsulfonyl)-8-azaspiro[4.5]decane, 78



fac-Ir(ppy)₃ (2.5 mg, 4 μ mol, 0.025 equiv.), **S46** (81 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **78** (55 mg, 0.11 mmol, 76%) as a pale yellow foam.

R_f = 0.70 (pentane / Et₂O, 9:1)

m.p. = 97-99 °C

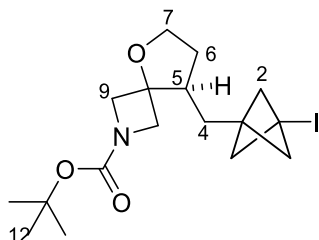
¹H NMR (400 MHz, CDCl₃) δ 7.87-7.69 (2H, m, ArH), 7.69-7.44 (3H, m, ArH), 2.96 (4H, m, H10), 2.16 (6H, s, H2), 1.92-1.66 (2H, m), 1.61-1.44 (m, 7H), 1.39-1.22 (m, 2H), 1.16-1.02 (m, 1H), 0.80 (dd, J = 12.9, 9.5 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 136.6, 132.8, 129.1, 127.7, 61.3, 48.3, 45.3, 44.2, 43.8, 40.3, 39.0, 37.9, 36.9 (2 overlapping peaks), 36.8, 31.5, 8.0.

HRMS (ESI⁺) Found $[M+H]^+$ = 486.0961; C₂₁H₂₉INO₂S requires 486.0958.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2914, 2360, 2342, 1353, 1168.

tert*-Butyl 8-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)-5-oxa-2-azaspiro[3.4]octane-2-carboxylate, **79*



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S50** (53 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:1) afforded **79** (42 mg, 0.10 mmol, 67%) as a colourless oil.

R_f = 0.31 (pentane / Et₂O, 2:1).

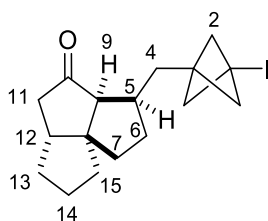
¹H NMR (400 MHz, CDCl₃) δ 4.00 (1H, dd, *J* = 9.3, 1.0 Hz, H9), 3.89-3.69 (5H, m, H7, H9), 2.29-2.21 (6H, m, H2), 2.09 (1H, dtd, *J* = 11.9, 7.3, 4.2 Hz, H6), 1.97-1.87 (2H, m, H4, H5), 1.54-1.44 (2H, m, H4, H6), 1.42 (9H, s, H12).

¹³C NMR (101 MHz, CDCl₃) δ 156.4, 80.2, 79.8, 66.3, 60.9, 60.2, 57.1, 47.5, 43.2, 32.4, 31.0, 28.5, 6.8.

HRMS (ESI⁺) Found [M+Na]⁺ = 442.0849; C₁₇H₂₆INO₃Na requires 442.0861.

IR (film) ν_{max}/cm⁻¹ 2975, 2877, 1698, 1391, 1174, 836.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)octahydrocyclopenta[*c*]pentalen-4(5*H*)-one, **80**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S51** (46 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **80** (40 mg, 0.11 mmol, 72%, 9:1 dr) as a colourless oil.

*Stereochemistry tentatively assigned through literature analogy.*¹⁰

major diastereoisomer:

R_f = 0.32 (pentane / Et₂O, 95:5)

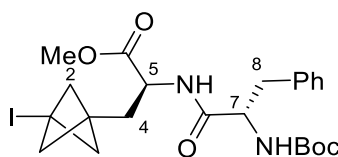
¹H NMR (400 MHz, CDCl₃) δ 2.39 (1H, dd, *J* = 18.3, 9.9 Hz, H11), 2.26-1.50 (19H, m), 1.37-1.23 (2H, m), 1.11 (app. qd, *J* = 12.3, 6.6 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 222.1, 62.3, 61.3, 59.0, 48.7, 48.1, 46.1, 42.8, 41.1, 40.9, 35.2, 33.6, 33.1, 25.9, 8.0.

HRMS (ESI⁺) Found [M+H]⁺ = 371.0871; C₁₇H₂₄IO requires 371.0866.

IR (film) ν_{max}/cm⁻¹ 2937, 1723, 1169, 824.

Boc-Phe-β-(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, **81**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S53** (71 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **81** (58 mg, 0.11 mmol, 71%) as a pale yellow solid.

R_f = 0.23 (pentane / Et₂O, 1:1)

m.p. = 89-91 °C

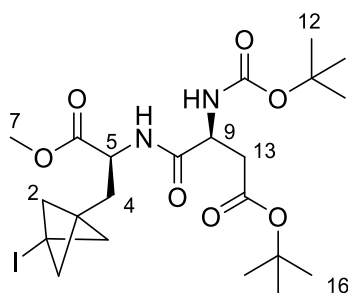
¹H NMR (400 MHz, CDCl₃) δ 7.39-7.22 (5H, m, ArH), 6.47 (1H, d, *J* = 7.5 Hz, NH), 5.05 (1H, d, *J* = 8.1 Hz, NH), 4.54 (1H, td, *J* = 7.5, 4.6 Hz, H7), 4.39 (1H, q, *J* = 7.1 Hz, H5), 3.73 (3H, s, OMe), 3.10 (2H, d, *J* = 7.5 Hz, H8), 2.23-2.08 (7H, m, H2, H4), 1.92 (1H, dd, *J* = 14.7, 7.1 Hz, H4), 1.48 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 171.7, 171.0, 155.5, 136.5, 129.4, 128.8, 127.2, 80.6, 60.8, 55.9, 52.6, 50.8, 45.2, 38.1, 34.1, 28.4, 6.1.

HRMS (ESI⁺) Found [M+H]⁺ = 543.1346; C₂₃H₃₂O₅N₂I requires 543.1350.

IR (film) ν_{max}/cm⁻¹ 3303, 2978, 1744, 1659, 1657, 1180, 842.

[α]_D²⁵ = 3.1° (c = 0.6, CHCl₃).

Boc-Asp(Ot-Bu)- β -(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, 82

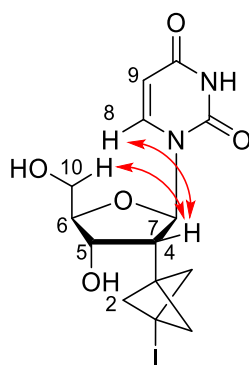
fac-Ir(ppy)₃ (2.5 mg, 4 μ mol, 0.025 equiv.), Boc-Asp(Ot-Bu)- β -iodo-Ala-OMe¹ (81 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **82** (72 mg, 0.13 mmol, 85%) as a white solid.

R_f = 0.19 (pentane / EtOAc, 4:1).

¹H NMR (400 MHz, CDCl₃) δ 7.07 (1H, d, J = 7.9 Hz, NH), 5.73 (1H, d, J = 8.5 Hz, NH), 4.53 (td, J = 7.5, 4.3 Hz, H5), 4.45 (q, J = 5.5 Hz, H9), 3.71 (3H, s, H7), 2.88 (1H, dd, J = 17.1, 4.5 Hz, H13), 2.57 (1H, dd, J = 17.1, 6.3 Hz, H13), 2.22 (6H, s, H2), 2.12 (1H, dd, J = 14.8, 4.3 Hz, H4), 1.93 (1H, dd, J = 14.7, 7.3 Hz, H4), 1.47 (9H, s, *t*-Bu), 1.45 (9H, s, *t*-Bu).

¹³C NMR (101 MHz, CDCl₃) δ 171.9, 171.6, 170.9, 155.7, 82.0, 80.7, 61.0, 52.6, 51.0, 50.8, 45.4, 37.0, 34.0, 28.5, 28.2, 6.3.

Spectroscopic data in agreement with that reported previously.¹

2'-(3-Iodobicyclo[1.1.1]pentan-1-yl)-2'-deoxyuridine, 83

fac-Ir(ppy)₃ (2.5 mg, 4 μ mol, 0.025 equiv.), 2'-iodo-2'-deoxyuridine¹ (53 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.25 mL, 0.9 M in Et₂O, 0.23 mmol, 1.5 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, CH₂Cl₂ / MeOH, 95:5) afforded **83** (45 mg, 0.11 mmol, 71%, 10:1 dr) as a pale yellow solid.

Stereochemistry assigned using the above indicated nOes.

minor diastereoisomer:

R_f = 0.20 (CH₂Cl₂ / MeOH, 9:1)

m.p. = 92-94 °C (decomp.)

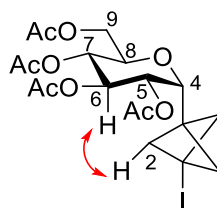
¹H NMR (400 MHz, CD₃OD) δ 7.94 (1H, d, *J* = 8.1 Hz, H8), 6.14 (1H, d, *J* = 8.9 Hz, H7), 5.72 (1H, dd, *J* = 8.1, 0.5 Hz, H9), 4.29 (1H, dd, *J* = 5.4, 1.7 Hz, H5), 3.92 (1H, td, *J* = 3.2, 1.7 Hz, H6), 3.69 (2H, dd, *J* = 3.3, 1.4 Hz, H10), 2.47 (1H, dd, *J* = 9.0, 5.4 Hz, H4), 2.40-2.26 (6H, m, H2).

¹³C NMR (101 MHz, CD₃OD) δ 165.8, 152.2, 142.3, 103.3, 89.1, 87.4, 74.7, 63.2, 61.9, 50.7, 45.7, 8.1.

HRMS (ESI⁺) Found [M+Na]⁺ = 443.0074; C₁₄H₁₇IN₂O₅Na requires 443.0074.

IR (film) ν_{max}/cm⁻¹ 3391, 2361, 1677, 1184, 1020.

2,3,4,6-Tetra-O-acetyl-1-deoxy-1-(3-iodobicyclo[1.1.1]pentan-1-yl)glucopyranose, **84**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S54** (69 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **84** (55 mg, 0.11 mmol, 70%, dr: 9:1) as a yellow solid.

Stereochemistry assigned using the above indicated nOes.

R_f = 0.12 (pentane / Et₂O, 1:1)

m.p. = 47-48 °C

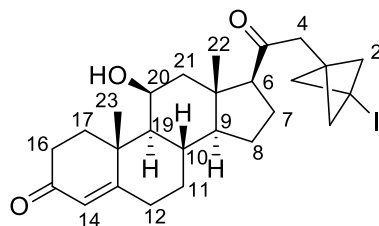
¹H NMR (400 MHz, CDCl₃) δ 5.33 (1H, dd, *J* = 9.6, 8.9 Hz, H6), 5.03 (1H, dd, *J* = 9.6, 6.0 Hz, H5), 4.91 (1H, t, *J* = 8.9 Hz, H7), 4.28-4.12 (2H, m, H4, H9), 4.12-3.95 (2H, m, H8, H9), 2.62-2.35 (6H, m, H2), 2.08 (3H, s, Me), 2.05 (3H, s, Me), 2.03 (3H, s, Me), 2.02 (3H, s, Me).

¹³C NMR (101 MHz, CDCl₃) δ 170.7, 170.0, 169.6, 169.6, 71.0, 71.0, 70.5, 69.7, 68.5, 62.4, 61.3, 47.3, 20.9, 20.8, 20.8, 20.8, 5.9.

HRMS (ESI⁺) Found [M+H]⁺ = 525.0616; C₁₉H₂₆IO₉ requires 525.0616.

IR (film) ν_{max}/cm⁻¹ 2920, 2359, 1746, 1368, 1221, 1035.

(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*S*)-11-Hydroxy-17-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetyl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one, **85**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S56** (69 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:1) afforded **85** (61 mg, 0.12 mmol, 78%) as a white solid.

R_f = 0.32 (pentane / Et₂O, 1:1)

m.p. = 137-139 °C

¹H NMR (400 MHz, CDCl₃) δ 5.66 (1H, d, *J* = 1.7 Hz, H14), 4.39 (1H, app. quin., *J* = 3.3 Hz, H20), 2.62-2.52 (2H, m, H4), 2.52-2.40 (2H, m), 2.38-2.27 (8H, m, H2), 2.26-2.05 (4H, m), 2.05-1.92 (2H, m), 1.83 (1H, td, *J* = 13.5, 4.6 Hz), 1.76-1.56 (3H, m), 1.43 (3H, s), 1.37-1.26 (2H, m), 1.16-0.93 (3H, m, H22), 0.86 (3H, s, H23).

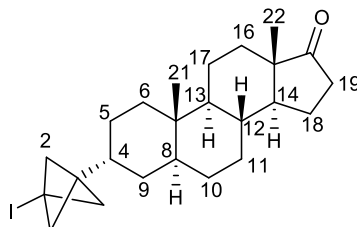
¹³C NMR (101 MHz, CDCl₃) δ 208.1, 199.6, 172.1, 122.5, 68.1, 63.5, 61.3, 57.6, 56.5, 48.4, 45.4, 43.8, 43.4, 39.3, 35.1, 33.9, 32.7, 32.1, 31.4, 24.4, 22.7, 21.1, 16.2, 6.7.

HRMS (CI⁺) Found [M+H]⁺ = 523.1680; C₂₆H₃₆IO₃ requires 523.1704.

IR (film) ν_{max}/cm⁻¹ 3506, 2914, 1703, 1653, 1172, 846.

[α]_D²⁵ = 157.0° (c = 0.5, CHCl₃).

(3*R*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-3-(3-Iodobicyclo[1.1.1]pentan-1-yl)-10,13-dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one, **86**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S57** (60 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.50 mL, 0.9 M in Et₂O, 0.45 mmol, 3.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography

(SiO₂, pentane / Et₂O, 1:0→95:5) afforded **86** (38 mg, 0.08 mmol, 54%) as a pale yellow solid.

Stereochemistry assigned using X-ray crystal structure.

R_f = 0.31 (pentane / Et₂O, 95:5)

m.p. = 103-105 °C

¹H NMR (400 MHz, CDCl₃) δ 2.43 (1H, dd, *J* = 19.2, 9.0 Hz, H19), 2.27 (6H, s, H2), 2.13-2.00 (1H, m, H19), 1.97-1.88 (1H, m, H18), 1.88-1.82 (1H, m, H4), 1.81-1.73 (2H, m, H16), 1.66-1.37 (7H, m, H5, H6, H9, H12, H17, H18), 1.31-1.13 (7H, m, H8, H10, H11, H14, H17), 1.05-0.90 (2H, m, H6, H9), 0.84 (3H, s, H22), 0.77 (3H, s, H21), 0.71-0.61 (1H, m, H13).

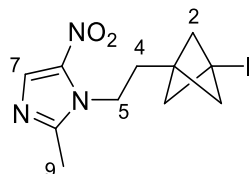
¹³C NMR (101 MHz, CDCl₃) δ 221.5, 61.4, 55.0, 52.4, 51.6, 47.9, 41.4, 36.2, 36.0, 35.2, 34.7, 34.3, 31.7, 31.1, 30.7, 28.8, 23.4, 21.9, 20.1, 14.0, 11.5, 7.9.

HRMS (CI⁺) Found [M+H]⁺ = 467.1801; C₂₄H₃₆IO requires 467.1805.

IR (film) ν_{max} /cm⁻¹ 2918, 1731, 1180, 865.

$[\alpha]_D^{25}$ = 69.4° (*c* = 0.4, CHCl₃).

1-(2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl)-2-methyl-5-nitro-1*H*-imidazole, **87**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S58** (42 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.50 mL, 0.9 M in Et₂O, 0.45 mmol, 3.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, Et₂O) afforded **87** (37 mg, 0.11 mmol, 71%) as a pale yellow solid.

R_f = 0.31 (Et₂O)

m.p. = 114-116 °C

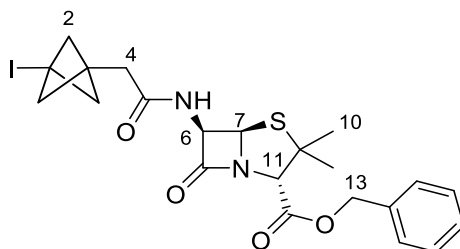
¹H NMR (400 MHz, (CD₃)₂CO) δ 7.87 (1H, s, H7), 4.42-4.25 (2H, m, H5), 2.47 (3H, s, H9), 2.34 (6H, s, H2), 2.11-2.01 (2H, m, H4).

¹³C NMR (101 MHz, (CD₃)₂CO) δ 151.2, 139.3, 133.4, 61.0, 46.4, 44.2, 32.4, 14.0, 7.4.

HRMS (ESI⁺) Found [M+H]⁺ = 348.0202; C₁₁H₁₅IN₃O₂ requires 348.0204.

IR (film) ν_{max} /cm⁻¹ 2987, 1529, 1470, 1360, 1184, 832.

Benzyl (2*S*,5*R*,6*R*)-6-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, **88**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S60** (71 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **88** (63 mg, 0.13 mmol, 78%) as a pale yellow solid.

R_f = 0.35 (pentane / Et₂O, 2:1)

m.p. = 69-71 °C

¹H NMR (400 MHz, CDCl₃) δ 7.48-7.33 (5H, m, ArH), 6.02 (1H, d, *J* = 8.9 Hz, NH), 5.65 (1H, dd, *J* = 8.9, 4.2 Hz, H6), 5.53 (1H, d, *J* = 4.2 Hz, H7), 5.28-5.07 (2H, m, H13), 4.45 (1H, s, H11), 2.49 (2H, s, H4), 2.32 (6H, s, H2), 1.62 (3H, s, H10), 1.42 (3H, s, H10).

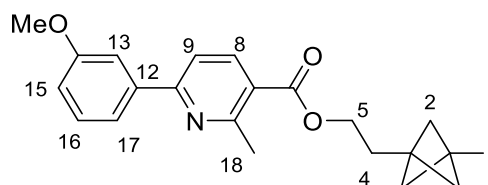
¹³C NMR (101 MHz, CDCl₃) δ 173.8, 168.7, 167.6, 134.7, 129.0, 128.9, 128.9, 70.7, 68.0, 67.7, 65.3, 61.0, 58.5, 43.9, 39.5, 31.7, 27.2, 5.7.

HRMS (ESI⁺) Found [M+H]⁺ = 541.0653; C₂₂H₂₅IN₂O₄S requires 541.0653.

IR (film) ν_{max}/cm⁻¹ 3308, 2971, 1781, 1745, 1667, 1176, 734.

[α]_D²⁵ = 133.2° (c = 0.5, CHCl₃).

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl 6-(3-methoxyphenyl)-2-methylnicotinate, **89**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S61** (60 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 3:1) afforded **89** (65 mg, 0.14 mmol, 94%) as a white solid.

R_f = 0.47 (pentane / Et₂O, 1:1)

m.p. = 84-86 °C

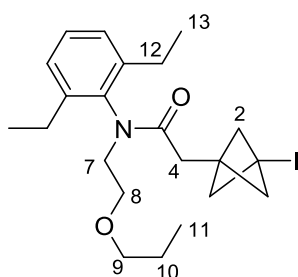
¹H NMR (400 MHz, CDCl₃) δ 8.21 (1H, d, *J* = 8.3 Hz, ArH), 7.70-7.57 (3H, m, ArH), 7.40 (1H, t, *J* = 8.1 Hz, H16), 7.00 (1H, ddd, *J* = 8.1, 2.6, 0.9 Hz, H15), 4.31 (2H, t, *J* = 6.4 Hz, H5), 3.90 (3H s, OMe), 2.91 (3H, s, H18), 2.30 (6H, s, H2), 2.02 (2H, t, *J* = 6.4 Hz, H4).

¹³C NMR (101 MHz, CDCl₃) δ 166.4, 160.3, 160.2, 159.2, 139.9, 139.3, 130.0, 123.3, 119.8, 117.7, 115.8, 112.7, 62.9, 60.9, 55.5, 46.0, 31.2, 25.5, 6.7.

HRMS (ESI⁺) Found [M+H]⁺ = 464.0712; C₂₁H₂₃INO₃ requires 464.0717.

IR (film) ν_{max}/cm⁻¹ 2971, 2924, 1700, 1586, 1283, 1177, 830.

N*-(2,6-Diethylphenyl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)-*N*-(2-propoxyethyl)acetamide, **90*



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S62** (60 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **90** (65 mg, 0.14 mmol, 92%) as a pale yellow oil.

R_f = 0.50 (pentane / Et₂O, 4:1)

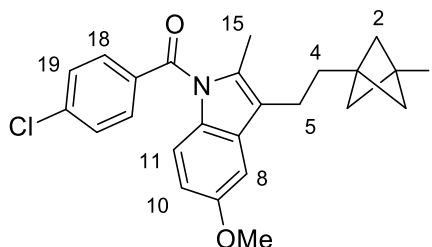
¹H NMR (400 MHz, CDCl₃) δ 7.32-7.27 (1H, m, ArH), 7.19-7.16 (2H, m, ArH), 3.70 (2H, t, *J* = 6.3 Hz, H7), 3.55 (2H, t, *J* = 6.3 Hz, H8), 3.30 (2H, t, *J* = 6.7 Hz, H9), 2.62-2.39 (4H, m, H12), 2.28 (6H, s, H2), 2.10 (2H, s, H4), 1.58-1.43 (2H, m, H10), 1.22 (6H, t, *J* = 7.6 Hz, H13), 0.84 (3H, t, *J* = 7.4 Hz, H11).

¹³C NMR (101 MHz, CDCl₃) δ 171.0, 141.4, 139.4, 128.6, 126.7, 72.8, 67.7, 61.3, 49.3, 44.3, 35.5, 23.4, 22.9, 14.3, 10.7, 7.3.

HRMS (ESI⁺) Found [M+H]⁺ = 470.1542; C₂₂H₃₃INO₂ requires 470.1550.

IR (film) ν_{max}/cm⁻¹ 2967, 2875, 1656, 1173, 843.

(4-Chlorophenyl)(3-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, **91**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S64** (60 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **91** (57 mg, 0.11 mmol, 73%) as a white solid.

R_f = 0.22 (pentane / Et₂O, 95:5)

m.p. = 97-99 °C

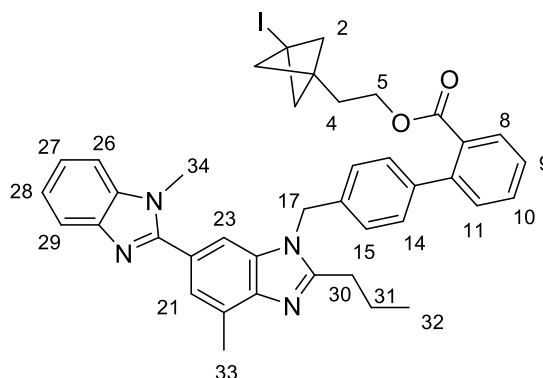
¹H NMR (400 MHz, CDCl₃) δ 7.66-7.61 (2H, m, ArH), 7.50-7.43 (2H, m, ArH), 6.88-6.83 (2H, m, ArH), 6.65 (1H, d, *J* = 9.0, 2.6 Hz, ArH), 3.84 (3H, s, OMe), 2.67-2.51 (2H, m, H5), 2.31 (3H, s, H15), 2.26 (6H, s, H2), 1.91-1.78 (2H, m, H4).

¹³C NMR (101 MHz, CDCl₃) δ 168.4, 155.9, 139.2, 134.3, 134.0, 131.2, 131.2, 131.0, 129.2, 118.9, 115.1, 110.7, 101.8, 60.4, 55.9, 48.3, 31.9, 21.4, 13.5, 7.5.

HRMS (ESI⁺) Found [M+H]⁺ = 520.0536; C₂₄H₂₄ClINO₂ requires 520.0535.

IR (film) ν_{max}/cm⁻¹ 2925, 2161, 1677, 1463, 830.

2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl 4'-((1,7'-dimethyl-2'-propyl-1*H*,3'*H*-[2,5'-bibenzo[*d*]imidazol]-3'-yl)methyl)-[1,1'-biphenyl]-2-carboxylate, **92**



fac-Ir(ppy)₃ (2.5 mg, 4 μmol, 0.025 equiv.), **S65** (100 mg, 0.15 mmol, 1.0 equiv.) and TCP (0.33 mL, 0.9 M in Et₂O, 0.30 mmol, 2.0 equiv.) in *t*-BuCN (1.5 mL) were submitted to **General Procedure 1** at room temperature for 16 h. Purification by column chromatography (SiO₂, EtOAc) afforded **92** (102 mg, 0.14 mmol, 93%) as a white solid.

R_f = 0.33 (EtOAc)

m.p. = 64-66 °C

¹H NMR (400 MHz, CDCl₃) δ 7.82-7.75 (2H, m, ArH), 7.54-7.48 (2H, m, ArH), 7.45-7.35 (3H, m, ArH), 7.32-7.27 (3H, m, ArH), 7.26-7.22 (2H, m, ArH), 7.13-7.08 (2H, m, ArH), 5.47 (2H, s, H17), 3.97 (2H, t, *J* = 6.2 Hz, H5), 3.82 (3H, s, H34), 2.99-2.90 (2H, m, H30), 2.77 (3H, s, H33), 2.02 (6H, s, H2), 1.94-1.84 (2H, m, H31), 1.59 (2H, t, *J* = 6.2 Hz, H4), 1.07 (3H, t, *J* = 7.4 Hz, H32).

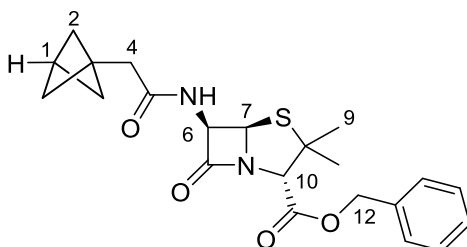
¹³C NMR (101 MHz, CDCl₃) δ 168.3, 156.6, 154.8, 143.3, 143.1, 141.7, 141.3, 136.8, 135.2, 135.0, 131.6, 131.0, 130.6, 129.9, 129.6, 129.2, 127.6, 126.1, 124.1, 124.0, 122.7, 122.5, 119.7, 109.7, 109.0, 62.8, 60.7, 47.2, 45.8, 32.0, 30.6, 30.0, 22.1, 17.1, 14.3, 6.9.

HRMS (ESI⁺) Found [M+H]⁺ = 735.2177; C₄₀H₄₀IN₄O₂ requires 735.2191.

IR (film) ν_{max}/cm⁻¹ 2965, 1717, 1450, 1282, 728.

b. Iodide Applications

Benzyl (2*S*,5*R*,6*R*)-6-(2-(bicyclo[1.1.1]pentan-1-yl)acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, **93**



To a solution of **88** (108 mg, 0.20 mmol, 1.0 equiv.) and tributyltin hydride (59 μ L, 0.22 mmol, 1.1 equiv.) in anhydrous THF (2 mL) at -78°C was added triethylborane (20 μ L, 1.0 M solution in hexane, 0.02 mmol, 0.1 equiv.). After 10 min at this temperature, $\text{Na}_2\text{S}_2\text{O}_3$ (2 mL, 10% aq.) and NaHCO_3 (2 mL, sat. aq.) were added. The resulting mixture was warmed to room temperature and extracted with Et_2O (3×5 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , pentane / Et_2O / Et_3N , 1:2:0.3) afforded **93** (60 mg, 0.15 mmol, 72%) as a colourless foam.

$R_f = 0.51$ (pentane / Et_2O , 1:2)

^1H NMR (400 MHz, CDCl_3) δ 7.41-7.34 (5H, m, ArH), 6.08 (1H, d, $J = 9.1$ Hz, NH), 5.72 (1H, dd, $J = 9.1, 4.2$ Hz, 6H), 5.53 (1H, d, $J = 4.2$ Hz, H7), 5.19 (2H, d, $J = 2.0$ Hz, H12), 4.46 (1H, s, H10), 2.50 (1H, s, H1), 2.43 (2H, s, H4), 1.81 (6H, s, H2), 1.63 (3H, s, H9), 1.42 (3H, s, H9).

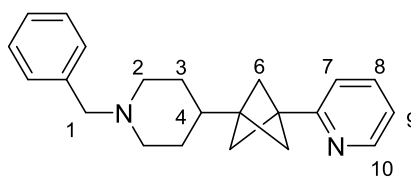
^{13}C NMR (101 MHz, CDCl_3) δ 174.2, 170.1, 167.6, 134.8, 128.9, 128.9, 128.8, 70.6, 68.2, 67.7, 65.1, 58.5, 51.3, 41.2, 40.7, 31.7, 28.2, 27.1.

HRMS (ESI^+) Found $[\text{M}+\text{H}]^+ = 415.1687$; $\text{C}_{22}\text{H}_{27}\text{O}_4\text{N}_2\text{S}$ requires 415.1686.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3288, 2966, 2871, 2361, 1784, 1664, 1202.

$[\alpha]_D^{25} = 142.5^{\circ}$ ($c = 0.6$, CHCl_3).

2-(3-(1-Benzylpiperidin-4-yl)bicyclo[1.1.1]pentan-1-yl)pyridine, **94**



To a solution of **45** (74 mg, 0.20 mmol, 1.0 equiv.) in anhydrous Et₂O (1 mL) at –78 °C was added *t*-BuLi (0.31 mL, 1.6 M in pentane, 0.50 mmol, 2.5 equiv.) dropwise. The resulting yellow heterogeneous solution was stirred for 1 h at –78 °C, then ZnCl₂ (0.26 mL, 1.9 M in 2-MeTHF, 0.50 mmol, 2.5 equiv.) was added dropwise. The resulting mixture was warmed to 0 °C and stirred for 30 min to give a white solution. In a separate vial, a suspension of Pd(dppf)Cl₂•CH₂Cl₂ (7 mg, 15 μmol, 5 mol%), 2-iodopyridine (82 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was sonicated for 3 min and added to the stirred solution of the organozinc reagent at 0 °C. The solution turned green instantly and the resulting mixture was heated at 55 °C for 16 h. After this time, the reaction mixture was cooled to room temperature and quenched with NH₄Cl (2 mL, sat. aq.). The aqueous phase was extracted with EtOAc (3 × 5 mL), and the combined organics were washed with brine, dried (MgSO₄) and concentrated *in vacuo*. Purification by column chromatography (SiO₂, CH₂Cl₂ / MeOH, 98:2→9:1) afforded **94** (48 mg, 0.15 mmol, 75%) as a yellow foam.

R_f = 0.25 (CH₂Cl₂ / MeOH, 95:5)

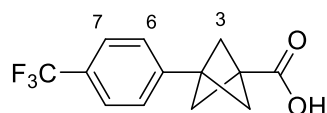
¹H NMR (400 MHz, CDCl₃) δ 8.53 (1H, ddd, *J* = 4.9, 1.8, 1.1 Hz, H10), 7.59 (1H, td, *J* = 7.7, 1.8 Hz, H8), 7.43-7.38 (2H, m, ArH), 7.38-7.28 (3H, m, ArH), 7.17 (1H, dt, *J* = 7.7, 1.1 Hz, H7), 7.10 (1H, ddd, *J* = 7.7, 4.9, 1.1 Hz, H9), 3.69 (2H, s, H1), 3.09 (2H, d, *J* = 10.7 Hz, H2), 2.15 (2H, td, *J* = 10.7, 5.2 Hz, H2), 1.95 (6H, s, H6), 1.69 (2H, m, H3), 1.52 (3H, m, H3, H4).

¹³C NMR (101 MHz, CD₃OD) δ 161.0, 149.5, 138.5, 137.9, 130.9, 129.3, 128.5, 123.1, 122.4, 64.2, 54.4, 50.6, 43.1, 42.4, 37.1, 29.0.

HRMS (ESI⁺) Found [M+H]⁺ = 319.2169; C₂₂H₂₇N₂ requires 319.2169.

IR (film) ν_{max} /cm⁻¹ 2966, 2926, 2863, 1588, 1173, 761.

3-(4-(Trifluoromethyl)phenyl)bicyclo[1.1.1]pentane-1-carboxylic acid, **95**



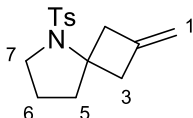
To a solution of **49** (60 mg, 0.18 mmol, 1.0 equiv.) in Et₂O (1.5 ml) cooled to -78°C , was added *t*-BuLi (0.27 ml, 1.6 M in pentane, 0.36 mmol, 2.5 equiv.). After stirring for 30 min, CO₂ (g) was bubbled through the solution for 30 min. The resulting solution was warmed to room temperature and quenched with NH₄Cl (5 mL, sat. aq.). The mixture was then acidified to pH 1 with HCl (1 M, aq.) and extracted with EtOAc (3 \times 10 ml), and the combined organic layers concentrated *in vacuo*. Purification by column chromatography (SiO₂, CH₂Cl₂ / MeOH, 95:5) afforded **95** (34 mg, 0.13 mmol, 73%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 7.67 (2H, d, J = 8.0 Hz, H7), 7.45 (2H, d, J = 8.0 Hz, H6), 2.26 (6H, s, H3).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.1, 144.3, 127.6 (q, J = 31.8 Hz), 127.0, 125.2 (q, J = 3.9 Hz), 124.4 (q, J = 271.9 Hz), 52.6, 40.7, 36.9.

Spectroscopic data in agreement with that reported previously.¹¹

2-Methylene-5-tosyl-5-azaspiro[3.4]octane, **96**



To a solution of **40** (20.3 mg, 0.05 mmol, 1.0 equiv.) in CH₂Cl₂ (2 ml) at -78°C was added AgSbF₆ (21 mg, 0.06 mmol, 1.2 equiv.). After 30 min at this temperature the reaction mixture was filtered through a SiO₂ pad (pentane / EtOAc, 9:1) to afford **96** (11.1 mg, 0.04 mmol, 80%) as a white solid.

R_f = 0.55 (pentane / EtOAc, 3:1)

m.p. = 69-71 $^{\circ}\text{C}$

¹H NMR (400 MHz, CDCl₃) δ 7.71 (2H, d, J = 8.2 Hz, ArH), 7.28 (2H, d, J = 8.2 Hz, ArH), 4.87-4.80 (2H, m, H1), 3.70-3.61 (2H, m, H3), 3.44 (2H, t, J = 6.7 Hz, H7), 2.52- 2.44 (2H, m, H3), 2.41 (3H, s, ArMe), 1.97 (2H, t, J = 6.7 Hz, H5), 1.78 (2H, app. quin., J = 6.7 Hz, H6).

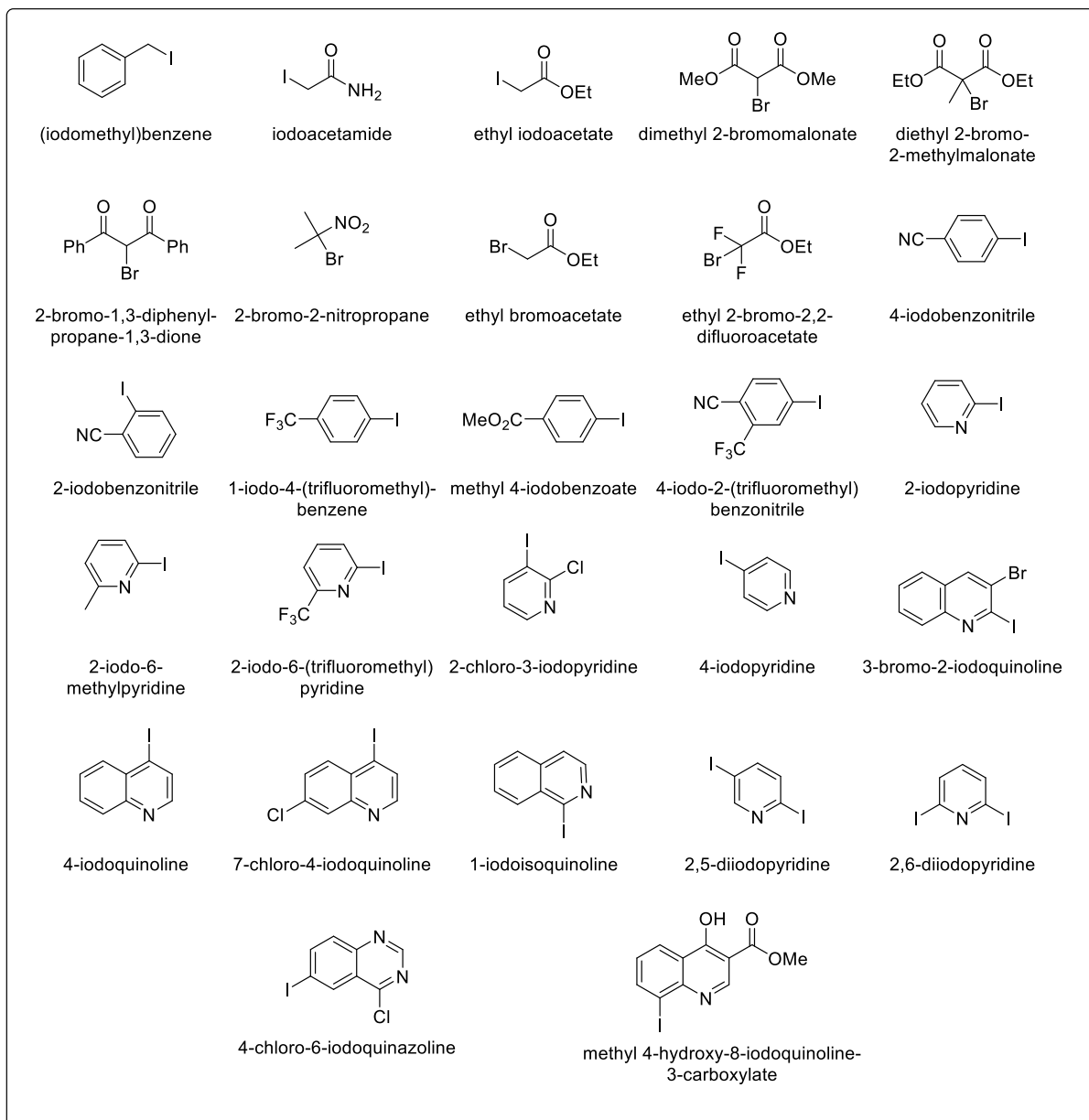
¹³C NMR (101 MHz, CDCl₃) δ 143.0, 141.6, 138.5, 129.7, 127.0, 106.6, 62.5, 50.2, 45.3, 40.7, 22.4, 21.6.

HRMS (ESI⁺) Found $[M+H]^+$ = 278.1210; C₁₅H₂₀O₂NS requires 278.1209.

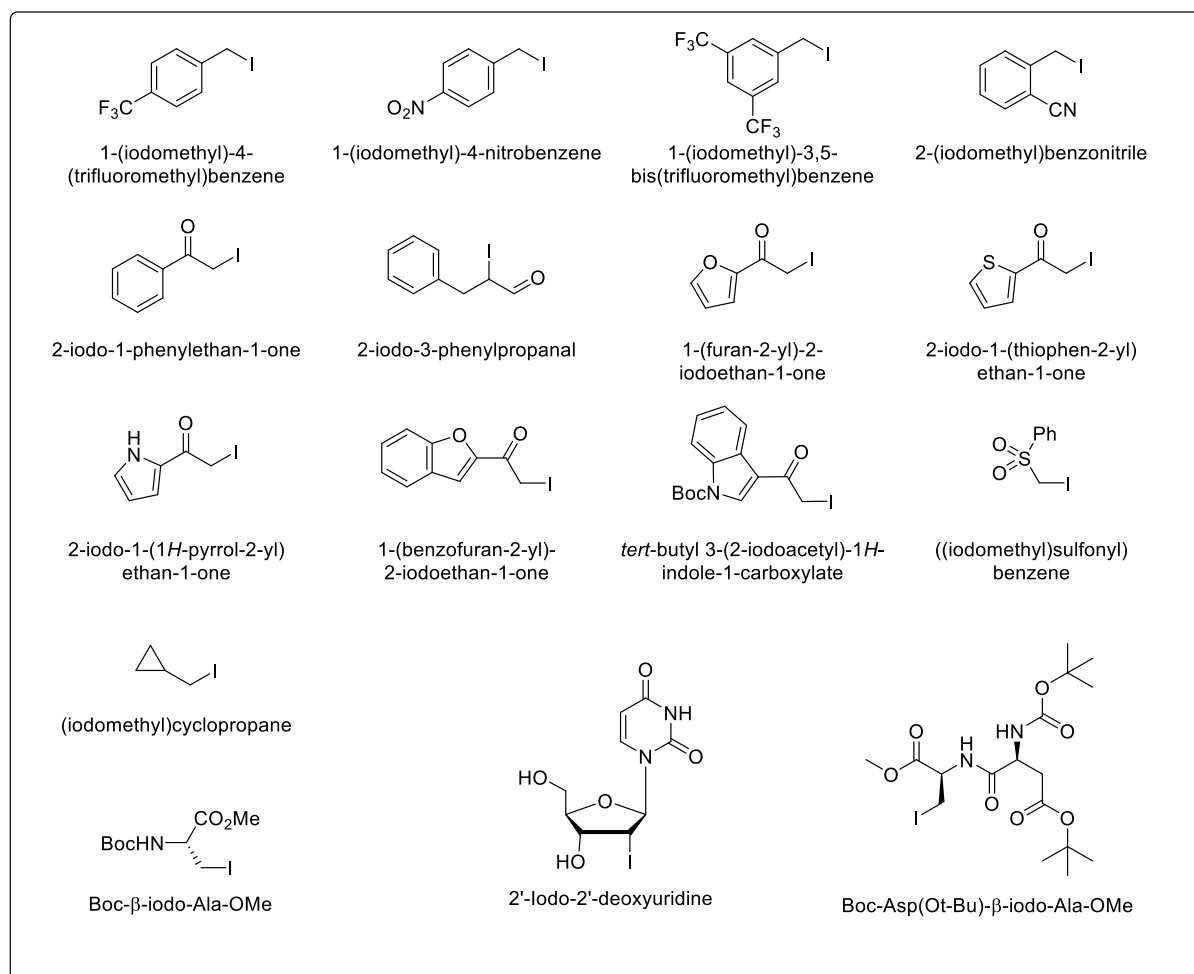
IR (film) ν_{max} /cm⁻¹ 2923, 1682, 1598, 1336, 1154, 667.

c. Synthesis of Iodide Precursors

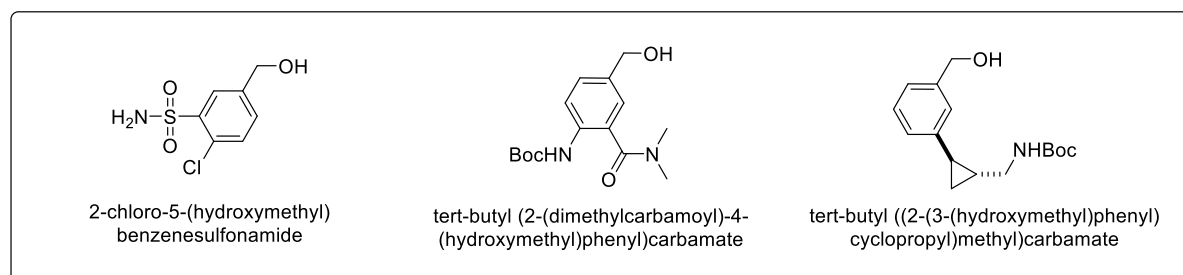
The following substrates were purchased from commercial suppliers.



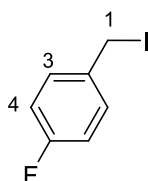
The synthesis of the following substrates have been previously reported by our group.¹



The following compounds were supplied by Pfizer:



1-Fluoro-4-(iodomethyl)benzene, S1



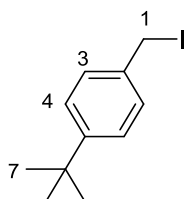
4-Fluorobenzyl bromide (125 μ L, 1.0 mmol, 1.0 equiv.) and NaI (299 mg, 2.0 mmol, 2.0 equiv.) were dissolved in acetone (6 mL) and submitted to **General Procedure 4** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:1) afforded **S1** (150 mg, 1.55 mmol, 64%) as a colourless solid.

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.31 (2H, m, ArH), 7.11-6.89 (2H, m, ArH), 4.44 (2H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 162.3 (d, J = 248.0 Hz), 135.3 (d, J = 3.1 Hz), 130.6 (d, J = 8.1 Hz), 115.9 (d, J = 22.2 Hz), 4.6.

Spectroscopic data in agreement with that reported previously.¹²

1-(*tert*-Butyl)-4-(iodomethyl)benzene, S2



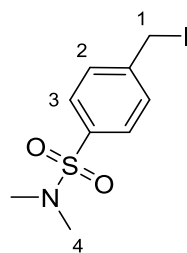
tert-Butylbenzyl bromide (718 mg, 3.2 mmol, 1.0 equiv.) and NaI (711 mg, 4.8 mmol, 1.5 equiv.) were dissolved in acetone (10 mL) and submitted to **General Procedure 4** at room temperature for 20 h. Purification by column chromatography (SiO₂, pentane) afforded **S2** (764 mg, 2.7 mmol, 85%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.31 (4H, m, H3, H4), 4.46 (2H, s, H1), 1.31 (9H, s, H7).

¹³C NMR (101 MHz, CDCl₃) δ 151.2, 136.3, 128.6, 125.9, 34.8, 31.4, 6.1.

Spectroscopic data in agreement with that reported previously.¹³

4-(Iodomethyl)-*N,N*-dimethylbenzenesulfonamide, **S3**



4-(Hydroxymethyl)-*N,N*-dimethylbenzenesulfonamide (215 mg, 1.00 mmol, 1.0 equiv.), triphenylphosphine (341 mg, 1.30 mmol, 1.3 equiv.), imidazole (102 mg, 1.50 mmol, 1.5 equiv.) and iodine (305 mg, 1.20 mmol, 1.2 equiv.) in CH₂Cl₂ (4 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 3:2) afforded **S3** (148 mg, 0.46 mmol, 46%) as a white solid.

R_f = 0.26 (pentane / Et₂O, 3:2)

m.p. = 100-101 °C

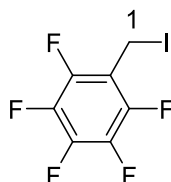
¹H NMR (500 MHz, CDCl₃) δ 7.73-7.68 (2H, m, H3), 7.55-7.51 (2H, m, H2), 4.47 (2H, s, H1), 2.72 (6H, s, H4).

¹³C NMR (126 MHz, CDCl₃) δ 144.5, 135.1, 129.5, 128.4, 38.1, 3.0.

HRMS (ESI⁺) Found [M+Na]⁺ = 347.9526; C₉H₁₂O₂NINaS requires 347.9526.

IR (film) ν_{\max} /cm⁻¹ 2920, 2848, 1340, 1160.

1,2,3,4,5-Pentafluoro-6-(iodomethyl)benzene, **S4**

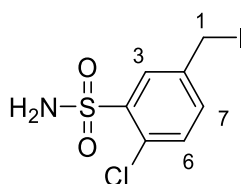


Pentafluorobenzyl bromide (546 mg, 1.9 mmol, 1.0 equiv.) and NaI (435 mg, 2.9 mmol, 1.5 equiv.) were dissolved in acetone (5 mL) and submitted to **General Procedure 4** at room temperature for 20 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:1) afforded **S4** (463 mg, 1.5 mmol, 79%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 4.36 (2H, br. s, H1).

Spectroscopic data in agreement with that reported previously.¹⁴

2-Chloro-5-(iodomethyl)benzenesulfonamide, S5



2-Chloro-5-(hydroxymethyl)benzenesulfonamide (222 mg, 1.0 mmol, 1.0 equiv.), triphenylphosphine (393 mg, 1.5 mmol, 1.5 equiv.), imidazole (102 mg, 1.5 mmol, 1.5 equiv.) and iodine (381 mg, 1.5 mmol, 1.5 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S5** (125 mg, 0.38 mmol, 38%) as a white solid.

R_f = 0.43 (CH₂Cl₂ / MeOH, 95:5)

m.p. = 180-182 °C

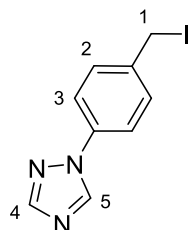
¹H NMR (400 MHz, CD₃OD) δ 8.10 (1H, d, J = 2.3 Hz, H3), 7.59 (1H, dd, J = 8.2, 2.3 Hz, H7), 7.51 (1H, d, J = 8.2 Hz, H6), 4.59 (2H, s, H1).

¹³C NMR (101 MHz, CD₃OD) δ 142.4, 141.3, 134.4, 133.1, 131.5, 130.6, 2.6.

HRMS (ESI⁺) Found $[M+Na]^+$ = 353.8824; C₇H₇O₂NCIISNa requires 353.8823.

IR (film) ν_{max}/cm^{-1} 3381, 3269, 1647, 1464, 1329, 1166, 698.

1-(4-(Iodomethyl)phenyl)-1H-1,2,4-triazole, S6



(4-(1H-1,2,4-Triazol-1-yl)phenyl)methanol (175 mg, 1.00 mmol, 1.0 equiv.), triphenylphosphine (341 mg, 1.30 mmol, 1.3 equiv.), imidazole (102 mg, 1.50 mmol, 1.5 equiv.) and iodine (305 mg, 1.20 mmol, 1.2 equiv.) in CH₂Cl₂ (4 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:3) afforded **S6** (56.8 mg, 0.20 mmol, 20%) as a pale yellow solid.

R_f = 0.10 (pentane / Et₂O, 2:3)

m.p. = 210-212 °C

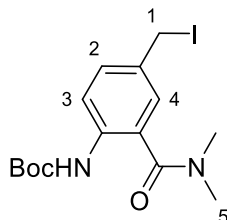
¹H NMR (500 MHz, CDCl₃) δ 8.55 (1H, s, H5), 8.11 (1H, s, H4), 7.65-7.59 (2H, m, H3), 7.54-7.51 (2H, m, H2), 4.49 (2H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 152.9, 140.9, 139.8, 136.4, 130.3, 120.5, 3.9.

HRMS (ESI⁺) Found [M+H]⁺ = 285.9836; C₉H₉N₃I requires 285.9836.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2922, 2851, 1524, 1276, 1153.

***tert*-Butyl (2-(dimethylcarbamoyl)-4-(iodomethyl)phenyl)carbamate, S7**



tert-Butyl (2-(dimethylcarbamoyl)-4-(hydroxymethyl)phenyl)carbamate (294 mg, 1.00 mmol, 1.0 equiv.), triphenylphosphine (341 mg, 1.30 mmol, 1.3 equiv.), imidazole (102 mg, 1.50 mmol, 1.5 equiv.) and iodine (305 mg, 1.20 mmol, 1.2 equiv.) in CH₂Cl₂ (4 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 3:2) afforded **S7** (71.6 mg, 0.18 mmol, 18%) as a yellow oil.

R_f = 0.17 (pentane / Et₂O, 3:2)

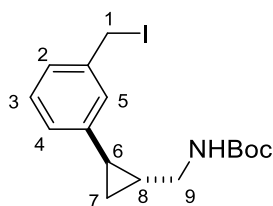
¹H NMR (500 MHz, CDCl₃) δ 8.16-8.04 (2H, m, H3 and NH), 7.36 (1H, dd, *J* = 8.6, 2.2 Hz, H2), 7.23 (1H, d, *J* = 2.2 Hz, H4), 4.42 (2H, s, H1), 3.08 (6H, br. d, *J* = 42.9 Hz, H5), 1.50 (9H, s, *t*-Bu).

¹³C NMR (126 MHz, CDCl₃) δ 169.9, 152.9, 137.3, 132.6, 131.0, 128.5, 123.6, 121.0, 80.9, 40.1, 35.6, 28.4, 5.3.

HRMS (ESI⁺) Found [M+Na]⁺ = 427.0488; C₁₅H₂₁O₃N₂INa requires 427.0489.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2925, 1727, 1630, 1518, 1392, 1240, 1155.

***tert*-Butyl ((-2-(3-(iodomethyl)phenyl)cyclopropyl)methyl)carbamate, S8**



tert-Butyl ((2-(3-(hydroxymethyl)phenyl)cyclopropyl)methyl)carbamate (277 mg, 1.00 mmol, 1.0 equiv.), triphenylphosphine (341 mg, 1.30 mmol, 1.3 equiv.), imidazole (102 mg, 1.50 mmol, 1.5 equiv.) and iodine (305 mg, 1.20 mmol, 1.2 equiv.) in CH₂Cl₂ (4 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **S8** (190 mg, 0.49 mmol, 49%) as a pale yellow oil.

R_f = 0.57 (pentane / Et₂O, 3:2)

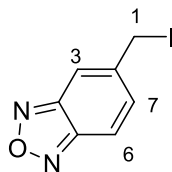
¹H NMR (400 MHz, CDCl₃) δ 7.20-7.15 (2H, m, ArH), 7.07-7.04 (1H, m, ArH), 6.93-6.88 (1H, m, ArH), 4.68 (1H, br. s, NH), 4.41 (2H, s, H1), 3.28-3.05 (2H, m, H9), 1.82-1.74 (1H, m, H8), 1.45 (9H, s, *t*-Bu), 1.33-1.27 (1H, m, H6), 0.97-0.86 (2H, m, H7).

¹³C NMR (126 MHz, CDCl₃) δ 156.0, 143.4, 139.4, 128.9, 126.4, 126.2, 125.5, 79.5, 44.8, 28.6, 23.3, 21.9, 14.5, 5.9.

HRMS (ESI⁺) Found [M+Na]⁺ = 410.0588; C₁₆H₂₂O₂NINa requires 410.0587.

IR (film) ν_{max}/cm⁻¹ 3354, 2976, 2929, 1697, 1509, 1167.

5-(Iodomethyl)benzo[*c*][1,2,5]oxadiazole, S9



2,1,3-Benzoxadiazol-5-ylmethanol (150 mg, 1.0 mmol, 1.0 equiv), triphenylphosphine (393 mg, 1.5 mmol, 1.5 equiv.), imidazole (102 mg, 1.5 mmol, 1.5 equiv.) and iodine (381 mg, 1.5 mmol, 1.5 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S9** (210 mg, 0.81 mmol, 81%) as a white solid.

R_f = 0.47 (pentane / Et₂O, 9:1)

m.p. = 102-104 °C

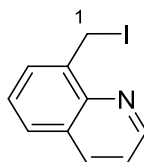
¹H NMR (400 MHz, CDCl₃) δ 7.81 (1H, dd, *J* = 9.3, 1.0 Hz, H6), 7.77-7.75 (1H, m, H3), 7.38 (1H, dd, *J* = 9.3, 1.5 Hz, H7), 4.47 (2H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 149.2, 148.5, 143.0, 133.8, 117.4, 113.9, 3.9.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max}/cm⁻¹ 2160, 2033, 1537, 819.

8-(Iodomethyl)quinoline, S10



3-(Bromomethyl)quinoline (222 mg, 1.00 mmol, 1.0 equiv.) and sodium iodide (225 mg, 1.50 mmol, 1.5 equiv.) in acetone (1 mL) were submitted to **General Procedure 4** for 20 h to afford **S10** (208 mg, 0.77 mmol, 77%) as a pale yellow solid.

R_f = 0.14 (pentane / Et₂O, 4:1)

m.p. = 84-85 °C

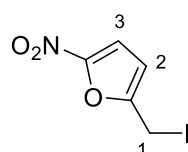
¹H NMR (500 MHz, CDCl₃) δ 9.03 (1H, dd, *J* = 4.2, 1.8 Hz, ArH), 8.16 (1H, dd, *J* = 8.3, 1.8 Hz, ArH), 7.84 (1H, dd, *J* = 7.1, 1.4 Hz, ArH), 7.77 (1H, dd, *J* = 8.3, 1.4 Hz, ArH), 7.48-7.42 (2H, m, ArH), 5.19 (2H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 149.9, 145.7, 137.9, 136.4, 129.9, 128.9, 128.3, 126.6, 121.8, 1.9.

HRMS (APCI⁺) Found [M+H]⁺ = 269.9775; C₁₀H₉NI requires 269.9774.

IR (film) ν_{max} /cm⁻¹ 1685, 1573, 1499, 1404, 1320, 1249.

2-(Iodomethyl)-5-nitrofuran, S11



3-(Bromomethyl)-5-nitrofuran (206 mg, 1.00 mmol, 1.0 equiv.) and sodium iodide (225 mg, 1.50 mmol, 1.5 equiv.) in acetone (1 mL) were submitted to **General Procedure 4** for 20 h to afford **S11** (189 mg, 0.75 mmol, 75%) as a dark orange oil.

R_f = 0.10 (pentane / Et₂O, 4:1)

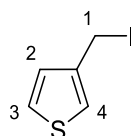
¹H NMR (500 MHz, CDCl₃) δ 7.24 (1H, d, *J* = 3.7 Hz, H3), 6.58 (1H, d, *J* = 3.7 Hz, H2), 4.42 (2H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 155.4, 151.6, 113.0, 111.4, -10.2.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max} /cm⁻¹ 3137, 1692, 1536, 1495, 1350, 1245.

3-(Iodomethyl)thiophene, S12



3-(Bromomethyl)thiophene (110 mg, 1.00 mmol, 1.0 equiv.) and sodium iodide (225 mg, 1.50 mmol, 1.5 equiv.) in acetone (1 mL) were submitted to **General Procedure 4** for 20 h to afford **S12** (210 mg, 0.94 mmol, 94%) as a pale yellow oil.

R_f = 0.74 (pentane / Et₂O, 7:3)

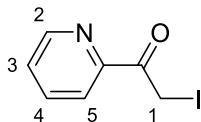
¹H NMR (500 MHz, CDCl₃) δ 7.29 (1H, dd, *J* = 5.0, 3.0 Hz, H3), 7.27-7.25 (1H, m, H4), 7.11 (1H, dd, *J* = 5.0, 1.4 Hz, H2), 4.47 (2H, s, H1).

¹³C NMR (126 MHz, CDCl₃) δ 139.3, 128.6, 126.7, 123.3, -1.1.

HRMS (EI⁺) Found [M-I]⁺ = 97.0103; C₅H₅S requires 97.0106.

IR (film) ν_{max} /cm⁻¹ 3098, 2905, 1683, 1565, 1428, 1153, 1080.

2-Iodo-1-(pyridin-2-yl)ethan-1-one, S13



1-(Pyridin-2-yl)ethan-1-one (0.11 mL, 1.0 mmol, 1.0 equiv.), CuO (80 mg, 1.0 mmol, 1.0 equiv.) and iodine (250 mg, 1.0 mmol, 1.0 equiv.) in methanol (4 mL) were submitted to **General Procedure 6**. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **S13** (21 mg, 0.09 mmol, 9%) as a yellow oil.

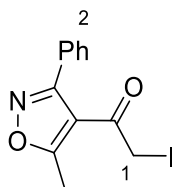
R_f = 0.43 (pentane / Et₂O, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 8.69 (1H, ddd, *J* = 4.7, 1.8, 1.1 Hz, H2), 8.10 (1H, dt, *J* = 7.7, 1.1 Hz, H5), 7.87 (1H, td, *J* = 7.7, 1.8 Hz, H4), 7.51 (1H, ddd, *J* = 7.7, 4.7, 1.1 Hz, H3), 4.69 (2H, s, H1).

¹³C NMR (101 MHz, CDCl₃) δ 194.6, 150.9, 149.2, 137.3, 127.8, 123.1, 1.9.

Spectroscopic data in agreement with that reported previously.¹⁵

2-Iodo-1-(5-methyl-3-phenylisoxazol-4-yl)ethan-1-one, S14



1-(5-Methyl-3-phenylisoxazol-4-yl)ethan-1-one (200 mg, 1.0 mmol, 1.0 equiv.), CuO (80 mg, 1.0 mmol, 1.0 equiv.) and iodine (250 mg, 1.0 mmol, 1.0 equiv.) in methanol (4 mL) were submitted to **General Procedure 6**. Purification by column chromatography (SiO₂, pentane / Et₂O, 4:1) afforded **S14** (0.24 g, 0.74 mmol, 74%) as a yellow oil.

R_f = 0.40 (pentane / Et₂O, 7:3)

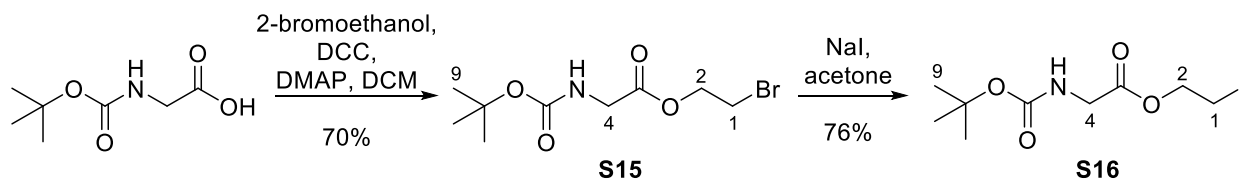
¹H NMR (500 MHz, CDCl₃) δ 7.57-7.49 (5H, m, PhH), 3.75 (2H, s, H1), 2.71 (3H, s, H2).

¹³C NMR (126 MHz, CDCl₃) δ 188.8, 176.5, 161.4, 130.6, 129.1, 129.1, 128.5, 114.1, 13.7, 6.1.

HRMS (ESI⁺) Found [M+H]⁺ = 327.9829; C₁₂H₁₁O₂NI requires 327.9829.

IR (film) ν_{max} /cm⁻¹ 1672, 1568, 1413, 1307, 699.

2-Iodoethyl (tert-butoxycarbonyl)glycinate, S16



To a solution of *N*-(tert-butoxycarbonyl)glycine (350 mg, 2.0 mmol, 1.0 equiv.), 2-bromoethanol (250 mg, 2.0 mmol, 1.0 equiv.) and DMAP (244 mg, 2.0 mmol, 1.0 equiv.) in CH₂Cl₂ (10 mL) was added DCC (454 mg, 2.2 mmol, 1.1 equiv.). After 12 h at room temperature, the mixture was diluted with water (10 mL). The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (2 × 15 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 4:1) afforded **S15** (399 mg, 1.4 mmol, 70%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.00 (1H, s, NH), 4.46 (2H, t, *J* = 6.2 Hz, H₂), 3.96 (2H, d, *J* = 5.7 Hz, H₄), 3.51 (2H, t, *J* = 6.2 Hz, H₁), 1.45 (9H, s, H₉).

¹³C NMR (101 MHz, CDCl₃) δ 170.2, 155.8, 80.3, 64.6, 42.4, 28.4, 28.3.

S15 (200 mg, 0.7 mmol, 1.0 equiv.) and NaI (531 mg, 3.6 mmol, 5.0 equiv.) were dissolved in acetone (10 mL) and submitted to **General Procedure 4** at reflux for 16 h. Purification by column chromatography (SiO₂, pentane / EtOAc, 9:1) afforded **S16** (178 mg, 0.5 mmol, 76%) as a colourless oil.

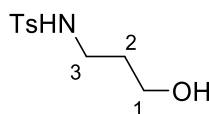
¹H NMR (400 MHz, CDCl₃) δ 5.00 (1H, d, *J* = 6.0 Hz, NH), 4.40 (2H, t, *J* = 6.9 Hz, H₂), 3.95 (2H, d, *J* = 6.0 Hz, H₄), 3.29 (2H, t, *J* = 6.9 Hz, H₁), 1.45 (9H, s, H₉).

¹³C NMR (101 MHz, CDCl₃) δ 170.0, 155.8, 80.3, 65.3, 42.5, 28.4, -0.2.

HRMS (ESI⁺) Found [M+Na]⁺ = 352.0016; C₉H₁₆O₄Na requires 352.0016.

IR (film) ν_{max}/cm⁻¹ 3369, 2977, 1754, 1700, 1159.

N-(3-Hydroxypropyl)-4-methylbenzenesulfonamide, S17



To a solution of 3-aminopropanol (2.0 g, 26.6 mmol, 1.3 equiv.) in CH₂Cl₂ (100 mL) at 0 °C was added triethylamine (2.5 mL, 25.0 mmol, 1.3 equiv.) and *p*-toluenesulfonyl chloride

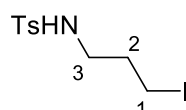
(3.8 g, 20.0 mmol, 1.0 equiv.). After 1 h, HCl (20 mL, 1 M aq.) was added, the layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo* to give **S17** (4.0 g, 17.4 mmol, 87%) as a yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.73 (2H, d, *J* = 8.0 Hz, ArH), 7.29 (2H, d, *J* = 8.0 Hz, ArH), 5.46 (1H, t, *J* = 6.2 Hz, NH), 3.69 (2H, q, *J* = 5.4 Hz, H1), 3.05 (2H, q, *J* = 6.2 Hz, H3), 2.51 (1H, t, *J* = 5.4 Hz, OH), 2.41 (3H, s, ArMe), 1.77-1.58 (2H, m, H2).

¹³C NMR (101 MHz, CDCl₃) δ 143.5, 136.8, 129.8, 127.1, 60.5, 41.0, 31.6, 21.6.

Spectroscopic data in agreement with that reported previously.¹⁶

***N*-(3-Iodopropyl)-4-methylbenzenesulfonamide, S18**



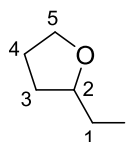
S17 (4.0 g, 17.4 mmol, 1.0 equiv.), triphenylphosphine (6.9 g, 26.1 mmol, 1.5 equiv.), imidazole (1.8 g, 26.1 mmol, 1.5 equiv.) and iodine (6.6 g, 26.1 mmol, 1.5 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / EtOAc, 4:1→0:1) afforded **S18** (4.6 mg, 13.6 mmol, 78%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.76 (2H, d, *J* = 8.0 Hz, ArH), 7.32 (2H, d, *J* = 8.0 Hz, ArH), 4.97 (1H, m, NH), 3.16 (2H, t, *J* = 6.6 Hz, H1), 3.03 (2H, q, *J* = 6.6 Hz, H3), 2.43 (3H, s, ArMe), 1.96 (2H, p, *J* = 6.6 Hz, H1).

¹³C NMR (101 MHz, CDCl₃) δ 143.8, 136.7, 129.9, 127.2, 43.5, 33.0, 21.7, 2.6.

Spectroscopic data in agreement with that reported previously.¹⁷

2-(Iodomethyl)tetrahydrofuran, S19



To a solution of Oxone® (1.23 g, 4.0 mmol, 2.0 equiv.) in MeCN (2 mL) and water (8 mL) was added a solution of 4-penten-1-ol (207 μL, 2.0 mmol, 1.0 equiv.) in MeCN (4 mL). After 2 h at room temperature, the reaction was diluted with water (20 mL) and Na₂S₂O₃ (10 mL, sat. aq.) then extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column

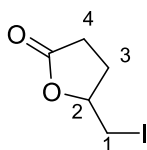
chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S19** (362 mg, 1.7 mmol, 85%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 4.08-3.90 (2H, m, H2, H5), 3.86-3.78 (1H, m, H5), 3.29-3.16 (2H, m, H1), 2.10 (1H, dddd, *J* = 12.2, 8.3, 6.8, 5.3 Hz, H3), 2.02-1.86 (2H, m, H4), 1.70-1.60 (1H, m, H3).

¹³C NMR (101 MHz, CDCl₃) δ 78.6, 69.0, 32.0, 26.2, 10.6.

Spectroscopic data in agreement with that reported previously.¹⁸

5-(Iodomethyl)dihydrofuran-2(3*H*)-one, **S20**



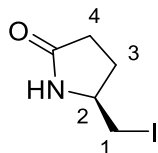
To a solution of Oxone[®] (1.23 g, 4.0 mmol, 2.0 equiv.) in MeCN (6 mL) and water (8 mL) was added a solution of 4-pentenoic acid (204 μL, 2.0 mmol, 1.0 equiv.) in MeCN (4 mL). After 2 h at room temperature, the reaction was diluted with water (20 mL) and Na₂S₂O₃ (10 mL, sat. aq.) then extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo* to give **S20** (227 mg, 2.0 mmol, 50%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 4.55 (1H, qd, *J* = 7.1, 4.4 Hz, H2), 3.41 (1H, dd, *J* = 10.4, 4.4 Hz, H1), 3.30 (1H, dd, *J* = 10.4, 7.1 Hz, H1), 2.72-2.41 (3H, m, H3, H4), 2.05-1.91 (1H, m, H3).

¹³C NMR (101 MHz, CDCl₃) δ 176.3, 78.5, 29.0, 28.2, 7.5.

Spectroscopic data in agreement with that reported previously.¹⁹

(*S*)-5-(Iodomethyl)pyrrolidin-2-one, **S21**



(*S*)-5-(Hydroxymethyl)pyrrolidin-2-one (333 mg, 2.9 mmol, 1.0 equiv.), triphenylphosphine (840 mg, 3.2 mmol, 1.1 equiv.), imidazole (497 mg, 7.3 mmol, 2.5 equiv.) and iodine (812 mg, 3.2 mmol, 1.1 equiv.) were submitted to **General Procedure 2**. Purification by

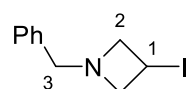
column chromatography (SiO₂, pentane / EtOAc, 4:1→0:1) afforded **S21** (555 mg, 2.5 mmol, 85%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 6.01 (1H, s, NH), 3.92-3.82 (1H, m, H2), 3.31-3.10 (2H, m, H1), 2.57-2.27 (3H, m, H3, H4), 1.89-1.77 (1H, m, H3).

¹³C NMR (101 MHz, CDCl₃) δ 178.7, 55.4, 30.5, 27.5, 11.6.

Spectroscopic data in agreement with that reported previously.²⁰

1-Benzyl-3-iodoazetidine, S22



1-Benzylazetidin-3-ol (0.25 g, 1.5 mmol, 1.0 equiv.), triphenylphosphine (0.51 g, 2.0 mmol, 1.3 equiv.), imidazole (0.15 g, 2.3 mmol, 1.5 equiv.) and iodine (0.46 g, 1.8 mmol, 1.2 equiv.) in CH₂Cl₂ (6 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 7:3) afforded **S22** (0.16 g, 0.58 mmol, 39%) as a pale yellow oil.

R_f = 0.17 (pentane / Et₂O, 4:1)

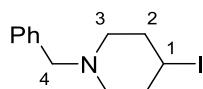
¹H NMR (500 MHz, CDCl₃) δ 7.34-7.22 (5H, m, PhH), 4.44 (1H, p, *J* = 6.8 Hz, H1), 3.95 (2H, td, *J* = 6.8, 2.0 Hz, H2), 3.71 (2H, s, H3), 3.57 (2H, td, *J* = 6.8, 2.0 Hz, H2).

¹³C NMR (126 MHz, CDCl₃) δ 137.6, 128.6, 128.6, 127.4, 66.4, 63.6, 5.3.

HRMS (ESI⁺) Found [M+H]⁺ = 274.0089; C₁₀H₁₃NI requires 274.0087.

IR (film) ν_{max} /cm⁻¹ 3027, 2951, 2829, 1494, 1453, 1362, 1214.

1-Benzyl-4-iodopiperidine, S23



1-Benzyl-4-hydroxypiperidine (0.38 g, 2.0 mmol, 1.0 equiv.), triphenylphosphine (0.68 g, 2.6 mmol, 1.3 equiv.), imidazole (0.20 g, 3.0 mmol, 1.5 equiv.) and iodine (0.61 g, 2.4 mmol, 1.2 equiv.) in CH₂Cl₂ (9 mL) were submitted to **General Procedure 3**. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S23** (0.31 g, 1.0 mmol, 51%) as a pale yellow oil.

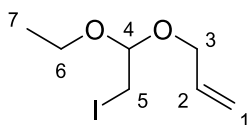
R_f = 0.29 (pentane / Et₂O, 4:1)

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.27 (4H, m, PhH), 7.28-7.23 (1H, m, PhH), 4.29 (1H, s, H1), 3.48 (2H, s, H4), 2.69-2.55 (2H, m, H3), 2.32-2.03 (6H, m, H2, H3).

¹³C NMR (101 MHz, CDCl₃) δ 138.4, 129.2, 128.4, 127.2, 63.3, 53.8, 38.4, 28.6.

Spectroscopic data in agreement with that reported previously.²¹

3-(1-Ethoxy-2-iodoethoxy)prop-1-ene, S24



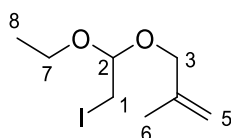
Allyl alcohol (0.20 mL, 3.00 mmol), ethyl vinyl ether (0.34 mL, 3.6 mmol) and *N*-iodosuccinimide (0.81 g, 3.6 mmol) in CH₂Cl₂ (5 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / EtOAc, 95:5) afforded **S24** (668 mg, 2.6 mmol, 87%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.92 (1H, ddt, *J* = 16.4, 10.8, 5.6 Hz, H2), 5.31 (1H, d, *J* = 17.1 Hz, H1), 5.19 (1H, d, *J* = 10.4 Hz, H1), 4.66 (1H, t, *J* = 5.5 Hz, H4), 4.19-4.10 (1H, m, H3), 4.09-4.01 (1H, m, H3), 3.67 (1H, app. quin., *J* = 7.2 Hz, H6), 3.56 (1H, app. quin., *J* = 7.2 Hz, H6), 3.23 (2H, d, *J* = 5.5 Hz, H5), 1.23 (3H, t, *J* = 7.2 Hz, H7).

¹³C NMR (101 MHz, CDCl₃) δ 134.2, 117.5, 101.3, 67.5, 62.3, 15.3, 5.4.

Spectroscopic data in agreement with that reported previously.²²

3-(1-Ethoxy-2-iodoethoxy)-2-methylprop-1-ene, S25



2-Methyl-2-propen-1-ol (0.3 mL, 3.6 mmol, 1.0 equiv.), ethyl vinyl ether (0.5 mL, 5.4 mmol, 1.5 equiv.) and *N*-iodosuccinimide (1.2 g, 5.4 mmol, 1.5 equiv.) in CH₂Cl₂ (5 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane) afforded **S25** (820 mg, 3.0 mmol, 84%) as a colourless oil.

*R*_f = 0.80 (pentane)

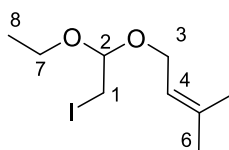
¹H NMR (400 MHz, CDCl₃) δ 5.04-4.97 (1H, m, H5), 4.94-4.86 (1H, m, H5), 4.69-4.61 (1H, m, H2), 4.07-3.91 (2H, m, H3), 3.74-3.51 (2H, m, H7), 3.24 (2H, d, *J* = 5.4 Hz, H1), 1.78 (3H, s, H6), 1.28-1.19 (3H, m, H8).

¹³C NMR (101 MHz, CDCl₃) δ 141.7, 112.9, 101.3, 70.5, 62.3, 19.8, 15.3, 5.4.

HRMS (CI⁺) Found [M+Na]⁺ = 293.0010; C₈H₁₅IO₂Na requires 293.0008

IR (film) *v*_{max}/cm⁻¹ 2975, 2912, 1449, 1116, 1052, 1029, 900.

1-(1-Ethoxy-2-iodoethoxy)-3-methylbut-2-ene, S26



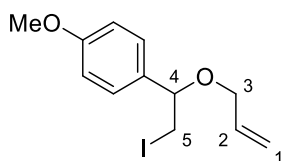
3-Methyl-2-buten-1-ol (0.3 mL, 3.0 mmol, 1.0 equiv.), ethyl vinyl ether (0.34 mL, 3.6 mmol, 1.2 equiv.) and *N*-iodosuccinimide (810 mg, 3.6 mmol, 1.2 equiv.) in CH₂Cl₂ (5 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane) afforded **S26** (731 mg, 2.6 mmol, 86%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.42-5.27 (1H, m, H4), 4.65 (1H, t, *J* = 5.5 Hz, H2), 4.09 (2H, qd, *J* = 11.2, 7.6 Hz, H3), 3.76-3.49 (2H, m, H7), 3.25-3.20 (2H, m, H1), 1.75 (3H, s, H6), 1.69 (3H, s, H6), 1.23 (3H, t, *J* = 7.0 Hz, H8).

¹³C NMR (101 MHz, CDCl₃) δ 137.9, 120.4, 101.2, 63.1, 62.0, 25.9, 18.2, 15.3, 5.7.

Spectroscopic data in agreement with that reported previously.²

1-(1-(Allyloxy)-2-iodoethyl)-4-methoxybenzene, S27



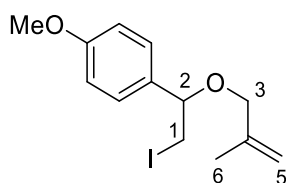
Allyl alcohol (0.51 mL, 7.5 mmol, 2.0 equiv.), 4-vinyl anisole (0.52 mL, 3.8 mmol, 1.0 equiv.) and *N*-iodosuccinimide (1.27 g, 5.6 mmol, 1.5 equiv.) in CH₂Cl₂ (25 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S27** (470 mg, 1.5 mmol, 39%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.24 (2H, d, *J* = 8.2 Hz, ArH), 6.90 (2H, d, *J* = 8.2 Hz, ArH), 5.92 (1H, ddt, *J* = 16.1, 10.6, 5.6 Hz, H2), 5.27 (1H, d, *J* = 17.1 Hz, H1), 5.19 (1H, d, *J* = 10.4 Hz, H1), 4.43 (1H, dd, *J* = 8.4, 4.7 Hz, H4), 3.98 (1H, dd, *J* = 12.9, 5.0 Hz, H3), 3.86-3.76 (1H, dd, *J* = 12.9, 5.0 Hz, H3), 3.81 (3H, s, OMe), 3.38 (1H, dd, *J* = 10.3, 4.7 Hz, H5), 3.30 (1H, dd, *J* = 10.3, 4.7 Hz, H5).

¹³C NMR (101 MHz, CDCl₃) δ 159.8, 134.5, 132.1, 128.0, 117.5, 114.2, 80.6, 70.1, 55.4, 11.1.

Spectroscopic data in agreement with that reported previously.⁵

1-(2-Iodo-1-((2-methylallyl)oxy)ethyl)-4-methoxybenzene, S28



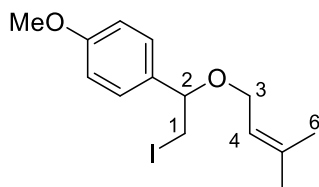
2-Methyl-2-propen-1-ol (0.25 mL, 3.0 mmol, 1.5 equiv.), 4-vinyl anisole (0.27 mL, 2.0 mmol, 1.0 equiv.) and *N*-iodosuccinimide (0.68 g, 3.0 mmol, 1.5 equiv.) in CH₂Cl₂ (10 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→95:5) afforded **S28** (470 mg, 1.55 mmol, 97%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.25-7.19 (2H, m, ArH), 6.94-6.86 (2H, m, ArH), 4.99-4.93 (1H, m, H5), 4.93-4.88 (1H, m, H5), 4.41 (1H, dd, *J* = 8.5, 4.5 Hz, H2), 3.86 (1H, d, *J* = 12.3 Hz, H3), 3.82 (3H, s, OMe), 3.70 (1H, d, *J* = 12.3 Hz, H3), 3.39 (1H, dd, *J* = 10.3, 8.5 Hz, H1), 3.30 (1H, dd, *J* = 10.3, 4.5 Hz, H1), 1.79 (3H, t, *J* = 1.2 Hz, H6).

¹³C NMR (101 MHz, CDCl₃) δ 159.8, 142.0, 132.2, 128.0, 114.2, 113.0, 80.5, 73.0, 55.4, 20.0, 10.9.

Spectroscopic data in agreement with that reported previously.⁵

1-(2-Iodo-1-((3-methylbut-2-en-1-yl)oxy)ethyl)-4-methoxybenzene, S29

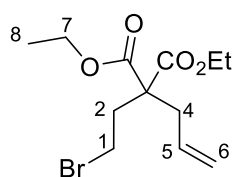


3-Methyl-2-buten-1-ol (0.76 mL, 7.5 mmol, 2.0 equiv.), 4-vinyl anisole (0.50 mL, 3.8 mmol, 1.0 equiv.) and *N*-iodosuccinimide (1.27 g, 5.6 mmol, 1.5 equiv.) in CH₂Cl₂ (25 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / Et₂O, 98:2) afforded **S29** (693 mg, 2.0 mmol, 53%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.27-7.12 (2H, m, ArH), 6.92-6.73 (2H, m, ArH), 5.35-5.27 (1H, m, H4), 4.33 (1H, dd, *J* = 8.3, 4.8 Hz, H2), 3.86-3.70 (5H, m, H3, OMe), 3.29 (1H, dd, *J* = 10.3, 8.3 Hz, H1), 3.21 (1H, dd, *J* = 10.3, 4.8 Hz, H1), 1.67 (3H, s, H6), 1.50 (3H, s, H6).

Spectroscopic data in agreement with that reported previously.⁵

Diethyl 2-allyl-2-(2-bromoethyl)malonate, **S30**



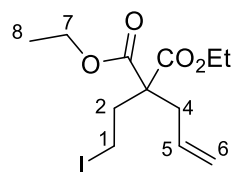
To an oven dried, nitrogen flushed flask was added anhydrous THF (20 mL) and NaH (480 mg of a 60% oil dispersion, 12.0 mmol, 1.2 equiv.). The suspension was cooled to 0 °C with stirring, and then diethyl allylmalonate (2.0 mL, 10.0 mmol, 1.0 equiv.) was added dropwise. The resulting mixture was stirred at 0 °C for 1 h, then 1,2-dibromoethane (1.7 mL, 20.0 mmol, 2.0 equiv.) was added and the resulting mixture was warmed to room temperature over 16 h. The mixture was quenched with NH₄Cl (10 mL, sat. aq.) and extracted with Et₂O (3 × 15 mL). The organic layer was dried (Na₂SO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 1:0→95:5) afforded **S30** (2.1 g, 0.67 mmol, 67%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.76-5.54 (1H, m, H5), 5.17-5.14 (1H, m, H6), 5.13-5.10 (1H, m, H6), 4.20 (4H, q, *J* = 7.1 Hz, H7), 3.35 (1H, dd, *J* = 9.0, 7.6 Hz, H1), 2.66 (2H, d, *J* = 7.5 Hz, H4), 2.53-2.37 (2H, m, H2), 1.26 (6H, t, *J* = 7.1 Hz, H8).

¹³C NMR (101 MHz, CDCl₃) δ 170.4, 132.0, 119.8, 61.7, 57.6, 37.9, 36.4, 27.2, 14.2.

Spectroscopic data in agreement with that reported previously.²³

Diethyl 2-allyl-2-(2-iodoethyl)malonate, **S31**



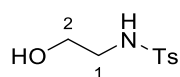
S30 (500 mg, 1.6 mmol, 1.0 equiv.) and NaI (480 mg, 3.2 mmol, 2.0 equiv.) were dissolved in acetone (5 mL) and submitted to **General Procedure 4** at reflux for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S31** (550 mg, 1.55 mmol, 97%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.64 (1H, ddt, *J* = 17.1, 9.7, 7.4 Hz, H5), 5.20-5.13 (1H, m, H6), 5.13-5.09 (1H, m, H6), 4.20 (4H, q, *J* = 7.2 Hz, H7), 3.13-3.06 (2H, m, H1), 2.64 (2H, dt, *J* = 7.4, 1.2 Hz, H4), 2.53-2.44 (2H, m, H2), 1.26 (6H, t, *J* = 7.1 Hz, H8).

¹³C NMR (101 MHz, CDCl₃) δ 170.2, 132.0, 119.7, 61.7, 59.2, 38.0, 37.6, 14.2, -2.3.

Spectroscopic data in agreement with that reported previously.²

***N*-(2-Hydroxyethyl)-4-methylbenzenesulfonamide, S32**



To a solution of ethanolamine (0.61 mL, 10.0 mmol, 1.0 equiv.) and *p*-toluenesulfonyl chloride (2.29 g, 15.0 mmol, 1.5 equiv.) in CH₂Cl₂ (5 mL) at 0 °C was added triethylamine (2.09 mL, 15.0 mmol, 1.5 equiv.) dropwise. The resulting mixture was stirred at room temperature for 24 h. After quenching with water, the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 3:7) afforded **S32** (1.42 g, 6.6 mmol, 66%) as a white solid.

R_f = 0.33 (pentane / EtOAc, 3:7)

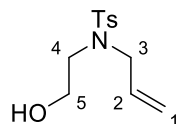
¹H NMR (400 MHz, CDCl₃) δ 7.75 (2H, d, *J* = 8.1 Hz, ArH), 7.29 (2H, d, *J* = 8.1 Hz, ArH), 5.53 (1H, t, *J* = 5.4 Hz, NH), 3.67 (2H, app. q, *J* = 5.4 Hz, H₂), 3.06 (2H, app. q, *J* = 5.4 Hz, H₁), 2.78 (1H, t, *J* = 5.4 Hz, OH), 2.41 (3H, s, ArMe).

¹³C NMR (101 MHz, CDCl₃) δ 143.7, 136.7, 129.9, 127.2, 61.4, 45.3, 21.6.

HRMS (ESI⁺) [M-H]⁺ = 214.0544; C₉H₁₂O₃NS requires 214.0543.

Spectroscopic data in agreement with that reported previously.²⁴

***N*-Allyl-*N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide, S33**



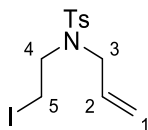
To a solution of **S32** (4.06 g, 18.9 mmol, 1.0 equiv.) in acetone (35 mL) was added K₂CO₃ (3.9 g, 28.4 mmol, 1.5 equiv.), KI (315 mg, 1.9 mmol, 0.1 equiv.) and allyl bromide (2.45 mL, 28.3 mmol, 1.5 equiv.). The resulting mixture was heated to reflux for 16 h. Water was added, and the aqueous layer was extracted with Et₂O (3 × 5 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 3:2) afforded **S33** (3.5 g, 13.6 mmol, 72%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.70 (2H, d, *J* = 7.7 Hz, ArH), 7.30 (2H, d, *J* = 7.7 Hz, ArH), 5.66 (1H, ddt, *J* = 16.5, 10.3, 6.0 Hz, H₂), 5.23-5.10 (2H, m, H₁), 3.83 (2H, d, *J* = 6.3 Hz, H₃), 3.71 (2H, t, *J* = 5.4 Hz, H₅), 3.22 (2H, t, *J* = 5.4 Hz, H₄), 2.42 (3H, s, ArMe).

¹³C NMR (101 MHz, CDCl₃) δ 143.7, 136.3, 133.1, 129.9, 127.4, 119.5, 61.1, 52.3, 49.8, 21.7.

Spectroscopic data in agreement with that reported previously.²⁵

***N*-Allyl-*N*-(2-iodoethyl)-4-methylbenzenesulfonamide, S34**



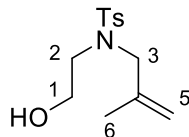
S33 (3.5 g, 13.7 mmol), triphenylphosphine (10.8 g, 41.0 mmol, 1.0 equiv.), imidazole (3.16 g, 46.5 mmol, 1.1 equiv.) and iodine (10.4 g, 41.0 mmol, 1.0 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / EtOAc, 4:1) afforded **S34** (3.15 g, 8.6 mmol, 63%) as a yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.69 (2H, d, J = 7.9 Hz, ArH), 7.31 (2H, d, J = 7.9 Hz, ArH), 5.66 (1H, ddt, J = 16.6, 10.7, 5.5 Hz, H2), 5.24-5.12 (2H, m, H1), 3.78 (2H, d, J = 6.3 Hz, H3), 3.71 (2H, t, J = 5.4 Hz, H4), 3.22 (2H, t, J = 5.4 Hz, H5), 2.42 (3H, s, ArMe).

¹³C NMR (101 MHz, CDCl₃) δ 143.8, 136.4, 133.0, 130.0, 127.2, 119.8, 51.8, 50.3, 21.7, 2.1.

Spectroscopic data in agreement with that reported previously.²

***N*-(2-Hydroxyethyl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide, S35**



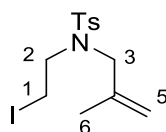
A solution of **S32** (500 mg, 2.3 mmol, 1.0 equiv.), 3-chloro-2-methyl-1-propene (0.28 mL, 2.8 mmol, 1.2 equiv.), K₂CO₃ (387 mg, 2.8 mmol, 1.2 equiv.) and KI (77 mg, 0.5 mmol, 0.2 equiv.) in acetone (10 mL) was heated at reflux for 16 h. The resulting mixture was concentrated *in vacuo* then water (5 mL) was added. The aqueous layer was extracted with Et₂O (3 \times 5 mL) and the combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo* to afford **S35** (600 mg, 2.2 mmol, 97%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.76-7.68 (2H, m, ArH), 7.36-7.28 (2H, m, ArH), 4.90-4.87 (1H, m, H5), 4.90-4.87 (1H, m, H5), 3.75-3.64 (4H, m, H1, H3), 3.20 (2H, t, J = 5.4 Hz, H2), 2.43 (3H, s, ArMe), 2.32-2.22 (1H, m, OH), 1.74 (3H, s, H6).

¹³C NMR (101 MHz, CDCl₃) δ 143.7, 141.0, 136.1, 129.9, 127.5, 114.9, 61.3, 56.4, 50.7, 21.7, 19.9.

Spectroscopic data in agreement with that reported previously.²⁶

N-(2-Iodoethyl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide, **S36**



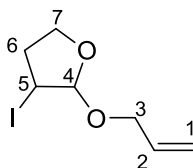
S35 (500 mg, 1.9 mmol, 1.0 equiv.), triphenylphosphine (970 mg, 3.7 mmol, 1.9 equiv.), imidazole (252 mg, 3.7 mmol, 1.9 equiv.) and iodine (939 mg, 3.7 mmol, 1.9 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1→4:1) afforded **S36** (523 mg, 1.4 mmol, 74%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.76-7.63 (2H, m, ArH), 7.37-7.29 (2H, m, ArH), 4.96-4.89 (1H, m, H5), 4.91-4.85 (1H, m, H5), 3.67 (2H, s, H3), 3.43-3.36 (2H, m, H2), 3.24-3.16 (2H, m, H1), 2.43 (3H, s, ArMe), 1.75-1.71 (3H, m, H6).

¹³C NMR (101 MHz, CDCl₃) δ 143.8, 140.7, 136.5, 130.0, 127.3, 115.4, 55.7, 51.0, 21.7, 19.9, 1.8.

Spectroscopic data in agreement with that reported previously.²

2-(Allyloxy)-3-iodotetrahydrofuran, **S37**



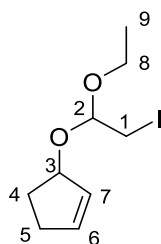
Allyl alcohol (0.5 mL, 7.4 mmol, 1.0 equiv.), 2,3-dihydrofuran (1.1 mL, 14.7 mmol, 2.0 equiv.) and *N*-iodosuccinimide (3.3 g, 14.7 mmol, 2.0 equiv.) in CH₂Cl₂ (15 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S37** (1.5 g, 5.7 mmol, 78%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.96-5.77 (1H, m, H2), 5.38 (1H, s, H4), 5.27 (1H, dq, *J* = 17.2, 1.5 Hz, H1), 5.18 (1H, dq, *J* = 10.4, 1.5 Hz, H1), 4.21-3.95 (5H, m, H3, H5, H7), 2.63 (1H, dtd, *J* = 14.2, 8.2, 6.3 Hz, H6), 2.20 (1H, dddd, *J* = 14.2, 7.0, 3.7, 2.3 Hz, H6).

¹³C NMR (101 MHz, CDCl₃) δ 134.2, 117.5, 110.0, 68.2, 67.2, 35.8, 24.7.

Spectroscopic data in agreement with that reported previously.²⁷

3-(1-Ethoxy-2-iodoethoxy)cyclopent-1-ene, S38



Cyclopent-2-en-1-ol (200 mg, 2.4 mmol, 1.0 equiv.), ethyl vinyl ether (0.5 mL, 4.8 mmol, 2.0 equiv.) and *N*-iodosuccinimide (1.1 g, 4.8 mmol, 2.0 equiv.) in CH₂Cl₂ (5 mL) were submitted to **General Procedure 5**. Purification by column chromatography (SiO₂, pentane / Et₂O, 99:1) afforded **S38** (480 mg, 1.7 mmol, 70%, dr = 1:1) as a pale-yellow oil.

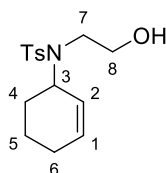
¹H NMR (400 MHz, CDCl₃) δ 6.05-6.01 (1H, m, C=C-H), 5.86-5.80 (1H, m, C=C-H), 4.84-4.77 (1H, m, 1H), 4.72 (q, *J* = 5.4 Hz, 1H), 3.74-3.51 (2H, m, H8), 3.28-3.18 (2H, m, H1), 2.58-2.41 (1H, m, H5), 2.34-2.08 (2H, m, H4, H5), 1.90-1.77 (1H, m, H4), 1.24 (3H, t, *J* = 7.0, H9).

¹³C NMR (101 MHz, CDCl₃) δ 136.1 (2 overlapping peaks), 131.2, 130.7, 101.6, 101.3, 82.6, 82.4, 61.9, 61.3, 31.2, 31.1, 31.0, 30.4, 15.3, 15.3, 6.4, 6.3.

HRMS (ESI⁺, CI⁺, EI⁺): Not found.

IR (film) ν_{max} /cm⁻¹ 2973, 2929, 1661, 1354, 1100, 1033.

N-(Cyclohex-2-en-1-yl)-*N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide, S39



To a solution of **S32** (520 mg, 2.4 mmol, 1.0 equiv.) in acetone (6 mL) was added K₂CO₃ (497 mg, 3.6 mmol, 1.5 equiv.), KI (40 mg, 0.24 mmol, 0.1 equiv.) and 3-bromocyclohex-1-ene (0.46 mL, 3.6 mmol, 1.5 equiv.). The resulting mixture was heated to reflux for 16 h. H₂O was added, and the aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 7:3) afforded **S39** (218 mg, 0.74 mmol, 31%) as a colourless oil.

R_f = 0.22 (pentane / EtOAc, 7:3)

¹H NMR (400 MHz, CDCl₃) δ 7.74 (2H, d, *J* = 8.3 Hz, ArH), 7.31 (2H, d, *J* = 8.3 Hz, ArH), 5.78 (1H, ddd, *J* = 7.5, 6.5, 4.1 Hz, H1), 4.98 (1H, dt, *J* = 10.3, 2.1 Hz, H2), 4.56-4.47 (1H,

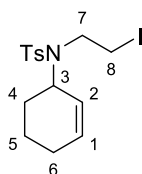
m, H3), 3.79 (2H, app. t, $J = 5.9$ Hz, H8), 3.25 (1H, dt, $J = 15.3, 5.9$ Hz, H7), 3.14 (1H, dt, $J = 15.3, 5.9$ Hz, H7), 2.96 (1H, s, OH), 2.42 (3H, s, ArMe), 1.98-1.82 (3H, m, H4, H6), 1.80-1.70 (1H, m, H5), 1.65-1.54 (1H, m, H5), 1.54-1.42 (1H, m, H4).

^{13}C NMR (101 MHz, CDCl_3) δ 143.5, 137.1, 133.0, 129.8, 127.2, 127.0, 63.2, 55.8, 46.2, 28.9, 24.4, 21.6, 21.5.

HRMS (ESI $^+$) Found $[\text{M}+\text{Na}]^+ = 318.1134$; $\text{C}_{15}\text{H}_{21}\text{O}_3\text{NNaS}$ requires 318.1134.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3523, 2936, 2361, 1598, 1334, 1160, 1087, 1045, 997, 968, 895, 871, 815, 761, 675.

N-(Cyclohex-2-en-1-yl)-*N*-(2-iodoethyl)-4-methylbenzenesulfonamide, **S40**



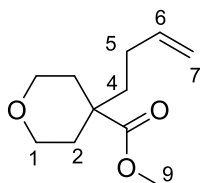
S39 (220 mg, 0.73 mmol, 1.0 equiv.), triphenylphosphine (580 mg, 2.2 mmol), imidazole (0.17 g, 2.5 mmol, 3.0 equiv.), 0.169 g, 2.49 mmol, 3.0 equiv.) and iodine (560 mg, 2.2 mmol, 3.0 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO_2 , pentane / EtOAc, 4:1) afforded **S40** (118 mg, 0.29 mmol, 40%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 7.72 (2H, d, $J = 7.8$ Hz, ArH), 7.31 (2H, d, $J = 7.8$ Hz, ArH), 5.80 (1H, d, $J = 10.2$ Hz, H1), 4.96 (1H, d, $J = 10.2$ Hz, H2), 4.48-4.40 (1H, m, H3), 3.52-3.36 (2H, m, H7, H8), 3.32-3.17 (2H, m, H7, H8), 2.43 (3H, s, ArMe), 2.00-1.84 (3H, m, H4, H6), 1.81-1.70 (1H, m, H5), 1.65-1.52 (1H, m, H5), 1.48-1.34 (1H, m, H4).

^{13}C NMR (101 MHz, CDCl_3) δ 143.7, 137.5, 133.4, 130.0, 127.2, 127.0, 55.5, 47.1, 29.4, 24.5, 21.7, 21.7, 5.0.

Spectroscopic data in agreement with that reported previously.²⁸

Methyl 4-(but-3-en-1-yl)tetrahydro-2H-pyran-4-carboxylate, **S41**



To a solution of diisopropylamine (2.1 mL, 15.0 mmol, 1.5 equiv.) in anhydrous THF (15 mL) at 0 °C was added *n*-BuLi (5.2 mL, 2.5 M solution in hexanes, 13.0 mmol,

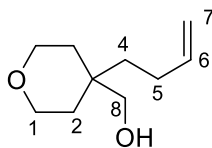
1.3 equiv.). After 10 min, the resulting solution was cooled to $-78\text{ }^{\circ}\text{C}$, then tetrahydropyran-4-carboxylic acid methyl ester (1.3 mL, 10.0 mmol, 1.0 equiv.) was added dropwise. After 1 h at this temperature, 4-bromobutene (1.5 mL, 15.0 mmol, 1.5 equiv.) was added and the resulting solution was slowly warmed to room temperature and stirred for 16 h. The mixture was quenched with NH_4Cl (20 mL, sat. aq.) and extracted with Et_2O ($3 \times 15\text{ mL}$). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , pentane / Et_2O , 9:1) afforded **S41** (1.7 g, 8.6 mmol, 86%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 5.81-5.64 (1H, m, H6), 5.02-4.91 (2H, m, H7), 3.81 (2H, dt, $J = 12.0, 3.3\text{ Hz}$, H1), 3.70 (3H, s, H9), 3.41 (2H, t, $J = 12.0\text{ Hz}$, H1), 2.15-2.02 (2H, m, H2), 2.01-1.89 (2H, m, H5), 1.66-1.56 (2H, m, H4), 1.55-1.44 (2H, m, H2).

^{13}C NMR (101 MHz, CDCl_3) δ 176.2, 138.0, 115.0, 65.6, 51.9, 44.9, 40.0, 34.4, 28.2.

Spectroscopic data in agreement with that reported previously.²⁹

(4-(But-3-en-1-yl)tetrahydro-2H-pyran-4-yl)methanol, **S42**



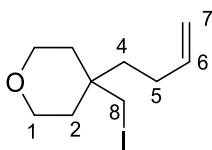
To a solution of **S41** (600 mg, 3.5 mmol, 1.0 equiv.) in anhydrous Et_2O (8 mL) at $0\text{ }^{\circ}\text{C}$ was added lithium aluminium hydride (1.3 mL, 4.0 M solution in Et_2O , 5.3 mmol, 1.5 equiv.). The reaction was stirred for 1 h at this temperature, then EtOAc was added dropwise until effervescence ceased. Rochelle's salt (10 mL, sat. aq.) was added and the resulting mixture was stirred vigorously overnight. The phases were separated, and the aqueous layer was extracted with Et_2O ($3 \times 15\text{ mL}$). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo* to afford **S42** (490 mg, 2.9 mmol, 82%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 5.84 (1H, ddt, $J = 16.8, 10.1, 6.5\text{ Hz}$, H6), 5.05 (1H, dq, $J = 17.1, 1.7\text{ Hz}$, H7), 4.97 (1H, ddt, $J = 10.1, 1.9, 1.3\text{ Hz}$, H7), 3.71-3.63 (4H, m, H1), 3.53 (2H, d, $J = 3.3\text{ Hz}$, H6), 2.08-1.99 (2H, m, H5), 1.60-1.39 (6H, m, H2, H4), 1.31 (1H, s, OH).

^{13}C NMR (101 MHz, CDCl_3) δ 139.2, 114.6, 67.3, 63.7, 35.2, 33.8, 32.6, 27.5.

Spectroscopic data in agreement with that reported previously.²⁹

4-(But-3-en-1-yl)-4-(iodomethyl)tetrahydro-2H-pyran, S43



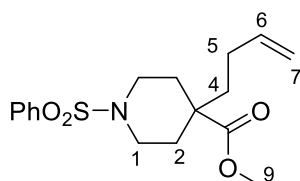
S42 (340 mg, 2.0 mmol, 1.0 equiv.), triphenylphosphine (574 mg, 2.2 mmol, 1.1 equiv.), imidazole (149 mg, 2.2 mmol, 1.1 equiv.) and iodine (556 mg, 2.2 mmol, 1.1 equiv.) in toluene (20 mL) were submitted to **General Procedure 2** at 80 °C for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S43** (330 mg, 1.2 mmol, 59%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.82 (1H, ddt, *J* = 17.0, 10.1, 6.6 Hz, H6), 5.06 (1H, dq, *J* = 17.0, 1.8 Hz, H7), 4.97 (1H, ddt, *J* = 10.1, 1.8, 1.4 Hz, H7), 3.73-3.56 (4H, m, H1), 3.28 (2H, s, H8), 2.01-1.90 (2H, m, H5), 1.66-1.49 (6H, m, H2, H4).

¹³C NMR (101 MHz, CDCl₃) δ 138.3, 115.0, 63.8, 36.6, 35.4, 33.4, 27.0, 19.9.

Spectroscopic data in agreement with that reported previously.²⁹

Methyl 4-(but-3-en-1-yl)-1-(phenylsulfonyl)piperidine-4-carboxylate, S44



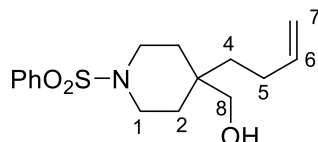
To a solution of diisopropylamine (1.1 mL, 7.5 mmol, 1.5 equiv.) in anhydrous THF (7.5 mL) at 0 °C was added *n*BuLi (2.6 mL, 2.5 M solution in hexanes, 6.5 mmol, 1.3 equiv.). After 10 min, the resulting solution was cooled to -78 °C, then methyl 1-(benzenesulfonyl)piperidine-4-carboxylate (1.4 g, 5.0 mmol, 1.0 equiv.) was added dropwise. After 1 h at this temperature, 4-bromobutene (0.76 mL, 7.5 mmol, 1.5 equiv.) was added and the resulting solution was slowly warmed to room temperature and stirred for 16 h. The mixture was quenched with NH₄Cl (10 mL, sat. aq.) and extracted with Et₂O (3 × 10 mL). The organic layer was dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S44** (1.7 g, 4.5 mmol, 90%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.74-7.67 (2H, m, ArH), 7.60-7.53 (1H, m, ArH), 7.52-7.46 (2H, m, ArH), 5.67 (1H, ddt, *J* = 16.7, 10.0, 6.5 Hz, H6), 4.98-4.88 (2H, m, H7), 3.64-3.57 (2H, m, H1), 3.55 (3H, s, H9), 2.35 (2H, td, *J* = 12.1, 2.5 Hz, H1), 2.23-2.14 (2H, m, H2), 1.93-1.84 (2H, m, H5), 1.59-1.46 (4H, m, H2, H4).

^{13}C NMR (101 MHz, CDCl_3) δ 175.3, 137.5, 136.3, 132.8, 129.1, 127.6, 115.1, 51.9, 44.9, 43.9, 39.5, 33.0, 28.3.

Spectroscopic data in agreement with that reported previously.²⁹

(4-(But-3-en-1-yl)-1-(phenylsulfonyl)piperidin-4-yl)methanol, **S45**



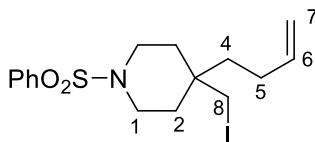
To a solution of **S44** (1.2 g, 3.5 mmol, 1.0 equiv.) in anhydrous Et_2O (8 mL) at 0 °C was added lithium aluminium hydride (1.3 mL of a 4.0 M solution in Et_2O , 5.3 mmol, 1.5 equiv.) dropwise. After 1 h at this temperature, EtOAc was added dropwise until effervescence ceased. Rochelle's salt (10 mL, sat. aq.) was added and the resulting mixture was stirred vigorously overnight. The phases were separated, and the aqueous layer was extracted with Et_2O (3×15 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo* to afford **S45** (1.0 g, 3.2 mmol, 91%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 7.79-7.73 (2H, m, ArH), 7.64-7.58 (1H, m, ArH), 7.57-7.51 (2H, m, ArH), 5.75 (1H, ddt, $J = 16.8, 10.3, 6.5$ Hz, H6), 5.04-4.95 (1H, m, H7), 4.94-4.90 (1H, m, H7), 3.36 (2H, d, $J = 4.8$ Hz, H8), 3.03 (4H, qdd, $J = 11.9, 7.2, 4.4$ Hz, H1), 2.04-1.89 (2H, m, H5), 1.64-1.46 (4H, m, H2), 1.38-1.28 (3H, m, H4, OH).

^{13}C NMR (101 MHz, CDCl_3) δ 138.8, 136.4, 132.9, 129.2, 127.7, 114.8, 66.5, 42.0, 35.3, 33.4, 31.3, 27.4.

Spectroscopic data in agreement with that reported previously.²⁹

4-(But-3-en-1-yl)-4-(iodomethyl)-1-(phenylsulfonyl)piperidine, **S46**



S45 (1.38 g, 4.5 mmol, 1.0 equiv.), triphenylphosphine (1.29 g, 4.9 mmol, 1.1 equiv.), imidazole (334 mg, 4.9 mmol, 1.1 equiv.) and iodine (1.24 g, 4.9 mmol, 1.1 equiv.) in toluene (50 mL) were submitted to **General Procedure 2** at 80 °C for 16 h. Purification by column chromatography (SiO_2 , pentane / Et_2O , 1:1) afforded **S46** (1.3 g, 3.1 mmol, 70%) as a colourless oil.

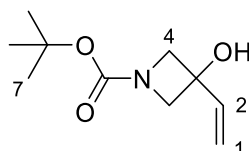
^1H NMR (400 MHz, CDCl_3) δ 7.83-7.71 (2H, m, ArH), 7.65-7.59 (1H, m, ArH), 7.58-7.50 (2H, m, ArH), 5.74 (1H, ddt, $J = 17.0, 10.1, 6.5$ Hz, H6), 5.00 (1H, dq, $J = 17.0, 1.5$ Hz, H7),

4.93 (1H, dq, $J = 10.1, 1.5$ Hz, H7), 3.12-3.02 (4H, m, H1, H8), 2.93 (2H, ddd, $J = 12.1, 7.8, 4.1$ Hz, H1), 1.94-1.82 (2H, m, H5), 1.73-1.57 (4H, m, H2), 1.40-1.32 (2H, m, H4).

^{13}C NMR (101 MHz, CDCl_3) δ 137.9, 136.4, 133.0, 129.3, 127.7, 115.1, 42.1, 36.5, 33.9, 33.5, 26.9, 18.1.

Spectroscopic data in agreement with that reported previously.²⁹

***tert*-Butyl 3-hydroxy-3-vinylazetidine-1-carboxylate, S47**



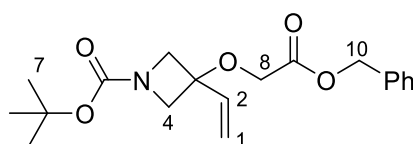
To a solution of 1-Boc-3-azetidinone (1.1 g, 6.4 mmol, 1.0 equiv.) in THF (50 mL) at -20 °C was added vinylmagnesium bromide (7 mL, 1.0 M solution in THF, 7.0 mmol, 1.1 equiv.). After 30 min at this temperature, NH_4Cl (30 mL, sat. aq.) was added. The mixture was warmed to room temperature and extracted with CH_2Cl_2 (3×20 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , pentane / Et_2O , 1:3) afforded **S47** (1.2 g, 6.0 mmol, 94%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 6.13 (1H, dd, $J = 17.3, 10.7$ Hz, H2), 5.36 (1H, dd, $J = 17.3, 0.8$ Hz, H1), 5.23-5.18 (1H, m, H1), 4.07-3.87 (4H, m, H4), 3.00-2.95 (1H, m, OH), 1.43 (9H, s, H7).

^{13}C NMR (101 MHz, CDCl_3) δ 156.6, 139.9, 114.1, 80.0, 70.1, 62.3, 28.5.

Spectroscopic data in agreement with that reported previously.³⁰

***tert*-Butyl 3-(2-(benzyloxy)-2-oxoethoxy)-3-vinylazetidine-1-carboxylate, S48**



To a solution of **S47** (1.2 g, 6.0 mmol, 1.0 equiv.) in anhydrous THF (50 mL) at 0 °C was added, portionwise, NaH (337 mg of a 60% dispersion in mineral oil, 8.4 mmol, 1.4 equiv.). The resulting mixture was warmed to room temperature and stirred for 30 min, then benzyl bromoacetate (1.3 mL, 8.4 mmol, 1.4 equiv.) was added. After 16 h at room temperature, the reaction was quenched with NH_4Cl (30 mL, sat. aq.) and extracted with Et_2O (3×20 mL). The organic layers were combined and washed with brine (20 mL). The organic layer was

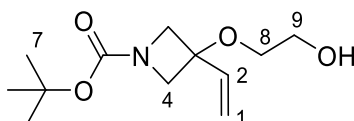
dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 3:1) afforded **S48** (1.8 g, 5.2 mmol, 87%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.41-7.29 (5H, m, ArH), 5.93 (1H, dd, *J* = 17.6, 10.7 Hz, H2), 5.40-5.35 (2H, m, H1), 5.19 (2H, s, H10), 4.06-3.89 (6H, m, H4, H8), 1.43 (9H, s, H7).

¹³C NMR (101 MHz, CDCl₃) δ 169.7, 156.5, 136.3, 135.3, 128.8, 128.7, 128.6, 118.2, 80.0, 75.9, 67.0, 62.6, 57.4, 28.5.

Spectroscopic data in agreement with that reported previously.³⁰

***tert*-Butyl 3-(2-hydroxyethoxy)-3-vinylazetidine-1-carboxylate, S49**



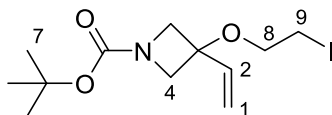
To a solution of **S48** (1.40 g, 4.0 mmol, 1.0 equiv.) in EtOH (15 mL) was added NaBH₄ (290 mg, 7.7 mmol, 1.9 equiv.). The mixture was heated at 60 °C for 16 h, then cooled to room temperature. The resultant mixture was concentrated *in vacuo* then dissolved in EtOAc (50 mL), and NH₄Cl (30 mL, sat. aq.) was added. After stirring for 10 min the phases were separated and the organic layer was washed with brine (20 mL). The organic layer was dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:3) afforded **S49** (740 mg, 3.0 mmol, 75%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.94 (1H, dd, *J* = 17.4, 10.9 Hz, H2), 5.37 (1H, d, *J* = 10.9 Hz, H1), 5.36 (1H, d, *J* = 17.4 Hz, H1), 3.98-3.89 (4H, m, H4), 3.77-3.72 (2H, m, H9), 3.41 (2H, dd, *J* = 5.1, 4.0 Hz, H8), 2.05-1.89 (1H, m, OH), 1.44 (9H, s, H7).

¹³C NMR (101 MHz, CDCl₃) δ 156.6, 137.3, 117.3, 79.9, 75.0, 65.3, 62.0, 57.7, 28.5.

Spectroscopic data in agreement with that reported previously.³⁰

***tert*-Butyl 3-(2-iodoethoxy)-3-vinylazetidine-1-carboxylate, S50**



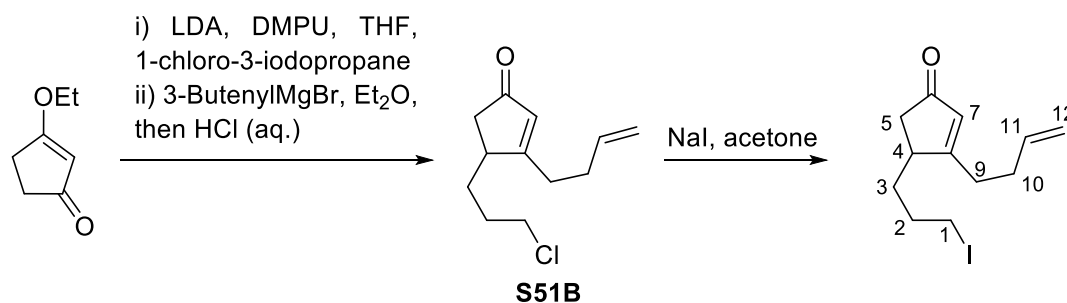
S49 (243 mg, 1.0 mmol, 1.0 equiv.), triphenylphosphine (393 mg, 1.5 mmol, 1.5 equiv.), imidazole (102 mg, 1.5 mmol, 1.5 equiv.) and iodine (381 mg, 1.5 mmol, 1.5 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S50** (200 mg, 0.6 mmol, 57%) as a colourless oil.

^1H NMR (400 MHz, CDCl_3) δ 5.94 (1H, dd, J = 17.4, 10.7 Hz, H2), 5.37 (1H, d, J = 10.7 Hz, H1), 5.36 (1H, d, J = 17.4 Hz, H1) 3.98-3.88 (4H, m, H4), 3.53 (2H, t, J = 6.7 Hz, H8), 3.22 (2H, t, J = 6.7 Hz, H9), 1.44 (9H, s, H7).

^{13}C NMR (101 MHz, CDCl_3) δ 156.6, 137.1, 117.5, 79.9, 65.2, 59.4, 57.9, 28.5, 2.9.

Spectroscopic data in agreement with that reported previously.³⁰

3-(But-3-en-1-yl)-4-(3-iodopropyl)cyclopent-2-en-1-one, **S51**



To a solution of diisopropylamine (2.3 mL, 16.7 mmol, 1.2 equiv.) in anhydrous THF (20 mL) at 0 °C was added *n*BuLi (9.3 mL of 1.8 M solution in hexanes, 16.7 mmol, 1.2 equiv.). After 10 mins the resulting solution was cooled to –78 °C, and a solution of 3-ethoxy-2-cyclopentenone (1.75 g, 13.9 mmol, 1.0 equiv.) in anhydrous THF (10 mL) was added. After 1 h at this temperature, a solution of 1-chloro-3-iodopropane (2.2 mL, 20.8 mmol, 1.5 equiv.) in DMPU (5 mL) was added. The resultant solution was allowed to warm to room temperature over 16 h, then water (50 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The organic layers were combined and washed with brine (20 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , CH_2Cl_2 / Et_2O , 9:1) afforded **S51A** (500 mg, 2.5 mmol, 18%) as a colourless oil.

To a solution of magnesium turnings (240 mg, 9.9 mmol, 4.0 equiv.) and iodine (1 crystal) in anhydrous Et_2O (20 mL) was added a few drops of 4-bromo-1-butene to initiate the reaction. 4-Bromo-1-butene (1 mL, 9.9 mmol, 4.0 equiv.) was then added dropwise and the resulting mixture was heated at reflux for 1 h. The resultant mixture was cooled to –10 °C then treated with **S51A** (500 mg, 2.5 mmol, 1.0 equiv.). After 16 h at room temperature, HCl (10 mL, 1 M aq.) was added. The mixture was then extracted with Et_2O (3 × 10 mL). The organic layers were combined and washed with brine (10 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , pentane / Et_2O , 4:1) afforded **S51B** (280 mg, 1.3 mmol, 53%) as a yellow oil.

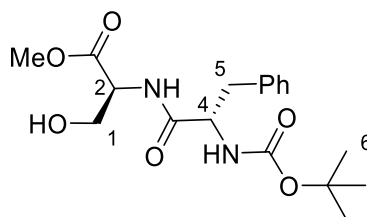
S51B (280 mg, 1.3 mmol, 1.0 equiv.) and NaI (592 mg, 4.0 mmol, 3.0 equiv.) were dissolved in acetone (8 mL) and submitted to **General Procedure 4** at reflux for 30 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **S51** (340 mg, 1.1 mmol, 86%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 5.99-5.94 (1H, m, H7), 5.88-5.73 (1H, m, H11), 5.08 (1H, dq, *J* = 17.1, 1.4 Hz, H12), 5.03 (1H, dq, *J* = 10.2, 1.4 Hz, H12), 3.26-3.13 (2H, m, H1), 2.87-2.79 (1H, m, H4), 2.62-2.50 (2H, m, H5, H9), 2.43-2.29 (3H, m, H9, H10), 2.08 (1H, dd, *J* = 18.6, 2.3 Hz, H5), 1.97-1.86 (1H, m, H3), 1.86-1.74 (2H, m, H2), 1.46-1.30 (1H, m, H3).

¹³C NMR (101 MHz, CDCl₃) δ 208.3, 183.9, 136.8, 130.0, 116.1, 42.3, 41.4, 33.5, 31.1, 30.6, 30.5, 6.3.

Spectroscopic data in agreement with that reported previously.¹⁰

Boc-Phe-Ser-OMe, S52



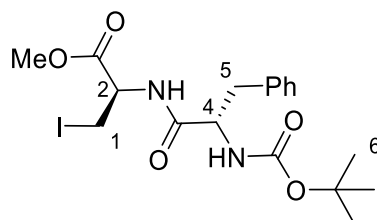
A solution of Boc-L-phenylalanine (4.4 g, 16.5 mmol, 1.1 equiv.), L-serine methyl ester hydrochloride (2.3 g, 15.0 mmol, 1.0 equiv.) and *N*-methylmorpholine (1.65 mL, 15.0 mmol, 1.0 equiv.) in CHCl₃ (20 mL) and DMF (10 mL) was cooled to 0 °C. DCC (3.1 g, 15.0 mmol, 1.0 equiv.) was added, and the resulting mixture was warmed to room temperature after 1 h and stirred at this temperature for 16 h. The resultant mixture was filtered and concentrated *in vacuo*. The residue was dissolved in EtOAc (50 mL) and washed with NaHCO₃ (30 mL, 0.5 M aq.), HCl (30 mL, 1 M aq.) and brine (30 mL). The organic layer was dried (MgSO₄) and filtered, then SiO₂ (10 g) was added and the mixture was concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / EtOAc, 3:7) afforded **S52** (3.1 g, 8.5 mmol, 57%) as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.11 (6H, m, ArH, NH), 5.34 (1H, d, *J* = 7.6 Hz, NH), 4.62 (1H, dt, *J* = 7.5, 3.6 Hz, H2), 4.43 (1H, q, *J* = 7.6 Hz, H4), 3.93-3.85 (2H, m, H1), 3.72 (3H, s, OMe), 3.55 (1H, t, *J* = 6.5 Hz, OH), 3.13 (1H, dd, *J* = 13.9, 5.9 Hz, H5), 2.98 (1H, dd, *J* = 13.9, 7.6 Hz, H5), 1.36 (9H, s, H6).

^{13}C NMR (101 MHz, CDCl_3) δ 172.0, 170.7, 155.9, 136.6, 129.4, 128.7, 127.0, 80.5, 62.8, 55.9, 54.9, 52.8, 38.3, 28.3.

Spectroscopic data in agreement with that reported previously.³¹

Boc-Phe- β -iodo-Ala-OMe, S53



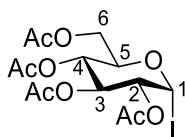
S52 (366 mg, 1.0 mmol, 1.0 equiv.), triphenylphosphine (393 mg, 1.5 mmol, 1.5 equiv.), imidazole (102 mg, 1.5 mmol, 1.5 equiv.) and iodine (381 mg, 1.5 mmol, 1.5 equiv.) were submitted to **General Procedure 2**. 2 h reaction time. Purification by column chromatography (SiO_2 , pentane / EtOAc, 2:1) afforded **S53** (277 mg, 0.6 mmol, 56%) as a colourless solid.

^1H NMR (400 MHz, CDCl_3) δ 7.34-7.20 (5H, m, ArH), 6.92-6.71 (1H, m, NH), 5.04-4.88 (1H, m, NH), 4.71 (1H, dt, $J = 7.4, 3.8$ Hz, H2), 4.51-4.33 (1H, m, H4), 3.77 (3H, s, OMe), 3.63-3.51 (2H, m, H1), 3.18-3.03 (2H, m, H5), 1.42 (9H, s, H6).

^{13}C NMR (101 MHz, CDCl_3) δ 171.3, 169.5, 155.5, 136.4, 129.4, 128.9, 127.2, 80.6, 55.7, 53.3, 52.7, 38.1, 28.4, 6.7.

Spectroscopic data in agreement with that reported previously.³²

2,3,4,6-Tetra-O-acetyl- α -D-glucopyranosyl iodide, S54



To a solution of D-glucose (1.0 g, 5.6 mmol, 1.0 equiv.) in acetic anhydride (2.7 mL, 28.6 mmol, 5.1 equiv.) at 0 °C was added iodine (0.1 g, 0.4 mmol, 0.07 equiv.). The mixture was warmed to room temperature and maintained at this temperature for 2 h. The mixture was diluted with CH_2Cl_2 (4 mL), then iodine (1.9 g, 7.3 mmol, 1.3 equiv.) and triethylsilane (1.2 mL, 7.8 mmol, 1.3 equiv.) were added. The mixture was heated at 40 °C for 2 h then cooled to room temperature and diluted with CH_2Cl_2 (20 mL), then treated with $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 \times 10 mL). The combined organic layers were washed with brine, dried (MgSO_4),

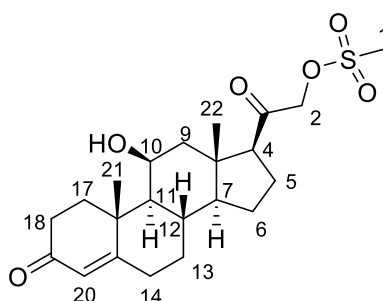
filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1) afforded **S54** (2.1 g, 4.6 mmol, 82%) as a yellow solid.

¹H NMR (400 MHz, CDCl₃) δ 6.98 (1H, d, *J* = 4.3 Hz, H1), 5.45 (1H, t, *J* = 9.7 Hz, H3), 5.17 (1H, dd, *J* = 10.3, 9.4 Hz, H4), 4.33 (1H, dd, *J* = 12.7, 4.1 Hz, H6), 4.19 (1H, dd, *J* = 9.9, 4.3 Hz, H2), 4.10 (1H, dd, *J* = 12.7, 2.2 Hz, H6), 4.04 (1H, dddd, *J* = 10.4, 4.2, 2.2, 0.7 Hz, H5), 2.09 (3H, s, Me), 2.08 (3H, s, Me), 2.04 (3H, s, Me), 2.02 (3H, s, Me).

¹³C NMR (101 MHz, CDCl₃) δ 170.6, 170.0, 169.7, 169.6, 75.0, 73.0, 71.8, 70.4, 67.0, 60.9, 21.0, 20.8, 20.7, 20.7.

Spectroscopic data in agreement with that reported previously.³³

Corticosterone methanesulfonate, **S55**



To a solution of corticosterone (208 mg, 0.6 mmol, 1.0 equiv.) in CH₂Cl₂ (5 mL) at 0 °C was added triethylamine (0.1 mL, 0.7 mmol, 1.2 equiv.) and methanesulfonyl chloride (0.6 mL, 0.7 mmol, 1.2 equiv.). After stirring for 2 h at 0 °C, the mixture was treated with NH₄Cl (5 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL) and the combined organic layers were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, Et₂O) afforded **S55** (180 mg, 0.4 mmol, 71%) as a white foam.

R_f = 0.20 (Et₂O)

¹H NMR (400 MHz, CDCl₃) δ 5.66 (1H, d, *J* = 1.7 Hz, H20), 4.86-4.64 (2H, m, H2), 4.41 (1H, p, *J* = 3.2 Hz, H10), 3.21 (3H, s, H1), 2.53-2.41 (3H, m), 2.38-2.30 (1H, m), 2.26-2.08 (4H, m), 2.05-1.94 (2H, m), 1.89-1.69 (3H, m), 1.61 (1H, dd, *J* = 13.7, 3.4 Hz), 1.47-1.34 (5H, m), 1.19-0.96 (3H, m), 0.93 (3H, s).

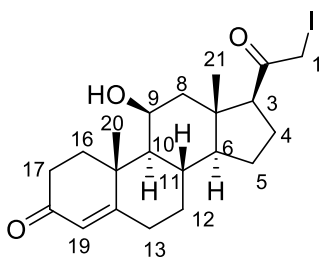
¹³C NMR (101 MHz, CDCl₃) δ 202.8, 199.5, 171.9, 122.5, 72.7, 67.9, 59.3, 57.7, 56.3, 47.9, 44.2, 39.3(2), 39.3(1), 35.1, 33.9, 32.7, 32.1, 31.5, 24.5, 22.6, 21.0, 16.0.

HRMS (ESI⁺) [*M*+Na]⁺ = 447.1807; C₂₂H₃₂O₆SNa requires 447.1812

IR (film) ν_{max}/cm⁻¹ 3345, 2941, 1733, 1646, 1356, 1170, 816.

[α]_D²⁵ = 212.7° (c = 0.1, CHCl₃)

11 β -Hydroxy-21-iodo-4-pregnene-3,20-dione, **S56**



S55 (140 mg, 0.33 mmol, 1.0 equiv.) and NaI (100 mg, 0.66 mmol, 2.0 equiv.) were dissolved in acetone (5 mL) and submitted to **General Procedure 4** at reflux for 1 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 2:1→1:1) afforded **S56** (120 mg, 0.26 mmol, 80%) as a colourless solid.

R_f = 0.4 (pentane / Et₂O, 2:1)

m.p. = 123-125 °C

¹H NMR (400 MHz, CDCl₃) 5.68 (1H, d, J = 1.7 Hz, H19), 4.42 (1H, p, J = 3.3 Hz, H9), 3.91-3.74 (2H, m, H1), 2.84 (1H, t, J = 9.0 Hz, H17), 2.54-2.41 (2H, m), 2.39-2.30 (1H, m), 2.29-2.09 (4H, m), 2.05-1.93 (2H, m), 1.90-1.72 (3H, m), 1.73-1.60 (1H, m), 1.44 (3H, s, H21), 1.43-1.34 (1H, m), 1.27-0.98 (4H, m), 0.93 (3H, s, H20).

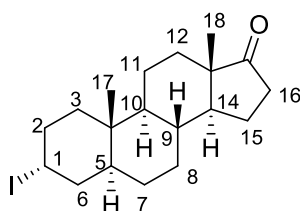
¹³C NMR (101 MHz, CDCl₃) δ 203.2, 199.5, 171.9, 122.6, 68.2, 60.3, 57.4, 56.5, 48.2, 43.9, 39.3, 35.2, 34.0, 32.7, 32.1, 31.5, 24.6, 24.0, 21.1, 16.2, 8.0.

HRMS (ESI⁺) $[M+H]^+$ = 457.1232; C₂₁H₃₀IO₃ requires 457.1234.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 3429, 2900, 1714, 1647, 1186, 1074.

$[\alpha]_D^{25}$ = 183.0° (c = 0.5, CHCl₃)

3 α -Iodo-5 α -androstan-17-one, **S57**



Epiandrosterone (436 mg, 1.5 mmol, 1.0 equiv.), triphenylphosphine (446 mg, 1.7 mmol, 1.1 equiv.), imidazole (75 mg, 1.7 mmol, 1.1 equiv.) and iodine (431 mg, 1.7 mmol, 1.1 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:0→9:1) afforded **S57** (550 mg, 1.4 mmol, 92%) as a white solid.

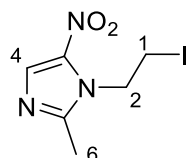
¹H NMR (400 MHz, CDCl₃) δ 4.98-4.89 (1H, m, H1), 2.44 (1H, ddd, J = 19.2, 9.0, 1.1 Hz, H16), 2.08 (1H, dt, J = 19.2, 9.0 Hz, H16), 2.00-1.88 (2H, m), 1.85-1.63 (5H, m), 1.60-1.40

(5H, m), 1.39-1.23 (5H, m), 1.15-1.04 (1H, m), 0.92 (1H, ddd, $J = 12.0, 10.4, 4.1$ Hz), 0.86 (3H, s, H18), 0.83 (3H, s, H17).

^{13}C NMR (101 MHz, CDCl_3) δ 221.4, 54.1, 51.6, 48.0, 42.2, 38.8, 37.7, 36.9, 36.0, 35.2, 34.5, 32.8, 31.7, 30.8, 27.6, 21.9, 20.2, 14.0, 13.5.

Spectroscopic data in agreement with that reported previously.³⁴

1-(2-Iodoethyl)-2-methyl-5-nitro-1*H*-imidazole, S58



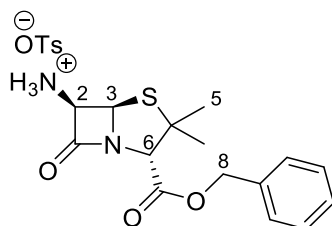
Metronidazole (500 mg, 2.9 mmol, 1.0 equiv.), triphenylphosphine (840 mg, 3.2 mmol, 1.1 equiv.), imidazole (497 mg, 7.3 mmol, 2.5 equiv.) and iodine (812 mg, 3.2 mmol, 1.1 equiv.) were submitted to **General Procedure 2**. Purification by column chromatography (SiO_2 , Et_2O / acetone, 95:5) afforded **S58** (600 mg, 2.1 mmol, 74%) as a white solid.

^1H NMR (400 MHz, CDCl_3) δ 7.98 (1H, s, H4), 4.63 (2H, t, $J = 7.0$ Hz, H2), 3.45 (2H, t, $J = 7.0$ Hz, H1), 2.57 (3, s, H6).

^{13}C NMR (101 MHz, CDCl_3) δ 150.5, 138.3, 133.5, 48.0, 14.9, 0.1, 0.0.

Spectroscopic data in agreement with that reported previously.^{35,36}

(+)-6-Aminopenicillanic acid benzyl ester tosylate salt, S59



To a solution of (+)-6-aminopenicillanic acid (1.9 g, 8.8 mmol, 1.0 equiv.) in CH_2Cl_2 (20 mL) was added Et_3N (2.5 mL, 17.6 mmol, 2.0 equiv.) followed by methyl acetoacetate (1.0 mL, 8.8 mmol, 1.0 equiv.). The mixture was stirred at room temperature for 3 h then concentrated *in vacuo*. The residue was dissolved in DMF (20 mL), benzyl bromide (1.1 mL, 8.8 mmol, 1.0 equiv.) was added, and the mixture was stirred at room temperature for 16 h. Et_2O (50 mL) was added and the organic layer was washed with brine (3×30 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. The residue was dissolved in acetone (20 mL), and *p*-toluenesulfonic acid monohydrate (1.95 g, 10.0 mmol, 1.1 equiv.) was added, and the mixture was stirred at room temperature for 1 h. The mixture

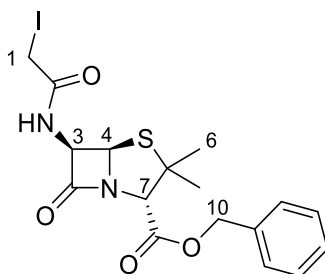
was then filtered, and the solid residue washed with Et₂O (50 mL) and pentane (50 mL). Drying *in vacuo* afforded **S59** (3.0 g, 6.3 mmol, 72%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.43 (3H, br. s, NH), 8.03-7.83 (7H, m, ArH), 7.69-7.55 (2H, m, ArH), 6.03 (1H, d, *J* = 4.3 Hz, H2), 5.77-5.67 (2H, m, H8), 5.63 (1H, d, *J* = 4.3 Hz, H3), 5.08 (1H, s, H6), 2.79 (3H, s, ArMe), 2.10 (3H, s, H5), 1.88 (3H, s, H5).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.7, 167.0, 145.4, 137.9, 135.1, 128.7, 128.6, 128.6, 128.2, 125.6, 69.8, 67.1, 65.2, 64.2, 57.2, 30.9, 26.6, 20.9.

Spectroscopic data in agreement with that reported previously.³⁷

Benzyl (2*S*,5*R*,6*R*)-6-(2-iodoacetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, S60



To a solution of **S59** (3.35 g, 7.0 mmol, 1.0 equiv.) in CH₂Cl₂ (35 mL) at 0 °C was added triethylamine (2.9 mL, 21.0 mmol, 3.0 equiv.) followed by chloroacetyl chloride (0.67 mL, 8.4 mmol, 1.2 equiv.). The reaction was stirred at 0 °C for 4 h, then NH₄Cl (20 mL, sat. aq.) was added. The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The organic layer was dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was dissolved in acetone (35 mL), NaI (3.15 g, 21.0 mmol, 3.0 equiv.) was added, and the mixture was stirred at room temperature for 16 h. The mixture was then concentrated *in vacuo*, and the residue was dissolved in CH₂Cl₂ (10 mL), washed with Na₂S₂O₃ (10 mL, 10% aq.) and brine (10 mL), dried (MgSO₄) and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 1:1→1:2) afforded **S60** (2.47 g, 5.2 mmol, 74%) as a pale yellow solid.

R_f = 0.50 (pentane / EtOAc, 2:1)

m.p. = 57-59 °C

¹H NMR (400 MHz, CDCl₃) δ 7.42-7.34 (5H, m, ArH), 6.67 (1H, d, *J* = 9.0 Hz, NH), 5.63 (1H, dd, *J* = 9.0, 4.2 Hz, H3), 5.58 (1H, d, *J* = 4.2 Hz, H4), 5.20 (2H, s, H10), 4.49 (1H, s, H7), 3.84-3.66 (2H, m, H1), 1.65 (3H, s, H6), 1.48-1.39 (3H, s, H6).

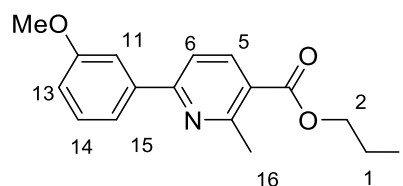
¹³C NMR (101 MHz, CDCl₃) δ 173.1, 167.5, 166.5, 134.8, 129.0, 128.9, 128.9, 70.6, 68.1, 67.7, 65.3, 59.4, 32.2, 27.0, -1.9.

HRMS (ESI⁺) [M+Na]⁺ = 496.9998; C₁₇H₁₉O₄N₂INaS requires 497.0002

IR (film) ν_{max}/cm⁻¹ 3375, 2958, 1784, 1736, 1687, 1519, 1213.

[α]_D²⁵ = 129.8° (c = 0.7, CHCl₃)

2-Iodoethyl 6-(3-methoxyphenyl)-2-methylnicotinate, S61



To a solution of 6-(3-methoxyphenyl)-2-methylnicotinic acid (487 mg, 2.0 mmol, 1.0 equiv.) in anhydrous CH₂Cl₂ (10 mL) at 0 °C was added 2-iodoethanol (0.3 mL, 4.0 mmol, 2.0 equiv.), DMAP (366 mg, 3.0 mmol, 1.5 equiv.) and EDCI (767 mg, 4.0 mmol, 2.0 equiv.). The resulting mixture was stirred at this temperature for 1 h, then NaHCO₃ (10 mL, sat. aq.) was added. The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The organic layer was dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1) afforded **S61** (600 mg, 1.5 mmol, 76%) as a white solid.

R_f = 0.5 (pentane / Et₂O, 1:1)

m.p. = 93-95 °C

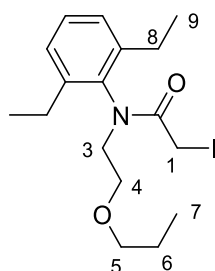
¹H NMR (400 MHz, CDCl₃) δ 8.33 (1H, d, *J* = 8.2 Hz, H5), 7.68-7.59 (3H, m, H6, H11, H15), 7.40 (1H, t, *J* = 7.9 Hz, H14), 7.00 (1H, ddd, *J* = 8.2, 2.6, 1.0 Hz, H13), 4.60 (2H, t, *J* = 6.6 Hz, H2), 3.90 (3H, s, OMe), 3.45 (2H, t, *J* = 6.6 Hz, H1), 2.93 (3H, s, H16).

¹³C NMR (101 MHz, CDCl₃) δ 165.9, 160.5, 160.2, 159.4, 139.9, 139.7, 130.0, 123.0, 119.9, 117.7, 115.8, 112.7, 65.2, 55.5, 25.6, 0.6.

HRMS (ESI⁺) [M+H]⁺ = 398.0245; C₁₆H₁₇O₃NI requires 398.0248

IR (film) ν_{max}/cm⁻¹ 2160, 2021, 1977, 1719, 1584, 1266, 778.

***N*-(2,6-Diethylphenyl)-2-iodo-*N*-(2-propoxyethyl)acetamide, S62**



Pretilachlor (936 mg, 3.0 mmol, 1.0 equiv.) and NaI (1.35 g, 9.0 mmol, 3.0 equiv.) were dissolved in acetone (15 mL) and submitted to **General Procedure 4** at room temperature for 16 h. Purification by column chromatography (SiO₂, pentane / Et₂O, 9:1→4:1) afforded **S62** (900 mg, 2.2 mmol, 74%) as a colourless oil.

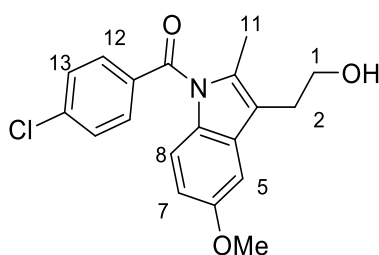
¹H NMR (400 MHz, CDCl₃) δ 7.34-7.28 (1H, m, ArH), 7.21-7.17 (2H, m, ArH), 3.74 (2H, t, *J* = 6.2 Hz, H3), 3.59 (2H, t, *J* = 6.2 Hz, H4), 3.47-3.45 (2H, m, H1), 3.30 (2H, t, *J* = 6.7 Hz, H5), 2.60 (4H, q, *J* = 7.5 Hz, H8), 1.54-1.44 (2H, m, H6), 1.25 (6H, t, *J* = 7.5 Hz, H9), 0.83 (3H, t, *J* = 7.5 Hz, H7).

¹³C NMR (101 MHz, CDCl₃) δ 168.5, 141.3, 139.2, 128.9, 126.8, 72.7, 67.3, 50.3, 23.7, 22.9, 14.3, 10.6, -1.8.

HRMS (ESI⁺) [*M*+H]⁺ = 404.1079; C₁₇H₂₇O₂NI requires 404.1081

IR (film) ν_{max}/cm⁻¹ 2964, 2874, 1655, 1456, 1110, 811.

(4-Chlorophenyl)(3-(2-hydroxyethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, S63



To a solution of indomethacin (1.0 g, 2.8 mmol, 1.0 equiv.) in anhydrous THF (10 mL) at 0 °C was added BH₃•DMS (1.55 mL, 2.0 M solution in THF, 3.1 mmol, 1.1 equiv.). The resulting mixture was warmed slowly to room temperature and maintained at this temperature for 16 h. MeOH (1 mL) was added and the resulting mixture was concentrated *in vacuo*. CH₂Cl₂ (20 mL) was added and the resulting mixture was washed with NaHCO₃ (20 mL, sat. aq.), HCl (10 mL, 2 M aq.) and brine (10 mL). The organic layer was dried (MgSO₄), filtered

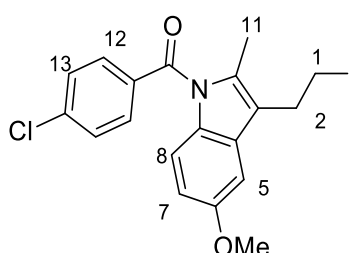
and concentrated *in vacuo*. Purification by column chromatography (SiO₂, CH₂Cl₂ / MeOH, 95:5) afforded **S63** (900 mg, 2.6 mmol, 94%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.69-7.60 (2H, m, H12), 7.51-7.42 (2H, m, H13), 6.95 (1H, d, *J* = 2.6 Hz, H5), 6.87 (1H, d, *J* = 9.0 Hz, H8), 6.66 (1H, dd, *J* = 9.0, 2.6 Hz, H7), 3.89-3.82 (5H, m, H1, OMe), 2.95 (2H, t, *J* = 6.7 Hz, H2), 2.37 (3H, s, H11), 1.60-1.48 (1H, m, OH).

¹³C NMR (101 MHz, CDCl₃) δ 168.4, 156.1, 139.3, 135.6, 134.1, 131.2, 131.2, 131.1, 129.2, 116.0, 115.2, 111.5, 101.4, 62.3, 55.9, 27.7, 13.5.

Spectroscopic data in agreement with that reported previously.³⁸

(4-Chlorophenyl)(3-(2-iodoethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, **S64**



S63 (344 mg, 1.0 mmol, 1.0 equiv.), triphenylphosphine (393 mg, 1.5 mmol, 1.5 equiv.), imidazole (102 mg, 1.5 mmol, 1.5 equiv.) and iodine (381 mg, 1.5 mmol, 1.5 equiv.) in CH₂Cl₂ (5 mL) were submitted to **General Procedure 2**. Purification by column chromatography (SiO₂, pentane / Et₂O, 95:5) afforded **S64** (425 mg, 0.9 mmol, 90%) as a pale yellow solid.

R_f = 0.2 (pentane / Et₂O, 9:1)

m.p. = 100-102 °C

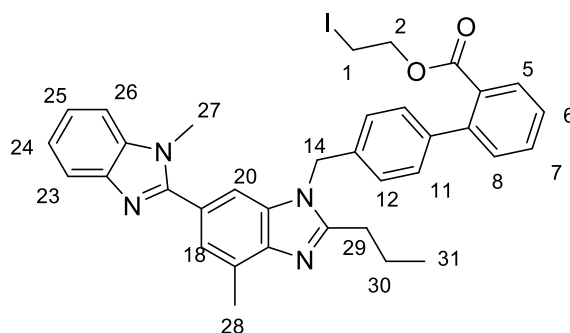
¹H NMR (400 MHz, CDCl₃) δ 7.73-7.59 (2H, m, H12), 7.52-7.43 (2H, m, H13), 6.91 (1H, d, *J* = 9.0 Hz, H8), 6.89 (1H, d, *J* = 2.6 Hz, H5), 6.68 (1H, dd, *J* = 9.0, 2.6 Hz, H7), 3.85 (3H, s, OMe), 3.39-3.33 (2H, m, H1), 3.29-3.23 (2H, m, H2), 2.35 (3H, s, H11).

¹³C NMR (101 MHz, CDCl₃) δ 168.5, 156.1, 139.4, 135.2, 134.0, 131.3, 131.1, 130.3, 129.3, 118.8, 115.2, 111.4, 101.1, 55.9, 29.0, 13.7, 4.3.

HRMS (ESI⁺) [*M*+*H*]⁺ = 454.0063; C₁₉H₁₈O₂NCII requires 454.0065

IR (film) *v*_{max}/cm⁻¹ 2160, 2031, 1978, 1673, 1327, 832.

Telmisartan 2-iodoethyl ester, S65



To a solution of telmisartan (129 mg, 0.25 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (3 mL) at 0 °C was added 2-iodoethanol (39 μL , 0.50 mmol, 2.0 equiv.), DMAP (46 mg, 0.38 mmol, 1.5 equiv.) and EDCI (96 mg, 0.50 mmol, 2.0 equiv.). The resulting mixture was stirred at room temperature for 4 h, then NaHCO_3 (5 mL, sat. aq.) was added. The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2 , EtOAc) afforded **S65** (160 mg, 0.24 mmol, 96%) as a white solid.

$R_f = 0.31$ (EtOAc)

m.p. = 86-88 °C

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.88 (1H, dd, $J = 7.7, 1.4$ Hz, ArH), 7.82-7.77 (1H, m, ArH), 7.52 (1H, td, $J = 7.6, 1.5$ Hz, ArH), 7.49-7.34 (4H, m, ArH), 7.32-7.21 (5H, m, ArH), 7.10-7.06 (2H, m, ArH), 5.45 (2H, s, H14), 4.26 (2H, t, $J = 6.7$ Hz, H2), 3.81 (3H, s, H27), 3.00 (2H, t, $J = 6.7$ Hz, H1), 2.97-2.91 (2H, m, H29), 2.77 (3H, s, H28), 1.99-1.83 (2H, m, H30), 1.07 (H, t, $J = 7.4$ Hz, H31).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.5, 156.6, 154.8, 143.3, 143.0, 142.2, 141.2, 136.8, 135.1, 135.0, 131.8, 131.0, 130.3, 130.0, 129.6, 129.2, 127.6, 126.0, 124.1, 124.0, 122.6, 122.4, 119.7, 109.7, 109.0, 65.1, 47.1, 32.0, 30.0, 22.1, 17.0, 14.3, -0.1.

HRMS (ESI $^+$) $[\text{M}+\text{H}]^+ = 669.1716$; $\text{C}_{35}\text{H}_{34}\text{O}_2\text{N}_4\text{I}$ requires 669.1721

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2960, 2032, 1978, 1722, 1450, 1242, 743.

6. Quantum Yield Experiments

a. Calibration of the Ferrioxalate Actinometer

The following method was followed based on that reported by Yoon *et al.*³⁹ For a comprehensive and up-to-date overview of the characterisation of photoredox mechanisms, see a review published by Melchiorre *et al.*⁴⁰

All actinometry was carried out in a dark room using an EvoluChem™ blue 18W LED and Teflon™-capped quartz cuvette (path length = 1.000 cm, V = 2.35 mL). UV/vis absorption measurements were carried out using a Perkin Elmer Lambda20 spectrometer.

A 0.15 M solution of ferrioxalate was prepared by dissolving 2.21 g of potassium ferrioxalate hydrate in 30 mL of 0.05 M H₂SO₄. This solution required careful handling to ensure it was not exposed to light where possible. A buffered solution of phenanthroline was prepared by dissolving 50 mg of phenanthroline and 11.25 g of sodium acetate in 50 mL of 0.5 M H₂SO₄. Each solution was sparged with N₂ for 10 min before use. To determine the photon flux of the spectrophotometer, 2.0 mL of the ferrioxalate solution was placed in a cuvette and irradiated for 90 seconds at $\lambda = 436$ nm at a distance of 10 cm from the light source. After irradiation, 0.35 mL of the phenanthroline solution was added to the cuvette. The solution was then allowed to rest for 1 h, before the absorbance of the solution was measured at 510 nm. A non-irradiated sample was also prepared and the absorbance at 510 nm measured. Conversion was calculated using equation 1.

$$\text{mol Fe}^{2+} = \frac{V \cdot \Delta A}{l \cdot \epsilon} \quad (\text{Equation 1})$$

Table 2. Values obtained for the moles of Fe²⁺ in the actinometer.

Run	l / cm	V / dm ³	ΔA / au	ϵ / dm ³ mol ⁻¹ cm ⁻¹	mol(Fe ²⁺)
1	1.000	0.00235	1.7634	11100	3.73×10^{-7}
2	1.000	0.00235	1.8459	11100	3.91×10^{-7}
Average					3.82×10^{-7}

Where V is the total volume (0.00235 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions (Figure 1), l is the path length (1.000 cm), and ϵ is the molar absorptivity at 510 nm ($11,100 \text{ L mol}^{-1} \text{ cm}^{-1}$). The photon flux can be calculated using equation 2.

$$flux = \frac{mol(Fe^{2+})}{\phi \cdot t \cdot f} \quad (\text{Equation 2})$$

Table 3. Values obtained for the photon flux of the actinometer.

Run	mol(Fe^{2+})	Φ	t / s	f	flux / einstein s^{-1}
1	3.73×10^{-7}	1.01	90	0.99877	4.11×10^{-9}
2	3.91×10^{-7}	1.01	90	0.99877	4.30×10^{-9}
Average	3.82×10^{-7}				4.21×10^{-9}

Φ is the quantum yield for the ferrioxalate actinometer (1.01 for a 0.15 M solution at $\lambda = 436 \text{ nm}$)⁴¹, t is the irradiation time (90.0 s), and f is the fraction of light absorbed at $\lambda = 436 \text{ nm}$ (0.99877, Figure 2). The fraction of light absorbed can be calculated using equation 3. The photon flux was calculated to be $4.21 \times 10^{-9} \text{ einstein s}^{-1}$.

$$f = 1 - 10^{-A} \quad (\text{Equation 3})$$

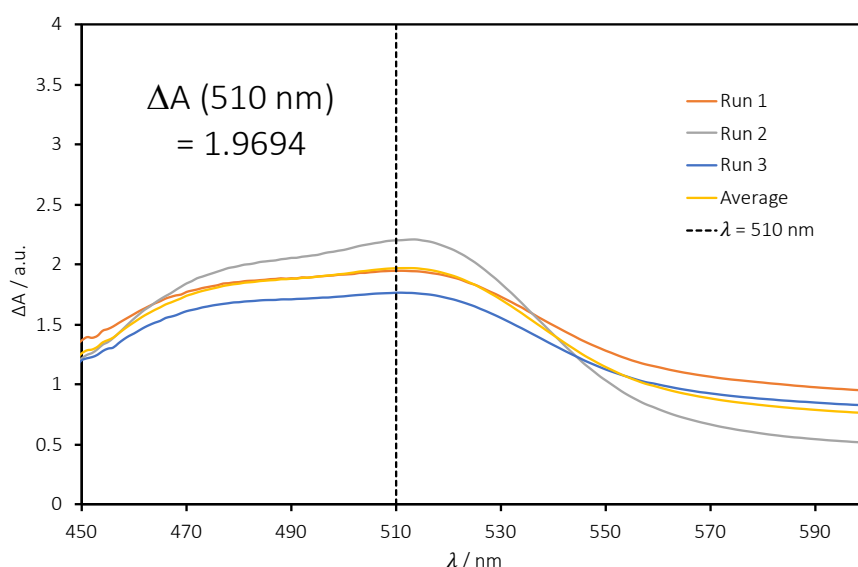


Figure 1. Difference plot for the absorption of the actinometer at $\lambda = 510 \text{ nm}$

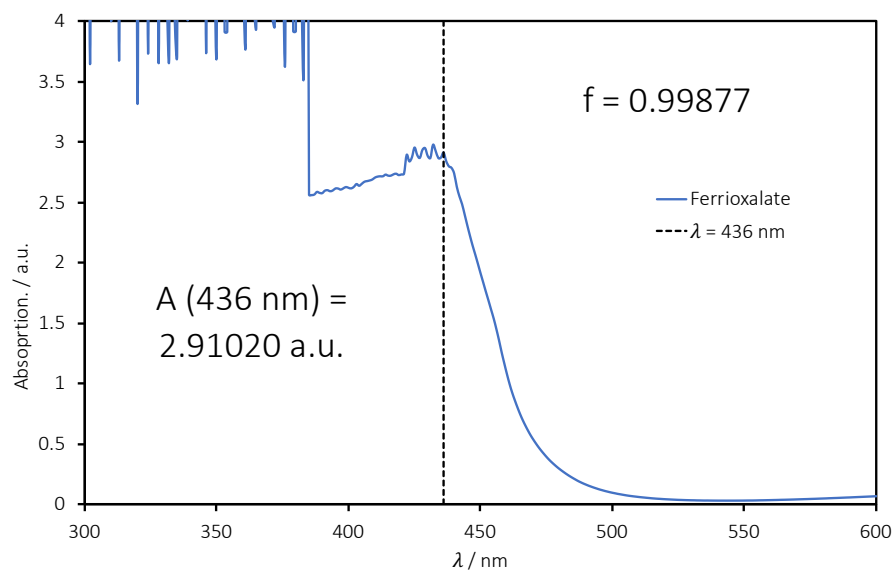


Figure 2. Measured fraction of light absorbed by ferrioxalate solution at $\lambda = 436 \text{ nm}$

b. Calibration of the Reaction Conditions

To measure quantum yields for the photoredox-catalysed radical addition of alkyl and aryl iodides to TCP, the fraction of light absorbed by the *fac*-Ir(ppy)₃ catalyst under the reaction conditions was measured via UV/Vis absorption at $\lambda = 436$ nm (Figure 3). A 4.8×10^{-4} M solution of *fac*-Ir(ppy)₃ was prepared by dissolving 2.5 mg of *fac*-Ir(ppy)₃ in 8 mL of *t*-BuCN and Et₂O (3 : 1, to mimic the reaction conditions). A 2.35 mL aliquot of this solution was used for subsequent measurements. The fraction of light absorbed by the catalyst at $\lambda = 436$ nm was found to be 0.95288.

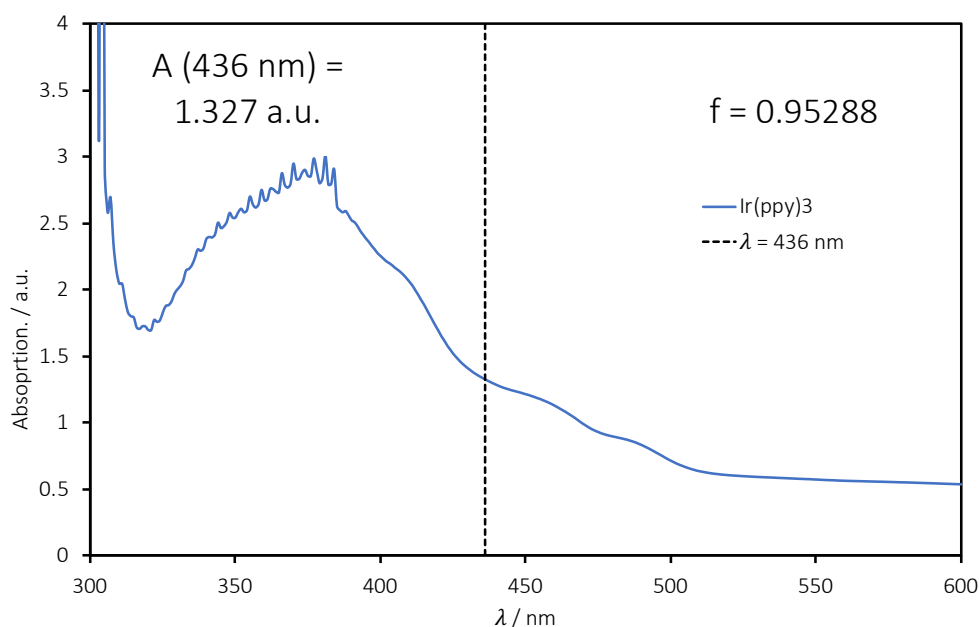


Figure 3. Fraction of light absorbed by *fac*-Ir(ppy)₃ in *t*-BuCN / Et₂O (3 : 1) at 4.8×10^{-4} M and $\lambda = 436$ nm

c. Measurement of Substrate Quantum Yields

To obtain quantum yields for each substrate, 0.15 mmol of substrate was dissolved in *t*-BuCN (4 mL) and Et₂O (1.4 mL). TCP (0.6 mL of a 0.5 M solution in Et₂O, 0.3 mmol) and *fac*-Ir(ppy)₃ (2.5 mg, 2.5 mol%) were added. This solution was degassed using three freeze-pump-thaw cycles (vacuum was only applied while the reaction mixture was frozen due to TCP volatility). A quartz cuvette was charged with 2.35 mL of this solution and irradiated for the indicated time at a distance of 10 cm from the light source. A 0.2 mL aliquot was removed and concentrated *in vacuo*, then diluted with CDCl₃ (0.5 mL). Conversion was measured using the ratio of starting material to all products observed in the ¹H NMR spectrum (400 MHz). The quantum yield can be calculated using equation 4.

$$\phi = \frac{\text{mol}(\text{products})}{\text{flux} \cdot t \cdot f} \quad (\text{Equation 4})$$

Substrate	t / s	Conversion / %	Yield / mol	ϕ^a
Ethyl iodoacetate	10	64%	2.80×10^{-5}	682 (32)
2-Iodopyridine	900	56%	2.46×10^{-5}	7.4 (1.5)
4-CF ₃ Iodobenzene	600	42%	1.82×10^{-5}	7.4 (0.39)
Benzyl iodide	1200	13%	5.97×10^{-6}	1.4 (0.41)

^aNumbers in brackets denote one standard deviation from the mean. The value of photon flux used in these calculations was 4.21×10^{-9} einstein s⁻¹. The value for the fraction of light absorbed was 0.95288.

Table 4. Quantum yields.

Discussion: From these data, ethyl iodoacetate was observed to have a very efficient turnover, suggesting the photocatalyst mainly serves as an initiator for the reaction. This is in good agreement with observations from reaction initiation using BEt₃ / O₂, where the reaction reached full conversion within seconds.¹

Pleasingly, where benzyl iodide showed poor reactivity under BEt₃/O₂ initiation, the use of photoredox catalysis resulted in a high-yielding reaction. The quantum yield of this reaction ($\phi \sim 1$), suggests *either* a poor chain process *or* inefficient initiation of the substrate. Addition of the *para* electron-withdrawing substituent CF₃ to the benzyl substrate increases the quantum yield almost 8-fold. 2-iodopyridine, a substrate also seen to be unsuccessful under BEt₃ / O₂ initiation, also works efficiently under this catalytic regime, with a quantum yield equivalent to that of 4-CF₃ iodobenzene.

d. Substrate UV/Vis Spectra

To validate the need for the photocatalyst, UV/vis spectra were obtained for each substrate at the reaction concentration to rule out initiation via homolytic cleavage of the C–I bond.

A quartz cuvette was charged with substrate (0.06 mmol), 1.6 mL *t*-BuCN and 0.8 mL Et₂O. A UV/vis absorption spectrum of this solution from 300–600 nm reveals that all substrates tested do not absorb light at 436 nm, suggesting direct photoexcitation of the substrate by the LED lamp does not play a part in the observed reaction (Figure 4).

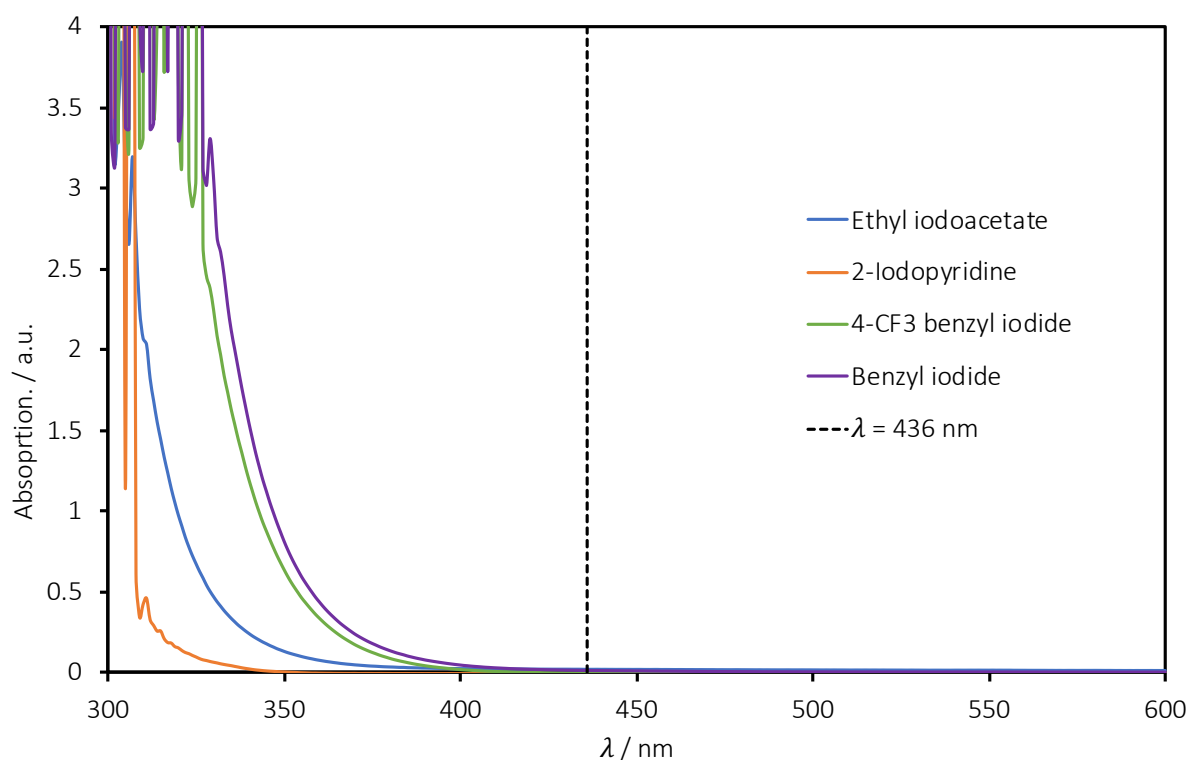


Figure 4. UV/vis spectrum of absorption of iodide substrates at $\lambda = 436$ nm

7. Computational Supplementary Information

a. Computational Methods.

Redox and Potential Energy Surface (PES) calculations were carried out using the ORCA suite of programs (versions 4.0.1 and 4.1.0 respectively).⁴² Tight criteria for both optimisation and SCF cycles were used for all structures (1×10^{-6} and 1×10^{-8} Hartrees, respectively). Resolution of identity (RI) was used to speed up the SCF process employing the RIJCOSX⁴³ approximation for exchange integrals and the Coulomb-fitting auxiliary basis set def2/J.⁴⁴ Single point calculations were obtained using GridX6. Implicit solvation was introduced employing the SMD model.⁴⁵⁻⁴⁷ As the reaction solvent *t*-BuCN ($\epsilon = 1.377$)⁴⁸ is not found in the SMD solvent library, acetonitrile (MeCN, $\epsilon = 1.344$),⁴⁹ which has similar properties, was used instead. Harmonic vibrational frequencies were calculated at the same level of theory to assign stationary points as either minima or transition structures, and to calculate the zero-point vibrational energy and thermal corrections. Grimme's quasi-RRHO approach was applied to obtain the vibrational entropy.⁵⁰

Redox Potential Calculations

A recent benchmarking study by Neese, Pantazis and co-workers found that the M06-2X and B2PLYP functionals in conjunction with the SMD solvation model provided the smallest root-mean-square error (RMSE) (0.12 eV and 0.25 eV, respectively) for the calculation of aqueous redox potentials of 19 small organic molecules.^{47,51} Following this protocol, redox potentials were calculated at the M06-2X⁵² and RI-B2PLYP^{53,54} levels of theory in combination with the def2-TZVPP basis set and the SMD solvation model, using the optimised TPSS/def2-TZVP geometries.^{45,46} It is worth noting that MP2 has been shown to reproduce the experimental geometry for [1.1.1]propellane and performs well in the description of corresponding cationic bicyclopentyl structures.⁵⁵ However, significant spin contamination is found due to the presence of low-lying excited states in the radical intermediates.^{56,57} Within this approach, the reduction potential is calculated using Equations 5 and 6.⁵⁸ The values of Faraday's constant and the SCE used were 23.061 kcal/V and 4.429 V respectively.⁵⁹

$$\Delta G_{\text{red}}^{\circ} = G_{\text{A}^{\bullet}, \text{solv}} - G_{\text{A}^{+}, \text{solv}} \quad (\text{Equation 5})$$

$$E_{1/2}^{\circ} = -\Delta G_{\text{red}}^{\circ} / nF \quad (\text{Equation 6})$$

Potential Energy Surface Calculations

Geometry optimizations were carried out at the RI-B2PLYP level of theory with the def2-TZVP basis set, using the SMD solvation model for MeCN. Iodine atoms were described using the ma-def2-TZVP basis set. The def2 basis set includes an effective core potential (ECP) description for I, with 28 electrons included in the core.^{60,61} Single-point energies were obtained at the RI-B2PLYP-D3BJ⁶² level of theory with the larger def2-QZVPP basis set (ma-def2-QZVPP on I), using the SMD solvation model for MeCN. Thermal corrections were applied from the optimisation level of theory. All species were corrected for 1 M standard state by adding $RT\ln(1/24.5) = 1.89 \text{ kcal mol}^{-1}$ to the calculated values.

b. Redox Potentials of Bicyclopentyl Radicals

The mechanism of this ATRA reaction is proposed to occur via initial reductive cleavage of the substrate C–I bond to afford an alkyl or aryl radical, followed by trapping of TCP to produce a bicyclopentyl radical. While quantum yield experiments indicate that formation of the BCP iodide is the dominant process (with regeneration of the alkyl / aryl radical), turnover of the catalyst requires reduction of $\text{Ir}^{\text{IV}}(\text{ppy})_3^+$ to complete the catalytic cycle (oxidative quenching pathway, Figure 5). Alternatively, reduction of $\text{Ir}^{\text{III}}(\text{ppy})_3^*$ by the BCP radical could also be imagined. To determine the feasibility of catalytic turnover via *either* an oxidative or reductive quenching pathway, redox potentials were calculated for a series of BCP radical/cation couples. The redox potential for the oxidation of a BCP radical to its corresponding cation coupled to the reduction of $\text{Ir}^{\text{IV}}(\text{ppy})_3/\text{Ir}^{\text{III}}(\text{ppy})_3$ and $\text{Ir}^{\text{III}}(\text{ppy})_3^*/\text{Ir}^{\text{II}}(\text{ppy})_3$ was then obtained, using experimental values for the iridium half-cells.⁶³ In all cases, a large positive redox cell potential was observed for the oxidation of each BCP radical to its corresponding cation, suggesting a favourable redox process capable of turning over the catalyst (Tables 5 and 6).

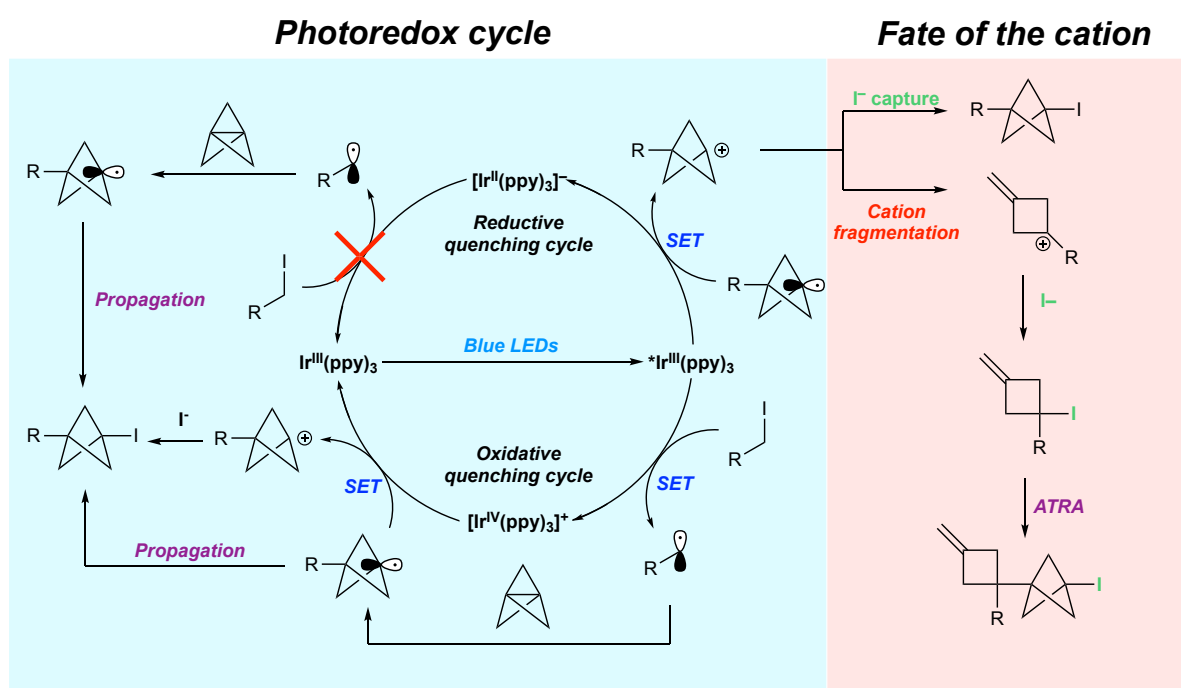


Figure 5. Proposed mechanistic cycle

Table 5. Calculated redox potentials for the oxidative (ox) and reductive (red) quenching paths shown in Figure 5.

Species	SMD(MeCN)-M06-2X/def2-TZVPP		SMD(MeCN)-B2PLYP/def2-TZVPP	
	E _{cell} (ox) / eV	E _{cell} (red) / eV	E _{cell} (ox) / eV	E _{cell} (red) / eV
<i>benzyl-BCP couple</i>	1.76	1.30	1.99	1.53
<i>p-CNphenyl-BCP couple</i>	1.75	1.29	2.07	1.61
<i>p-CNbenzyl-BCP couple</i>	1.70	1.24	1.92	1.46
<i>p-Mebenzyl-BCP couple</i>	1.75	1.29	1.99	1.53
<i>p-MeObenzyl-BCP couple</i>	2.06	1.60	2.31	1.85
<i>p-MeOphenyl-BCP couple</i>	2.49	2.03	2.91	2.45
<i>p-NH₂benzyl-BCP couple</i>	2.45	1.99	2.65	2.19
<i>p-OHbenzyl-BCP couple</i>	2.02	1.56	2.25	1.79
<i>p-NH₂phenyl-BCP couple</i>	2.92	2.46	3.31	2.85
<i>p-OHphenyl-BCP couple</i>	2.46	2.00	2.86	2.40
<i>phenyl-BCP couple</i>	2.15	1.69	2.55	2.09
<i>pyr-2-BCP couple</i>	1.78	1.32	2.08	1.62
<i>pyr-3-BCP couple</i>	1.86	1.40	2.15	1.69
<i>pyr-4-BCP couple</i>	1.63	1.17	1.92	1.46

Table 6. Experimental reduction potentials for each redox process for *fac*-Ir(ppy)₃.⁶³

Ir(ppy) ₃ redox states	Mechanism	Expt E° (vs SCE) / eV
3* → 2	Reductive	0.31
3* → 4	Oxidative	-1.73
3 → 2	Reductive	-2.19
4 → 3	Oxidative	0.77

Structures of Calculated Species

The test set of BCP radicals in this study was chosen to represent substrates with varying electronic characteristics, and to mirror some of those that have been subject to the photoredox reaction. Figure 6 displays the calculated reduction potentials, referenced to the SCE.

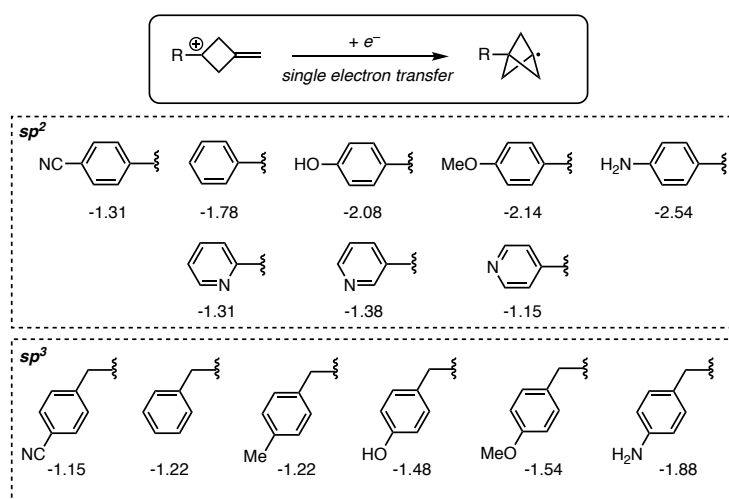


Figure 6. Reduction potentials (eV vs SCE) for all substrates calculated in this study at the SMD(MeCN)-**RI-B2PLYP**/def2-TZVPP//SMD(MeCN)-/TPSS/def2-TZVP level of theory. Values are reported in Table 8.

The structure of each cation derived from the corresponding BCP radical via SET to the Ir(IV) complex was found to depend on the electronics of the transannular substituent (Figure 7). Three different states were observed: bent (**B**), planar, (**P**) and spiro (**S**). For two sp^3 substituents (Table 7, entries 1 and 2), both **B** and **S** were observed, with the spirocyclic phenonium cation **S** being favoured in both cases. For *p*-nitrobenzyl substitution, only **B** was observed. In the case of electron-withdrawing sp^2 substituents, both **B** and **P** were observed (Table 7, entries 3–6), with **P** preferred in all cases. For the remaining sp^3 species, only **S** was observed, and in the case of sp^2 species, only **P** was observed.

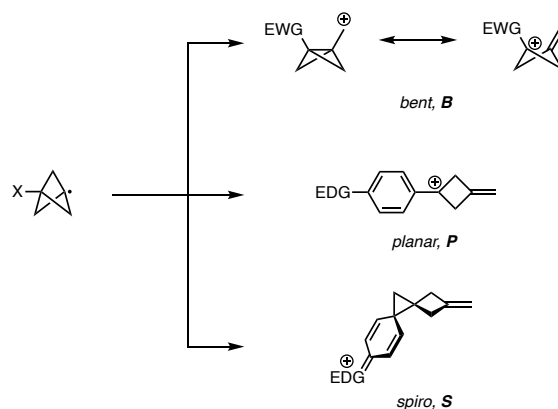


Figure 7. Depictions of BCP radical and corresponding oxidised species

Table 7. Relative free energy (ΔG , in kcal mol⁻¹) between the alternative states (B = bent , P= planar, S = spiro) found for the bicyclopentyl cations described in Figure 7. Negative values indicate the former is more stable. Complete free energy data is reported in Table 12.

Entry	Species	ΔG (RI-B2PLYP)	ΔG (M06-2X)
1	<i>Benzyl: S vs B</i>	-0.3	0.8
2	<i>p-Mebenzyl: S vs B</i>	-2.8	-2.6
3	<i>p-CN phenyl: P vs B</i>	-5.0	-3.0
4	<i>2-pyridyl: P vs B</i>	-5.1	-2.5
5	<i>3-pyridyl: P vs B</i>	-5.4	-3.9
6	<i>4-pyridyl: P vs B</i>	-4.7	-2.1

BCP Radicals

The oxidation process for all BCP radicals tested falls below the cut-off for both the oxidative and reductive quenching pathways (-0.77 and -0.31 eV respectively, Figures 8 and 9). From these results, and the observation of bicyclobutyl iodide byproducts, it is feasible that the BCP radical is the species responsible for catalytic turnover.

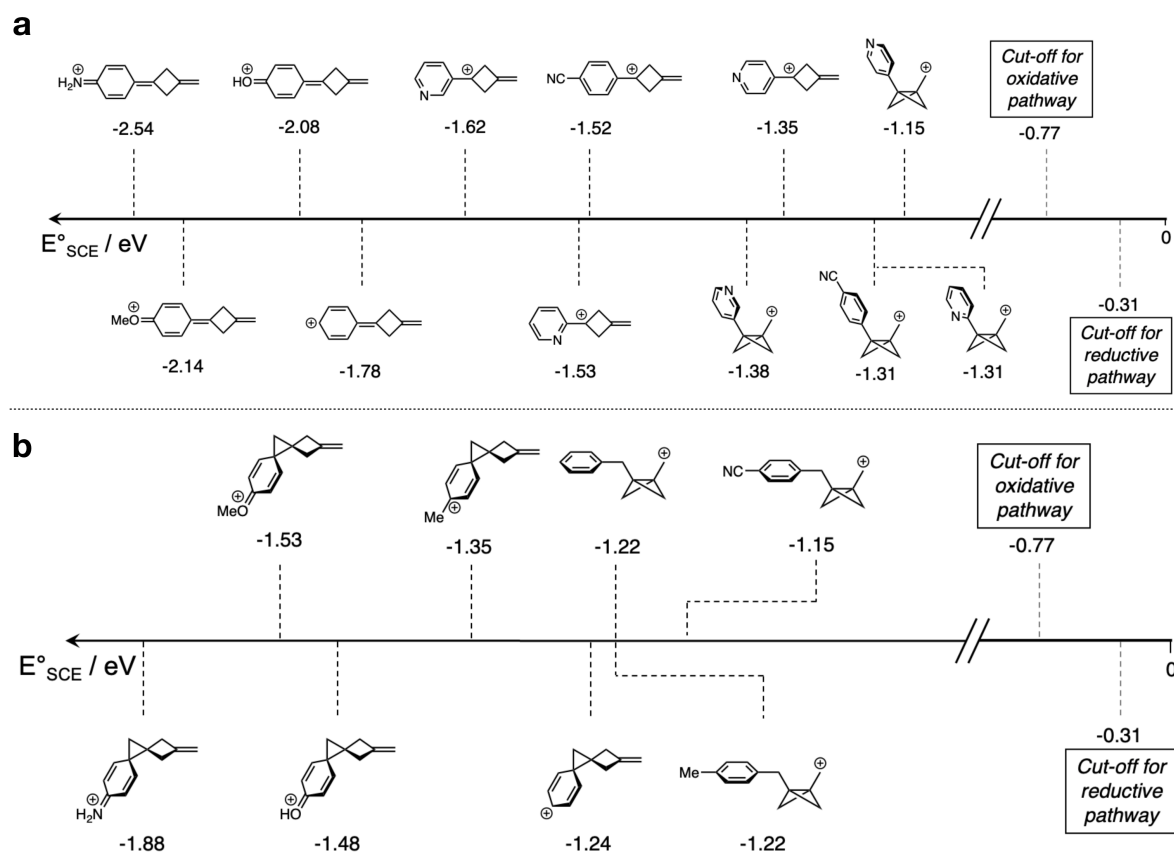


Figure 8. Comparative scale for the reduction of **a**, phenyl/pyridyl-derived bicyclobutyl cation/BCP radical and exomethylenecyclobutyl cation/BCP radical couples and **b**, benzyl-derived bicyclobutyl cation/BCP radical and spiro-exomethylenecyclobutyl phenonium cation/BCP radical couples. Values obtained at the SMD(MeCN)-**RI-B2PLYP**/def2-TZVPP//SMD(MeCN)-**TPSS**/def2-TZVP level of theory. Values are reported in Table 8.

Table 8. Gibbs free energy (ΔG) and reduction potentials ($E_{1/2}$) for redox couples with SMD(MeCN)-**RI-B2PLYP**/def2-TZVPP and SMD(MeCN)-**M06-2X**/def2-TZVPP for geometries and thermochemistry from SMD(MeCN)-**TPSS**/def2-TZVP. All energies are reported in kcal mol⁻¹.

Species	E_{el}(RI-B2PLYP/def2-TZVPP)				E_{el}(M06-2X/def2-TZVPP)			
	ΔE_{el}	ΔG	$E_{1/2}$ / eV	$E_{1/2}$ (SCE) / eV	ΔE_{el}	ΔG	$E_{1/2}$ / eV	$E_{1/2}$ (SCE) / eV
<i>benzyl-BCP couple</i>	-74.7	-74.0	3.21	-1.22	-81.1	-80.4	3.49	-0.94
<i>p-CNphenyl-BCP couple</i>	-73.4	-72.0	3.12	-1.31	-82.0	-80.6	3.50	-0.93
<i>p-CNbenzyl-BCP couple</i>	-76.6	-75.6	3.28	-1.15	-82.7	-81.8	3.55	-0.88
<i>p-Mebenzyl-BCP couple</i>	-74.2	-73.9	3.20	-1.22	-80.9	-80.6	3.50	-0.93
<i>p-MeObenzyl-BCP couple</i>	-66.9	-66.7	2.89	-1.53	-73.5	-73.3	3.18	-1.25
<i>p-MeOphenyl-BCP couple</i>	-53.6	-52.8	2.29	-2.14	-64.3	-63.5	2.75	-1.68
<i>p-NH₂benzyl-BCP couple</i>	-58.7	-58.9	2.55	-1.88	-64.1	-64.3	2.79	-1.64
<i>p-OHbenzyl-BCP couple</i>	-68.0	-68.1	2.95	-1.48	-74.2	-74.4	3.22	-1.20
<i>p-NH₂phenyl-BCP couple</i>	-44.8	-43.6	1.89	-2.54	-54.8	-53.6	2.32	-2.11
<i>p-OHphenyl-BCP couple</i>	-54.7	-54.1	2.34	-2.08	-64.9	-64.3	2.79	-1.64
<i>phenyl-BCP couple</i>	-62.7	-61.1	2.65	-1.78	-73.0	-71.5	3.10	-1.33
<i>pyr-2-BCP couple</i>	-72.9	-72.0	3.12	-1.31	-80.8	-79.9	3.47	-0.96
<i>pyr-3-BCP couple</i>	-71.3	-70.3	3.05	-1.38	-79.3	-78.2	3.39	-1.04
<i>pyr-4-BCP couple</i>	-76.1	-75.7	3.28	-1.15	-83.7	-83.3	3.61	-0.82
<i>pyr-2-but-cat/BCP rad couple</i>	-69.6	-66.9	2.90	-1.53	-80.1	-77.4	3.36	-1.07
<i>pyr-3-but-cat/BCP rad couple</i>	-67.2	-64.8	2.81	-1.62	-76.6	-74.3	3.22	-1.21
<i>pyr-4-but-cat/BCP rad couple</i>	-73.5	-71.0	3.08	-1.35	-83.8	-81.2	3.52	-0.91
<i>p-CNphenyl-but-cat/BCP rad couple</i>	-69.4	-67.1	2.91	-1.52	-80.0	-77.6	3.37	-1.06
<i>benzyl-spiro-cat/BCP rad couple</i>	-74.6	-73.6	3.19	-1.24	-82.1	-81.1	3.52	-0.91
<i>p-Mebenzyl-spiro-cat/BCP rad couple</i>	-71.9	-71.1	3.08	-1.35	-78.8	-78.0	3.38	-1.05

TCP Oxidation & Reduction

Degradation of TCP under the reaction conditions by the photocatalyst *fac*-Ir(ppy)₃ is shown to be unlikely due to the unfavourable redox cell potentials for all combinations of electron transfer couples (Figure 9).

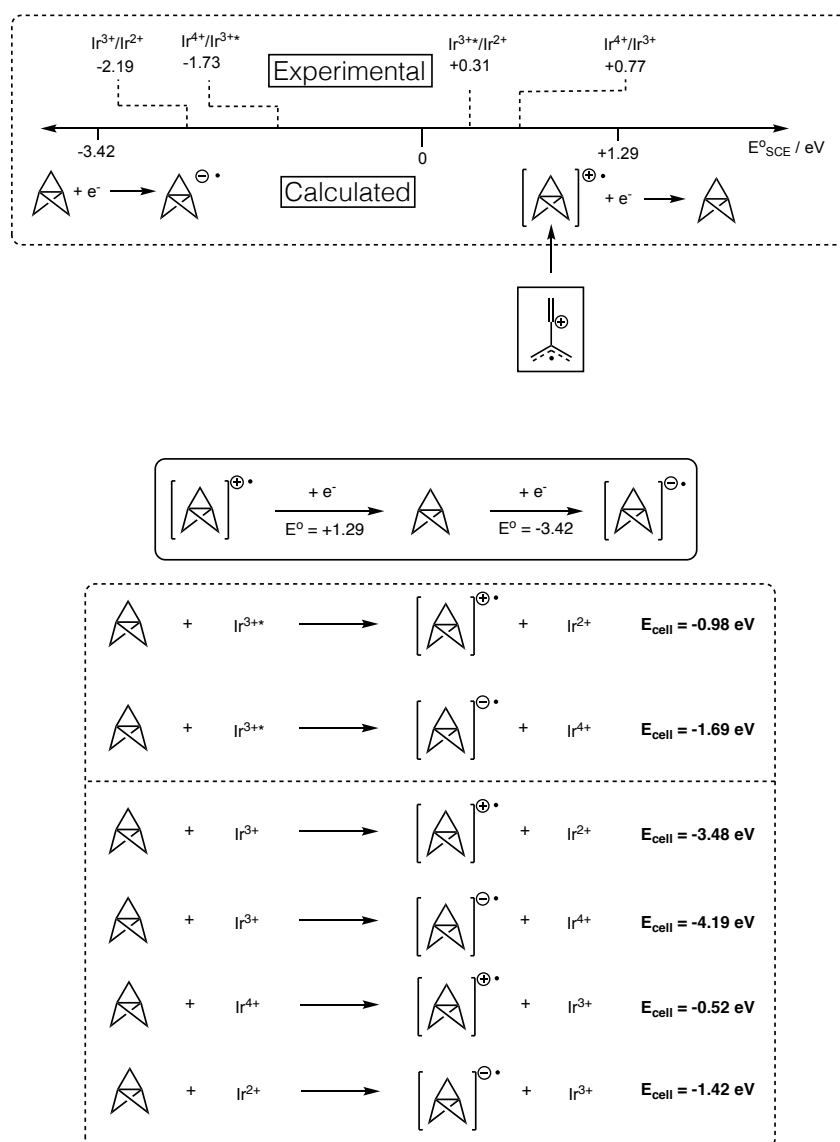


Figure 9. a, Reduction potentials for TCP compared with literature experimental values for *fac*-Ir(ppy)₃ in MeCN, calculated at the SMD(MeCN)-RI-B2PLYP/def2-TZVPP//SMD(MeCN)-TPSS/def2-TZVP level of theory. **B,** Cell potentials calculated by the combination of the corresponding TCP / Ir(ppy)₃ redox processes. Values are reported in Table 14.

c. Radical Reactivity of TCP

Addition of carbon-centred radicals across the bridgehead bond in TCP and the further reactivity of BCP radicals has been studied computationally by Uchiyama⁶⁴ and Anderson¹, using DFT. These studies formed the starting point for the calculations described here. An activation barrier of 11.4 kcal mol⁻¹ was calculated for the addition of the 4-pyridyl radical **B** to TCP (Figure 10). This is followed by iodine atom abstraction ($\Delta G^\ddagger = 11.8$ kcal mol⁻¹), which completes the ATRA reaction. Turnover of the catalyst can result from the oxidation of the BCP radical **C** to give bent bicyclobutyl cation **E**, with a thermodynamic driving force of 44.4 kcal mol⁻¹.

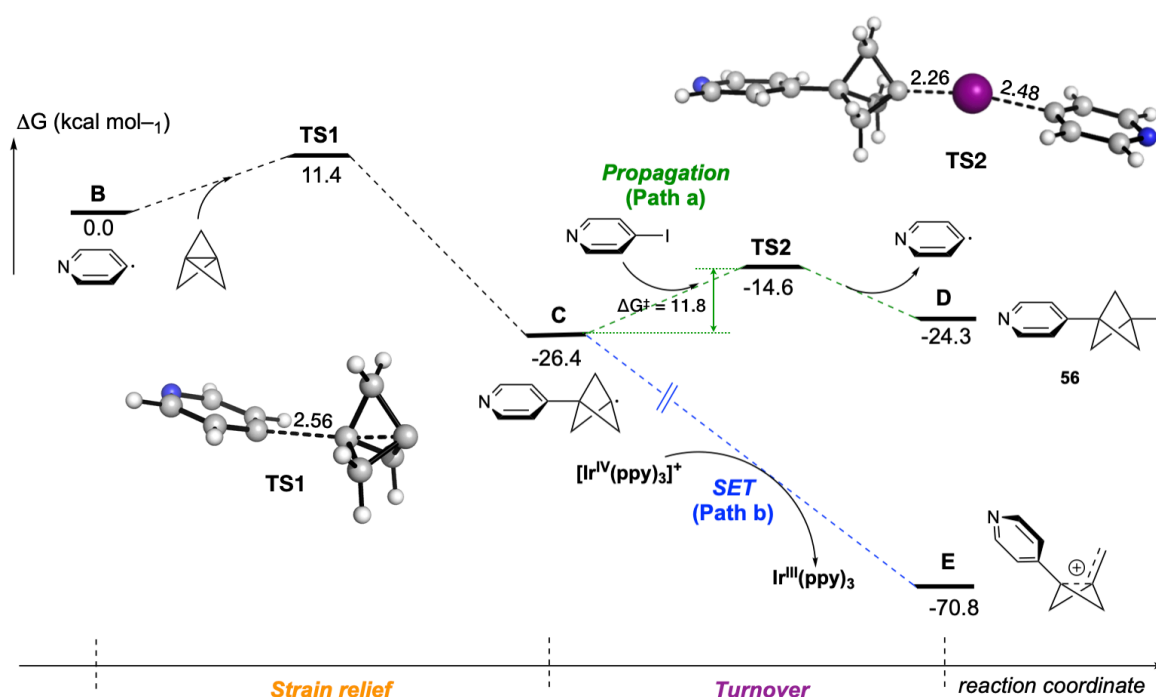


Figure 10. Radical reactivity of TCP with the 4-pyridyl radical. Calculations at SMD(MeCN)-RI-B2PLYP-D3BJ/def2-QZVPP//SMD(MeCN)-RI-B2PLYP/def2-TZVP. Values are tabulated in Table 9.

d. Reactions of BCP Cations with Iodide

While oxidation of the BCP radical has been shown to be feasible, whether the reaction of the newly-formed bent cyclopentyl cation with iodide could form a BCP iodide **M8** is not clear from experiment. Several pathways can be envisaged to compete with this process, with the potential to form either a bicyclobutyl iodide **M11** or exomethylene cyclobutyl iodide **M3/M4**. Experimental observation of 4-pyridyl cyclobutyl iodide (Figure 11) provides a starting point for the computational analysis of the PES responsible for the reactivity of BCP cations with iodide.

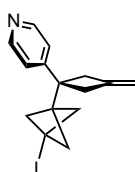


Figure 11. *Exo*-methylene cyclobutyl double-ATRA adduct observed experimentally

Calculations on a simple system with transannular methyl substitution were first used to identify key intermediates and transition states. Substituting methyl for 4-pyridyl for the analogous key competing processes was used to compare directly with the experimental observations.

Methyl substituent

The full PES that considers all intermediate structures and transition states is shown in Figure 12. The dominating pathway (solid black line) is that from bent bicyclobutyl cation **M1** to cyclobutyl iodide **M3**. This is proposed to commence via flattening of the cyclobutyl ring ($\Delta G^\ddagger = 0.9 \text{ kcal mol}^{-1}$). This low-barrier unimolecular step will dominate over all competing bimolecular processes. Subsequent C–I bond formation drives this equilibrium to the cyclobutyl iodide **M3/M4**. Bicyclo[1.1.0]butyl iodide **M11** and products derived from the subsequent reaction ATRA reaction are not observed experimentally (Figure 12, left grey). The pathway *via* **TS3** (dashed black line) requires significant distortion of the carbocyclic cation, which results in increased strain in the transition state, and is therefore disfavoured by $13.3 \text{ kcal mol}^{-1}$ compared with the dominant pathway.

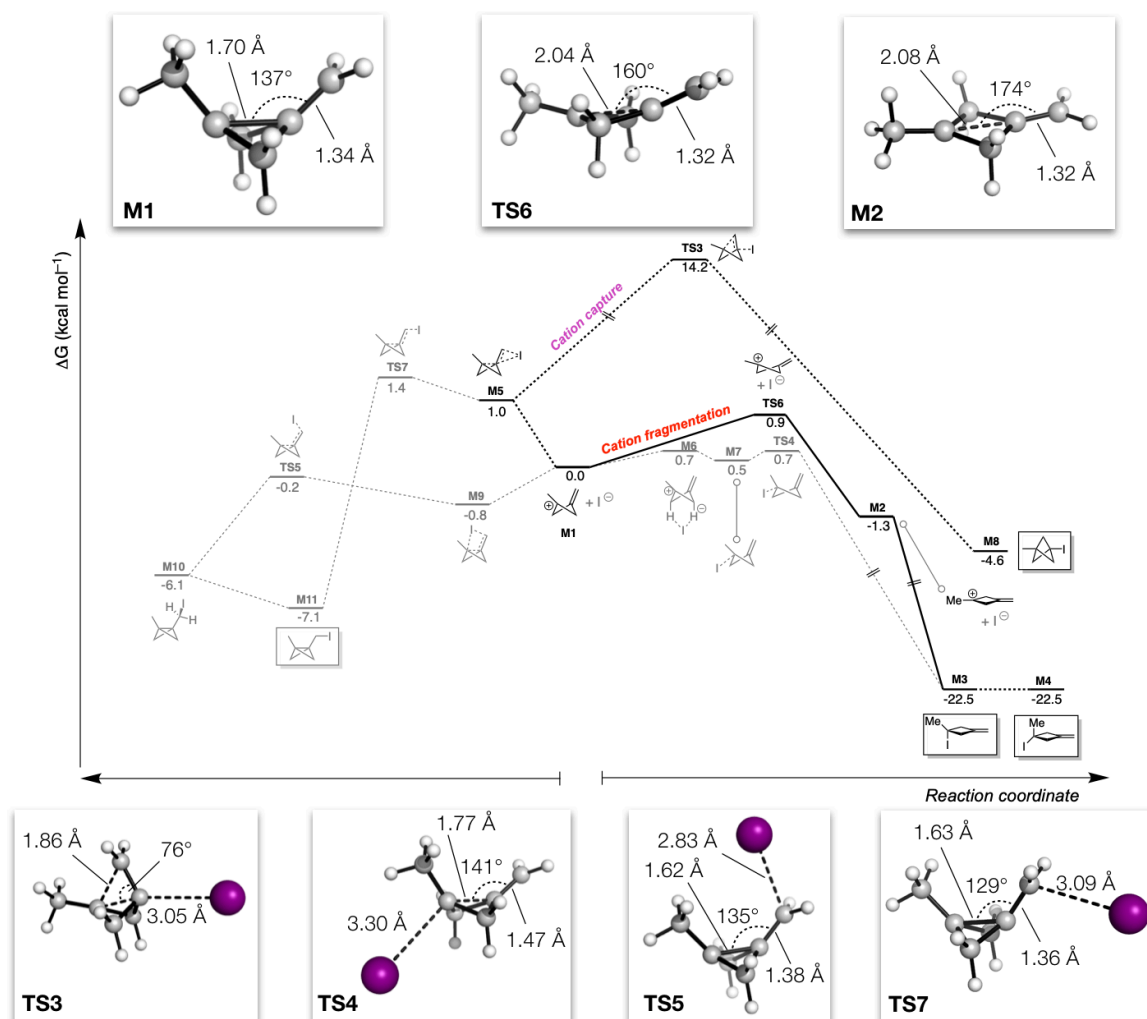


Figure 12. Gibbs Free energy profile for the reaction of iodide with bicyclobutyl cation **M1**. Solid line denotes favoured pathway. Dashed black line denotes the path leading to BCP iodide. Grey dashed lines denote all other disfavoured pathways. Calculations at SMD(MeCN)-RI-B2PLYP-D3BJ/def2-QZVPP//SMD(MeCN)-RI-B2PLYP/def2-TZVP. Values are tabulated in Table 9.

4-pyridyl substituent

To demonstrate the bias for the formation of cyclobutyl iodide **G** to correlate with the experimental observation, a computational investigation of the 4-pyridyl BCP cation **E** was undertaken. The pathway favoured in the initial investigation with methyl substitution was compared with the bicyclopentyl iodide-forming step, from bent cyclobutyl cation **E** to either BCP iodide **D** or cyclobutyl iodide **G** (Figure 13). The results of this study suggest all bent cations formed will result in the formation of cyclobutyl iodide **F** due to the large difference in activation barriers between the two pathways ($\Delta\Delta G^\ddagger = 13.2$ kcal mol⁻¹).

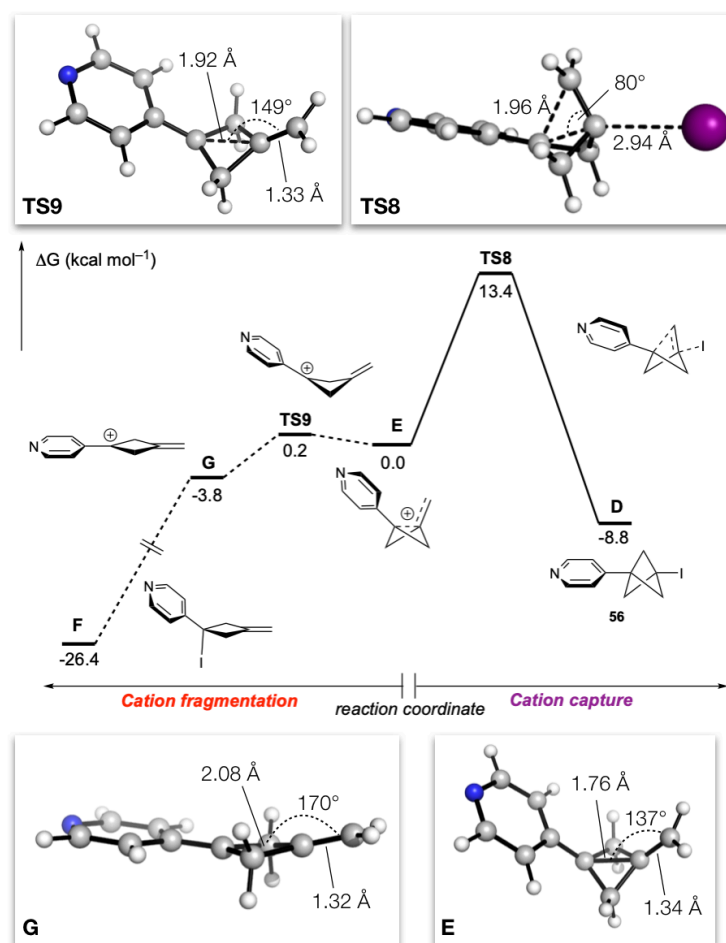


Figure 13. Calculated free energy pathways for the addition of iodide to bicyclobutyl cation **E**. Calculations at SMD(MeCN)-RI-B2PLYP-D3BJ/def2-QZVPP//SMD(MeCN)-RI-B2PLYP/def2-TZVP. Values are relative to cation **E**, and are tabulated in Table 9.

Table 9. Relative electronic energies (ΔE_{el}) and Gibbs free energy (ΔG) in kcal mol⁻¹ for methyl and pyridyl PES presented in Figures 10, 12 and 13. Calculations at the SMD(MeCN)-**RI-B2PLYP-D3BJ**/def2-QZVPP//SMD(MeCN)-**RI-B2PLYP**/def2-TZVP. Absolute energies are presented in Table 16.

PES	Species	ΔE_{el}	ΔG	
<i>Methyl</i>	<i>M1 + I-</i>	0.0	0.0	
	<i>M2 + I-</i>	1.0	-1.3	
	<i>M3</i>	-29.4	-22.5	
	<i>M4</i>	-29.6	-22.5	
	<i>M5</i>	-3.8	1.0	
	<i>M6</i>	-3.9	0.7	
	<i>M7</i>	-4.0	0.5	
	<i>M8</i>	-12.9	-4.6	
	<i>M9</i>	-5.6	-0.8	
	<i>M10</i>	-12.9	-6.1	
	<i>M11</i>	-14.0	-7.1	
	<i>TS3</i>	7.7	14.2	
	<i>TS4</i>	-4.2	0.7	
	<i>TS5</i>	-5.9	-0.2	
	<i>TS6 + I-</i>	2.6	0.9	
<i>TS7</i>	-4.5	1.4		
<i>4-Pyridyl</i>	B + <i>TCP + pyrI + I-</i>	0.0	0.0	
	<i>TS1 + pyrI + I-</i>	0.7	11.4	
	C + <i>pyrI + I-</i>	-40.0	-26.4	
	<i>TS2 + I-</i>	-39.6	-14.6	
	D + <i>pyr rad + I-</i>	-38.3	-24.3	
	E + <i>I- + pyr-I</i>	-	-70.8	0.0
	<i>TS8 + pyr-I</i>	-	-57.4	13.4
	D + <i>pyr-I</i>	-	-79.6	-8.8
	<i>TS9 + I- + pyrI</i>	-	-70.6	0.2
	G + <i>I- + pyrI</i>	-	-74.6	-3.8
	F + <i>pyr-I</i>	-	-97.2	-26.4
	$\Delta G_{ox}(Ir^{IV}/Ir^{III}) = -119.89414$			

e. Energetics and Thermodynamic Quantities

Redox potential calculations

Table 10. Absolute electronic energies (E_{el}), zero-point energy (ZPE), enthalpy (H), quasi-harmonic entropies (Tqh-S), total thermal correction (T_{corr}) and quasi-harmonic Gibbs energy (qh-G) (in Hartrees) for each species in the redox process, calculated at the SMD(MeCN)-TPSS/def2-TZVP level of theory. Thermochemistry was evaluated at 298.15 K and 1 M.

TPSS/def2-TZVP	E_{el}	ZPE	H	Tqh-S	Total corr	qh-G
<i>benzyl-BCP-cat</i>	-465.10729	0.20859	-464.88670	0.04704	0.17355	-464.93374
<i>benzyl-BCP-rad</i>	-465.22798	0.20953	-465.00738	0.04582	0.17478	-465.05320
<i>p-CNphenyl BCP-cat</i>	-518.07174	0.17917	-517.88016	0.04816	0.14341	-517.92832
<i>p-CNphenyl-BCP-rad</i>	-518.19027	0.18018	-517.99940	0.04523	0.14564	-518.04463
<i>p-CNbenzyl-BCP-cat</i>	-557.40255	0.20700	-557.18169	0.05132	0.16954	-557.23301
<i>p-CNbenzyl-BCP-rad</i>	-557.52688	0.20815	-557.30585	0.04999	0.17105	-557.35583
<i>p-Mebenzyl-BCP-cat</i>	-504.44567	0.23517	-504.19744	0.04926	0.19896	-504.24670
<i>p-Mebenzyl-BCP-rad</i>	-504.56511	0.23625	-504.31589	0.04986	0.19936	-504.36575
<i>p-MeObenzyl-BCP-cat</i>	-579.70643	0.24072	-579.45131	0.05208	0.20303	-579.50340
<i>p-MeObenzyl-BCP-rad</i>	-579.81552	0.24117	-579.56060	0.05166	0.20326	-579.61226
<i>p-MeOphenyl-BCP-cat</i>	-540.39121	0.21204	-540.16577	0.05020	0.17524	-540.21597
<i>p-MeOphenyl-BCP-rad</i>	-540.47996	0.21315	-540.25435	0.04907	0.17654	-540.30342
<i>p-NH₂benzyl-BCP-cat</i>	-520.52287	0.22561	-520.28428	0.04881	0.18978	-520.33309
<i>p-NH₂benzyl-BCP-rad</i>	-520.61935	0.22559	-520.38124	0.04866	0.18944	-520.42991
<i>p-OHbenzyl-BCP-cat</i>	-540.38391	0.21317	-540.15801	0.04839	0.17751	-540.20640

<i>p</i> -OHbenzyl-BCP-rad	-540.49468	0.21334	-540.26906	0.04836	0.17727	-540.31741
<i>p</i> -NH ₂ phenyl-BCP-cat	-481.20885	0.19723	-480.99961	0.04724	0.16200	-481.04685
<i>p</i> -NH ₂ phenyl-BCP-rad	-481.28388	0.19755	-481.07598	0.04401	0.16389	-481.11999
<i>p</i> -OHphenyl-BCP-cat	-501.06846	0.18436	-500.87232	0.04662	0.14952	-500.91894
<i>p</i> -OHphenyl-BCP-rad	-501.15909	0.18530	-500.96281	0.04577	0.15051	-501.00858
phenyl-BCP-cat	-425.78813	0.17968	-425.59854	0.04259	0.14700	-425.64113
phenyl-BCP-rad	-425.89217	0.18166	-425.70164	0.04112	0.14941	-425.74276
pyr-2-BCP-cat	-441.82351	0.16932	-441.64383	0.04346	0.13623	-441.68729
pyr-2-BCP-rad	-441.94058	0.16979	-441.76202	0.04099	0.13758	-441.80300
pyr-3-BCP-cat	-441.82322	0.16898	-441.64368	0.04411	0.13543	-441.68778
pyr-3-BCP-rad	-441.93861	0.17037	-441.75864	0.04284	0.13713	-441.80148
pyr-4-BCP-cat	-441.81744	0.16920	-441.63786	0.04350	0.13608	-441.68135
pyr-4-BCP-rad	-441.93971	0.17009	-441.75998	0.04304	0.13669	-441.80302
pyr-2-but-cat	-441.82604	0.16705	-441.64819	0.04456	0.13330	-441.69275
pyr-3-but-cat	-441.82732	0.16716	-441.64932	0.04457	0.13343	-441.69389
pyr-4-but-cat	-441.81921	0.16646	-441.64182	0.04482	0.13258	-441.68663
<i>p</i> -CNphenyl-but-cat	-518.07569	0.17767	-517.88545	0.04834	0.14190	-517.93379
benzyl-spiro-cat	-465.10653	0.20824	-464.88634	0.04693	0.17326	-464.93327
<i>p</i> -Mebenzyl-spiro-cat	-504.44775	0.23504	-504.19894	0.05077	0.19804	-504.24971

Table 11. Change in absolute energy (ΔE_{el}), enthalpy (ΔH), quasi-harmonic entropies ($T\Delta S$) and quasi-harmonic Gibbs energy (ΔG) (all values stated in kcal mol⁻¹) for each redox couple calculated at the SMD(MeCN)-TPSS/def2-TZVP level of theory. Thermochemistry was evaluated at 298.15 K and 1 M.

TPSS/def2-TZVP	ΔE_{el}	ΔH	$T\Delta S$	ΔG
<i>benzyl-BCP couple</i>	-75.7	-75.7	-0.8	-75.0
<i>p-CNphenyl-BCP couple</i>	-74.4	-74.8	-1.8	-73.0
<i>p-CNbenzyl-BCP couple</i>	-78.0	-77.9	-0.8	-77.1
<i>p-Mebenzyl-BCP couple</i>	-75.0	-74.3	0.4	-74.7
<i>p-MeObenzyl-BCP couple</i>	-68.5	-68.6	-0.3	-68.3
<i>p-MeOphenyl-BCP couple</i>	-55.7	-55.6	-0.7	-54.9
<i>p-NH₂benzyl-BCP couple</i>	-60.5	-60.8	-0.1	-60.8
<i>p-OHbenzyl-BCP couple</i>	-69.5	-69.7	0.0	-69.7
<i>p-NH₂phenyl-BCP couple</i>	-47.1	-47.9	-2.0	-45.9
<i>p-OHphenyl-BCP couple</i>	-56.9	-56.8	-0.5	-56.2
<i>phenyl-BCP couple</i>	-65.3	-64.7	-0.9	-63.8
<i>pyr-2-BCP couple</i>	-73.5	-74.2	-1.5	-72.6
<i>pyr-3-BCP couple</i>	-72.4	-72.1	-0.8	-71.3
<i>pyr-4-BCP couple</i>	-76.7	-76.6	-0.3	-76.3
<i>pyr-2-but-cat/BCP rad couple</i>	-71.9	-71.4	-2.2	-69.2
<i>pyr-3-but-cat/BCP rad couple</i>	-69.8	-68.6	-1.1	-67.5
<i>pyr-4-but-cat/BCP rad couple</i>	-75.6	-74.2	-1.1	-73.0
<i>p-CNphenyl-but-cat/BCP rad couple</i>	-71.9	-71.5	-2.0	-69.6
<i>benzyl-spiro-cat/BCP rad couple</i>	-76.2	-76.0	-0.7	-75.3
<i>p-Mebenzyl-spiro-cat/BCP rad couple</i>	-73.6	-73.4	-0.6	-72.8

Table 12. Absolute electronic energies (E_{el}) and corrected quasi-harmonic Gibbs energy (qh-G) (in Hartrees) for each species in the redox processes, calculated at the SMD(MeCN)-**RI-B2PLYP**/def2-TZVPP and SMD(MeCN)-**M06-2X**/def2-TZVPP levels of theory. Geometries and thermochemistry from SMD(MeCN)-**TPSS**/def2-TZVP were used to calculate E_{el} and qh-G.

Species	E_{el} (RI-B2PLYP/def2-TZVPP)	qh-G	E_{el} (M06-2X/def2-TZVPP)	qh-G
<i>benzyl-BCP-cat</i>	-464.65640	-464.48285	-464.80857	-464.63501
<i>benzyl-BCP-rad</i>	-464.77549	-464.60071	-464.93787	-464.76309
<i>p-CNphenyl BCP-cat</i>	-517.59313	-517.44972	-517.74945	-517.60604
<i>p-CNphenyl-BCP-rad</i>	-517.71015	-517.56451	-517.88015	-517.73451
<i>p-CNbenzyl-BCP-cat</i>	-556.88550	-556.71595	-557.05983	-556.89029
<i>p-CNbenzyl-BCP-rad</i>	-557.00751	-556.83646	-557.19165	-557.02060
<i>p-Mebenzyl-BCP-cat</i>	-503.95541	-503.75644	-504.12076	-503.92179
<i>p-Mebenzyl-BCP-rad</i>	-504.07358	-503.87422	-504.24962	-504.05026
<i>p-MeObenzyl-BCP-cat</i>	-579.16690	-578.96387	-579.34850	-579.14547
<i>p-MeObenzyl-BCP-rad</i>	-579.27349	-579.07023	-579.46562	-579.26236
<i>p-MeOphenyl-BCP-cat</i>	-539.89172	-539.71648	-540.05250	-539.87727
<i>p-MeOphenyl-BCP-rad</i>	-539.97709	-539.80054	-540.15494	-539.97840
<i>p-NH₂benzyl-BCP-cat</i>	-520.03263	-519.84285	-520.20196	-520.01218
<i>p-NH₂benzyl-BCP-rad</i>	-520.12612	-519.93668	-520.30405	-520.11461
<i>p-OHbenzyl-BCP-cat</i>	-539.88890	-539.71139	-540.05707	-539.87956
<i>p-OHbenzyl-BCP-rad</i>	-539.99722	-539.81995	-540.17535	-539.99808

<i>p</i> -NH ₂ phenyl-BCP-cat	-480.75844	-480.59644	-480.90619	-480.74419
<i>p</i> -NH ₂ phenyl-BCP-rad	-480.82983	-480.66594	-480.99347	-480.82958
<i>p</i> -OHphenyl-BCP-cat	-500.61359	-500.46407	-500.76111	-500.61159
<i>p</i> -OHphenyl-BCP-rad	-500.70075	-500.55024	-500.86461	-500.71410
phenyl-BCP-cat	-425.37891	-425.23191	-425.51057	-425.36357
phenyl-BCP-rad	-425.47877	-425.32936	-425.62696	-425.47754
pyr-2-BCP-cat	-441.40601	-441.26979	-441.54173	-441.40550
pyr-2-BCP-rad	-441.52211	-441.38454	-441.67043	-441.53285
pyr-3-BCP-cat	-441.40631	-441.27088	-441.54202	-441.40659
pyr-3-BCP-rad	-441.52001	-441.38288	-441.66832	-441.53118
pyr-4-BCP-cat	-441.39996	-441.26388	-441.53622	-441.40014
pyr-4-BCP-rad	-441.52121	-441.38452	-441.66962	-441.53293
pyr-2-but-cat	-441.41122	-441.27793	-441.54275	-441.40945
pyr-3-but-cat	-441.41299	-441.27956	-441.54625	-441.41282
pyr-4-but-cat	-441.40401	-441.27143	-441.53613	-441.40356
<i>p</i> -CNphenyl-but-cat	-517.59953	-517.45763	-517.75271	-517.61081
benzyl-spiro-cat	-464.65666	-464.48340	-464.80707	-464.63381
<i>p</i> -Mebenzyl-spiro-cat	-503.95902	-503.76098	-504.12398	-503.92594

Table 13. Absolute electronic energies (E_{el}), zero point energy (ZPE), enthalpy (H), quasi-harmonic entropies (Tqh-S), total thermal correction (T_{corr}) and quasi-harmonic Gibbs energy (qh-G) (in Hartrees) for TCP oxidation and reduction, calculated at the SMD(MeCN)-**TPSS**/def2-TZVP level of theory. Thermochemistry was evaluated at 298.15 K and 1 M.

Species	E_{el}	ZPE	H	Tqh-S	Total corr	qh-G
<i>TCP</i>	-194.14299	0.09163	-194.04635	0.03033	0.06631	-194.07667
<i>TCP radical anion</i>	-194.18166	0.08861	-194.08800	0.03105	0.06261	-194.11905
<i>TCP radical cation</i>	-193.92370	0.08415	-193.83243	0.03530	0.05597	-193.86773

Table 14. Absolute electronic energies (E_{el}) and corrected quasi-harmonic Gibbs energy (qh-G) (in Hartrees) for TCP oxidation and reduction, calculated at the SMD(MeCN)-**M06-2X**/def2-TZVPP and SMD(MeCN)-**RI-B2PLYP**/def2-TZVPP levels of theory. Geometries and thermochemistry from SMD(MeCN)-**TPSS**/def2-TZVP were used to calculate E_{el} and qh-G.

Species	$E_{\text{el}}(\text{M06-2X/def2-TZVPP})$	qh-G	$E_{\text{el}}(\text{RI-B2PLYP/def2-TZVPP})$	qh-G
<i>TCP</i>	-194.02091	-193.95460	-193.94439	-193.87808
<i>TCP radical anion</i>	-194.05318	-193.99057	-193.97844	-193.91583
<i>TCP radical cation</i>	-193.77951	-193.72354	-193.72401	-193.66804

Bicyclopentyl cation PES

Table 15. Absolute electronic energies (E_{el}), zero point energy (ZPE), enthalpy (H), quasi-harmonic entropies (Tqh-S), total thermal correction (T_{corr}) and quasi-harmonic Gibbs energy (qh-G) (in Hartrees) for each species on the PES, calculated at the SMD(MeCN)-**RI-B2PLYP**/def2-TZVP level of theory. Thermochemistry was evaluated at 298.15 K and 1 M.

Species	E_{el}	ZPE	H	Tqh-S	Total corr	qh-G	TS Freq ^a
<i>iodide</i>	-297.72310	0.00000	-297.71980	0.01921	-0.01590	-297.73900	
<i>B</i>	-247.48156	0.07573	-247.40066	0.03313	0.04777	-247.43379	
<i>C</i>	-441.45095	0.17341	-441.26814	0.04354	0.13927	-441.31168	
<i>E</i>	-441.33015	0.17264	-441.14740	0.04405	0.13870	-441.19145	
<i>F</i>	-441.33365	0.17038	-441.15279	0.04499	0.13587	-441.19778	
<i>G</i>	-739.09914	0.17353	-738.91378	0.04936	0.13600	-738.96314	
<i>D</i>	-739.07566	0.17577	-738.88881	0.04808	0.13877	-738.93688	
<i>pyr-I</i>	-545.10934	0.07830	-545.02436	0.03835	0.04663	-545.06271	
<i>TS1</i>	-441.38835	0.16965	-441.20918	0.04448	0.13469	-441.25366	-65.0
<i>TS2</i>	-986.55558	0.25152	-986.28728	0.06124	0.20706	-986.34852	-109.6
<i>TS8</i>	-739.03810	0.17348	-738.85289	0.04974	0.13547	-738.90263	-287.0
<i>TS9</i>	-441.32964	0.17153	-441.14864	0.04287	0.13813	-441.19151	-59.5
<i>M1</i>	-233.64748	0.13034	-233.50966	0.03700	0.10082	-233.54666	
<i>M2</i>	-233.64613	0.12701	-233.51119	0.03784	0.09710	-233.54903	
<i>M3</i>	-531.41208	0.13215	-531.27118	0.04203	0.09888	-531.31321	
<i>M4</i>	-531.41253	0.13243	-531.27138	0.04198	0.09917	-531.31336	
<i>M5</i>	-531.37556	0.13067	-531.23572	0.04419	0.09565	-531.27991	

<i>M6</i>	-531.37537	0.13028	-531.23586	0.04421	0.09530	-531.28007	
<i>M7</i>	-531.37514	0.13021	-531.23561	0.04435	0.09518	-531.27996	
<i>M8</i>	-531.38697	0.13406	-531.24479	0.04091	0.10128	-531.28569	
<i>M9</i>	-531.37701	0.13044	-531.23740	0.04400	0.09562	-531.28140	
<i>M10</i>	-531.38664	0.13272	-531.24499	0.04284	0.09881	-531.28784	
<i>M11</i>	-531.38949	0.13287	-531.24772	0.04282	0.09895	-531.29054	
<i>TS3</i>	-531.35564	0.13241	-531.21436	0.04305	0.09822	-531.25742	-255.5
<i>TS4</i>	-531.37418	0.13029	-531.23468	0.04369	0.09581	-531.27837	-97.5
<i>TS5</i>	-531.37602	0.13102	-531.23619	0.04281	0.09702	-531.27900	-102.4
<i>TS6</i>	-233.64378	0.12724	-233.50954	0.03609	0.09814	-233.54564	-37.2
<i>TS7</i>	-531.37501	0.13139	-531.23483	0.04285	0.09733	-531.27768	-54.3

^a Imaginary frequencies are denoted with a minus sign

Table 16. Electronic energy and Gibbs free energy for methyl and pyridyl PES with SMD(MeCN)-**RI-B2PLYP-D3BJ**/def2-QZVPP for geometries and thermochemistry from SMD(MeCN)-**RI-B2PLYP**/def2-TZVP. All energies are reported in kcal mol⁻¹.

PES	Species	E_{el}	qh-G
<i>methyl</i>	<i>M1</i>	-233.69569	-233.59487
	<i>M2</i>	-233.69412	-233.59702
	<i>M3</i>	-531.52081	-531.42193
	<i>M4</i>	-531.52112	-531.42195
	<i>M5</i>	-531.48008	-531.38443
	<i>M6</i>	-531.48025	-531.38495
	<i>M7</i>	-531.48041	-531.38523
	<i>M8</i>	-531.49458	-531.39331
	<i>M9</i>	-531.48292	-531.38731
	<i>M10</i>	-531.49452	-531.39571
	<i>M11</i>	-531.49627	-531.39732
	<i>TS3</i>	-531.46167	-531.36345
	<i>TS4</i>	-531.48072	-531.38491
	<i>TS5</i>	-531.48345	-531.38643
	<i>TS6</i>	-233.69159	-233.59345
	<i>TS7</i>	-531.48109	-531.38376
<i>4-pyridyl</i>	<i>Iodide</i>	-297.77829	-297.79419
	<i>B</i>	-247.52347	-247.47570
	<i>C</i>	-441.53482	-441.39555
	<i>E</i>	-441.41281	-441.27411
	<i>F</i>	-441.41597	-441.28010
	<i>G</i>	-739.24322	-739.10722
	<i>D</i>	-739.21804	-739.07927
	<i>pyr-I</i>	-545.20931	-545.16268
	<i>TS1</i>	-441.47000	-441.33531
	<i>TS2</i>	-986.74351	-986.53645
	<i>TS8</i>	-739.17937	-739.04390
	<i>TS9</i>	-441.41187	-441.27374

f. Optimised Cartesian Coordinates

Cartesian coordinates (in xyz format) for computed stationary points can be found in the ZIP folder provided.

8. X-ray Crystallography

Low temperature single crystal X-ray diffraction data were collected for **76** and **86** using I19-1 at the Diamond Light Source⁶⁵ at 100 K. These data were reduced using CrysAlisPro, solved using SuperFlip⁶⁶ and the structures were refined using CRYSTALS.^{67,68}

The Flack x parameter^{69,70} was refined for **86** and had a value -0.028(14). Bayesian analysis of the Bijvoet pairs was also carried out using all the data used in the refinement.⁷¹ This gave the Hooft y parameter (-0.041(7)), the P2 probability (the likelihood that the hand is correct given the crystal was enantiopure), and the P3 probability (the likelihood that the hand is correct given the crystal was enantiopure or racemic). These data (see below) indicate a high probability that the handedness of the model is correct.

Further details about the refinements are documented in the CIF. The crystallographic data have been deposited with the CCDC as entries CCDC 1905036–1905037.

Table 17. Crystal data and structure refinement for **76**.

CCDC Identification code	1905036	
Empirical formula	C ₂₀ H ₂₆ I ₁ N ₁ O ₂ S ₁	
Formula weight	471.40	
Temperature	100 K	
Wavelength	0.68890 Å	
Crystal system	Monoclinic	
Space group	P 2 ₁ /c	
Unit cell dimensions	a = 12.2416(7) Å	α = 90°.
	b = 20.4922(11) Å	β = 91.862(5)°.
	c = 7.9382(4) Å	γ = 90°.
Volume	1990.30(19) Å ³	
Z	4	
Density (calculated)	1.573 Mg/m ³	
Absorption coefficient	1.727 mm ⁻¹	
F(000)	952	
Crystal size	0.085 x 0.010 x 0.005 mm ³	
Theta range for data collection	1.613 to 25.584°.	
Index ranges	-15 ≤ h ≤ 15, -25 ≤ k ≤ 25, -9 ≤ l ≤ 9	
Reflections collected	28866	
Independent reflections	4086 [R(int) = 0.172]	
Completeness to theta = 25.584°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.99 and 0.49	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4070 / 0 / 226	
Goodness-of-fit on F ²	0.9900	
Final R indices [I > 2σ(I)]	R ₁ = 0.0861, wR ₂ = 0.2199	
R indices (all data)	R ₁ = 0.1421, wR ₂ = 0.2630	
Largest diff. peak and hole	3.00 and -1.52 e.Å ⁻³	

Table 18. Crystal data and structure refinement for **86**.

CCDC Identification code	1905037	
Empirical formula	C ₂₄ H ₃₅ I ₁ O ₁	
Formula weight	466.45	
Temperature	100 K	
Wavelength	0.68890 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.30332(4) Å	α = 90°.
	b = 11.85008(9) Å	β = 90°.
	c = 28.71209(18) Å	γ = 90°.
Volume	2144.64(3) Å ³	
Z	4	
Density (calculated)	1.445 Mg/m ³	
Absorption coefficient	1.503 mm ⁻¹	
F(000)	960	
Crystal size	0.04 x 0.02 x 0.02 mm ³	
Theta range for data collection	1.802 to 36.089°.	
Index ranges	-10 ≤ h ≤ 10, -19 ≤ k ≤ 19, -46 ≤ l ≤ 48	
Reflections collected	46658	
Independent reflections	10443 [R(int) = 0.0577]	
Completeness to theta = 32.119°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.97 and 0.74	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	10425 / 0 / 236	
Goodness-of-fit on F ²	0.9998	
Final R indices [I > 2σ(I)]	R1 = 0.0367, wR2 = 0.0948	
R indices (all data)	R1 = 0.0402, wR2 = 0.0967	
Largest diff. peak and hole	2.06 and -1.18 e.Å ⁻³	
Absolute structure parameter (Flack)	-0.028(14) for 4447 Friedel pairs	
Absolute structure parameter (Hooft)	-0.041(7) for 4318 Friedel pairs	
Hooft probability analysis	P2(correct) > 99.9999%, P3(correct) > 99.9999%	

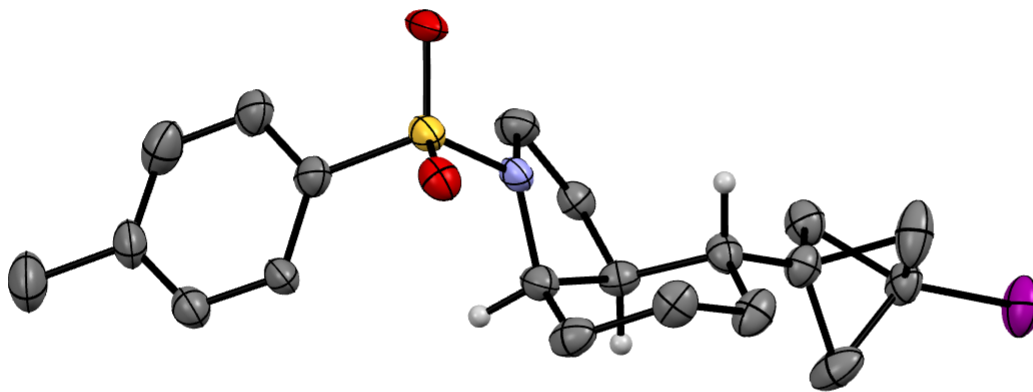


Figure 14: Solid state structure of **76**. Displacement ellipsoid plots are drawn at 30% probability. Hydrogen atoms, except those at the stereocentres, have been removed for clarity

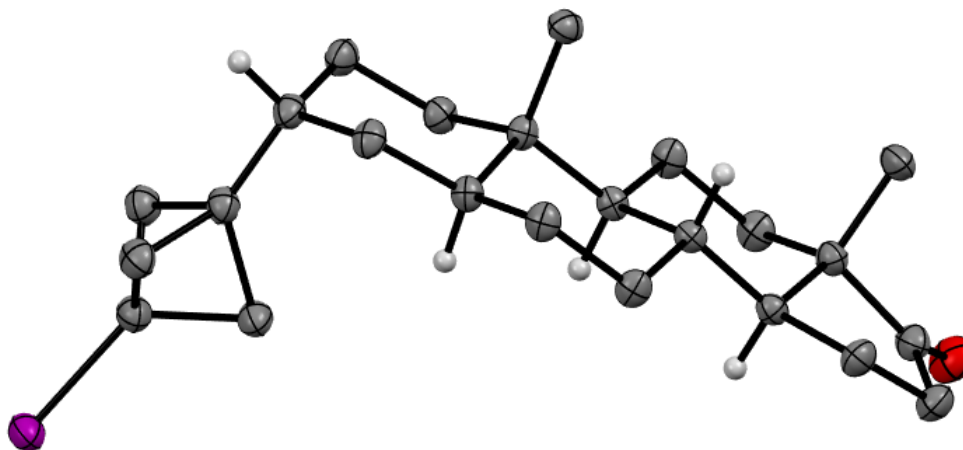


Figure 15: Solid state structure of **86**. Displacement ellipsoid plots are drawn at 50% probability. Hydrogen atoms, except those at the stereocentres, have been removed for clarity.

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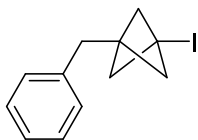
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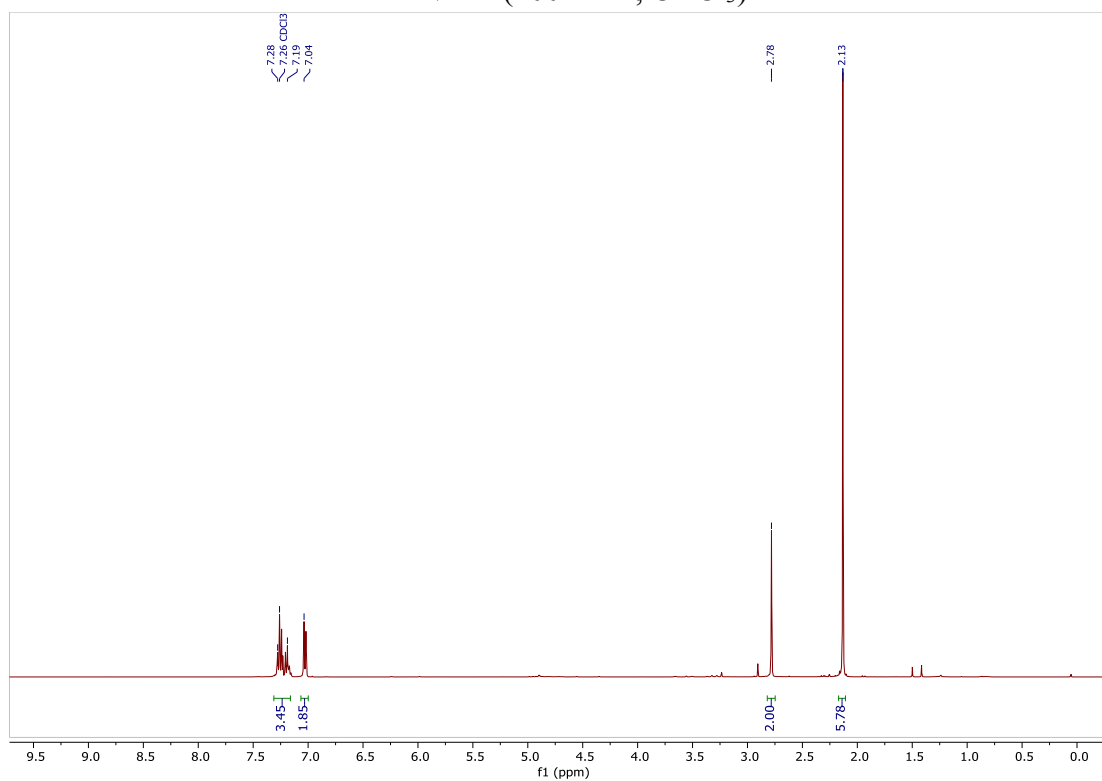
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10. Copies of NMR spectra

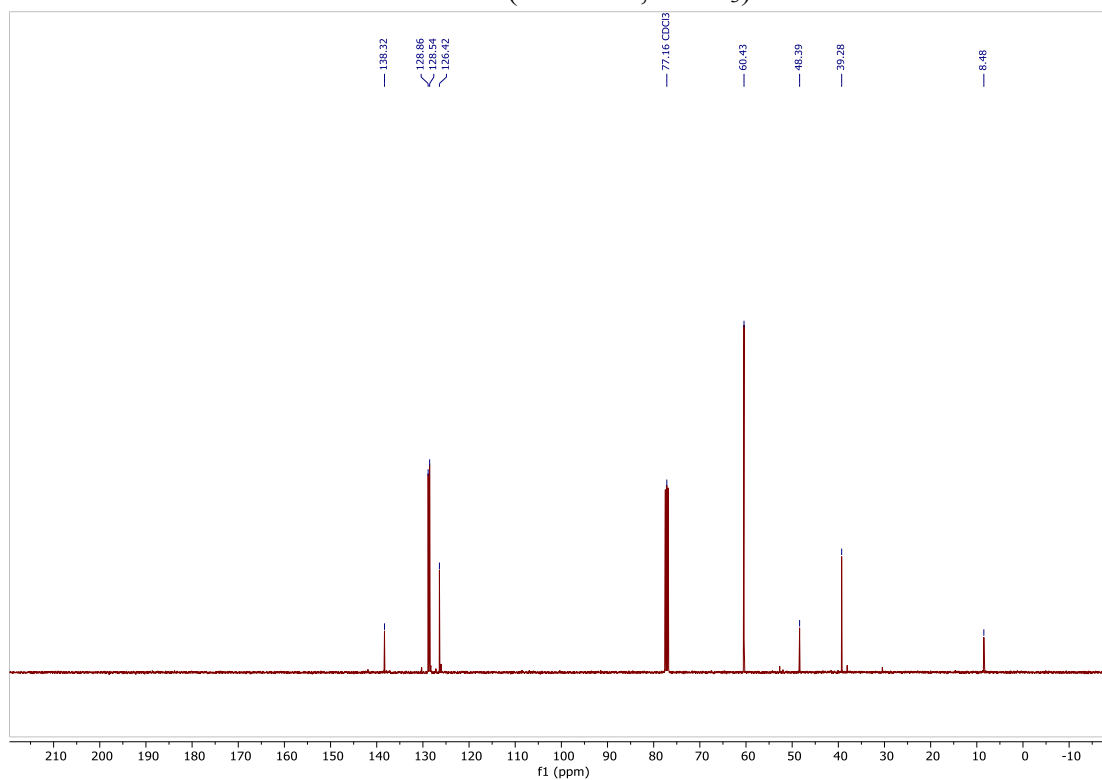
1-Benzyl-3-iodobicyclo[1.1.1]pentane, **3**



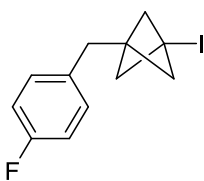
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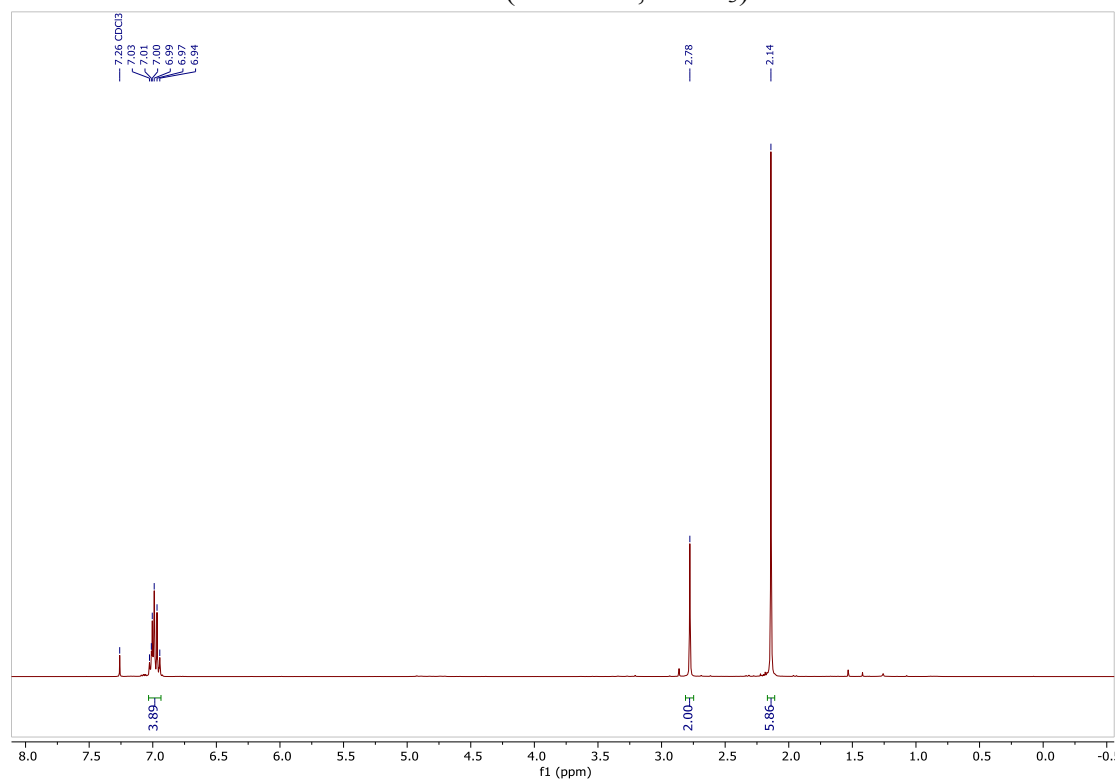
^{13}C NMR (101 MHz, CDCl_3)



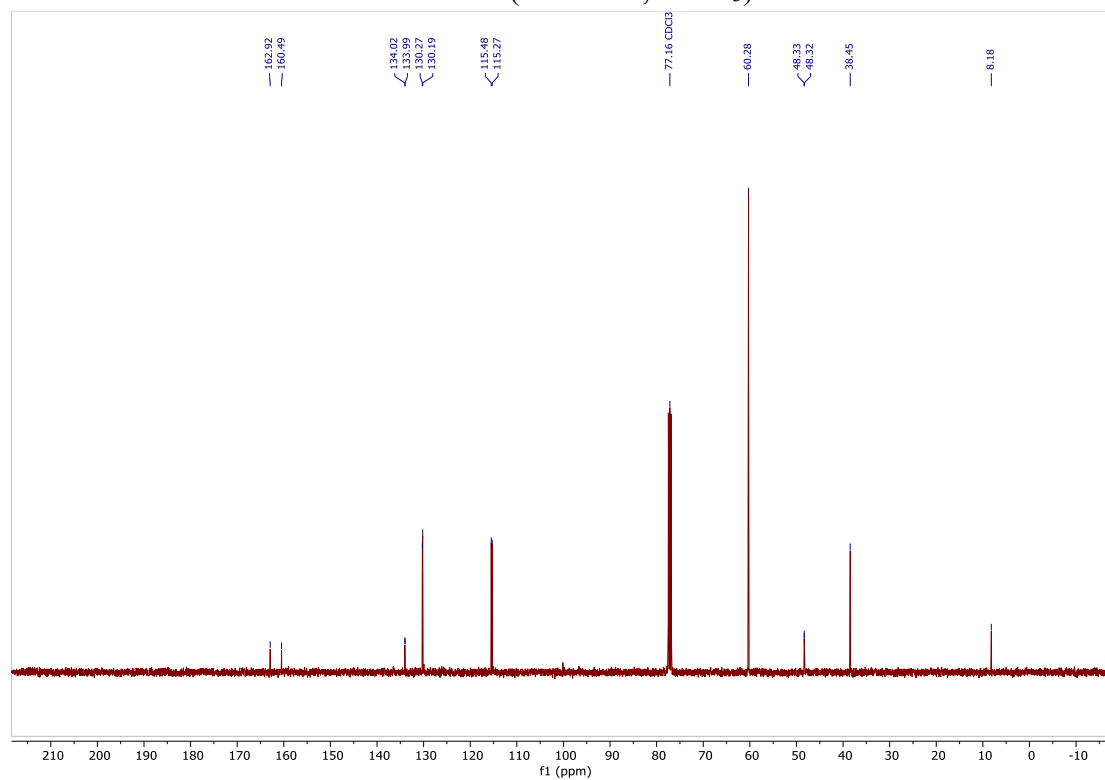
1-(4-Fluorobenzyl)-3-iodobicyclo[1.1.1]pentane, 4



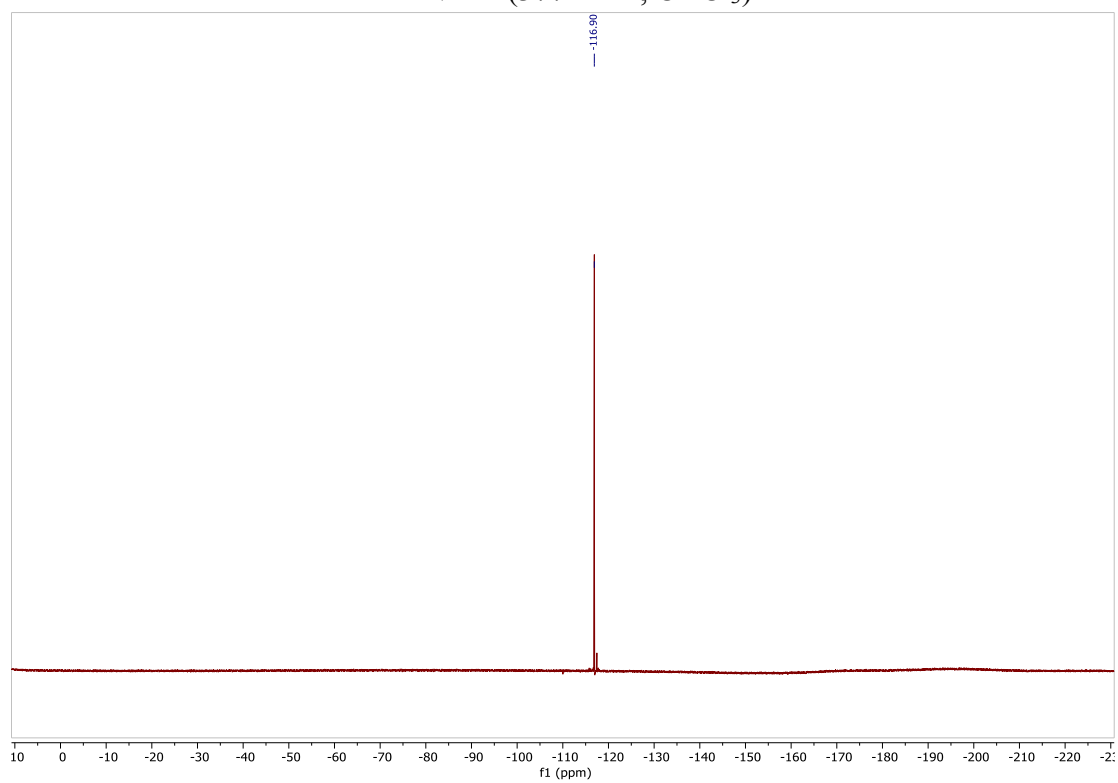
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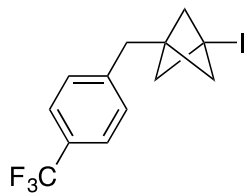
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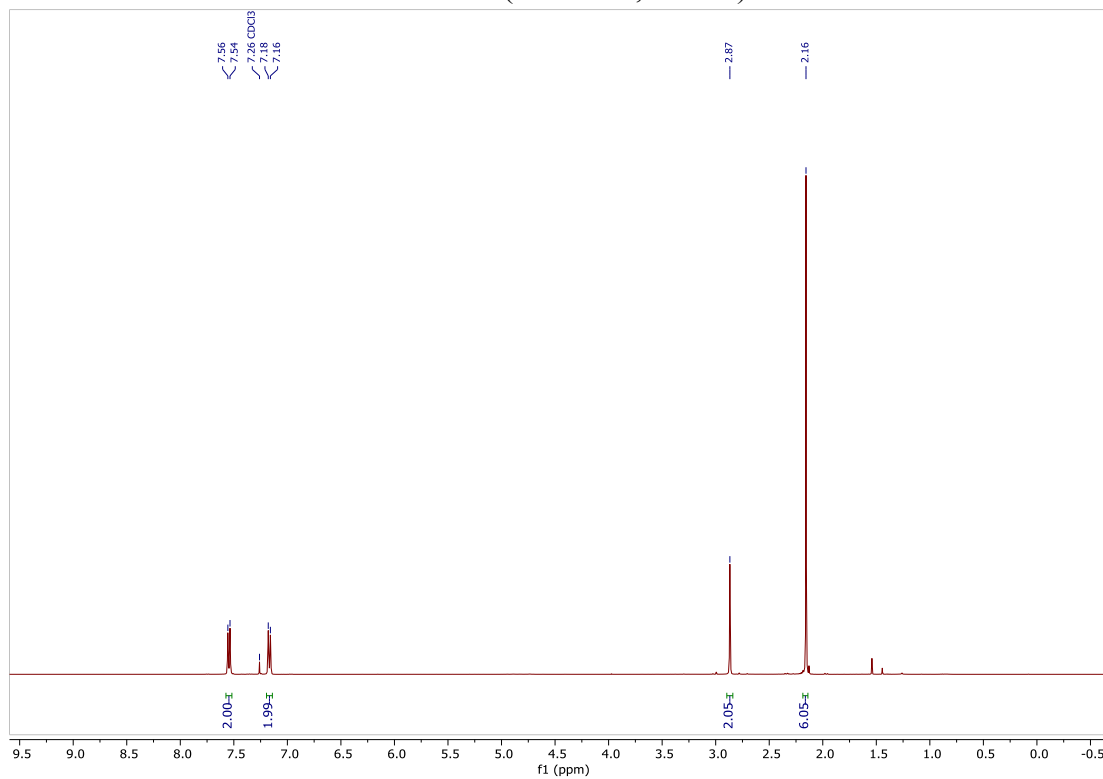
^{19}F NMR (377 MHz, CDCl_3)



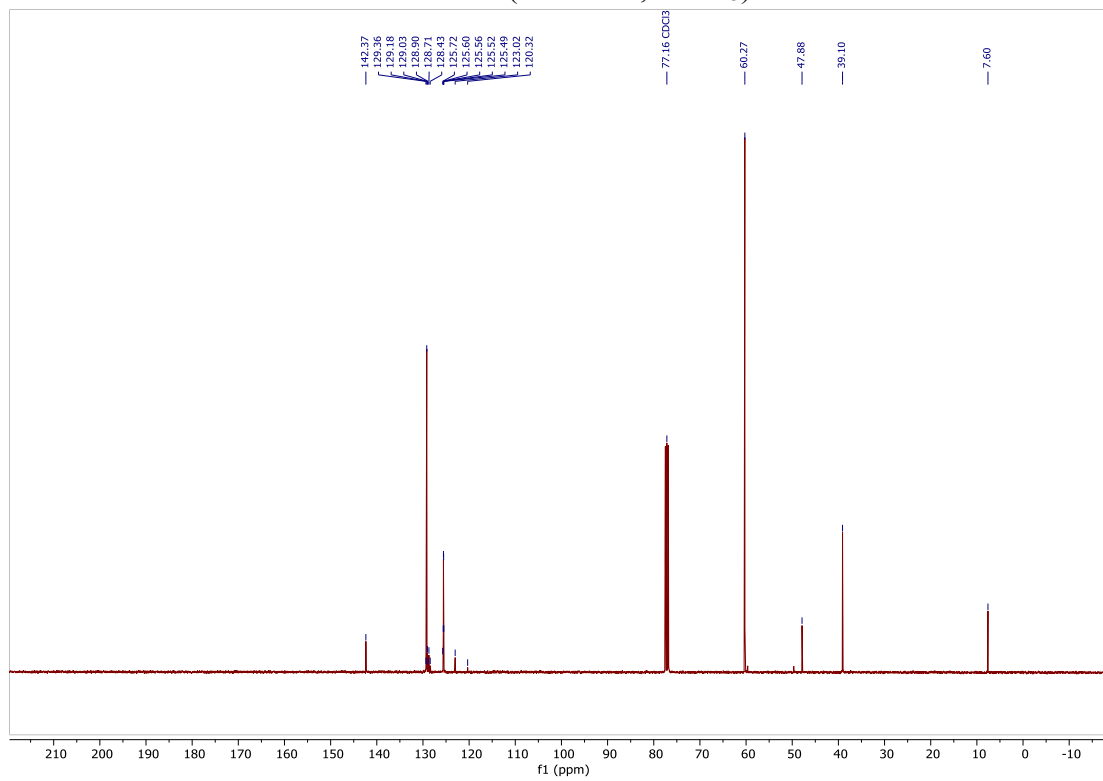
1-Iodo-3-(4-(trifluoromethyl)benzyl)bicyclo[1.1.1]pentane, 5



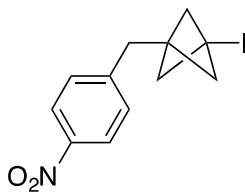
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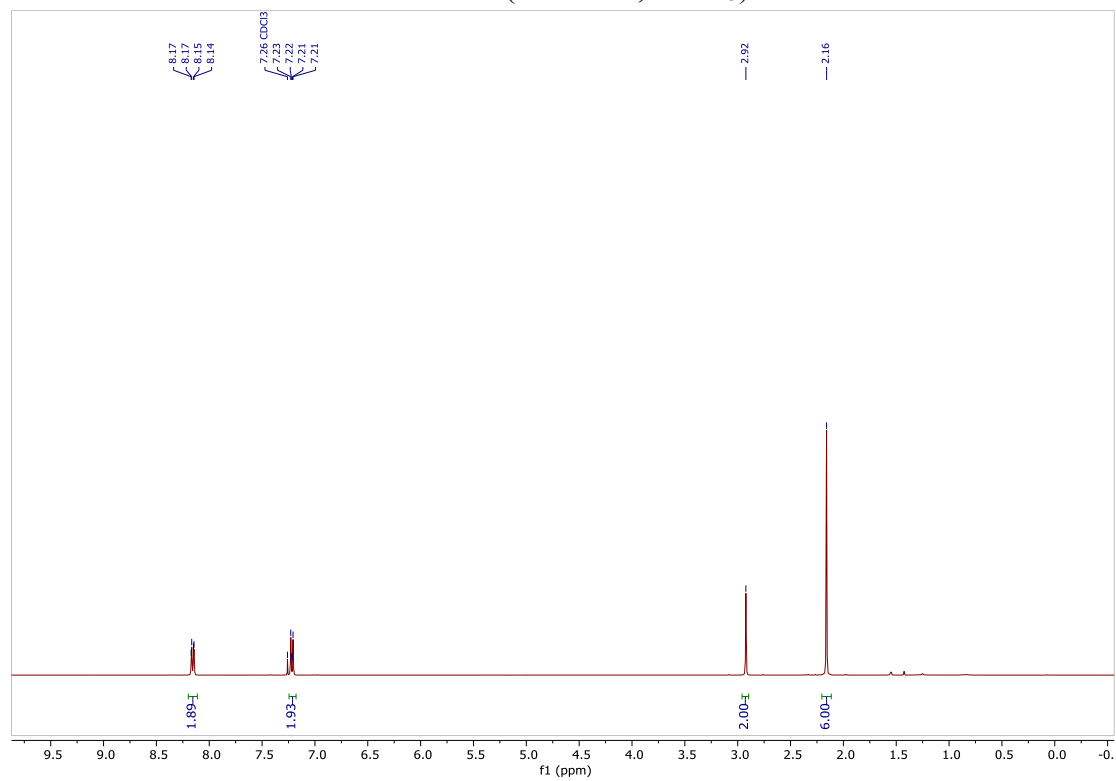
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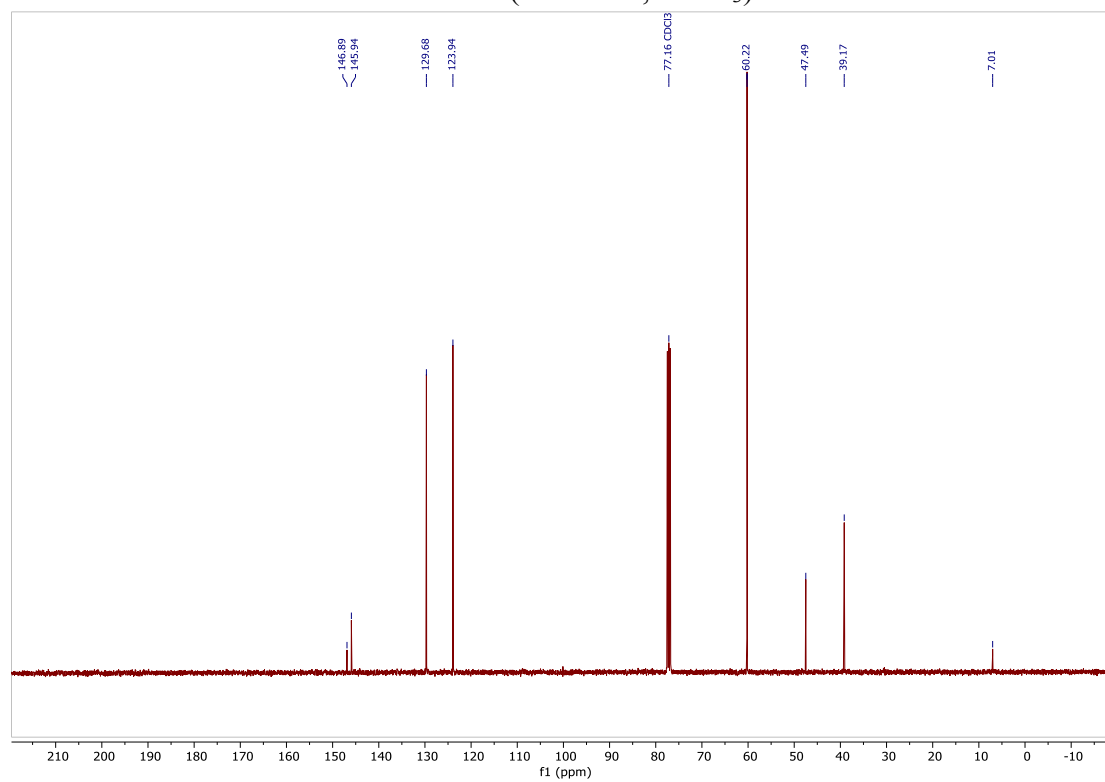
1-Iodo-3-(4-nitrobenzyl)bicyclo[1.1.1]pentane, 6



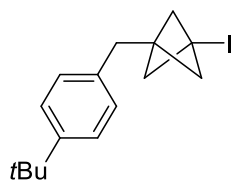
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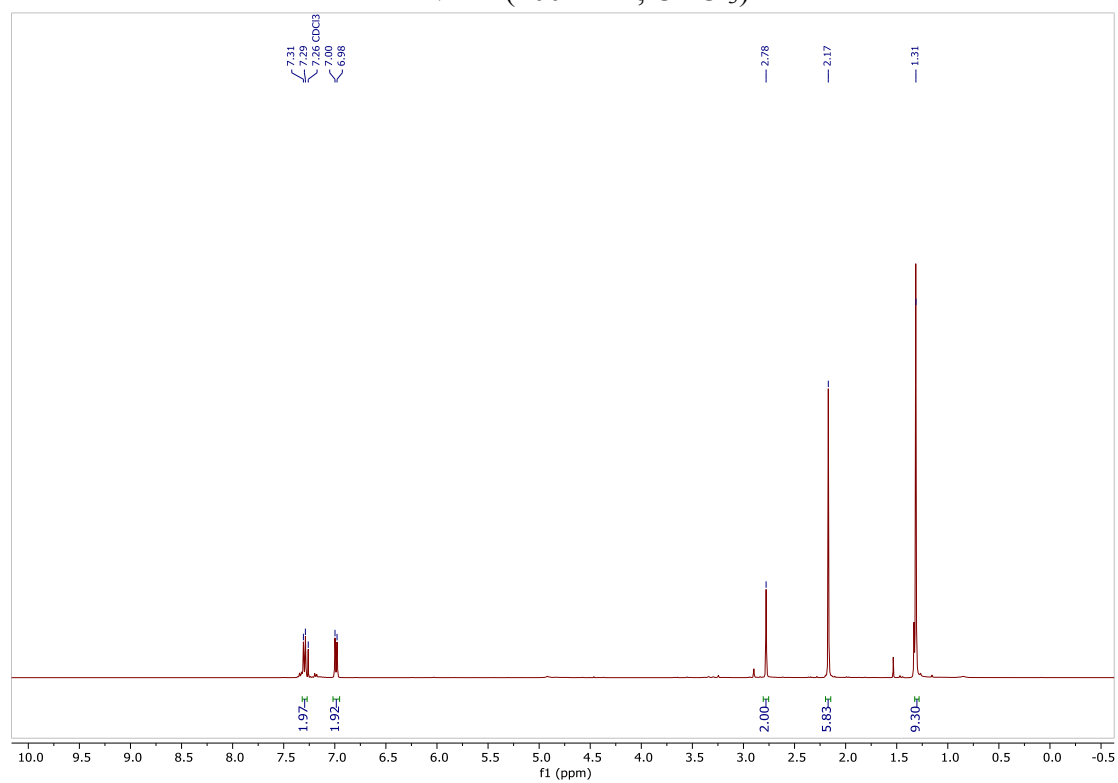
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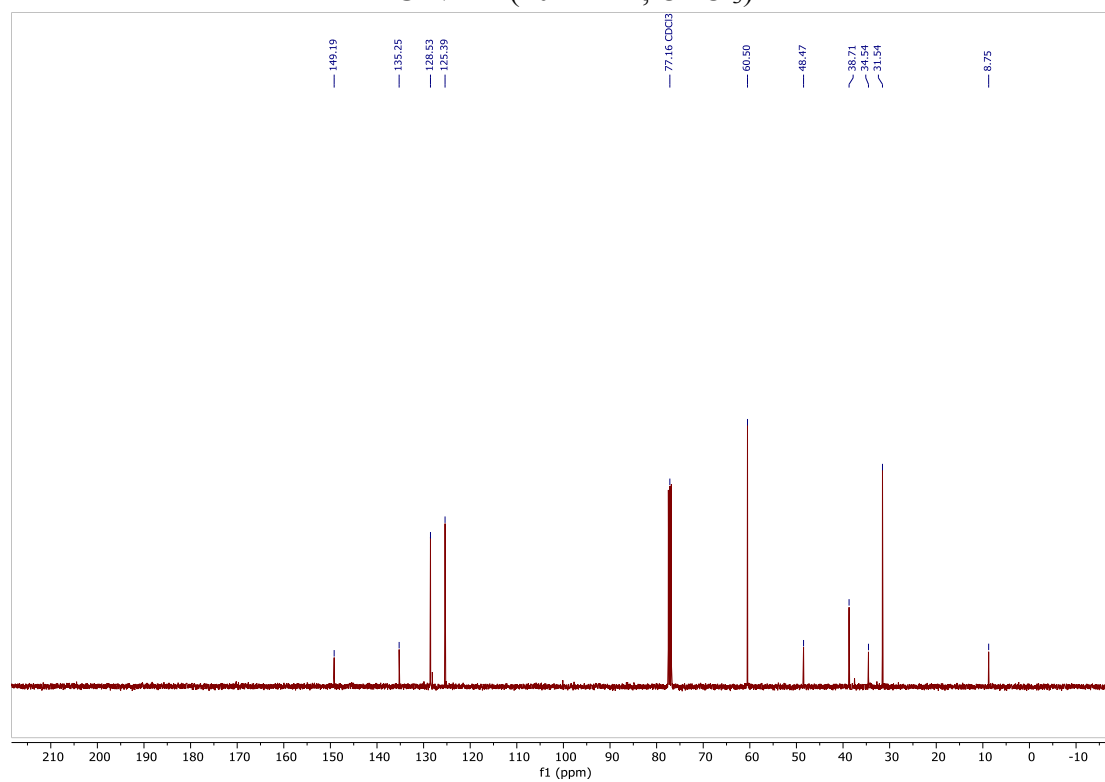
1-(4-(*tert*-Butyl)benzyl)-3-iodobicyclo[1.1.1]pentane, 7



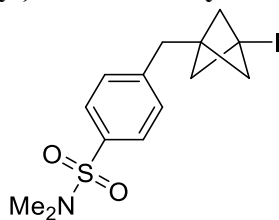
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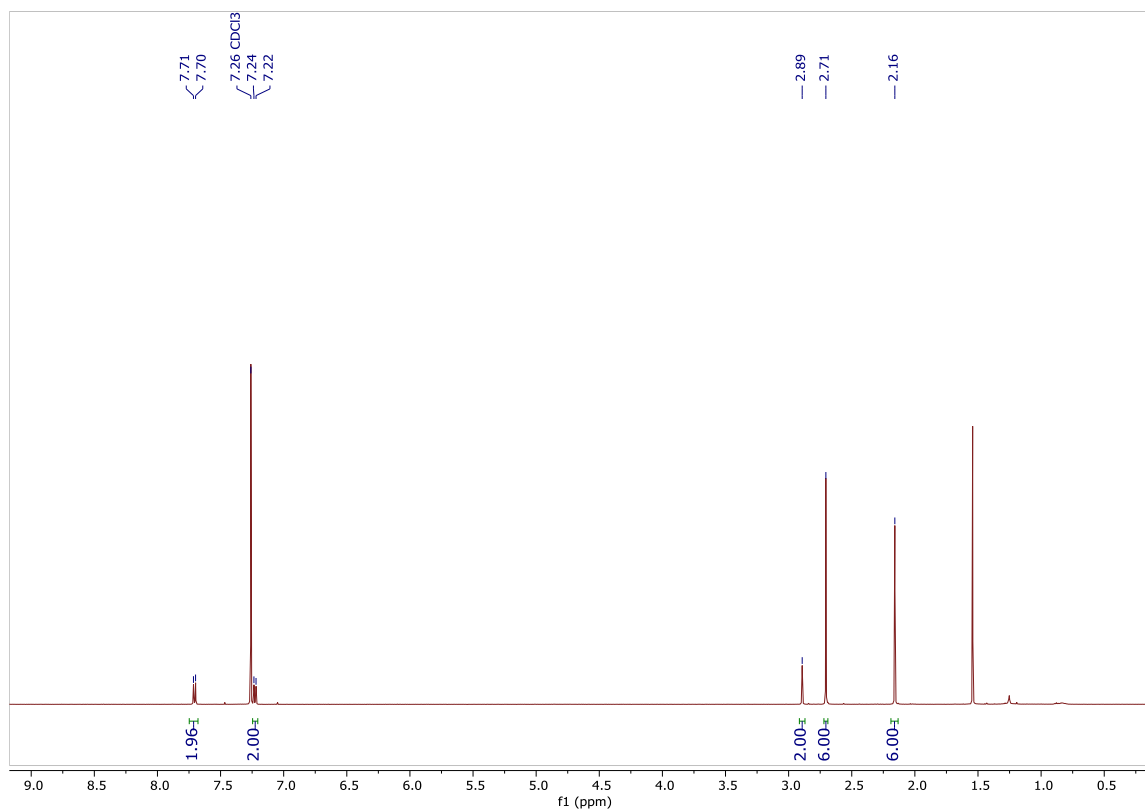
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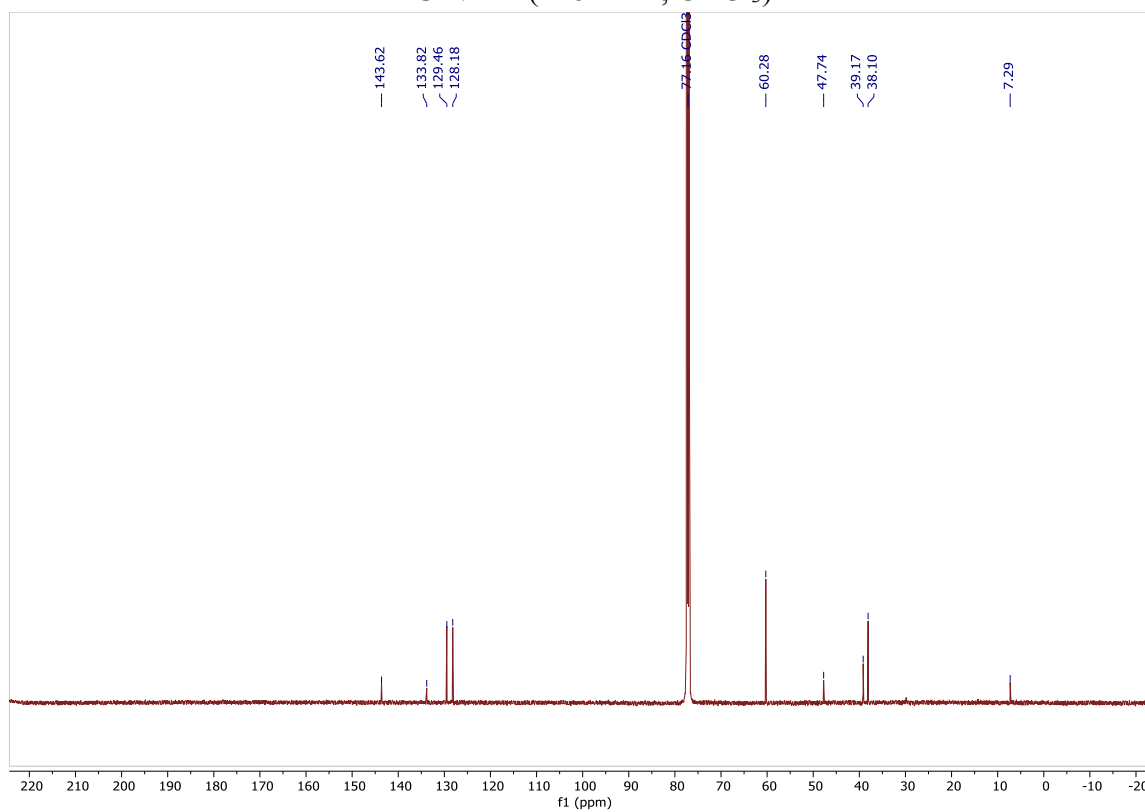
4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-*N,N*-dimethylbenzenesulfonamide, 8



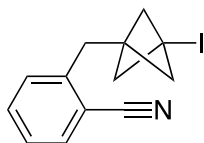
^1H NMR (500 MHz, CDCl_3)



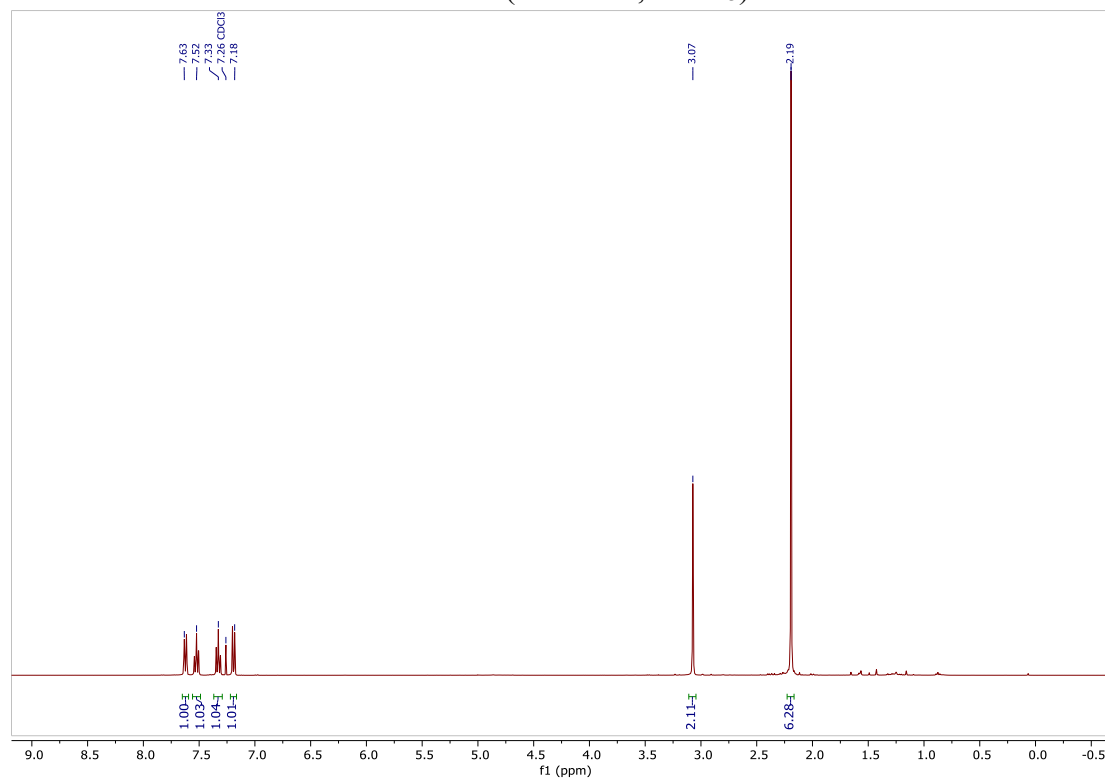
^{13}C NMR (126 MHz, CDCl_3)



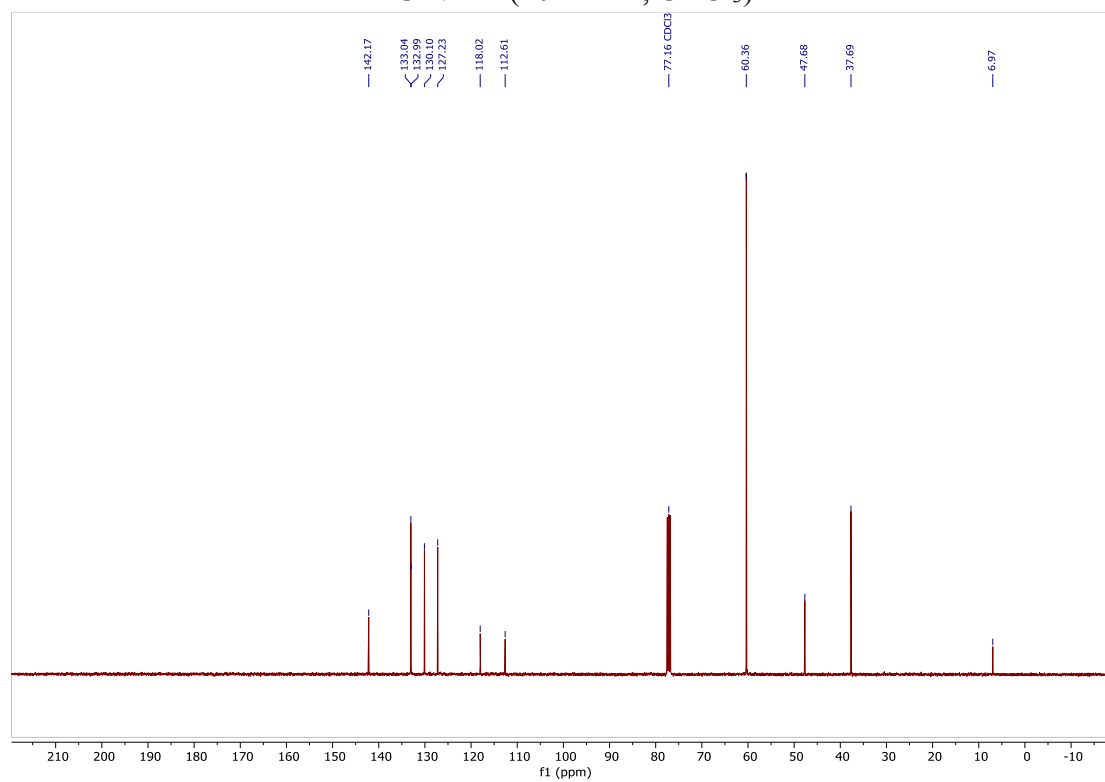
2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)benzonitrile, 9



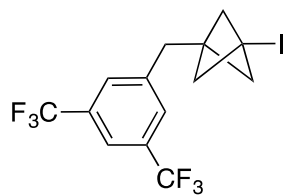
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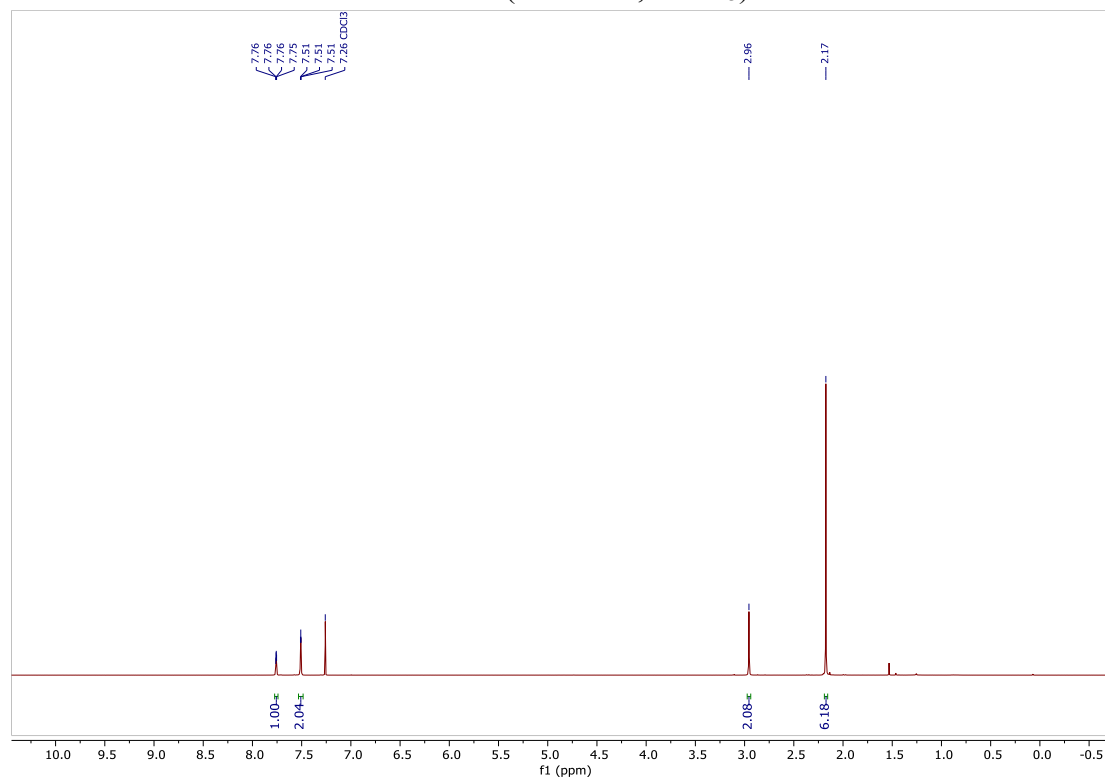
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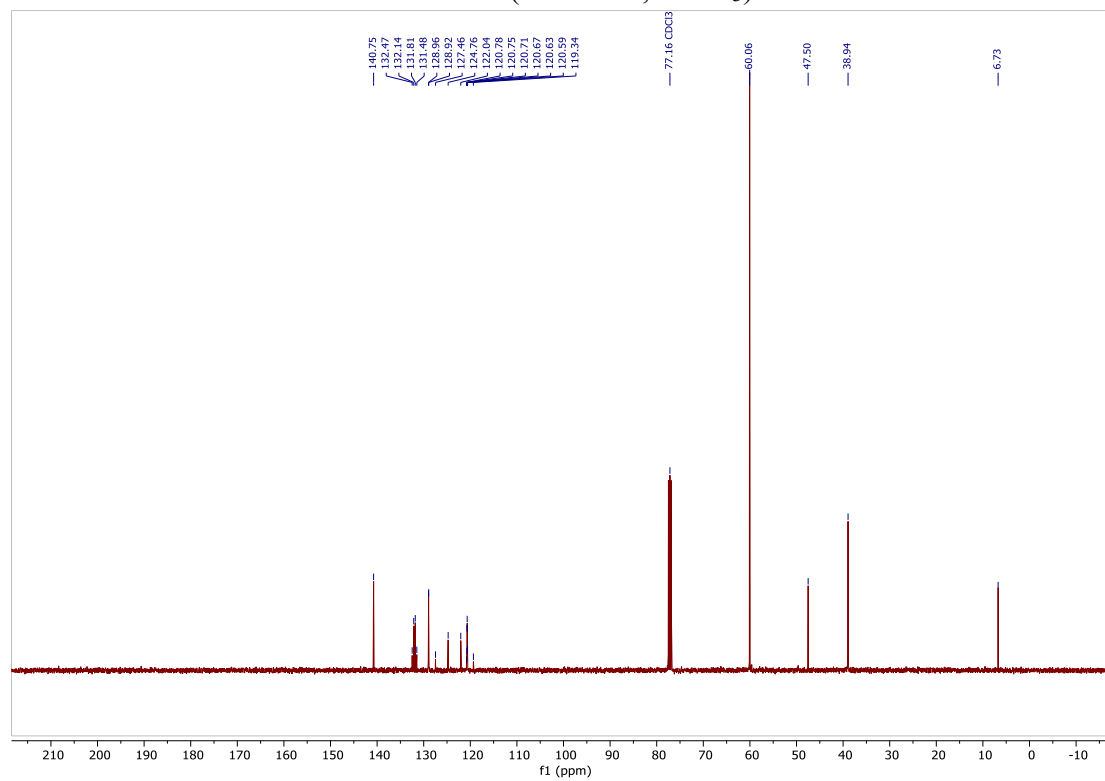
1-(3,5-Bis(trifluoromethyl)benzyl)-3-iodobicyclo[1.1.1]pentane, 10



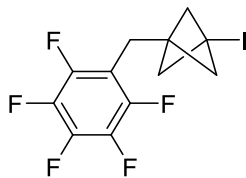
^1H NMR (400 MHz, CDCl_3)



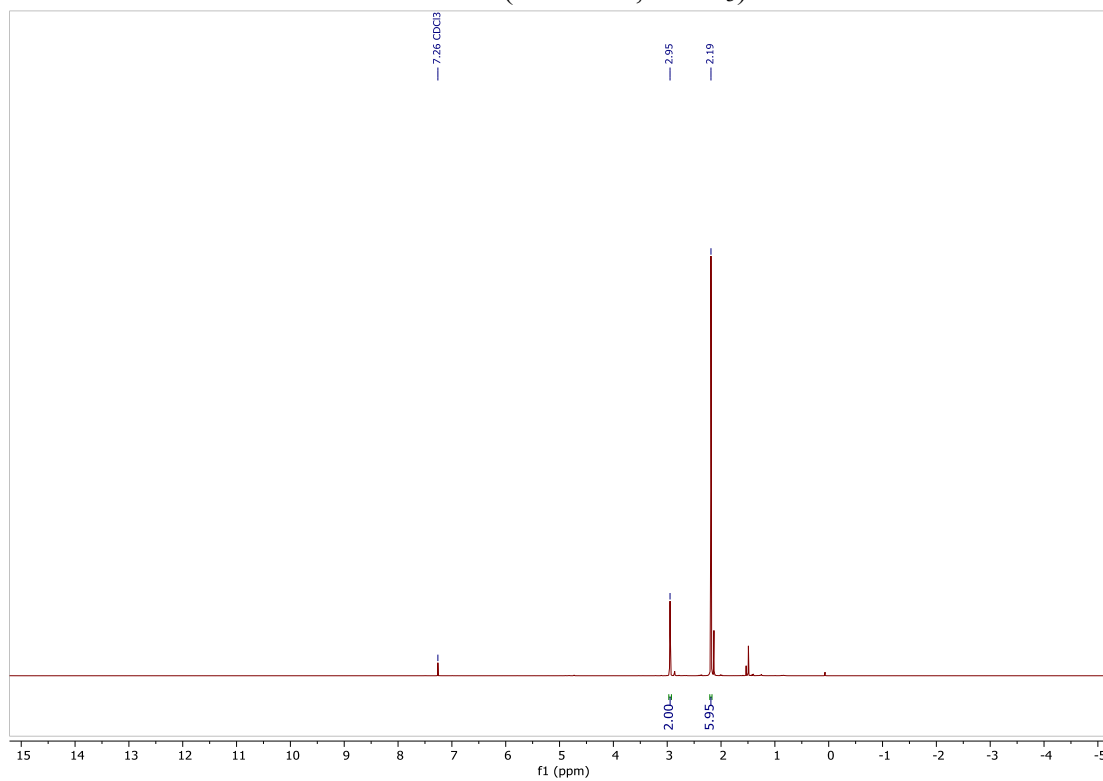
^{13}C NMR (101 MHz, CDCl_3)



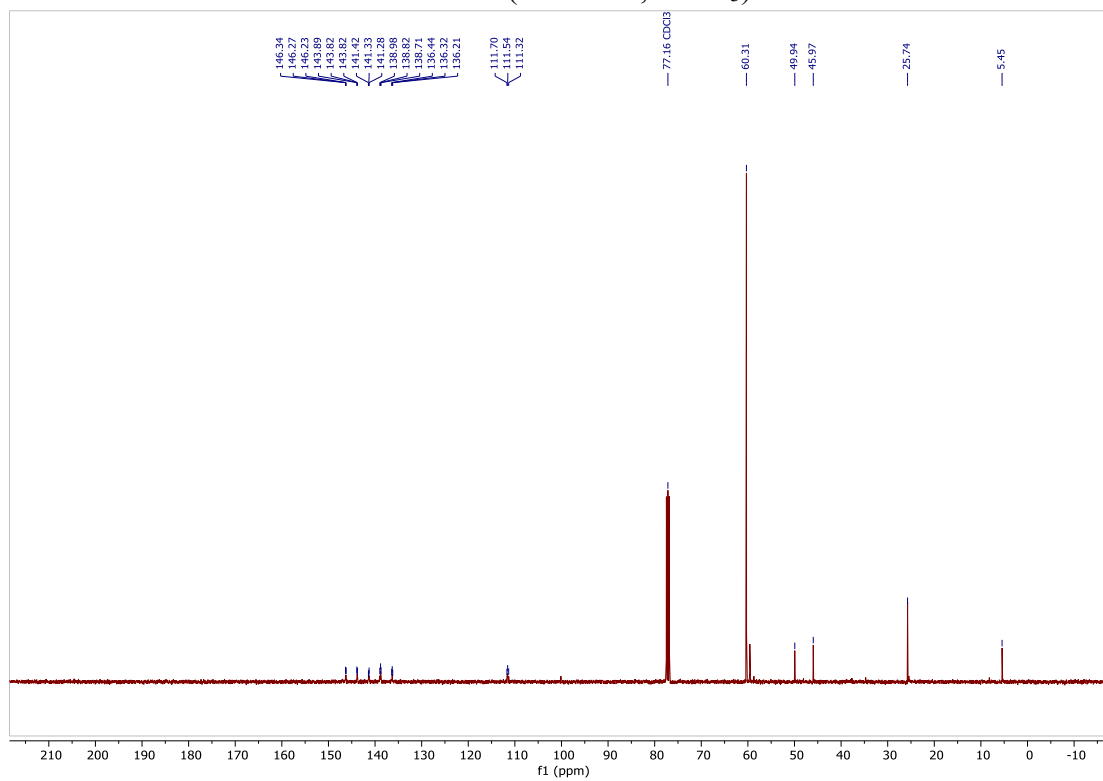
1-Iodo-3-((perfluorophenyl)methyl)bicyclo[1.1.1]pentane, 11



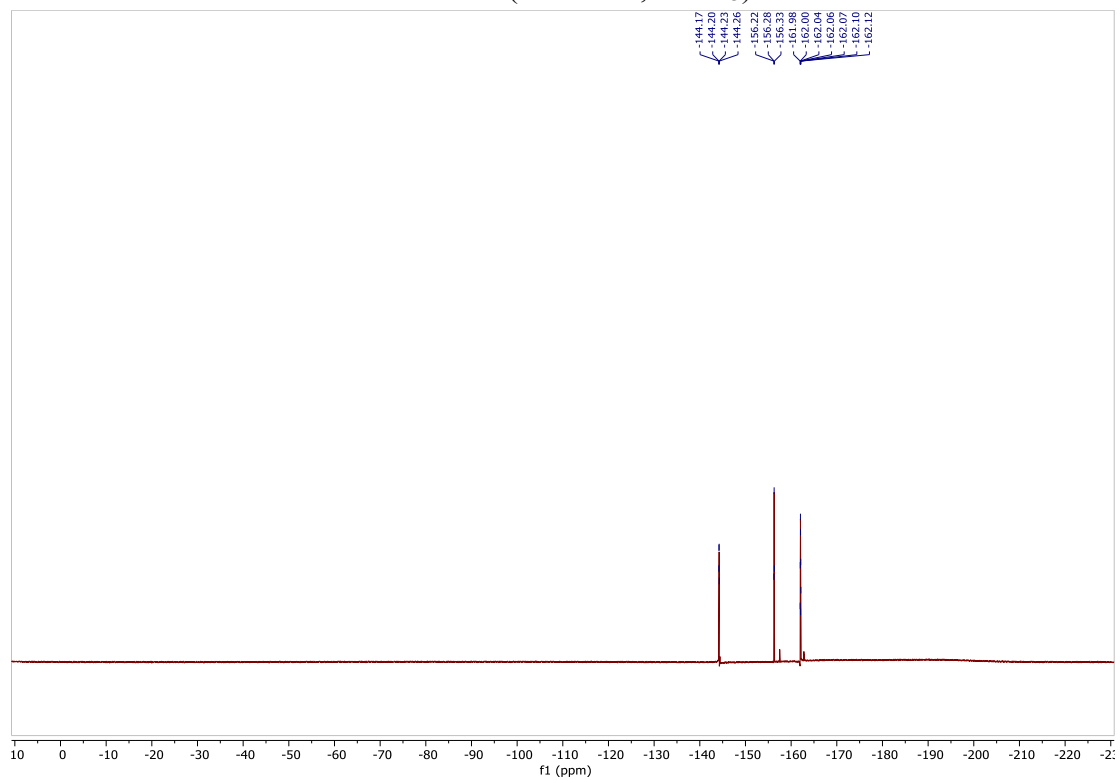
^1H NMR (400 MHz, CDCl_3)



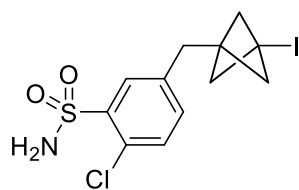
^{13}C NMR (101 MHz, CDCl_3)



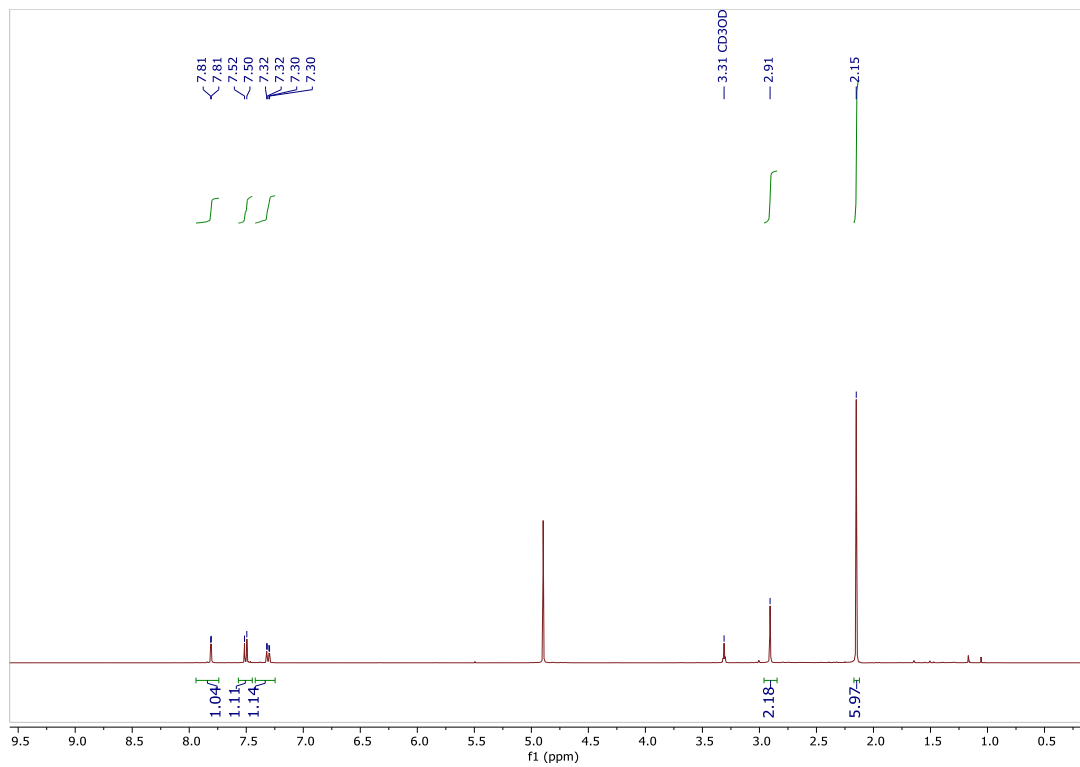
^{19}F NMR (377 MHz, CDCl_3)



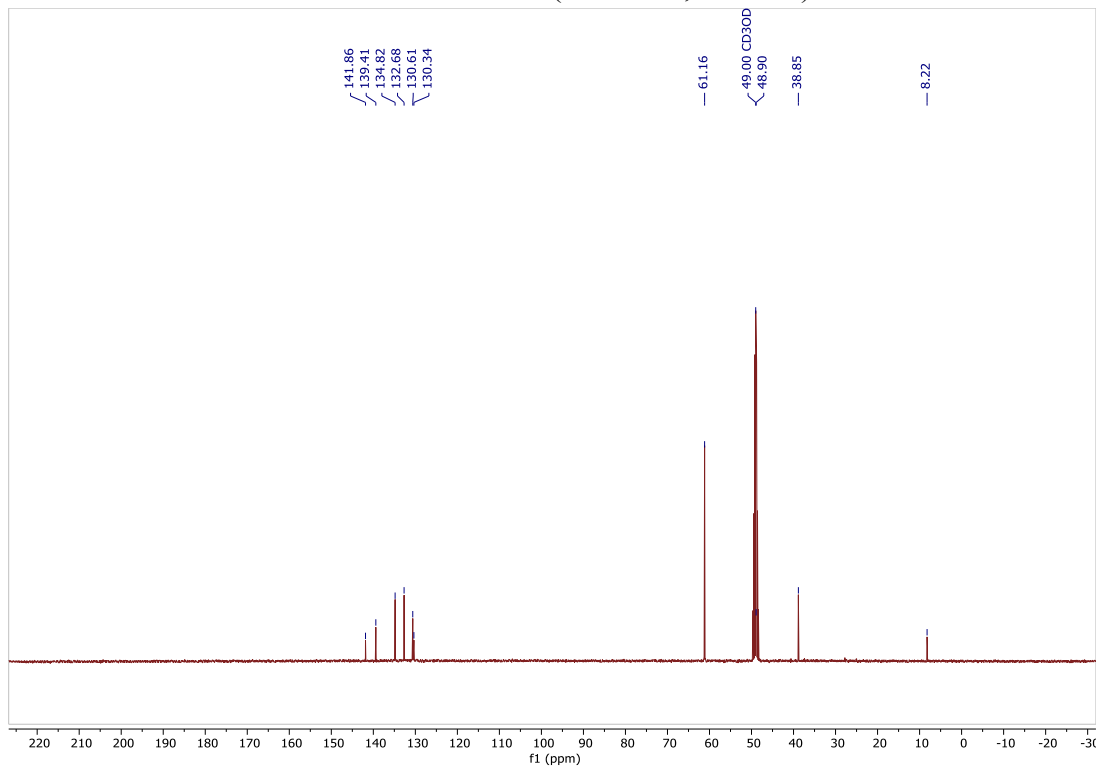
2-Chloro-5-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)benzenesulfonamide, 12



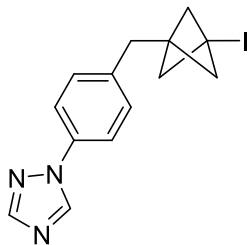
^1H NMR (400 MHz, CD_3OD)



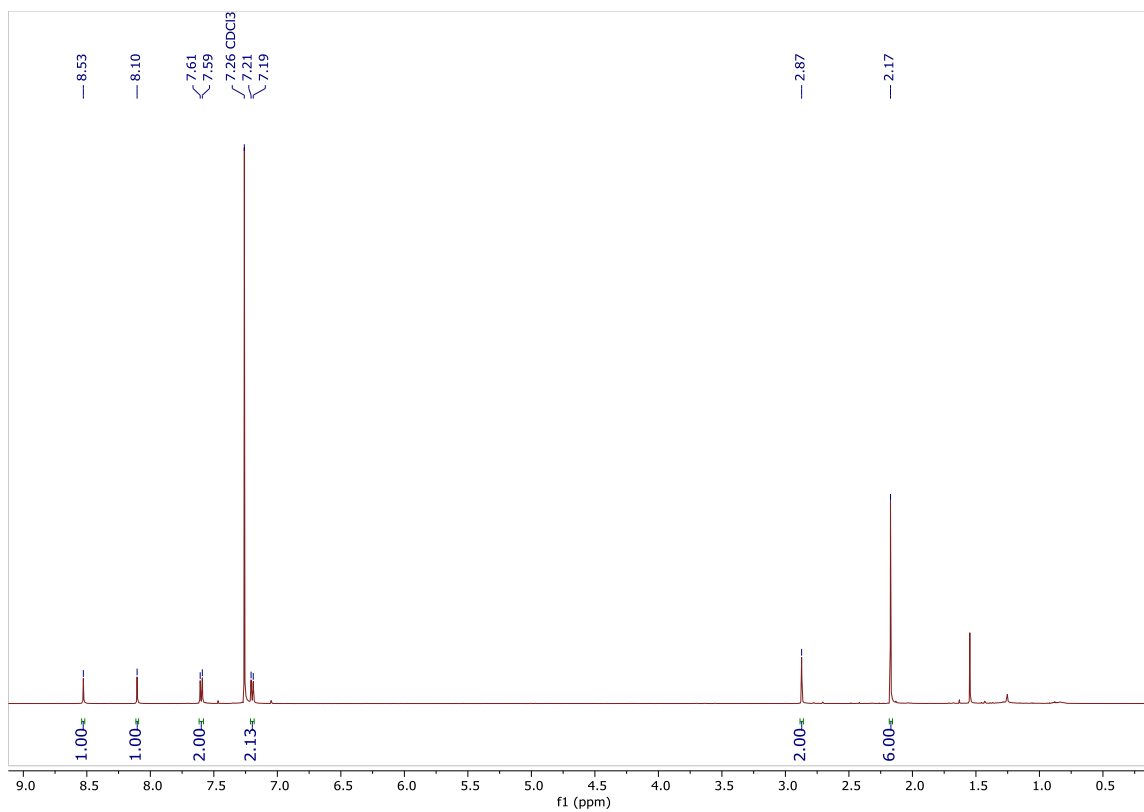
^{13}C NMR (101 MHz, CD_3OD)



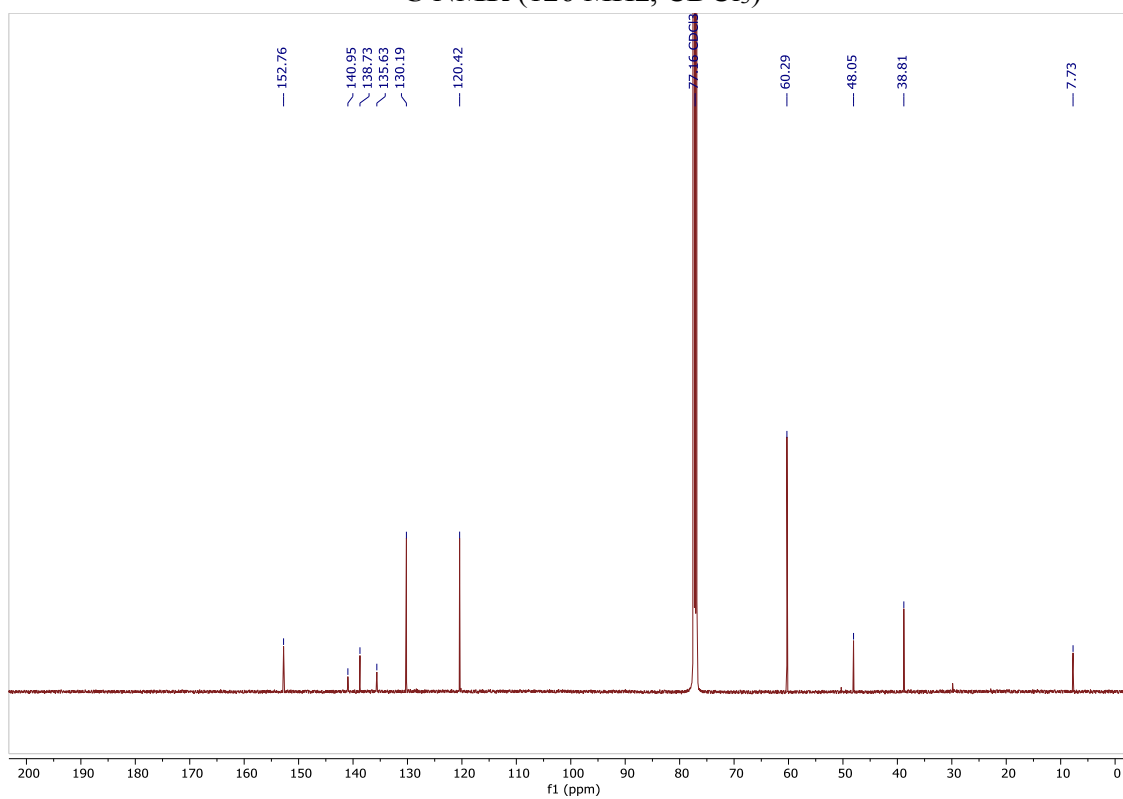
1-(4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl)-1*H*-1,2,4-triazole, 13



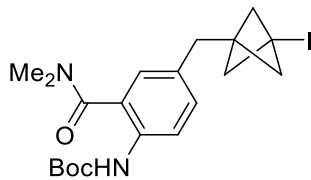
¹H NMR (500 MHz, CDCl₃)



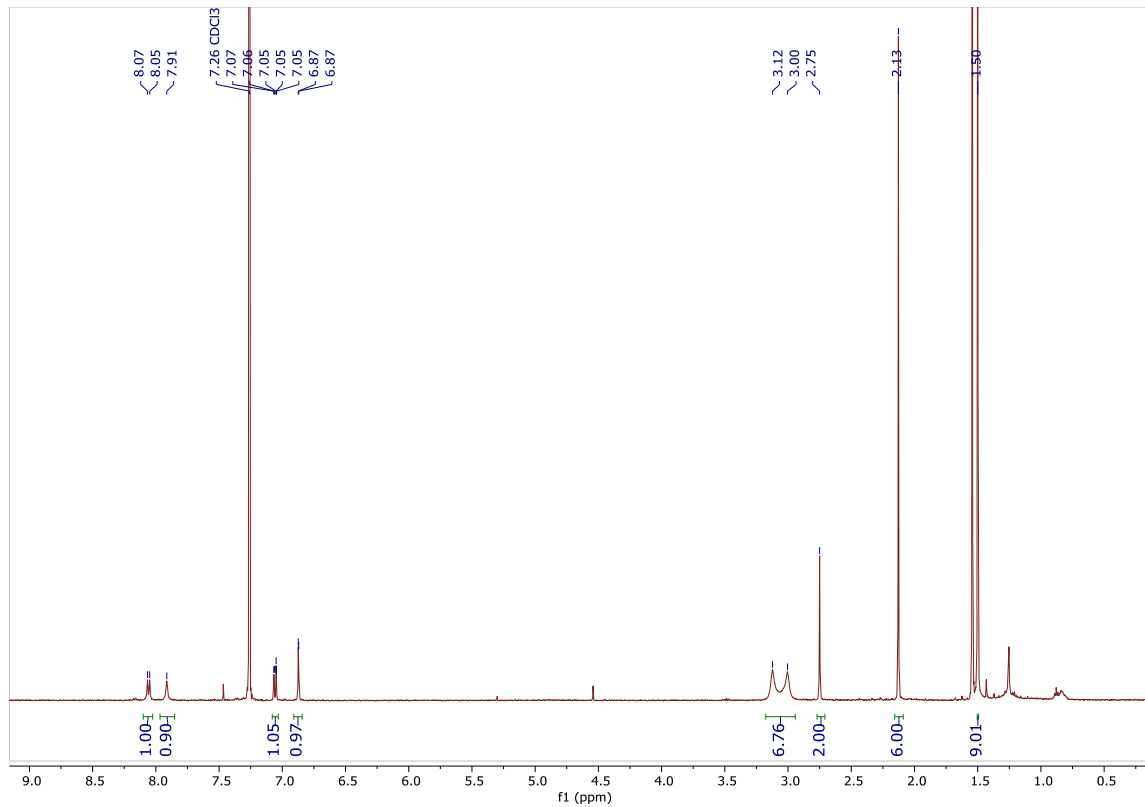
¹³C NMR (126 MHz, CDCl₃)



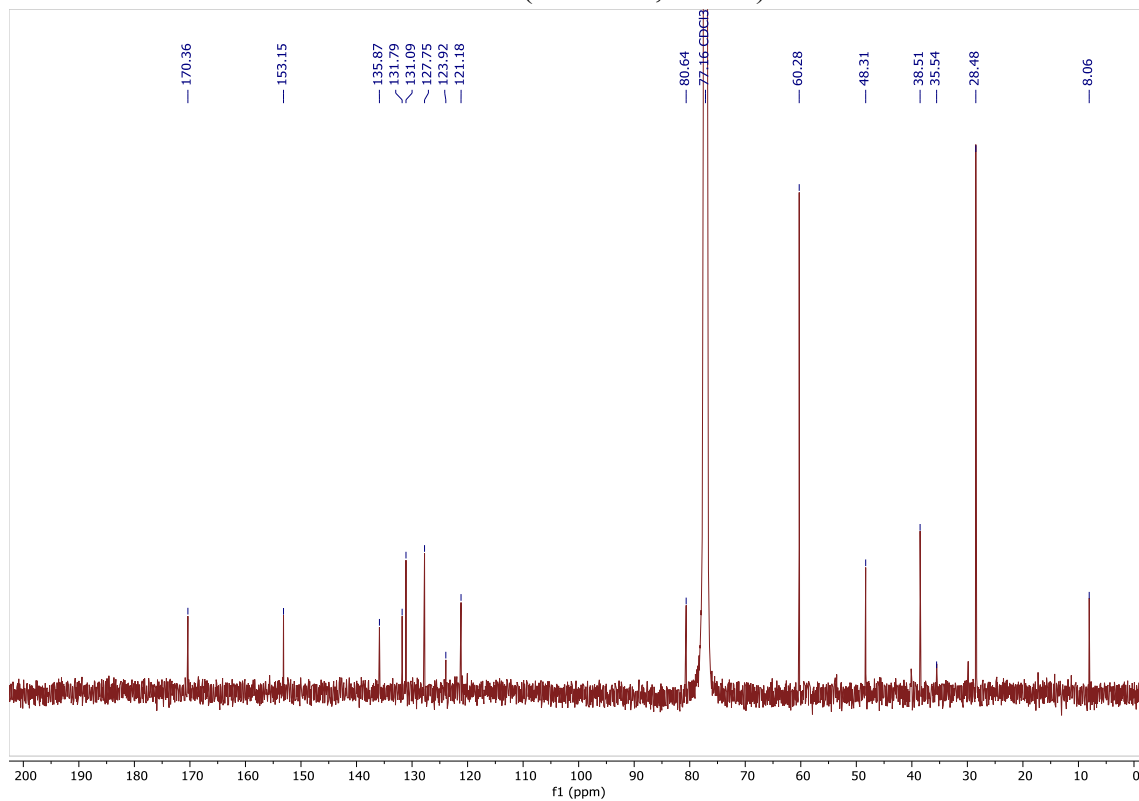
***tert*-Butyl (2-(dimethylcarbamoyl)-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl)carbamate, 14**



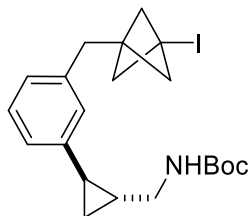
^1H NMR (500 MHz, CDCl_3)



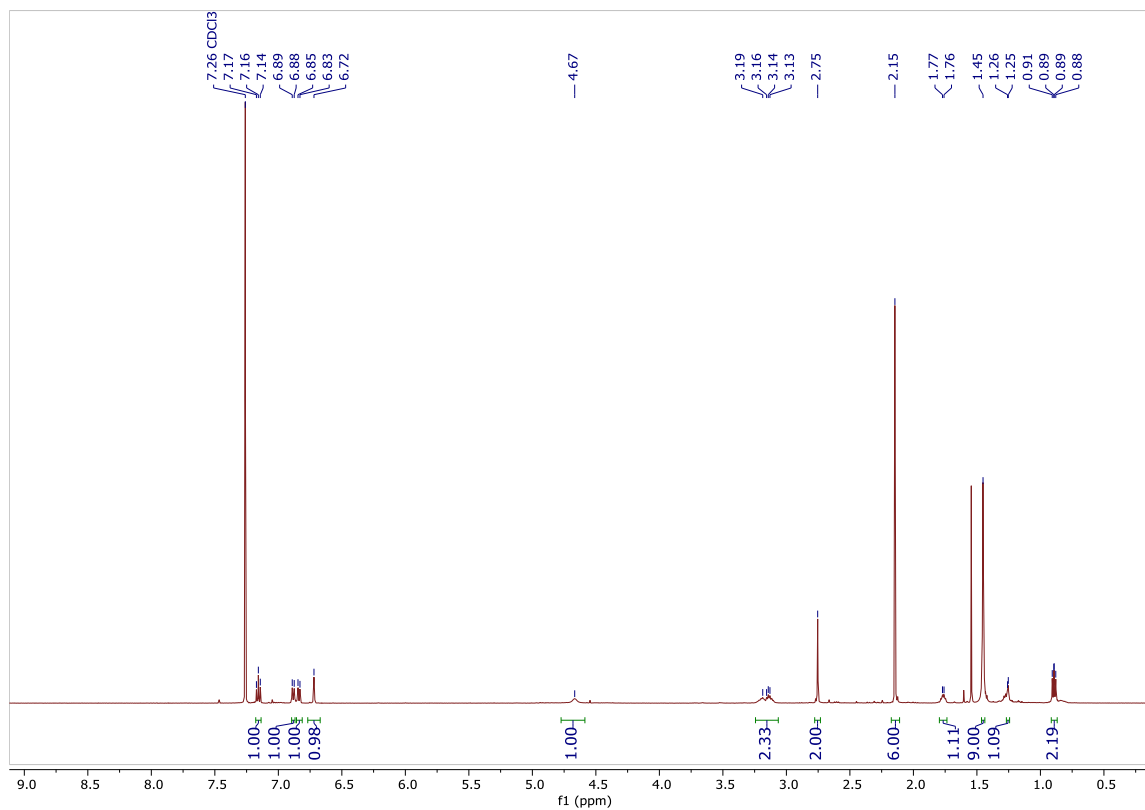
^{13}C NMR (126 MHz, CDCl_3)



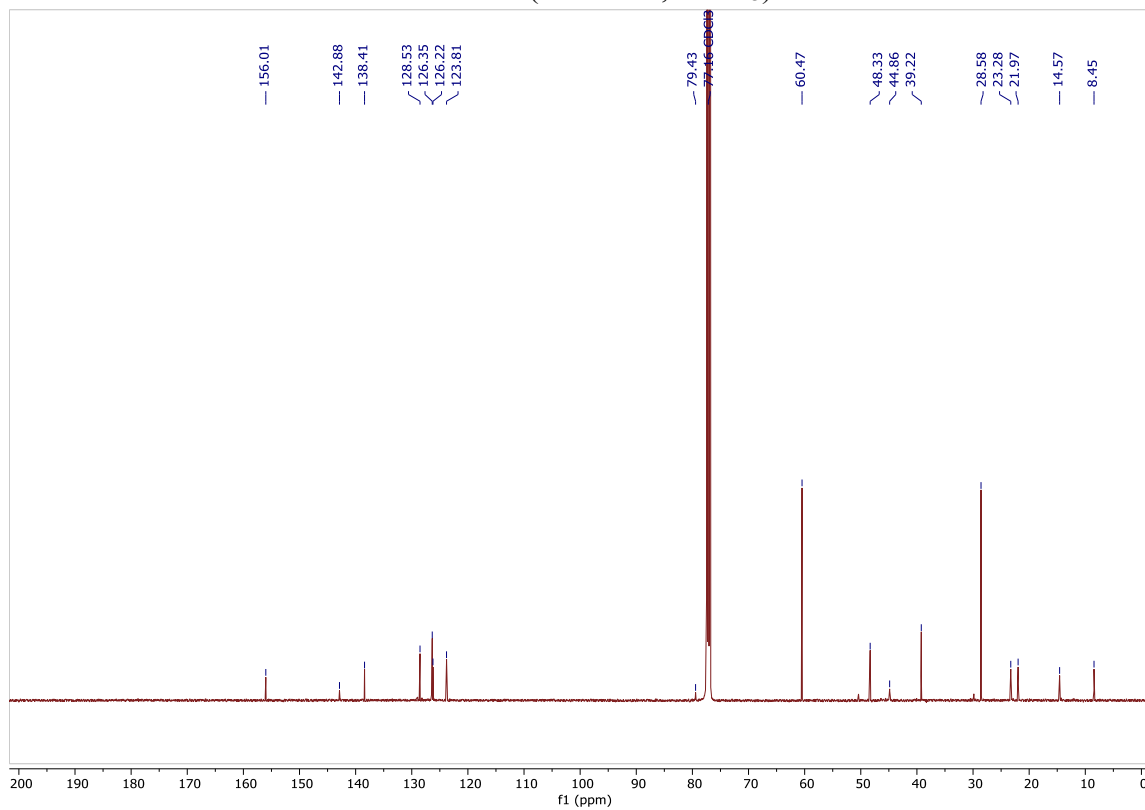
***tert*-Butyl ((2-(3-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)phenyl)cyclopropyl)methyl)carbamate, 15**



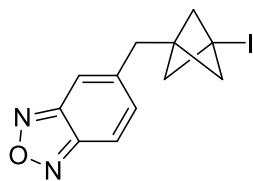
^1H NMR (500 MHz, CDCl_3)



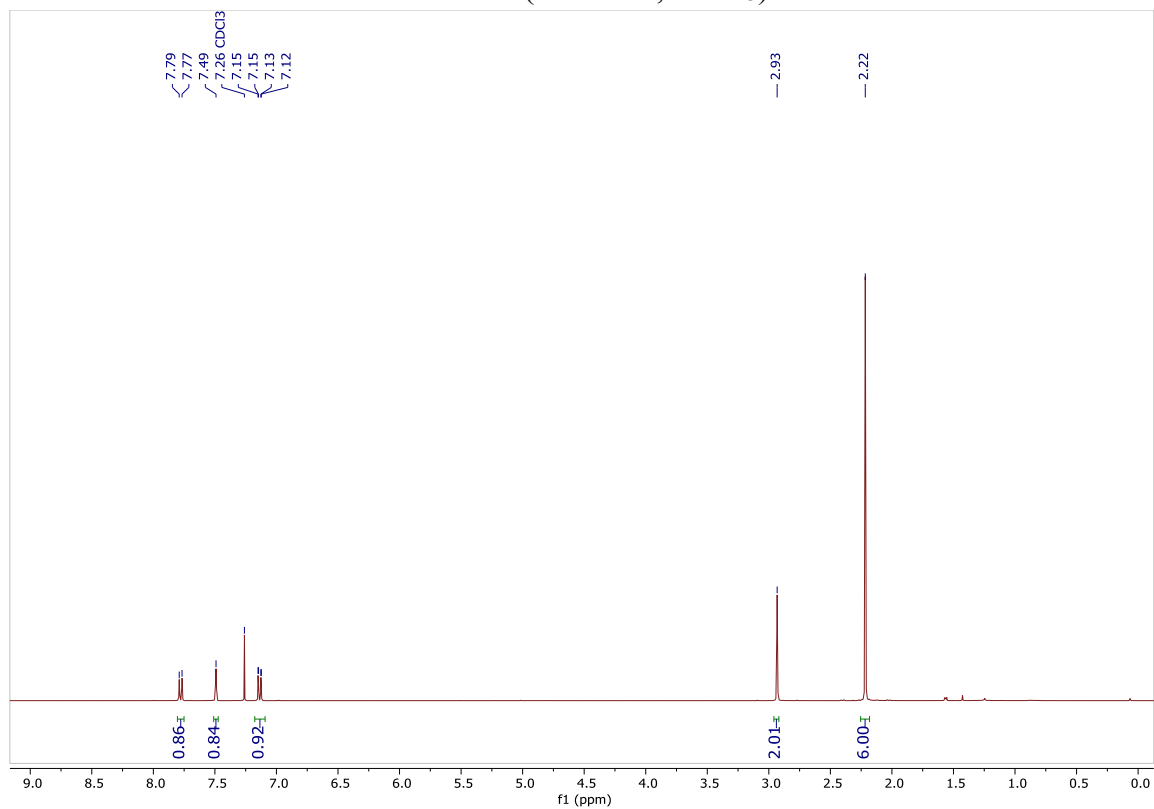
^{13}C NMR (126 MHz, CDCl_3)



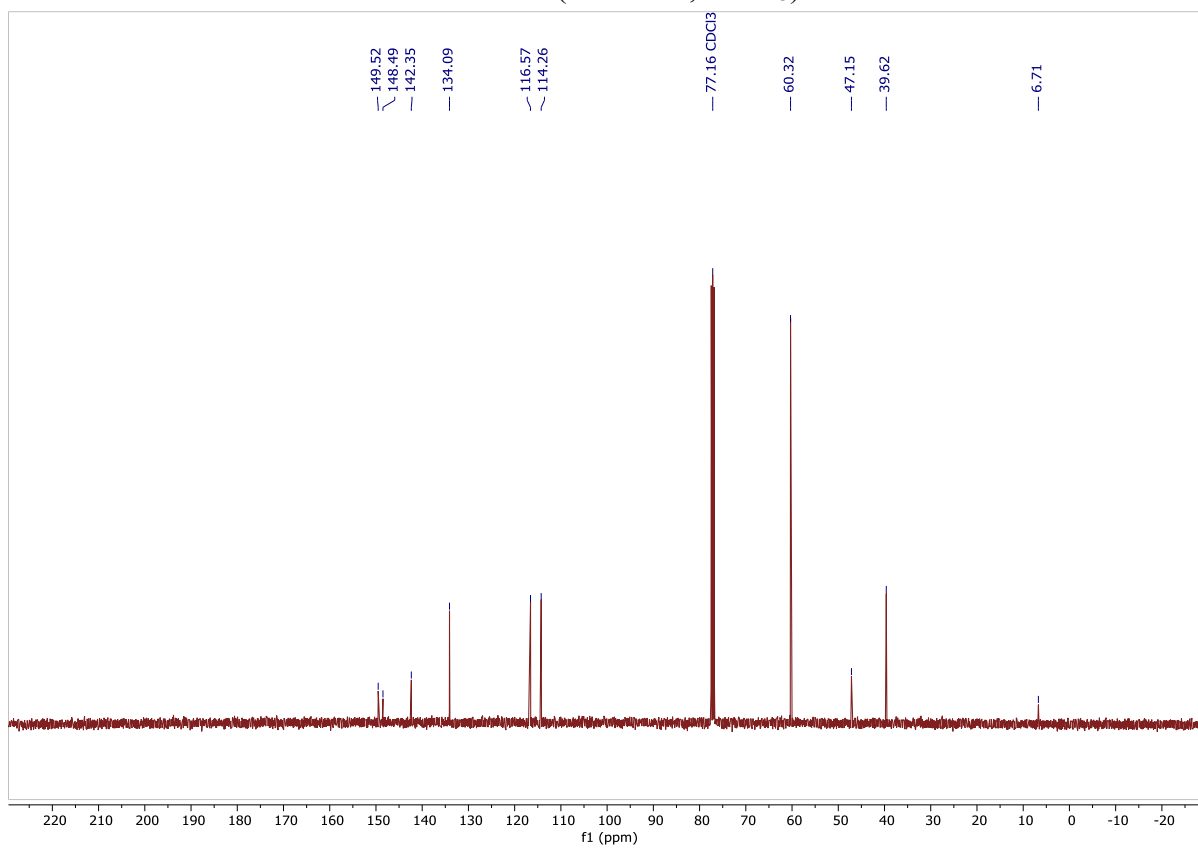
5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)benzo[c][1,2,5]oxadiazole, 16



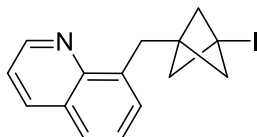
^1H NMR (400 MHz, CDCl_3)



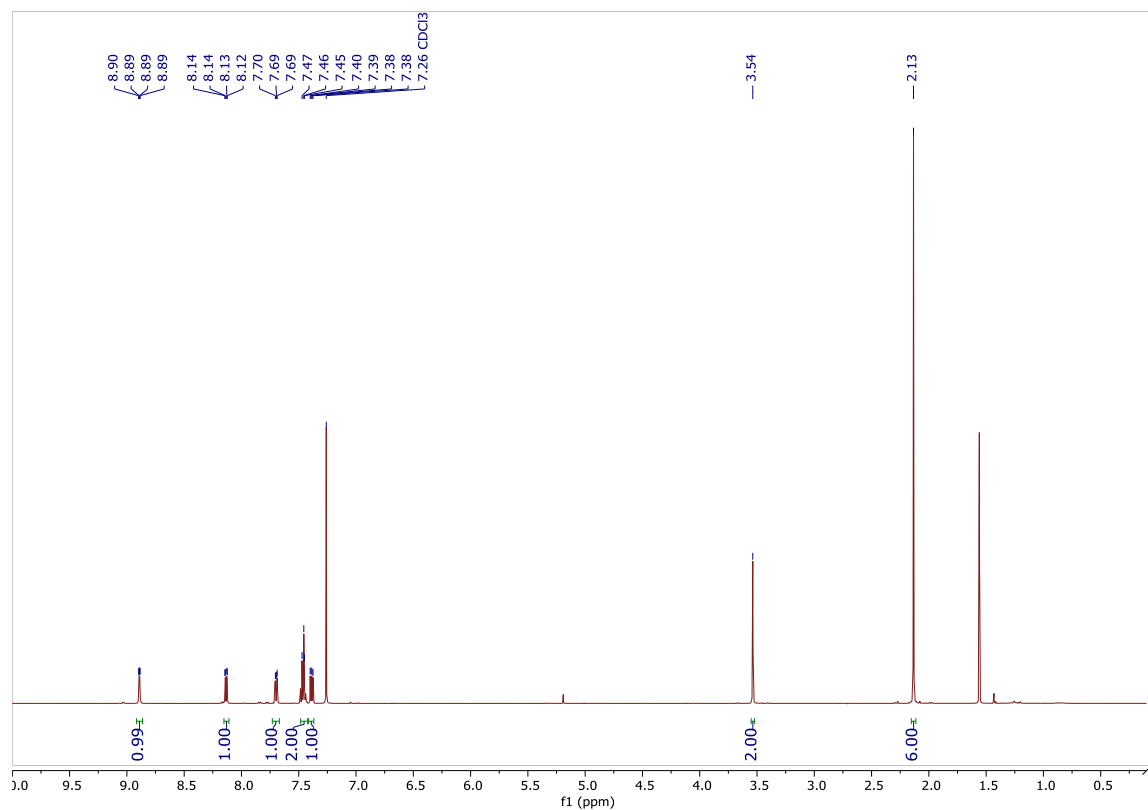
^{13}C NMR (101 MHz, CDCl_3)



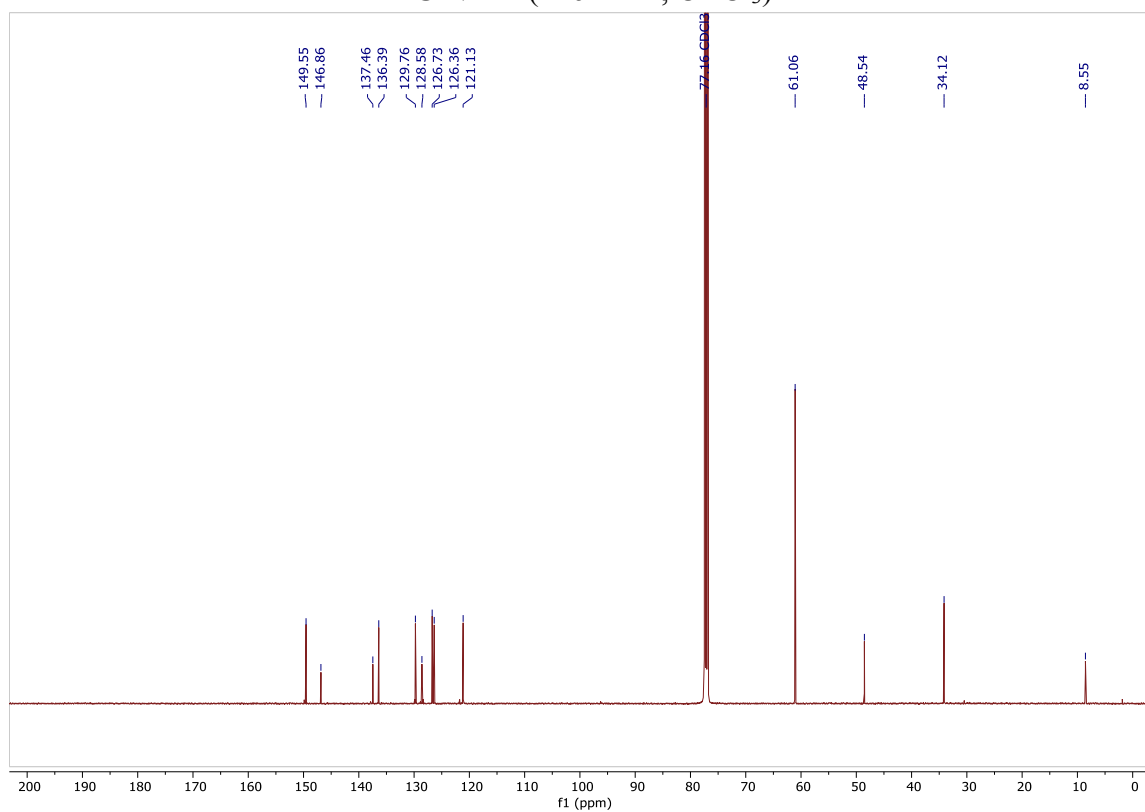
8-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)quinoline, 17



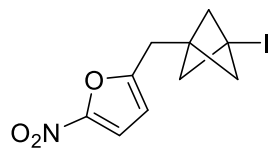
^1H NMR (500 MHz, CDCl_3)



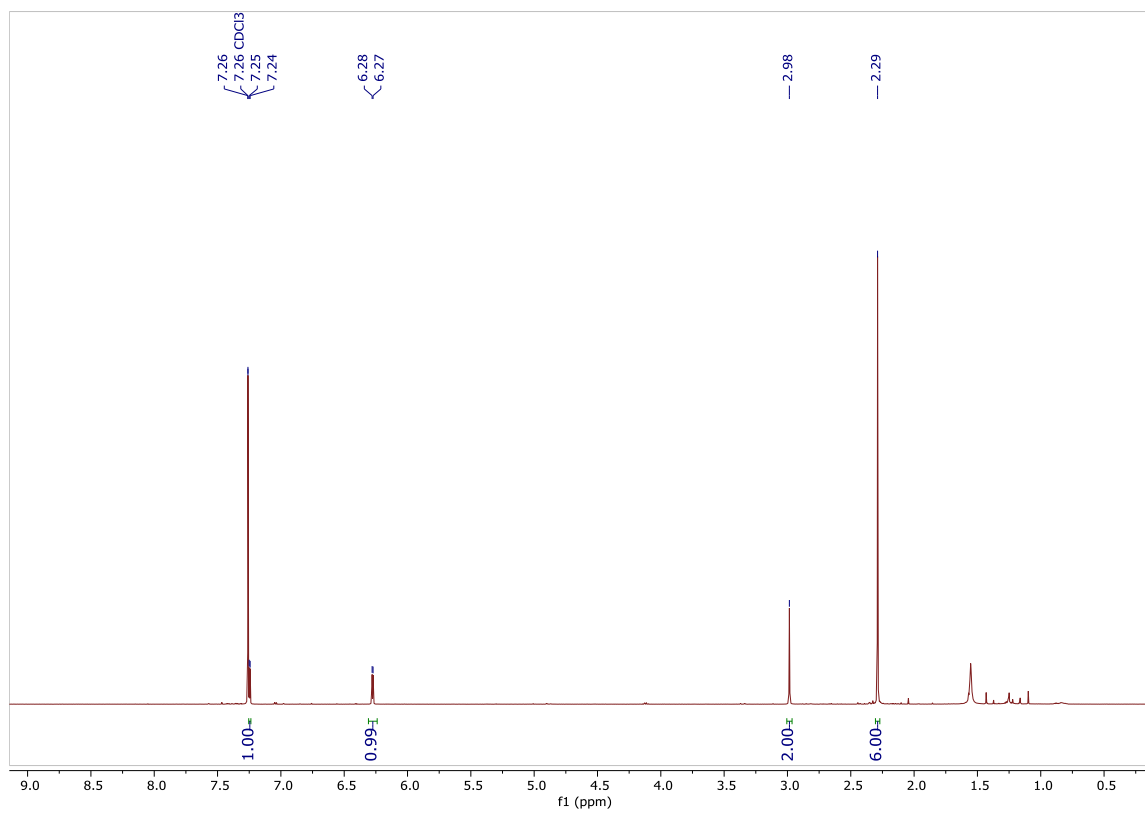
^{13}C NMR (126 MHz, CDCl_3)



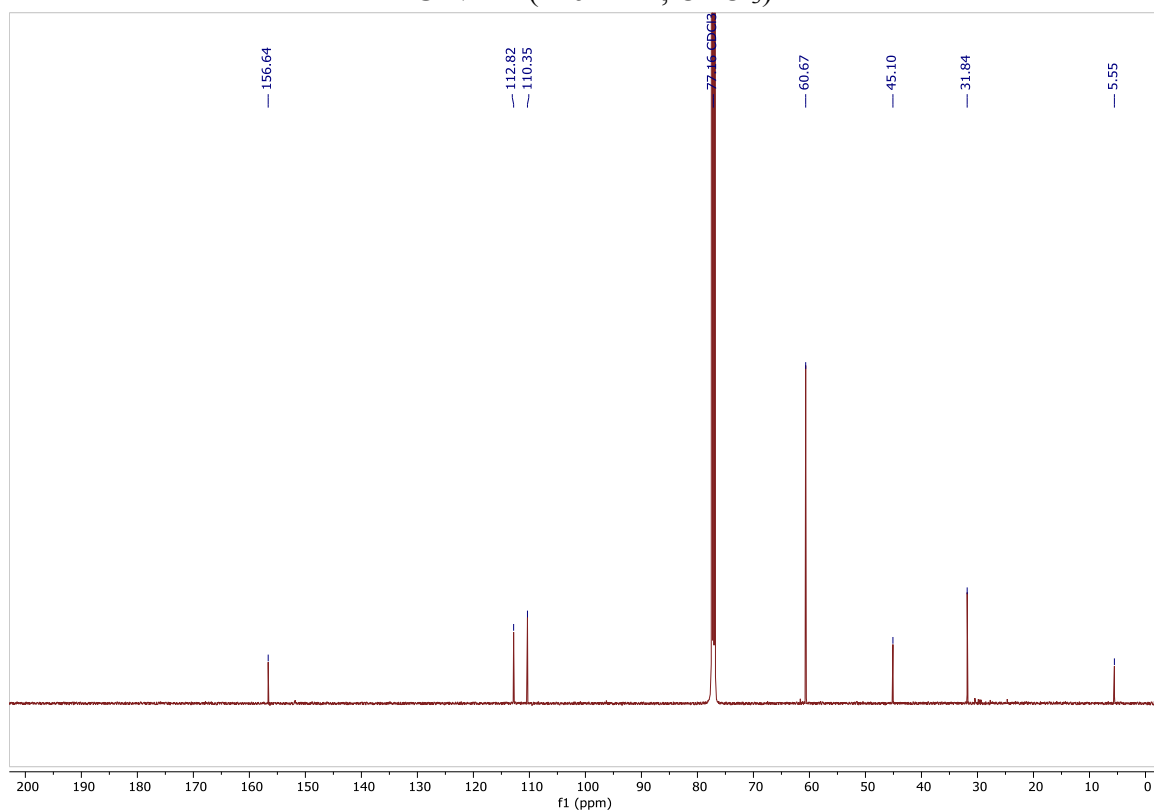
2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-5-nitrofuran, 18



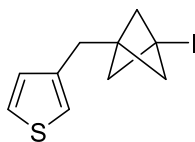
^1H NMR (500 MHz, CDCl_3)



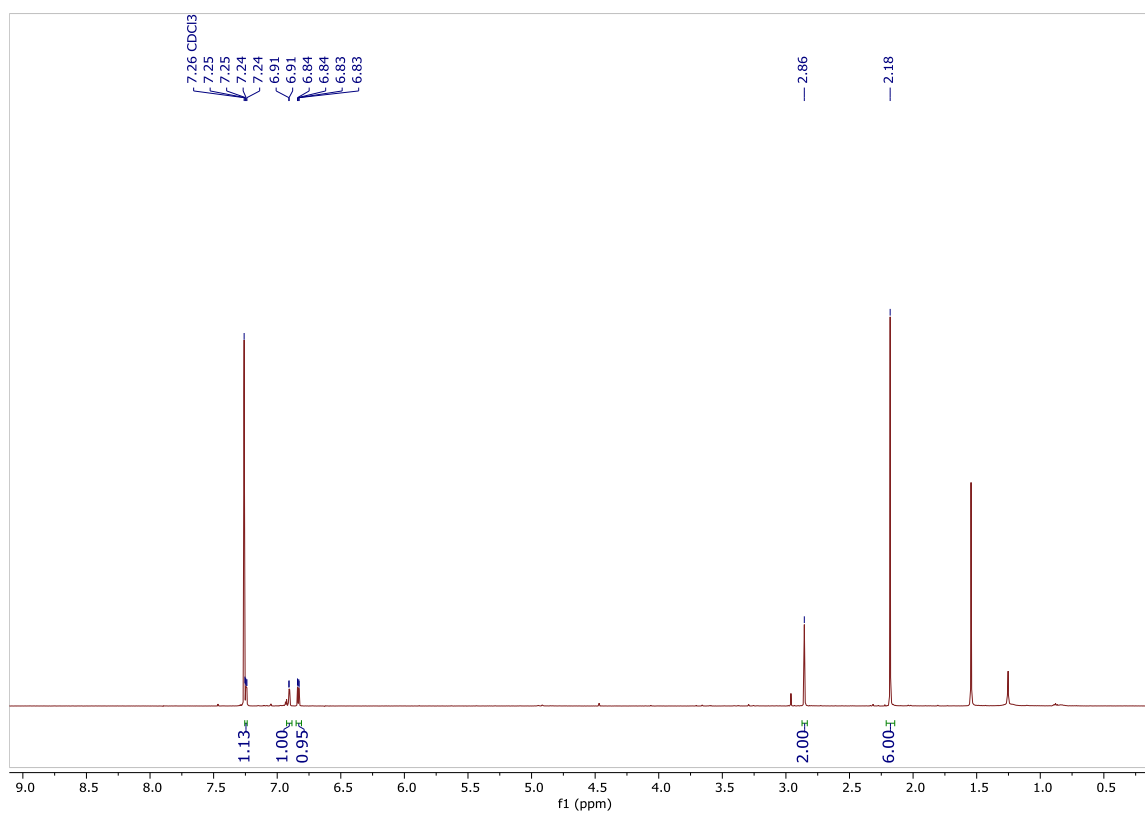
^{13}C NMR (126 MHz, CDCl_3)



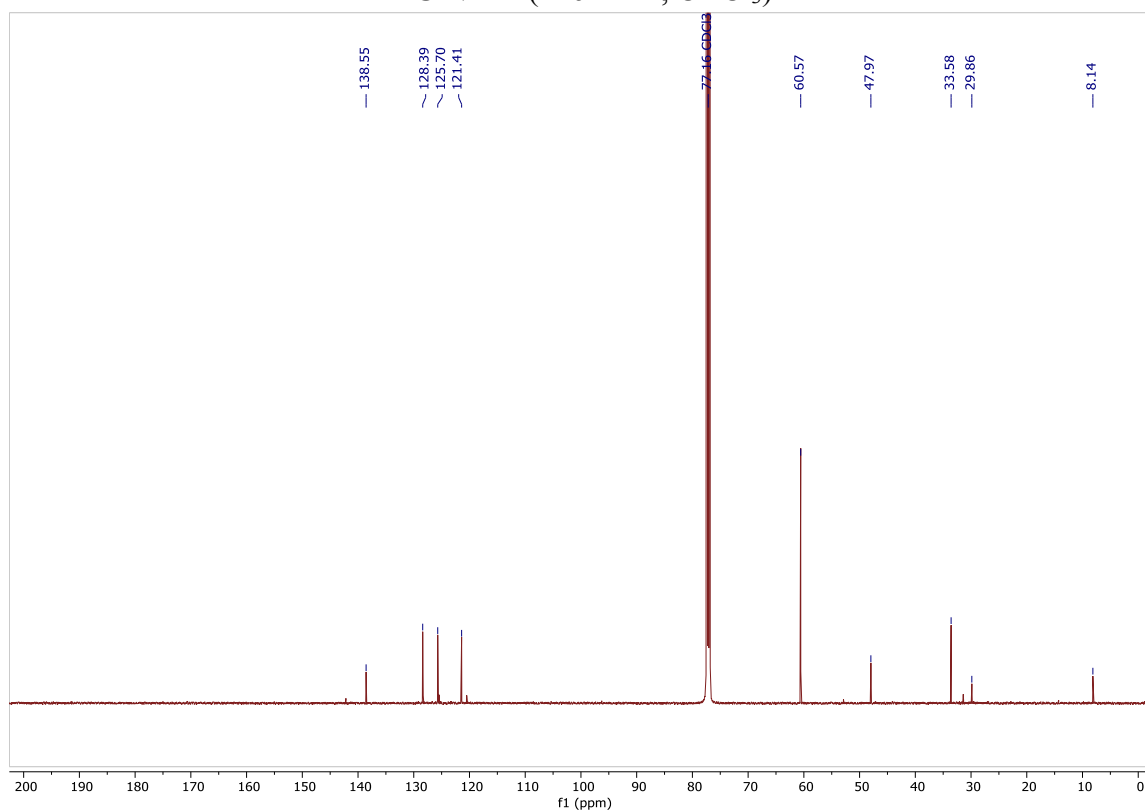
3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)thiophene, 19



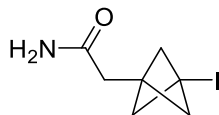
^1H NMR (500 MHz, CDCl_3)



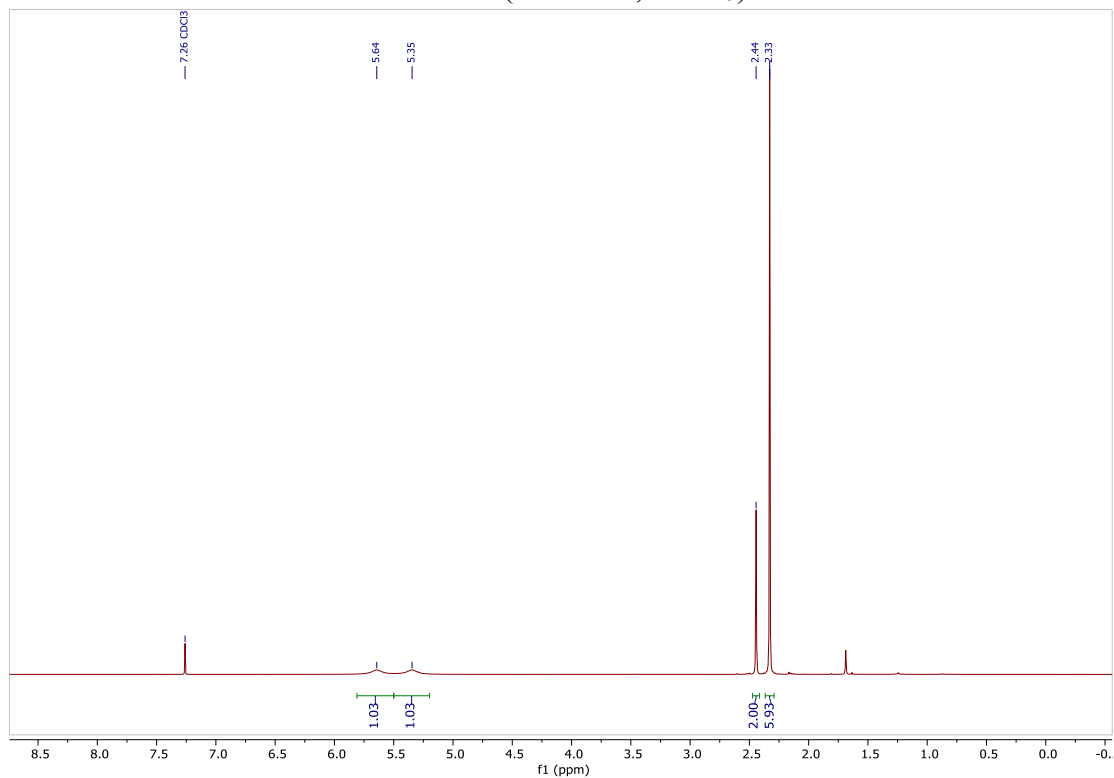
^{13}C NMR (126 MHz, CDCl_3)



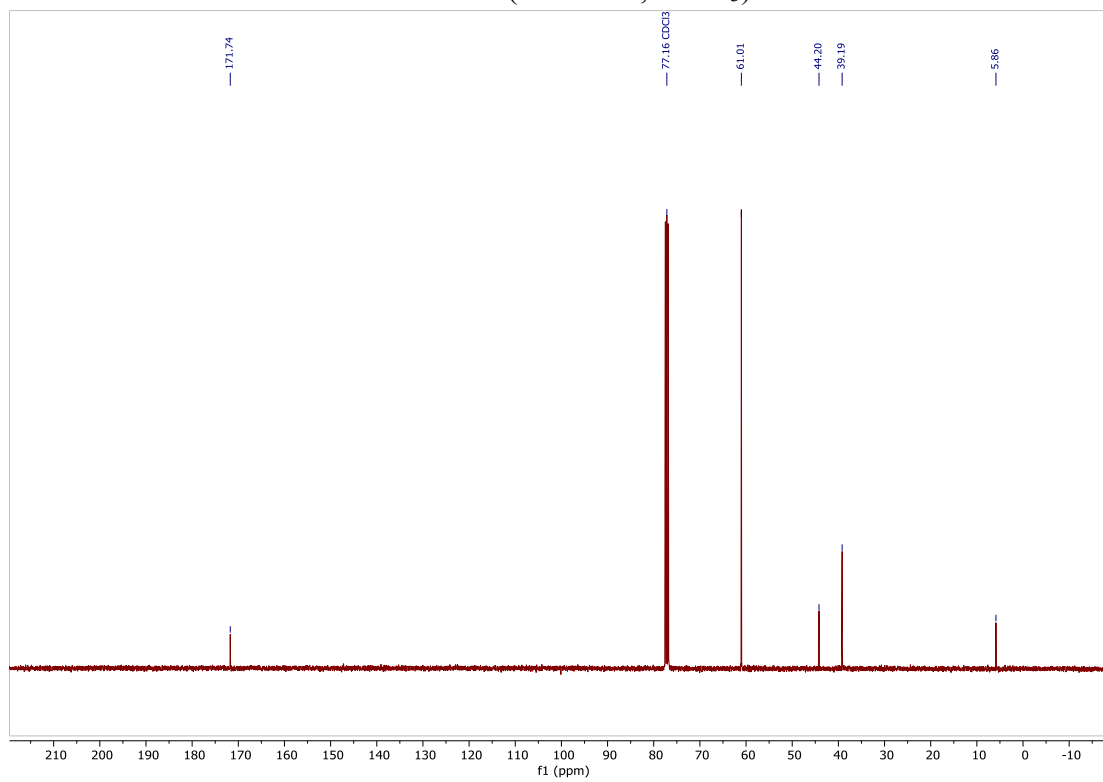
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)acetamide, 20



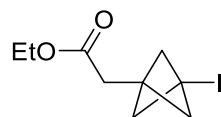
^1H NMR (400 MHz, CDCl_3)



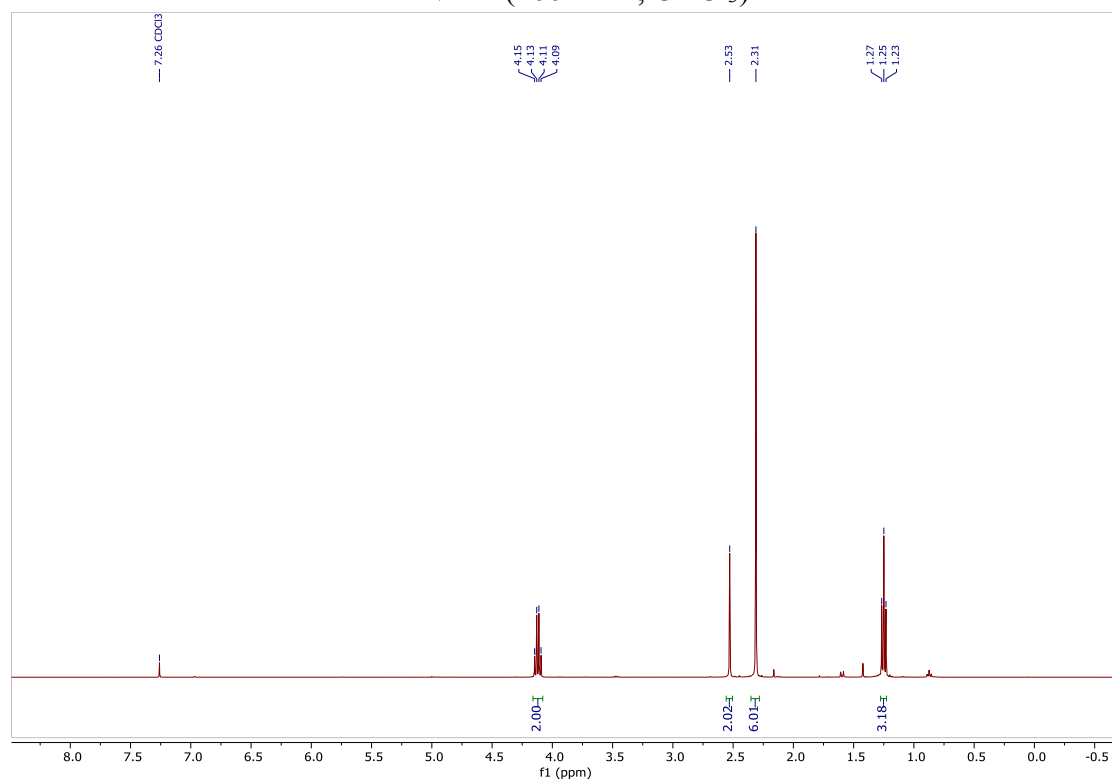
^{13}C NMR (101 MHz, CDCl_3)



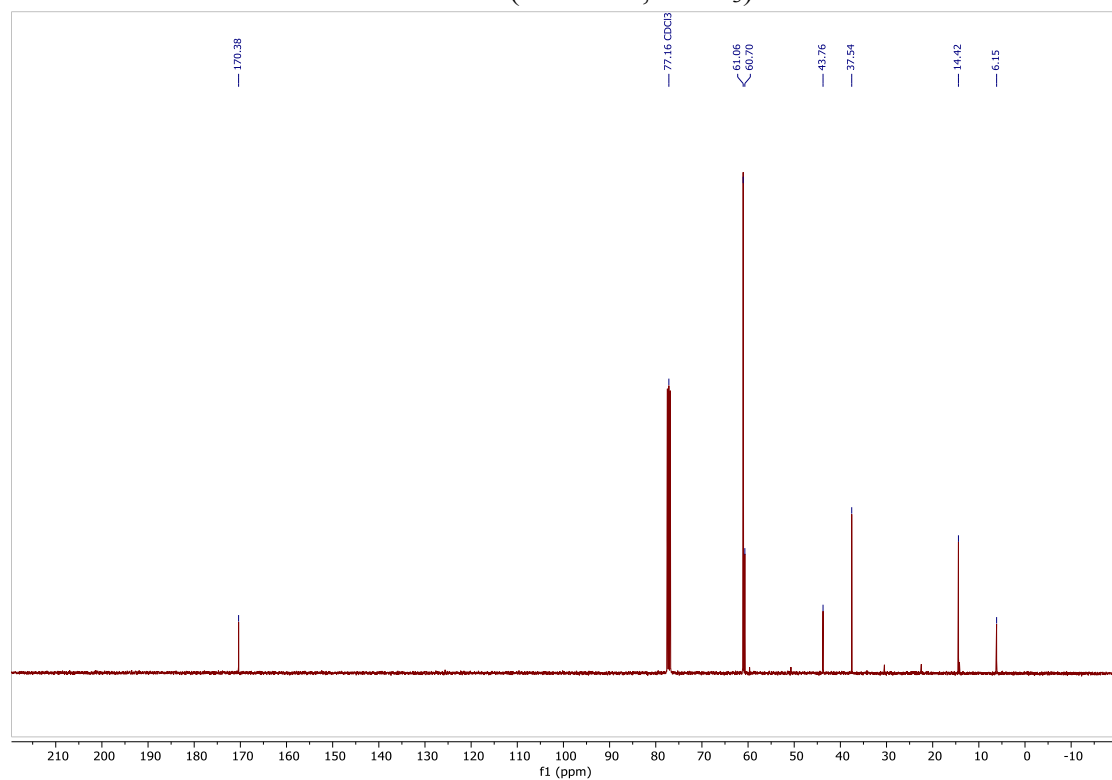
Ethyl 2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetate, 21



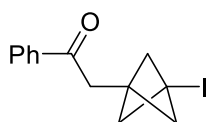
^1H NMR (400 MHz, CDCl_3)



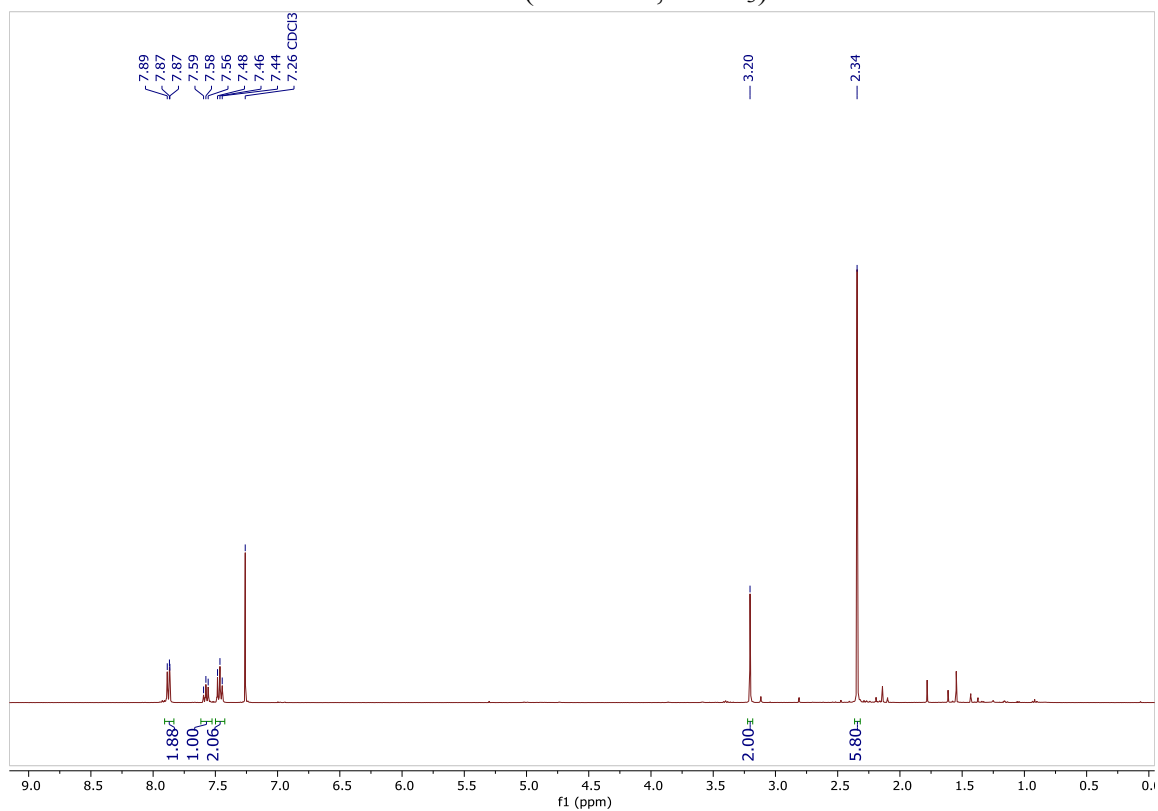
^{13}C NMR (101 MHz, CDCl_3)



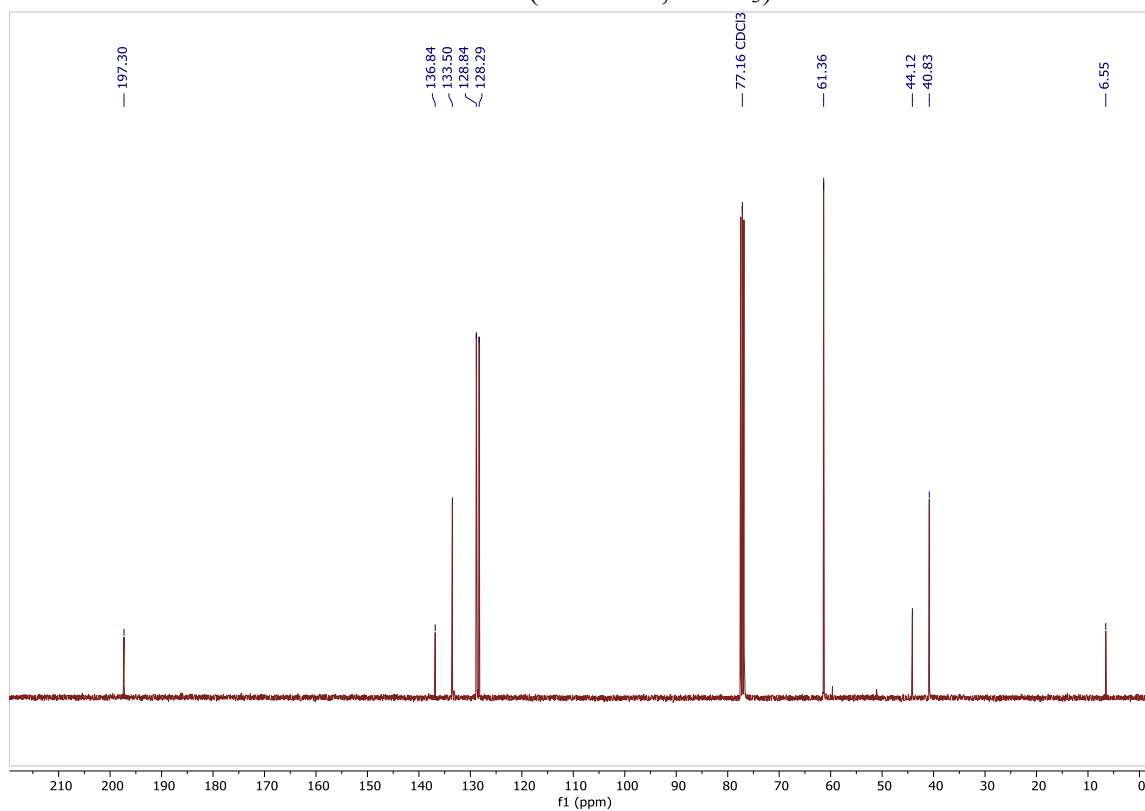
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-phenylethan-1-one, 22



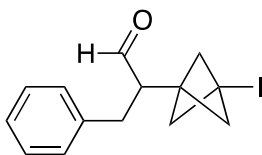
^1H NMR (400 MHz, CDCl_3)



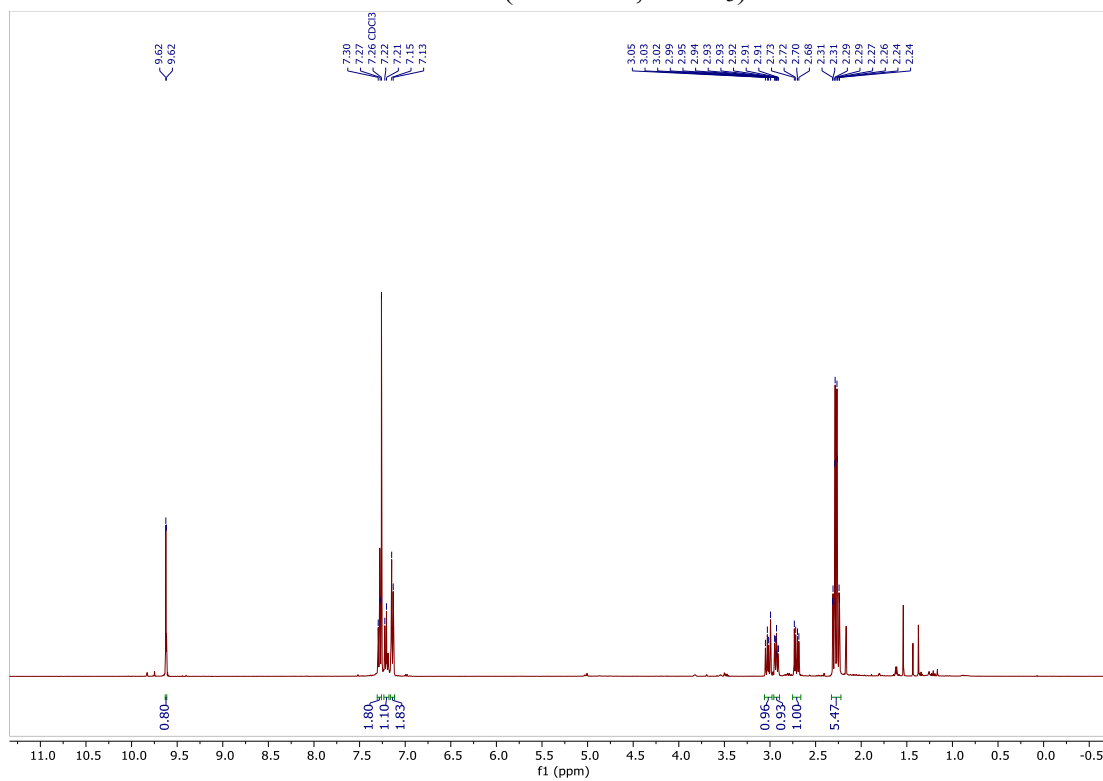
^{13}C NMR (101 MHz, CDCl_3)



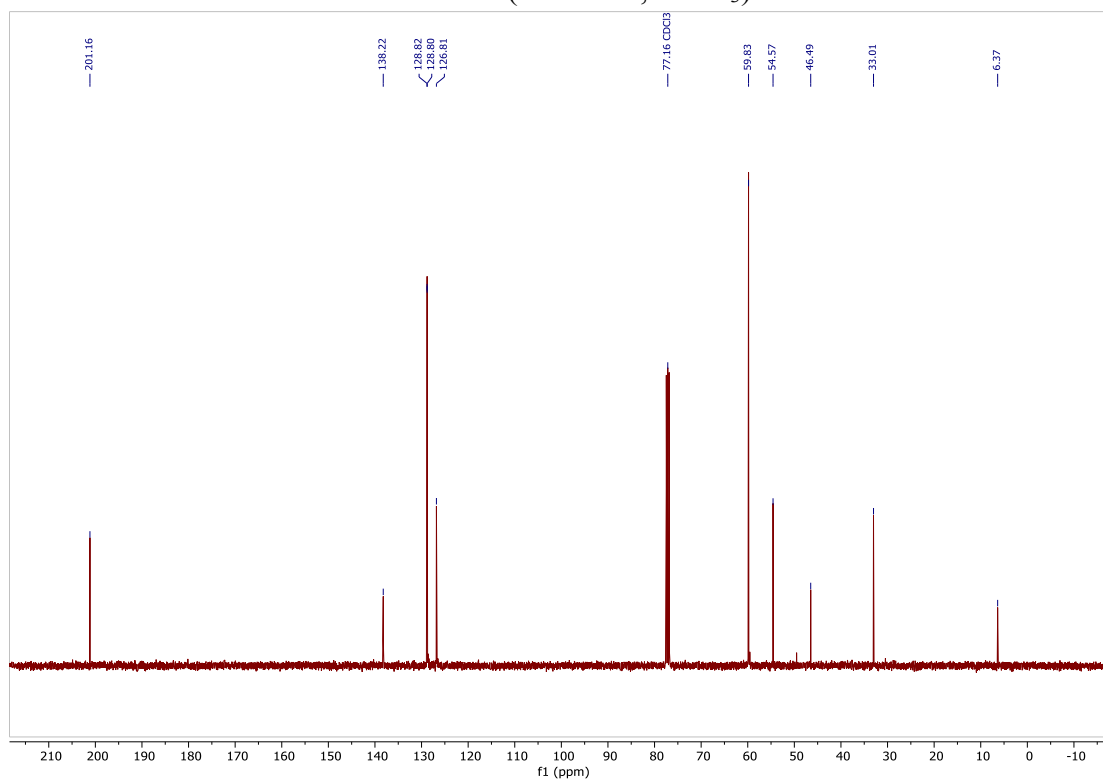
Iodo-3-2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-3-phenylpropanal, 23



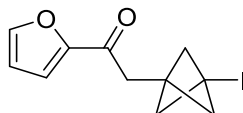
¹H NMR (400 MHz, CDCl₃)



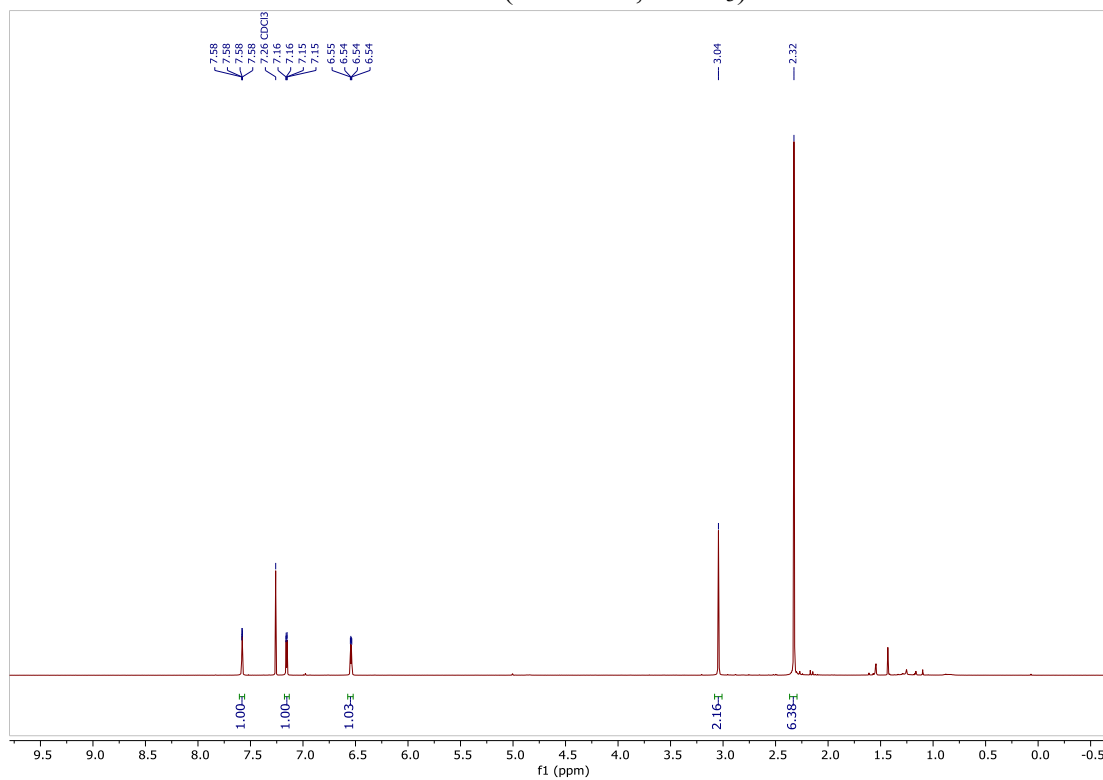
¹³C NMR (101 MHz, CDCl₃)



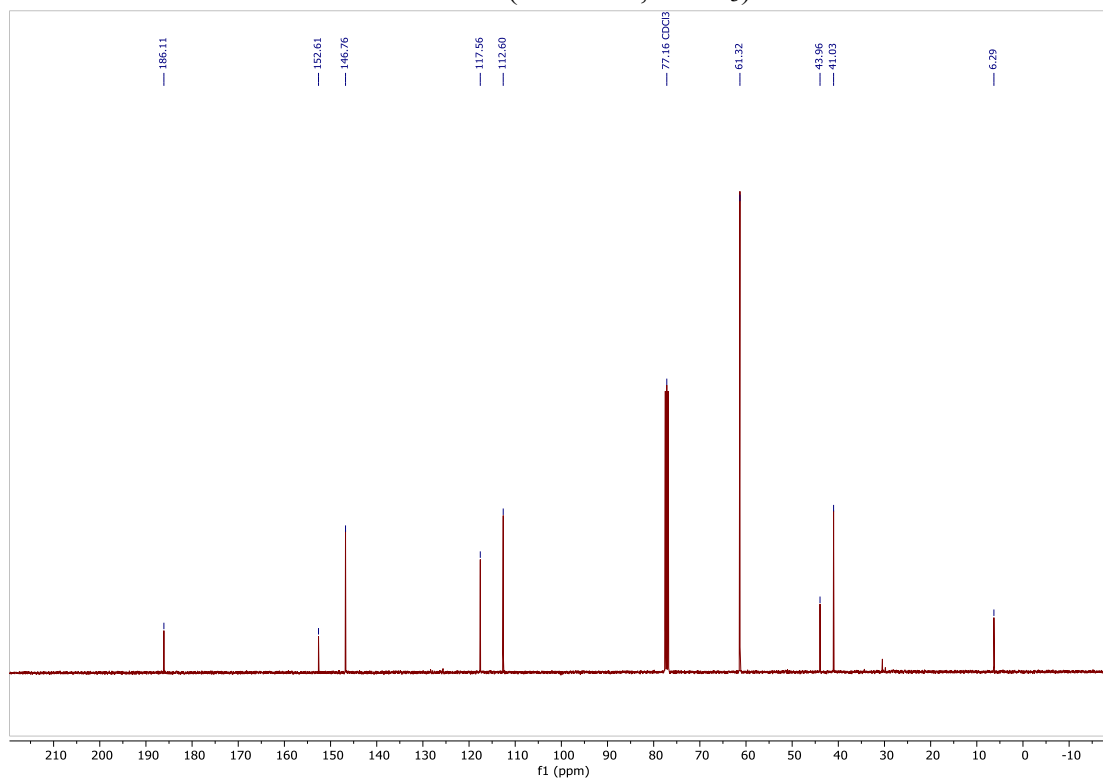
1-(Furan-2-yl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethan-1-one, 24



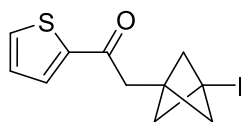
^1H NMR (400 MHz, CDCl_3)



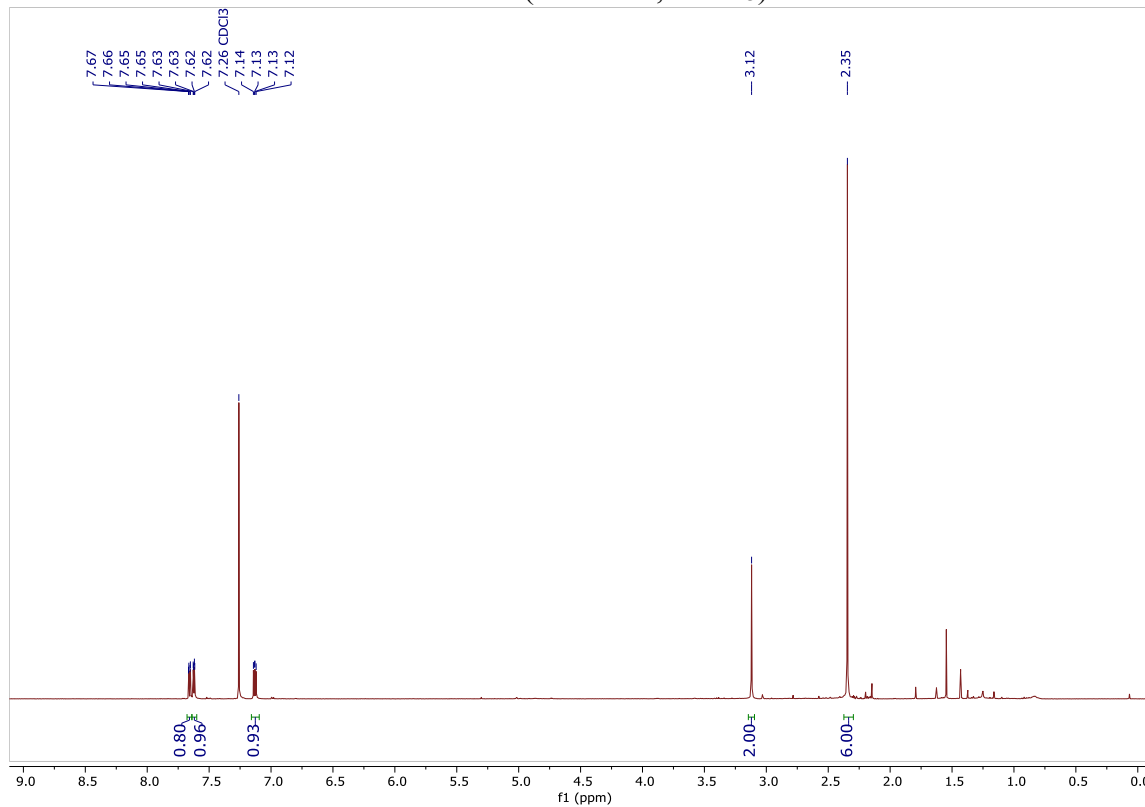
^{13}C NMR (101 MHz, CDCl_3)



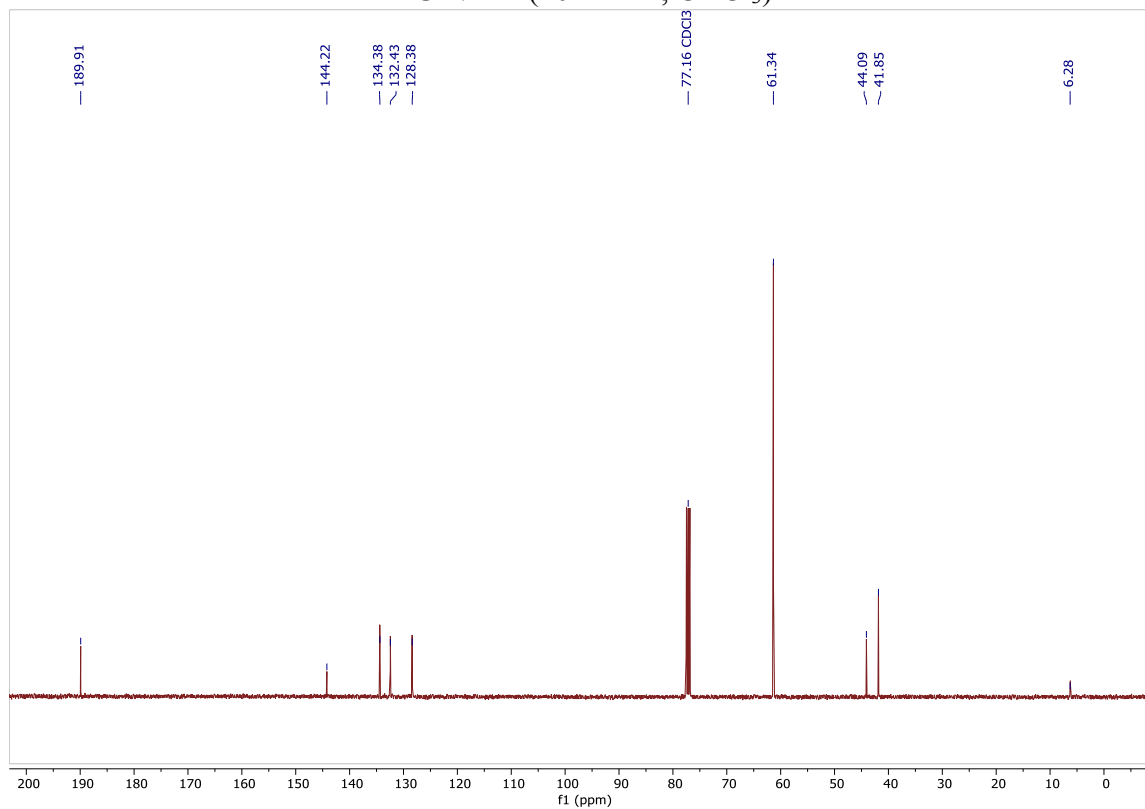
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(thiophen-2-yl)ethan-1-one, 25



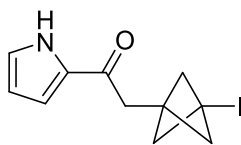
^1H NMR (400 MHz, CDCl_3)



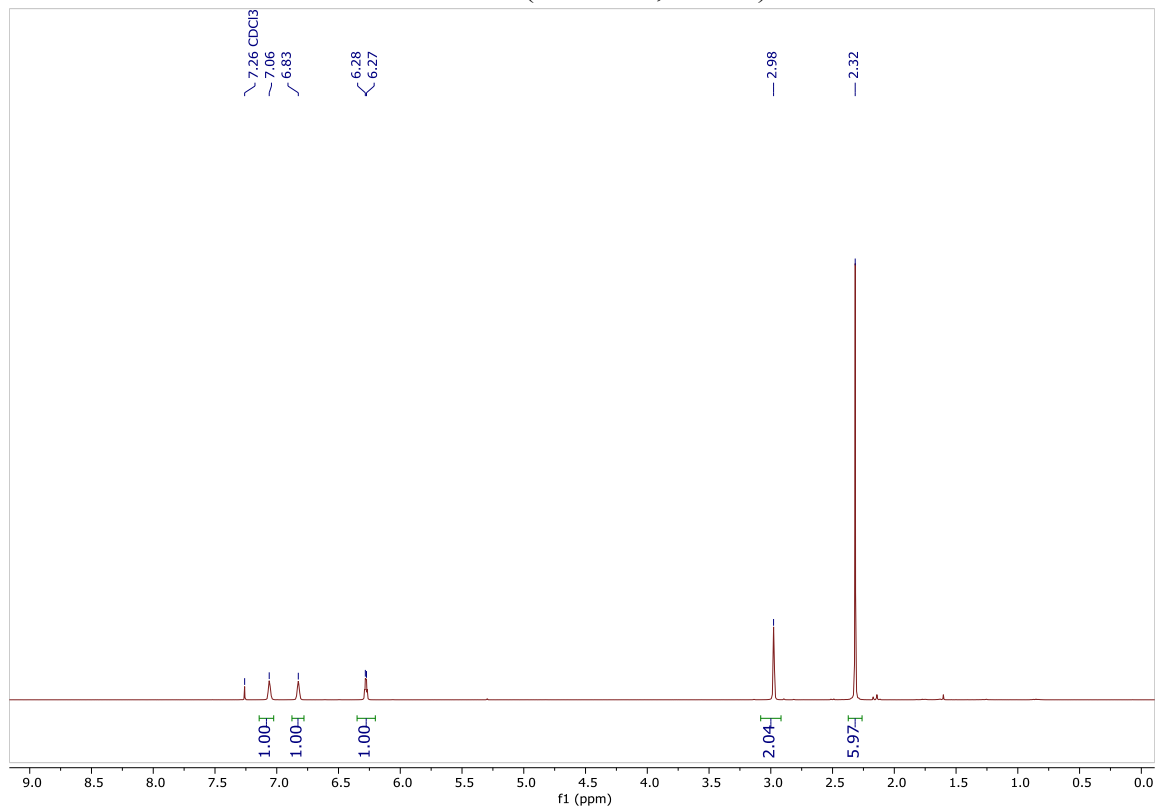
^{13}C NMR (101 MHz, CDCl_3)



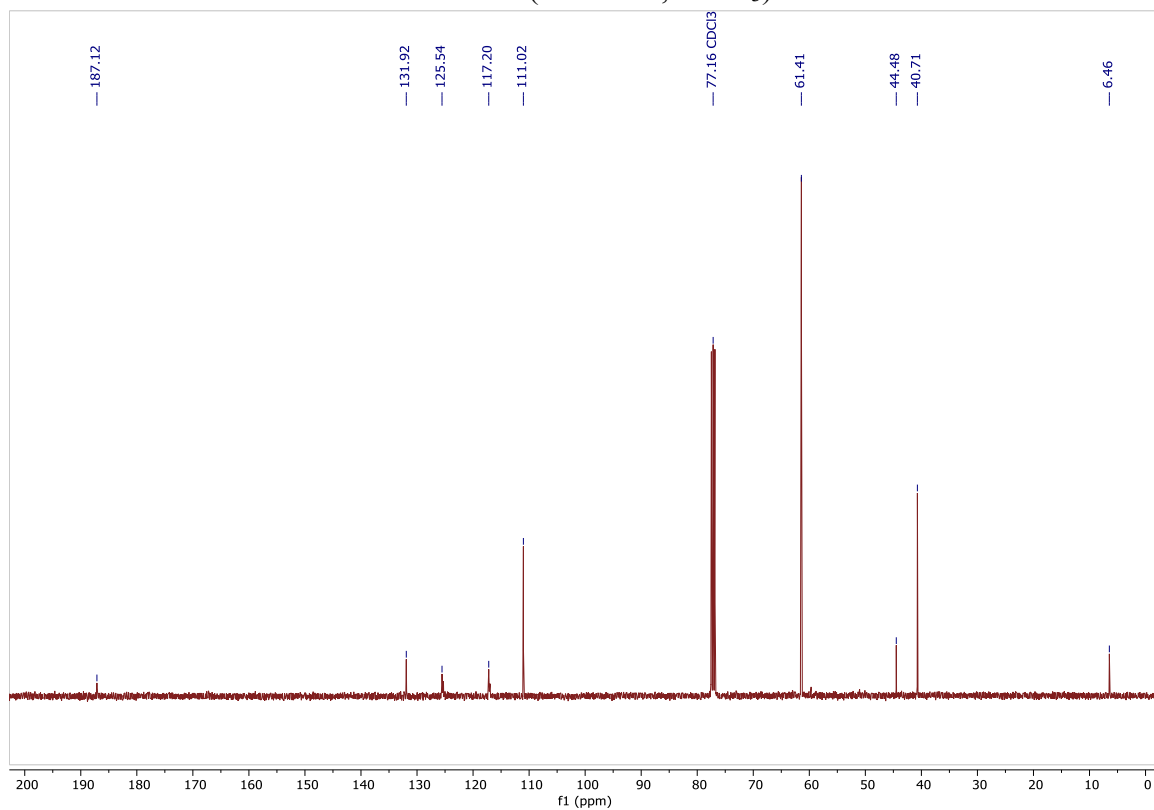
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(1*H*-pyrrol-2-yl)ethan-1-one, 26



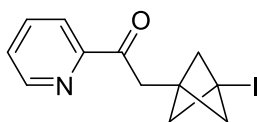
^1H NMR (400 MHz, CDCl_3)



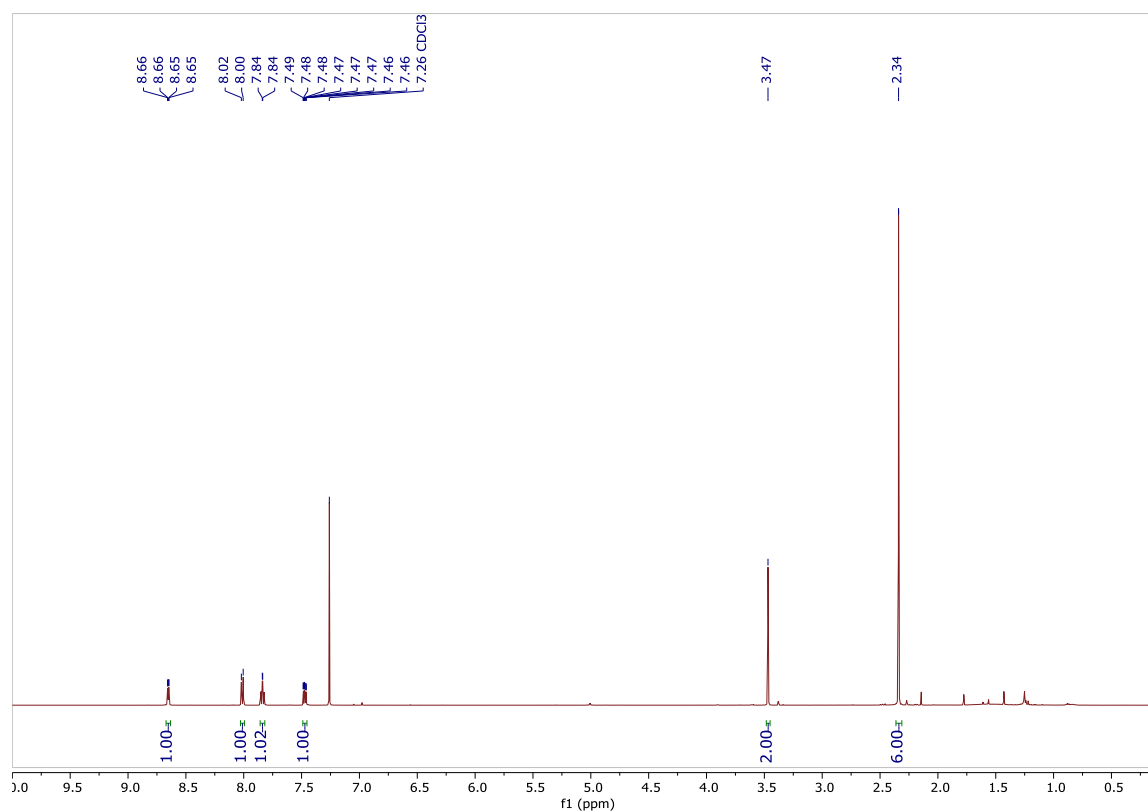
^{13}C NMR (101 MHz, CDCl_3)



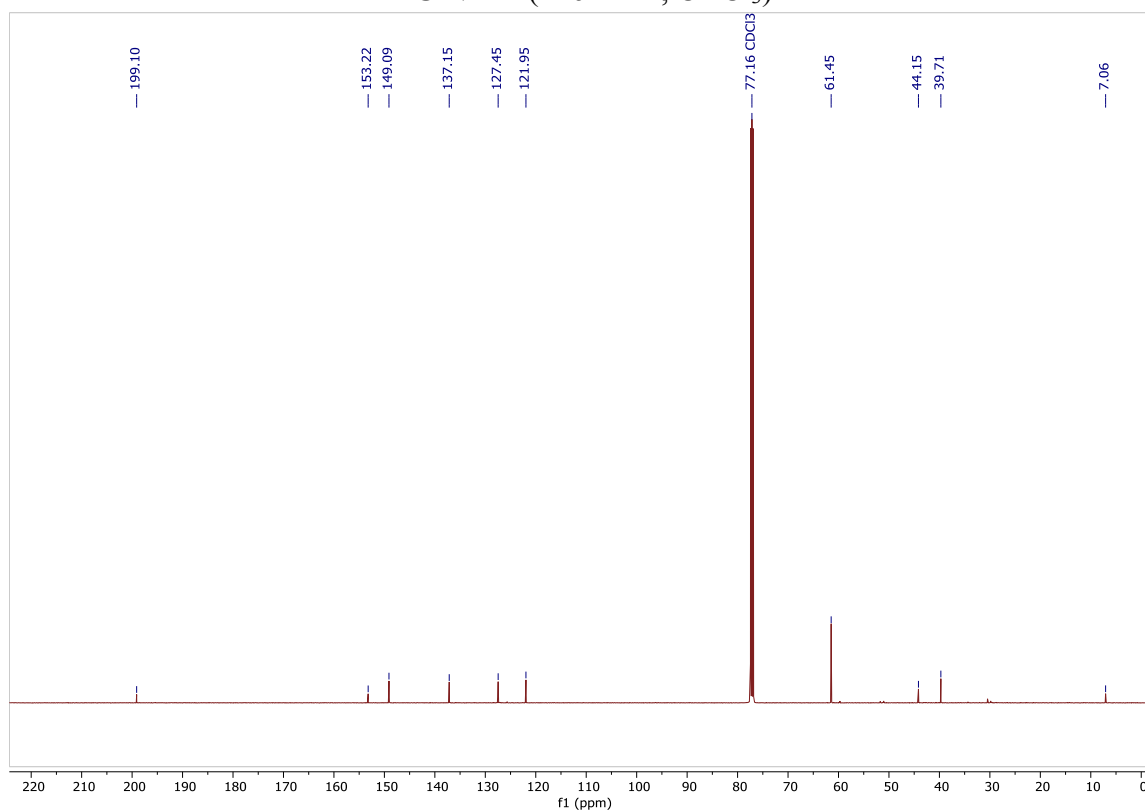
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(pyridin-2-yl)ethan-1-one, 27



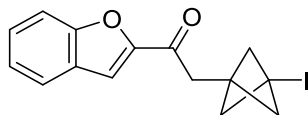
^1H NMR (500 MHz, CDCl_3)



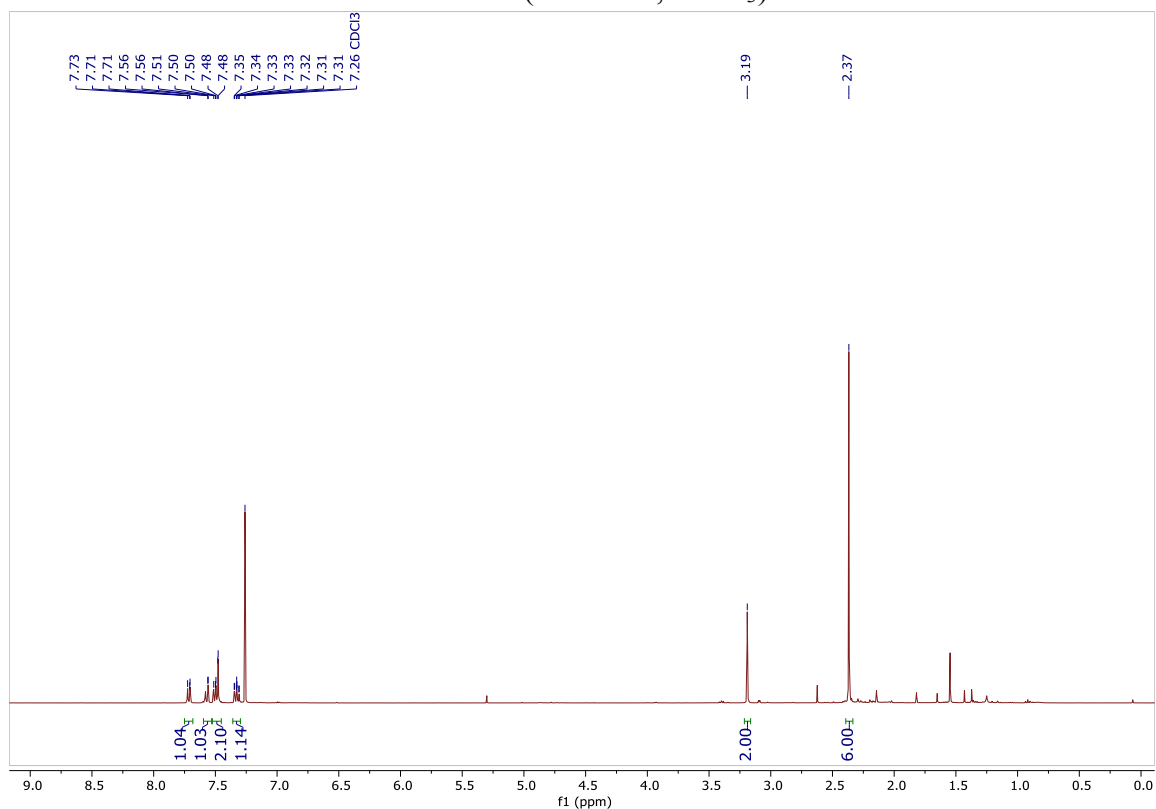
^{13}C NMR (126 MHz, CDCl_3)



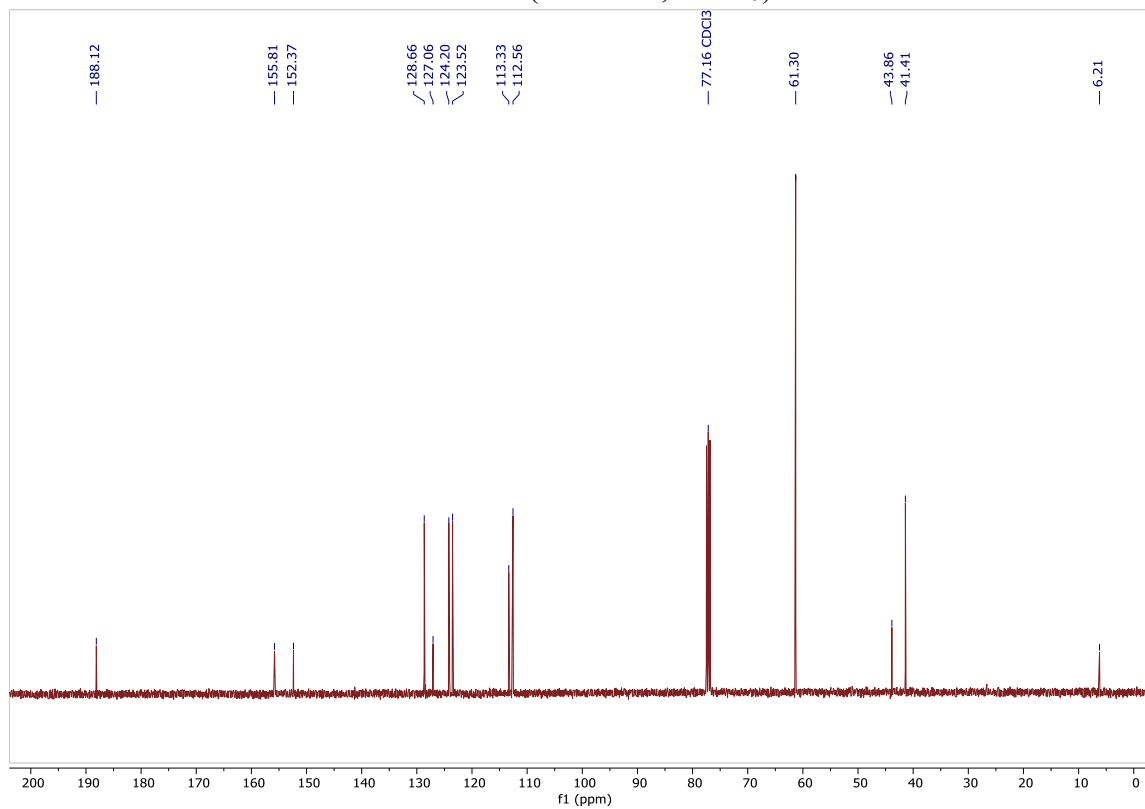
1-(Benzofuran-2-yl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethan-1-one, 28



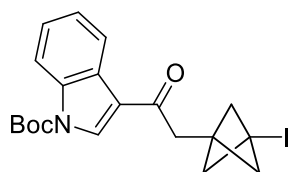
^1H NMR (400 MHz, CDCl_3)



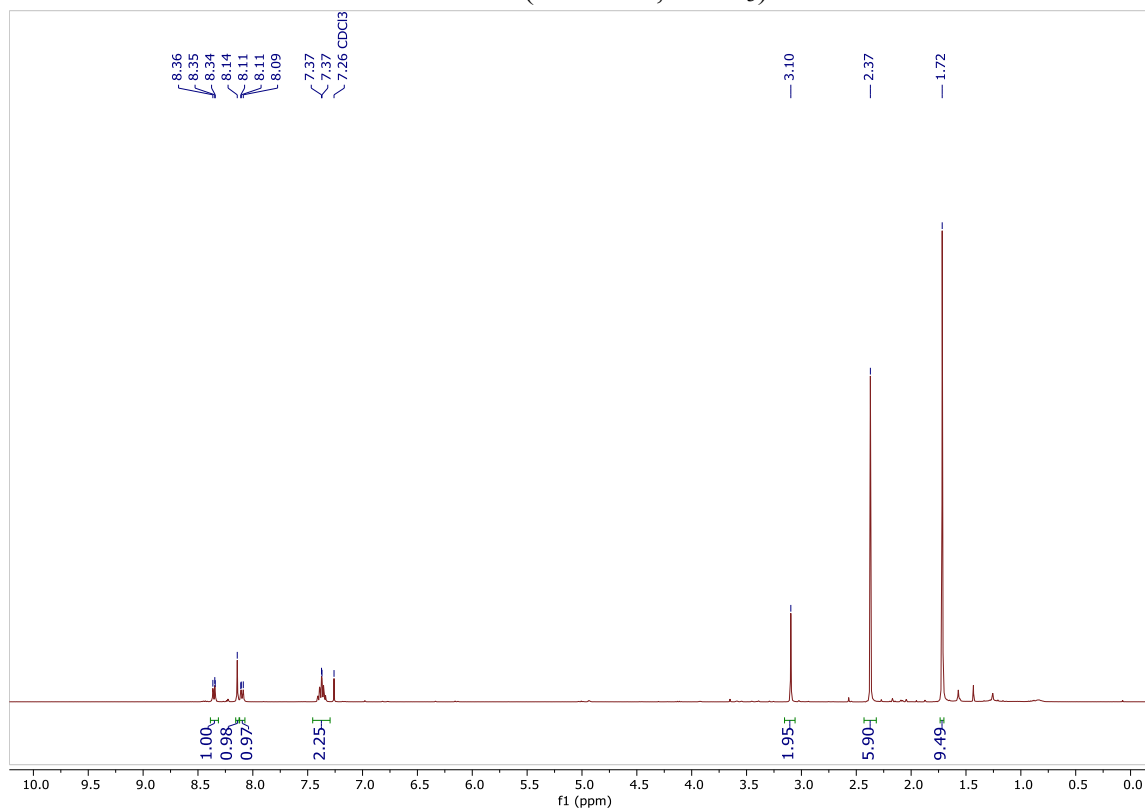
^{13}C NMR (101 MHz, CDCl_3)



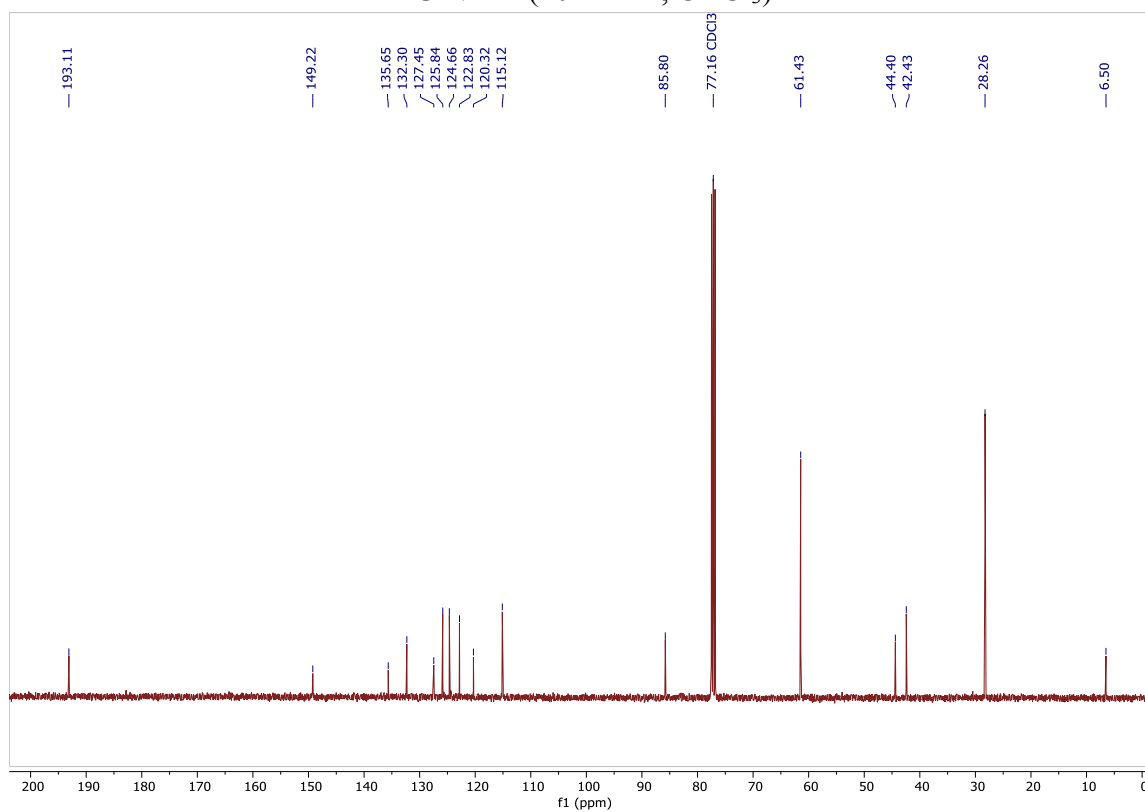
***tert*-Butyl 2-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetyl)-1*H*-indole-1-carboxylate, 29**



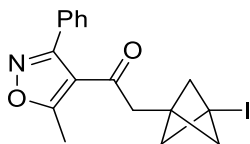
¹H NMR (400 MHz, CDCl₃)



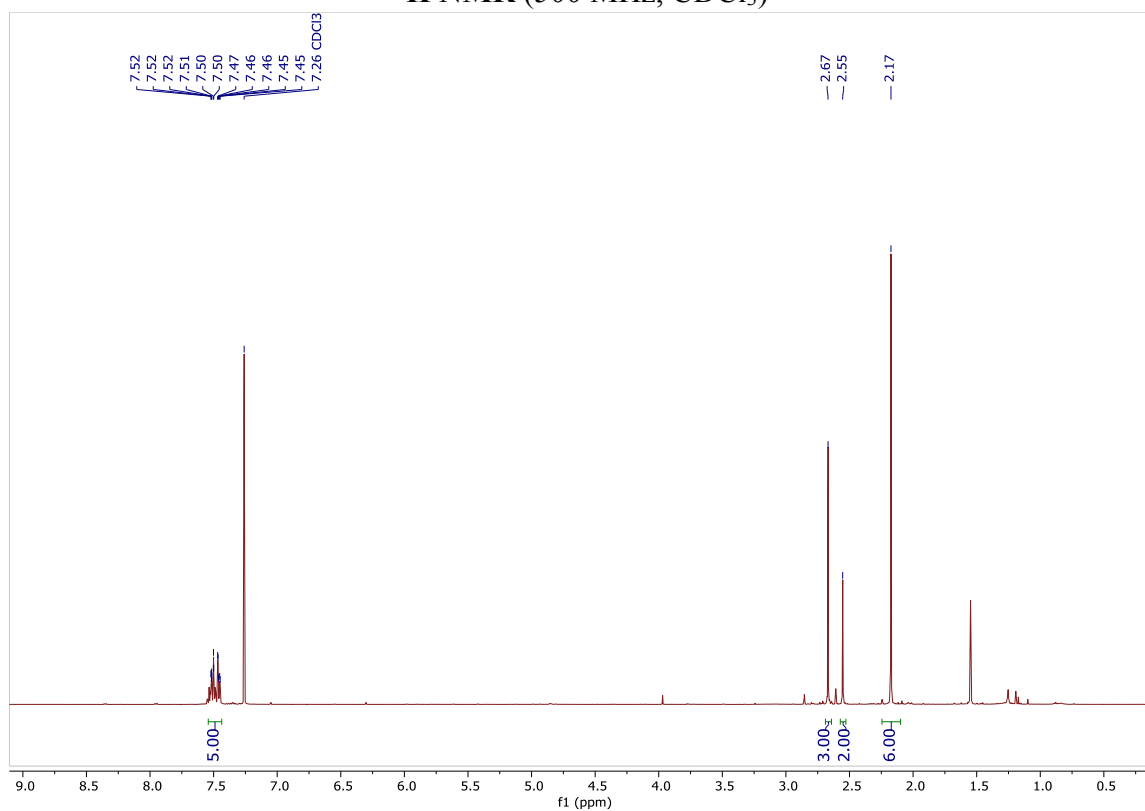
¹³C NMR (101 MHz, CDCl₃)



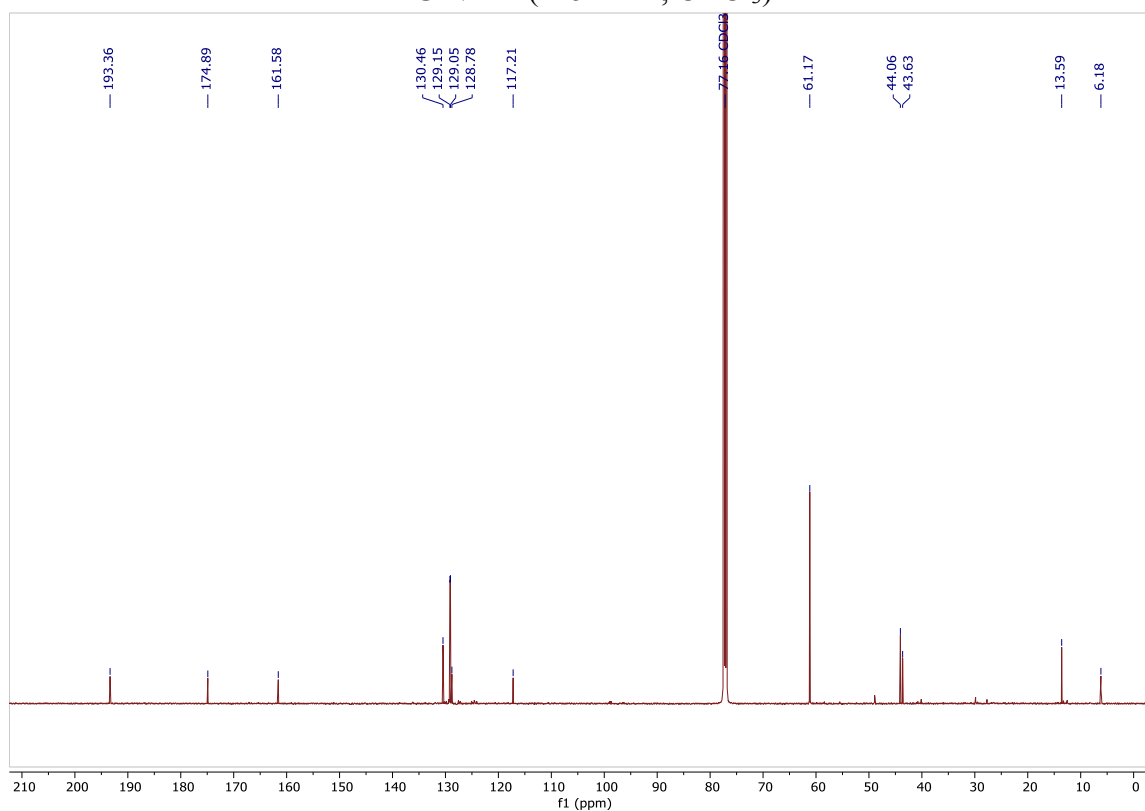
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-(5-methyl-3-phenylisoxazol-4-yl)ethan-1-one, 30



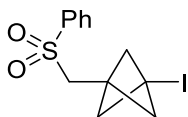
^1H NMR (500 MHz, CDCl_3)



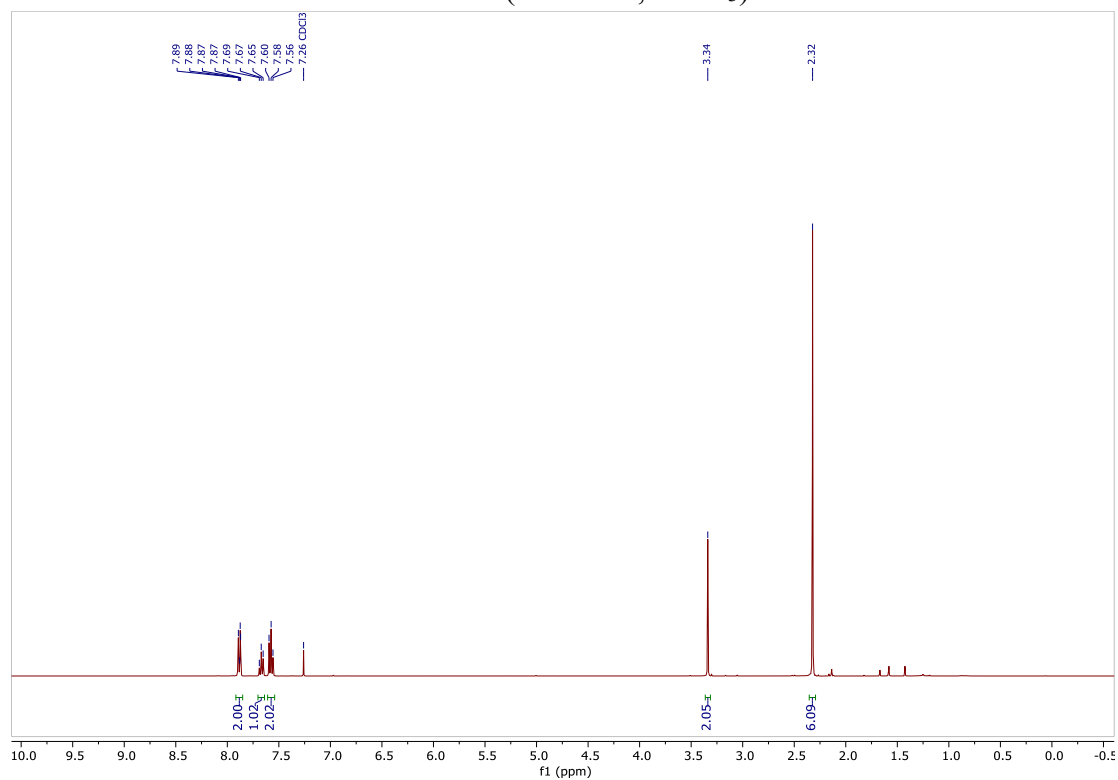
^{13}C NMR (125 MHz, CDCl_3)



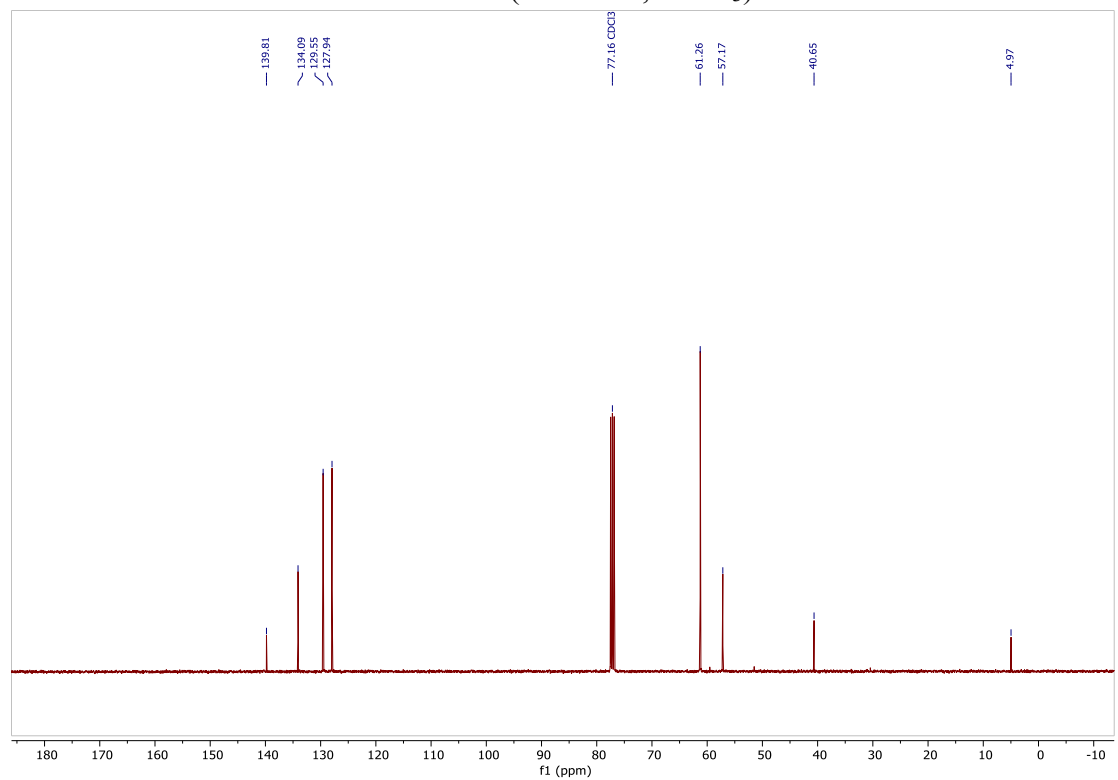
((Phenylsulfonyl)methyl)bicyclo[1.1.1]pentane, 31



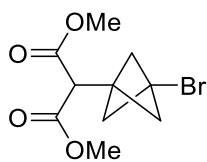
^1H NMR (400 MHz, CDCl_3)



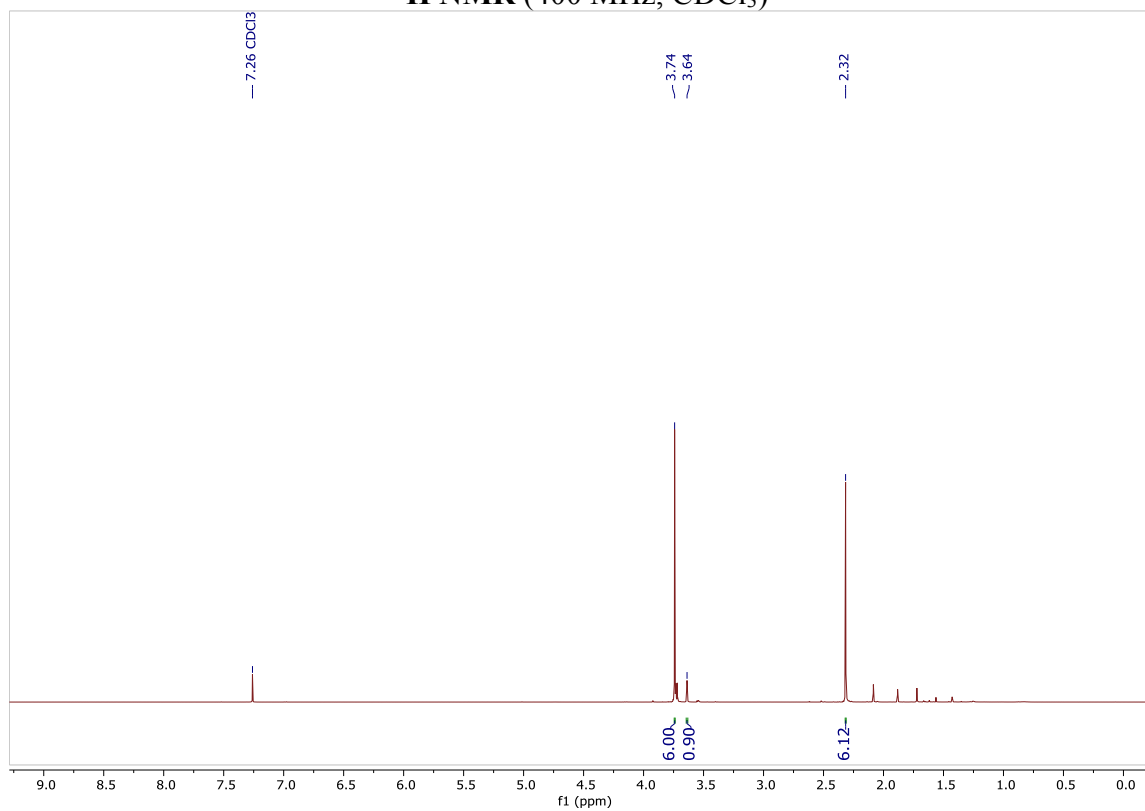
^{13}C NMR (101 MHz, CDCl_3)



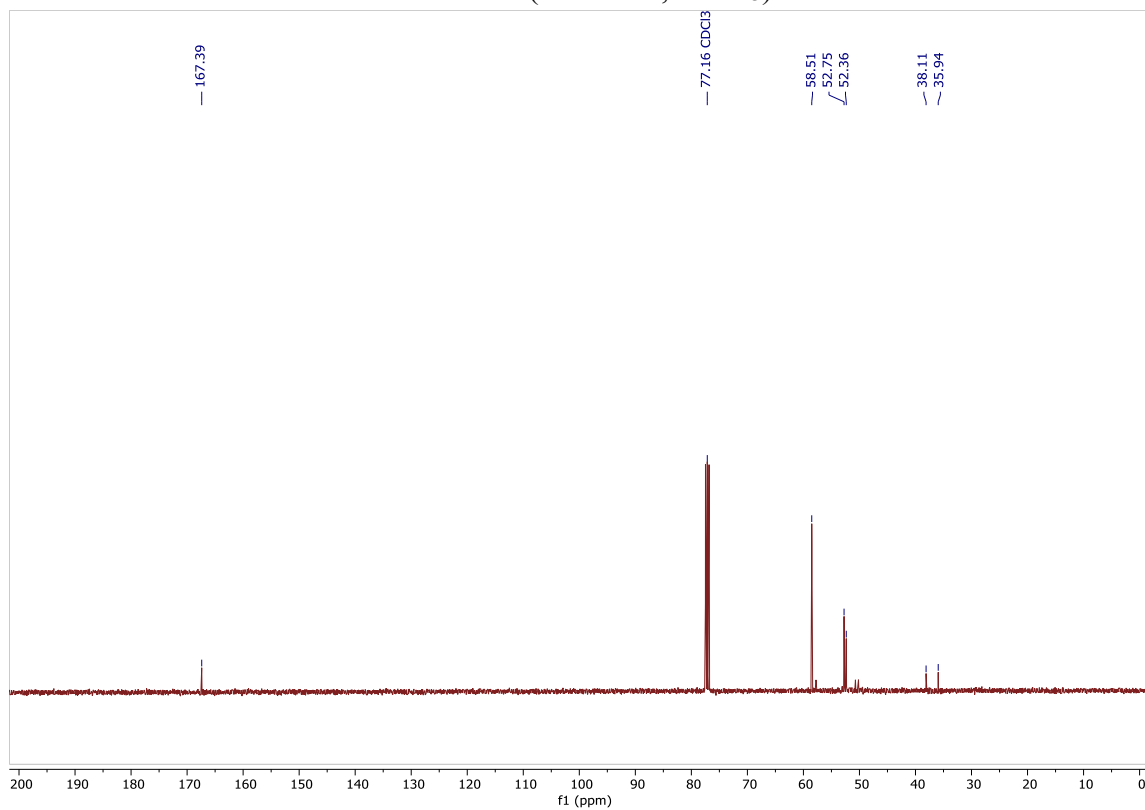
Dimethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)malonate, 32



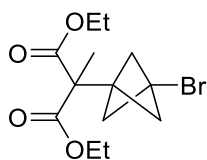
^1H NMR (400 MHz, CDCl_3)



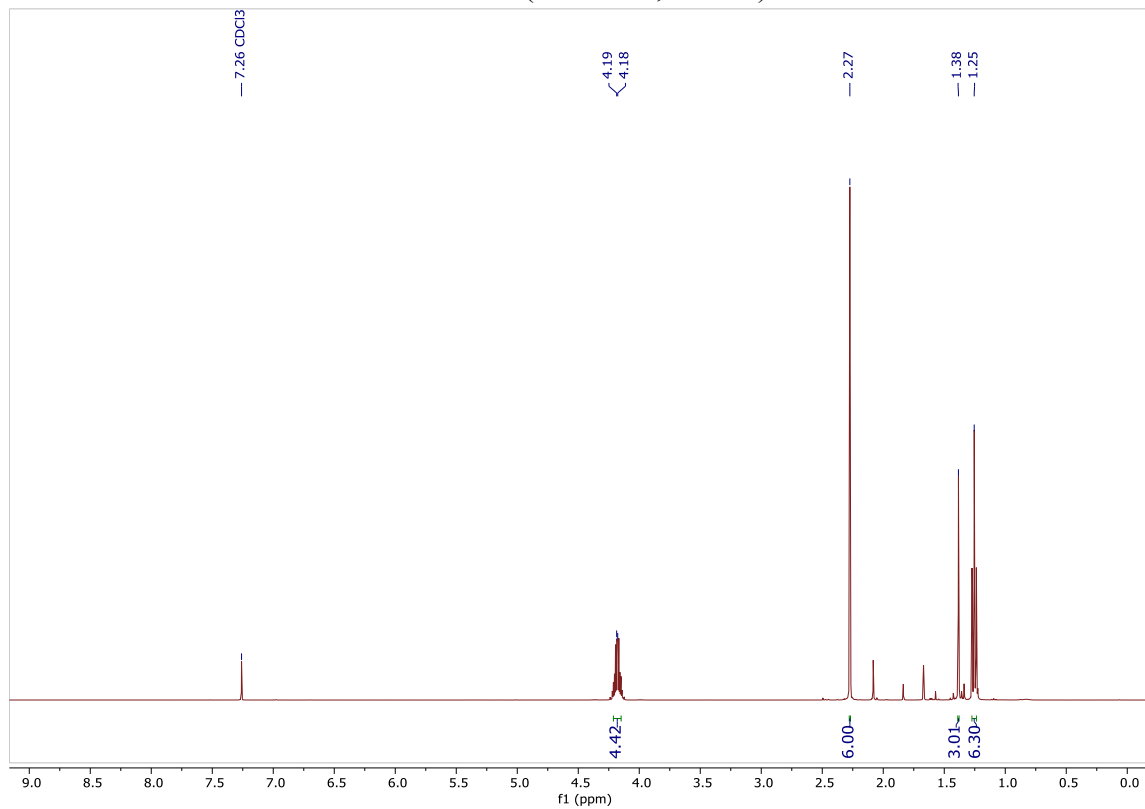
^{13}C NMR (101 MHz, CDCl_3)



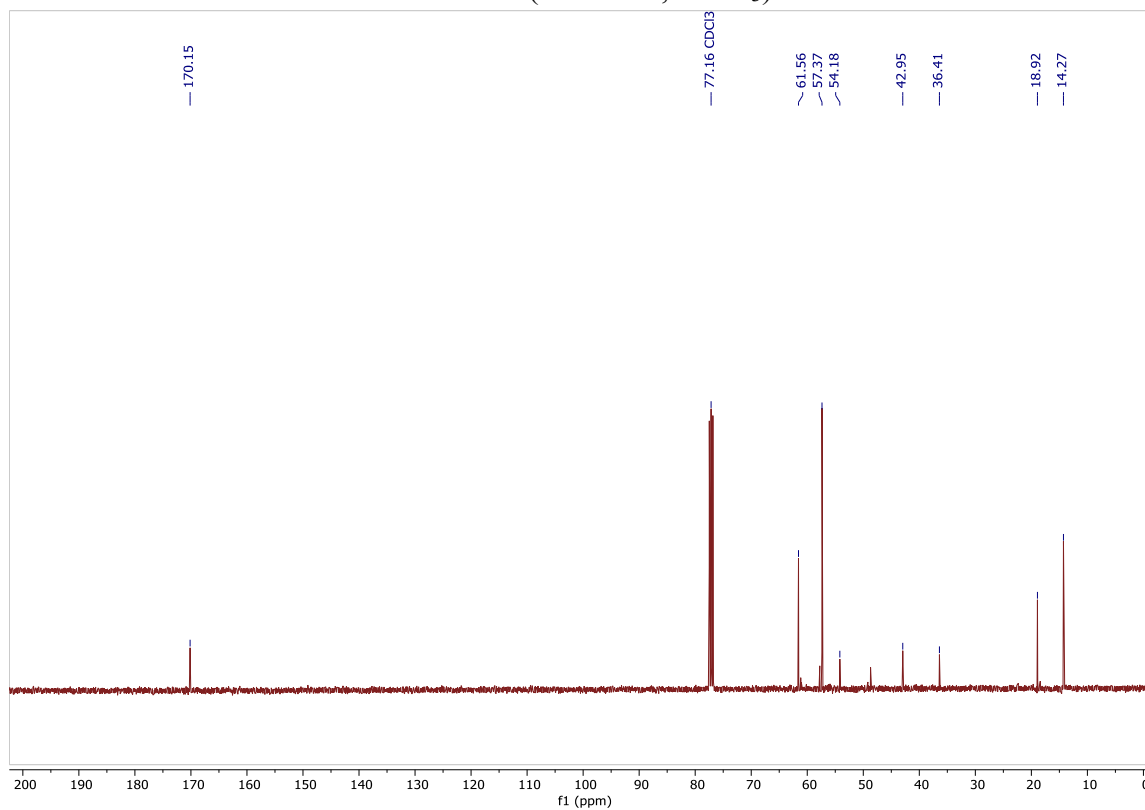
Diethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)-2-methylmalonate, 33



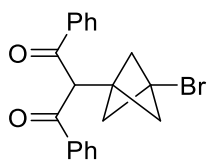
^1H NMR (400 MHz, CDCl_3)



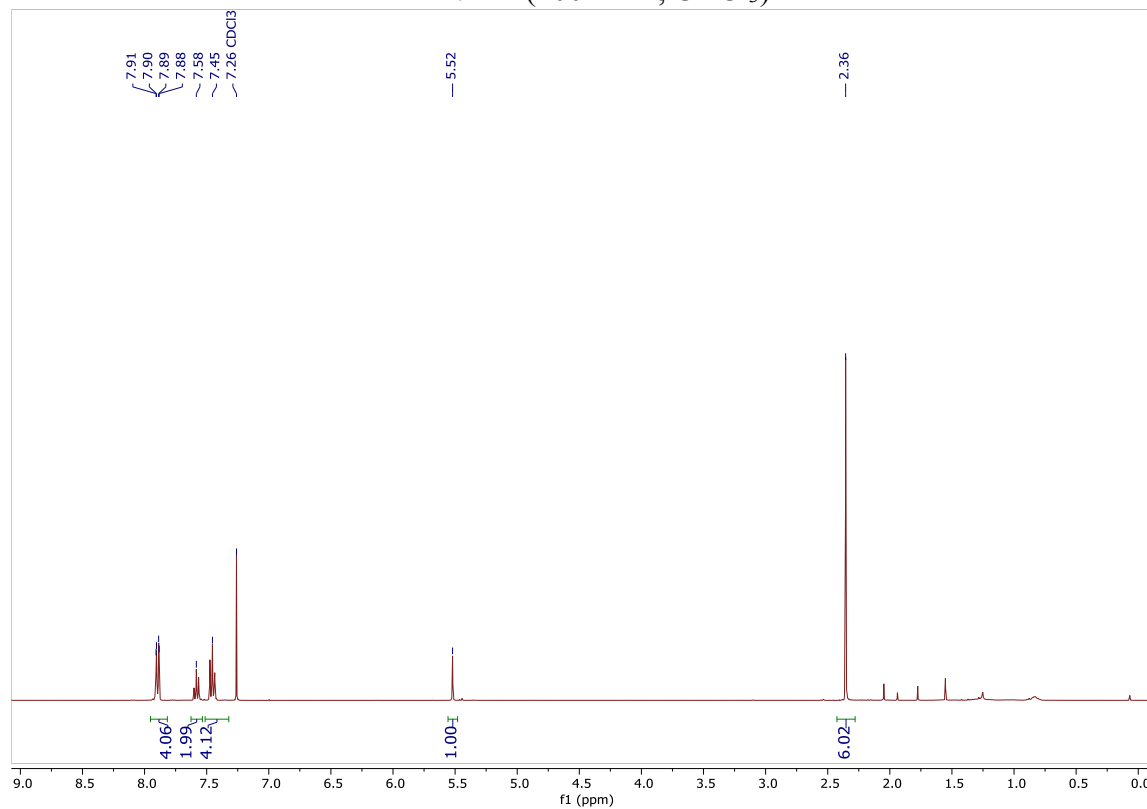
^{13}C NMR (101 MHz, CDCl_3)



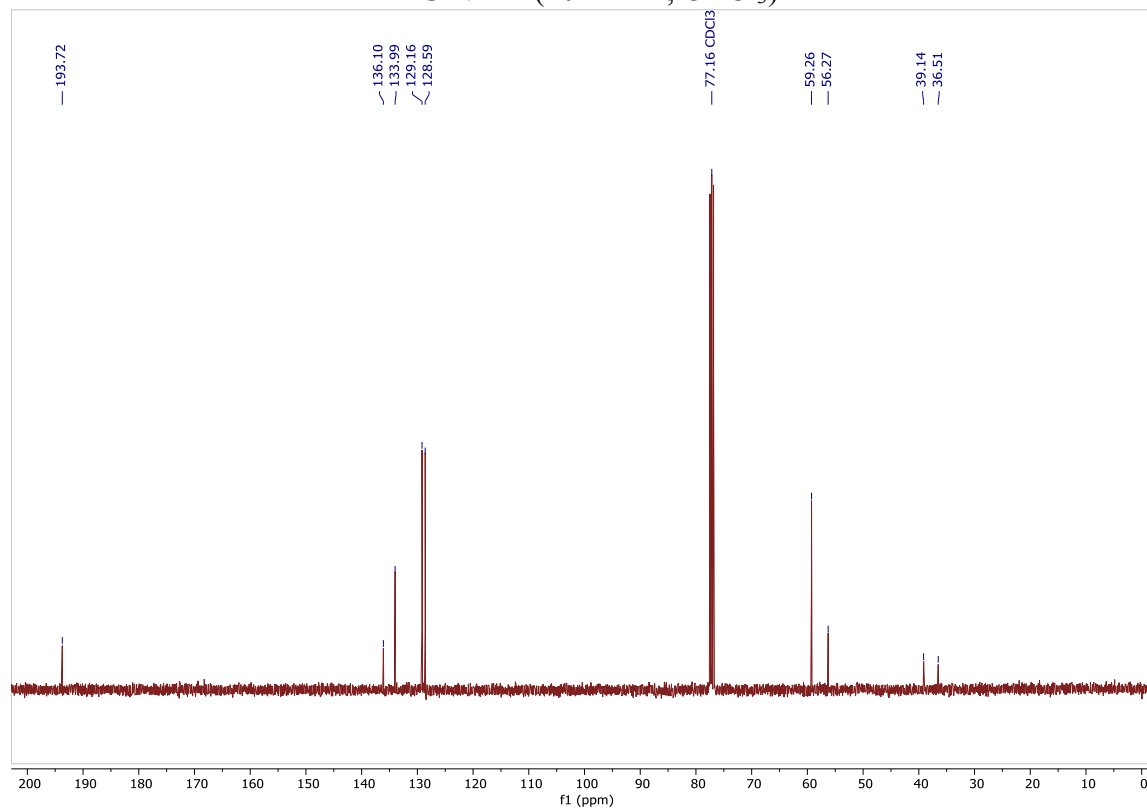
2-(3-Bromobicyclo[1.1.1]pentan-1-yl)-1,3-diphenylpropane-1,3-dione, 34



^1H NMR (400 MHz, CDCl_3)



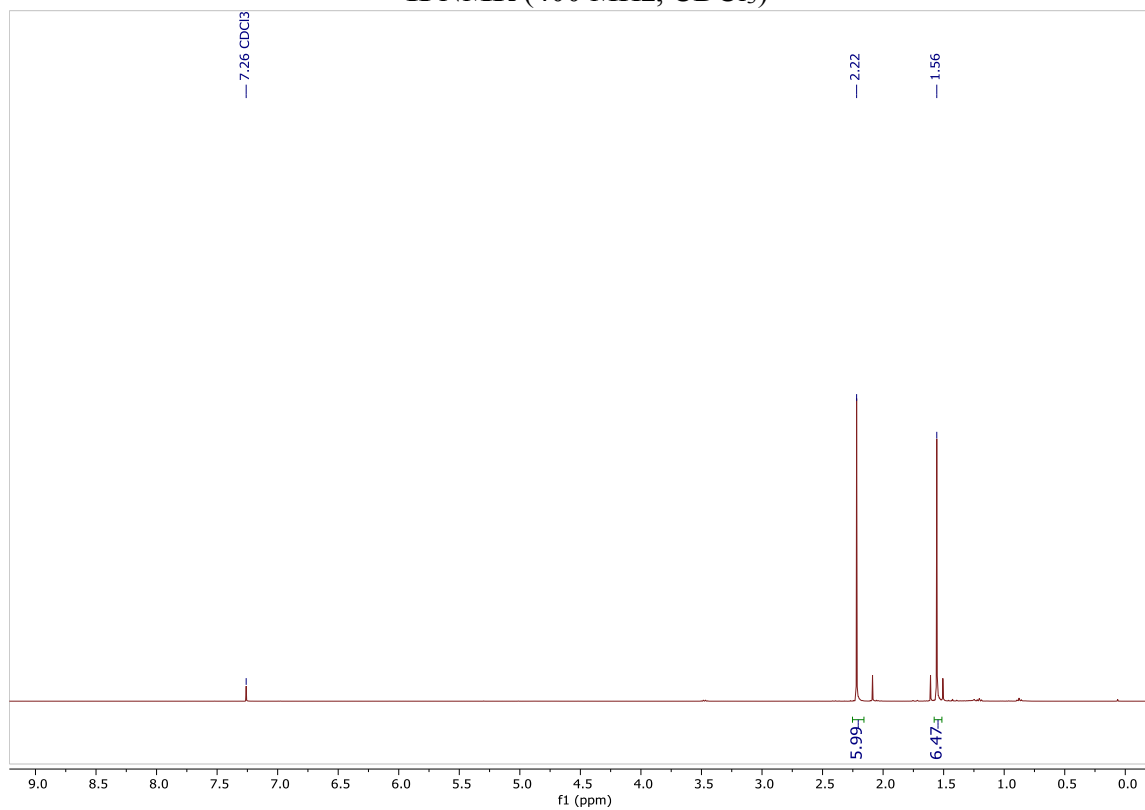
^{13}C NMR (101 MHz, CDCl_3)



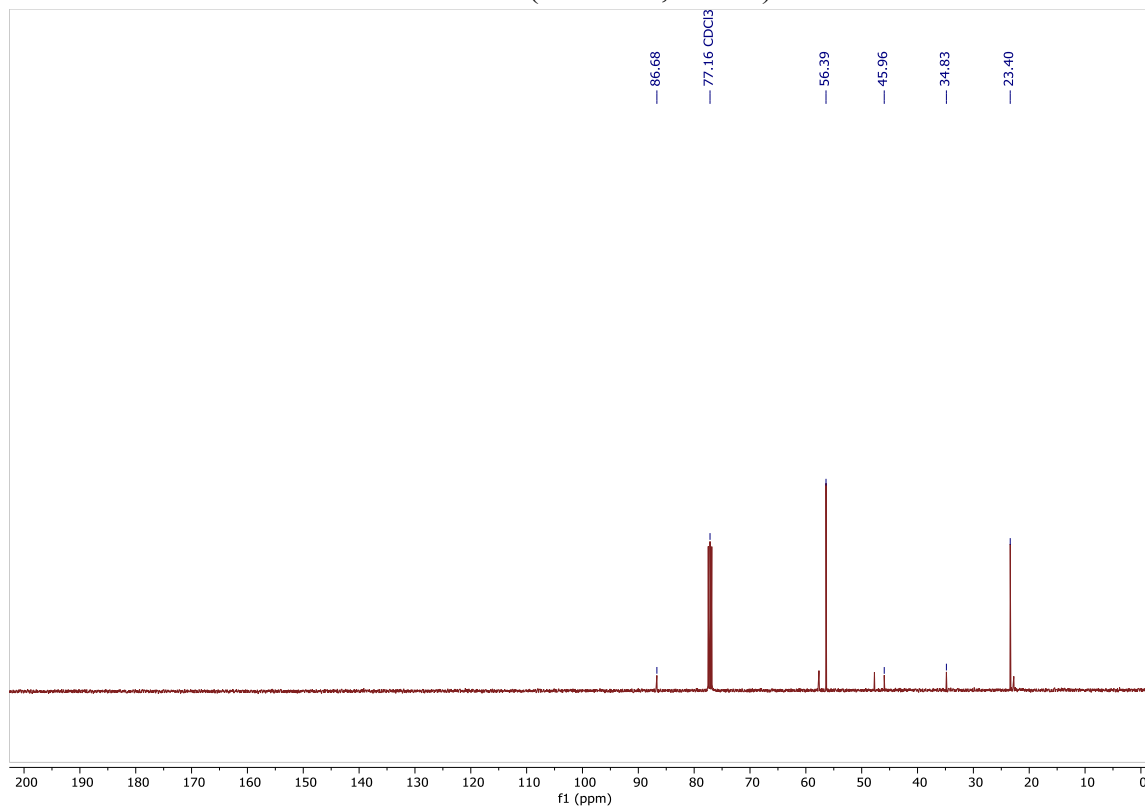
1-Bromo-3-(2-nitropropan-2-yl)bicyclo[1.1.1]pentane, 35



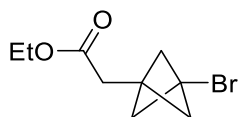
^1H NMR (400 MHz, CDCl_3)



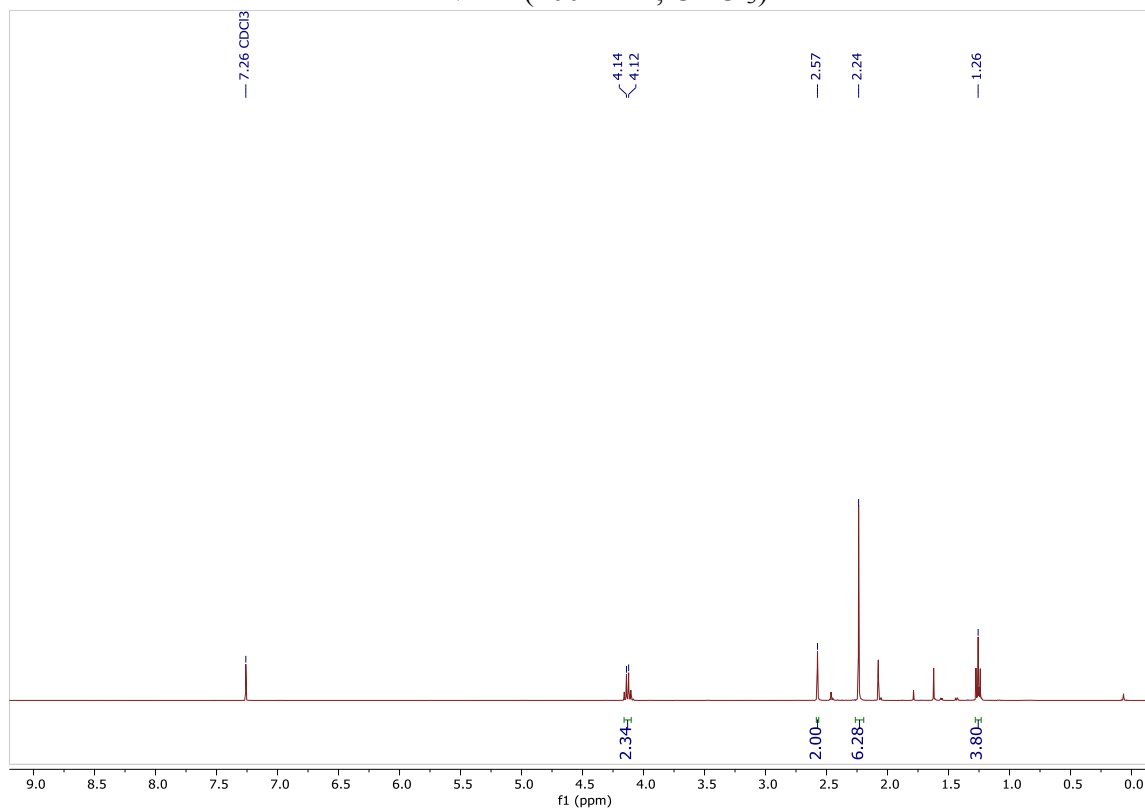
^{13}C NMR (101 MHz, CDCl_3)



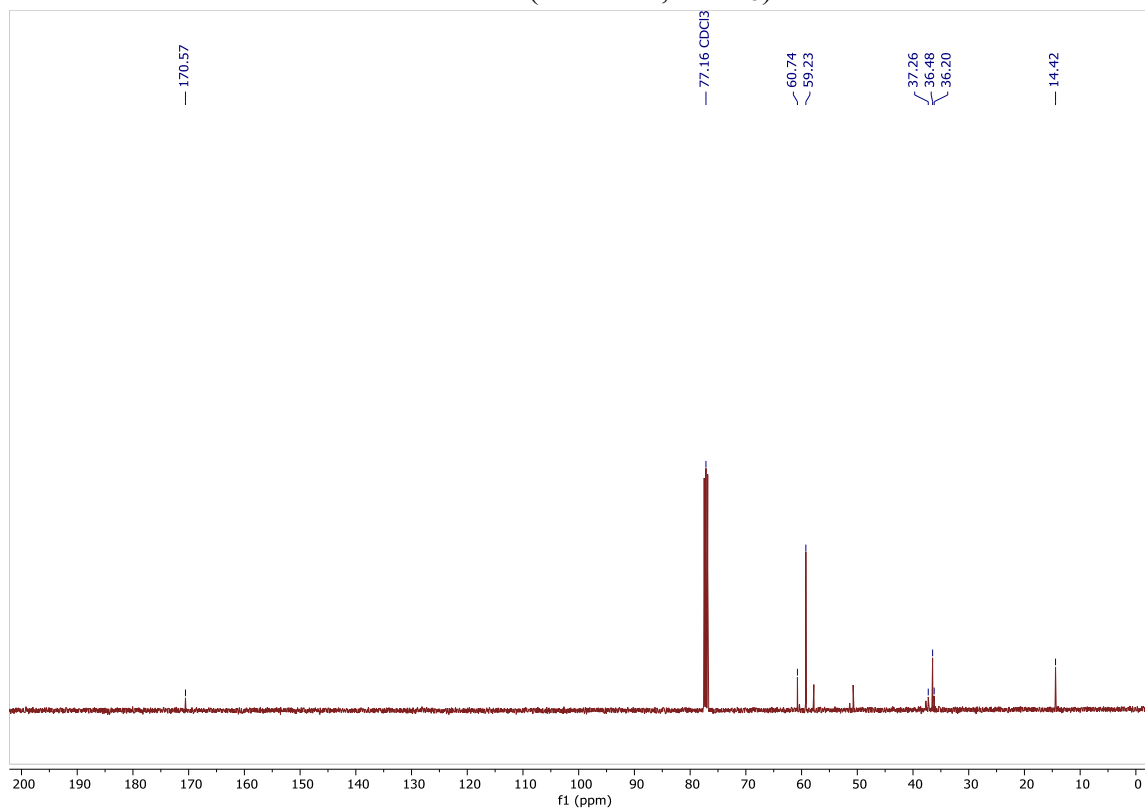
Ethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)acetate, 36



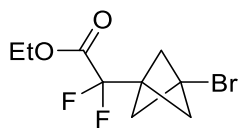
^1H NMR (400 MHz, CDCl_3)



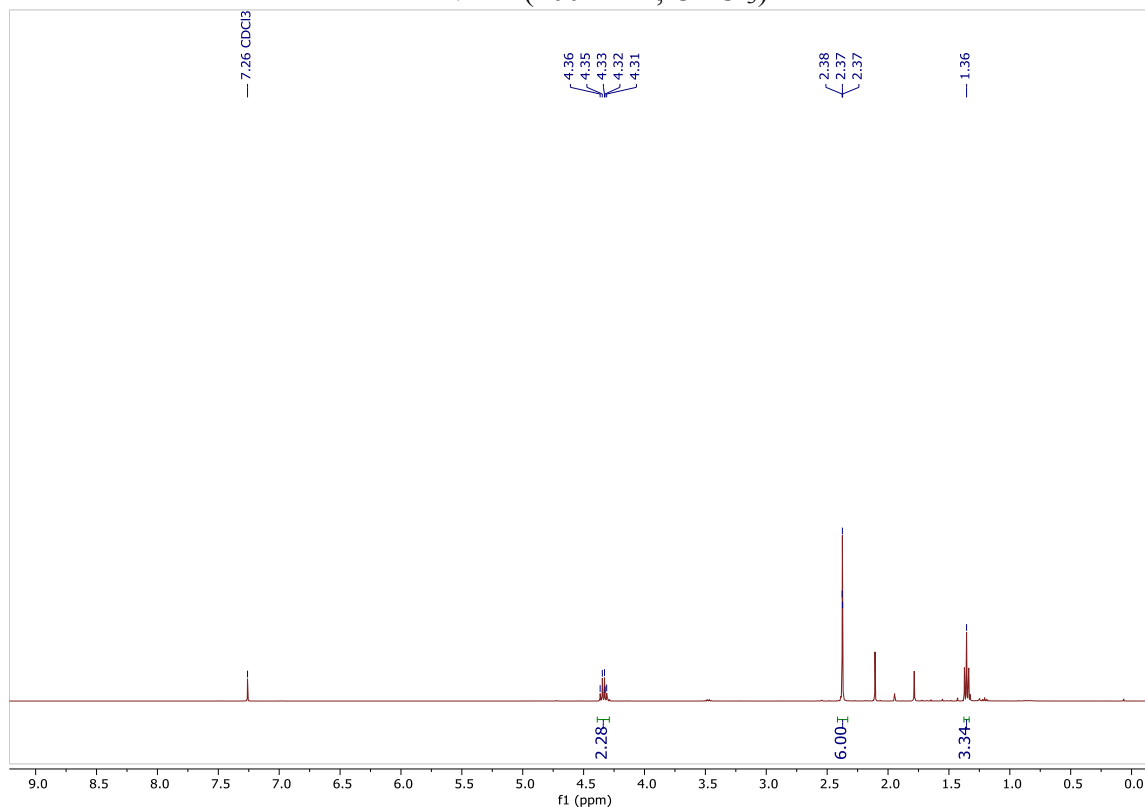
^{13}C NMR (101 MHz, CDCl_3)



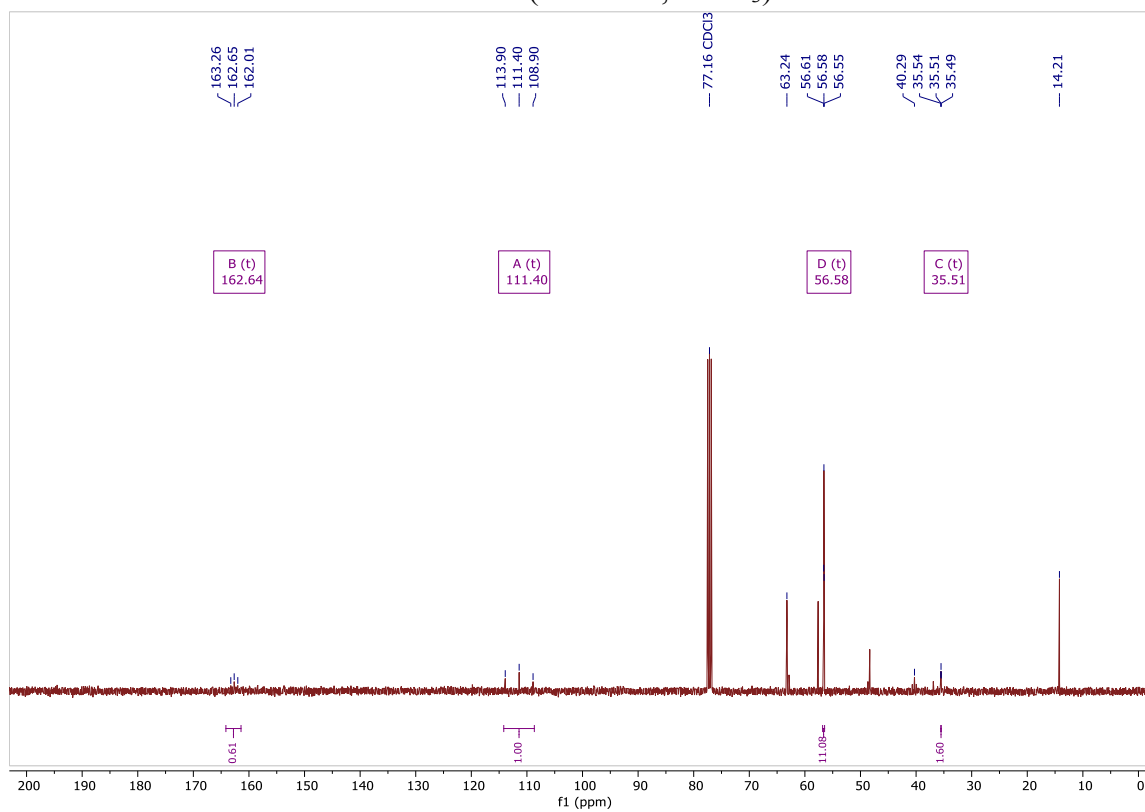
Ethyl 2-(3-bromobicyclo[1.1.1]pentan-1-yl)-2,2-difluoroacetate, 37



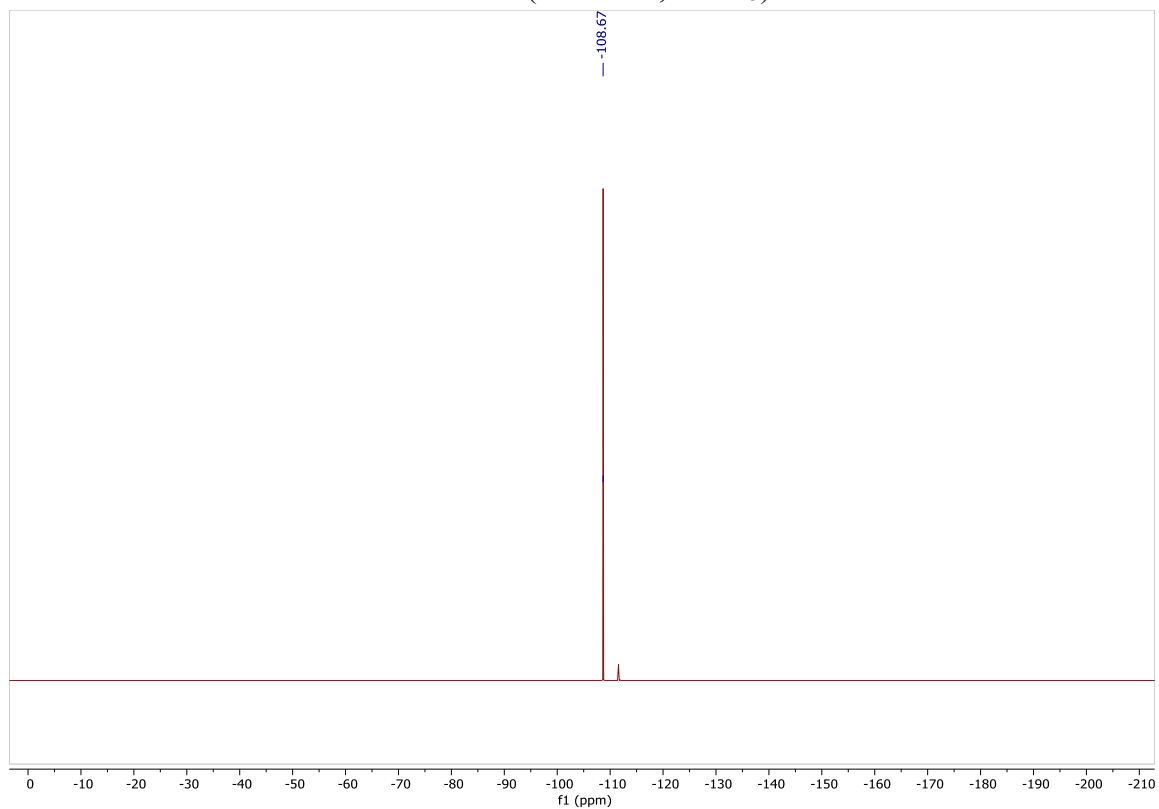
^1H NMR (400 MHz, CDCl_3)



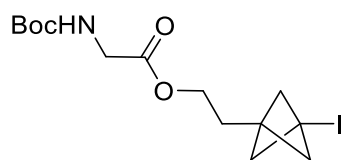
^{13}C NMR (101 MHz, CDCl_3)



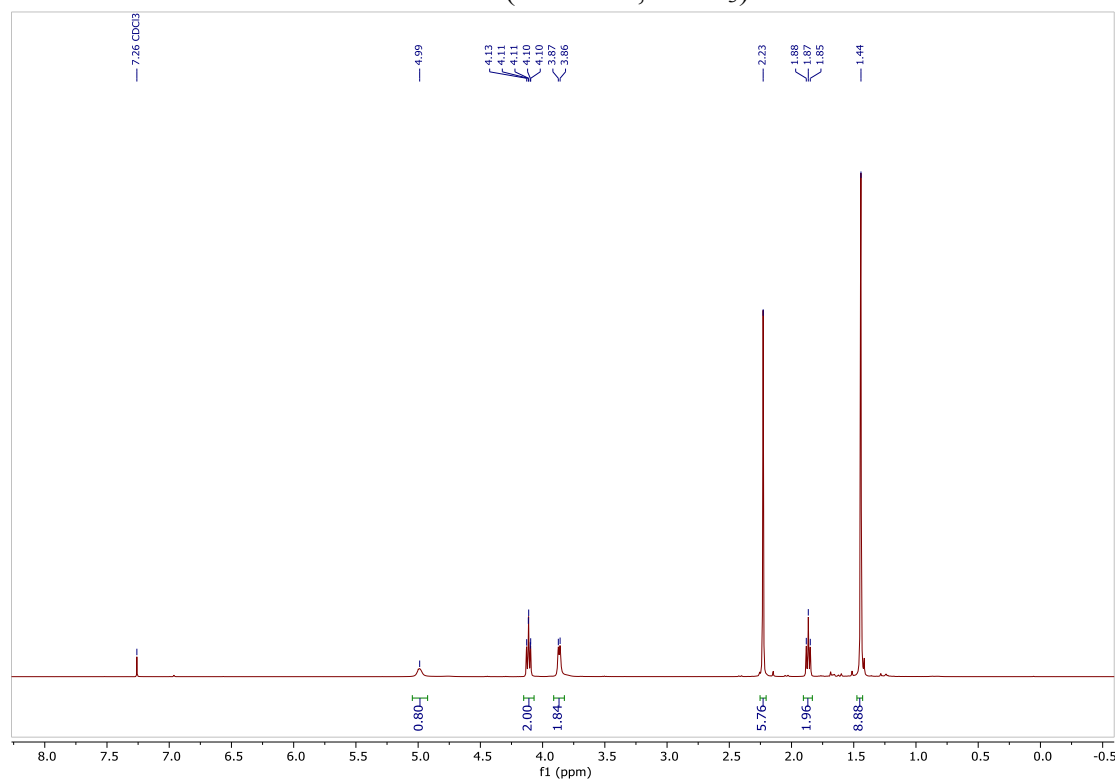
^{19}F NMR (377 MHz, CDCl_3)



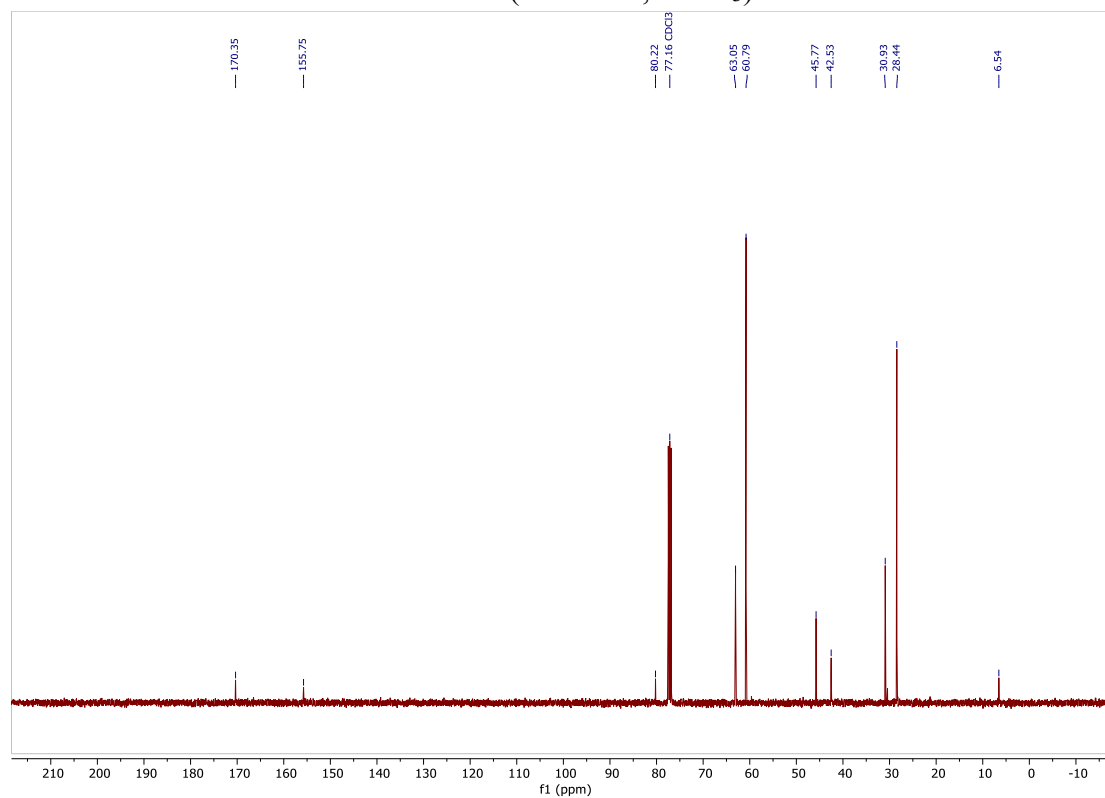
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl (tert-butoxycarbonyl)glycinate, 38



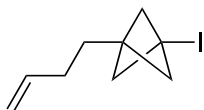
^1H NMR (400 MHz, CDCl_3)



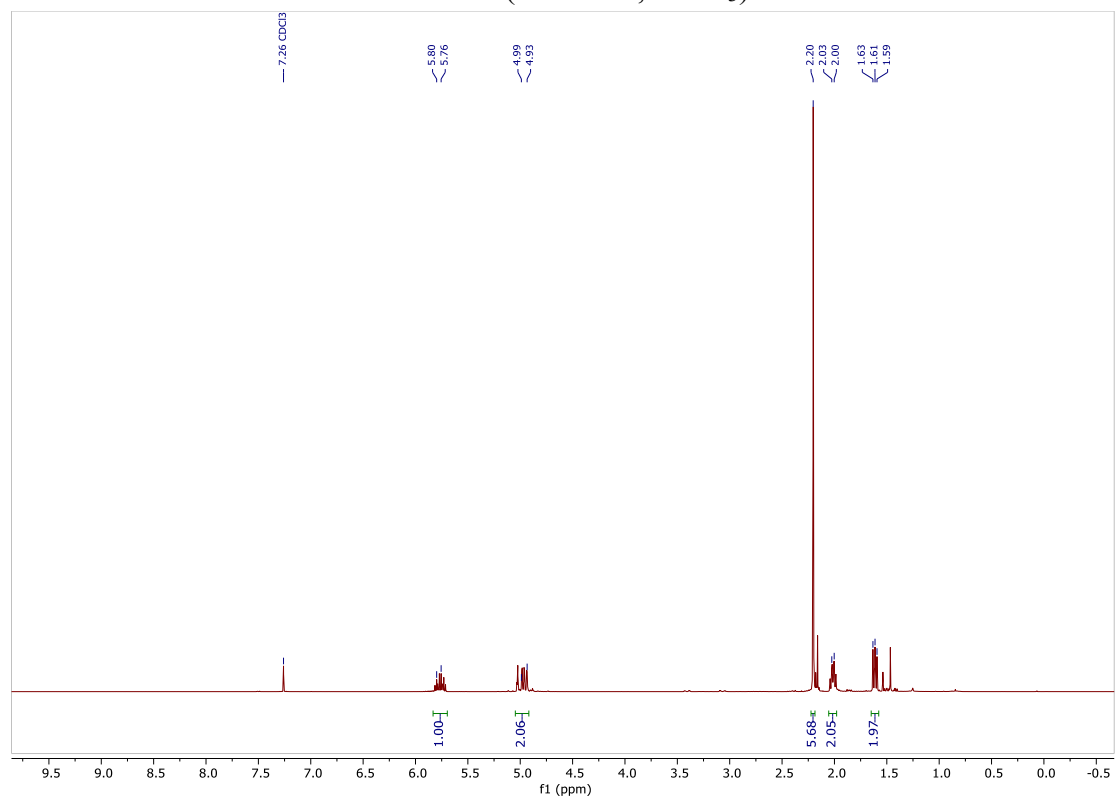
^{13}C NMR (101 MHz, CDCl_3)



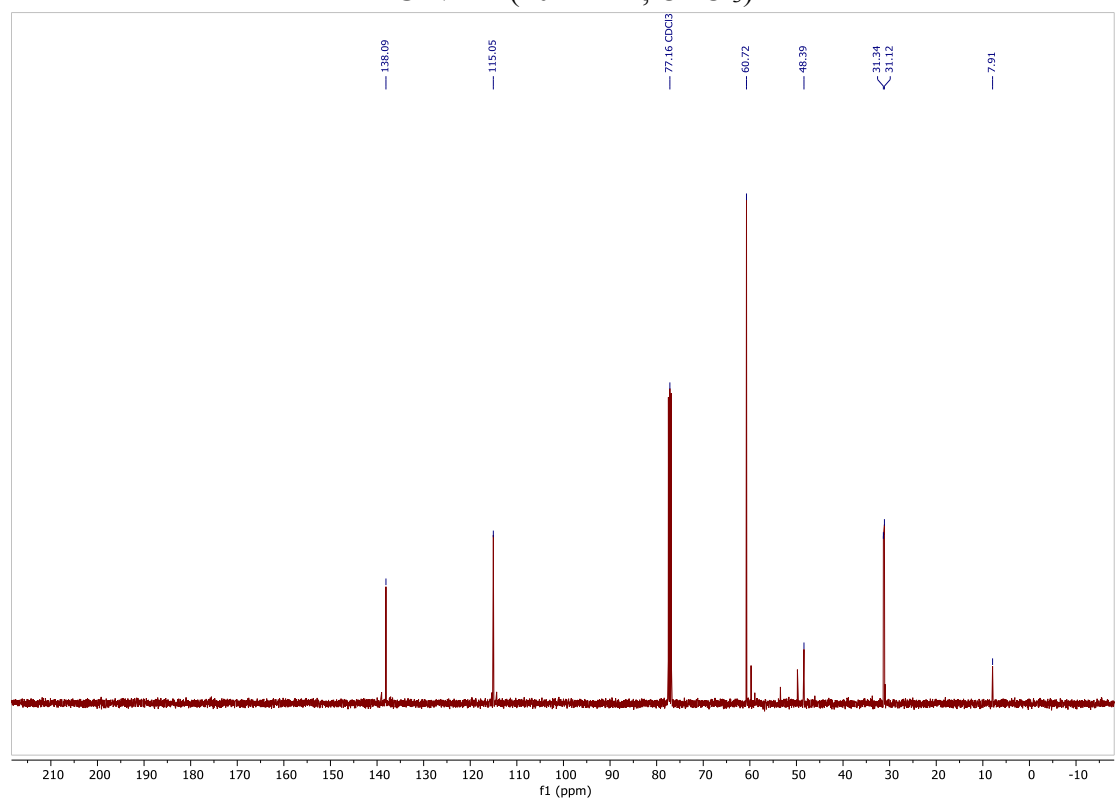
1-(But-3-en-1-yl)-3-iodobicyclo[1.1.1]pentane, 39



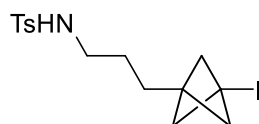
^1H NMR (400 MHz, CDCl_3)



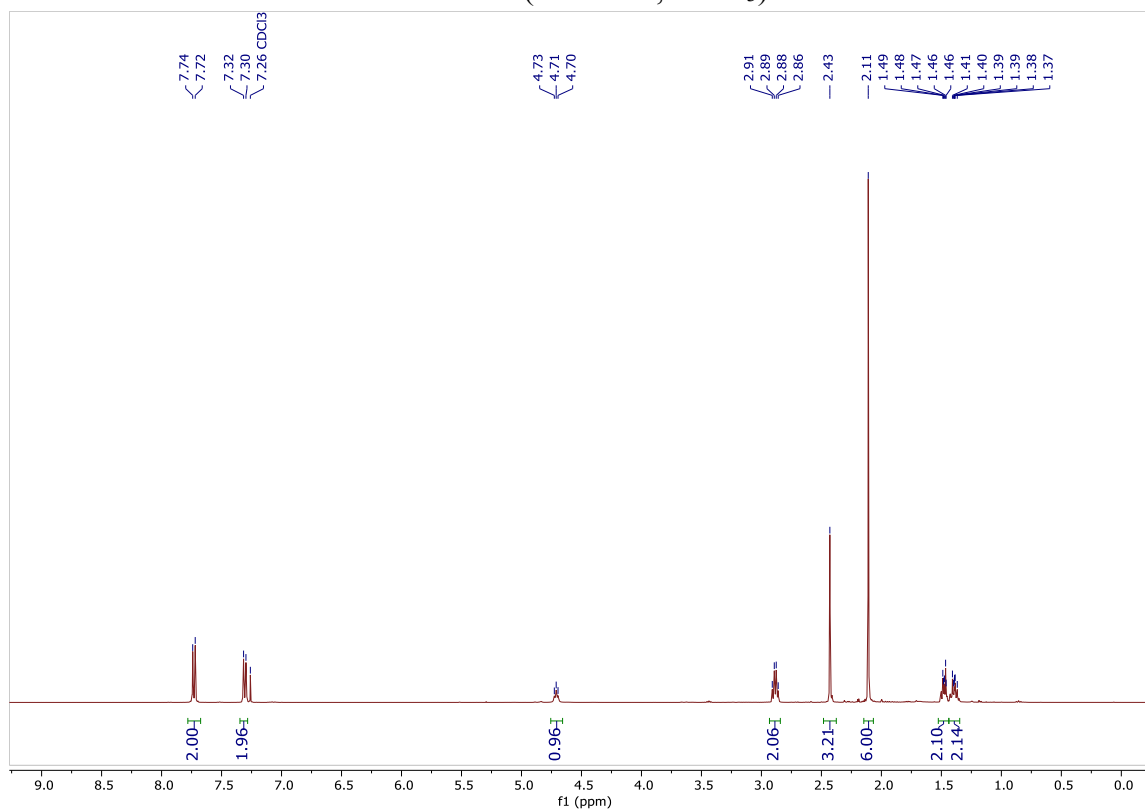
^{13}C NMR (101 MHz, CDCl_3)



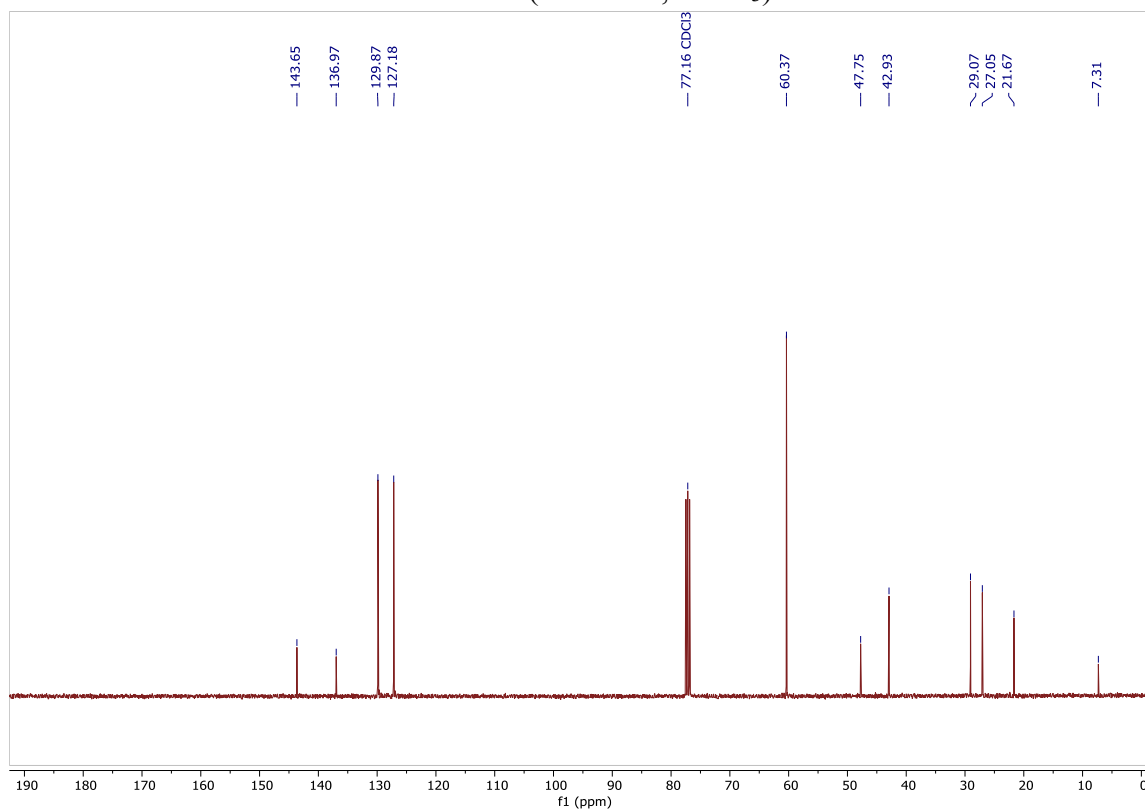
***N*-(3-(3-Iodobicyclo[1.1.1]pentan-1-yl)propyl)-4-methylbenzenesulfonamide, 40**



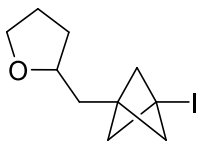
¹H NMR (400 MHz, CDCl₃)



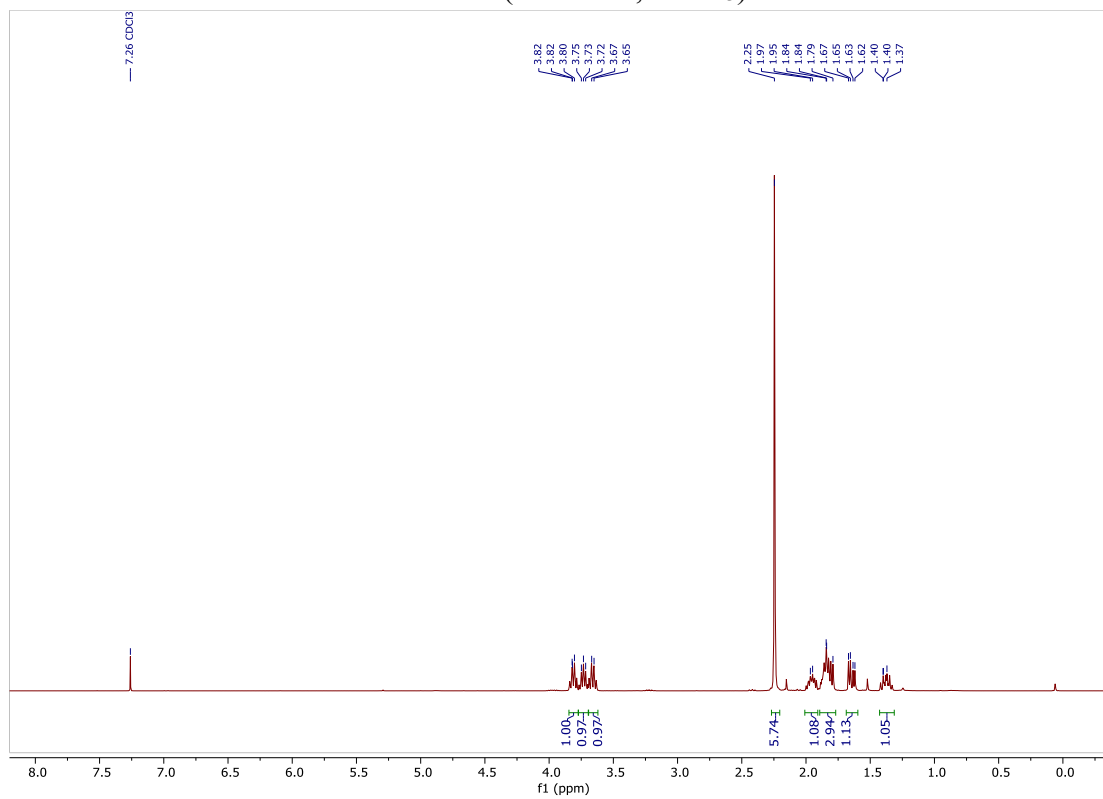
¹³C NMR (101 MHz, CDCl₃)



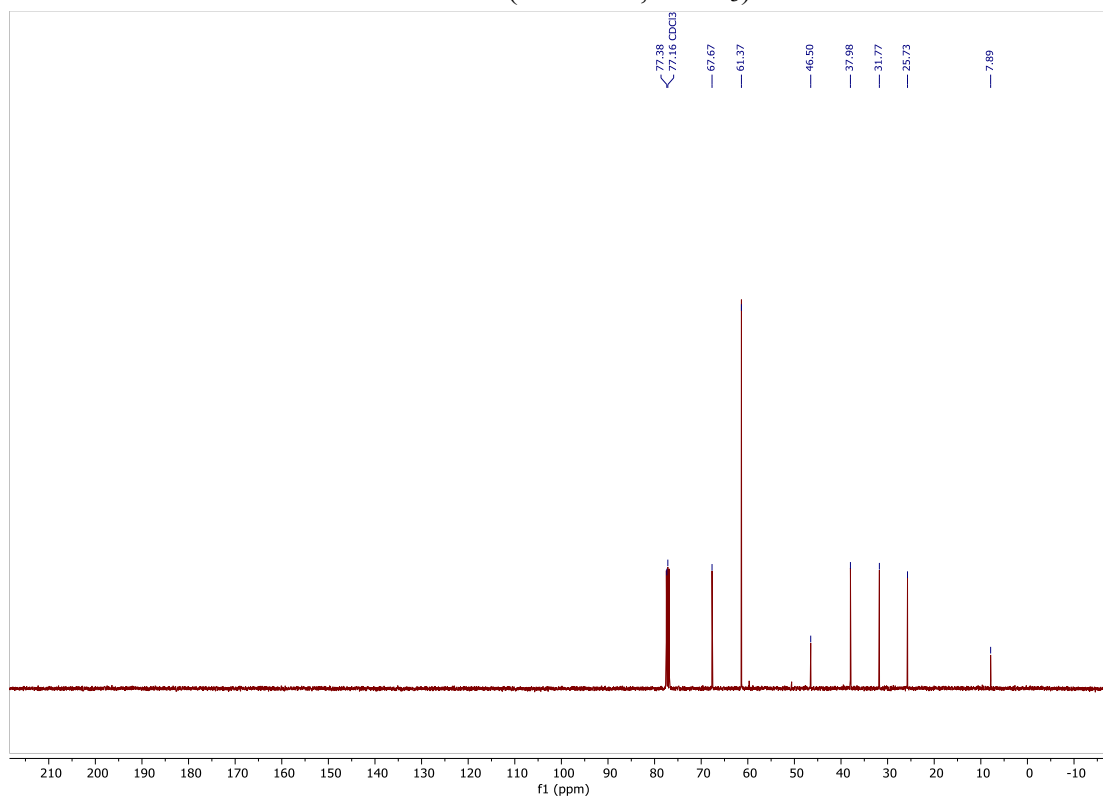
2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)tetrahydrofuran, 41



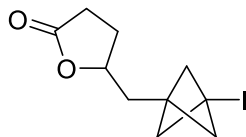
^1H NMR (400 MHz, CDCl_3)



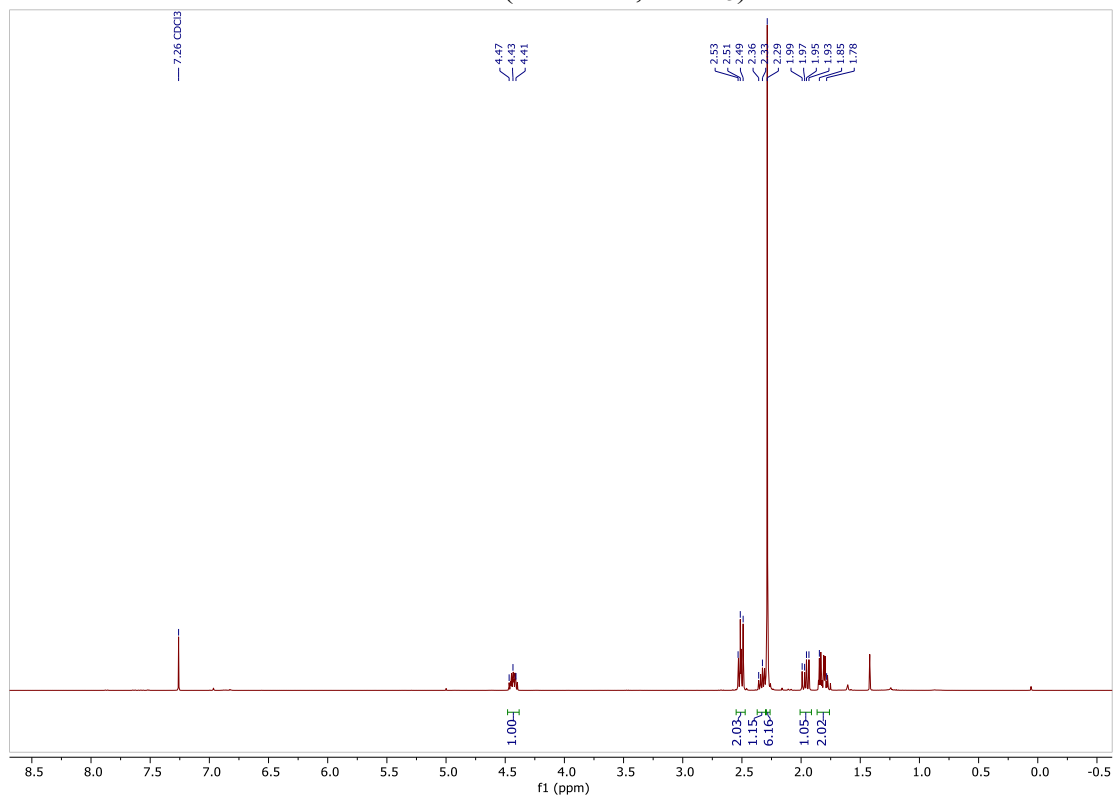
^{13}C NMR (101 MHz, CDCl_3)



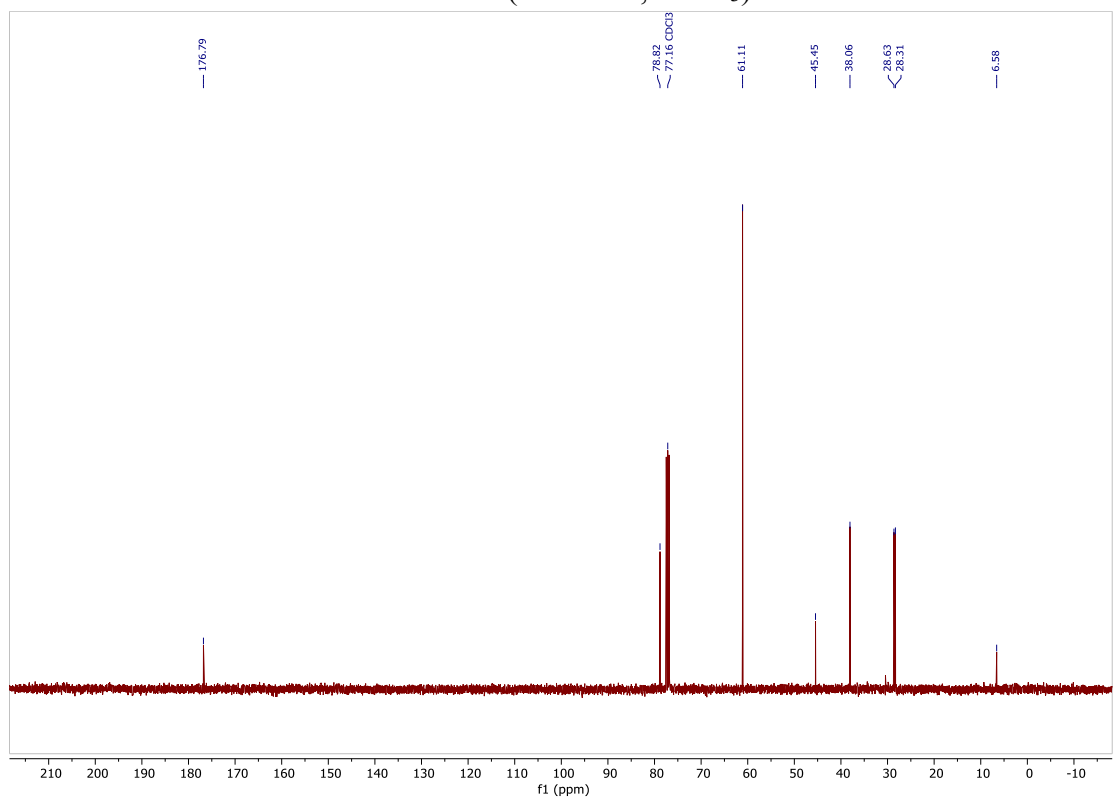
5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)dihydrofuran-2(3H)-one, 42



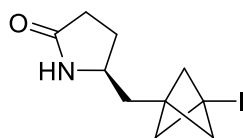
^1H NMR (400 MHz, CDCl_3)



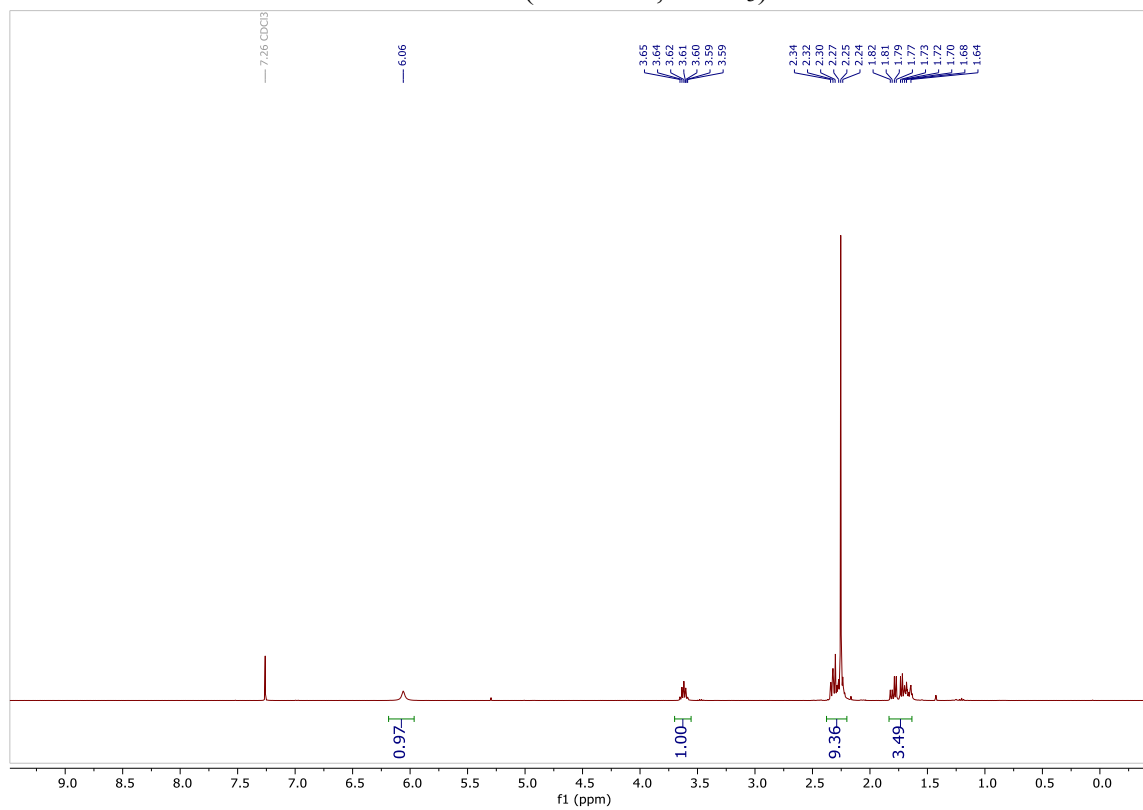
^{13}C NMR (101 MHz, CDCl_3)



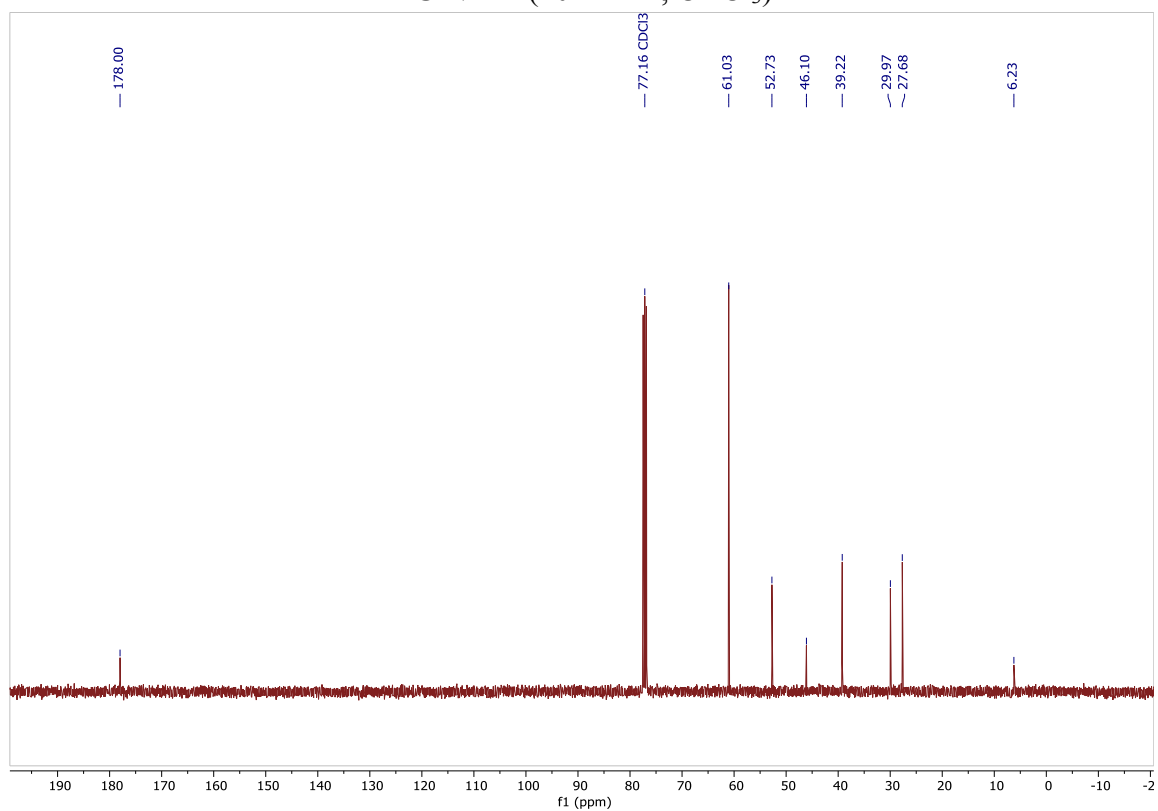
(S)-5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)pyrrolidin-2-one, 43



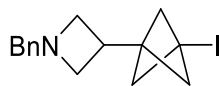
^1H NMR (400 MHz, CDCl_3)



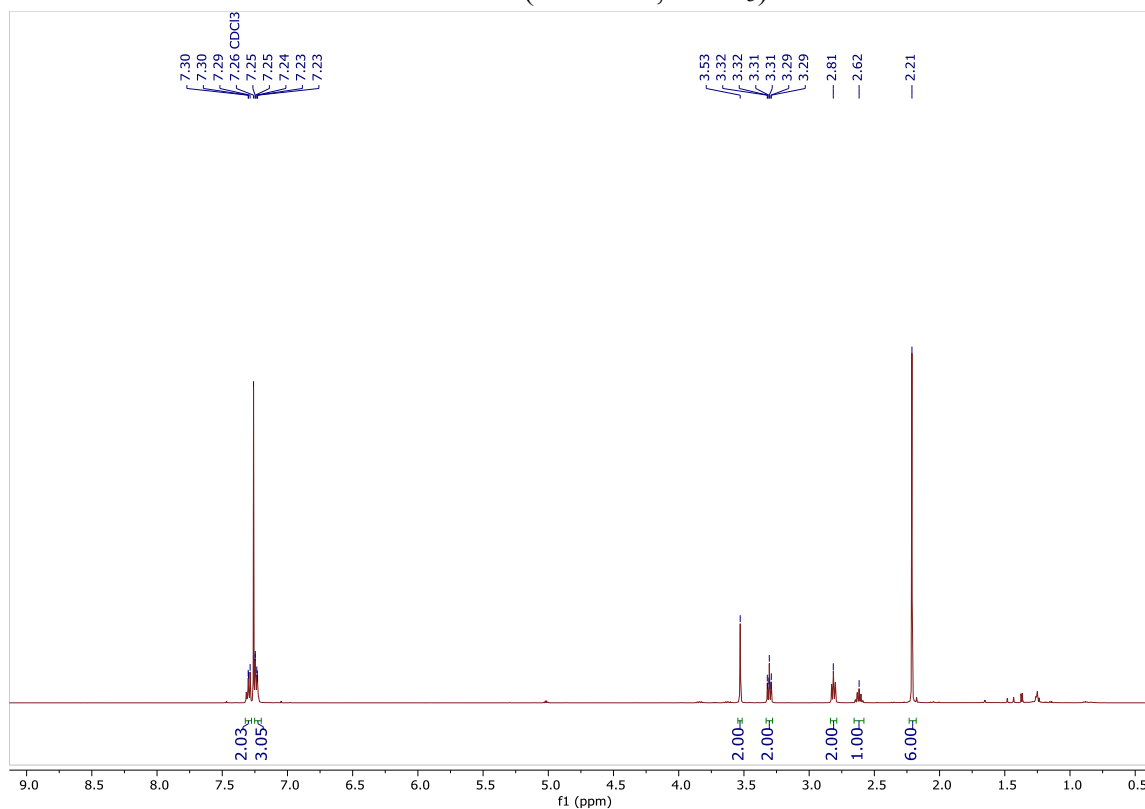
^{13}C NMR (101 MHz, CDCl_3)



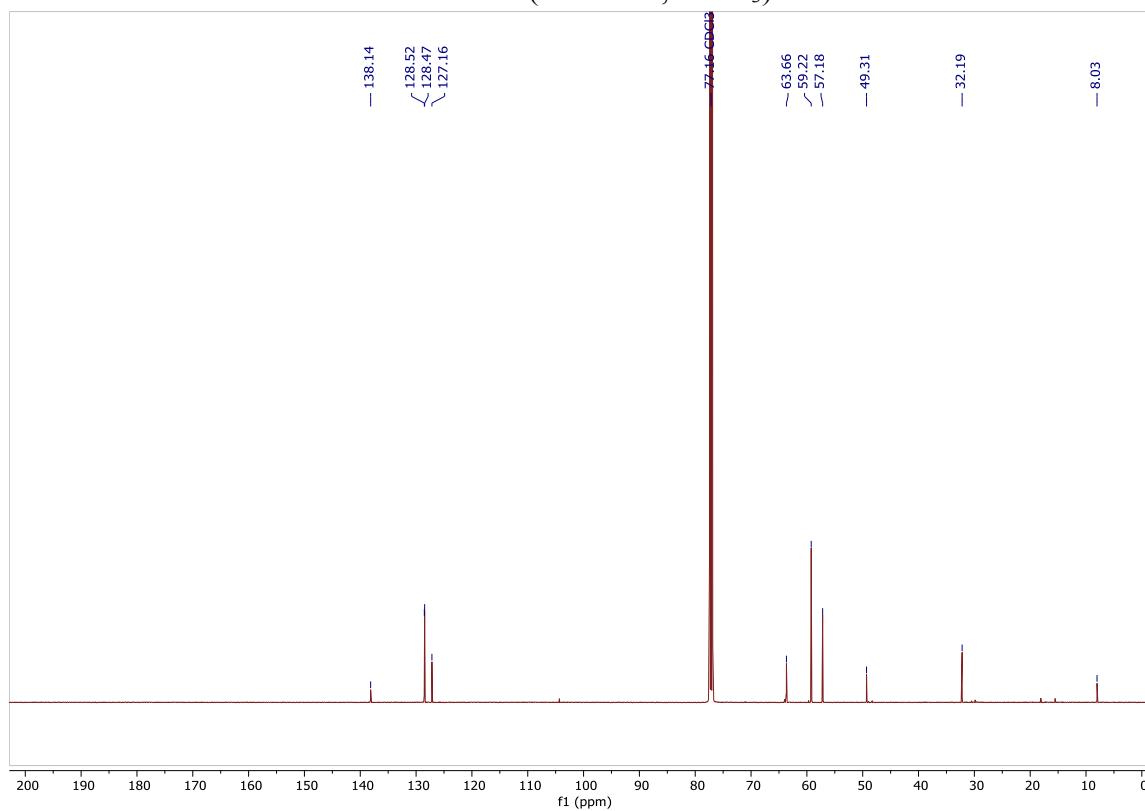
1-Benzyl-3-(3-iodobicyclo[1.1.1]pentan-1-yl)azetidine, 44



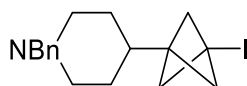
^1H NMR (500 MHz, CDCl_3)



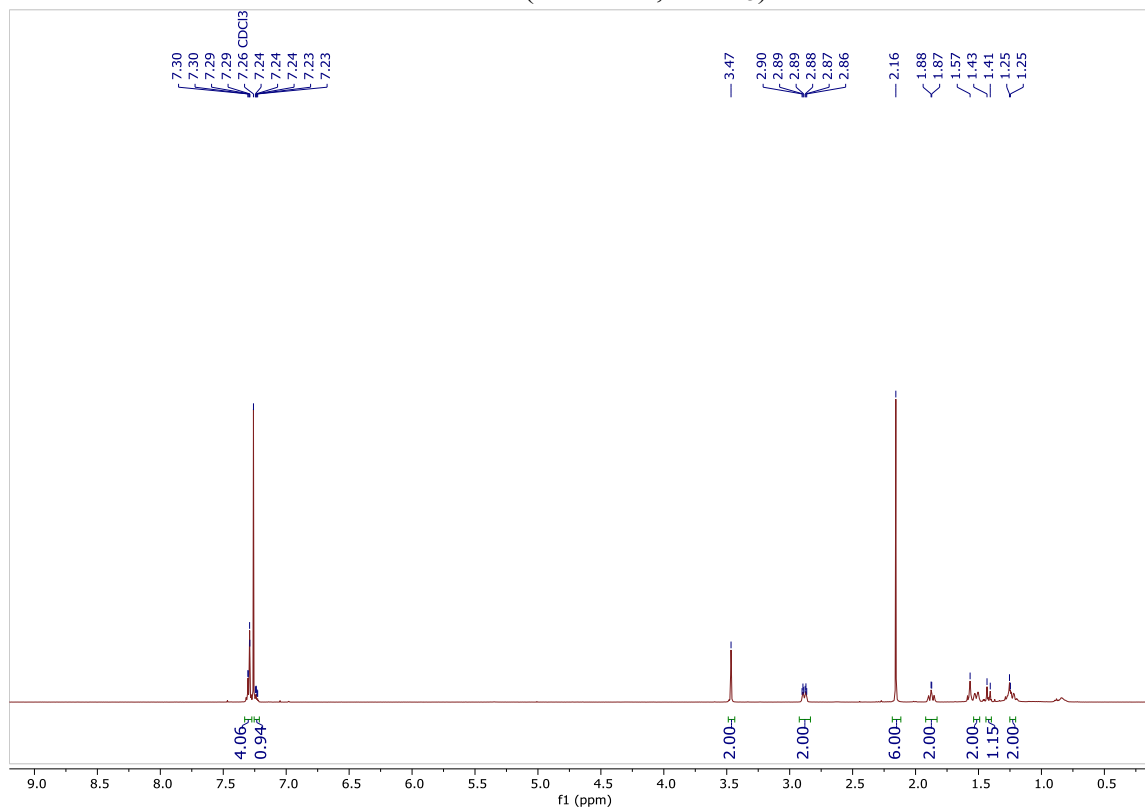
^{13}C NMR (125 MHz, CDCl_3)



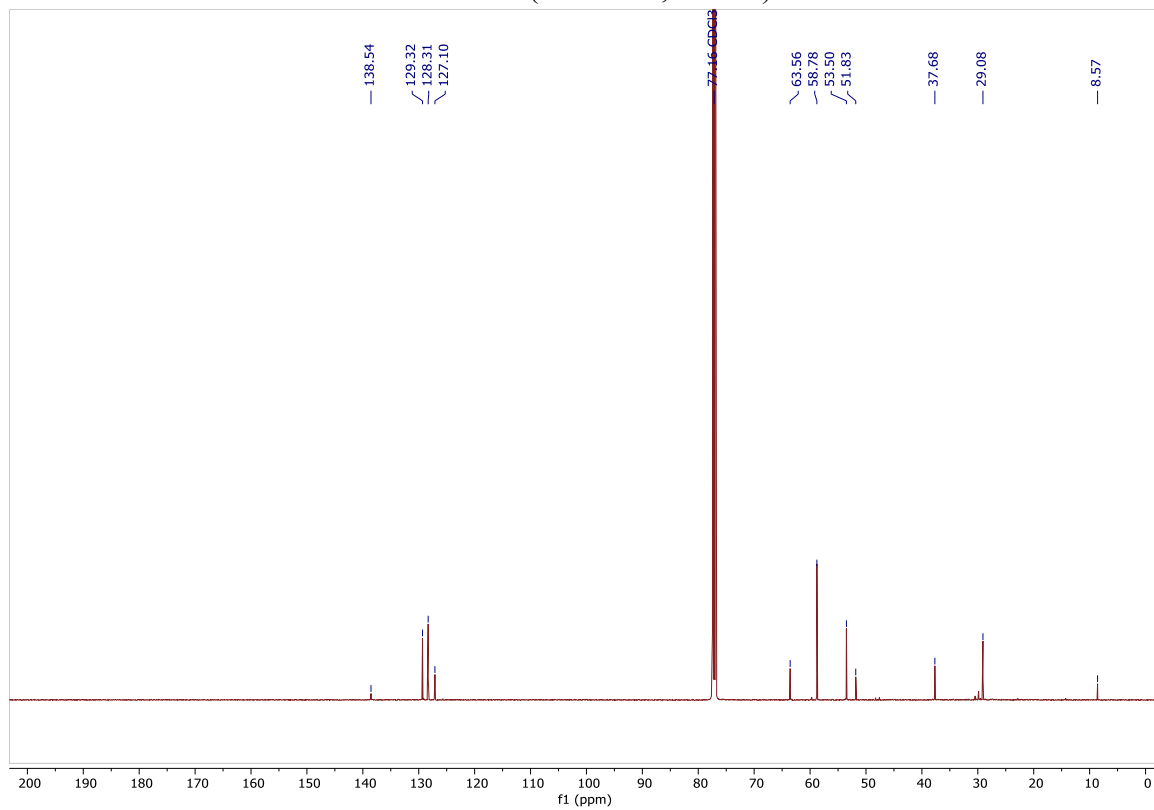
1-Benzyl-4-(3-iodobicyclo[1.1.1]pentan-1-yl)piperidine, 45



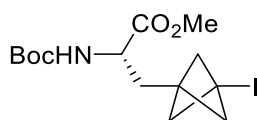
^1H NMR (500 MHz, CDCl_3)



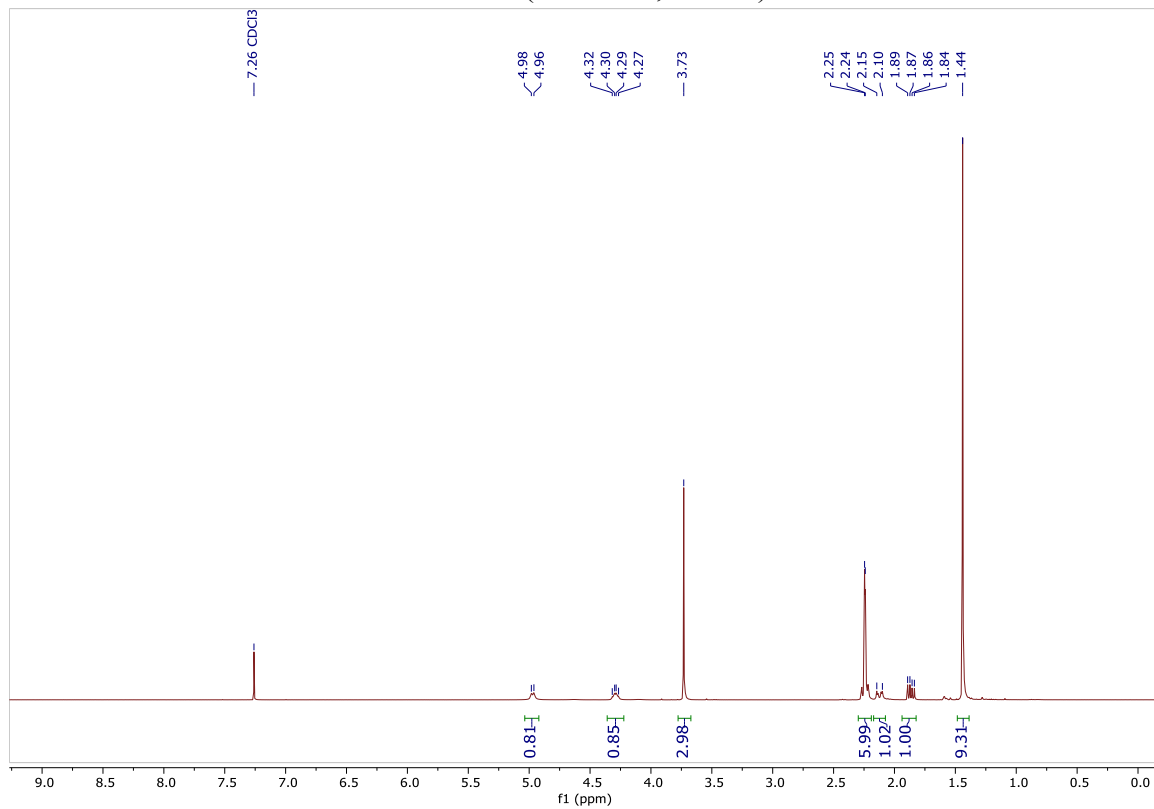
^{13}C NMR (125 MHz, CDCl_3)



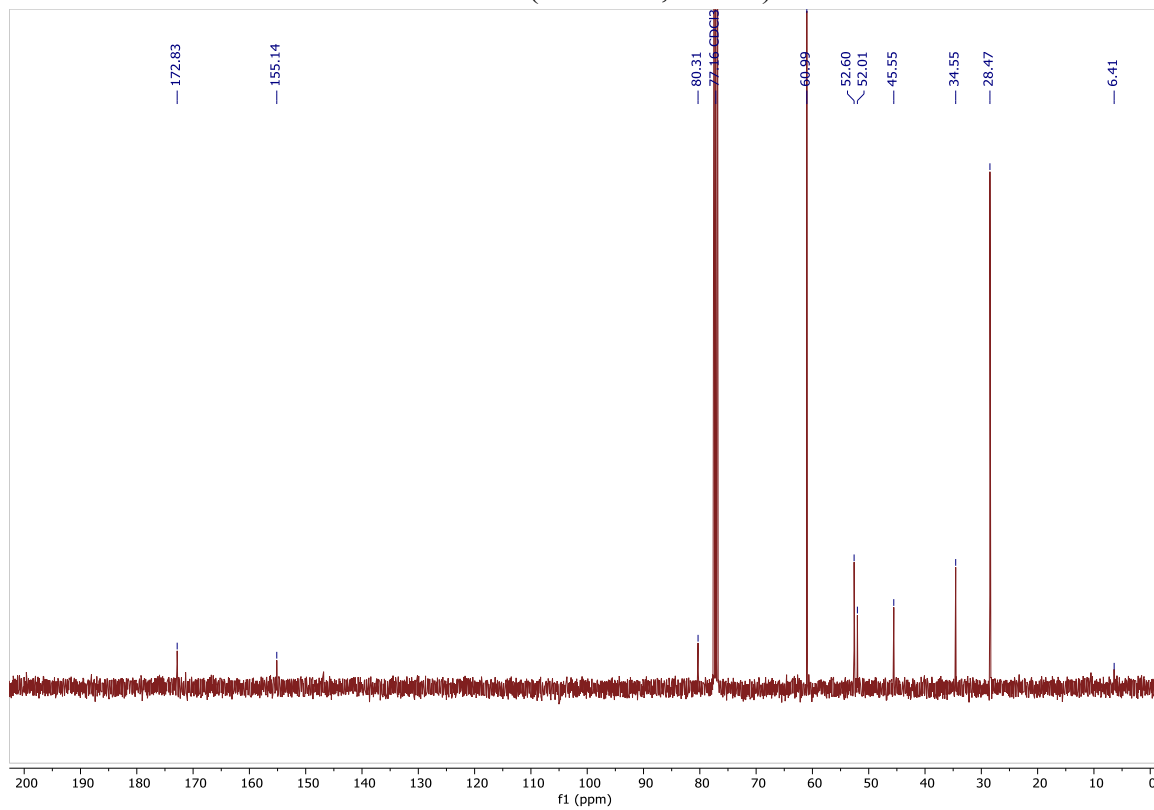
***N*-Boc- β -(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, 46**



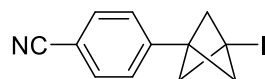
^1H NMR (400 MHz, CDCl_3)



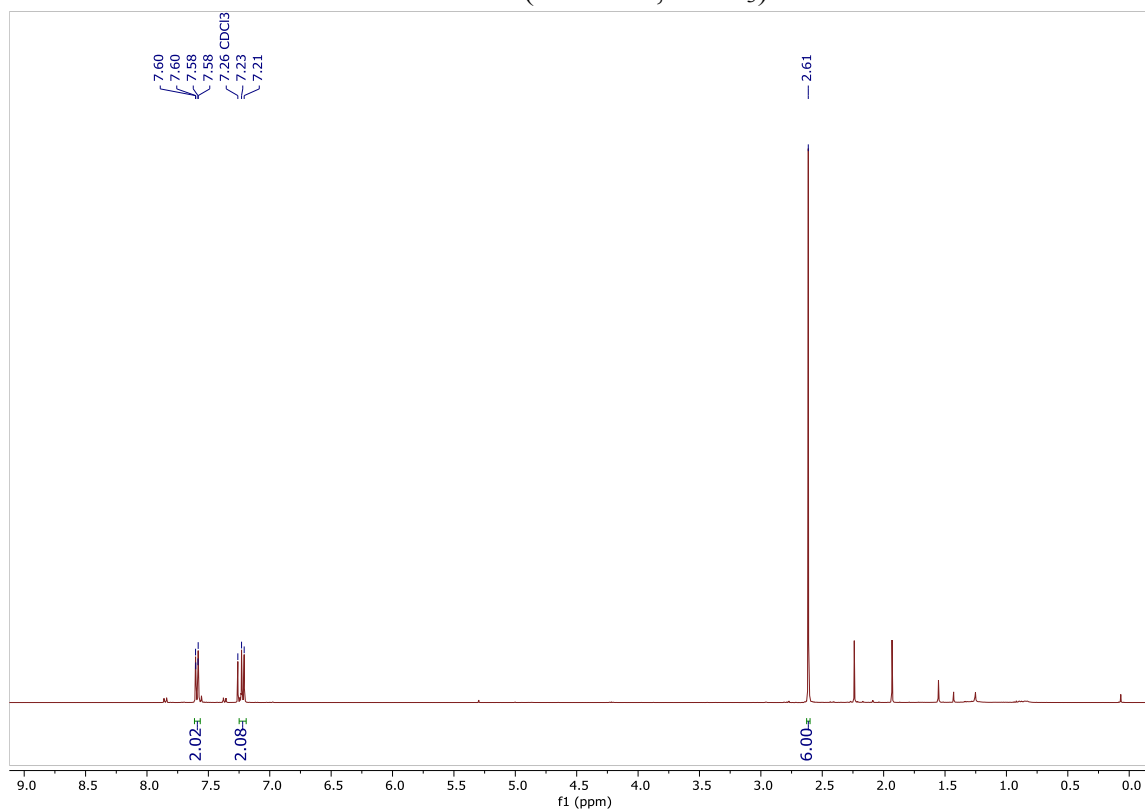
^{13}C NMR (101 MHz, CDCl_3)



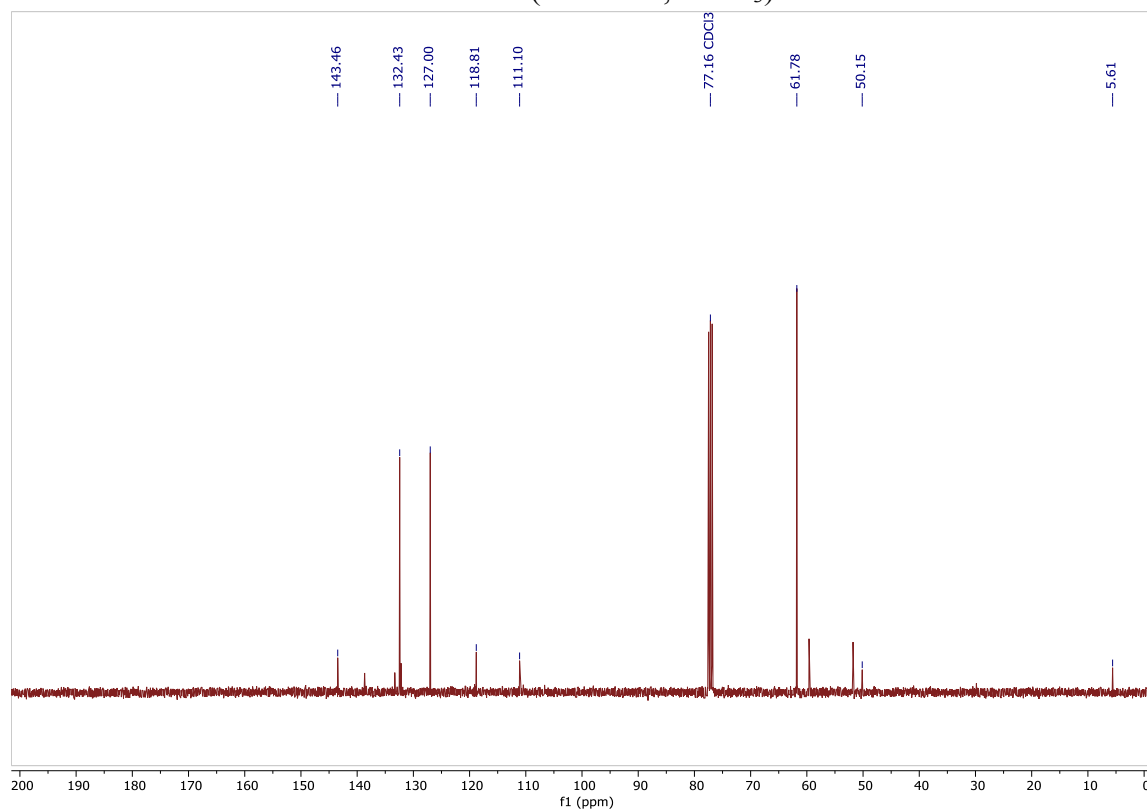
4-(3-Iodobicyclo[1.1.1]pentan-1-yl)benzonitrile, 47



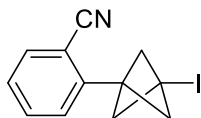
^1H NMR (400 MHz, CDCl_3)



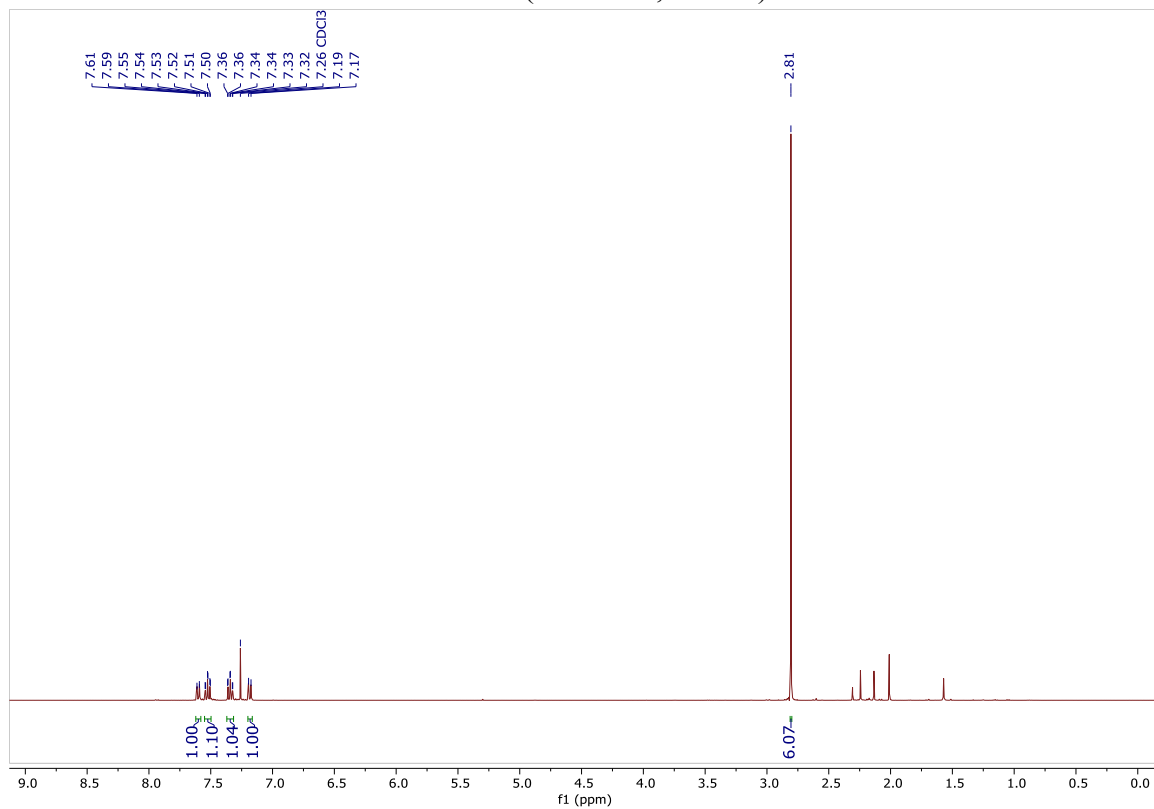
^{13}C NMR (101 MHz, CDCl_3)



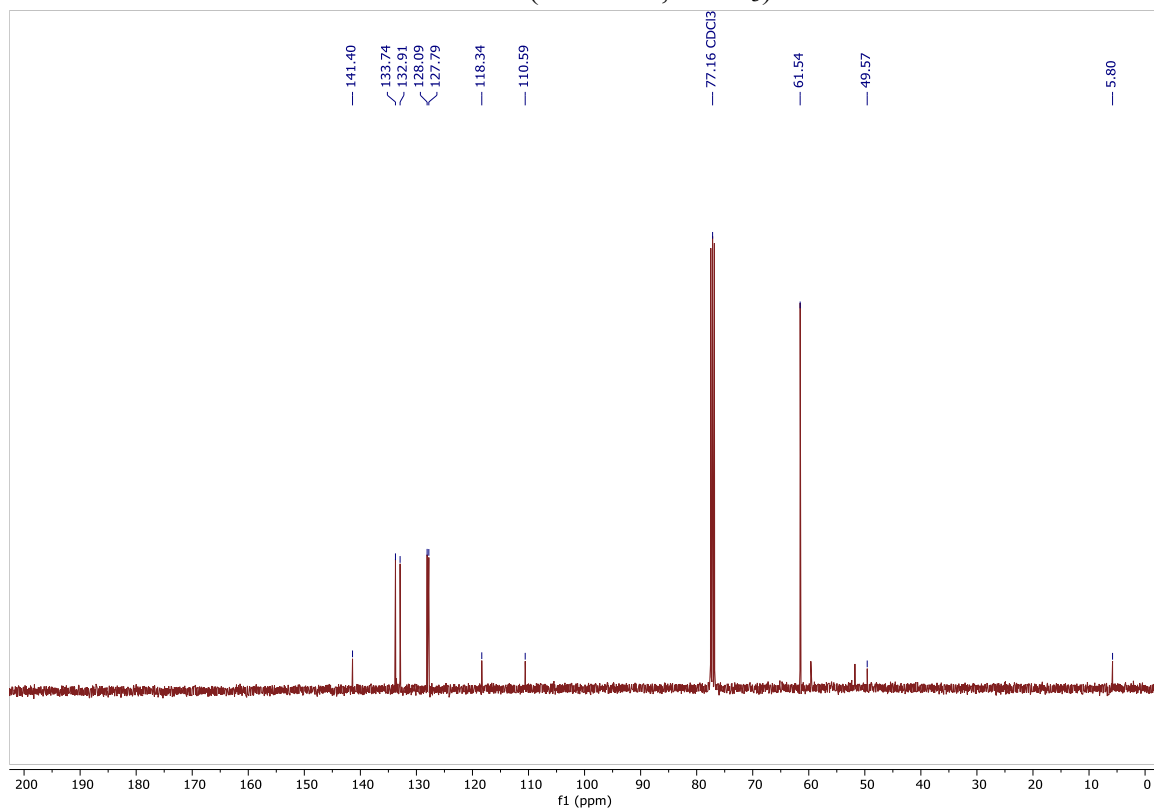
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)benzonitrile, 48



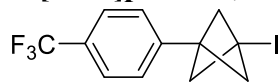
^1H NMR (400 MHz, CDCl_3)



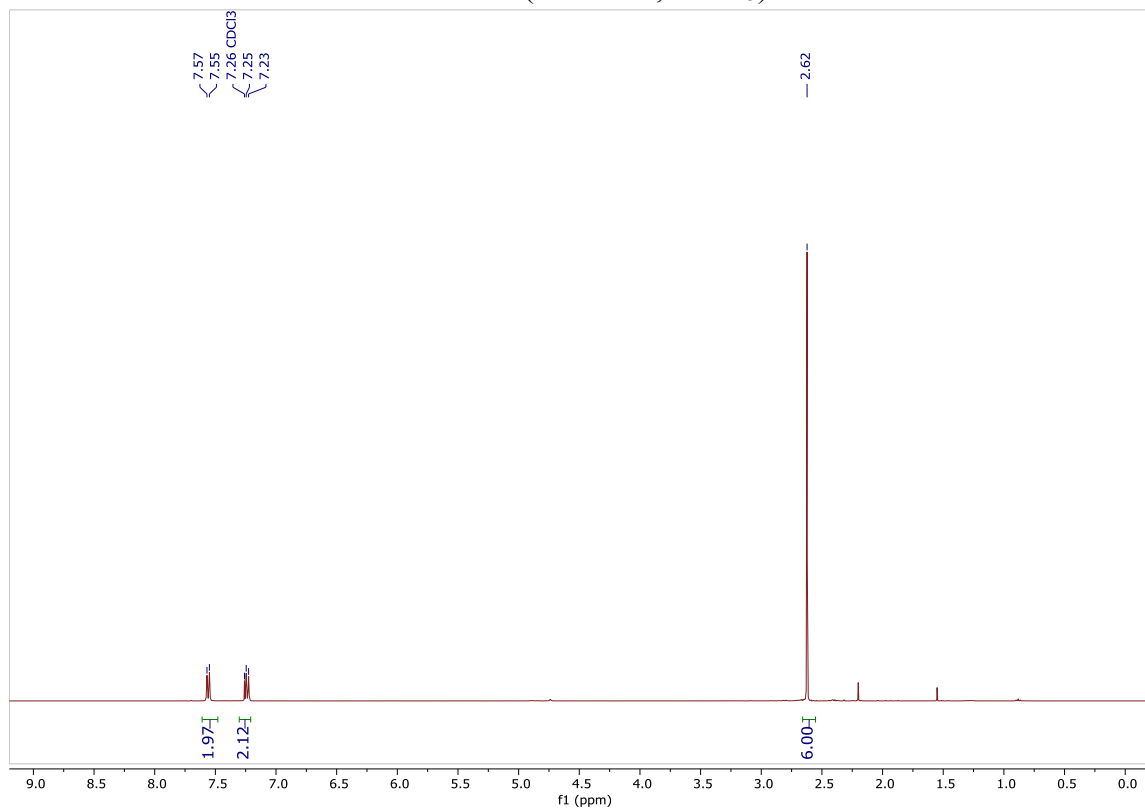
^{13}C NMR (101 MHz, CDCl_3)



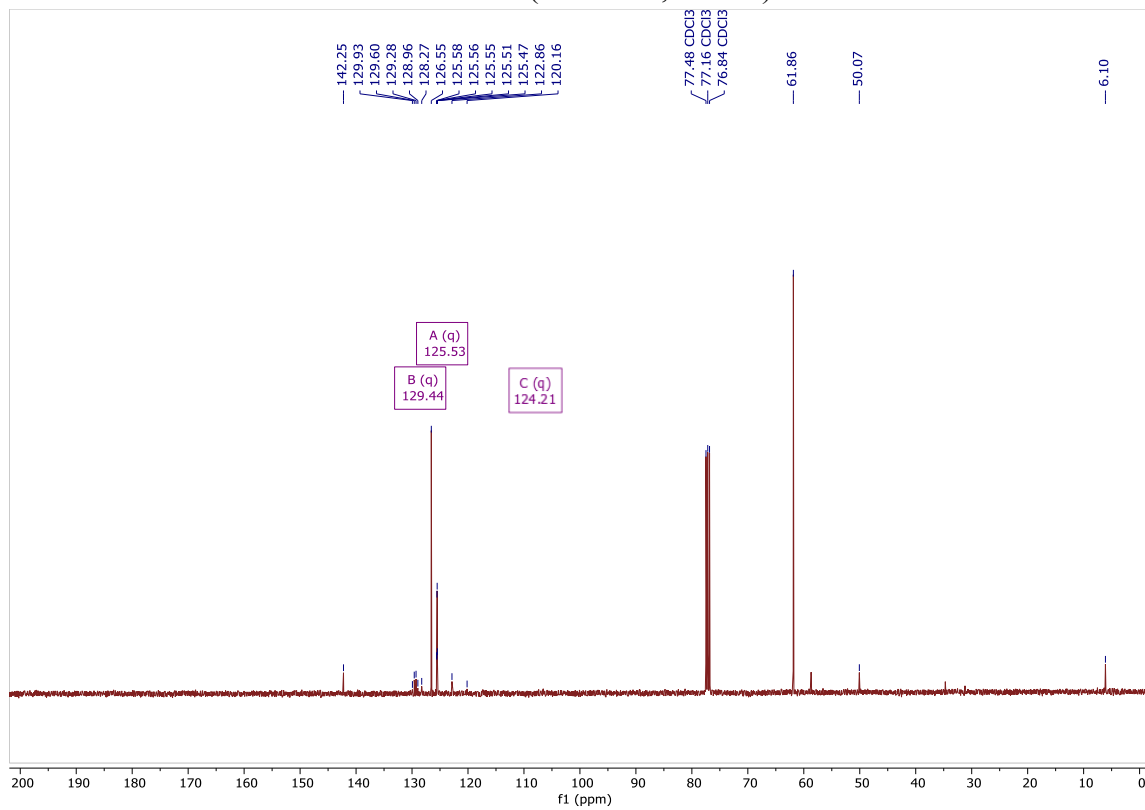
1-Iodo-3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.1]pentane, 49



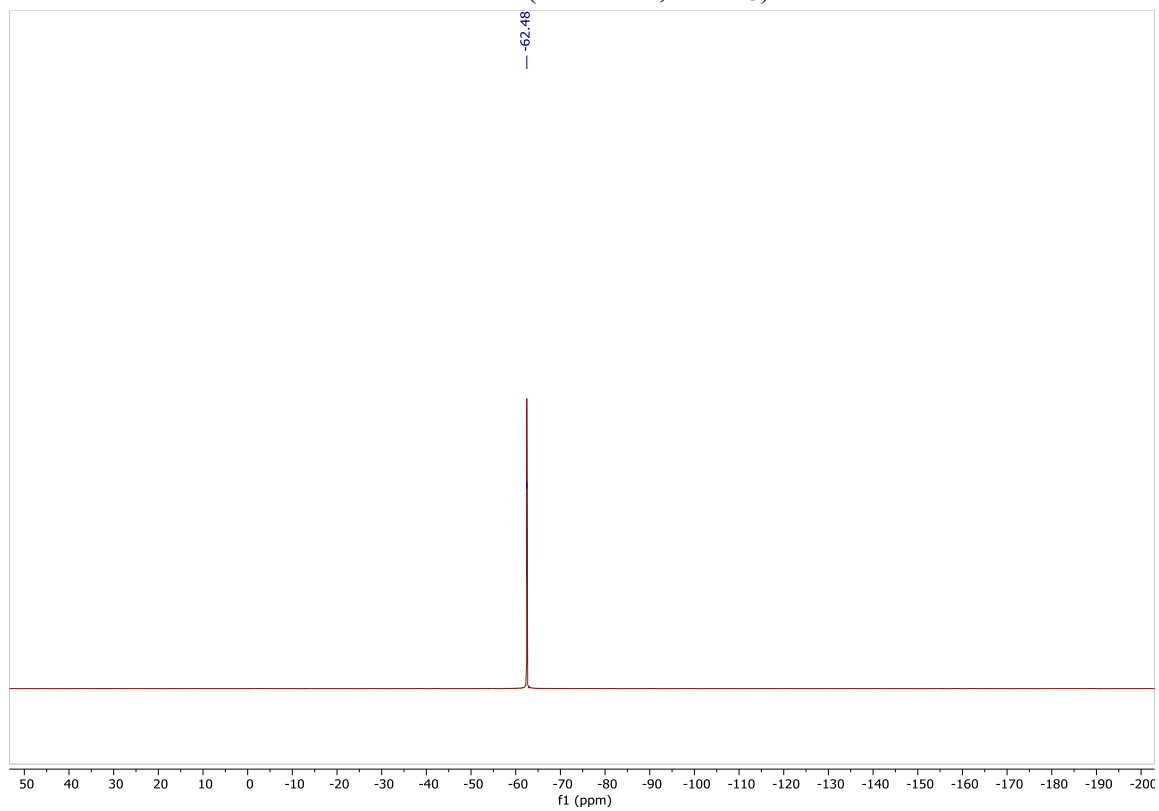
^1H NMR (400 MHz, CDCl_3)



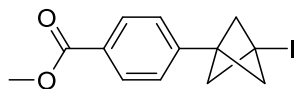
^{13}C NMR (101 MHz, CDCl_3)



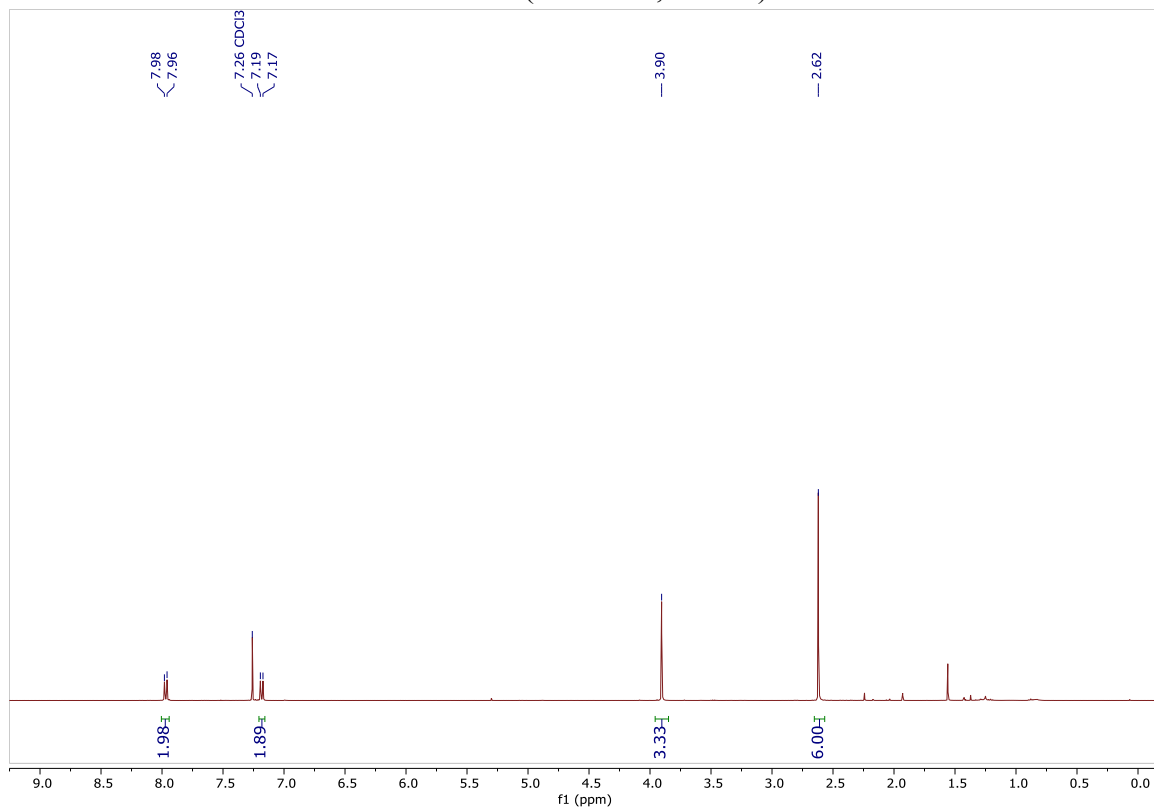
^{19}F NMR (377 MHz, CDCl_3)



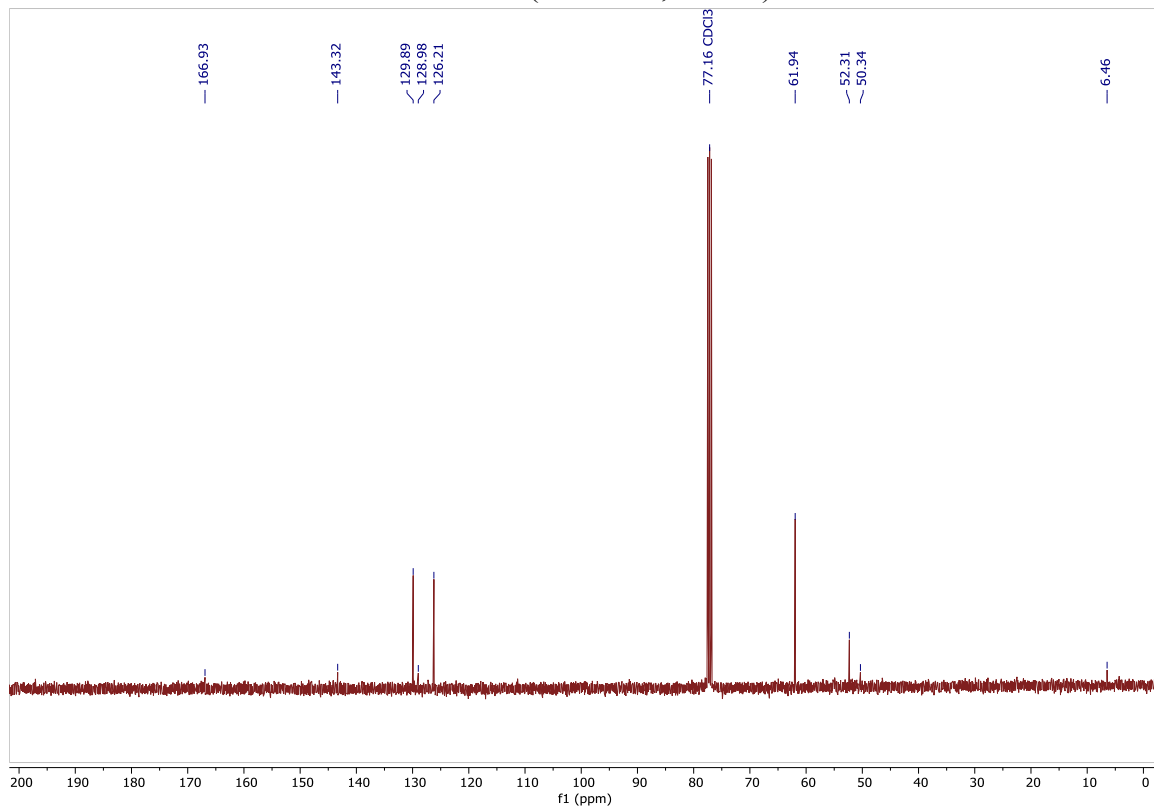
Methyl 4-(3-iodobicyclo[1.1.1]pentan-1-yl)benzoate, 50



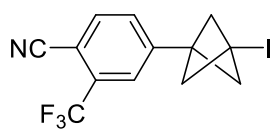
^1H NMR (400 MHz, CDCl_3)



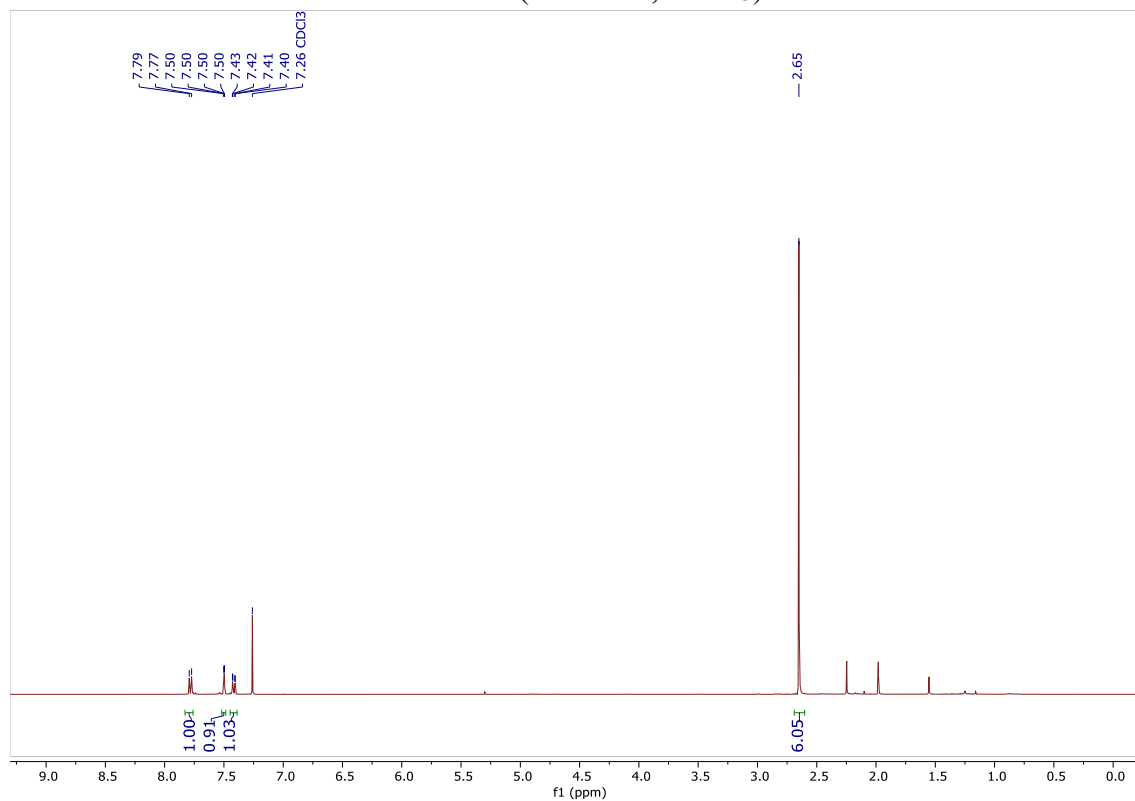
^{13}C NMR (101 MHz, CDCl_3)



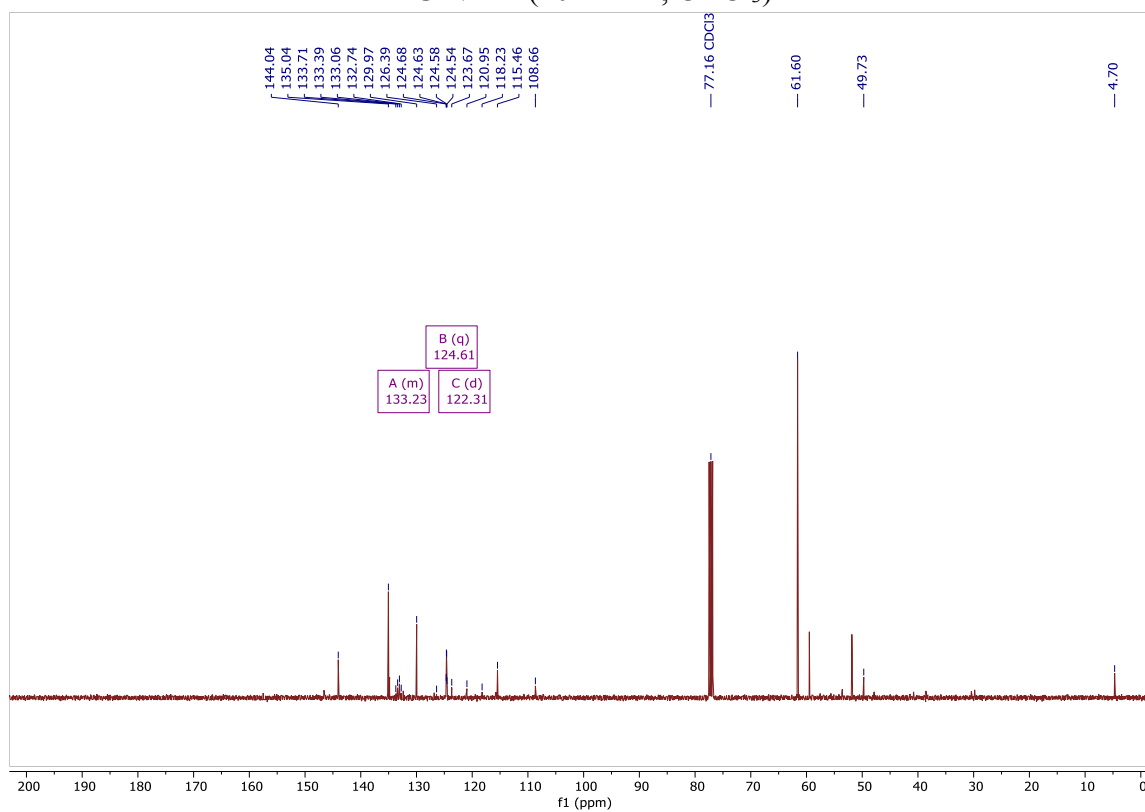
4-(3-Iodobicyclo[1.1.1]pentan-1-yl)-2-(trifluoromethyl)benzonitrile, 51



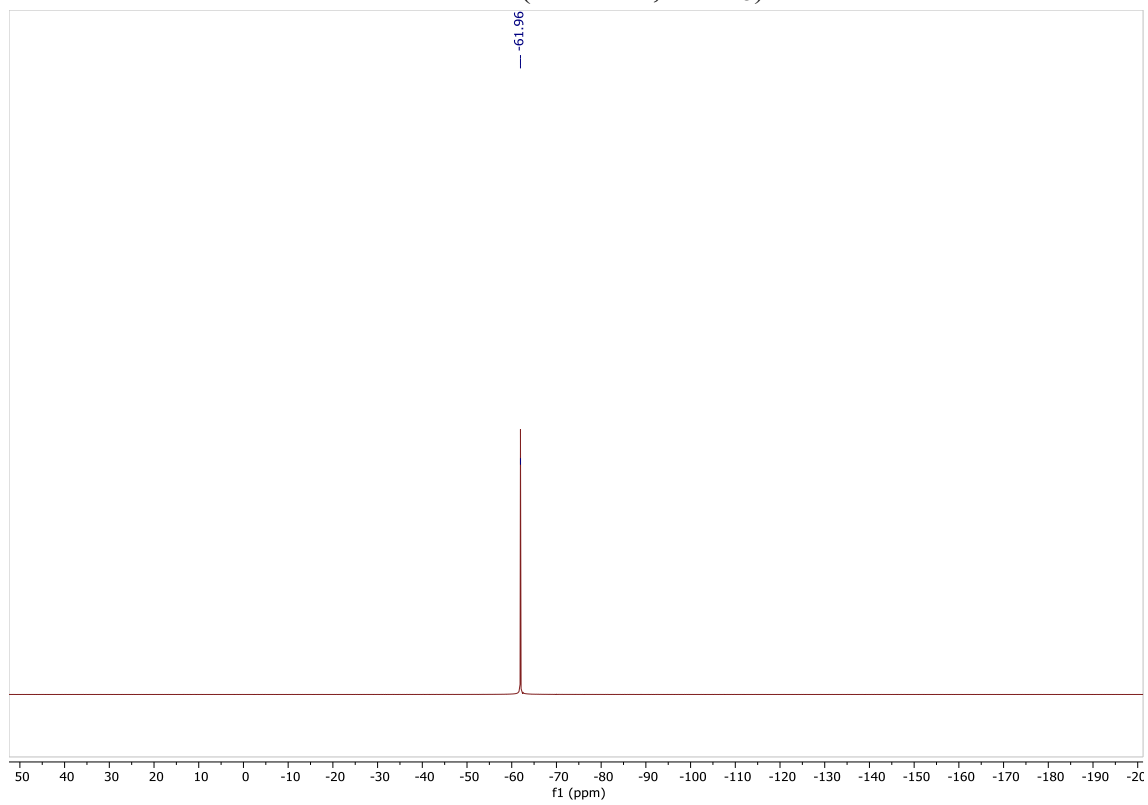
¹H NMR (400 MHz, CDCl₃)



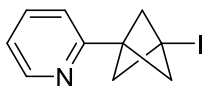
¹³C NMR (101 MHz, CDCl₃)



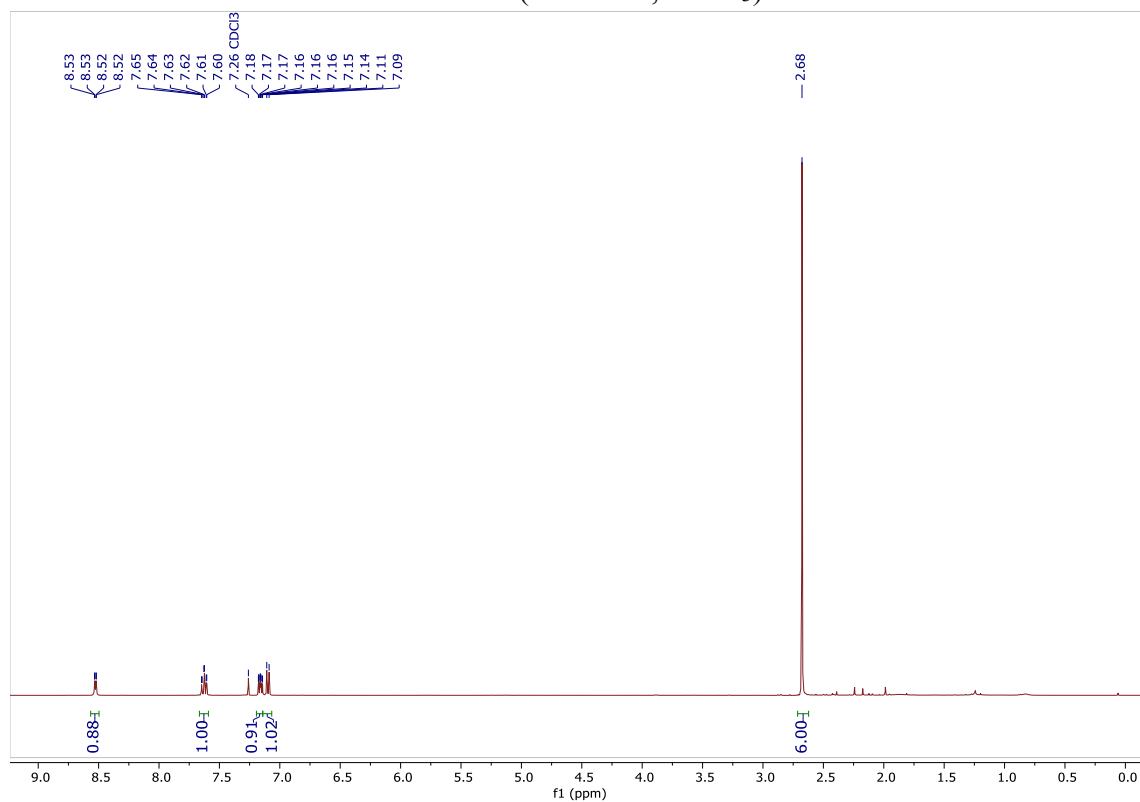
^{19}F NMR (377 MHz, CDCl_3)



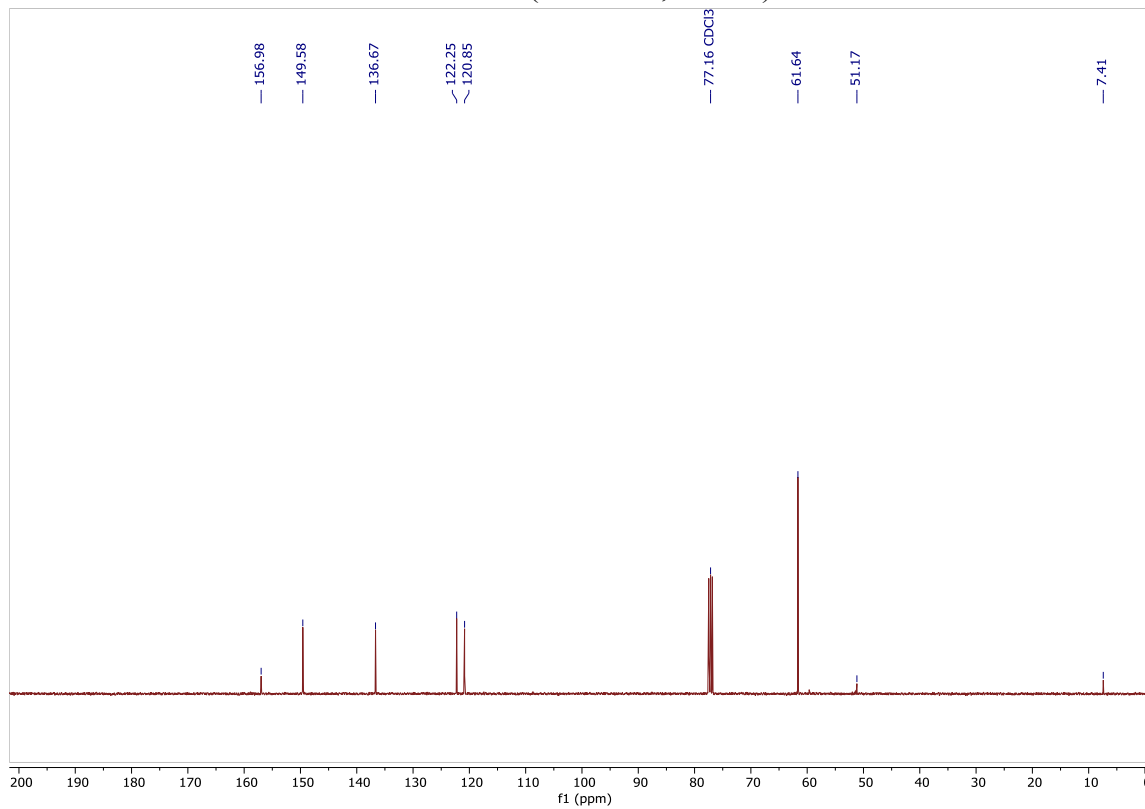
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)pyridine, 52



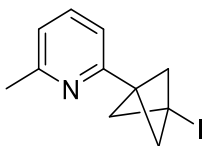
¹H NMR (400 MHz, CDCl₃)



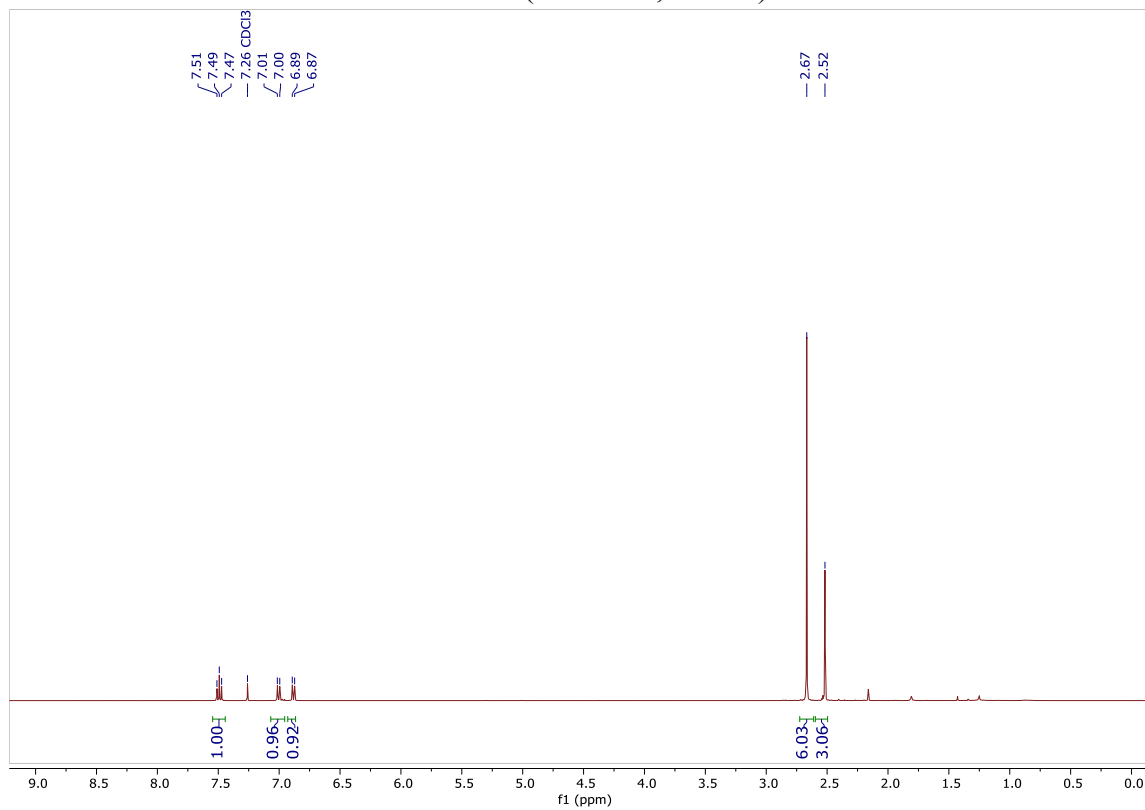
¹³C NMR (101 MHz, CDCl₃)



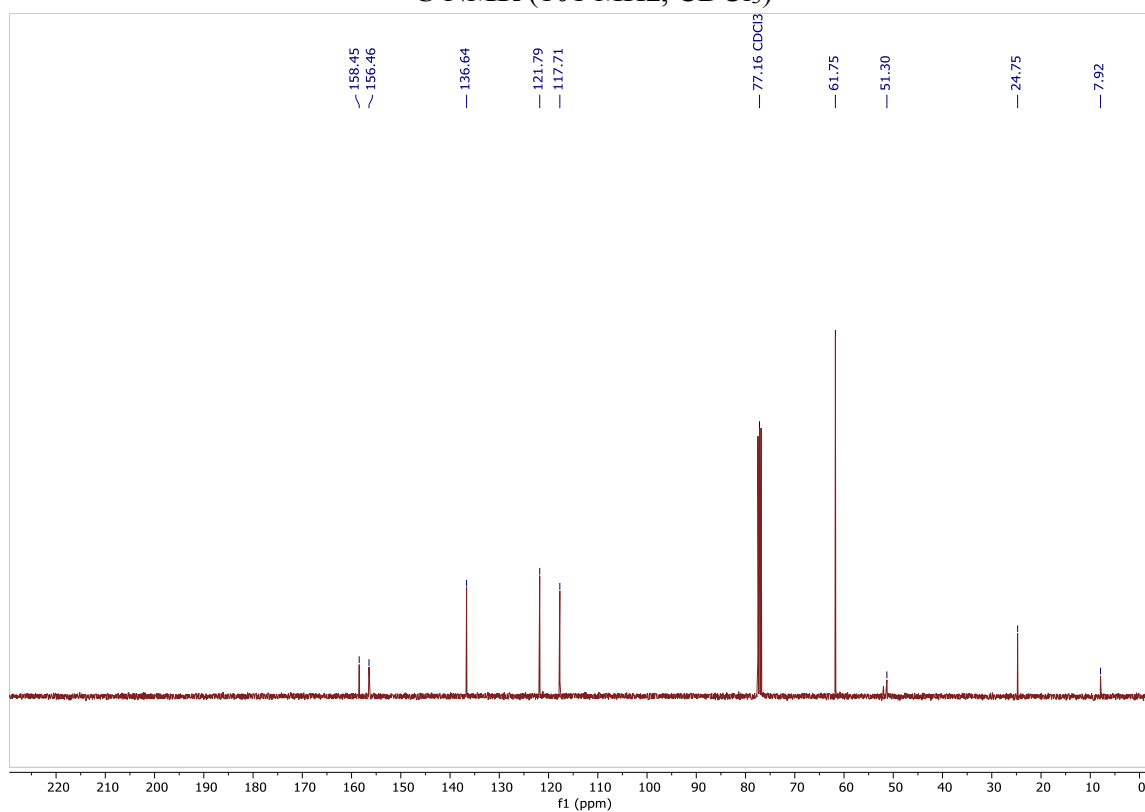
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-6-methylpyridine, 53



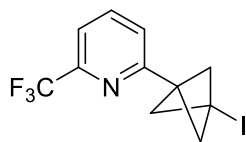
¹H NMR (400 MHz, CDCl₃)



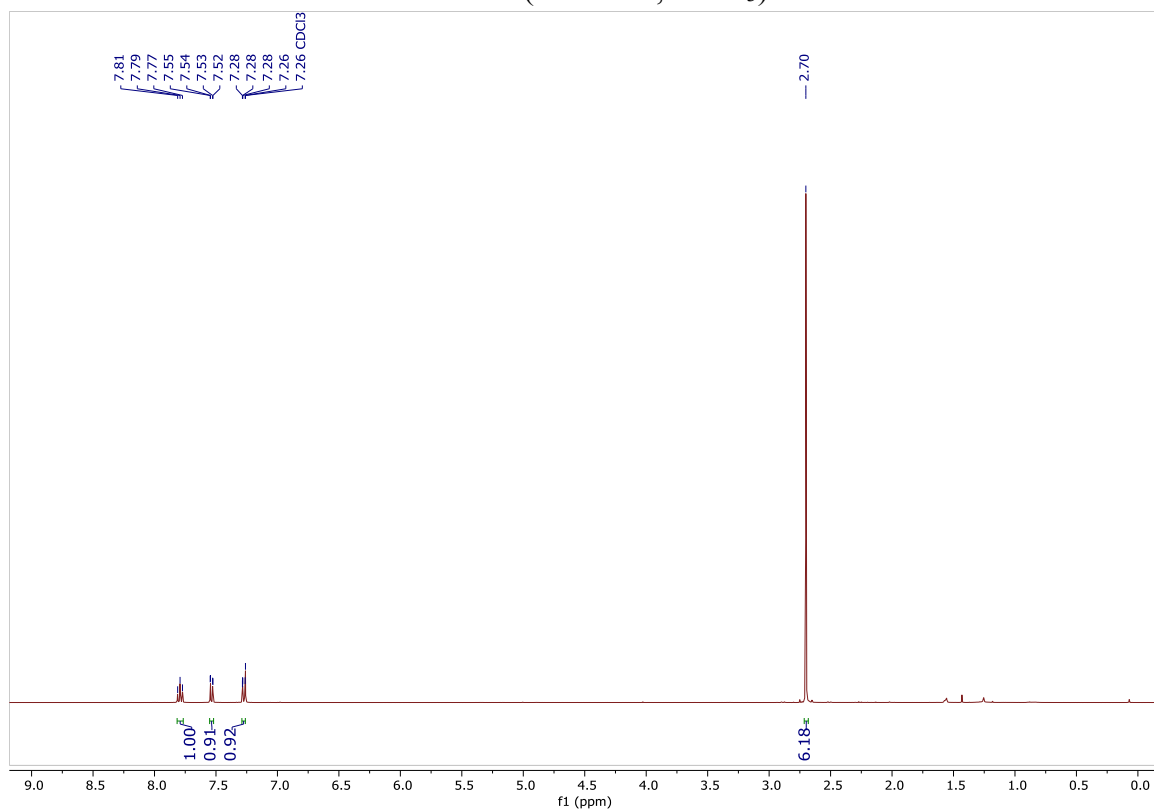
¹³C NMR (101 MHz, CDCl₃)



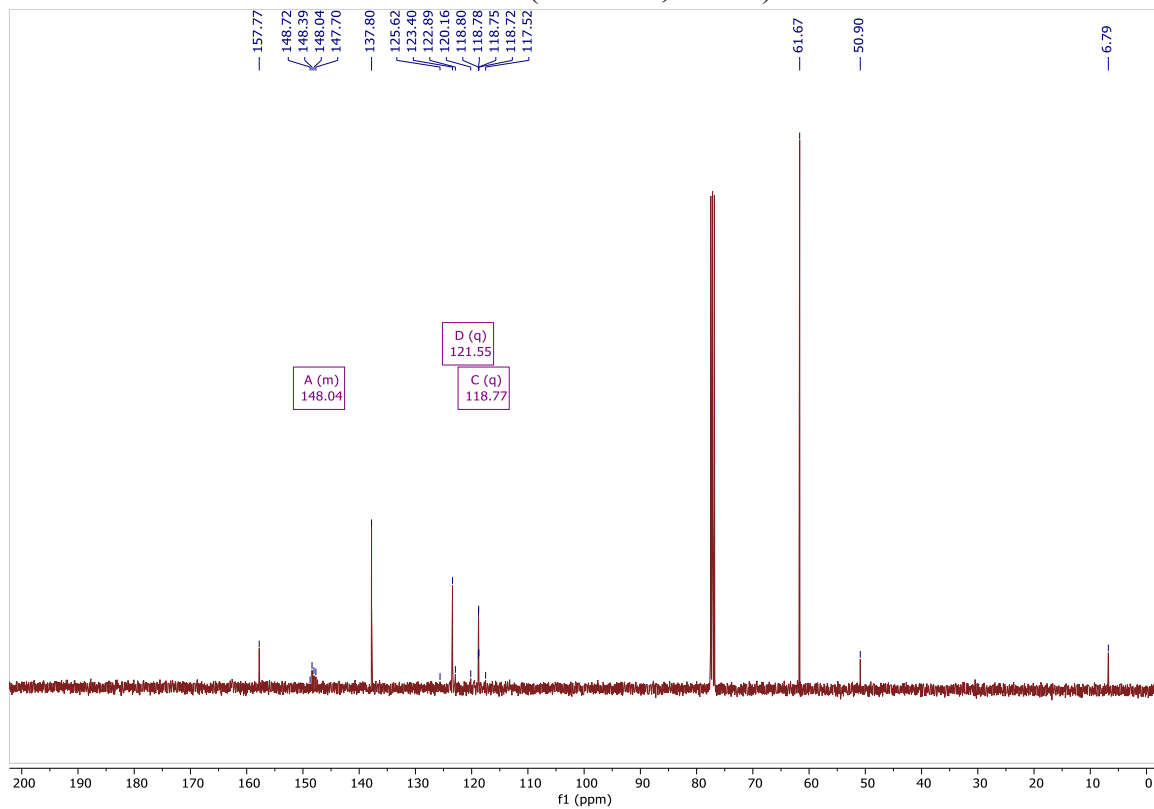
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)-6-(trifluoromethyl)pyridine, 54



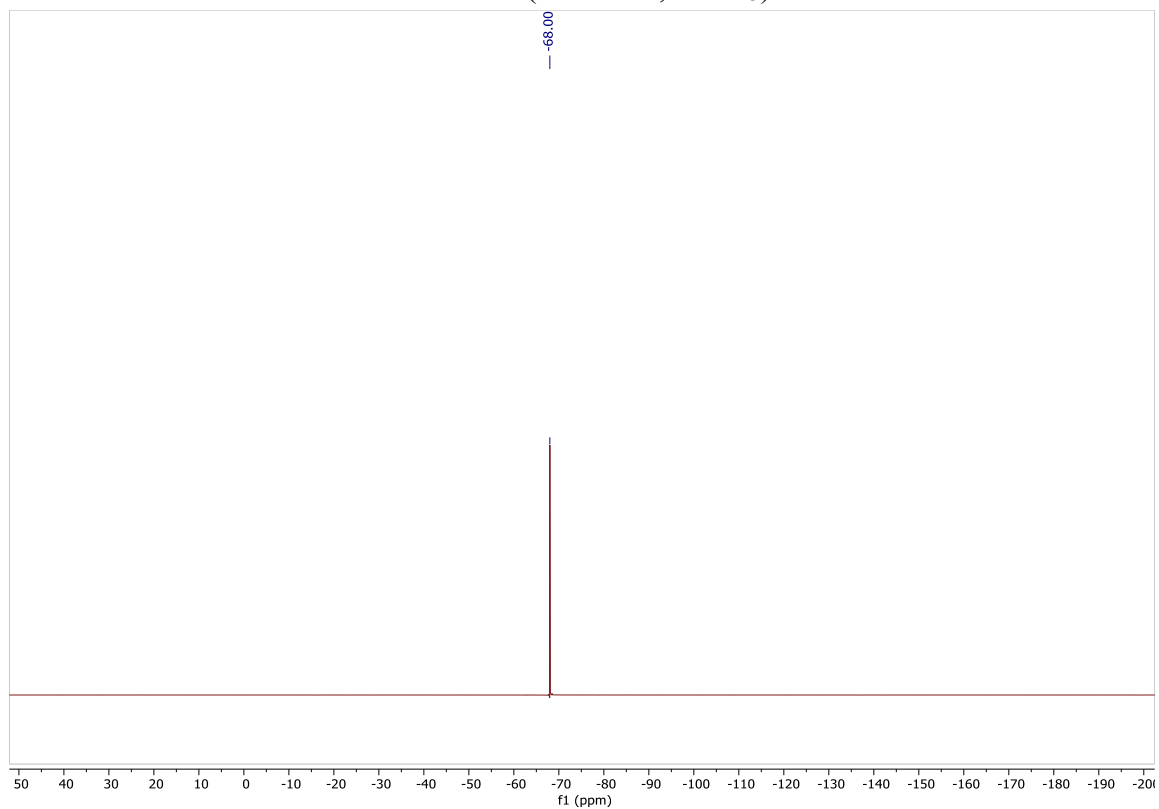
^1H NMR (400 MHz, CDCl_3)



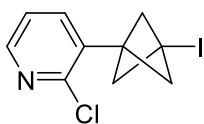
^{13}C NMR (101 MHz, CDCl_3)



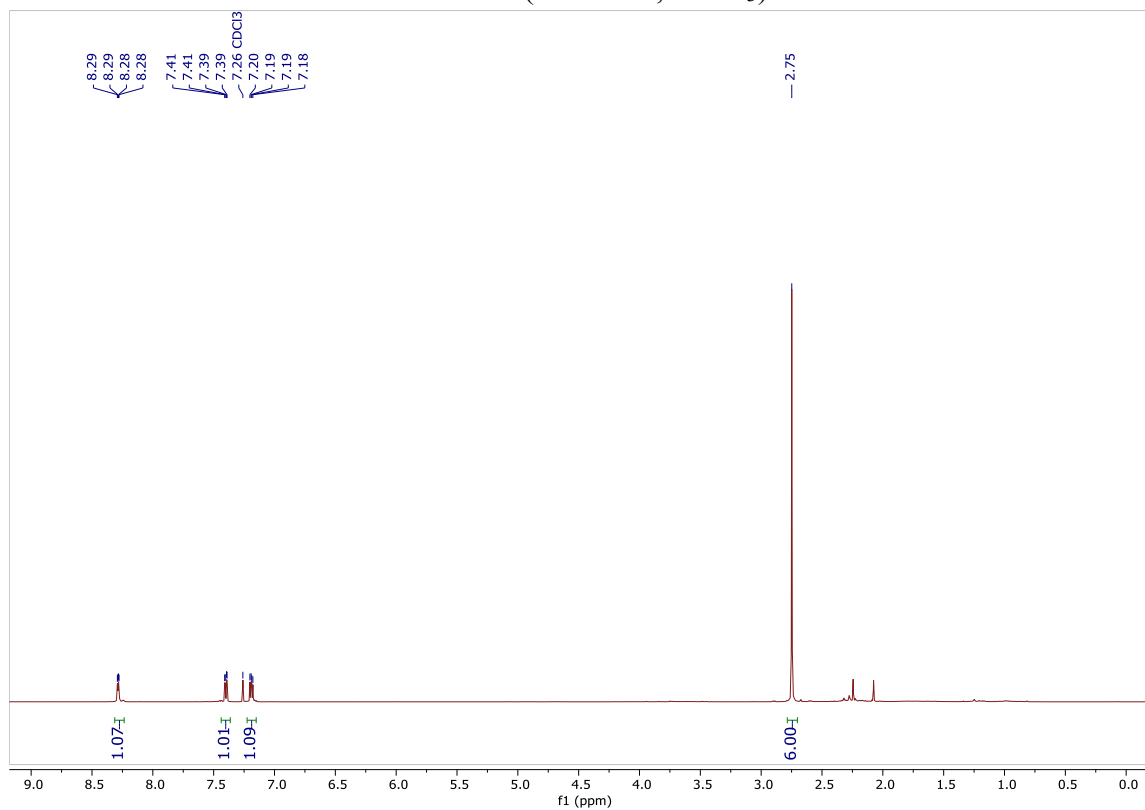
^{19}F NMR (377 MHz, CDCl_3)



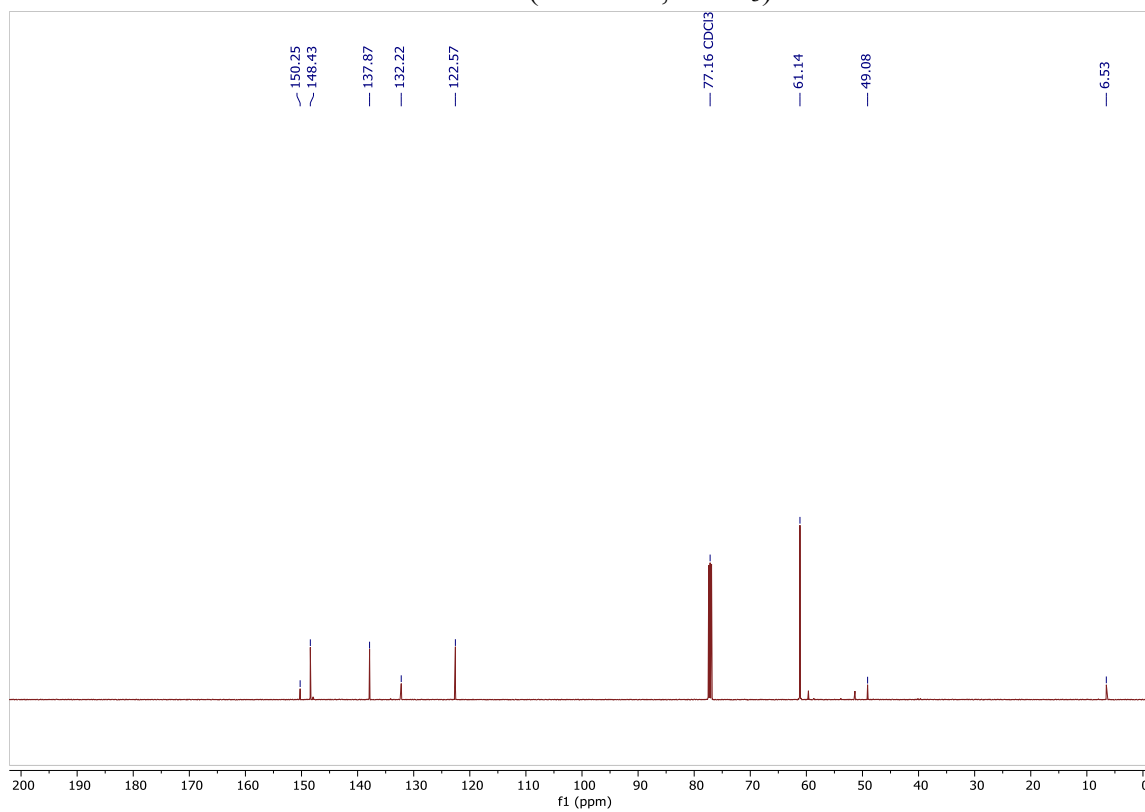
3-Chloro-2-(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, 55



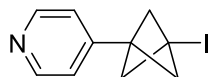
^1H NMR (500 MHz, CDCl_3)



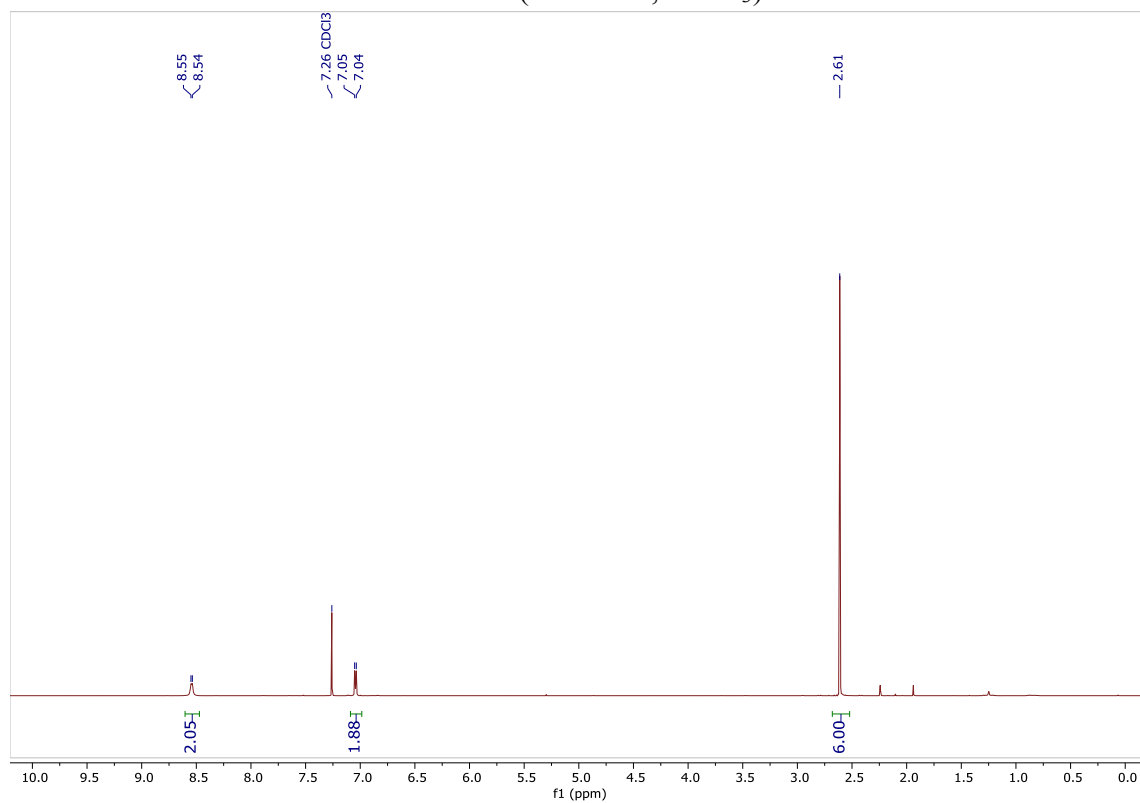
^{13}C NMR (125 MHz, CDCl_3)



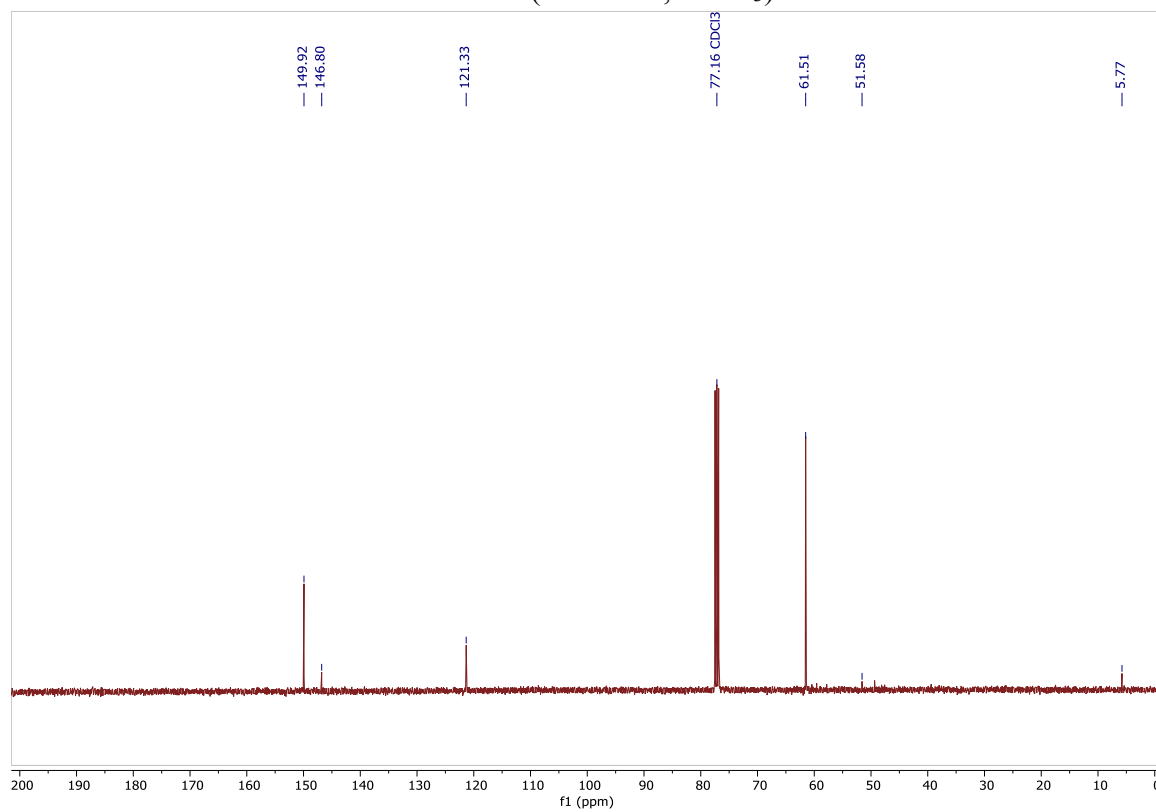
4-(3-Iodobicyclo[1.1.1]pentan-1-yl)pyridine, 56



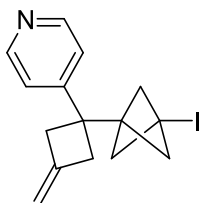
¹H NMR (400 MHz, CDCl₃)



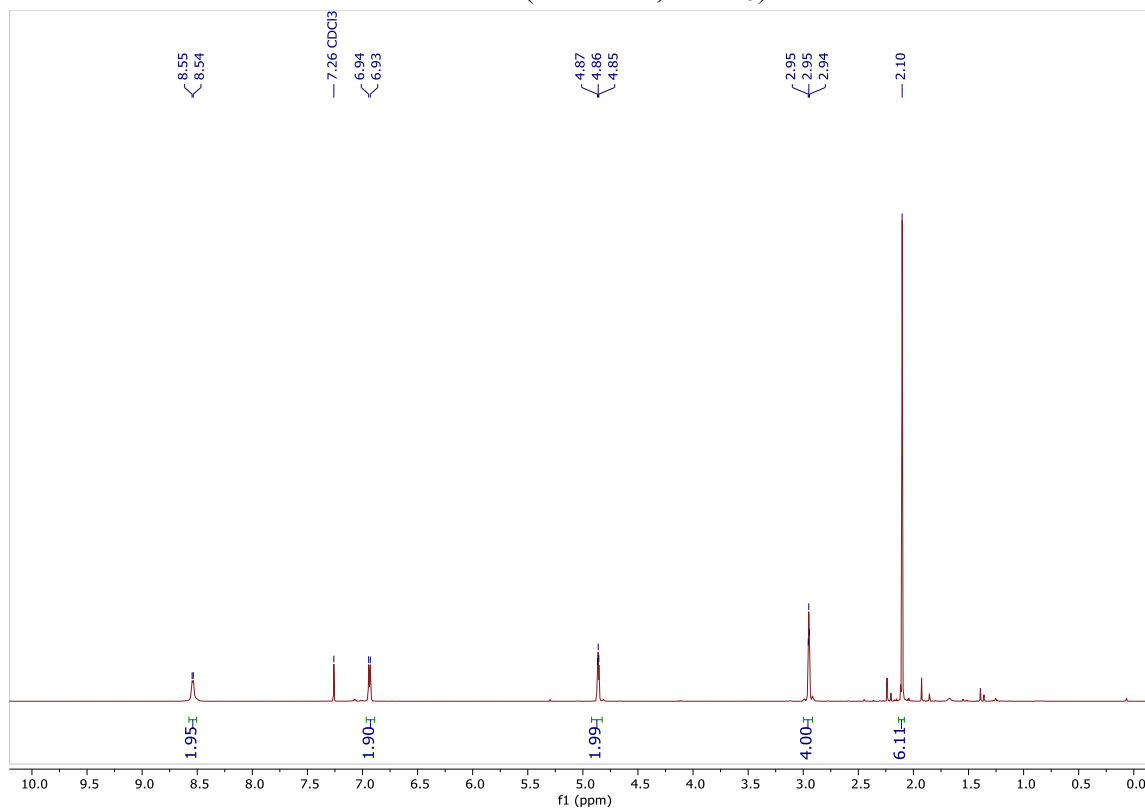
¹³C NMR (101 MHz, CDCl₃)



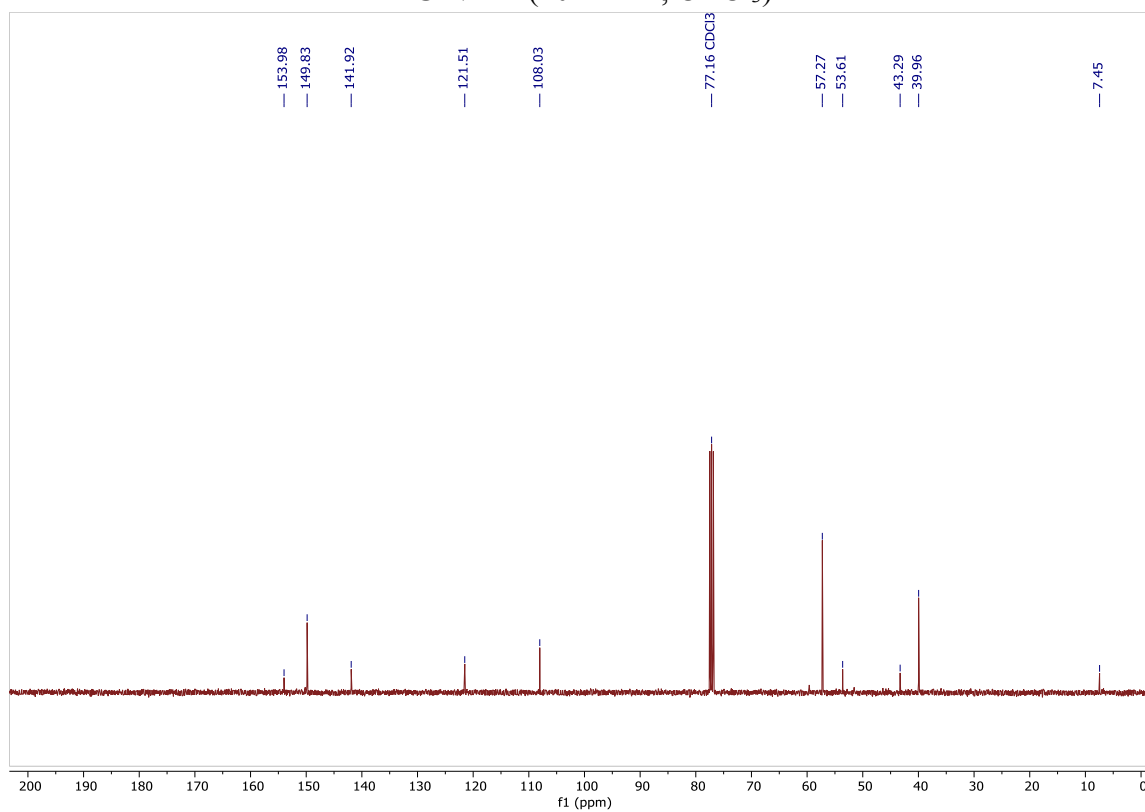
4-(1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-3-methylenecyclobutyl)pyridine, 97



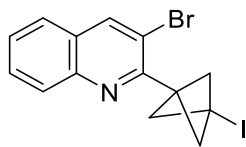
¹H NMR (400 MHz, CDCl₃)



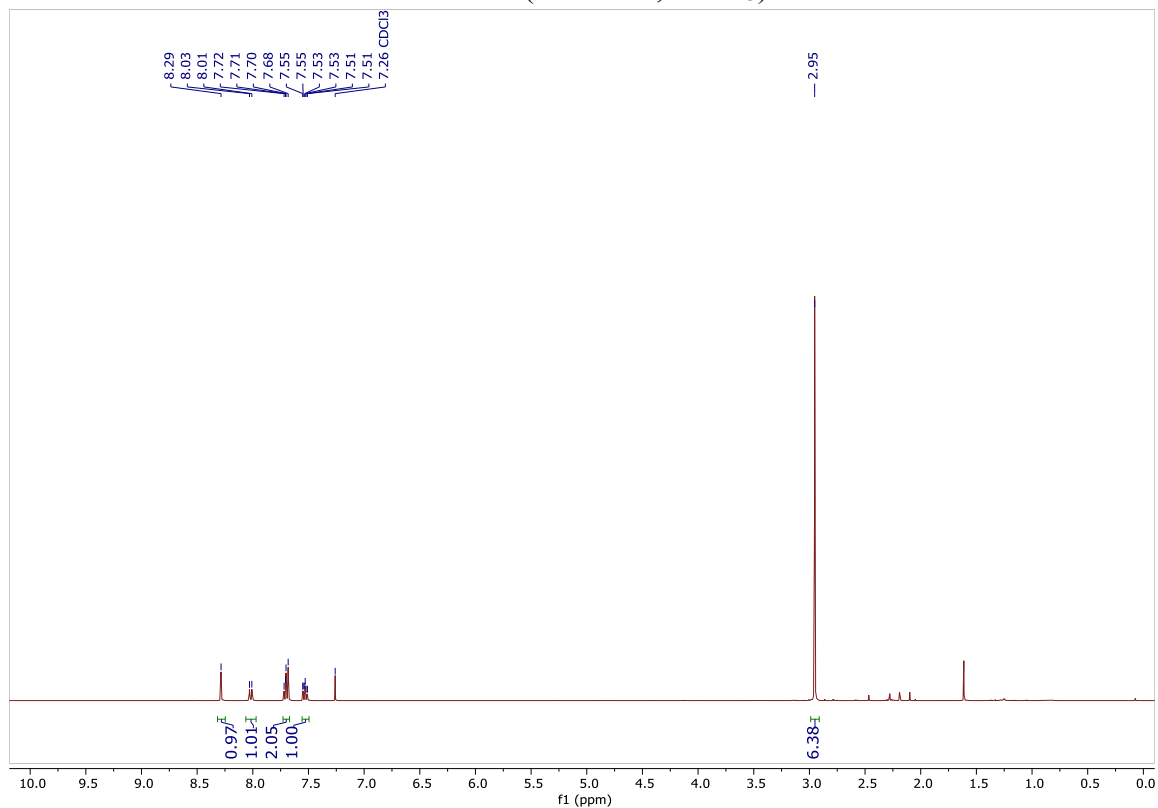
¹³C NMR (101 MHz, CDCl₃)



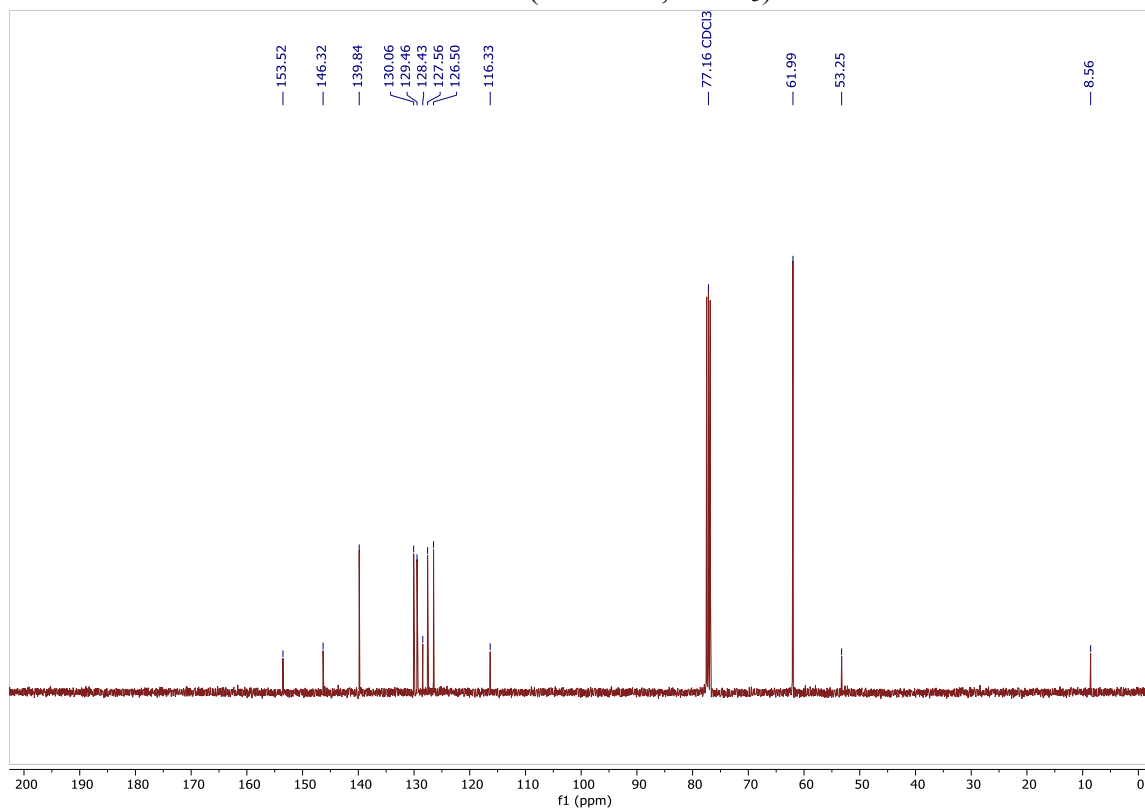
3-Bromo-2-(3-iodobicyclo[1.1.1]pentan-1-yl)quinolone, 57



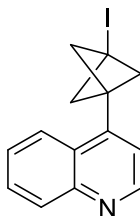
^1H NMR (400 MHz, CDCl_3)



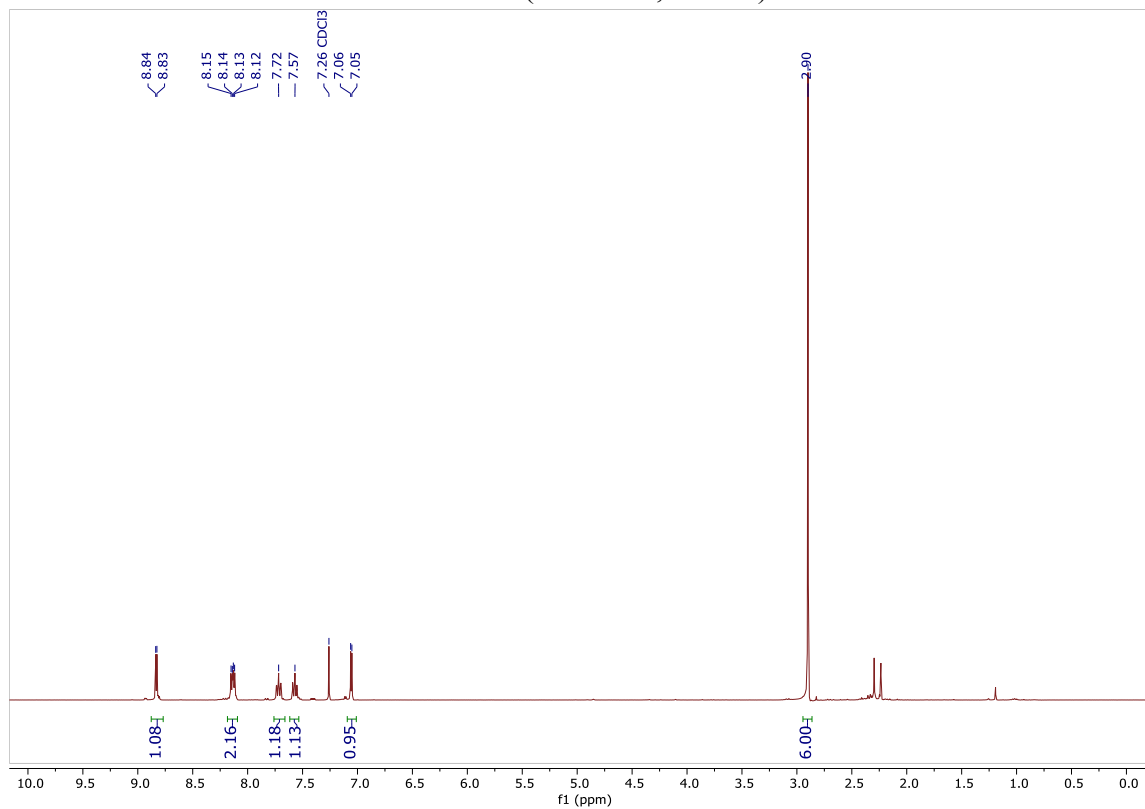
^{13}C NMR (101 MHz, CDCl_3)



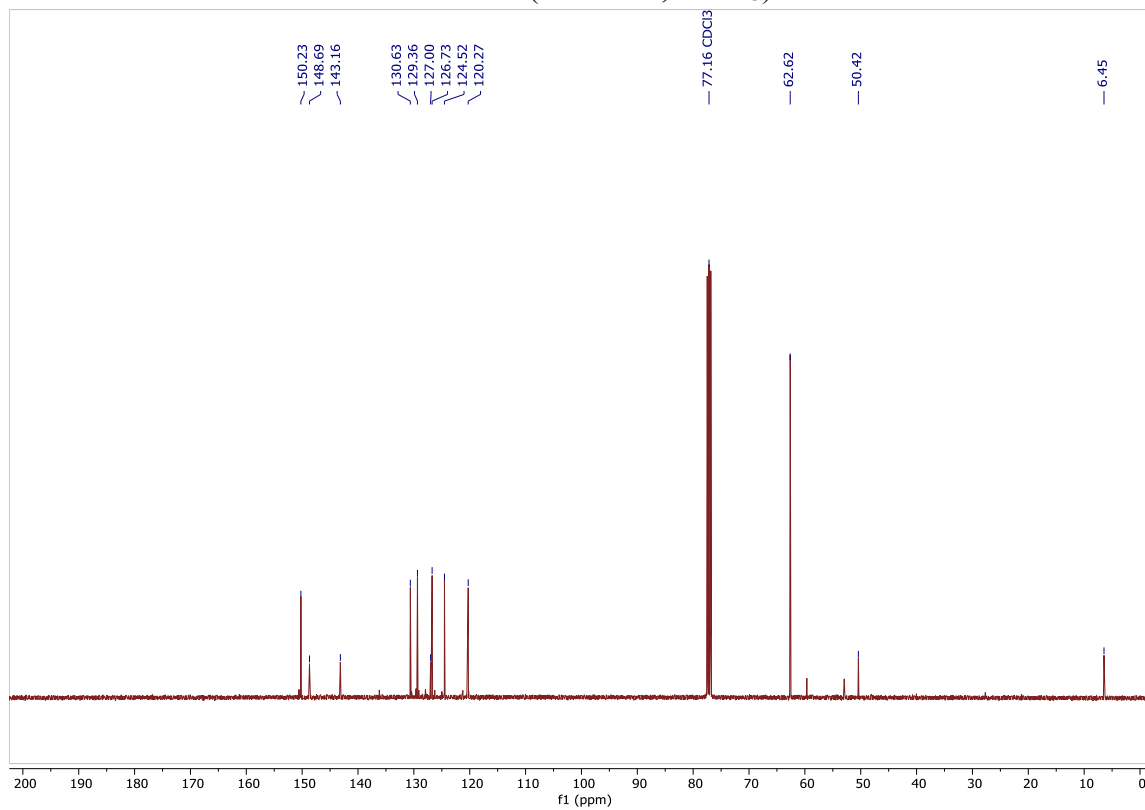
4-(3-Iodobicyclo[1.1.1]pentan-1-yl)quinoline, **58**



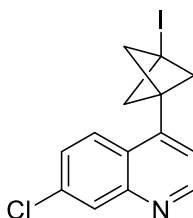
^1H NMR (400 MHz, CDCl_3)



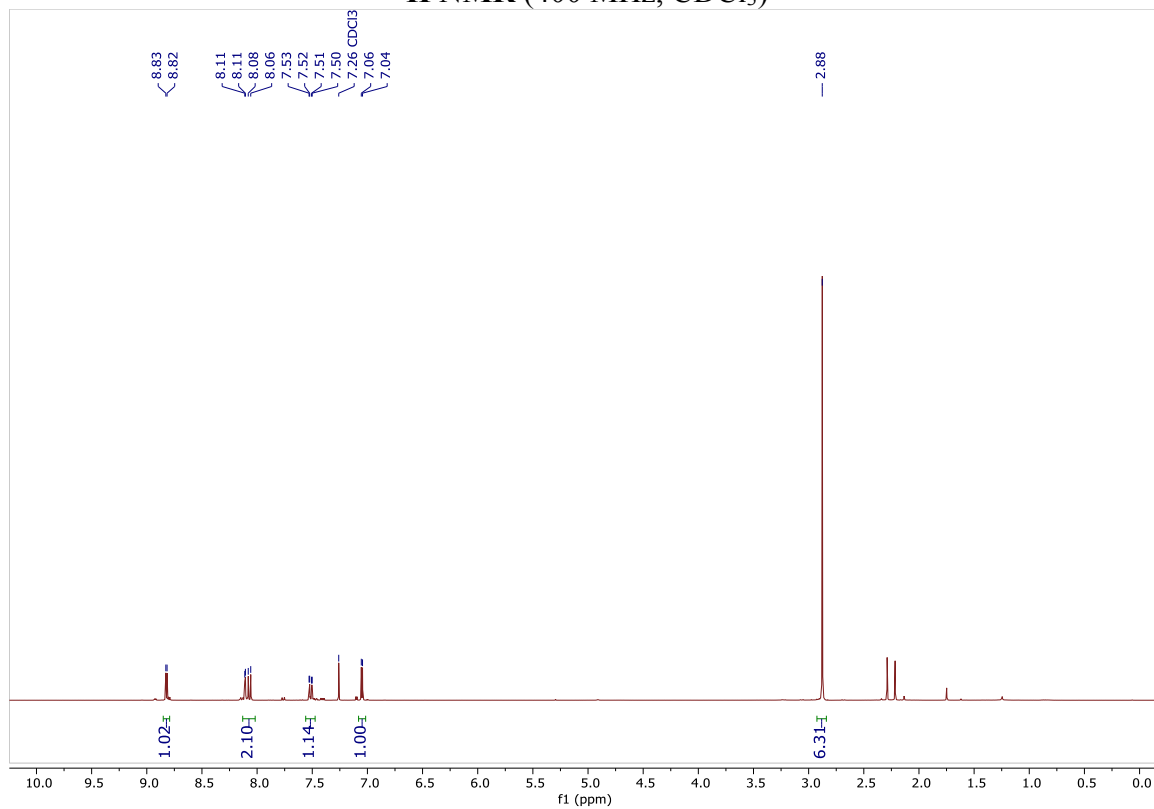
^{13}C NMR (101 MHz, CDCl_3)



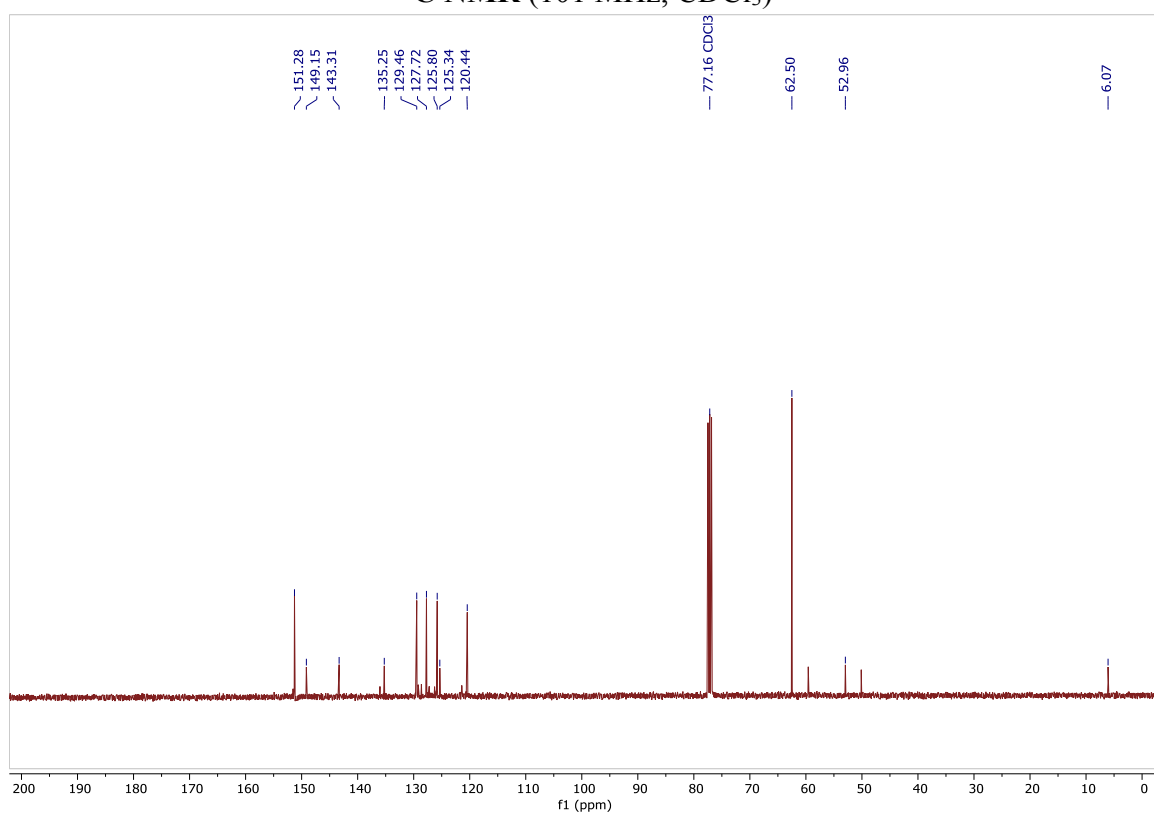
7-Chloro-4-(3-iodobicyclo[1.1.1]pentan-1-yl)quinolone, 59



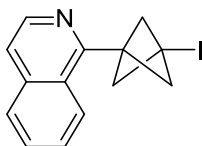
¹H NMR (400 MHz, CDCl₃)



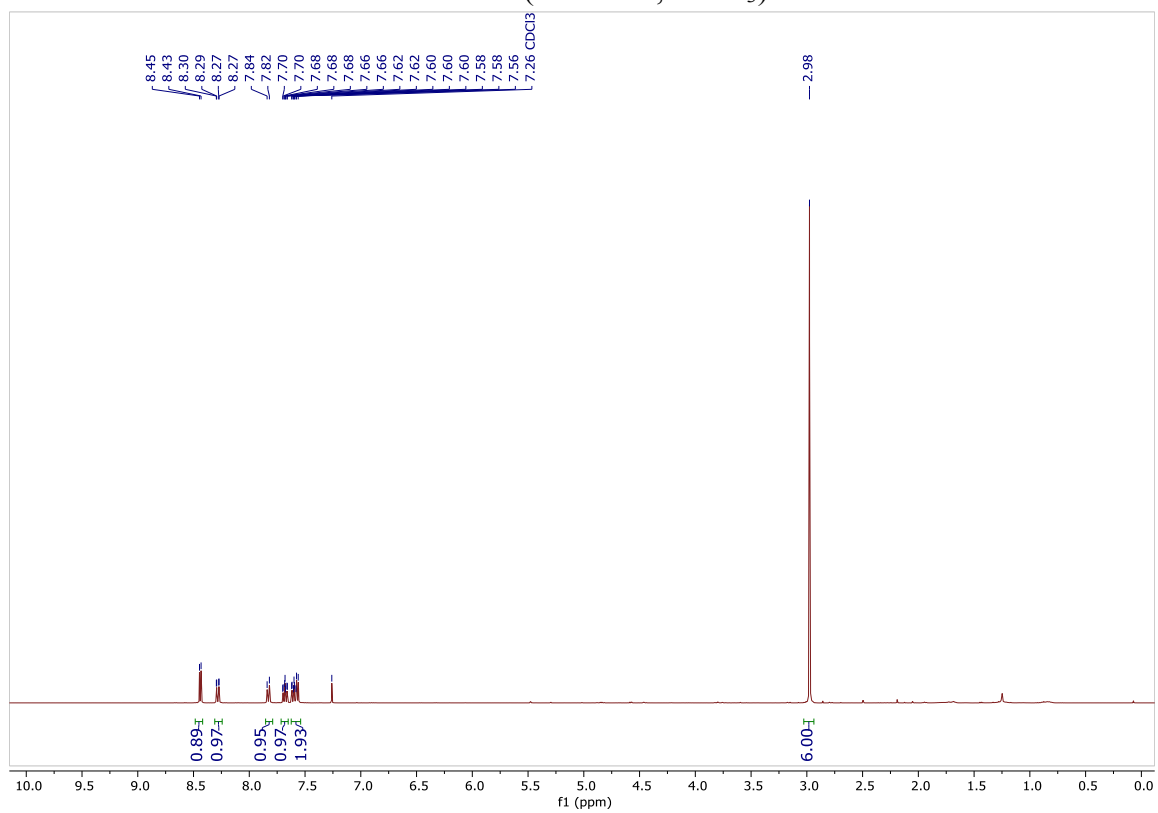
¹³C NMR (101 MHz, CDCl₃)



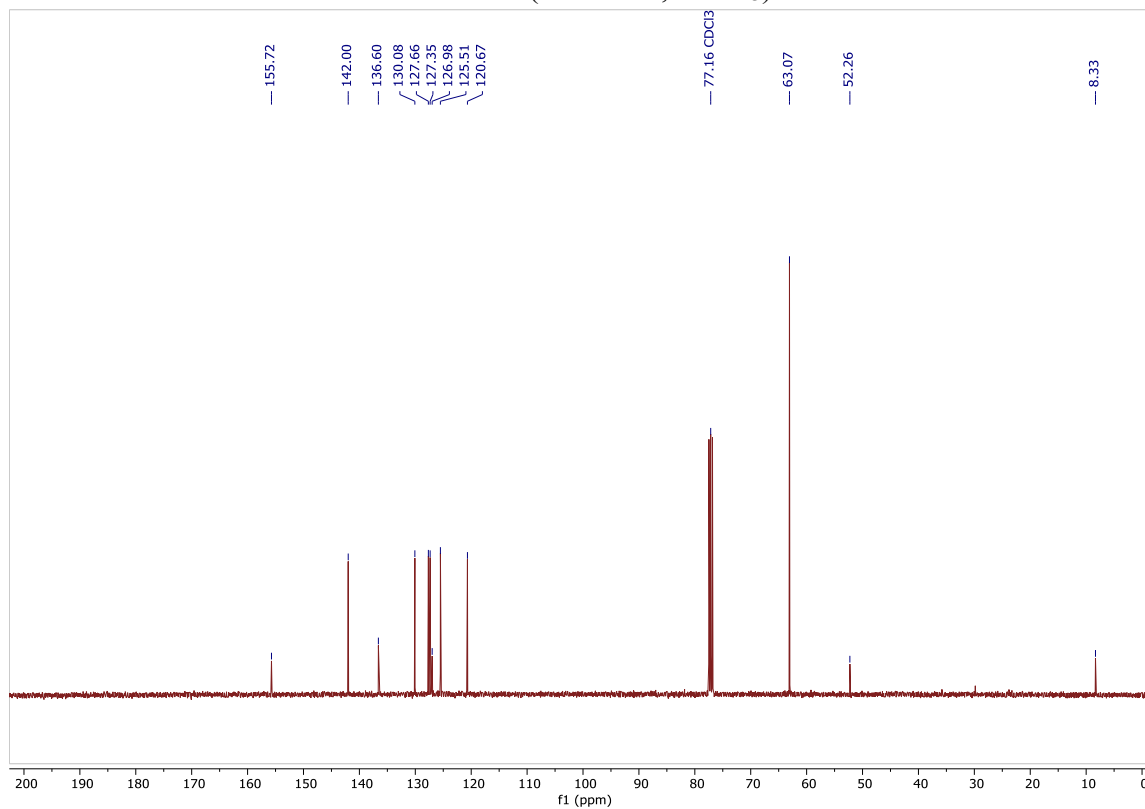
1-(3-Iodobicyclo[1.1.1]pentan-1-yl)isoquinoline, 60



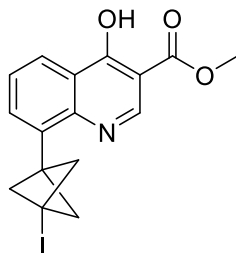
¹H NMR (400 MHz, CDCl₃)



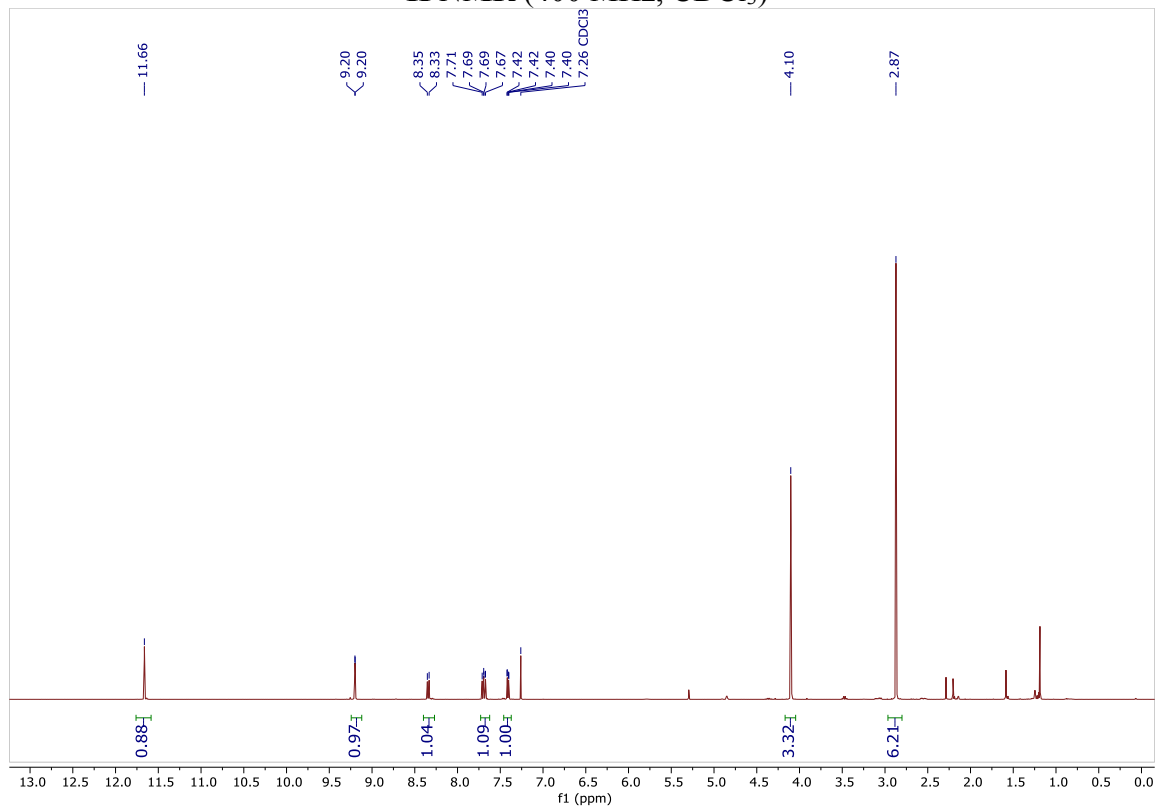
¹³C NMR (101 MHz, CDCl₃)



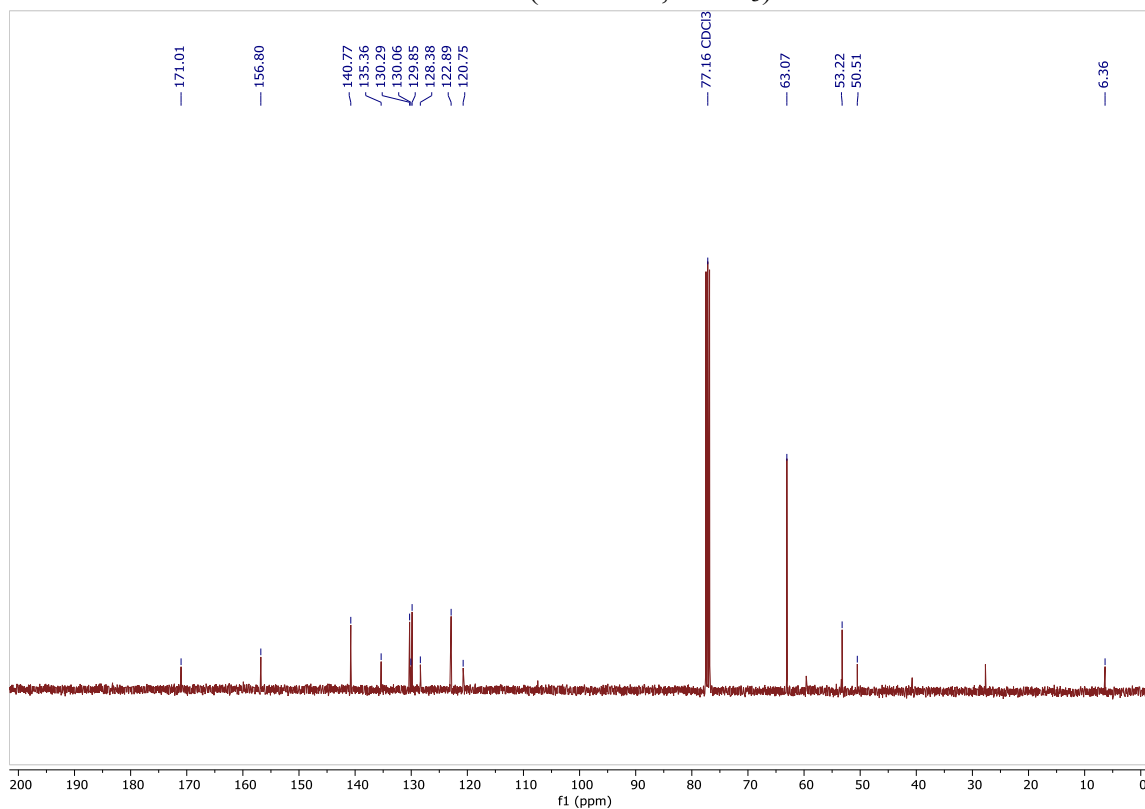
Methyl 4-hydroxy-8-(3-iodobicyclo[1.1.1]pentan-1-yl)quinoline-3-carboxylate, 61



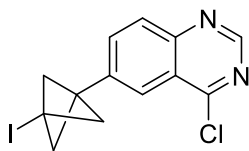
^1H NMR (400 MHz, CDCl_3)



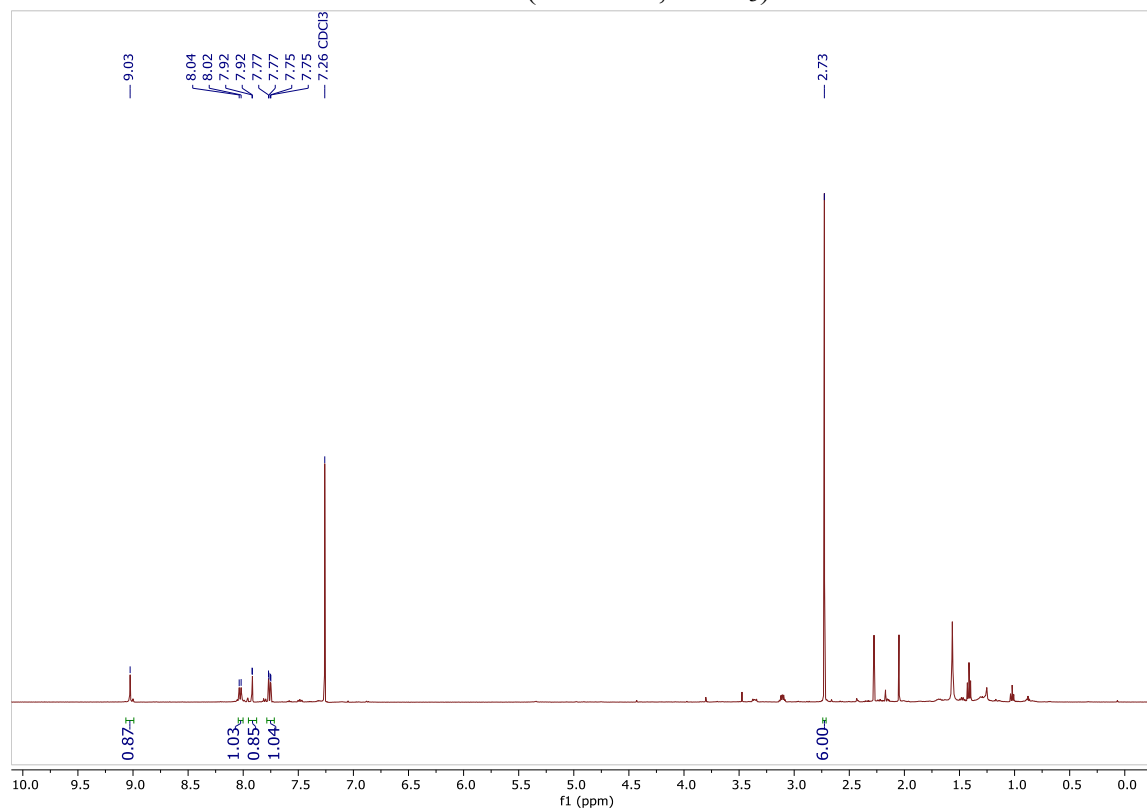
^{13}C NMR (101 MHz, CDCl_3)



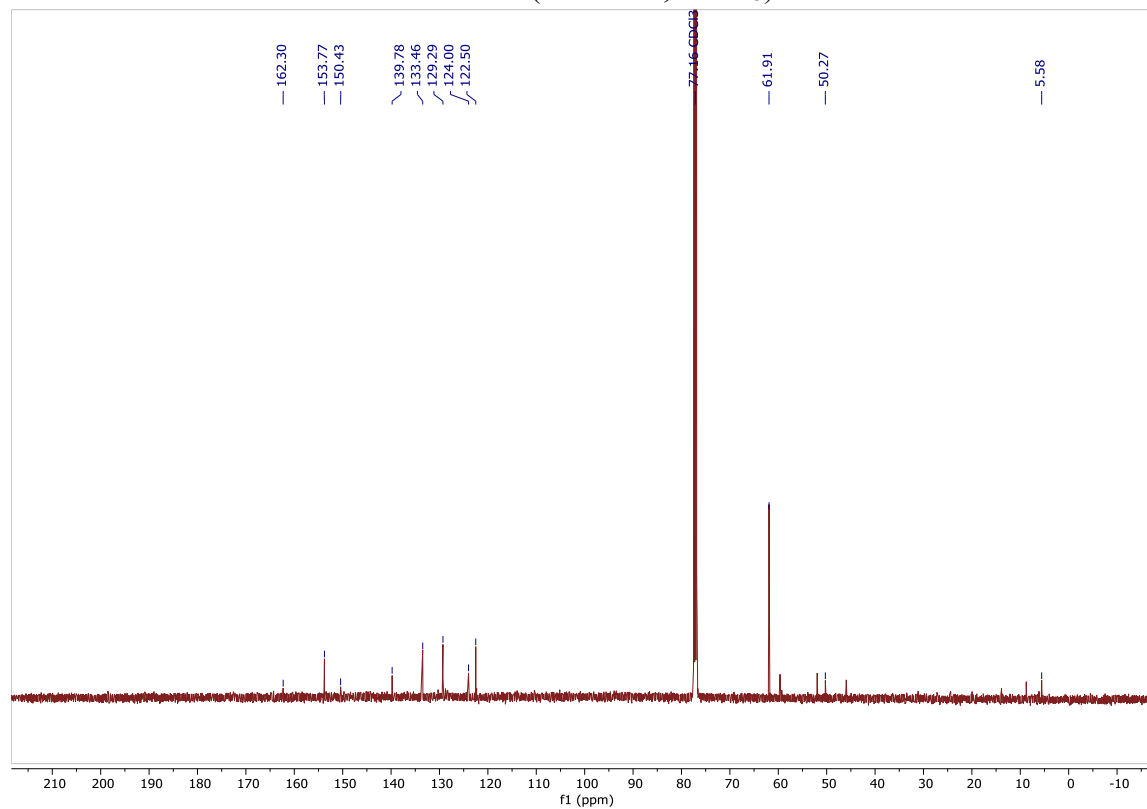
4-Chloro-6-(3-iodobicyclo[1.1.1]pentan-1-yl)quinazoline, 62



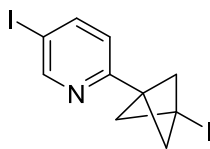
^1H NMR (500 MHz, CDCl_3)



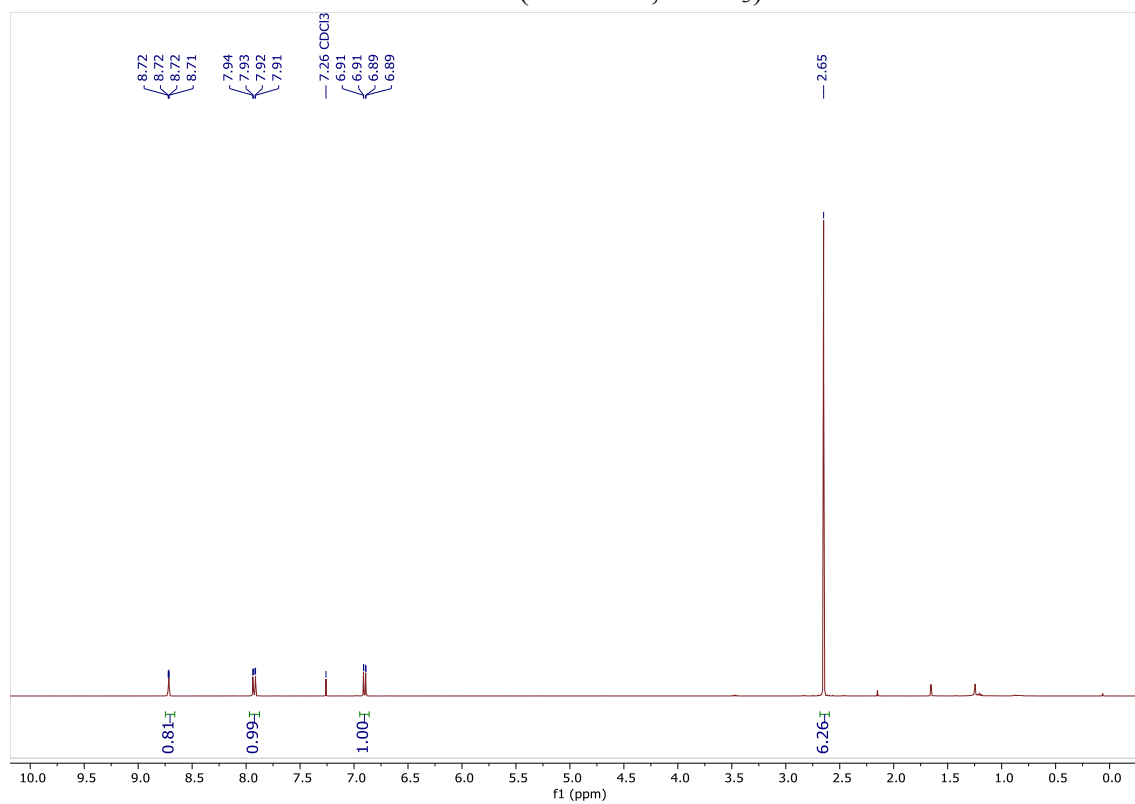
^{13}C NMR (125 MHz, CDCl_3)



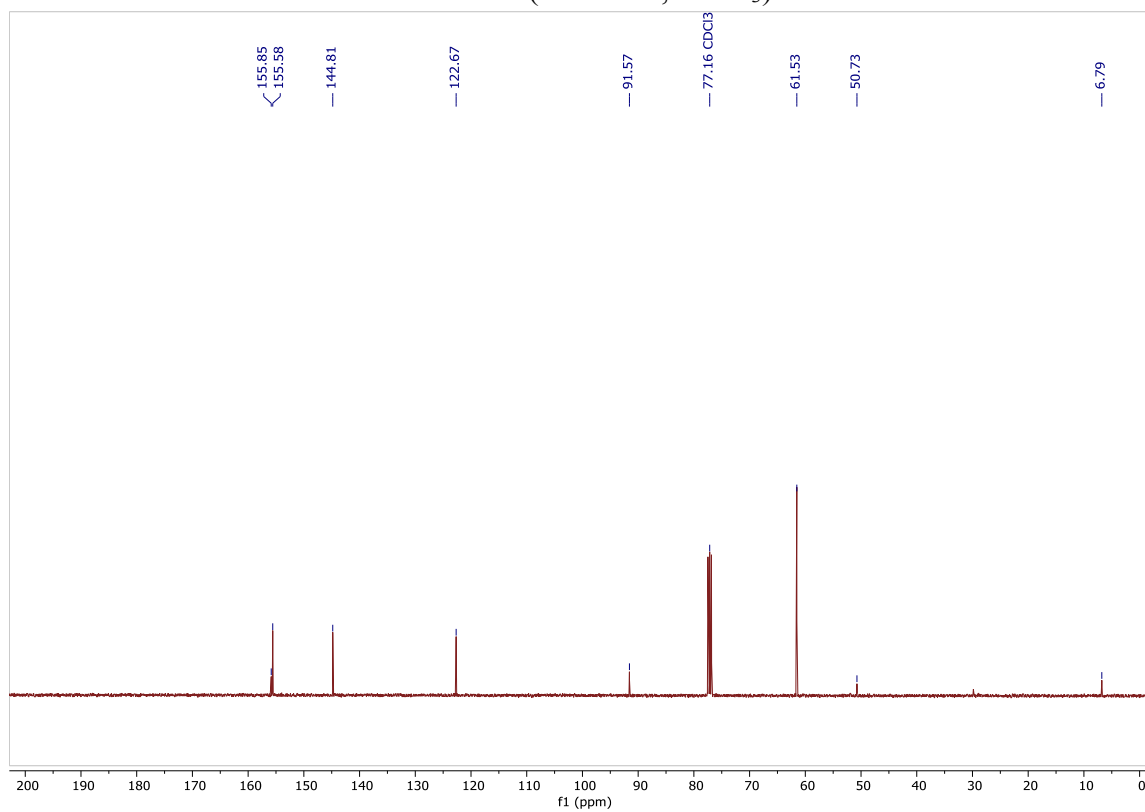
5-Iodo-2-(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, 63



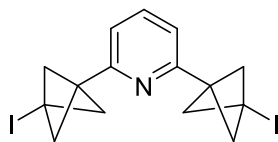
^1H NMR (400 MHz, CDCl_3)



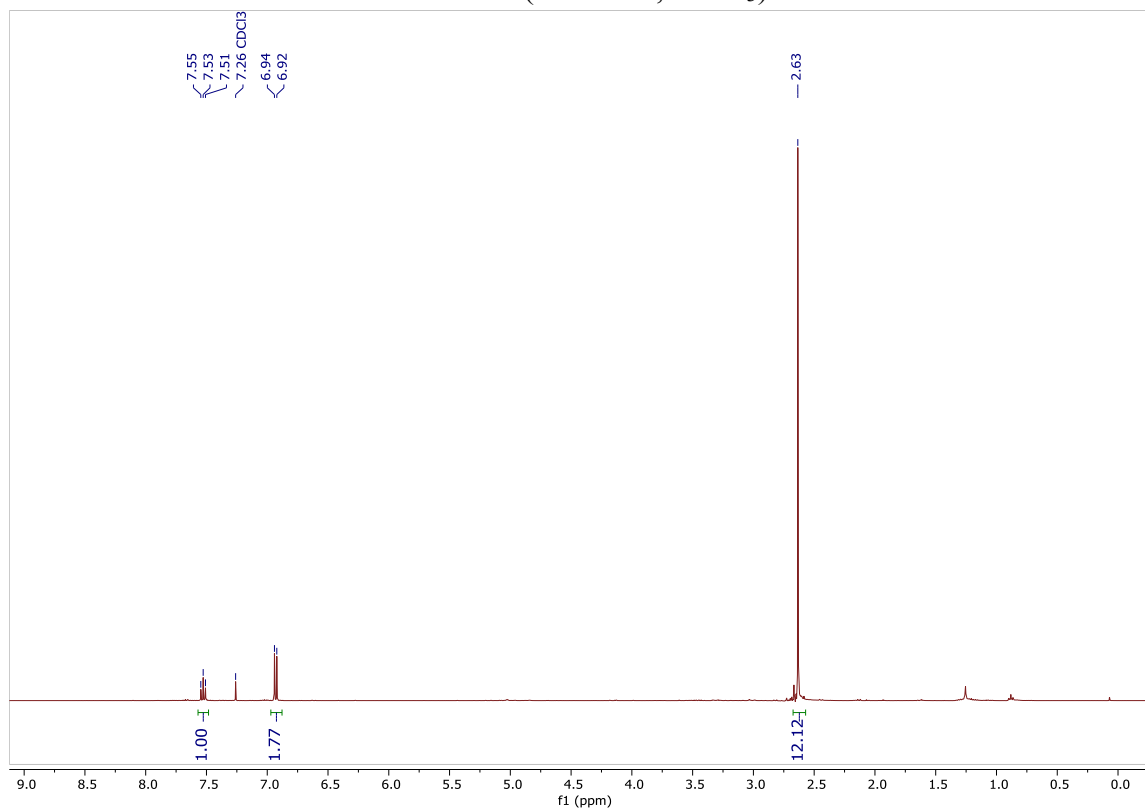
^{13}C NMR (101 MHz, CDCl_3)



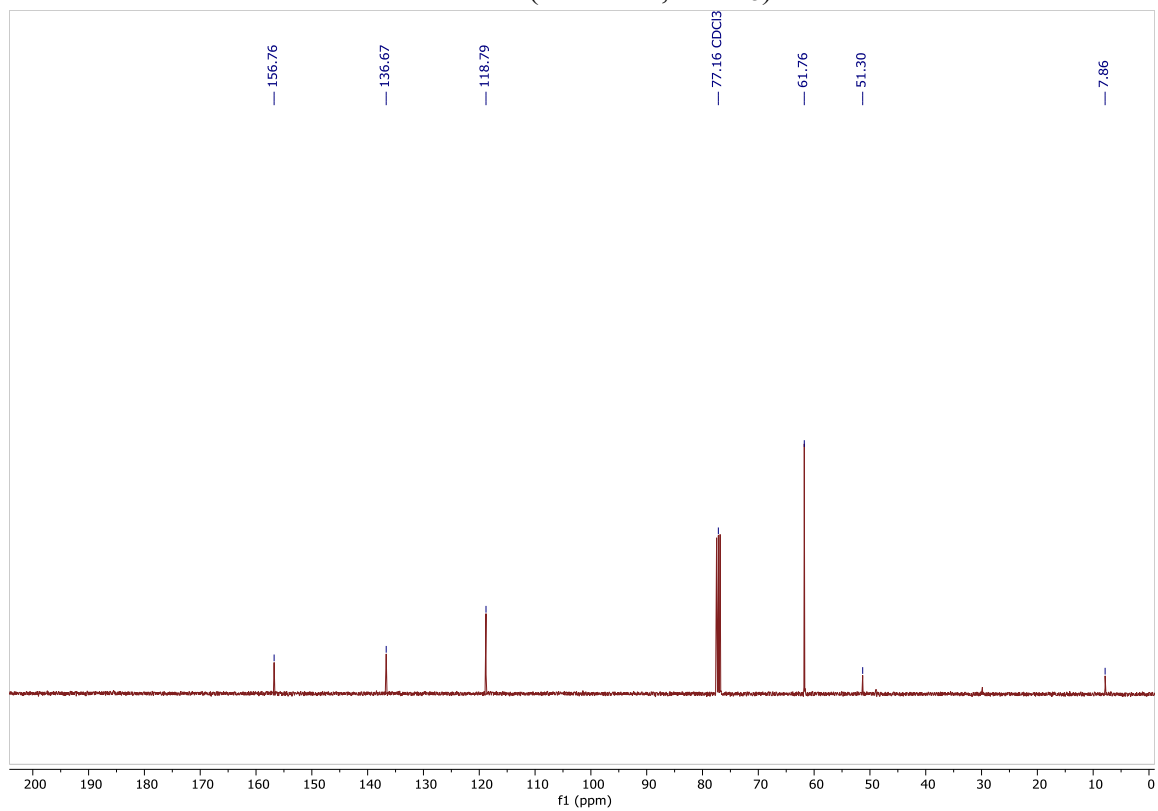
2,6-Bis(3-iodobicyclo[1.1.1]pentan-1-yl)pyridine, 64



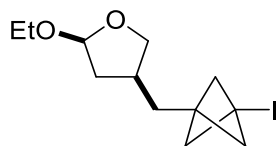
^1H NMR (400 MHz, CDCl_3)



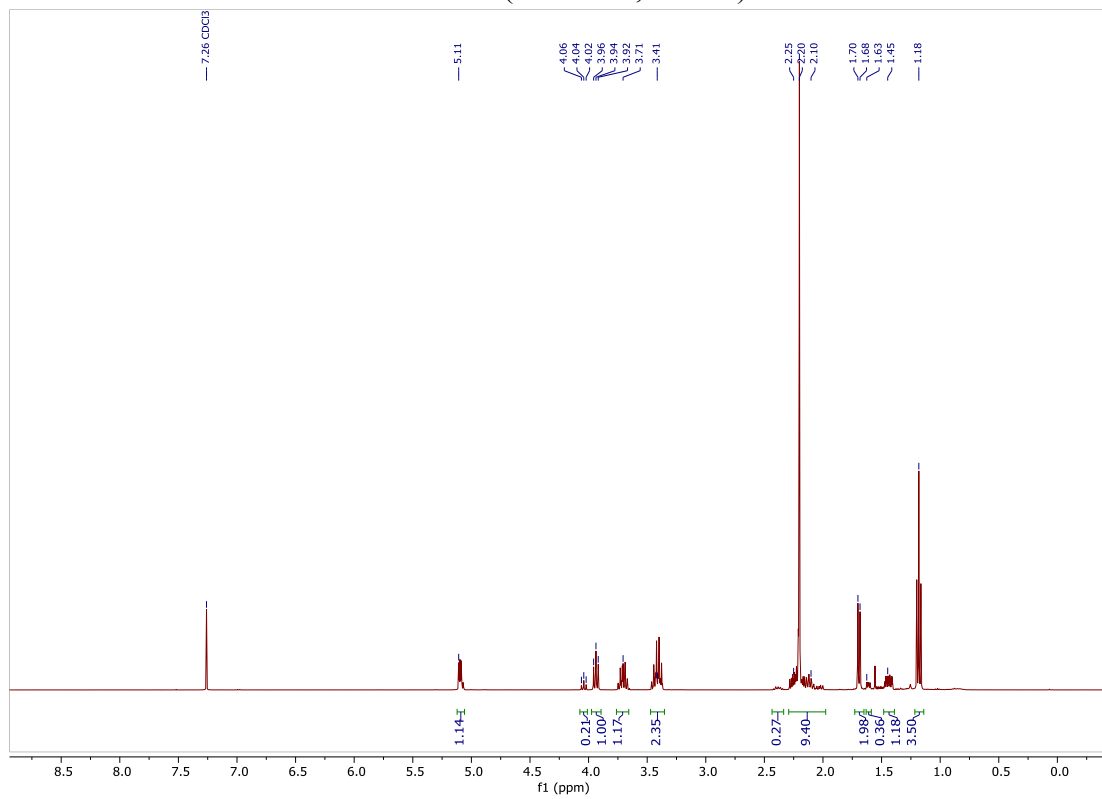
^{13}C NMR (101 MHz, CDCl_3)



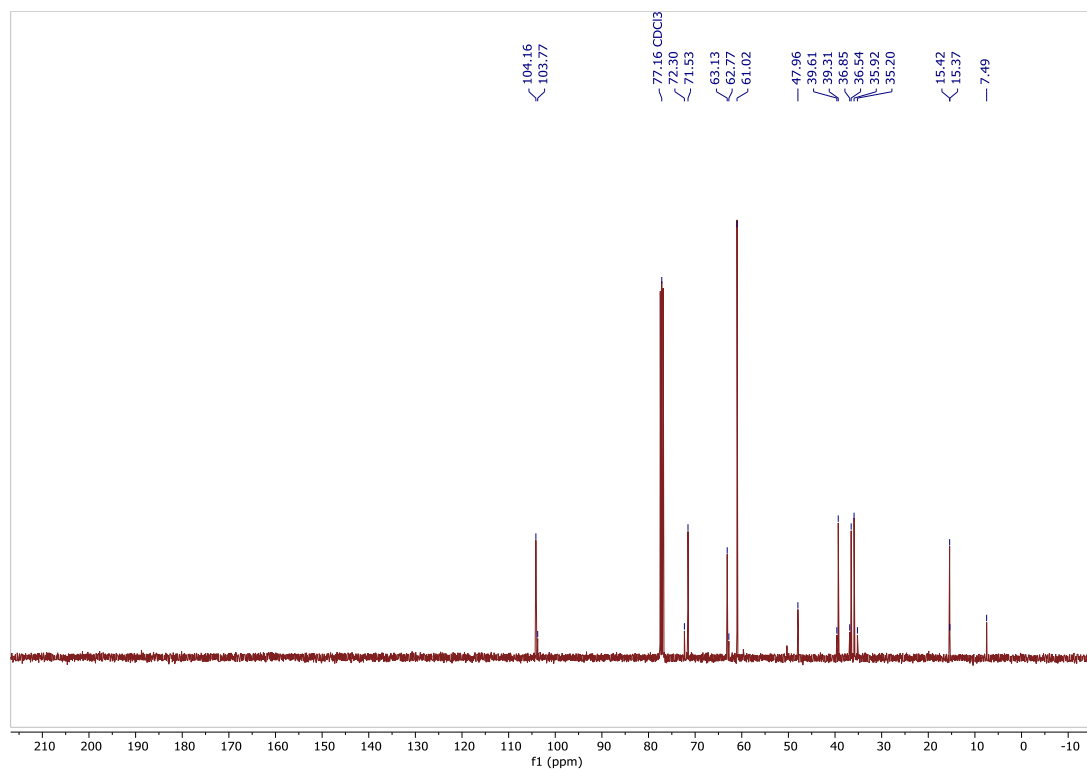
2-Ethoxy-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)tetrahydrofuran, 65



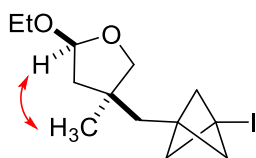
^1H NMR (400 MHz, CDCl_3)



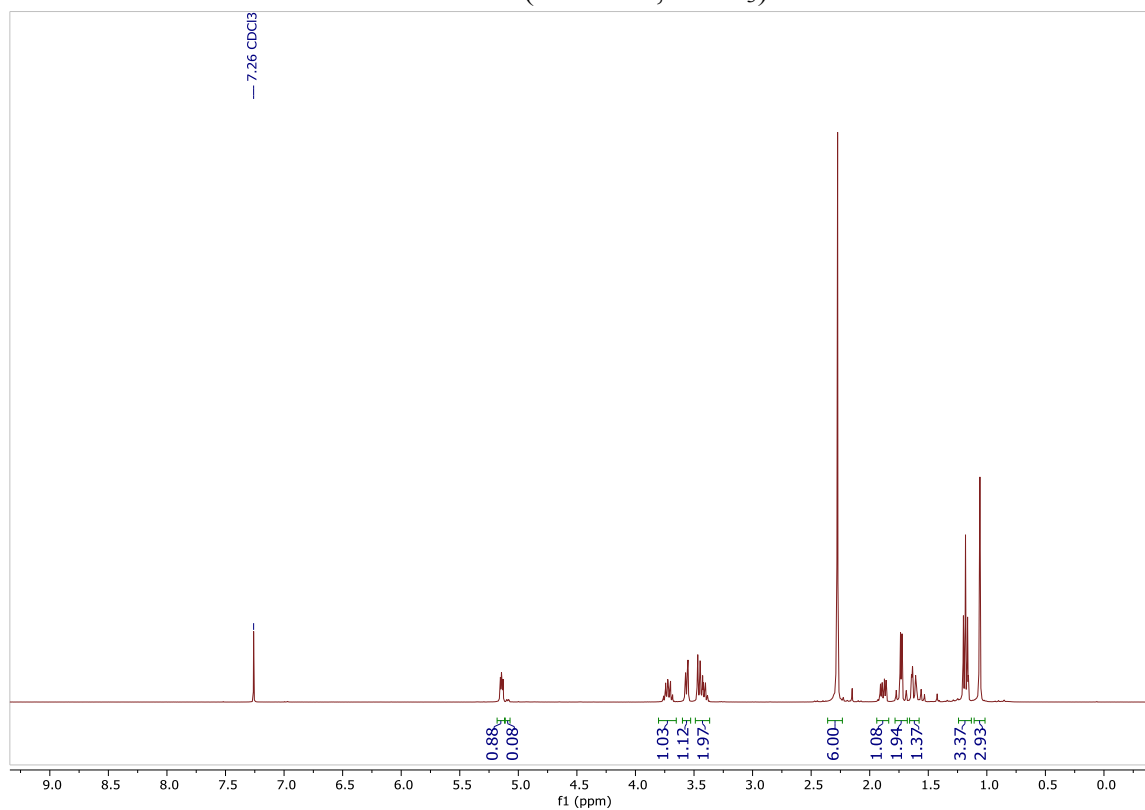
^{13}C NMR (101 MHz, CDCl_3)



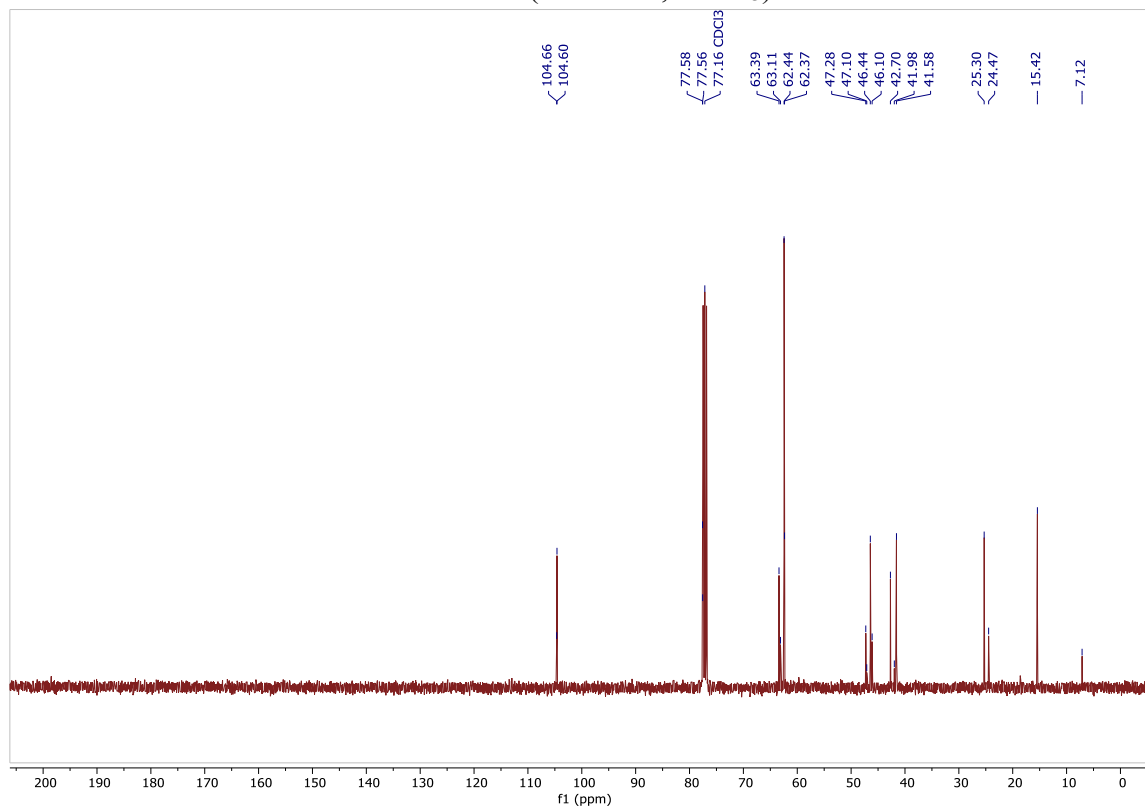
2-Ethoxy-4-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)-4-methyltetrahydrofuran, 66



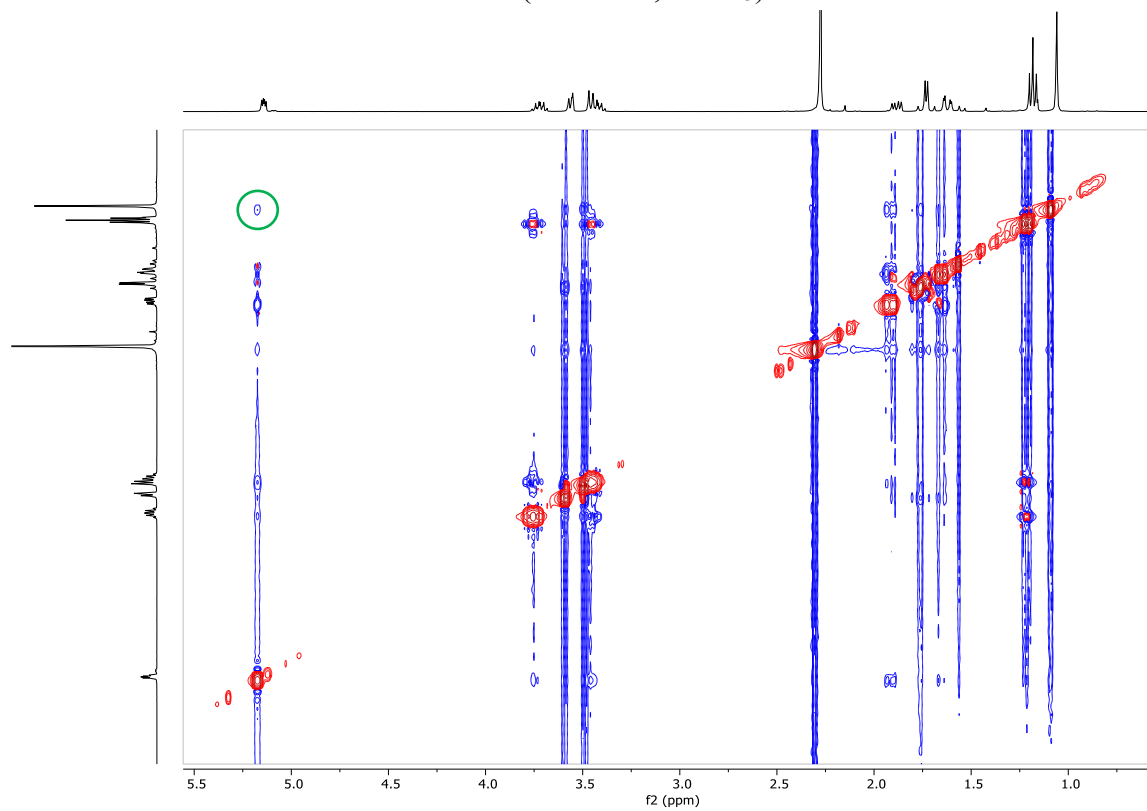
^1H NMR (400 MHz, CDCl_3)



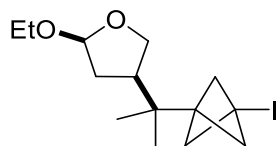
^{13}C NMR (101 MHz, CDCl_3)



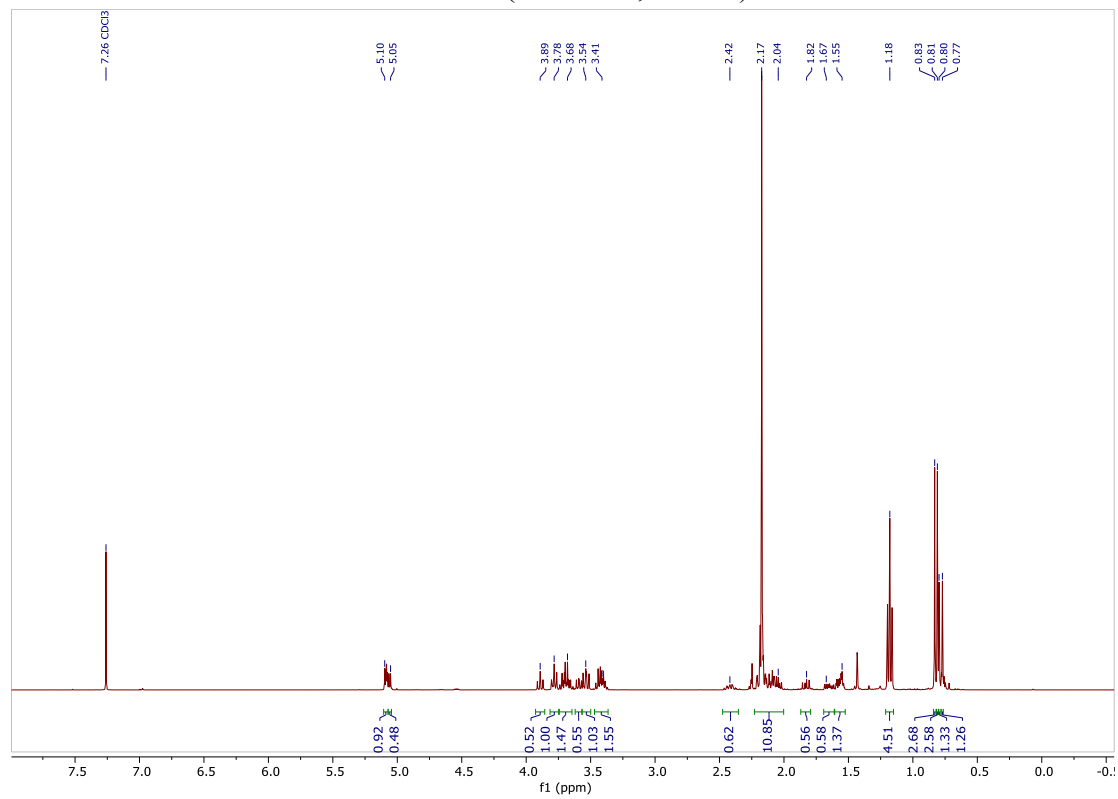
NOESY (400 MHz, CDCl₃)



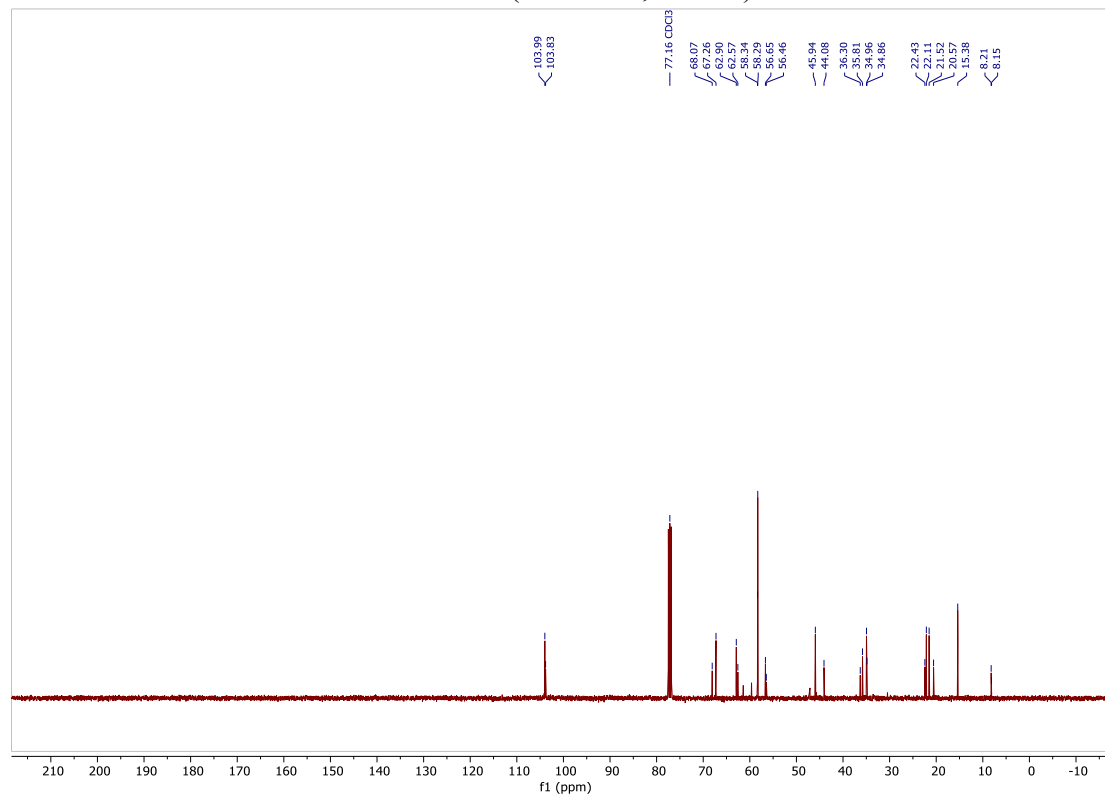
2-Ethoxy-4-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)propan-2-yl)tetrahydrofuran, 67



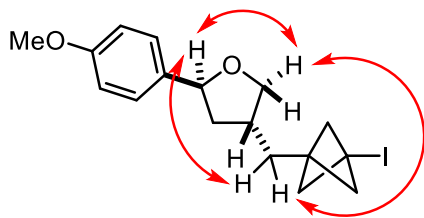
^1H NMR (400 MHz, CDCl_3)



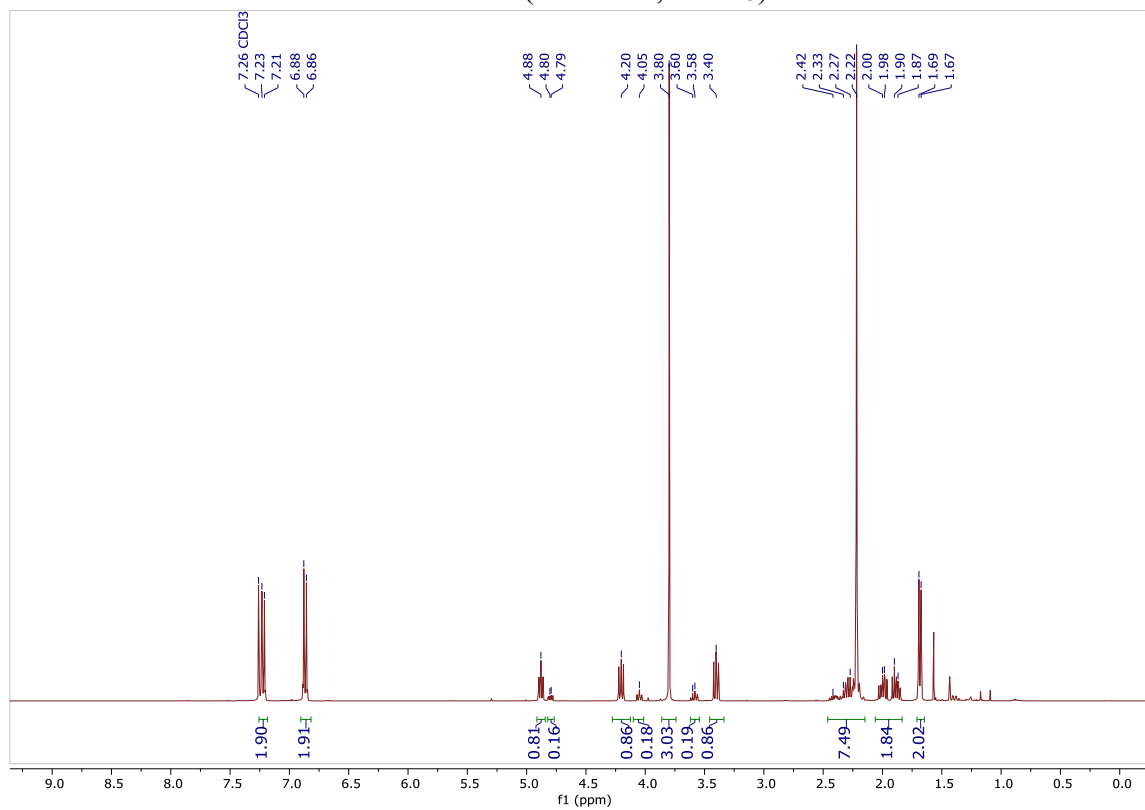
^{13}C NMR (101 MHz, CDCl_3)



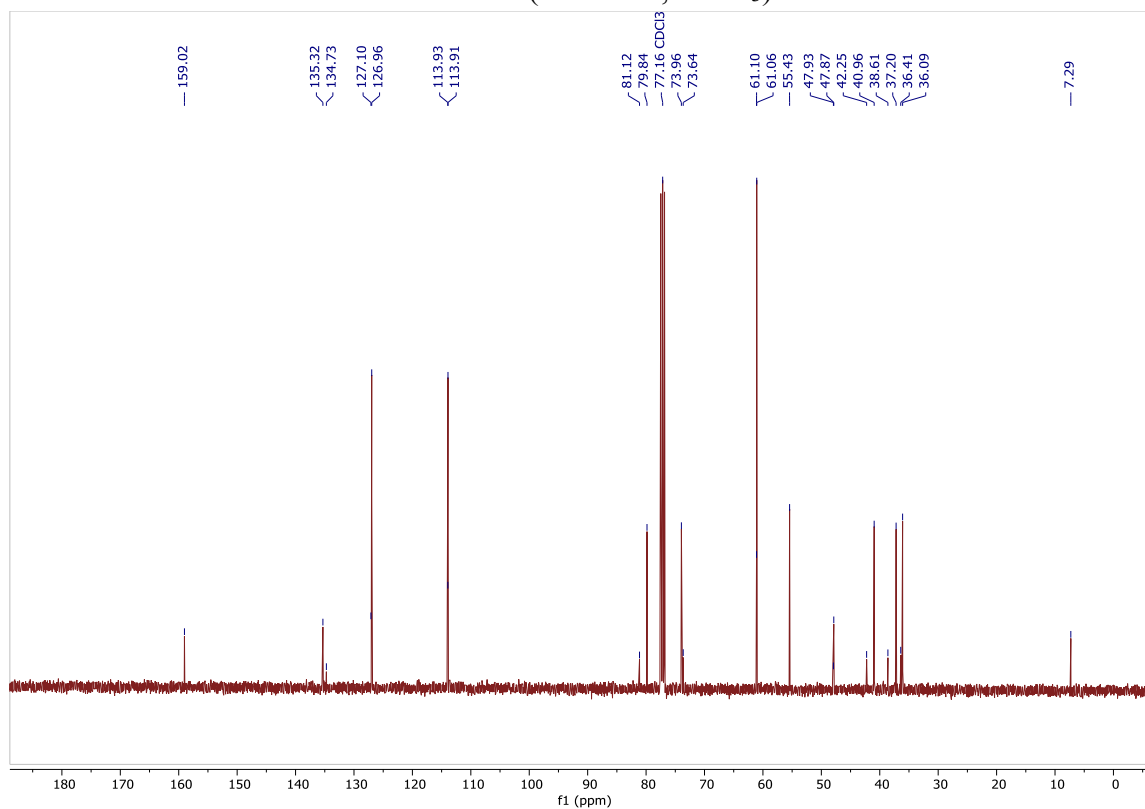
4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-2-(4-methoxyphenyl)tetrahydrofuran, 68



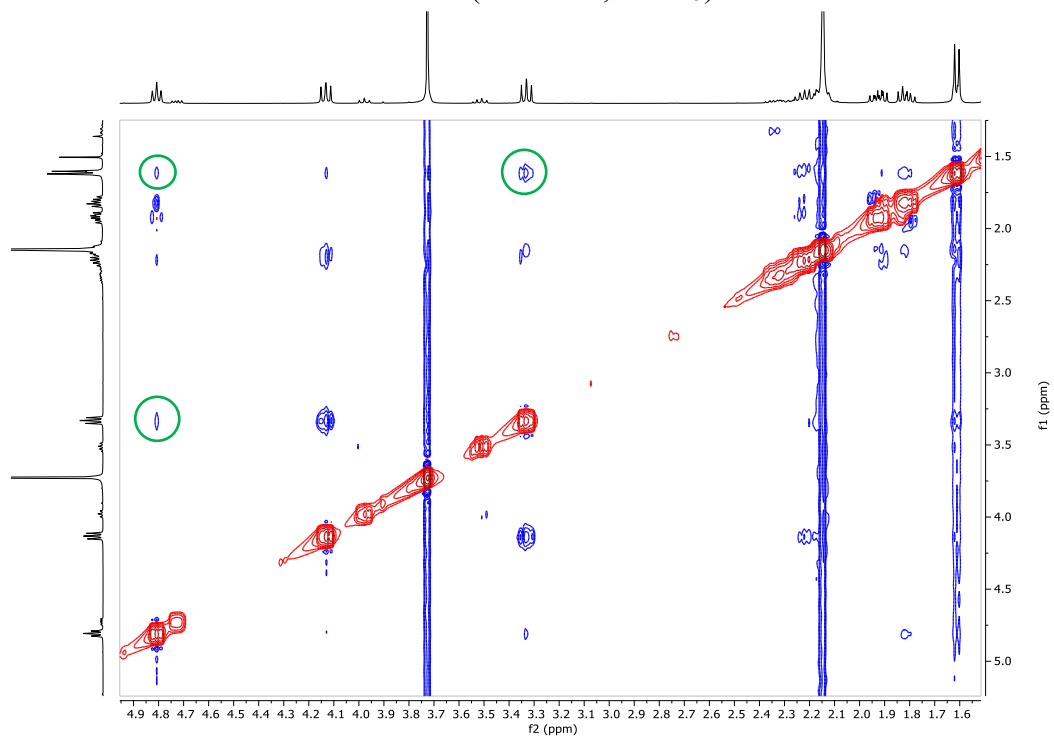
^1H NMR (400 MHz, CDCl_3)



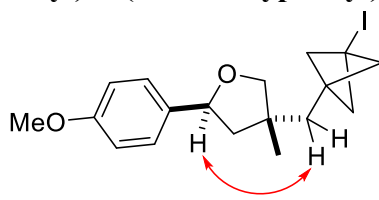
^{13}C NMR (101 MHz, CDCl_3)



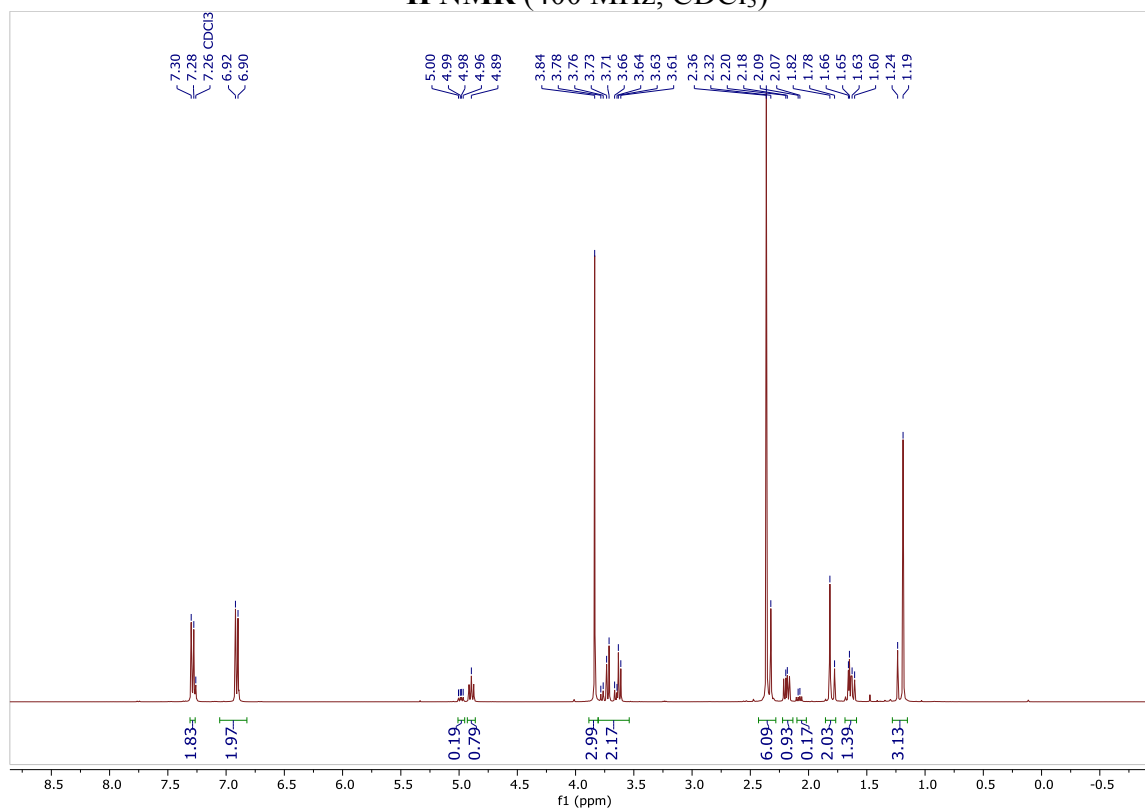
NOESY (400 MHz, CDCl₃)



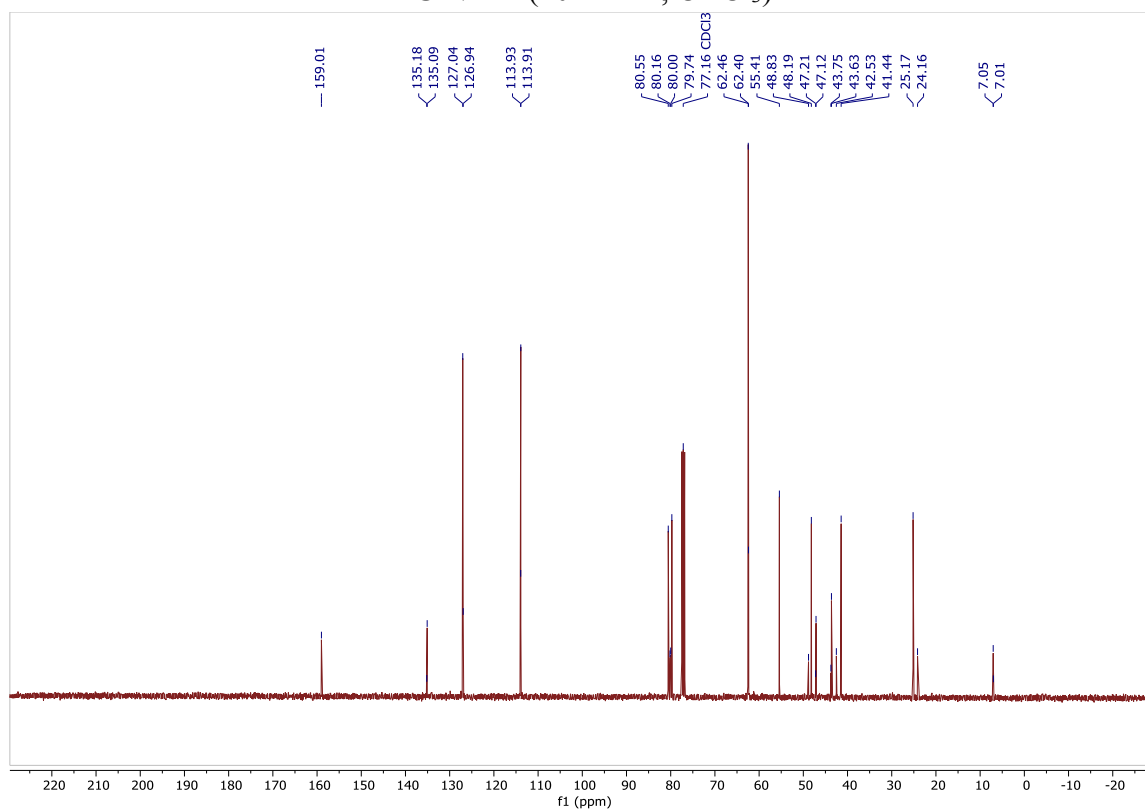
4-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-2-(4-methoxyphenyl)-4-methyltetrahydrofuran, 69



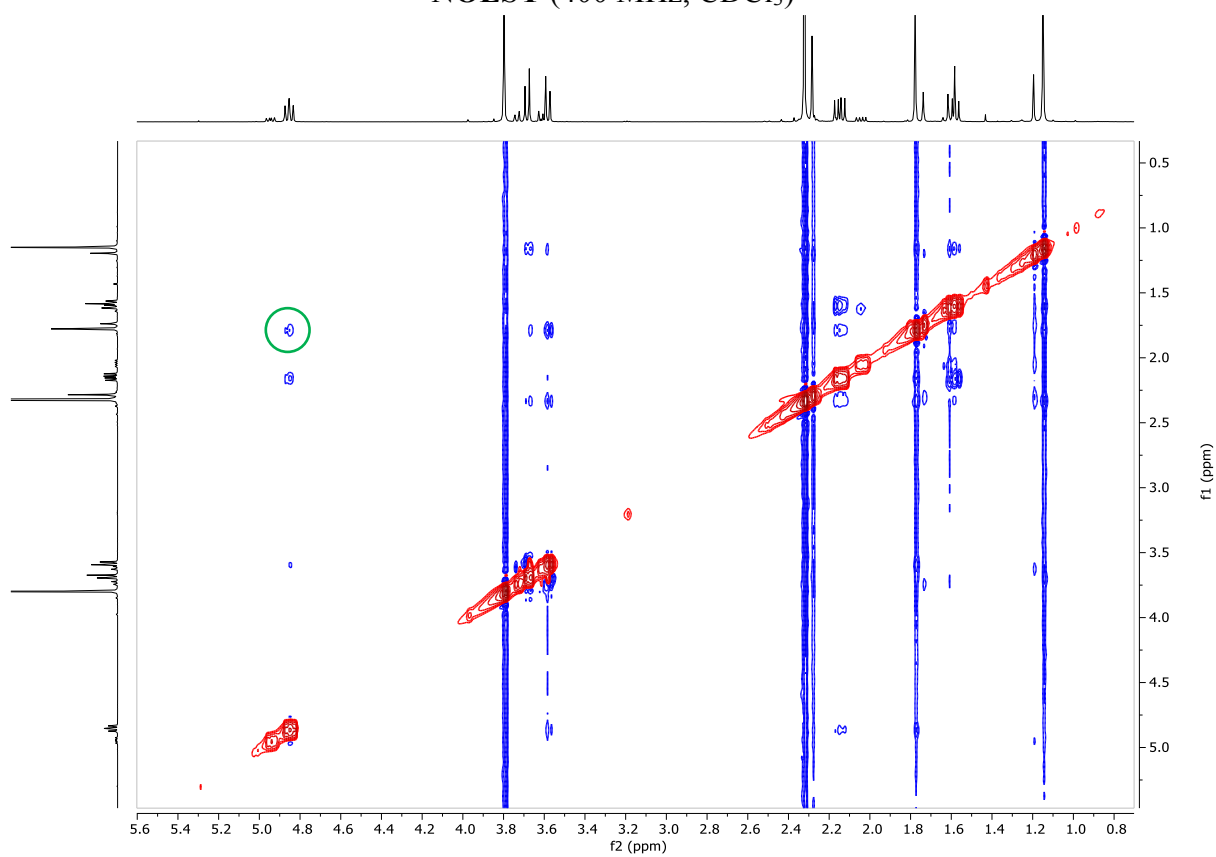
^1H NMR (400 MHz, CDCl_3)



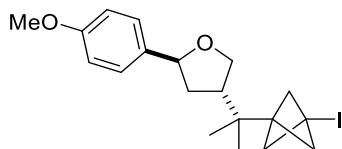
^{13}C NMR (101 MHz, CDCl_3)



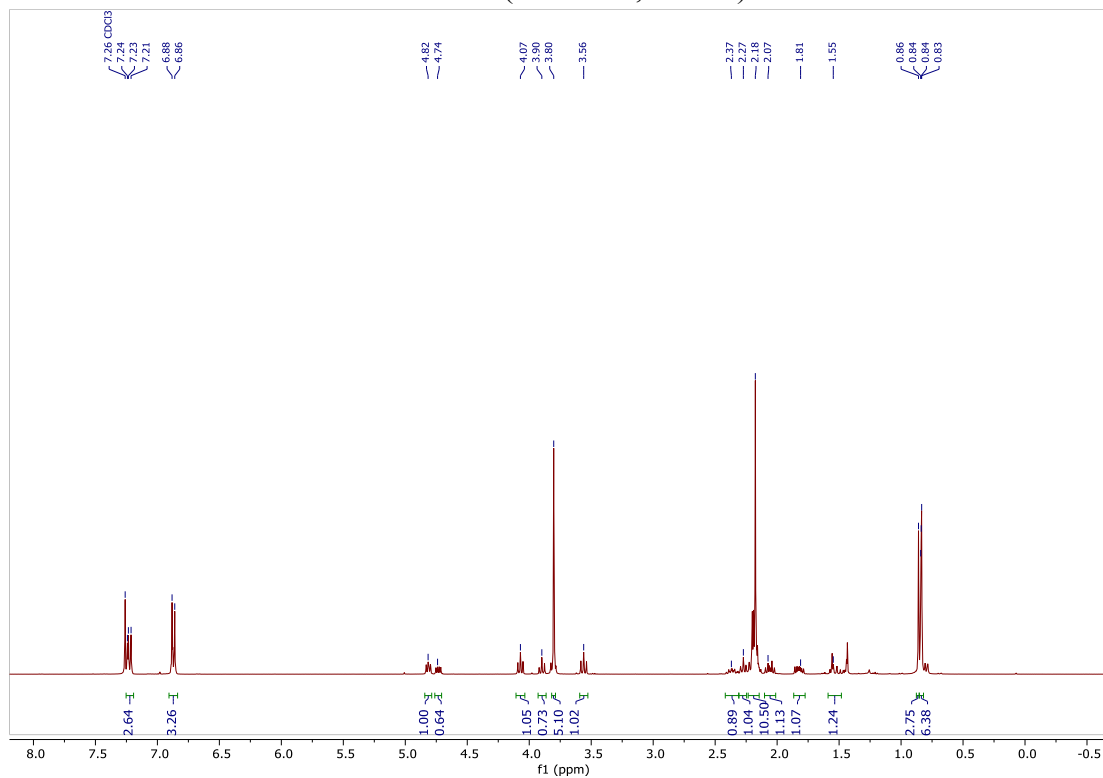
NOESY (400 MHz, CDCl₃)



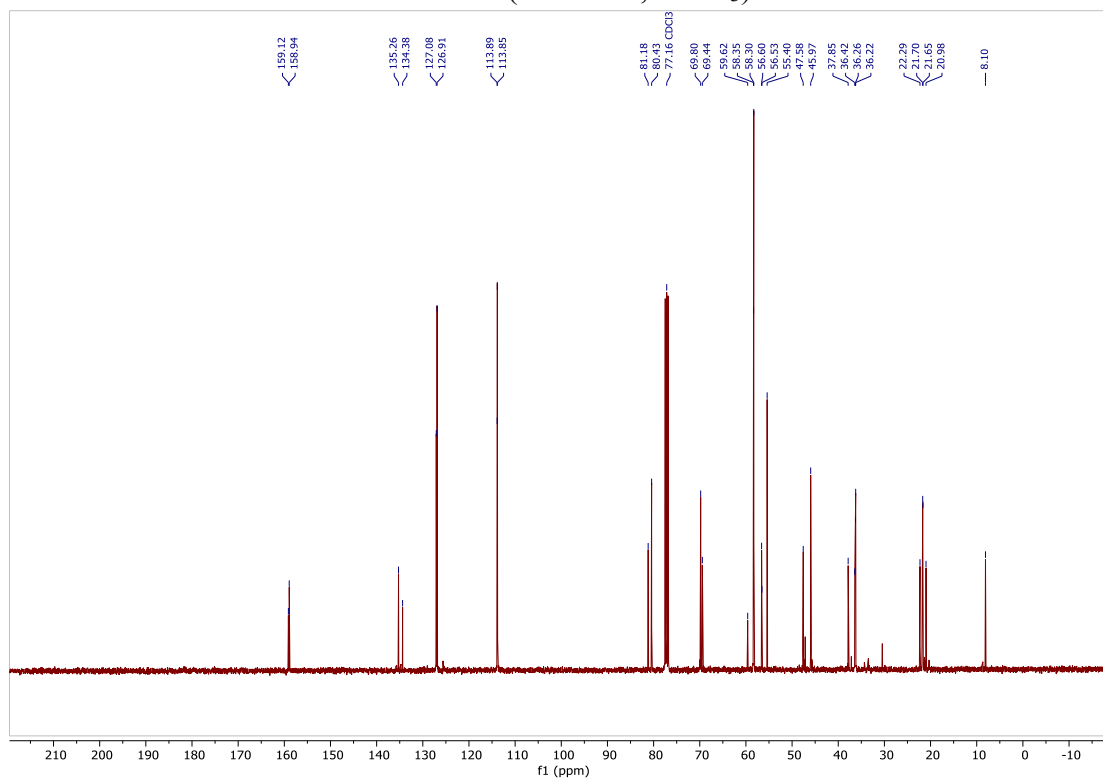
4-(2-(3-Iodobicyclo[1.1.1]pentan-1-yl)propan-2-yl)-2-(4-methoxyphenyl)tetrahydrofuran, 70



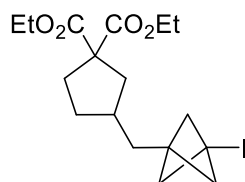
¹H NMR (400 MHz, CDCl₃)



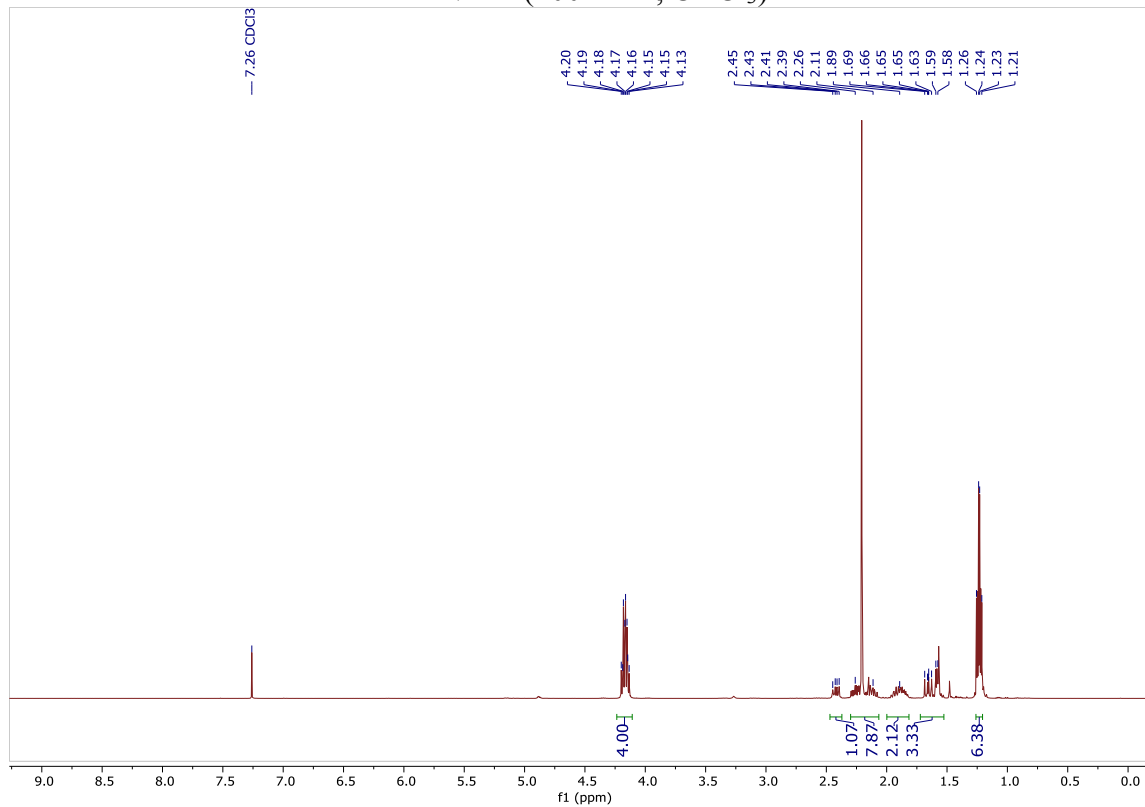
¹³C NMR (101 MHz, CDCl₃)



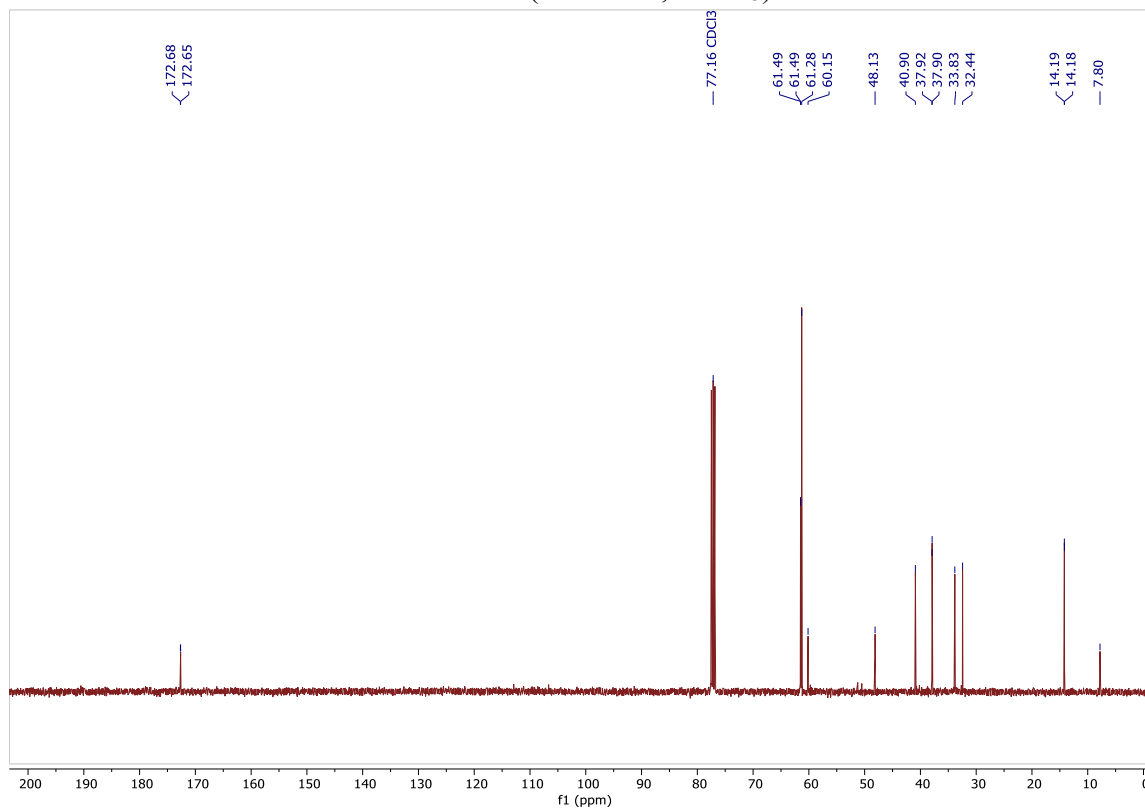
Diethyl 3-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)cyclopentane-1,1-dicarboxylate, 71



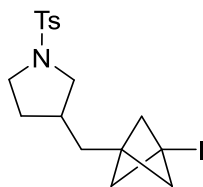
^1H NMR (400 MHz, CDCl_3)



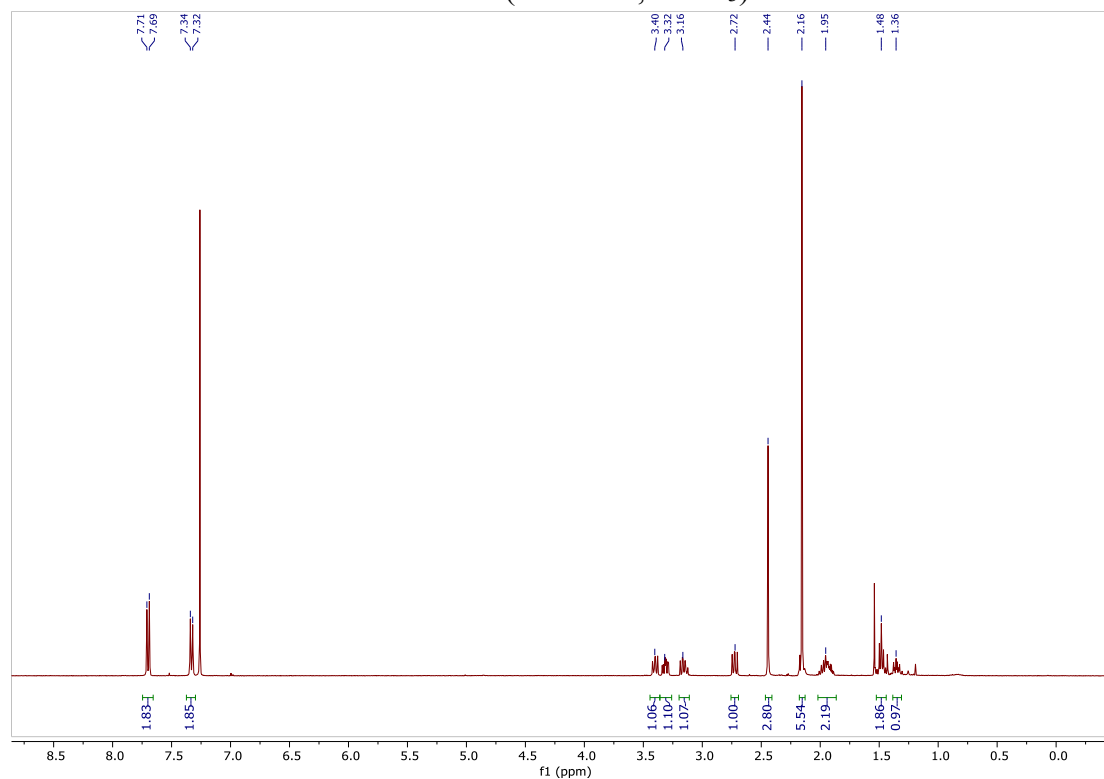
^{13}C NMR (101 MHz, CDCl_3)



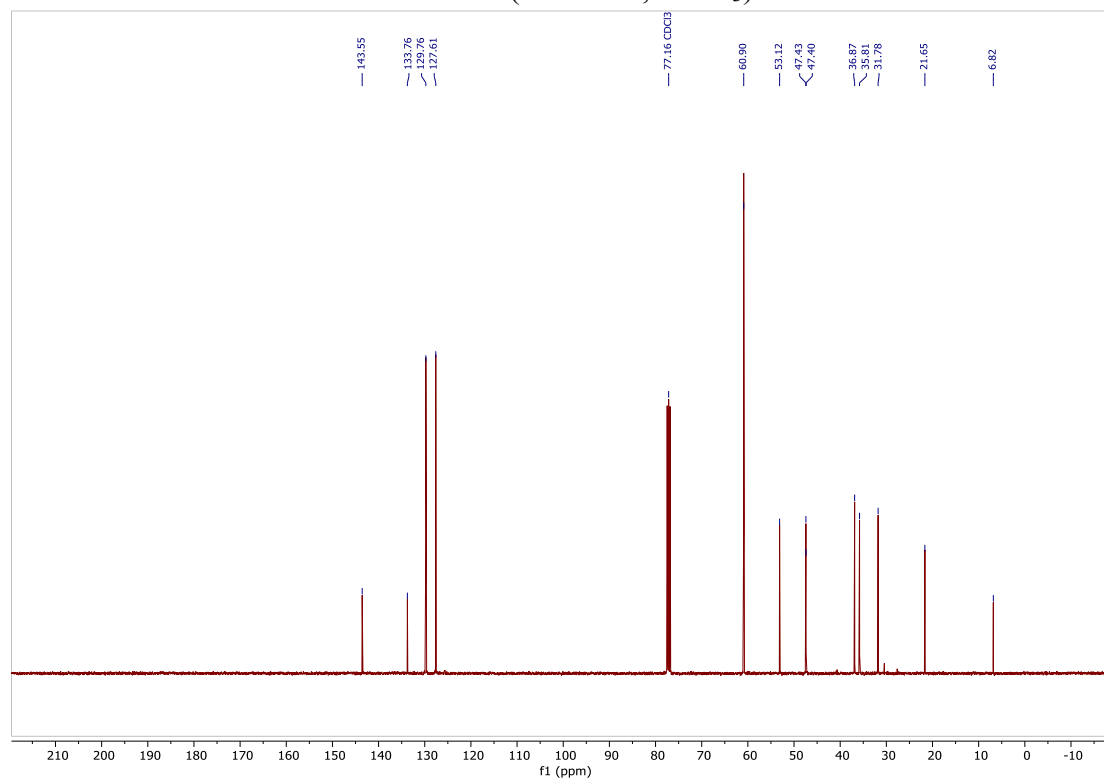
3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-1-tosylpyrrolidine, 72



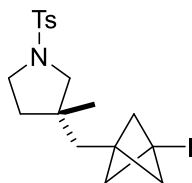
^1H NMR (400 MHz, CDCl_3)



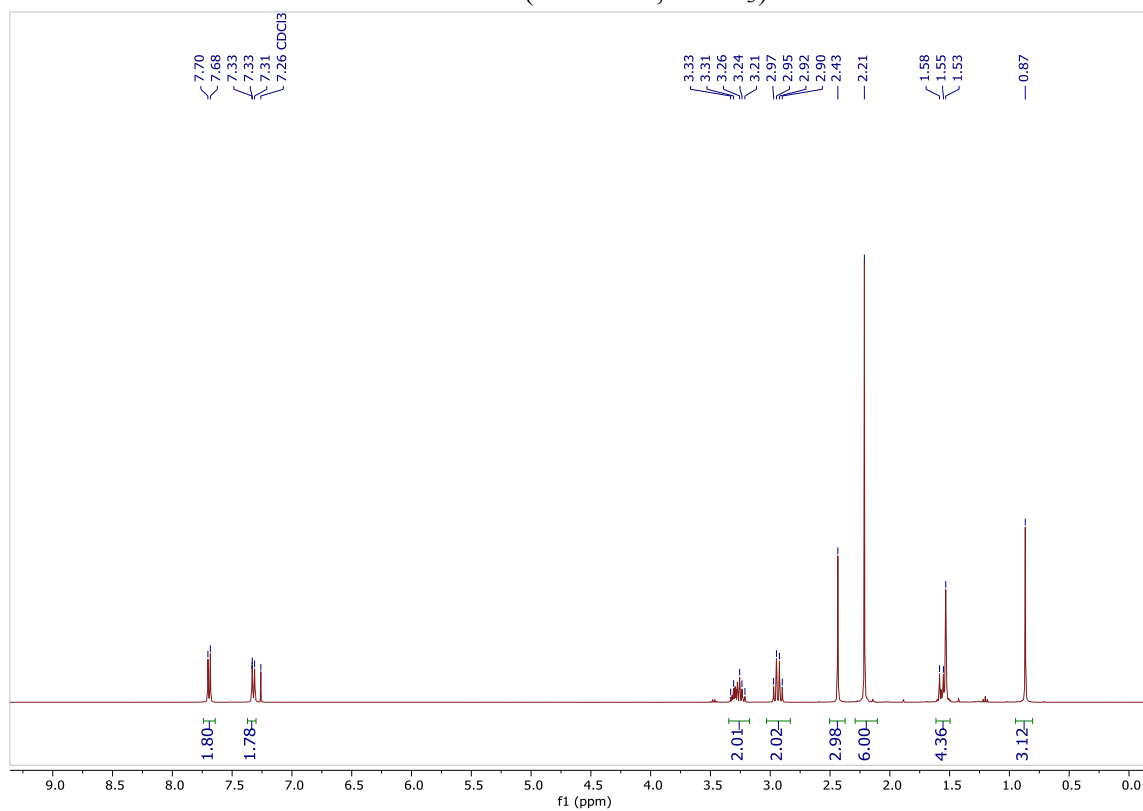
^{13}C NMR (101 MHz, CDCl_3)



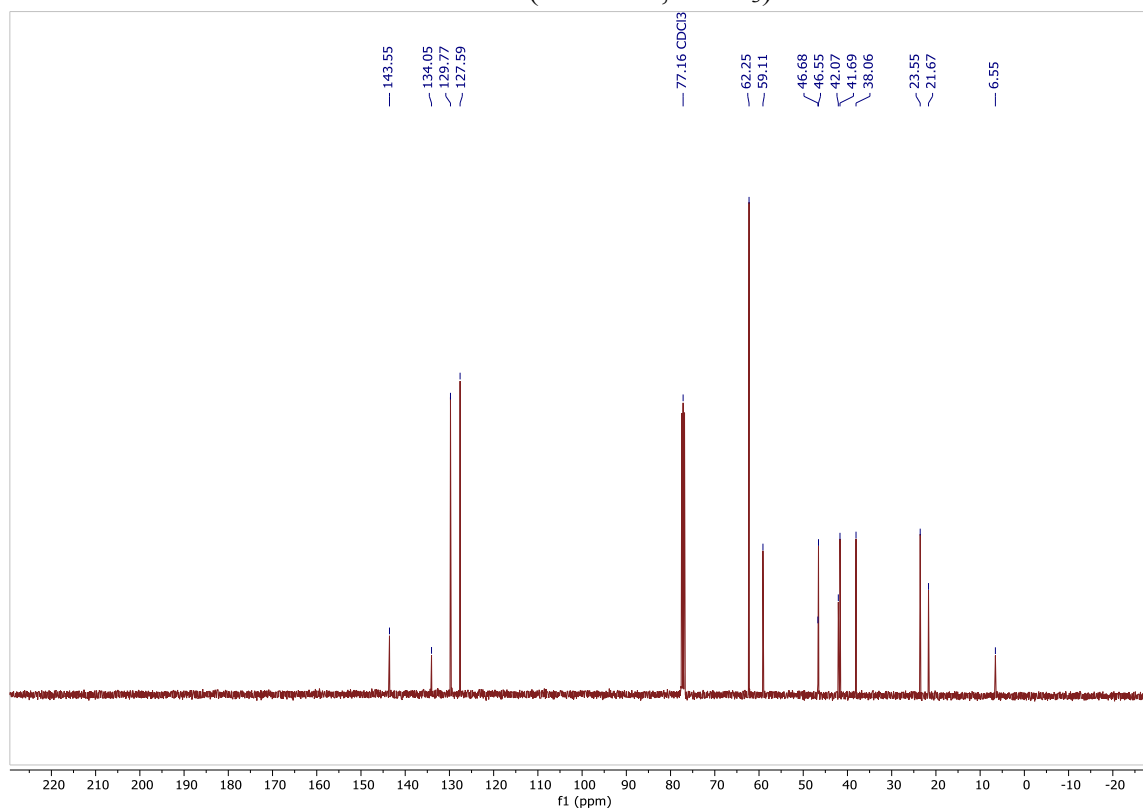
3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-3-methyl-1-tosylpyrrolidine, 73



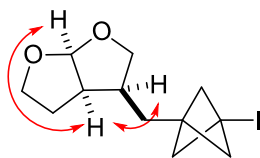
^1H NMR (400 MHz, CDCl_3)



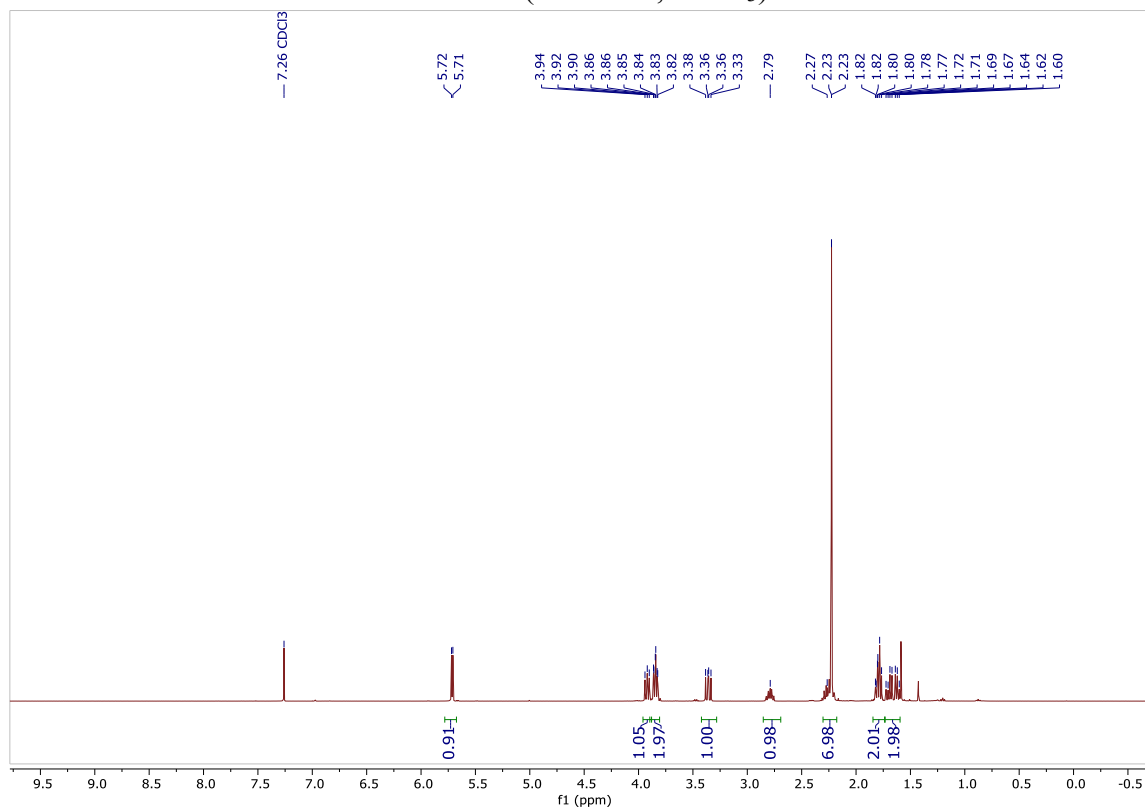
^{13}C NMR (101 MHz, CDCl_3)



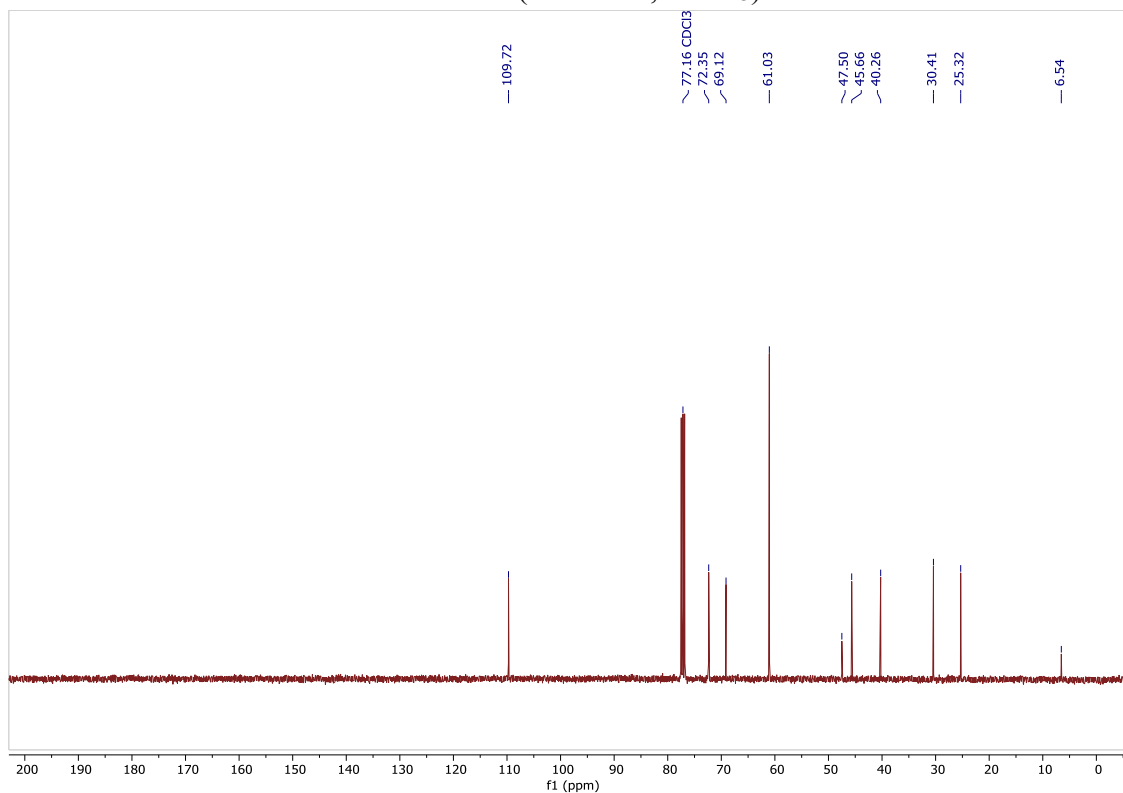
3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)hexahydrofuro[2,3-*b*]furan. 74



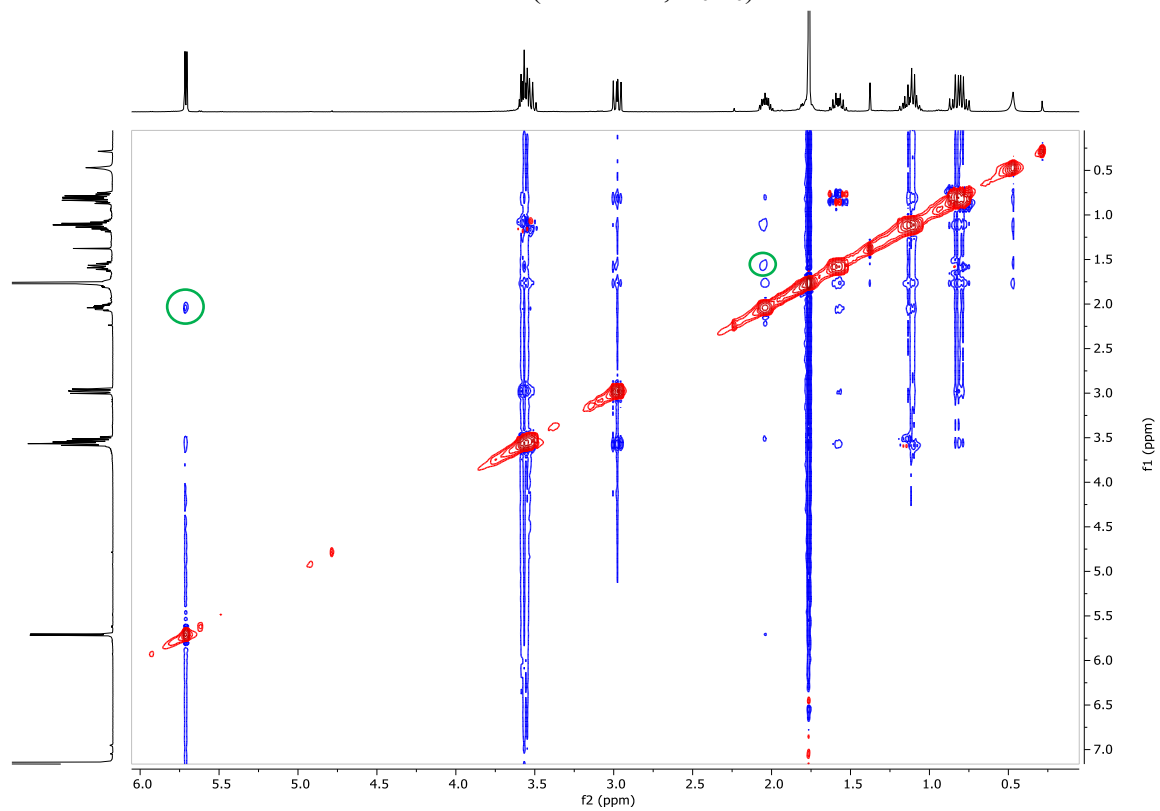
^1H NMR (400 MHz, CDCl_3)



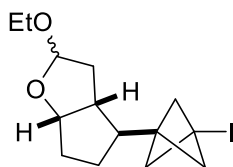
^{13}C NMR (101 MHz, CDCl_3)



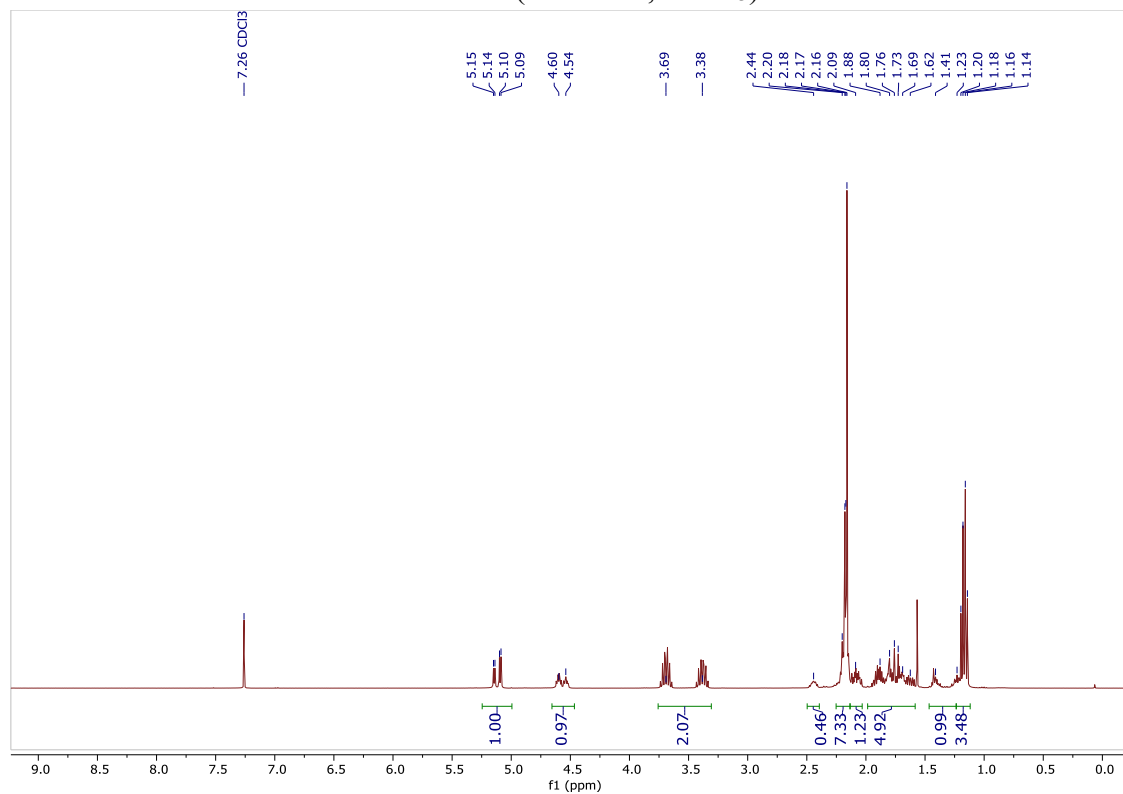
NOESY (400 MHz, C₆D₆)



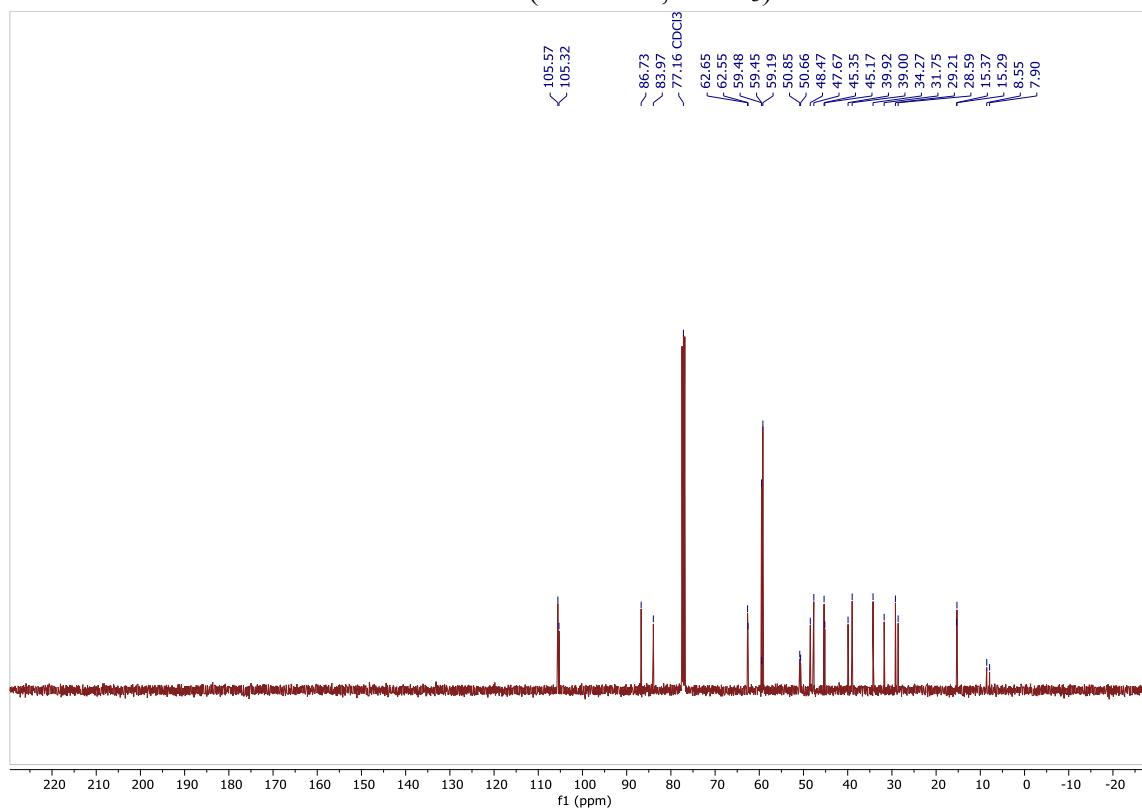
2-Ethoxy-4-(3-iodobicyclo[1.1.1]pentan-1-yl)hexahydro-2*H*-cyclopenta[*b*]furan, 75



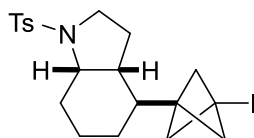
^1H NMR (400 MHz, CDCl_3)



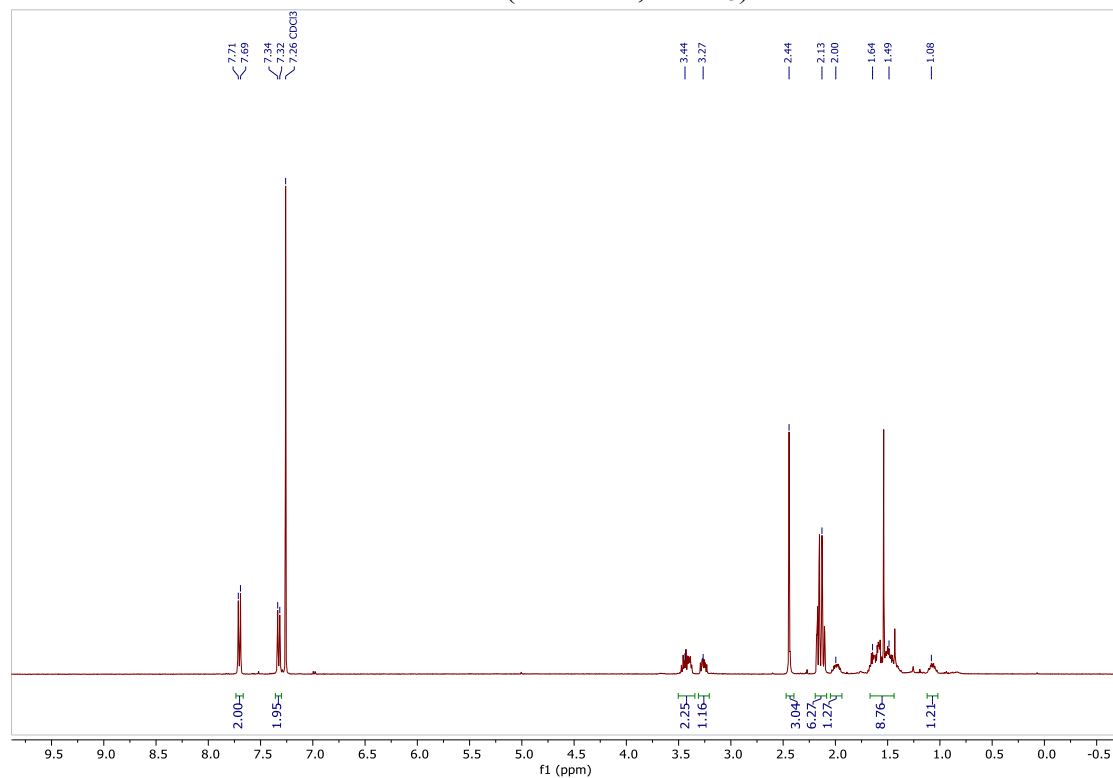
^{13}C NMR (101 MHz, CDCl_3)



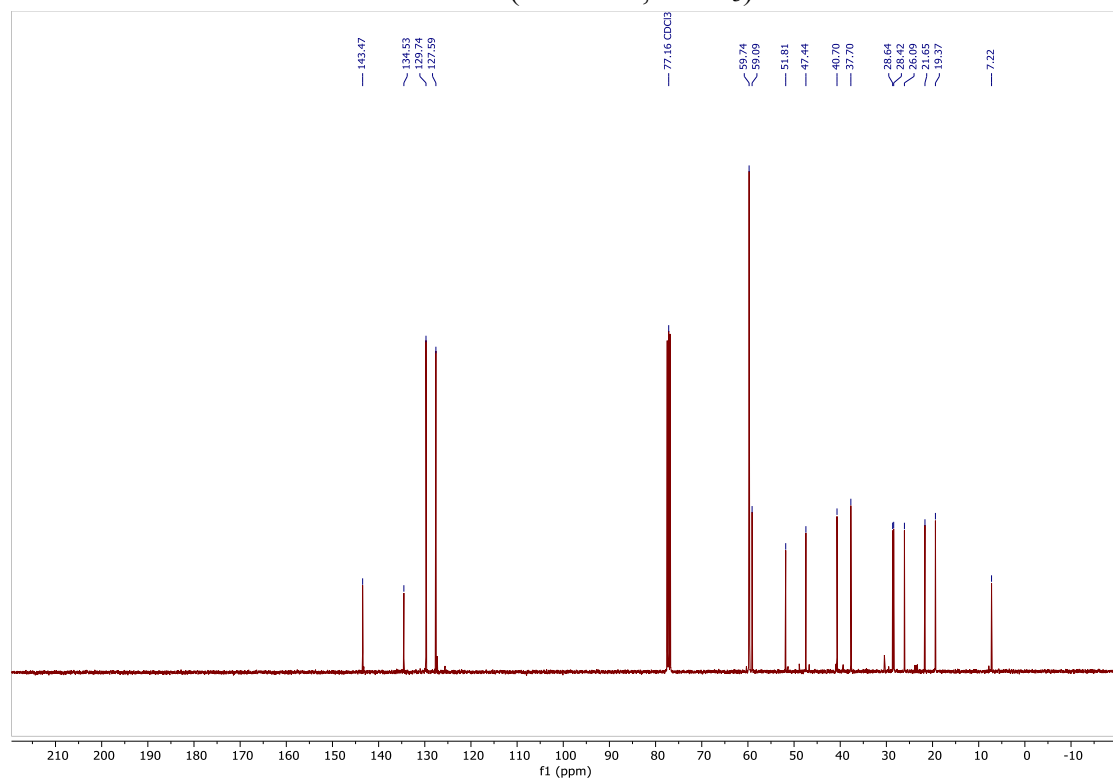
4-(3-Iodobicyclo[1.1.1]pentan-1-yl)-1-tosyloctahydro-1*H*-indole, 76



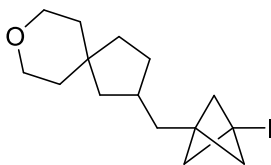
^1H NMR (400 MHz, CDCl_3)



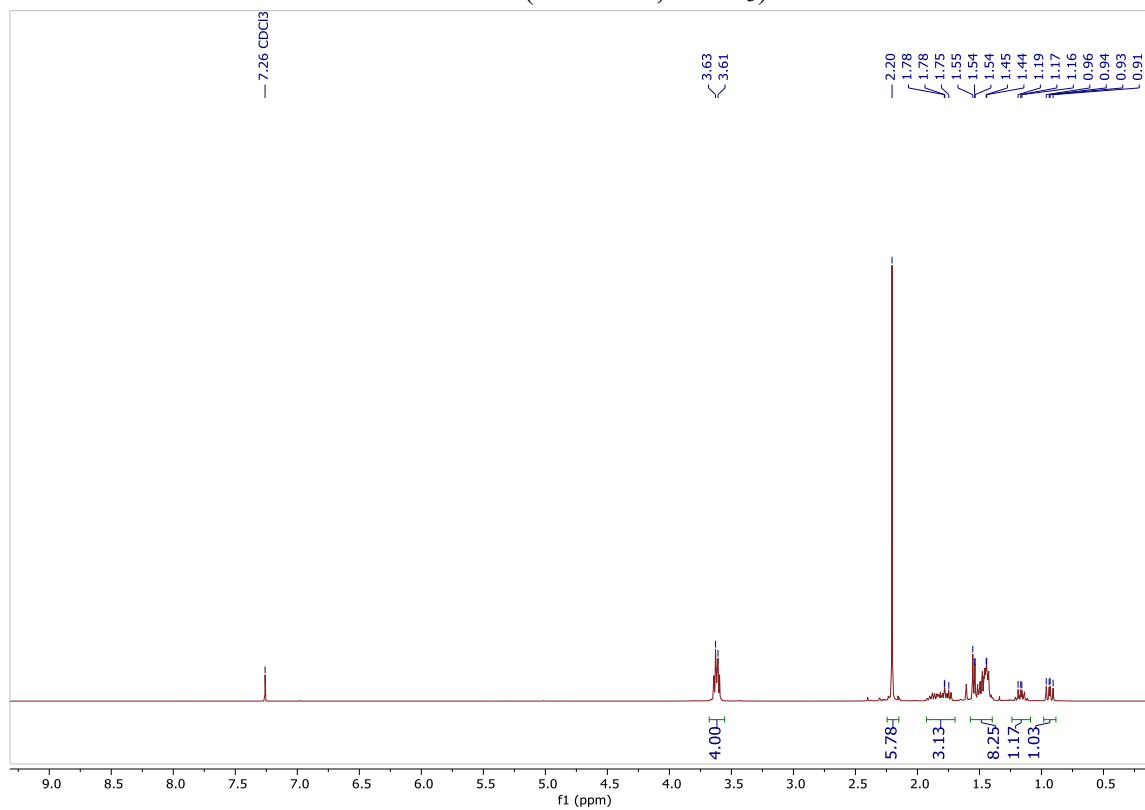
^{13}C NMR (101 MHz, CDCl_3)



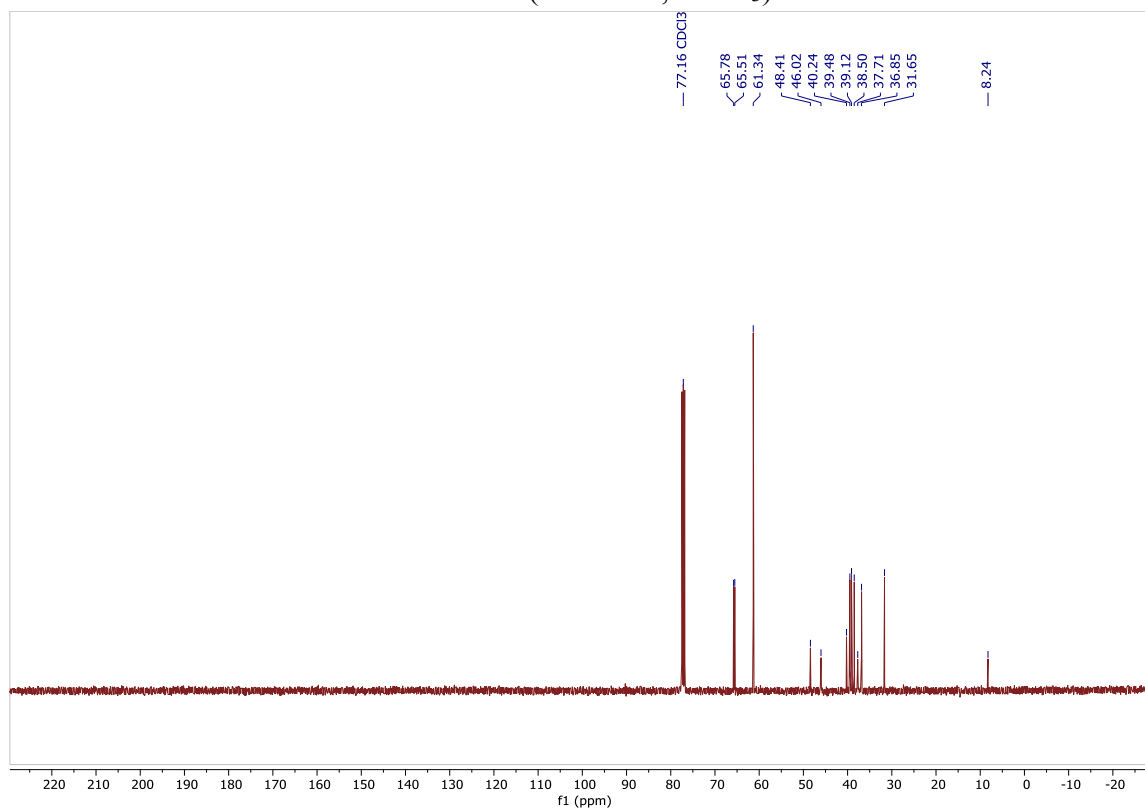
2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-8-oxaspiro[4.5]decane, 77



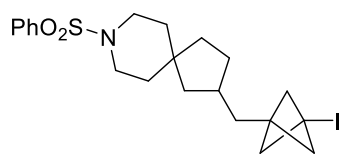
^1H NMR (400 MHz, CDCl_3)



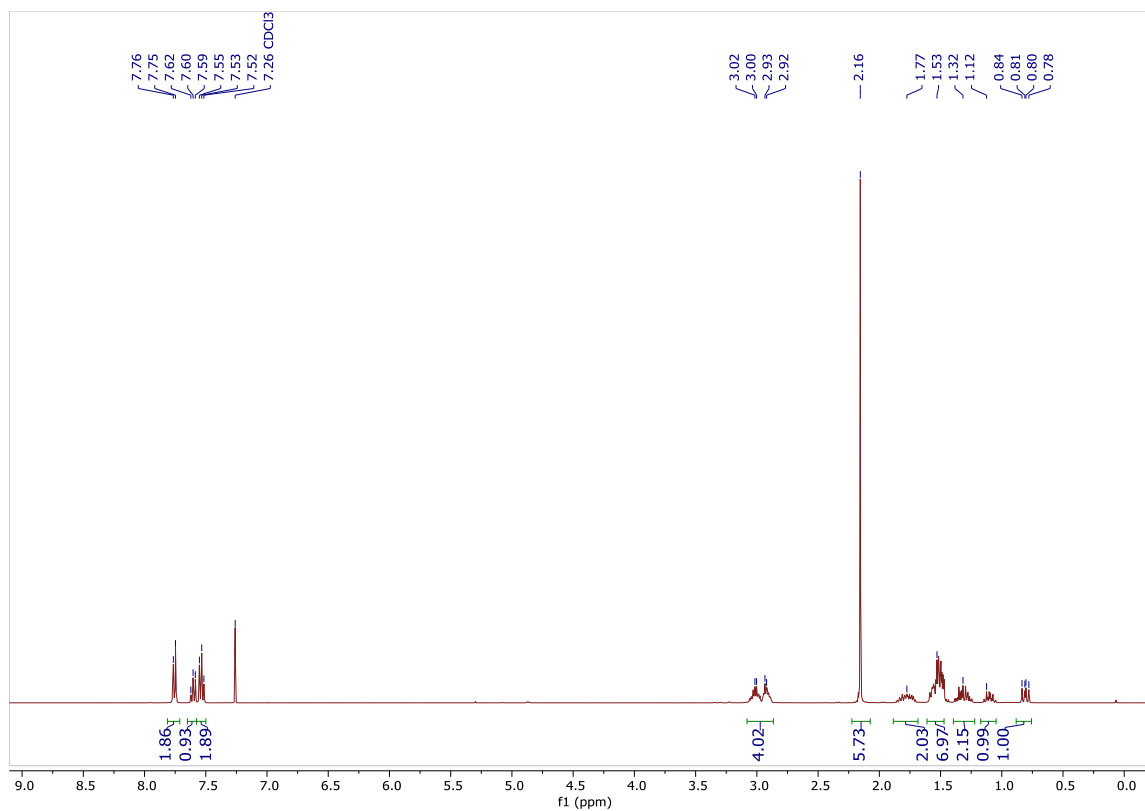
^{13}C NMR (101 MHz, CDCl_3)



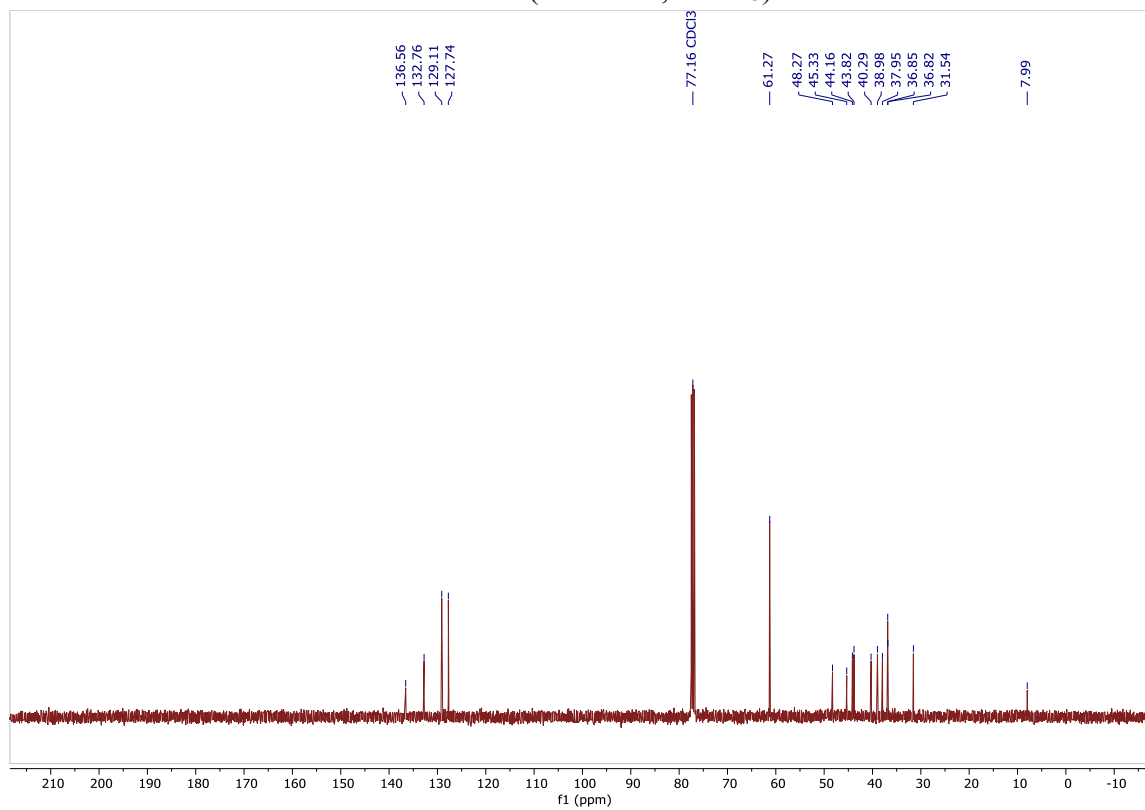
2-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-8-(phenylsulfonyl)-8-azaspiro[4.5]decane, 78



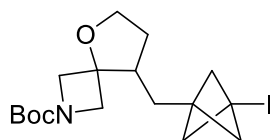
^1H NMR (400 MHz, CDCl_3)



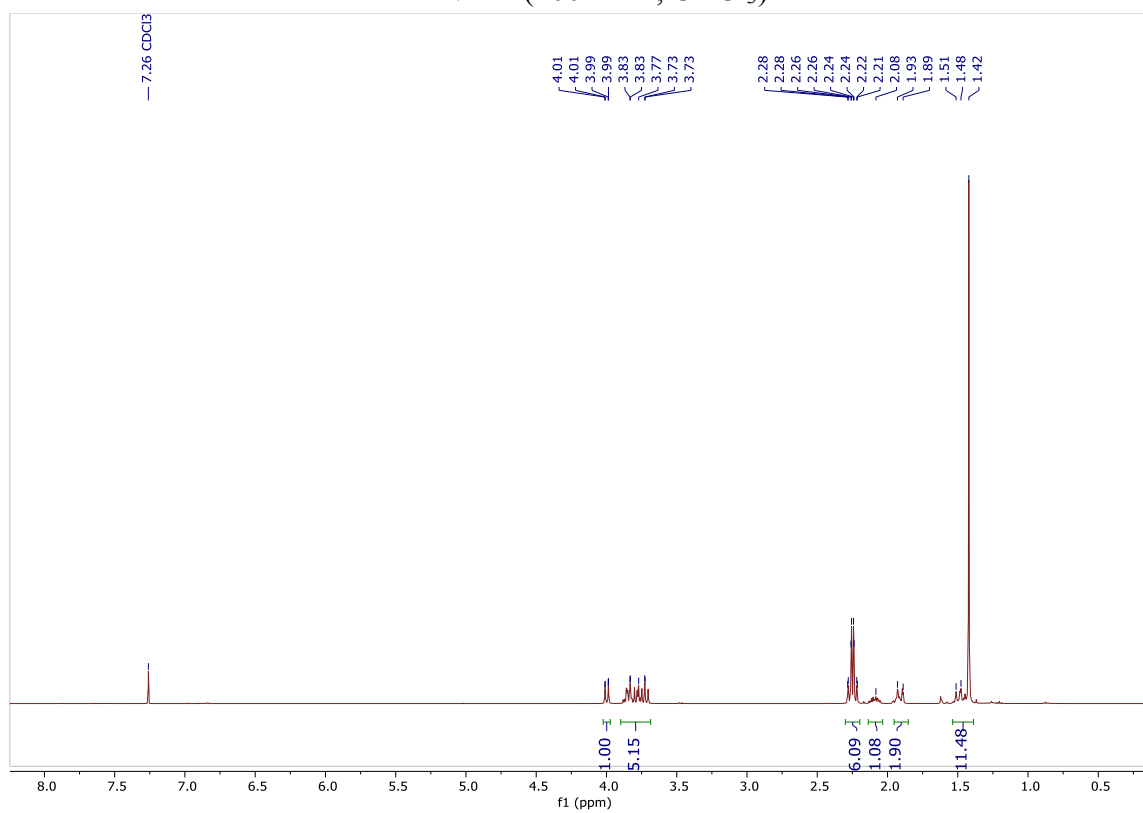
^{13}C NMR (101 MHz, CDCl_3)



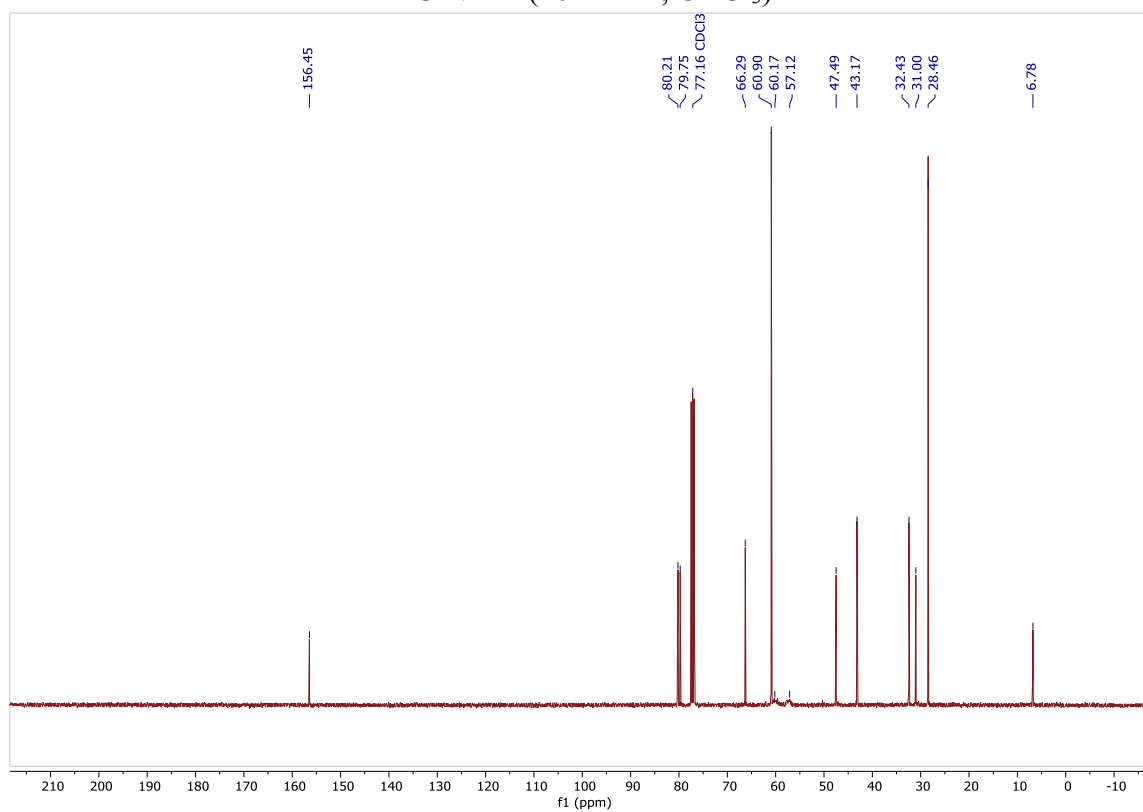
***tert*-Butyl 8-((3-iodobicyclo[1.1.1]pentan-1-yl)methyl)-5-oxa-2-azaspiro[3.4]octane-2-carboxylate, 79**



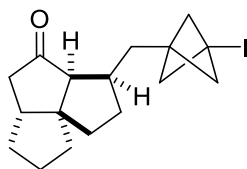
^1H NMR (400 MHz, CDCl_3)



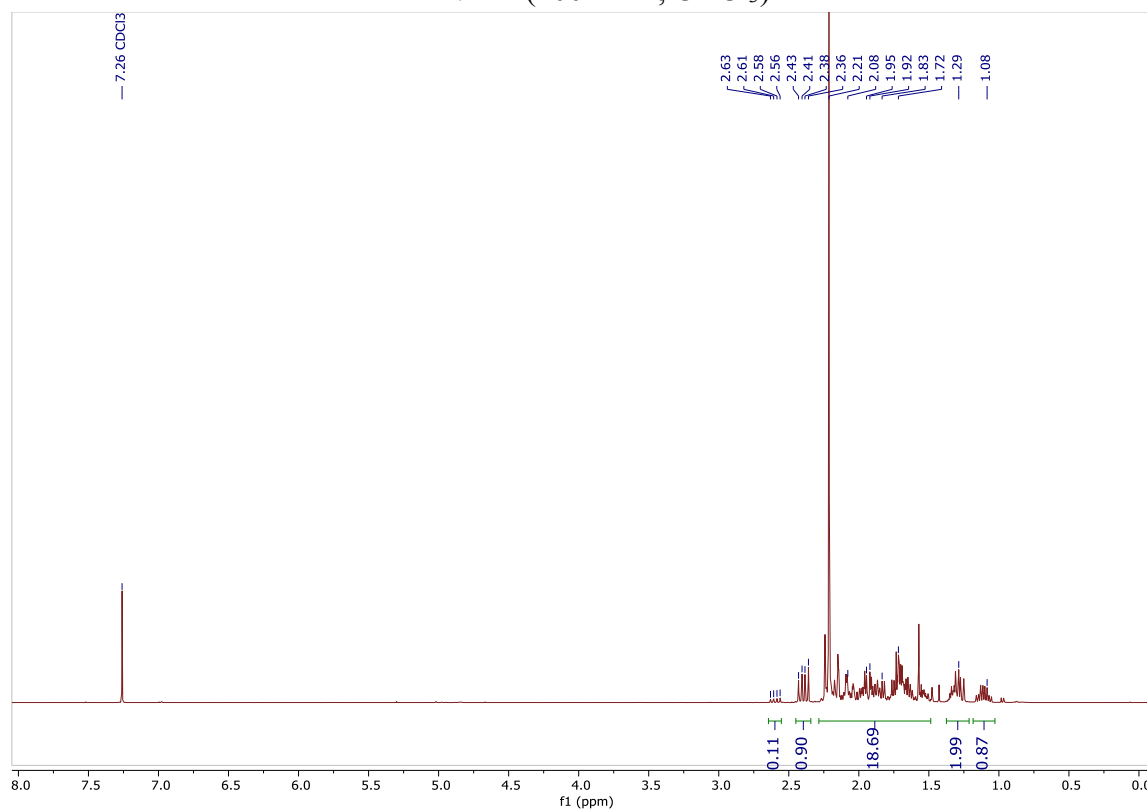
^{13}C NMR (101 MHz, CDCl_3)



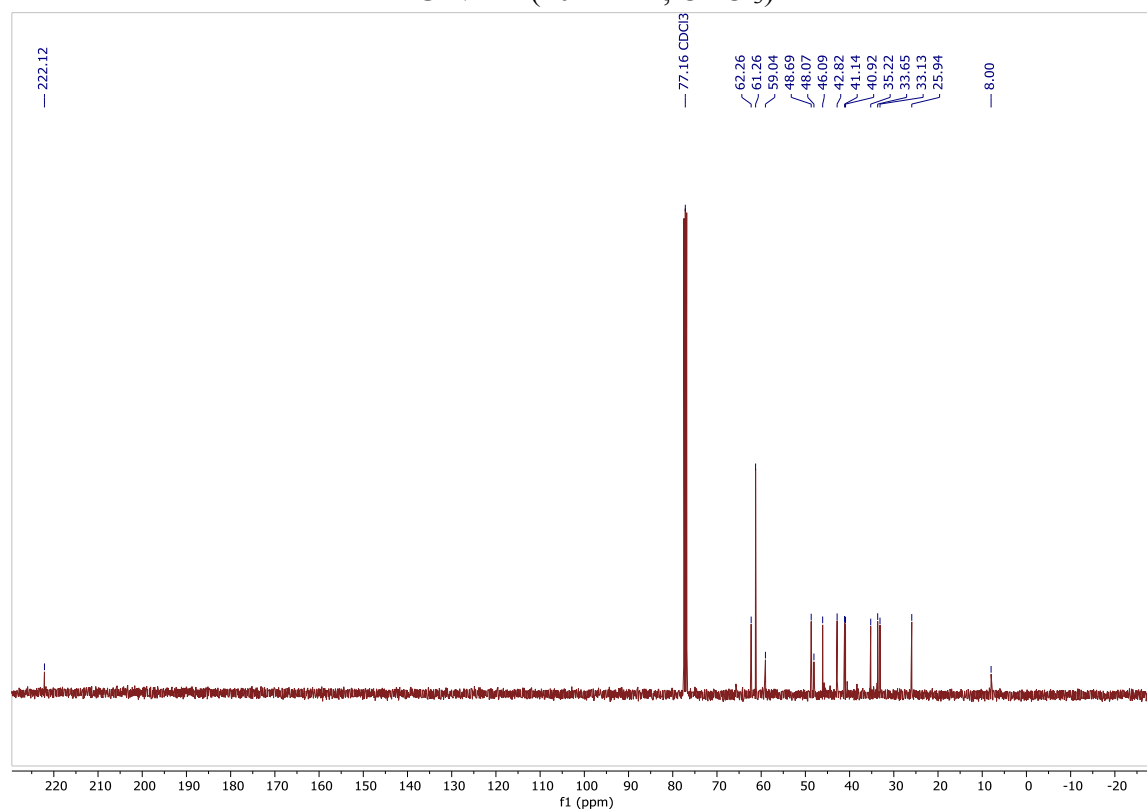
3-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)octahydrocyclopenta[*c*]pentalen-4(5*H*)-one, 80



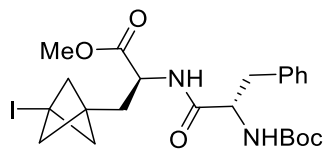
^1H NMR (400 MHz, CDCl_3)



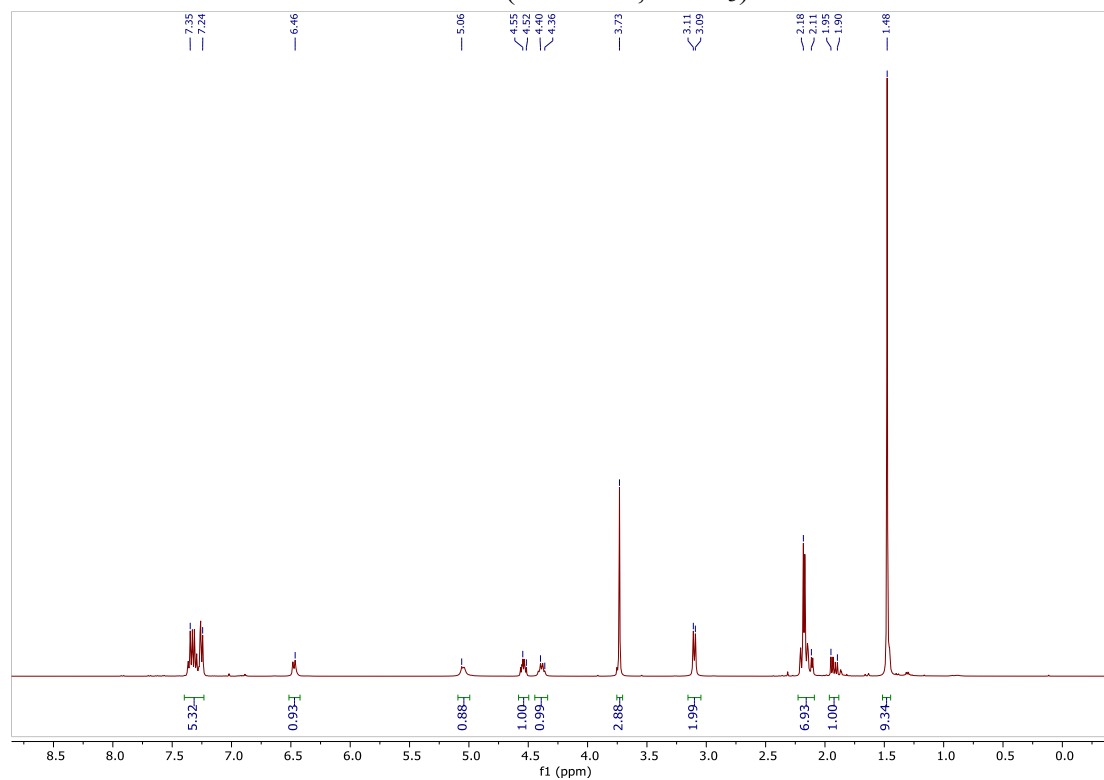
^{13}C NMR (101 MHz, CDCl_3)



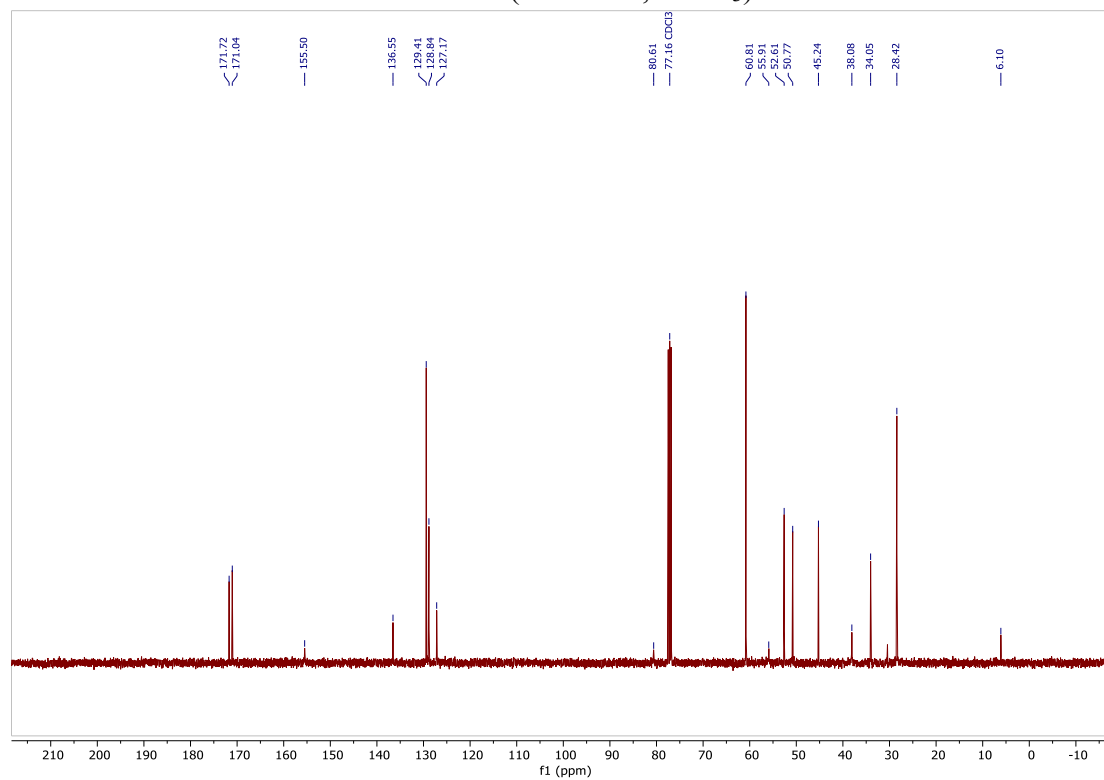
Boc-Phe- β -(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, 81



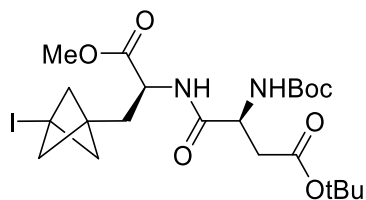
^1H NMR (400 MHz, CDCl_3)



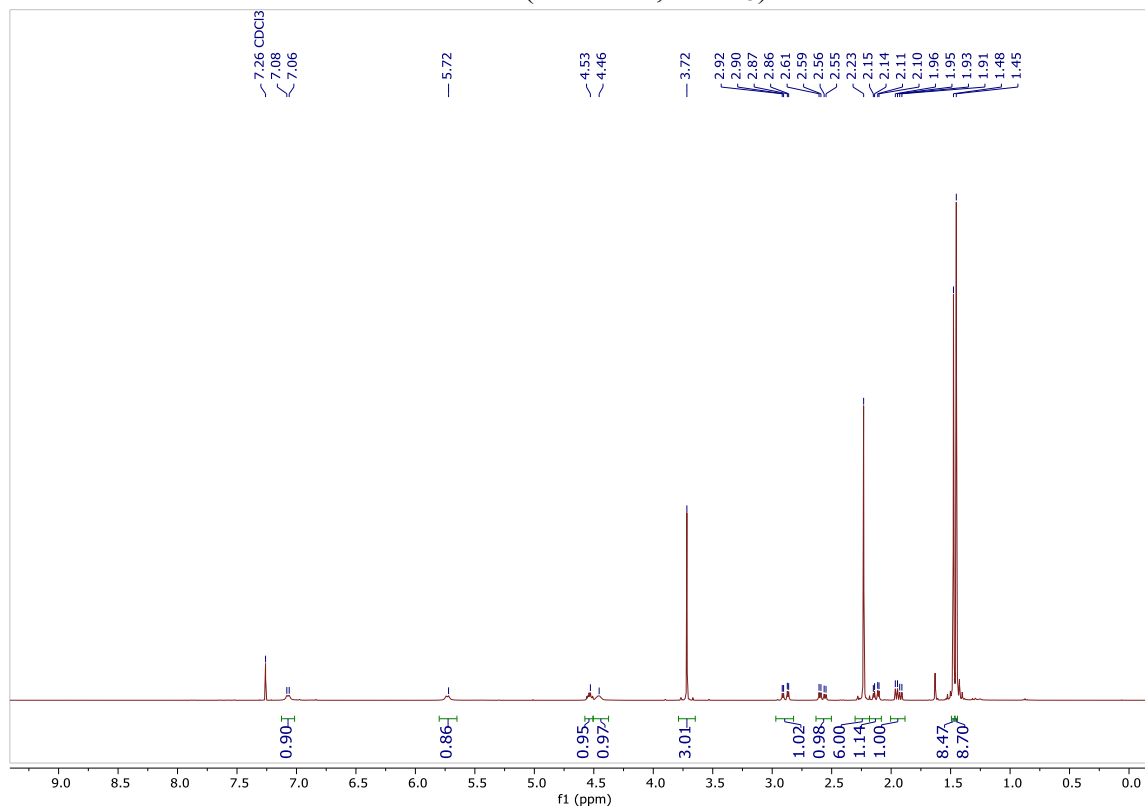
^{13}C NMR (101 MHz, CDCl_3)



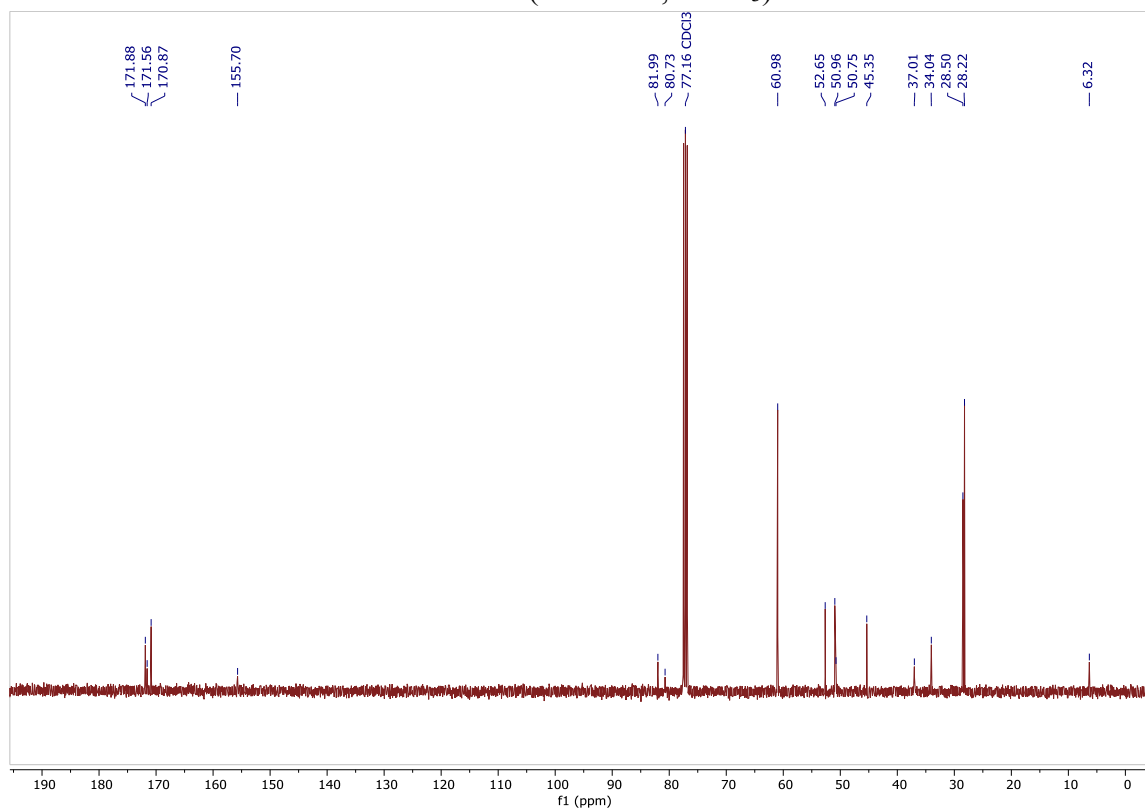
Boc-Asp(OtBu)- β -(3-iodobicyclo[1.1.1]pentan-1-yl)Ala-OMe, 82



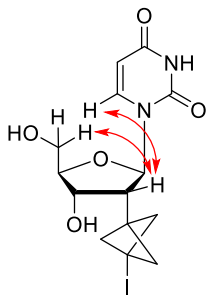
^1H NMR (400 MHz, CDCl_3)



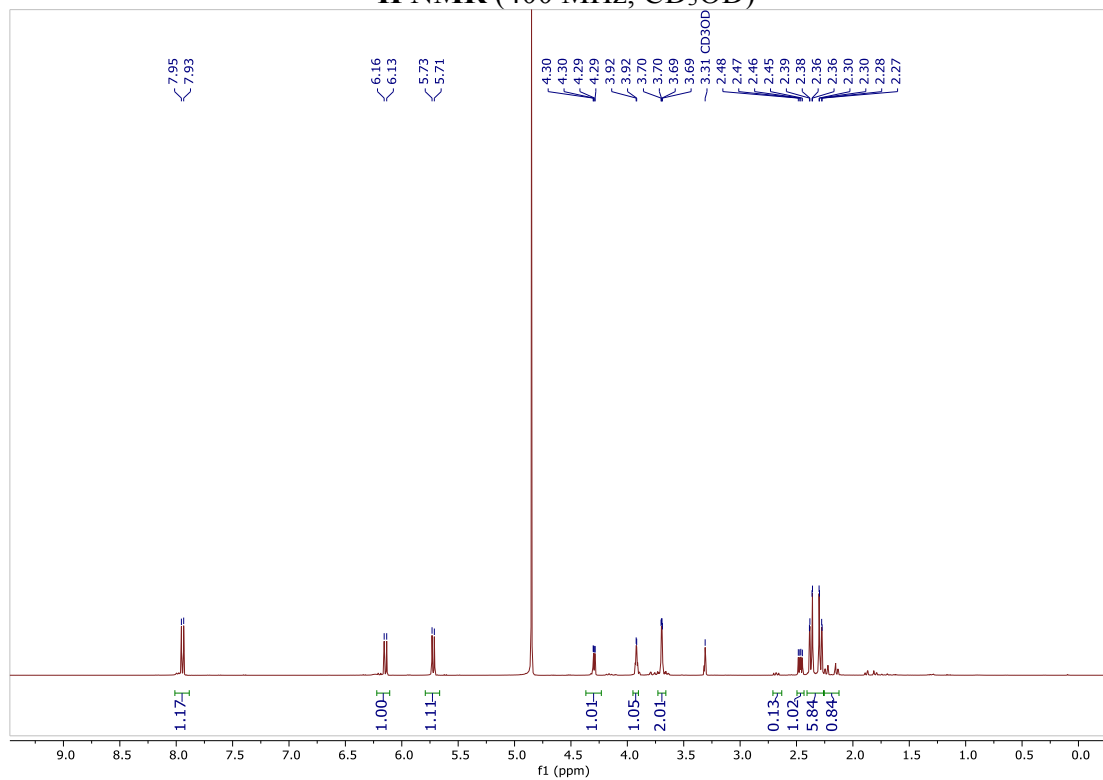
^{13}C NMR (101 MHz, CDCl_3)



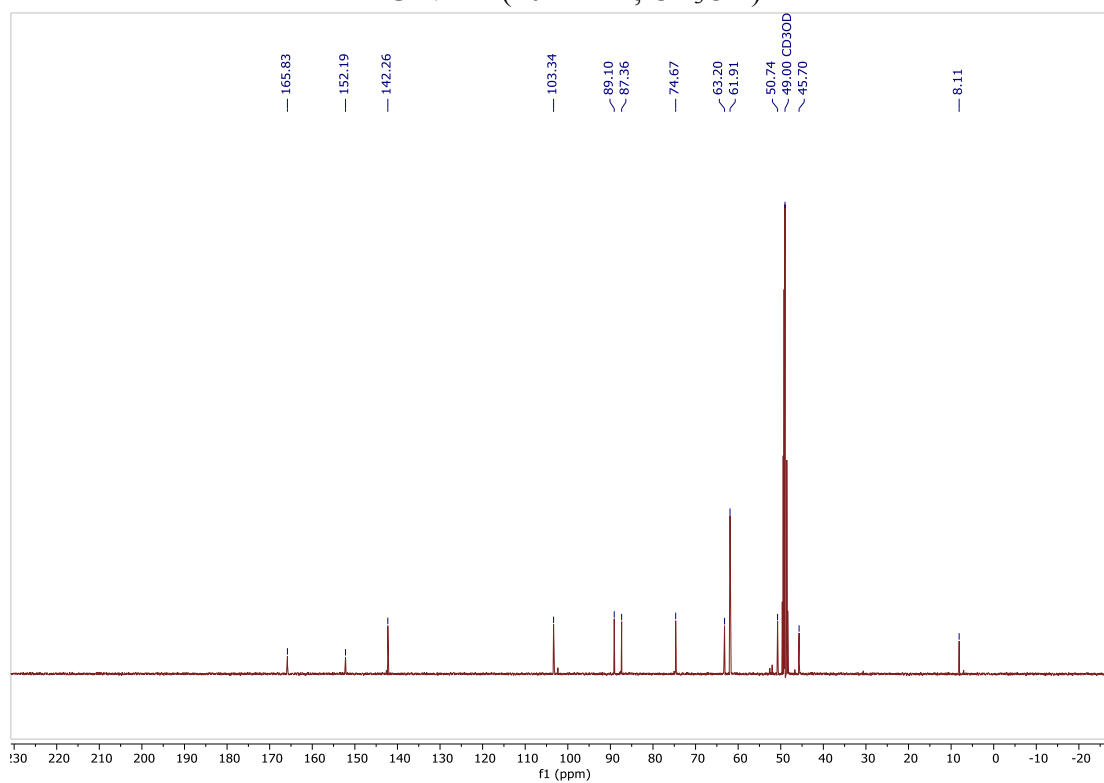
2'-(3-Iodobicyclo[1.1.1]pentan-1-yl)-2'-deoxyuridine, 83



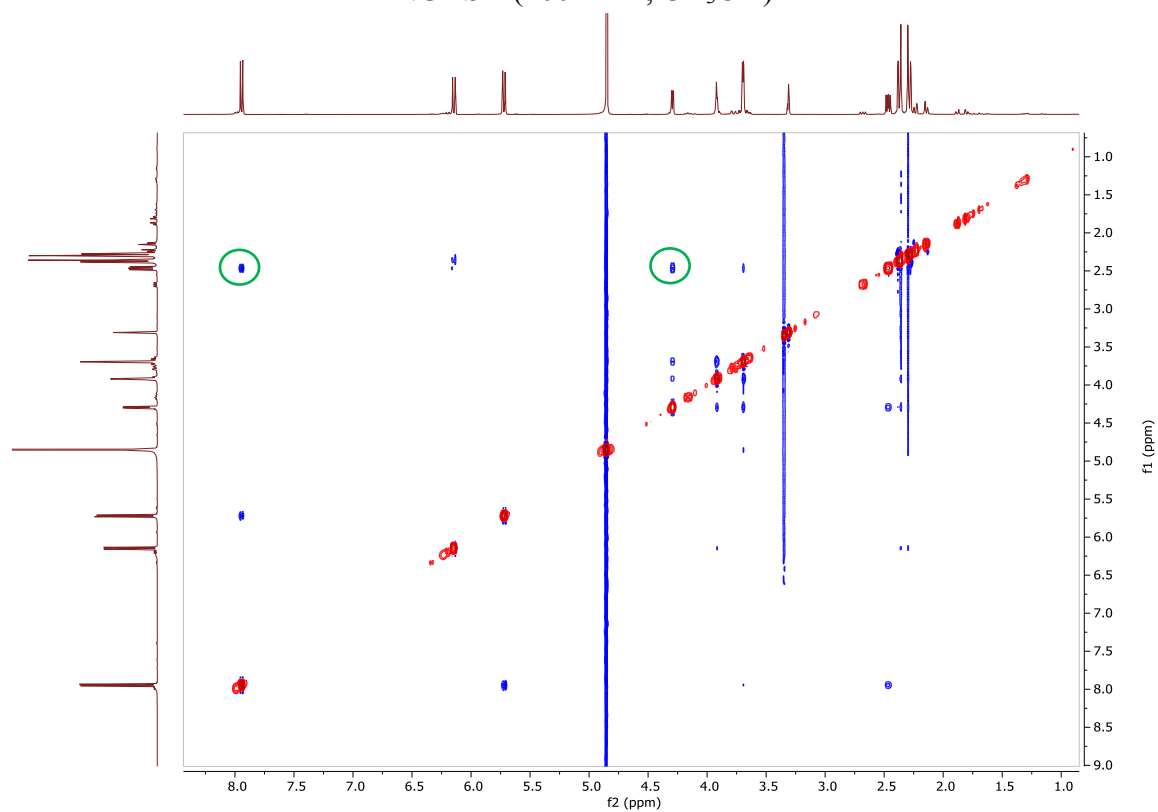
¹H NMR (400 MHz, CD₃OD)



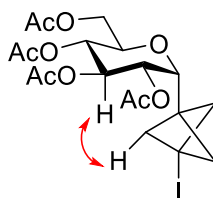
¹³C NMR (101 MHz, CD₃OD)



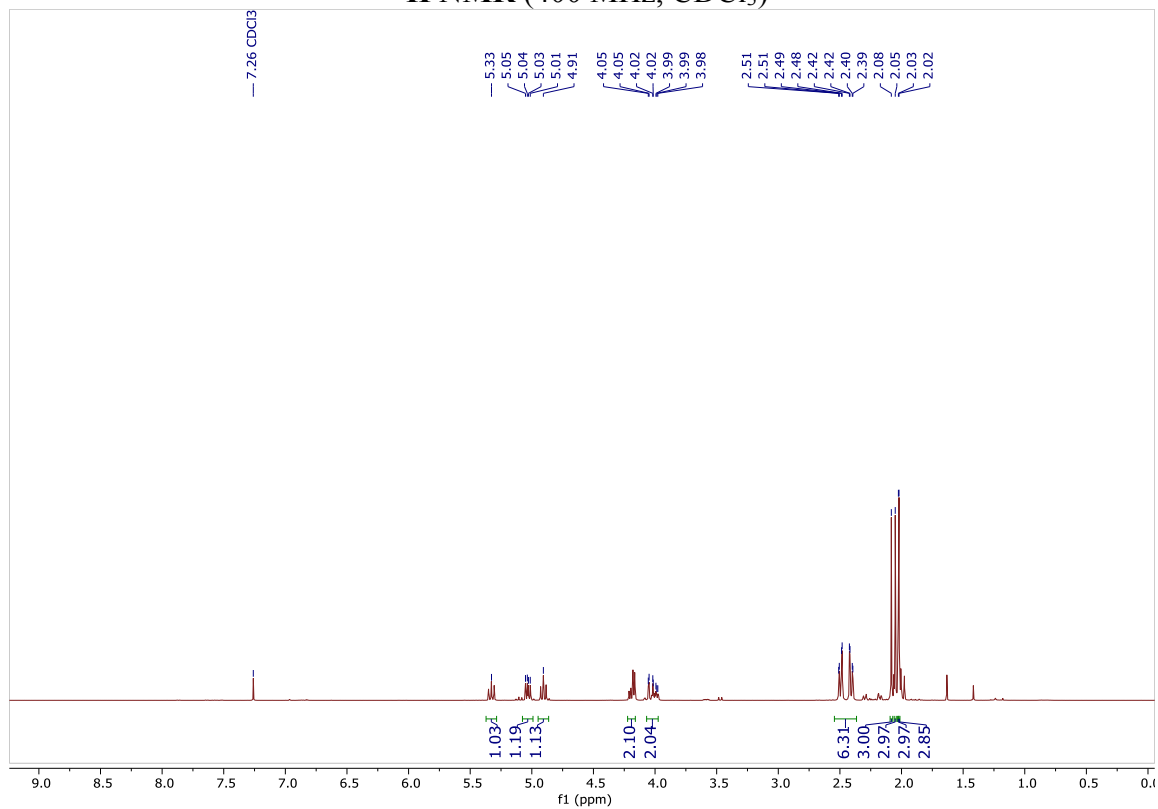
NOESY (400 MHz, CD₃OD)



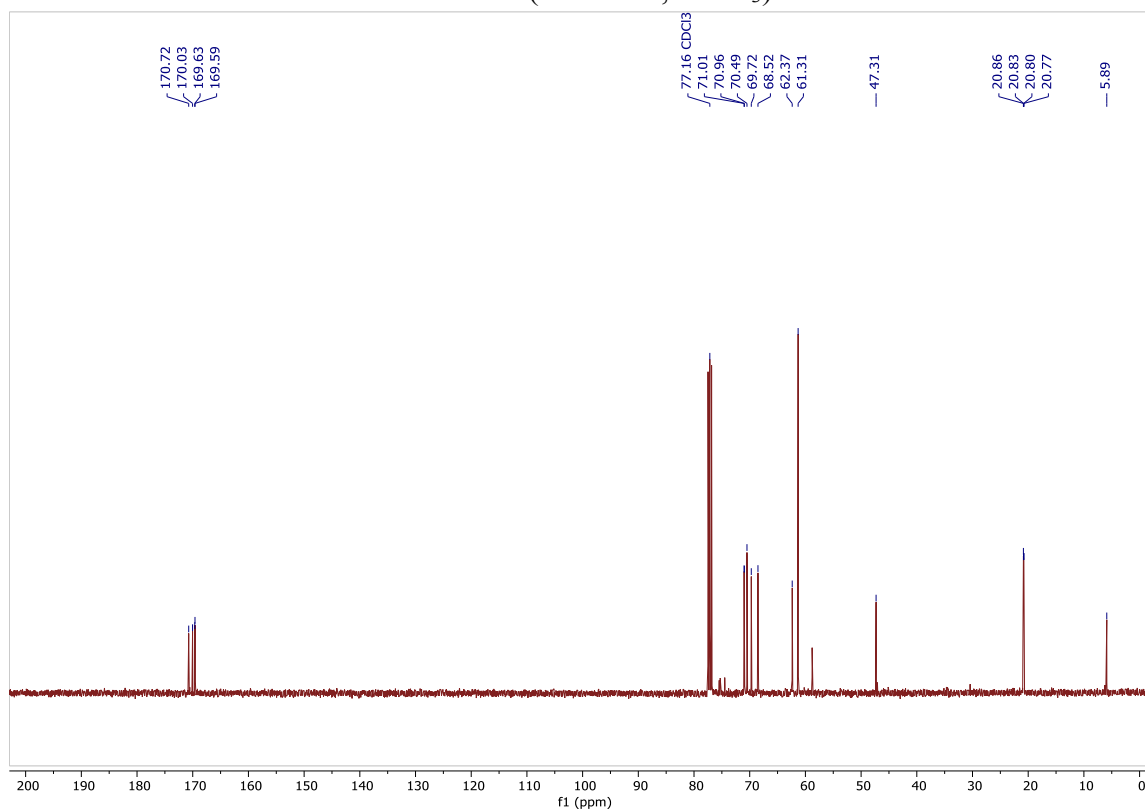
2,3,4,6-Tetra-O-acetyl-1-deoxy-1-(3-iodobicyclo[1.1.1]pentan-1-yl)glucopyranose, 84



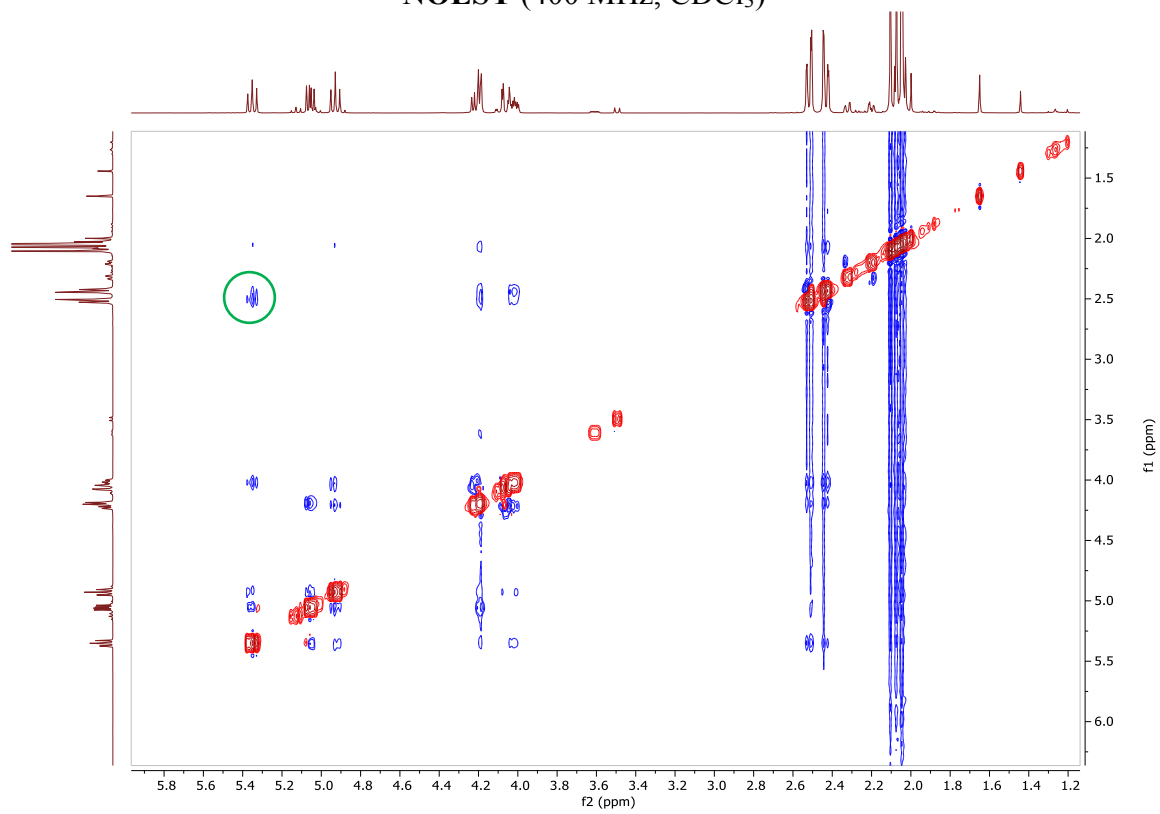
^1H NMR (400 MHz, CDCl_3)



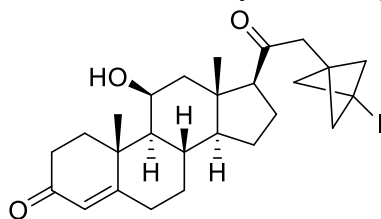
^{13}C NMR (101 MHz, CDCl_3)



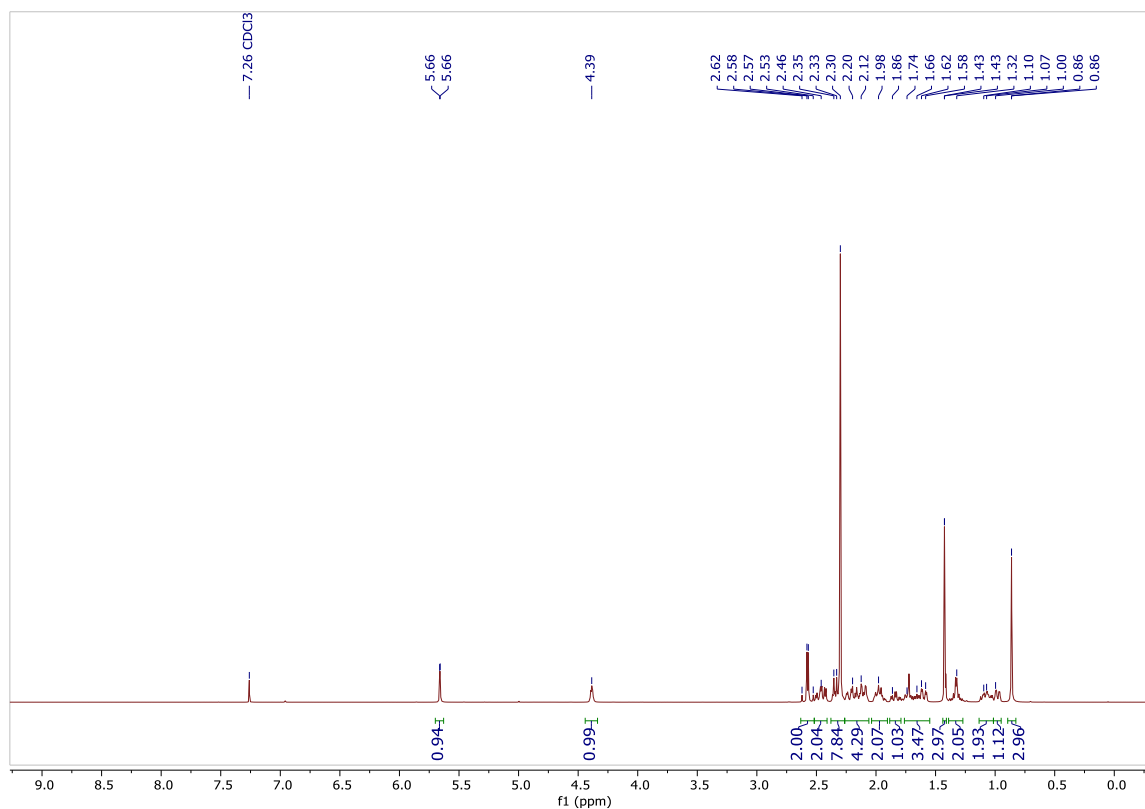
NOESY (400 MHz, CDCl₃)



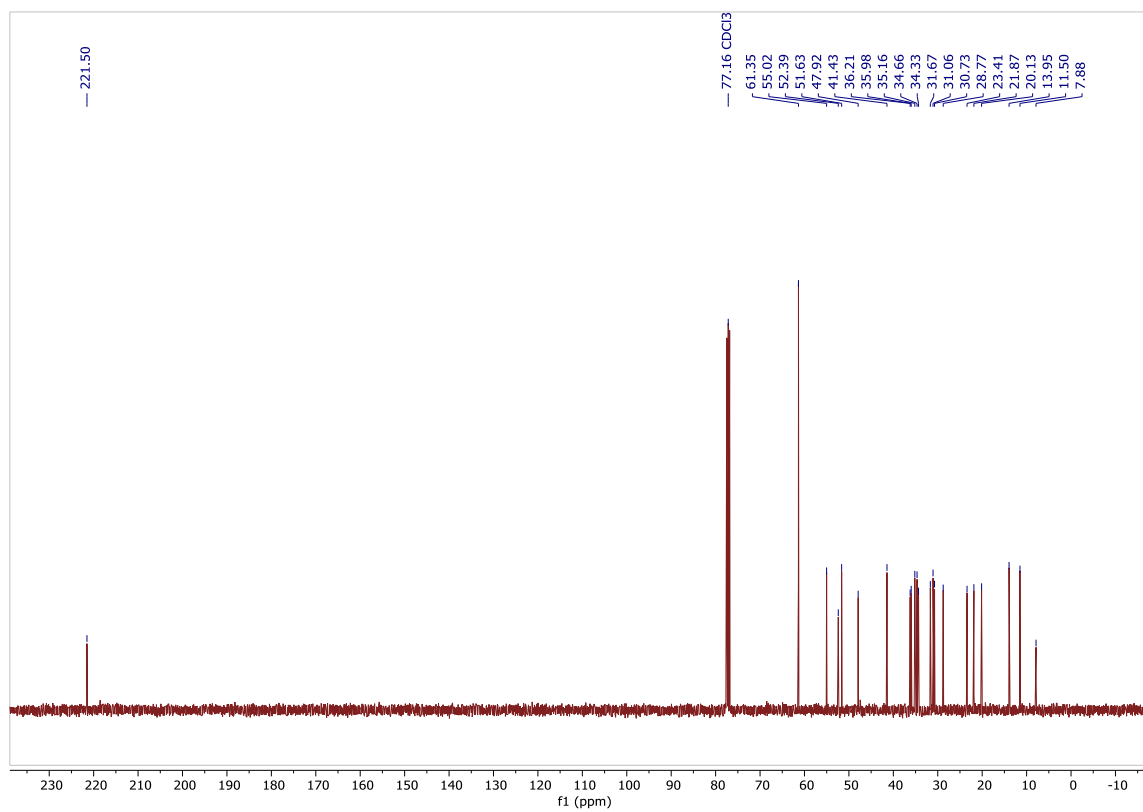
(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*S*)-11-Hydroxy-17-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetyl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one, 85



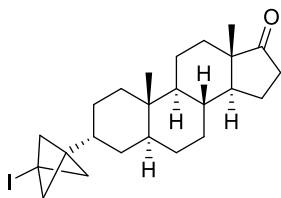
¹H NMR (400 MHz, CDCl₃)



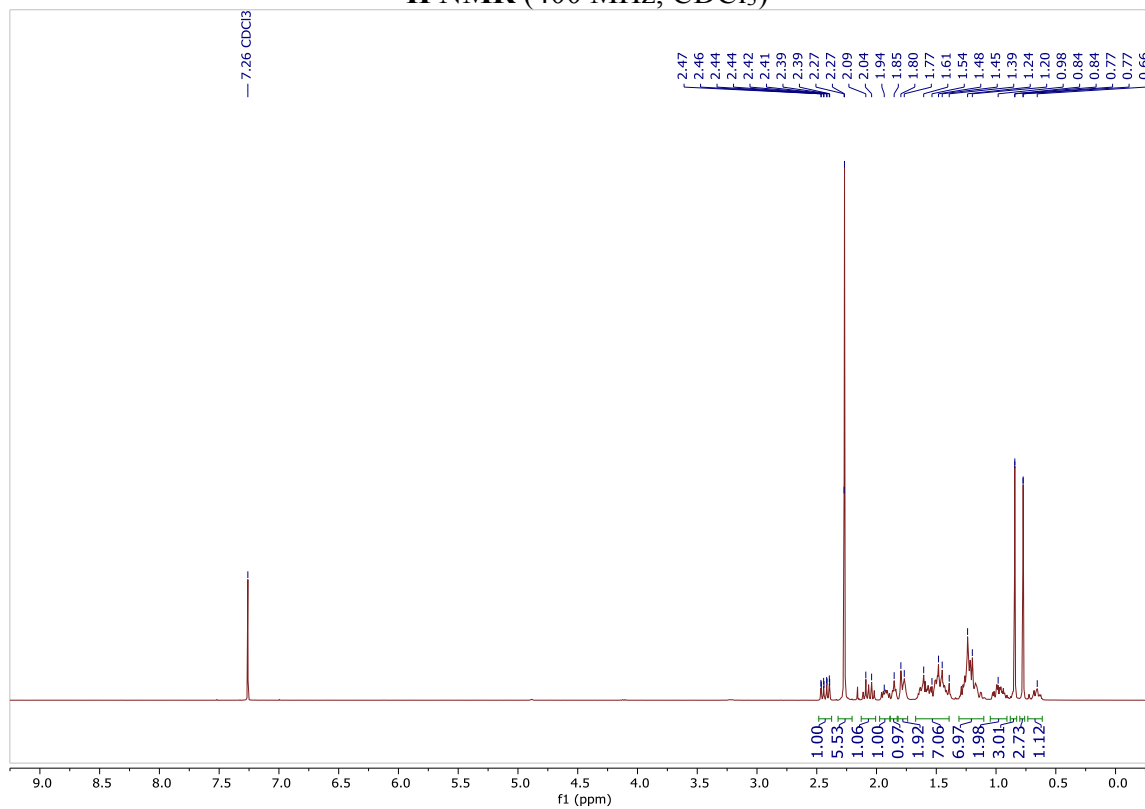
^{13}C NMR (101 MHz, CDCl_3)



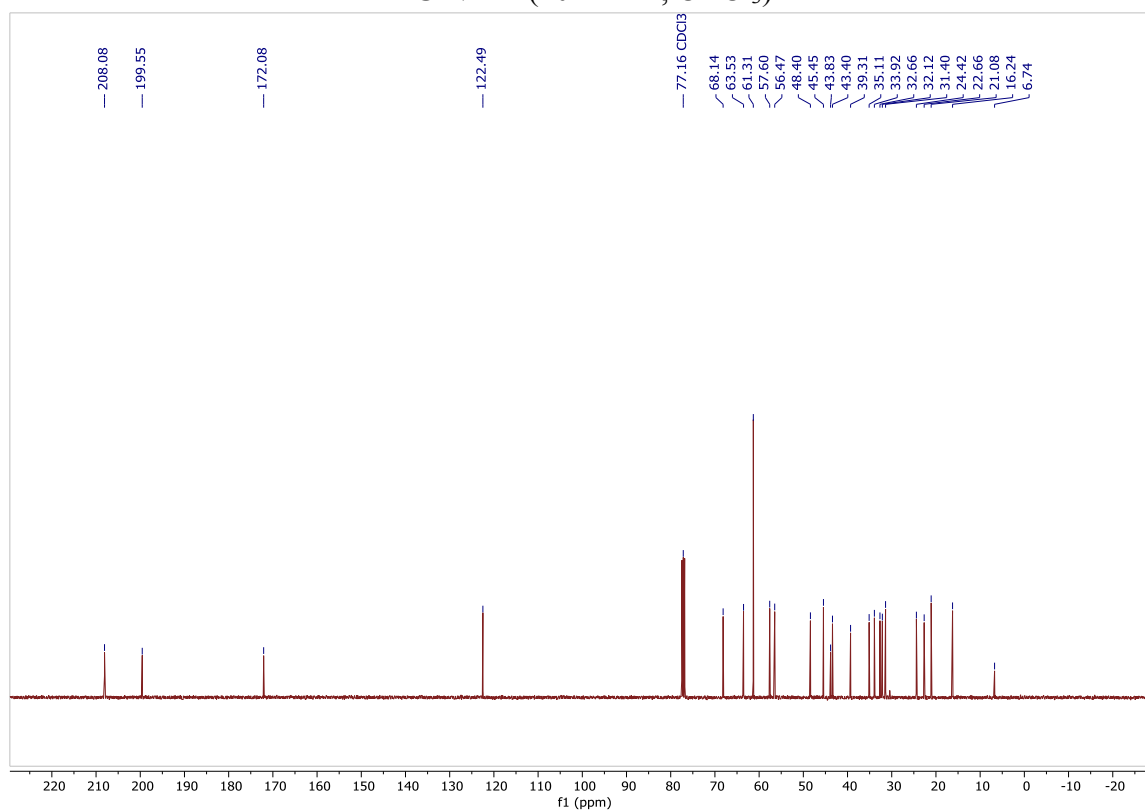
(3*R*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-3-(3-Iodobicyclo[1.1.1]pentan-1-yl)-10,13-dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one, 86



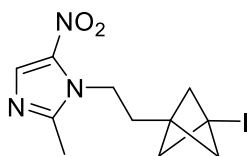
¹H NMR (400 MHz, CDCl₃)



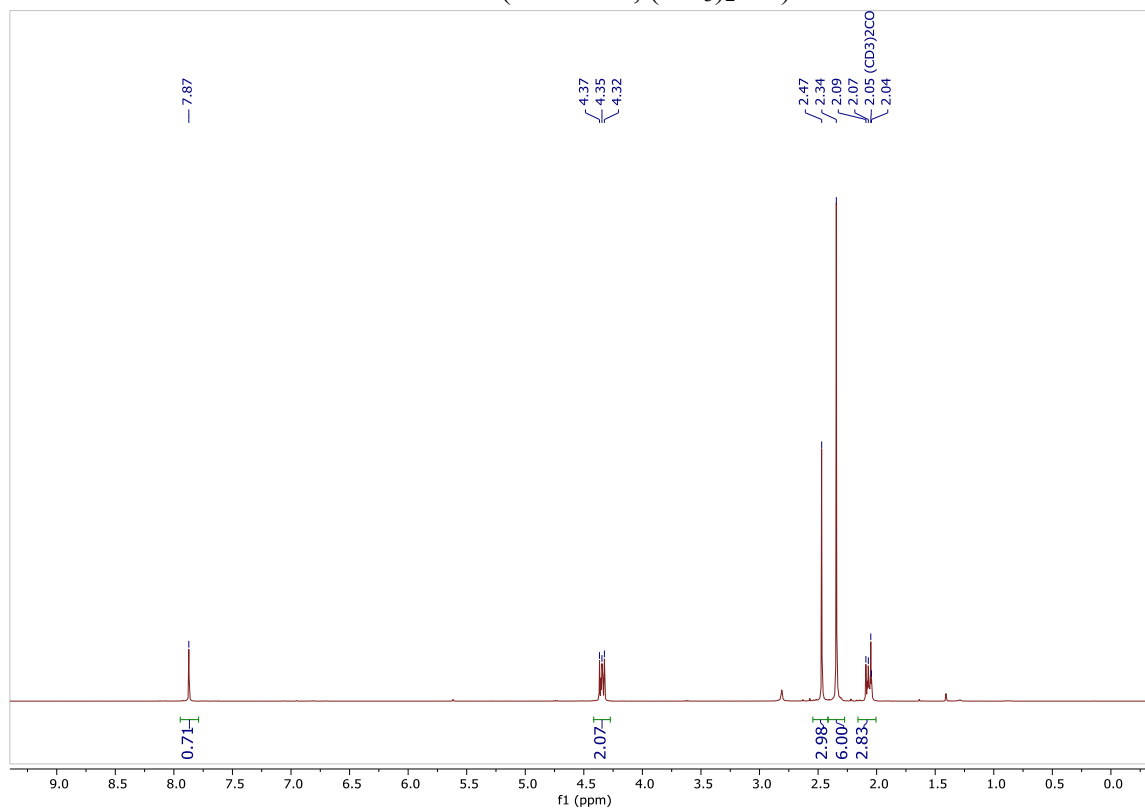
¹³C NMR (101 MHz, CDCl₃)



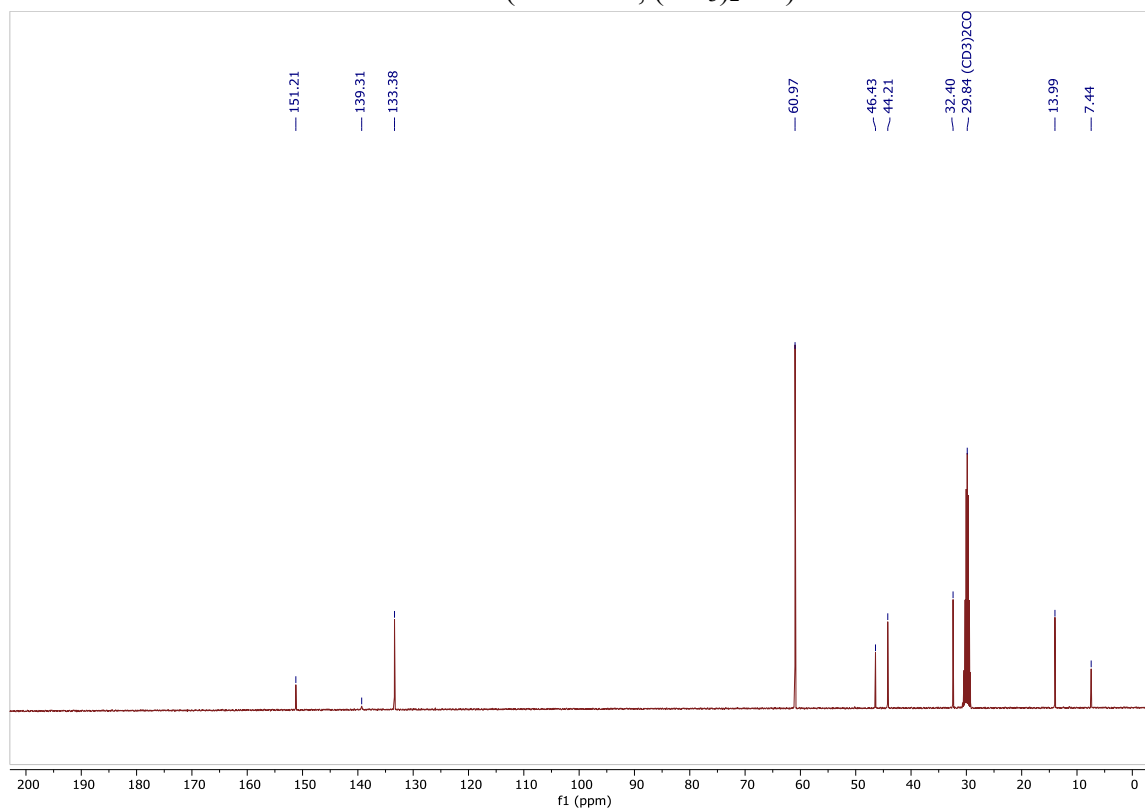
1-(2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl)-2-methyl-5-nitro-1*H*-imidazole, 87



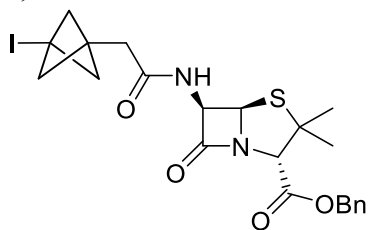
^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$)



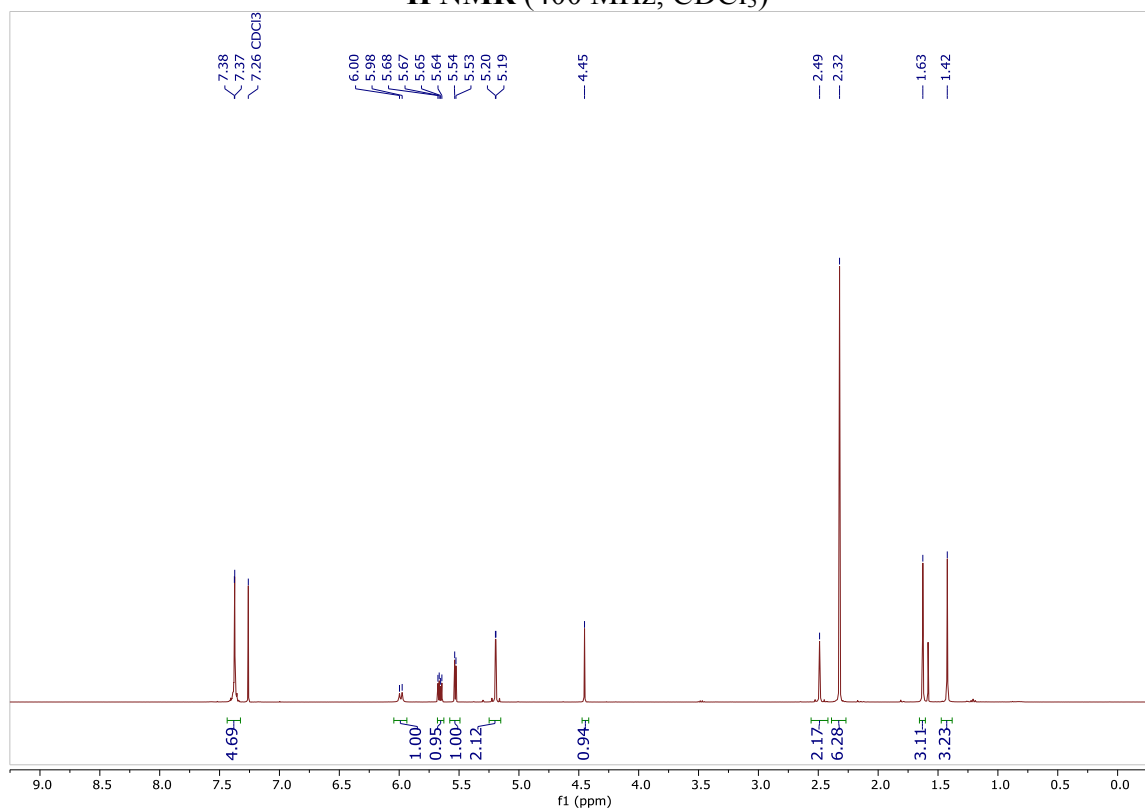
^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$)



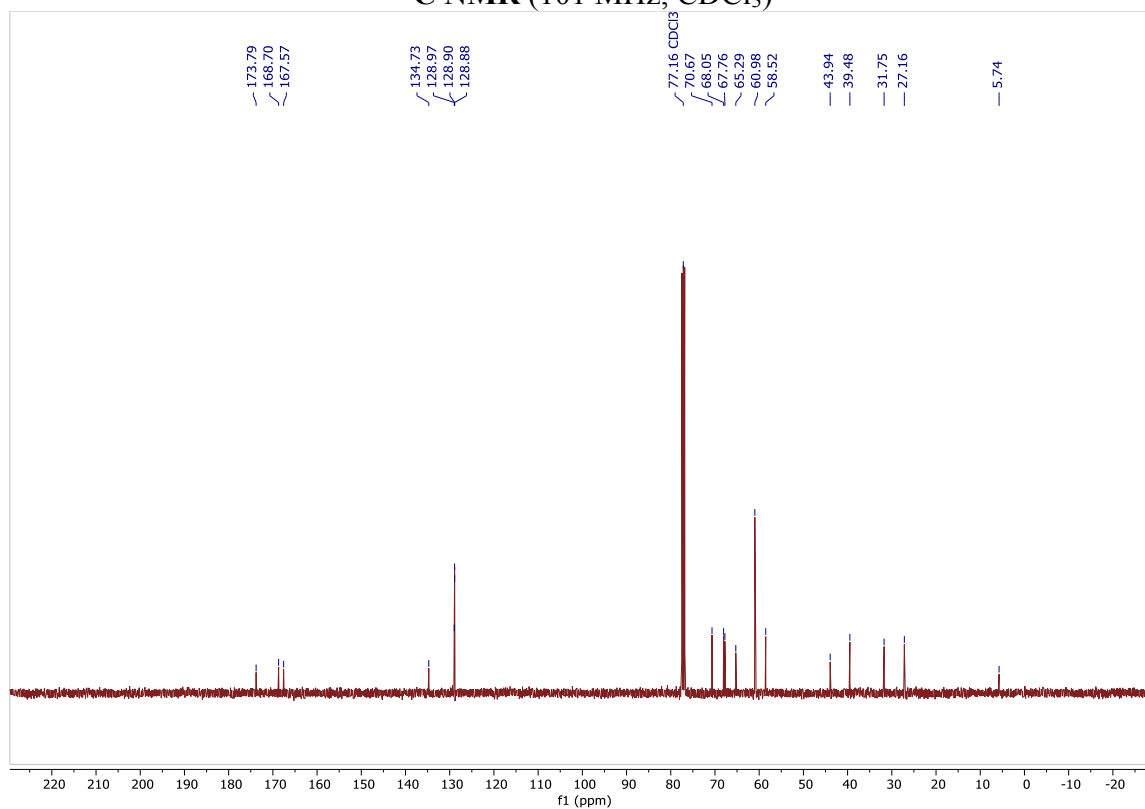
Benzyl (2S,5R,6R)-6-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, 88



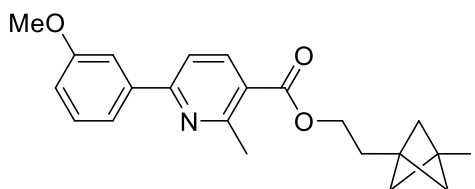
^1H NMR (400 MHz, CDCl_3)



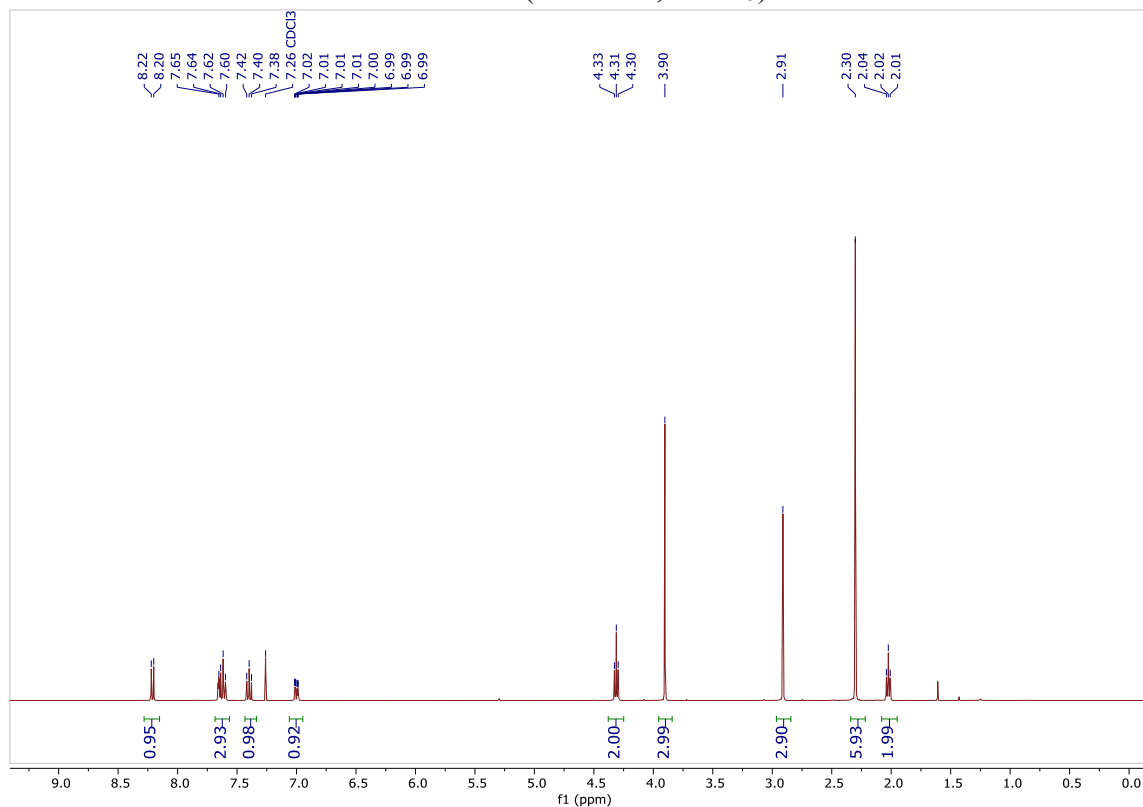
^{13}C NMR (101 MHz, CDCl_3)



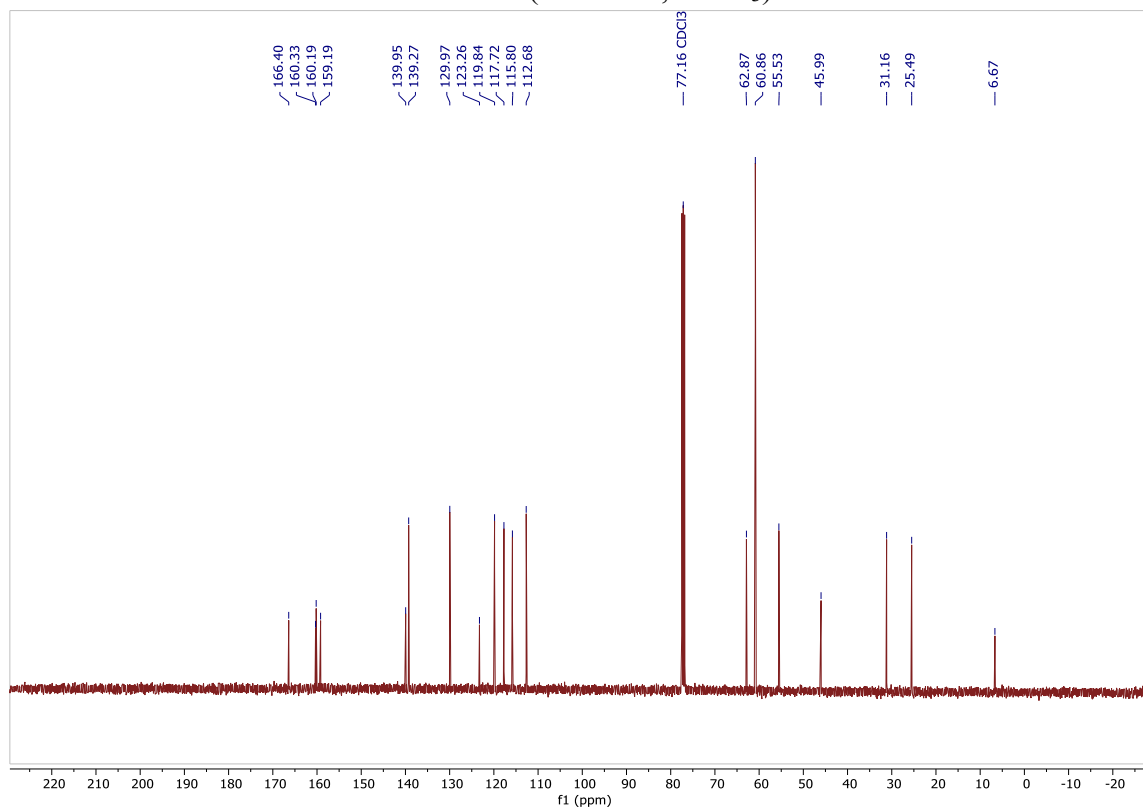
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl 6-(3-methoxyphenyl)-2-methylnicotinate, 89



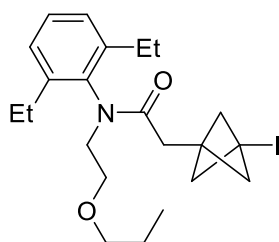
^1H NMR (400 MHz, CDCl_3)



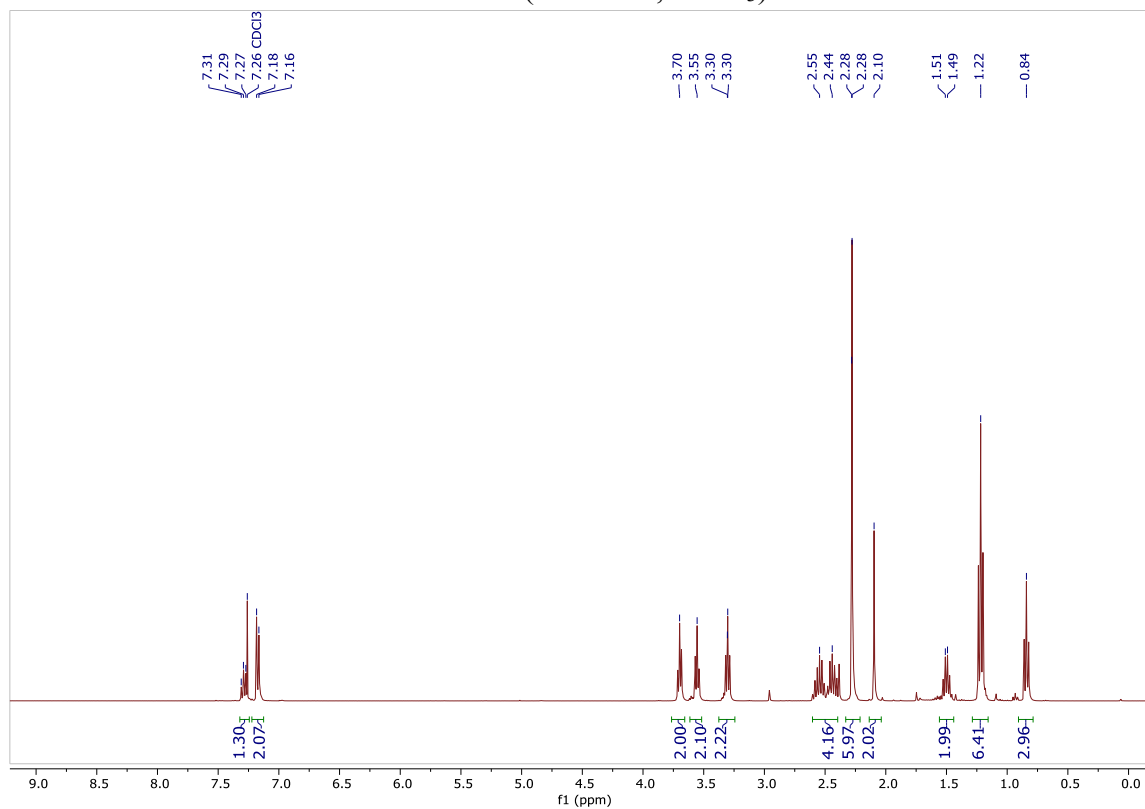
^{13}C NMR (101 MHz, CDCl_3)



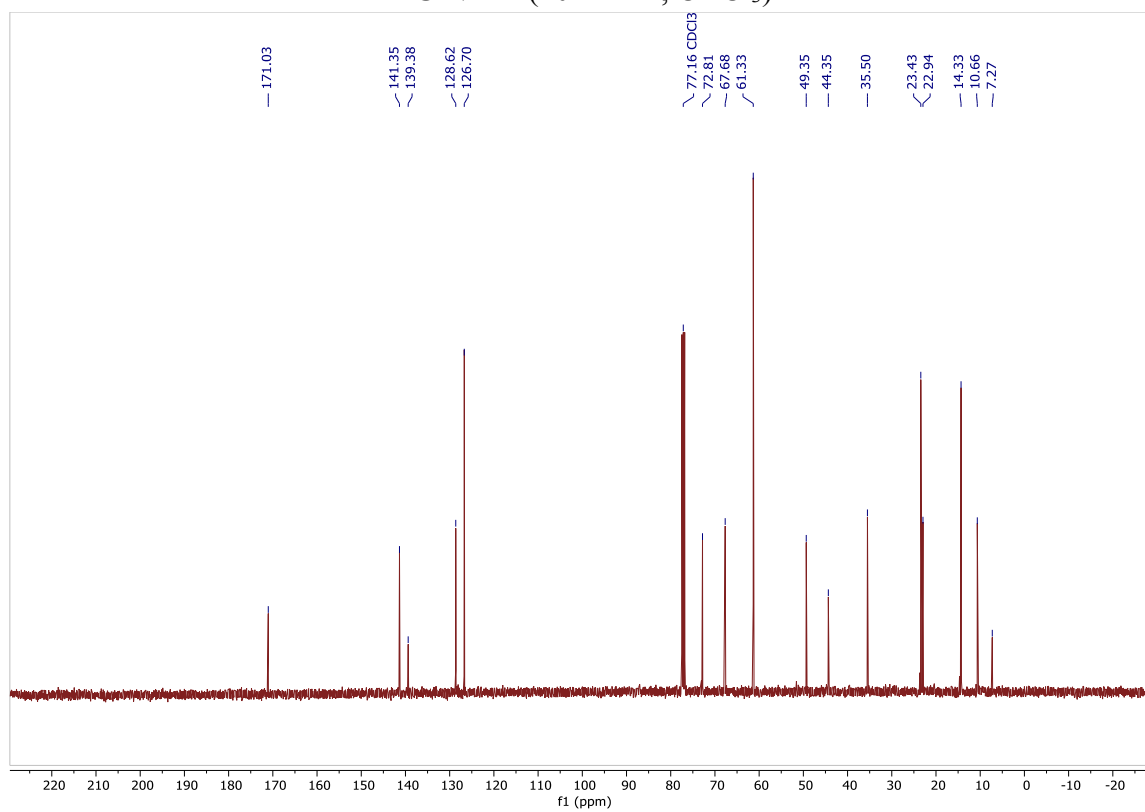
***N*-(2,6-Diethylphenyl)-2-(3-iodobicyclo[1.1.1]pentan-1-yl)-*N*-(2-propoxyethyl)acetamide, 90**



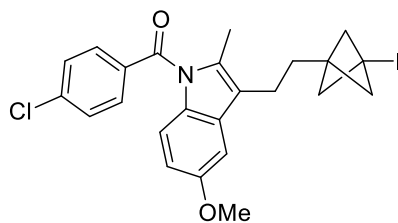
^1H NMR (400 MHz, CDCl_3)



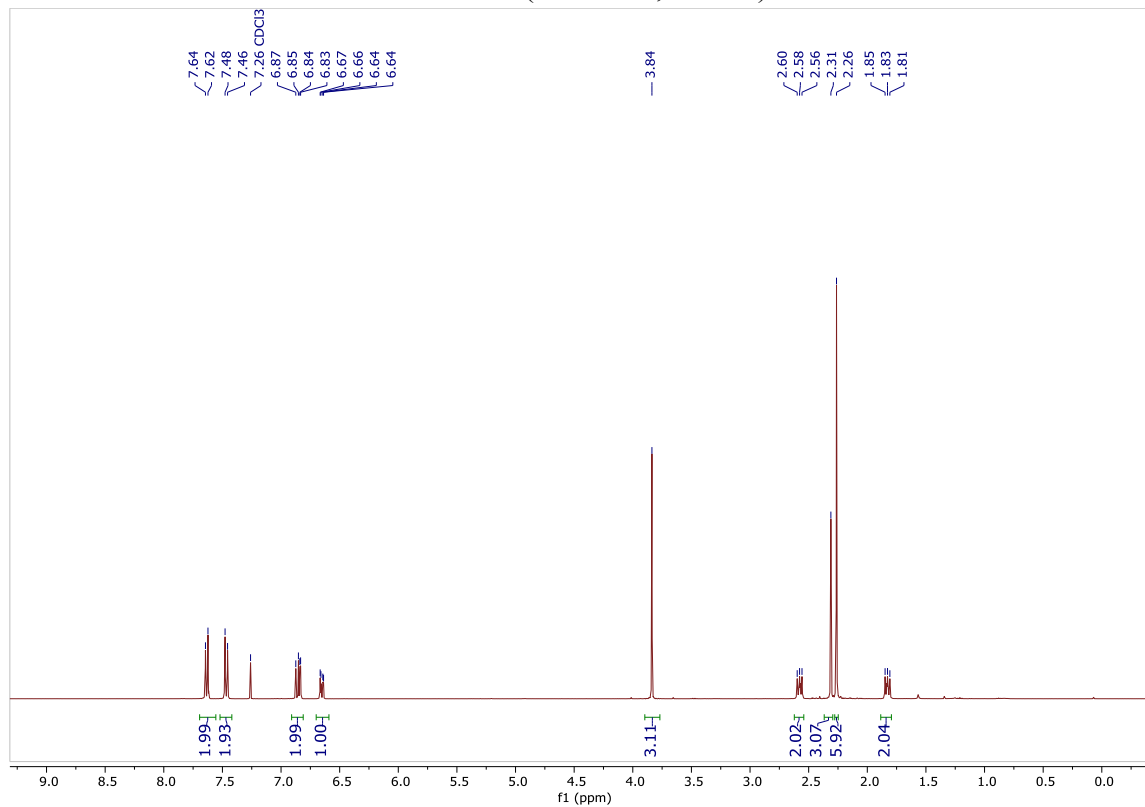
^{13}C NMR (101 MHz, CDCl_3)



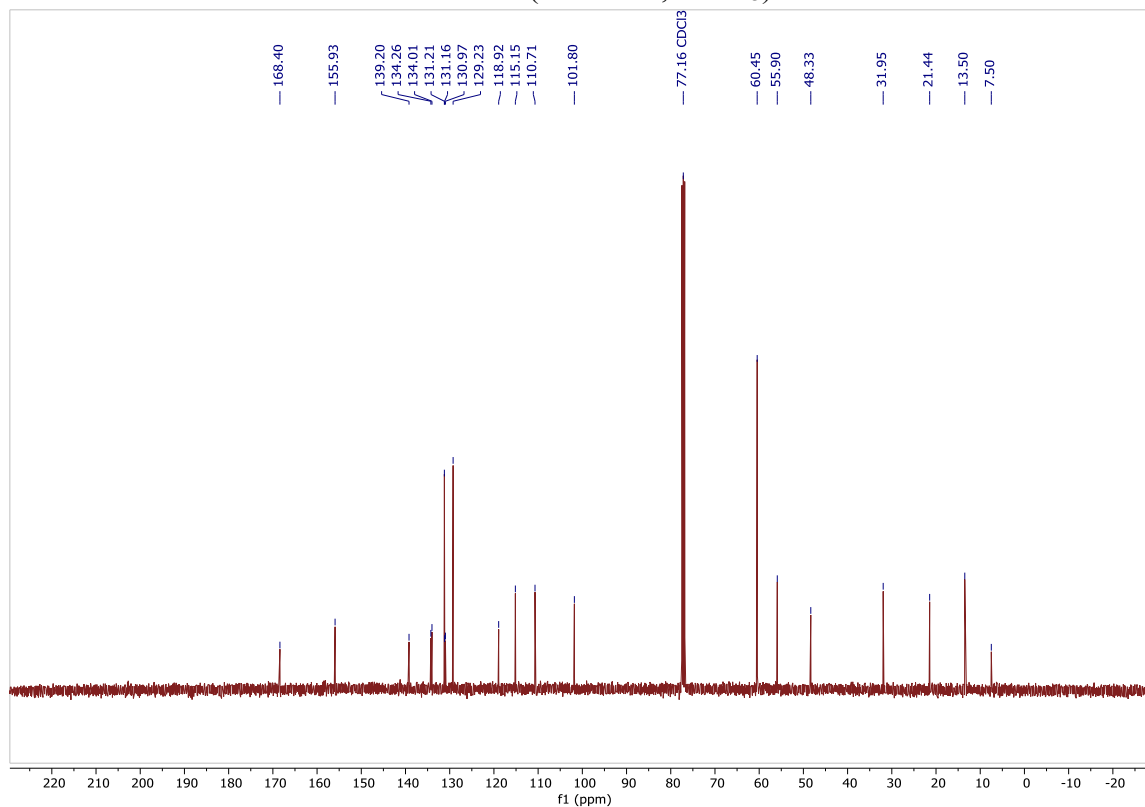
(4-Chlorophenyl)(3-(2-(3-iodobicyclo[1.1.1]pentan-1-yl)ethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, 91



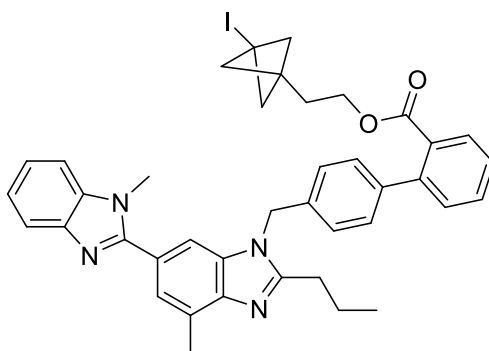
^1H NMR (400 MHz, CDCl_3)



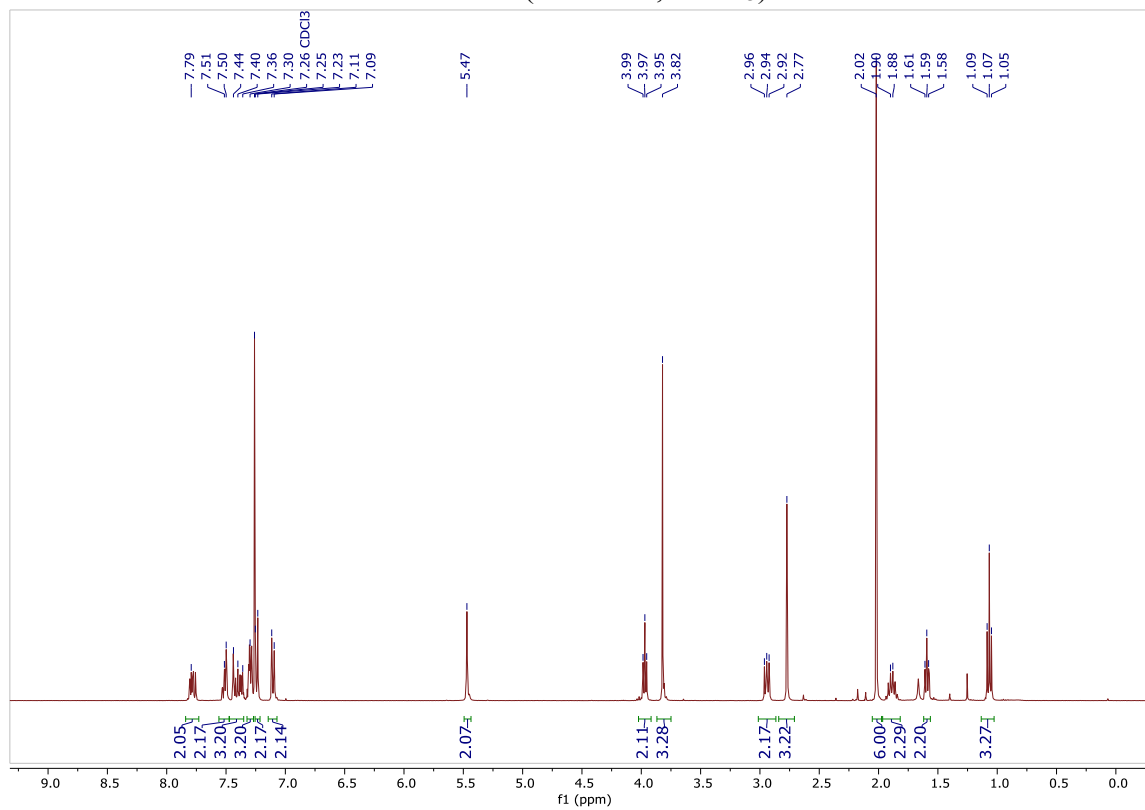
^{13}C NMR (101 MHz, CDCl_3)



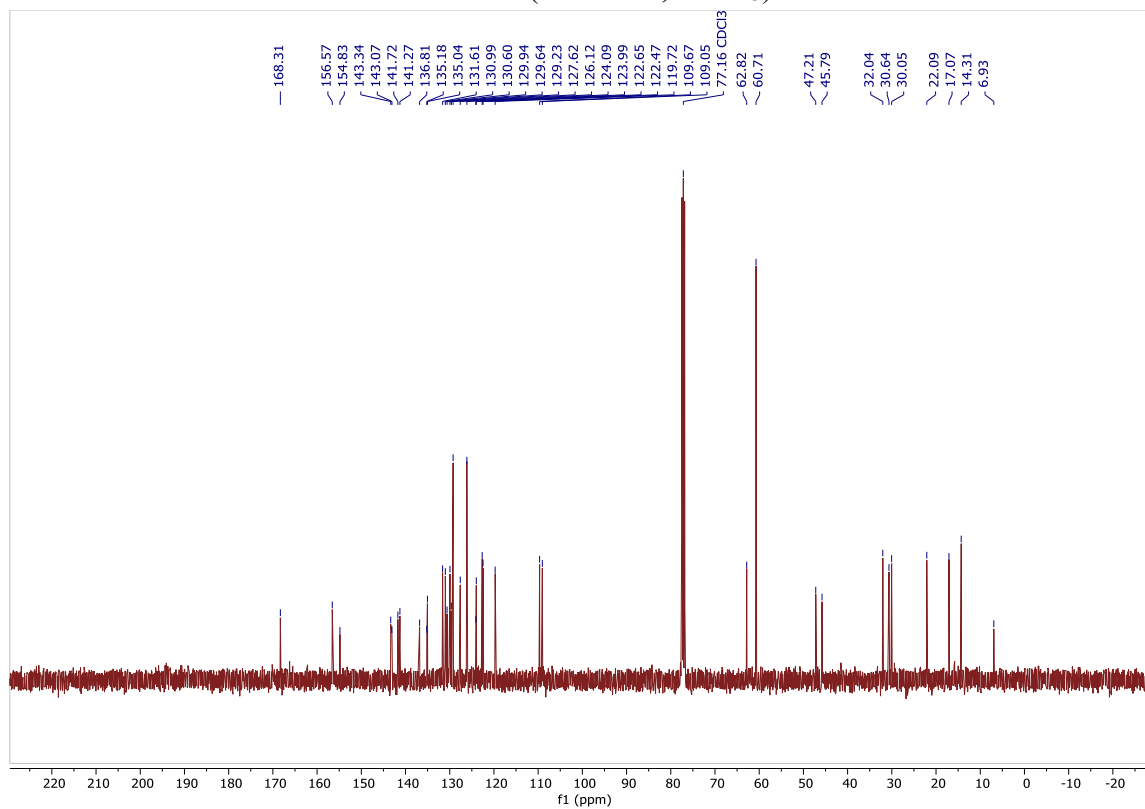
2-(3-Iodobicyclo[1.1.1]pentan-1-yl)ethyl 4'-((1,7'-dimethyl-2'-propyl-1*H*,3'*H*-[2,5-bibenzo[*d*]imidazol]-3'-yl)methyl)-[1,1'-biphenyl]-2-carboxylate, 92



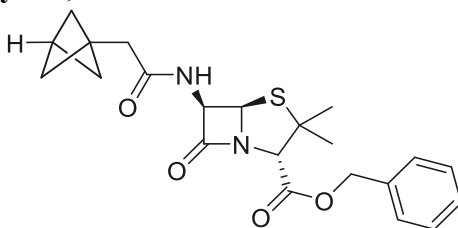
¹H NMR (400 MHz, CDCl₃)



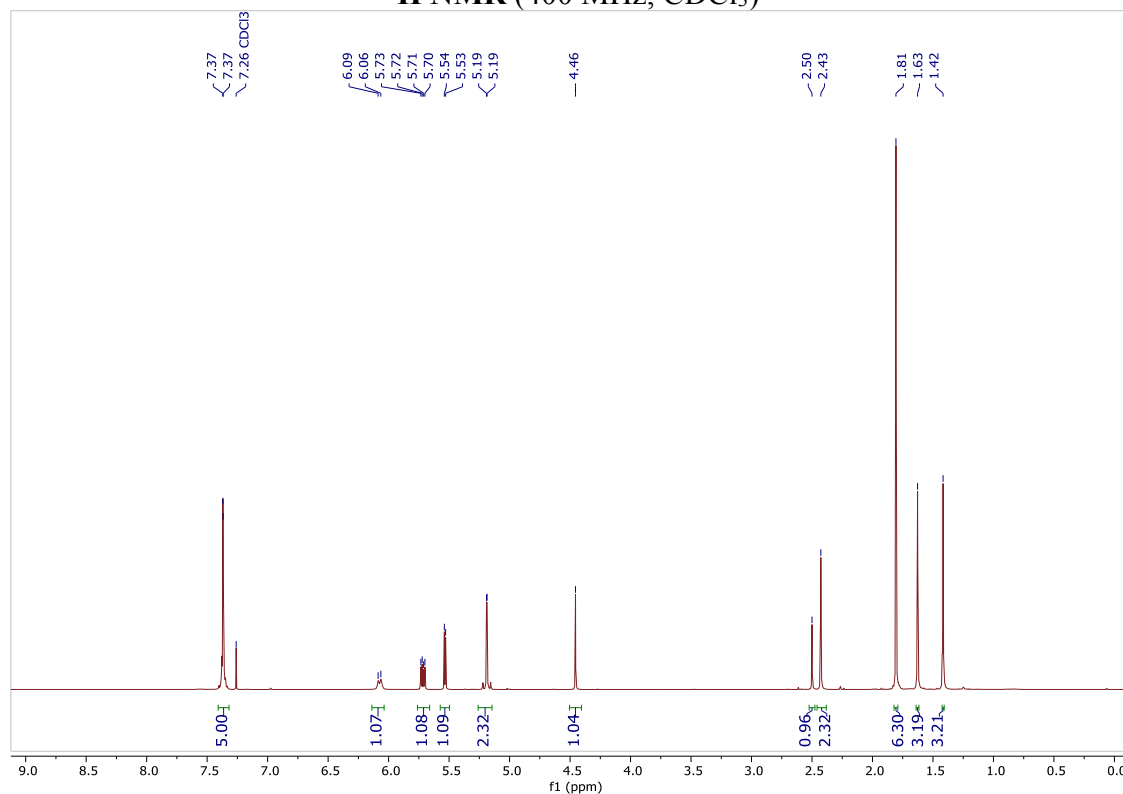
^{13}C NMR (101 MHz, CDCl_3)



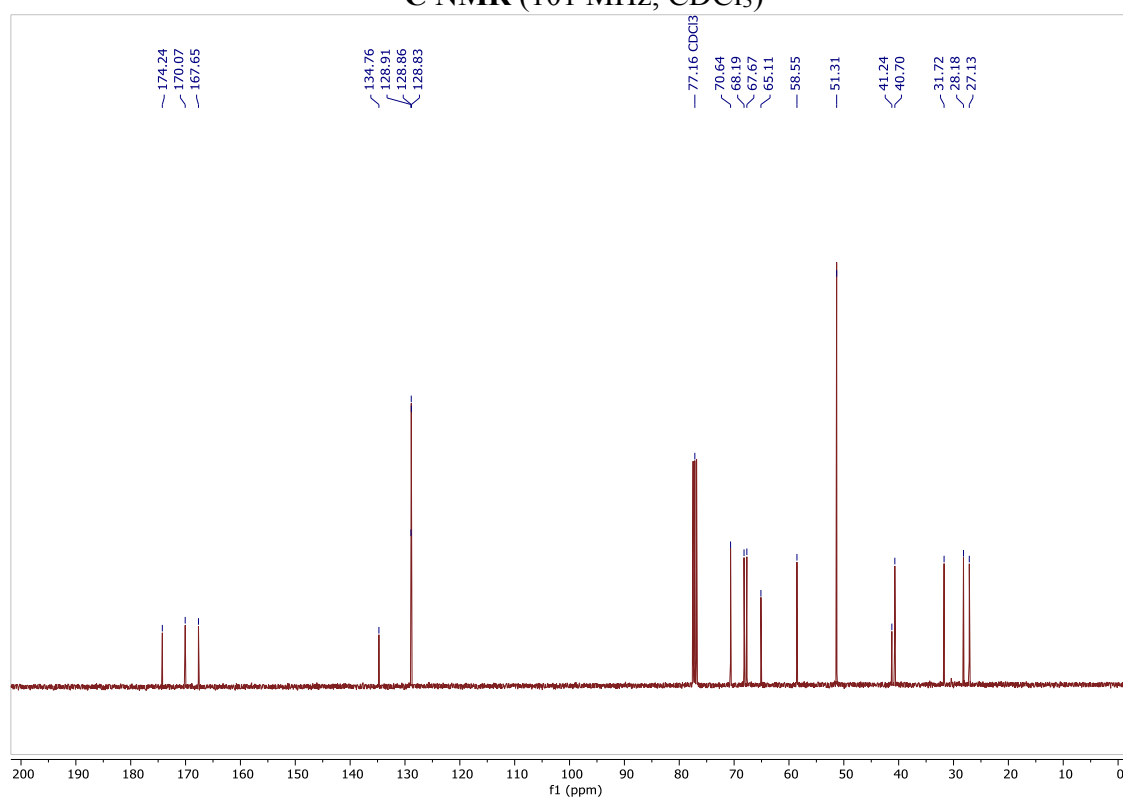
Benzyl (2*S*,5*R*,6*R*)-6-(2-(bicyclo[1.1.1]pentan-1-yl)acetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, 93



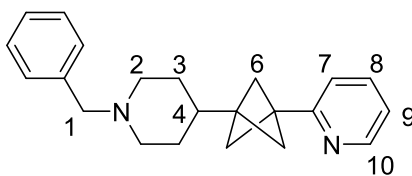
¹H NMR (400 MHz, CDCl₃)



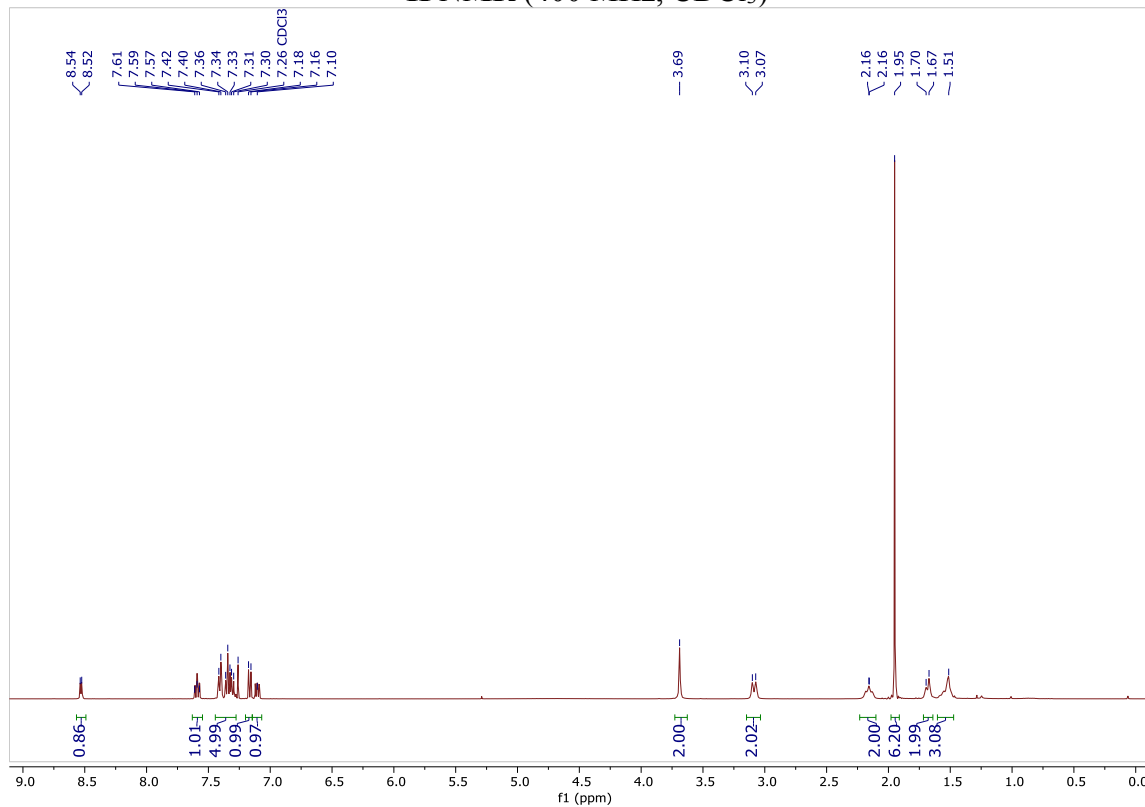
¹³C NMR (101 MHz, CDCl₃)



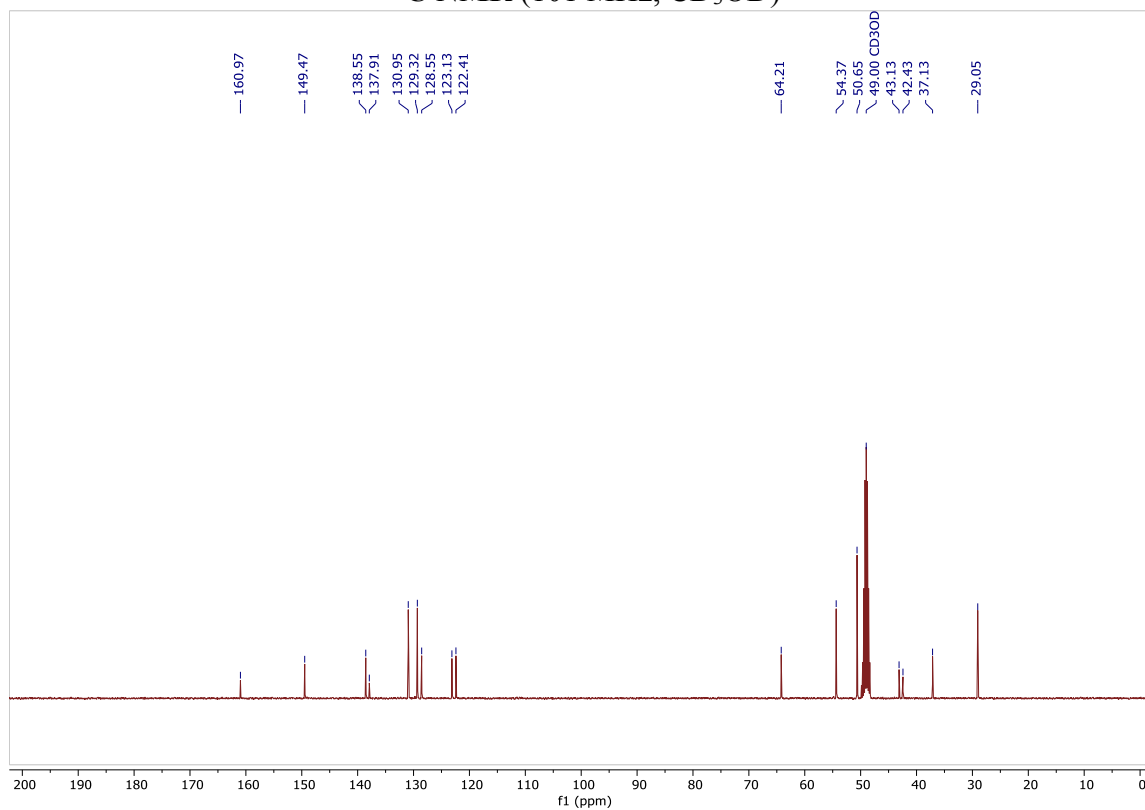
2-(3-(1-Benzylpiperidin-4-yl)bicyclo[1.1.1]pentan-1-yl)pyridine, **94**



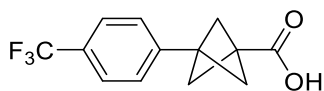
^1H NMR (400 MHz, CDCl_3)



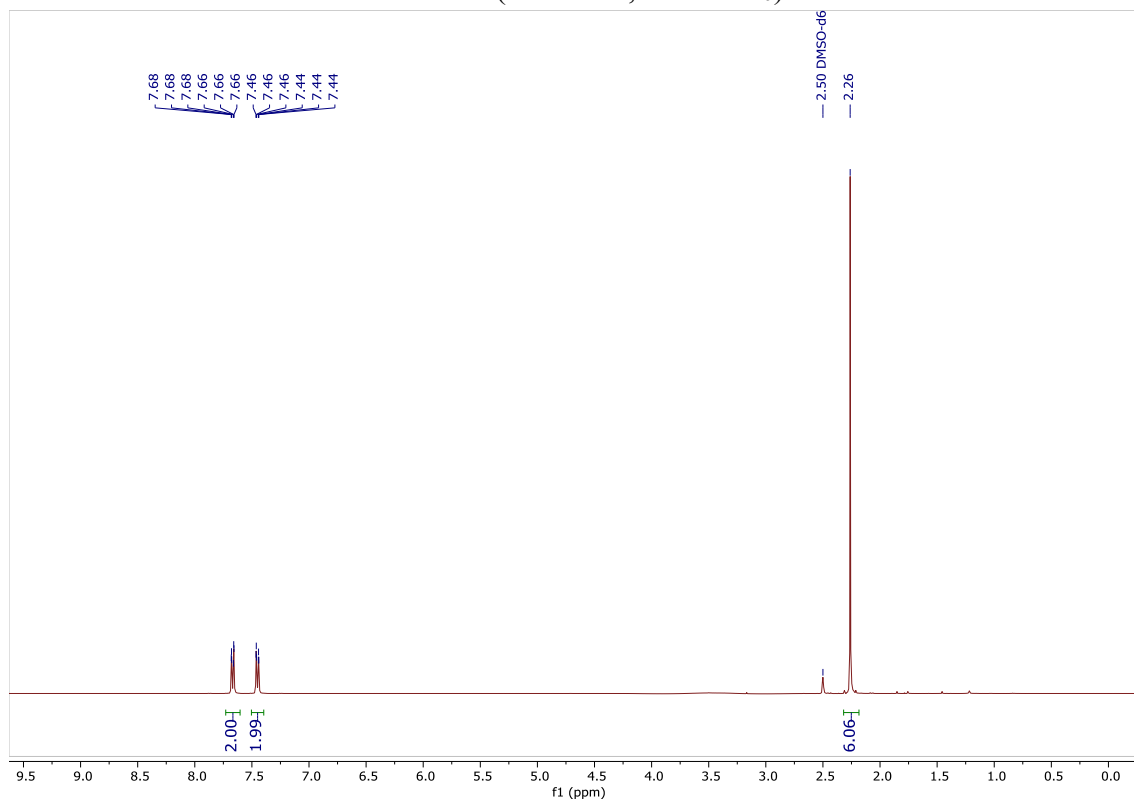
^{13}C NMR (101 MHz, CD_3OD)



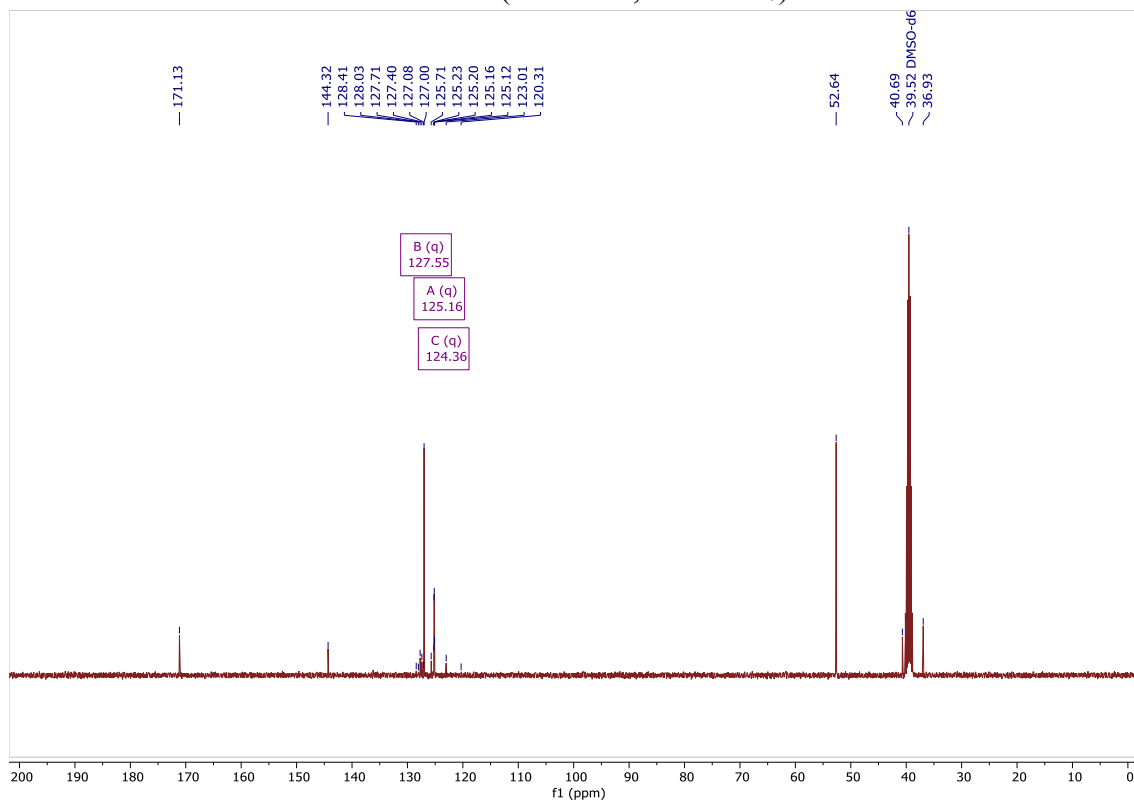
3-(4-(Trifluoromethyl)phenyl)bicyclo[1.1.1]pentane-1-carboxylic acid, 95



^1H NMR (400 MHz, DMSO- d_6)



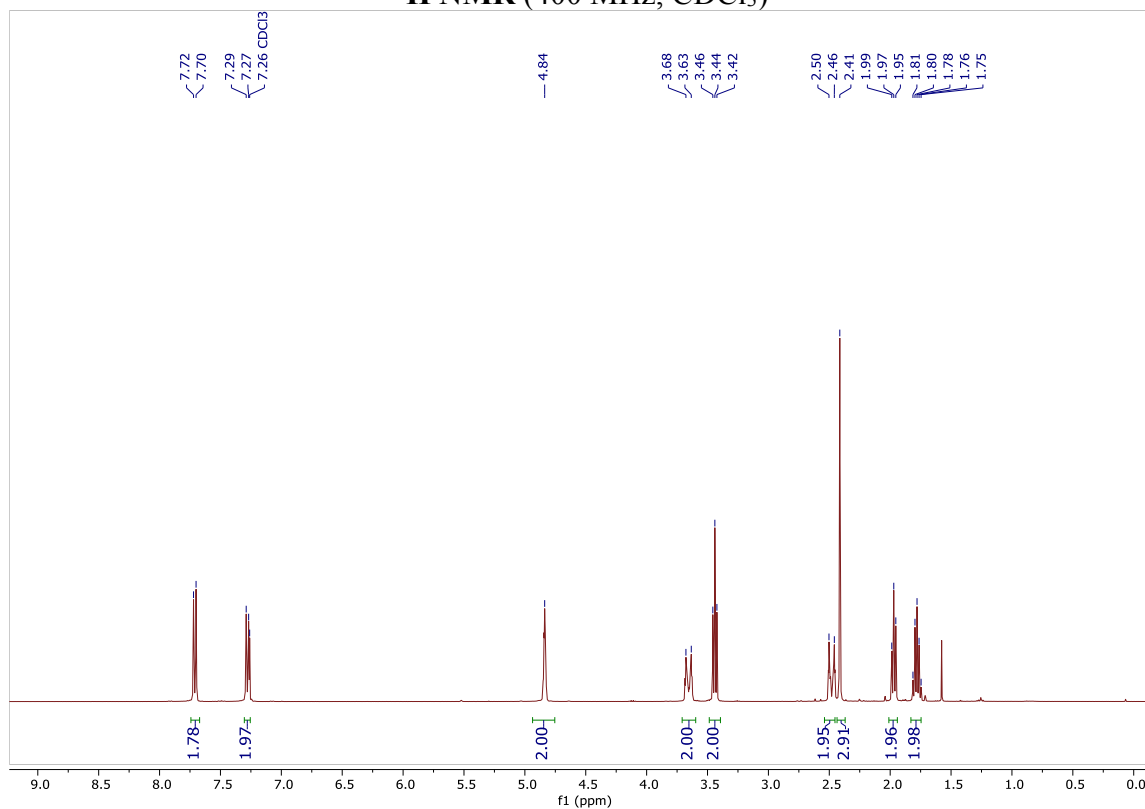
^{13}C NMR (101 MHz, DMSO- d_6)



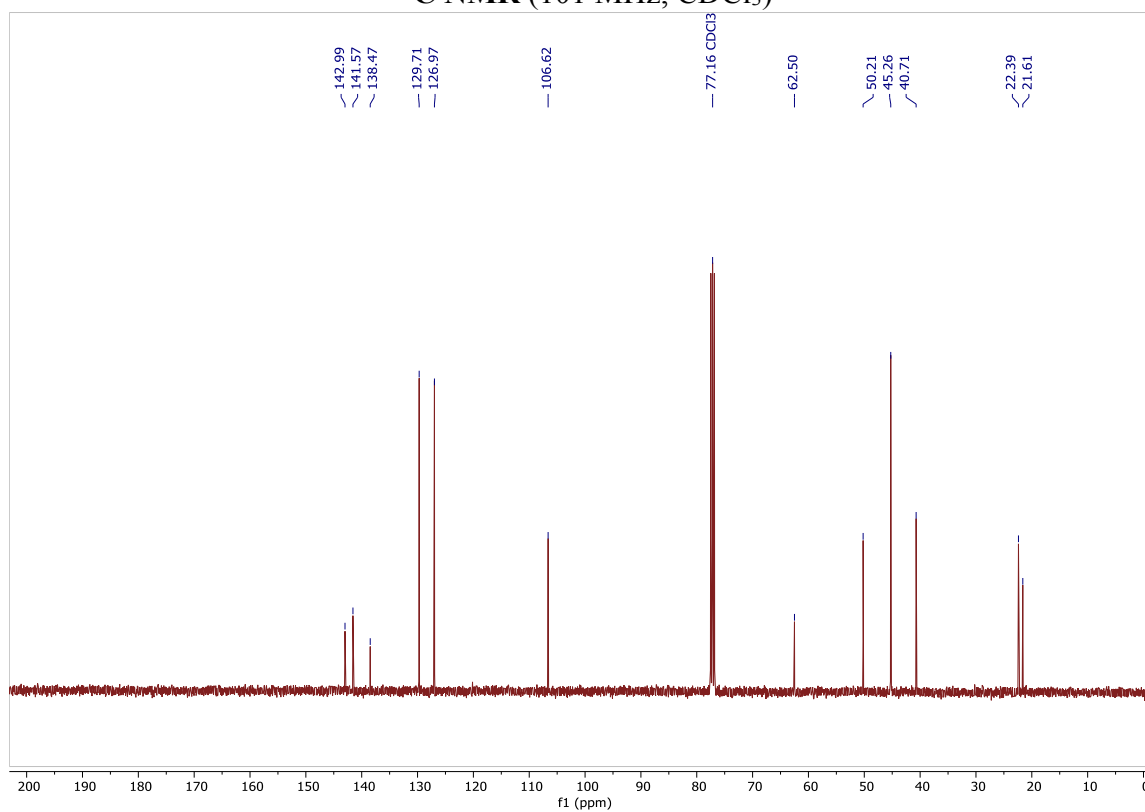
2-Methylene-5-tosyl-5-azaspiro[3.4]octane, 96



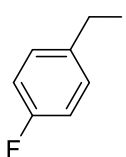
^1H NMR (400 MHz, CDCl_3)



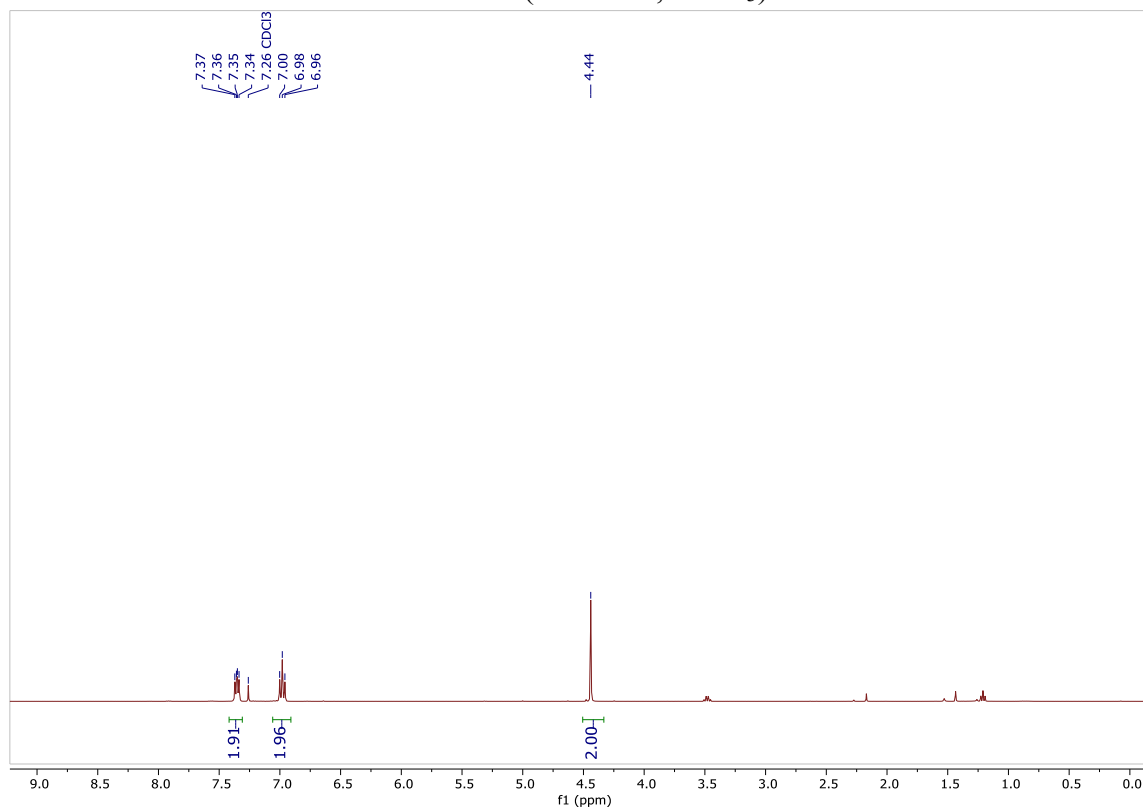
^{13}C NMR (101 MHz, CDCl_3)



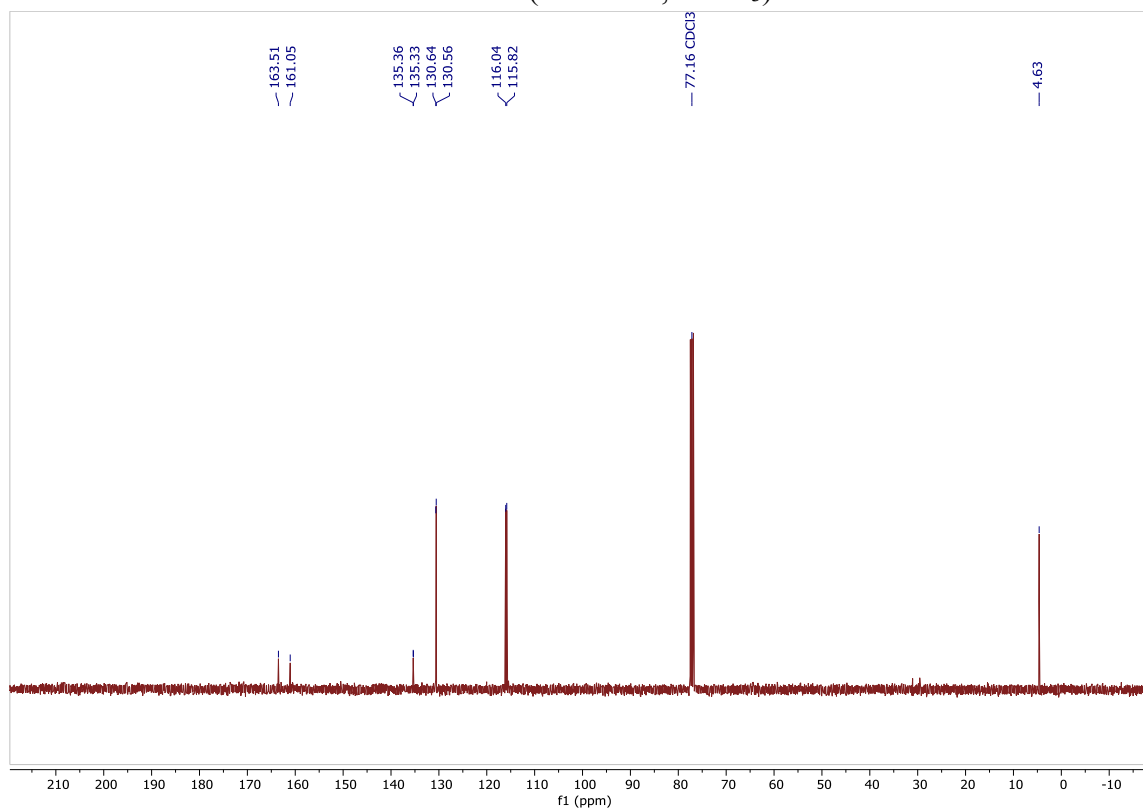
1-Fluoro-4-(iodomethyl)benzene, S1



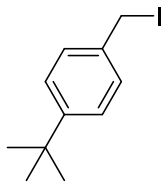
^1H NMR (400 MHz, CDCl_3)



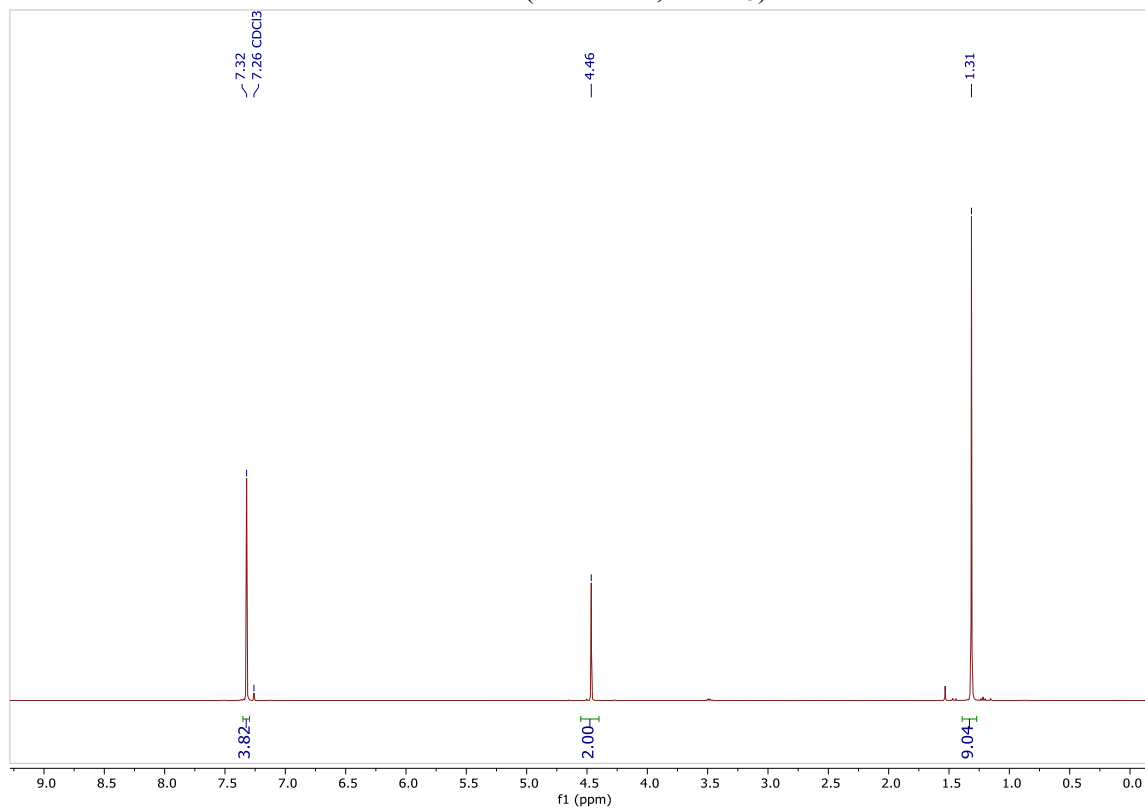
^{13}C NMR (101 MHz, CDCl_3)



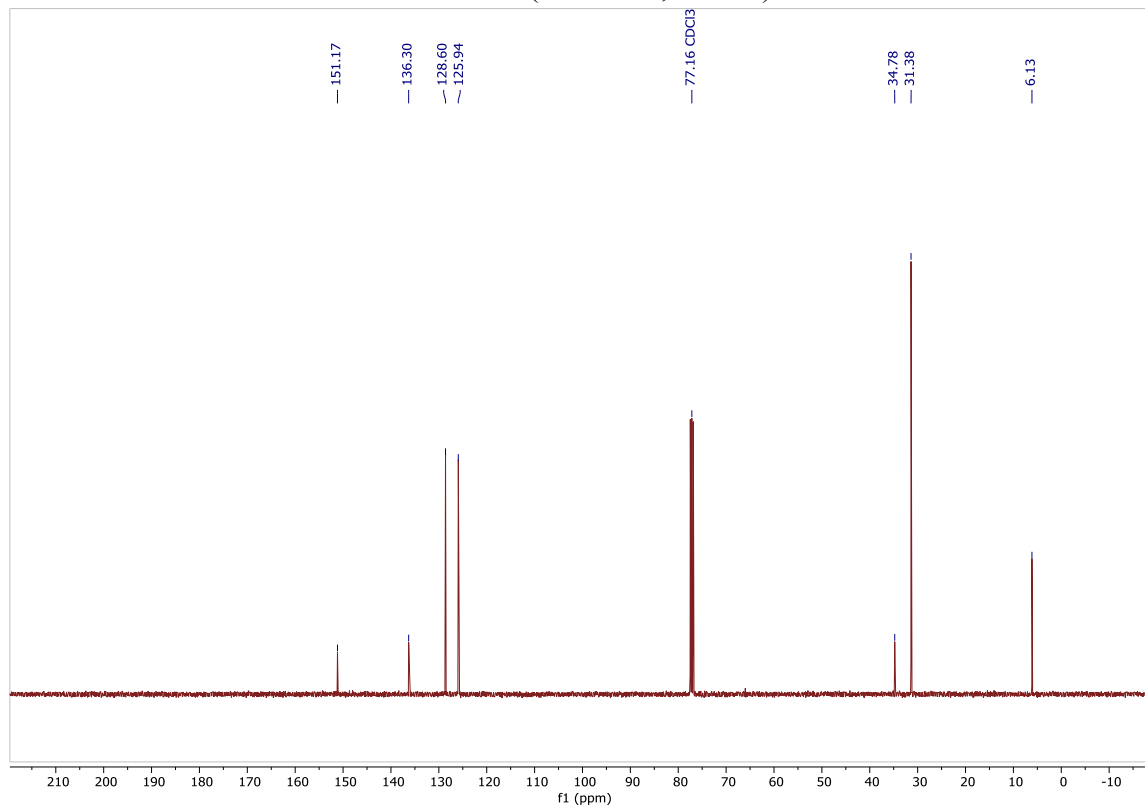
1-(*tert*-Butyl)-4-(iodomethyl)benzene, S2



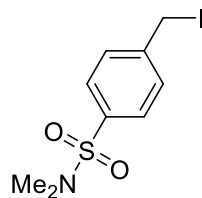
^1H NMR (400 MHz, CDCl_3)



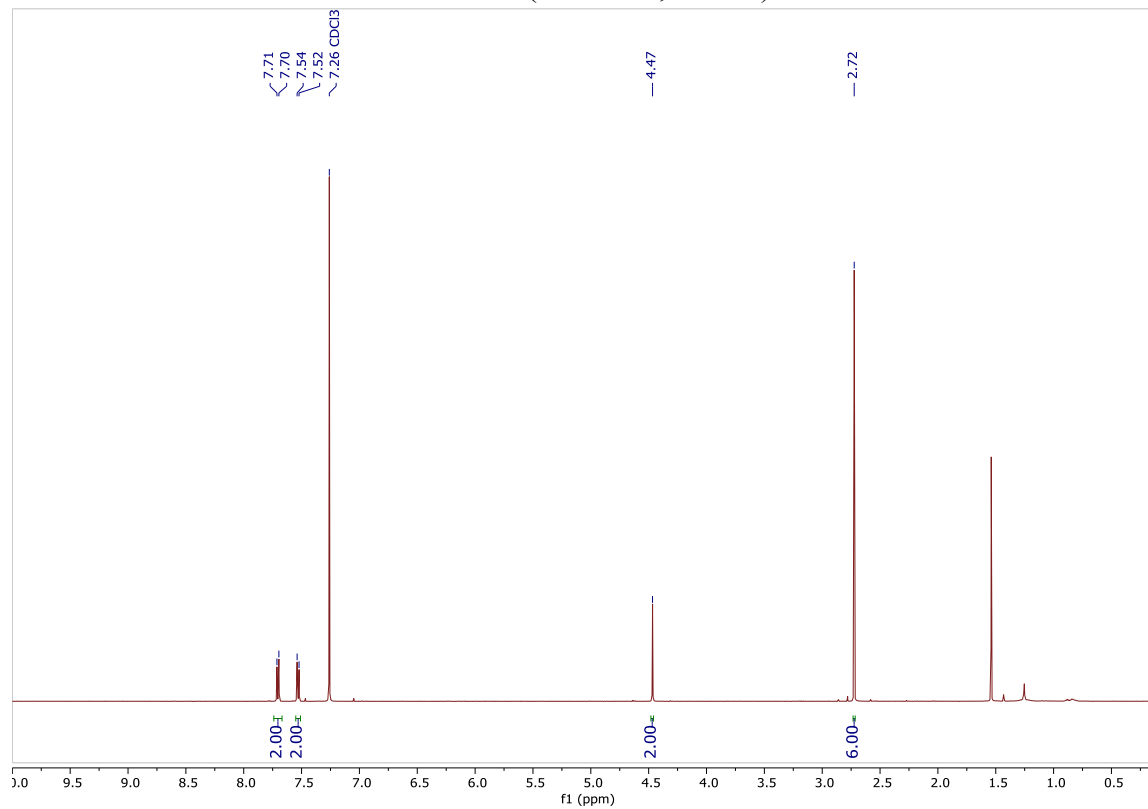
^{13}C NMR (101 MHz, CDCl_3)



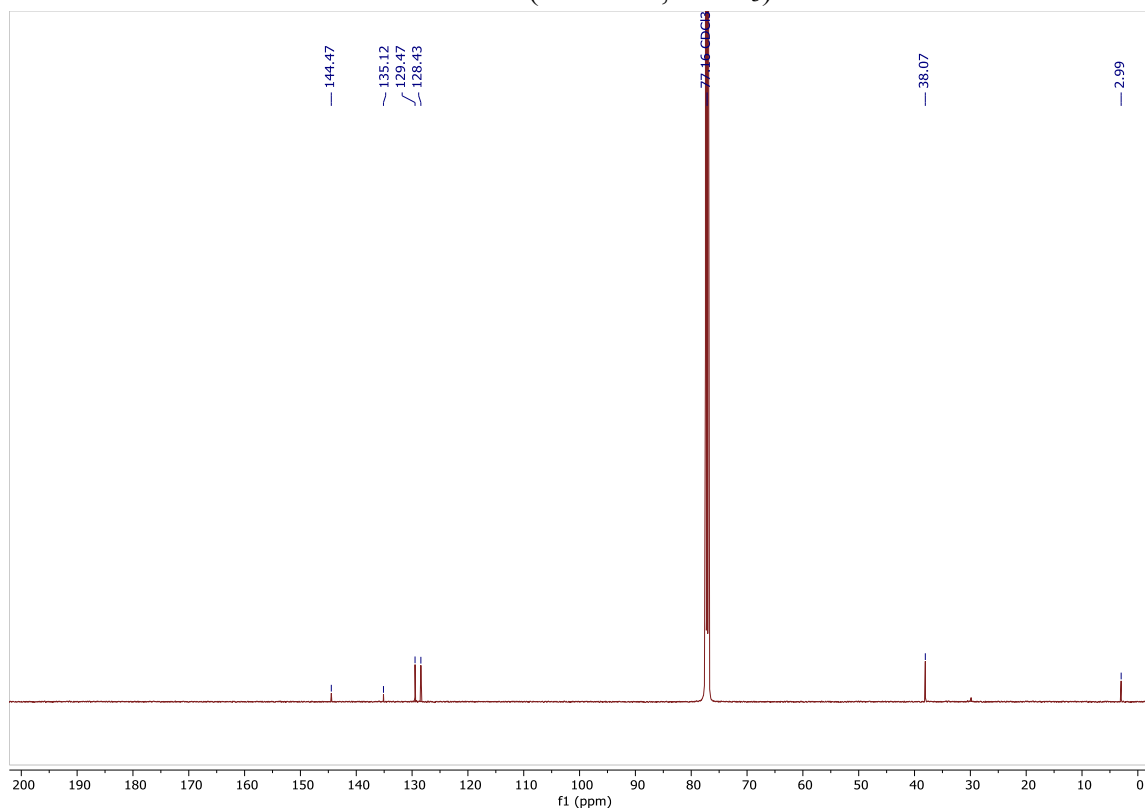
4-(Iodomethyl)-*N,N*-dimethylbenzenesulfonamide, S3



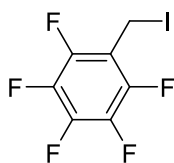
^1H NMR (500 MHz, CDCl_3)



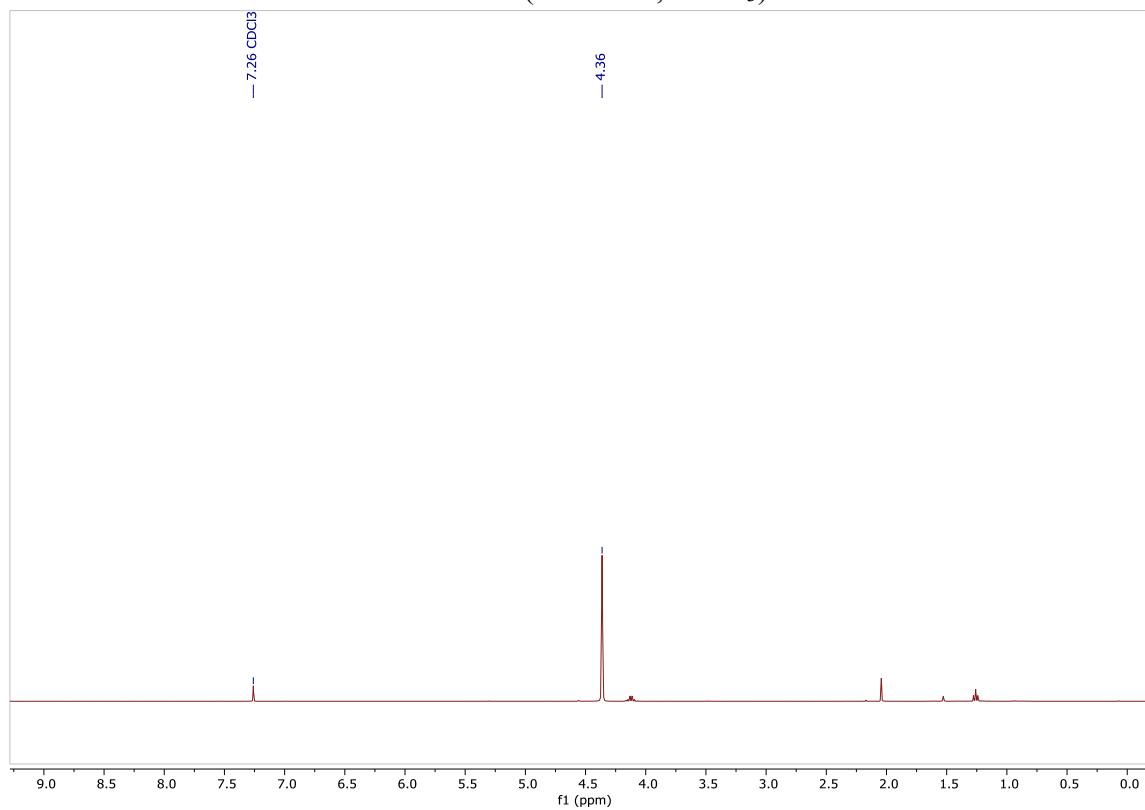
^{13}C NMR (125 MHz, CDCl_3)



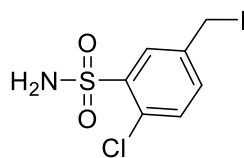
1,2,3,4,5-Pentafluoro-6-(iodomethyl)benzene, S4



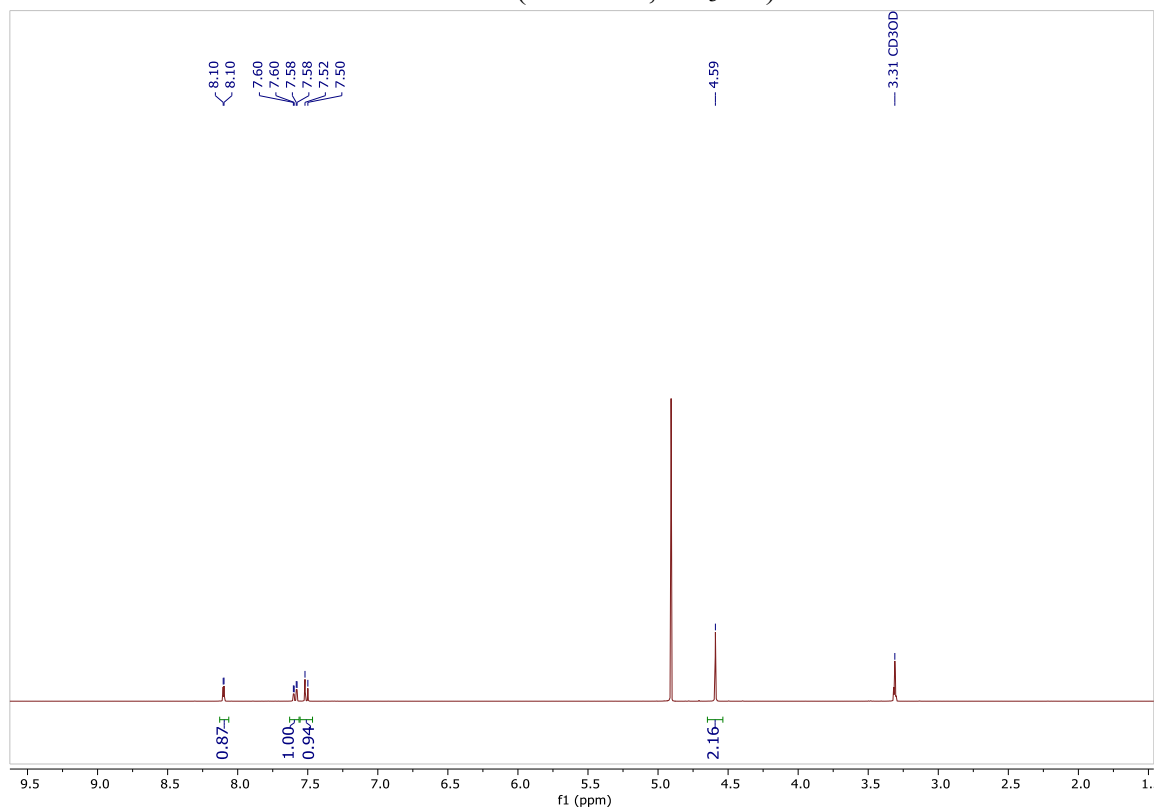
^1H NMR (400 MHz, CDCl_3)



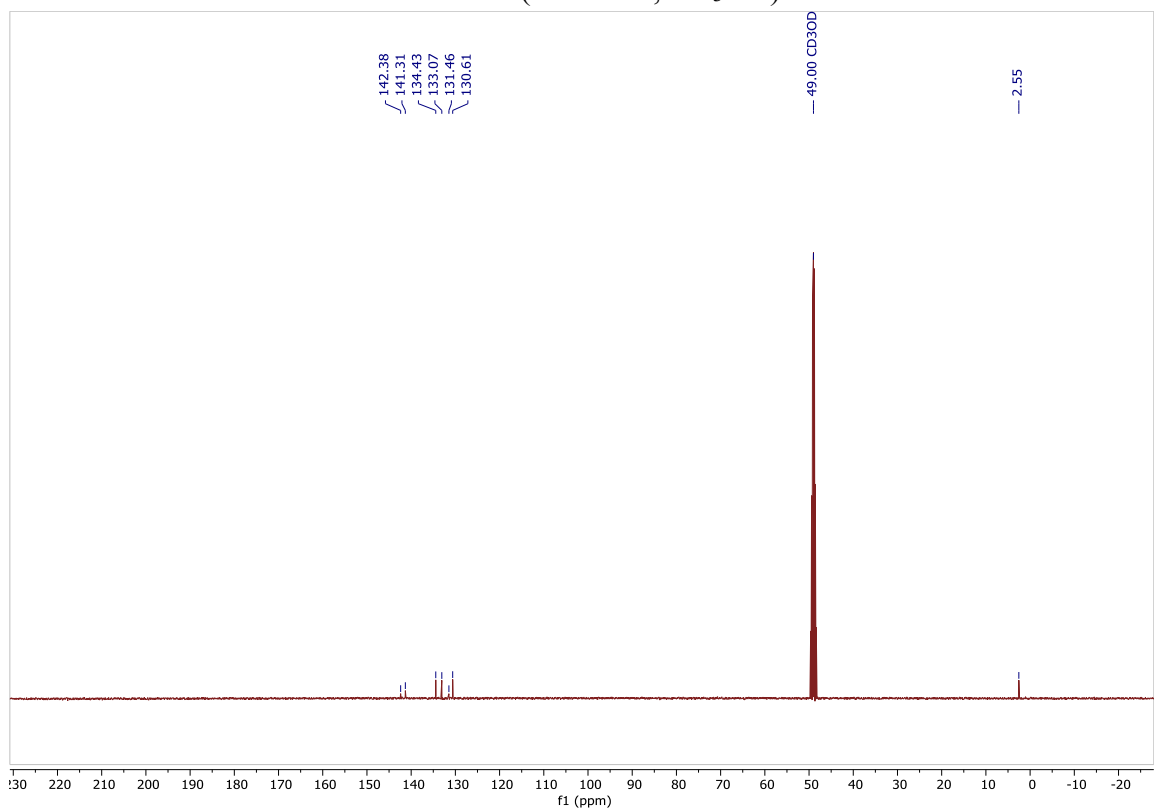
2-Chloro-5-(iodomethyl)benzenesulfonamide, S5



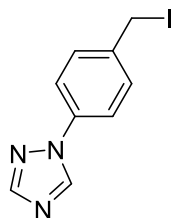
^1H NMR (400 MHz, CD_3OD)



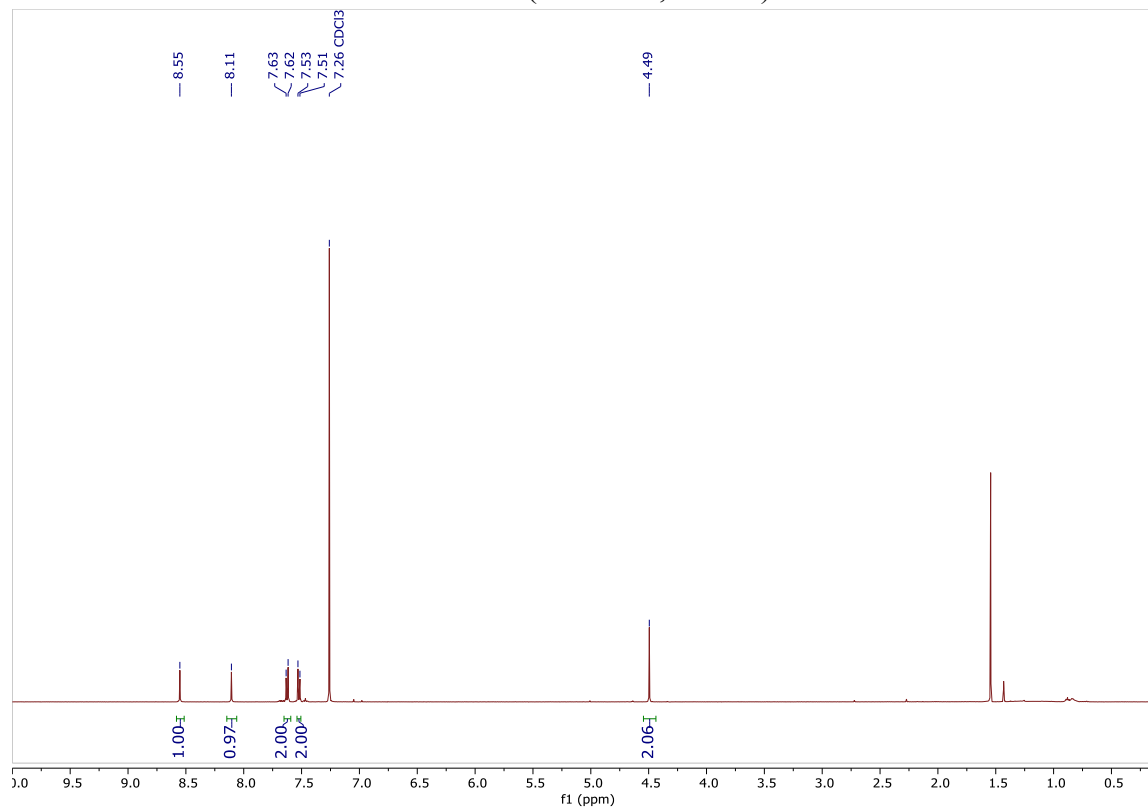
^{13}C NMR (101 MHz, CD_3OD)



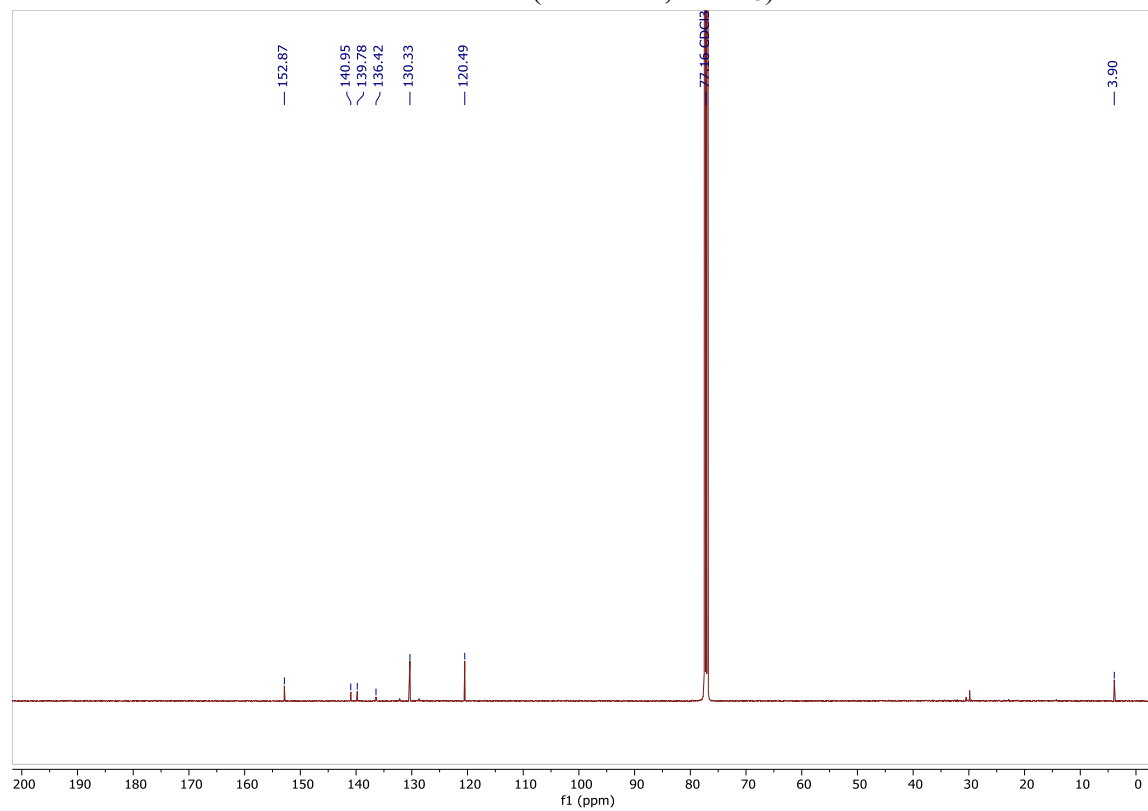
1-(4-(Iodomethyl)phenyl)-1*H*-1,2,4-triazole, S6



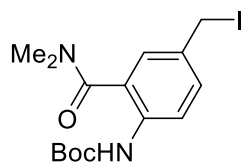
¹H NMR (500 MHz, CDCl₃)



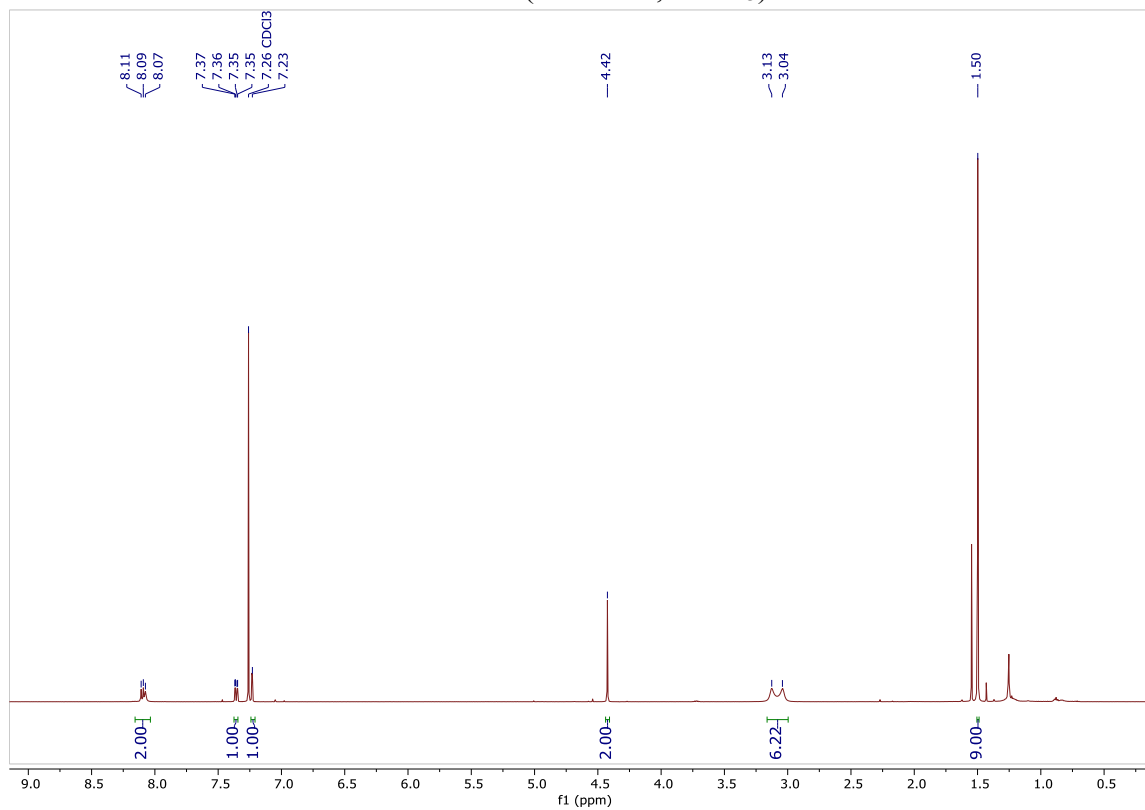
¹³C NMR (125 MHz, CDCl₃)



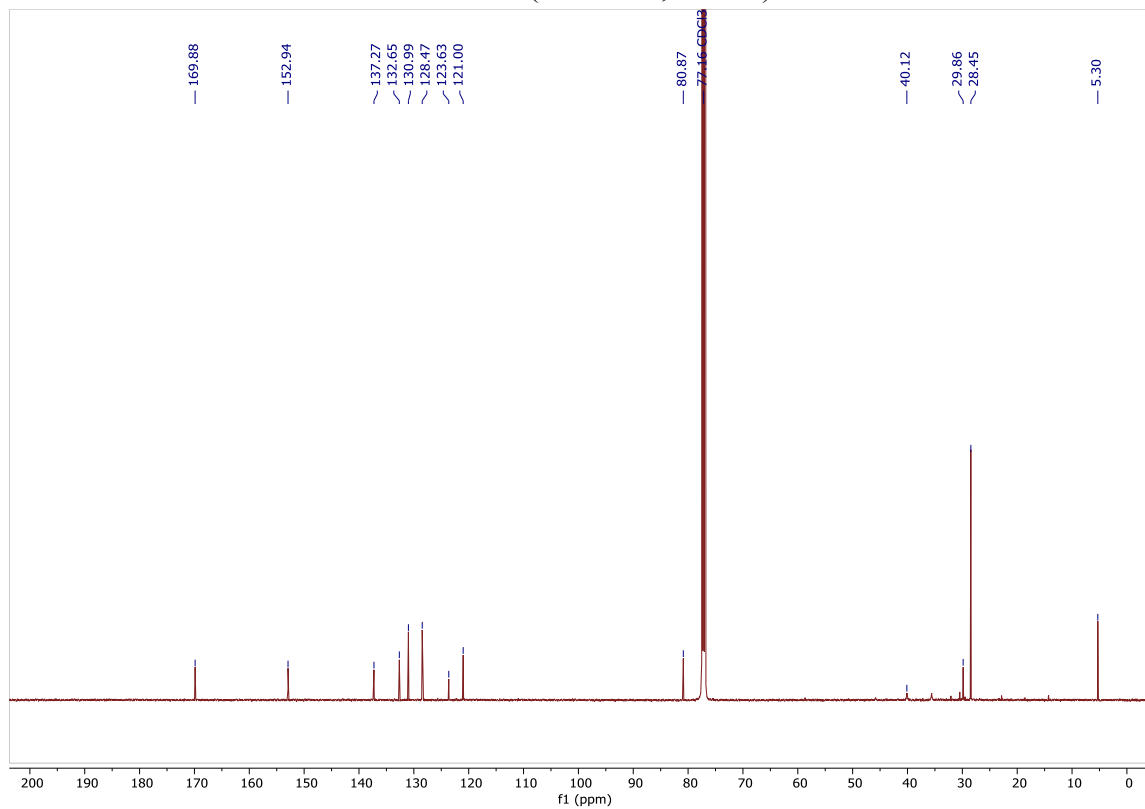
***tert*-Butyl (2-(dimethylcarbamoyl)-4-(iodomethyl)phenyl)carbamate, S7**



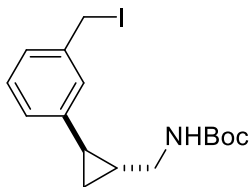
^1H NMR (500 MHz, CDCl_3)



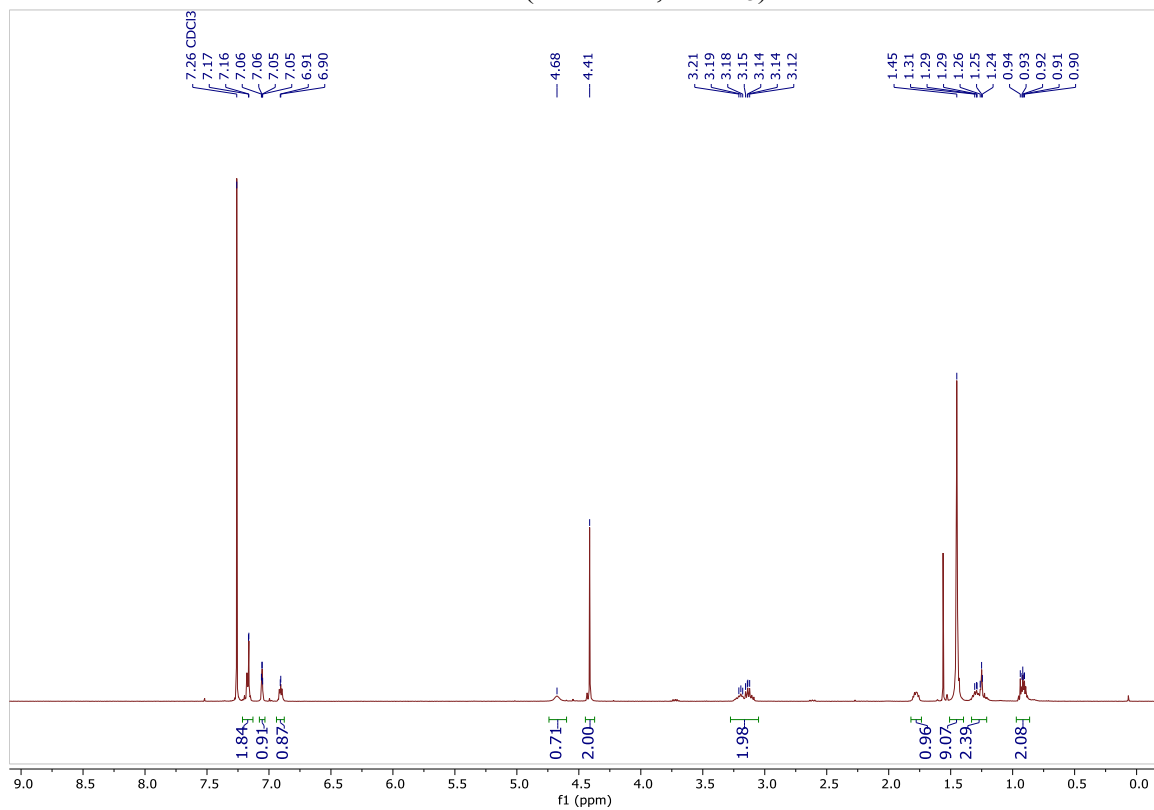
^{13}C NMR (125 MHz, CDCl_3)



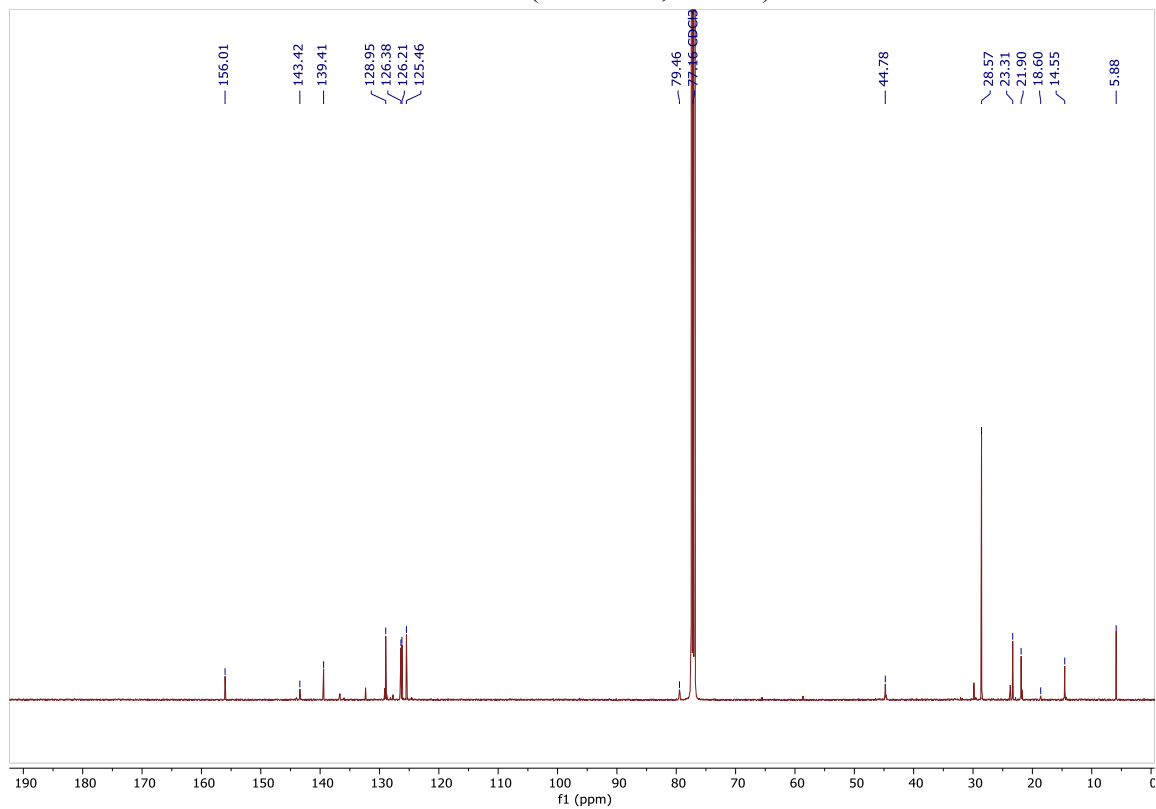
***tert*-Butyl ((-2-(3-(iodomethyl)phenyl)cyclopropyl)methyl)carbamate, S8**



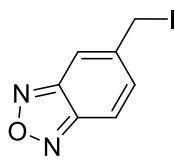
^1H NMR (500 MHz, CDCl_3)



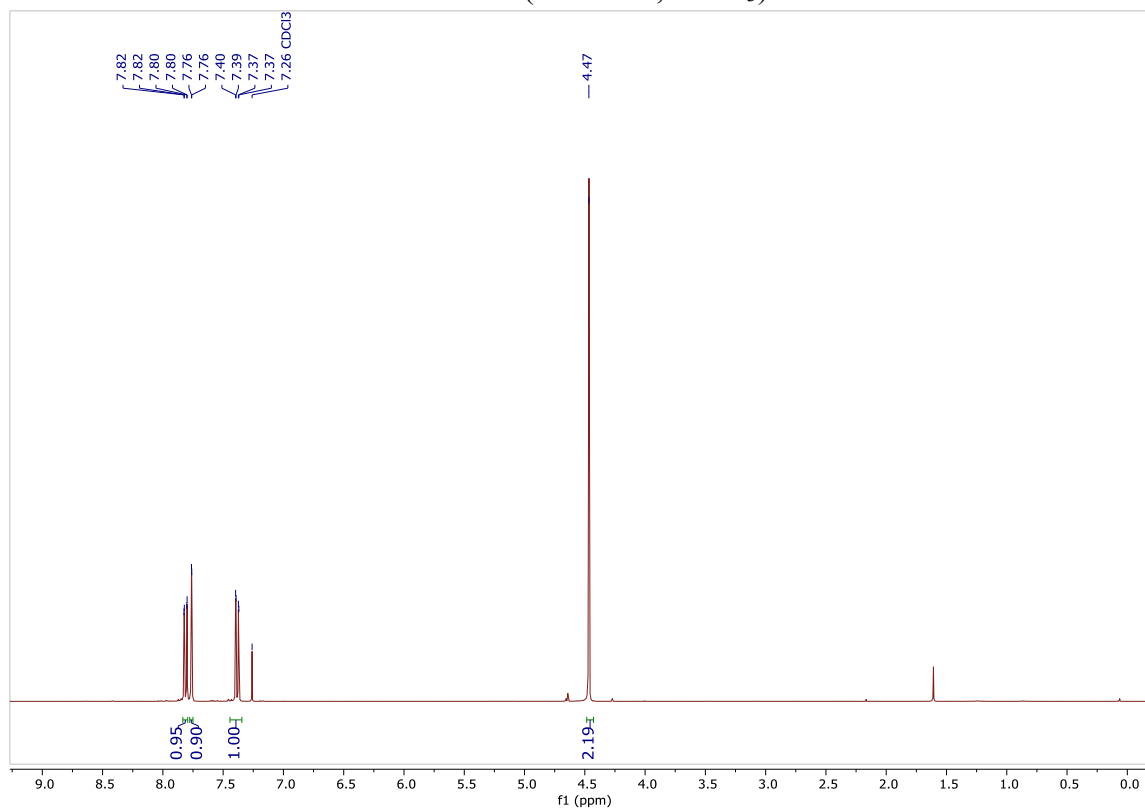
^{13}C NMR (125 MHz, CDCl_3)



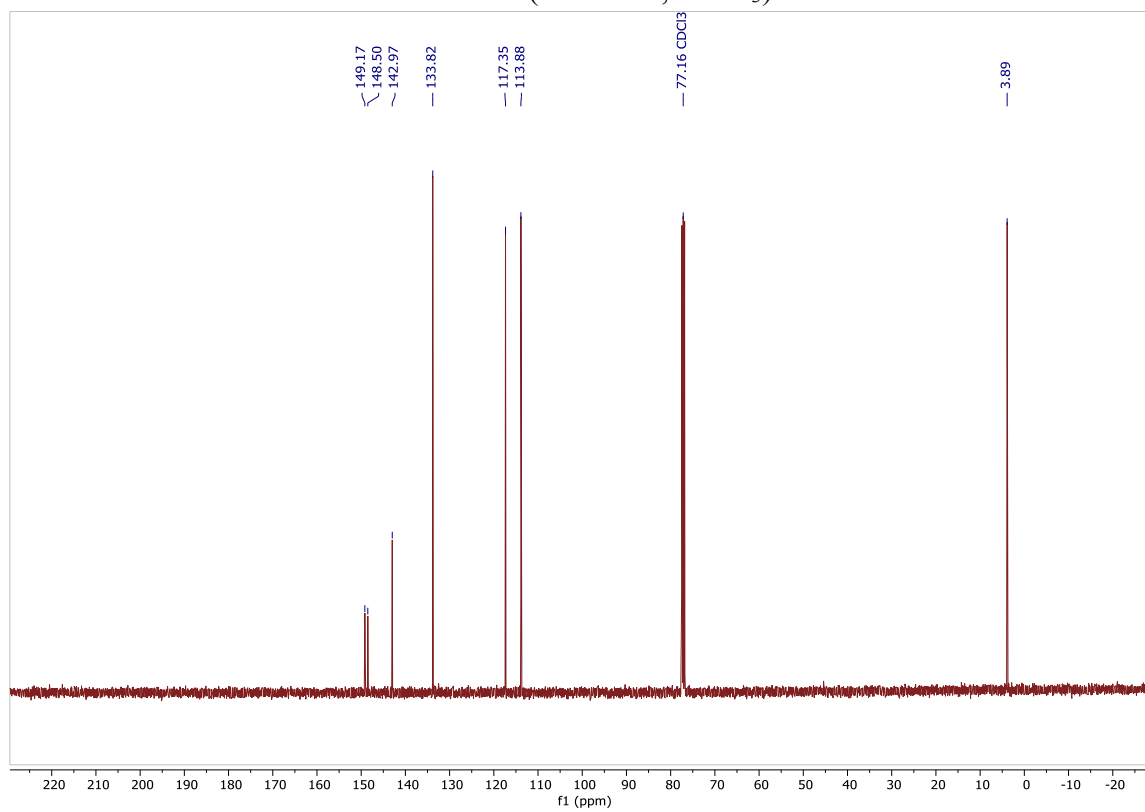
5-(Iodomethyl)benzo[c][1,2,5]oxadiazole, S9



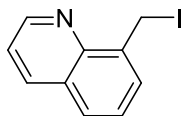
^1H NMR (400 MHz, CDCl_3)



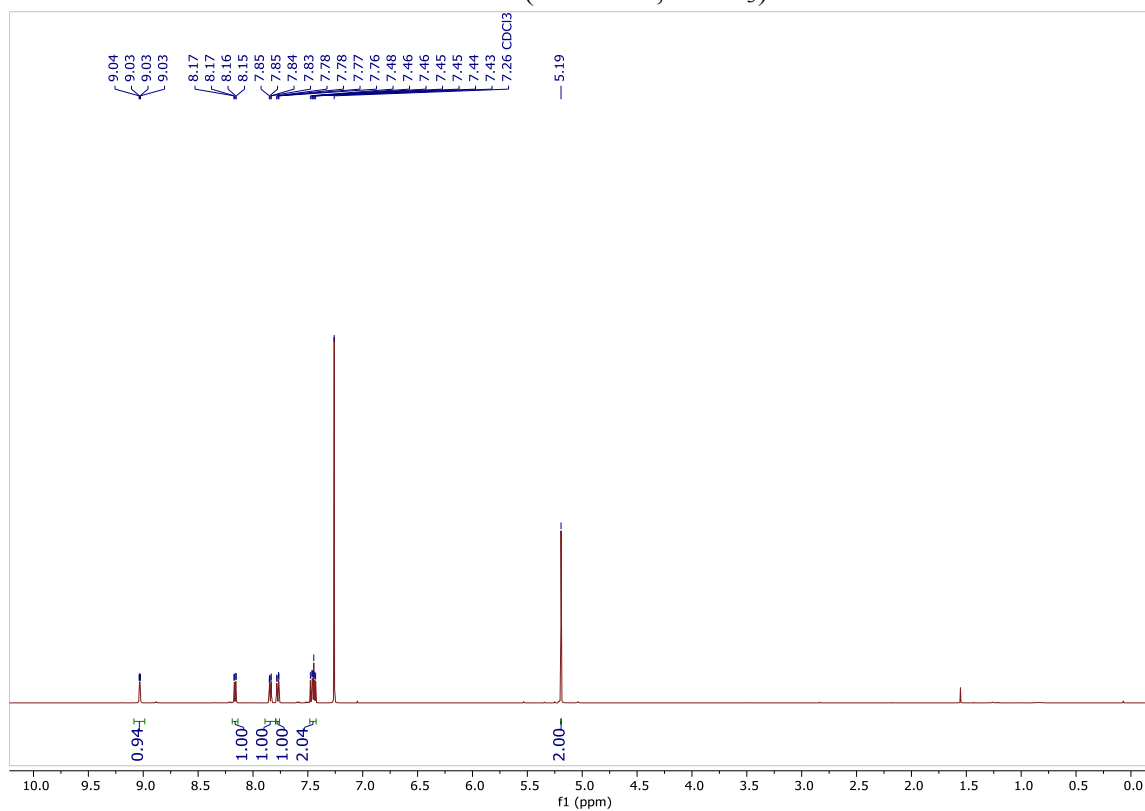
^{13}C NMR (101 MHz, CDCl_3)



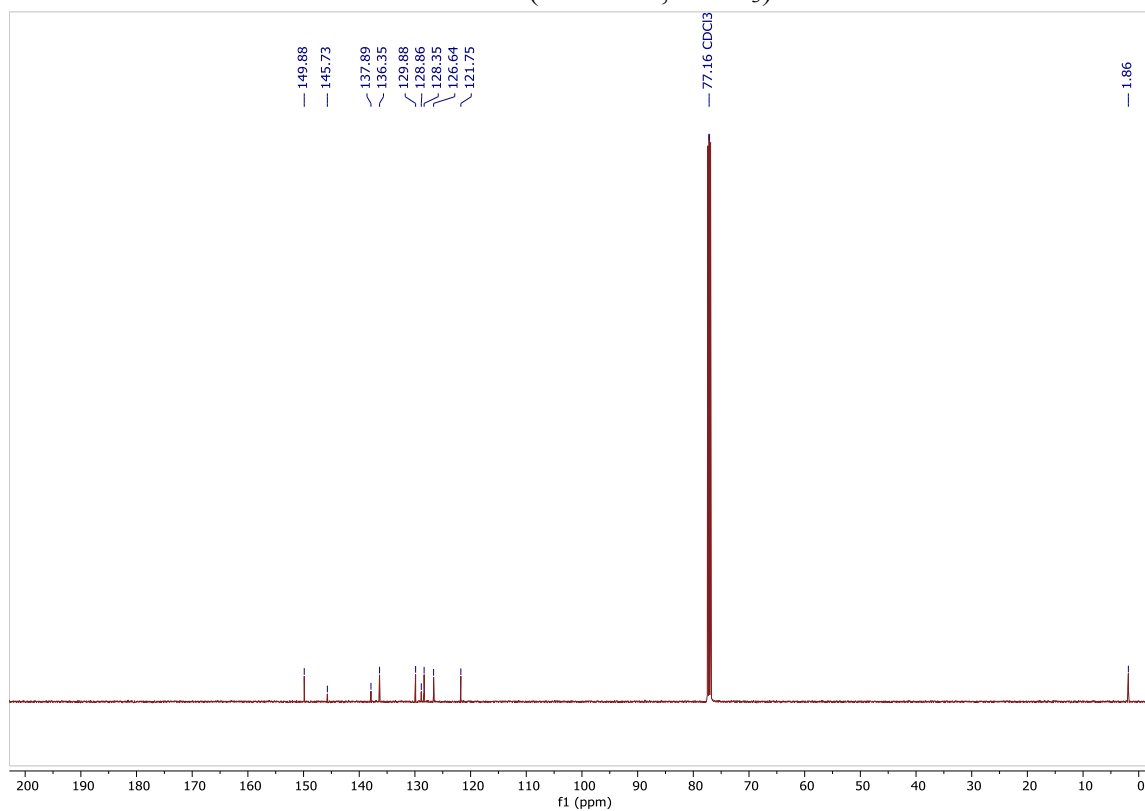
8-(Iodomethyl)quinoline, S10



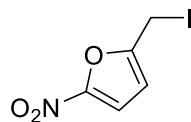
^1H NMR (500 MHz, CDCl_3)



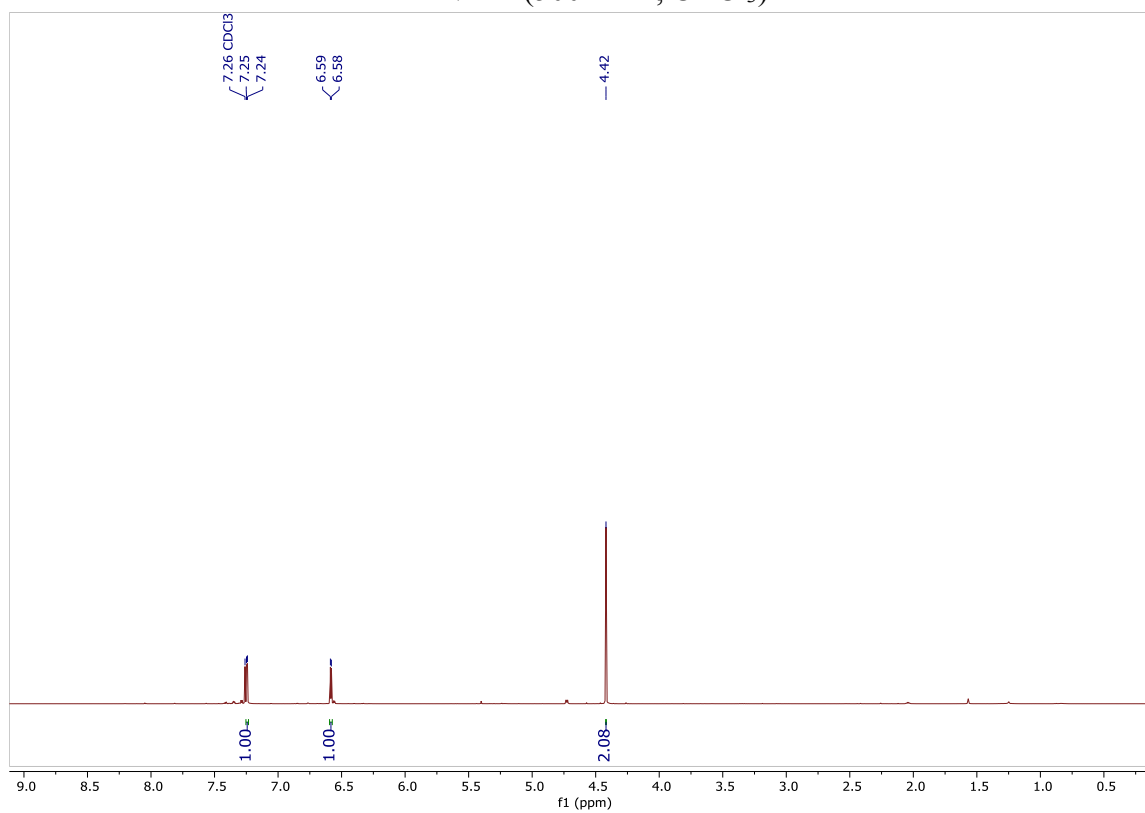
^{13}C NMR (125 MHz, CDCl_3)



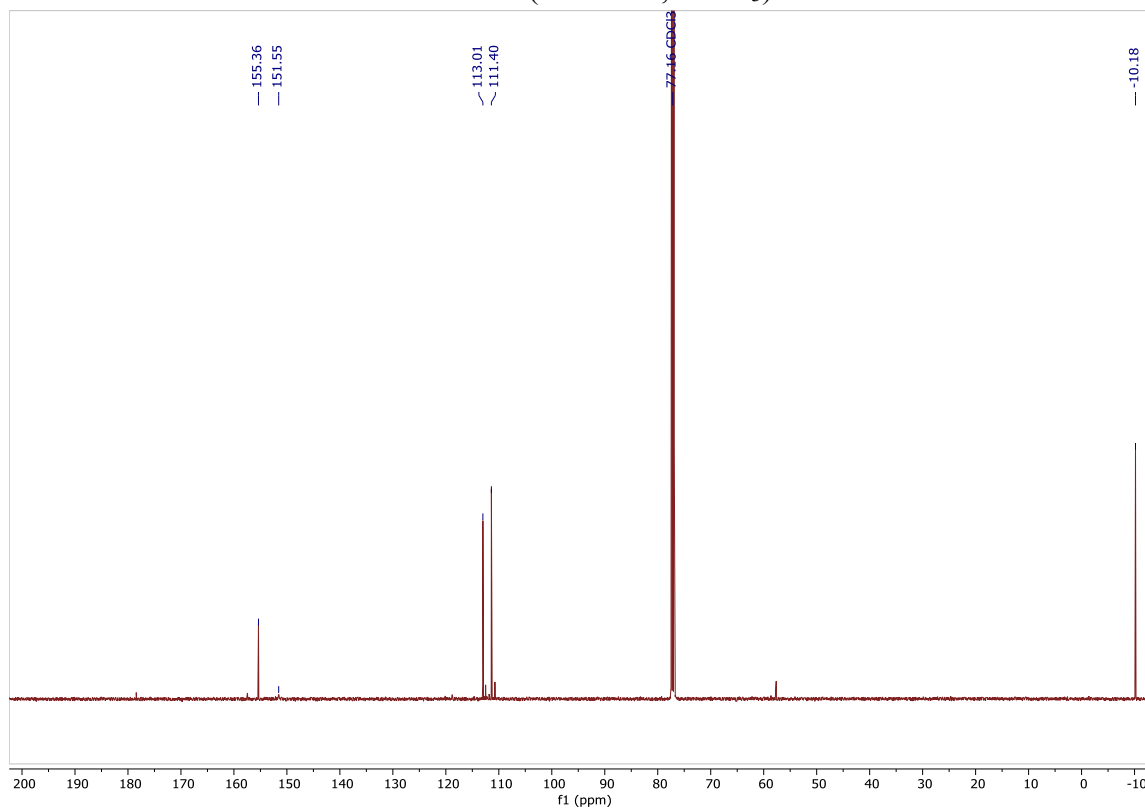
2-(Iodomethyl)-5-nitrofuran, S11



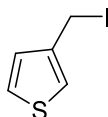
^1H NMR (500 MHz, CDCl_3)



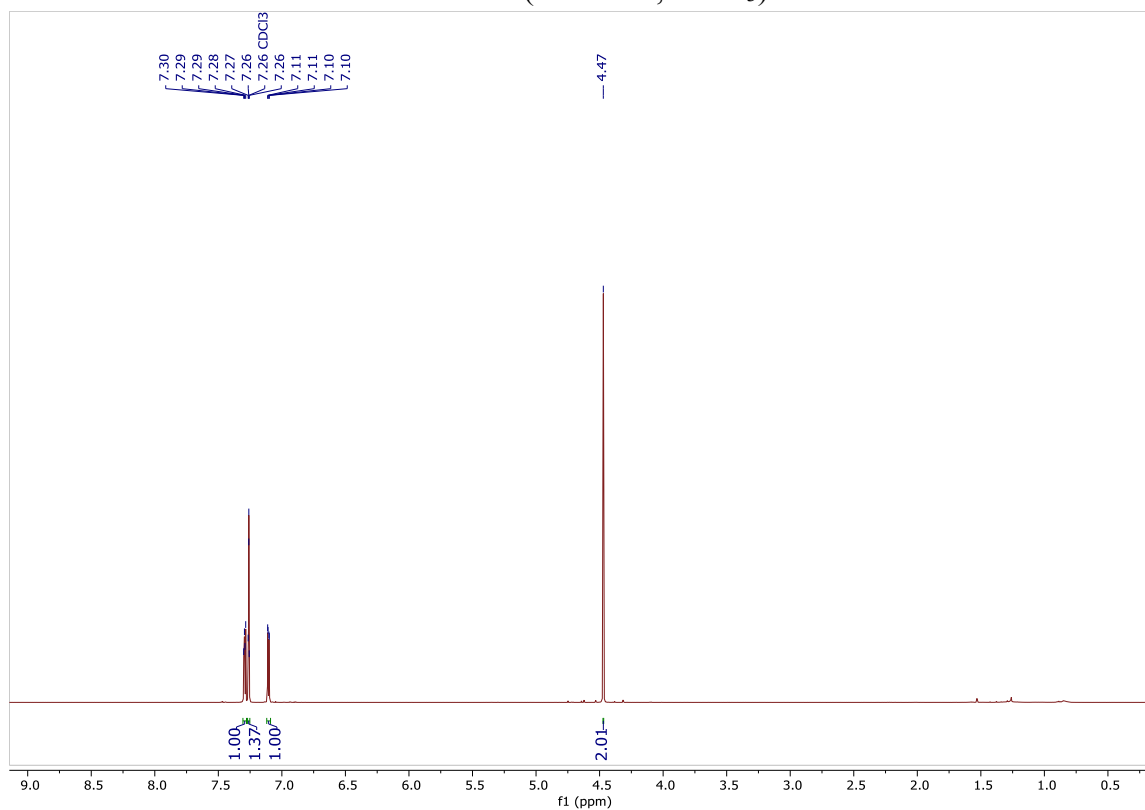
^{13}C NMR (125 MHz, CDCl_3)



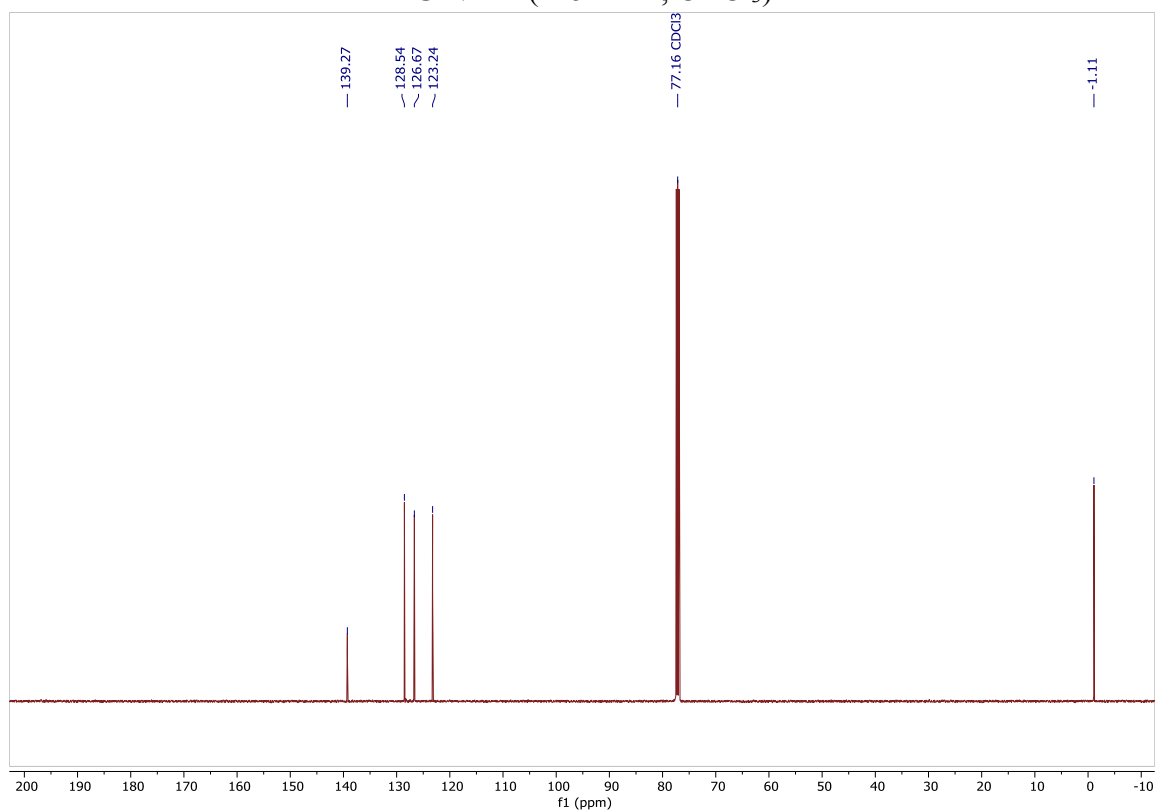
3-(Iodomethyl)thiophene, S12



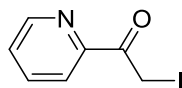
^1H NMR (500 MHz, CDCl_3)



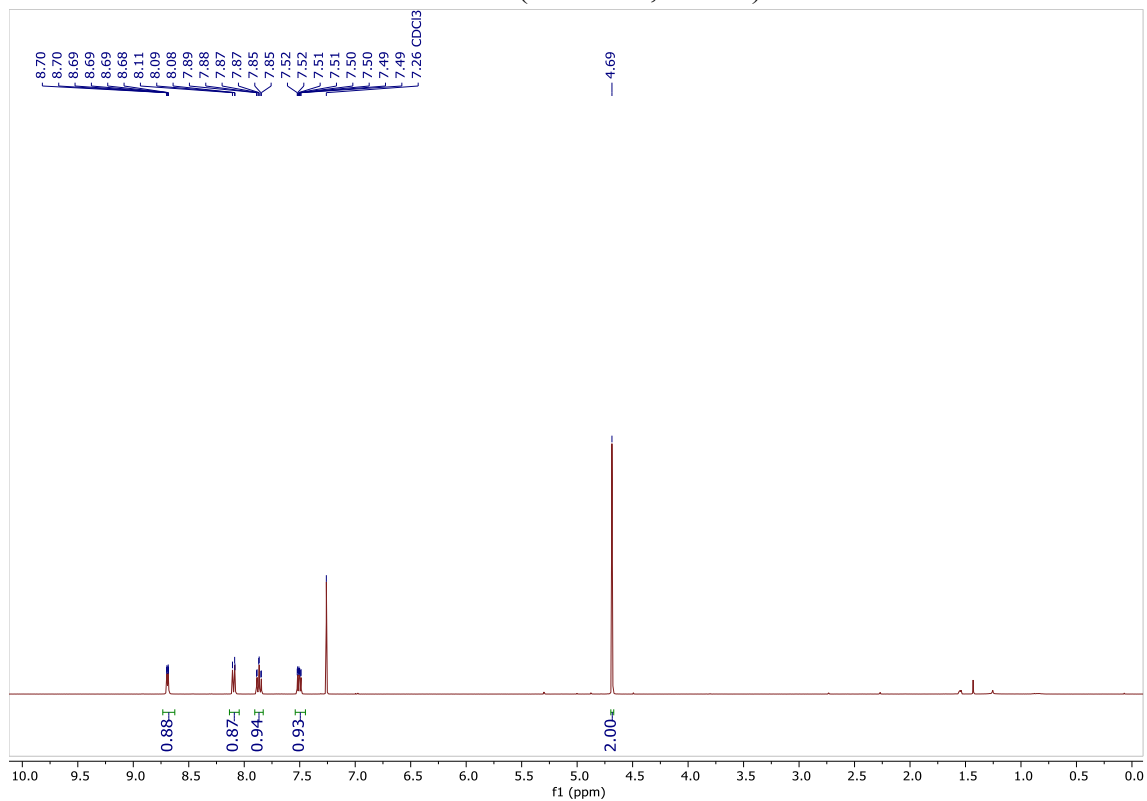
^{13}C NMR (125 MHz, CDCl_3)



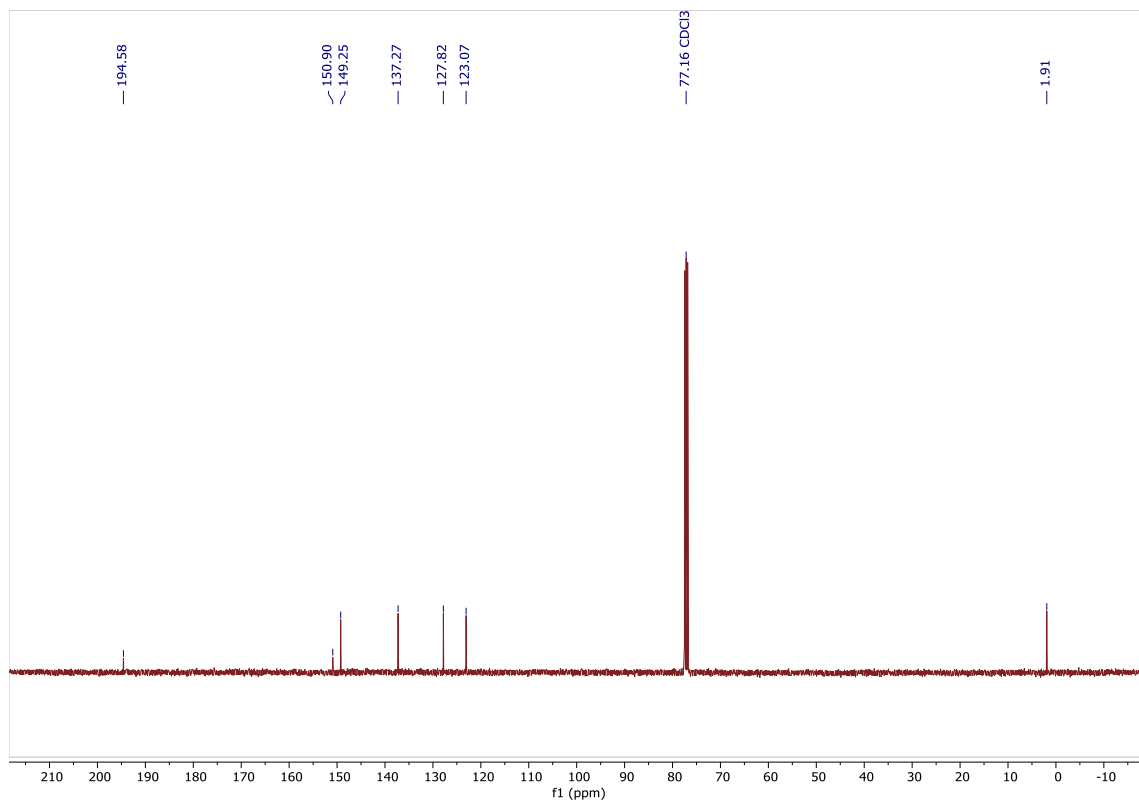
Iodo-1-(pyridin-2-yl)ethan-1-one, S13



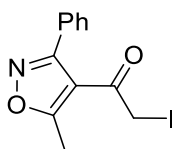
¹H NMR (400 MHz, CDCl₃)



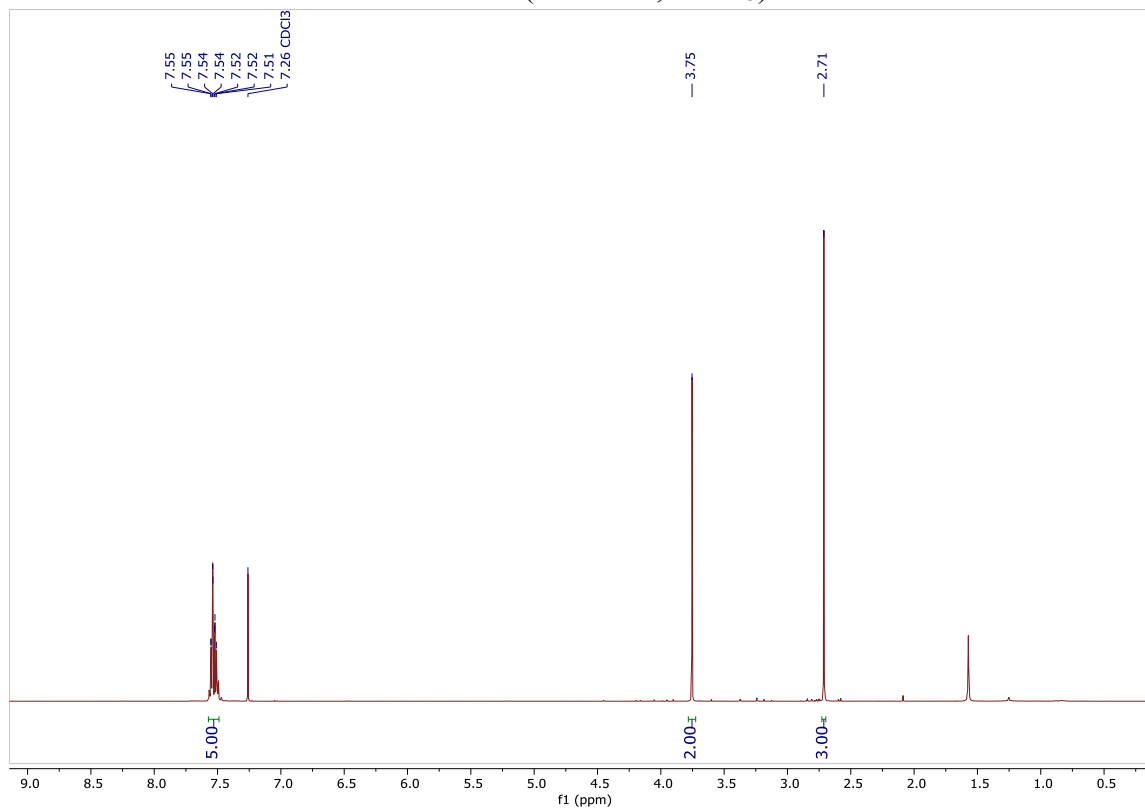
¹³C NMR (101 MHz, CDCl₃)



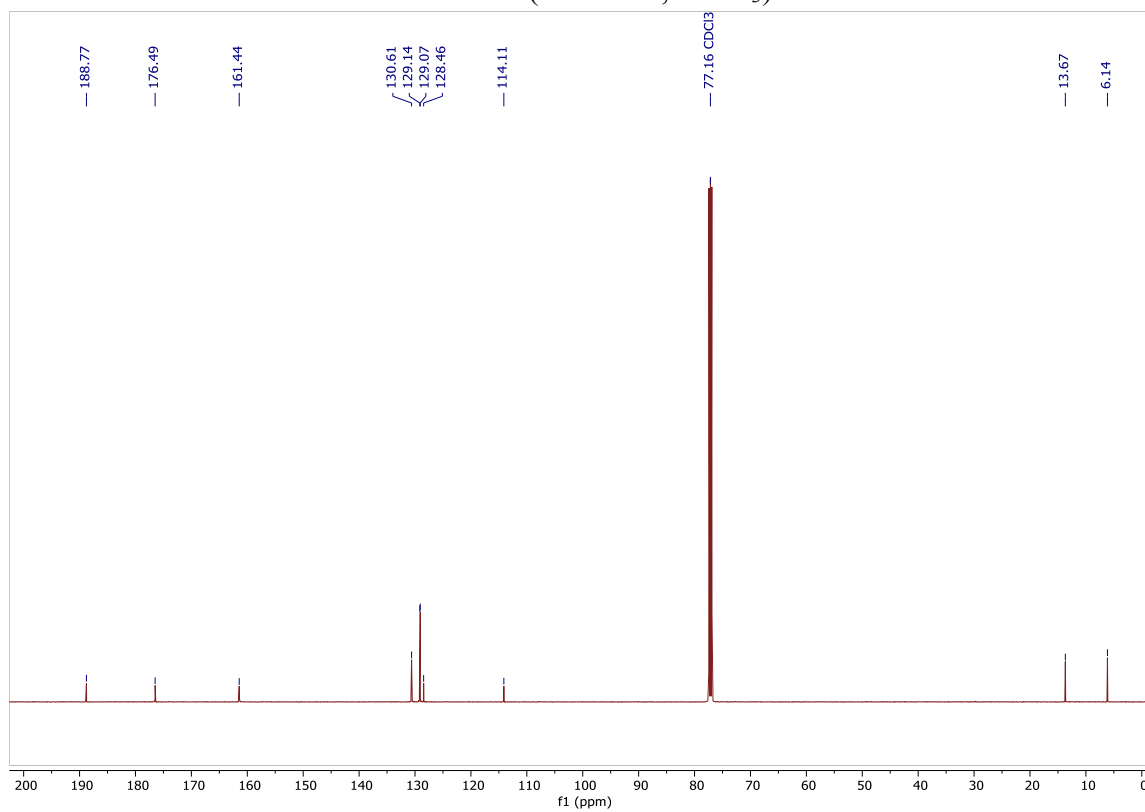
2-Iodo-1-(5-methyl-3-phenylisoxazol-4-yl)ethan-1-one, S14



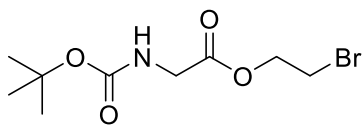
^1H NMR (500 MHz, CDCl_3)



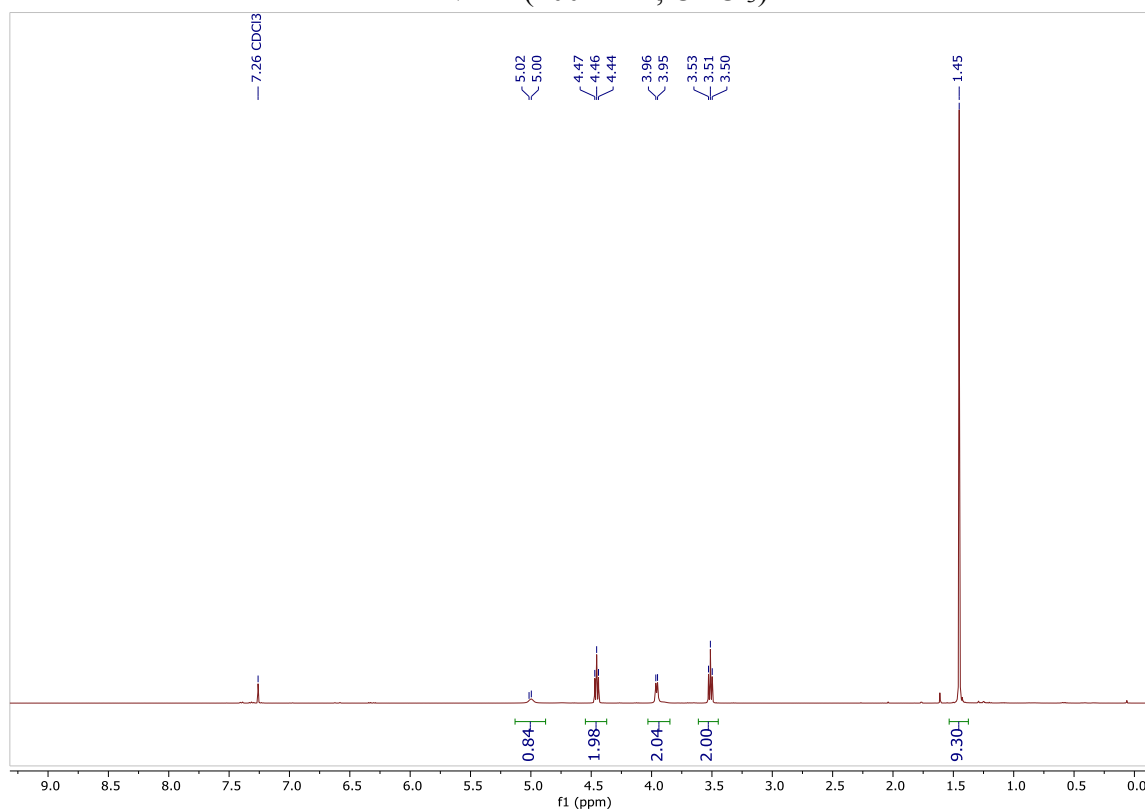
^{13}C NMR (125 MHz, CDCl_3)



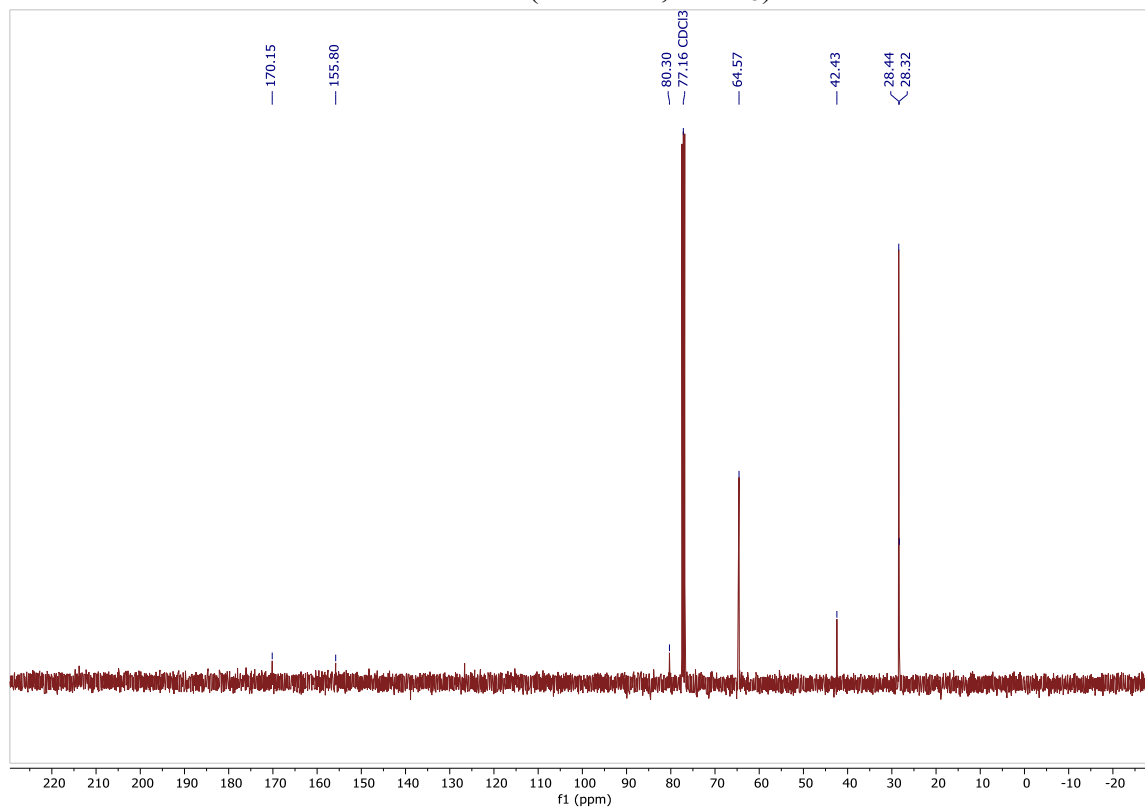
2-Bromoethyl (tert-butoxycarbonyl)glycinate, S15



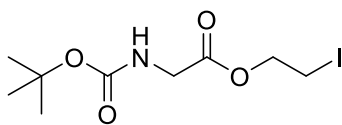
^1H NMR (400 MHz, CDCl_3)



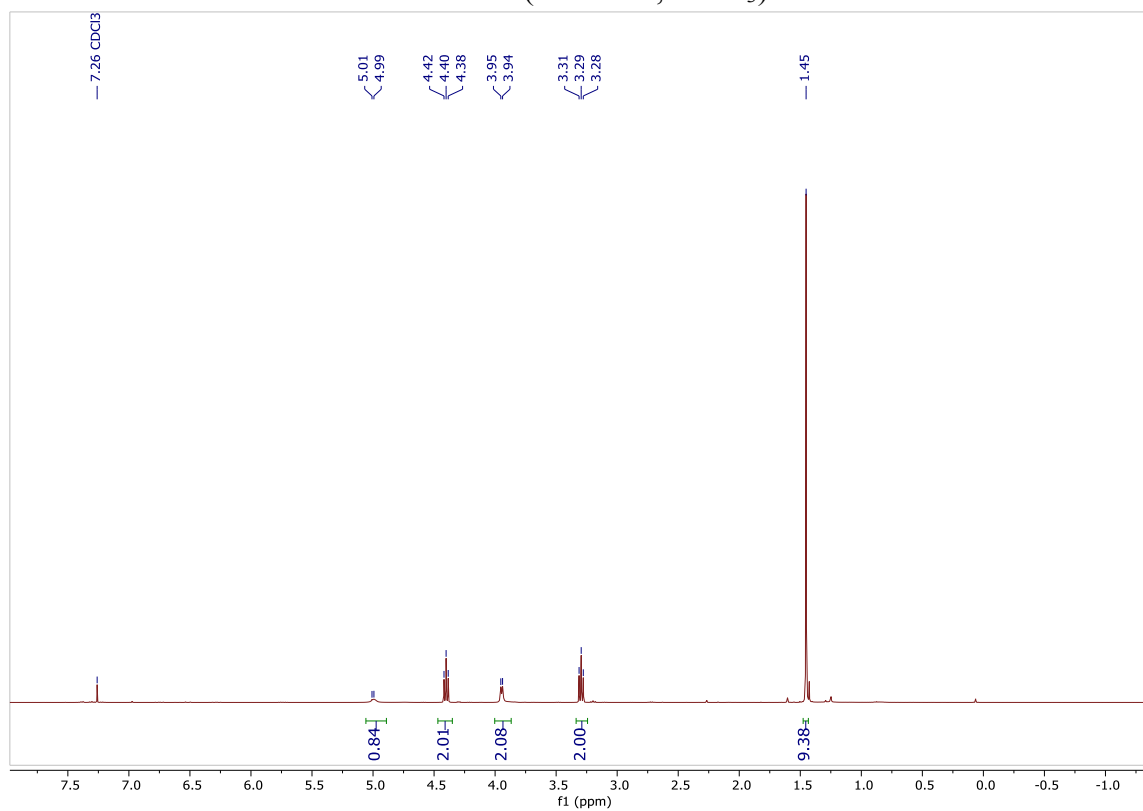
^{13}C NMR (101 MHz, CDCl_3)



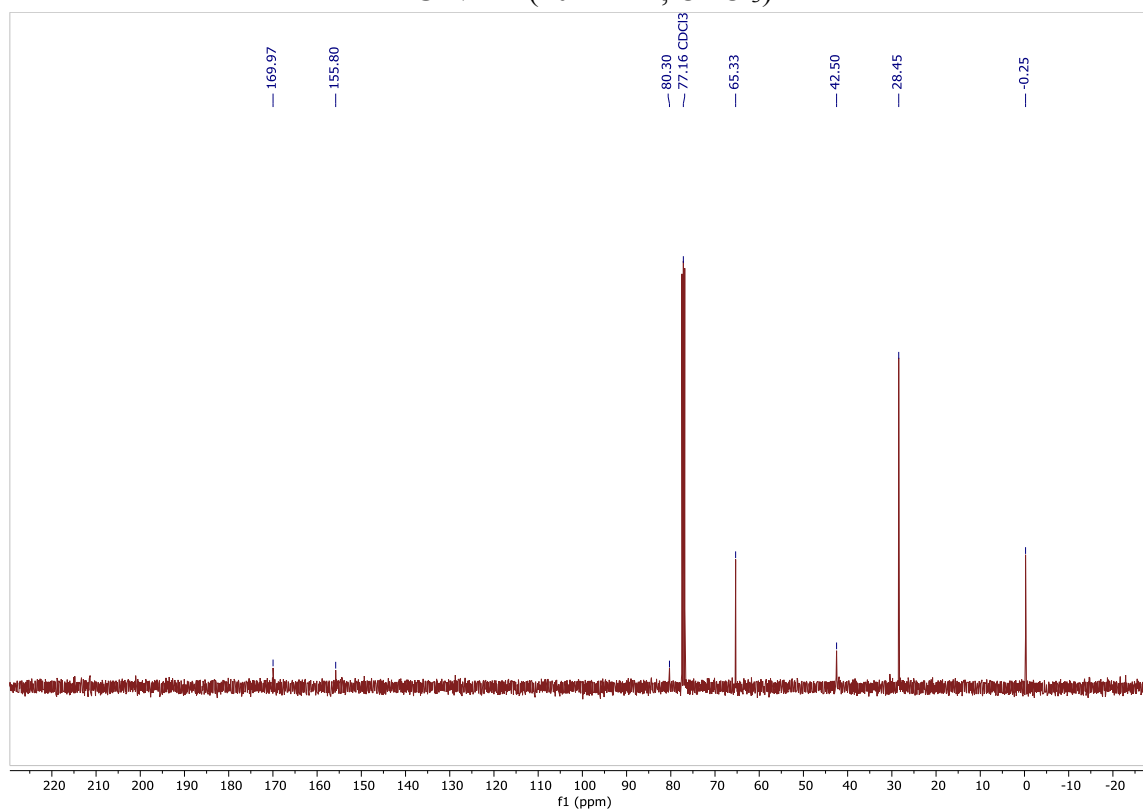
2-Iodoethyl (tert-butoxycarbonyl)glycinate, S16



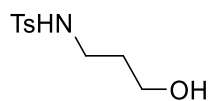
^1H NMR (400 MHz, CDCl_3)



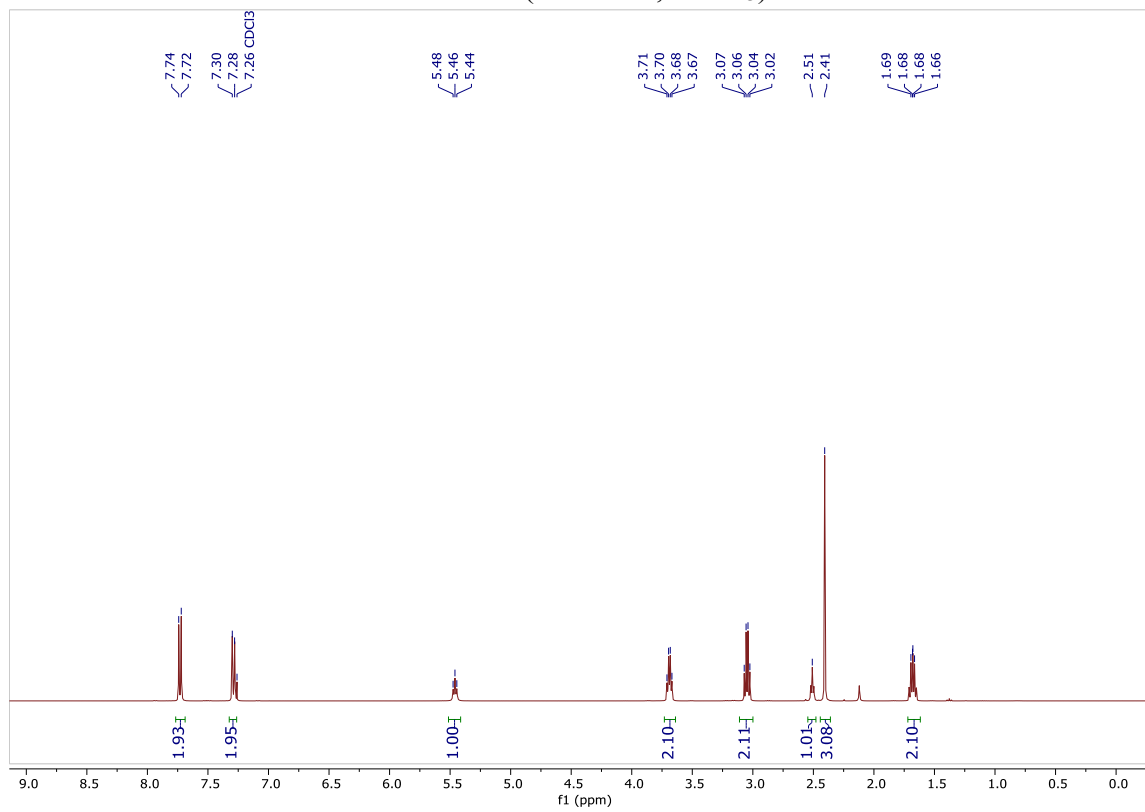
^{13}C NMR (101 MHz, CDCl_3)



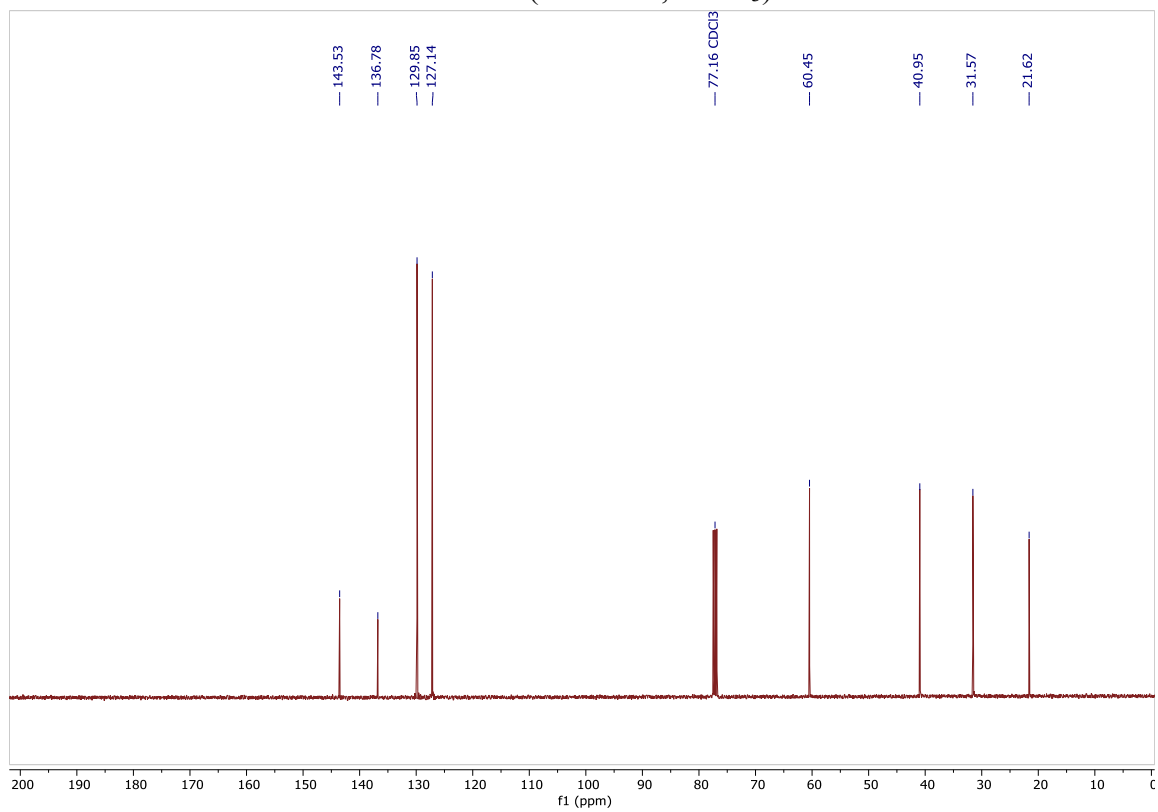
***N*-(3-Hydroxypropyl)-4-methylbenzenesulfonamide, S17**



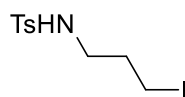
^1H NMR (400 MHz, CDCl_3)



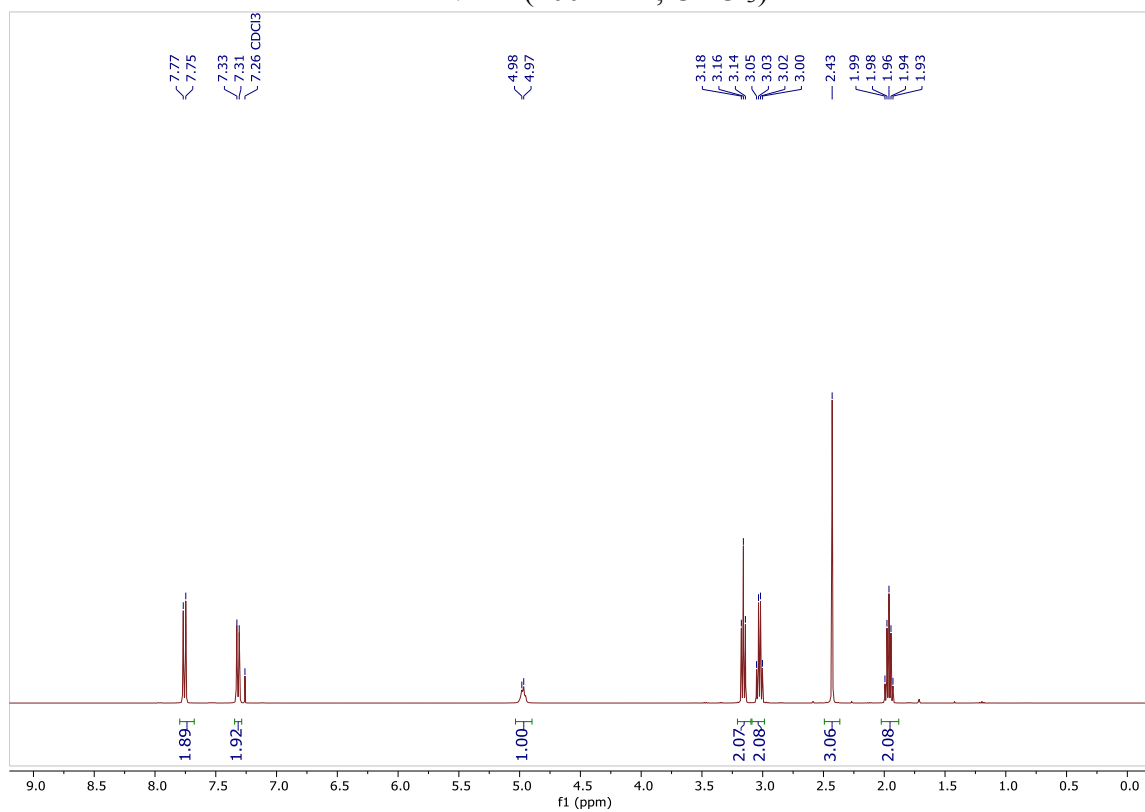
^{13}C NMR (101 MHz, CDCl_3)



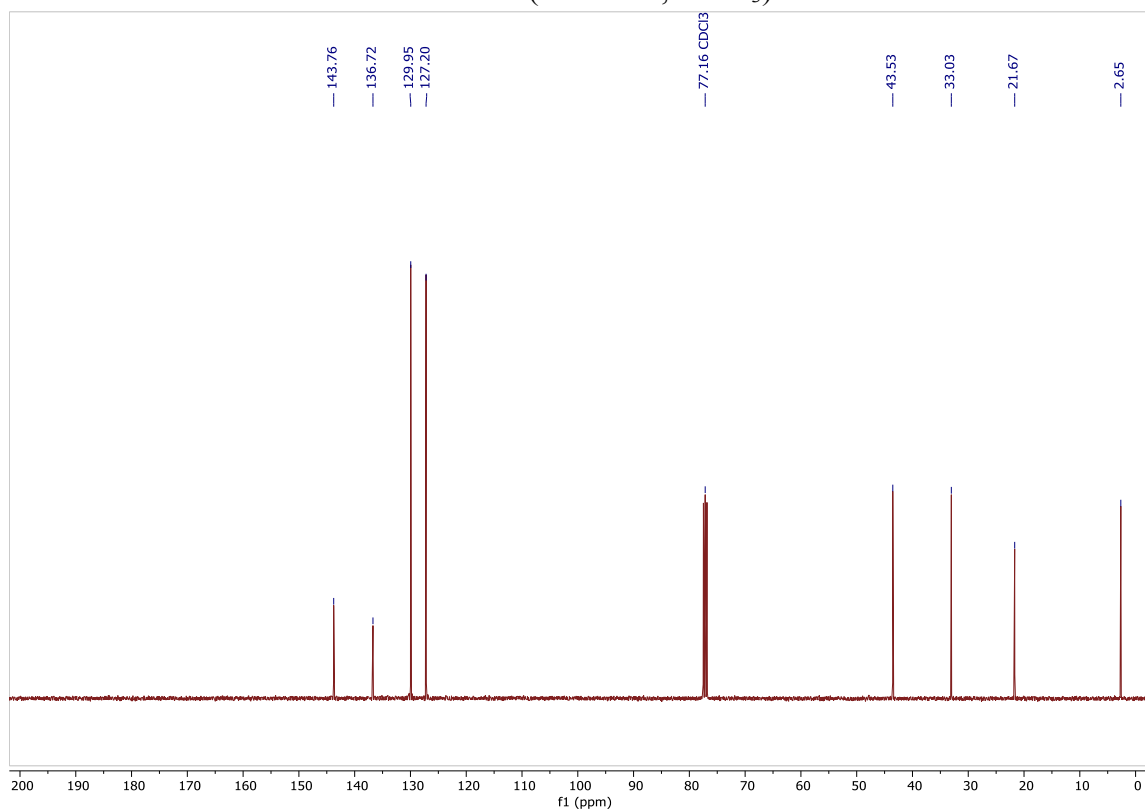
***N*-(3-Iodopropyl)-4-methylbenzenesulfonamide, S18**



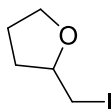
¹H NMR (400 MHz, CDCl₃)



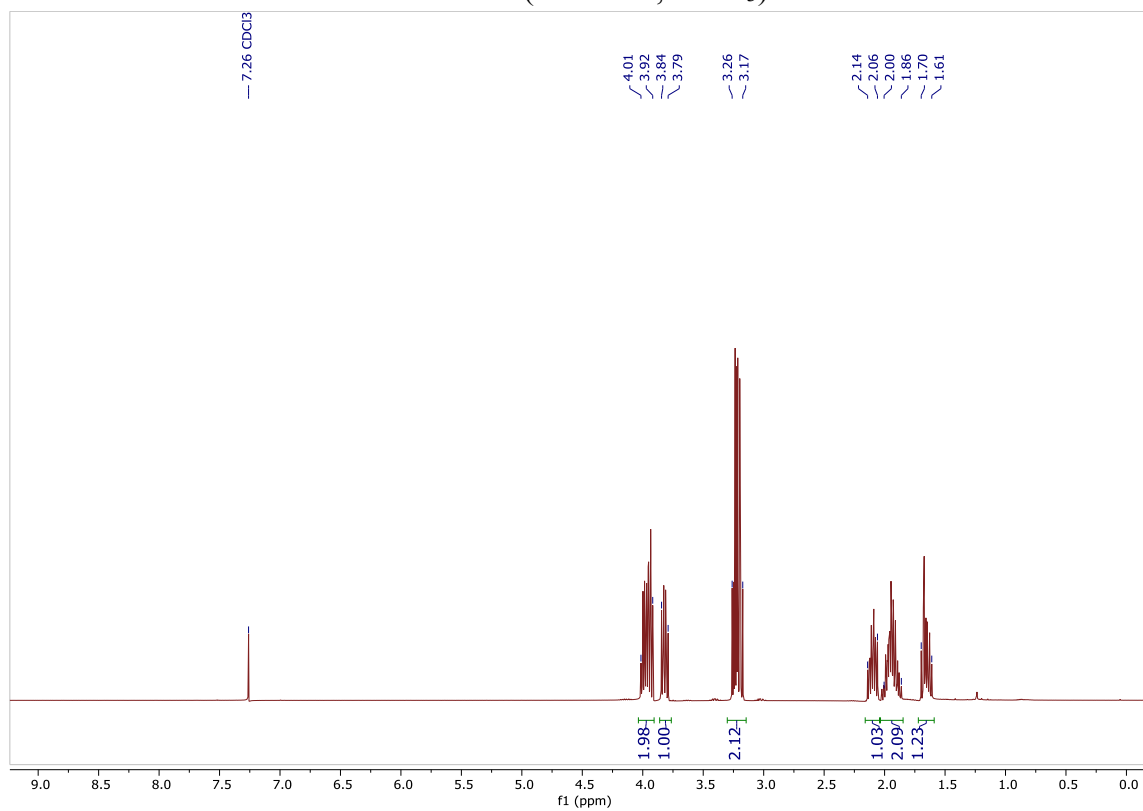
¹³C NMR (101 MHz, CDCl₃)



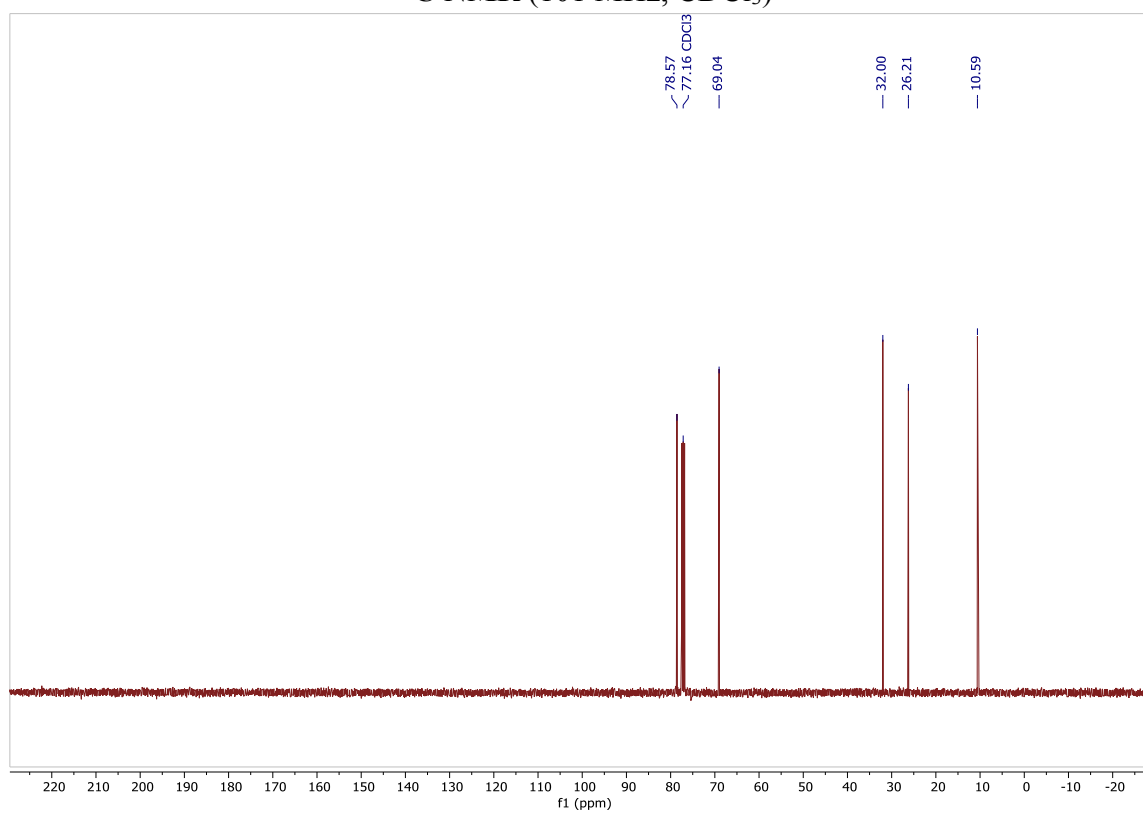
2-(Iodomethyl)tetrahydrofuran, S19



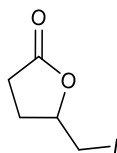
^1H NMR (400 MHz, CDCl_3)



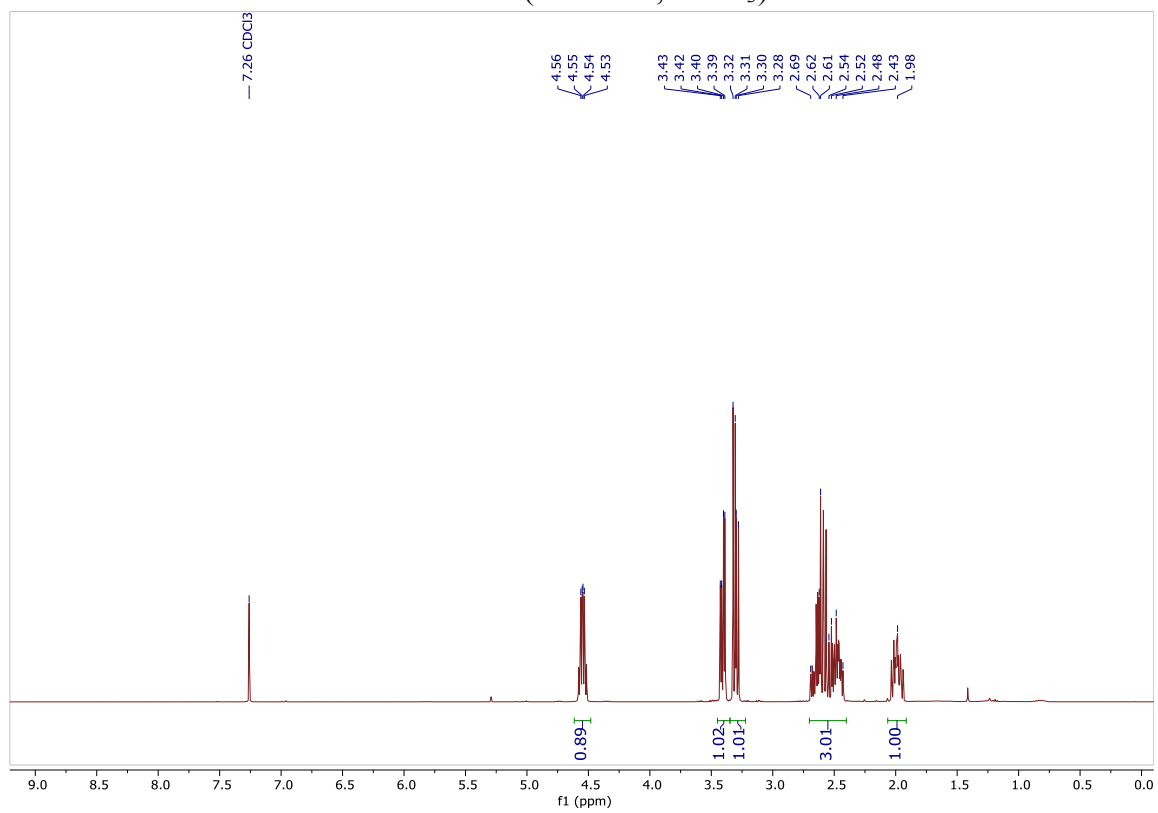
^{13}C NMR (101 MHz, CDCl_3)



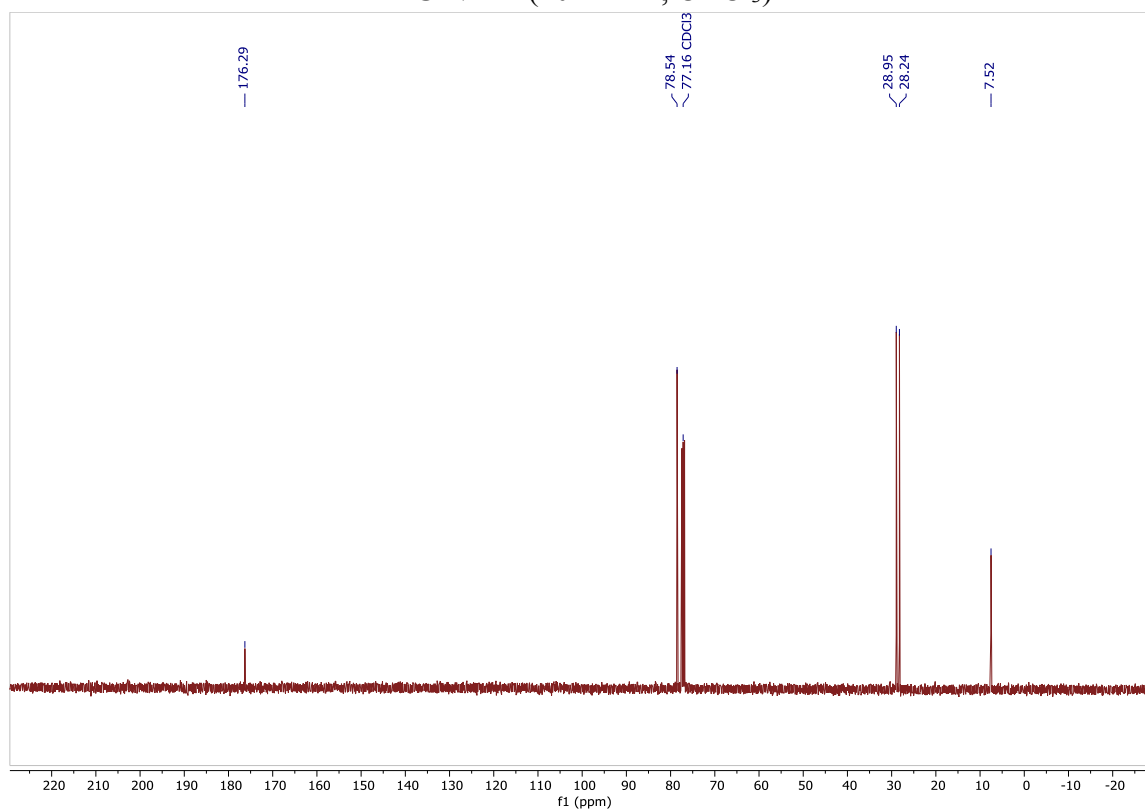
5-(Iodomethyl)dihydrofuran-2(3H)-one, S20



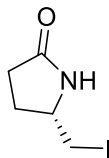
^1H NMR (400 MHz, CDCl_3)



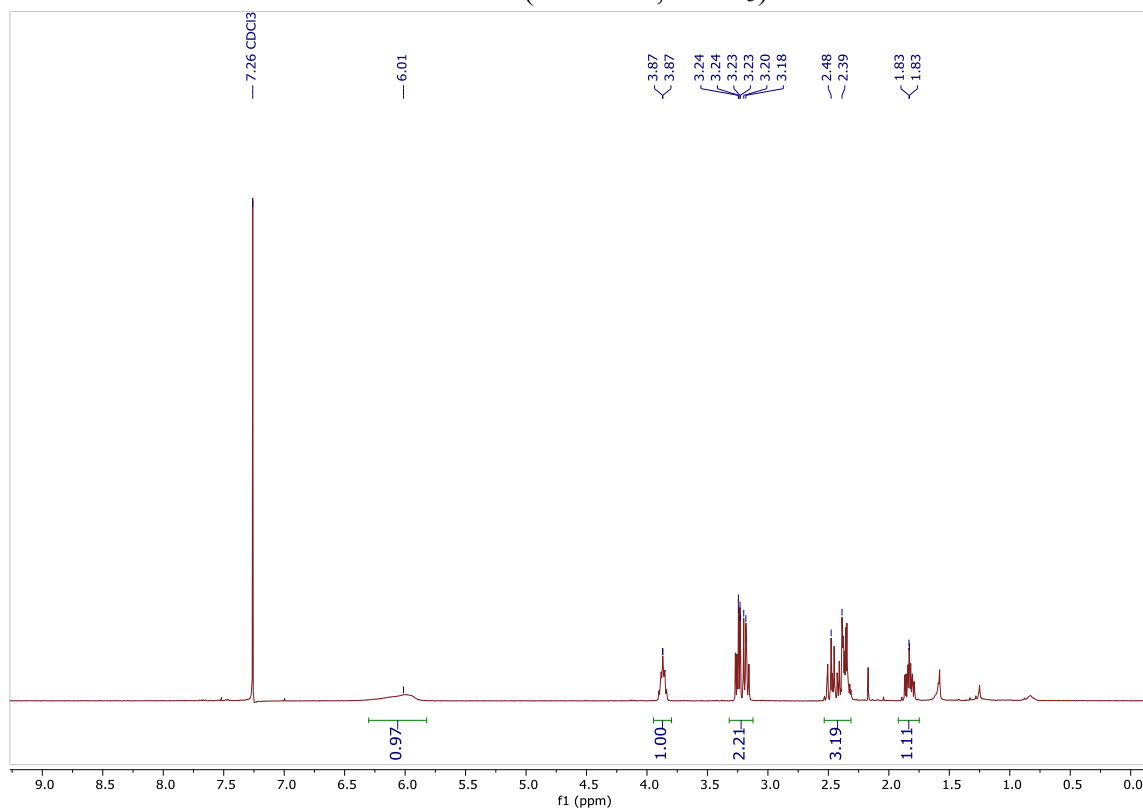
^{13}C NMR (101 MHz, CDCl_3)



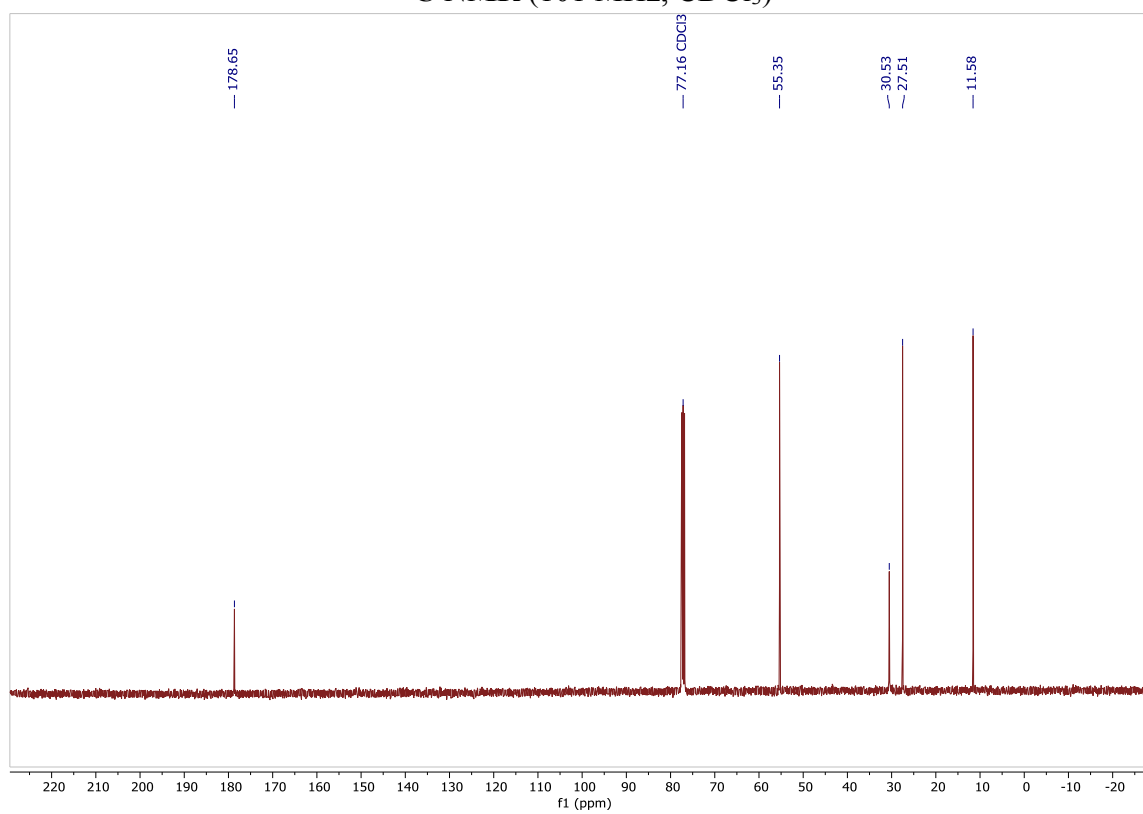
(S)-5-(Iodomethyl)pyrrolidin-2-one, S21



^1H NMR (400 MHz, CDCl_3)



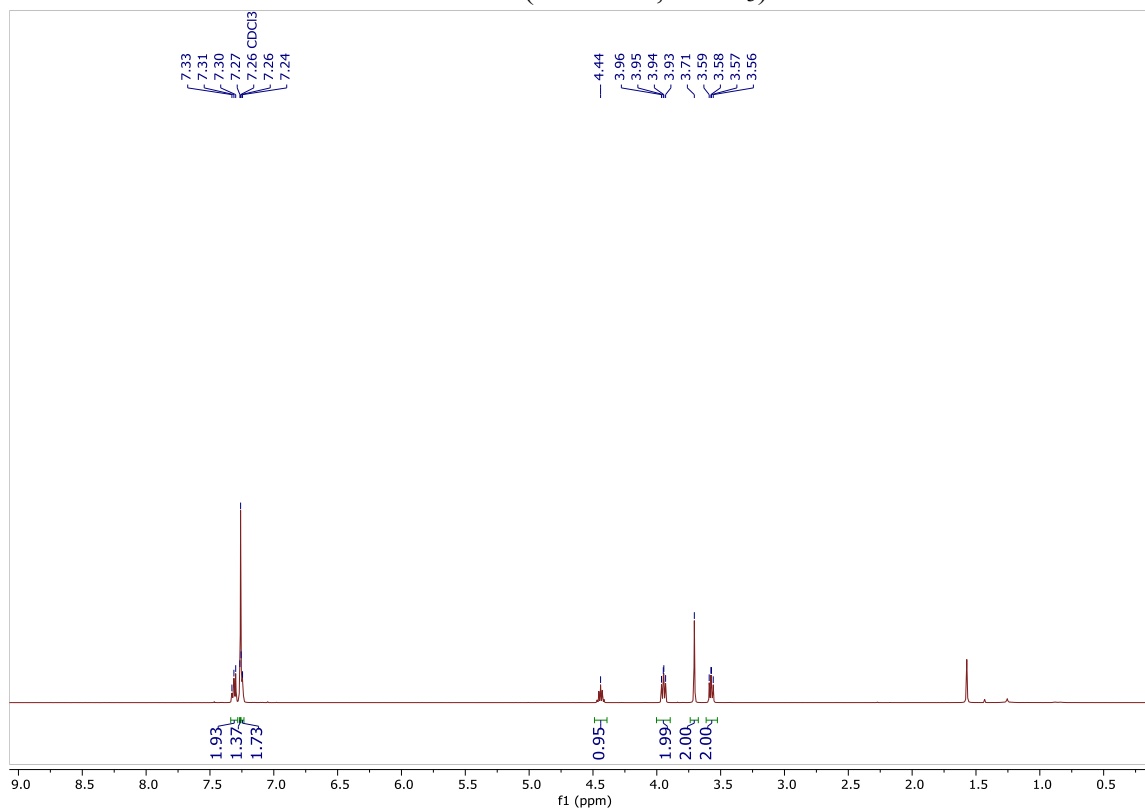
^{13}C NMR (101 MHz, CDCl_3)



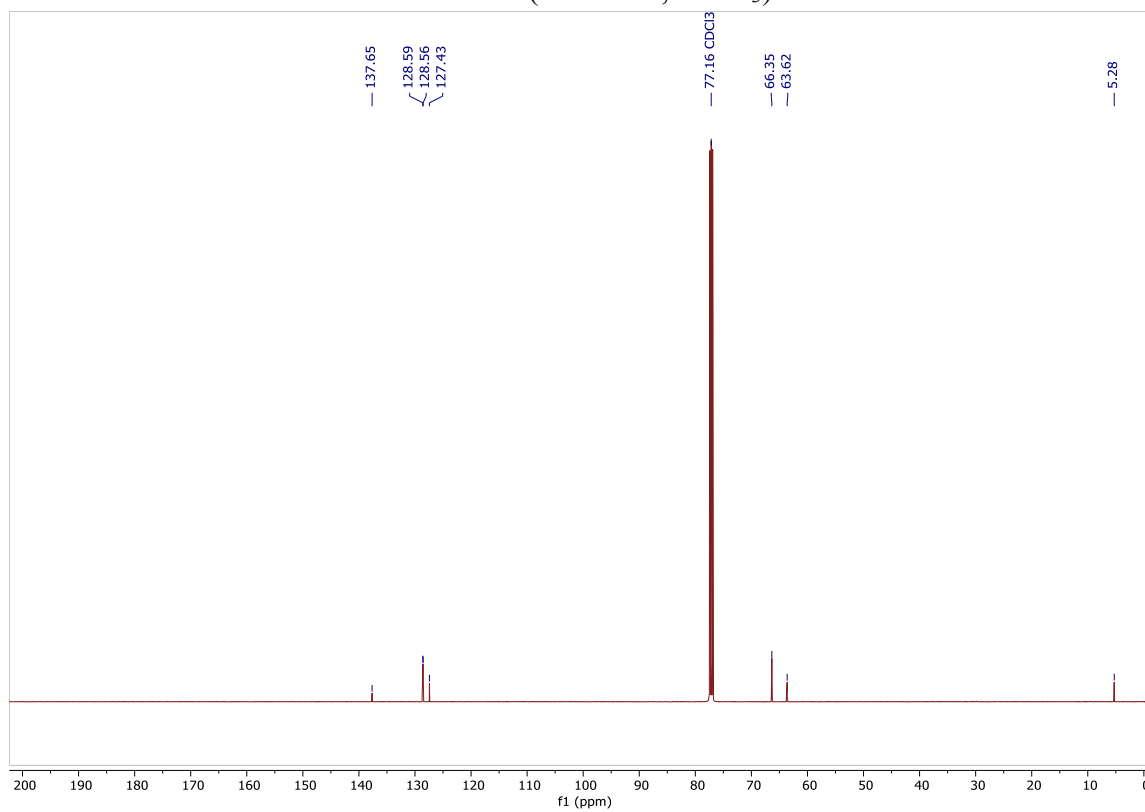
1-Benzyl-3-iodoazetidine, S22



^1H NMR (500 MHz, CDCl_3)



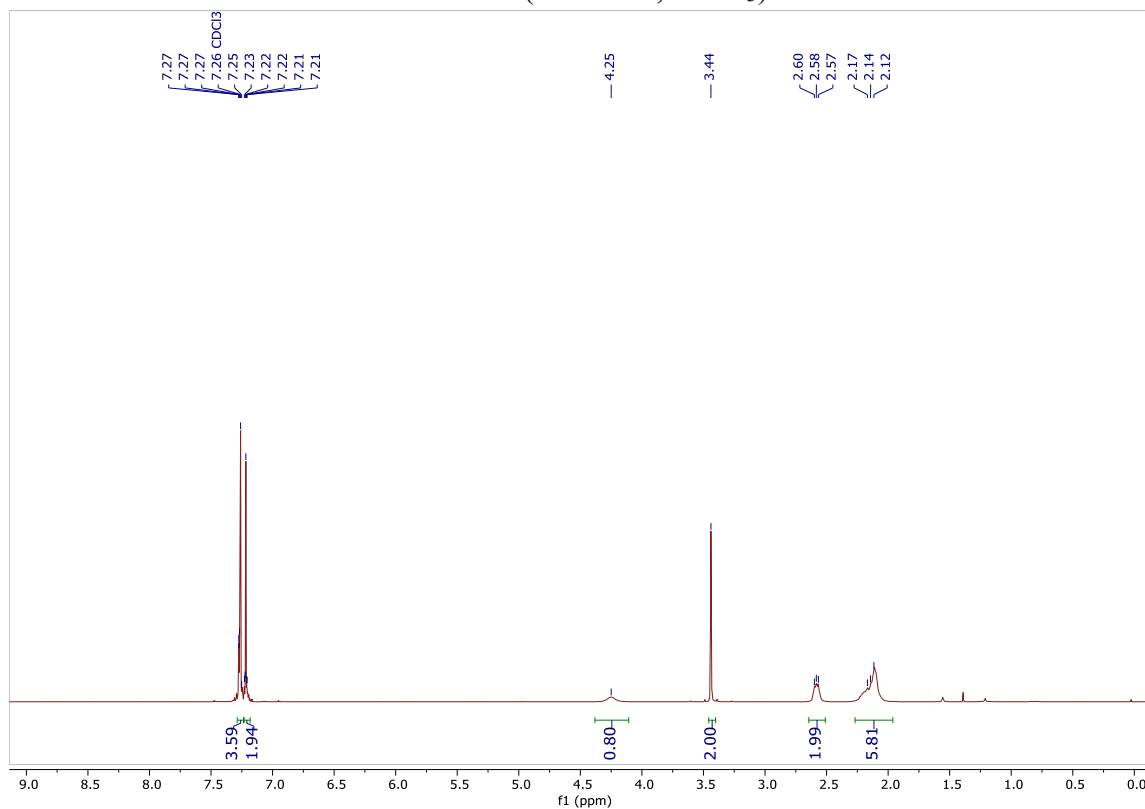
^{13}C NMR (125 MHz, CDCl_3)



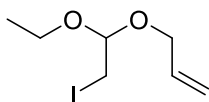
1-Benzyl-4-iodopiperidine, S23



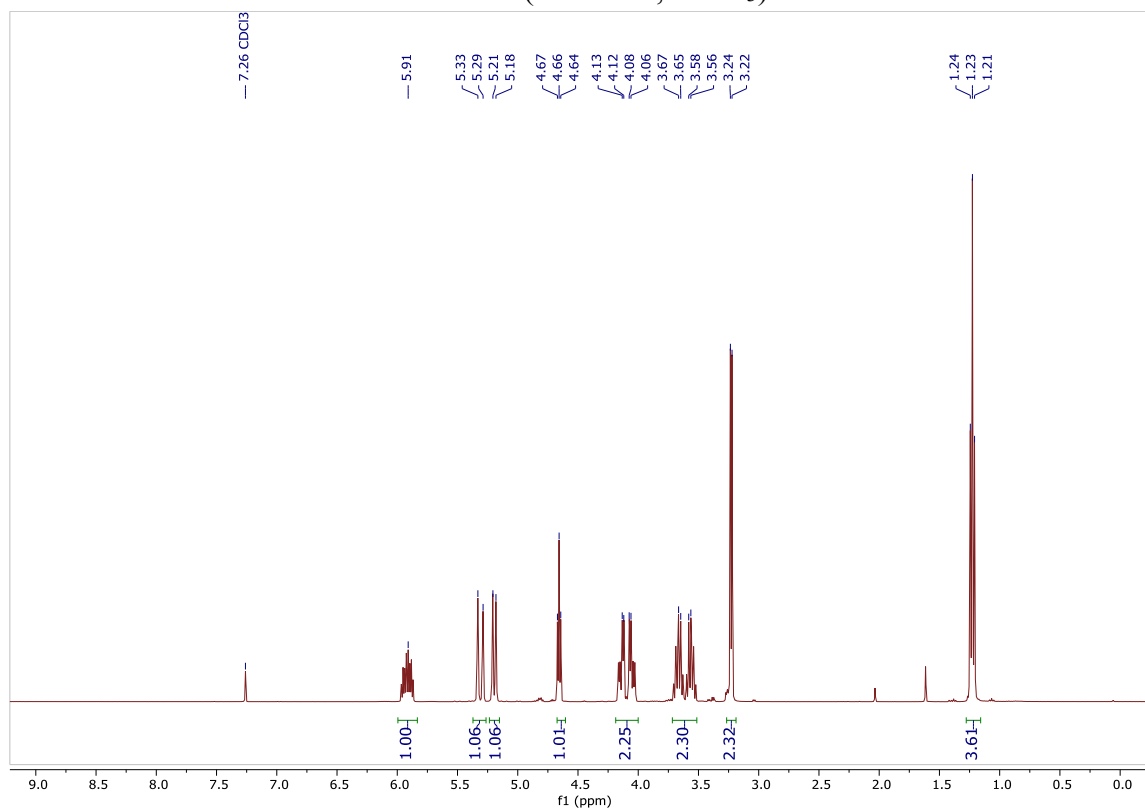
¹H NMR (500 MHz, CDCl₃)



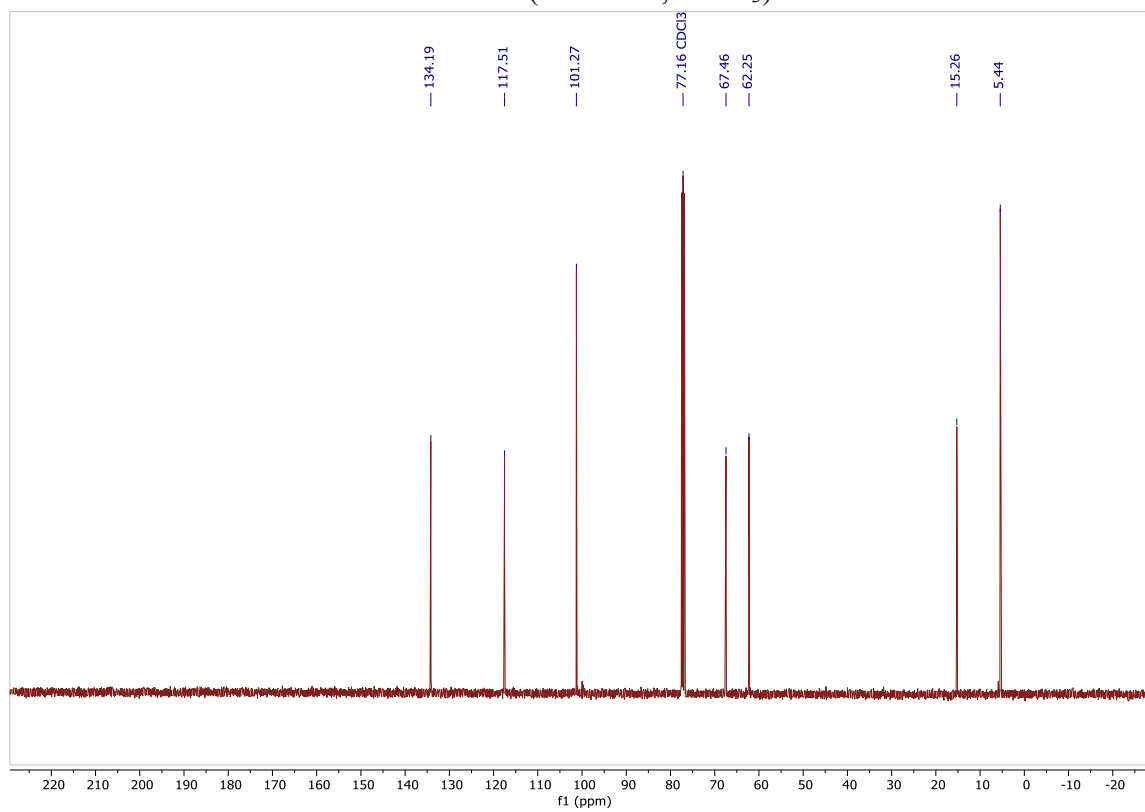
3-(1-Ethoxy-2-iodoethoxy)prop-1-ene, S24



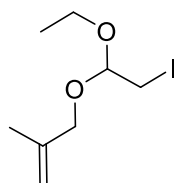
^1H NMR (400 MHz, CDCl_3)



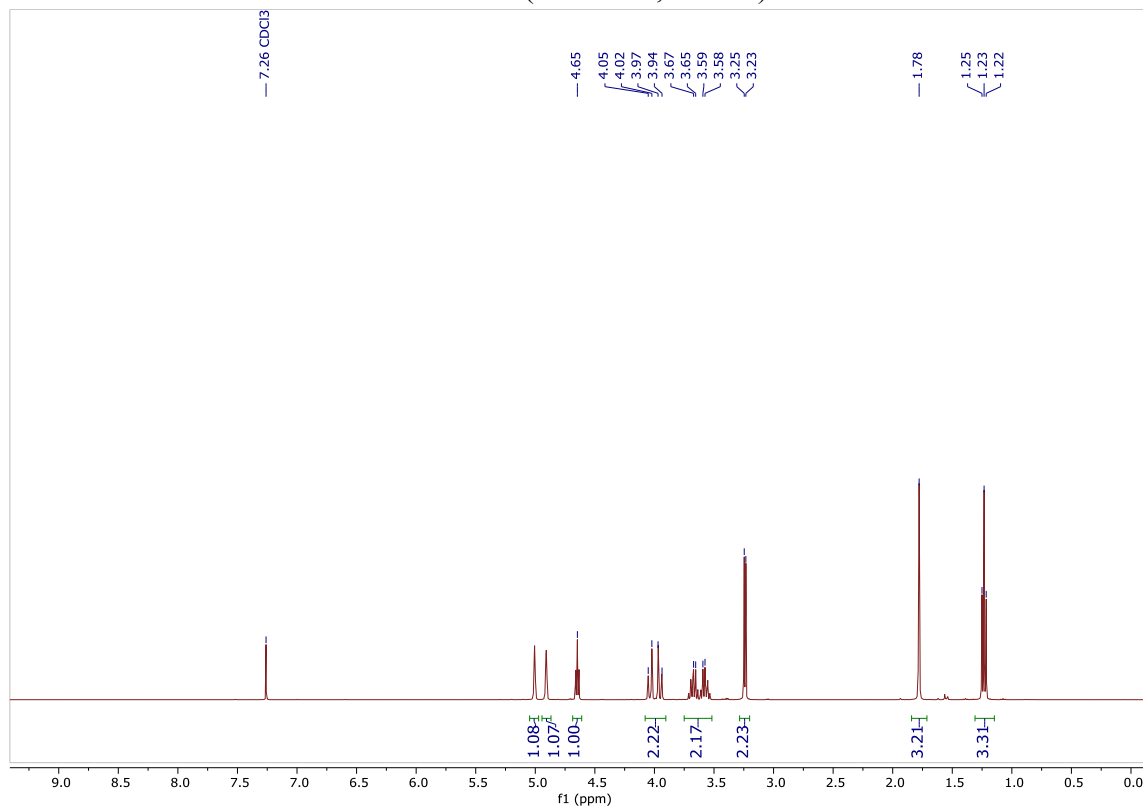
^{13}C NMR (101 MHz, CDCl_3)



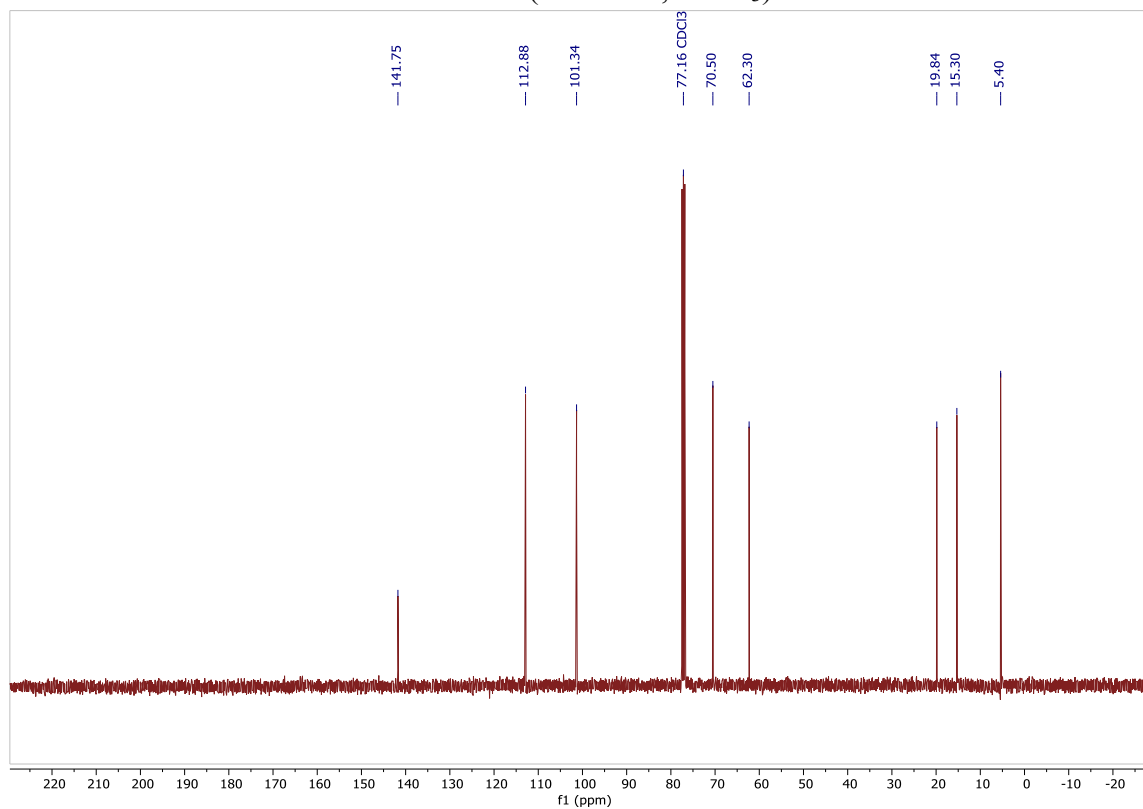
3-(1-Ethoxy-2-iodoethoxy)-2-methylprop-1-ene, S25



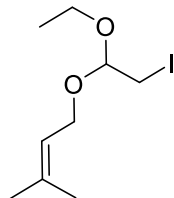
^1H NMR (400 MHz, CDCl_3)



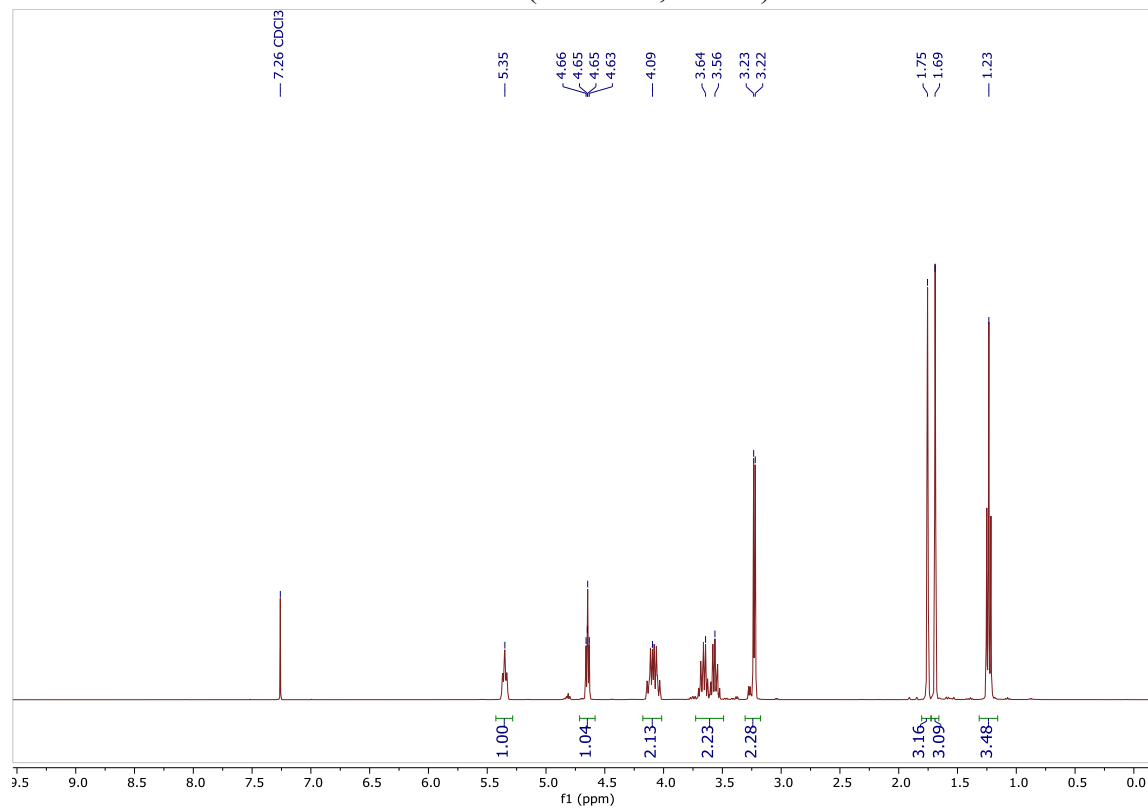
^{13}C NMR (101 MHz, CDCl_3)



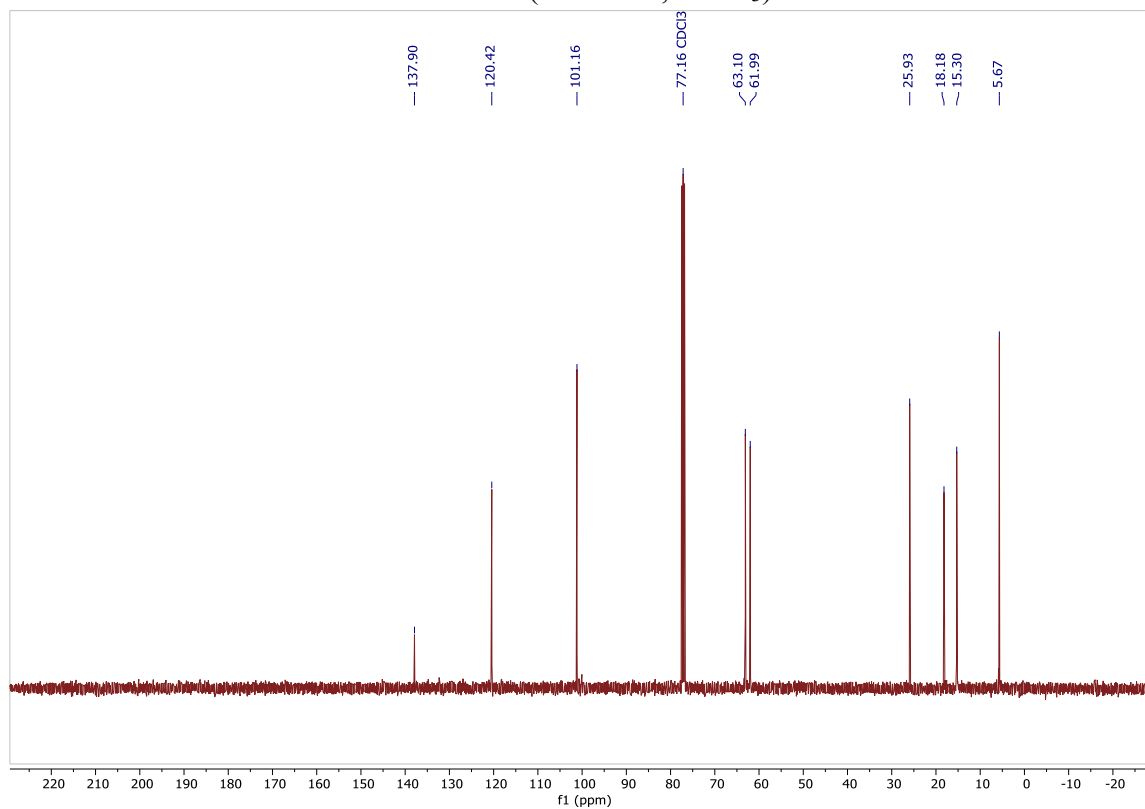
1-(1-Ethoxy-2-iodoethoxy)-3-methylbut-2-ene, S26



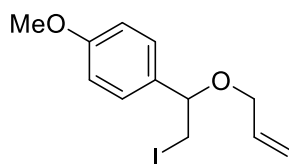
^1H NMR (400 MHz, CDCl_3)



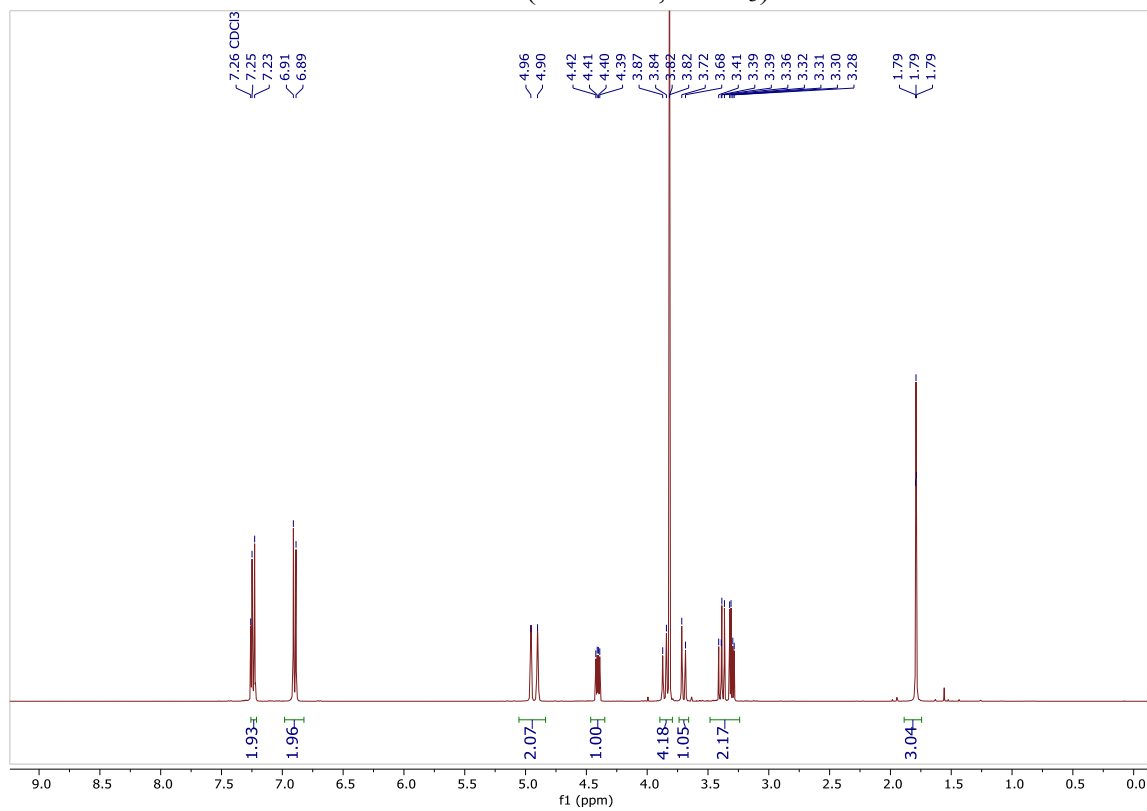
^{13}C NMR (101 MHz, CDCl_3)



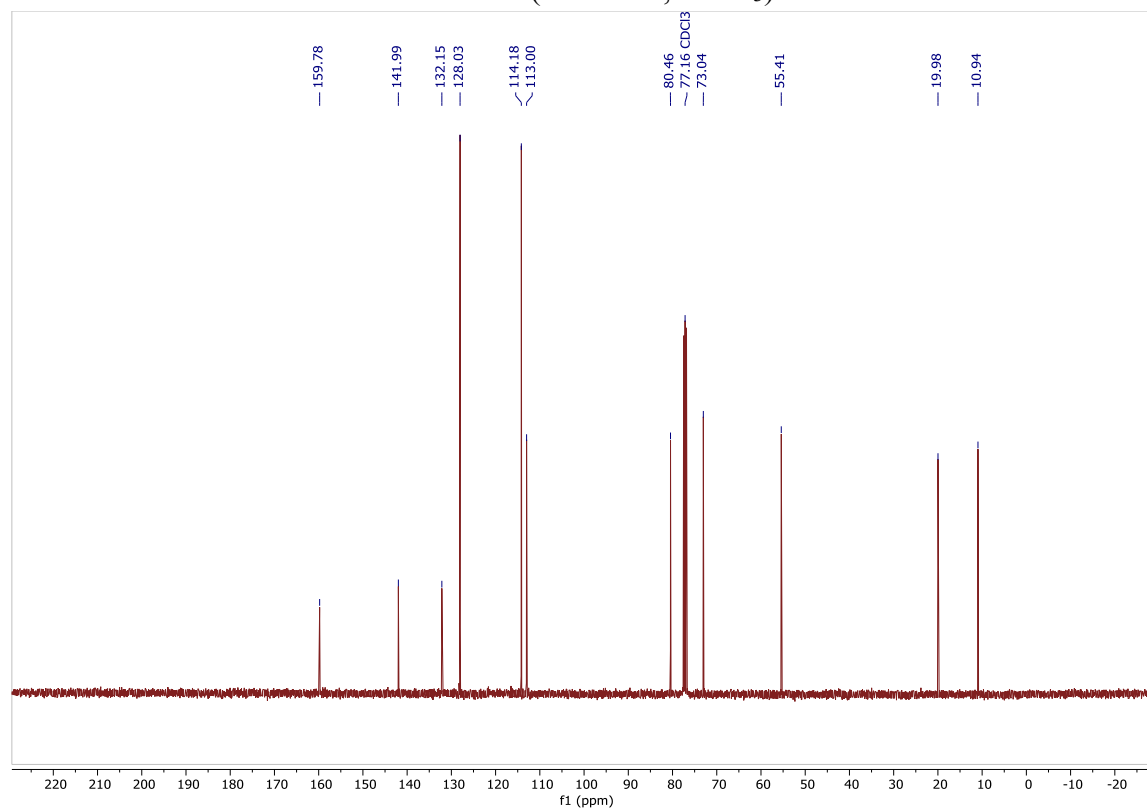
1-(1-(Allyloxy)-2-iodoethyl)-4-methoxybenzene, S27



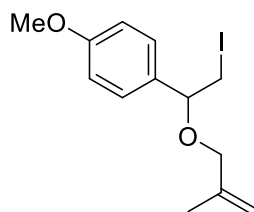
^1H NMR (400 MHz, CDCl_3)



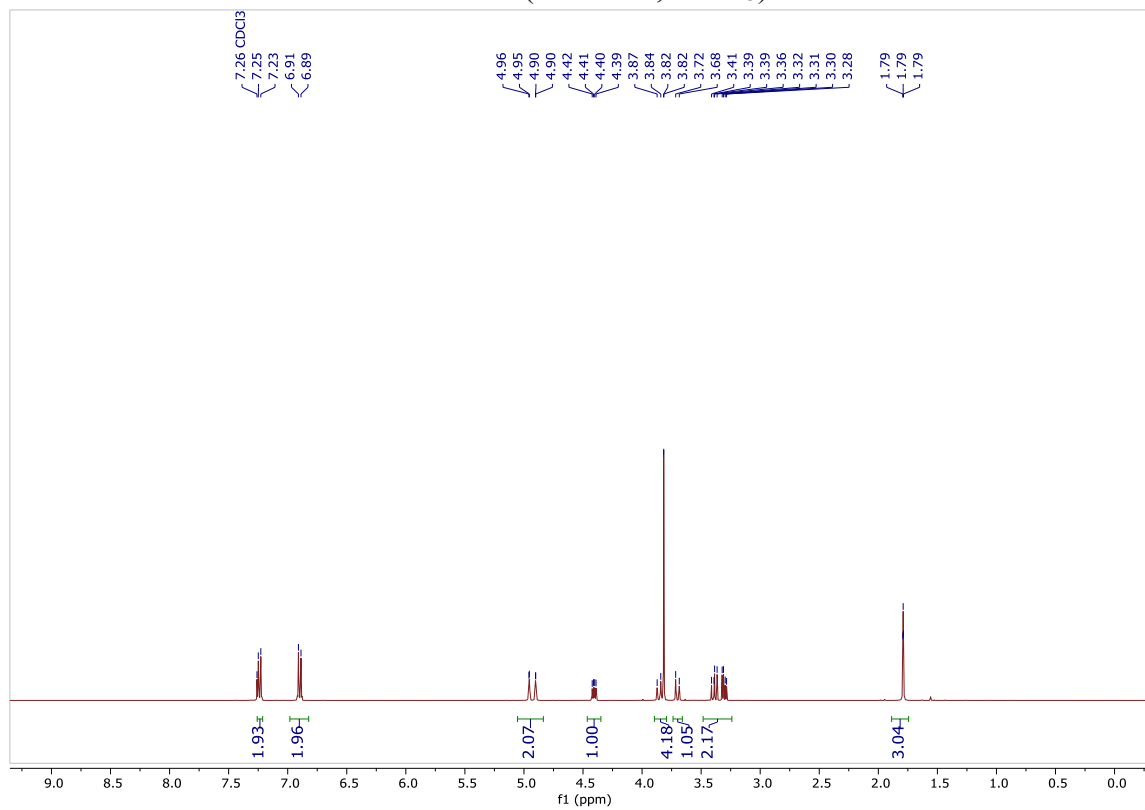
^{13}C NMR (101 MHz, CDCl_3)



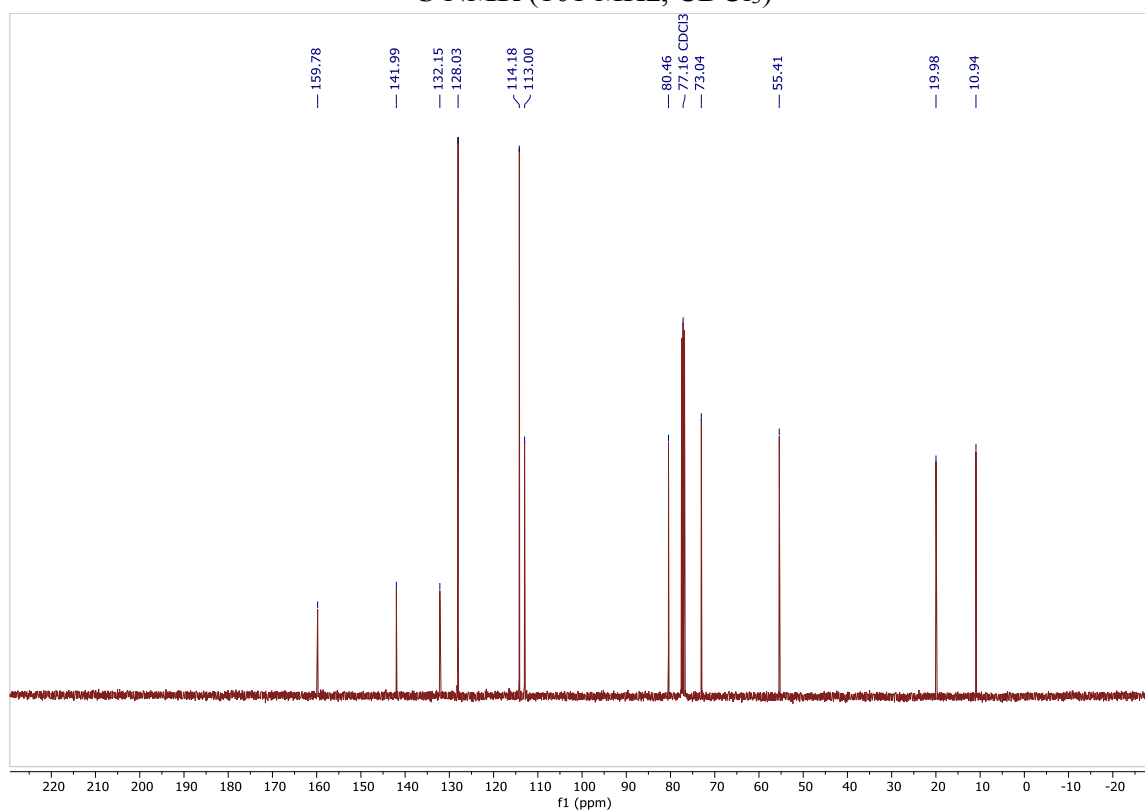
1-(2-Iodo-1-((2-methylallyl)oxy)ethyl)-4-methoxybenzene, S28



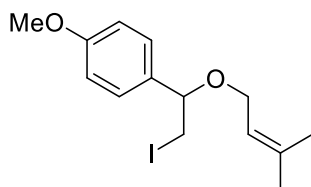
^1H NMR (400 MHz, CDCl_3)



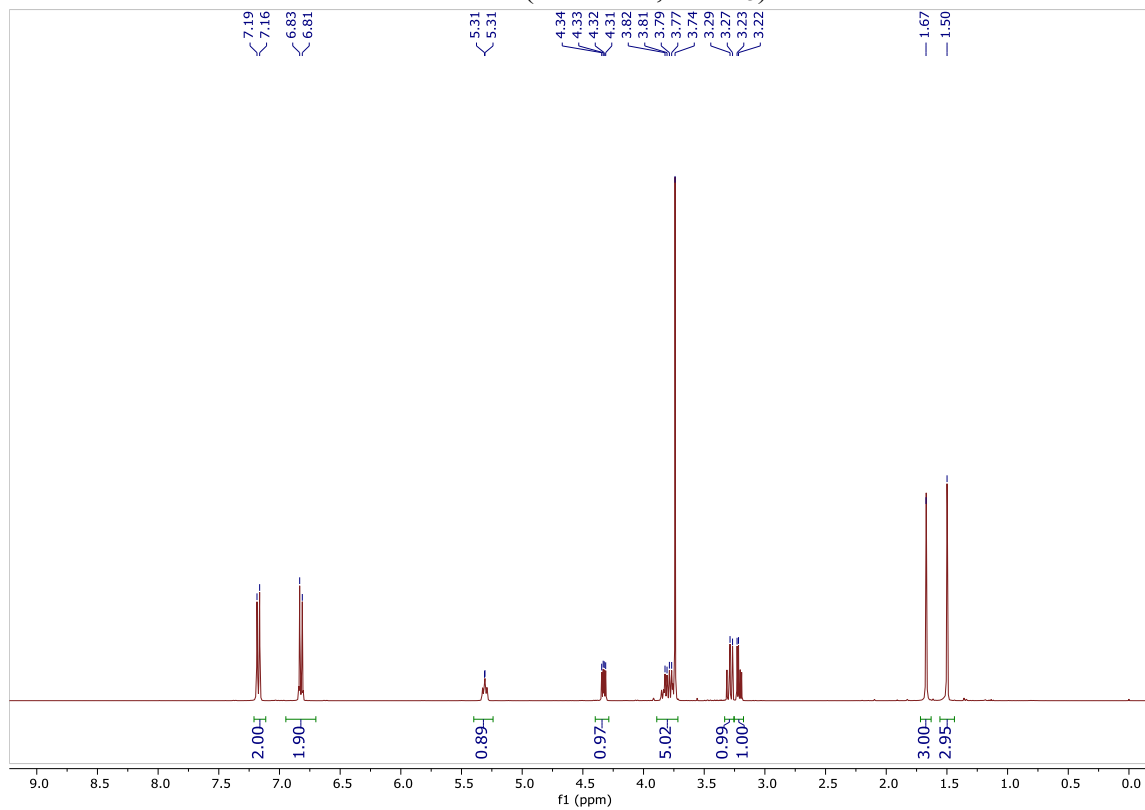
^{13}C NMR (101 MHz, CDCl_3)



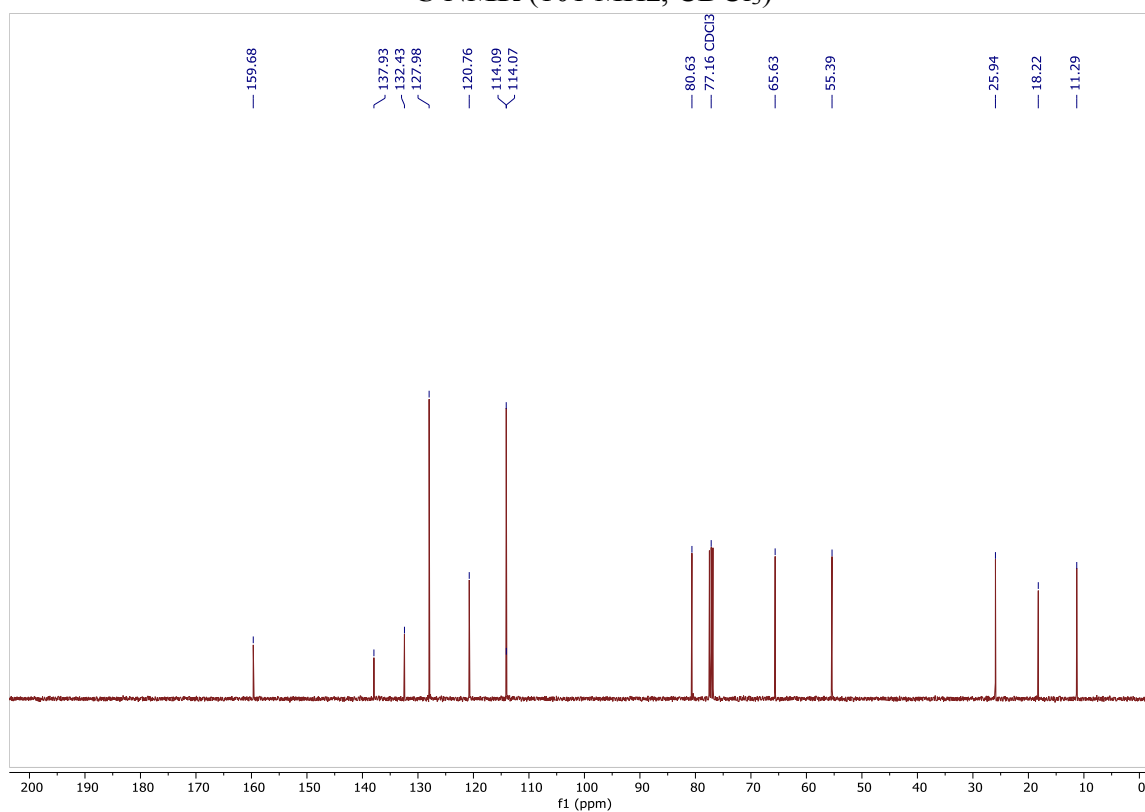
1-(2-Iodo-1-((3-methylbut-2-en-1-yl)oxy)ethyl)-4-methoxybenzene, S29



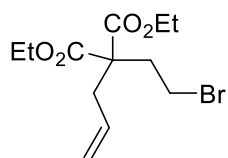
^1H NMR (400 MHz, CDCl_3)



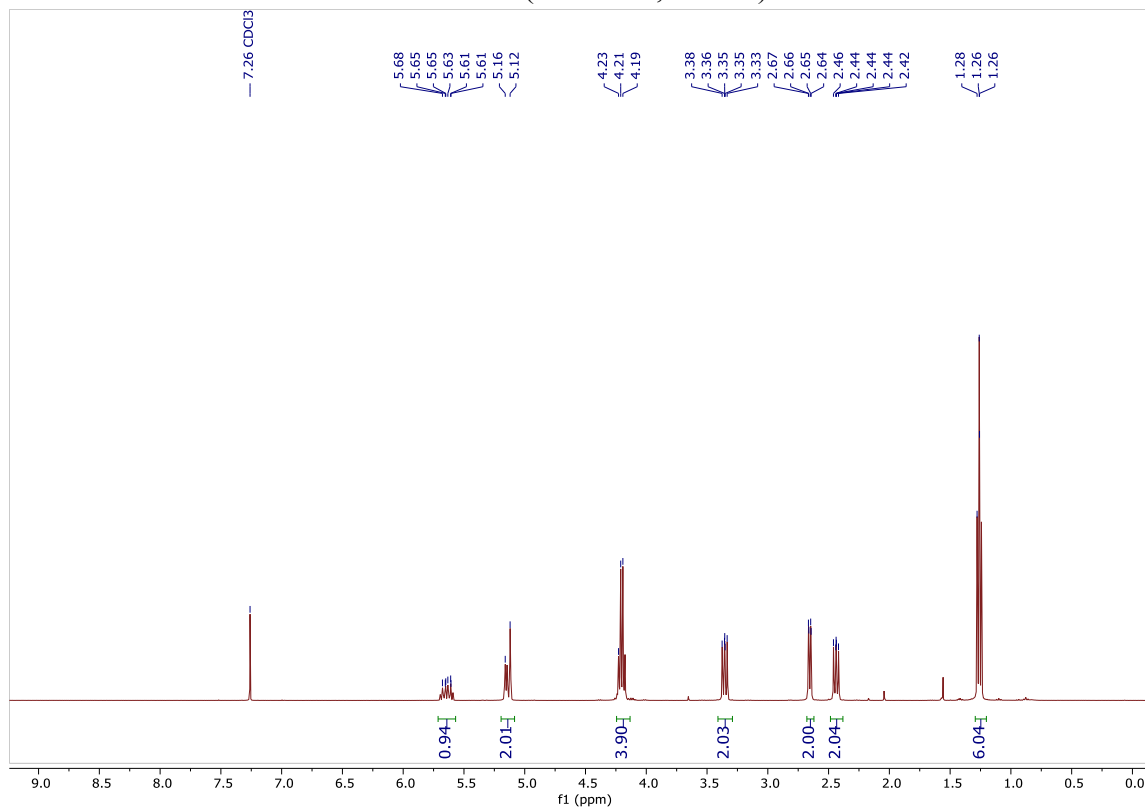
^{13}C NMR (101 MHz, CDCl_3)



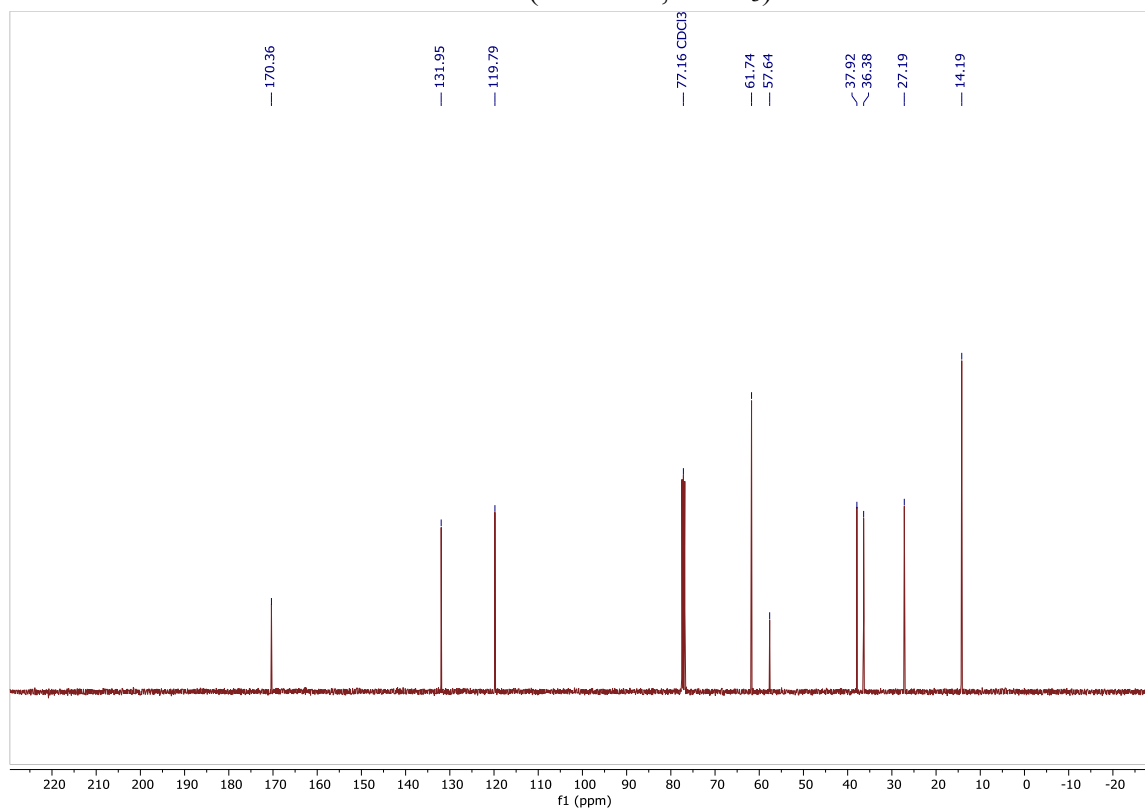
Diethyl 2-allyl-2-(2-bromoethyl)malonate, S30



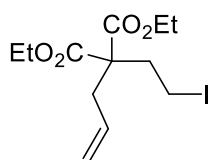
^1H NMR (400 MHz, CDCl_3)



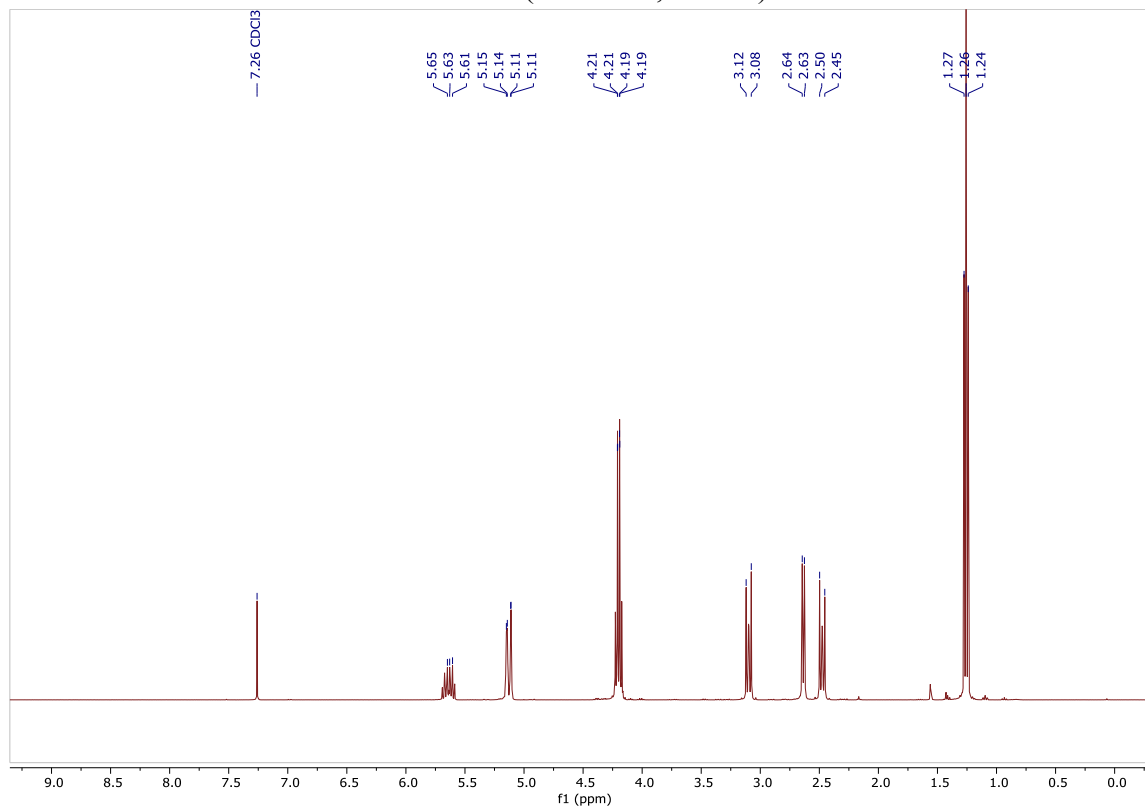
^{13}C NMR (101 MHz, CDCl_3)



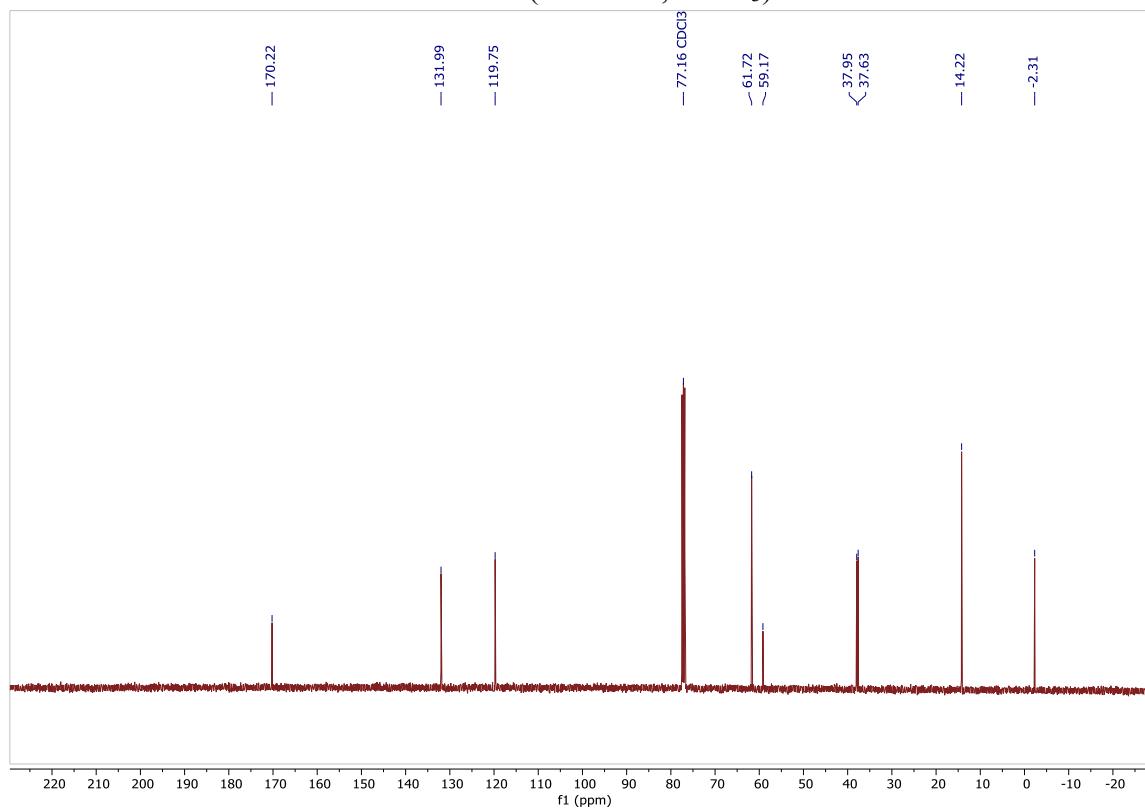
Diethyl 2-allyl-2-(2-iodoethyl)malonate, S30



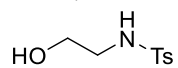
^1H NMR (400 MHz, CDCl_3)



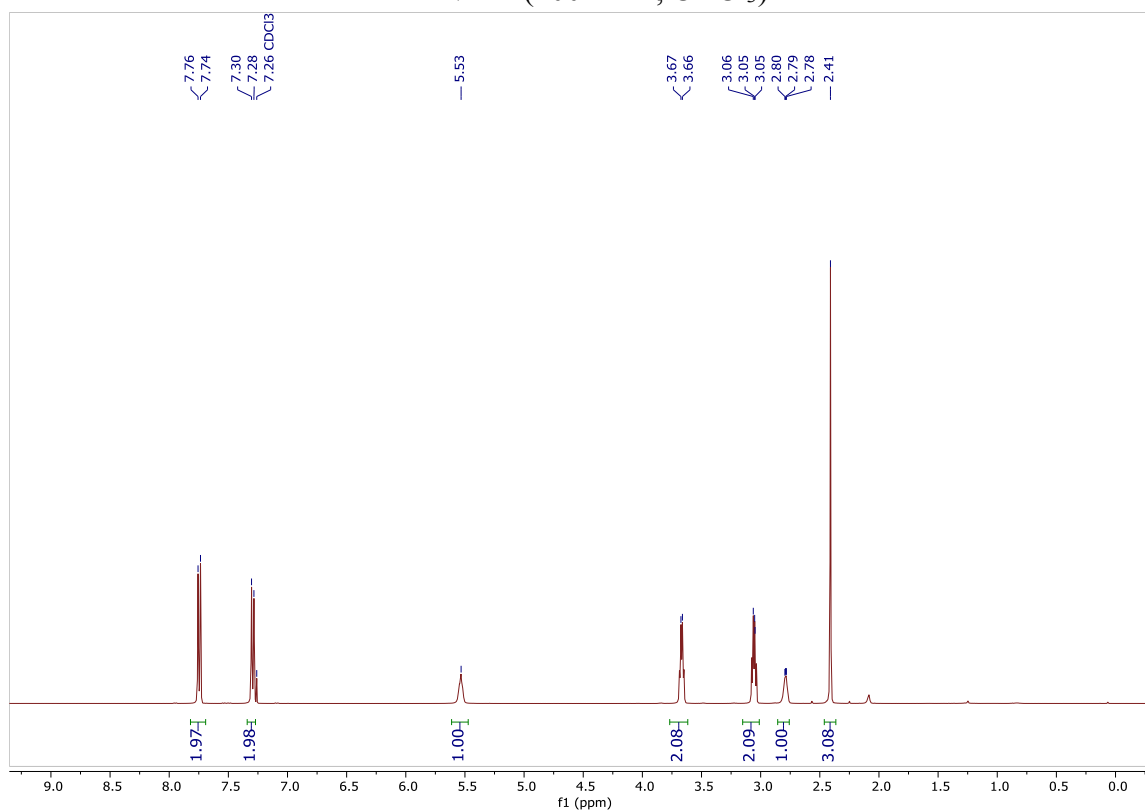
^{13}C NMR (101 MHz, CDCl_3)



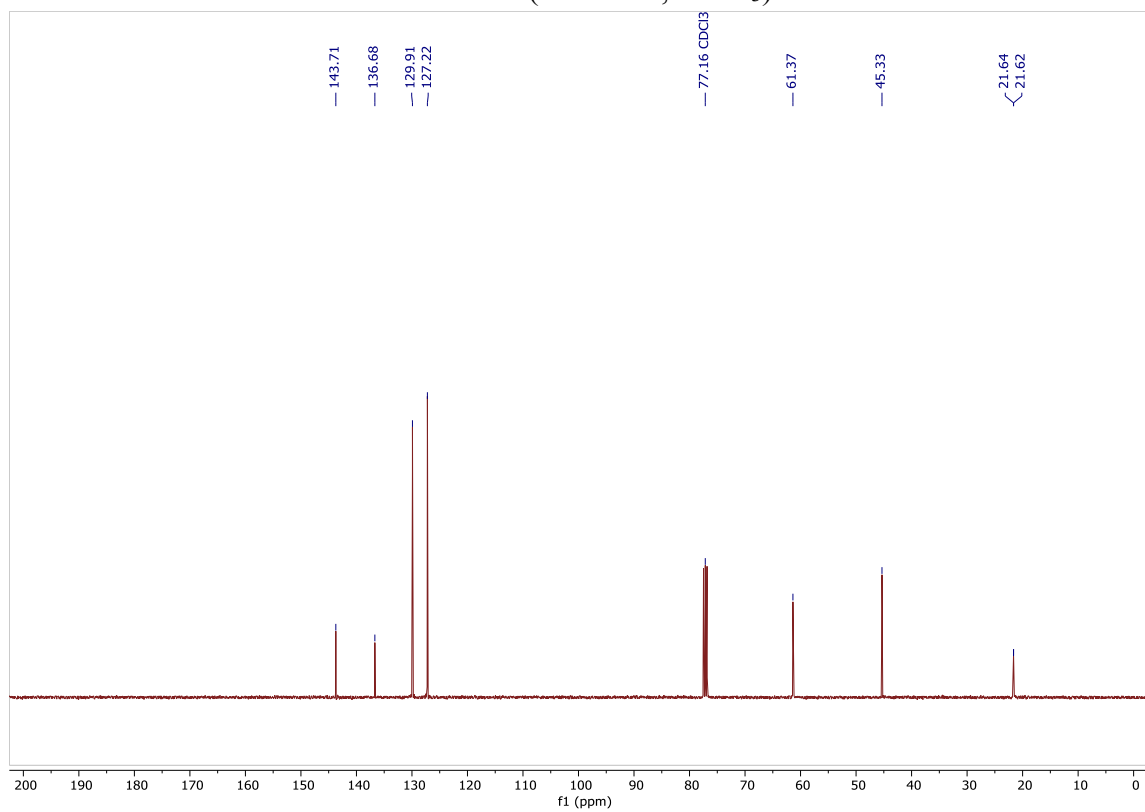
***N*-(2-Hydroxyethyl)-4-methylbenzenesulfonamide, S32**



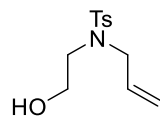
¹H NMR (400 MHz, CDCl₃)



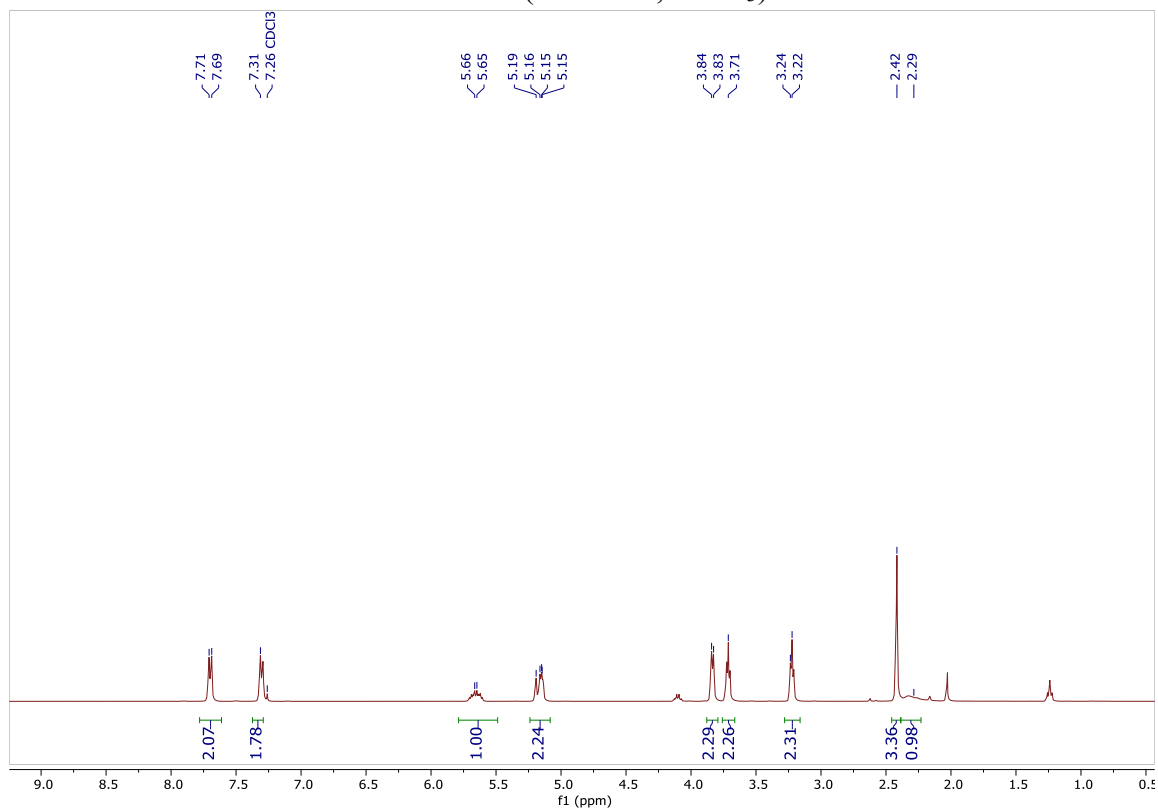
¹³C NMR (101 MHz, CDCl₃)



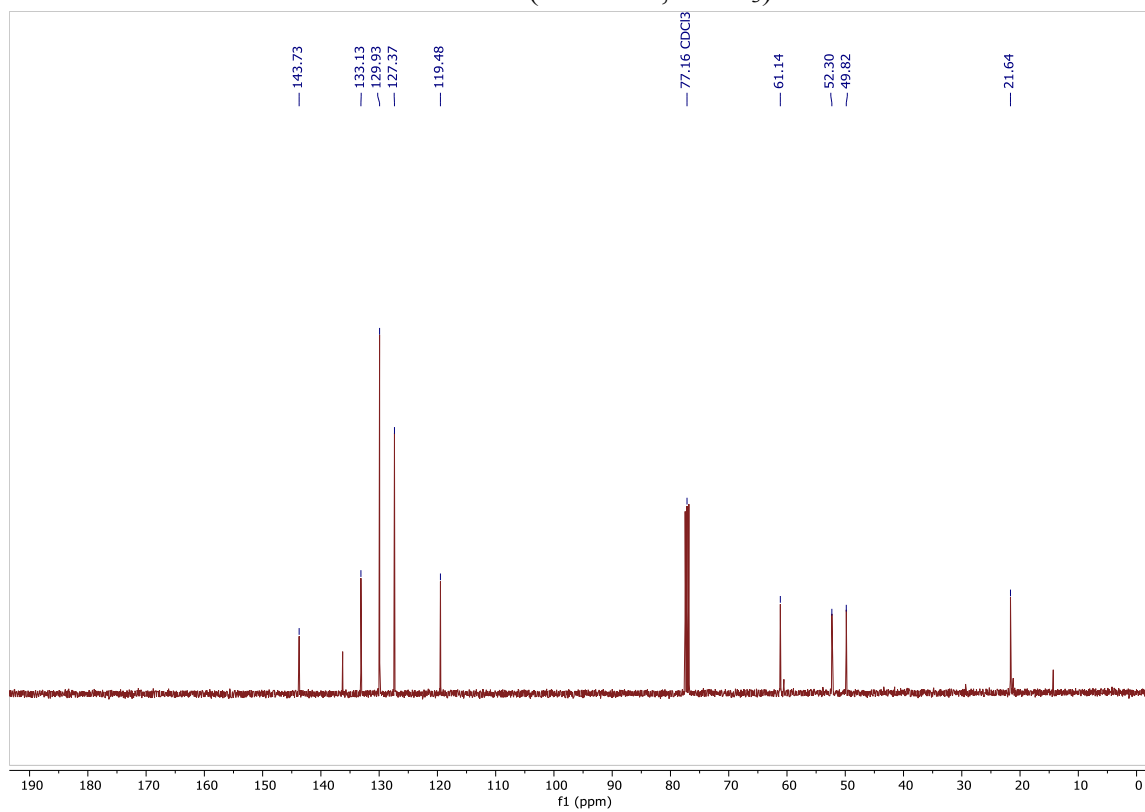
***N*-Allyl-*N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide, S33**



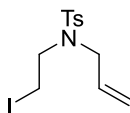
¹H NMR (400 MHz, CDCl₃)



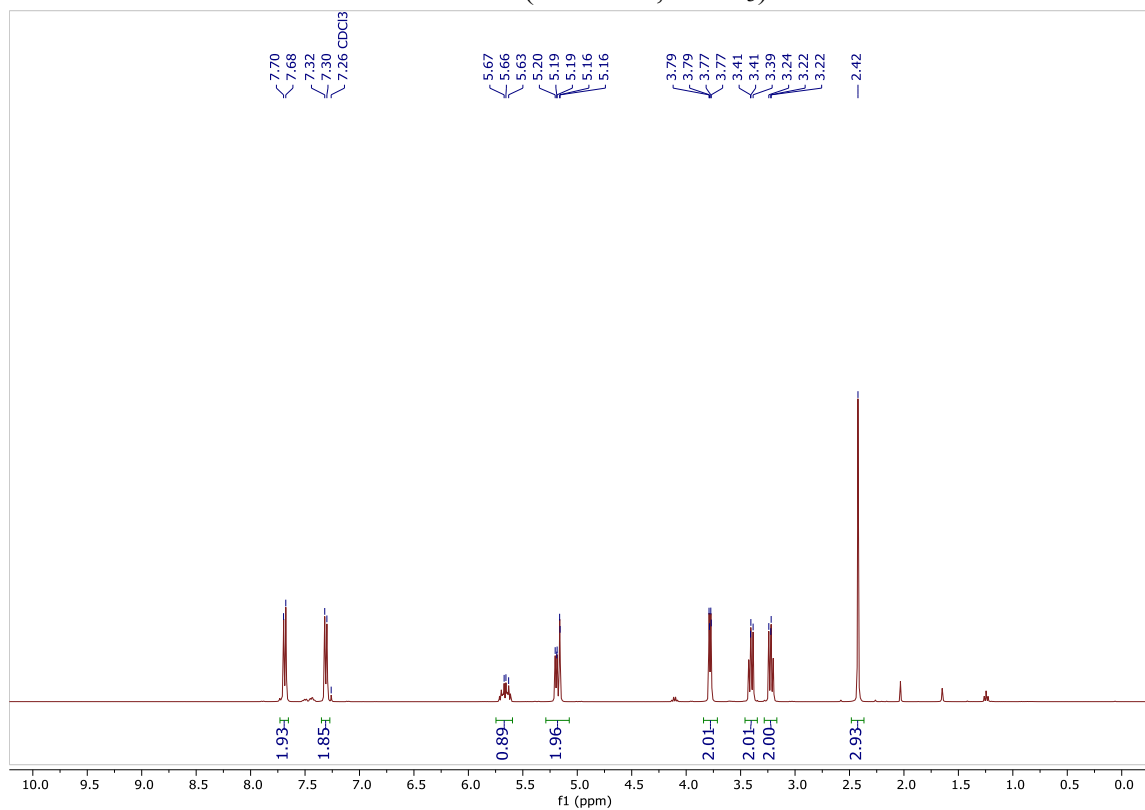
¹³C NMR (101 MHz, CDCl₃)



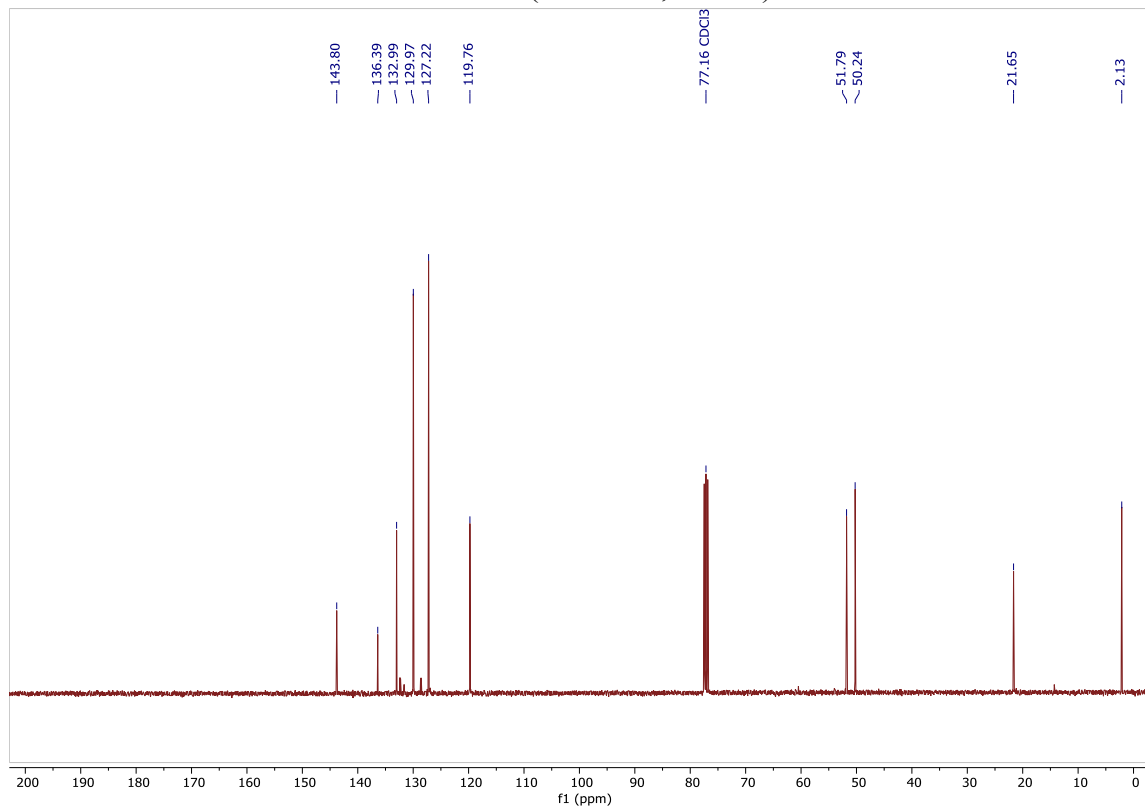
***N*-Allyl-*N*-(2-iodoethyl)-4-methylbenzenesulfonamide , S34**



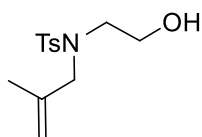
^1H NMR (400 MHz, CDCl_3)



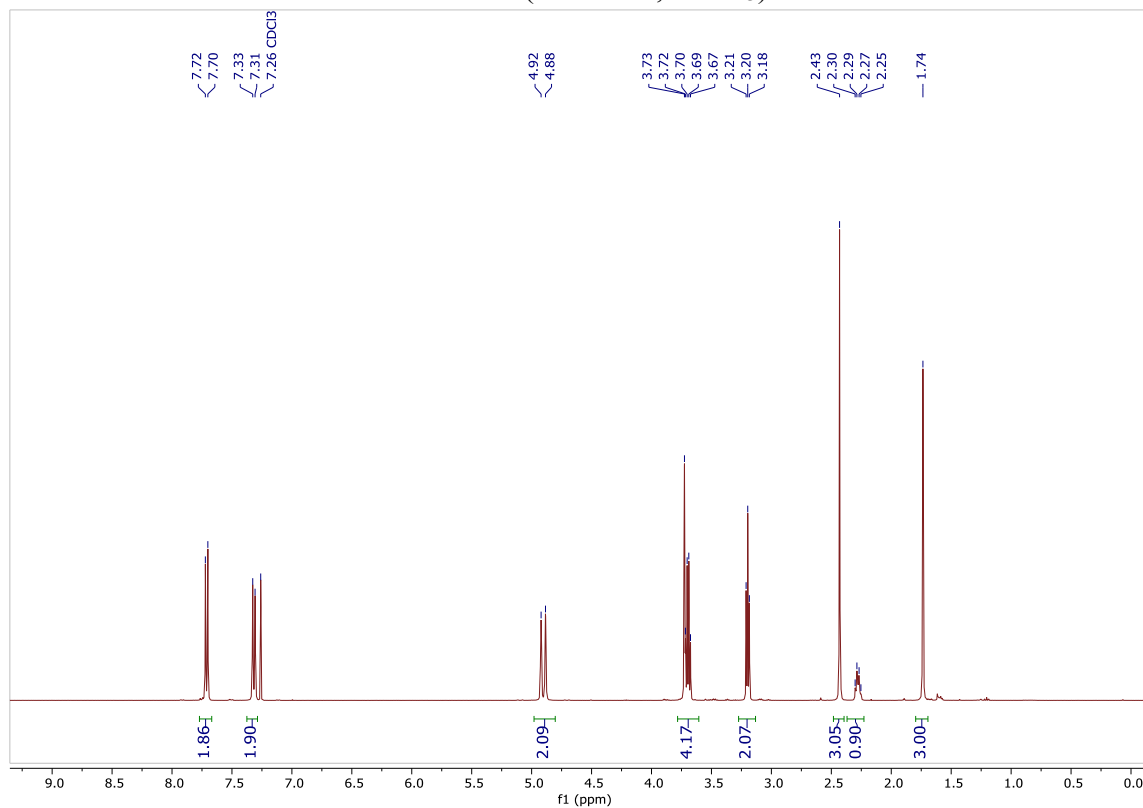
^{13}C NMR (101 MHz, CDCl_3)



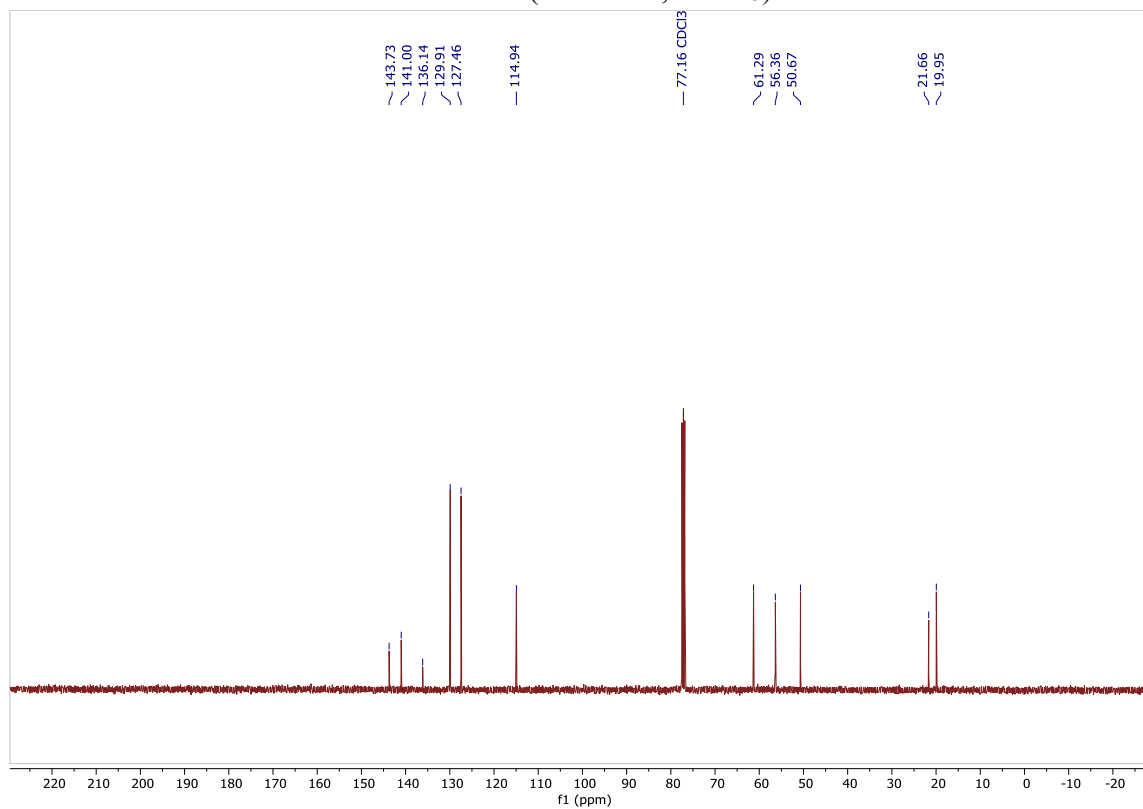
***N*-(2-Hydroxyethyl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide, S35**



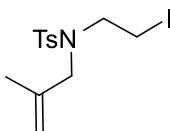
^1H NMR (400 MHz, CDCl_3)



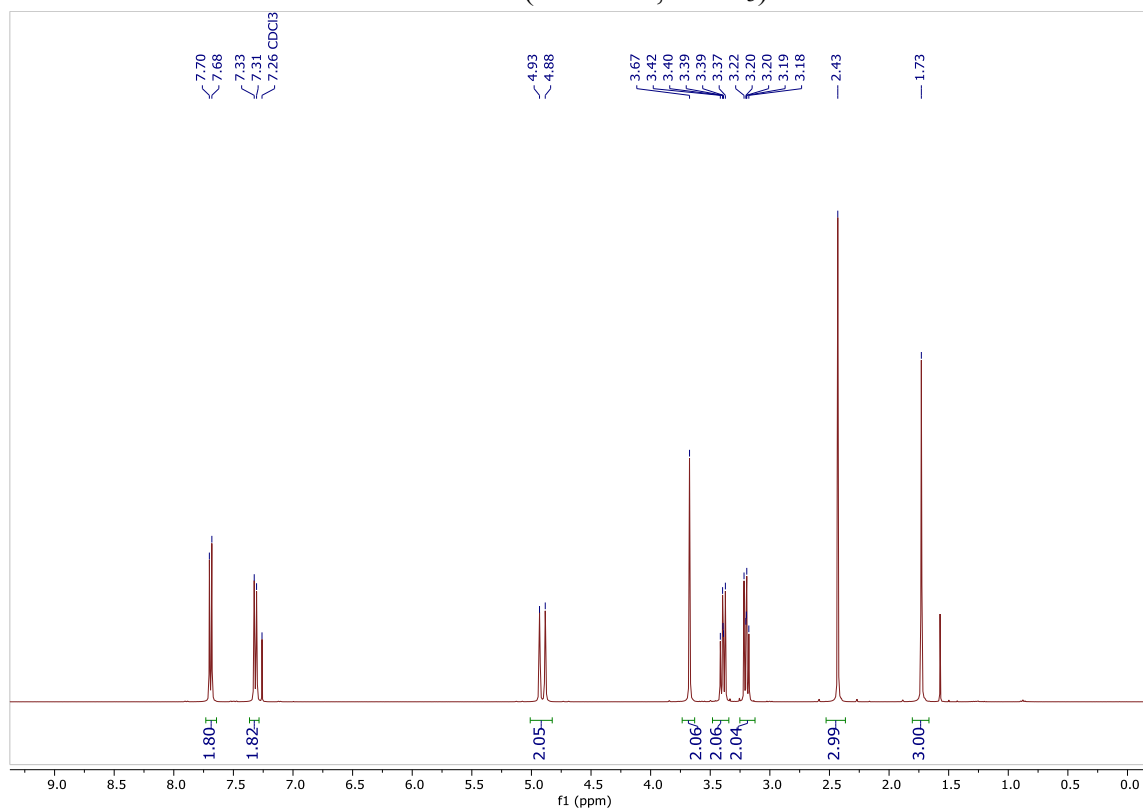
^{13}C NMR (101 MHz, CDCl_3)



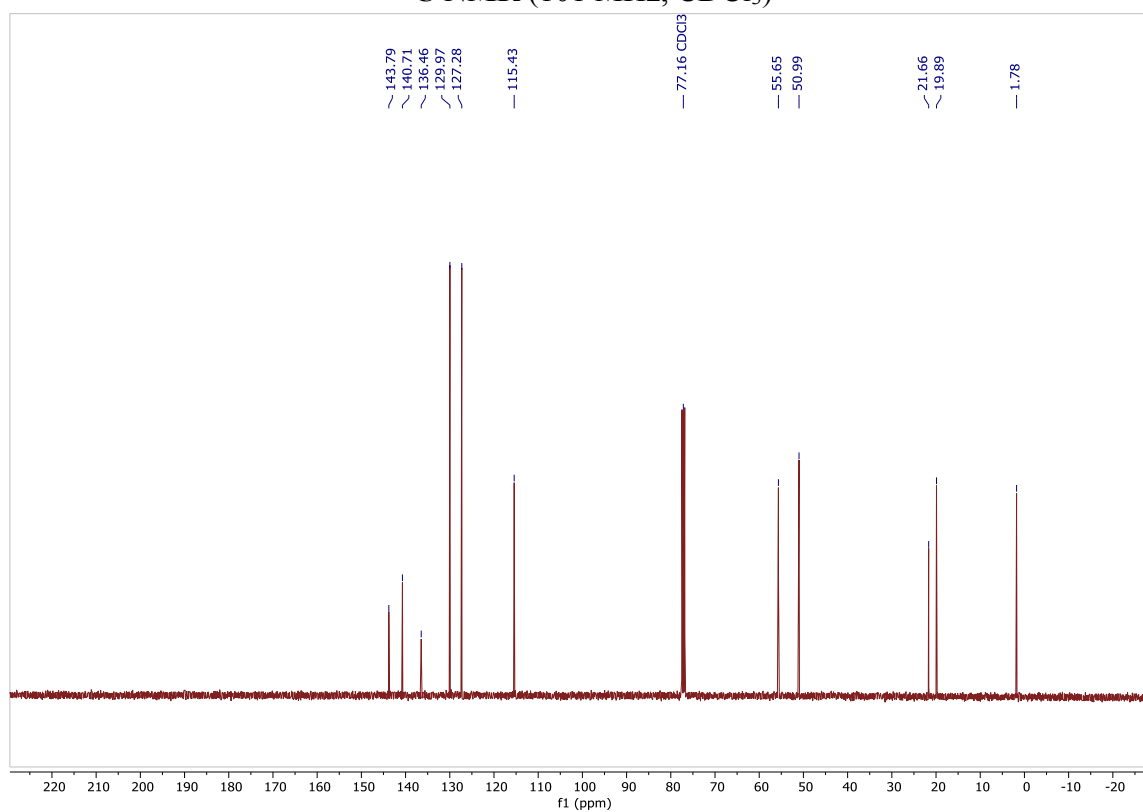
***N*-(2-Iodoethyl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide, S36**



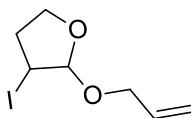
^1H NMR (400 MHz, CDCl_3)



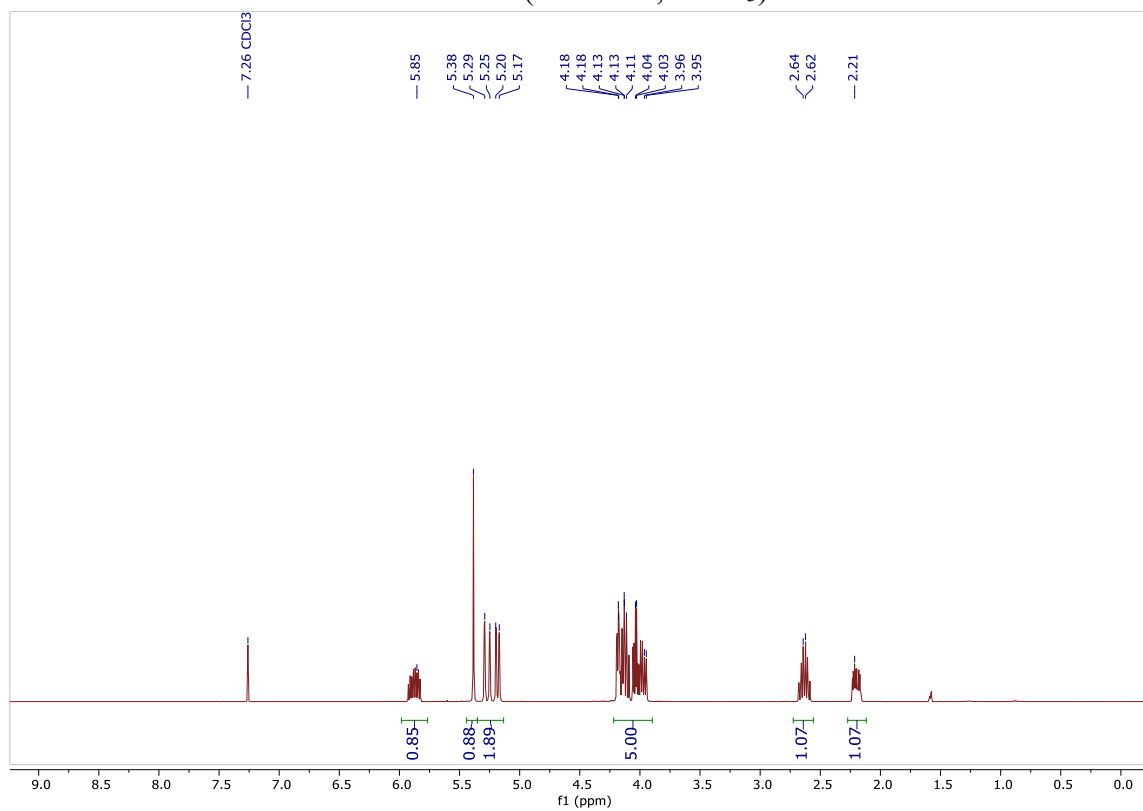
^{13}C NMR (101 MHz, CDCl_3)



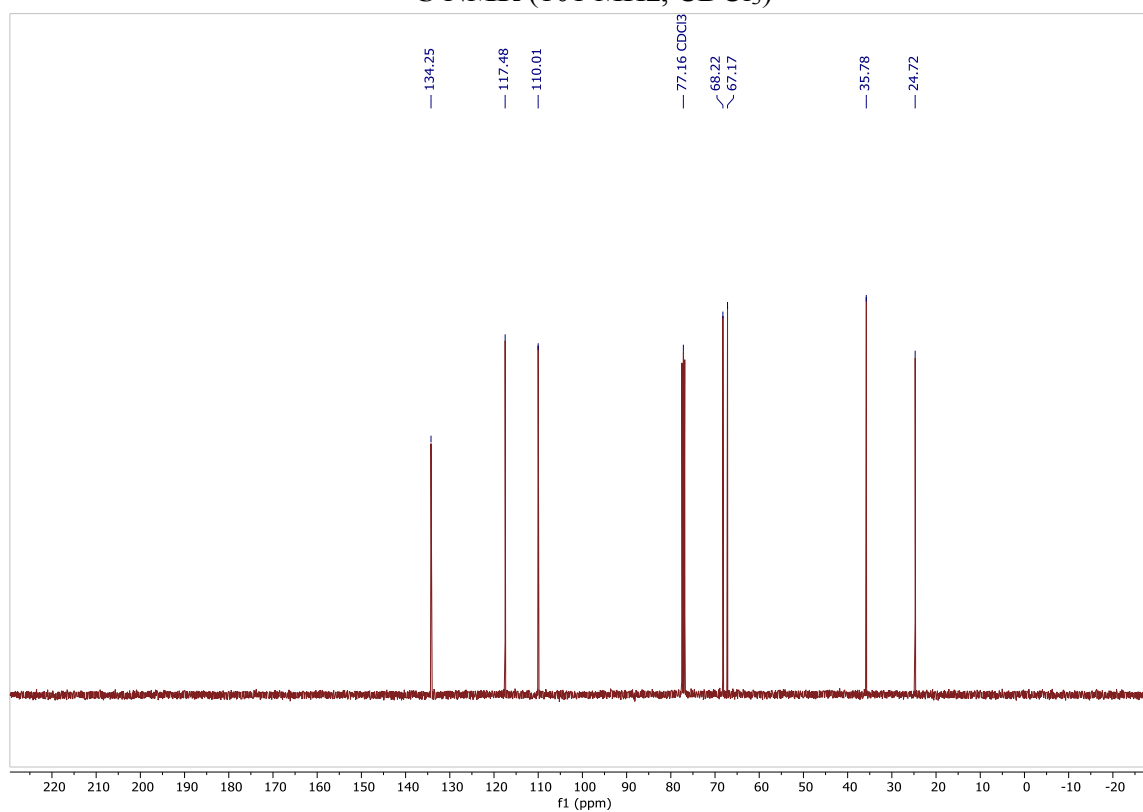
2-(Allyloxy)-3-iodotetrahydrofuran, S37



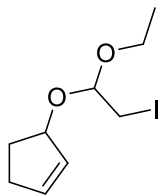
^1H NMR (400 MHz, CDCl_3)



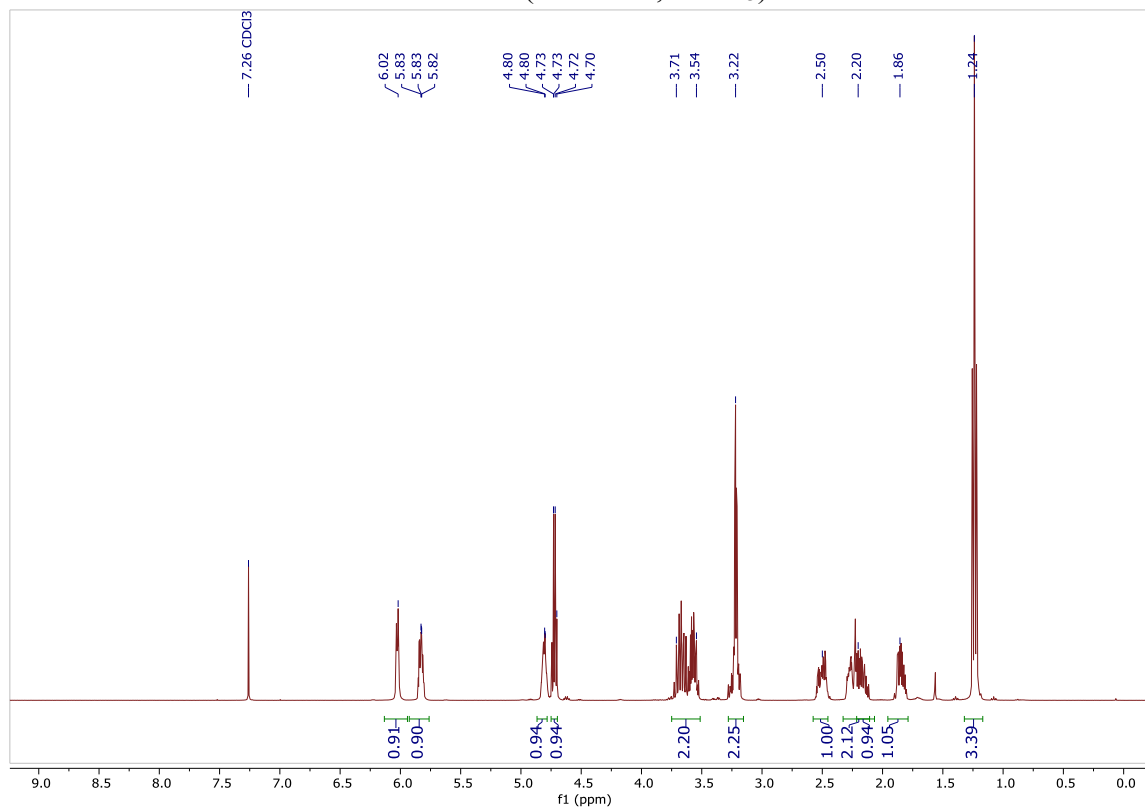
^{13}C NMR (101 MHz, CDCl_3)



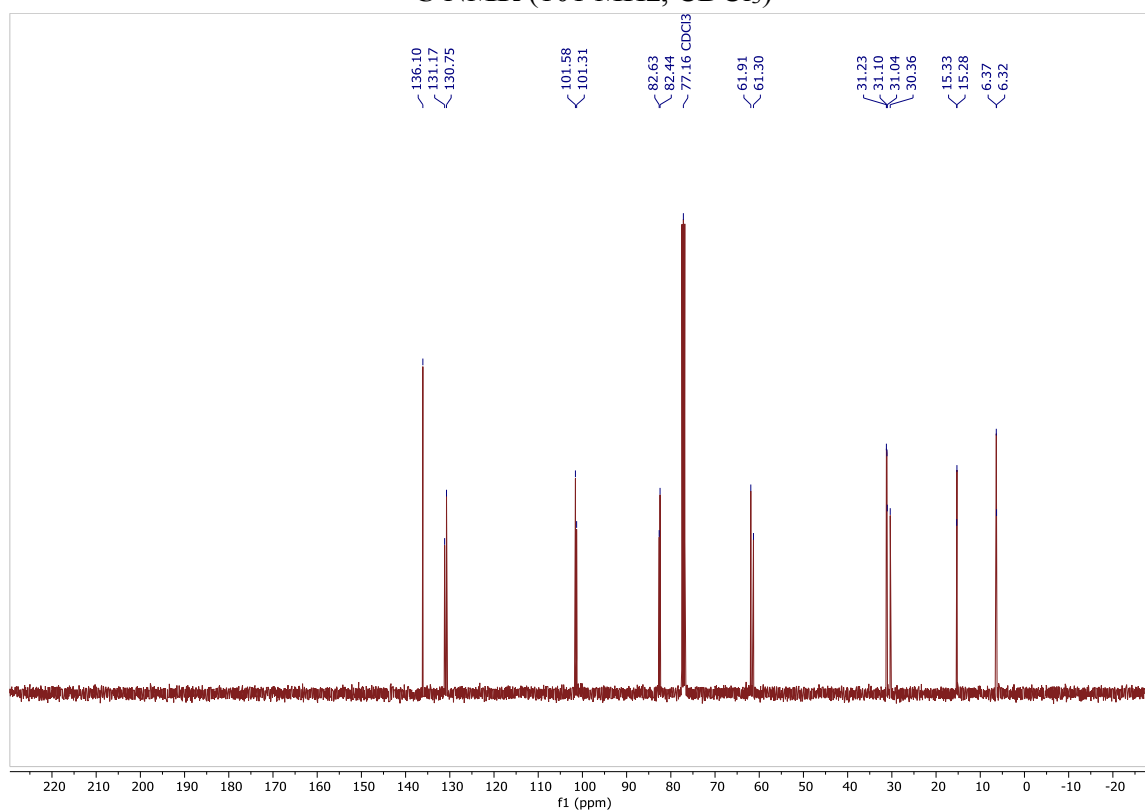
3-(1-Ethoxy-2-iodoethoxy)cyclopent-1-ene, S38



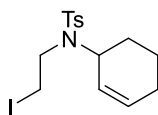
^1H NMR (400 MHz, CDCl_3)



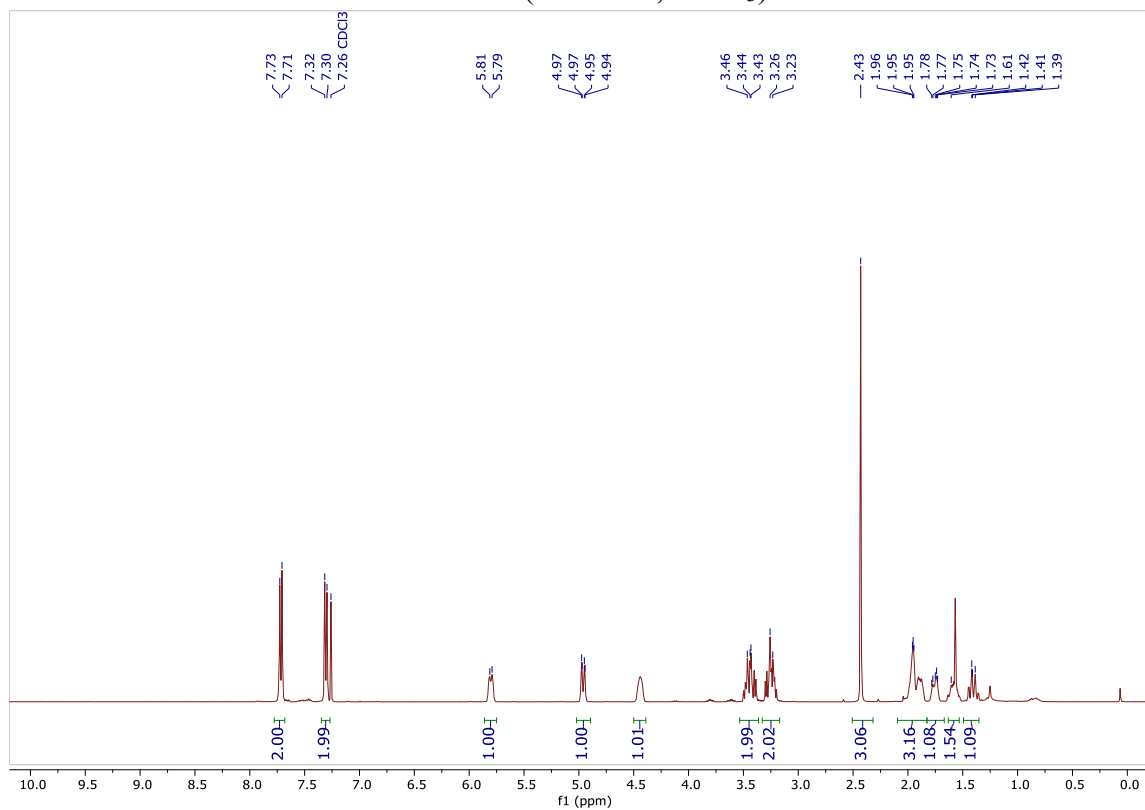
^{13}C NMR (101 MHz, CDCl_3)



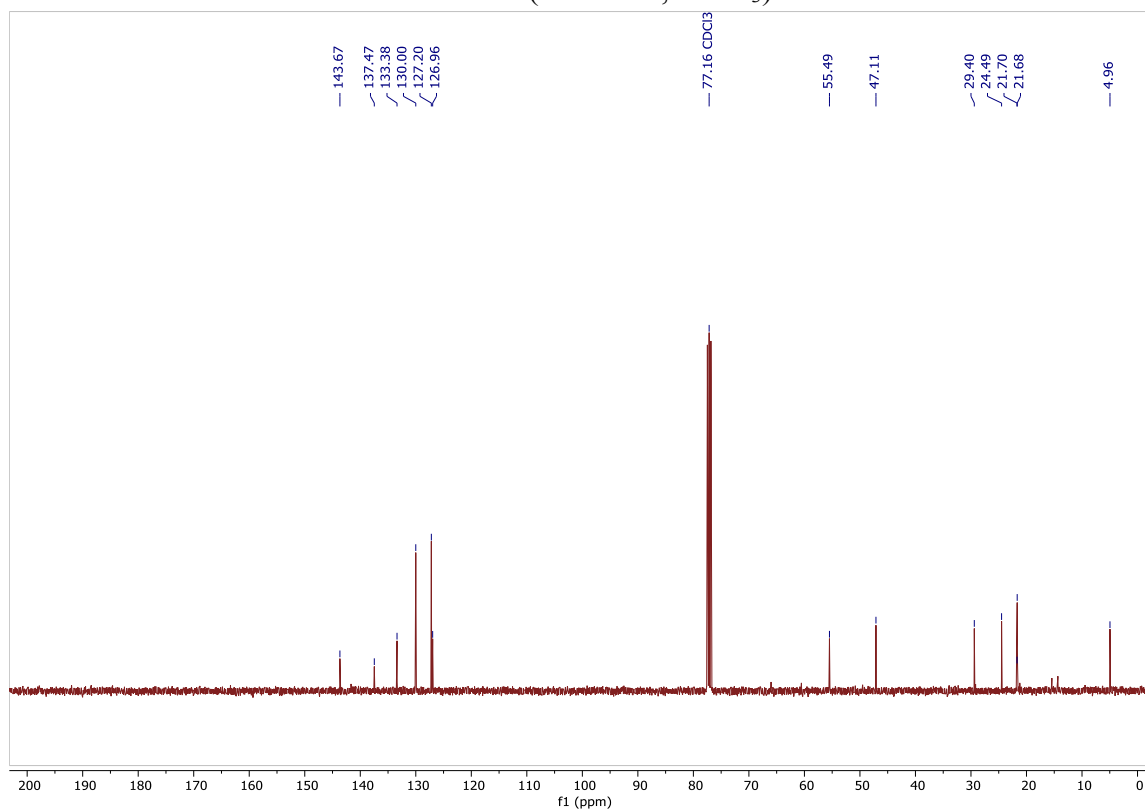
***N*-(Cyclohex-2-en-1-yl)-*N*-(2-iodoethyl)-4-methylbenzenesulfonamide, S40**



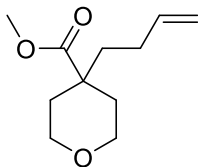
¹H NMR (400 MHz, CDCl₃)



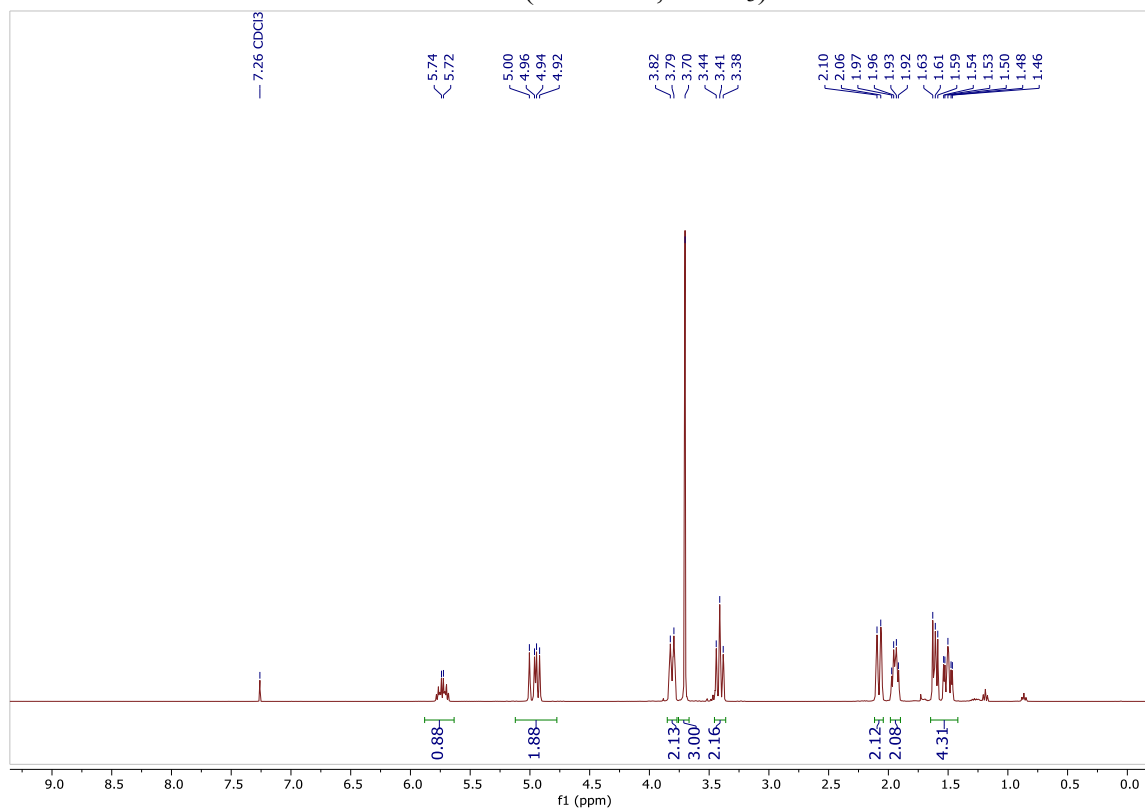
¹³C NMR (101 MHz, CDCl₃)



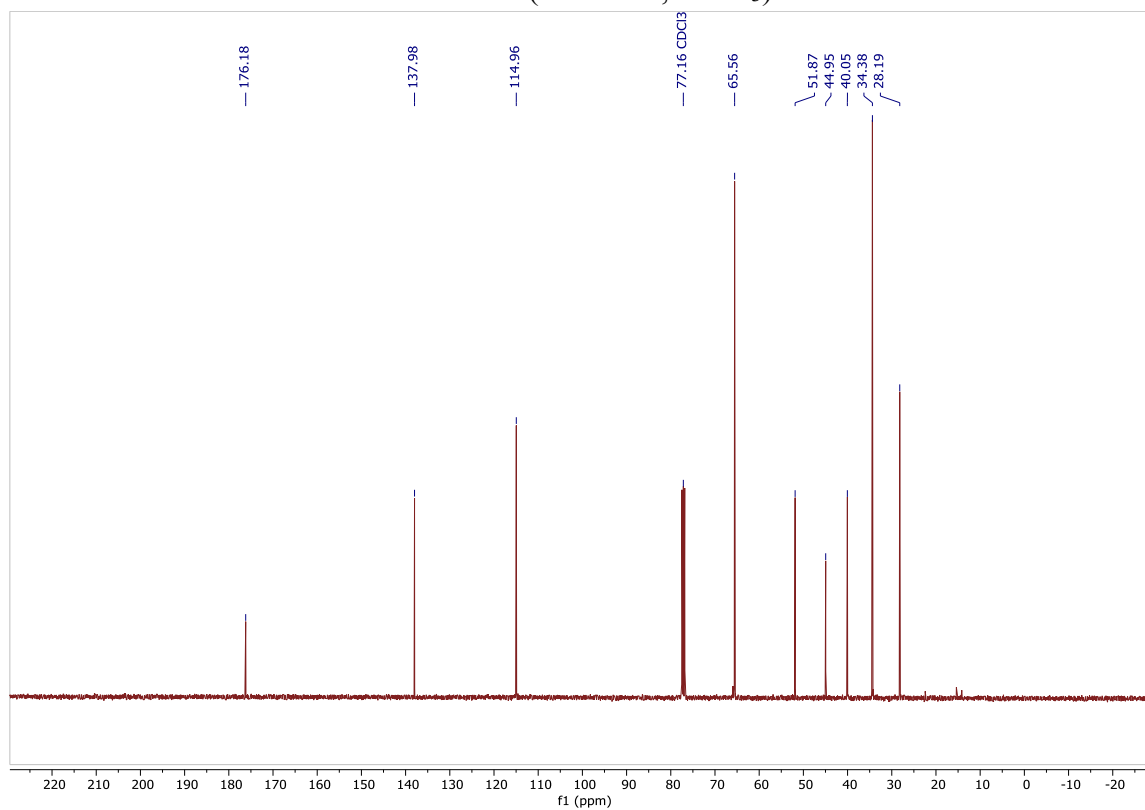
Methyl 4-(but-3-en-1-yl)tetrahydro-2H-pyran-4-carboxylate, S41



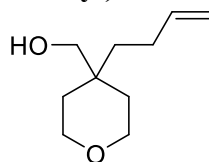
^1H NMR (400 MHz, CDCl_3)



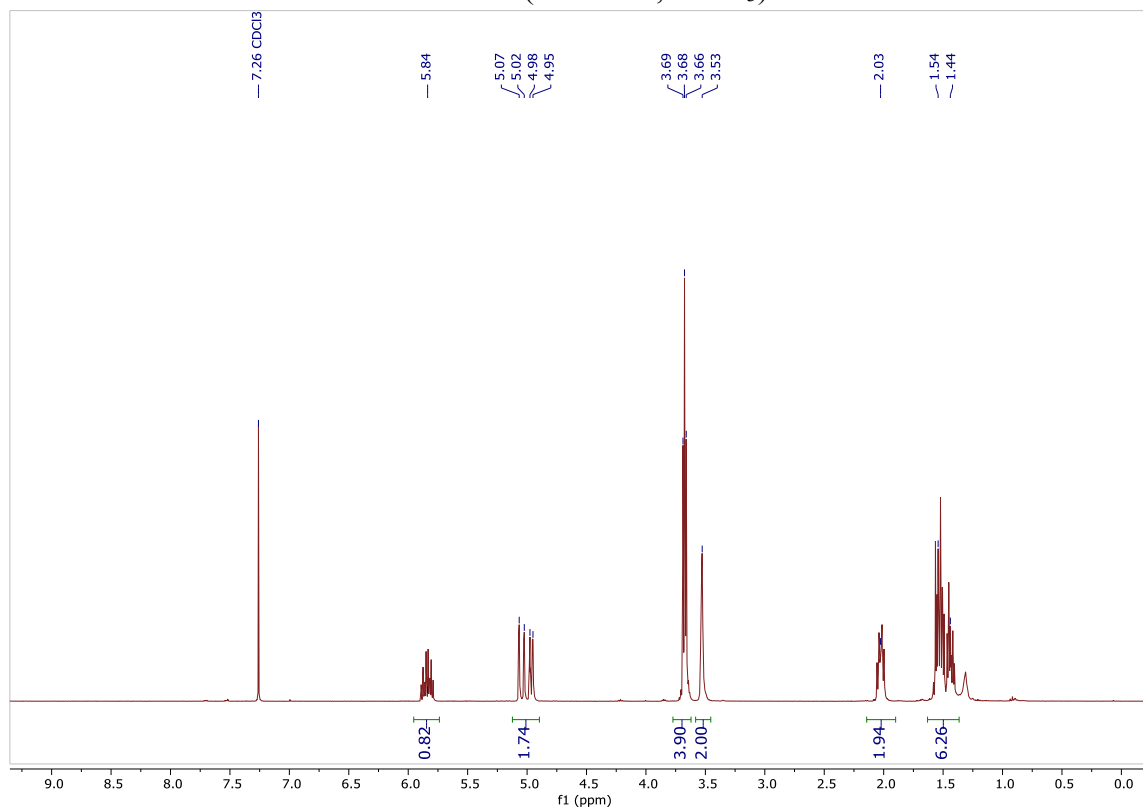
^{13}C NMR (101 MHz, CDCl_3)



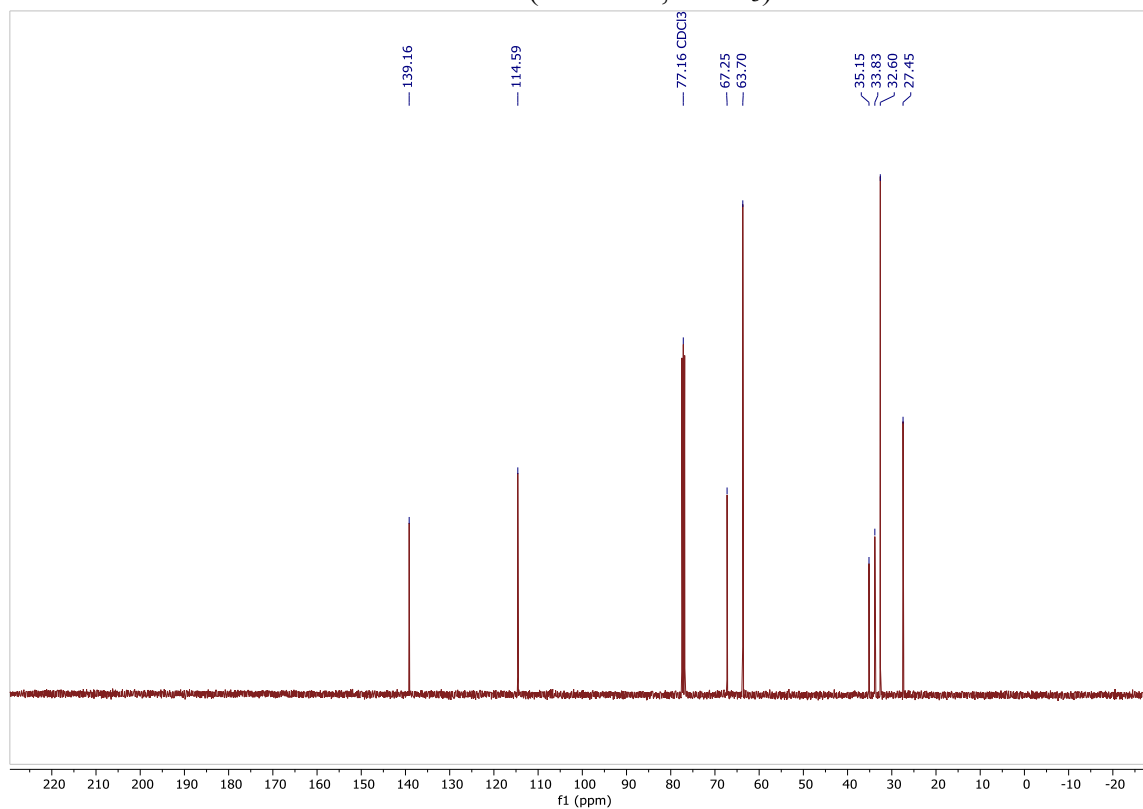
(4-(But-3-en-1-yl)tetrahydro-2H-pyran-4-yl)methanol, S42



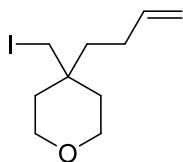
¹H NMR (400 MHz, CDCl₃)



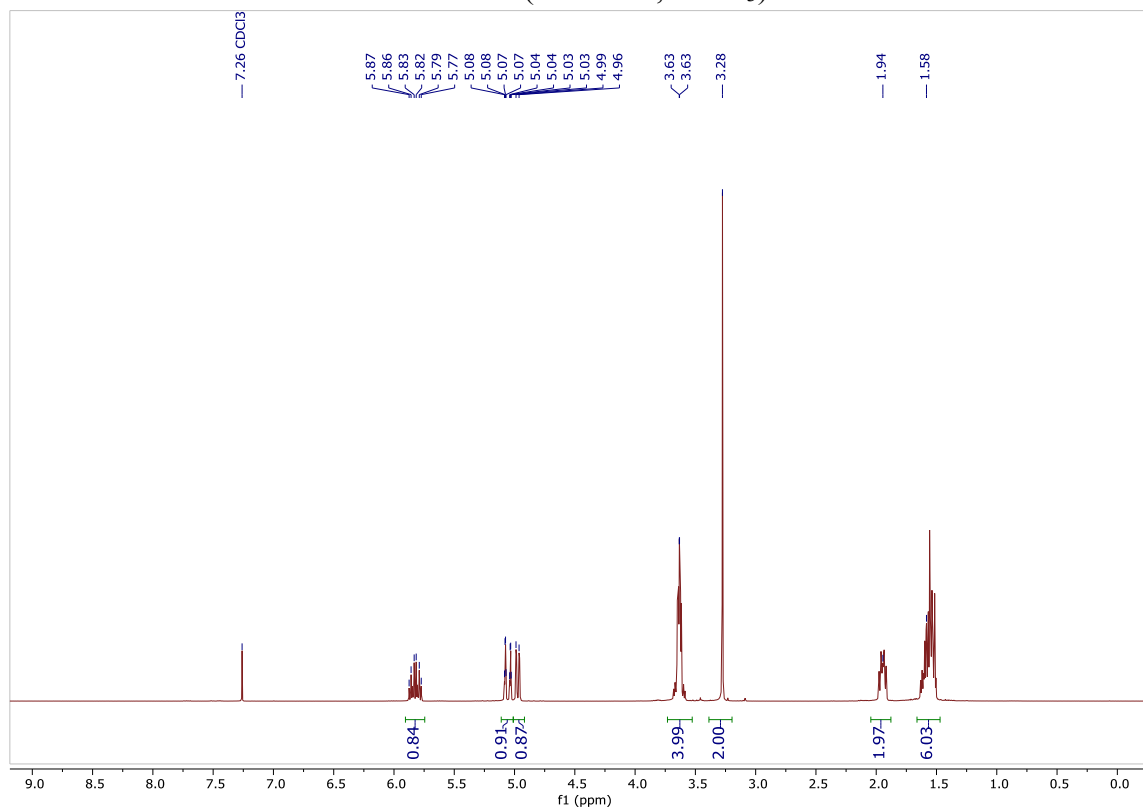
¹³C NMR (101 MHz, CDCl₃)



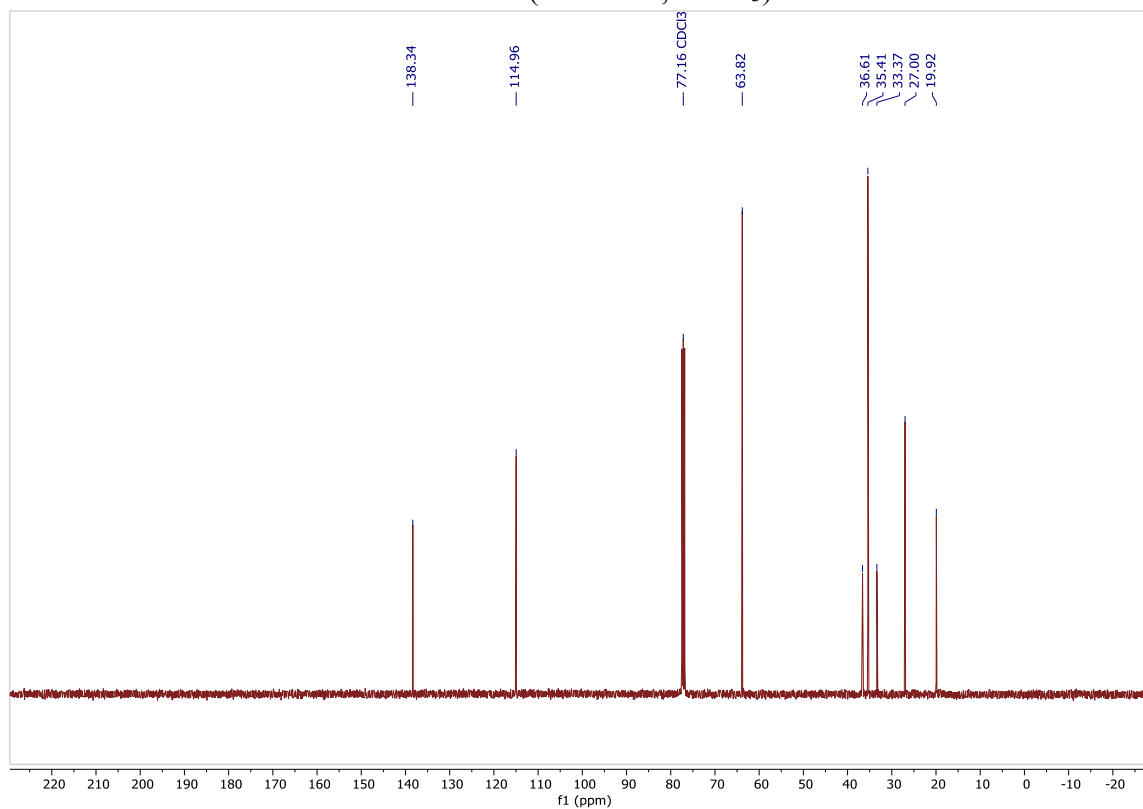
4-(But-3-en-1-yl)-4-(iodomethyl)tetrahydro-2H-pyran, S43



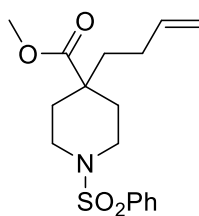
^1H NMR (400 MHz, CDCl_3)



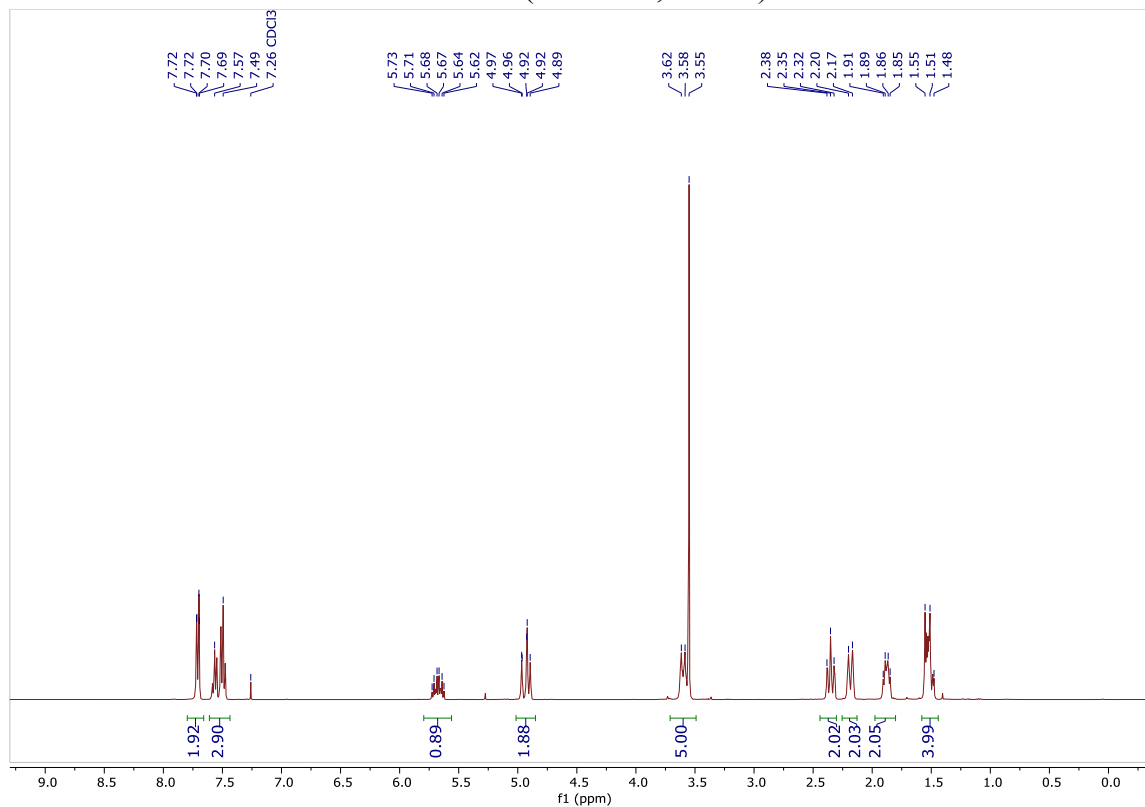
^{13}C NMR (101 MHz, CDCl_3)



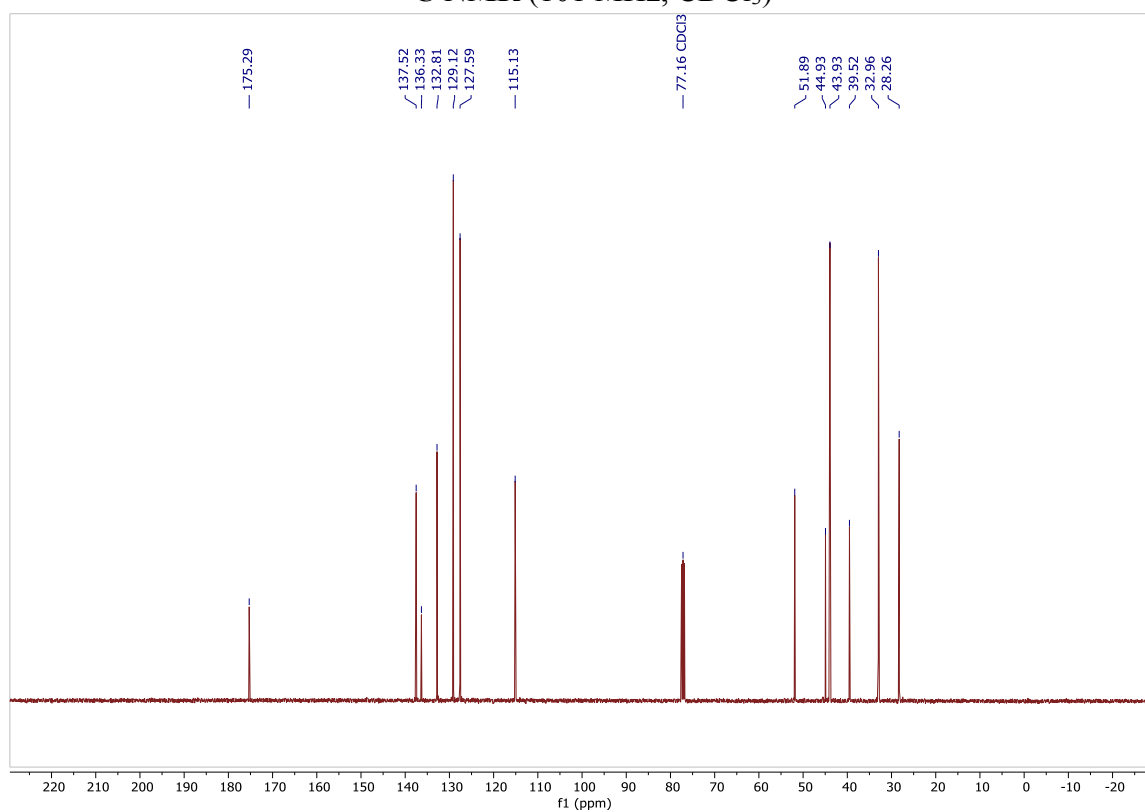
Methyl 4-(but-3-en-1-yl)-1-(phenylsulfonyl)piperidine-4-carboxylate, S44



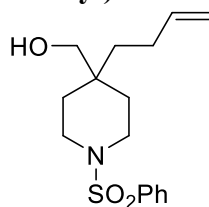
^1H NMR (400 MHz, CDCl_3)



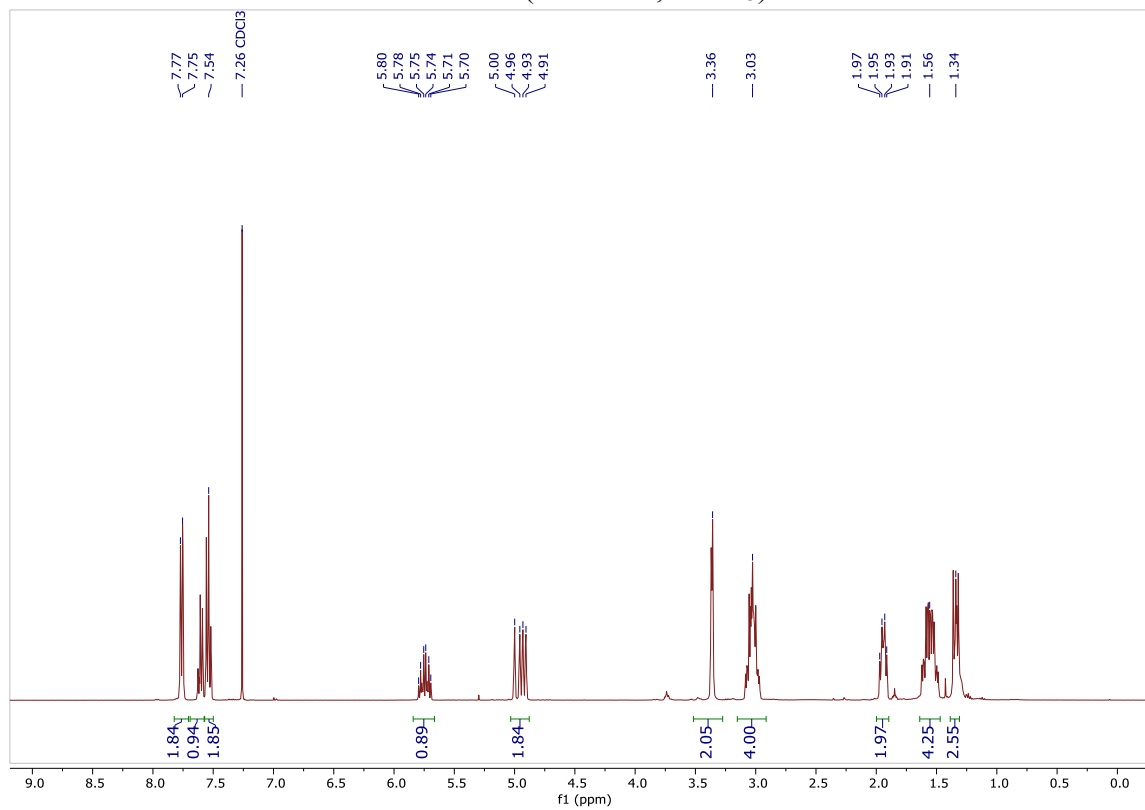
^{13}C NMR (101 MHz, CDCl_3)



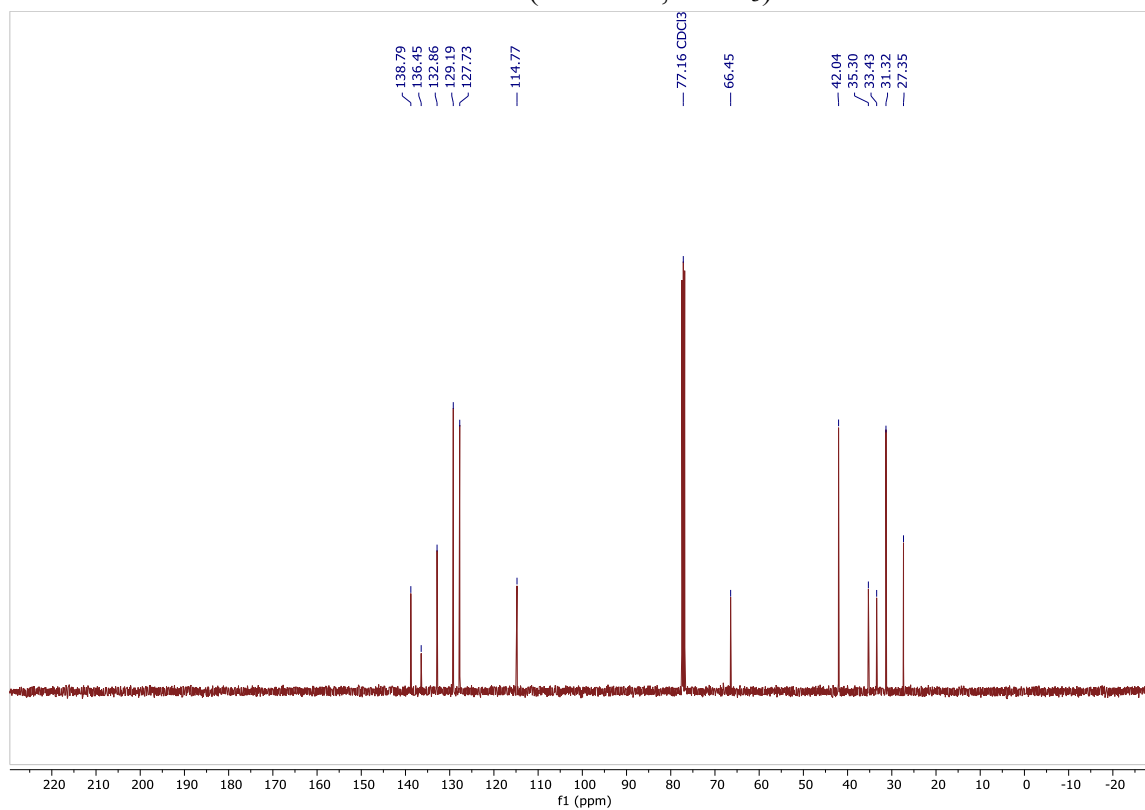
(4-(But-3-en-1-yl)-1-(phenylsulfonyl)piperidin-4-yl)methanol, S45



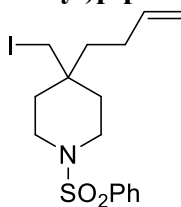
^1H NMR (400 MHz, CDCl_3)



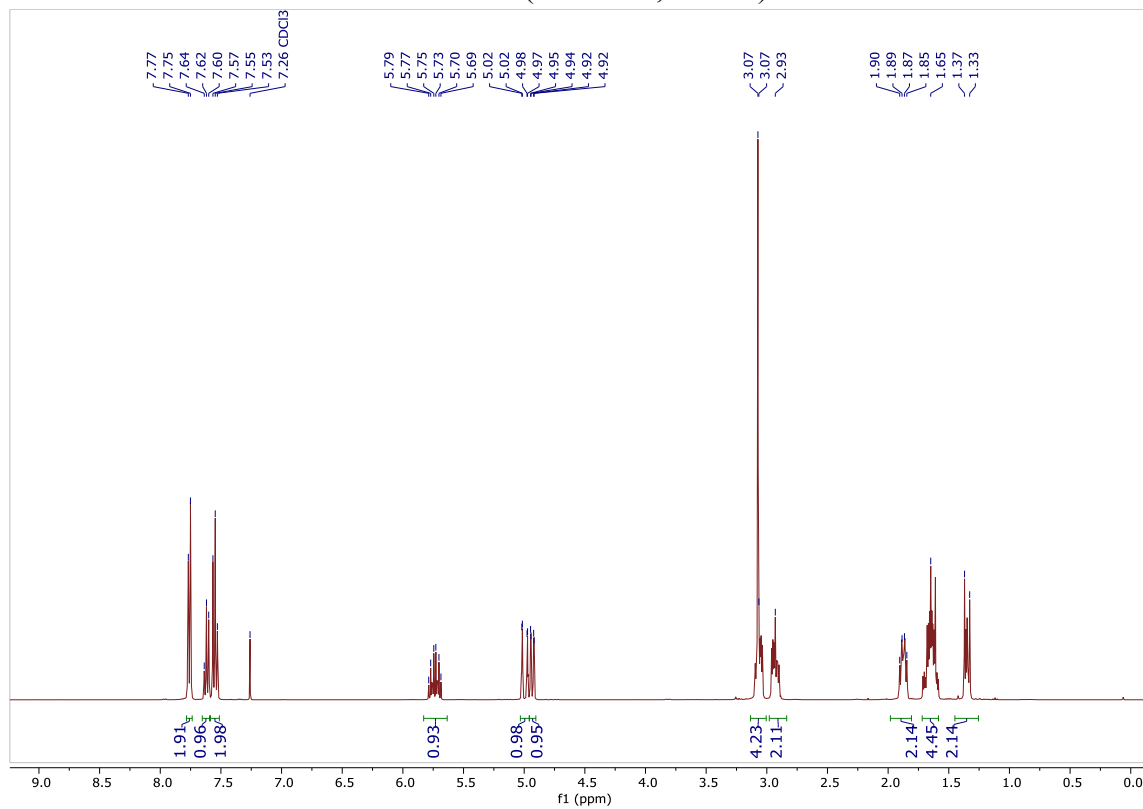
^{13}C NMR (101 MHz, CDCl_3)



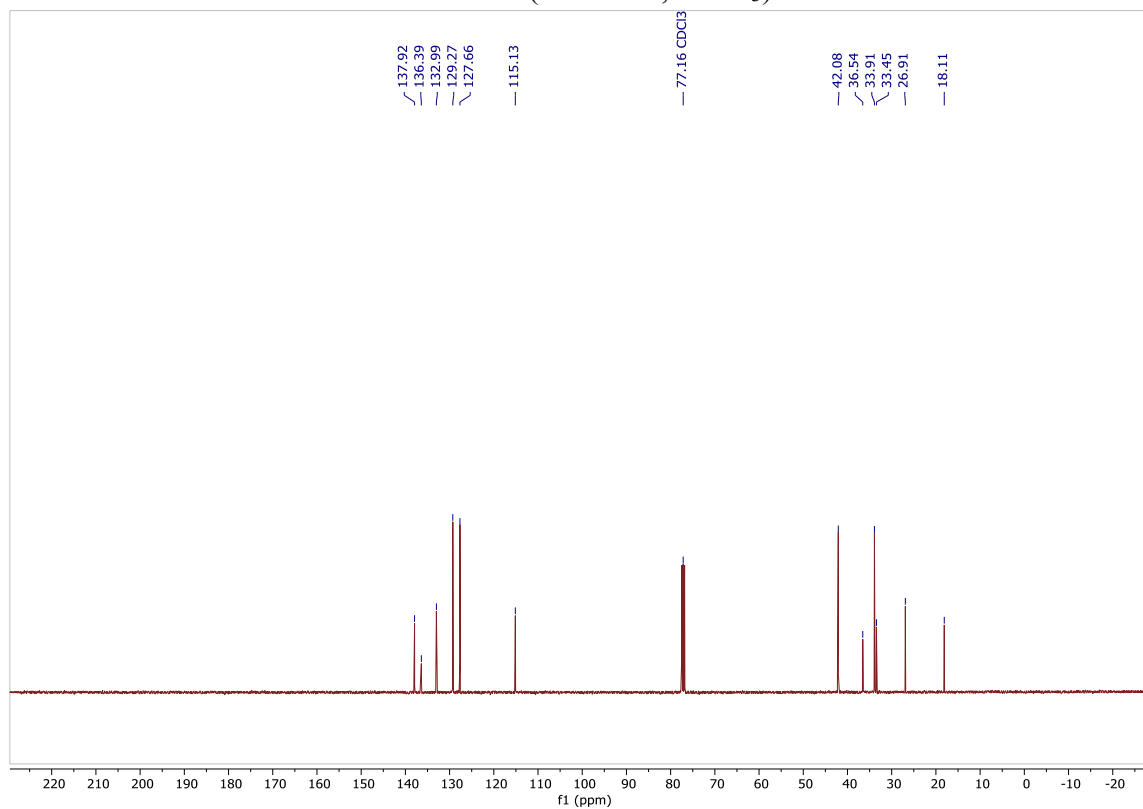
4-(But-3-en-1-yl)-4-(iodomethyl)-1-(phenylsulfonyl)piperidine, S46



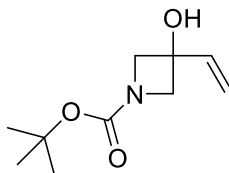
^1H NMR (400 MHz, CDCl_3)



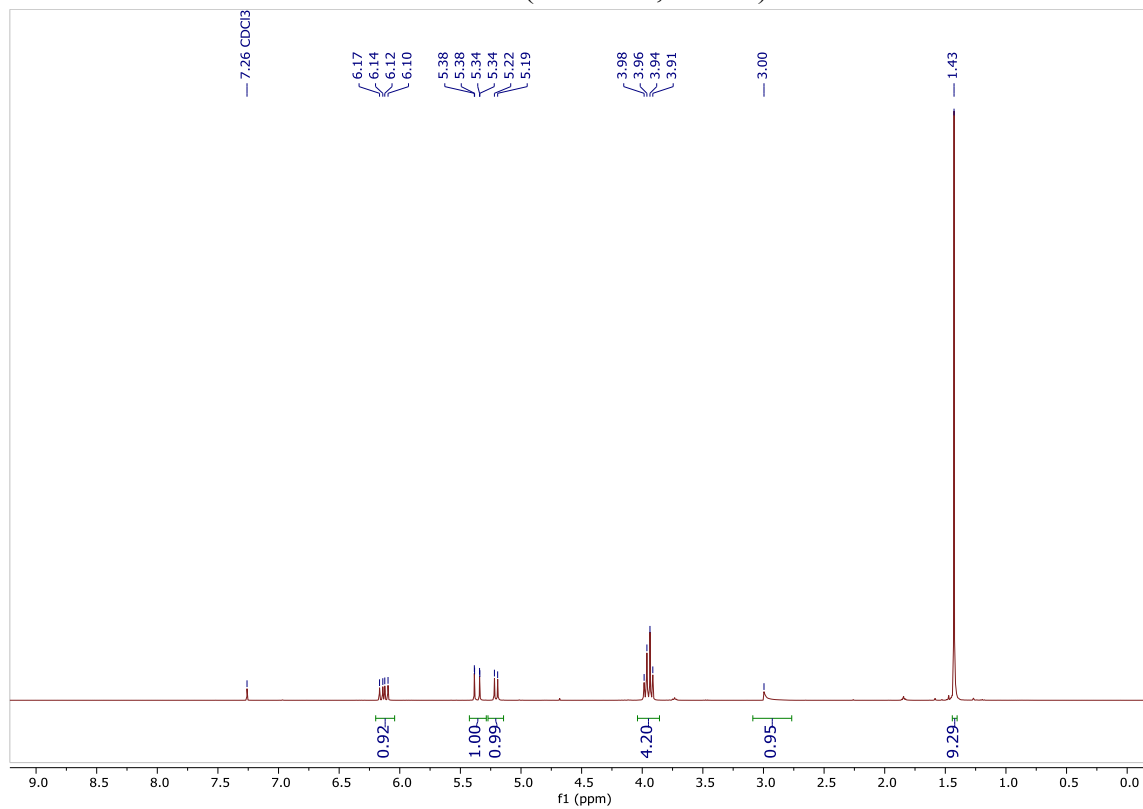
^{13}C NMR (101 MHz, CDCl_3)



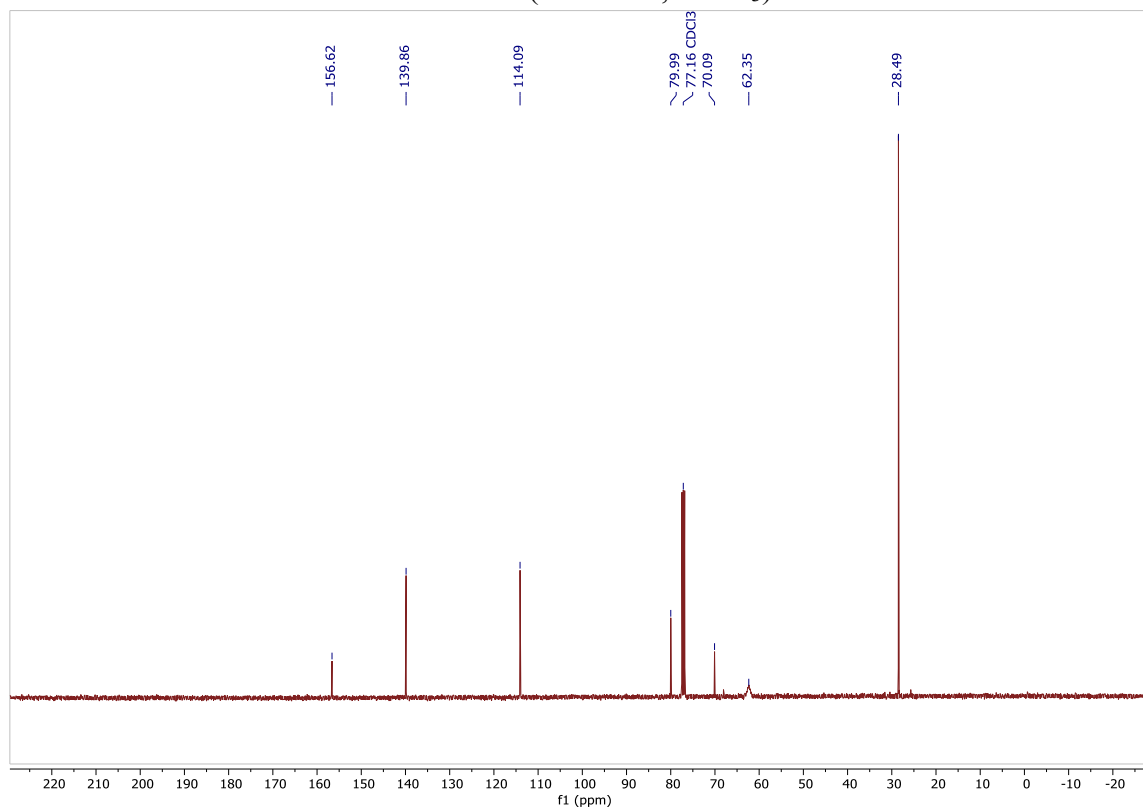
***tert*-Butyl 3-hydroxy-3-vinylazetidine-1-carboxylate, S47**



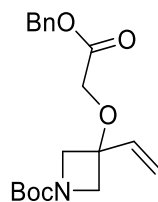
^1H NMR (400 MHz, CDCl_3)



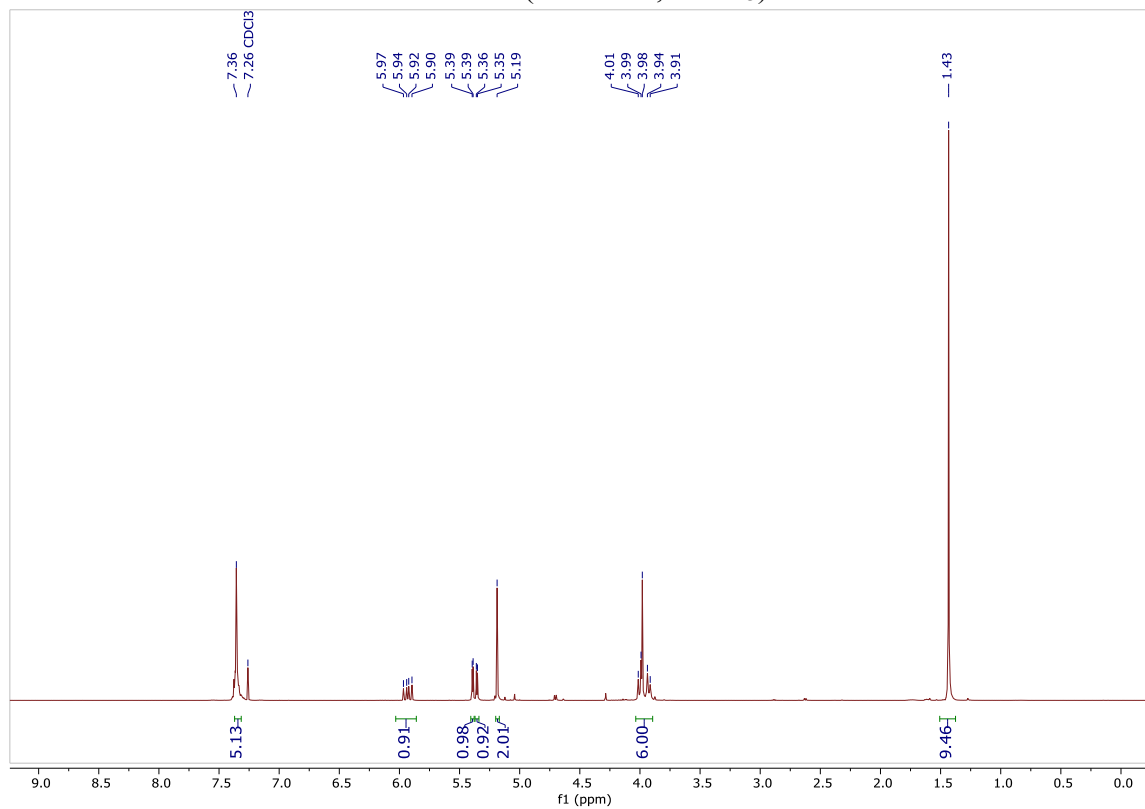
^{13}C NMR (101 MHz, CDCl_3)



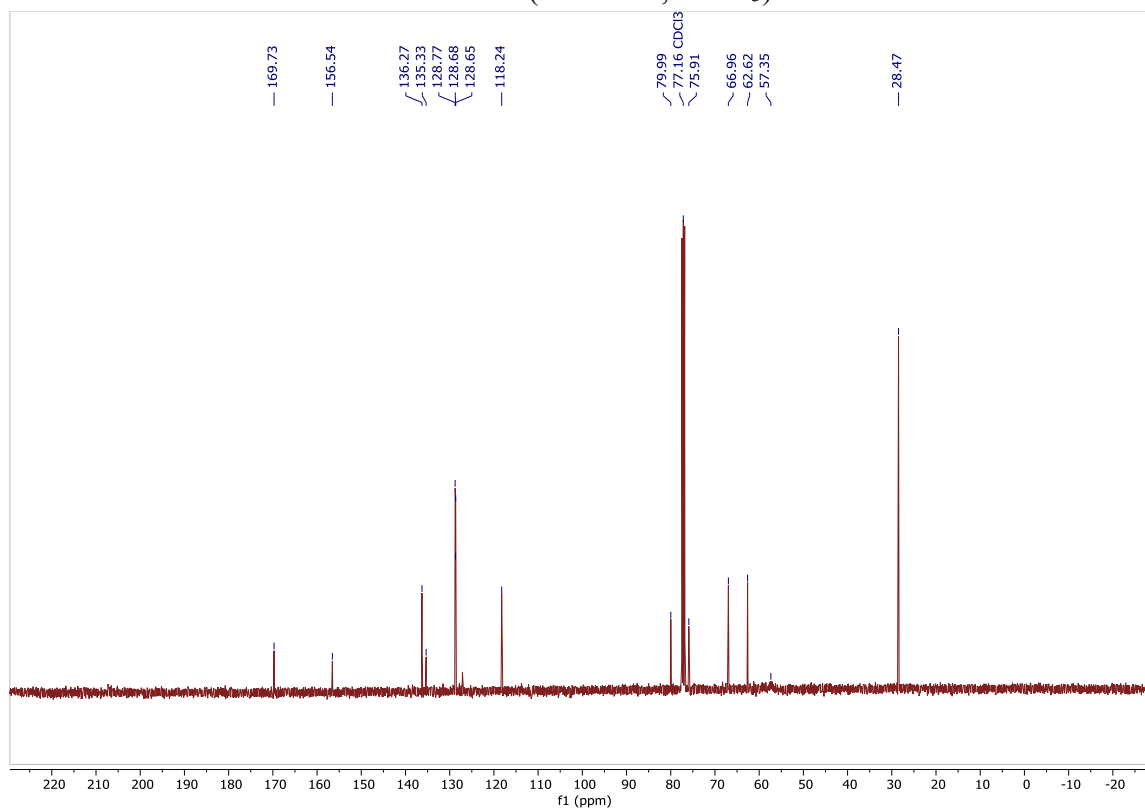
***tert*-Butyl 3-(2-(benzyloxy)-2-oxoethoxy)-3-vinylazetidine-1-carboxylate, S48**



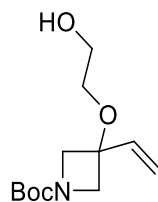
^1H NMR (400 MHz, CDCl_3)



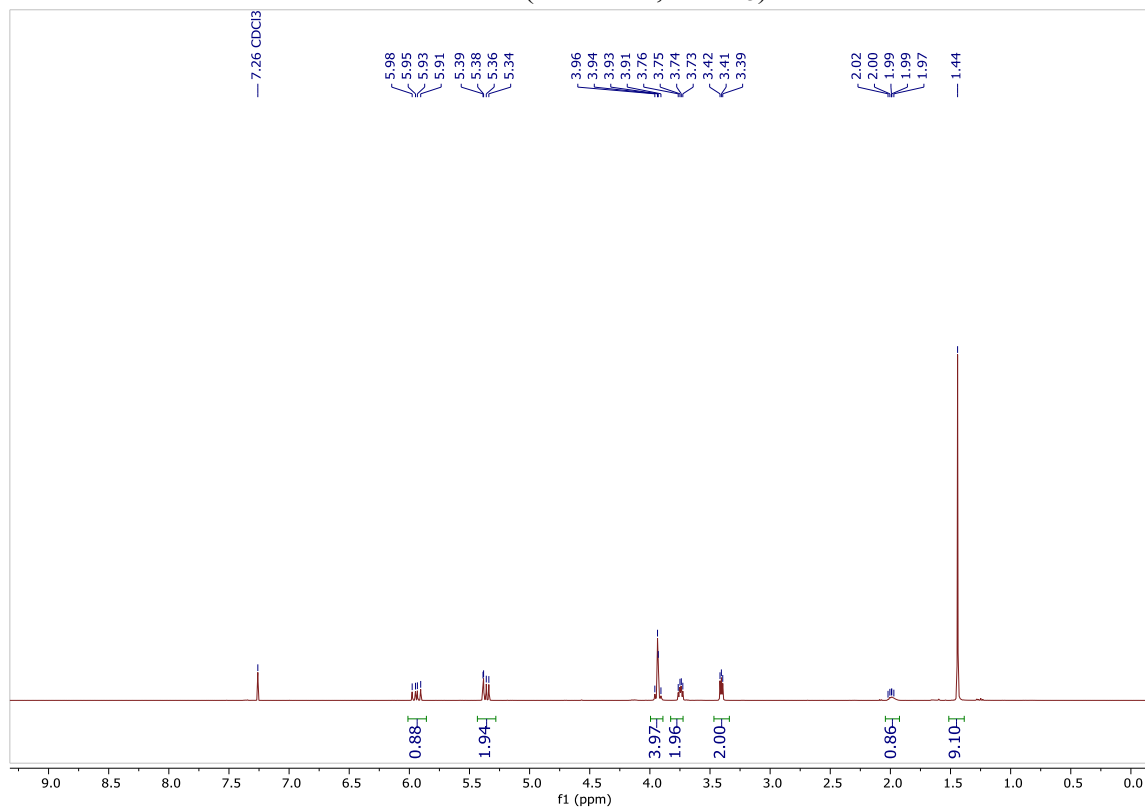
^{13}C NMR (101 MHz, CDCl_3)



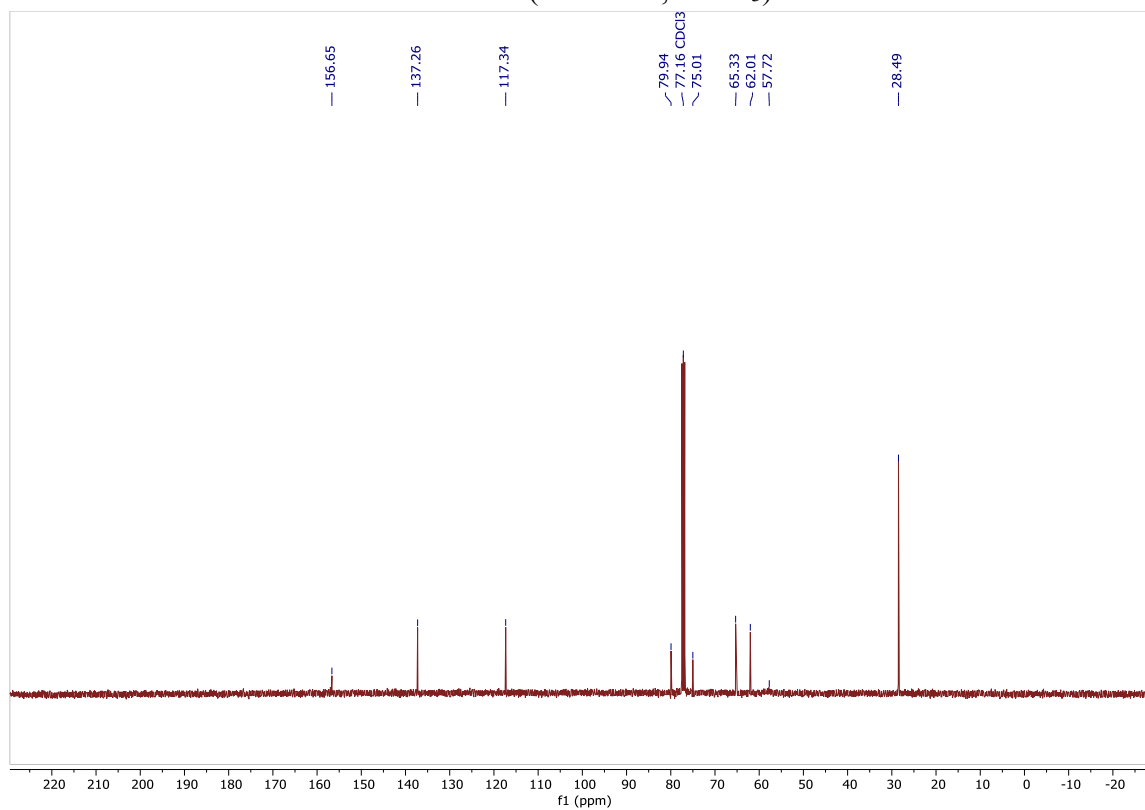
***tert*-Butyl 3-(2-hydroxyethoxy)-3-vinylazetidine-1-carboxylate, S49**



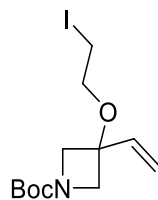
¹H NMR (400 MHz, CDCl₃)



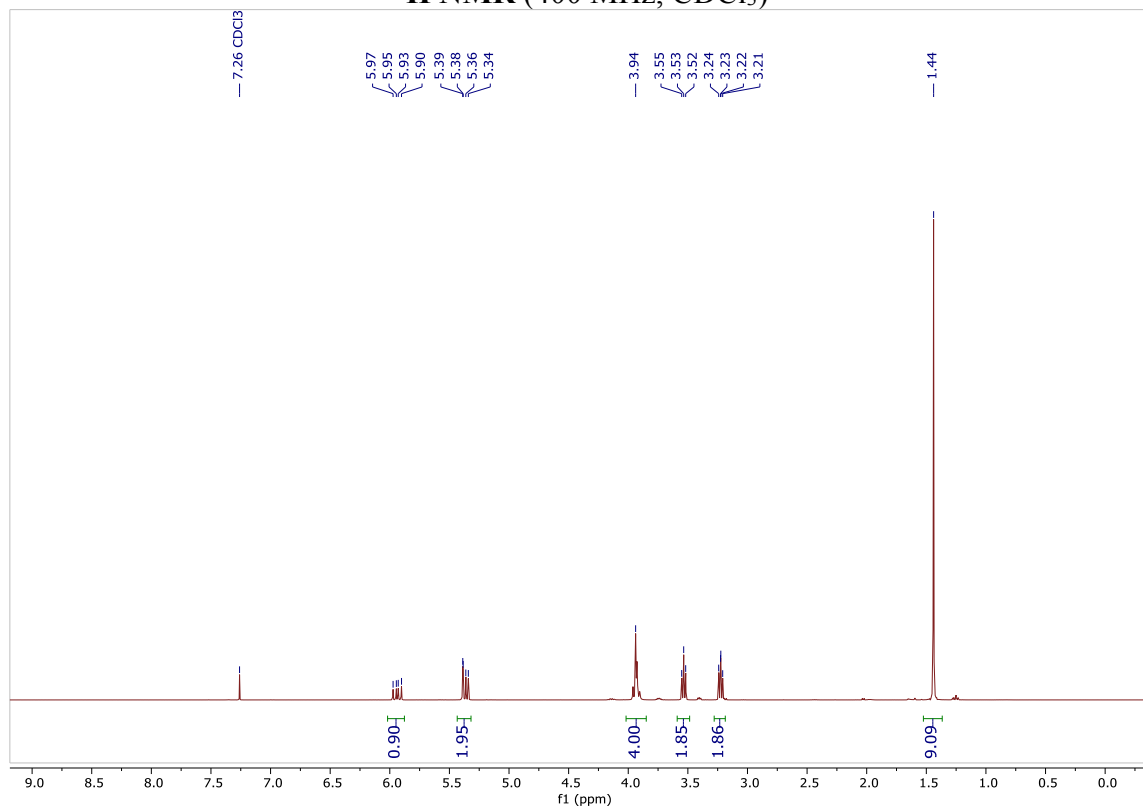
¹³C NMR (101 MHz, CDCl₃)



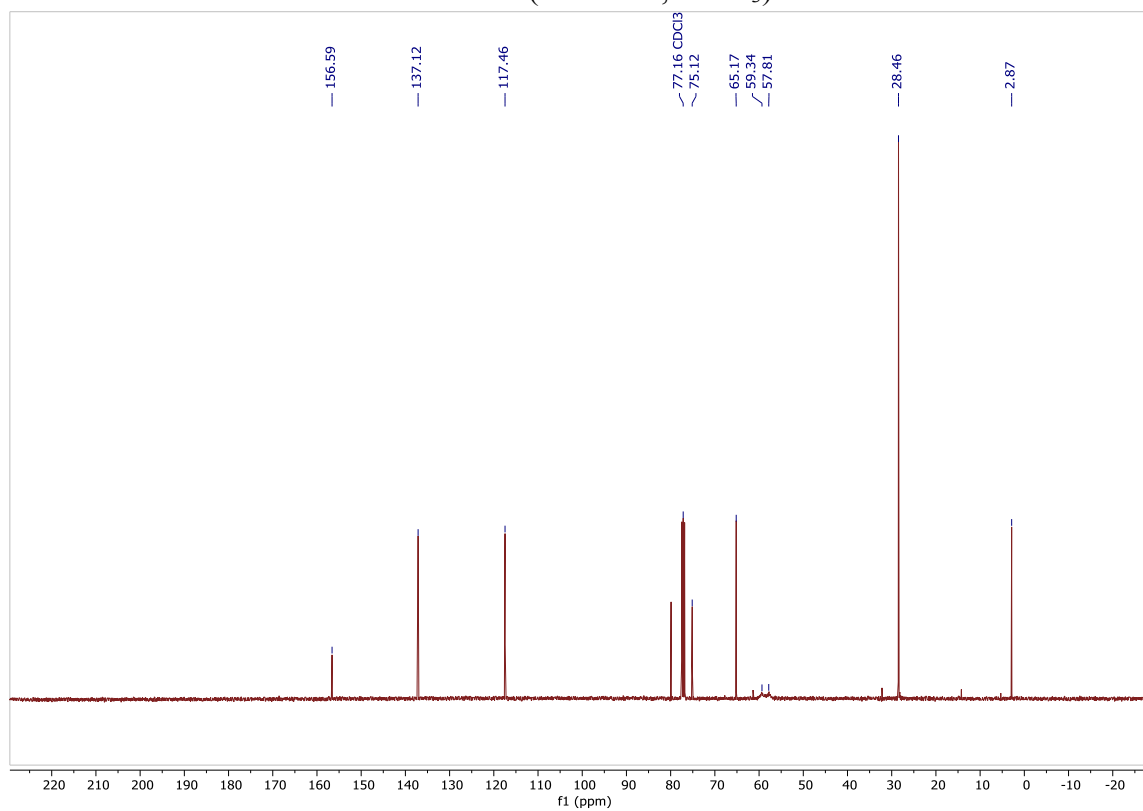
***tert*-Butyl 3-(2-iodoethoxy)-3-vinylazetidine-1-carboxylate, S50**



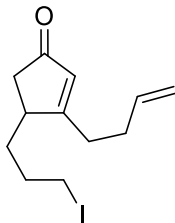
^1H NMR (400 MHz, CDCl_3)



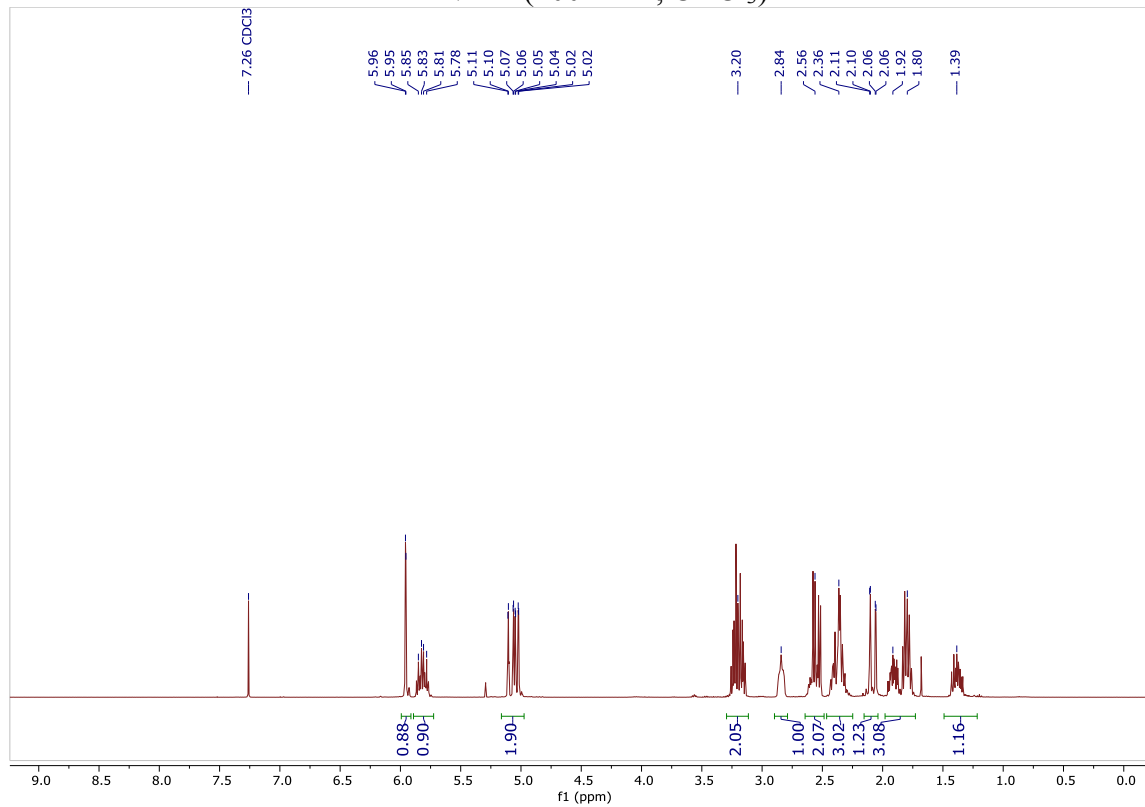
^{13}C NMR (101 MHz, CDCl_3)



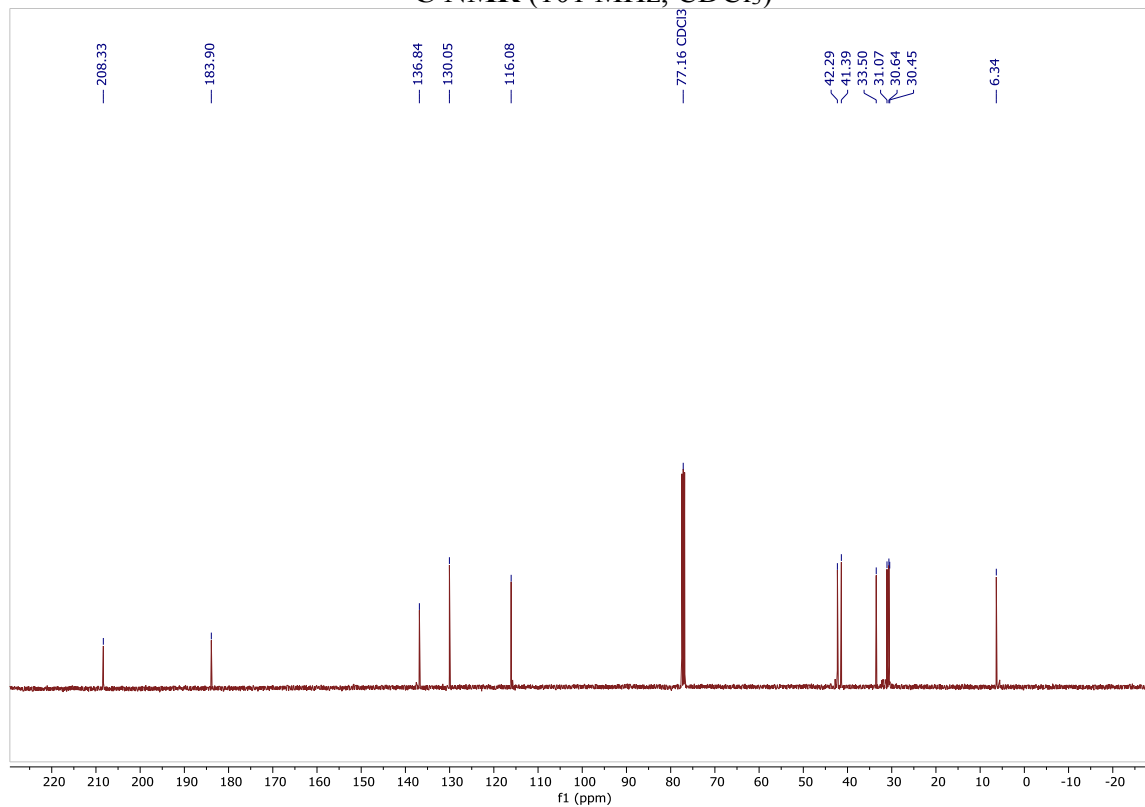
3-(But-3-en-1-yl)-4-(3-iodopropyl)cyclopent-2-en-1-one, S51



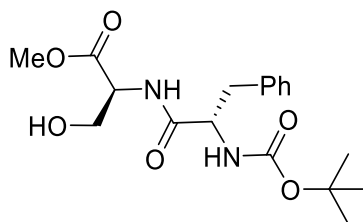
^1H NMR (400 MHz, CDCl_3)



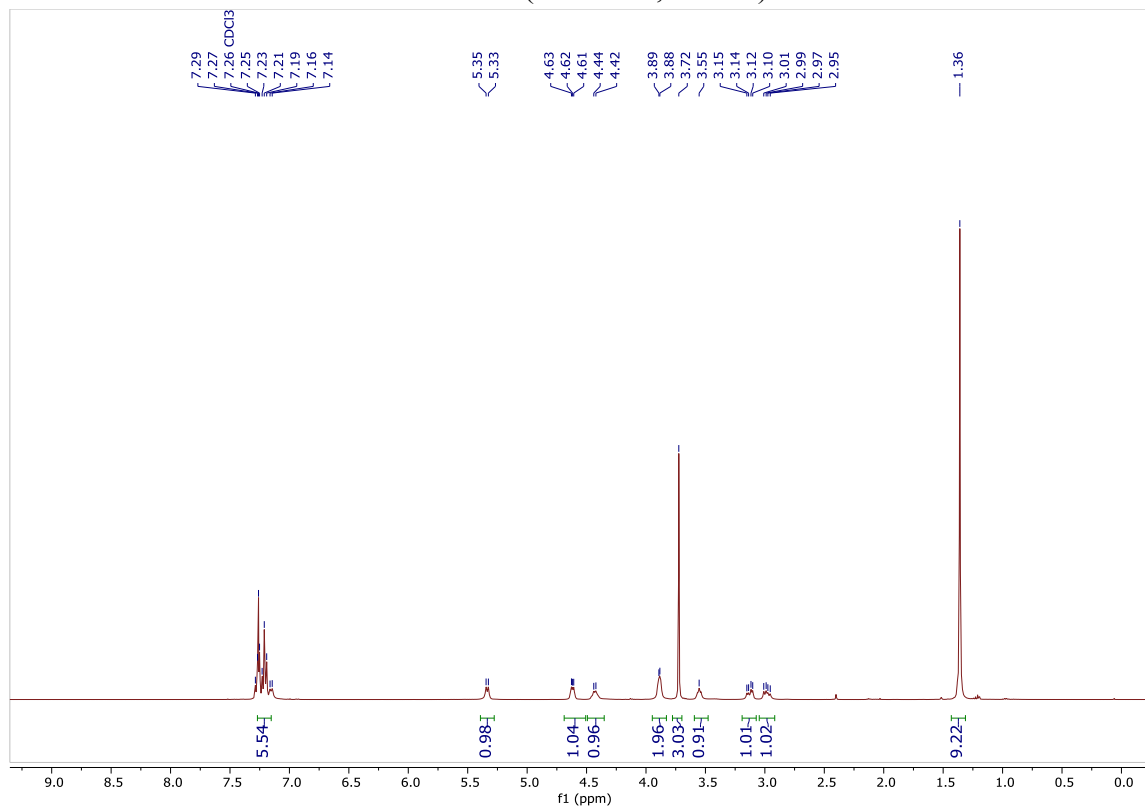
^{13}C NMR (101 MHz, CDCl_3)



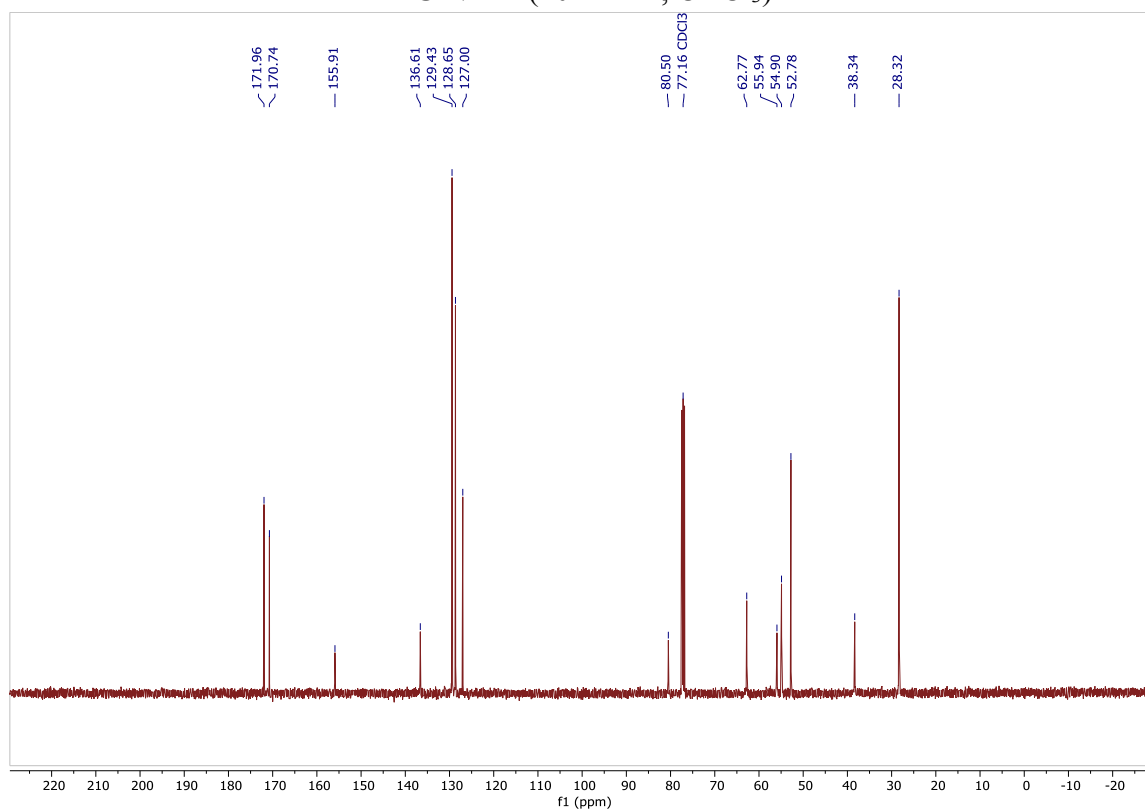
Boc-Phe-Ser-OMe, S52



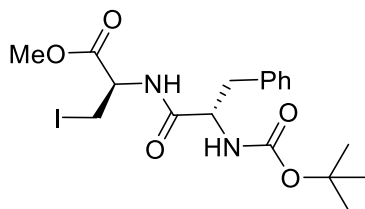
^1H NMR (400 MHz, CDCl_3)



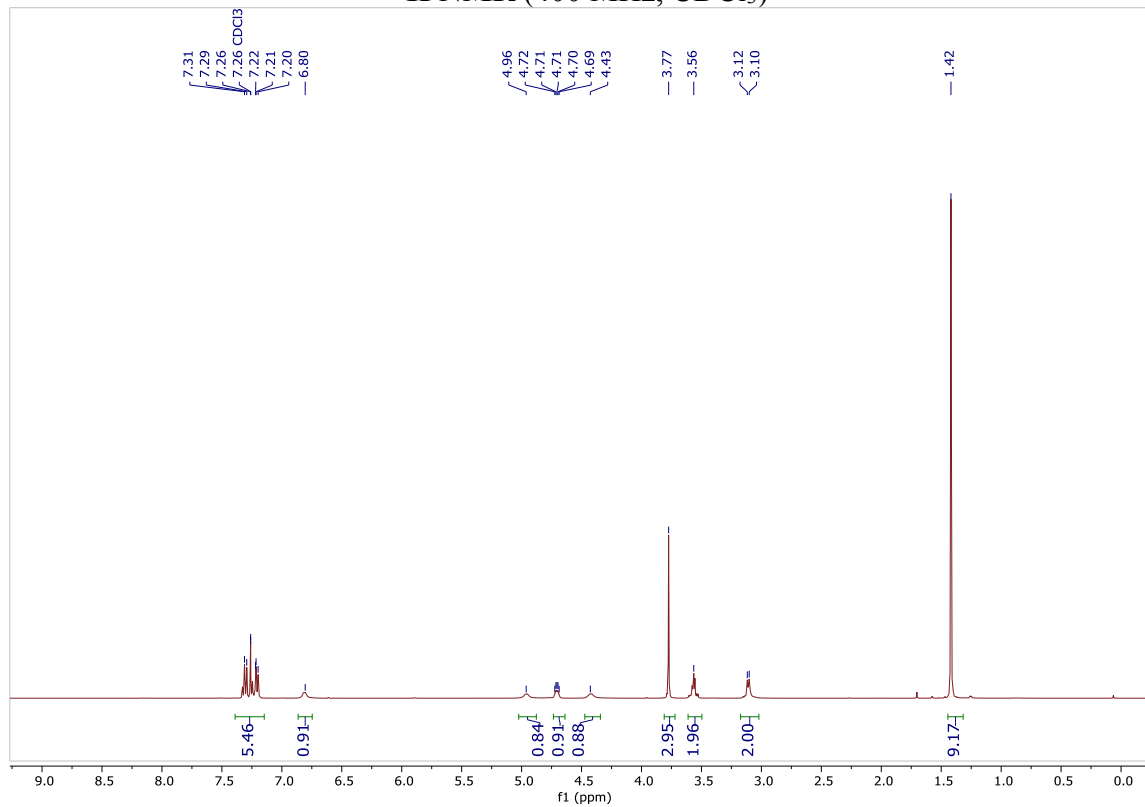
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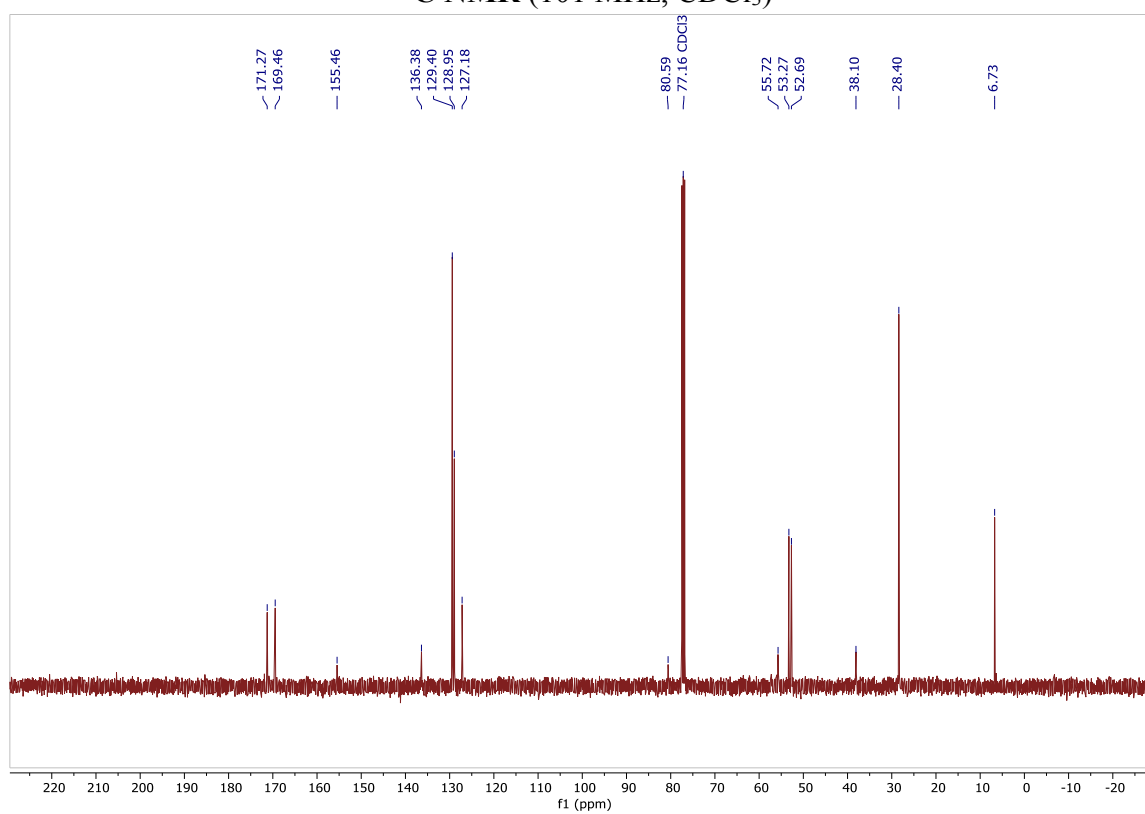
Boc-Phe-β-iodo-Ala-OMe, S53



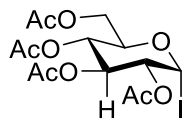
¹H NMR (400 MHz, CDCl₃)



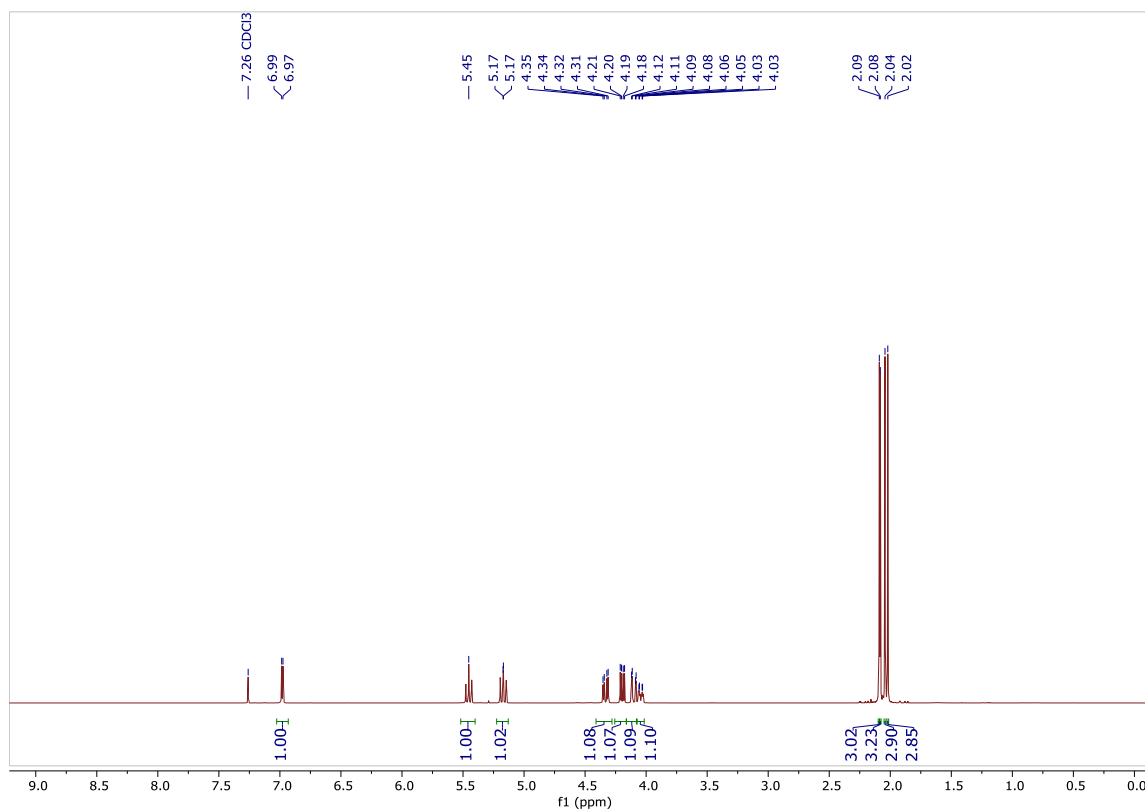
¹³C NMR (101 MHz, CDCl₃)



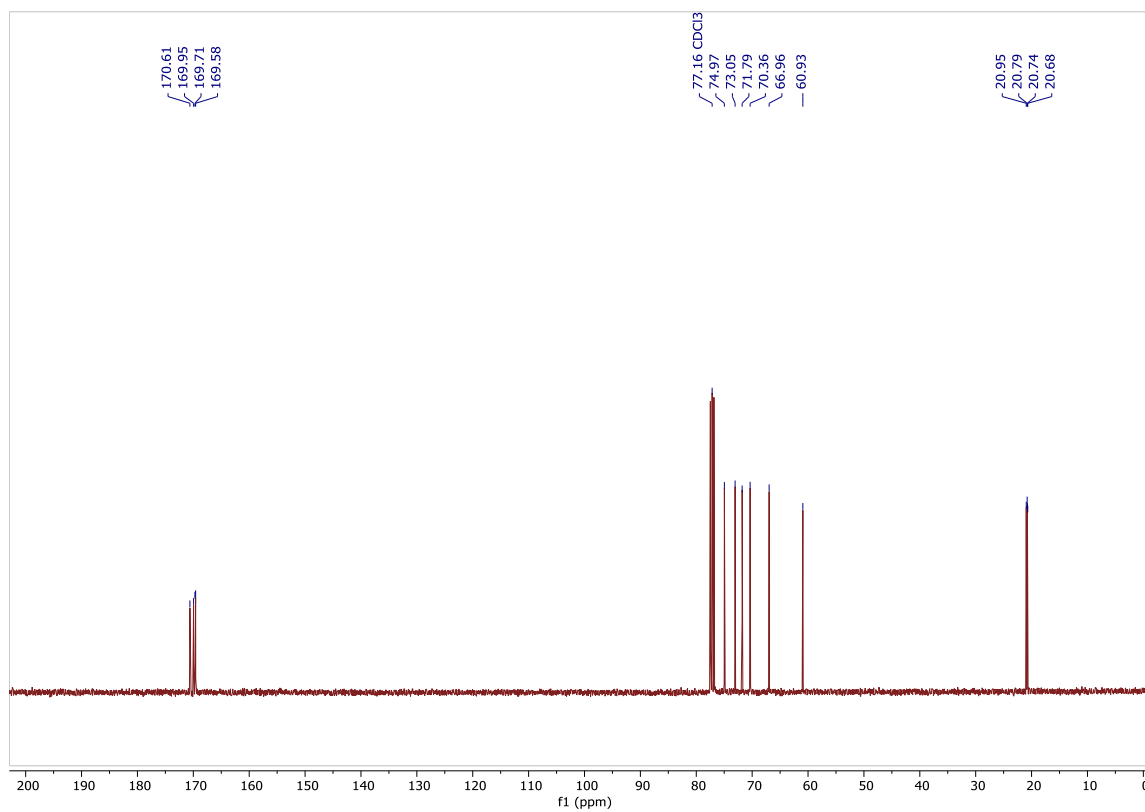
2,3,4,6-Tetra-O-acetyl- α -D-glucopyranosyl iodide, S54



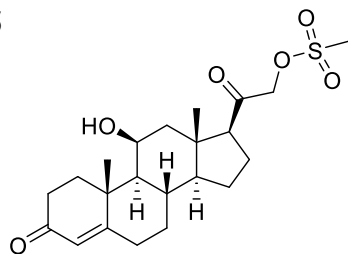
^1H NMR (400 MHz, CDCl_3)



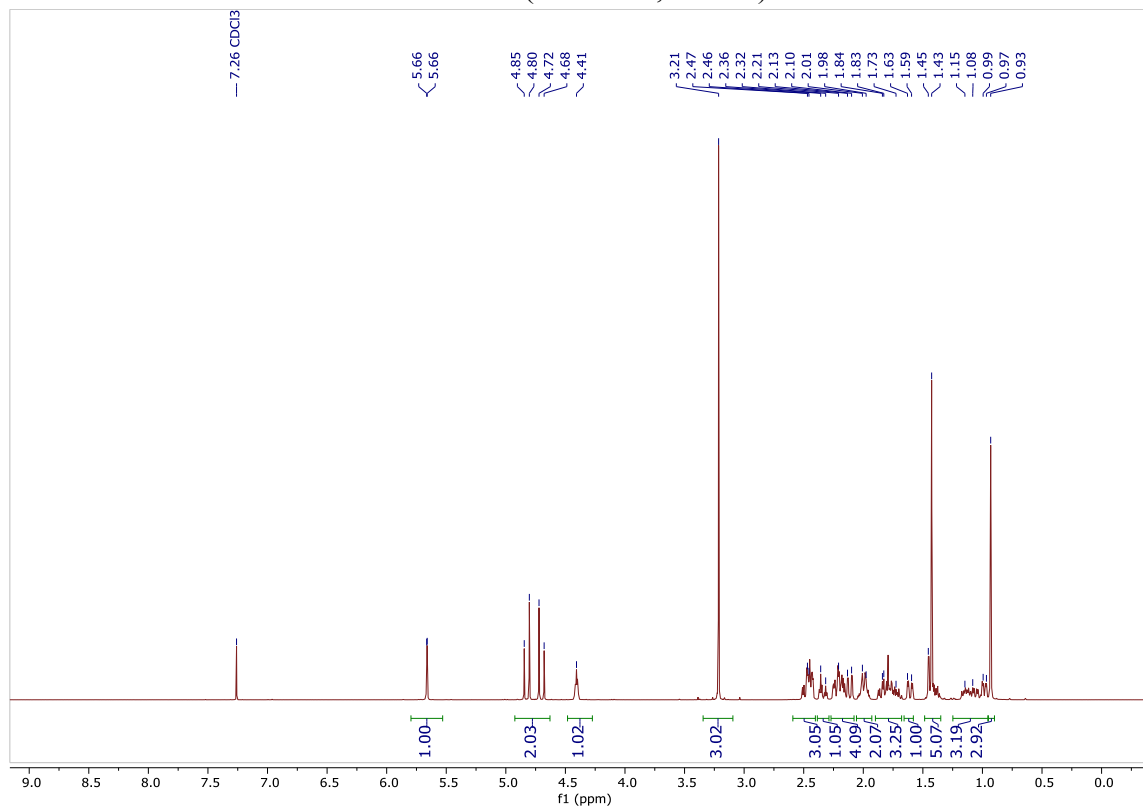
^{13}C NMR (101 MHz, CDCl_3)



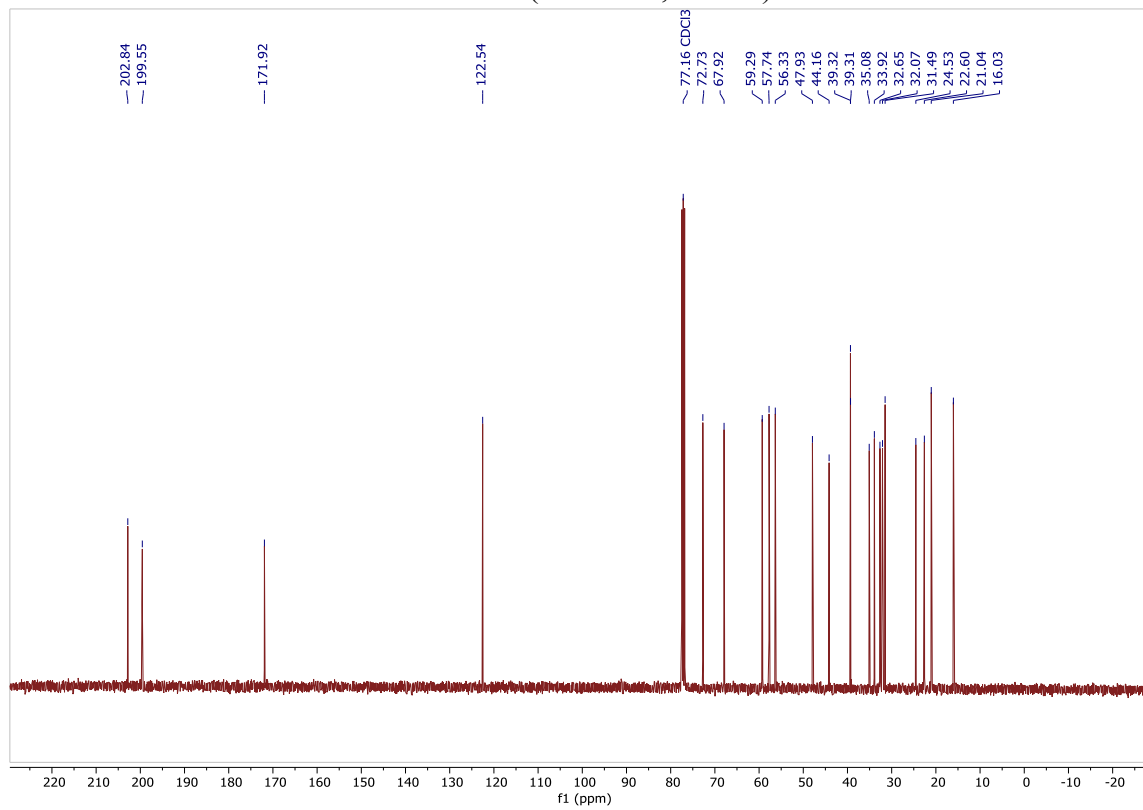
Corticosterone methanesulfonate, S55



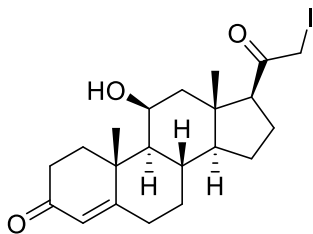
^1H NMR (400 MHz, CDCl_3)



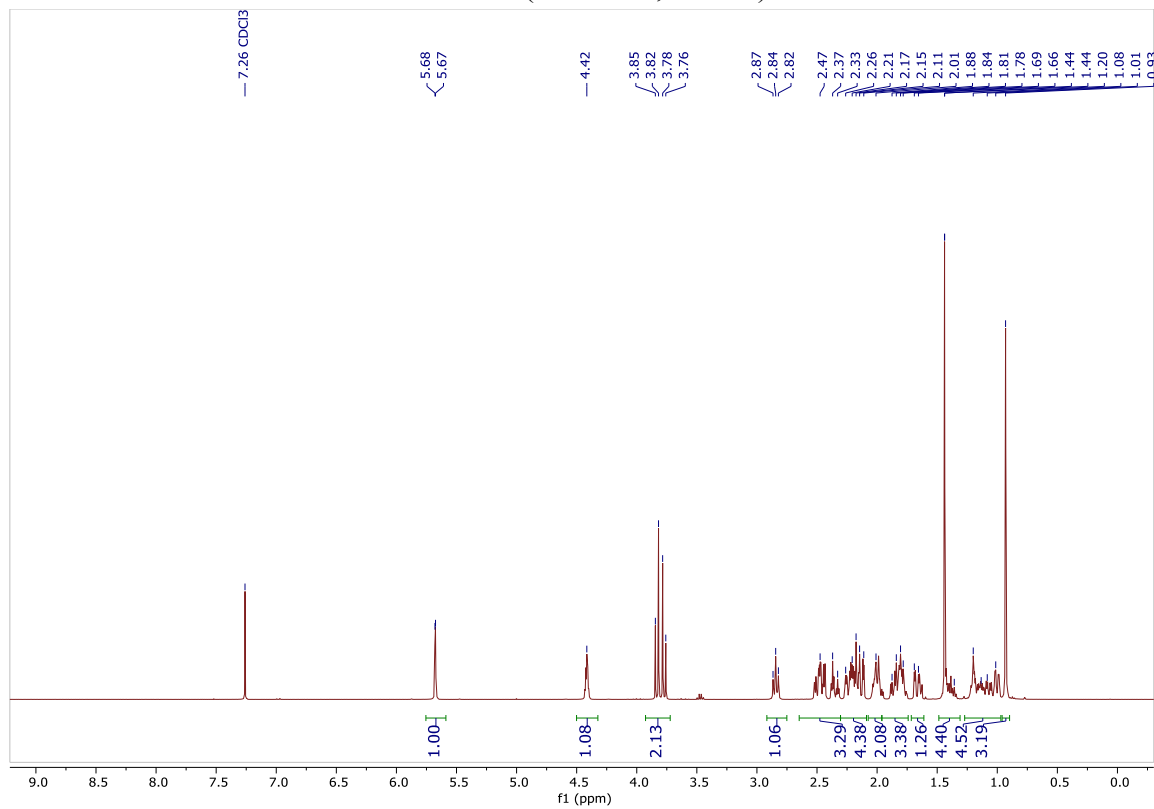
^{13}C NMR (101 MHz, CDCl_3)



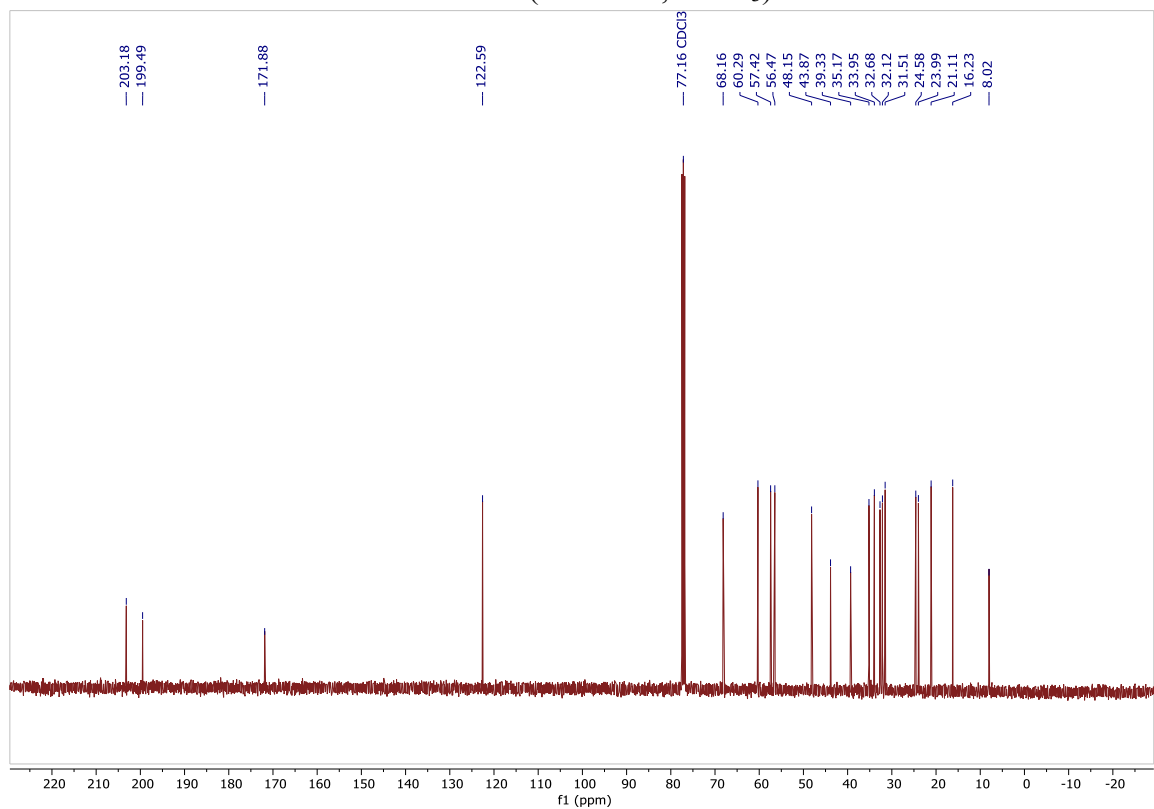
11 β -Hydroxy-21-iodo-4-pregnene-3,20-dione, S56



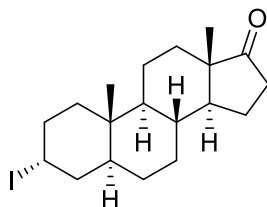
^1H NMR (400 MHz, CDCl_3)



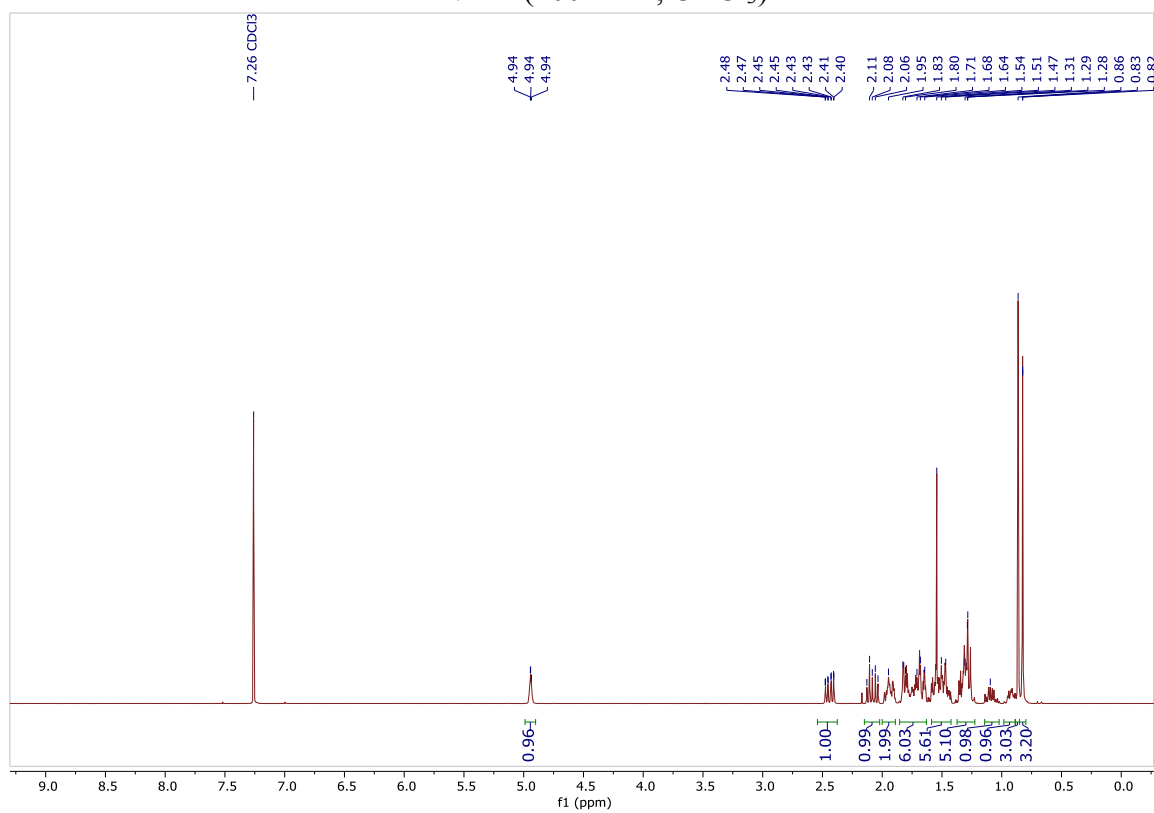
^{13}C NMR (101 MHz, CDCl_3)



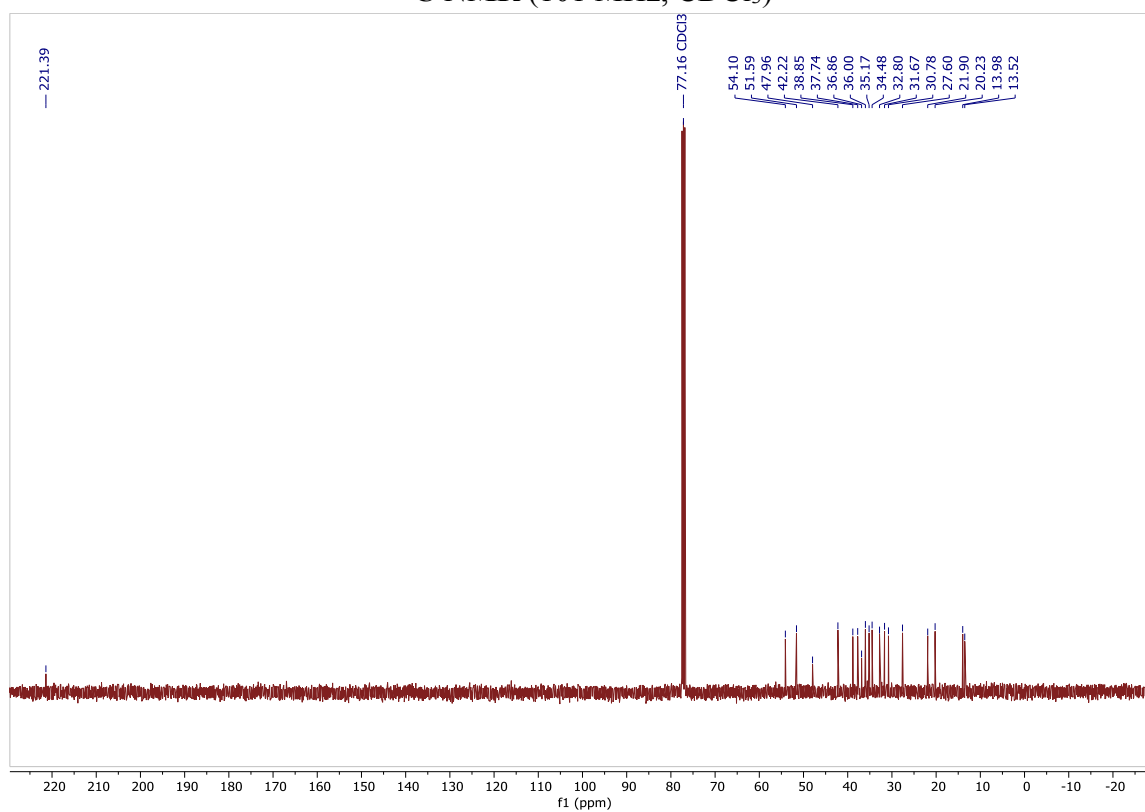
3 α -Iodo-5 α -androstan-17-one, S57



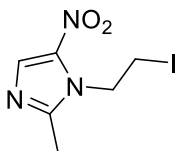
^1H NMR (400 MHz, CDCl_3)



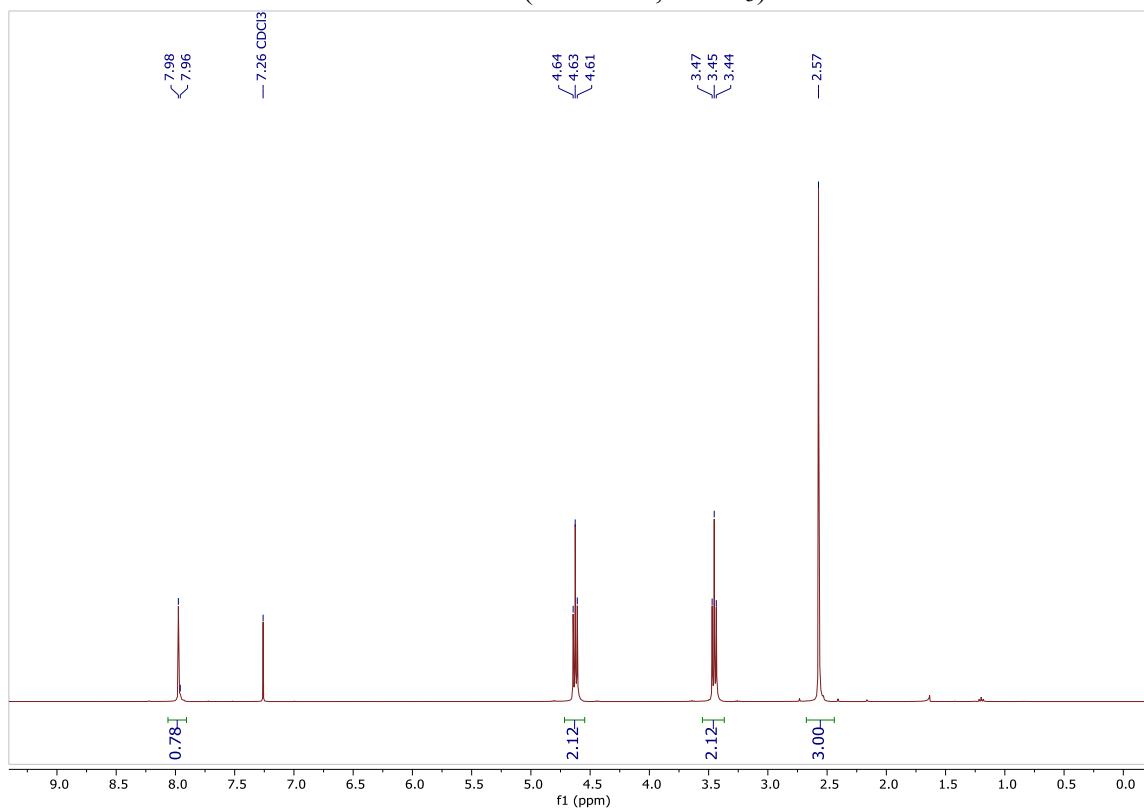
^{13}C NMR (101 MHz, CDCl_3)



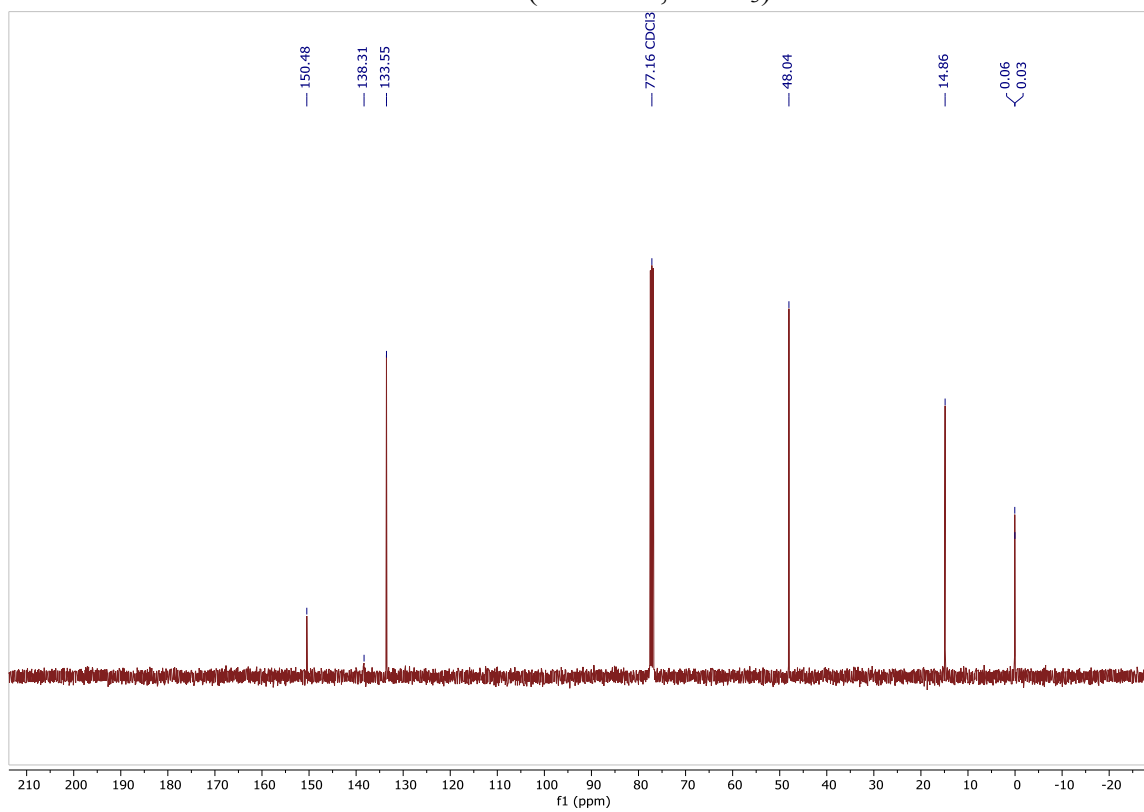
1-(2-Iodoethyl)-2-methyl-5-nitro-1*H*-imidazole, S58



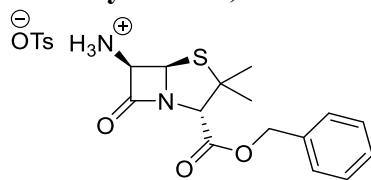
¹H NMR (400 MHz, CDCl₃)



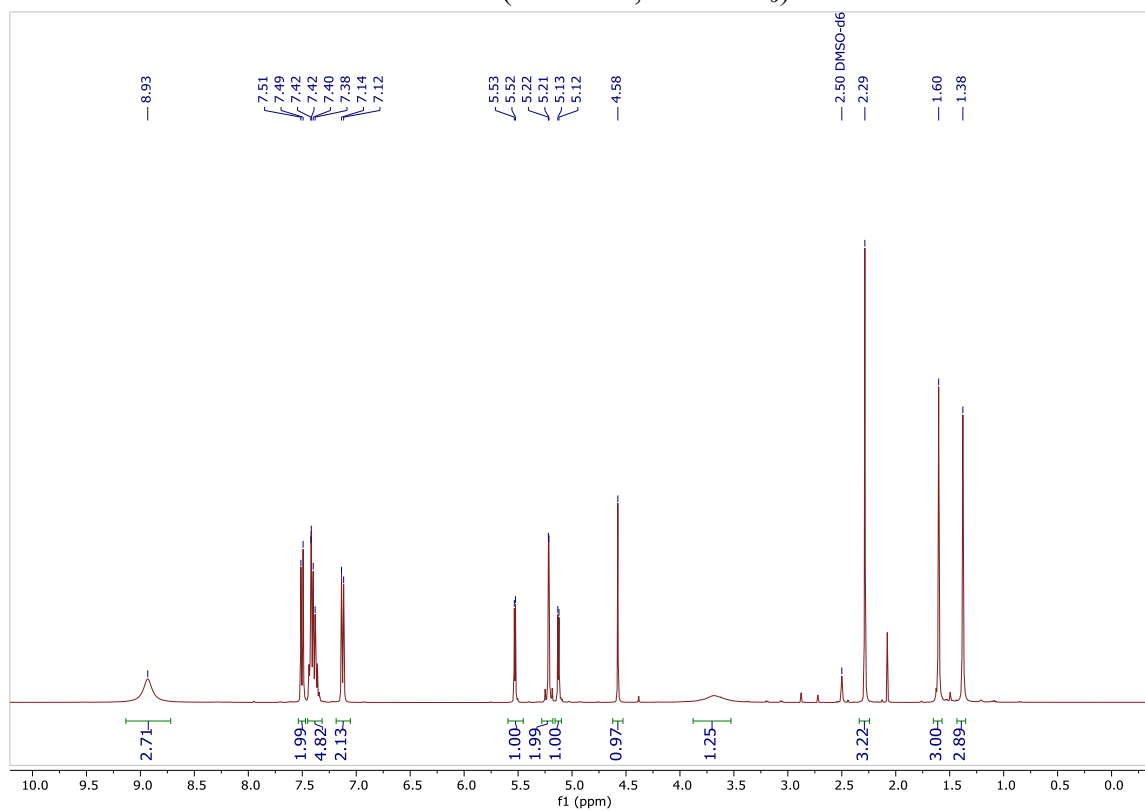
¹³C NMR (101 MHz, CDCl₃)



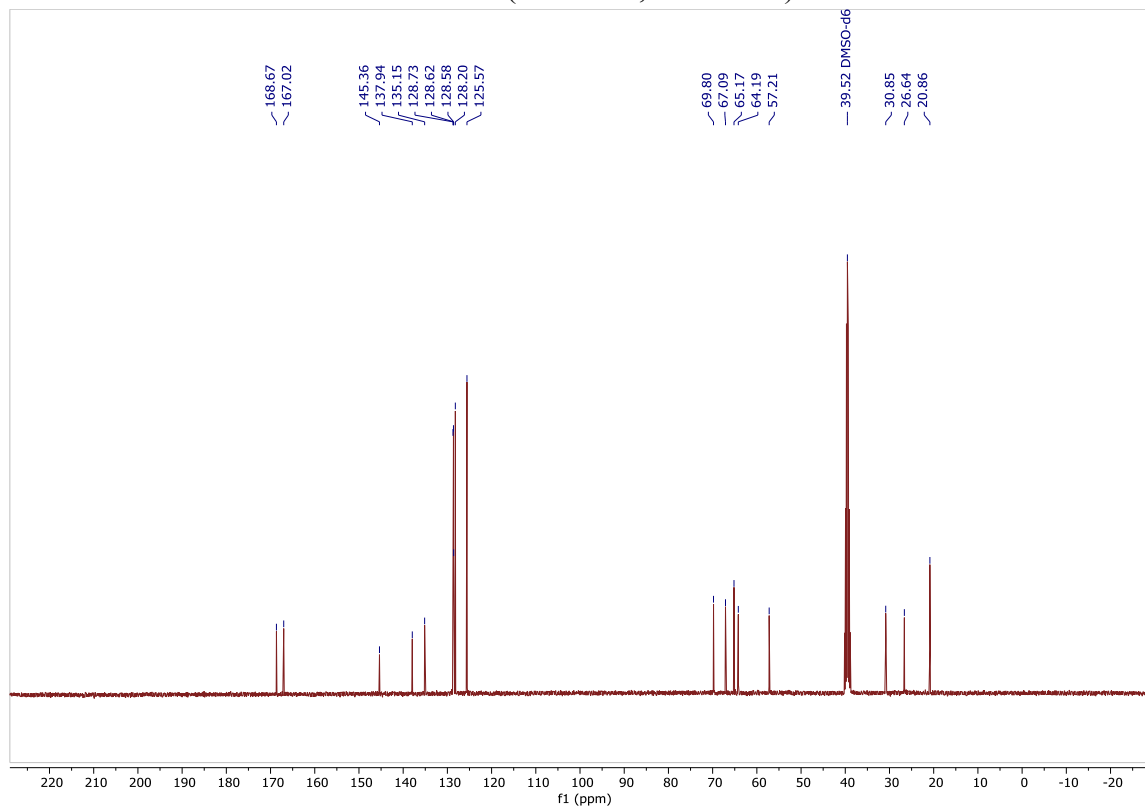
(+)-6-Aminopenicillanic acid benzyl ester tosylate salt, S59



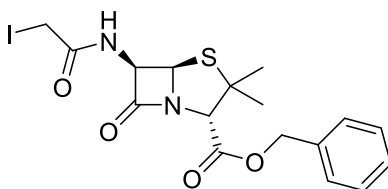
^1H NMR (400 MHz, DMSO- d_6)



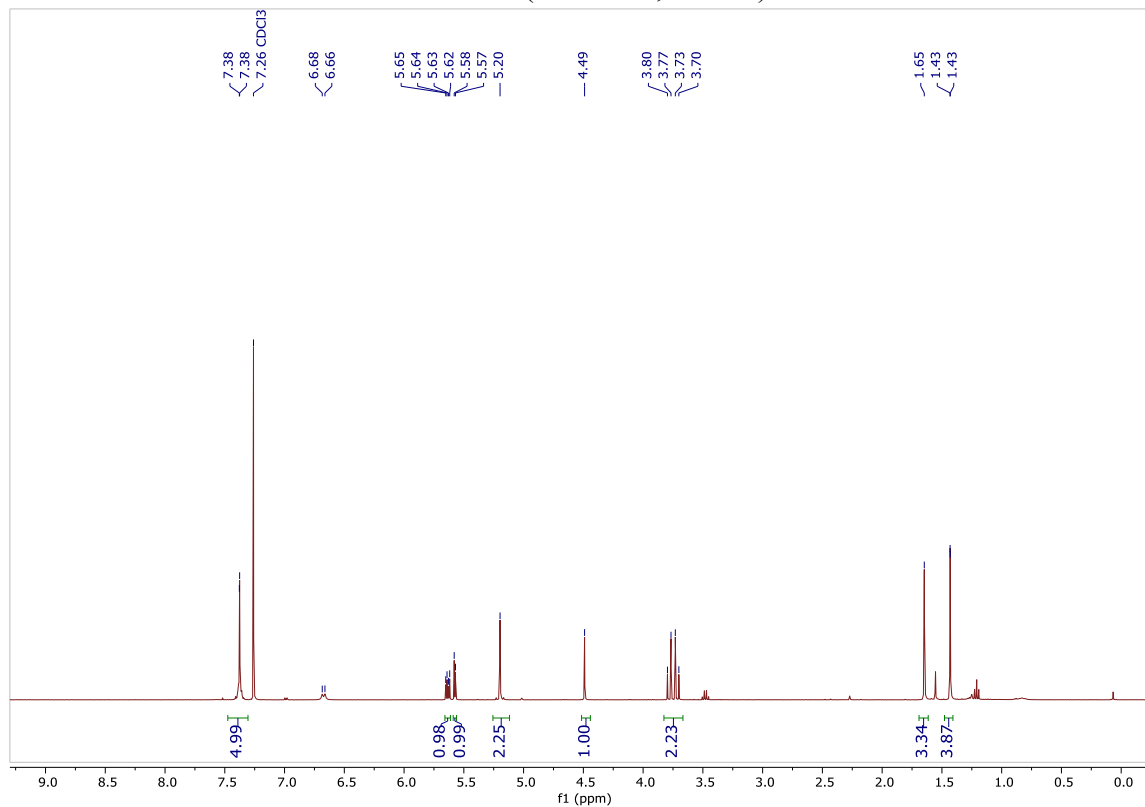
^{13}C NMR (101 MHz, DMSO- d_6)



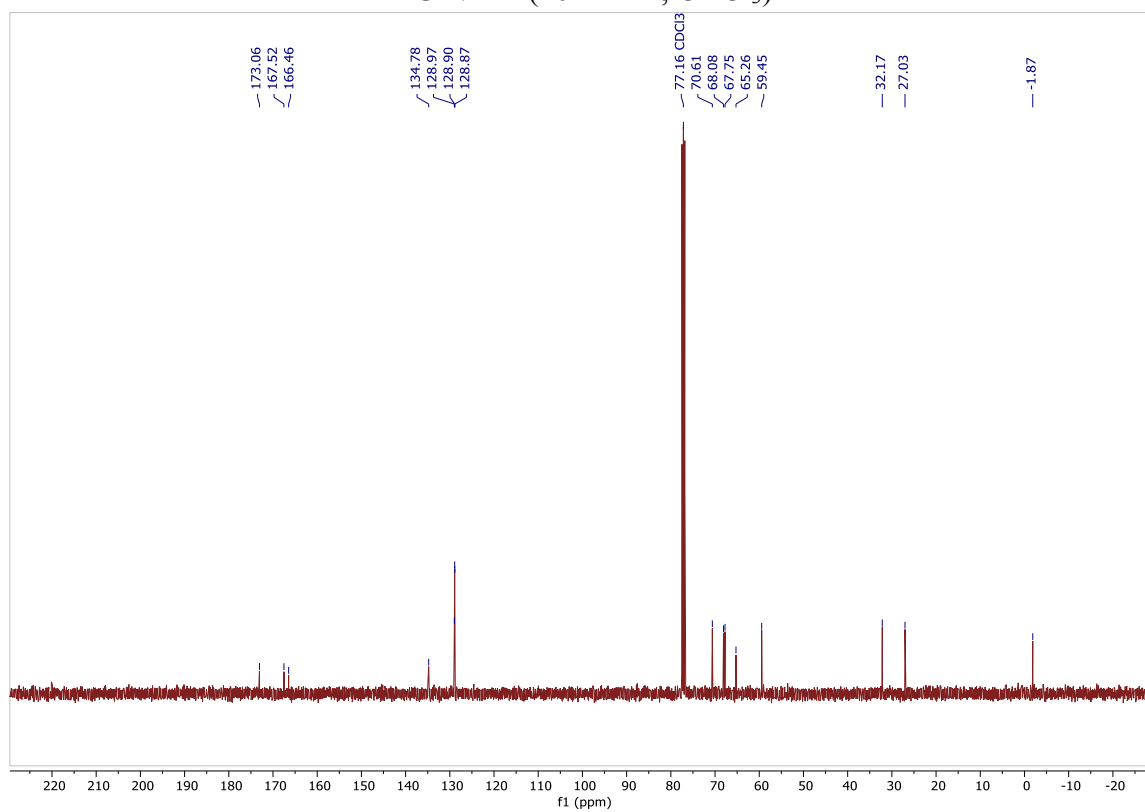
Benzyl (2*S*,5*R*,6*R*)-6-(2-iodoacetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate, S60



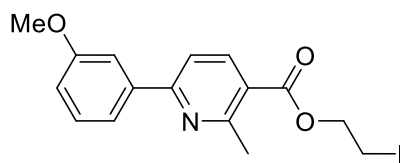
¹H NMR (400 MHz, CDCl₃)



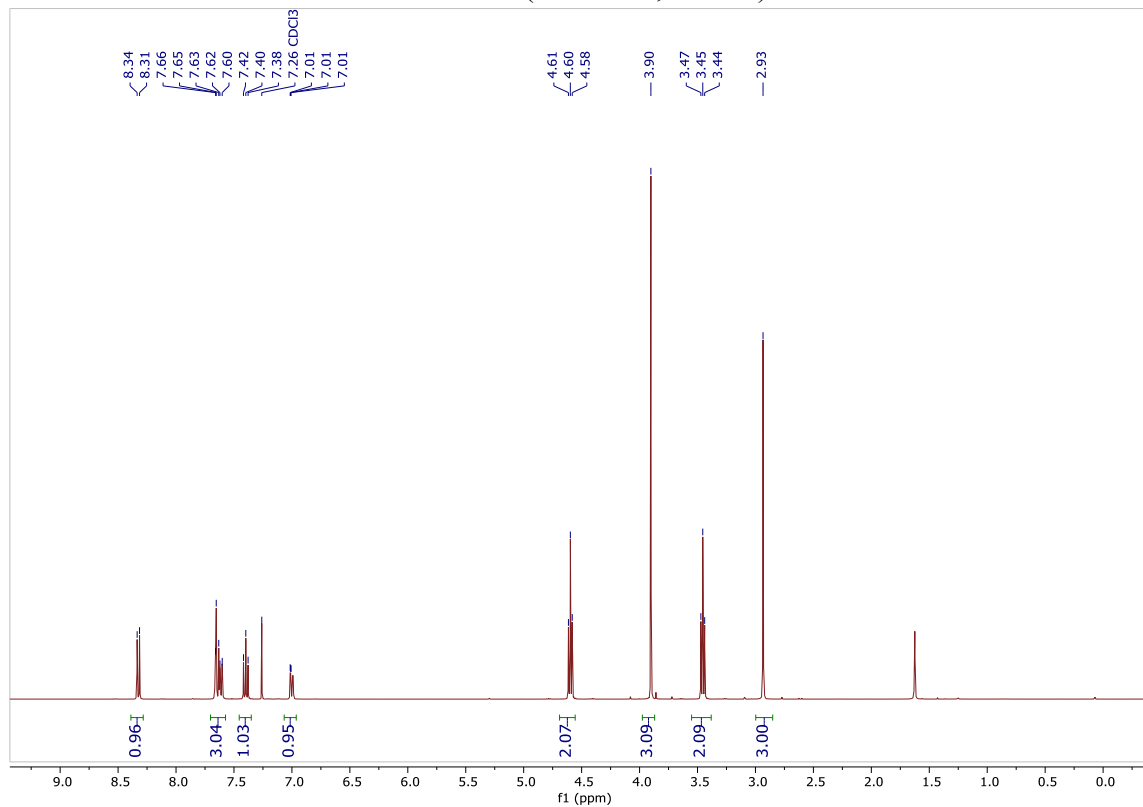
¹³C NMR (101 MHz, CDCl₃)



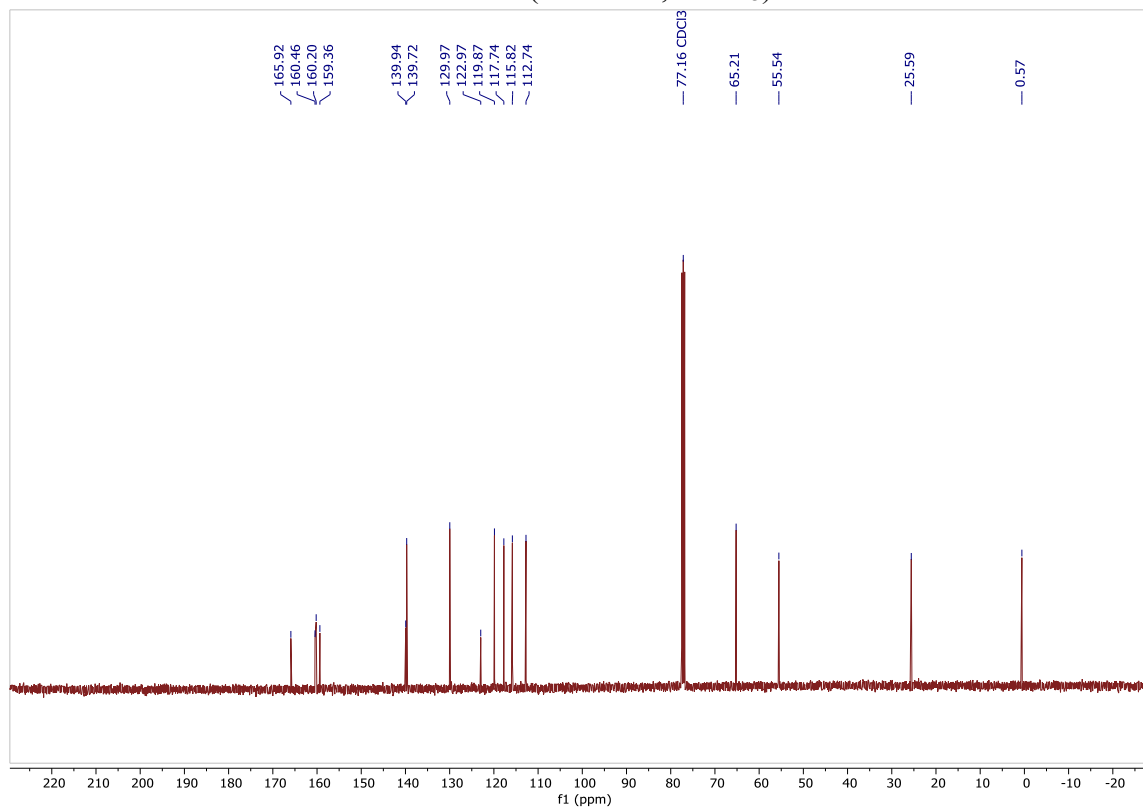
2-Iodoethyl 6-(3-methoxyphenyl)-2-methylnicotinate, S61



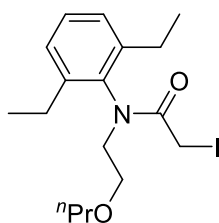
^1H NMR (400 MHz, CDCl_3)



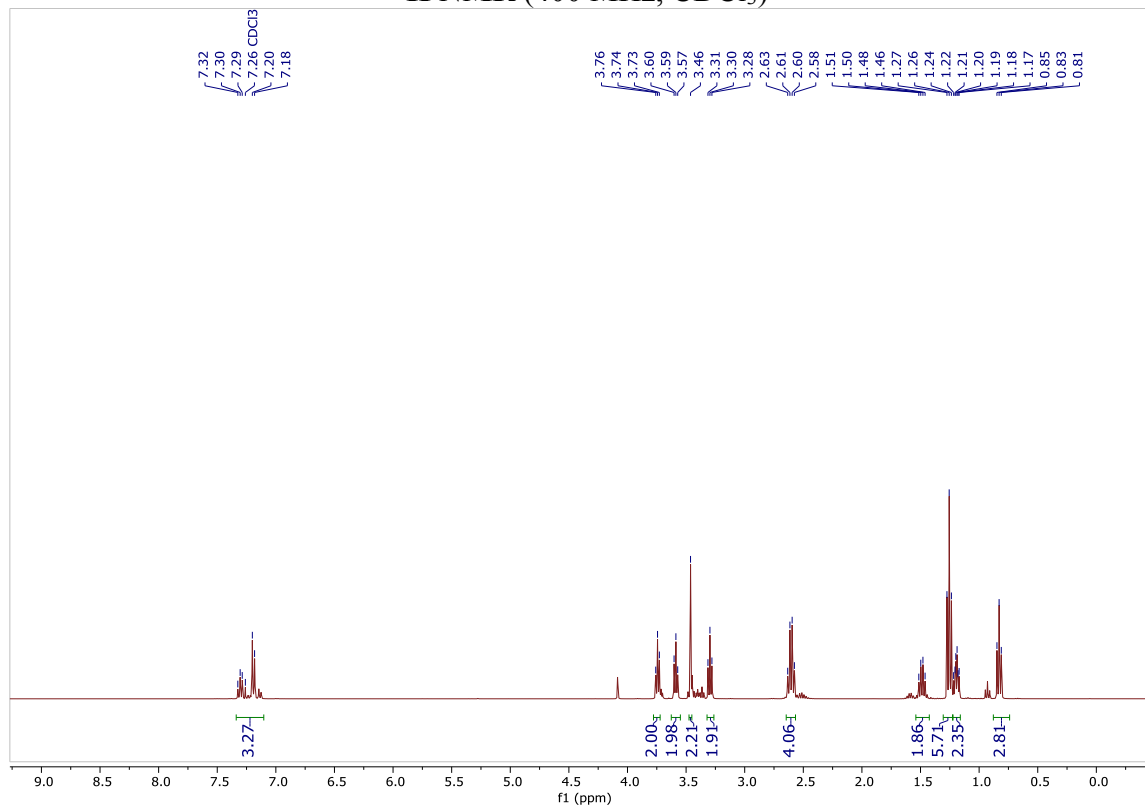
^{13}C NMR (101 MHz, CDCl_3)



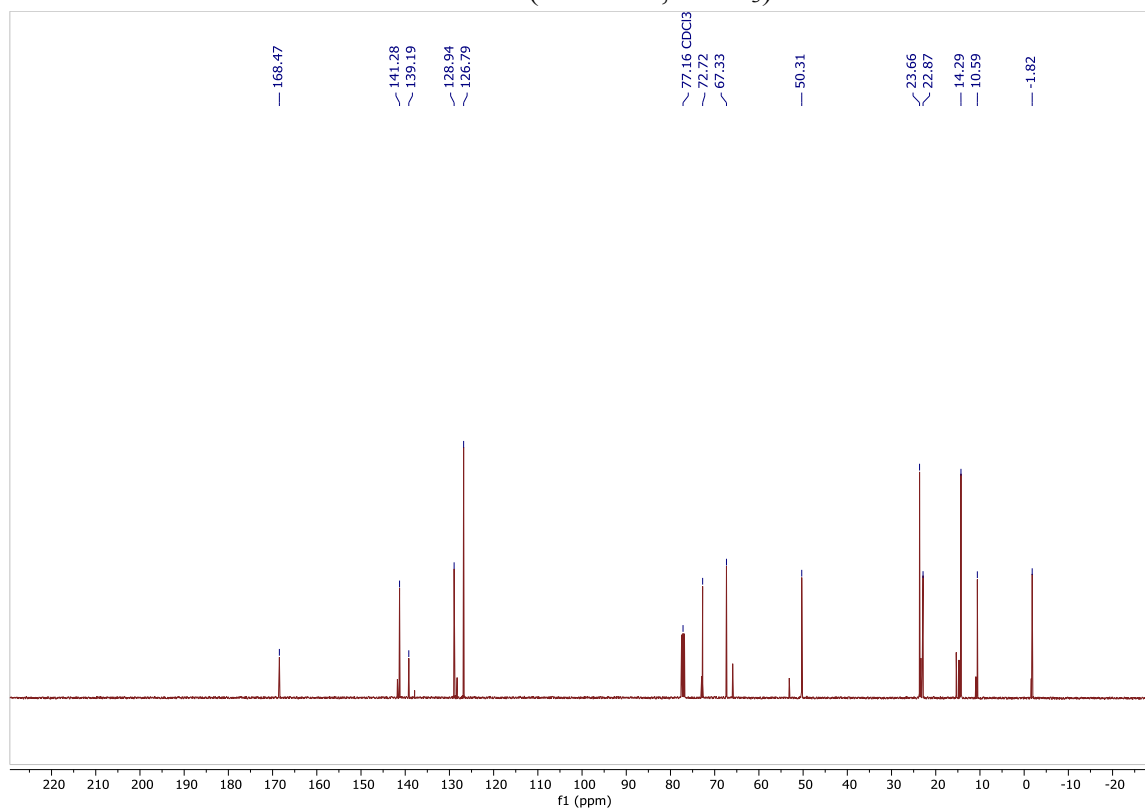
***N*-(2,6-Diethylphenyl)-2-iodo-*N*-(2-propoxyethyl)acetamide, S62**



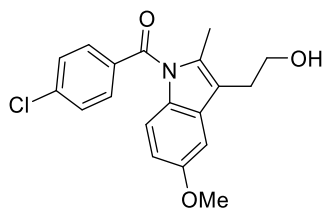
^1H NMR (400 MHz, CDCl_3)



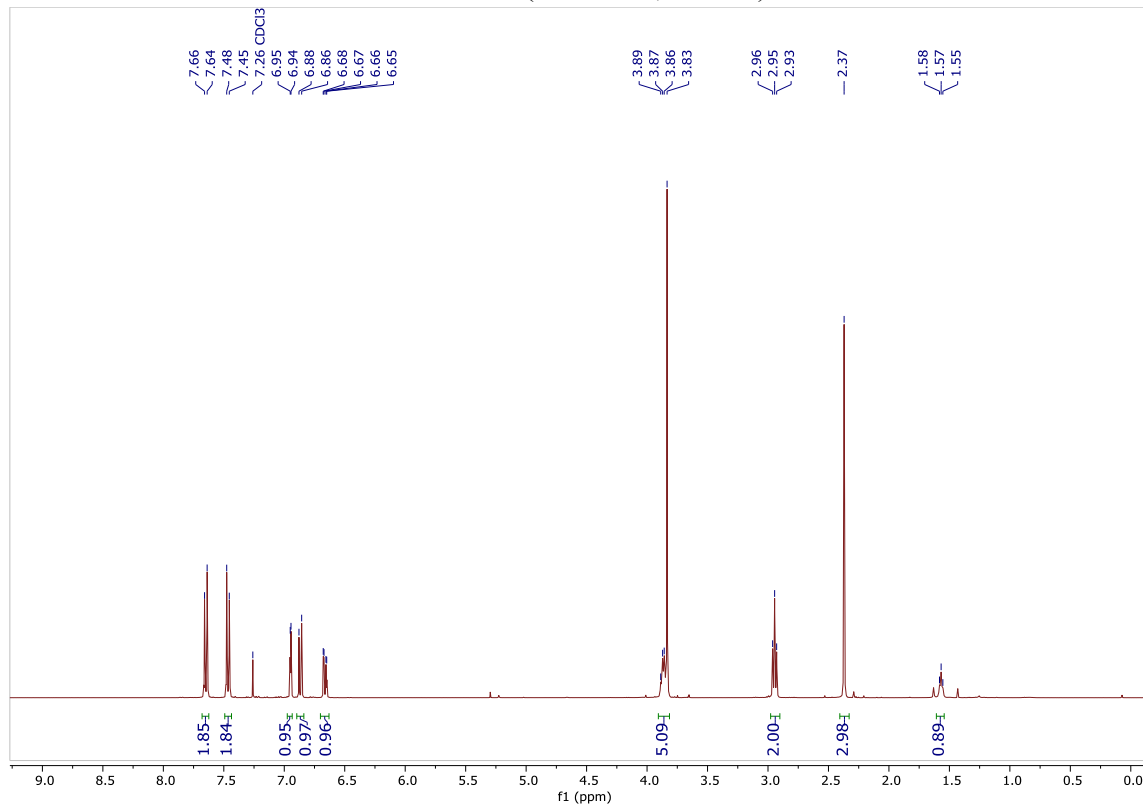
^{13}C NMR (101 MHz, CDCl_3)



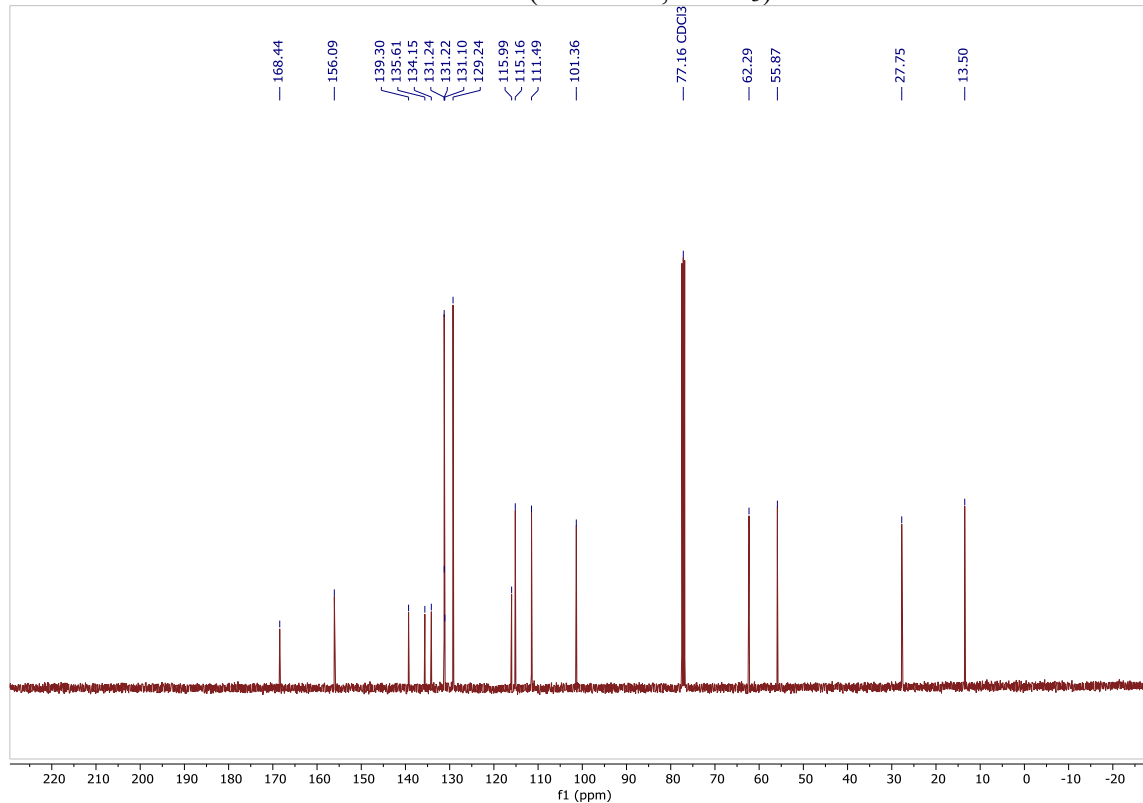
(4-Chlorophenyl)(3-(2-hydroxyethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, S63



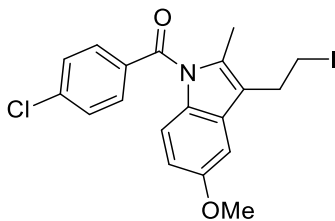
^1H NMR (400 MHz, CDCl_3)



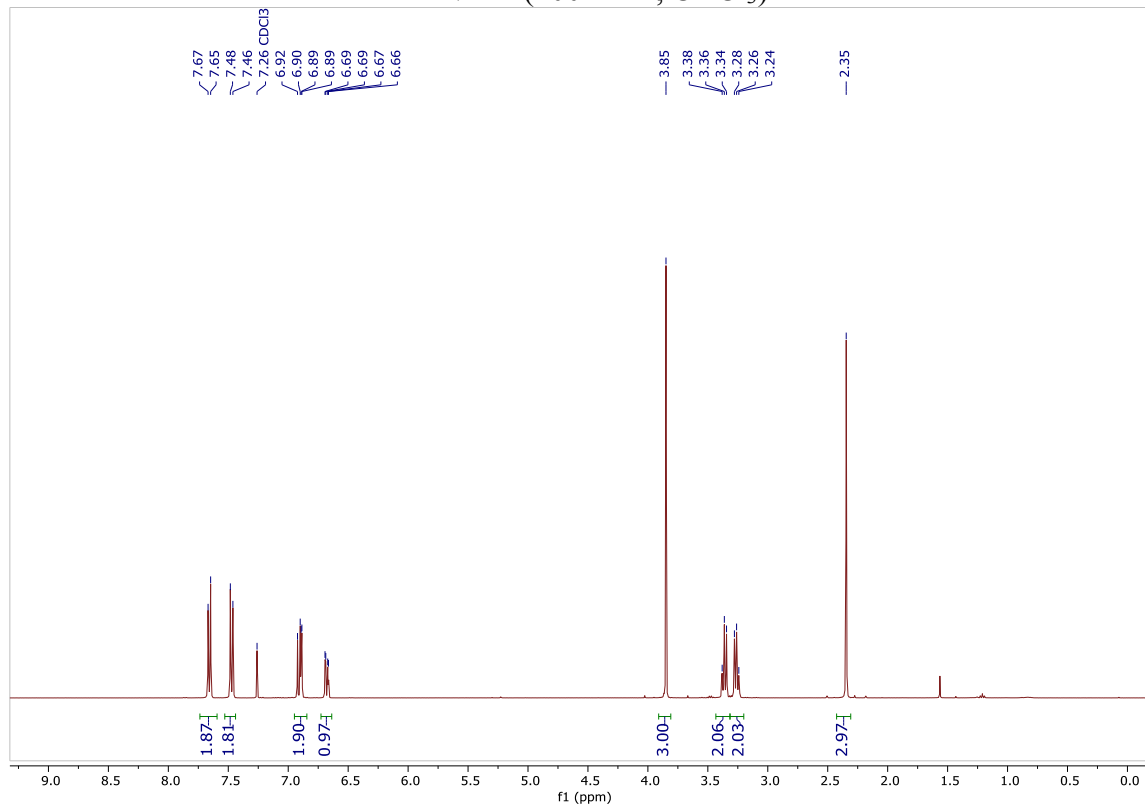
^{13}C NMR (101 MHz, CDCl_3)



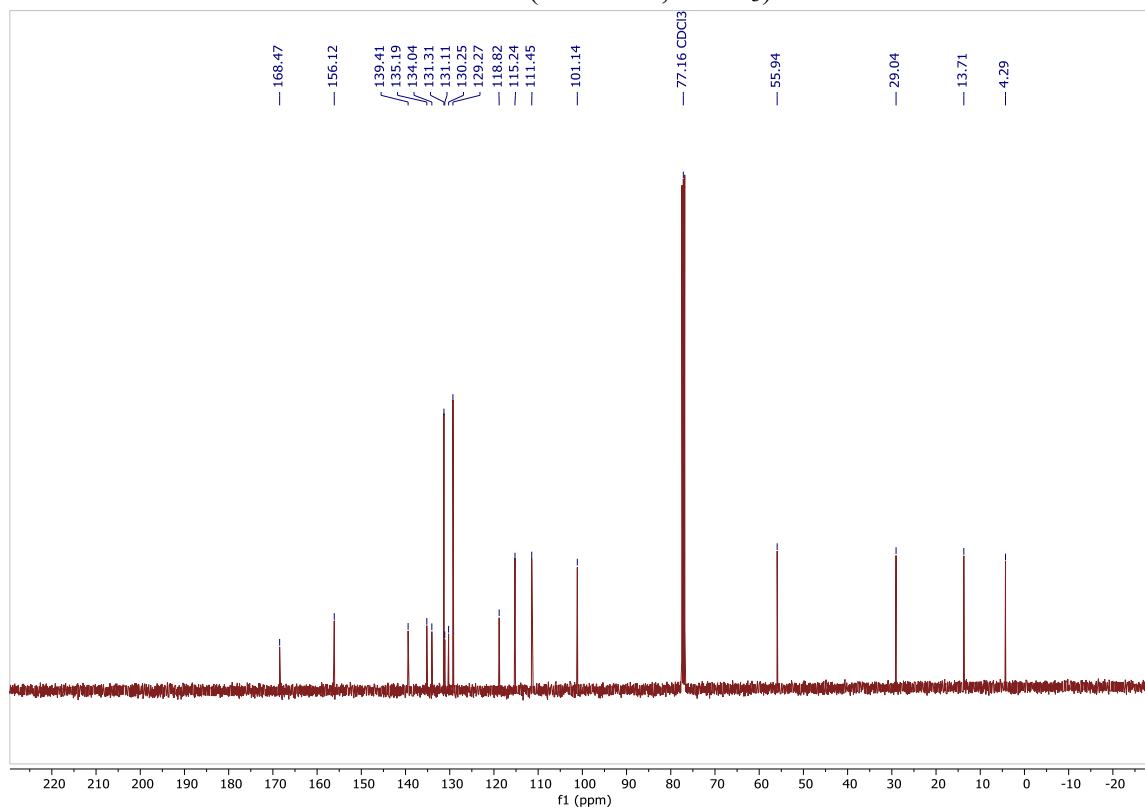
(4-Chlorophenyl)(3-(2-iodoethyl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone, S64



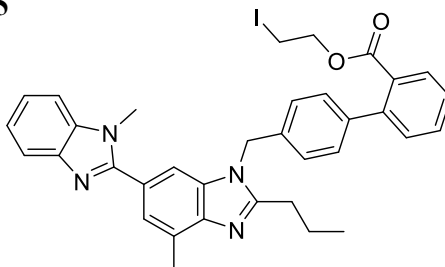
¹H NMR (400 MHz, CDCl₃)



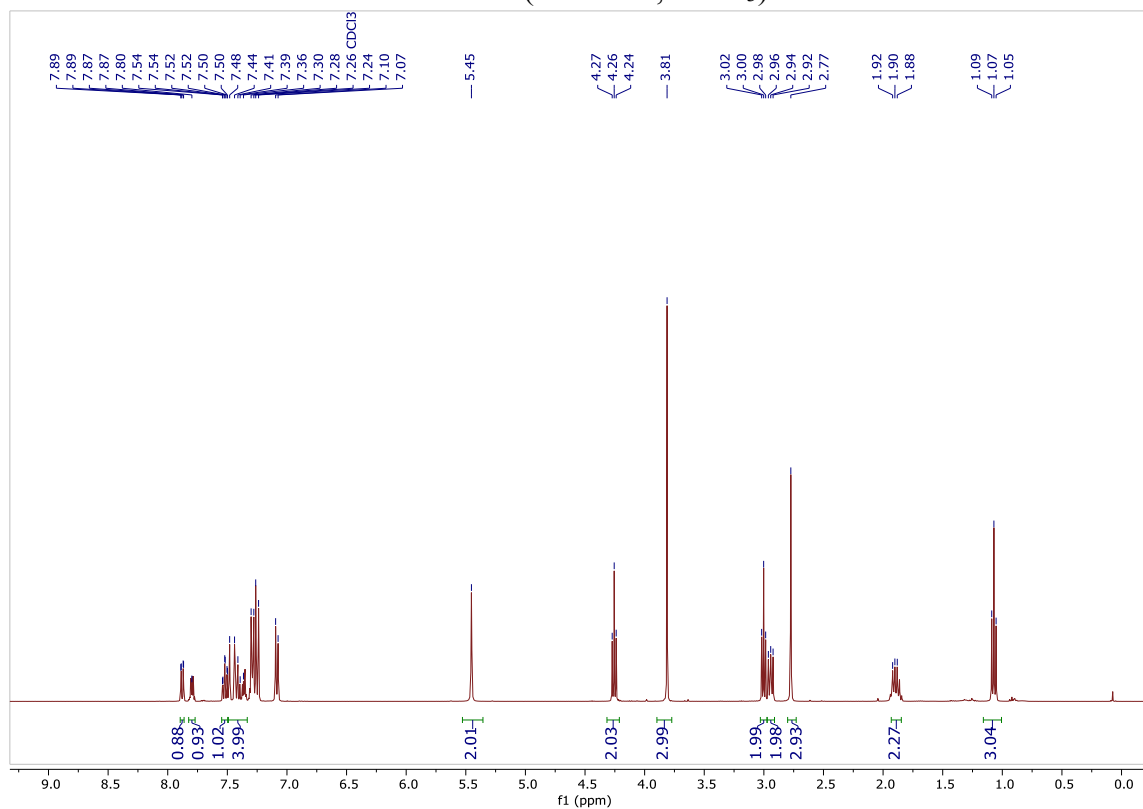
¹³C NMR (101 MHz, CDCl₃)



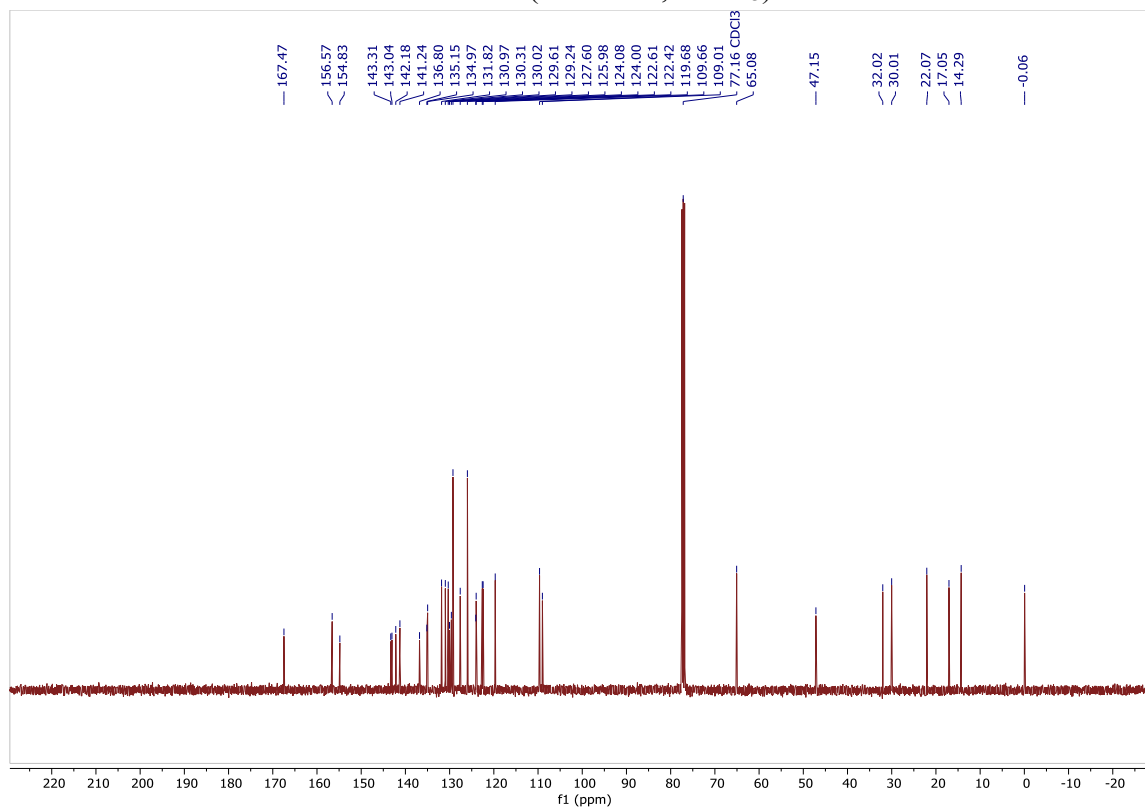
Telimisartan 2-iodoethyl ester, S65



^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (101 MHz, CDCl_3)



Supporting Information.pdf (36.08 MiB)

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checkCIF (full publication check) running

checkCIF/PLATON (full publication check)

Structure factors have been supplied for datablock(s) 77, 87

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No syntax errors found.
Please wait while processing

[CIF dictionary](#)
[Interpreting this report](#)

[Structure factor report](#)

Datablock: 77

Bond precision:	C-C = 0.0148 Å	Wavelength=0.68890
Cell:	a=12.2416(7) b=20.4922(11) c=7.9382(4)	
	alpha=90 beta=91.862(5) gamma=90	
Temperature: 100 K		

	Calculated	Reported
Volume	1990.30(19)	1990.30(19)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C20 H26 I N O2 S	C20 H26 I1 N1 O2 S1
Sum formula	C20 H26 I N O2 S	C20 H26 I1 N1 O2 S1
Mr	471.38	471.40
Dx, g cm ⁻³	1.573	1.573
Z	4	4
Mu (mm ⁻¹)	1.567	1.727
F000	952.0	952.0
F000'	950.79	
h,k,lmax	15,25,9	15,25,9
Nref	4103	4086
Tmin,Tmax		0.490,0.990
Tmin'		

Correction method= # Reported T Limits: Tmin=0.490 Tmax=0.990
AbsCorr = MULTI-SCAN

Data completeness= 0.996 Theta(max)= 25.584
R(reflections)= 0.0861(2314) wR2(reflections)= 0.2630(4070)
S = 0.990 Npar= 226

The following ALERTS were generated. Each ALERT has the format
[test-name_ALERT_alert-type_alert-level](#).
Click on the hyperlinks for more details of the test.

🟡 Alert level B

[PLAT910_ALERT_3_B](#) Missing # of FCF Reflection(s) Below Theta(Min). 16 Note

🟡 Alert level C

[RINTA01_ALERT_3_C](#) The value of Rint is greater than 0.12
Rint given 0.172

PLAT020_ALERT_3_C The Value of Rint is Greater Than 0.12	0.172 Report
PLAT084_ALERT_3_C High wR2 Value (i.e. > 0.25)	0.26 Report
PLAT234_ALERT_4_C Large Hirshfeld Difference C2 --C5 .	0.17 Ang.
PLAT241_ALERT_2_C High 'MainMol' Ueq as Compared to Neighbors of	C3 Check
PLAT241_ALERT_2_C High 'MainMol' Ueq as Compared to Neighbors of	C5 Check
PLAT242_ALERT_2_C Low 'MainMol' Ueq as Compared to Neighbors of	C2 Check
PLAT242_ALERT_2_C Low 'MainMol' Ueq as Compared to Neighbors of	C4 Check

PLAT342_ALERT_3_C	Low Bond Precision on C-C Bonds	0.01482	Ang.
PLAT906_ALERT_3_C	Large K Value in the Analysis of Variance	8.597	Check
PLAT906_ALERT_3_C	Large K Value in the Analysis of Variance	2.014	Check

Alert level G

ABSMU01_ALERT_1_G	Calculation of _exptl_absorpt_correction_mu not performed for this radiation type.		
PLAT083_ALERT_2_G	SHELXL Second Parameter in WGHT Unusually Large	10.94	Why ?
PLAT092_ALERT_4_G	Check: Wavelength Given is not Cu,Ga,Mo,Ag,In Ka	0.68890	Ang.
PLAT343_ALERT_2_G	Unusual sp3 Angle Range in Main Residue for		C2 Check
PLAT343_ALERT_2_G	Unusual sp3 Angle Range in Main Residue for		C4 Check
PLAT793_ALERT_4_G	Model has Chirality at C7 (Centro SPGR)		R Verify

And 2 other PLAT793 Alerts

PLAT793_ALERT_4_G	Model has Chirality at C11 (Centro SPGR)		R Verify
PLAT793_ALERT_4_G	Model has Chirality at C12 (Centro SPGR)		S Verify

PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L= 0.600	18	Note
PLAT960_ALERT_3_G	Number of Intensities with I < - 2*sig(I) ...	3	Check
PLAT984_ALERT_1_G	The I-f' = -0.7740 Deviates from the B&C-Value	-0.4882	Check

And 3 other PLAT984 Alerts

PLAT984_ALERT_1_G	The N-f' = 0.0040 Deviates from the B&C-Value	0.0056	Check
PLAT984_ALERT_1_G	The O-f' = 0.0070 Deviates from the B&C-Value	0.0101	Check
PLAT984_ALERT_1_G	The S-f' = 0.1050 Deviates from the B&C-Value	0.1187	Check

PLAT985_ALERT_1_G	The I-f'' = 1.7190 Deviates from the B&C-Value	1.7230	Check
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- 0 **ALERT level A** = Most likely a serious problem - resolve or explain
 1 **ALERT level B** = A potentially serious problem, consider carefully
 11 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
 15 **ALERT level G** = General information/check it is not something unexpected

- 6 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
 7 ALERT type 2 Indicator that the structure model may be wrong or deficient
 8 ALERT type 3 Indicator that the structure quality may be low
 6 ALERT type 4 Improvement, methodology, query or suggestion
 0 ALERT type 5 Informative message, check

Datablock: 87

Bond precision: C-C = 0.0030 A Wavelength=0.68890
 Cell: a=6.30332(4) b=11.85008(9) c=28.71209(18)
 alpha=90 beta=90 gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2144.65(3)	2144.64(3)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C24 H35 I O	C24 H35 I1 O1
Sum formula	C24 H35 I O	C24 H35 I1 O1
Mr	466.42	466.45
Dx, g cm-3	1.445	1.445
Z	4	4
Mu (mm-1)	1.366	1.503
F000	960.0	960.0
F000'	958.30	
h,k,lmax	10,20,49	10,19,48
Nref	11226[6277]	10443
Tmin,Tmax		0.740,0.970
Tmin'		

Correction method= # Reported T Limits: Tmin=0.740 Tmax=0.970

AbsCorr = MULTI-SCAN

Data completeness= 1.66/0.93 Theta(max)= 36.089

R(reflections)= 0.0367(9448) wR2(reflections)= 0.0967(10425)

S = 1.000 Npar= 236

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

PLAT910 ALERT 3 B Missing # of FCF Reflection(s) Below Theta(Min). 17 Note

PLAT915_ALERT_3_C No Flack x Check Done: Low Friedel Pair Coverage 90 %

[ABSMU01_ALERT_1_G](#) Calculation of _exptl_absorpt_correction_mu
not performed for this radiation type.

[PLAT092_ALERT_4_G](#) Check: Wavelength Given is not Cu,Ga,Mo,Ag,In Ka 0.68890 Ang.

[PLAT142_ALERT_4_G](#) s.u. on b - Axis Small or Missing 0.00009 Ang.

[PLAT143_ALERT_4_G](#) s.u. on c - Axis Small or Missing 0.00018 Ang.

[PLAT343_ALERT_2_G](#) Unusual sp3 Angle Range in Main Residue for C2 Check

[PLAT343_ALERT_2_G](#) Unusual sp3 Angle Range in Main Residue for C4 Check

[PLAT431_ALERT_2_G](#) Short Inter HL..A Contact I1 ..025 . 3.18 Ang.

1/2-x,1-y,-1/2+z = 2_564 Check

[PLAT791_ALERT_4_G](#) Model has Chirality at C7 (Chiral SPGR) R Verify

And 6 other PLAT791 Alerts

PLAT791_ALERT_4_G	Model has Chirality at C10	(Chiral SPGR)	S Verify
PLAT791_ALERT_4_G	Model has Chirality at C12	(Chiral SPGR)	S Verify
PLAT791_ALERT_4_G	Model has Chirality at C16	(Chiral SPGR)	R Verify
PLAT791_ALERT_4_G	Model has Chirality at C17	(Chiral SPGR)	S Verify
PLAT791_ALERT_4_G	Model has Chirality at C20	(Chiral SPGR)	S Verify
PLAT791_ALERT_4_G	Model has Chirality at C21	(Chiral SPGR)	S Verify

PLAT912 ALERT 4 G	Missing # of FCF Reflections Above Sth/L= 0.600	265	Note
PLAT913 ALERT 3 G	Missing # of Very Strong Reflections in FCF	1	Note
PLAT984 ALERT 1 G	The I-f'=- 0.7740 Deviates from the B&C-Value	-0.4882	Check
PLAT984 ALERT 1 G	The O-f'= 0.0070 Deviates from the B&C-Value	0.0101	Check
PLAT985 ALERT 1 G	The I-f''= 1.7190 Deviates from the B&C-Value	1.7230	Check

```
0 ALERT level A = Most likely a serious problem - resolve or explain
1 ALERT level B = A potentially serious problem, consider carefully
1 ALERT level C = Check. Ensure it is not caused by an omission or oversight
19 ALERT level G = General information/check it is not something unexpected
```

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4 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
11 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

```

checkCIF publication errors

PUBL024_ALERT 1 A The number of authors is greater than 9.
Please specify the role of each of the co-authors
for your paper.

1 **ALERT level A** = Data missing that is essential or data in wrong format
0 **ALERT level G** = General alerts. Data that may be required is missing

Publication of your CIF

You should attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the nature of your study may justify the reported deviations from journal submission requirements and the more serious of these should be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. *checkCIF* was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

If level A alerts remain, which you believe to be justified deviations, and you intend to submit this CIF for publication in a journal, you should additionally insert an explanation in your CIF using the Validation Reply Form (VRF) below. This will allow your explanation to be considered as part of the review process.

Validation response form

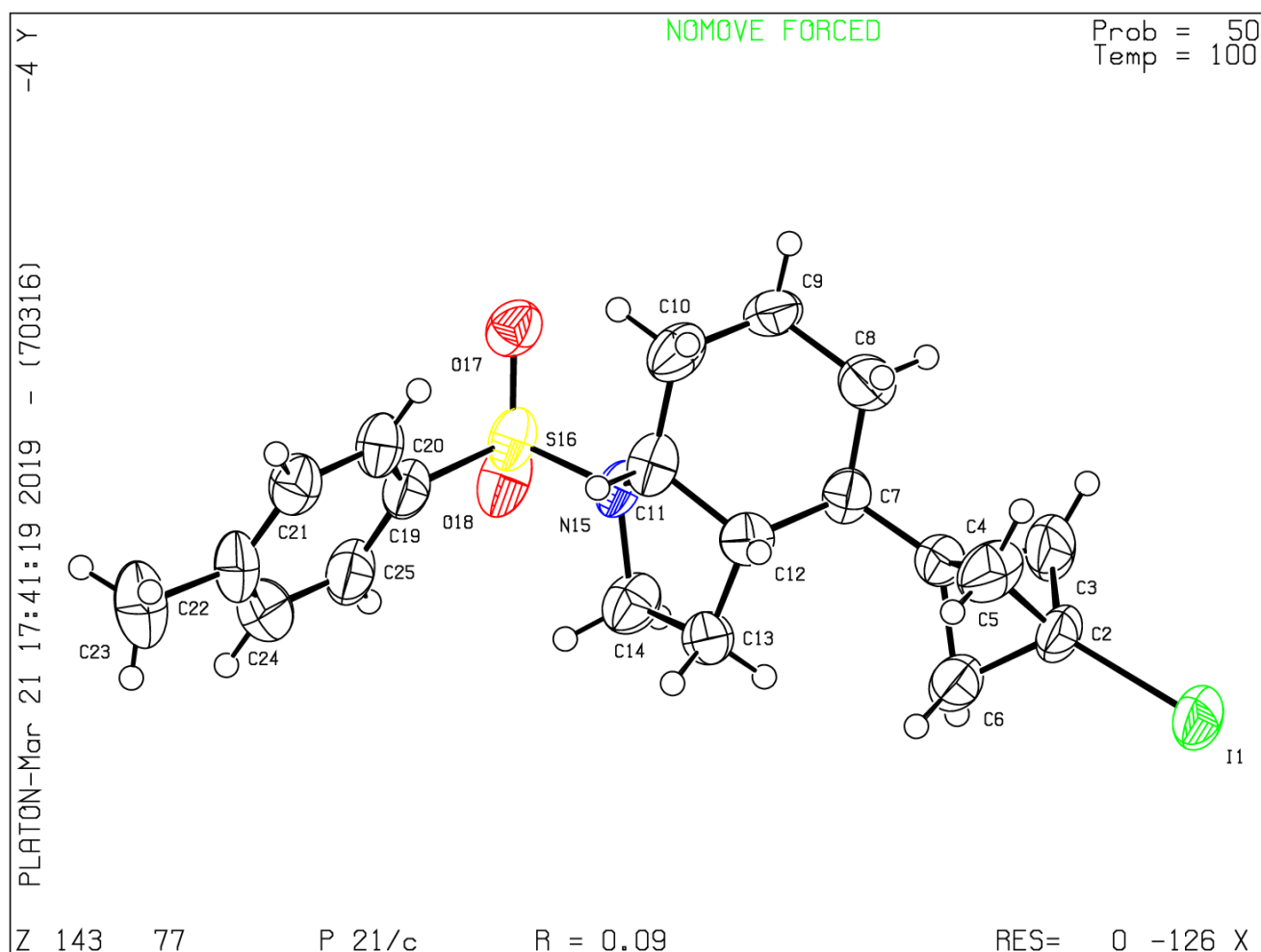
Please find below a validation response form (VRF) that can be filled in and pasted into your CIF.

```
# start Validation Reply Form
_vrf_PUBL024_GLOBAL
;
PROBLEM: The number of authors is greater than 9.
RESPONSE: ...
;
# end Validation Reply Form
```

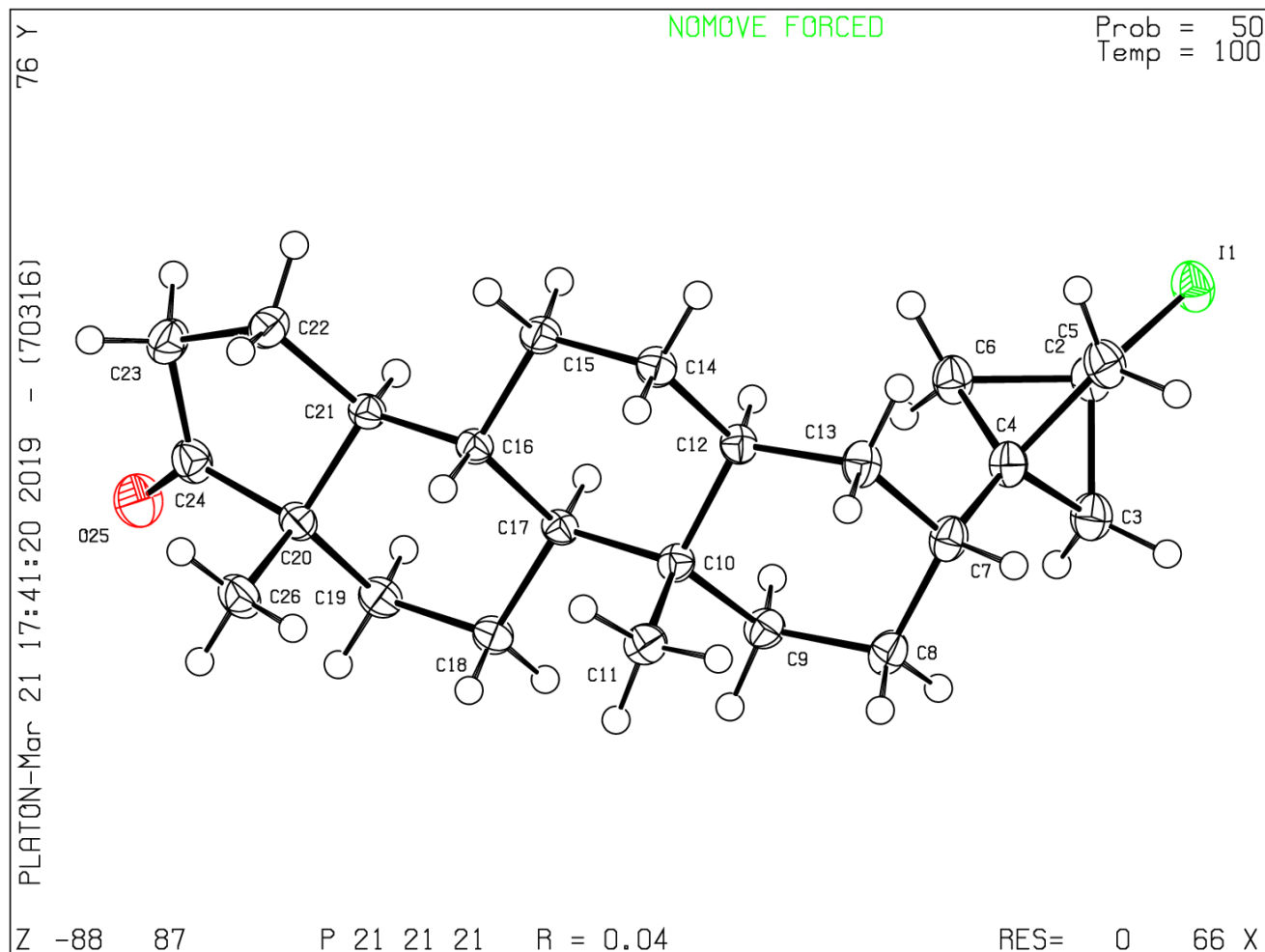
If you wish to submit your CIF for publication in Acta Crystallographica Section C or E, you should upload your CIF via [the web](#). If you wish to submit your CIF for publication in IUCrData you should upload your CIF via [the web](#). If your CIF is to form part of a submission to another IUCr journal, you will be asked, either during electronic [submission](#) or by the Co-editor handling your paper, to upload your CIF via our web site.

PLATON version of 17/03/2019; check.def file version of 04/03/2019

Datablock 77 - ellipsoid plot



Datablock 87 - ellipsoid plot



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Other files

CrystallographicData.cif (49.70 KiB)

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OptimisedCartesianCoordinates.zip (38.20 KiB)

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