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Iminophosphoranes are reported as convenient precursors to amides, ureas, carbamates and other carbonyl-containing molecules through CO_2 -fixation. Key to this transformation with stable isotopes and carbon-11 is interception of the reactive isocyanate intermediate. Automated synthesis and isolation of PET radiopharmaceuticals is achieved.

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Interrupted Aza-Wittig Reactions Using Iminophosphoranes to Synthesize ^{11}C -Carbonyls

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Abstract

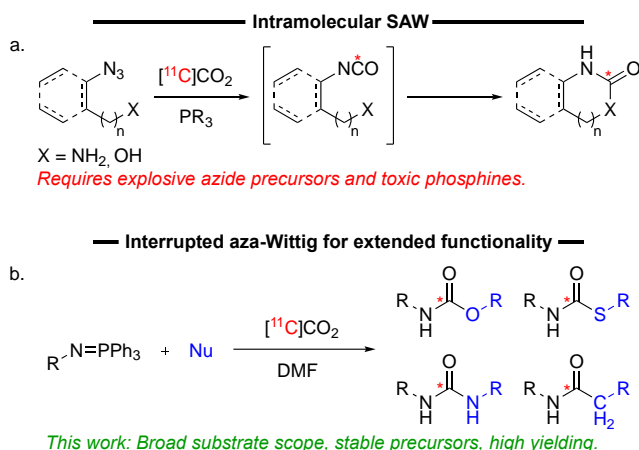
Carbonyls are frequently found in bioactive compounds due to their propensity for hydrogen bonding and synthetic utility in functional group manipulations. Carbon-11 (^{11}C) is routinely incorporated into small molecule radiotracers for positron emission tomography (PET) imaging. Herein, we report a high-yielding, direct CO_2 -fixation methodology coupling structurally diverse iminophosphoranes with various nucleophiles to synthesize ureas, carbamates, thiocarbamates, and amides, and which is amenable for ^{11}C radiolabeling. The success of this strategy relies upon the interception of an isocyanate intermediate of sequential aza-Wittig reactions using a suitable nucleophile. This methodology is practical, as demonstrated by the synthesis of >35 products and isolation of the radiopharmaceuticals [^{11}C]URB694 (13% radiochemical yield, $69\text{ GBq}\cdot\mu\text{mol}^{-1}$) and [^{11}C]glibenclamide (62% RCY, $59\text{ GBq}\cdot\mu\text{mol}^{-1}$), within 17 minutes and 21 minutes from [^{11}C] CO_2 , respectively.

Introduction

Positron emission tomography (PET) is a non-invasive molecular imaging modality used to evaluate biological processes *in vivo* with short-lived radionuclides. PET radiopharmaceuticals are used to diagnose metastatic and cardiovascular diseases, conduct non-invasive pathology studies to detect biomarkers of neurodegeneration, and to probe molecular and functional mechanisms in living systems.¹ Carbon-11 (^{11}C , $t_{1/2} = 20.4\text{ min}$) is prized for isotopic labeling of biomolecules and pharmaceuticals, and is routinely incorporated into PET imaging agents for both research and clinical applications.^{2,3} Currently, a lack of diverse methods for directly incorporating [^{11}C] CO_2 into complex molecules has limited its use.⁴ Consequently, [^{11}C] CO_2 is most often converted into reactive secondary precursors such as [^{11}C] CH_3I or [^{11}C] CH_3OTf , which are accompanied by elongated processing times and significant reductions in radiochemical yield due

to sub-quantitative conversions.⁵⁻⁸ Isocyanates are valuable synthetic intermediates that can be readily converted into pharmaceutically-relevant functional groups such as carbamates, ureas, and amides.^{9,10} Conventional approaches to synthesizing ¹¹C-isocyanates rely on stepwise trapping of [¹¹C]CO₂ with amines, followed by dehydration using phosphoryl chloride (POCl₃) or Mitsunobu-type conditions.^{4,11,12} Importantly, the former strategy displays poor tolerance towards anilines and the highly acidic conditions pose challenges for maintaining efficient trapping of [¹¹C]CO₂ in solution. The latter technique has displayed improved utility for synthesizing asymmetrical ureas¹² and also amides using either Grignard reagents¹³ or organozinc coupling reactions,¹⁴ though high mass loading of azo reagents and phosphines may complicate radiotracer purification. Each strategy requires careful control of temperature and reagent concentrations during sequential reaction steps in order to prevent formation of complex mixtures of symmetrical byproducts and heterocycles.^{11,15} Iminophosphoranes have been shown to undergo the aza-Wittig reaction directly with CO₂ to produce isocyanates in high yields.¹⁶ Indeed, similar reactivity towards carbonyl containing functional groups has been exploited in the synthesis of complex alkaloids such as (-)-dendrobine and a myriad heterocyclic drugs and natural products.^{17,18} In the context of ¹¹C, the commercially available precursor *N*-(triphenylphosphoranylidene)aniline was previously reported to prepare acyclic ¹¹C-ureas from [¹¹C]CO₂ in moderate radiochemical yields (RCYs).¹⁹ Del Vecchio *et al.* deployed *o*-azidoanilines and azido alcohols with dimethylphenylphosphine to synthesize cyclic ureas and carbamates, including oxatomide, domperidone, and zolmitriptan in useful yields through a proposed intramolecular Staudinger aza-Wittig sequence (SAW, Scheme 1a) upon heating to 70 °C.^{20,21} An intermolecular variant of this reaction produced a linear carbamate in low RCY at much higher temperature.

We aimed to develop conditions that are high yielding and selective for C–O, C–N, C–C, and C–S bond formation and would be amenable for one-pot $[^{11}\text{C}]\text{CO}_2$ -fixation to prepare radiopharmaceuticals and novel tracer candidates. Through the synthesis of functionalized iminophosphorane precursors, this approach would obviate the need for highly acidic POCl_3 , Mitsunobu reagents, explosive azide precursors, and toxic phosphines used in current methodologies, enhancing the substrate versatility and practicality of this method for good manufacturing practices (GMP) environments (Scheme 1b). Herein, we describe a versatile and efficient approach to carbonyl ligation using iminophosphorane- CO_2 -fixation coupled with intermolecular nucleophilic addition. This method is effective for synthesizing acyclic products with stable isotopes under mild conditions and is suitable for automated synthesis and ^{11}C radiolabeling. We demonstrate a broad substrate scope, high functional group tolerance, and practical application for the synthesis and isolation of radiopharmaceuticals.



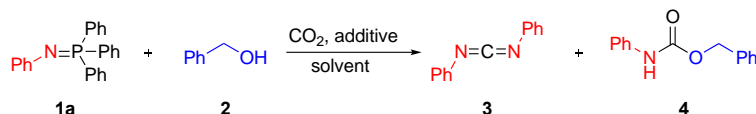
Scheme 1. Synthetic approaches to iminophosphorane $[^{11}\text{C}]\text{CO}_2$ -fixation.

Results and Discussion

At the outset, we focused on developing a nucleophilic coupling strategy to iminophosphorane- CO_2 fixation conditions using stable isotopes, since no such straightforward high yielding

procedure for this coupling has been reported.¹⁶ First, CO₂ was bubbled into a heated toluene solution containing *N*-(triphenylphosphoranylidene)aniline (**1a**) until complete consumption of the iminophosphorane, followed by the addition of benzyl alcohol (**2**).

Table 1. Optimization of reaction conditions



Entry	Solvent	[2] (mM)	3 yield (%)	4 yield (%)
1 ^{a,b}	toluene	100	77	6
2 ^{a,b}	toluene	150	77	6
3 ^{a,c}	toluene	100	42	36
4 ^{a,c}	toluene	250	0	84
5 ^d	toluene	250	0	70
6 ^d	1,4-dioxane	250	0	72
7 ^d	DMF	250	0	75
8 ^d	ACN	250	0	78
9 ^{d,e}	ACN	250	0	84
10 ^{d,f}	ACN	250	0	70

^aYields obtained by UPLC/MS. Reactions performed in toluene at 110 °C. ^bNucleophile added after iminophosphorane consumption.

^cNucleophile added at *t* = 0. ^dConditions: **2** (0.625 mmol), solvent (2.5 mL), 85 °C; then **1** (100 mM, 2.5 mL) added over 1 h. Reaction time: 2 hr. Isolated yields. ^eDBU (2.6 equiv). ^fBEMP (2.6 equiv.)

Low yield of the desired product **4** (6%) was observed using stepwise addition (Table 1, entry 1). The observed major product was the symmetrical *N,N'*-diphenylcarbodiimide (CDI, **3**), likely formed by a second aza-Wittig coupling reaction to the isocyanate intermediate.¹⁸ The ratio of **4**:**3** increased to 0.9:1 when the nucleophile was present from the beginning of the reaction (entry 3). Increasing the concentration of **2** led to exclusive formation of **4** in 84% yield (entry 4). This suggests that short-lived free isocyanates are formed in the presence of iminophosphoranes, subject to two competing reaction pathways: CDI formation and carbamate formation. Thus, at high

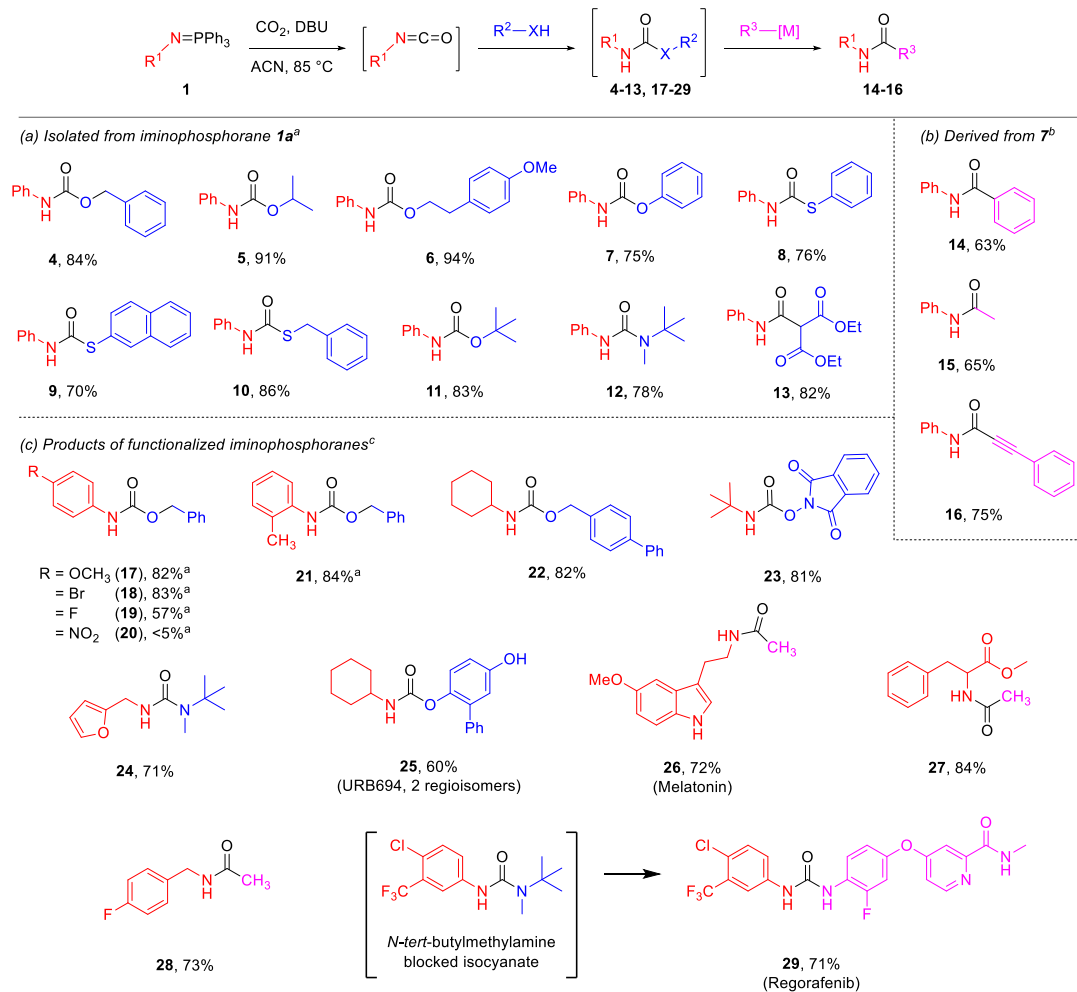
concentrations of an intercepting nucleophile, it is possible to selectively divert the reaction towards intermolecular ligation. Carbamate **4** could be prepared and isolated in good yields from hydrocarbon, ethereal, and polar solvents using similar conditions (entries 5–8). With our primary focus on establishing easily translatable conditions to ^{11}C radiochemistry, we were delighted to find that two common CO_2 trapping bases, amidine DBU and phosphazene BEMP (2.6 equiv.), significantly increased the rate of formation of **4**, concomitant with moderate impacts in yield (entries 9–10, table S1). These effects are likely due to the increased availability of soluble CO_2 in the form of activated complexes.^{22,23}

We assessed the compatibility of the iminophosphorane- CO_2 -fixation method with a diverse scope of nucleophiles (Scheme 2a). Under our developed conditions, carbamates derived from benzyl, isopropyl, and 4-methoxyphenethyl alcohol were isolated in 84–94% yields (**4-6**). In contrast, phenyl carbamates and thiocarbamates (**7-9**) required higher nucleophile concentrations to achieve yields in excess of 70%, likely due to their propensity for elimination. Benzyl mercaptan also proved to be a compatible nucleophile, forming the corresponding thiocarbamate **10** in excellent yield (86%). Sterically hindered nucleophiles such as *tert*-butanol yielded product **11** (83%) in high yield, and *N*-methyl-*N*-*tert*-butylamine also provided the urea **12** in 78% yield. We were gratified to find that amides such as **13** (82%) could be accessed directly by carbon-carbon bond formation using diethyl malonate. Despite this success, some nucleophiles were found to be incompatible with the interrupted aza-Wittig conditions, including Grignard reagents, and phenylacetylene. However, a number of our synthesized products (**7-9**, **11-12**) stand in as blocked isocyanates, and facilitate indirect nucleophilic substitution (Scheme 2b).²⁴ *In situ* formed *O*-phenylcarbamate **7** could be successfully transformed to amides **14-16**, all in moderate to good

yields based on iminophosphorane **1a**. Overall, both direct and indirect nucleophilic substitutions are robust, and further open the door to selective C-C bond formation using iminophosphoranes.

We next investigated the scope of functionalized aryl iminophosphoranes synthesized by the Kirsanov reaction and isolated by our modified general procedure (Scheme 2c, see ESI for details).¹⁸ First, CBz-protected products (**17-21**) were isolated to determine sensitivity to electronic and steric features of iminophosphoranes under the optimized conditions. Electron-rich arenes, aryl bromides, and *ortho*-substitution (**17-18**, **21**) were all well-tolerated in comparison with electron-deficient iminophosphoranes (**19-20**). Alkyl iminophosphoranes afforded products such as carbamate **22** (82%) and blocked isocyanates **23-24** in good yields. The utility of this method for biopharmaceuticals was assessed by targeting the fatty acid amide hydrolase inhibitor URB694 (**25**), melatonin (**26**), and the oral multi-kinase inhibitor regorafenib (**29**). Hydroquinone carbamate **25** was isolated as a mixture of regioisomers in 60% yield.¹¹ Indirect substitution using phenol-blocked isocyanates yielded melatonin **26** (72%), phenylalanine derivative **27** (84%), and electron-deficient amide **28** (73%). Finally, the urea regorafenib **29** was synthesized first by direct nucleophilic coupling, though indirect substitution using an *N-tert*-butylmethanamine blocked isocyanate intermediate better facilitated purification of **29** in 71% overall yield.²⁵

Scheme 2: Interrupted aza-Wittig for Extended Functionality: Reaction Scope

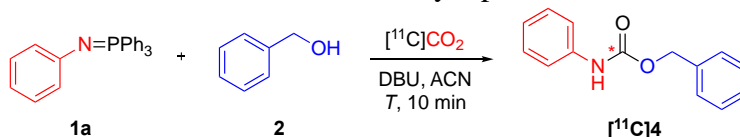


^aConditions: **1** (0.25 mmol), R²-XH (2.5 equiv.), DBU (2.6 equiv.), ACN (2.5 mL), reflux; isolated yields. ^b PhOH (10 equiv.), R³-MgX (20 equiv.) or R³-SH (2.5 equiv.) or PhCCH (12 equiv.), THF. ^c R²-XH (10 equiv.), LHMDS (0.99 equiv.), THF. See ESI for detailed procedures.

Satisfied with the iminophosphorane-CO₂ nucleophilic coupling methodology using stable isotopes, we were determined to apply this method to carbon-11 radiochemistry. Since [¹¹C]CO₂ is the limiting reagent in these processes (typically <1 μmol), reconsideration of reaction

conditions to produce [^{11}C]**4** was required (Table 2). First, we focused on the influence of the concentration of **1a** on product yield using high concentrations of DBU and benzyl alcohol in ACN (entry 1). We noted a low 13% RCY with these initial conditions, mainly due to a large excess of unreacted [^{11}C]CO₂. Increasing the concentration of **1a** (entries 2–3) led to maximum 32% RCY and reducing the concentration of DBU to 100 mM enhanced the selectivity toward [^{11}C]**4** (entry 4–5). Increasing the reaction temperature in DMF to 100 °C resulted in 65% RCY (entries 6–7). Finally, increasing the concentration of nucleophile **2** further improved the selectivity of [^{11}C]**4**, leading to a 91% RCY (entries 7–9). Trapping efficiencies of [^{11}C]CO₂ during the optimization of [^{11}C]**4** were all greater than 90%.

Table 2. Radiochemistry Optimization



Entry	<i>T</i> (°C)	[1a] (mM)	[2] (mM)	[DBU] (mM)	RCY ^a (%)
1	65	7	200	200	13
2	65	70	200	200	32
3	65	100	200	200	29
4	65	70	200	150	39
5	65	70	200	100	56
6 ^b	65	70	200	100	62
7 ^b	100	70	200	100	65
8 ^b	100	70	600	100	78
9 ^b	100	70	1200	100	91

^aRadiochemical yield calculated from relative integration of HPLC-UV chromatogram. ^bReaction performed in DMF.

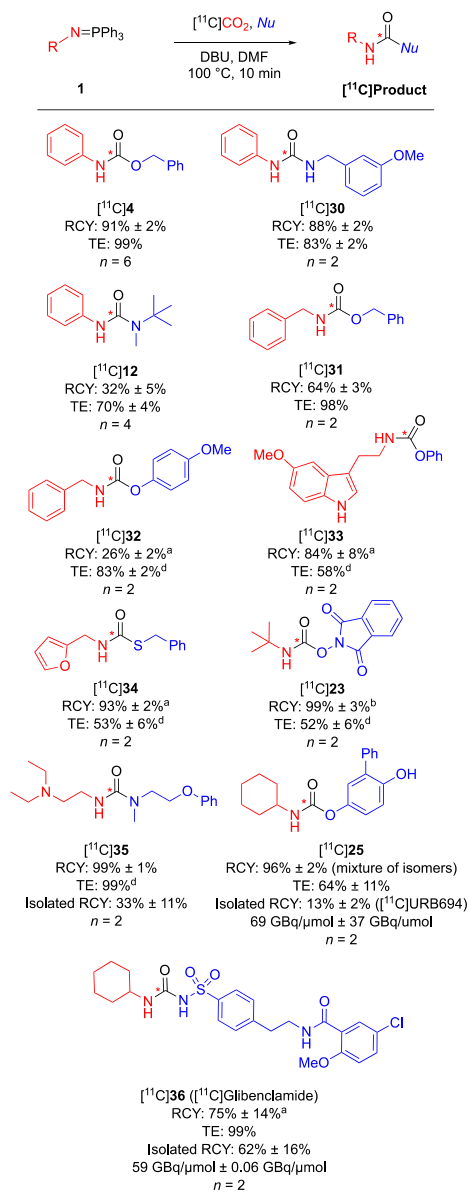
Structurally diverse iminophosphoranes were also used to successfully radiolabel compounds using this procedure (Scheme 3). Aniline derived products using iminophosphorane **1a** include labeled urea [^{11}C]**30** in 88% RCY, and blocked isocyanate [^{11}C]**12** in 32% RCY. Using

benzyl iminophosphorane, *O*-benzyl carbamate [^{11}C]**31** was formed in 64% yield. By substituting DABCO for DBU, *O*-aryl carbamate [^{11}C]**32** (26%), 5-methoxytryptamine carbamate [^{11}C]**33** (84%), and thiocarbamate [^{11}C]**34** (93%) could be radiolabeled, with trapping efficiencies ranging from 53–83%. We suspect that mildly basic conditions and higher nucleophile concentrations improve the yields of **32-34** due to their sensitivity towards low temperature elimination.²⁶ From *tert*-butyl iminophosphorane, *N*-hydroxysuccinimide-derived [^{11}C]**23** (99%) was also efficiently radiolabeled.

To further demonstrate the practicality of this technique [^{11}C]**35**, an experimental antiarrhythmic compound, also containing the β -glucocerebrosidase activating moiety *N*-methyl-*N*-(2-phenoxyethyl)amine, was isolated using a fully automated method (see ESI).^{27,28} [^{11}C]**35** was labeled with 99% RCY starting from 15.7 GBq of [^{11}C]CO₂, and obtained in an isolated yield of 33% \pm 10.6% (2.7 \pm 0.4 GBq) within 22 min from [^{11}C]CO₂ delivery. The fatty acid amide hydrolase inhibitor [^{11}C]URB694 ([^{11}C]**25**, [^{11}C]CURB) is used in clinical research studies to investigate psychiatric illnesses and alcohol use disorder, and was prepared from cyclohexyliminophosphorane in 96% \pm 2% RCY (2:3 regioselectivity).^{29,30} From 25.9 GBq of [^{11}C]CO₂, 1.9 GBq \pm 0.7 GBq of [^{11}C]CURB was obtained as the major isomer in 99% radiochemical purity, with an isolated decay corrected yield of 13% \pm 2%, and a molar activity of 69 GBq $\cdot\mu\text{mol}^{-1}$ \pm 37 GBq $\cdot\mu\text{mol}^{-1}$ within 17 min from [^{11}C]CO₂ delivery. Lastly, the clinically approved sulfonylurea glibenclamide, currently used in the treatment of diabetes mellitus type 2, and shown to reduce tissue damage in preclinical models for CNS injuries, was synthesized with 75% \pm 14% RCY.³¹ [^{11}C]Glibenclamide ([^{11}C]**36**) is a substrate for organic anion-transporting polypeptide (OATP) transporter and can be used to study the integrity of the blood-brain barrier by non-invasive PET imaging.^{32,33} This radiopharmaceutical, which is currently synthesized in

two-steps using $[^{11}\text{C}]\text{CH}_3\text{OTf}$, was efficiently labeled using an iminophosphorane precursor directly from $[^{11}\text{C}]\text{CO}_2$.³⁴ Following purification 7.4 ± 1.9 GBq of $[^{11}\text{C}]\text{glibenclamide}$ was obtained with an isolated decay corrected yield of $62 \pm 16\%$ from 25.9 GBq of $[^{11}\text{C}]\text{CO}_2$, and a molar activity of 59 ± 0.06 GBq $\cdot\mu\text{mol}^{-1}$ within 21 minutes from the beginning of synthesis.

Scheme 3: Carbon-11 Substrate Scope



^a DBU replaced with DABCO. ^b DBU replaced with LHMDs. ^c KO^tBu. ^d $[^{11}\text{C}]\text{CO}_2$ trapped at -60 °C. See ESI for detailed procedures. * indicates position of ^{11}C .

Conclusion

In conclusion, we have developed a methodology to synthesize several stable and radiolabeled functional groups using the interrupted aza-Wittig approach. The advantages of this method include direct [^{11}C]CO₂-fixation using stable iminophosphorane precursors prepared from commercially available amines, diverse functional group selectivity, and applicability to relevant PET imaging agents. Radiopharmaceuticals are synthesized under mild reaction conditions with rapid synthesis times and using automated procedures to represent a novel strategy for labeling biologically relevant molecules. We anticipate this method contributing to the accessibility of in-demand radiopharmaceuticals such as [^{11}C]CURB and [^{11}C]glibenclamide, among others.

Supporting Information

Characterization data; experimental procedures; preparation of precursors; NMR spectra for compounds

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Notes

The authors declare no competing financial interest.

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SUPPORTING INFORMATION

Interrupted Aza-Wittig Reactions Using Iminophosphoranes to Prepare ^{11}C -Carbonyls

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Section 1: General Information

All chemicals and solvents used were bought commercially and were not further purified unless indicated otherwise. All CO₂ fixation reactions were carried out by bubbling CO₂ (balloon) through the solution. CO₂ was passed through a drying tube filled with Drierite in order to obtain anhydrous CO₂. All other reactions were routinely carried out under inert (argon or nitrogen) atmosphere. All solvents used were anhydrous. Anhydrous 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was obtained by reflux in KOH pellets, and distilled under reduced pressure. Reaction products were confirmed using ¹H-NMR, ¹³C-NMR, and mass spectrometry. Purification of reaction products was carried out by flash column chromatography using silica gel unless stated otherwise. Analytical thin layer chromatography (TLC) was performed on aluminum or glass backing. ¹H-NMR spectra obtained using Bruker AVANCE 300 or Bruker AVANCE 400. Spectral data are reported in ppm using solvent as the reference (CDCl₃ at 7.26 ppm for ¹H NMR and DMSO at 2.50 ppm). ¹H NMR data was reported as: multiplicity (ap = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constant(s) in Hz. Low resolution mass spectrometry was performed using Waters Xevo TQD with an Acquity UPLC H-Class Plus system. High resolution mass spectrometry was performed using a Kratos Concept – Magnetic Sector Electron Impact Mass Spectrometer. Radiolabeled products were synthesized using Synthra Melplus Research module. All products generated were characterized in accordance to the literature.

Sigma-Aldrich: *N*-(triphenylphosphoranylidene)aniline; triphenylphosphine dibromide; benzyl alcohol; 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine; 2-propanol; thiophenol; phenol; diethyl malonate; 4-bromoaniline; 4-fluoroaniline; furfurylamine; methyl magnesium bromide solution (3.0 M in diethyl ether); phenyl magnesium bromide solution (3.0 M in diethyl ether); benzylamine; *N*-methyl-2-phenoxyethanamine; phenylacetylene; 2-phenyl hydroquinone; phenylisocyanate; 5-chloro-2-methoxy-*N*-[2-(4-sulfamoylphenyl)ethyl]benzamide; *N*-butyllithium solution (1.6 M) in hexanes.

Oakwood Chemical: 1,8-diazabicyclo[5.4.0]undec-7-ene; 2-(4-methoxyphenyl)ethanol; 4-nitroaniline; cyclohexylamine; *tert*-butylamine; triethylamine; 3-methoxybenzylamine; 1,2,4-triazole-3-thiol

Alfa Aesar: Benzyl mercaptan; *tert*-butyl alcohol; *N*-*tert*-butylmethylamine; *p*-Anisidine; *o*-toluidine; 4-fluorobenzylamine; 3-chloro-4-(trifluoromethyl)aniline; 4-(4-amine-3-fluorophenoxy)-*N*-methylpicolinamide; *N*-hydroxyphthalamide.

Acros Organics: 5-methoxytryptamine; *L*-phenylalanine methyl ester hydrochloride; *N,N*-diethylethylenediamine; 2-Naphthalenethiol.

Tokyo Chemical Company: Glibenclamide

Section 2: Synthetic Procedures

1. Synthesis of iminophosphoranes.

A flame dried flask was equipped with a magnetic stir bar and charged with triphenylphosphine dibromide (0.6 mmol) under inert atmosphere and dissolved in DCM (2.0 mL). The flask was placed in an ice bath, and a solution containing the corresponding amine (0.6 mmol) and triethylamine (0.6 mmol) in DCM (2 mL) was added to the reactor in a dropwise manner over 10 minutes. The reaction was stirred at room temperature for 4 hours. The solvent was removed under reduced pressure, and anhydrous THF (10 mL) was added to the residue. The solution was filtered through a Celite plug, and the concentrated under reduced pressure. A sufficient volume of chloroform was added to solubilize the residue, and hexane was added to precipitate the product. The product was re-precipitated five or more times to remove unwanted triphenylphosphine oxide (TPPO).

Note: Amine hydrochlorides (0.6 mmol) were first dissolved in DCM (2.0 mL) and 1.1 equiv. of triethylamine was added. After stirring the reaction medium at room temperature for 30 min, ammonium salts were removed by adding Et₂O followed by filtration over a celite pad. Solvents were removed by rotary evaporation under reduced pressure and the afforded free amines were used without further purification.

2. Synthesis of carbamate and thiocarbamate products.

A flame dried flask was charged with the corresponding nucleophile (0.25 mmol), DBU (0.65 mmol), and ACN (2.5 mL). The mixture was brought to reflux, and CO₂ was bubbled through the solution for 10 minutes, prior to the addition of iminophosphorane (IMP). A solution containing IMP (0.25 mmol) in ACN (2 mL) was added dropwise over one hour to the reaction mixture. CO₂ was bubbled continuously throughout the reaction until completion. The contents of the flask were concentrated under reduced pressure and re-suspended in 5 mL of DCM. The solution was extracted with saturated NH₄⁺Cl⁻ (3 x 10 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure and purified by flash column chromatography using a 0-25% hexane/ethyl acetate gradient.

Note: Blocked isocyanate products (**7–9, 11–12**) and products of alkyl iminophosphoranes (**22–23, 25**) use 2.5 mmol of nucleophile (10 equiv.) and are not subjected to solvent-solvent extraction unless mentioned otherwise. The concentrated residue is immediately purified by flash column chromatography using a 0-25% hexane/ethyl acetate gradient.

3. Synthesis of urea products.

A flame dried flask was charged with an amine nucleophile (0.50 mmol), DBU (0.25 mmol), and ACN (2.5 mL). CO₂ was bubbled through this solution for 10 minutes, followed by the addition of a solution containing iminophosphorane (0.25 mmol) in ACN (2 mL), added dropwise over 20 minutes at room temperature. The contents of the flask were concentrated under reduced pressure and purified by flash chromatography using a 0-25% hexane/ethyl acetate gradient.

4. Synthesis of amides using Grignards via blocked isocyanate intermediates.

A flame dried round bottom flask was charged with the corresponding blocking nucleophile (2.5 mmol), DBU (0.65 mmol), and THF (2.5 mL). The mixture was brought to reflux, and CO₂ was bubbled through the solution for 10 minutes. A solution containing IMP (0.25 mmol) in THF (2 mL) was added dropwise over one hour to the reaction mixture. CO₂ was bubbled continuously throughout the reaction until completion. The reaction solution was sparged with argon for five minutes and added dropwise to a cooled flask containing Grignard (5 mmol) dissolved in THF (2 mL). The reaction was left to stir overnight and quenched with methanol (15 mL). The contents of the flask were concentrated under reduced

pressure, re-suspended in DCM, and extracted with NH_4^+Cl^- (3 x 20 mL), water (3 x 15 mL) and brine (3 x 15 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure and purified by flash column chromatography using a 0-25% hexane/ethyl acetate gradient.

5. Synthesis of amides using phenylacetylene.

A flame dried round bottom flask was charged with phenylacetylene (2.5 mmol) dissolved in THF (5 mL) and cooled to -78°C . n-Butyllithium (2.45 mmol) was added dropwise to the solution. The solution was left to stir for 2 hrs. The reaction was brought to room temperature, and the contents of this flask were added dropwise to a separate flask containing the prepared blocked isocyanate using procedure 4. The reaction was left to stir at room temperature for 2 hours. The contents of the flask were concentrated under reduced pressure, resuspended in DCM (5 mL), and extracted with ammonium chloride (3 x 15 mL), water (3 x 15 mL), brine (1 x 15 mL) and dried over magnesium sulfate. The product was purified by flash chromatography using a hexane/ethyl acetate gradient.

6. Synthesis of amides using diethyl malonate.

A flame dried round bottom flask was charged with diethylmalonate (10 mmol) and dissolved in THF (5 mL). The flask was cooled to -78°C , and LHMDs (2.45 mmol) was added dropwise. The reaction was left to stir for 2 hrs. The solution was brought to room temperature, and 1.25 mL of the solution was added to a separate flask that was charged with DBU (0.65 mmol) and THF (1.25 mL). The reaction was heated to reflux, and CO_2 was bubbled into the reaction for 5 minutes. A solution of IMP (0.25 mmol) dissolved in THF (2 mL) was added dropwise to the reaction mixture over 1 hr. CO_2 was bubbled continuously into the reaction until completion. The contents of the flask were concentrated under reduced pressure and purified by flash column chromatography using a 0-25% hexane/ethyl acetate gradient.

7. Deprotonation of alkyl iminophosphorane salts.

The iminophosphorane salt (0.25 mmol) was added to a 5-mL flame dried round bottom flask and dissolved in THF (2.5 mL). The flask was cooled to 0°C using an ice-water bath, and KHMDS was added to the solution (0.245 mmol). The reaction was left to stir for 5 minutes and brought to room temperature for use.

8. Synthesis of carbon-11 radiolabeled products.

Using the Synthra Melplus Research module, iminophosphorane (28.29 μmol), DBU (40 μmol), and nucleophile (483 μmol) were dissolved in 400 μL of DMF and loaded into reactor 1. DMF or ACN (1 mL) was loaded into vial A1. Carbon-11 (CO_2) ($[^{11}\text{C}]\text{CO}_2$), generated by the bombardment of a gas target filled with pressurized N_2/O_2 mixture using a Siemens 11 MeV cyclotron, at 55 μA for 2 minutes, and was directed to a steel coil cooled at -180°C . The reactor was cooled to -60°C prior to heating the coil to 25°C . $[^{11}\text{C}]\text{CO}_2$ was bubbled into the solution at 5 mL/min. The reactor was heated to 100°C for 10 minutes, and solvent from vial A1 was added to the reactor to dilute the mixture. The solution was transferred to a glass vial, and analyzed by radioHPLC. Integration of radiation detector chromatograms on analytical HPLC informed radiochemical yields, and products were identified by co-injection of nonradioactive standards. Isolated yields were determined by decay correcting the activity to the end of synthesis (EoS). Analytical HPLC conditions for radiolabeled products (unless otherwise stated): 50% ACN / 50% 0.1 M AMF for 2 minutes, then gradient to 95% ACN/ 5% 0.1 M AMF to 12 minutes, 65% ACN/35% 0.1 M AMF to 13 minutes, then gradient to 20% ACN/ 80% 0.1 M AMF to 20 minutes.

9. Radiosynthesis of [¹¹C]35

A solution of iminophosphorane **1o** (2.19 μmol in 200 μL of DMF) was prepared, and DBU (2.18 μmol) was added ten minutes prior to end-of-bombardment. The solution of iminophosphorane and a solution of N-methyl-2-phenoxyethanamine (0.12 mmol in 200 μL of DMF) were loaded into the reaction vessel and tightly sealed two minutes prior to end-of-bombardment. [¹¹C]CO₂ was trapped at -180 °C. The trap was heated to 25 °C, and [¹¹C]CO₂ was released under a stream of helium at 3 mL/min to bubble into the reaction vessel until peak activity. The reactor was heated to 100 °C for 1 min and quenched with 800 μL of H₂O. The solution was injected onto an HPLC column for purification. HPLC conditions: Nucleodur C18 Pyramid 7 μm, 250 x 10 mm eluted with 30% ACN/70% 0.1 M AMF at 5 mL/min. The product was collected, and the identity was established by co-injection with the non-radioactive standard using an analytical HPLC.

10. Radiosynthesis of [¹¹C]25b ([¹¹C]URB694)

DMF was degassed using five freeze-thaw cycles prior to use. 2-Phenyl-1,4-dihydroquinone was purified by flash column chromatography (0-25% hexanes/ethyl acetate) on the day of use. A solution of iminophosphorane **1g** (2.27 μmol in 100 μL of DMF, 0.01 mg/μL) was prepared, and DBU (2.27 μmol) was added two minutes prior to end-of-bombardment. The solution was mixed under argon for one minute, and 25 μL of this solution was added to a vial containing 2-phenyl-1,4-dihydroquinone (80.5 μmol) in 125 μL of DMF. This precursor solution was loaded into the reaction vessel and tightly sealed. A stream of helium was swept through the reaction vessel after loading. [¹¹C]CO₂ was trapped at -180 °C. The trap was heated to 25 °C, and [¹¹C]CO₂ was released under a stream of helium at 3 mL/min to bubble into the reaction vessel until peak activity. The reactor was heated to 100 °C for 2 min and quenched with 800 μL of mobile phase. The solution was injected onto an HPLC column for purification. HPLC conditions: Nucleodur C18 Pyramid 7 μm, 250 x 10 mm eluted with 70% MeOH/30% H₂O containing 1% formic acid at 7 mL/min. The product was collected, and the identity was established by co-injection with the cold standard using an analytical HPLC.

11. Radiosynthesis of [¹¹C]36 ([¹¹C]Glibenclamide)

DMF was degassed using five freeze-thaw cycles prior to use. A solution of iminophosphorane **1g** (2.27 μmol in 100 μL of DMF) was prepared, and 27.5 μL of DABCO (1.22 μmol, 0.02 mg/μL solution in DMF) was added two minutes prior to the end-of-bombardment. The solution was stirred for 30 seconds, and 25 μL of this solution was added to the reactor. 5-Chloro-2-methoxy-N-[2-(4-sulfamoylphenyl)ethyl]benzamide (40.66 μmol) was dissolved in 125 μL of DMF and added to a Teflon sealed vial under inert atmosphere containing potassium *tert*-butoxide (40 μmol), also mixed 2 minutes prior to the end-of-bombardment. The solution was loaded into the reaction vessel and tightly sealed. A stream of helium was swept through the reaction vessel after loading. [¹¹C]CO₂ was trapped at -180 °C. The trap was heated to 25 °C, and [¹¹C]CO₂ was released under a stream of helium at 3 mL/min to bubble into the reaction vessel until peak activity. The reactor was heated to 100 °C for 2 min and quenched with 800 μL of mobile phase. The solution was injected onto an HPLC column for purification. HPLC conditions: Nucleodur C18 Pyramid 7 μm, 250 x 10 mm eluted with 55% ACN/45% H₂O containing 0.1% TFA at 5 mL/min for 10 minutes, then switched to 75% ACN/25% H₂O + 0.1% TFA for 3 minutes. The product was collected, and the identity was established by co-injection with the cold standard using an analytical HPLC.

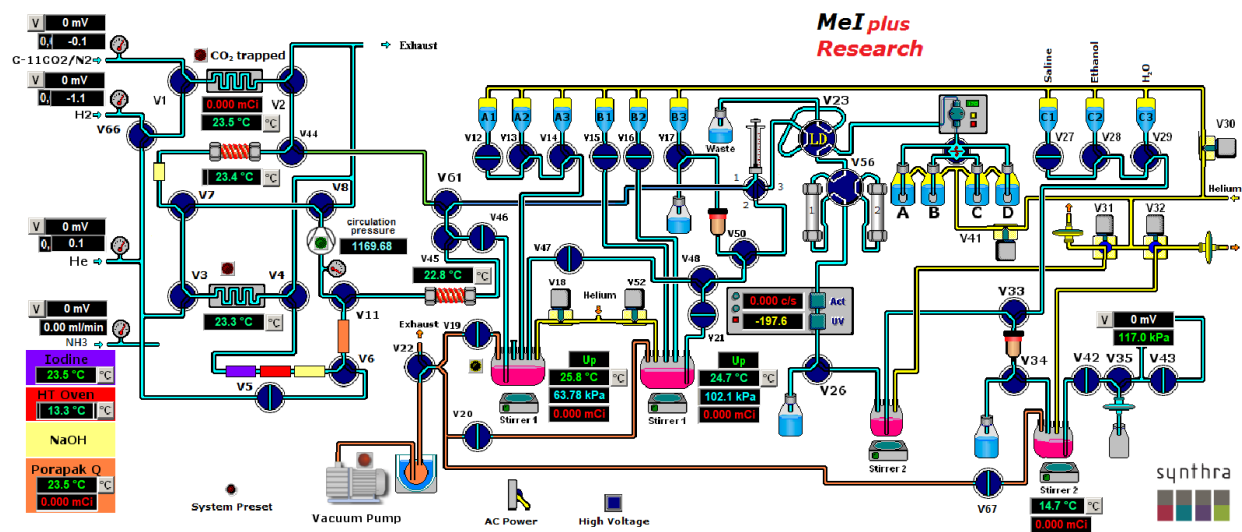
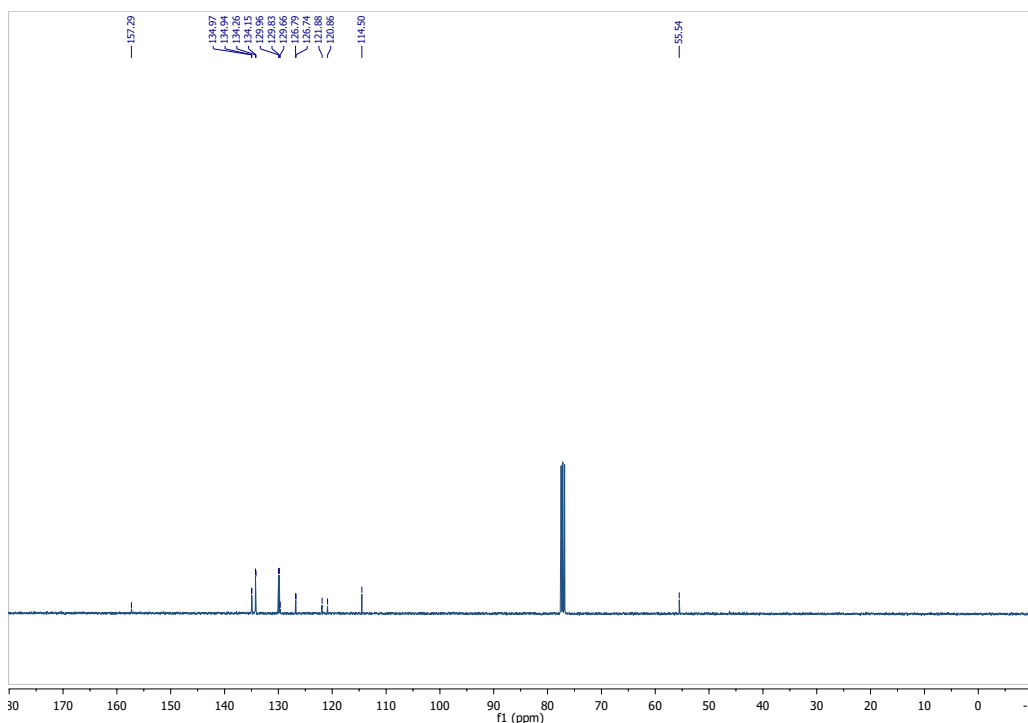
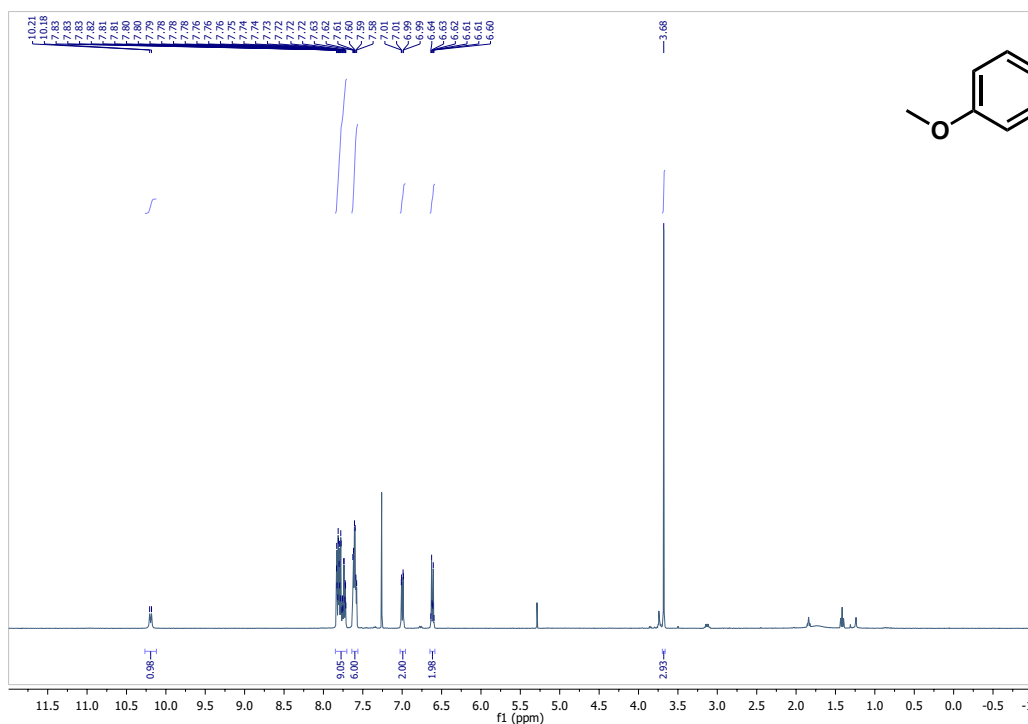
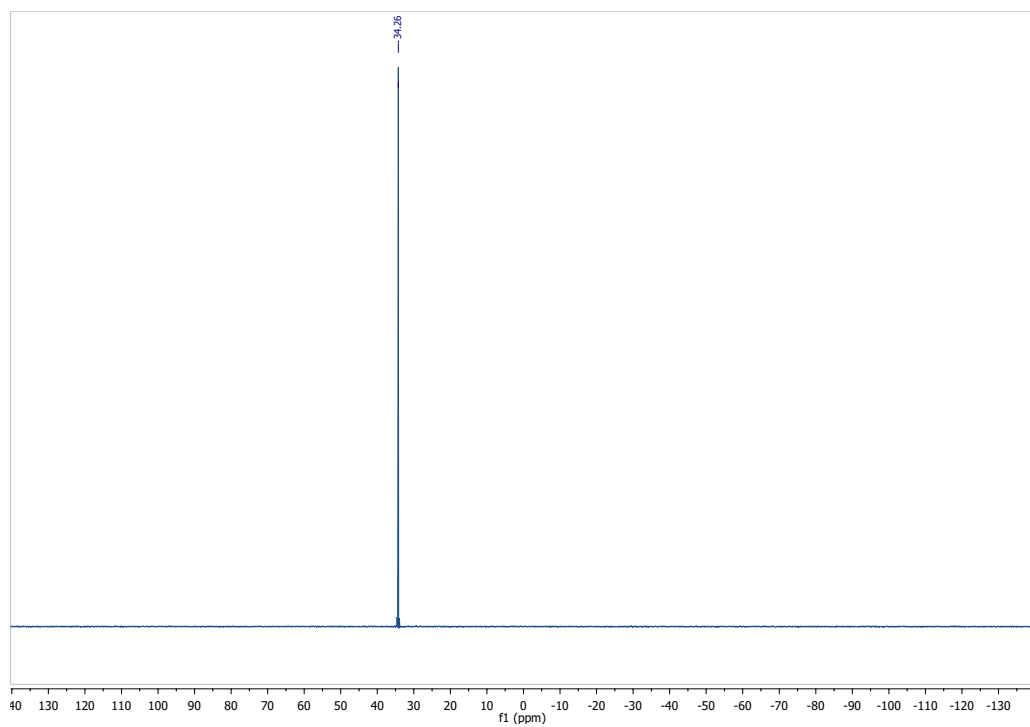


Figure S1. Synthra Melplus Research apparatus scheme.

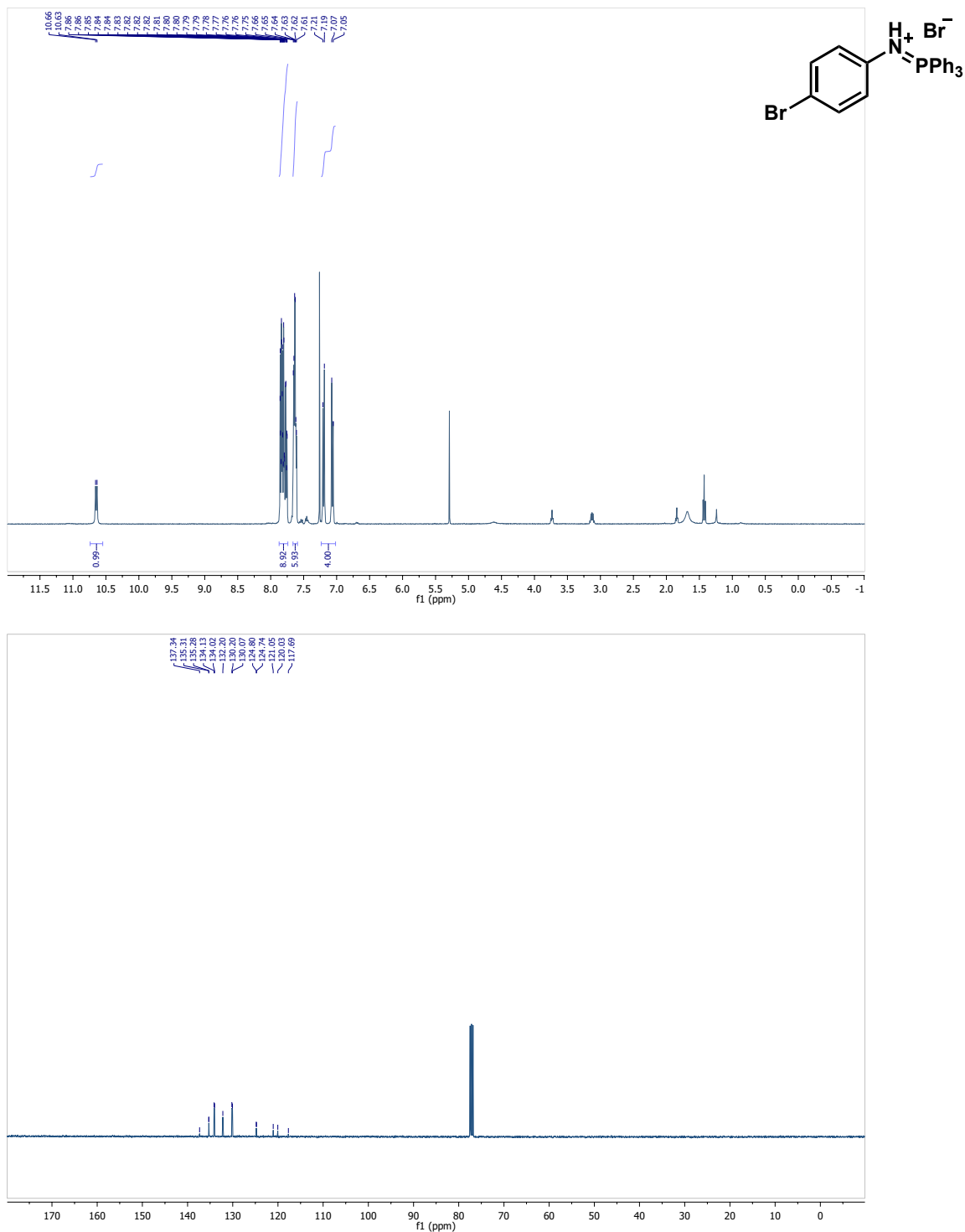
1b. 4-methoxy-N-(triphenylphosphanylidene)anilinium bromide

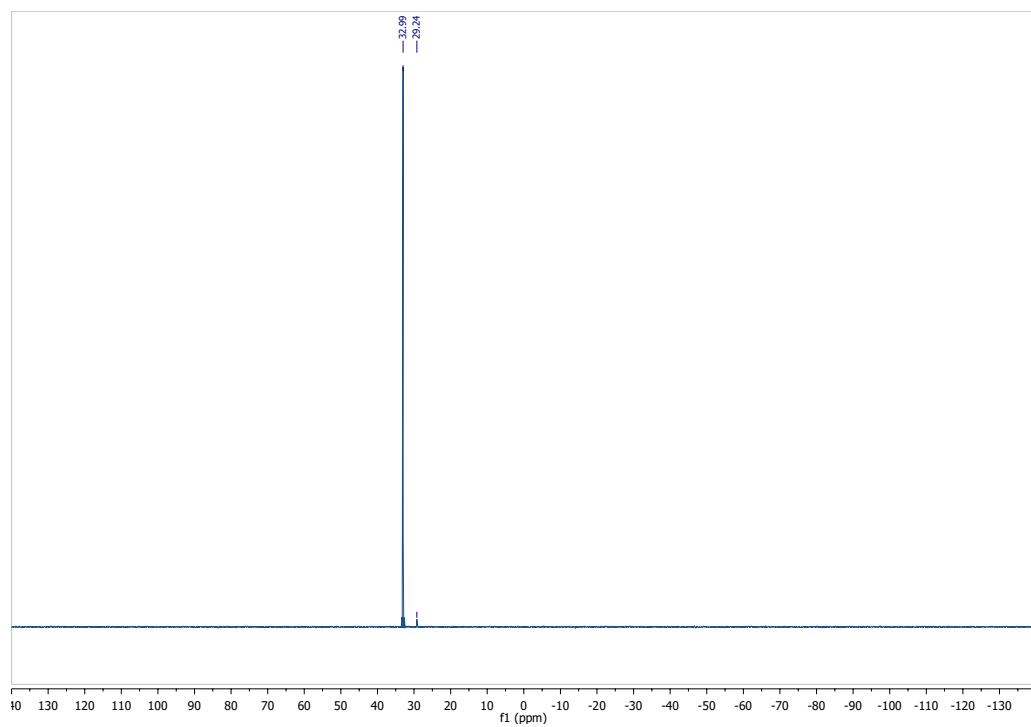
COc1ccc([NH+]#P)(c1)[Br-]



1c. 4-bromo-N-(triphenylphosphanylidene)anilinium bromide

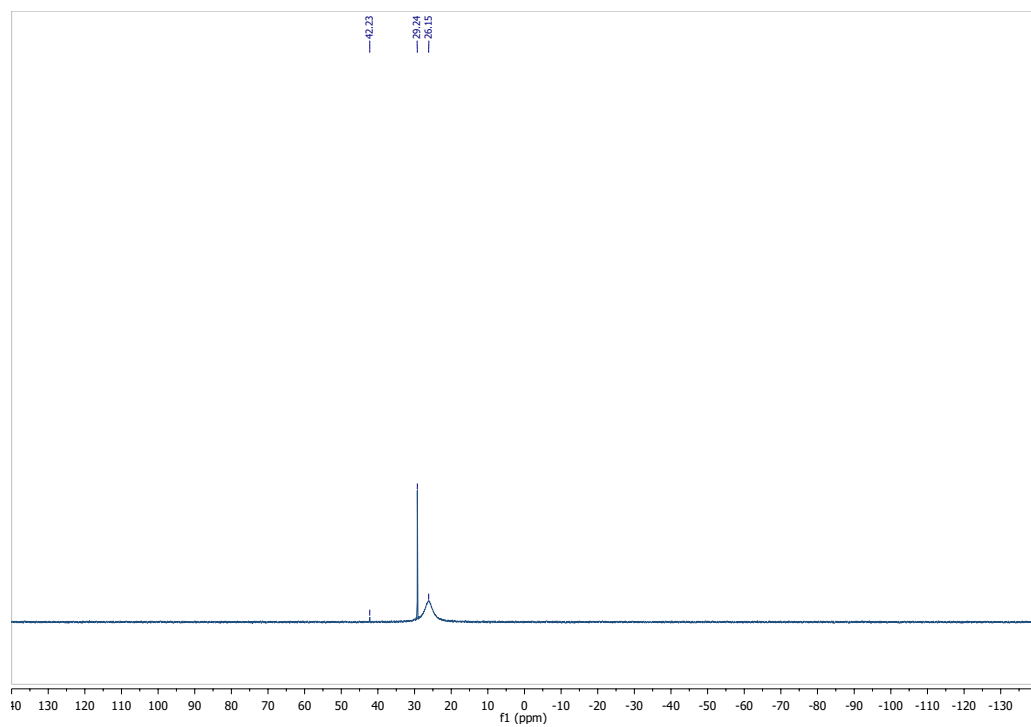
Followed the general procedure (1), product obtained as a white solid (209 mg, yield 68%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 10.65 (d, 1H), 7.86–7.75 (m, 9H), 7.66–7.61 (m, 6 H), 7.13 (dd, 4H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 137.3, 135.3, 134.1, 132.2, 130.1, 124.8, 120.5, 117.7. $^{31}\text{P-NMR}$ (162 MHz, CDCl_3): δ 32.99 (s, 1P), 29.24 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{24}\text{H}_{20}\text{NBrP}$ as 432.0517, $[\text{M}+\text{H}]$ found as 432.0504.





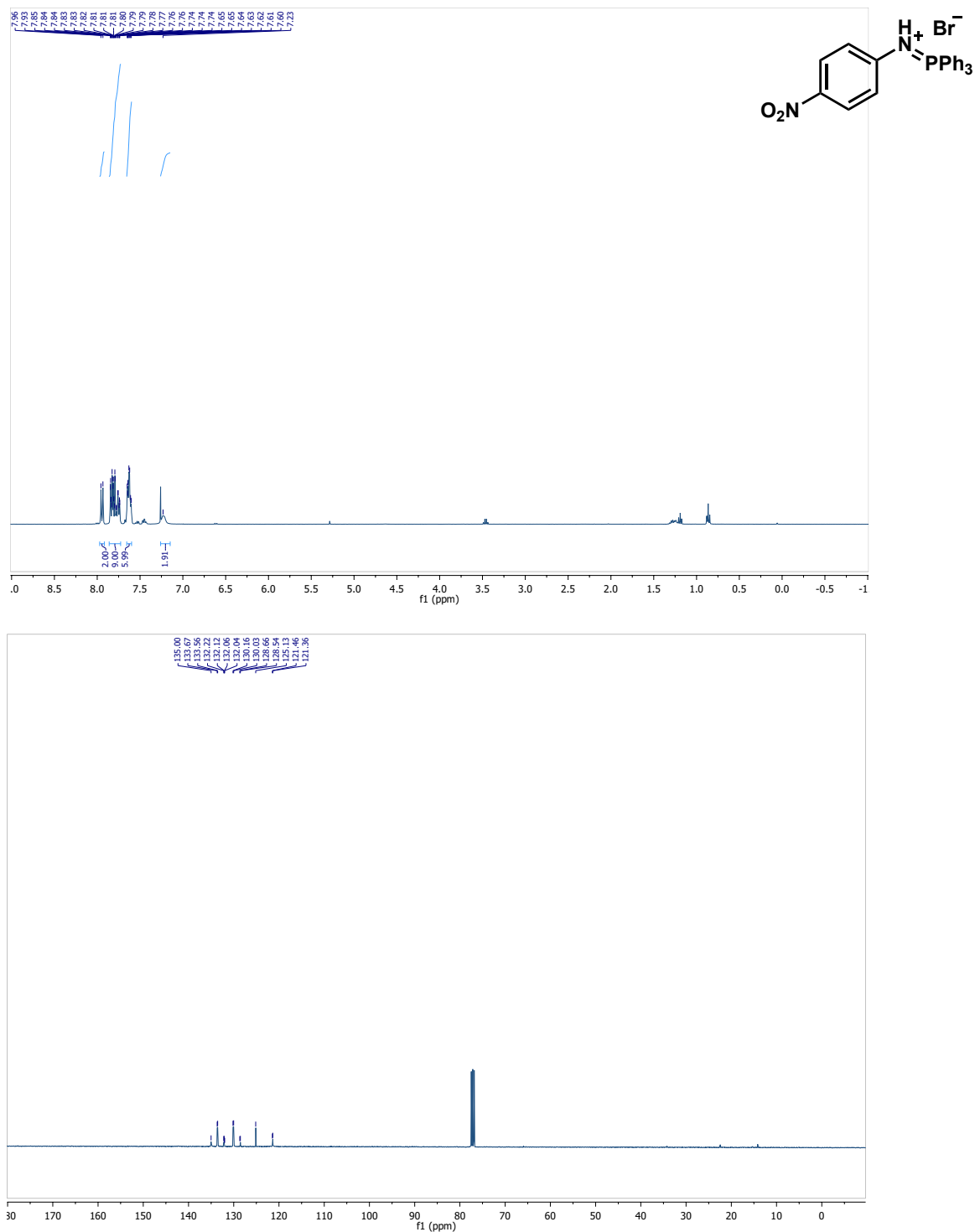
Followed the general procedure (1), product obtained as an off-white solid (44 mg, yield 17%). ¹H-NMR (400 MHz, CDCl₃): δ 7.79 (m, 6H), 7.69 (m, 3H), 7.57 (m, 6H), 6.97 (m, 2H), 6.75 (m, 2H). ¹³C-NMR (100 MHz, CDCl₃): 134.3, 133.7, 132.1, 129.7, 128.6, 125.5, 123.6, 115.7. ³¹P-NMR (162 MHz, CDCl₃): δ 42.23 (s, 1P), 29.24 (s, 1P), 26.15 (s, 1P). MS (ESI⁺): Calculated C₂₄H₂₀NFP as 372.1317, [M+H]⁺ found as 372.1307.

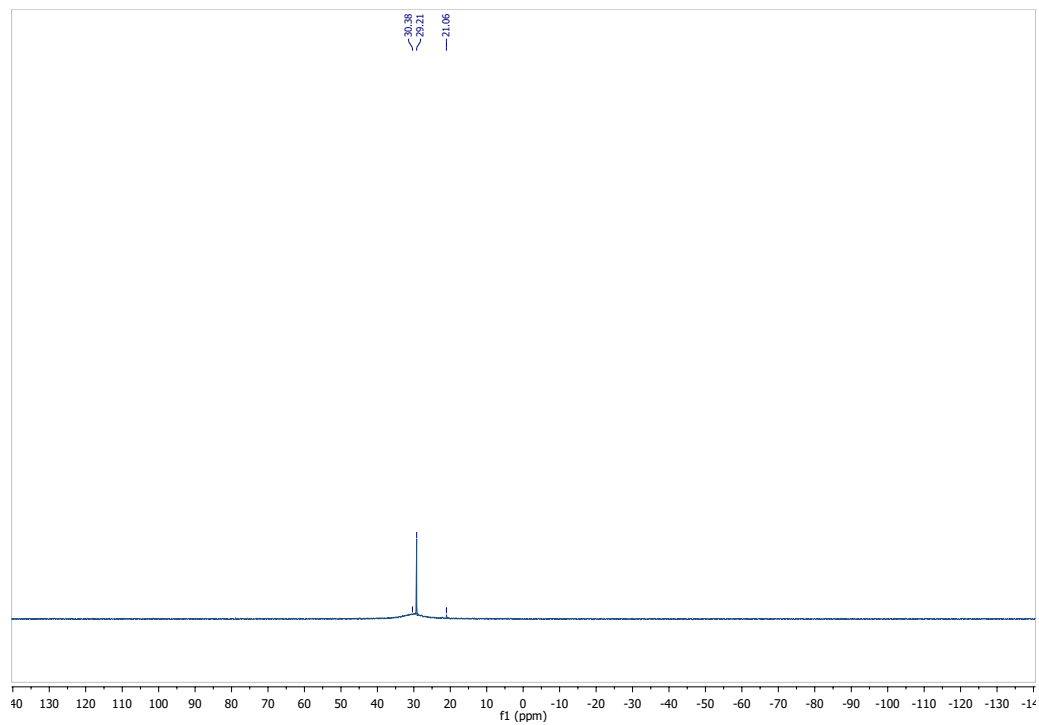




1e. 4-nitro-N-(triphenylphosphanylidene)anilinium bromide

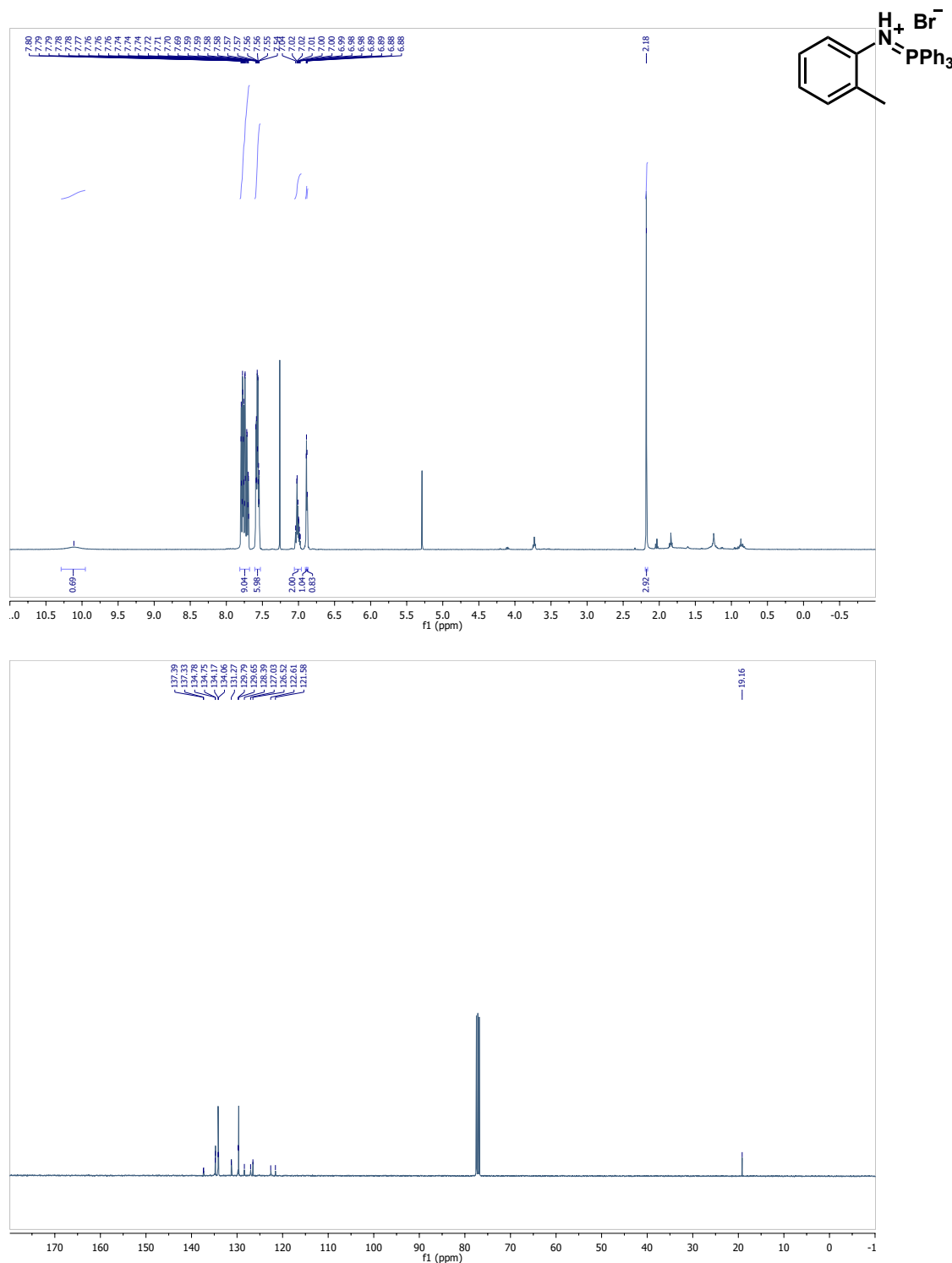
Followed the general procedure (1), product obtained as a yellow solid (230 mg, yield 80%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.95 (m, 2H), 7.85–7.74 (m, 9H), 7.63 (m, 6H), 7.23 (s, 2H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 135.0, 133.6, 132.2, 132.1, 130.1, 128.6, 125.1, 121.4. $^{31}\text{P-NMR}$ (162 MHz, CDCl_3): δ 30.38 (s, 1P), 29.21 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_2\text{P}$ as 399.1262, $[\text{M}+\text{H}]$ found as 399.1248.

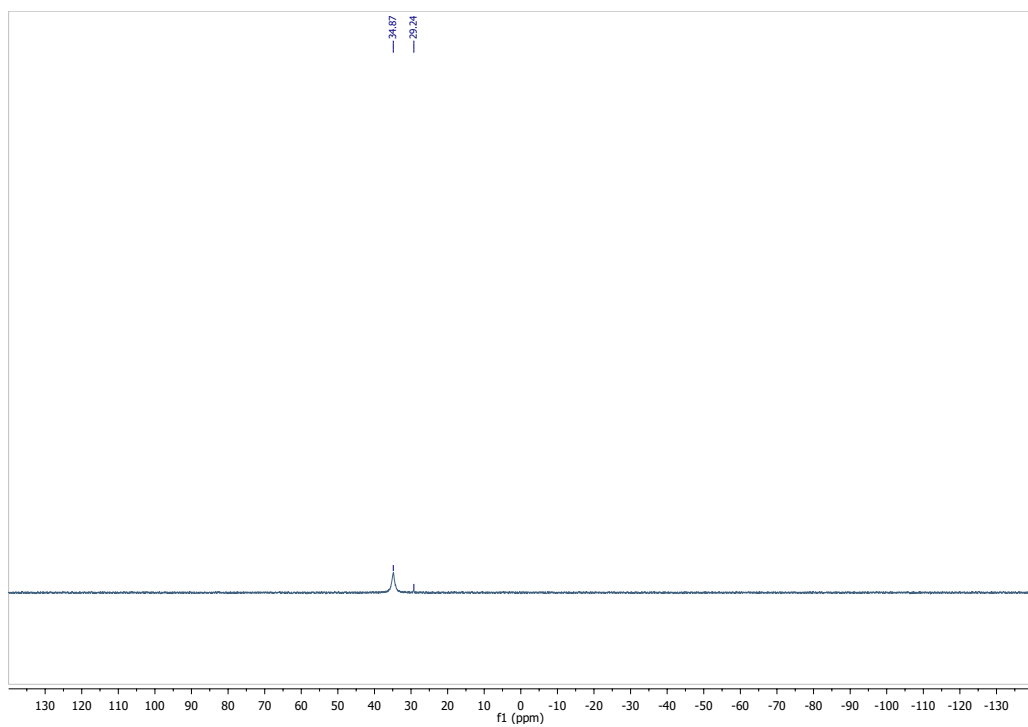




1f. 2-methyl-N-(triphenylphosphanylidene)anilinium bromide

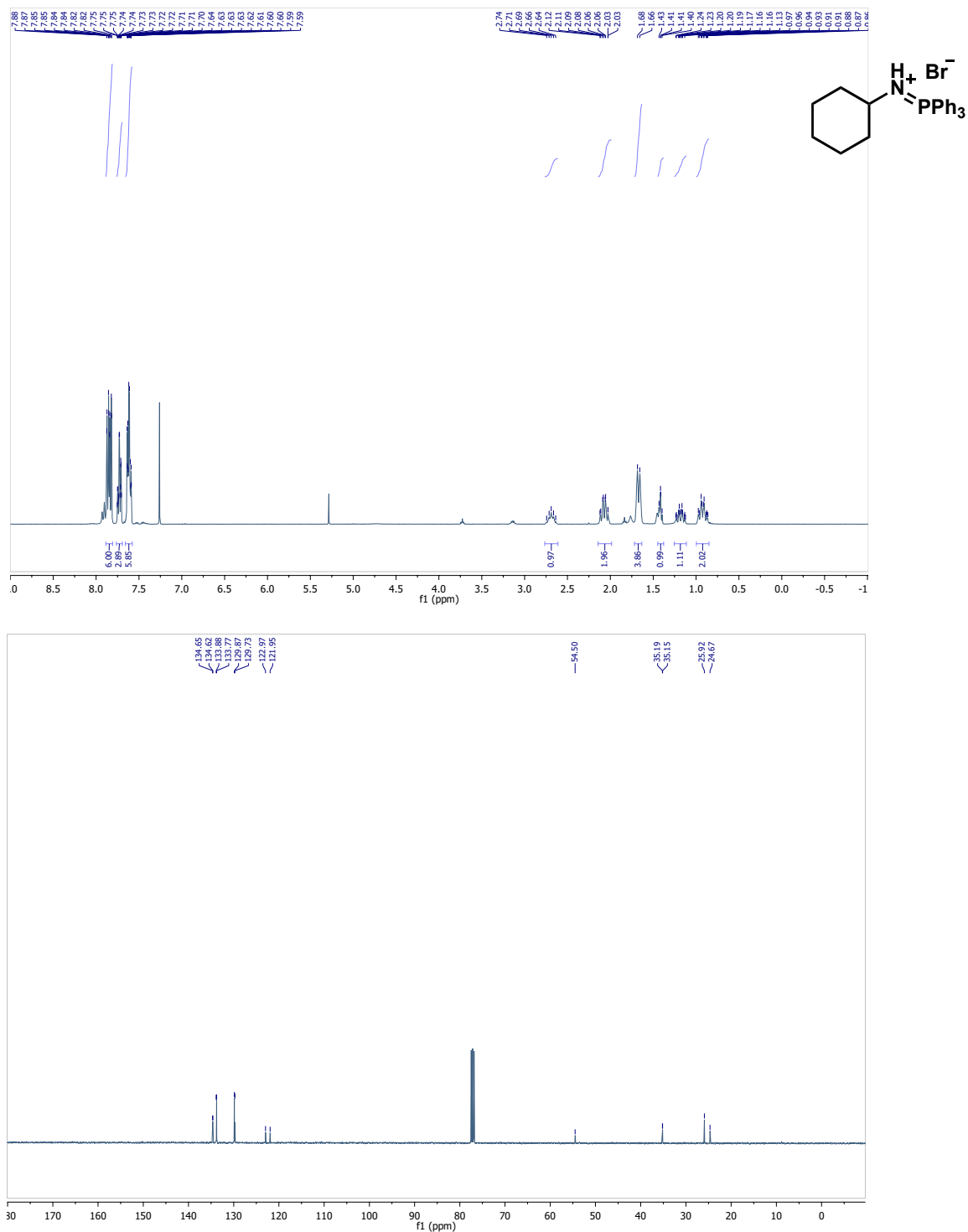
Followed the general procedure (1), product obtained as a white solid (76 mg, yield 28%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 10.11 (s, 1H), 7.80–7.58 (m, 9H), 7.59–7.54 (m, 6H), 7.04–6.98 (m, 2H), 6.89 (d, 1H), 6.88 (d, 1H), 2.18 (s, 3H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 137.4, 134.8, 134.1, 131.3, 129.7, 127.7, 126.5, 122.1, 19.2. $^{31}\text{P-NMR}$ (162 MHz, CDCl_3): δ 34.87 (s, 1P), 29.24 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{25}\text{H}_{23}\text{NP}$ as 368.1568, $[\text{M}+\text{H}]$ found as 368.1555.

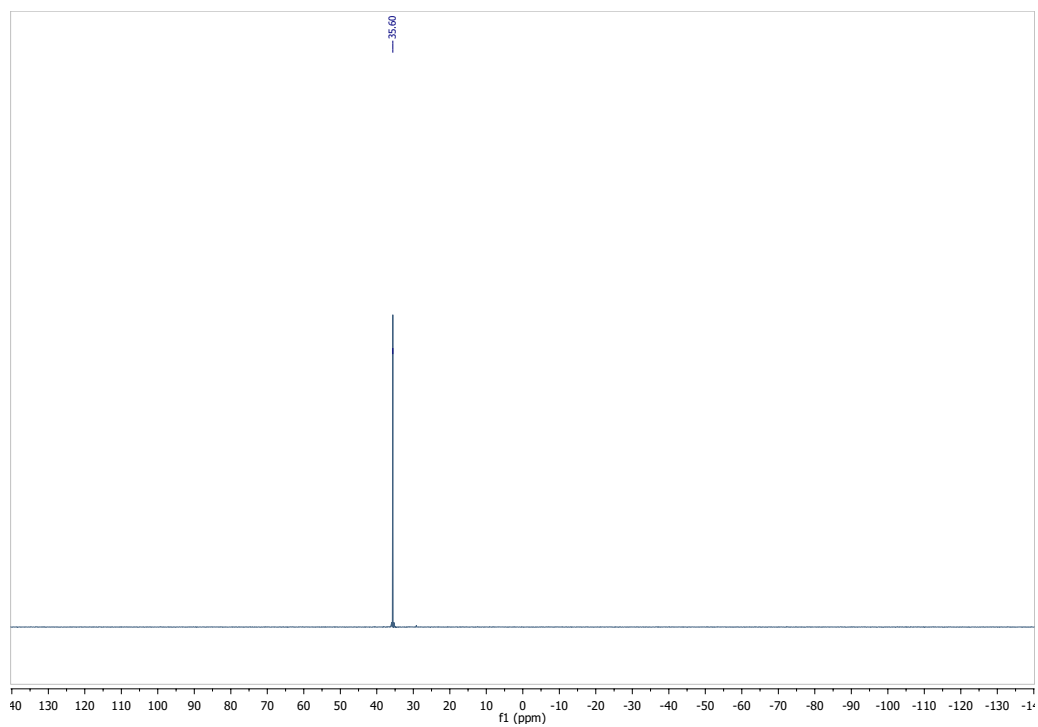




1g. N-(triphenylphosphanylidene)cyclohexanaminium bromide

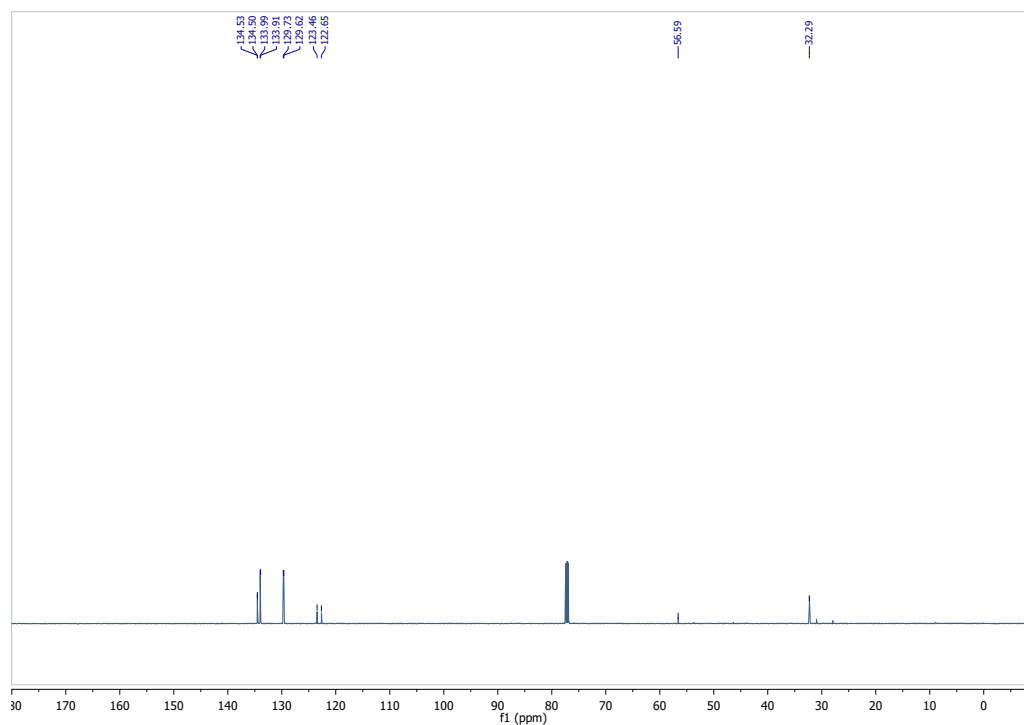
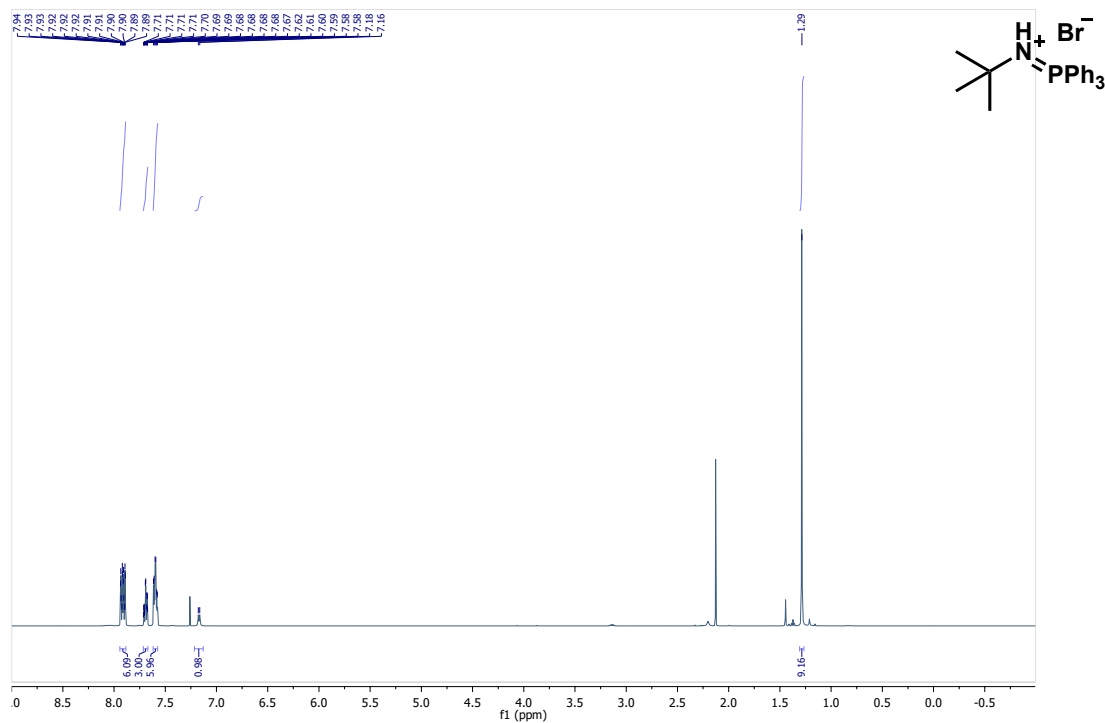
Followed the general procedure (1), product obtained as a white solid (147 mg, yield 56%). ^1H -NMR (400 MHz, CDCl_3): δ 7.88–7.82 (m, 6H), 7.75–7.70 (m, 3H), 7.64–7.59 (m, 6H), 2.69 (m, 1H), 2.12–2.03 (m, 2H), 1.67 (d, 4H), 1.42 (dd, 1H), 1.18 (m, 1H), 0.92 (m, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 134.6, 133.8, 129.8, 122.5, 54.5, 35.2, 25.9, 24.7. ^{31}P -NMR (162 MHz, CDCl_3): δ 35.60 (s, 1P). MS (ESI+): Calculated $\text{C}_{24}\text{H}_{27}\text{NP}$ as 360.1881, $[\text{M}+\text{H}]$ found as 360.1879.

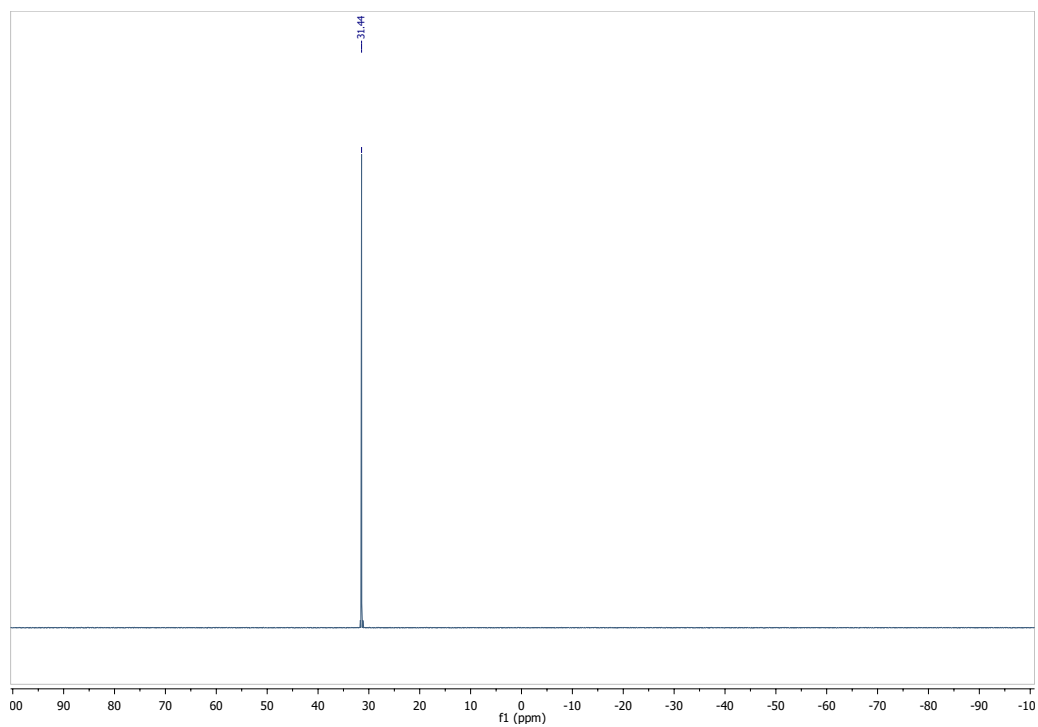




1h. tert-butyl(triphenylphosphanylidene)azanium bromide

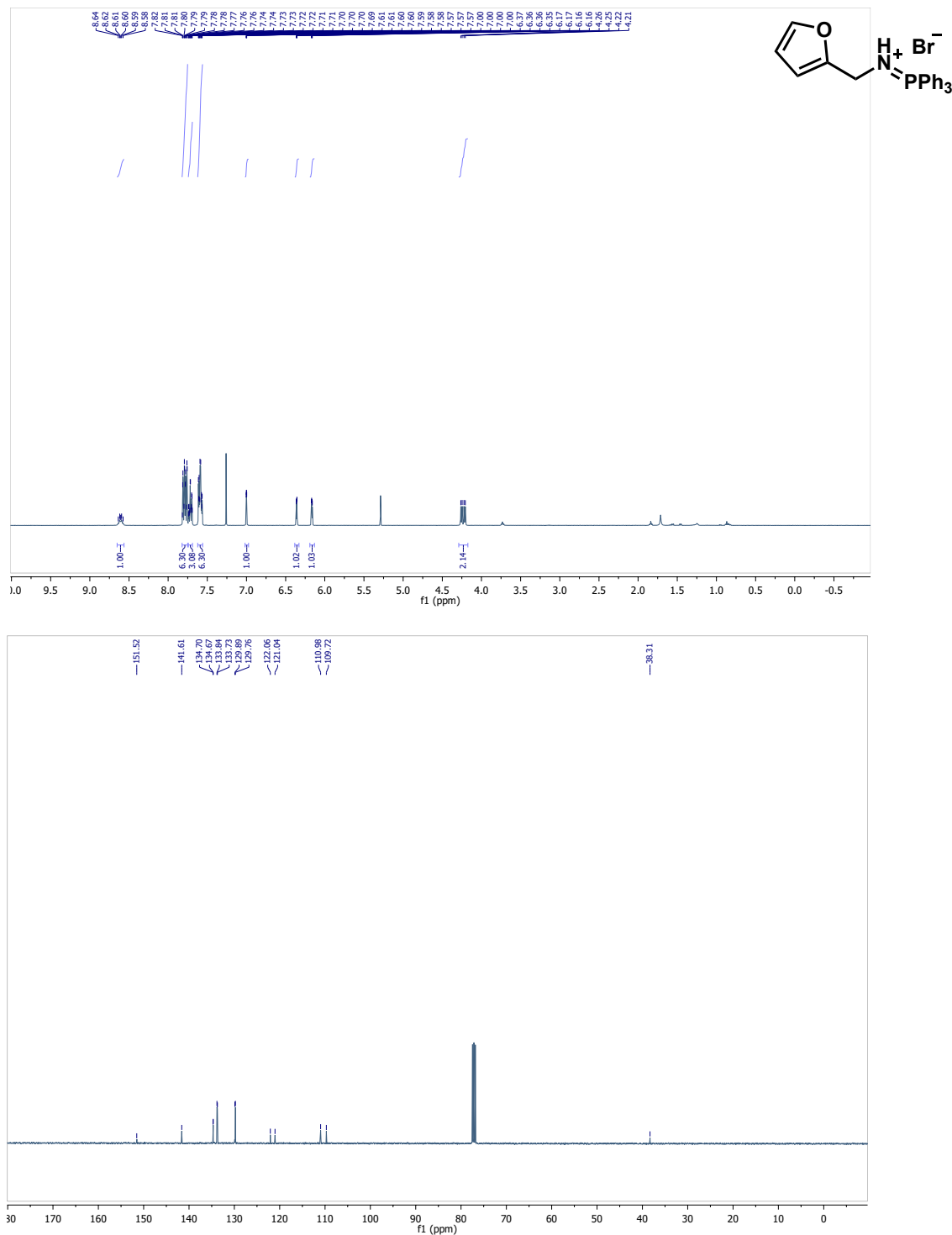
Followed the general procedure (1), product obtained as a white solid (47 mg, yield 19%). ^1H -NMR (400 MHz, CDCl_3): δ 7.94–7.89 (m, 6H), 7.71–7.67 (m, 3H), 7.62–7.58 (m, 6H), 7.17 (d, 1H), 1.29 (s, 9H). ^{13}C -NMR (100 MHz, CDCl_3): 134.5, 134.0, 129.7, 123.1, 56.6, 32.3. ^{31}P -NMR (162 MHz, CDCl_3): δ 31.44 (s, 1P). MS (ESI+): Calculated $\text{C}_{22}\text{H}_{25}\text{NP}$ as 334.1725, $[\text{M}+\text{H}]$ found as 334.1703.

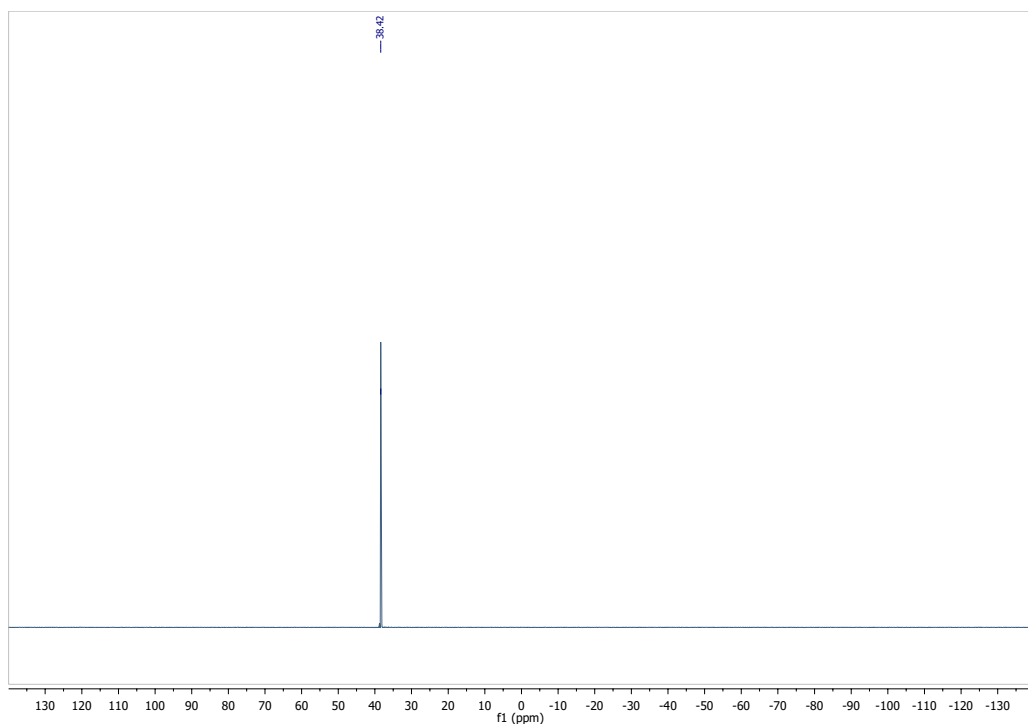




1i. [(furan-2-yl)methyl](triphenylphosphanylidene)azanium bromide

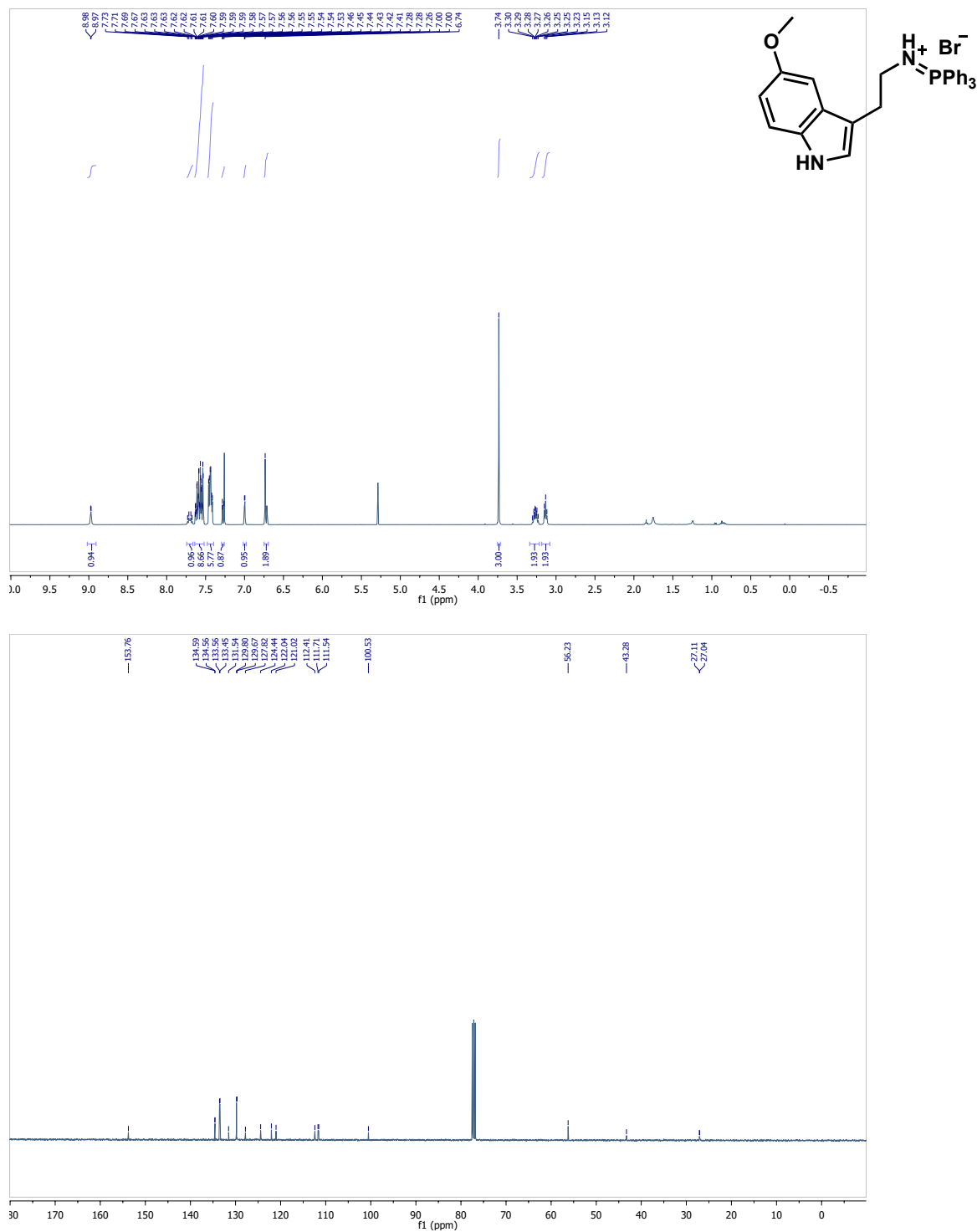
Followed the general procedure (1), product obtained as a white solid (142 mg, yield 54%). ^1H -NMR (400 MHz, CDCl_3): δ 8.61 (m, 1H), 7.82–7.76 (m, 6H), 7.74–7.69 (m, 3H), 7.61–7.57 (m, 6H), 7.00 (dd, 1H), 6.36 (dd, 1H), 6.17 (dd, 1H), 4.24 (dd, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 151.5, 141.6, 134.7, 133.8, 129.8, 121.6, 111.0, 109.7, 38.3. ^{31}P -NMR (162 MHz, CDCl_3): δ 38.42 (s, 1P). MS (ESI+): Calculated $\text{C}_{23}\text{H}_{21}\text{NPO}$ as 358.1361, $[\text{M}+\text{H}]$ found as 358.1364.

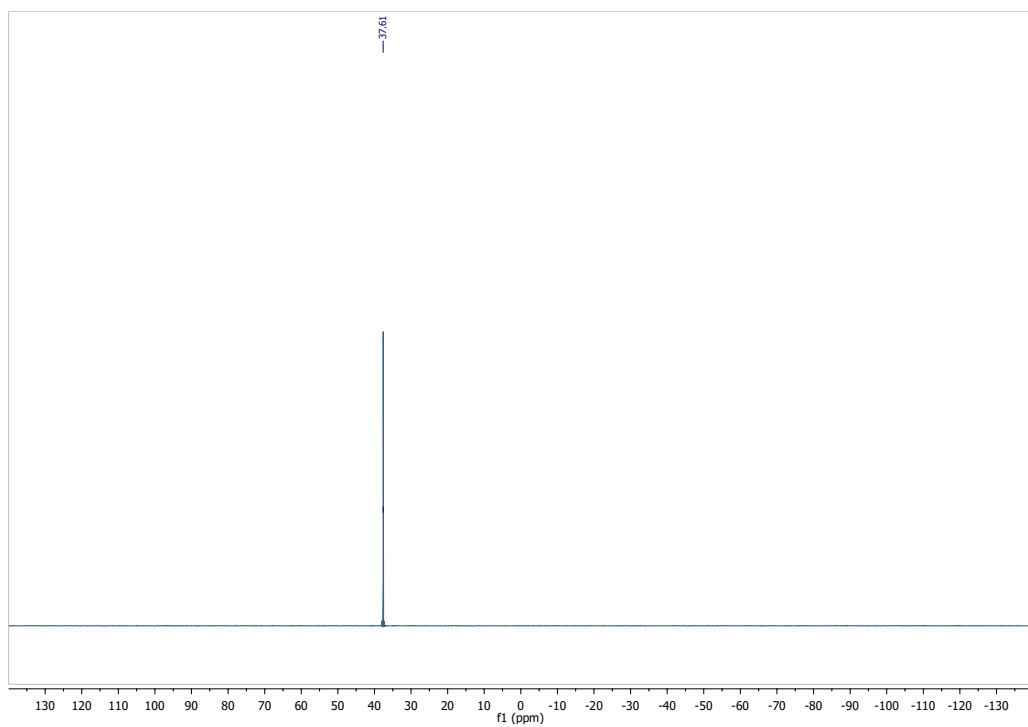


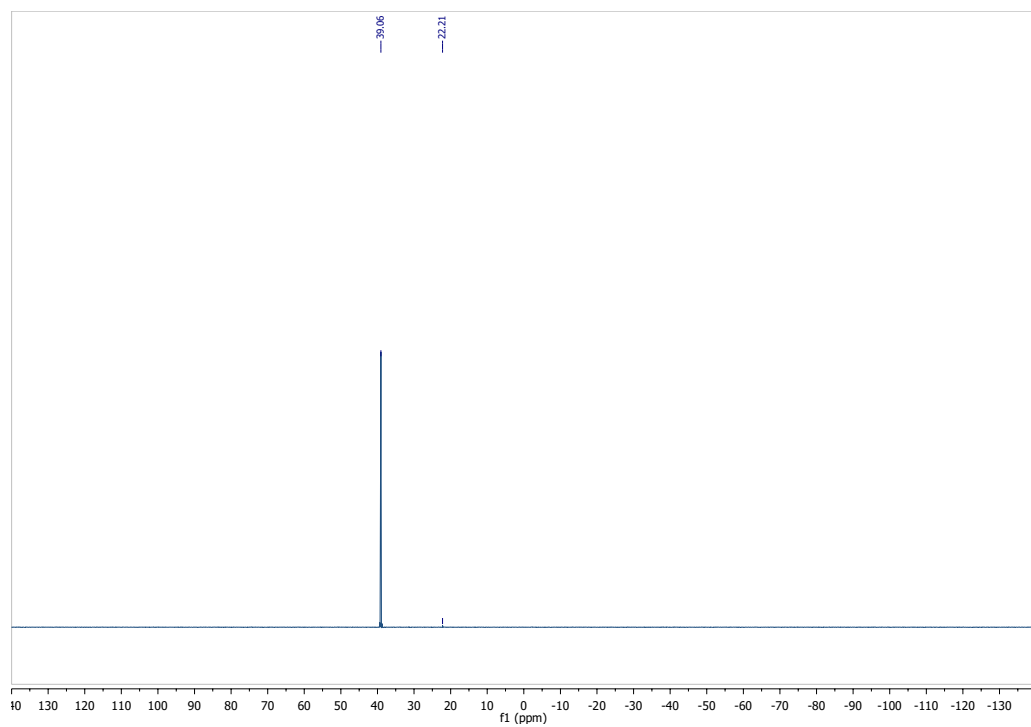


1j. [2-(5-methoxy-1H-indol-3-yl)ethyl](triphenylphosphanylidene)azanium bromide

Followed the general procedure (1), product obtained as a white solid (143 mg, yield 45%). ^1H -NMR (400 MHz, CDCl_3): δ 8.98 (d, 1H), 7.70 (dd, 1H), 7.63–7.53 (m, 9H), 7.46–7.41 (m, 6H), 7.27 (dd, 1H), 7.00 (dd, 1H), 6.74 (s, 1H), 3.74 (s, 3H), 3.27 (m, 2H), 3.14 (dd, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 153.8, 134.6, 133.5, 131.5, 129.7, 127.8, 124.4, 121.5, 112.4, 111.7, 111.5, 100.5, 56.2, 43.3, 27.1. ^{31}P -NMR (162 MHz, CDCl_3): δ 37.61 (s, 1P). MS (ESI $^+$): Calculated $\text{C}_{29}\text{H}_{28}\text{N}_2\text{PO}$ as 451.1939, $[\text{M}+\text{H}]$ found as 451.1922.

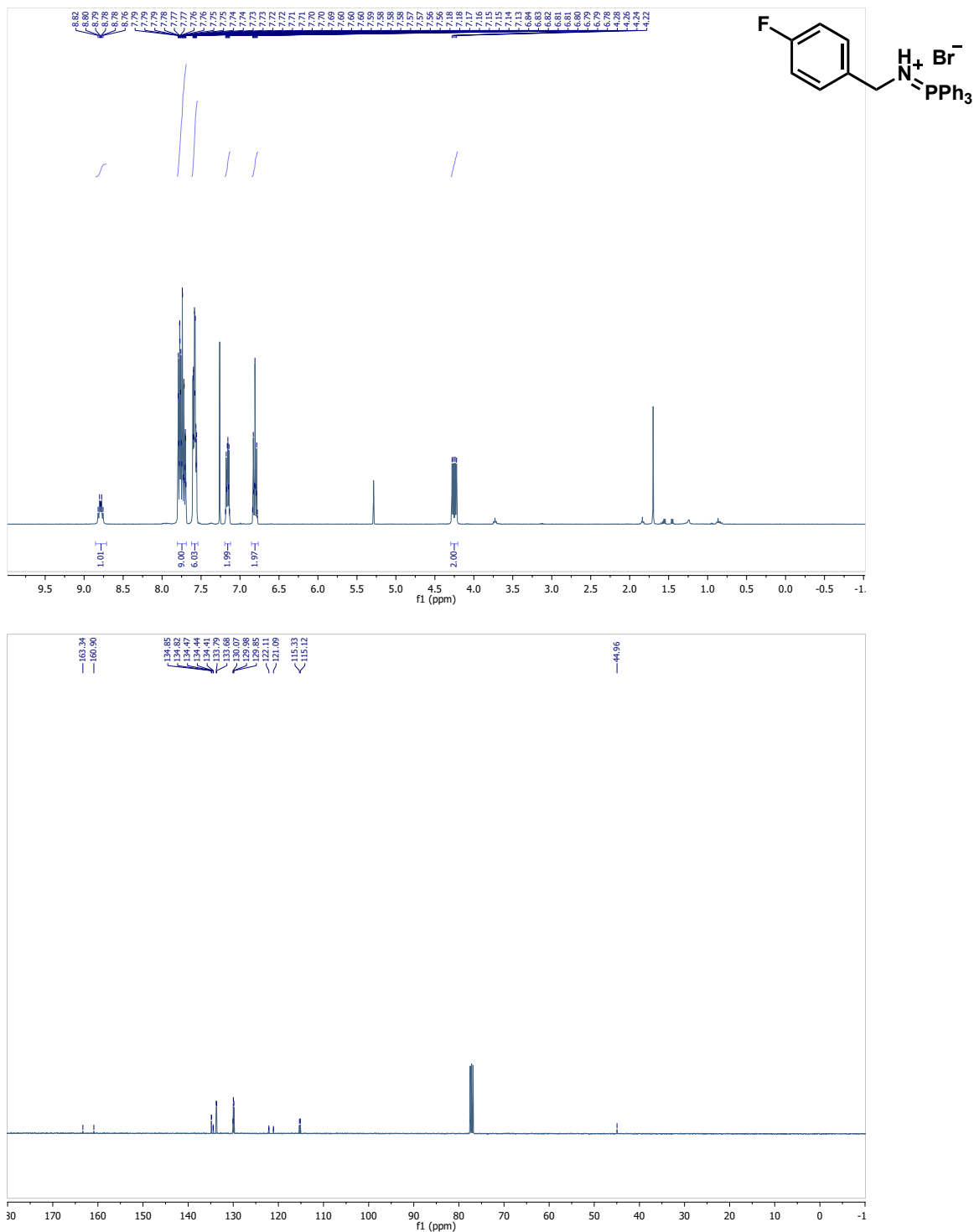


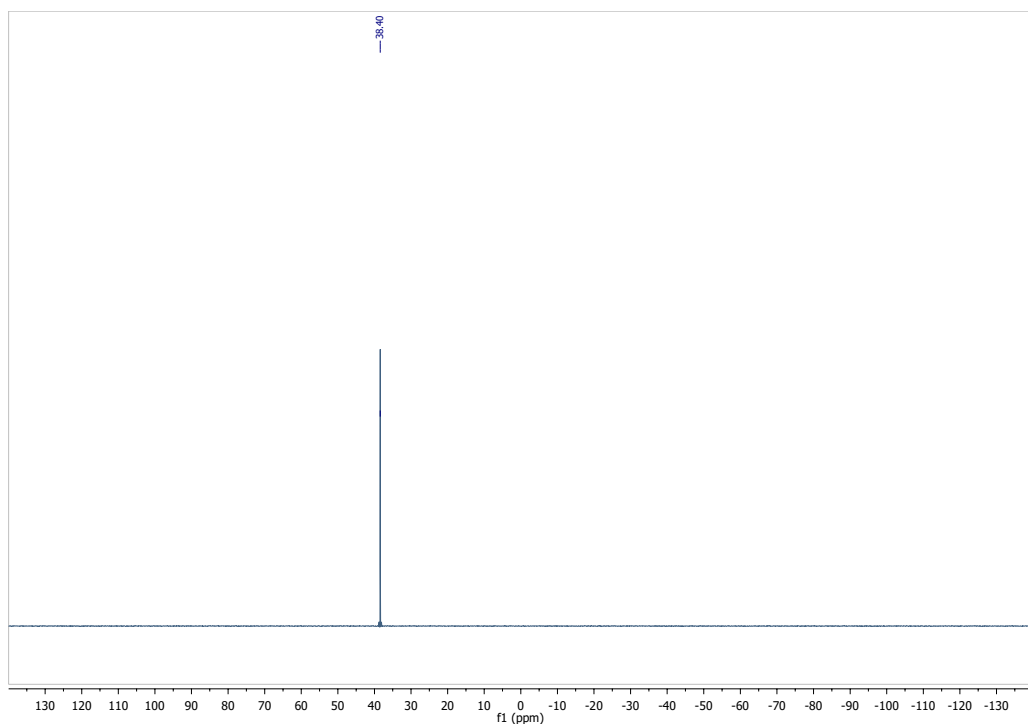




11. [(4-fluorophenyl)methyl](triphenylphosphanyliden)azanium bromide

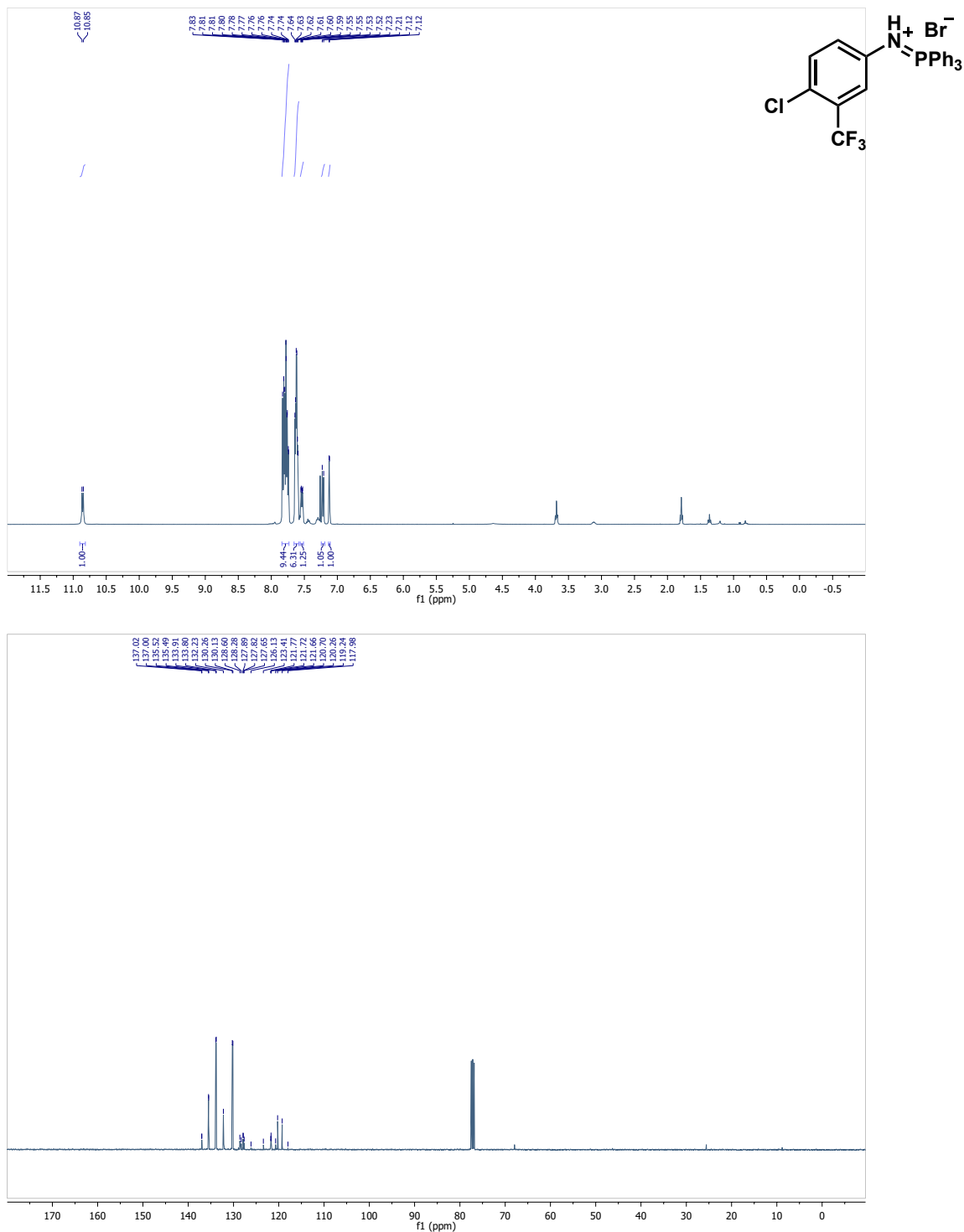
Followed the general procedure (1), product obtained as a white solid (100 mg, yield 36%). ^1H -NMR (400 MHz, CDCl_3): δ 8.79 (m, 1H), 7.79–7.70 (m, 9H), 7.60–7.56 (m, 6H), 7.18–7.13 (m, 2H), 6.84–6.78 (m, 2H), 4.25 (dd, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 162.1, 134.8, 134.4, 133.8, 130.1, 129.9, 121.6, 115.2, 45.0. ^{31}P -NMR (162 MHz, CDCl_3): δ 38.40 (s, 1P). MS (ESI+): Calculated $\text{C}_{25}\text{H}_{22}\text{NPF}$ as 386.1474 [M+H] found as 386.1492.

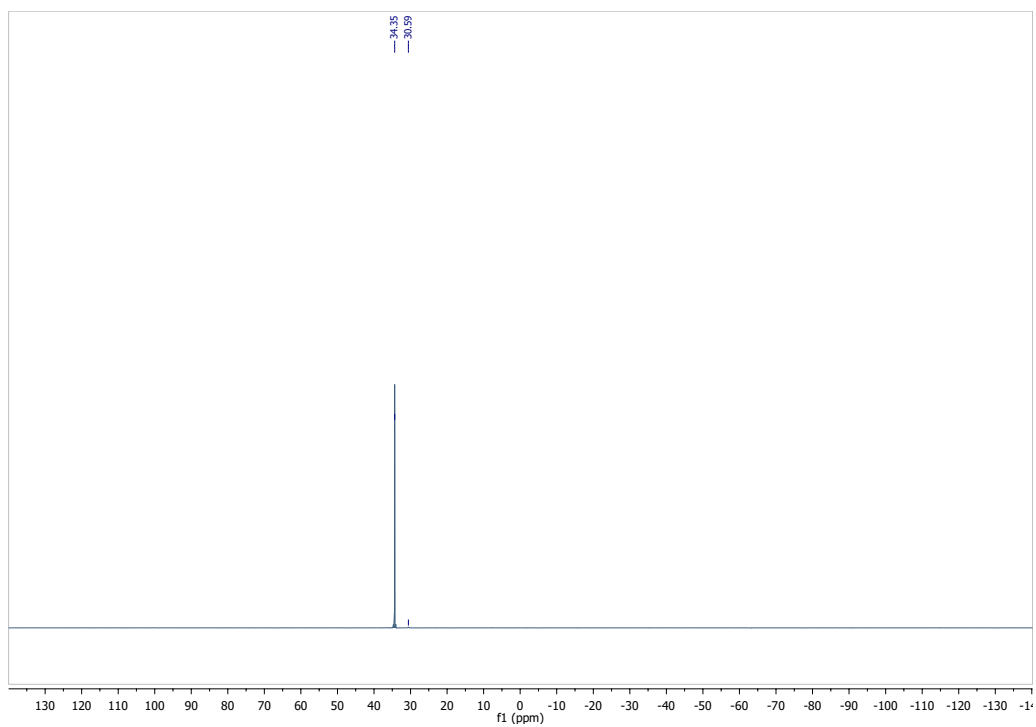




1m. 4-chloro-3-(trifluoromethyl)-N-(triphenylphosphanylidene)anilinium bromide

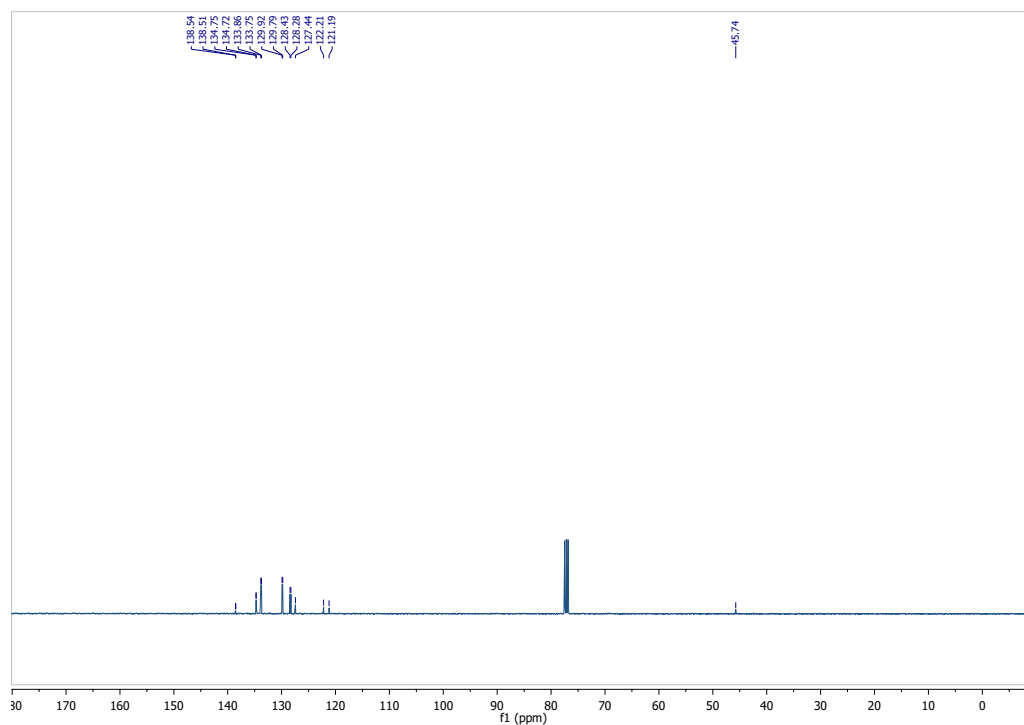
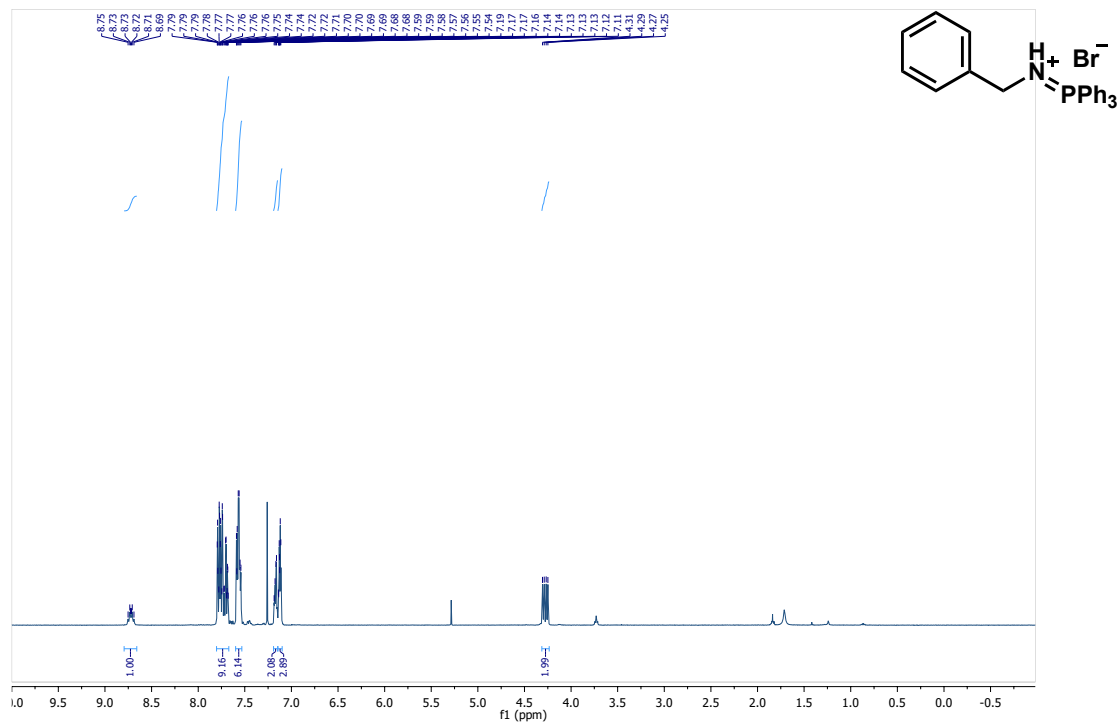
Followed the general procedure (1), product obtained as a white solid (171 mg, yield 53%). ^1H -NMR (400 MHz, CDCl_3): δ 10.86 (d, 1H), 7.83–7.74 (m, 9H), 7.64–7.59 (m, 6H), 7.54 (dd, 1H), 7.22 (d, 1H), 7.12 (d, 1H). ^{13}C -NMR (100 MHz, CDCl_3): 137.0, 135.5, 133.9, 132.2, 130.2, 128.4, 127.9, 127.7, 122.1, 121.7, 119.8. ^{31}P -NMR (162 MHz, CDCl_3): δ 34.35 (s, 1P), 30.59 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{25}\text{H}_{19}\text{NF}_3\text{Cl}$ as 456.0896, $[\text{M}+\text{H}]$ found as 456.0886.

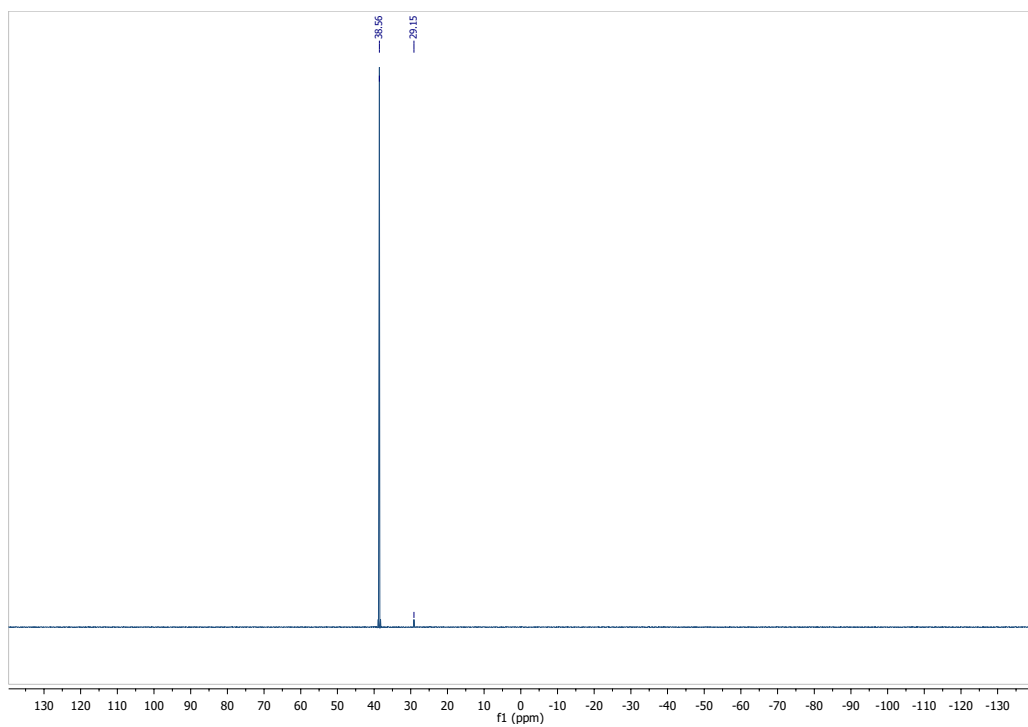




1n. benzyl(triphenylphosphanyliden)azanum bromide

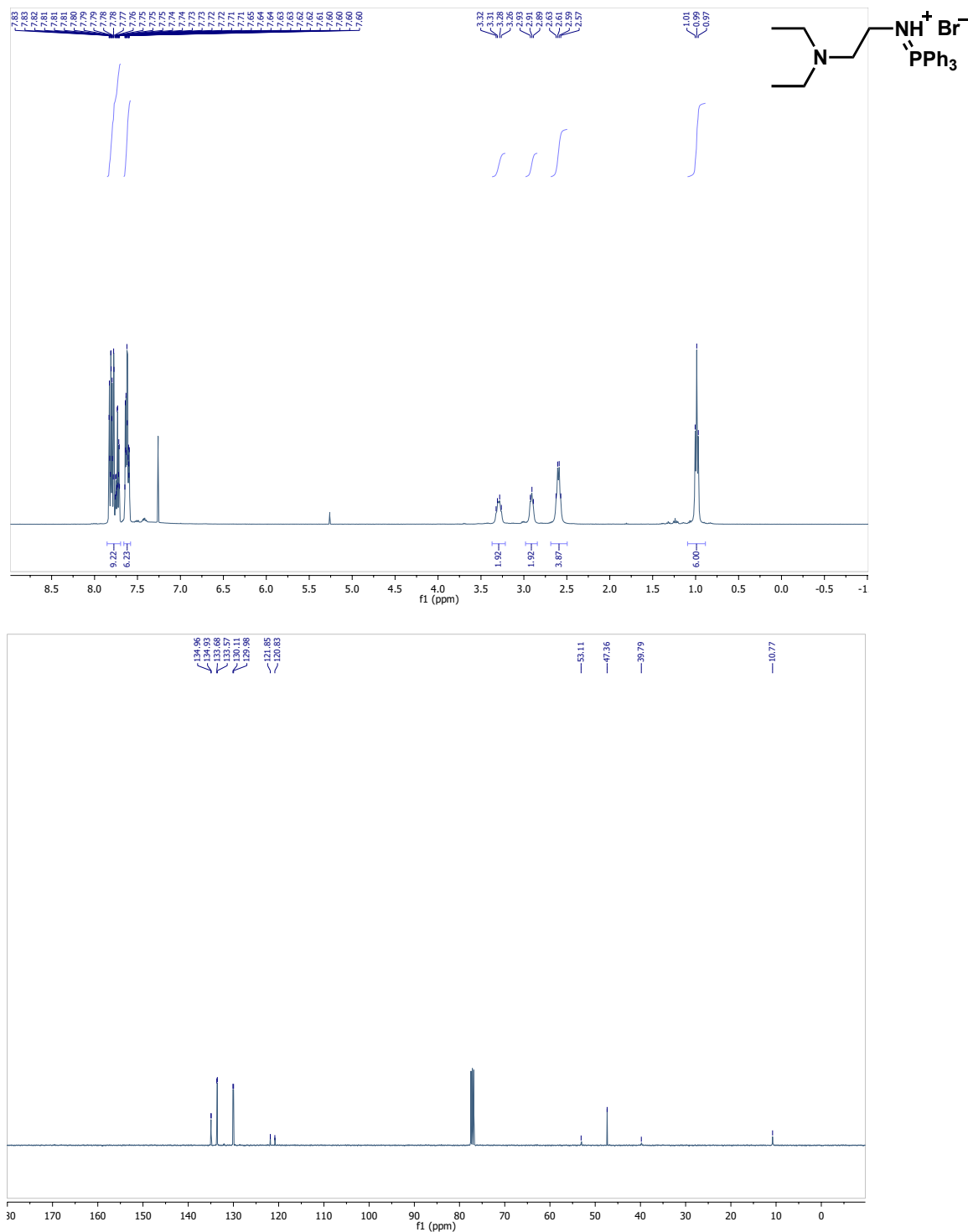
Followed the general procedure (1), product obtained as a white solid (199 mg, yield 74%). ^1H -NMR (400 MHz, CDCl_3): δ 8.72 (m, 1H), 7.74 (m, 9H), 7.57 (m, 6H), 7.18 (m, 2H), 7.13 (m, 3H), 4.28 (dd, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 138.5, 134.7, 133.8, 129.9, 128.4, 128.3, 127.4, 121.7, 45.7. ^{31}P -NMR (162 MHz, CDCl_3): δ 38.56 (s, 1P), 29.15 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{25}\text{H}_{23}\text{NP}$ as 368.1568, $[\text{M}+\text{H}]$ found as 368.1574.

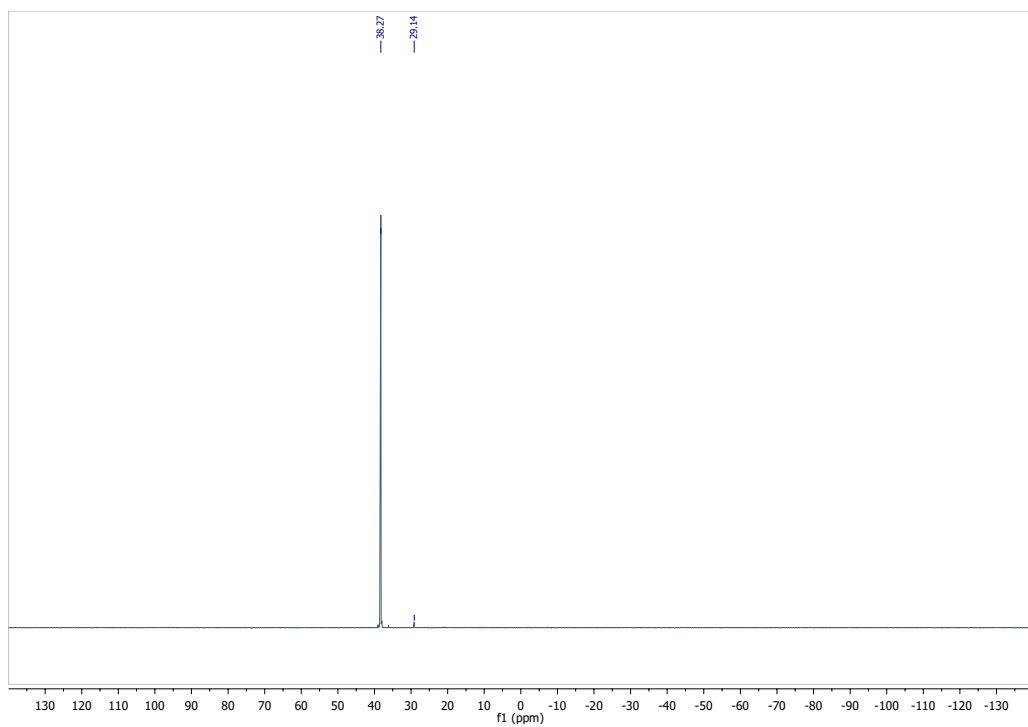




1o. [2-(diethylamino)ethyl](triphenylphosphanylidene)azanum bromide

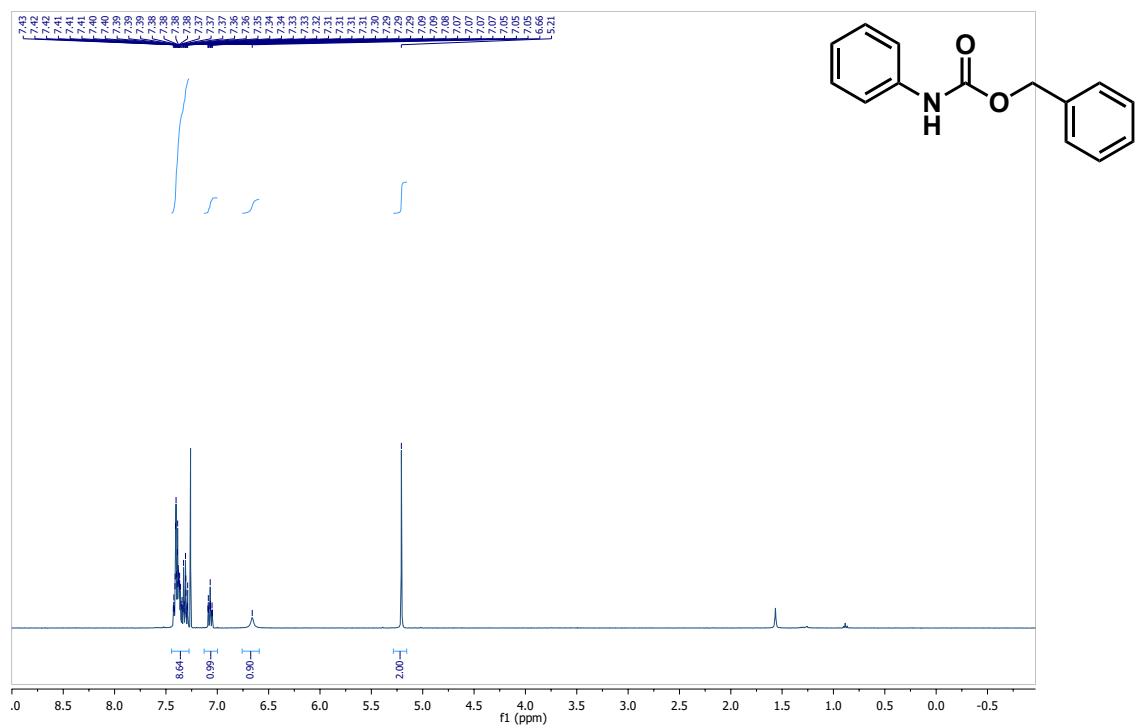
Followed the general procedure (**1**), product obtained as a sticky yellow solid (113 mg, yield 41%). ^1H -NMR (400 MHz, CDCl_3): δ 7.83–7.71 (m, 9H), 7.65–7.60 (m, 6H), 3.29 (dd, 2H), 2.91 (t, 2H), 2.60 (dd, 4H), 0.99 (t, 6H). ^{13}C -NMR (100 MHz, CDCl_3): 134.9, 133.6, 130.0, 121.3, 53.1, 47.4, 39.8, 10.8. ^{31}P -NMR (162 MHz, CDCl_3): δ 38.27 (s, 1P), 29.14 (s, 1P, TPPO). MS (ESI+): Calculated $\text{C}_{24}\text{H}_{30}\text{N}_2\text{P}$ as 377.2147, $[\text{M}+\text{H}]$ found as 377.2166.





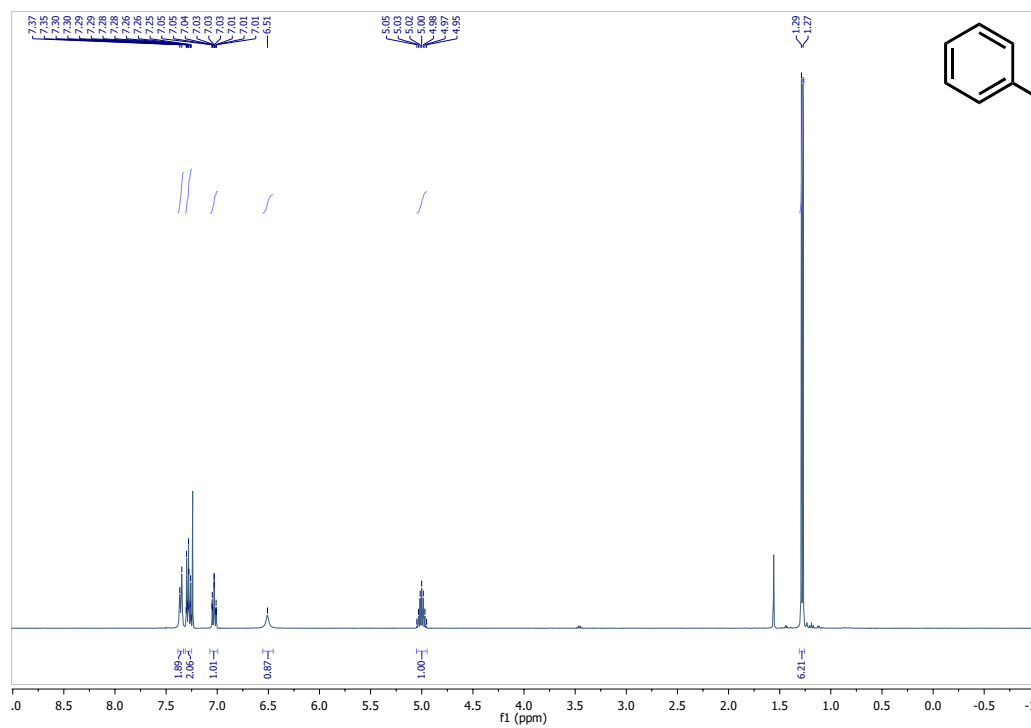
4. benzyl N-phenylcarbamate

Followed the general procedure (2), product obtained as a white powder (23 mg, yield 84%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.43–7.29 (m, 9H), 7.07 (m, 1H), 6.66 (s, 1H), 5.21 (s, 2H). MS (ESI+): Calculated $\text{C}_{14}\text{H}_{13}\text{NO}_2$ as 227.09, $[\text{M}+\text{H}]$ found as 228.02. Characterized in accordance to the literature.¹



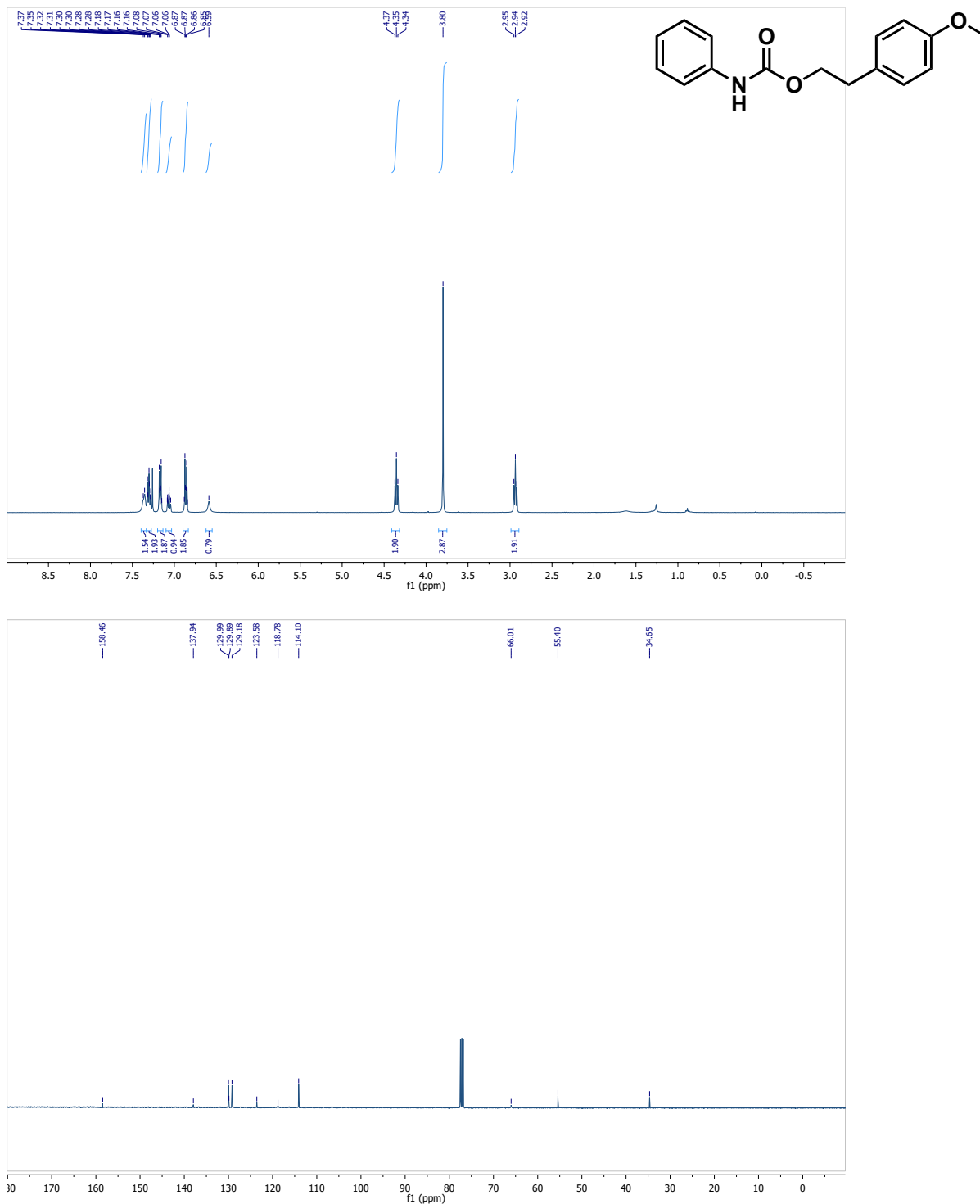
5. propan-2-yl N-phenylcarbamate

Followed the general procedure (2), product obtained as a white powder (41 mg, yield 91%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.36 (d, 2H), 7.28 (m, 2H), 7.03 (m, 1H), 6.51 (s, 1H), 5.00 (sept, 1H), 1.28 (d, 6H). MS (ESI+): Calculated $\text{C}_{10}\text{H}_{13}\text{NO}_2$ as 179.09, $[\text{M}+\text{H}]$ found as 180.08. Characterized in accordance to the literature.²



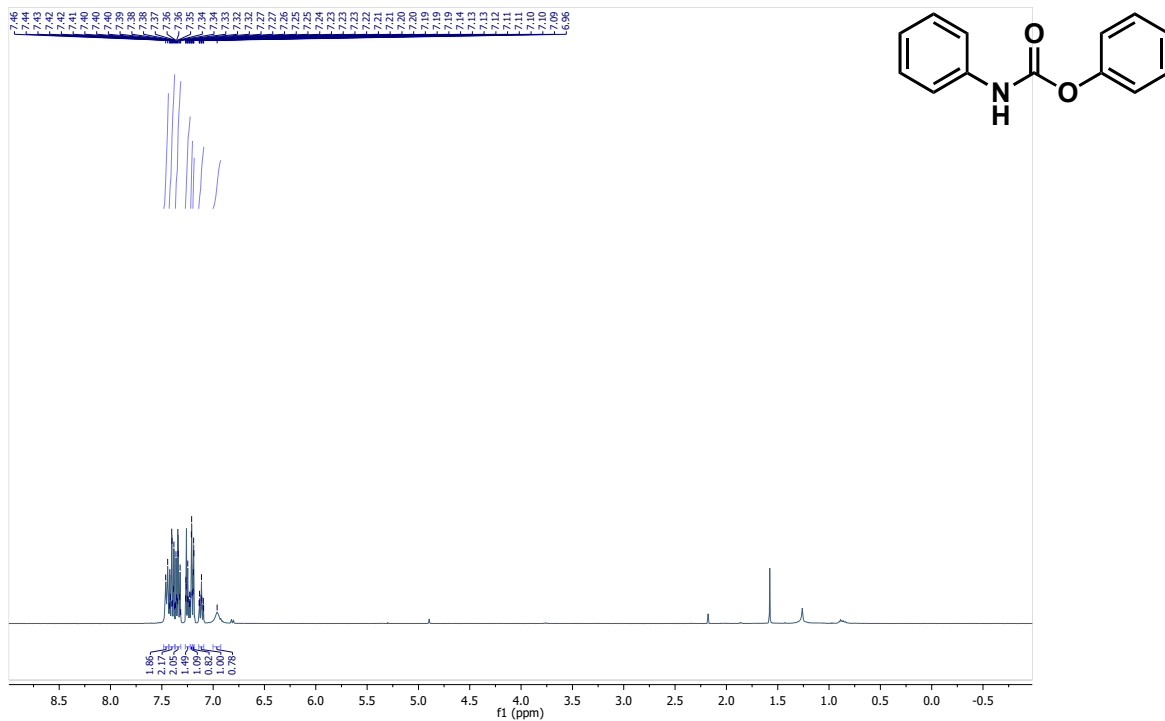
6. 2-(4-methoxyphenyl)ethyl N-phenylcarbamate

Followed the general procedure (2), product obtained as a white powder (64 mg, yield 94%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.36 (d, 2H), 7.30 (m, 2H), 7.17 (m, 2H), 7.06 (m, 1H), 6.86 (m, 2H), 6.59 (s, 1H), 3.36 (dd, 2H), 3.80 (s, 3H), 2.94 (dd, 2H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 158.5, 137.9, 130.0, 129.9, 129.2, 123.6, 118.8, 114.1, 66.0, 55.4, 34.7. MS (ESI+): Calculated $\text{C}_{16}\text{H}_{17}\text{NO}_3\text{Na}$ as 294.1106, $[\text{M}+\text{H}]$ found as 294.1088.



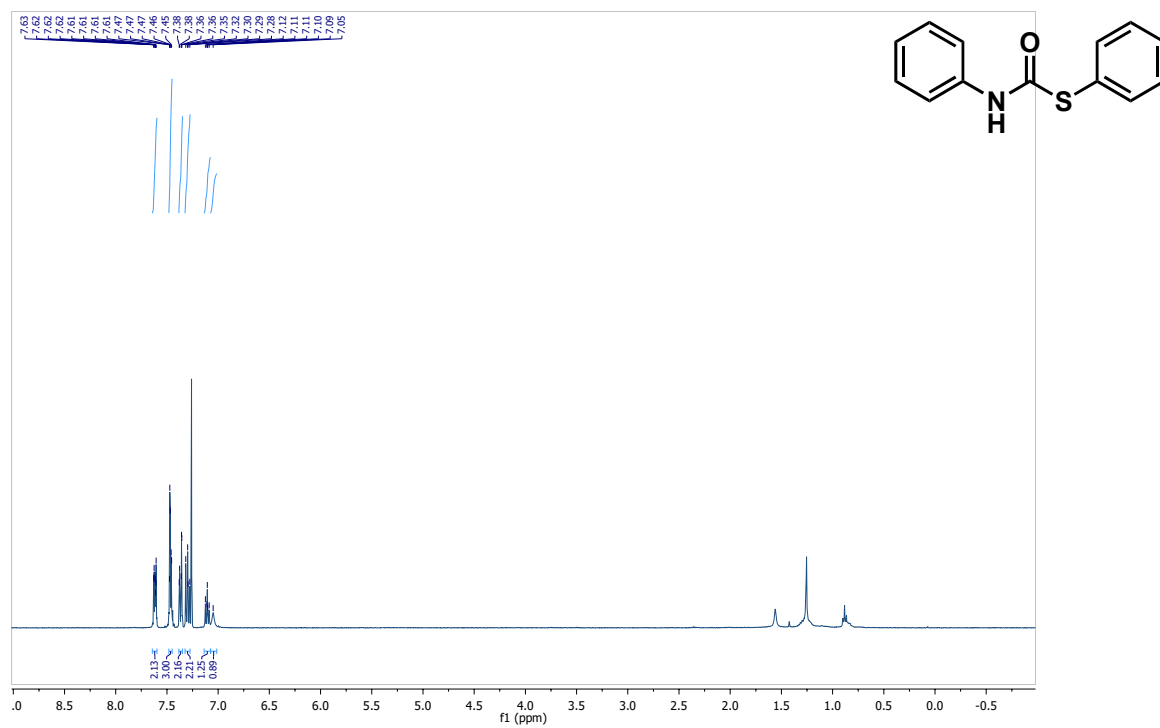
7. phenyl N-phenylcarbamate

Followed the general procedure (2), using 10 equiv. of phenol. Product obtained as a white powder (40 mg, yield 75%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.45 (d, 2H), 7.41 (m, 2H), 7.35 (m, 2H), 7.25 (m, 1H), 7.21 (dd, 1H), 7.20 (dd, 1H), 7.12 (m, 1H), 6.96 (s, 1H). MS (ESI $^+$): Calculated $\text{C}_{13}\text{H}_{11}\text{NO}_2$ as 213.08, $[\text{M}+\text{H}]$ found as 214.26. Characterized in accordance to the literature.³



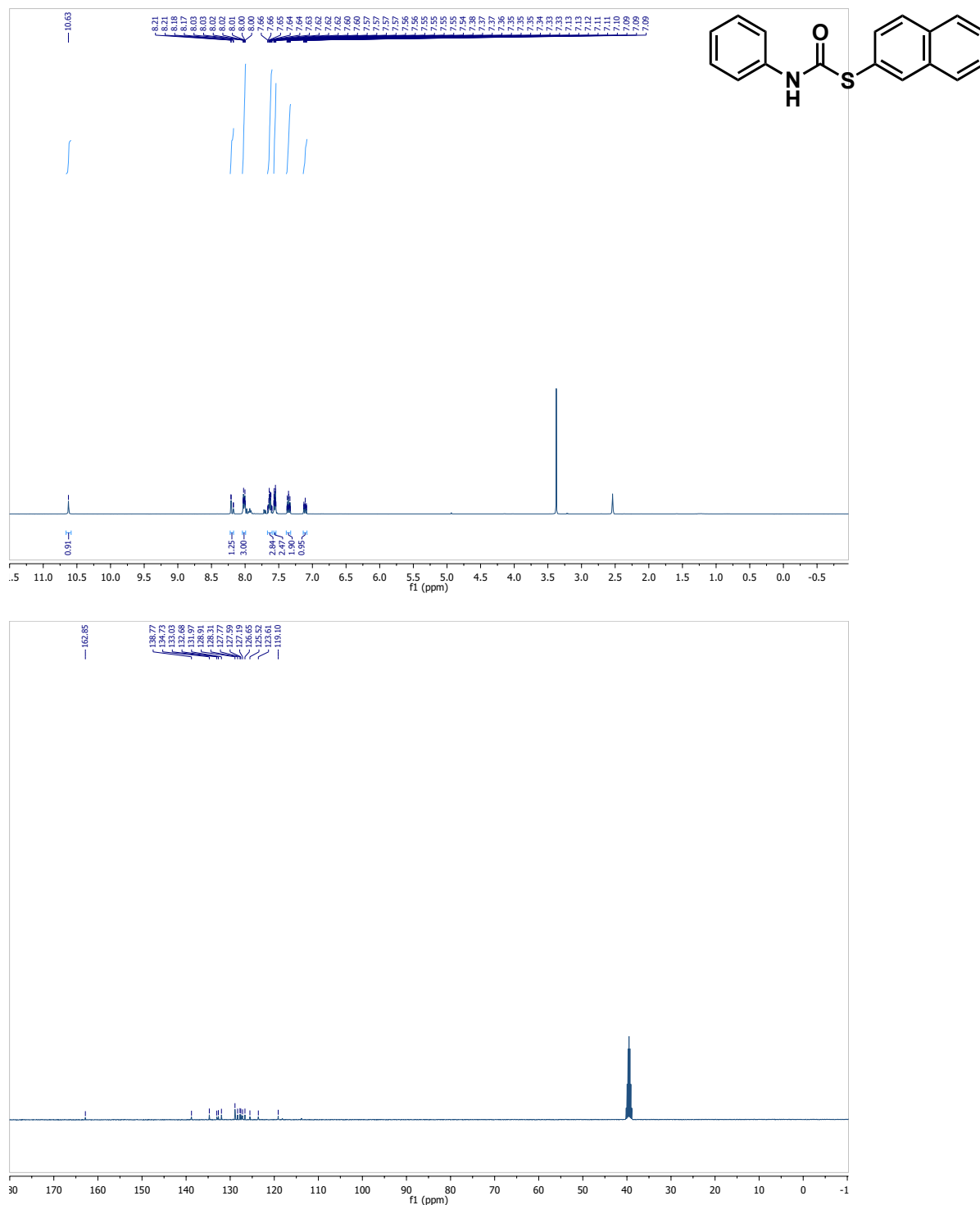
8. N-phenyl-1-(phenylsufanyl)formamide

Followed the general procedure (2), using 10 eqv. of thiophenol. Product obtained as a white powder (43.5 mg, yield 76%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.62 (m, 2H), 7.46 (m, 3H), 7.37 (m, 2H), 7.30 (m, 2H), 7.11 (m, 1H), 7.05 (s, 1H). MS (ESI+): Calculated $\text{C}_{13}\text{H}_{11}\text{NOS}$ as 229.06, $[\text{M}+\text{H}]$ found as 230.11. Characterized in accordance to the literature.⁴



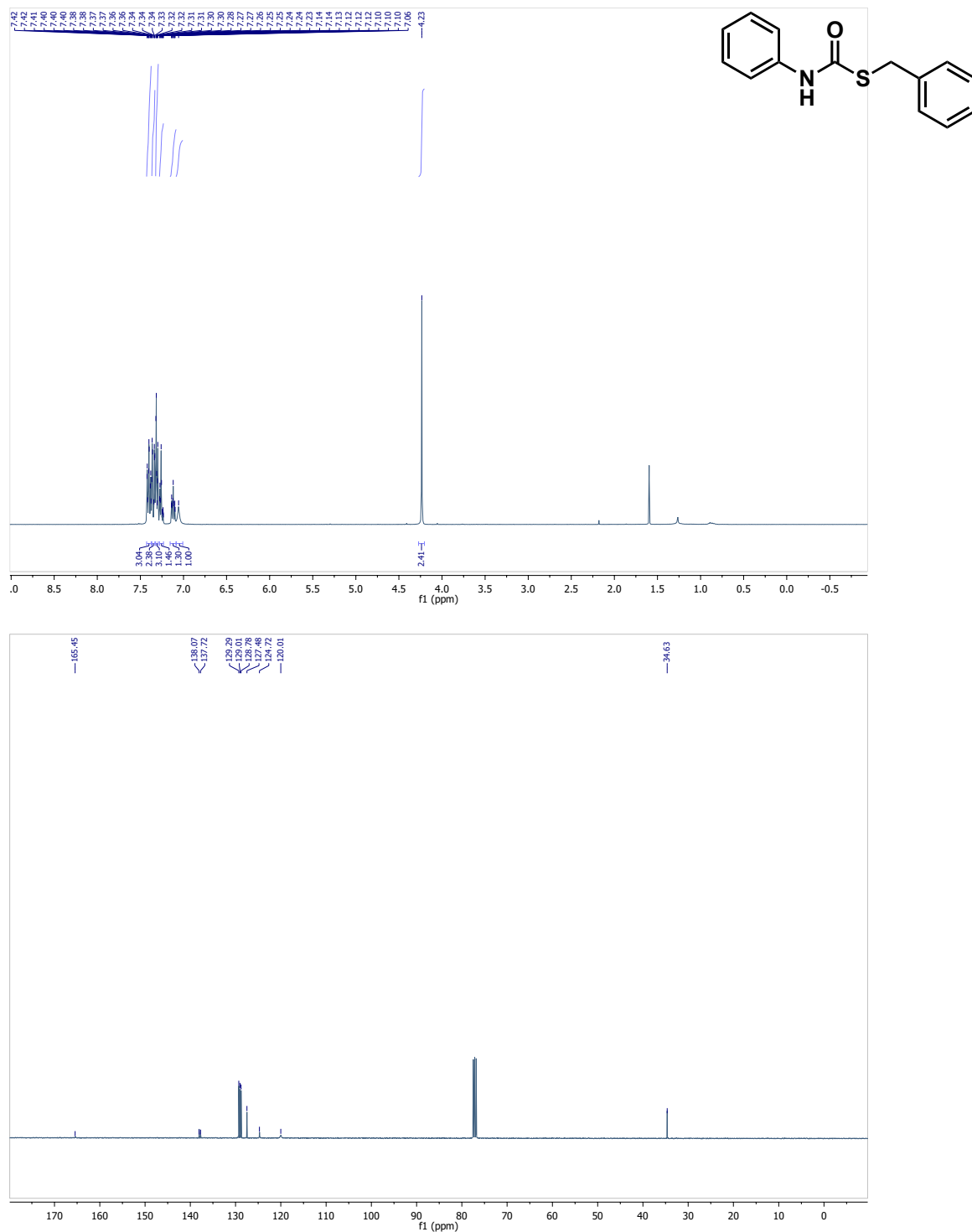
9. 1-(naphthalen-2-ylsulfanyl)-N-phenylformamide

Followed the general procedure (2), using 10 equiv. of 2-naphthalenethiol product obtained as a white powder (49 mg, yield 70%). ^1H -NMR (400 MHz, DMSO): δ 10.63 (s, 1H), 8.19 (dd, 1H), 8.02 (m, 3H), 7.63 (m, 3H), 7.56 (m, 2H), 7.36 (m, 2H), 7.11 (m, 1H). ^{13}C -NMR (100 MHz, DMSO): 162.9, 138.8, 134.7, 133.0, 132.7, 132.0, 128.9, 128.3, 127.8, 127.6, 127.2, 126.7, 125.6, 123.6, 119.1. MS (ESI+): Calculated $\text{C}_{17}\text{H}_{13}\text{NOS}$ as 279.07, $[\text{M}+\text{H}]$ found as 280.26. Characterized in accordance to the literature.⁴



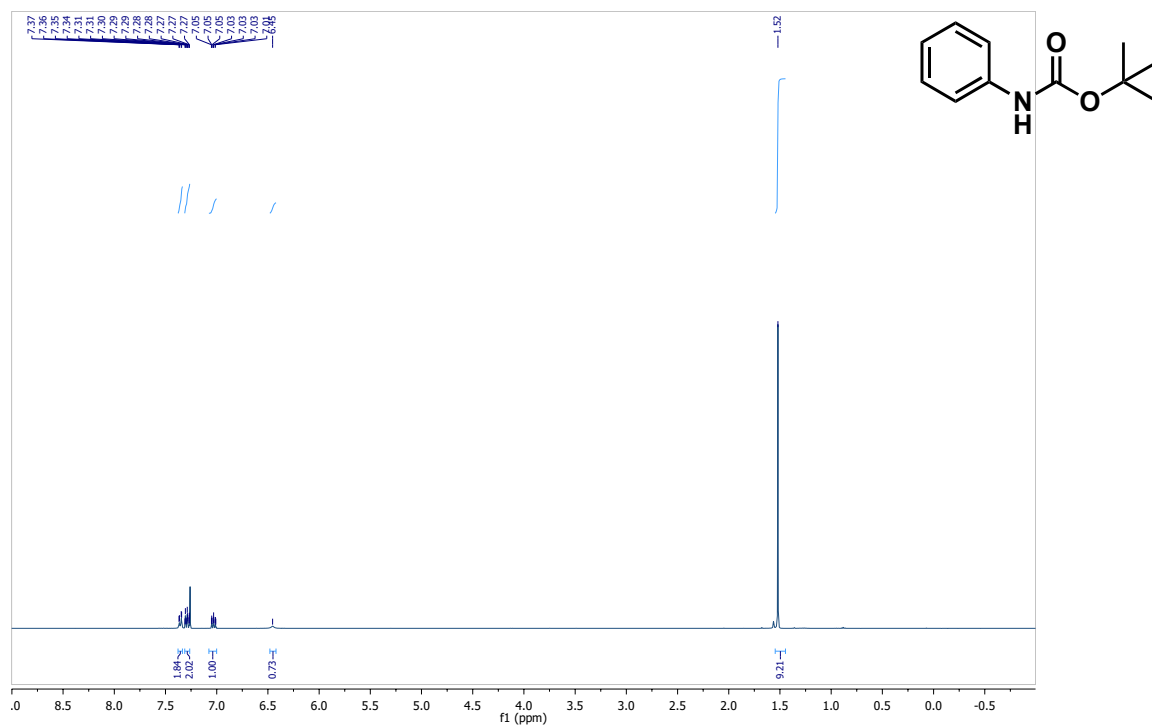
10. N-phenyl(benzylsufanyl)formamide

Followed the general procedure (2), product obtained as a white powder (66.5 mg, yield 86%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.40 (m, 3H), 7.35 (m, 2H), 7.31 (m, 3H), 7.26 (m, 1H), 7.12 (m, 1H), 7.06 (s, 1H), 4.23 (s, 2H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 165.5, 138.1, 137.8, 129.3, 129.0, 128.8, 127.5, 124.7, 120.0, 34.6. MS (ESI+): Calculated $\text{C}_{14}\text{H}_{13}\text{NOS}$ as 243.07, $[\text{M}+\text{H}]$ found as 244.13. Characterized in accordance to the literature.⁴



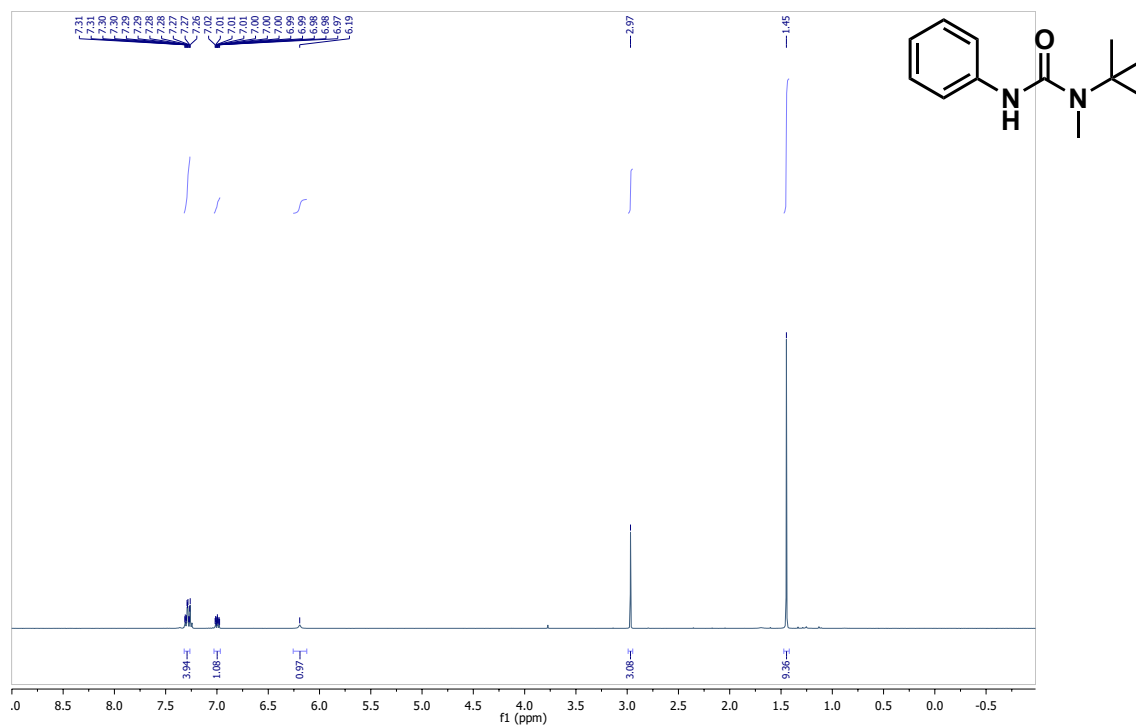
11. *tert*-butyl N-phenylcarbamate

Followed the general procedure (2), using 10 equiv. of *tert*-butyl alcohol. Product obtained as a white powder (40 mg, yield 83%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.36 (m, 2H), 7.29 (m, 2H), 7.03 (m, 1H), 6.45 (s, 1H), 1.52 (s, 9H). MS (ESI+): Calculated $\text{C}_{11}\text{H}_{15}\text{NO}_2$ as 193.11, $[\text{M}+\text{H}]$ found as 194.14. Characterized in accordance to the literature.⁵



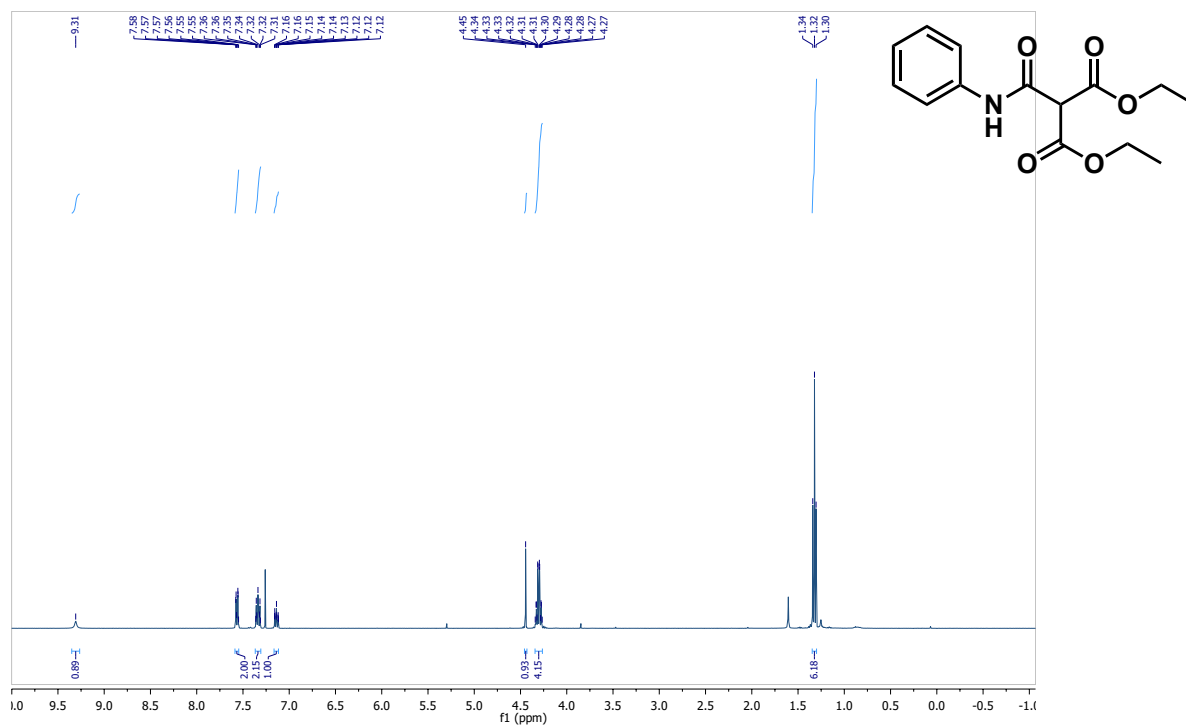
12. 3-tert-butyl-3-methyl-1-phenylurea

Followed the general procedure (**3**), product obtained as a white powder (40 mg, yield 78%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.29 (m, 4H), 7.00 (m, 1H), 6.19 (s, 1H), 2.97 (s, 3H), 1.45 (s, 9H). MS (ESI $^+$): Calculated $\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}$ as 206.14, $[\text{M}+\text{H}]$ found as 207.14. Characterized in accordance to the literature.⁶



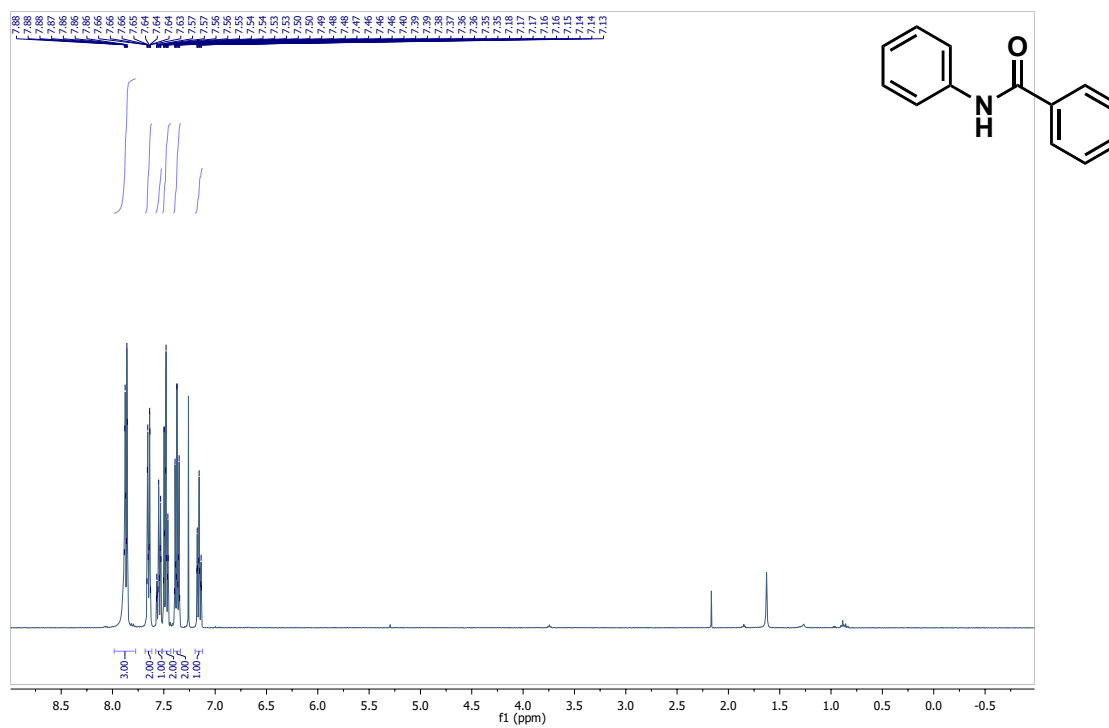
13. 1,3-diethyl 2-(phenylcarbamoyl)propanedioate

Followed the general procedure (6), product obtained as a white powder (57 mg, yield 82%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 9.31 (s, 1H), 7.57 (m, 2H), 7.34 (m, 2H), 7.14 (m, 1H), 4.45 (s, 1H), 4.31 (m, 4H), 1.32 (t, 6H). MS (ESI+): Calculated $\text{C}_{14}\text{H}_{17}\text{NO}_5\text{Na}$ as 302.1004, $[\text{M}+\text{H}]$ found as 302.0982.



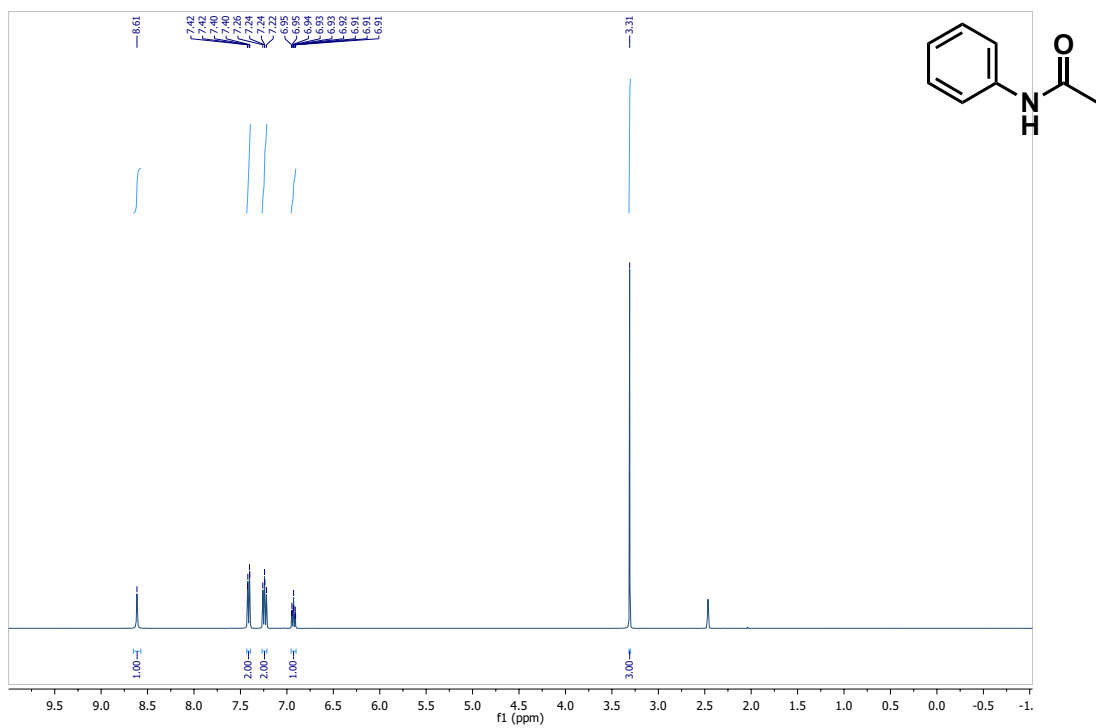
14. N-phenylbenzamide

Followed the general procedure (4), product obtained as a white powder (31 mg, yield 63%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.87 (m, 3H), 7.65 (m, 2H), 7.55 (m, 1H), 7.48 (m, 2H), 7.38 (m, 2H), 7.16 (m, 1H). MS (ESI+): Calculated $\text{C}_{13}\text{H}_{11}\text{NO}$ as 197.08, $[\text{M}+\text{H}]$ found as 198.16. Characterized in accordance to the literature.¹³



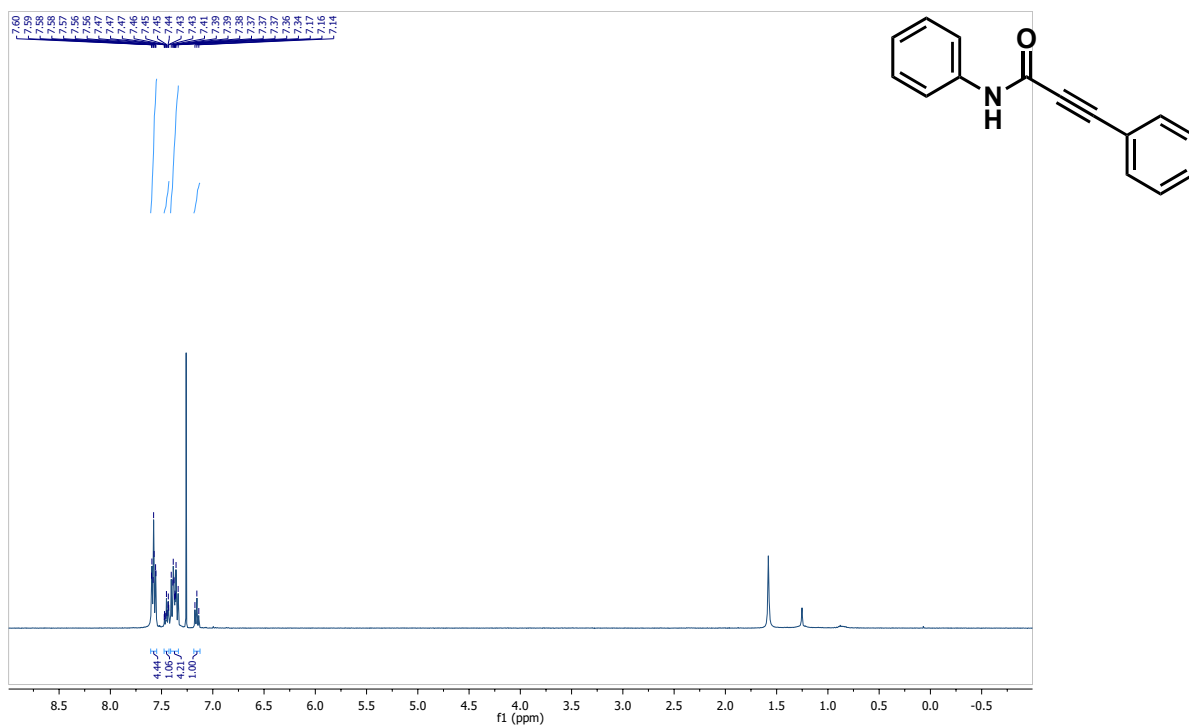
15. N-phenylacetamide

Followed the general procedure (**4**), product obtained as a white solid (32 mg, yield 65%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 8.61 (s, 1H), 7.41 (m, 2H), 7.24 (m, 2H), 6.93 (m, 1H), 3.31 (s, 3H). MS (ESI+): Calculated $\text{C}_8\text{H}_9\text{NO}$ as 135.07, $[\text{M}+\text{H}]$ found as 136.14. Characterized in accordance to the literature.¹⁴



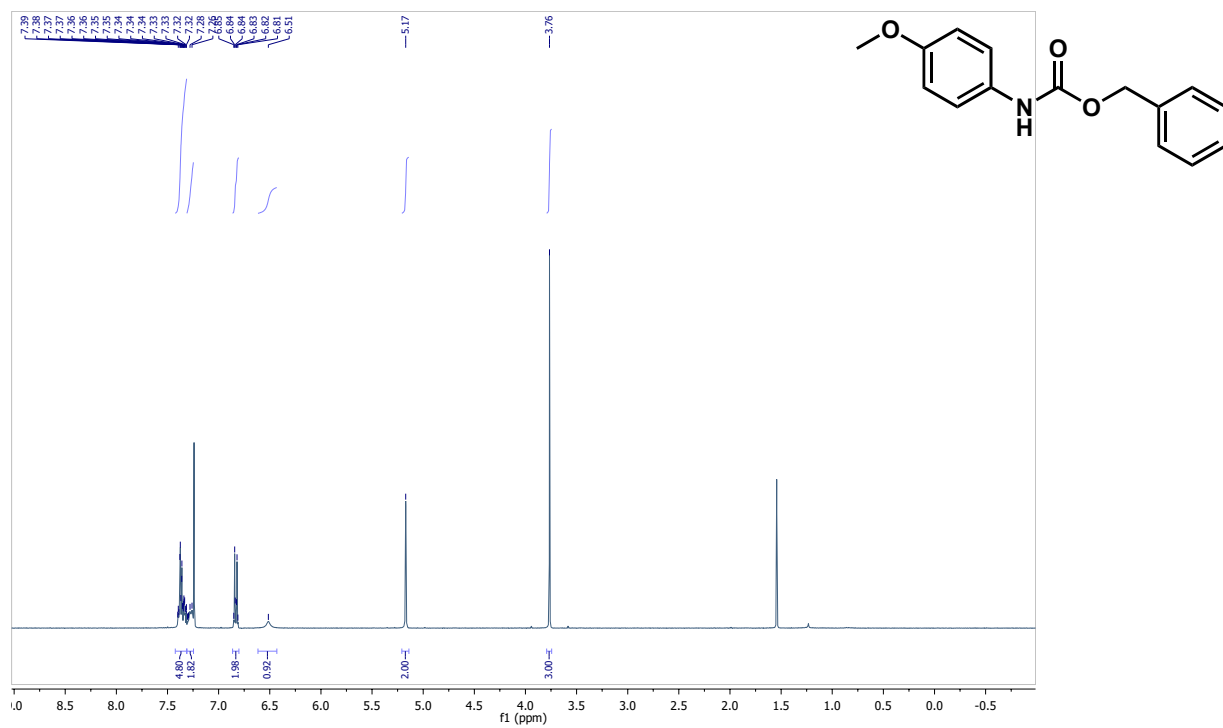
16. N,3-diphenylprop-2-ynamide

Followed the general procedure (5), product obtained as a brown solid (41.5 mg, yield 75%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.58 (m, 4H), 7.45 (m, 1H), 7.38 (m, 4H), 7.15 (m, 1H). MS (ESI+): Calculated $\text{C}_{15}\text{H}_{11}\text{NO}$ as 221.08, $[\text{M}+\text{H}]$ found as 222.09. Characterized in accordance to the literature.¹⁵



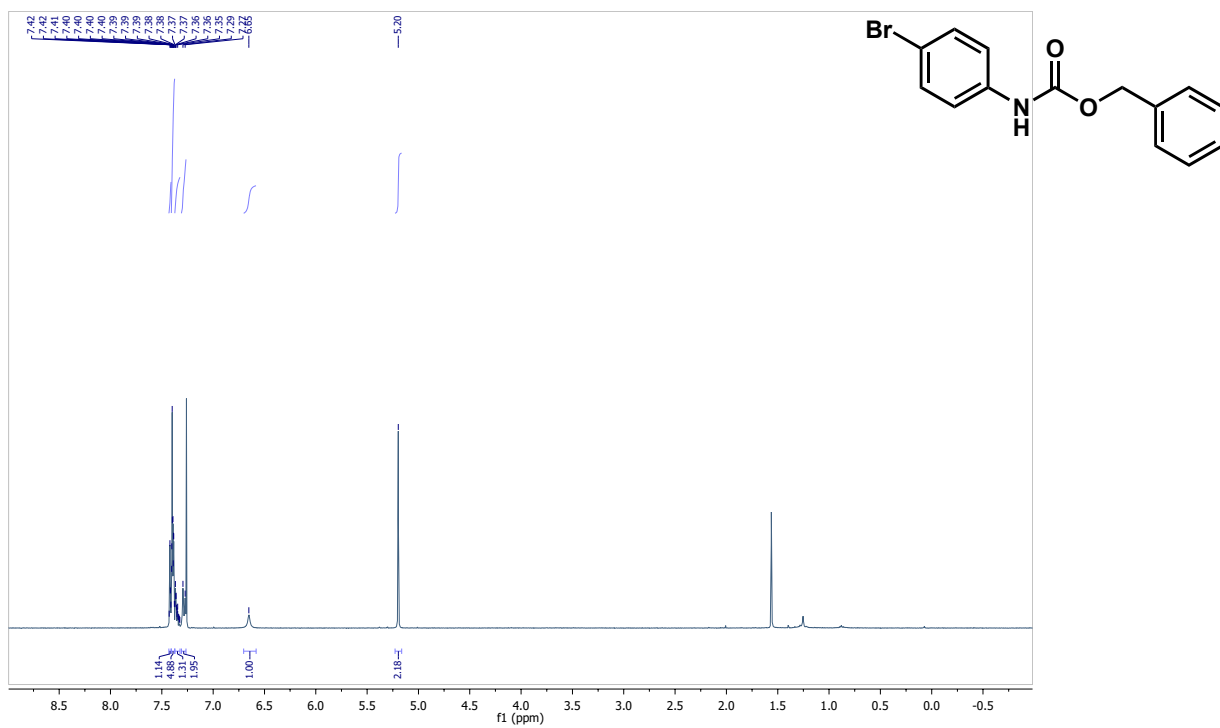
17. benzyl N-(4-methoxyphenyl)carbamate

Followed the general procedure (2), product obtained as a white powder (53 mg, yield 82%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.40–7.32 (m, 5H), 7.30–7.26 (m, 2H), 6.83 (m, 2H), 6.51 (s, 1H), 5.17 (s, 2H), 3.76 (s, 3H). MS (ESI+): Calculated $\text{C}_{15}\text{H}_{15}\text{NO}_3$ as 257.11, $[\text{M}+\text{H}]$ found as 258.20. Characterized in accordance to the literature.¹



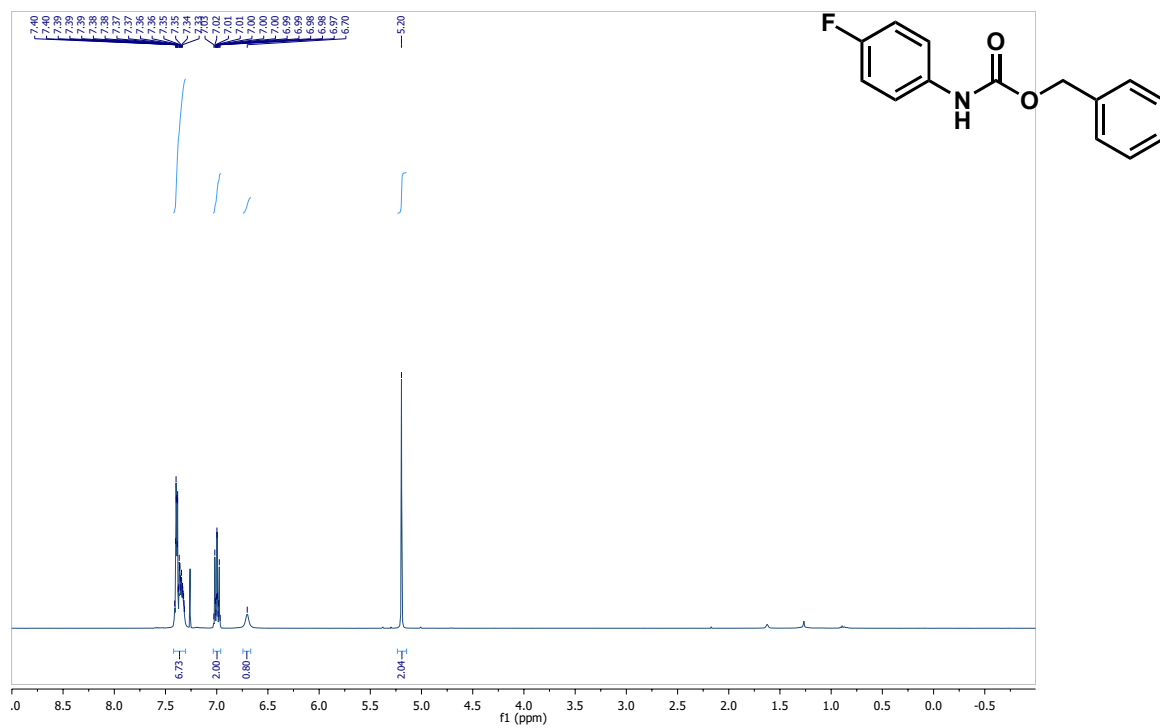
18. benzyl N-(4-bromophenyl)carbamate

Followed the general procedure (2), product obtained as a white powder (64 mg, yield 83%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.42 (m, 1H), 7.39 (m, 5H), 7.35 (m, 1H), 7.28 (d, 2H), 6.65 (s, 1H), 5.20 (s, 2H). MS (ESI $^+$): Calculated $\text{C}_{14}\text{H}_{12}\text{BrNO}_2$ as 305.01, $[\text{M}+\text{H}]$ found as 306.19. Characterized in accordance to the literature.¹



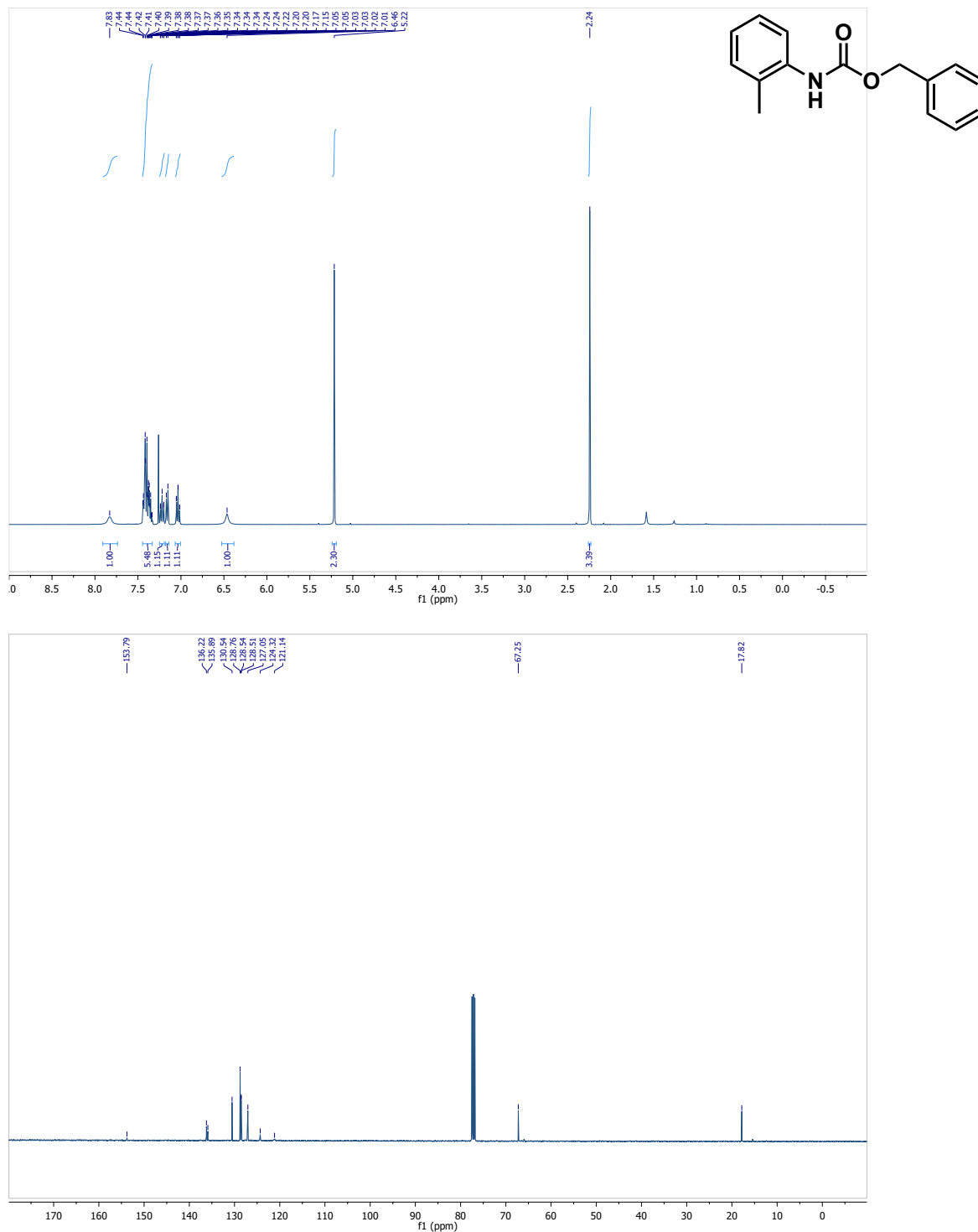
19. benzyl N-(4-fluorophenyl)carbamate

Followed the general procedure (2), product obtained as a white powder (35 mg, yield 57%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.41–7.32 (m, 7H), 7.00 (m, 2H), 6.70 (s, 1H), 5.20 (s, 2H). MS (ESI+): Calculated $\text{C}_{14}\text{H}_{12}\text{FNO}_2$ as 245.09, $[\text{M}+\text{H}]$ found as 246.06. Characterized in accordance to the literature.¹



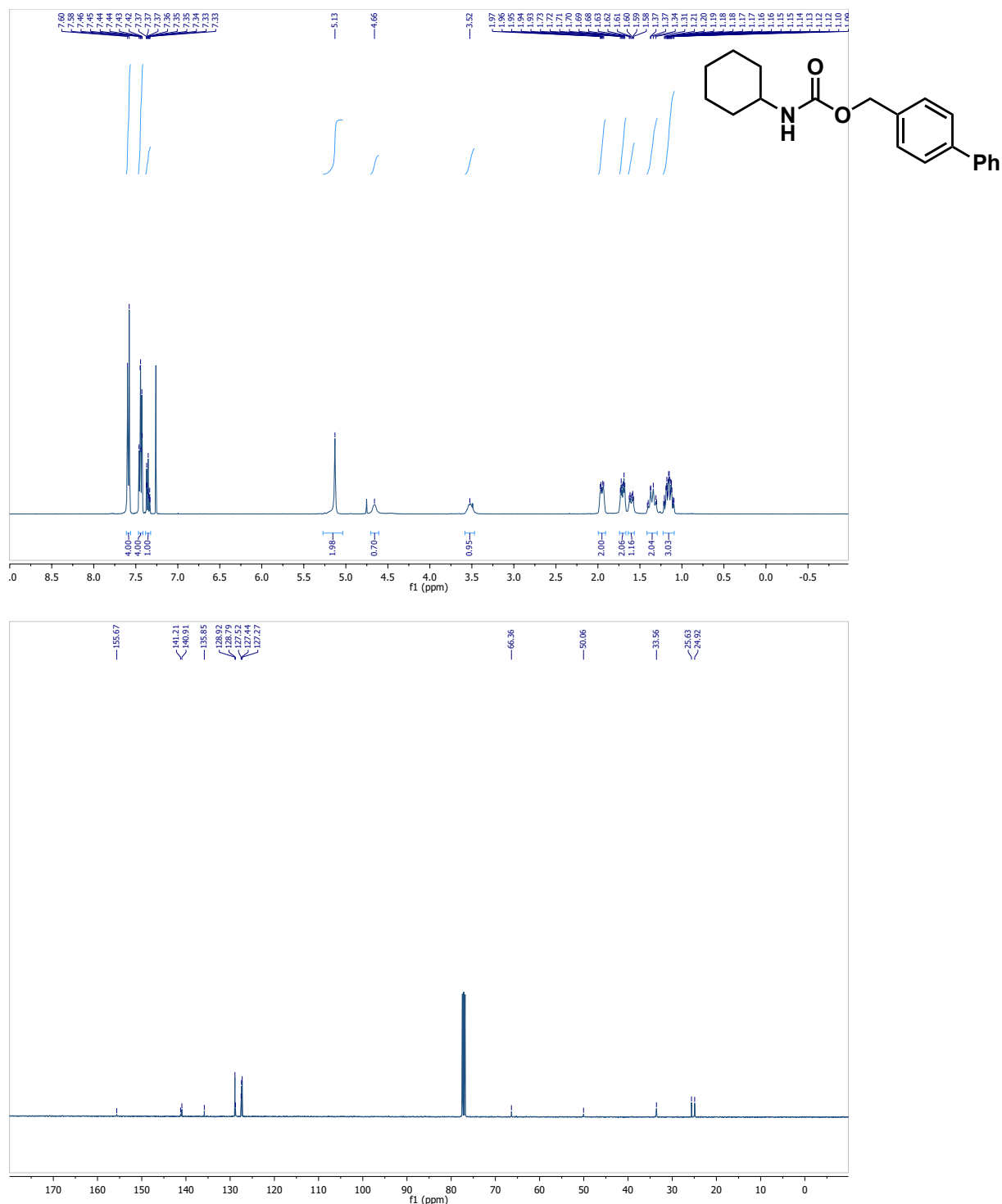
21. benzyl N-(2-methylphenyl)carbamate

Followed the general procedure (2), product obtained as a white powder (51 mg, yield 84%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.83 (s, 1H), 7.44–7.34 (m, 5H), 7.22 (m, 1H), 7.16 (d, 1H), 7.03 (m, 1H), 6.46 (s, 1H), 5.22 (s, 2H), 2.24 (s, 3H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 153.8, 136.2, 135.9, 130.5, 128.8, 128.5, 128.5, 127.1, 124.3, 121.1, 67.3, 17.8. MS (ESI+): Calculated $\text{C}_{15}\text{H}_{15}\text{NO}_2$ as 241.11, $[\text{M}+\text{H}]$ found as 242.17. Characterized in accordance to the literature.²



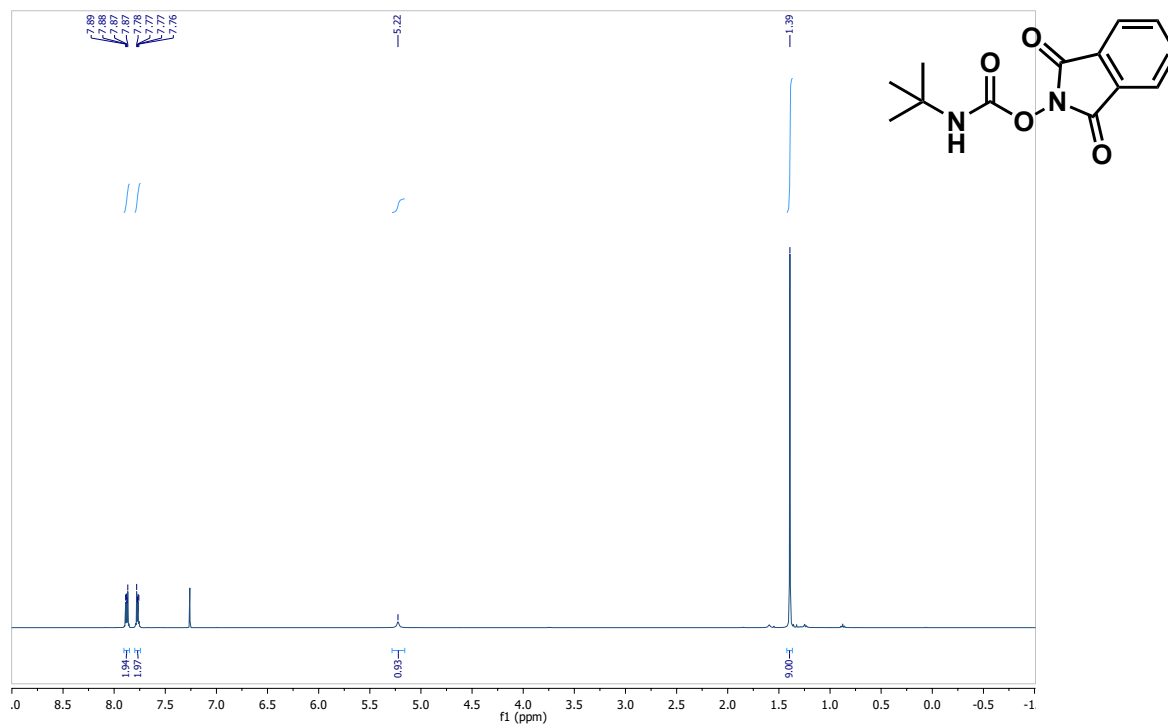
22. [(1,1'-biphenyl)-4-yl]methyl N-cyclohexylcarbamate

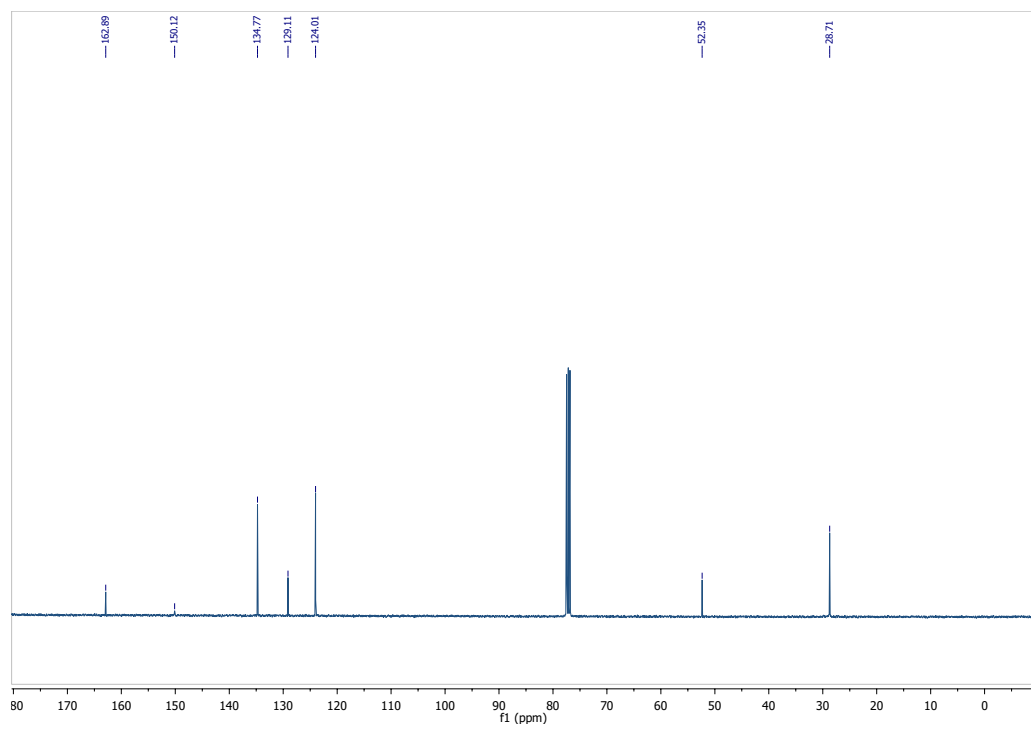
Followed the general procedure **7**, then procedure **2**, using 10 equiv. of 4-biphenylmethanol. The reaction was performed at reflux temperature in THF (2.5 mL). DBU was not used. Product obtained as a white powder (64 mg, yield 82%). ^1H -NMR (400 MHz, CDCl_3): δ 7.59 (m, 4H), 7.44 (m, 4H), 7.35 (m, 1H), 5.13 (s, 2H), 4.66 (s, 1H), 3.52 (s, 1H), 1.95 (m, 2H), 1.71 (m, 2H), 1.61 (m, 2H), 1.36 (m, 2H), 1.15 (m, 2H). ^{13}C -NMR (100 MHz, CDCl_3): 155.7, 141.2, 140.9, 135.9, 128.9, 128.8, 127.5, 127.4, 127.3, 66.4, 50.1, 33.6, 25.6, 24.9. MS (ESI $^+$): Calculated $\text{C}_{20}\text{H}_{23}\text{NO}_2\text{Na}$ as 332.1626, $[\text{M}+\text{H}]$ found as 332.1635.



23. 1,3-dioxo-2,3-dihydro-1H-isoindol-2-yl N-tert-butylcarbamate

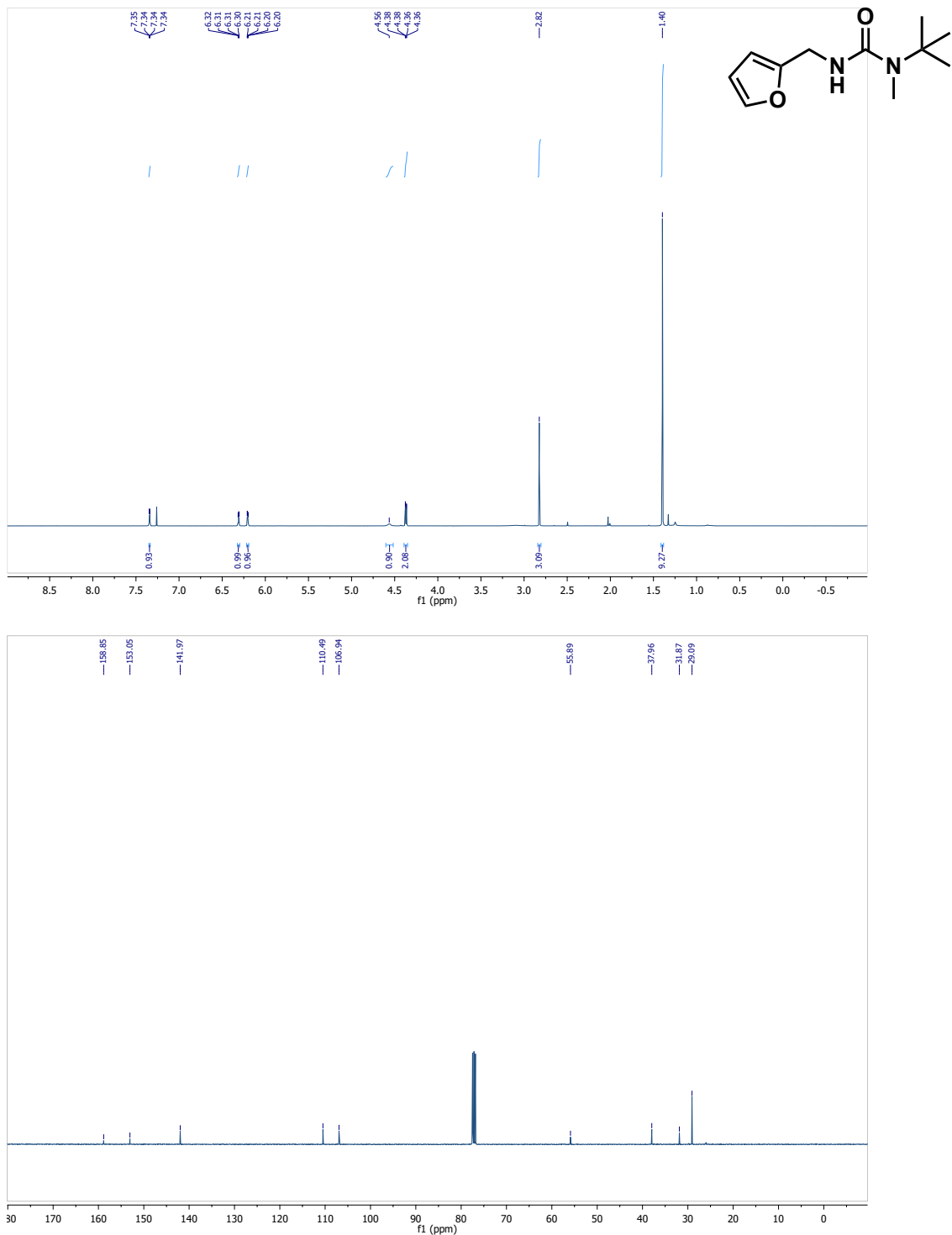
Followed the general procedure **7**, then procedure **2** using 10 equiv. of *N*-hydroxyphthalimide (NHP). NHP was dissolved in THF (2.5 mL), and 10 equiv. of NEt_3 was added. The reaction was performed at reflux temperature in THF (2.5 mL). DBU was not used. The solvent was removed under reduced pressure, and the residue was dissolved in 10 mL of DCM. Solvent extraction was performed, and the organic layer was extracting using saturated NH_4^+Cl^- (3 x 5 mL), 10% Na_2CO_3 (2 x 5 mL), and water (2 x 5 mL). The solvent was removed under reduced pressure, and the product was purified by flash chromatography using silica gel (0-25% hexane/ethyl acetate). Product obtained as a white powder (54 mg, yield 81%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.88 (m, 2H), 7.77 (m, 2H), 5.22 (s, 1H), 1.39 (s, 9H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 162.9, 150.1, 134.8, 129.1, 124.0, 52.4, 28.7. MS (ESI+): Calculated $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_4$ as 262.10, $[\text{M}+\text{H}]$ found as 263.11.





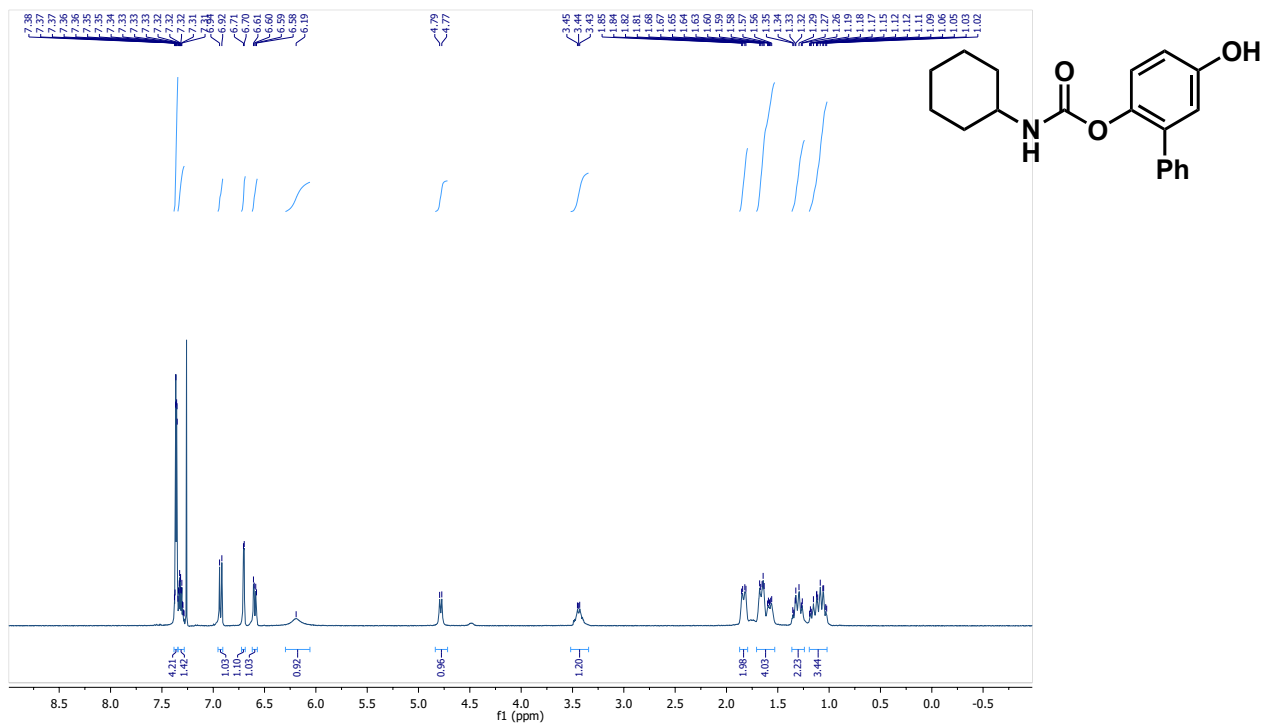
24. 3-tert-butyl-1-[(furan-2-yl)methyl]-3-methylurea

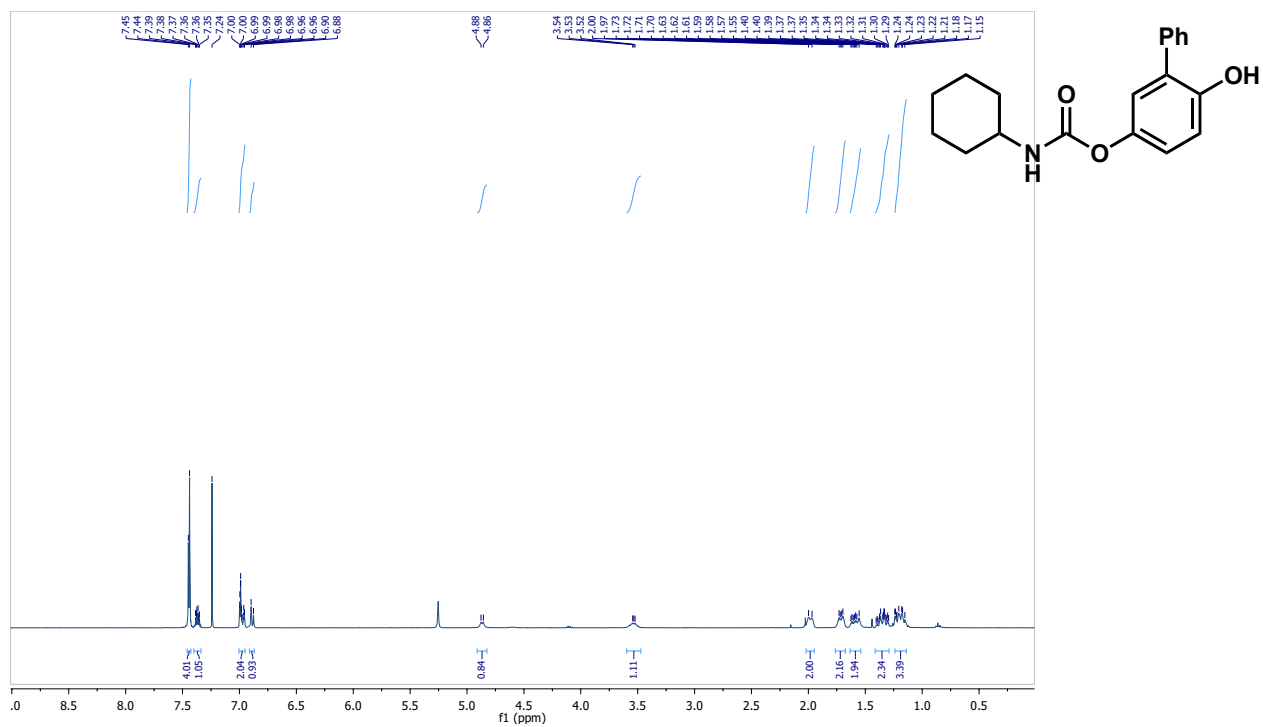
Followed the general procedure (**3**), product obtained as a white powder (37.5 mg, yield 71%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.35 (dd, 1H), 6.31 (dd, 1H), 6.21 (dd, 1H), 4.56 (s, 1H), 4.37 (dd, 2H), 2.82 (s, 3H), 1.40 (s, 9H). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 158.9, 153.1, 142.0, 110.5, 106.9, 55.9, 38.0, 31.9, 29.1. MS (ESI+): Calculated $\text{C}_{11}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}$ as 233.1266, $[\text{M}+\text{H}]$ found as 233.1261.



25. 5-hydroxy-(1,1'-biphenyl)-2-yl N-cyclohexylcarbamate

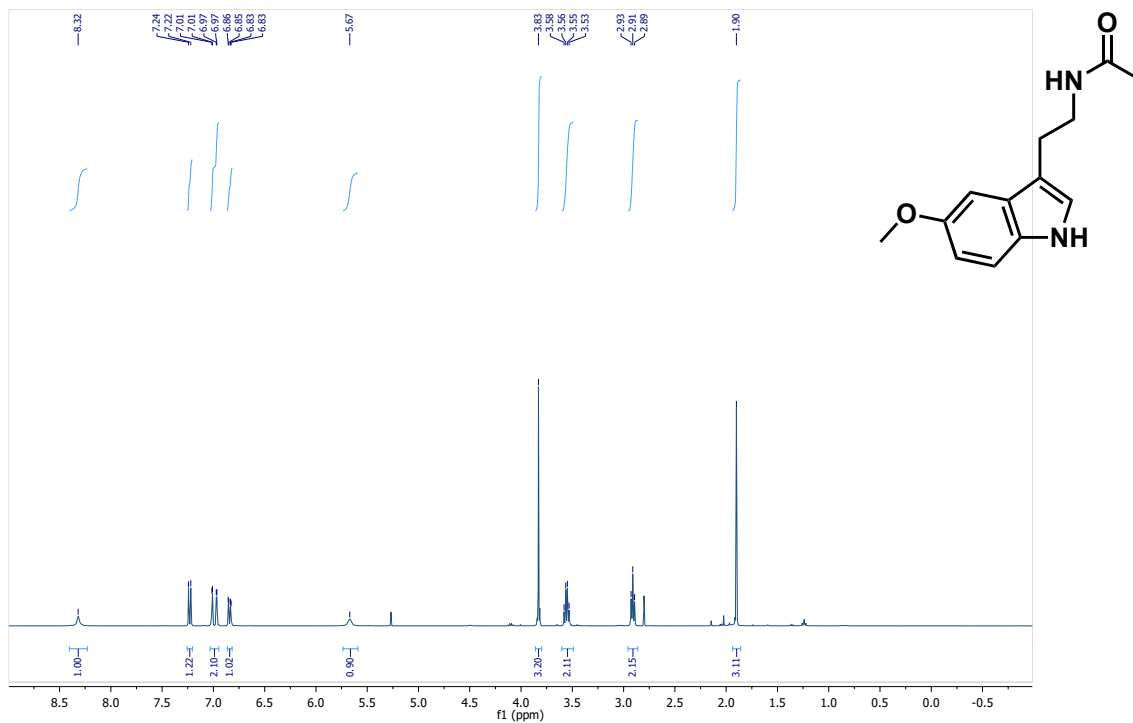
Followed the general procedure 7, then procedure 2 using 10 equiv. of 2-phenyl-1,4-dihydroquinone. The reaction was performed at reflux temperature in THF (2.5 mL). DBU was not used. The obtained product was hydrolyzed in accordance with the literature, and a mixture of isomers was obtained (186 mg, yield 60%). Isomers were separated by prep-HPLC using a Phenomenex C18, 10 μ M, 250x10 column with 70:30 MeOH/H₂O + 1% formic acid at 10 mL/min. Obtained isomer 1 as a white powder (160 mg, 85%), obtained isomer 2 as a white powder (26.5 mg, 14%). Isomer 1 ¹H-NMR (400 MHz, CDCl₃): δ 7.36 (m, 4H), 7.31 (m, 1H), 6.93 (d, 1H), 6.71 (d, 1H), 6.60 (dd, 1H), 6.19 (s, 1H), 4.78 (d, 1H), 3.44 (m, 1H), 1.83 (m, 2H), 1.68–1.56 (m, 4H), 1.31 (m, 2H), 1.10 (m, 2H). MS (ESI⁺): Calculated C₁₉H₂₁NO₃ as 311.15, [M+H]⁺ found as 312.20. Isomer 2 ¹H-NMR (400 MHz, CDCl₃): δ 7.45 (d, 4H), 7.37 (m, 1H), 6.98 (m, 2H), 6.89 (d, 1H), 4.87 (d, 1H), 3.53 (m, 1H), 1.99 (d, 2H), 1.72 (m, 2H), 1.69 (m, 2H), 1.35 (m, 2H), 1.20 (m, 2H). MS (ESI⁺): Calculated C₁₉H₂₁NO₃ as 311.15, [M+H]⁺ found as 312.18. Characterized in accordance to the literature.⁷





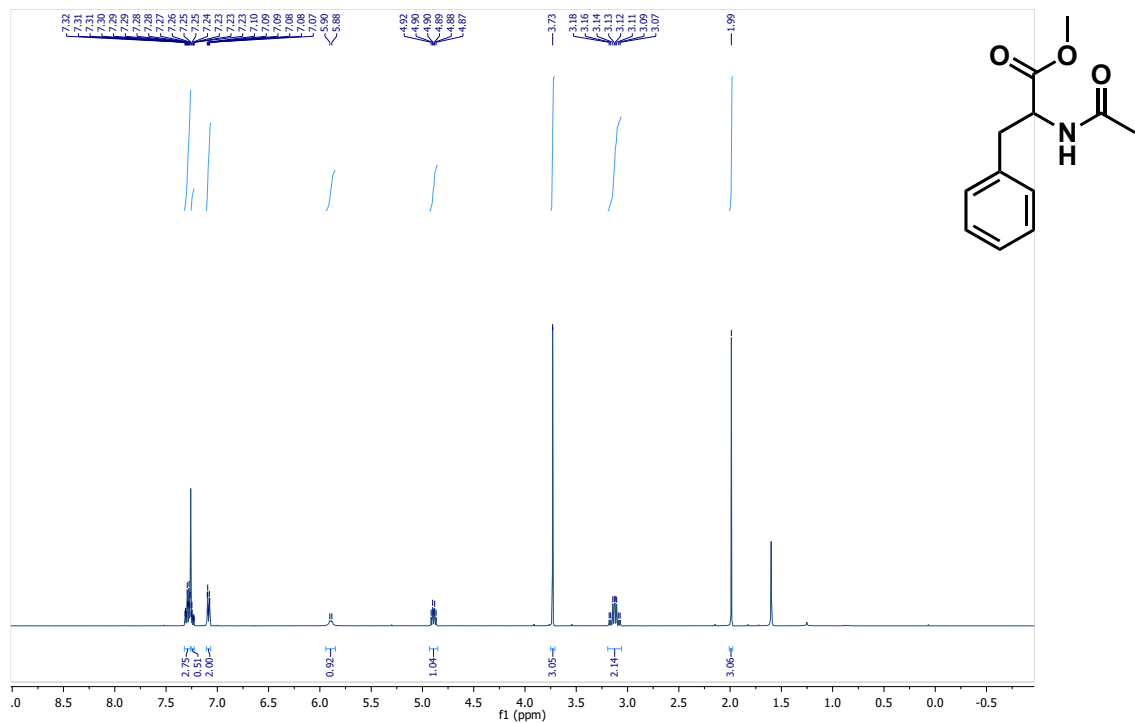
26. N-[2-(5-methoxy-1H-indol-3-yl)ethyl]acetamide

Followed the general procedure **7**, then procedure **4**. Flash column chromatography at 0–80% hexanes/ethyl acetate. Product obtained as a brown oil (42 mg, yield 72%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 8.32 (s, 1H), 7.23 (d, 1H), 6.99 (dd, 2H), 6.85 (dd, 1H), 5.67 (s, 1H), 3.83 (s, 3H), 3.56 (q, 2H), 2.91 (t, 2H), 1.90 (s, 3H). MS (ESI+): Calculated $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_2$ as 232.12, $[\text{M}+\text{H}]$ found as 233.15. Characterized in accordance to the literature.¹⁶



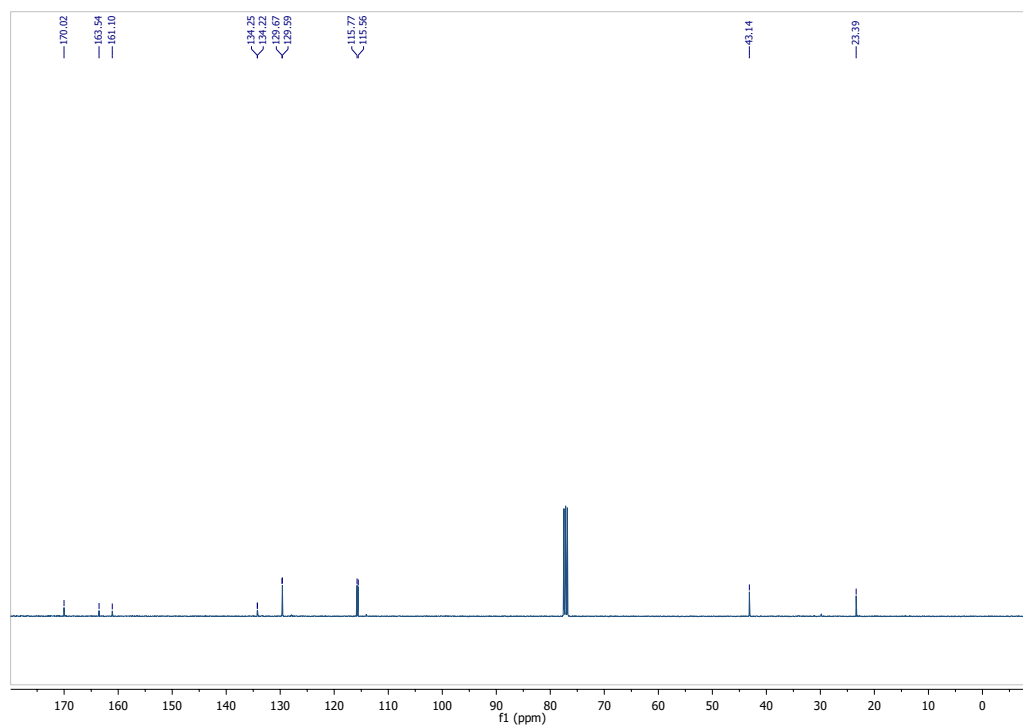
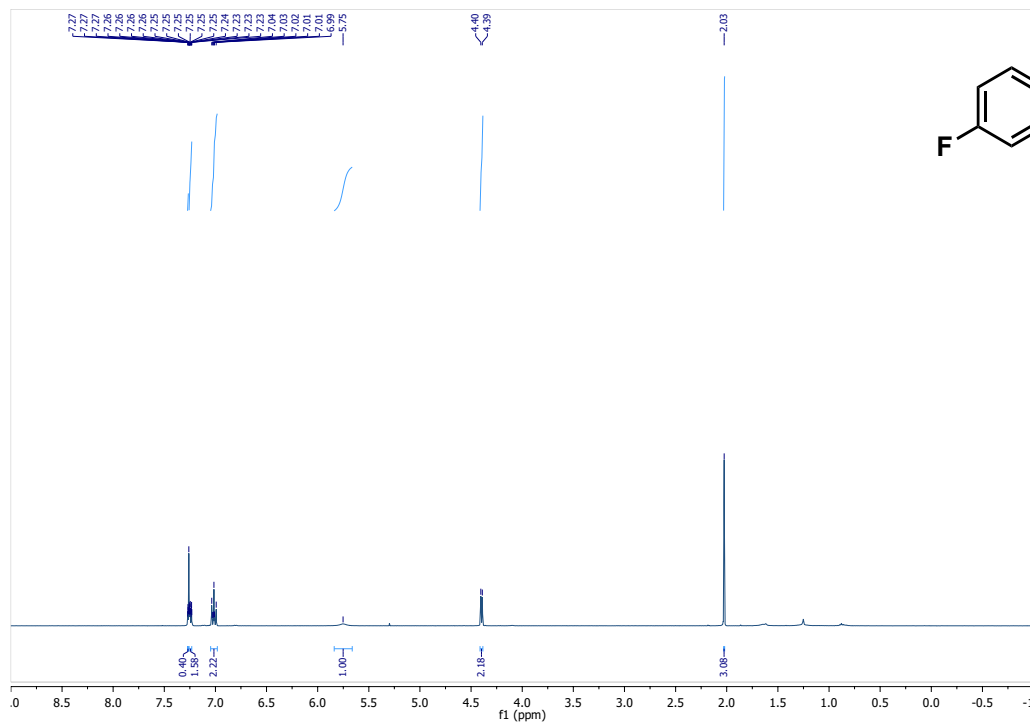
27. methyl 2-acetamido-3-phenylpropanoate

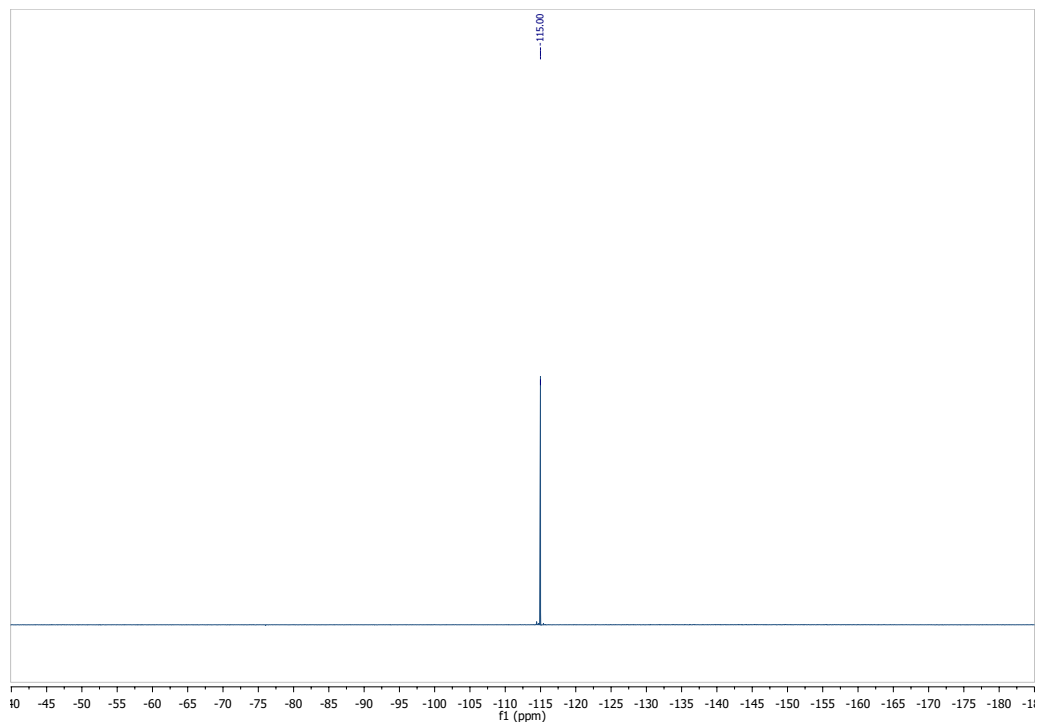
Followed the general procedure **7**, then procedure **4**. Product obtained as a white powder (46.5 mg, yield 84%). ^1H -NMR (400 MHz, CDCl_3): δ 7.32–7.23 (m, 3H), 7.09 (m, 2H), 5.89 (d, 1H), 4.90 (m, 1H), 3.73 (s, 3H), 3.13 (m, 2H), 1.99 (s, 3H). MS (ESI+): Calculated $\text{C}_{12}\text{H}_{15}\text{NO}_3$ as 221.11, $[\text{M}+\text{H}]$ found as 222.09. Characterized in accordance to the literature.¹⁷



28. N-[(4-fluorophenyl)methyl]acetamide

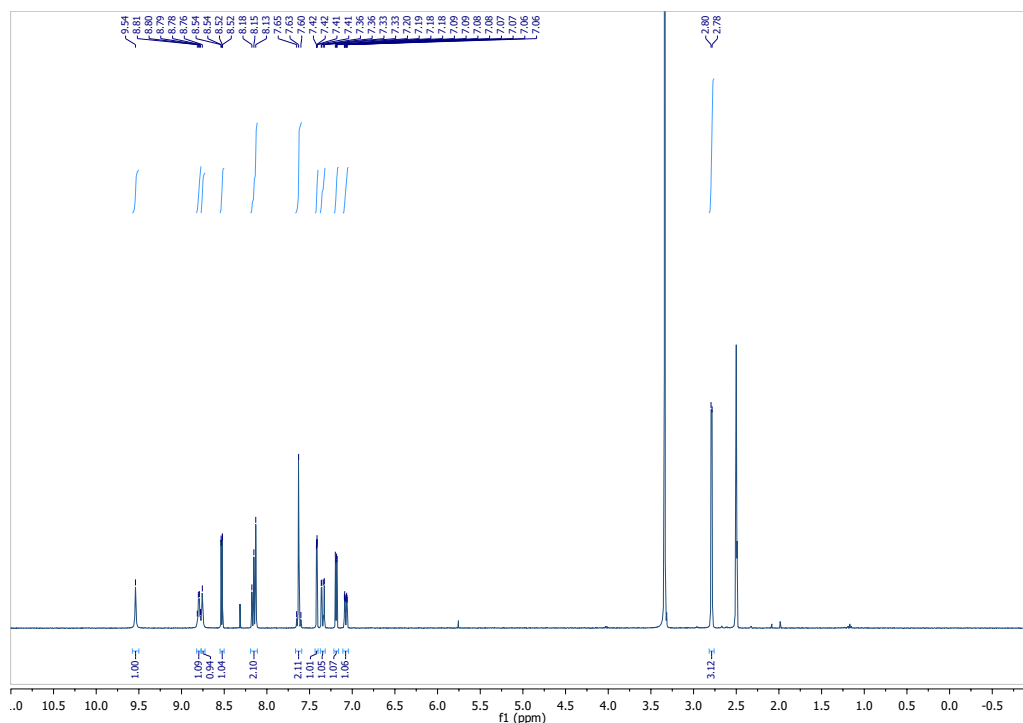
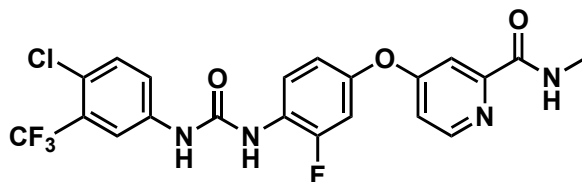
Followed the general procedure **7**, then procedure **4**. Product obtained as a white powder (30.5 mg, yield 73%). ^1H -NMR (400 MHz, CDCl_3): δ 7.25 (m, 2H), 7.02 (m, 2H), 5.75 (s, 1H), 4.40 (d, 2H), 2.03 (s, 3H). ^{13}C -NMR (100 MHz, CDCl_3): 170.0, 162.3, 134.2, 129.6, 115.7, 43.1, 23.4. ^{19}F -NMR (376 MHz, CDCl_3): -115.00 (s, 1F). MS (ESI⁺): Calculated $\text{C}_9\text{H}_{10}\text{FNO}$ as 167.07, $[\text{M}+\text{H}]$ found as 167.94. Characterized in accordance to the literature.¹⁵

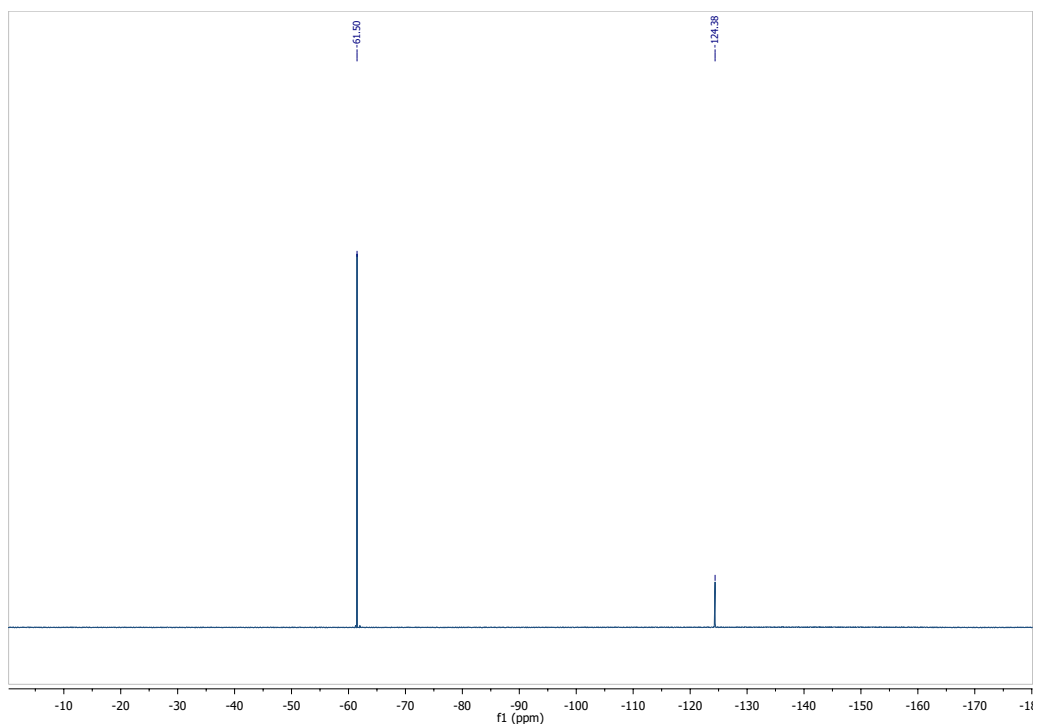




29. 4-[4-({[4-chloro-3-(trifluoromethyl)phenyl]carbamoyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide

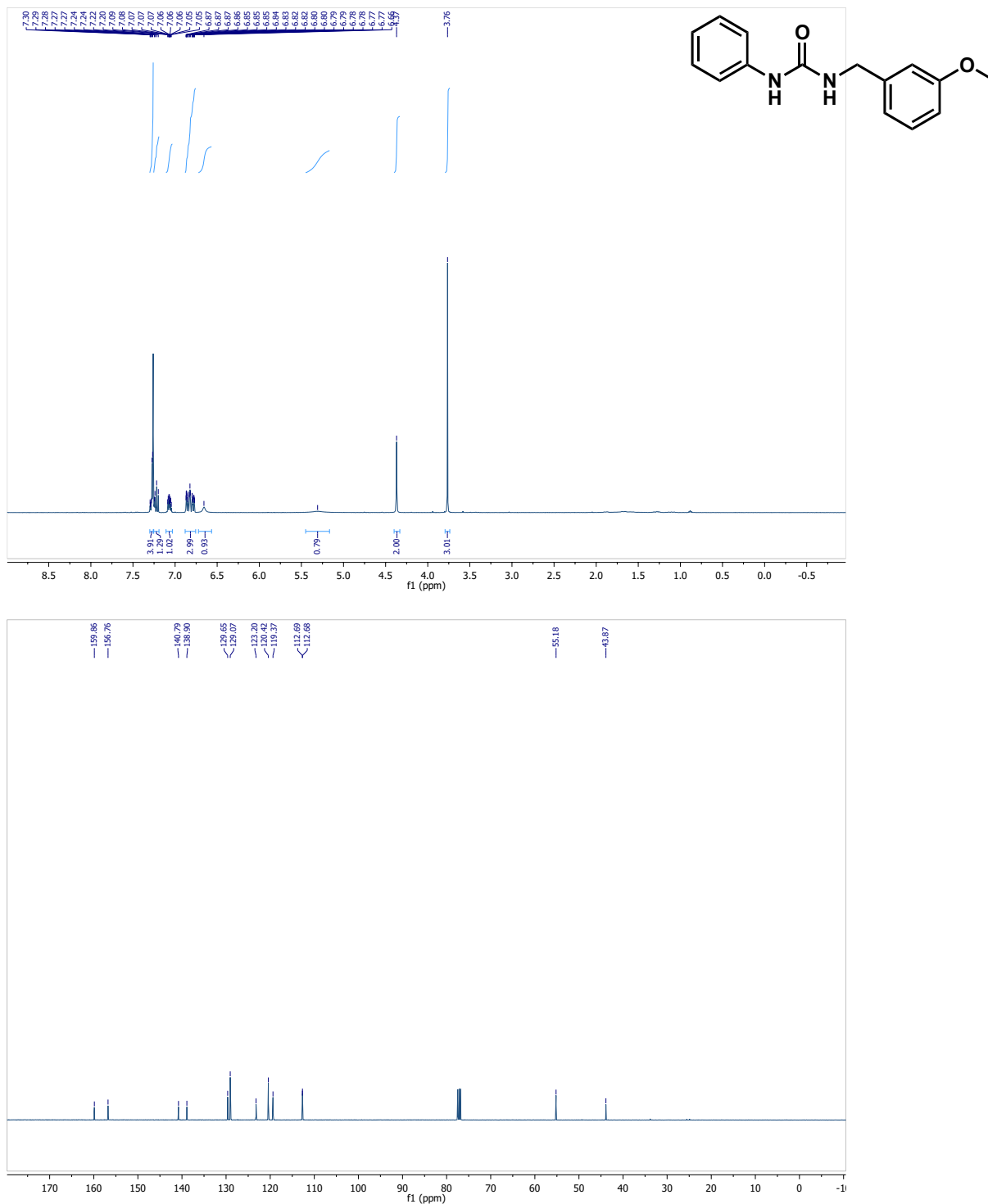
Followed the general procedure (3) to obtain the urea derived from N-tert-butylmethylamine. The intermediate was dissolved in toluene (0.25 M), and 1.5 equiv. of 4-(4-amine-3-fluorophenoxy)-N-methylpicolinamide was added. The reaction was heated to reflux until completion. Flash column chromatography performed using a gradient of 0–10% DCM/MeOH. Product obtained as a white powder (85 mg, yield 71%). ¹H-NMR (400 MHz, CDCl₃): δ 9.54 (s, 1H), 8.80 (q, 1H), 8.76 (s, 1H), 8.53 (dd, 1H), 8.16 (m, 2H), 7.63 (m, 2H), 7.42 (dd, 1H), 7.35 (dd, 1H), 7.19 (dd, 1H), 7.08 (m, 1H), 2.79 (d, 3H). ¹⁹F-NMR (376 MHz, CDCl₃): -61.50 (s, 3F), -124.38 (s, 1F). MS (ESI⁺): Calculated C₂₁H₁₅ClF₄N₄O₃ as 482.08, [M+H]⁺ found as 483.14. Characterized in accordance to the literature.¹⁸





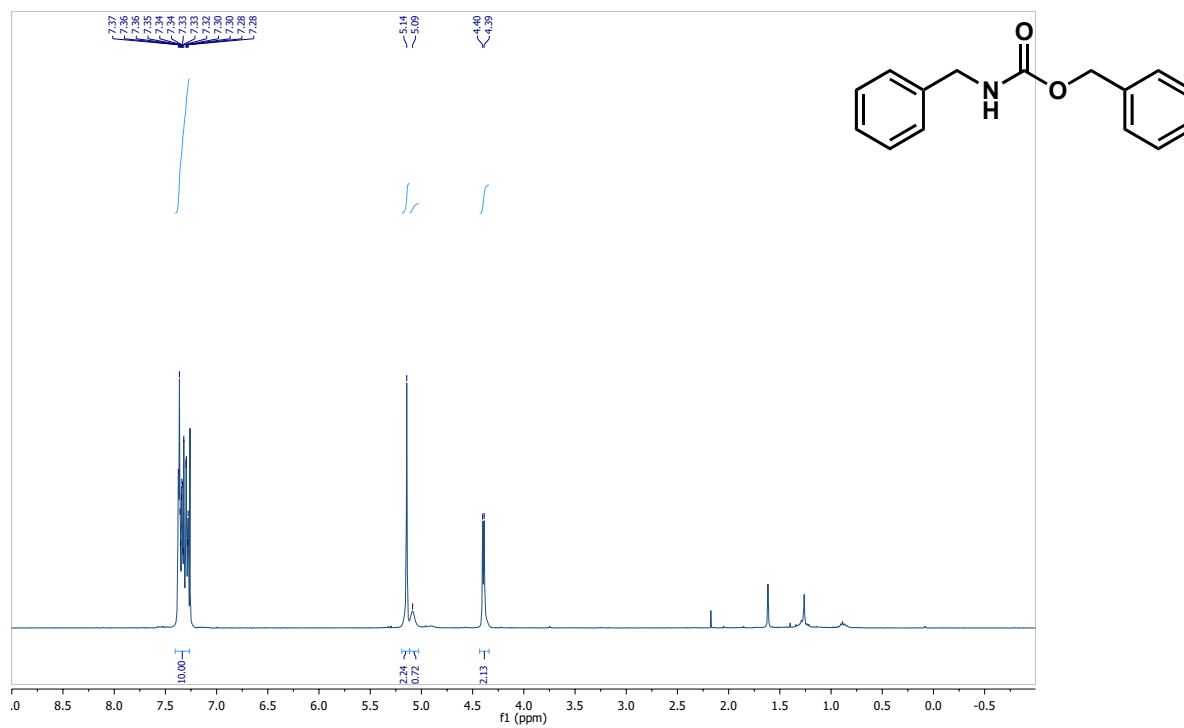
30. 1-[(3-methoxyphenyl)methyl]-3-phenylurea

Followed the procedure described by Murray et al.,⁸ product obtained as a white powder (56 mg, yield 88%). ¹H-NMR (400 MHz, CDCl₃): δ 7.29 (m, 4H), 7.22 (m, 1H), 7.07 (m, 1H), 6.82 (m, 3H), 6.66 (s, 1H), 5.31 (s, 1H), 4.37 (s, 2H), 3.76 (s, 3H). ¹³C-NMR (100 MHz, CDCl₃): 159.9, 156.8, 140.8, 138.9, 129.7, 129.1, 123.2, 120.4, 119.4, 112.7, 112.7, 55.2, 43.9. MS (ESI+): Calculated C₁₅H₁₆N₂O₂Na as 279.1109, [M+H]⁺ found as 279.1128.



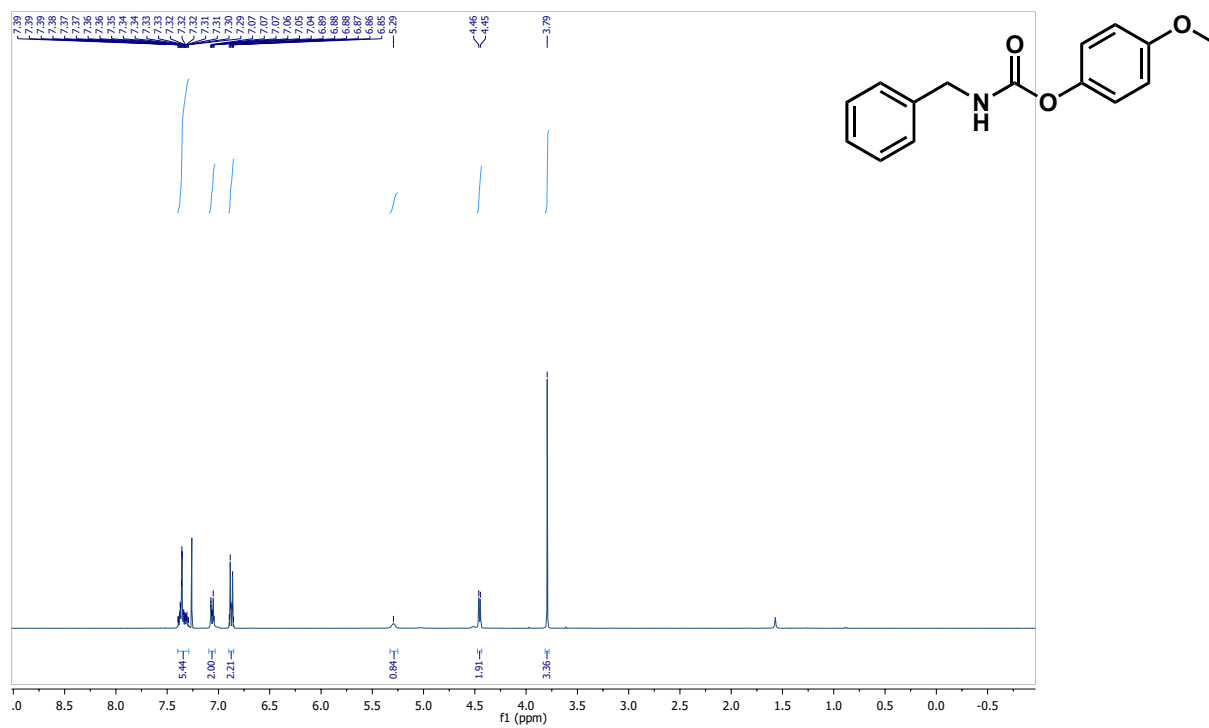
31. benzyl N-benzylcarbamate

Followed the general procedure (2), product obtained as a white powder (43 mg, yield 72%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.33 (m, 10H), 5.14 (s, 2H), 5.09 (s, 1H), 4.40 (d, 2H). MS (ESI+): Calculated $\text{C}_{15}\text{H}_{15}\text{NO}_2$ as 241.11, $[\text{M}+\text{H}]$ found as 242.17. Characterized in accordance to the literature.¹



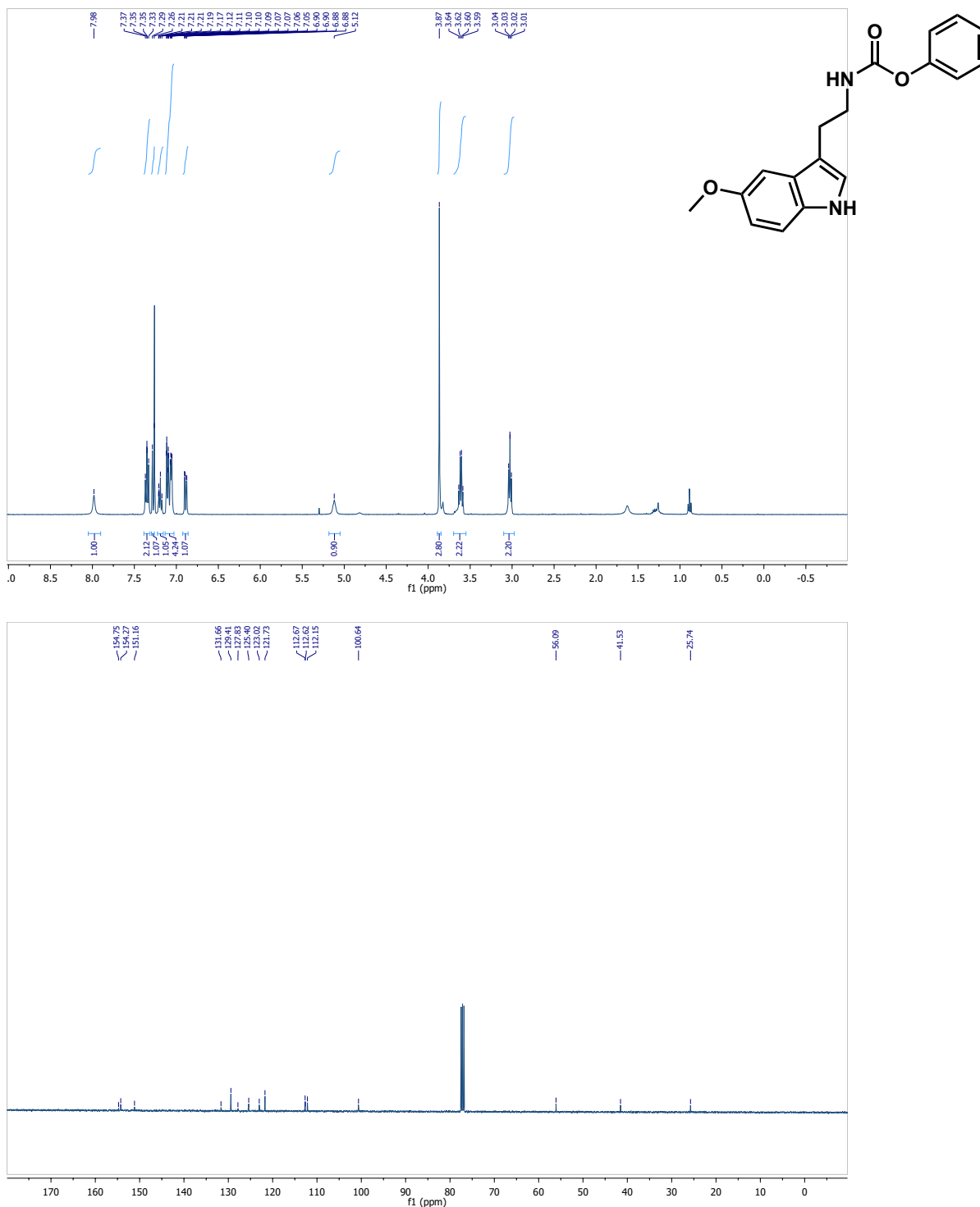
32. 4-methoxyphenyl N-benzylcarbamate

Followed the procedure described by Krátký M. et al.,⁹ product obtained as a white powder (81 mg, yield 92%). ¹H-NMR (400 MHz, CDCl₃): δ 7.34 (m, 5H), 7.06 (m, 2H), 6.87 (m, 2H), 5.29 (s, 1H), 4.46 (d, 2H), 3.79 (s, 3H). MS (ESI+): Calculated C₁₅H₁₅NO₃ as 257.11, [M+H]⁺ found as 258.16. Characterized in accordance to the literature.¹⁰



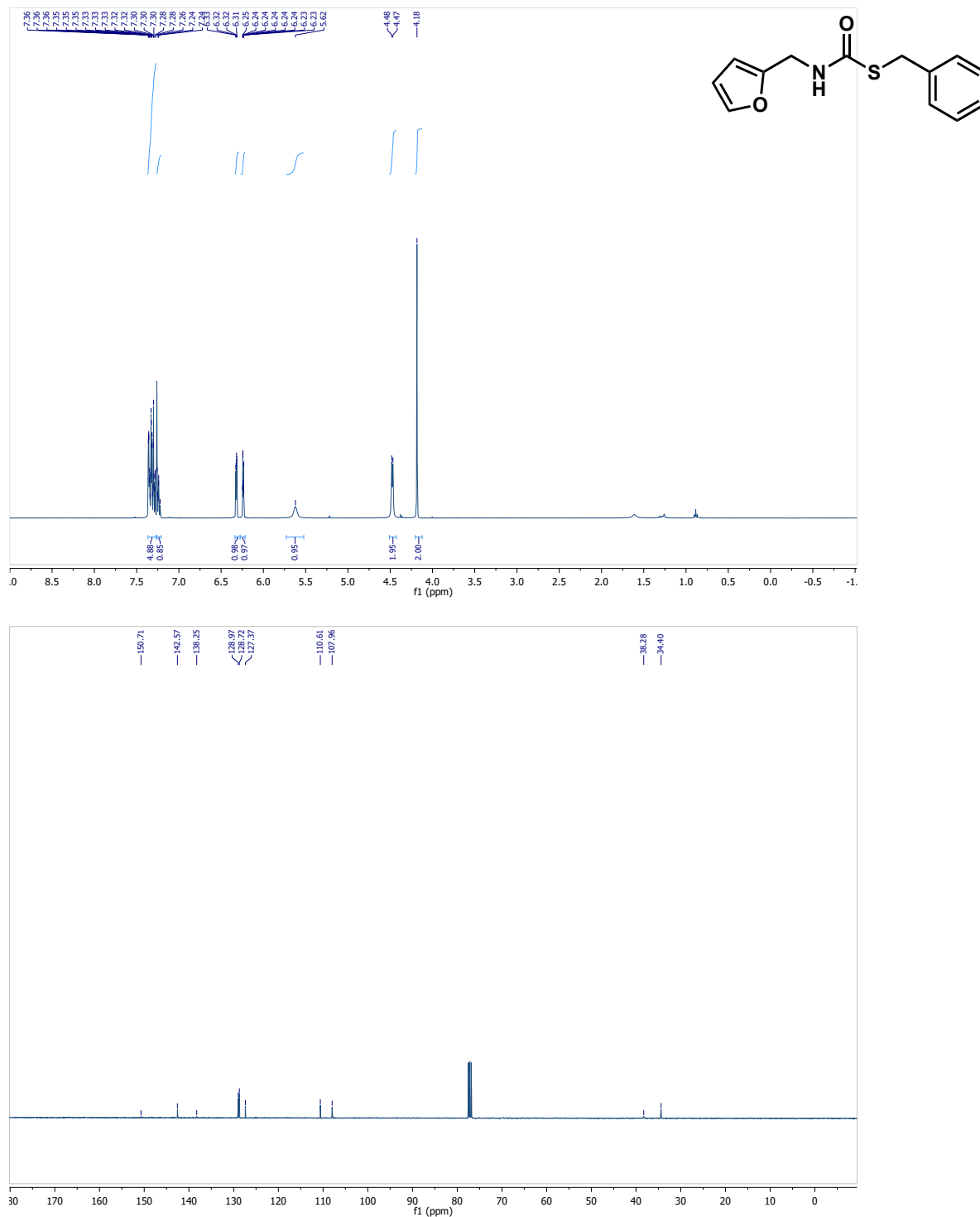
33. phenyl N-[2-(5-methoxy-1H-indol-3-yl)ethyl]carbamate

Followed the procedure described by Zhou Y. et al.,¹¹ product obtained as a light yellow solid (60 mg, yield 74%). ¹H-NMR (400 MHz, CDCl₃): δ 7.98 (s, 1H), 7.35 (m, 2H), 7.26 (d, 1H), 7.19 (m, 1H), 7.09 (m, 4H), 6.89 (dd, 1H), 5.12 (s, 1H), 3.87 (s, 3H), 3.62 (m, 2H), 3.03 (m, 2H). ¹³C-NMR (100 MHz, CDCl₃): 154.8, 154.3, 151.2, 131.7, 129.4, 127.8, 125.4, 123.0, 121.7, 112.7, 112.6, 112.2, 100.6, 56.1, 41.5, 25.7. MS (ESI+): Calculated C₁₈H₁₈N₂O₃Na as 333.1215, [M+H]⁺ found as 333.1205. Characterized in accordance to the literature.



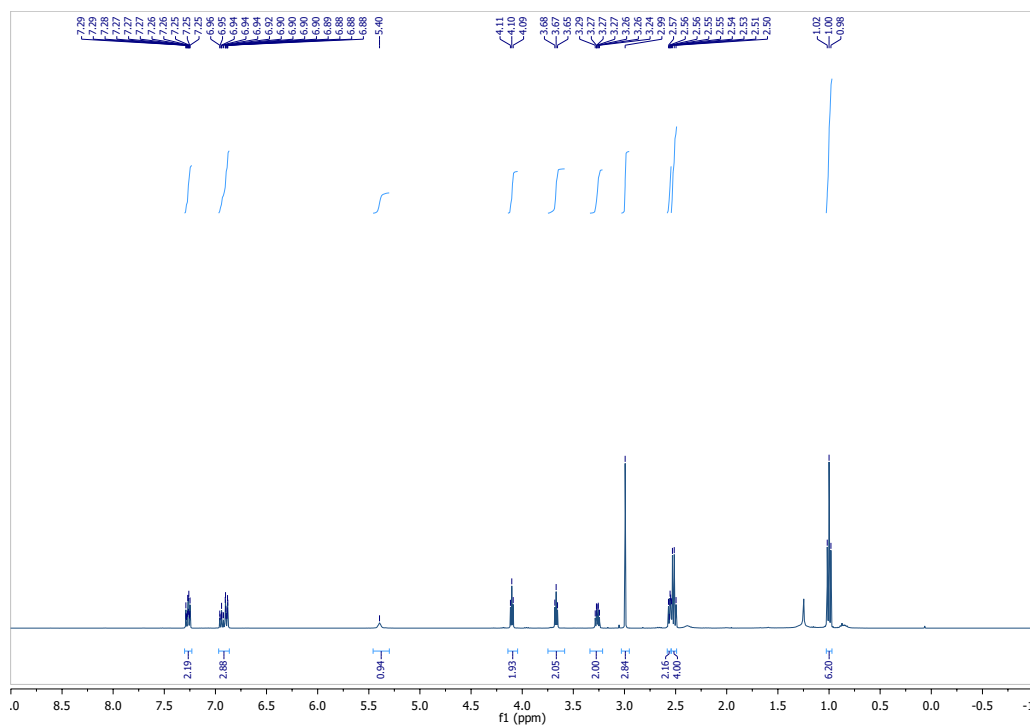
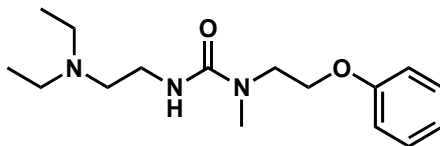
34. N-[(furan-2-yl)methyl](benzylsulfanyl)formamide

Followed the procedure described by Zhou Y. et al.,¹¹ product obtained as a white powder (63 mg, yield 25%). ¹H-NMR (400 MHz, CDCl₃): δ 7.32 (m, 5H), 7.24 (m, 1H), 6.32 (m, 1H), 6.24 (m, 1H), 5.62 (s, 1H), 4.48 (d, 2H), 4.18 (s, 2H). ¹³C-NMR (100 MHz, CDCl₃): 150.7, 142.6, 138.3, 129.0, 128.7, 127.4, 110.6, 108.0, 38.3, 34.4. MS (ESI+): Calculated C₁₃H₁₃NO₂SN_a as 270.0565, [M+H]⁺ found as 270.0571.



35. 3-[2-(diethylamino)ethyl]-1-methyl-1-(2-phenoxyethyl)urea

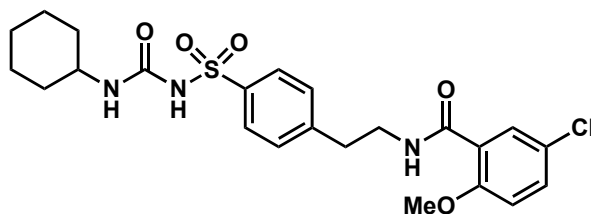
Followed the procedure described by Zhou Y. et al.,¹¹ product obtained as an oil (42 mg, yield 27%). ¹H-NMR (400 MHz, CDCl₃): δ 7.27 (m, 2H), 6.92 (m, 3H), 5.40 (s, 1H), 4.10 (t, 2H), 3.67 (t, 2H), 3.27 (m, 2H), 2.99 (s, 3H), 2.56 (m, 2H), 2.52 (m, 4H), 1.00 (t, 6H). MS (ESI+): Calculated C₁₆H₂₇N₃O₂ as 293.21, [M+H]⁺ found as 294.24. Characterized in accordance to the literature.¹²



Section 4: Radiochemistry

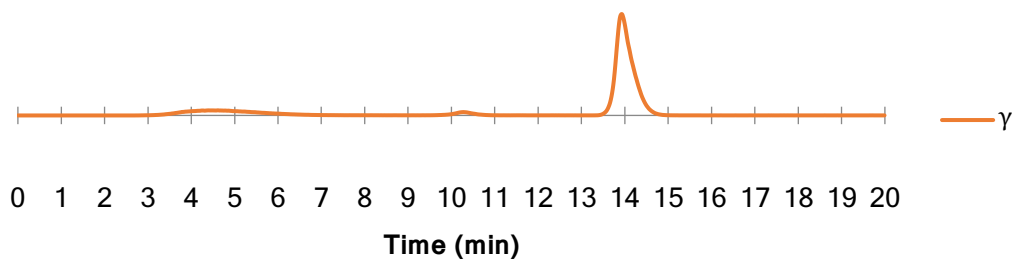
The peaks indicated by solid arrows are present in the chromatograms following co-injection of products with additional nonradioactive standard. The differences in elution times are due to UV-Vis and radiation detectors placed in series, and in all cases were consistent with delays observed at the time of acquisition. Due to modifications of the radioHPLC system, these delays have varied over the course of this project.

Example:



RCY: $75 \pm 14\%$, TE: 99%
 $n = 2$

Radiochemical Yield (RCY) determined based on integration of the peaks by radioHPLC.



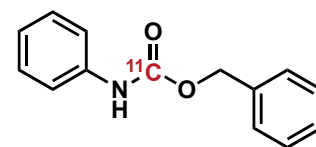
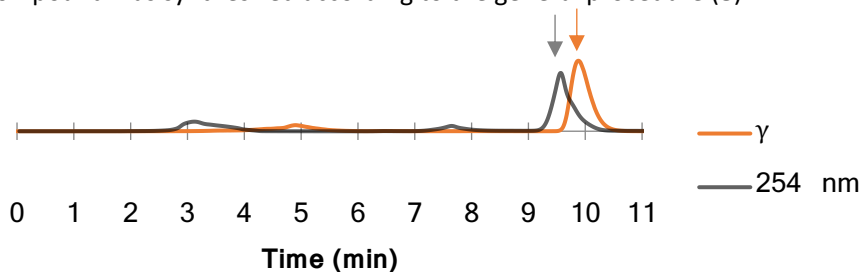
Retention Time (min)	Area ($\mu\text{V} \cdot \text{sec}$)	% Area	d.c. Area	d.c. % Area
4.614	5,426,465	15.60%	6,350,537	12%
10.275	905,203	2.60%	1,284,783	2%
13.927	28,444,819	81.79%	45,723,732	86%

Trapping Efficiency (TE) determined based on the activity readings collected at the reactor and the CO₂ trap.

$$TE = \frac{d.c. A_{\text{reactor}}}{A_{\text{trap}}} \times 100\% = \frac{640 \text{ mCi at 18:01}}{690 \text{ mCi at 17:59}} \times 100\% = \frac{685 \text{ mCi at 17:59}}{690 \text{ mCi at 17:59}} \times 100\% = 99\%$$

[¹¹C]4 (benzyl N-phenylcarbamate)

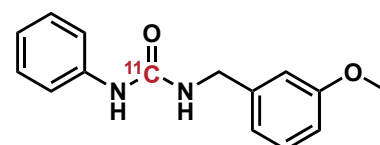
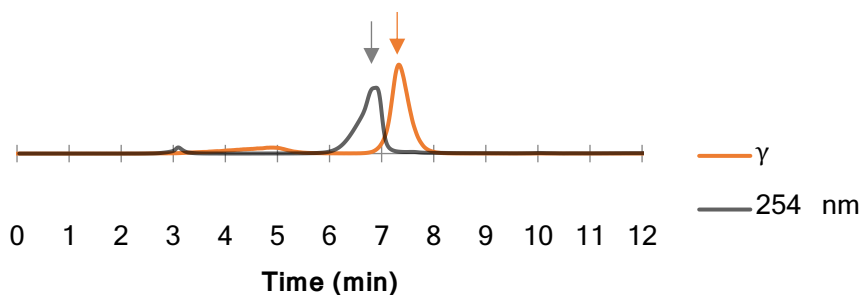
Compound was synthesized according to the general procedure (8).



RCY: $91 \pm 2\%$, TE: 99%
 $n = 6$

[¹¹C]30 (1-[(3-methoxyphenyl)methyl]-3-phenylurea)

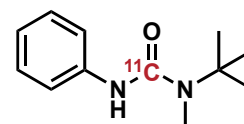
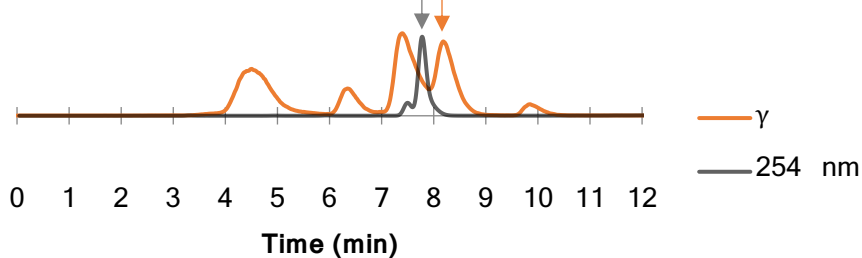
Compound was synthesized according to the general procedure (8).



RCY: $88 \pm 2\%$, TE: $83 \pm 2\%$
 $n = 2$

[¹¹C]12 (3-tert-butyl-3-methyl-1-phenylurea)

Compound was synthesized according to the general procedure (8)

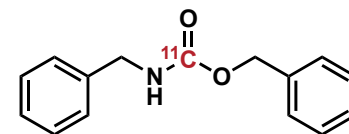
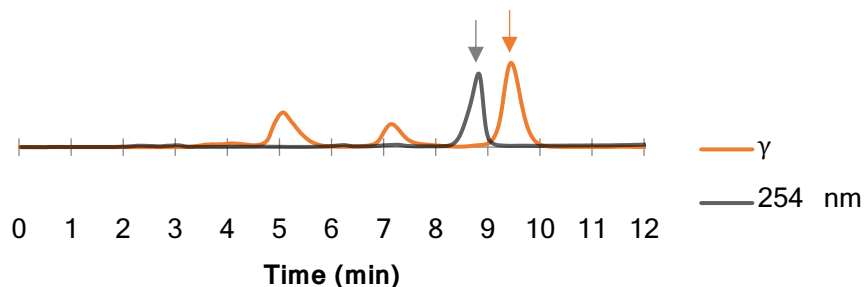


RCY: $32 \pm 5\%$, TE: $70 \pm 4\%$
 $n = 2$

[¹¹C]31 (benzyl N-benzylcarbamate)

Compound was synthesized according to the general procedure (8).

Exceptional conditions: Iminophosphorane **1o** (7.83 μmol).

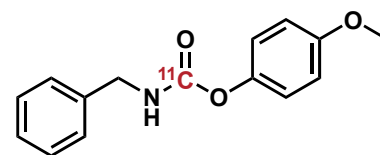
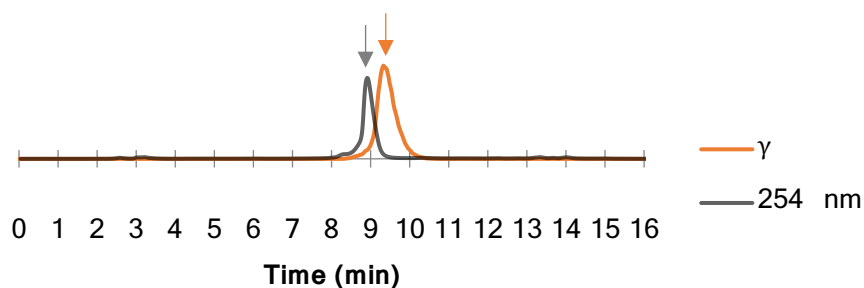


RCY: $64 \pm 3\%$, TE: $98 \pm 3\%$
 $n = 2$

[¹¹C]32 (4-methoxyphenyl N-benzylcarbamate)

Compound was synthesized according to the general procedure (8).

Exceptional conditions: Iminophosphorane **1o** (7.83 μmol), phenol (560 μmol), DABCO (160 μmol), no DBU. CO₂ trapped at -60 °C.



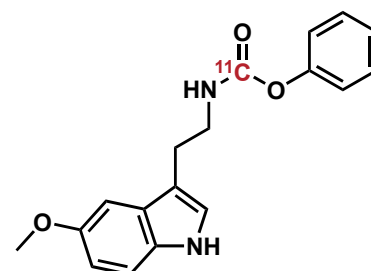
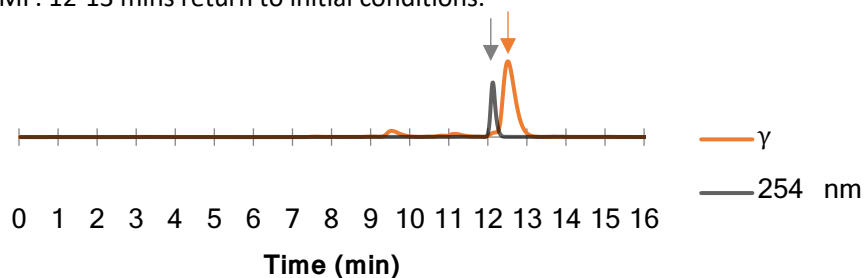
RCY: $26 \pm 2\%$, TE: $83 \pm 2\%$
 $n = 2$

[¹¹C]33 (phenyl-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]carbamate)

Compound was synthesized according to the general procedure (8).

Exceptional conditions: Iminophosphorane **1j** (7.53 μmol), phenol (1300 μmol), DABCO (16.04 μmol), no DBU. Reaction run for 2 min. CO₂ trapped at -60 °C.

Analytical HPLC Conditions: 0-2 mins at 20% ACN / 80% 0.1 M AMF. 2-10 mins gradient to 80% ACN / 20% 0.1 M AMF. 10-12 mins at 80% ACN / 20% 0.1 M AMF. 12-13 mins return to initial conditions.

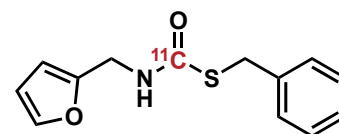
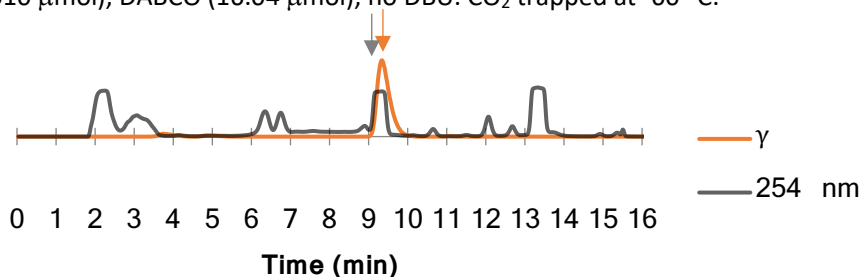


RCY: $84 \pm 8\%$, TE: 58%
 $n = 2$

[¹¹C]34 (N-[(furan-2-yl)methyl](benzylsufanyl)formamide)

Compound was synthesized according to the general procedure (8).

Exceptional conditions: Iminophosphorane **1j** (9.13 μmol), benzyl mercaptan (510 μmol), DABCO (16.04 μmol), no DBU. CO₂ trapped at -60 °C.

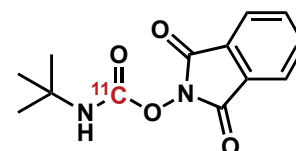
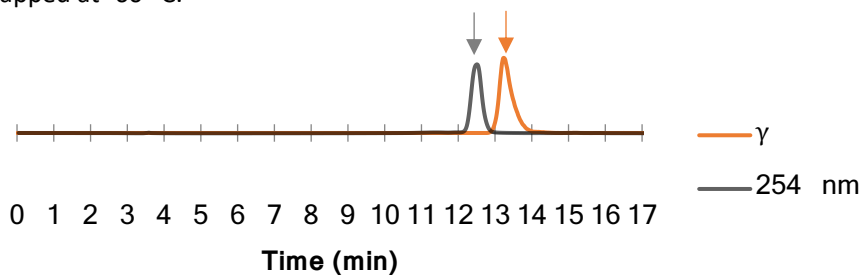


RCY: 93 ± 2%, TE: 53 ± 6%
n = 2

[¹¹C]23 (1,3-dioxo-2,3-dihydro-1H-isoindol-2-yl N-tert-butylcarbamate)

Compound was synthesized according to the general procedure (8).

Exceptional conditions: Iminophosphorane **1h** (11.9 μmol), LHMDs (11.7 μmol), N-hydroxyphthalimide (510 μmol), NEt₃ (510 μmol), no DBU. CO₂ trapped at -60 °C.



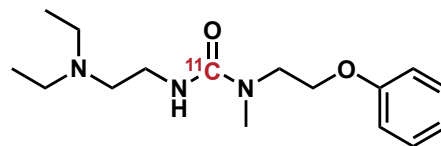
RCY: 99 ± 3%, TE: 52 ± 6%
n = 2

[¹¹C]35 (3-[2-(diethylamino)ethyl]-1-methyl-1-(2-phenoxyethyl)urea)

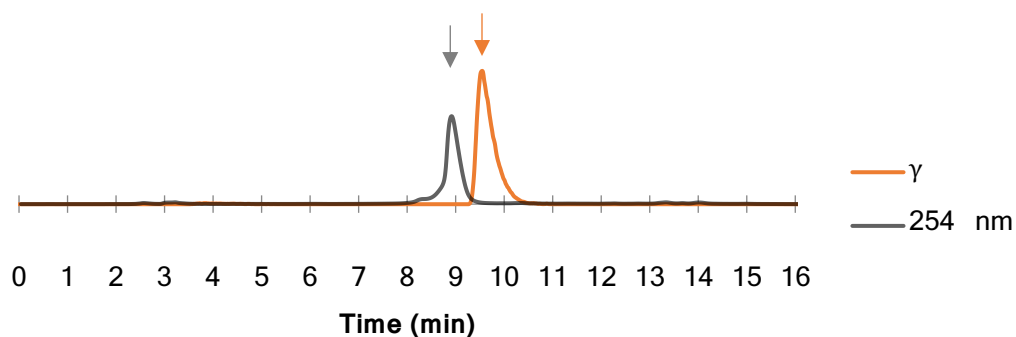
Compound was synthesized using procedure 9.

Exceptional conditions: Iminophosphorane **1p** (8.75 μmol), N-methyl-2-phenoxyethanamine (87.5 μmol), DBU (8.71 μmol). CO₂ trapped at -60 °C.

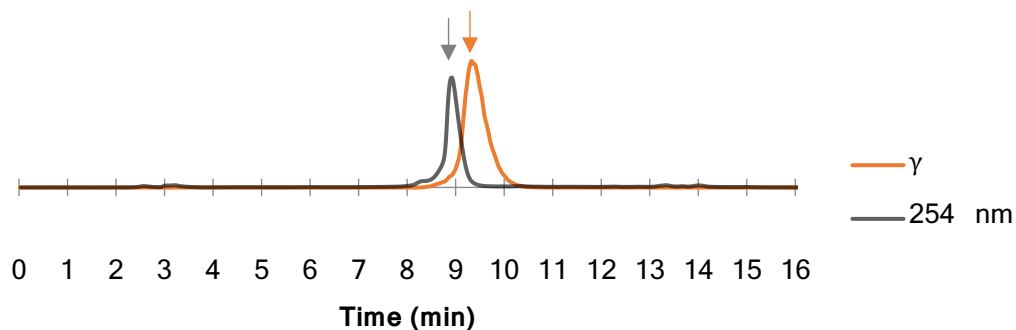
Analytical HPLC Conditions: 0-2 mins at 20% ACN / 80% 0.1 M AMF. 2-10 min gradient to 65% ACN / 35% 0.1 M AMF. 10-12 min 65% ACN / 35% 0.1 M AMF. 12-13 min return to initial conditions.



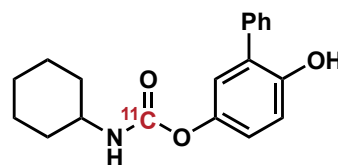
RCY: 99 ± 1%, **TE:** 99%
n = 2



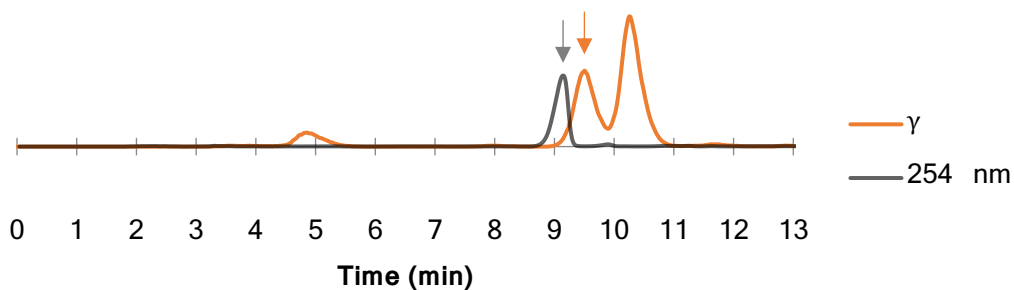
Isolated RCY: 33 ± 11%



[¹¹C]25 (5-hydroxy-(1,1'-biphenyl)-2-yl N-cyclohexylcarbamate)
 Compound was synthesized using procedure 10.

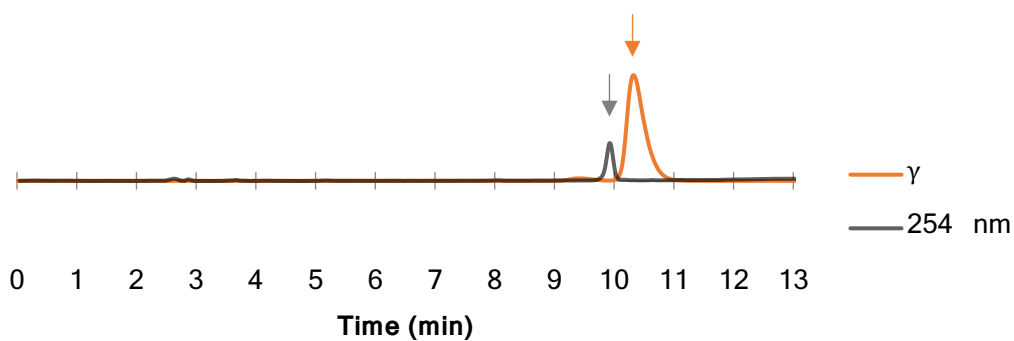


RCY: $96 \pm 1\%$, **TE:** $64 \pm 11\%$
 (as a mixture of isomers)
 $n = 2$



[¹¹C]URB694:

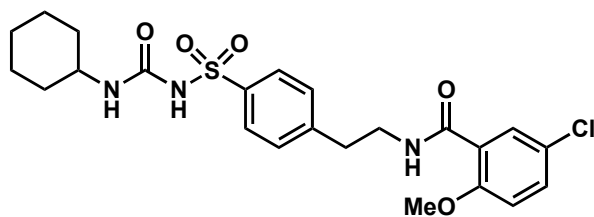
Isolated RCY: $13 \pm 2\%$, **Molar Activity:** 69 ± 37 GBq/ μ mol ($n = 2$)



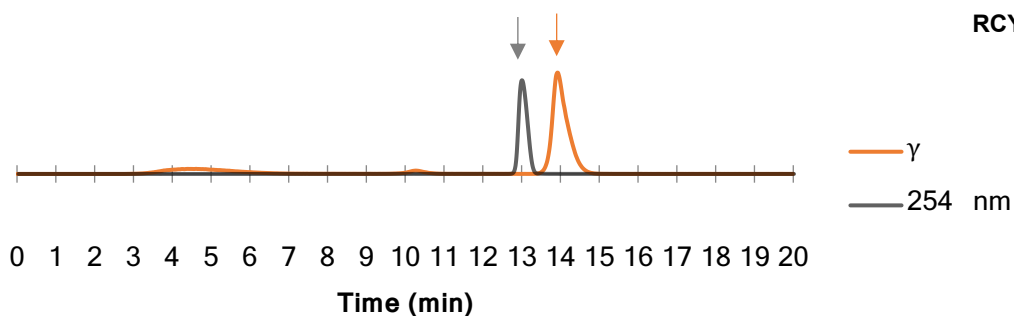
[¹¹C]36 (5-chloro-N-[2-4-[[[(cyclohexylcarbonyl)amino]sulfonyl]phenyl]ethyl]-2-methoxybenzamide)

Compound was synthesized using procedure 11.

Analytical HPLC Conditions: 0-2 mins at 20% ACN / 80% 0.1 M AMF. 2-10 min gradient to 65% ACN / 35% 0.1 M AMF. 10-12 min 65% ACN / 35% 0.1 M AMF. 12-13 min return to initial conditions.

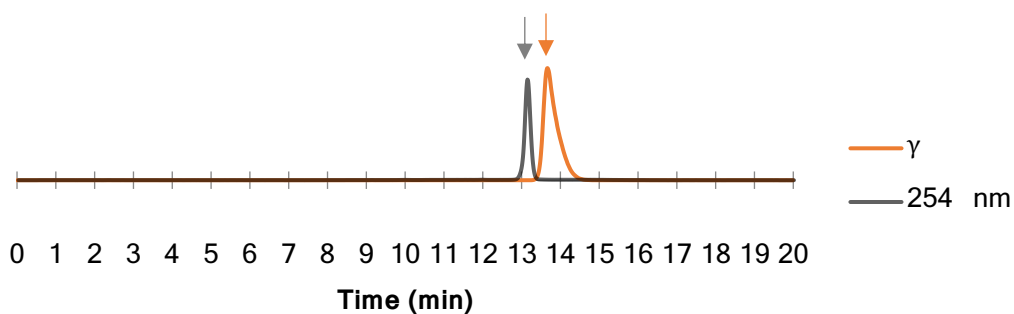


RCY: $75 \pm 14\%$, **TE:** 99%
n = 2

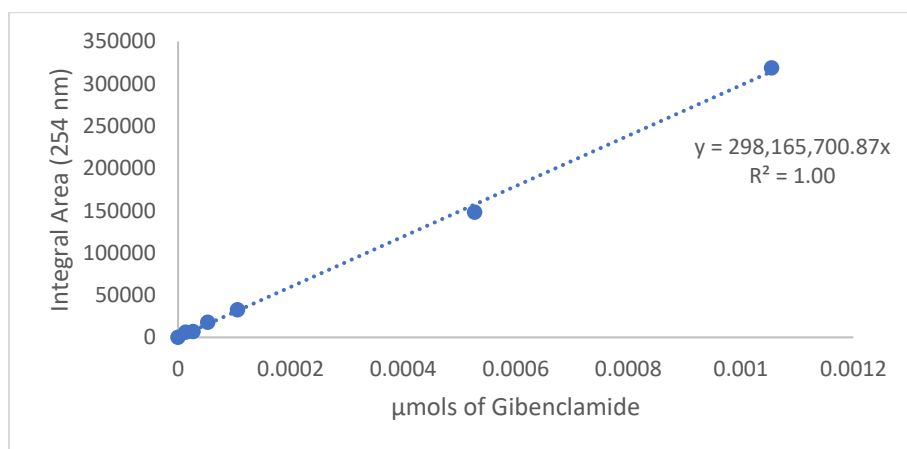
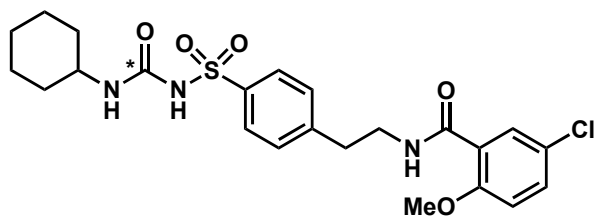
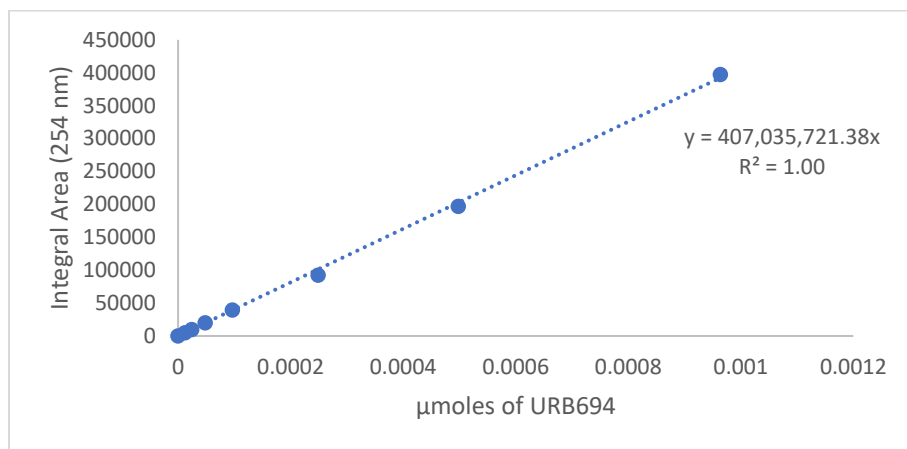
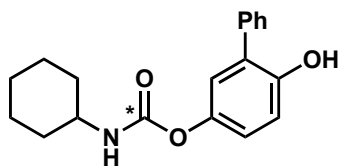


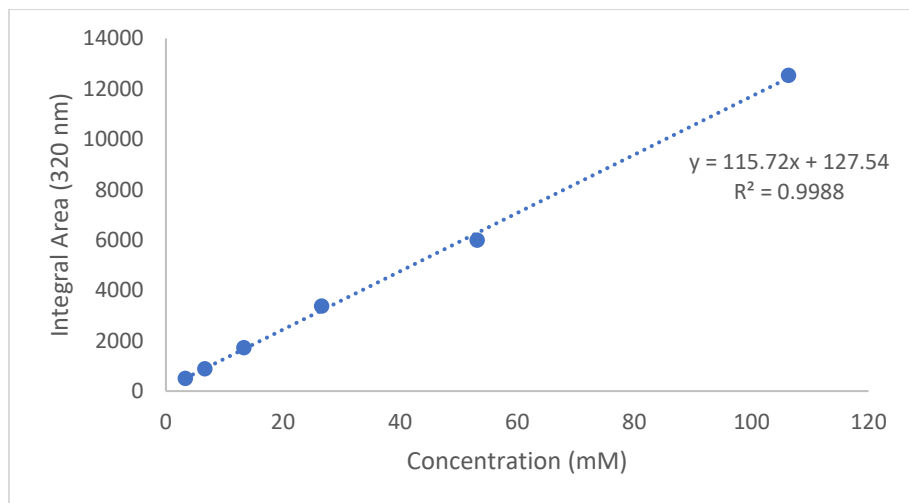
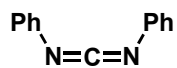
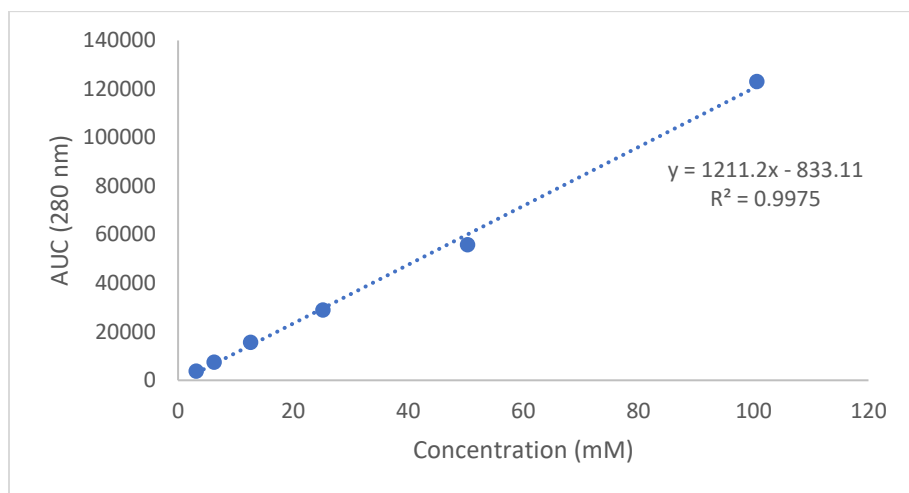
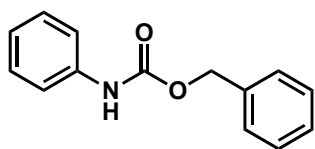
[¹¹C]Glibenclamide:

Isolated RCY: $62 \pm 16\%$, **Molar Activity:** 59 ± 0.06 GBq/ μ mol (*n* = 2)



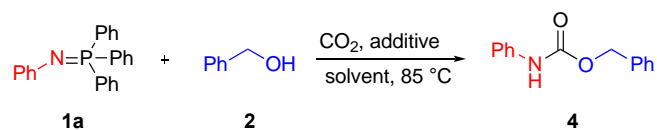
Section 5: Standard Curves





Section 6: Optimization Table

Table S1. Solvent and additive screening^a



Entry	Solvent	Additive	Rxn time ^b	Yield
1	Toluene	-	2h	70%
2	Dioxane	-	2h	72%
3	DMF	-	2h	75%
4	DMSO	-	2h	64%
5	THF	-	2h	72%
6	ACN	-	2h	78%
7	ACN	DBU	1h	84%
8	ACN	BEMP	1h	70%
9	ACN	DMAP	2h	65%
10	ACN	Pyridine	2h	72%
11	ACN	K ₂ CO ₃	2h	75%

^aReaction conditions: **1** (0.25mmol), **2** (1.25mmol), additives (0.55mmol), dry solvent (2.5mL). Isolated yield.

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