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Asymmetric cyclopropane synthesis currently requires bespoke strategies, methods, substrates and reagents, even when targeting similar compounds. This limits the speed and chemical space available for discovery campaigns. Here we introduce a practical and versatile diazocompound, and we demonstrate its performance in the first unified asymmetric synthesis of functionalized cyclopropanes. We found that the redox-active leaving group in this reagent enhances the reactivity and selectivity of geminal carbene transfer. This effect enabled the asymmetric cyclopropanation of a wide range of olefins including unactivated aliphatic alkenes, enabling the 3-step total synthesis of (–)-dictyopterene A. This unified synthetic approach delivers high enantioselectivities that are independent of the stereoelectronic properties of the functional groups transferred. Our results demonstrate that orthogonally-differentiated diazocompounds are viable and advantageous equivalents of single-carbon chirons.

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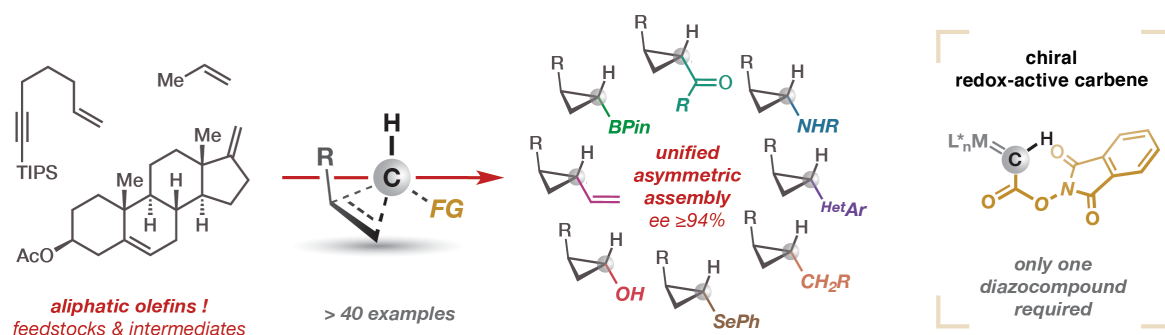
General Cyclopropane Assembly *via* Enantioselective Redox-Active Carbene Transfer to Aliphatic Olefins

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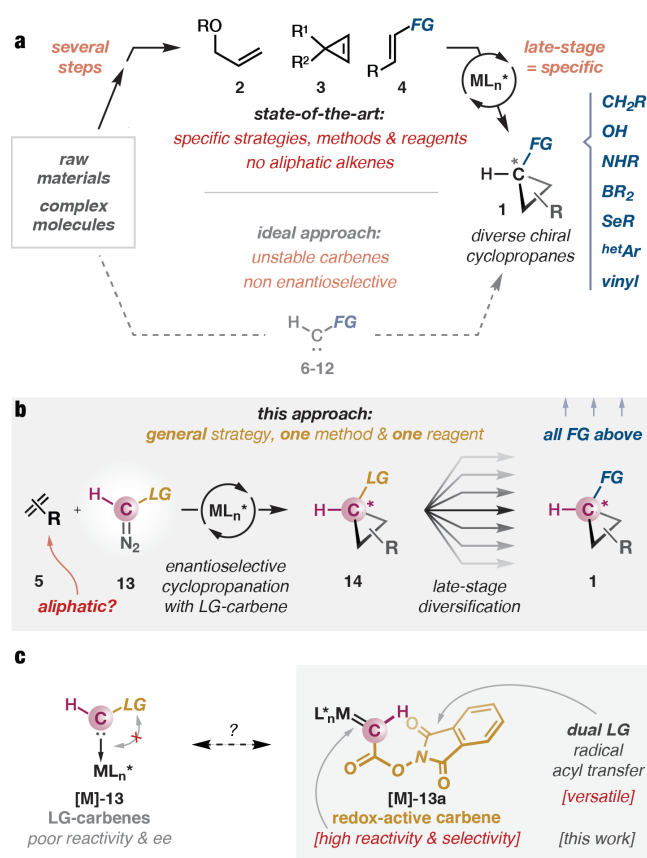


Abstract: Asymmetric cyclopropane synthesis currently requires bespoke strategies, methods, substrates and reagents, even when targeting similar compounds. This limits the speed and chemical space available for discovery campaigns. Here we introduce a practical and versatile diazocompound, and we demonstrate its performance in the first unified asymmetric synthesis of functionalized cyclopropanes. We found that the redox-active leaving group in this reagent enhances the reactivity and selectivity of geminal carbene transfer. This effect enabled the asymmetric cyclopropanation of a wide range of olefins including unactivated aliphatic alkenes, enabling the 3-step total synthesis of (–)-dictyopterene A. This unified synthetic approach delivers high enantioselectivities that are independent of the stereoelectronic properties of the functional groups transferred. Our results demonstrate that orthogonally-differentiated diazocompounds are viable and advantageous equivalents of single-carbon chirons.

Cyclopropanes have attracted the attention of chemists for decades. The high strain and unique bonding of these carbocycles display enhanced conformational control and oxidative resistance that have been exploited in organic synthesis,^[1a] asymmetric catalysis^[1b] and medicinal chemistry.^[1c] Cyclopropanes are common in advanced total syntheses both as structural elements in challenging natural products,^[1d] and as enabling instruments to drive creative disconnections.^[1e] Different asymmetric syntheses of functionalized cyclopropanes **1** have thus been developed (Scheme 1a).^{[2],[3]} However, similar targets with different peripheral functionality still require discrete strategies based on specific reagents, catalysts, and substrates that are elaborated over several steps from raw sources. The key enantioselective step on these routes are often based on allylic alcohols **2**,^[4] 1,1-disubstituted cyclopropenes **3**,^[5] or electron-deficient alkenes **4**.^[6] Simple unfunctionalized olefins (**5**) are abundant feedstocks and frequent in complex intermediates but only some classes can engage in asymmetric cyclopropanation using advanced metal catalysts,^[7] or engineered enzymes.^[8] While electron-rich alkenes and styrenes are efficient in these reactions, the most common aliphatic alkenes^[9] are poorly reactive, and problematic in asymmetric catalysis because of their structural flexibility and weak dispersive interactions.^[10] Although elegant approaches have been documented,^[7b, 7c, 8c, 8d] the asymmetric cyclopropanation of aliphatic olefins is yet to be achieved with a general and simple catalytic system.^[7b-i, 10] Importantly, many interesting functionalized carbenes **6-12** (FG- $\ddot{\text{C}}\text{-H}$; Scheme 1a, bottom) are still unsuitable for cyclopropanation reactions: alkyl-,^[11a, 11b] hydroxy-,^[11c] amino-,^[11d] boryl-,^[11e] selenyl-,^[11f] heteroaryl-,^[11g] or alkenyl-methylenes^[11h] are either unstable or prone to oligomerization. As a result, the syntheses of the cyclopropanes bearing these functions are lengthy and specific, typically requiring overmanipulation of other cyclopropane intermediates.^[5, 6d, 6e, 11e, 12]

We conceived a unified strategy^[13] to comprehensively address the enantioselective formal transfer of carbenes **6-12** to alkene feedstocks **5** through a two-stage process (Scheme 1b): (1) enantioselective cyclopropanation of **5** with a diazocompound featuring a leaving group (**13**); and (2) diversification of the resulting intermediates **14**. This late-stage functionalization is critical to access chiral products with identical enantioselectivity regardless of their specific functionality. Unlike current tailored syntheses, this approach simplifies the optimization of the enantioselective step using a single carbene precursor. However, leaving group-

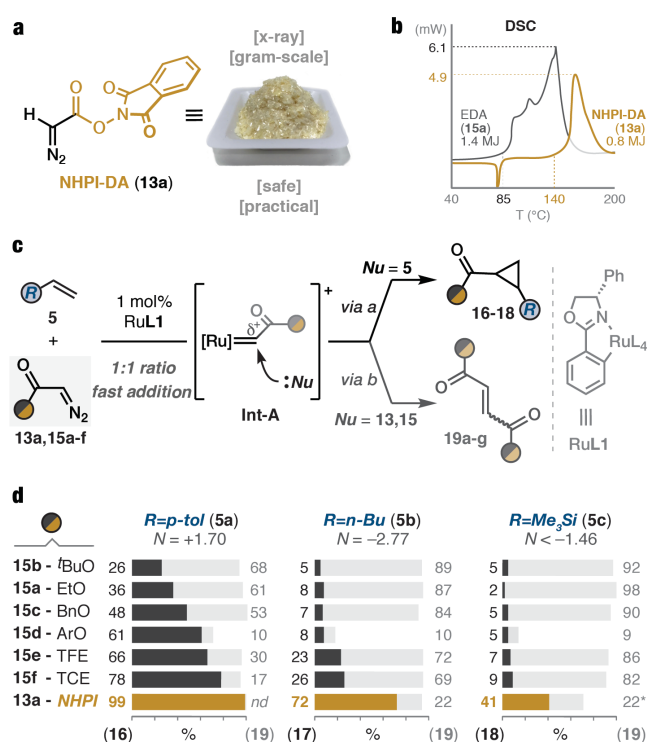
functionalized carbenes **[M]-13** (Scheme 1c) are known to be poorly reactive, and non-enantioselective. Their precursors tend to undergo substitution prior to the carbene transfer, and require additional stabilizing groups.^[14] We envisioned that redox-active carbenes bearing an *N*-hydroxyphthalimide ester leaving group **[M]-13a** (LG = CONHPI; Scheme 1c) could become equivalent to *all* the distinct carbenes **6-12**, due to the dual capacity of NHPI esters to act as acyl electrophile^[15] and carbon-centered radical precursors. The latter manifold is vividly expanding into new C-C,^[16] C-N,^[17] C-O^[18] or C-B^[19] bond forming reactions. This diversity is beyond the reach of current divergent strategies towards chiral cyclopropanes.^{[20][21a]} Despite the versatility of NHPI esters, their orthogonality to metal-carbenes was unknown, and a logical concern when considering their facile irreversible fragmentation upon activation with various transition metals and/or visible light.^[16-19]



Scheme 1. State-of-the-art, concept and challenges towards the unified assembly of diverse chiral cyclopropanes.

After extensive experimentation, we found that the designed *N*-hydroxyphthalimidoyl diazoacetate reagent (NHPI-DA, **13a**; Scheme 2a)^[22] can be isolated in gram-amounts as a

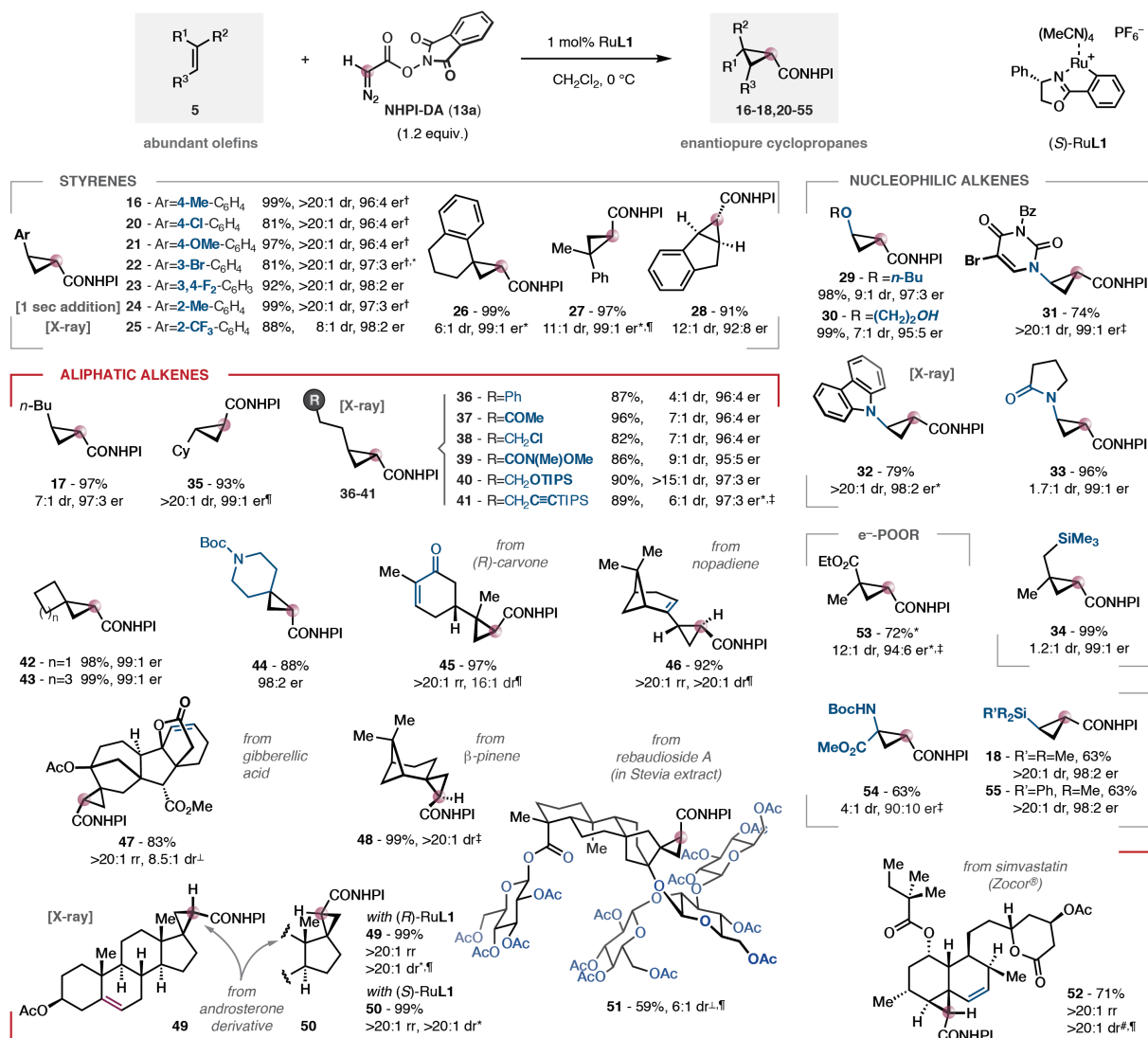
crystalline solid that is bench-stable for months. NHPI-DA (**13a**) does not require solution storage, and thus allows for easier handling. It also displays higher stability than the benchmark ethyl diazoacetate, as evidenced by DSC (EDA, **15a**; Scheme 2b). Initial evaluation of NHPI-DA (**13a**) in cyclopropanation reactions using common rhodium, copper and palladium catalysts^[2] displayed low efficiency and selectivity (Table S3), as anticipated for this challenging transformation (*vide supra*). Fortunately, we discovered that NHPI-DA (**13a**) is effective in combination with the electron-rich metallacyclic ruthenium catalyst **RuL1**^[22] (Scheme 2c), displaying a remarkable cyclopropanation selectivity over the competing dimerization pathway (**16-18/19**). We compared this intrinsic selectivity against various conventional diazo reagents with different steric and electronic properties (**15a-f**). For this study, we used equimolar conditions without slow addition of the carbene precursors to minimize any substrate-specific bias. Model olefins **5a-c** with distinct nucleophilicities (N ;^[23] Scheme 2d), were used as representative substrates. Using styrene (**5a**, $N = +1.70$), it was found that NHPI-DA (**13a**) outperforms diazocompounds **15a-f**. More importantly, this trend is accentuated when exploring more challenging olefins, such as 1-hexene (**5b**, $N = -2.77$) and vinyltrimethylsilane (**5c**, $N < -1.46$), which are cyclopropanated with NHPI-DA in 72% and 41% yield, respectively (<26% and <9% yield using **15a-f**). This effect can be rationalized by the stronger electron-withdrawing effect of the ester moiety in **13a**, which allows less reactive olefins to effectively compete for the electrophilic carbene **Int-A** (Scheme 2c).



Scheme 2. Properties and performance of NHPI-DA (**13a**). Conditions: **5** (0.1 mmol), RuL1 (1 mol%), diazocompound (0.1 mmol; 1 s addition time), CH₂Cl₂, 0 °C; DSC, differential scanning calorimetry; EDA, ethyl diazoacetate; ArO, 2,6-di-(*tert*-butyl)-4-methylphenoxy; TFE, 2,2,2-trifluoroethoxy; TCE, 2,2,2-trichloroethoxy. Supplementary crystallographic data: CCDC 1851523 (**13a**).

Although RuL1 is a competent catalyst in asymmetric cyclopropanation,^[21] we have found that NHPI-DA (**13a**) expands its scope into an unprecedentedly wide selection of alkenes with surprisingly high enantioselectivities (Scheme 3).^[2] Functionalized styrenes with various substitution patterns lead, without slow addition, to redox-active cyclopropanes **16,20-28** in excellent yields, and with high diastereo- and enantioselectivities. Different nucleophilic enol ethers smoothly produce push-pull products **29,30**, even in the presence of a primary alcohol (no O–H insertion observed). Various types of enamines (**31-33**) or an allylic silane (**34**), are also efficiently cyclopropanated. Aliphatic olefins are challenging substrates in enantioselective cyclopropanation,^[7, 10] but to our delight, non-coordinating and structurally flexible alkenes furnished cyclopropanes **17,35** with high diastereo- and enantioselectivity under standard conditions. We explored the functional group tolerance of this method in these series using unactivated olefins equipped with a pendant arene (**36**), ketone (**37**), chloride (**38**), Weinreb amide (**39**), alcohol derivative (**40**) and alkyne (**41**), observing high enantioselectivity in all cases. Methylenecycloalkanes produce the interesting spiro-cyclopropane building blocks **42,43**. Additionally, protected amines (**44**) were also tolerated. As far as we are aware, the NHPI-DA / RuL1 combination is the simplest homogeneous system to achieve highly enantioselective cyclopropanation on a wide range of aliphatic alkenes.^[7, 8, 10] Natural unactivated olefin feedstocks offer an opportunity to explore its performance in complex settings. Complete discrimination between olefins of different nucleophilicity (including enones and 1,3-dienes) enables the selective modification of carvone, nopadiene, and gibberellic acid (**45-47**). Olefins at hindered positions in the pinane (**48**) and steroid (**49-50**) frameworks are also suitable in smooth cyclopropanations. In the latter, either enantiomer of the catalyst RuL1 can be used to access alternative diastereomers **49** and **50** with complete facial discrimination. This system is also primed for late-stage functionalization of macromolecular natural glycosides and pharmaceuticals that would be problematic with existing biocatalysts,^[8] like rebaudioside A obtained from a *Stevia* extract (**51**) and the cholesterol-regulating drug simvastatin (Zocor®) (**52**). Electron-poor olefins produce the

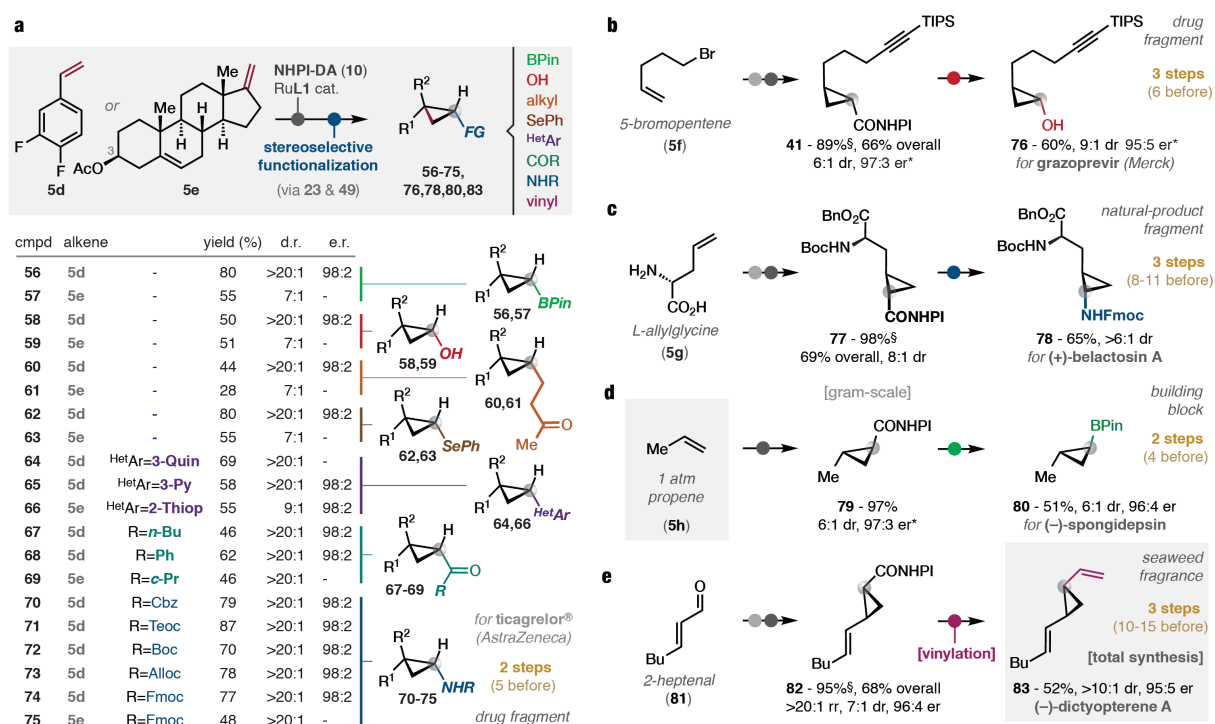
differentiated bis-carboxylate **53** and the cyclopropyl amino acid derivative **54**. Silylcyclopropanes **18,55** are also obtained with high diastereo- and enantioselectivity from vinylsilanes, despite their high steric bulk.



Scheme 3. Scope of the enantioselective cyclopropanation with NHPI-DA (**13a**). Conditions: **5** (1.0 equiv.), **13a** (1.2 equiv., 40 min addition time), catalyst *(S)*-RuL1 (1 mol%), CH₂Cl₂, 0 °C. [†] **13a** (1 s addition time), catalyst (2 mol%). [‡] **13a** (6 h addition time), catalyst (2 mol%). [⊥] **13a** (3 equiv., 16 h addition time), catalyst (3 mol%), rt. [¶] **13a** (3 equiv., 24 h addition time), catalyst (5 mol%), rt. [¶] catalyst *(R)*-RuL1. ^{*} Absolute stereochemistry confirmed. See Supporting Information for experimental details. Supplementary crystallographic data: CCDC 1851521 (**22**), 1851524 (**32**), 1851525 (**41**), 1851522 (**50**).

We explored the synthetic potential of enantioenriched redox-active cyclopropane scaffolds derived from the representative olefins **5d,e** (Scheme 4a). Upon decarboxylation, these are versatile precursors of catecholboronates^[19b] that can be readily converted into pinacolboronates **56-57** or oxidized to cyclopropanols **58-59**. Radical decarboxylative

alkylation (**60,61**) and selenation (**62,63**)^[24] yield enantioenriched alkyl- and selenylcyclopropane products. To the best of our knowledge, this represents the first enantioselective synthesis of selenyl cyclopropanes. Basic and electron-rich heteroaromatics can be installed through telescoped cross-coupling with the corresponding bromides or lithiated heterocycles^[25] (see **64-66**). Taking advantage of the capacity of NHPI esters as acyl donors,^[15] we added Grignard nucleophiles to produce the corresponding alkyl- and arylketones **67-69**. We also developed a direct Curtius amination protocol towards cyclopropylamines **70-75**, including the ticagrelor® fragments **70-74**.^[26] It is important to highlight that the synthesis of products **56-75** did not require neither an individual synthesis of suitable carbene precursors, nor custom catalysts to accommodate their diverse functionalities. These results illustrate the unique versatility of enantioenriched redox-active cyclopropane carboxylates, now accesible in one-step from feedstock alkenes using NHPI-DA (**13a**).



Scheme 4. Synthesis of unrelated enantioenriched functionalized cyclopropanes *via* redox-active intermediates. See Supporting Information for experimental details. [†]C-3 acetate cleaved. * Absolute stereochemistry confirmed. [§] Yield of the cyclopropanation step. Yields are calculated on the isolated product. Bpin, boronic acid pinacol ester; ^{Het}Ar, heteroaryl; FG, functional group; 3-Quin, quinoline-3-yl; 3-Py, pyridine-3-yl; 2-Thiop, thiophene-2-yl; Cbz, benzyloxycarbonyl; Teoc, (2-(trimethylsilyl)ethoxycarbonyl); Alloc, allyloxycarbonyl; Fmoc, fluorenylmethyloxycarbonyl; Bn, benzyl.

With these results in hand, we explored the valorization of simple feedstocks in the synthesis of relevant chiral cyclopropanes (Scheme 4b-d). As such, 4-bromobutene (**5f**) can be transformed in a three-step process into the enantioenriched cyclopropanol fragment **76** of the drug grazoprevir®.^[27] *L*-allylglycine (**5g**) can be utilized to produce **77**, which can be transformed into the cyclopropylamine fragment **78** of the bioactive natural product (+)-belactosin A (Scheme 4c).^[28] Moreover, propene gas (**5h**), the simplest pro-chiral aliphatic olefin, leads efficiently on a gram-scale to **79** en-route to the enantiopure cyclopropylboronate building block **80**, used in the total synthesis of (–)-spongidepsin (Scheme 4d).^[29] After olefination of the inexpensive 2-heptenal (**81**; Scheme 4e), the resulting 1,3-diene, is cyclopropanated to yield **82** and further vinylated using a telescoped Zweifel process^[25b, 30] into the divinylcyclopropane natural product dictyopterene A (**83**).^[31] To put these results in perspective, it is important to highlight that the synthesis of the diverse cyclopropane fragments in commercial drugs (**70-74,76**), natural products (**78,80**), and the shortest total synthesis of **83** invariably required 2-3 steps from feedstock materials, utilizing a single strategy, carbene precursor (**13a**) and catalyst (Ru**L1**). If step count is used to illustrate the tactical value of this new scheme, previous strategies for the asymmetric synthesis of products **70-74,76,78,80,83** required at least twice as many, and up to 15 steps (see Scheme 4) using custom methods, materials, and reagents. This has been realized through the 2-step enantioselective formal transfer of carbenes **6-12**, which is unprecedented to the best of our knowledge. The current momentum of redox-active ester chemistry and the rich reactivity of carbene transfer suggest future synthetic upgrades of this technology, some of which are underway in our laboratories.

In summary, NHPI-DA (**13a**) is a practical, safe, and crystalline methine precursor that provides a comprehensive solution to the enantioselective formal transfer of various functionalized methylenes. This reagent (i) renders the synthesis of custom and unstable carbene reagents unnecessary, (ii) simplifies the optimization of the asymmetric carbene transfer step, and (iii) enables the synthesis of targets with distinct functionalities with the same enantioselectivity and conceptual approach. The unexpected synergistic effect between the geminal redox-active ester and carbene functions enables the general asymmetric cyclopropanation of challenging aliphatic alkenes. Moreover, the NHPI ester function has the unique capacity to promote both acyl-transfer and radical derivatization reactions that

enhance the synthetic utility of the resulting enantioenriched cyclopropane intermediates. NHPI-DA (**13a**) provides the foundation for further asymmetric assembly of ubiquitous carbon stereocenters from single carbon units: their simplest retrosynthetic chirons.

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Conflict of interest

A priority patent application has been filed (1850940-6), where A.M., M.M.-M., M.C. and E.M.-C. are listed as inventors.

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General Cyclopropane Assembly *via* Enantioselective Redox-Active Carbene Transfer to Aliphatic Olefins

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¹³ C NMR (101 MHz, CDCl ₃) for compound 45	230
COSY NMR (400 MHz, CDCl ₃) for compound 45	231
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COSY NMR (400 MHz, CDCl ₃) for compound 49	253
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¹ H NMR (400 MHz, CDCl ₃) for compound 50	255
¹³ C NMR (101 MHz, CDCl ₃) for compound 50	256
COSY NMR (400 MHz, CDCl ₃) for compound 50	257
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¹³ C NMR (101 MHz, CDCl ₃) for compound 60	308
¹⁹ F NMR (376MHz, CDCl ₃) for compound 60	309
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¹³ C NMR (101 MHz, CDCl ₃) for compound 62	313
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1. General experimental

Materials. All reactions were carried out using oven-dried glassware under an atmosphere of argon (99.999%). Dry solvents were obtained using a solvent purifier equipped with activated alumina columns. All solvents used in work-up procedures, silica gel column chromatography, HPLC analysis and/or purification were obtained from commercial suppliers and used without further purification. When appropriate, degassing of anhydrous solvent was performed by bubbling Ar for 30 minutes under sonication. Reagents were obtained from commercially available sources and used as received unless stated otherwise. Catalysts **(S)-**, **(R)-Ru-L1(CH₃CN)₄PF₆** and **Ru-L2(CH₃CN)₄PF₆** were prepared as described by Iwasa.^[1] Catalysts **(S)-Rh₂(L3)₄**,^[2] and **(S)-Rh₂(L4)₄**,^[3] were prepared according to the indicated literature procedure.

Commercially available alkenes were purchased from Sigma-Aldrich, Fluorochem, TCI or Acros Organics. Liquid alkenes were quickly distilled, using a Hickman head, prior to use. Other alkene substrates were synthesized following the literature procedures indicated in the corresponding cyclopropanation reaction. The olefins **5e,s,ac,an** were prepared as described below (See Section 2.1.2). Rebaudioside-A (>97% pure) was obtained from Steviago® Stevia sweetener extract. Propene (99.5%) was obtained from Sigma-Aldrich Messer® CANGas.

Chromatography. Thin layer chromatography (TLC) was carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as visualizing agent and a vanillin or KMnO₄ solution and heat as developing agent. Flash silica gel chromatography was performed using Normasil 60 VWR Chemicals (60 Å, particle size 0.040-0.063 mm) or E. Merck silica gel (60 Å, particle size 0.043-0.063 mm).

Gas chromatography was performed on a Shimadzu GC-2010 Plus Gas Chromatograph coupled with a GCMS-QP2020 Mass Spectrometer and a FID detector (FID-2010Plus) and an Agilent HP-5MS, 30 m x 0.25 mm fused silica (film = 0.25 µm) capillary column.

Semi-preparative High-Performance Liquid Chromatography (HPLC) was performed on an Agilent 1100 series Liquid Chromatograph, equipped with a UV diode array and a Pursuit XRs 10-Si, 250 x 21.2 mm, normal phase column.

Determination of Enantiomeric Purity: HPLC analysis on chiral stationary phase was performed on an Agilent 1200-series instrument, employing Daicel Chiralpak columns IA, IB, IC, ID, IF and AS-H, or a Waters e2695 separation module, using Daicel Chiralpak IA, IB

and IC chiral columns. SFC on chiral stationary phase was performed on a Waters UPC2 device (supercritical CO₂ + polar solvent), equipped with a UV-Vis diode array; employing columns YMC SA (IA), Lux A1 (AD), Lux C4, (S,S)-Whelk-O1 and Chiralpak IG (columns dimensions = 150 mm x 4.6 mm, 3 Å particle size) or Chiralpak IG (column dimensions = 250 mm x 4.6 mm, 3 Å particle size). GC on chiral stationary phase was performed on a Varian 450-GC Gas Chromatograph coupled with a Varian 200-MS Mass Spectrometer equipped with a Macherey-Nagel Hydrodex-B-6TBDM, 25m x 0.25 mm capillary column. The specific conditions of these analyses are detailed along the characterization details of the relevant compound. HPLC, SFC and GC traces were compared to racemic samples prepared using **Ru-L2(CH₃CN)₄PF₆** as the catalyst.

Characterization. NMR spectra for the characterization of new compounds were recorded, unless stated otherwise, at 25°C on Bruker 400 Ultrashield (400/101/376 MHz ¹H/¹³C/¹⁹F), Bruker 500 Ultrashield (500/126/471/95 MHz ¹H/¹³C/¹⁹F/⁷⁷Se), 600 Ultrashield (600/151 MHz ¹H/¹³C) or Oxford AS500 (500/126/471 MHz ¹H/¹³C/¹⁹F) instruments. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in CDCl₃ (δ_H = 7.26 and δ_C = 77.16 ppm), CD₃CN (δ_H = 1.94 and δ_C = 1.32 ppm), C₆D₆ (δ_H = 7.16 and δ_C = 128.06 ppm) or CD₂Cl₂ (δ_H = 5.32 and δ_C = 53.84 ppm) as internal reference, or Ph₂Se₂ (δ_{Se} = 464.0 ppm)^[4] as an external reference, and coupling constants (*J*) are given in hertz (Hz). Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, br: broad, m: multiplet), coupling constants (*J* in Hz) and integration. Carbon multiplicities were assigned by DEPT and edited HSQC techniques. NMR spectra for ¹³C, ⁷⁷Se and ¹⁹F we recorded decoupled from ¹H.

High-resolution mass spectra (HRMS) were determined with a Bruker Daltonics microTOF Mass Spectrometer using electrospray ionization source (ESI). Melting points (m.p.) were measured on a Stuart SMP50 apparatus and are uncorrected. Specific optical rotation was measured on a Rudolph Research Analytical Autopol IV polarimeter and is reported as follows: [α]_D^T (concentration in g per 100 mL, solvent).

Experimental details. Reactions were performed in common pyrex round bottom flasks, microwave vials 2 - 8 ml (VWR or Biotage[®]), or 5 - 20 ml flat bottom vials (Cronus, SMI-LabHut Ltd. or VWR[®]) crimped on top with 20 mm Sil/PTFE Septa. Reaction temperatures were maintained using Thermowatch-controlled silicone oil baths, dry ice-acetone, water-ice baths or an Immersion Cooler (Julabo-FT902) equipped with temperature controller. Slow

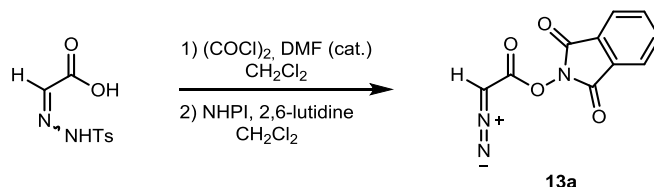
additions were performed using Landgraf HLL LA-30 or Harvard Apparatus Pump11Elite syringe pumps. Photoinduced reactions were performed using a photoreactor consisting in a blue LEDs strip foiled in a crystallising dish, as reported by Aggarwal and coworker.^[5]

UV-Vis: UV-vis measurements were carried out on a Varian Cary 50 Bio UV-Visible spectrophotometer equipped with silicon diode detectors and Xe pulse lamp single source.

2. Experimental Procedures

2.1. Synthesis of starting materials

2.1.1. Synthesis of 1,3-dioxoisindolin-2-yl 2-diazoacetate (**13a**)



To a suspension of 2-(2-tosylhydrazono)acetic acid^[6] (5 g, 20.6 mmol) in dry CH₂Cl₂ (150 mL), DMF (64 μ L, 0.83 mmol, 0.04 equiv) was added under Ar. The suspension was placed in an ice-water bath and stirred for 10 minutes. Then, oxalyl chloride (2.6 mL, 30.9 mmol, 1.5 equiv) was added dropwise over 30 minutes (gas evolution observed). (*Note: this step should be performed in a well-ventilated fumehood*). After the addition, the mixture was stirred at 0 °C for 20 minutes before the ice-bath was removed. The mixture was stirred at room temperature overnight.^[7] During the process gas evolution ceased and the suspended solid completely dissolved (*Note: more efficient reactivity was observed when the starting hydrazone was used as a fine powder*). Volatiles were removed by rotatory evaporation and fresh dry CH₂Cl₂ (100 mL) was added. The pale yellow or colorless solution was placed in an ice-bath again under Ar again. Then, a briefly sonicated solution of *N*-hydroxyphthalimide (NHPI, 6.72 g, 41.2 mmol, 2 equiv) and 2,6-lutidine (7.2 mL, 61.8 mmol, 3.0 equiv) in dry CH₂Cl₂ (50 mL) was added slowly. The reaction was allowed to reach room temperature over 30 minutes and further stirred for 4 hours at this temperature. Then, the volume of CH₂Cl₂ was reduced to a *ca.* 20% by rotatory evaporation, and the crude yellow oil was purified by column chromatography (eluent CHCl₃/petroleum ether 30:70 to 70:30 or heptane/CH₂Cl₂/EtOAc 70:20:10 to 60:25:15). The solvent was removed *in vacuo*, the off-white solid was washed with a mixture of 20% Et₂O in petroleum ether (2 x 100 mL) and dried, to yield **13a** as an amorphous solid. This solid can be further purified by crystallization. The product was dissolved in the minimum amount of dichloromethane and layered with petroleum ether. After 12 hours, the pale yellow needles were filtered, washed with petroleum ether. The mother liquor was subjected to rotatory evaporation and the crystallization process was repeated again, leaving the mixture to stand for 24 hours (longer

periods may be detrimental for the purity). The crystals from the two batches were combined affording pure **13a** (2.62 g, 55% yield).

Appearance: pale yellow crystals.

M.p.: 154.4 °C (decomp.)

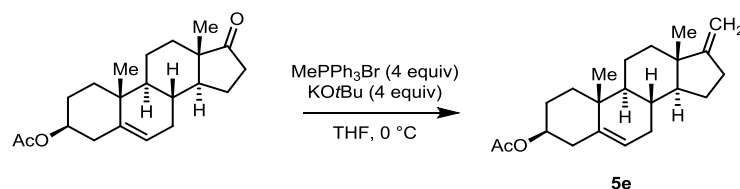
TLC R_f = 0.4 (CHCl_3). It develops red using vanillin staining solution and it is UV-active.

^1H NMR (500 MHz, CDCl_3) δ = 7.92 – 7.86 (m, 2H), 7.82 – 7.75 (m, 2H), 5.17 (br s, 1 H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 163.2 (C_q), 162.2 (C_q), 135.0 (CH), 129.0 (C_q), 124.2 (CH), 45.2 (CH) ppm.

2.1.2. Synthesis of starting alkenes

Synthesis of androsterone derivative (5e)



In an oven-dried flask methyl triphenylphosphoniumbromide (4.95 g, 13.87 mmol, 4.0 equiv) was dissolved in dry THF (25 mL). The solution was cooled down to 0 °C and KOtBu (1.56 g, 13.87 mmol, 4.0 equiv) was added. The resulting yellow suspension was stirred at 0 °C for 1 hour. Then, a solution of acetyl-prasterone^[8] (1.15 g, 3.47 mmol, 1.0 equiv) in THF (5 mL) was added dropwise. After the addition, the mixture was stirred overnight while it reached room temperature. The suspension was filtered through Celite, washed with CH_2Cl_2 and the filtrate was concentrated by rotatory evaporation. The resulting yellow oil was purified by column chromatography (EtOAc/petroleum ether 2:98), yielding pure alkene **5e** (923 mg, 2.81 mmol, 81% yield).

Appearance: white solid.

M.p.: 102.6 °C - 103.8 °C

TLC R_f = 0.55 (Et_2O /petroleum ether 1:9)

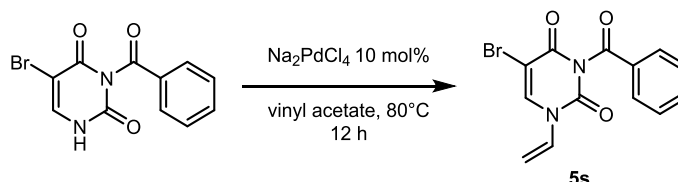
^1H NMR (500 MHz, CDCl_3) δ = 5.38 (dt, J = 4.6, 1.8 Hz, 1H), 4.67 – 4.55 (m, 3H), 2.50 (ddq, J = 17.1, 10.0, 2.2 Hz, 1H), 2.38 – 2.20 (m, 3H), 2.06 – 1.99 (m, 1H), 2.03 (s, 3H), 1.92 – 1.80 (m, 3H), 1.76 – 1.44 (m, 6H), 1.35 – 1.23 (m, 2H), 1.18 – 1.10 (m, 1H), 1.04 (s, 3H), 1.05 – 0.94 (m, 2H), 0.79 (s, 3H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 170.6 (C_q), 161.8 (C_q), 139.9 (C_q), 122.6 (CH), 101.1 (CH_2), 74.0 (CH), 54.8 (CH_3), 50.4 (CH), 44.0 (C_q), 38.3 (CH_2), 37.2 (CH_2), 36.9 (C_q), 35.7

(CH₂), 31.92 (CH), 31.85 (CH₂), 29.5 (CH₂), 27.9 (CH₂), 24.4 (CH₂), 21.6 (CH₃), 21.1 (CH₂), 19.5 (CH₃), 18.4 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₂₂H₃₂O₂+Na]⁺ 351.2300; found: 351.2281.

Synthesis of 3-benzoyl-5-bromo-1-vinylpyrimidine-2,4(1H,3H)-dione (5s)



Adapted from Dulcere and co-workers.^[9]

Under argon atmosphere, sodium tetrachloropalladate (26.9 mg, 0.091 mmol, 0.1 equiv) and 3-benzoyl-5-bromopyrimidine-2,4(1H,3H)-dione^[10] (270 mg, 0.915 mmol, 1 equiv) were added in a microwave vial, then vinyl acetate (1.80 mL) was added and the mixture was stirred at 80°C for 12h. The crude was filtered through a syringe filter, then concentrated under vacuum and purified by flash chromatography (EtOAc:CH₂Cl₂ 1:99) to afford the pure product **5s** as a light brown solid (250 mg, 85%).

Appearance: light brown solid.

M.p.: 166.6 °C - 169.1 °C

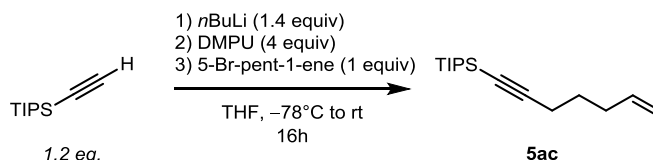
TLC R_f = 0.3 (EtOAc/petroleum ether 1:2)

¹H NMR (400 MHz, CDCl₃) δ = 7.96 – 7.89 (m, 3H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.51 (dd, *J* = 8.3, 7.4 Hz, 2H), 7.11 (dd, *J* = 15.9, 9.0 Hz, 1H), 5.23 (dd, *J* = 15.9, 2.6 Hz, 1H), 5.06 (dd, *J* = 9.0, 2.7 Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 167.2 (C_q), 157.8 (C_q), 147.7 (C_q), 138.4 (CH), 135.6 (CH), 130.9 (C_q), 130.7 (CH), 129.4 (CH), 129.2 (CH), 103.1 (CH₂), 98.4 (C_q) ppm.

HRMS (ESI-TOF) calc'd for [C₁₃H₉BrN₂O₃+Na]⁺: 342.9689; found: 342.9689.

Synthesis of hept-6-en-1-yn-1-yltriisopropylsilane (5ac)



Adapted from Wulff and co-workers.^[11]

Under argon atmosphere, ethynyltriisopropylsilane (2.429 mL, 12 mmol, 1.2 equiv) was dissolved in dry THF (30 mL). The mixture was cooled to –78 °C and butyllithium (5.60 mL, 14.00 mmol, 2.5 M in hexane, 1.4 equiv) was added dropwise and the mixture stirred at –78 °C for 30 minutes. 1,3-Dimethyltetrahydropyrimidin-2(1H)-one (DMPU, 4.84 mL, 40.0

mmol, 4 equiv) was added and the mixture was stirred for 15 minutes, then 5-bromopent-1-ene (1.185 mL, 10.00 mmol, 1 equiv) was added dropwise to the solution. The mixture was left stirring overnight at rt and poured into a mixture of water:diethyl ether 1:1 (4 mL) and extracted. The water phase was extracted with diethyl ether (20 mL), then the combined organic phases were washed with water (4 x 20 mL) and brine, dried over Na₂SO₄ and concentrated under vacuum. The crude mixture was purified by flash chromatography (pentane) to afford the final product **5ac** as a colourless oil (1.86 g, 74% yield).

Appearance: colorless oil

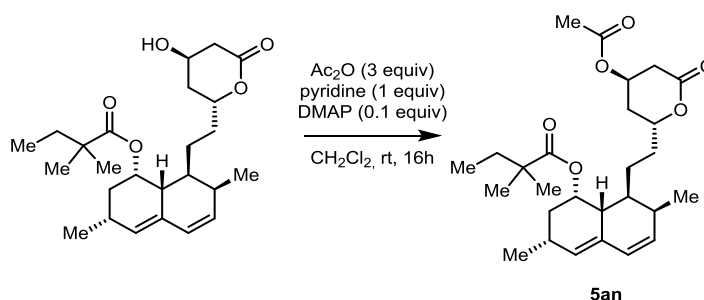
TLC R_f = 0.9 (Pentane).

¹H NMR (400 MHz, CDCl₃) δ = 5.80 (ddt, *J* = 17.0, 10.1, 6.8 Hz, 1H), 5.08 – 4.95 (m, 2H), 2.27 (t, *J* = 7.0 Hz, 2H), 2.23 – 2.15 (m, 2H), 1.62 (p, *J* = 7.1 Hz, 2H), 1.09 – 1.04 (m, 21H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 138.1 (CH), 115.3 (CH₂), 108.9 (C_q), 80.5 (C_q), 32.9 (CH₂), 28.3 (CH₂), 19.4 (CH₂), 18.8 (CH₃), 11.5 (CH) ppm.

HRMS (ESI-TOF) calc'd for [C₁₆H₃₀Si+K]⁺ 289.1748; found: 289.1755.

Synthesis of simvastatin acetate (**5an**)



Under argon atmosphere, acetic anhydride (101 μL, 1.075 mmol, 3 equiv) and pyridine (28.9 μL, 0.358 mmol, 1 equiv) were dissolved in dry dichloromethane (1.2 mL). The mixture was stirred at rt for 10 minutes, then simvastatin (150 mg, 0.358 mmol) and 4-dimethylaminopyridine (DMAP; see figure above) (4.38 mg, 0.036 mmol, 0.1 equiv) were added and the mixture was left stirring overnight at room temperature. The solvent was removed and the product was purified by flash chromatography (EtOAc/pentane 1:3) to afford the final product **5an** as a white solid (162 mg, 98% yield).

Appearance: white solid.

m.p.: 46.1 °C - 48.1 °C

TLC R_f = 0.69 (EtOAc/petroleum ether 3:7)

¹H NMR (400 MHz, CDCl₃) δ = 5.97 (d, *J* = 9.7 Hz, 1H), 5.76 (dd, *J* = 9.6, 6.1 Hz, 1H), 5.49 (bt, *J* = 3.1 Hz, 1H), 5.34 (q, *J* = 3.2 Hz, 1H), 5.26 – 5.20 (m, 1H), 4.51 – 4.42 (m, 1H), 2.81 – 2.65 (m, 2H), 2.47 – 2.38 (m, 1H), 2.38 – 2.30 (m, 1H), 2.29 – 2.21 (m, 1H), 2.07 (s, 3H), 2.04 – 2.01 (m, 1H), 1.96 – 1.92 (m, 2H), 1.87 – 1.61 (m, 4H), 1.60 – 1.51 (m, 2H), 1.51 – 1.39 (m, 2H), 1.32 – 1.22 (m, 1H), 1.11 (s, 3H), 1.10 (s, 3H), 1.06 (d, *J* = 7.5 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.5 Hz, 3H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 177.8 (C_q), 170.1 (C_q), 168.9 (C_q), 132.9 (CH), 131.6 (C_q), 129.9 (CH), 128.5 (CH), 76.8 (CH), 68.1 (CH), 65.6 (CH), 43.1 (C_q), 37.6 (CH), 36.8 (CH), 35.5 (CH₂), 33.4 (CH₂), 33.3 (CH₂), 33.2 (CH₂), 32.9 (CH₂), 30.8 (CH), 27.4 (CH), 24.9 (CH₃), 24.8 (CH₃), 24.5 (CH₂), 23.1 (CH₃), 21.2 (CH₃), 14.0 (CH₃), 9.4 (CH₃) ppm.

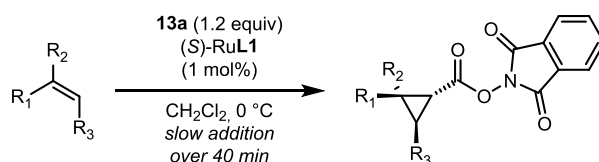
HRMS (ESI-TOF) calc'd for [C₂₇H₄₀O₆+Na]⁺: 483.2717; found: 483.2722.

2.2. Enantioselective Synthesis of Cyclopropyl Redox-Active Esters

As a general guideline, when testing the reaction on a new substrate, it is recommended to start with general procedure A. In general, styrenes, aliphatic olefins, terminal dienes and vinyl- and silyl ethers are expected to give satisfactory results under those conditions. If dimerization of **13a** appears to be a major problem (i.e. if the substrate is not nucleophilic enough), general procedure B is usually able to overcome the issue. For poorly reactive substrates (very electron poor or sterically hindered olefins) general procedure C is recommended. If full conversion of the olefin is required (e.g. when the starting material and the cyclopropane have similar R_f 's) general procedure C is also recommended.

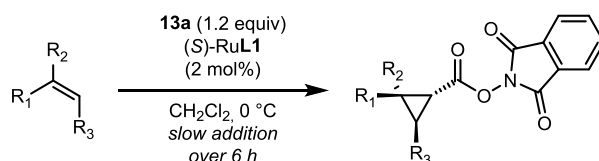
2.2.1. General procedures for the enantioselective cyclopropanations:

General procedure A for the synthesis of cyclopropyl redox-active esters:



To a solution of (S)-RuL1(CH_3CN) $_4\text{PF}_6$ (0.01 equiv) and alkene (1 equiv) in dry CH_2Cl_2 (final concentration in CH_2Cl_2 : 0.1 M) at $0\text{ }^\circ\text{C}$, a solution of **13a** (0.2 M or 0.3 M, 1.2 equiv) in dry CH_2Cl_2 was added over 40 minutes using an addition pump. Alternatively, when employing styrenes **5a**, **5i-k**, **5l** as a substrate, **13a** was added in one portion. Once the addition was completed, the reaction was monitored by TLC. After consumption of the diazocompound, volatiles were removed *in vacuo* and the crude mixture was analyzed by ^1H NMR in order to determine the diastereomeric ratio. When specified, the NMR yield was also determined using 1,1,2,2-tetrachloroethane as internal standard. The crude cyclopropane was purified by column chromatography using the indicated eluent system unless stated otherwise.

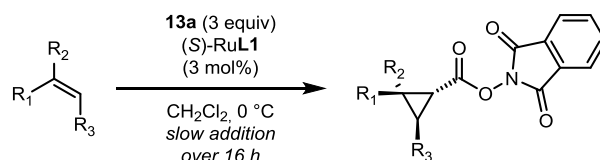
General procedure B for the synthesis of cyclopropyl redox-active esters:



To a solution of (S)-RuL1(CH_3CN) $_4\text{PF}_6$ (0.02 equiv) and alkene (1 equiv) in dry CH_2Cl_2 (final concentration in CH_2Cl_2 : 0.1 M) at $0\text{ }^\circ\text{C}$, a solution of **13a** (0.2 M or 0.3 M, 1.2 equiv) in dry CH_2Cl_2 was added over 6 hours using an addition pump. Once the addition was

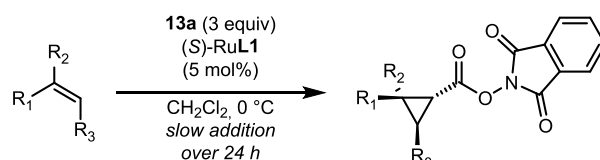
completed, the reaction was monitored by TLC. After consumption of the diazocompound, volatiles were removed *in vacuo* and the crude mixture was analyzed by ^1H NMR in order to determine the diastereomeric ratio. When specified, the NMR yield was also determined using 1,1,2,2-tetrachloroethane as internal standard. The crude cyclopropane was purified by column chromatography using the indicated eluent system unless stated otherwise.

General procedure C for the synthesis of cyclopropyl redox-active esters:



To a solution of **(S)-RuL1(CH₃CN)₄PF₆** (0.03 equiv) and alkene (1 equiv) in dry CH₂Cl₂ (final concentration in CH₂Cl₂: 0.05 M) at *rt*, a solution of **13a** (0.2 M, 3 equiv) in dry CH₂Cl₂ was added over 16 hours using an addition pump. Once the addition was completed, the reaction was monitored by TLC. After consumption of the diazocompound, volatiles were removed *in vacuo* and the crude mixture was analyzed by ^1H NMR in order to determine the diastereomeric ratio. When specified, the NMR yield was also determined using 1,1,2,2-tetrachloroethane as internal standard. The crude cyclopropane was purified by column chromatography using the indicated eluent system unless stated otherwise.

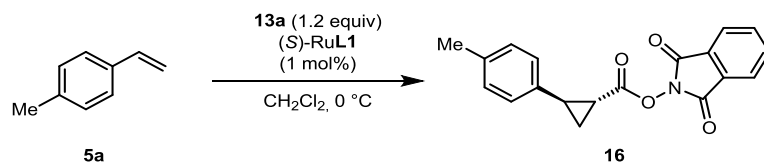
General procedure D for the synthesis of cyclopropyl redox-active esters:



To a solution of **(S)-RuL1(CH₃CN)₄PF₆** (0.05 equiv) and alkene (1 equiv) in dry CH₂Cl₂ (final concentration in CH₂Cl₂: 0.05 M) at *rt*, a solution of **13a** (0.2 M, 3 equiv) in dry CH₂Cl₂ was added over 24 hours using an addition pump. Once the addition was completed, the reaction was monitored by TLC. After consumption of the diazocompound, volatiles were removed *in vacuo* and the crude mixture was analyzed by ^1H NMR in order to determine the diastereomeric ratio. When specified, the NMR yield was also determined using 1,1,2,2-tetrachloroethane as internal standard. The crude cyclopropane was purified by column chromatography using the indicated eluent system unless stated otherwise.

2.2.2. Synthesis and characterization of chiral cyclopropyl redox-active cyclopropanes:

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(*p*-tolyl)cyclopropane-1-carboxylate (**16**)



General procedure A was applied using **13a** (0.36 mmol, 1.8 mL, 1.2 equiv), olefin **5a** (0.3 mmol, 35.5 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.003 mmol, 1.9 mg, 0.01 equiv). **13a** was added in one portion. The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **16** as a white solid (95 mg, 99% yield, d.r.>20:1). Compound (*R,R*)-**16** was obtained with a 95.7:4.3 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 14.6 min, τ_{minor} = 13.1 min.

Appearance: white solid.

m.p.: 129.4 °C - 131.5 °C

TLC R_f = 0.44 (petroleum ether/ EtOAc 4:1).

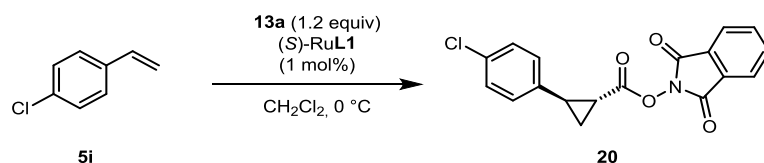
$[\alpha]_{20}^D = -310.0$ ($c = 1.0$, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.94 – 7.86 (m, 2H), 7.83 – 7.75 (m, 2H), 7.14 (d, $J = 7.7$ Hz, 2H), 7.07 (d, $J = 8.1$ Hz, 2H), 2.76 (ddd, $J = 9.3, 6.9, 4.1$ Hz, 1H), 2.34 (s, 3H), 2.18 (ddd, $J = 8.4, 5.2, 4.1$ Hz, 1H), 1.80 (dt, $J = 9.3, 5.0$ Hz, 1H), 1.61 (ddd, $J = 8.4, 6.9, 4.9$ Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 169.9 (C_q), 162.1 (C_q), 137.0 (C_q), 135.5 (C_q), 134.9 (CH), 129.4 (CH), 129.0 (C_q), 126.4 (CH), 124.1 (CH), 28.3 (CH), 21.2 (CH₃), 21.0 (CH), 18.5 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₉H₁₅NO₄+Na]⁺: 344.0893; found: 344.0897.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(4-chlorophenyl)cyclopropane-1-carboxylate (**20**)



General procedure A was applied using **13a** (0.36 mmol, 1.8 mL, 1.2 equiv), olefin **5i** (0.3 mmol, 41.6 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.003 mmol, 1.9 mg, 0.01 equiv).

13a was added in one portion. The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **20** as a white solid (83.4 mg, 81% yield, d.r.>20:1). Compound (*R,R*)-**20** was obtained with a 96.3:3.7 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 13.7 min, τ_{minor} = 12.2 min.

Appearance: white solid.

m.p.: 133.9 °C - 136.4 °C

TLC R_f = 0.33 (petroleum ether/ EtOAc 4:1).

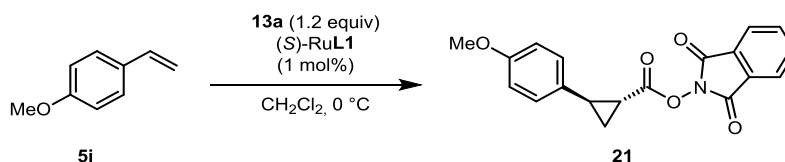
$[\alpha]_{20}^D = +287.7$ ($c = 1.0$, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.95 – 7.85 (m, 2H), 7.85 – 7.75 (m, 2H), 7.30 (d, $J = 8.5$ Hz, 2H), 7.11 (d, $J = 8.5$ Hz, 2H), 2.75 (ddd, $J = 9.3, 6.9, 4.1$ Hz, 1H), 2.19 (ddd, $J = 8.4, 5.1, 4.1$ Hz, 1H), 1.83 (dt, $J = 9.3, 5.1$ Hz, 1H), 1.60 (ddd, $J = 8.5, 6.9, 5.1$ Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 169.7 (C_q), 162.1 (C_q), 137.1 (C_q), 135.0 (CH), 133.1 (C_q), 129.0 (C_q), 129.0 (CH), 128.0 (CH), 124.2 (CH), 27.7 (CH), 21.1 (CH), 18.5 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₈H₁₂ClNO₄+Na]⁺: 364.0347; found: 364.0334.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(4-methoxyphenyl)cyclopropane-1-carboxylate (**21**)



General procedure A was applied using **13a** (0.36 mmol, 1.8 mL, 1.2 equiv), olefin **5j** (0.3 mmol, 40.3 mg, 1.0 equiv) and (*S*)-**RuL1**(CH₃CN)₄PF₆ (0.003 mmol, 1.9 mg, 0.01 equiv). **13a** was added in one portion. The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **21** as a white solid (98.1 mg, 97% yield, d.r.>20:1). Compound (*R,R*)-**21** was obtained with a 96.2:3.8 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 13.2 min, τ_{minor} = 11.5 min.

Appearance: white solid.

m.p.: 111.7 °C - 113.8 °C

TLC R_f = 0.33 (petroleum ether/ EtOAc 4:1).

$[\alpha]_{20}^D = +312.8$ ($c = 1.0$, CHCl₃).

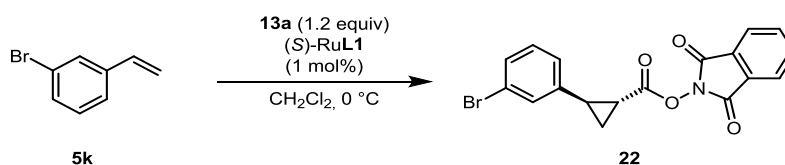
¹H NMR (400 MHz, CDCl₃) δ = 7.95 – 7.85 (m, 2H), 7.84 – 7.74 (m, 2H), 7.11 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 3.81 (s, 3H), 2.75 (ddd, $J = 9.3, 6.9, 4.1$ Hz, 1H), 2.14 (ddd,

$J = 8.3, 5.2, 4.1$ Hz, 1H), 1.79 (dt, $J = 9.3, 5.0$ Hz, 1H), 1.59 (ddd, $J = 8.4, 7.0, 4.9$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 169.9$ (C_q), 162.1 (C_q), 159.0 (C_q), 134.9 (CH), 130.6 (C_q), 129.2 (C_q), 127.8 (CH), 124.1 (CH), 114.3 (CH), 55.5 (CH_3), 28.0 (CH), 20.9 (CH), 18.3 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{19}\text{H}_{15}\text{NO}_5 + \text{Na}]^+$: 360.0842; found: 360.0839.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(3-bromophenyl)cyclopropane-1-carboxylate (22)*



General procedure A was applied using **13a** (0.36 mmol, 1.8 mL, 1.2 equiv), olefin **5k** (0.3 mmol, 54.9 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.003 mmol, 1.9 mg, 0.01 equiv). **13a** was added in one portion. The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **22** as a white solid (94.3 mg, 81% yield, d.r. >20:1). Compound (*R,R*)-**22** was obtained with a 97.3:2.7 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 14.0$ min, $\tau_{\text{minor}} = 15.0$ min.

Appearance: white solid.

m.p.: 125.1 °C - 126.9 °C

TLC $R_f = 0.25$ (petroleum ether/ EtOAc 4:1).

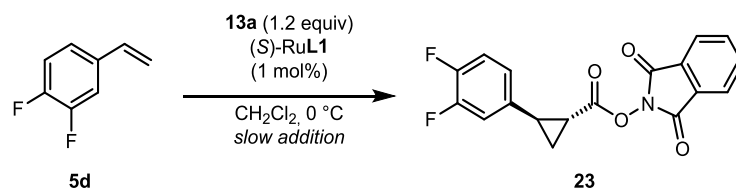
$[\alpha]_{20}^D = -248.1$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.95 - 7.85$ (m, 2H), 7.84 - 7.76 (m, 2H), 7.42 - 7.37 (m, 1H), 7.32 - 7.30 (m, 1H), 7.20 (t, $J = 7.8$ Hz, 1H), 7.14 - 7.09 (m, 1H), 2.75 (ddd, $J = 9.4, 6.8, 4.1$ Hz, 1H), 2.22 (ddd, $J = 8.5, 5.3, 4.2$ Hz, 1H), 1.84 (dt, $J = 9.3, 5.2$ Hz, 1H), 1.62 (ddd, $J = 8.5, 6.8, 5.1$ Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3) $\delta = 169.6$ (C_q), 162.0 (C_q), 141.0 (C_q), 135.0 (CH), 130.4 (CH), 130.3 (CH), 129.7 (CH), 129.1 (C_q), 125.4 (CH), 124.2 (CH), 122.9 (C_q), 27.7 (CH), 21.1 (CH), 18.4 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{18}\text{H}_{12}\text{BrNO}_4 + \text{Na}]^+$: 407.9842; found: 407.9839.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(2,3-difluorophenyl)cyclopropane-1-carboxylate (**23**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5d** (0.4 mmol, 56.1 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **23** as a white solid (126 mg, 92% yield, d.r. >20:1). Compound (*R,R*)-**23** was obtained with a 98.3:1.7 enantiomeric ratio determined by HPLC using a Chiralpak-ID column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 17.9 min, τ_{minor} = 15.1 min.

Appearance: white solid.

m.p.: 131.0 °C - 132.9 °C

TLC R_f = 0.37 (petroleum ether/ EtOAc 4:1).

$[\alpha]_{20}^D$ = -242.3 (c = 1.0, CHCl₃).

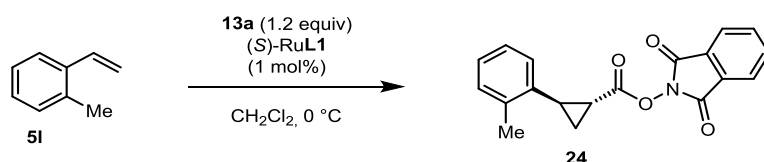
¹H NMR (400 MHz, CDCl₃) δ = 7.94 – 7.86 (m, 2H), 7.84 – 7.76 (m, 2H), 7.12 (dt, J = 10.1, 8.3 Hz, 1H), 7.02 – 6.89 (m, 2H), 2.74 (ddd, J = 9.4, 6.8, 4.1 Hz, 1H), 2.18 (ddd, J = 8.5, 5.3, 4.2 Hz, 1H), 1.83 (dt, J = 9.3, 5.2 Hz, 1H), 1.58 (ddd, J = 9.3, 5.2 Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 169.3 (C_q), 161.2 (C_q), 150.4 (dd, J = 248.8, 12.8 Hz, C_F), 149.3 (dd, J = 247.9, 12.6 Hz, C_F), 135.5 (dd, J = 5.8, 3.7 Hz, C_q), 134.8 (CH), 128.9 (C_q), 124.0 (CH), 122.7 (dd, J = 6.3, 3.6 Hz, CH), 117.5 (d, J = 17.4 Hz, CH), 115.5 (d, J = 17.7 Hz, CH), 27.2 (CH), 20.9 (CH), 18.2 (CH₂) ppm.

¹⁹F NMR (377 MHz, CDCl₃) δ = -137.1 (d, $^3J_{\text{FF}}$ = 21.1 Hz), -139.7 (d, $^3J_{\text{FF}}$ = 21.3 Hz).

HRMS (ESI-TOF) calc'd for [C₁₈H₁₁F₂NO₄+Na]⁺: 366.0548; found: 366.0550.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(*o*-tolyl)cyclopropane-1-carboxylate (**24**)



General procedure A was applied using **13a** (0.36 mmol, 1.8 mL, 1.2 equiv), olefin **5l** (0.3 mmol, 35.5 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.003 mmol, 1.9 mg, 0.01 equiv). **13a** was added in one portion. The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **24** as a white solid (96 mg, 99% yield,

d.r.>20:1). Compound (*R,R*)-**24** was obtained with a 97.4:2.6 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 11.6$ min, $\tau_{\text{minor}} = 10.7$ min.

Appearance: white solid.

m.p.: 140.5 °C - 142.3 °C.

TLC $R_f = 0.34$ (petroleum ether/ EtOAc 4:1).

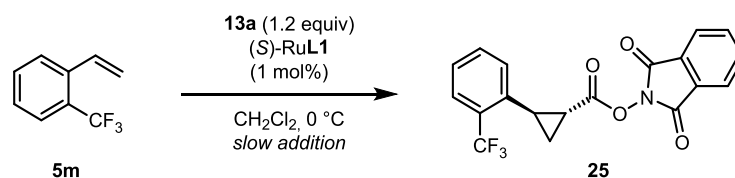
$[\alpha]_{20}^D = -239.3$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.95 - 7.85$ (m, 2H), 7.84 – 7.76 (m, 2H), 7.24 – 7.10 (m, 3H), 7.06 (dd, $J = 7.0, 1.7$ Hz, 1H), 2.77 (ddd, $J = 9.2, 7.2, 4.4$ Hz, 1H), 2.49 (s, 3H), 2.05 (ddd, $J = 8.3, 5.1, 4.4$ Hz, 1H), 1.83 (dt, $J = 9.2, 4.9$ Hz, 1H), 1.70 (ddd, $J = 8.2, 7.2, 4.8$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 170.3$ (C_q), 162.2 (C_q), 138.7 (C_q), 136.5 (C_q), 134.9 (CH), 130.3 (CH), 129.1 (C_q), 127.5 (CH), 126.2 (CH), 126.1 (CH), 124.1 (CH), 27.5 (CH), 19.7 (CH_3), 19.7 (CH), 16.5 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{19}\text{H}_{15}\text{NO}_4 + \text{Na}]^+$: 344.0893; found: 344.0892.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(2-(trifluoromethyl)phenyl)cyclopropane-1-carboxylate (25)*



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5m** (0.4 mmol, 60.3 mg, 1.0 equiv) and (*S*)-**RuL1**(CH_3CN) $_4\text{PF}_6$ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **25** as a white solid (115.2 mg, 88% yield, d.r. 8:1). Compound (*R,R*)-**25** was obtained with a 98.0:2.0 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 11.8$ min, $\tau_{\text{minor}} = 11.1$ min.

Appearance: white solid.

m.p.: 112.8 °C - 115.2 °C.

TLC $R_f = 0.22$ (petroleum ether/ EtOAc 4:1).

$[\alpha]_{20}^D = -205.4$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.98 - 7.88$ (m, 2H), 7.86 – 7.78 (m, 2H), 7.75 – 7.69 (m, 1H), 7.54 (t, $J = 7.7$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 1H), 7.25 (d, $J = 7.8$ Hz, 1H), 3.11 (d, $J =$

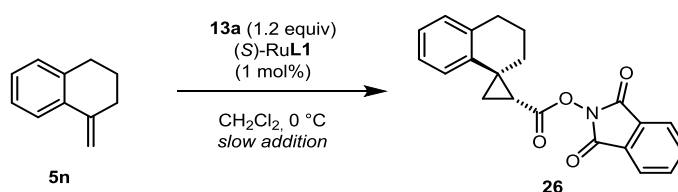
10.5 Hz, 1H), 2.27 (dt, $J = 8.7, 4.9$ Hz, 1H), 1.90 (dt, $J = 9.4, 5.2$ Hz, 1H), 1.77 – 1.69 (m, 1H) ppm.

^{13}C NMR (100 MHz, CDCl_3) $\delta = 169.5$ (C_q), 161.9 (C_q), 136.5 (q, $J = 1.6$ Hz, C_q), 134.9 (CH), 132.2 (CH), 130.46 (q, $J = 30.5$ Hz, C_q), 129.1 (C_q), 127.5 (CH), 127.4 (CH), 126.45 (q, $J = 5.7$ Hz, CH), 124.40 (q, $J = 273.9$ Hz, C_q), 124.1 (CH), 25.30 (q, $J = 2.2$ Hz, CH), 20.49 (d, $J = 0.9$ Hz, CH), 17.1 (CH).

^{19}F NMR (377 MHz, CDCl_3) $\delta = -60.32$ (major), -60.63 (minor).

HRMS (ESI-TOF) calc'd for $[\text{C}_{19}\text{H}_{12}\text{F}_3\text{NO}_4 + \text{Na}]^+$: 398.0611; found: 398.0612.

Synthesis of tetrahydronaphthalene **26**



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5n**^[12] (0.4 mmol, 57.7 mg, 1.0 equiv) and **(S)-RuL1**(CH_3CN)₄ PF_6 (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 9:1), affording pure **26** as a white solid (139 mg, 99%, d.r. 6:1). Additionally, compound **26** can be obtained as a single diastereoisomer by column chromatography (CH_2Cl_2 /Petroleum Ether 1:1). Compound (*R,R*)-**26** was obtained with a 98.6:1.4 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 12.5$ min, $\tau_{\text{minor}} = 17.4$ min.

Appearance: white solid.

m.p.: 162.1 °C - 164.9 °C

TLC $R_f = 0.35$ (petroleum ether/ EtOAc 4:1) / $R_f = 0.58$ (CH_2Cl_2 /Petroleum Ether 3:2).

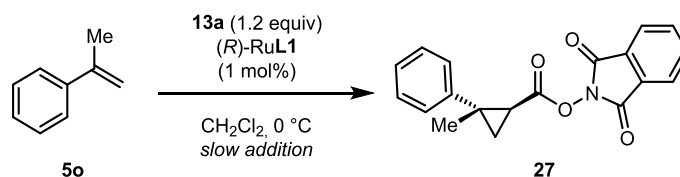
$[\alpha]_{20}^{\text{D}} = -359.9$ ($c = 1.0$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) $\delta = 7.93 - 7.83$ (m, 2H), 7.82 – 7.75 (m, 2H), 7.19 – 7.09 (m, 3H), 6.82 – 6.77 (m, 1H), 3.02 – 2.79 (m, 2H), 2.28 (dd, $J = 8.2, 6.5$ Hz, 1H), 2.13 – 1.89 (m, 5H), 1.71 (dd, $J = 6.5, 5.5$ Hz, 1H) ppm.

^{13}C NMR (126 MHz, CDCl_3) $\delta = 167.7$ (C_q), 162.2 (C_q), 138.5 (C_q), 138.0 (C_q), 134.8 (CH), 129.4 (CH), 129.1 (C_q), 126.58 (CH), 126.55 (CH), 124.0 (CH), 121.8 (CH), 32.3 (C_q), 30.4 (CH_2), 28.9 (CH), 27.7 (CH_2), 23.7 (CH_2), 21.9 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{21}\text{H}_{17}\text{NO}_4 + \text{Na}]^+$: 370.1055; found: 370.1038.

Synthesis of 1,3-dioxoisindolin-2-yl (1*S*,2*S*)-2-methyl-2-phenylcyclopropane-1-carboxylate (**27**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5o** (0.4 mmol, 43.7 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **27** as a white solid (125 mg, 97% yield, d.r. 11:1). Compound (*S,S*)-**27** was obtained with a 99.4:0.6 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 12.4 min, τ_{minor} = 11.1 min.

Appearance: white solid.

m.p.: 100.5 °C - 102.4 °C

TLC R_f = 0.37 (petroleum ether/ EtOAc 4:1).

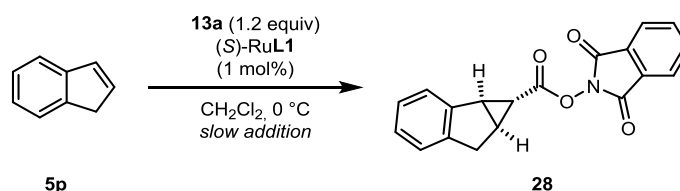
$[\alpha]_{20}^D$ = -275.1 (c = 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.96 – 7.87 (m, 2H), 7.84 – 7.76 (m, 2H), 7.41 – 7.33 (m, 4H), 7.30 – 7.23 (m, 1H), 2.30 (dd, J = 8.3, 5.9 Hz, 1H), 1.74 (dd, J = 8.3, 5.0 Hz, 1H), 1.65 – 1.60 (m, 4H) ppm.

¹³C NMR (101 MHz, CDCl₃): δ = 168.7 (C_q), 162.3 (C_q), 144.6 (C_q), 134.9 (CH), 129.1 (C_q), 128.8 (CH), 127.5 (CH), 127.2 (CH), 124.1 (CH), 33.6 (C_q), 24.7 (CH), 22.6 (CH₂), 20.2 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₁₉H₁₅NO₄+Na]⁺: 344.0893; found: 344.0894.

Synthesis of indene derivative **28**



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5p** (0.4 mmol, 33.7 mg, 1.0 equiv) and (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **28** as a white solid (116.4 mg, 91% yield, d.r. 12:1). Compound (*R,R,S*)-**28** was obtained with a 91.8:8.2 enantiomeric ratio determined by SFC using a LUX A1 column [10% EtOH in CO₂, 120 bar, 3.5 mL/min]: τ_{major} = 3.9 min, τ_{minor} = 3.5 min.

Appearance: white solid.

m.p.: 159.1 °C - 162.2 °C

TLC R_f = 0.55 (petroleum ether/ EtOAc 4:1).

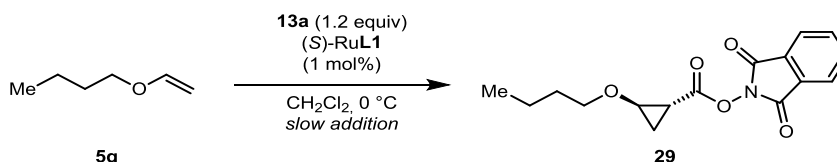
$[\alpha]_{20}^D = -169.75$ ($c = 0.77$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.96 – 7.86 (m, 2H), 7.85 – 7.75 (m, 2H), 7.48 – 7.43 (m, 1H), 7.24 – 7.17 (m, 3H), 3.37 (dd, $J = 17.8, 6.2$ Hz, 1H), 3.26 – 3.14 (m, 2H), 2.70 (td, $J = 6.1, 3.2$ Hz, 1H), 1.53 (t, $J = 2.8$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 168.9 (C_q), 162.2 (C_q), 142.5 (C_q), 141.5 (C_q), 134.9 (CH), 129.1 (C_q), 127.2 (CH), 126.8 (CH), 125.5 (CH), 124.6 (CH), 124.1 (CH), 36.4 (CH), 35.6 (CH_2), 28.8 (CH), 27.4 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{19}\text{H}_{13}\text{NO}_4 + \text{Na}]^+$: 342.0737; found: 342.0734.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-butoxycyclopropane-1-carboxylate (29)*



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5q** (0.4 mmol, 40.1 mg, 1.0 equiv) and (S)-RuL1(CH₃CN)₄PF₆ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/ EtOAc 4:1), affording pure **29** as a white solid (119 mg, 98% yield, d.r. 9:1). Compound (*R,R*)-**29** was obtained with a 97.3:2.7 enantiomeric ratio determined by HPLC using a Chiralpak-ID column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 14.0$ min, $\tau_{\text{minor}} = 12.4$ min.

Appearance: white solid.

m.p.: 63.5 °C - 64.8 °C

TLC R_f = 0.41 (petroleum ether/ EtOAc 4:1).

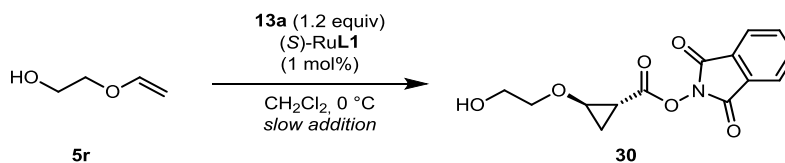
$[\alpha]_{20}^D = -98.9$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.92 – 7.84 (m, 2H), 7.81 – 7.74 (m, 2H), 3.79 (ddd, $J = 6.7, 4.7, 2.0$ Hz, 1H), 3.65 (tt, $J = 6.6, 3.2$ Hz, 2H), 2.07 (ddd, $J = 9.4, 6.1, 1.9$ Hz, 2H), 1.67 – 1.48 (m, 5H), 1.39 (ddt, $J = 14.5, 9.6, 7.3$ Hz, 2H), 0.94 (t, $J = 7.4$ Hz, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 169.0 (C_q), 162.1 (C_q), 134.9 (CH), 129.1 (C_q), 124.1 (CH), 71.7 (CH), 62.7 (CH_2), 31.5 (CH), 19.4 (CH_2), 18.6 (CH_2), 17.6 (CH_2), 14.0 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{16}\text{H}_{17}\text{NO}_5 + \text{Na}]^+$: 326.0999; found: 326.0995.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(2-hydroxyethoxy)cyclopropane-1-carboxylate (**30**)



General procedure A was applied using **13a** (0.36 mmol, 1.2 mL, 1.2 equiv), olefin **5r** (0.3 mmol, 26.4 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.003 mmol, 1.9 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (EtOAc/petroleum ether 1:1), affording pure **30** as a white wax (86 mg, 99% yield, d.r. 7:1). Compound (*R,R*)-**30** was obtained with a 95.1:4.9 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 13.3 min, τ_{minor} = 11.1 min.

Appearance: white wax.

TLC R_f = 0.28 (EtOAc/petroleum ether 1:1).

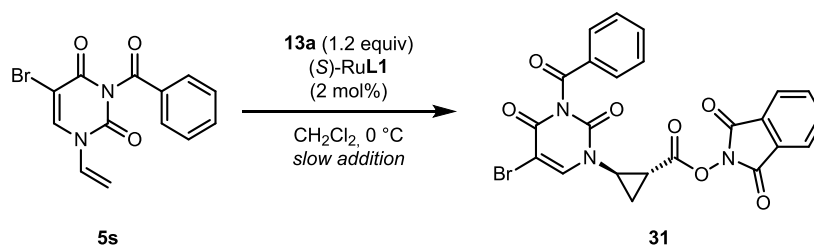
$[\alpha]_{20}^D$ = -63.4 (c = 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.92 – 7.82 (m, 2H), 7.81 – 7.75 (m, 2H), 3.87 (ddd, J = 6.6, 4.6, 2.0 Hz, 1H), 3.84 – 3.68 (m, 4H), 2.13 (ddd, J = 9.5, 6.2, 2.0 Hz, 1H), 1.99 (bs, 1H), 1.63 – 1.50 (m, 2H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 168.8 (C_q), 162.1 (C_q), 134.9 (CH), 129.0 (C_q), 124.1 (CH), 72.8 (CH₂), 62.8 (CH), 61.6 (CH₂), 18.6 (CH), 17.6 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₄H₁₃NO₆+Na]⁺: 314.0635; found: 314.0628.

Synthesis of uracil derivative **31**



General procedure B was applied using **13a** (0.36 mmol, 1.2 mL, 1.2 equiv), olefin **5s** (0.3 mmol, 96.0 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.006 mmol, 3.8 mg, 0.02 equiv). The crude product was purified by silica gel chromatography (EtOAc/petroleum ether 1:1), affording pure **31** as a white solid (116 mg, 74% yield, d.r. >20:1). Compound (*R,S,R*)-**31** was obtained with a 99.0:1.0 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (40:60), 1.0 mL/min]: τ_{major} = 21.4 min, τ_{minor} = 19.9 min.

Appearance: white solid.

m.p.: 132.3 °C - 134.9 °C.

TLC R_f = 0.10 (petroleum ether/EtOAc 7:3)

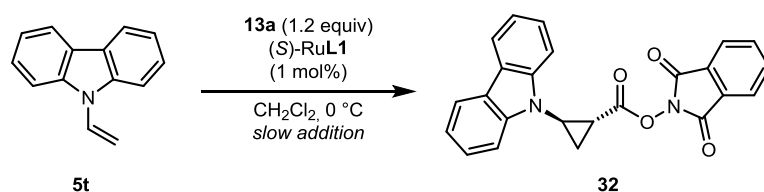
$[\alpha]_{20}^D = -156.5$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.92 (d, $J = 7.1$, 2H), 7.90 – 7.86 (m, 2H), 7.83 – 7.77 (m, 2H), 7.70 (s, 1H), 7.69 – 7.63 (m, 1H), 7.56 – 7.47 (m, 2H), 3.75 (ddd, $J = 8.0$, 5.3, 3.0 Hz, 1H), 2.53 (ddd, $J = 9.5$, 6.2, 3.0 Hz, 1H), 1.93 (dt, $J = 7.8$, 6.4 Hz, 1H), 1.84 (ddd, $J = 9.7$, 6.6, 5.3 Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 167.6 (C_q), 167.3 (C_q), 161.7 (C_q), 158.0 (C_q), 149.3 (C_q), 142.7 (CH), 135.6 (CH), 135.1 (CH), 131.0 (C_q), 130.8 (CH), 129.4 (CH), 128.8 (C_q), 124.3 (CH), 97.1 (C_q), 39.4 (CH), 19.7 (CH), 17.1 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{23}\text{H}_{14}\text{BrN}_3\text{O}_7 + \text{Na}]^+$: 545.9907; found: 545.9912.

Synthesis of 1,3-dioxoisindolin-2-yl (1R,2R)-2-(9H-carbazol-9-yl)cyclopropane-1-carboxylate (32)



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5t** (0.4 mmol, 77 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 30 minutes at 0 °C. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 9:1 to 3:1), affording pure **32** as a pale yellow solid (125 mg, 79% yield, d.r. >20:1). Compound (*R,R*)-**32** was obtained with a 98.4:1.6 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 15.1$ min, $\tau_{\text{minor}} = 12.1$ min.

Appearance: pale yellow solid.

m.p.: 198 °C (decomp.)

TLC R_f = 0.38 (petroleum ether/EtOAc 4:1)

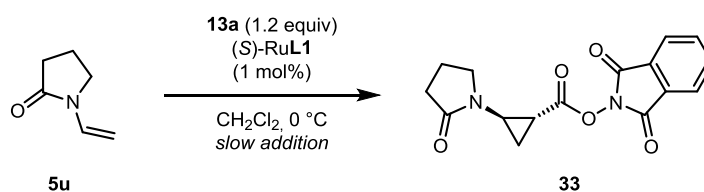
$[\alpha]_{20}^D = -350.2$ ($c = 0.69$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ = 8.08 (dt, $J = 7.8$, 0.9 Hz, 2H), 7.97 – 7.92 (m, 2H), 7.86 – 7.80 (m, 2H), 7.68 (dd, $J = 8.2$, 0.8 Hz, 2H), 7.54 (ddd, $J = 8.3$, 7.2, 1.2 Hz, 2H), 7.33 – 7.27 (m, 2H), 3.99 (ddd, $J = 7.7$, 5.3, 2.8 Hz, 1H), 2.57 (ddd, $J = 9.0$, 6.0, 2.7 Hz, 1H), 2.25 (dt, $J = 7.4$, 5.7 Hz, 1H), 2.11 (dt, $J = 9.2$, 5.5 Hz, 1H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 168.6 (C_q), 161.8 (C_q), 140.6 (C_q), 134.9 (CH), 128.9 (C_q), 126.25 (CH), 124.1 (CH), 123.3 (C_q), 120.4 (CH), 120.1 (CH), 109.8 (CH), 34.8 (CH), 19.8 (CH), 17.6 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₂₄H₁₆N₂O₄+Na]⁺ 419.1002; found 419.1008.

Synthesis of 1,3-dioxoisindolin-2-yl (1R)-2-(2-oxopyrrolidin-1-yl)cyclopropane-1-carboxylate (33)



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5u** (0.4 mmol, 44.5 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 30 minutes at 0 °C. The crude cyclopropyl redox-active ester **33** was obtained as a mixture of diastereoisomers (d.r. 1.7:1). This mixture was purified by column chromatography on silica gel (EtOAc/petroleum ether 6:1), allowing for the separation of both diastereoisomers. Fast eluting *trans*-**33a** was obtained in 60% yield (76.2 mg, d.r. >20:1) and slow eluting *cis*-**33b** was obtained in 36% yield (44.8 mg, >20:1 dr). Compound (*R,R*)-**33a** was obtained with a 98.5:1.5 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (70:30), 1.0 mL/min]: τ_{major} = 19.2 min, τ_{minor} = 14.8 min.

Appearance: white solid.

m.p.: 115.9 °C - 117.3 °C.

TLC R_f = 0.43 (EtOAc)

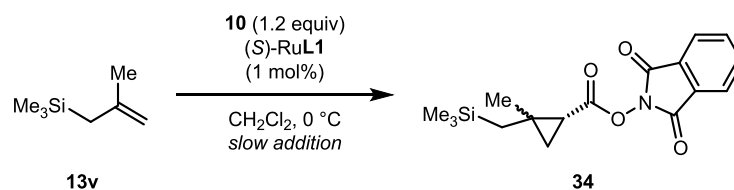
[α]₂₀^D = -126.4 (*c* = 0.5, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ = (for major diast **33a**) 7.92 – 7.85 (m, 2H), 7.81 – 7.76 (m, 2H), 3.46 – 3.33 (m, 3H), 2.42 (t, *J* = 7.8 Hz, 2H), 2.20 (ddd, *J* = 9.1, 5.8, 3.1 Hz, 1H), 2.12 – 1.98 (m, 2H), 1.89 (dt, *J* = 9.2, 5.8 Hz, 1H), 1.74 (dt, *J* = 8.2, 5.9 Hz, 1H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = (for major diast **33a**) 176.0 (C_q), 169.0 (C_q), 161.9 (C_q), 134.9 (CH), 129.0 (C_q), 124.2 (CH), 47.7 (CH₂), 36.3 (CH), 31.8 (CH₂), 18.2 (CH₂), 16.9 (CH), 16.4 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₆H₁₄N₂O₅+Na]⁺ 337.0795; found 337.0811.

Synthesis allyl silane derivative **34**



General procedure A was applied using **10** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5v** (0.4 mmol, 51.3 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **34** as a colorless oil (130.6 mg, 99% yield, d.r. 1.2:1). HPLC analysis of the mixture of the two diastereomers **34a,34b** gave the following results: compound **34a** was obtained with a 98.8:1.2 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (95:5), 1.0 mL/min]: $\tau_{\text{major}} = 8.2$ min, $\tau_{\text{minor}} = 9.1$ min. Compound **34b** was obtained with a 99.1:0.9 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (95:5), 1.0 mL/min]: $\tau_{\text{major}} = 10.6$ min, $\tau_{\text{minor}} = 11.9$ min.

Appearance: colorless oil.

TLC $R_f = 0.69$ (petroleum ether/EtOAc 4:1).

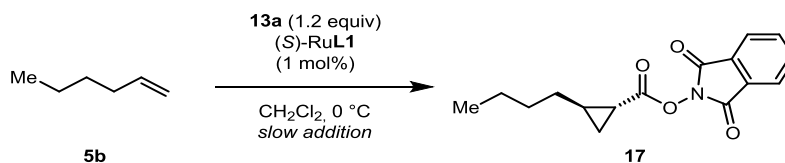
$[\alpha]_{20}^D = -138.6$ ($c = 1.0$, CHCl₃).

¹H NMR (400 MHz, CDCl₃) $\delta = 7.91 - 7.85$ (m, 2H_{34a} + 2H_{34b}), 7.81 – 7.75 (m, 2H_{34a} + 2H_{34b}), 1.83 – 1.77 (m, 1H_{34a} + 1H_{34b}), 1.31 – 1.28 (m, 3H_{34b}, 3H_{34a}), 1.26 – 1.20 (d, $J = 7.3$ Hz, 1H_{34a} + 2H_{34b}), 1.14 (dd, $J = 7.9, 4.6$ Hz, 1H_{34a}), 0.96 (s, 2H_{34b}), 0.88 (d, $J = 34.7$ Hz, 1H_{34a}), 0.84 (d, $J = 34.7$ Hz, 1H_{34a}), 0.13 (s, 9H_{34b}), 0.08 (s, 9H_{34a}) ppm.

¹³C NMR (100 MHz, CDCl₃) $\delta = 169.1$ (C_q), 169.0 (C_q), 162.4 (C_q), 134.8 (CH), 129.2 (C_q), 129.2 (C_q), 124.0 (CH), 124.0 (CH), 30.1 (CH₂), 29.5 (C_q), 28.9 (C_q), 27.1 (CH₃), 25.3 (CH₂), 25.0 (CH₂), 24.9 (CH), 24.6 (CH), 19.6 (CH₂), 19.0 (CH₃), -0.1 (CH₃), -0.2 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₁₇H₂₁NO₄Si+Na]⁺: 354.1132; found: 354.1135.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-butylcyclopropane-1-carboxylate (**17**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5b** (0.4 mmol, 33.7 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **17** as a white solid (111.8 mg, 97% yield, d.r. 7:1). Compound (*R,R*)-**17** was

obtained with a 96.7:3.3 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 12.1$ min, $\tau_{\text{minor}} = 10.2$ min.

Appearance: white solid.

m.p.: 69.1 °C - 70.4 °C.

TLC $R_f = 0.47$ (petroleum ether/EtOAc 4:1).

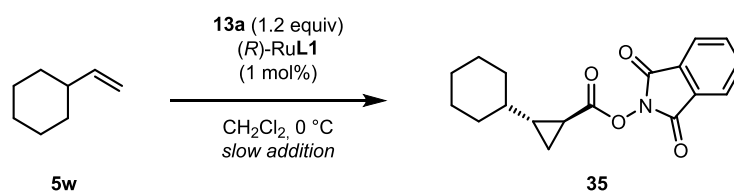
$[\alpha]_{20}^D = -98.6$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.92 - 7.85$ (m, 2H), $7.81 - 7.75$ (m, 2H), 1.70 (dt, $J = 8.3$, 4.3 Hz, 1H), $1.68 - 1.57$ (m, 1H), $1.55 - 1.23$ (m, 7H), 1.02 (ddd, $J = 8.3$, 6.8 , 4.4 Hz, 1H), 0.92 (t, $J = 7.1$ Hz, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 170.8$ (CH_q), 162.2 (CH_q), 134.8 (CH), 129.1 (C_q), 124.1 (CH), 32.7 (CH_2), 31.1 (CH_2), 25.6 (CH), 22.4 (CH_2), 17.8 (CH_2), 17.3 (CH), 14.1 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{16}\text{H}_{17}\text{NO}_4 + \text{Na}]^+$: 310.1050; found: 310.1038.

Synthesis of 1,3-dioxoisindolin-2-yl (1S,2R)-2-cyclohexylcyclopropane-1-carboxylate (35)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5w** (0.4 mmol, 44.1 mg, 1.0 equiv) and **(R)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **35** as a white solid (117 mg, 93% yield, d.r. >20:1). Compound (*S,R*)-**35** was obtained with a 98.9:1.1 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 8.4$ min, $\tau_{\text{minor}} = 10.8$ min.

Appearance: white solid.

m.p.: 140.6 °C - 142.0 °C.

TLC $R_f = 0.28$ (petroleum ether/EtOAc 4:1).

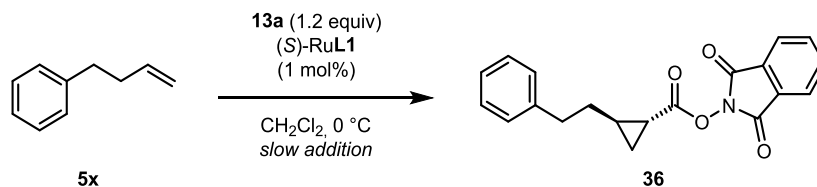
$[\alpha]_{20}^D = +114.0$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3): $\delta = 7.92 - 7.85$ (m, 2H), $7.82 - 7.75$ (m, 2H), $1.90 - 1.84$ (m, 1H), $1.79 - 1.71$ (m, 4H), $1.68 - 1.63$ (m, 1H), $1.53 - 1.46$ (m, 1H), 1.38 (app. dt, $J = 9.0$, 4.5 Hz, 1H), $1.24 - 1.10$ (m, 5H), 1.06 (ddd, $J = 8.2$, 6.8 , 4.4 Hz, 1H), $0.92 - 0.78$ (m, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.9 (C_q), 162.2 (C_q), 134.8 (CH), 129.2 (C_q), 124.0 (CH), 41.5 (CH), 32.6 (CH_2), 32.3 (CH_2), 32.0 (CH), 26.5 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 16.2 (CH_2), 16.0 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{18}\text{H}_{19}\text{NO}_4+\text{Na}]^+$: 336.1206; found: 336.1198.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-phenethylcyclopropane-1-carboxylate (**36**)*



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5x** (0.4 mmol, 52.9 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **36** as a white solid (117 mg, 87% yield, d.r. 4:1). Compound (*R,R*)-**36** was obtained with a 96.4:3.6 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 17.4 min, τ_{minor} = 15.5 min.

Appearance: white solid.

m.p.: 78.6 °C - 79.4 °C.

TLC R_f = 0.30 (petroleum ether/EtOAc 4:1).

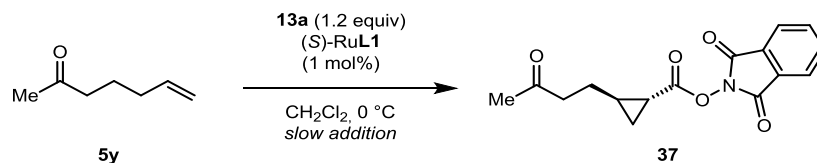
$[\alpha]_{20}^D = -91.4$ (c = 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3): δ = 7.94 – 7.84 (m, 2H), 7.82 – 7.72 (m, 2H), 7.34 – 7.27 (m, 2H), 7.25 – 7.17 (m, 3H), 2.79 (t, J = 7.3 Hz, 2H), 1.80 – 1.59 (m, 4H), 1.41 (dt, J = 8.8, 4.6 Hz, 1H), 1.01 (ddd, J = 8.2, 6.5, 4.5 Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.6 (C_q), 162.2 (C_q), 141.3 (C_q), 134.8 (CH), 129.1 (C_q), 128.7 (CH), 126.2 (CH), 124.1 (CH), 35.4 (CH_2), 35.0 (CH_2), 25.0 (CH), 17.6 (CH_2), 17.3 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{20}\text{H}_{17}\text{NO}_4+\text{Na}]^+$: 358.1050; found: 358.1042.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(3-oxobutyl)cyclopropane-1-carboxylate (**37**)*



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5y** (0.4 mmol, 52.9 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1),

affording pure **37** as a white solid (87 mg, 96% yield, d.r. 7:1). Compound (*R,R*)-**37** was obtained with a 96.5:3.5 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 22.0$ min, $\tau_{\text{minor}} = 19.6$ min.

Appearance: white solid.

m.p.: 88.8 °C - 98.8 °C.

TLC $R_f = 0.18$ (petroleum ether/EtOAc 4:1).

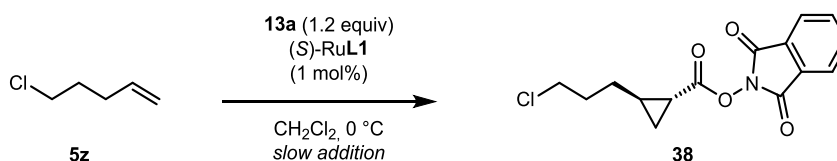
$[\alpha]_{20}^D = -60.3$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3): $\delta = 7.90 - 7.85$ (m, 2H), $7.81 - 7.75$ (m, 2H), 2.63 (t, $J = 7.1$ Hz, 2H), 2.20 (s, 3H), $1.78 - 1.53$ (m, 4H), 1.42 (dt, $J = 8.9, 4.6$ Hz, 1H), 1.06 (ddd, $J = 8.4, 6.3, 4.6$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 207.9$ (C_q), 170.4 (C_q), 162.2 (C_q), 134.9 (CH), 129.1 (C_q), 124.1 (CH), 42.7 (CH_2), 30.4 (CH_3), 26.9 (CH_2), 24.9 (CH), 17.5 (CH_2), 17.4 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{16}\text{H}_{15}\text{NO}_5 + \text{Na}]^+$: 324.0842; found: 324.0835.

*Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*R*)-2-(3-chloropropyl)cyclopropane-1-carboxylate (**38**)*



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5z** (0.4 mmol, 41.8 mg, 1.0 equiv) and (*S*)-**RuL1**(CH_3CN) $_4\text{PF}_6$ (0.004 mmol, 2.5 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 1 additional hour at 0 °C before purification. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 9:1), affording pure **38** as a white solid (101 mg, 82% yield, d.r. 7:1). Compound (*R,R*)-**38** was obtained with a 96.4:3.6 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 14.3$ min, $\tau_{\text{minor}} = 13.1$ min.

Appearance: white solid.

m.p.: 76.2 – 78.5 °C.

TLC $R_f = 0.43$ (petroleum ether/EtOAc 4:1).

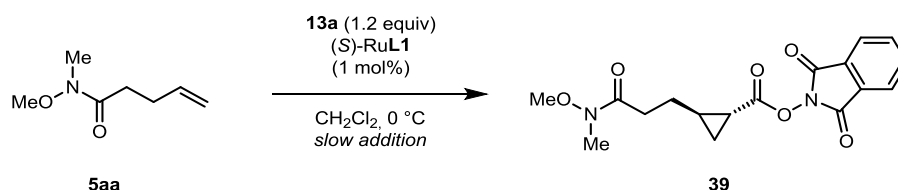
$[\alpha]_{20}^D = -92.7$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) (major diast.) $\delta = 7.91 - 7.83$ (m, 2H), $7.80 - 7.75$ (m, 2H), 3.63 (t, $J = 6.4$ Hz, 2H), $2.00 - 1.91$ (m, 2H), 1.76 (ddd, $J = 8.3, 4.7, 3.6$ Hz, 1H), $1.69 - 1.50$ (m, 3H), $1.49 - 1.39$ (m, 1H), 1.07 (ddd, $J = 8.2, 6.2, 4.4$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.5 (C_q), 162.1 (C_q), 134.9 (CH), 129.1 (C_q), 124.1 (CH), 44.4 (CH_2), 31.8 (CH_2), 29.9 (CH_2), 24.5 (CH), 17.3 (CH), 17.2 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{15}\text{H}_{14}\text{ClNO}_4+\text{Na}]^+$: 330.0504; found: 330.0510.

Synthesis of Weinreb amide derivative **39**



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5aa**^[13] (0.4 mmol, 57.3 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 4 additional hours at 0 °C before purification. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 2:1 to 1:1), affording pure **39** as a white solid (119 mg, 86% yield, d.r. 9:1). (Note: the diastomeric ratio was determined using HPLC analysis due to the broad ^1H -NMR signals produced by rotameric equilibria). Compound (*R,R*)-**39** was obtained with a 95.5:4.5 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 12.9 min, τ_{minor} = 12.1 min.

Appearance: white solid.

m.p.: 76.2 – 77.9 °C.

TLC R_f = 0.29 (EtOAc/petroleum ether 1:1).

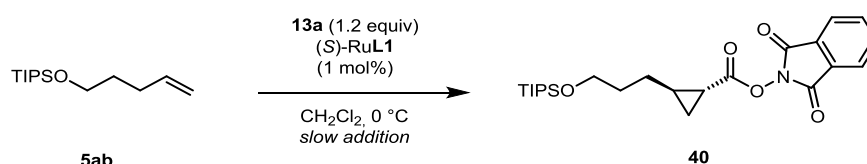
$[\alpha]_{20}^D$ = –91.4 (c = 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.88 – 7.81 (m, 2H), 7.79 – 7.73 (m, 2H), 3.75 – 3.62 (m, 3H), 3.23 – 3.14 (m, 3H), 2.66 – 2.52 (m, 2H), 1.85 – 1.56 (m, 4H), 1.45 – 1.32 (m, 1H), 1.13 – 1.01 (m, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 173.5 (C_q), 170.5 (C_q), 162.1 (C_q), 134.8 (CH), 129.1 (C_q), 124.0 (CH), 61.5 (CH_3), 32.3 (CH_3), 31.1 (CH_2), 28.0 (CH_2), 24.9 (CH), 17.6 (CH_2), 17.3 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_6+\text{Na}]^+$: 369.1057; found: 369.1063.

Synthesis of protected alcohol **40**



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5ab**^[14] (0.4 mmol, 97.0 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.004 mmol, 2.5 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 1 additional hour at 0 °C before purification. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 9:1), affording pure **40** as a colorless oil (160 mg, 90% yield, d.r. >15:1). Compound (*R,R*)-**40** was obtained with a 96.8:3.2 enantiomeric ratio determined by HPLC using Chiralpak-IF column [*i*-hexane/*i*-PrOH (98:2), 1.0 mL/min]: $\tau_{\text{major}} = 13.6$ min, $\tau_{\text{minor}} = 15.8$ min.

Appearance: colorless oil.

TLC $R_f = 0.61$ (petroleum ether/EtOAc 4:1).

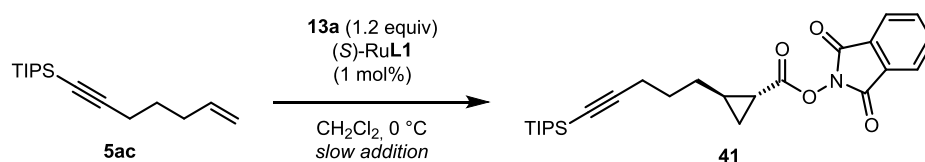
$[\alpha]_{20}^D = -68.7$ ($c = 1.0$, CHCl₃).

¹H NMR (400 MHz, CDCl₃) $\delta = 7.89 - 7.83$ (m, 2H), 7.79 – 7.73 (m, 2H), 3.74 (t, $J = 6.0$ Hz, 2H), 1.76 – 1.55 (m, 5H), 1.46 – 1.38 (m, 2H), 1.13 – 0.97 (m, 22H) ppm.

¹³C NMR (101 MHz, CDCl₃) $\delta = 170.7$ (C_q), 162.2 (C_q), 134.8 (CH), 129.1 (C_q), 124.0 (CH), 62.6 (CH₂), 32.2 (CH₂), 29.3 (CH₂), 25.3 (CH), 18.2 (CH₃), 17.7 (CH₂), 17.3 (CH), 12.1 (CH) ppm.

HRMS (ESI-TOF) calc'd for [C₂₄H₃₅NSiO₅+Na]⁺: 468.2177; found: 458.2175.

Synthesis of alkyne **41**



General procedure B was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5ac** (0.4 mmol, 100 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.008 mmol, 5 mg, 0.02 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 5:1), affording pure **41** as a white solid (161 mg, 89% yield, d.r. 6:1). Compound (*R,R*)-**41** was obtained with a 96.9:3.1 enantiomeric ratio determined by HPLC using Chiralpak-IF column [*i*-hexane/*i*-PrOH (95:5), 1.0 mL/min]: $\tau_{\text{major}} = 9.2$ min, $\tau_{\text{minor}} = 10.0$ min. Compound (*R,R*)-**41** was obtained as a single diastereoisomer by semi-preparative HPLC purification using a Pursuit XRs 10-Si column [*i*-hexane/MTBE (85:15), 9.0 mL/min].

Appearance: White solid.

m.p.: 65.3 °C - 67.1 °C.

TLC $R_f = 0.65$ (petroleum ether/EtOAc 5:1).

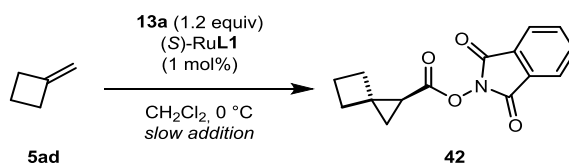
$[\alpha]_{20}^D = -64.2$ ($c = 1.0$, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.93 – 7.84 (m, 2H), 7.82 – 7.75 (m, 2H), 2.36 (t, J = 6.6 Hz, 2H), 1.78 – 1.58 (m, 6H), 1.53 – 1.38 (m, 2H), 1.13 – 0.98 (m, 21H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 170.7 (C_q), 162.2 (C_q), 134.8 (CH), 129.1 (C_q), 124.1 (CH), 108.4 (C_q), 81.1 (C_q), 31.7 (CH₂), 28.1 (CH₂), 24.9 (CH), 19.5 (CH₂), 18.8 (CH₃), 17.6 (CH), 17.2 (CH₂), 11.4 (CH) ppm.

HRMS (ESI-TOF) calc'd for [C₂₆H₃₅NO₄Si+Na]⁺: 476.2235; found: 476.2235.

Synthesis of 1,3-dioxoisindolin-2-yl (S)-spiro[2.3]hexane-1-carboxylate (42)



General procedure A was applied using **13a** (0.36 mmol, 1.2 mL, 1.2 equiv), olefin **5ad** (0.3 mmol, 20.4 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.003 mmol, 1.9 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **42** as a colorless oil (79.6 mg, 98% yield). Compound (S)-**42** was obtained with a 99.3:0.7 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 10.0 min, τ_{minor} = 8.8 min.

Appearance: colorless oil.

TLC R_f = 0.38 (petroleum ether/EtOAc 4:1).

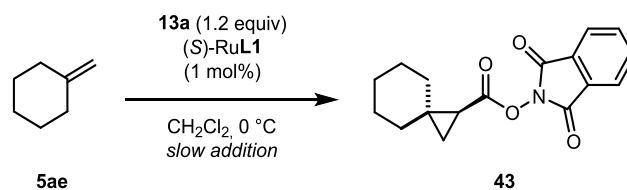
$[\alpha]_{20}^D$ = -140.9 (c = 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.92 – 7.85 (m, 2H), 7.82 – 7.75 (m, 2H), 2.47 – 2.34 (m, 2H), 2.23 – 2.05 (m, 4H), 1.93 (dd, J = 8.4, 5.3 Hz, 1H), 1.40 (t, J = 5.1 Hz, 1H), 1.33 (dd, J = 8.4, 5.0 Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 168.9 (C_q), 162.4 (C_q), 134.8 (CH), 129.2 (C_q), 124.1 (CH), 33.2 (C_q), 30.3 (CH₂), 27.5 (CH₂), 23.0 (CH₂), 22.1 (CH), 16.6 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₅H₁₃NO₄+Na]⁺: 294.0737; found: 294.0741.

Synthesis of 1,3-dioxoisindolin-2-yl (S)-spiro[2.5]octane-1-carboxylate (43)



General procedure A was applied using **13a** (0.36 mmol, 1.2 mL, 1.2 equiv), olefin **5ae** (0.3 mmol, 28.9 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.003 mmol, 1.9 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1),

affording pure **43** as a colourless oil (89.7 mg, 99% yield). Compound (S)-**43** was obtained with a 99.1:0.9 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 12.3$ min, $\tau_{\text{minor}} = 10.6$ min.

Appearance: colourless oil.

TLC $R_f = 0.56$ (petroleum ether/EtOAc 4:1).

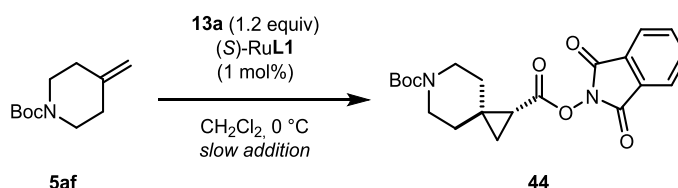
$[\alpha]_{20}^D = -165.9$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.93 - 7.85$ (m, 2H), $7.82 - 7.74$ (m, 2H), 1.79 (dd, $J = 7.8$, 5.4 Hz, 1H), $1.71 - 1.51$ (m, 8H), $1.52 - 1.41$ (m, 1H), $1.41 - 1.32$ (m, 1H), 1.28 (t, $J = 5.0$ Hz, 1H), 1.15 (dd, $J = 7.8$, 4.6 Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 169.0$ (C_q), 162.4 (C_q), 134.8 (CH), 129.2 (C_q), 124.0 (CH), 37.3 (CH_2), 34.2 (C_q), 28.9 (CH_2), 26.1 (CH_2), 25.8 (CH_2), 25.4 (CH_2), 23.1 (CH_2), 22.8 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{17}\text{H}_{17}\text{NO}_4 + \text{Na}]^+$: 322.1050; found: 322.1048.

Synthesis of 6-(tert-butyl) 1-(1,3-dioxoisindolin-2-yl) (S)-6-azaspiro[2.5]octane-1,6-dicarboxylate (44)



General procedure A was applied using **13a** (0.45 mmol, 2.25 mL, 1.2 equiv), olefin **5af**^[15] (0.375 mmol, 74 mg, 1.0 equiv) and (S)-**RuL1**(CH_3CN)₄**PF**₆ (0.00375 mmol, 2.4 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 7:3), affording pure **44** as a white solid (132.5 mg, 88% yield). Compound (S)-**44** was obtained with a 98.0:2.0 enantiomeric ratio determined by HPLC using Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 7.6$ min, $\tau_{\text{minor}} = 8.1$ min.

Appearance: white solid.

m.p.: 78.2 °C - 81.1 °C.

TLC $R_f = 0.21$ (petroleum ether/EtOAc 7:3).

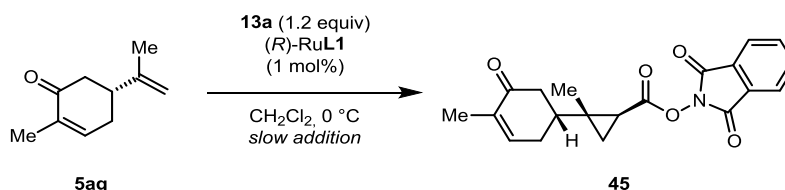
$[\alpha]_{20}^D = -137.6$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.93 - 7.85$ (m, 2H), $7.83 - 7.75$ (m, 2H), $3.77 - 3.53$ (m, 2H), $3.47 - 3.34$ (m, 2H), 1.91 (dd, $J = 8.0$, 5.4 Hz, 1H), $1.78 - 1.56$ (m, 2H), $1.52 - 1.20$ (m, 13H).

^{13}C NMR (101 MHz, CDCl_3) δ = 168.6 (C_q), 162.2 (C_q), 154.9 (C_q), 134.9 (CH), 129.2 (C_q), 124.1 (CH), 79.7 (C_q), 43.4 (CH_2), 36.2 (CH_2), 31.8 (C_q), 28.6 (CH_3), 22.2 (CH_2), 21.8 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_6+\text{Na}]^+$: 423.1527; found: 423.1529.

Synthesis of (*R*)-carvone derivative (**45**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5ag** (0.4 mmol, 601 mg, 1.0 equiv) and (*R*)-**RuL1**(CH_3CN) $_4\text{PF}_6$ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 2:1), affording pure (+)-**45** as a white solid (138 mg, 97% yield, d.r. >16:1).

Appearance: white solid.

m.p.: 76.2 °C - 78.3 °C.

TLC R_f = 0.16 (petroleum ether/EtOAc 4:1).

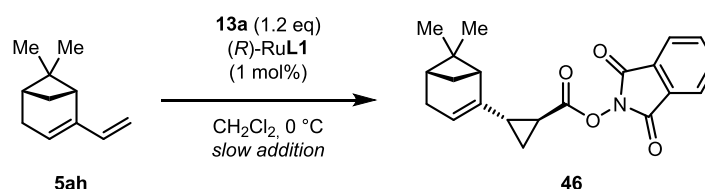
$[\alpha]_{20}^D$ = +196.4 (c = 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.90 – 7.84 (m, 2H), 7.81 – 7.74 (m, 2H), 6.77 (tt, J = 3.2, 1.5 Hz, 1H), 2.55 – 2.37 (m, 4H), 1.86 (dd, J = 8.2, 5.5 Hz, 1H), 1.77 (d, J = 1.8 Hz, 3H), 1.51 (dddd, J = 13.4, 9.2, 6.4, 4.3 Hz, 1H), 1.30 (t, J = 5.3 Hz, 1H), 1.22 (s, 3H), 1.18 (dd, J = 8.2, 5.0 Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 199.2 (C_q), 168.3 (C_q), 162.2 (C_q), 144.5 (CH), 135.8 (C_q), 134.9 (CH), 129.0 (C_q), 124.1 (CH), 45.7 (CH), 41.7 (CH_2), 32.0 (C_q), 29.3 (CH_2), 23.0 (CH), 22.3 (CH_2), 15.8 (CH_3), 12.6 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{20}\text{H}_{19}\text{NO}_5+\text{Na}]^+$: 376.1155; found: 376.1154.

Synthesis of nopadiene derivative (**46**)



General procedure A was applied using **13a** (0.178 mmol, 0.6 mL, 1.2 equiv), olefin **5ah**^[16] (0.148 mmol, 22 mg, 1.0 equiv) and (*R*)-**RuL1**(CH_3CN) $_4\text{PF}_6$ (0.0015 mmol, 0.95 mg, 0.01

equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure (+)-**46** as a colorless oil (48 mg, 92% yield, d.r. >20:1).

Appearance: colorless oil.

TLC R_f = 0.56 (petroleum ether/EtOAc 4:1).

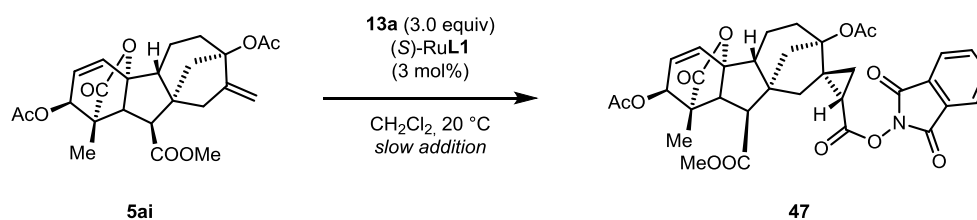
$[\alpha]_{20}^D$ = +98.0 (c = 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.91 – 7.86 (m, 2H), 7.81 – 7.75 (m, 2H), 5.47 – 5.41 (m, 1H), 2.39 (dt, J = 8.7, 5.6 Hz, 1H), 2.35 – 2.16 (m, 2H), 2.14 – 2.08 (m, 1H), 1.95 – 1.84 (m, 2H), 1.47 (dt, J = 9.2, 4.8 Hz, 1H), 1.34 – 1.23 (m, 5H), 1.20 (d, J = 8.7 Hz, 1H), 0.81 (s, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.4 (C_q), 162.2 (C_q), 144.4 (C_q), 134.8 (CH), 129.1 (C_q), 124.1 (CH), 119.5 (CH), 43.2 (CH), 41.0 (CH), 38.0 (C_q), 31.5 (CH_2), 31.4 (CH_2), 29.6 (CH), 26.3 (CH_3), 21.3 (CH_3), 16.5 (CH), 14.8 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{21}\text{H}_{21}\text{NO}_4 + \text{Na}]^+$: 374.1363; found: 374.1364.

Synthesis of gibberellic acid derivative (**47**)



General procedure C was applied using **13a** (1.6 mmol, 6.0 mL, 3.0 equiv), olefin **5ai**^[17] (0.40 mmol, 178 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.012 mmol, 7.6 mg, 0.03 equiv). After the addition, the mixture was allowed to react for 6 additional hour at 20 °C. The crude product was purified by silica gel chromatography (EtOAc/petroleum ether 3:7 to 1:1), affording pure (+)-**47** as a white solid (215 mg, 83% yield, d.r. 8.5:1).

Appearance: white solid.

m.p.: 144.8 – 146.2 °C.

TLC R_f = 0.33 (EtOAc/petroleum ether 1:1).

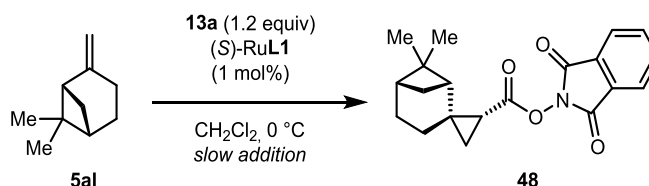
$[\alpha]_{20}^D$ = +48.0 (c = 1.0, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ = 7.90 – 7.82 (m, 2H), 7.81 – 7.75 (m, 2H), 6.39 (d, J = 9.3 Hz, 1H), 5.87 (dd, J = 9.3, 3.8 Hz, 1H), 5.32 (d, J = 3.8 Hz, 1H), 3.83 (s, 3H), 3.34 (d, J = 11.1 Hz, 1H), 2.81 (d, J = 11.1 Hz, 1H), 2.75 (dd, J = 11.2, 2.5 Hz, 1H), 2.49 (dd, J = 9.1, 5.6 Hz, 1H), 2.28 – 2.20 (m, 1H), 2.10 – 2.02 (m, 9H), 1.91 – 1.83 (m, 1H), 1.81 (d, J = 13.2 Hz, 1H), 1.75 (dddd, J = 11.6, 6.5, 5.1, 2.4 Hz, 1H), 1.57 (dd, J = 9.1, 5.0 Hz, 1H), 1.50 (dd, J = 13.2, 2.4 Hz, 1H), 1.38 (t, J = 5.3 Hz, 1H), 1.14 (s, 3H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 177.1 (C_q), 172.0 (C_q), 170.2 (C_q), 169.5 (C_q), 168.3 (C_q), 162.0 (C_q), 134.9 (CH), 134.3 (CH), 129.3 (CH), 129.0 (C_q), 124.1 (CH), 90.0 (C_q), 82.5 (C_q), 70.3 (CH), 53.3 (CH), 52.7 (CH_3), 52.3 (C_q), 51.9 (CH), 51.2 (C_q), 51.0 (CH), 42.2 (CH_2), 41.6 (C_q), 41.4 (CH_2), 33.1 (CH_2), 21.9 (CH_3), 21.8 (CH), 20.9 (CH_3), 19.9 (CH_2), 17.4 (CH_2), 14.5 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{34}\text{H}_{33}\text{NO}_{12}+\text{Na}]^+$: 670.1895; found: 670.1921.

Synthesis of β -pinene derivative (**48**)



General procedure B was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5al** (0.4 mmol, 54.5 mg, 1.0 equiv) and **(S)-RuL1**(CH_3CN) $_4\text{PF}_6$ (0.008 mmol, 5 mg, 0.02 equiv). After the addition the mixture was diluted with 1 mL of pentane and quickly filtered through a plug of silica, eluting with a 9:1 mixture of CH_2Cl_2 :pentane. *The product quickly decomposes during flash chromatography, filtration on silica proved to be the best way to obtain the pure product with no observable decomposition.* The filtrate was concentrated under vacuum to afford pure (–)-**48** as a white solid (134 mg, 99% yield, d.r. >20:1).

Appearance: white solid.

m.p.: 93.4 °C - 94.9 °C.

TLC R_f = 0.59 (petroleum ether/EtOAc 4:1).

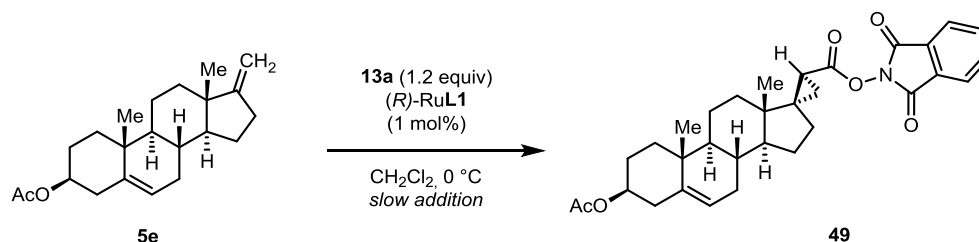
$[\alpha]_{20}^D = -146.4$ ($c = 1.0$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ = 7.89 – 7.85 (m, 2H), 7.79 – 7.75 (m, 2H), 2.40 – 2.21 (m, 2H), 2.03 – 1.98 (m, 1H), 1.98 – 1.88 (m, 2H), 1.87 (t, $J = 5.5$ Hz, 1H), 1.74 (dd, $J = 7.8, 6.0$ Hz, 1H), 1.62 (d, $J = 10.4$ Hz, 1H), 1.43 (ddd, $J = 14.8, 9.1, 2.2$ Hz, 1H), 1.37 (dd, $J = 7.9, 4.9$ Hz, 1H), 1.33 (dd, $J = 6.0, 4.9$ Hz, 1H), 1.22 (s, 3H), 0.95 (s, 3H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 168.6 (C_q), 162.3 (C_q), 134.8 (CH), 129.2 (C_q), 124.0 (CH), 43.5 (CH), 40.6 (CH), 40.3 (C_q), 35.5 (C_q), 28.2 (CH_2), 26.8 (CH_2), 26.7 (CH_2), 26.4 (CH_3), 24.3 (CH_2), 22.6 (CH), 21.7 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{20}\text{H}_{21}\text{NO}_4+\text{Na}]^+$: 362.1363; found: 362.1363.

Synthesis of androsterone derivative, with (*R*)-RuL1 (**49**)



General procedure A was applied using **13a** (0.4 mmol, 2.4 mL, 1.2 equiv), olefin **5e** (0.40 mmol, 131 mg, 1.0 equiv) and (*R*)-RuL1(CH₃CN)₄PF₆ (0.004 mmol, 2.6 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 1 additional hour at 0 °C. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 3:1), affording pure (+)-**49** as a white solid (212 mg, 99% yield, d.r. >20:1).

Appearance: white solid.

m.p.: 194°C (decomp.)

TLC R_f = 0.5 (petroleum ether/EtOAc 7:3).

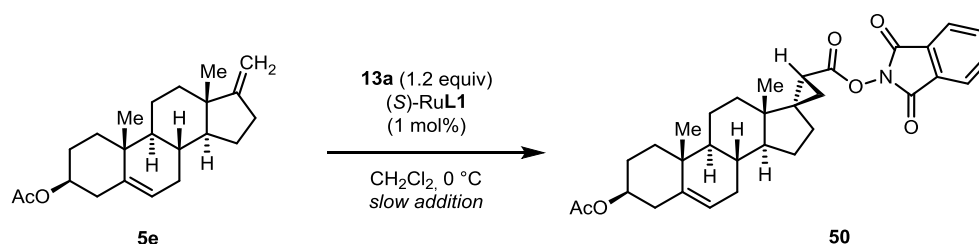
[α]₂₀^D = +50.5 (*c* = 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.90 – 7.84 (m, 2H), 7.80 – 7.73 (m, 2H), 5.40 – 5.38 (m, 1H), 4.61 (tdd, *J* = 10.4, 6.3, 4.1 Hz, 1H), 2.38 – 2.29 (m, 2H), 2.17 (ddd, *J* = 13.8, 10.7, 2.5 Hz, 1H), 2.10 – 2.01 (m, 4H), 1.90 – 1.78 (m, 4H), 1.69 – 1.22 (m, 9H), 1.19 – 1.12 (m, 3H), 1.04 – 0.95 (m, 5H), 0.93 (s, 3H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 170.6 (C_q), 169.9 (C_q), 162.4 (C_q), 139.8 (C_q), 134.8 (CH), 129.2 (C_q), 124.0 (CH), 122.5 (CH), 74.0 (CH), 54.8 (CH), 50.2 (CH), 44.8 (C_q), 42.0 (C_q), 38.2 (CH₂), 37.2 (CH₂), 36.8 (C_q), 33.2 (CH₂), 32.7 (CH), 31.9 (CH₂), 29.5 (CH₂), 27.9 (CH₂), 24.7 (CH₂), 21.6 (CH₃), 21.3 (CH₂), 20.6 (CH₂), 19.5 (CH₃), 18.4 (CH), 17.3 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₃₂H₃₇NO₆+Na]⁺: 554.2513; found: 554.2532.

Synthesis of androsterone derivative, with (*S*)-RuL1 (**50**)



General procedure A was applied using **13a** (0.365 mmol, 1.8 mL, 1.2 equiv), olefin **5e** (0.30 mmol, 100 mg, 1.0 equiv) and (*S*)-RuL1(CH₃CN)₄PF₆ (0.003 mmol, 1.9 mg, 0.01 equiv). After the addition, the mixture was allowed to react for 1 additional hour at 0 °C. The crude

product was purified by silica gel chromatography (petroleum ether/EtOAc 3:1), affording pure (–)-**50** as a white solid (160 mg, 99% yield, d.r. >20:1).

Appearance: white solid.

m.p.: 182 °C (decomp.)

TLC R_f = 0.36 (petroleum ether/EtOAc 4:1).

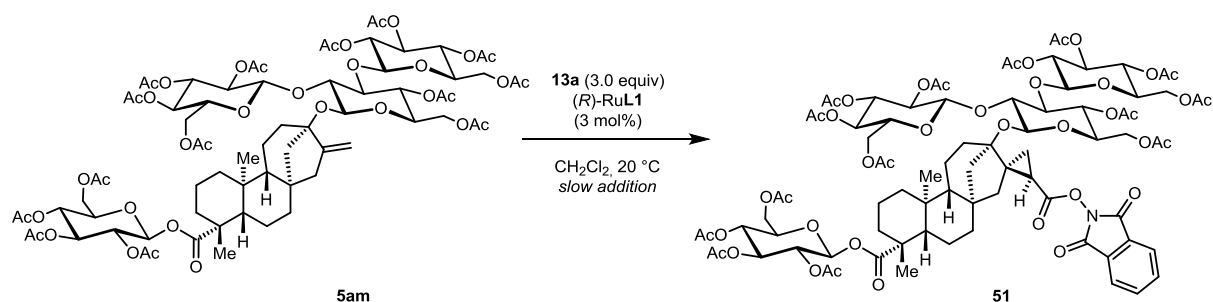
$[\alpha]_{20}^D = -211.8$ ($c = 0.5$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.89 – 7.82 (m, 2H), 7.79 – 7.67 (m, 2H), 5.38 (d, $J = 4.7$ Hz, 1H), 4.65 – 4.53 (m, 1H), 2.38 – 2.26 (m, 2H), 2.14 (dd, $J = 8.4, 5.4$ Hz, 1H), 2.09 – 2.02 (m, 1H), 2.02 (s, 3H), 1.94 – 0.97 (m, 18H), 1.02 (s, 3H), 0.84 (s, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.6 (C_q), 169.1 (C_q), 162.3 (C_q), 139.6 (C_q), 134.8 (CH), 129.1 (C_q), 124.0 (CH), 122.6 (CH), 74.0 (CH), 54.6 (CH), 49.9 (CH), 45.4 (C_q), 42.4 (C_q), 38.2 (CH_2), 37.1 (CH_2), 36.8 (C_q), 33.8 (CH_2), 32.6 (CH), 31.9 (CH_2), 27.9 (CH_2), 27.5 (CH_2), 25.3 (CH_2), 21.6 (CH_3), 20.7 (CH_2), 20.4 (CH), 19.4 (CH_3), 17.4 (CH_3), 15.9 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{32}\text{H}_{37}\text{NO}_6 + \text{Na}]^+$: 554.2513; found: 554.2516.

Synthesis of Rebaudioside A derivative (**51**)



General procedure C was applied using **13a** (0.4 mmol, 2.67 mL, 2.0 equiv, 0.15 M), olefin **5am**^[18] (0.20 mmol, 311 mg, 1.0 equiv) and **(R)-RuL1(CH₃CN)₄PF₆** (0.006 mmol, 3.8 mg, 0.03 equiv). After the addition, the mixture an aliquote was analyzed by ^1H NMR showing a 2:1 ratio between cyclopropanated product and starting material. Then, a solution of **10** (0.2 mmol, 1 mL, 1.0 equiv, 0.2 M) was added over 4 hours. After the addition, the mixture was allowed to react for 6 additional hour at 20 °C. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 7:3 to 1:1) affording pure (–)-**51** as a white solid (208 mg, 59% yield, d.r. 6:1).

Appearance: white solid.

m.p.: 140-145 °C.

TLC R_f = 0.33 (EtOAc/petroleum ether 3:2).

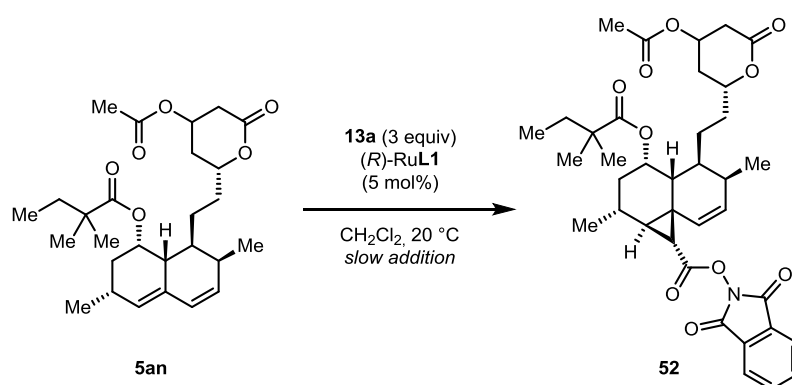
$[\alpha]_{20}^D = -6.60$ ($c = 1.0$, CHCl_3).

^1H NMR (500 MHz, C_6D_6) $\delta = 7.34 - 7.22$ (m, 2H), 6.79 – 6.69 (m, 2H), 5.92 (d, $J = 8.0$ Hz, 1H), 5.56 (t, $J = 9.3$ Hz, 1H), 5.50 – 5.24 (m, 10H), 5.12 (dd, $J = 11.2, 7.2$ Hz, 2H), 4.82 – 4.70 (m, 2H), 4.48 (dd, $J = 12.4, 4.7$ Hz, 1H), 4.32 (dd, $J = 12.3, 5.2$ Hz, 1H), 4.29 – 4.18 (m, 2H), 4.19 – 4.09 (m, 2H), 4.06 – 3.97 (m, 2H), 3.88 (dd, $J = 8.9, 7.5$ Hz, 1H), 3.80 – 3.72 (m, 2H), 3.66 (ddd, $J = 10.1, 4.8, 2.4$ Hz, 1H), 3.28 – 3.14 (m, 1H), 2.41 (d, $J = 11.4$ Hz, 1H), 2.34 (dd, $J = 8.3, 6.0$ Hz, 1H), 2.25 (dd, $J = 8.4, 4.0$ Hz, 1H), 2.21 (s, 3H), 2.05 – 1.56 (m, 51H), 1.54 – 1.49 (m, 1H), 1.47 – 1.38 (m, 1H), 1.32 – 1.22 (m, 1H), 1.14 – 1.11 (m, 1H), 1.13 (s, 3H), 0.98 (s, 3H), 0.91 – 0.74 (m, 3H) ppm.

^{13}C NMR (126 MHz, C_6D_6) $\delta = 175.8$ (C_q), 170.5 (C_q), 170.2 (C_q), 170.2 (C_q), 170.1 (C_q), 170.1 (C_q), 167.0 ($\text{C}_q \times 2$), 169.9 (C_q), 169.8 (C_q), 169.4 (C_q), 169.3 (C_q), 169.2 (C_q), 169.2 (C_q), 169.1 (C_q), 169.0 (C_q), 162.8 (C_q), 134.1 (CH), 129.4 (C_q), 123.8 (CH), 100.5 (CH), 99.4 (CH), 97.1 (CH), 91.6 (CH), 83.8 (C_q), 80.7 (CH), 79.3 (CH), 73.9 (CH), 73.6 (CH), 73.5 (CH), 72.9 (CH), 72.9 (CH), 72.8 (CH $\times 2$), 72.5 (CH), 71.9 (CH), 71.5 (CH), 68.6 (CH), 68.5 (CH), 68.5 (CH), 67.8 (CH), 62.6 (CH_2), 62.1 (CH_2), 61.6 (CH_2), 61.1 (CH_2), 56.5 (CH), 53.9 (CH), 46.6 (CH_2), 44.4 (C_q), 43.8 (CH_2), 43.5 (C_q), 41.8 (CH_2), 40.3 (CH_2), 39.9 (C_q), 39.7 (C_q), 38.1 (CH_2), 35.0 (CH_2), 28.9 (CH_3), 22.4 (CH_2), 21.3 (CH_2), 21.0 (CH_3), 20.8 ($2 \times \text{CH}_3$), 20.8 (CH_3), 20.7 (CH_3), 20.6 (CH), 20.5 (CH_3), 20.4 (CH_3), 20.3 (CH_3), 20.3 ($3 \times \text{CH}_3$), 20.2 (CH_3), 20.1 (CH_3), 19.9 (CH_2), 19.8 (CH_3), 19.5 (CH_2), 16.4 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{82}\text{H}_{103}\text{NO}_{41} + \text{Na}]^+$: 1780.5898; found: 1780.5908.

Synthesis of Simvastatin derivative (**52**)



General procedure D was applied using **13a** (1.2 mmol, 6 mL, 3 equiv), olefin **5an** (0.4 mmol, 184 mg, 1.0 equiv) and (*R*)-**RuL1**(CH_3CN) $_4\text{PF}_6$ (0.02 mmol, 13 mg, 0.05 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 55:45), affording pure (+)-**52** as a white solid (186 mg, 71% yield, d.r. >20:1).

Appearance: white solid.

TLC R_f = 0.38 (EtOAc/petroleum ether 1:1).

m.p.: 82.3 °C - 84.4 °C.

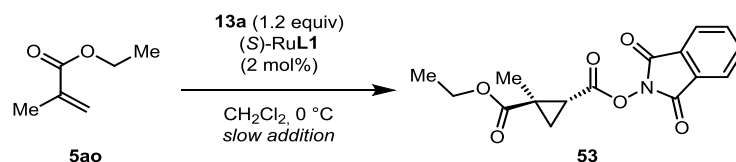
$[\alpha]_{20}^D = +95.4$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.96 – 7.84 (m, 2H), 7.82 – 7.75 (m, 2H), 5.76 (dd, $J = 9.6$, 3.8 Hz, 1H), 5.35 – 5.27 (m, 1H), 5.15 (bd, $J = 2.3$ Hz, 1H), 5.04 (bdd, $J = 9.7$, 1.8 Hz, 1H), 4.67 – 4.57 (m, 1H), 2.85 – 2.66 (m, 2H), 2.56 – 2.46 (m, 1H), 2.23 – 2.15 (m, 1H), 2.11 – 2.00 (m, 5H), 1.96 – 1.87 (m, 2H), 1.82 – 1.65 (m, 2H), 1.65 – 1.41 (m, 7H), 1.40 – 1.28 (m, 1H), 1.21 (d, $J = 7.4$ Hz, 3H), 1.10 (s, 6H), 1.04 (d, $J = 7.3$ Hz, 3H), 0.81 (t, $J = 7.4$ Hz, 3H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 177.6 (C_q), 170.2 (C_q), 169.2 (C_q), 166.8 (C_q), 162.3 (C_q), 134.9 (CH), 134.3 (CH), 132.1 (CH), 128.9 (C_q), 124.0 (CH), 76.9 (CH), 73.5 (CH), 65.8 (CH), 42.8 (C_q), 41.4 (CH), 35.5 (CH_2), 35.1 (CH_2), 34.4 (CH), 34.4 (CH), 34.3 (CH_2), 33.2 (CH_2), 32.8 (CH_2), 30.2 (C_q), 29.9 (CH), 27.4 (CH), 26.2 (CH_3), 24.7 (CH_3), 24.7 (CH_3), 24.2 (CH_2), 21.3 (CH), 21.2 (CH_3), 15.9 (CH_3), 9.4 (CH_3).

HRMS (ESI-TOF) calc'd for $[\text{C}_{37}\text{H}_{45}\text{NO}_{10} + \text{Na}]^+$: 686.2936; found: 686.2930.

Synthesis of 2-(1,3-dioxoisindolin-2-yl) 1-ethyl (1R,2R)-1-methylcyclopropane-1,2-dicarboxylate (53)



General procedure B was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5ao** (0.4 mmol, 45.7 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.008 mmol, 5 mg, 0.02 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **53** as a colorless oil (91.8 mg, 72% yield, d.r. 12:1). Compound (*R,R*)-**53** was obtained with a 94.3:5.7 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 10.1$ min, $\tau_{\text{minor}} = 11.7$ min.

Appearance: colorless oil.

TLC R_f = 0.34 (petroleum ether/EtOAc 4:1).

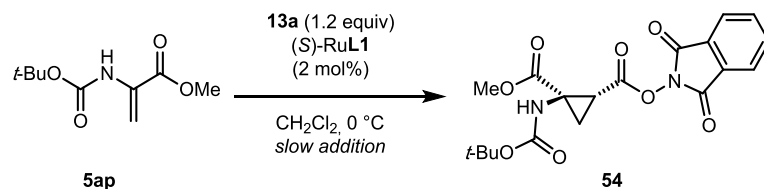
$[\alpha]_{20}^D = -156.0$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.91 – 7.85 (m, 2H), 7.82 – 7.75 (m, 2H), 4.19 (q, $J = 7.1$, 2H), 2.69 (dd, $J = 8.7$, 6.4 Hz, 1H), 1.81 (dd, $J = 8.7$, 4.5 Hz, 1H), 1.50 (s, 3H), 1.46 (dd, $J = 6.4$, 4.5 Hz, 1H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 172.5 (C_q), 167.4 (C_q), 162.0 (C_q), 134.9 (CH), 129.0 (C_q), 124.1 (CH), 61.9 (CH_2), 29.2 (C_q), 24.5 (CH), 22.6 (CH_2), 14.3 (CH), 13.2 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{16}\text{H}_{15}\text{NO}_6+\text{Na}]^+$: 340.0792; found: 340.0783.

Synthesis of protected aminoester **54**



General procedure B was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5ap**^[19] (0.4 mmol, 80 mg, 1.0 equiv) and **(S)-RuL1**(CH_3CN) $_4\text{PF}_6$ (0.008 mmol, 5 mg, 0.02 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 3:2), affording pure **54** as a white solid (101.3 mg, 63% yield, d.r. 4:1). Compound (*R,R*)-**54** was obtained with a 90.0:10.0 enantiomeric ratio determined by HPLC using a Chiralpak-IB column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: τ_{major} = 16.4 min, τ_{minor} = 13.6 min.

Appearance: white solid.

m.p.: 78.2 °C - 80.1 °C.

TLC R_f = 0.2 (petroleum ether/EtOAc 7:3).

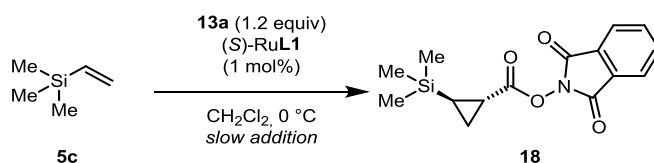
$[\alpha]_{20}^D$ = -113.5 (c = 1.0, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.92 – 7.86 (m, 2H), 7.82 – 7.76 (m, 2H), 5.36 (s, 1H), 3.77 (s, 3H), 3.07 – 2.94 (m, 1H), 2.16 – 2.08 (m, 1H), 2.02 – 1.93 (m, 1H), 1.43 (s, 9H) ppm.

^{13}C NMR (101 MHz, CDCl_3) δ = 170.4 (C_q), 165.3 (C_q), 161.7 (C_q), 155.5 (C_q), 134.9 (CH), 129.0 (C_q), 124.1 (CH), 80.8 (C_q), 53.4 (CH_3), 41.5 (C_q), 28.3 (CH_3), 26.1 (CH), 22.8 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_8+\text{Na}]^+$: 427.1112; found: 427.1111.

Synthesis of 1,3-dioxoisindolin-2-yl (1*S*,2*R*)-2-(trimethylsilyl)cyclopropane-1-carboxylate (**18**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5c** (0.4 mmol, 40 mg, 1.0 equiv) and **(S)-RuL1**(CH_3CN) $_4\text{PF}_6$ (0.004 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1) affording pure **18** as a colorless oil (76 mg, 63% yield, d.r. >20:1). Compound (*S,R*)-**18** was

obtained with a 98.4:1.6 enantiomeric ratio determined by HPLC using a Chiralpak-IF column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 9.4$ min, $\tau_{\text{minor}} = 7.8$ min.

Appearance: colorless oil.

TLC $R_f = 0.63$ (petroleum ether/EtOAc 4:1).

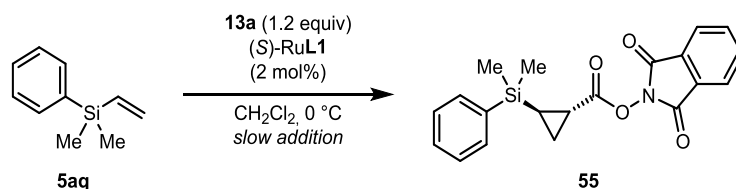
$[\alpha]_{20}^D = -104.2$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.91 - 7.85$ (m, 2H), $7.81 - 7.75$ (m, 2H), 1.79 (ddd, $J = 7.4, 5.9, 4.0$ Hz, 1H), 1.48 (dt, $J = 11.0, 3.8$ Hz, 1H), 1.05 (ddd, $J = 8.8, 7.4, 3.6$ Hz, 1H), 0.70 (ddd, $J = 11.0, 8.7, 6.0$ Hz, 1H), 0.06 (s, 9H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 171.6$ (C_q), 162.2 (C_q), 134.8 (CH), 129.1 (C_q), 124.1 (CH), 14.3 (CH_2), 13.9 (CH), 12.2 (CH), -2.6 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{15}\text{H}_{17}\text{NO}_4\text{Si} + \text{Na}]^+$: 326.0819; found: 326.0821.

Synthesis of 1,3-dioxoisindolin-2-yl (1S,2R)-2-(dimethyl(phenyl)silyl)cyclopropane-1-carboxylate (55)



General procedure A was applied using **13a** (0.48 mmol, 2.4 mL, 1.2 equiv), olefin **5aq** (0.4 mmol, 64.9 mg, 1.0 equiv) and **(S)-RuL1(CH₃CN)₄PF₆** (0.008 mmol, 5 mg, 0.02 equiv). The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **55** as a colorless oil (92 mg, 63% yield, d.r. >20:1). Compound (*S,R*)-**55** was obtained with a 98.3:1.7 enantiomeric ratio determined by HPLC using a Chiralpak-IF column [*i*-hexane/*i*-PrOH (95:5), 1.0 mL/min]: $\tau_{\text{major}} = 15.9$ min, $\tau_{\text{minor}} = 14.1$ min.

Appearance: colorless oil.

TLC $R_f = 0.60$ (petroleum ether/EtOAc 4:1).

$[\alpha]_{20}^D = -130.5$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) $\delta = 7.90 - 7.84$ (m, 2H), $7.80 - 7.74$ (m, 2H), $7.58 - 7.53$ (m, 2H), $7.43 - 7.38$ (m, 3H), 1.80 (ddd, $J = 7.4, 6.0, 4.1$ Hz, 1H), 1.53 (dt, $J = 10.9, 3.9$ Hz, 1H), 1.04 (ddd, $J = 8.7, 7.4, 3.6$ Hz, 1H), 0.89 (ddd, $J = 10.9, 8.6, 5.9$ Hz, 1H), 0.34 (s, 3H), 0.33 (s, 3H) ppm.

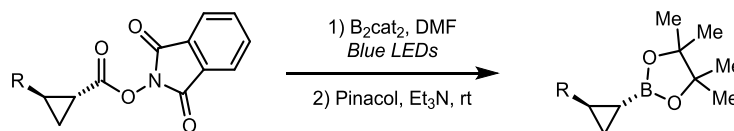
^{13}C NMR (101 MHz, CDCl_3) $\delta = 171.5$ (C_q), 162.1 (C_q), 136.4 (C_q), 134.8 (CH), 134.0 (CH), 129.7 (CH), 129.1 (C_q), 128.2 (CH), 124.1 (CH), 14.1 (CH_2), 14.1 (CH), 11.2 (CH), -3.7 (CH_3), -4.0 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{20}\text{H}_{19}\text{NO}_4\text{Si}+\text{Na}]^+$: 388.0976; found: 388.0972.

2.3. Derivatization of redox-active cyclopropanes

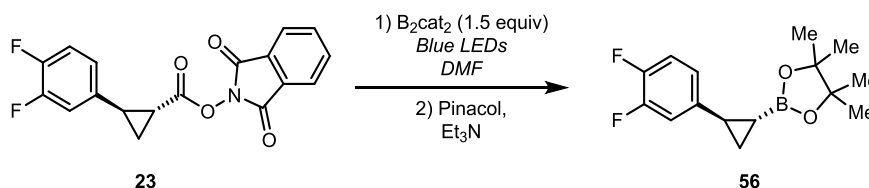
2.3.1. Synthesis of cyclopropylboronates

General procedure E for the synthesis of cyclopropylboronates:



This procedure has been modified from the original protocol developed by Aggarwal.^[5] An 8 mL vial was charged with a stirring bar, redox-active ester (0.2 mmol, 1 equiv) and 2,2'-bibenzo[d][1,3,2]dioxaborole (B_2cat_2 , 71.3 mg, 0.3 mmol, 1.5 equiv), and degassed DMF (2.0 mL, 0.1 M) was added. Then, Ar was flushed to displace the air in the vial. (*Note: According to the original procedure, it is very important to purge the vial headspace with Ar or N_2 prior to initiating the photoinduced borylation reaction*). The vial was capped and the mixture was stirred under blue LED lights. After the time indicated for each example, the lights were removed, the solution was allowed to cool to room temperature and a solution of 2,3-dimethylbutane-2,3-diol (pinacol, 94.5 mg, 0.80 mmol, 4 equiv) in Et_3N (0.7 mL) was added. The resulting brown solution was stirred for 1.5 hours. The reaction mixture was diluted with Et_2O (30 mL), H_2O (10 mL) and NH_4Cl (saturated aqueous solution, 10 mL). Phases were separated and the aqueous phase was extracted twice with Et_2O (2 x 30 mL). The combined organic layers were concentrated by rotatory evaporation, yielding crude cyclopropylboronate. The crude material was purified by column chromatography on silica gel using the indicated eluent. (*Note: column chromatography purification should be performed very quickly to avoid decomposition of the cyclopropylboronate on silica gel*). Desired products stain bright blue with vanillin staining solution.

Synthesis of 2-((1R,2R)-2-(3,4-difluorophenyl)cyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**56**)



General procedure E was applied using **23** (68.7 mg, 0.2 mmol, 1.0 equiv) and B_2cat_2 (B_2cat_2 , 71.3 mg, 0.3 mmol, 1.5 equiv) in DMF (2.0 mL) for 6 hours. The crude product was purified

by silica gel chromatography (petroleum ether/Et₂O 95:5), affording pure **56** as a colorless oil (45 mg, 80% yield, d.r.>20:1). (*R,R*)-**56** was obtained with a 97.7:2.3 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (99.5:0.5), 1.0 mL/min]: $\tau_{\text{major}} = 4.2$ min, $\tau_{\text{minor}} = 4.7$ min.

Appearance: colorless oil.

TLC $R_f = 0.55$ (petroleum ether/Et₂O 95:5).

$[\alpha]_{20}^D = -106.0$ ($c = 1.12$, CHCl₃).

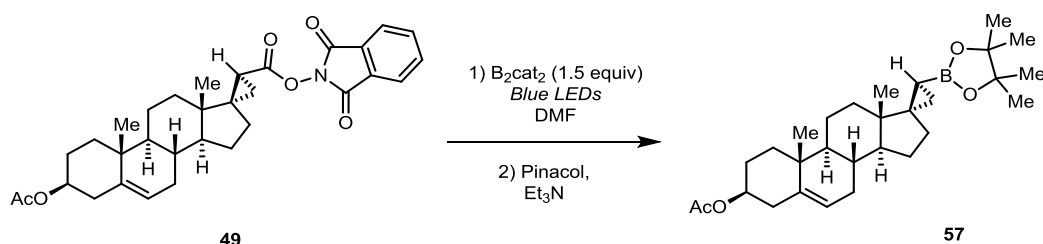
¹H NMR (400 MHz, CDCl₃) $\delta = 7.00$ (dt, $J = 10.3, 8.4$ Hz, 1H), 6.84 (ddd, $J = 11.7, 7.6, 2.2$ Hz, 1H), 6.79 (ddt, $J = 8.1, 3.8, 1.7$ Hz, 1H), 2.05 (dt, $J = 8.1, 5.4$ Hz, 1H), 1.25 (s, 6H), 1.24 (s, 6H), 1.15 (ddd, $J = 8.2, 6.9, 3.9$ Hz, 1H), 0.97 – 0.84 (m, 1H), 0.26 – 0.17 (m, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) $\delta = 150.4$ (dd, $J = 247.0, 12.8$ Hz, C_F), 148.6 (dd, $J = 245.1, 12.8$ Hz, C_F), 140.7 (dd, $J = 5.8, 3.6$ Hz, C_q), 121.7 (dd, $J = 5.9, 3.3$ Hz, CH), 116.9 (d, $J = 17.2$ Hz, CH), 114.6 (d, $J = 17.5$ Hz, CH), 83.5 (C_q), 24.9 (CH₃), 24.9 (CH₃), 21.3 (CH), 15.0 (CH₂), 6.0 (CH) ppm.

¹⁹F NMR (377 MHz, CDCl₃) $\delta = -138.70$ (d, $^3J_{\text{FF}} = 21.4$ Hz), -142.66 (d, $^3J_{\text{FF}} = 21.4$ Hz) ppm.

MS (200 °C, 70 eV, m/e): 181 (M⁺-C₆H₁₁O, 100%), 280 (M⁺, 55%), 83 (M⁺-C₉H₈BF₂O₂, 50%), 153 (M⁺-C₆H₁₂BO₂, 41%).

Synthesis of the cyclopropyl boronate derived from androsterone (**57**)



General procedure E was applied using **49** (80 mg, 0.15 mmol, 1.0 equiv) and B₂cat₂ (B₂cat₂, 53.5 mg, 0.225 mmol, 1.5 equiv) in DMF (1.5 mL) for 6 hours. The crude product was purified by silica gel chromatography (petroleum ether/Et₂O 9:1), affording pure (–)-**57** as a white solid (38.7 mg, 55% yield, d.r. 6.9:1).

Appearance: white solid.

m.p.: 177 °C (decomp.)

TLC $R_f = 0.75$ (Petroleum Ether/EtOAc 4:1).

$[\alpha]_{20}^D = -30.5$ ($c = 1.12$, CHCl₃).

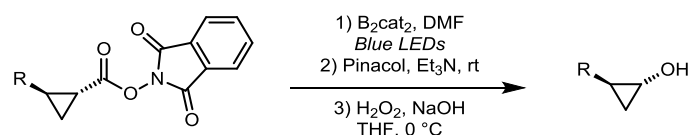
¹H NMR (400 MHz, CDCl₃) δ = 5.38 (d, J = 5.0 Hz, 1H), 4.65 – 4.55 (m, 1H), 2.37 – 2.25 (m, 2H), 2.08 – 1.95 (m, 5H), 1.90 – 1.81 (m, 2H), 1.81 – 1.73 (m, 1H), 1.64 – 1.39 (m, 6H), 1.31 – 1.25 (m, 14H), 1.15 – 0.90 (m, 8H), 0.77 (s, 3H), 0.40 (dd, J = 7.1, 3.3 Hz, 1H), –0.17 (dd, J = 9.9, 7.1 Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 170.7 (C_q), 139.8 (C_q), 122.8 (CH), 82.9 (C_q), 74.1 (CH), 54.5 (CH), 50.5 (CH), 41.7 (C_q), 38.6 (C_q), 38.3 (CH₂), 37.2 (CH₂), 36.9 (C_q), 32.8 (CH), 32.7 (CH₂), 32.1 (CH₂), 31.7 (CH₂), 27.9 (CH₂), 25.32 (CH₃), 25.30 (CH₂), 24.7 (CH₃), 21.6 (CH₃), 20.7 (CH₂), 19.5 (CH₃), 17.7 (CH₂), 17.3 (CH₃), 0.54 (CH) ppm.

HRMS (ESI-TOF) calc'd for [C₂₉H₄₅BO₄+Na]⁺: 491.3303; found: 491.3310.

2.3.2. Synthesis of cyclopropanols

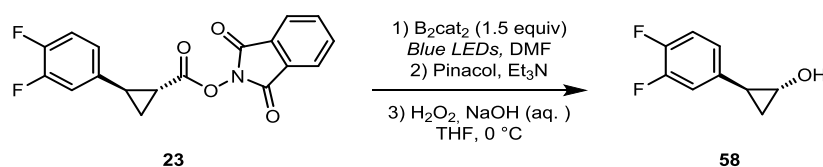
General procedure F for the synthesis of cyclopropanols:



This procedure has been modified from the original protocol developed by Aggarwal.^[5] An 8 mL vial was charged with a stirring bar, redox-active ester (0.15 mmol, 1 equiv) and 2,2'-bibenzo[*d*][1,3,2]dioxaborole (B₂cat₂, 53.5 mg, 0.23 mmol, 1.5 equiv), and degassed DMF (1.5 mL, 0.1 M) was added. Then, Ar was flushed to displace the air in the vial. (*Note: According to the original procedure, it is very important to purge the vial headspace with Ar or N₂ prior to initiating the photoinduced borylation reaction*). The vial was capped and the mixture was stirred under blue LED lights. After the time indicated for each example, the lights were removed, the solution was allowed to cool to room temperature and a solution of 2,3-dimethylbutane-2,3-diol (pinacol, 71.0 mg, 0.60 mmol, 4 equiv) in Et₃N (0.45 mL) was added. (*Note: the pinacol transesterification and the extraction are not required and may be substituted by a direct addition of H₂O₂ (186 μ L, 1.8 mmol, 12 equiv) in the DMF reaction mixture if the purification of the cyclopropanols is not problematic*). The resulting brown solution was stirred for 1.5 hours. The reaction mixture was transferred into separating funnel containing H₂O (10 mL) and NH₄Cl (saturated aqueous solution, 10 mL). The mixture was extracted with pentane (3 x 25 mL) and volatiles were removed *in vacuo*. The organic residue was transferred to an 8 mL vial and dissolved in THF (1 mL). Then, the vial was placed in an ice/water bath. After 10 minutes, 30% wt aqueous H₂O₂ (62 μ L, 0.6 mmol, 4 equiv) was added, followed by aqueous 3 M NaOH (0.1 mL, 0.3 mmol, 2 equiv). A white precipitate

appeared over time. The mixture was stirred until no pinacol boronate was observed by TLC (typically 30 minutes). The mixture was diluted with H₂O (20 mL) and extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (50 mL) and dried over Na₂SO₄. The crude cyclopropane was purified by column chromatography using the indicated eluent.

Synthesis of (1R,2S)-2-(3,4-difluorophenyl)cyclopropan-1-ol (58)



General procedure F was applied using **23** (51.3 mg, 0.15 mmol, 1.0 equiv) and B₂cat₂ (B₂cat₂, 54 mg, 0.23 mmol, 1.5 equiv) in DMF (1.5 mL) for 6 hours. Cyclopropyl boronate **56** was formed by adding pinacol (71 mg, 0.6 mmol, 4 equiv) dissolved in Et₃N (0.45 mL). Extraction with pentane afforded crude cyclopropylboronate **56**, which was oxidized as described above. The crude product was purified by silica gel chromatography (Petroleum Ether/EtOAc 4:1), affording pure **58** as a colorless oil (12.8 mg, 50% yield, d.r. >20:1). (*R,R*)-**58** was obtained with a 98.3:1.7 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: $\tau_{\text{major}} = 4.9$ min, $\tau_{\text{minor}} = 5.2$ min. Characterization data are consistent with those reported in the literature for the racemic compound.^[20] (*Note: this compound is unstable and it decomposes over time under air at room temperature. The decomposition is accelerated when it is dissolved in chloroform and under HPLC conditions*).

Appearance: colorless oil.

TLC R_f = 0.4 (Petroleum Ether/EtOAc 7:3).

$[\alpha]_{20}^D = -98.2$ (*c* = 0.1, CHCl₃).

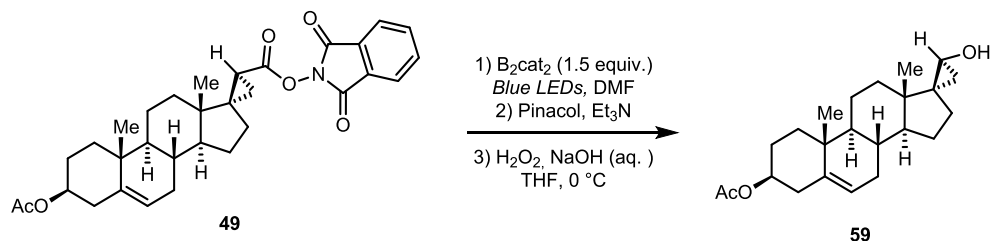
¹H NMR (500 MHz, CD₂Cl₂) δ = 7.05 (dt, *J* = 10.4, 8.4 Hz, 1H), 6.84 – 6.74 (m, 2H), 3.54 (ddd, *J* = 6.3, 3.6, 2.4 Hz, 1H), 2.24 (s, 1H), 2.04 (ddd, *J* = 10.1, 6.3, 2.5 Hz, 1H), 1.25 (ddd, *J* = 10.0, 6.2, 3.6 Hz, 1H), 0.98 (dd, *J* = 12.8, 6.4 Hz, 1H) ppm.

¹³C NMR (126 MHz, CD₂Cl₂) δ = 150.7 (dd, *J* = 246.4, 12.9 Hz, C_F), 148.6 (dd, *J* = 244.6, 12.8 Hz, C_F), 139.3 (dd, *J* = 5.8, 3.6 Hz, C_q), 122.4 (dd, *J* = 6.1, 3.8 Hz, CH), 117.4 (d, *J* = 17.4 Hz, CH), 115.0 (d, *J* = 17.6 Hz, CH), 55.7 (CH), 25.2 (CH), 18.3 (CH₂) ppm.

¹⁹F NMR (377 MHz, CD₂Cl₂) δ = -139.4 (d, ³*J*_{FF} = 21.1 Hz), -143.5 (d, ³*J*_{FF} = 21.1 Hz) ppm.

MS (200 °C, 70 eV, m/e): 127 ($M^+ - C_2H_3O$, 100%), 128 ($M^+ - C_2H_2O$, 55%), 170 (M^+ , 50%), 114 ($M^+ - C_3H_4O$, 38%), 101 ($M^+ - C_4H_5O$, 32%).

Synthesis of the cyclopropanol derived from androsterone (59)



General procedure F was applied using **49** (80.0 mg, 0.15 mmol, 1.0 equiv) and B_2cat_2 (B_2cat_2 , 54 mg, 0.23 mmol, 1.5 equiv) in DMF (1.5 mL) for 6 hours. Cyclopropyl boronate **57** was formed by adding pinacol (71 mg, 0.6 mmol, 4 equiv) dissolved in Et_3N (0.45 mL). Extraction with Et_2O afforded crude cyclopropylboronate **57**, which was oxidized as described above. Crude **59** (d.r. 6.9:1) was purified by silica gel chromatography (pentane/ $EtOAc$ 9:1 to 4:1), affording pure (–)-**59** as a yellow oil (27.4 mg, 51% yield, d.r. 18:1).

Appearance: yellow oil.

TLC R_f = 0.55 (Petroleum Ether/ $EtOAc$ 7:3).

$[\alpha]_{20}^D = -72.8$ ($c = 1.0$, $CHCl_3$).

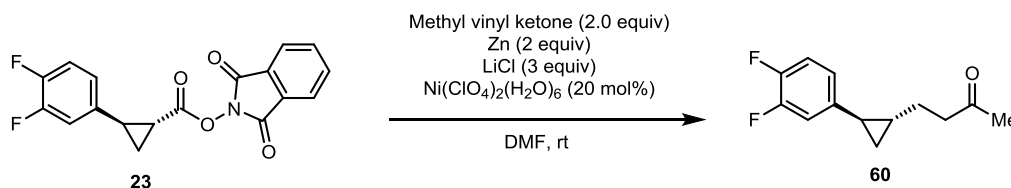
1H NMR (500 MHz, $CDCl_3$) δ = 5.38 (dd, $J = 4.7, 2.8$ Hz, 1H), 4.60 (dddd, $J = 11.5, 10.1, 6.1, 4.1$ Hz, 1H), 3.28 (dd, $J = 7.2, 3.5$ Hz, 1H), 2.37 – 2.26 (m, 2H), 2.20 – 2.12 (m, 1H), 2.07 – 2.02 (m, 4H), 1.89 – 1.78 (m, 3H), 1.68 – 1.27 (m, 9H), 1.17 – 1.11 (m, 1H), 1.02 (s, 3H), 1.00 – 0.85 (m, 4H), 0.81 (s, 3H), 0.21 (dd, $J = 5.7, 3.4$ Hz, 1H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.7 (C_q), 139.8 (C_q), 122.7 (CH), 74.1 (CH), 55.6 (CH), 51.7 (CH), 50.3 (CH), 40.8 (C_q), 38.3 (CH_2), 37.5 (C_q), 37.2 (CH_2), 36.9 (C_q), 34.4 (CH_2), 32.4 (CH), 32.1 (CH_2), 28.4 (CH_2), 27.9 (CH_2), 24.9 (CH_2), 21.6 (CH_3), 20.6 (CH_2), 19.8 (CH_2), 19.5 (CH_3), 16.8 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[C_{23}H_{34}O_3 + Na]^+$: 381.2400; found: 381.2394.

2.3.3. Synthesis of alkylcyclopropanes

Synthesis of 4-((1*R*,2*R*)-2-(3,4-difluorophenyl)cyclopropyl)butan-2-one (**60**)



Redox-active cyclopropane **23** (0.3 mmol, 103 mg, 1.0 equiv), zinc powder (0.62 mmol, 41 mg, 2.0 equiv), LiCl (0.93 mmol, 40 mg, 3.0 equiv), and Ni(ClO₄)₂·(H₂O)₆ (0.062 mmol, 23 mg, 20 mol%) were charged in a microwave vial equipped with a PTFE-lined stir bar. DMF was then charged (0.75 mL, final concentration 0.4 M) along with methyl vinyl ketone (0.62 mmol, 52 μ L, 2.0 equiv). The reaction mixture was stirred at 800 rpm overnight at room temperature. To the reaction mixture, 5 mL of deionized water were added, and the resulting mixture was extracted 3 times with 5 mL of Et₂O. The organic fractions were collected, dried over Na₂SO₄ and filtered through a Pasteur pipette packed with silica gel. The filtrate was evaporated *in vacuo*, and the residue was purified by silica gel chromatography (petroleum ether/Et₂O 6:1), affording pure **60** as a yellow oil (31 mg, 44% yield, d.r. >20:1). Compound (*R,R*)-**60** was obtained with a 97.9:2.1 enantiomeric ratio determined by HPLC using a Chiralpak-ID column [*i*-hexane/*i*-PrOH (95:5), 1.0 mL/min]: $\tau_{\text{major}} = 6.9$ min, $\tau_{\text{minor}} = 7.2$ min.

Appearance: yellow oil.

$[\alpha]_{20}^D = +57.4$ ($c = 0.35$, CHCl₃).

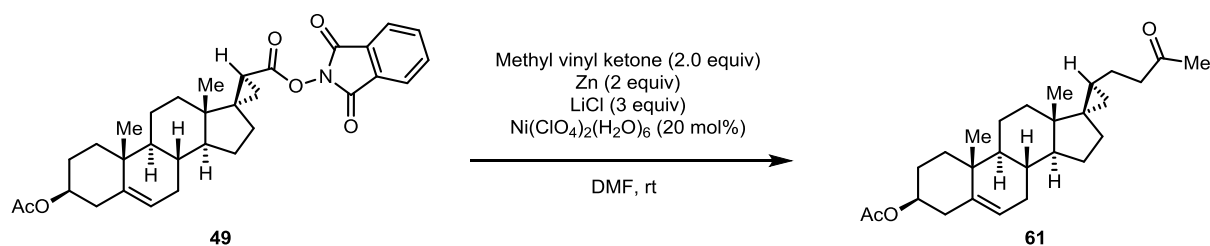
¹H NMR (400 MHz, CDCl₃) δ = 7.00 (dt, $J = 10.2, 8.4$ Hz, 1H), 6.82 – 6.71 (m, 2H), 2.57 (t, $J = 7.3$ Hz, 2H), 2.15 (s, 3H), 1.70 – 1.56 (m, 3H), 1.03 – 0.94 (m, 1H), 0.85 – 0.74 (m, 2H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 208.7 (C_q), 150.7 (dd, $J = 184.9, 12.8$ Hz, C_F), 148.2 (dd, $J = 182.8, 12.8$ Hz, C_F), 140.6 (dd, $J = 5.8, 3.6$ Hz, C_q), 121.7 (dd, $J = 6.0, 3.4$ Hz, CH), 117.0 (d, $J = 16.9$ Hz, CH), 114.4 (d, $J = 17.4$ Hz, CH), 43.3 (CH₂), 30.3 (CH₃), 28.4 (CH₂), 23.3 (CH), 22.8 (d, $J = 1.8$ Hz, CH), 16.2 (CH₂) ppm.

¹⁹F NMR (377 MHz, CDCl₃) δ = –138.6 (d, $^3J_{\text{FF}} = 21.2$ Hz), –142.9 (d, $^3J_{\text{FF}} = 21.7$ Hz) ppm.

HRMS (ESI-TOF) calc'd for [C₁₃H₁₄F₂O + Na]⁺: 247.0905; found: 247.0908.

Synthesis of the alkylcyclopropane derived from androsterone (**61**)



Redox-active cyclopropane **49** (0.3 mmol, 160 mg, 1.0 equiv), zinc powder (0.62 mmol, 41 mg, 2.0 equiv), LiCl (0.93 mmol, 40 mg, 3.0 equiv), and $\text{Ni(ClO}_4)_2 \cdot (\text{H}_2\text{O})_6$ (0.062 mmol, 23 mg, 20 mol%) were charged in a microwave vial equipped with a PTFE-lined stir bar. DMF was then charged (0.75 mL, final concentration 0.4 M) along with methyl vinyl ketone (0.62 mmol, 52 μL , 2.0 equiv). The reaction mixture was stirred at 800 rpm overnight at room temperature. To the reaction mixture, 5 mL of deionized water were added, and the resulting mixture was extracted 3 times with 5 mL of diethyl ether. The organic fractions were collected, dried over Na_2SO_4 and filtered through a Pasteur pipette packed with silica gel. Finally, the silica in the pipette was washed thoroughly with chloroform and the filtrates were evaporated *in vacuo*, and the residue was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure (–)-**61** as a white solid (35 mg, 28% yield, d.r. 7:1).

Appearance: white solid.

m.p.: 116.0 – 119.1 $^{\circ}\text{C}$

$[\alpha]_{25}^{\text{D}} = -54.8$ ($c = 0.3$, CHCl_3)

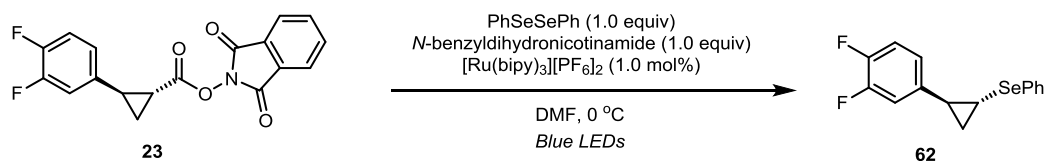
^1H NMR (500 MHz, CDCl_3) $\delta = 5.41 - 5.35$ (m, 1H), 4.66 – 4.55 (m, 1H), 2.51 (t, $J = 7.6$ Hz, 2H), 2.35 – 2.28 (m, 2H), 2.15 (s, 3H), 2.07 – 1.93 (m, 6H), 1.90 – 1.74 (m, 3H), 1.66 – 0.76 (m, 16H), 0.80 (dd, $J = 9.0, 4.4$ Hz, 1H), 0.73 (s, 3H), 0.48 (dtd, $J = 9.0, 7.2, 5.7$ Hz, 1H), –0.28 (dd, $J = 5.7, 4.4$ Hz, 1H) ppm

^{13}C NMR (126 MHz, CDCl_3) $\delta = 209.3$ (C_q), 170.6 (C_q), 139.7 (C_q), 122.6 (CH), 74.0 (CH), 55.0 (CH), 50.4 (CH), 44.3 (CH_2), 41.0 (C_q), 38.2 (CH_2), 37.1 (CH_2), 36.8 (C_q), 36.1 (C_q), 33.2 (CH_2), 32.5 (CH), 32.0 (CH_2), 30.0 (CH_3), 29.0 (CH_2), 27.8 (CH_2), 25.5 (CH_2), 25.1 (CH_2), 21.5 (CH_3), 20.6 (CH_2), 19.4 (CH_3), 17.3 (CH_2), 16.9 (CH_3), 16.5 (CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{27}\text{H}_{40}\text{O}_3 + \text{Na}]^+$: 435.2870; found: 435.2883.

2.3.4. Synthesis of selenylcyclopropanes

Synthesis of ((1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl)(phenyl)selane (**62**)



Redox-active cyclopropane **23** (103 mg, 0.300 mmol, 1.0 equiv), *N*-benzyl-1,4-dihydronicotinamide (64.0 mg, 0.300 mmol, 1.0 equiv), 1,2-diphenyldiselenane (PhSeSePh, 47.0 mg, 0.150 mmol, 1.0 equiv), and [Ru(bipy)₃][PF₆]₂ (2.7 mg, 3.11 μmol, 1.0 mol%) were charged in a culture tube equipped with a PTFE-coated stir bar.^[21] The tube was introduced to a N₂-filled dry box and 9.0 mL of DMF were charged. Once the solvent was charged, the tube was sealed with a PTFE-lined screw cap, and removed from the box. The tube was placed in an *i*-PrOH bath cooled to 0 °C, and the reaction mixture was exposed to blue LED light overnight. To the reaction mixture, 5 mL of deionized water were added, and the resulting mixture was extracted 3 times with 10 mL of diethyl ether. The organic fractions were collected, dried over Na₂SO₄ and filtered through a Pasteur pipette packed with silica gel. The filtrate was evaporated *in vacuo*, and the residue was purified by silica gel chromatography (pentane), affording pure **62** as a yellow oil (55 mg, 59% yield, d.r. >20:1). Compound (*R,R*)-**62** was obtained with a 98.3:1.7 enantiomeric ratio determined by HPLC using a Chiralpak OJ-H column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 8.2 min, τ_{minor} = 9.4 min.

Note on characterization: the ⁷⁷Se NMR chemical shift of **62** is consistent with that of a selene, as opposed to a selenoxide, which appear farther downfield in the region of δ > 800 ppm.^[22] Oxidation of the selene is an unavoidable artifact that takes place during ionization using ESI. Other ionization techniques were unsuccessful.

Appearance: yellow oil.

[α]_{27.1}^D = −49.1 (*c* = 0.35, CHCl₃)

¹H NMR (400 MHz, CDCl₃) δ = 7.51 – 7.43 (m, 2H), 7.32 – 7.22 (m, 3H), 7.08 (dt, *J* = 10.2, 8.3 Hz, 1H), 6.91 – 6.78 (m, 2H), 2.52 (ddd, *J* = 8.2, 5.4, 4.2 Hz, 1H), 2.24 (ddd, *J* = 9.5, 5.7, 4.1 Hz, 1H), 1.50 (dt, *J* = 8.2, 5.8 Hz, 1H), 1.42 (dt, *J* = 8.9, 5.6 Hz, 1H) ppm.

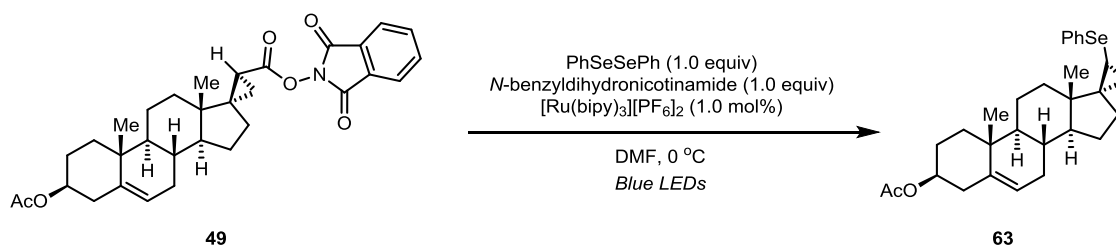
¹³C NMR (101 MHz, CDCl₃) δ = 150.5 (dd, *J* = 247.9, 12.8 Hz, CF), 149.0 (dd, *J* = 246.4, 12.8 Hz, CF), 138.6 (dd, *J* = 5.9, 3.7 Hz, C_q), 131.7 (C_q), 131.0 (CH), 129.3 (CH), 126.7 (CH), 122.0 (dd, *J* = 6.1, 3.5 Hz, CH), 117.3 (d, *J* = 17.3 Hz, CH), 114.8 (d, *J* = 17.4 Hz, CH), 26.4 (d, *J* = 1.6 Hz, CH), 18.2 (CH₂), 17.2 (s, *J* = 100.4 Hz satellites, CH) ppm.

¹⁹F NMR (377 MHz, CDCl₃) δ = −137.8 (d, ³J_{FF} = 21.7 Hz), −141.4 (d, ³J_{FF} = 21.1 Hz) ppm.

⁷⁷Se NMR (95 MHz, CDCl₃) δ = 397.2 ppm.

HRMS (ESI-TOF) calc'd for [C₁₅H₁₂F₂OSe+Na]⁺: 348.9914; found: 348.9910.

Synthesis of the selenylcyclopropane derived from androsterone (63)



Compound **49** (159 mg, 0.300 mmol, 1.0 equiv), *N*-benzyl-1,4-dihydronicotinamide (64.0 mg, 0.300 mmol, 1.0 equiv), 1,2-diphenyldiselenane (47.0 mg, 0.150 mmol, 1.0 equiv), and [Ru(bipy)₃][PF₆]₂ (2.7 mg, 3.11 μmol, 1.0 mol%) were charged in a culture tube equipped with a PTFE-coated stir bar. The tube was introduced to a N₂-filled dry box and 9.0 mL of DMF were charged. Once the solvent was charged, the tube was sealed with a PTFE-lined screw cap, and removed from the box. The tube was placed in an *i*-PrOH bath cooled to 0 °C, and the reaction mixture was exposed to blue LED light overnight. To the reaction mixture, 5 mL of deionized water were added, and the resulting mixture was extracted 3 times with 10 mL of ethyl acetate. The organic fractions were collected, dried over Na₂SO₄ and filtered through a Pasteur pipette packed with silica gel. The filtrate was evaporated *in vacuo*, and the residue was purified by silica gel chromatography (petroleum ether/Et₂O 95:5), affording pure (−)-**63** as a white solid (90 mg, 60% yield, d.r. 1.4:1.0).

Note on characterization: the ⁷⁷Se NMR chemical shift of (−)-**63** is consistent with that of a selenane, as opposed to a selenoxide, which appear farther downfield in the region of δ > 800 ppm.^[22] Oxidation of the selenane is an unavoidable artifact that takes place during ionization using ESI. Other ionization techniques were unsuccessful.

Appearance: white solid.

m.p.: 129.7 – 135.1 °C

[α]₂₅^D = −46.6 (*c* = 0.8, CHCl₃)

¹H NMR (400 MHz, CDCl₃) δ = 7.55 – 7.45 (m, 2H), 7.28 – 7.15 (m, 3H), 5.38 (d, *J* = 4.8 Hz, 1H), 4.71 – 4.48 (m, 1H), 2.41 – 2.24 (m, 3H), 2.23 – 2.13 (m, 1H), 2.07 – 1.97 (m, 4H), 1.91 – 1.73 (m, 3H), 1.66 – 1.05 (m, 12H), 1.04 – 0.94 (m, 4H), 0.93 (s, 3H, **63b**), 0.90 – 0.79 (m, 1H, **63b**), 0.78 (s, 3H, **63a**), 0.48 (t, *J* = 5.2 Hz, 1H, **63a**) ppm.

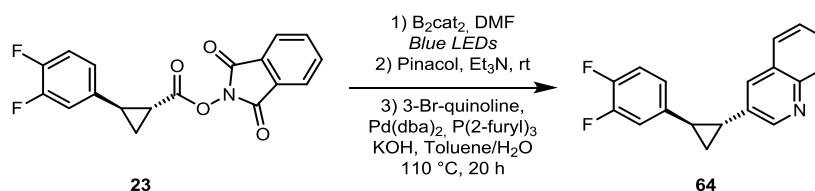
^{13}C NMR (101 MHz, CDCl_3) (for the mixture of **63a** and **63b**) δ = 170.8 (C_q), 139.8 (C_q), 139.7 (C_q), 133.5 (C_q), 132.6 (C_q), 130.8 (CH), 129.7 (CH), 129.0 (CH), 129.0 (CH), 126.1 (CH), 125.7 (CH), 122.7 (CH), 122.6 (CH), 74.0 (CH), 74.0 (CH), 55.9 (CH), 55.2 (CH), 50.1 (CH), 50.0 (CH), 42.6 (C_q), 41.6 (C_q), 38.6 (C_q), 38.3 (C_q), 38.2 (C_q), 37.1 (CH_2), 37.1 (CH_2), 36.8 (C_q), 36.7 (C_q), 35.8 (CH_2), 33.3 (CH_2), 32.6 (CH), 32.4 (CH), 32.0 (CH_2), 32.0 (CH_2), 31.9 (CH_2), 27.8 (CH_2), 25.5 (CH_2), 25.2 (CH_2), 22.8 (CH_2), 21.7 (CH_3), 21.6 (CH_2), 20.6 (CH_2), 20.5 (CH_2), 19.5 (CH_3), 17.9 (CH), 17.2 (CH_3), 16.6 (CH_3), 16.1 (CH) ppm.

^{77}Se NMR (95 MHz, CDCl_3) δ = 328.20 (**63**), 312.22 (**63**) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{29}\text{H}_{38}\text{O}_2\text{Se} + \text{Na}]^+$: 521.1931; found: 521.1918

2.3.5. Synthesis of arylcyclopropanes

*Synthesis of 3-((1R,2R)-2-(3,4-difluorophenyl)cyclopropyl)quinoline (**64**)*



This procedure has been modified from the original protocol developed by Aggarwal.^[5] An 8 mL vial was charged with a stirring bar, redox-active ester **23** (51.5 mg, 0.15 mmol, 1.0 equiv) and 2,2'-bibenzo[*d*][1,3,2]dioxaborole (B_2cat_2 , 53.5 mg, 0.23 mmol, 1.5 equiv), and degassed DMF (1.5 mL, 0.1 M) was added. Then, Ar was flushed to displace the air in the vial. (Note: According to the original procedure, it is very important to purge the vial headspace with Ar or N_2 prior to initiating the photoinduced borylation reaction). The vial was capped and the mixture was stirred under blue LED lights during 6 hours. After this time, the lights were removed, the solution was allowed to cool to room temperature and a solution of 2,3-dimethylbutane-2,3-diol (pinacol, 71.0 mg, 0.60 mmol, 4 equiv) in Et_3N (0.45 mL) was added. The resulting brown solution was stirred for 1.5 hours. The reaction mixture was transferred into a separating funnel containing H_2O (10 mL) and NH_4Cl (saturated aqueous solution, 10 mL). The mixture was extracted with pentane (3 x 25 mL) and volatiles were removed *in vacuo* (Note: extraction with other solvents, such as Et_2O or EtOAc led to lower yields). The resulting organic residue was transferred to a MW vial and $\text{Pd}(\text{dba})_2$ (4.3 mg, 0.0075 mmol, 0.05 equiv) and $\text{P}(\text{2-furyl})_3$ (3.5 mg, 0.015 mmol, 0.1 equiv) were added to the vial before sealing it. The reaction vessel was flushed with Ar, and toluene (3 mL), aqueous 3 M KOH (0.3 mL, 0.9 mmol, 6 equiv) and 3-bromoquinoline (125 mg, 0.6 mmol, 4 equiv) were added. The resulting biphasic red mixture was stirred at room temperature for 10

minutes, while it became yellow. Then, the vial was placed in an oil bath at 110 °C and stirred for 16 hours. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure **64** as a yellow solid (29 mg, 69% yield, d.r. >20:1). (*R,R*)-**64** was obtained with a 97.9:2.1 enantiomeric ratio determined by HPLC using a Chiralpak-ID column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 12.4$ min, $\tau_{\text{minor}} = 10.6$ min.

Appearance: yellow solid.

m.p.: 61 – 63 °C.

TLC $R_f = 0.3$ (petroleum ether/EtOAc 4:1).

$[\alpha]_{20}^D = -358.9$ ($c = 0.8$, CHCl_3).

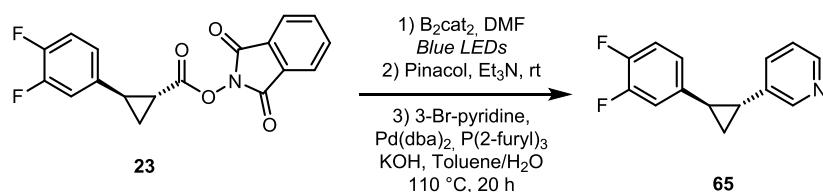
^1H NMR (400 MHz, CDCl_3) $\delta = 8.79$ (d, $J = 2.3$ Hz, 1H), 8.08 (dd, $J = 8.4, 1.0$ Hz, 1H), 7.79 (d, $J = 2.3$ Hz, 1H), 7.76 (dd, $J = 8.1, 1.4$ Hz, 1H), 7.66 (ddd, $J = 8.4, 6.9, 1.5$ Hz, 1H), 7.53 (ddd, $J = 8.1, 6.9, 1.2$ Hz, 1H), 7.09 (dt, $J = 10.2, 8.3$ Hz, 1H), 6.96 (ddd, $J = 11.4, 7.5, 2.2$ Hz, 1H), 6.91 (ddt, $J = 8.0, 3.7, 1.7$ Hz, 1H), 2.34 – 2.23 (m, 2H), 1.61 (dt, $J = 8.8, 5.8$ Hz, 1H), 1.52 (dt, $J = 8.7, 5.8$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 150.5$ (dd, $J = 248.0, 12.8$ Hz, C_F), 150.4 (CH), 147.1 (C_q), 149.0 (dd, $J = 246.4, 12.7$ Hz, C_F), 138.9 (dd, $J = 5.8, 3.7$ Hz, C_q), 134.7 (C_q), 131.2 (CH), 129.4 (CH), 128.9 (CH), 128.1 (C_q), 127.4 (CH), 127.0 (CH), 122.1 (dd, $J = 6.1, 3.5$ Hz, CH), 117.3 (d, $J = 17.2$ Hz, CH), 114.8 (d, $J = 17.6$ Hz, CH), 27.3 (CH), 25.7 (CH), 18.0 (CH_2) ppm.

^{19}F NMR (377 MHz, CDCl_3) $\delta = -137.8$ (d, $^3J_{\text{FF}} = 21.1$ Hz), -141.5 (d, $^3J_{\text{FF}} = 21.2$ Hz) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{18}\text{H}_{13}\text{F}_2\text{N}+\text{H}]^+$: 282.1089; found: 282.1102.

Synthesis of 3-((1*R*,2*R*)-2-(3,4-difluorophenyl)cyclopropyl)pyridine (**65**)



This procedure has been modified from the original protocol developed by Aggarwal.^[5] An 8 mL vial was charged with a stirring bar, redox-active ester **23** (51.5 mg, 0.15 mmol, 1.0 equiv) and 2,2'-bibenzo[*d*][1,3,2]dioxaborole (B_2cat_2 , 53.5 mg, 0.23 mmol, 1.5 equiv), and degassed DMF (1.5 mL, 0.1 M) was added. Then, Ar was flushed to displace the air in the vial. (Note: According to the original procedure, it is very important to purge the vial headspace with Ar or N_2 prior to initiating the photoinduced borylation reaction). The vial was capped and the mixture was stirred under blue LED lights during 6 hours. After this time,

the lights were removed, the solution was allowed to cool to room temperature and a solution of 2,3-dimethylbutane-2,3-diol (pinacol, 71.0 mg, 0.60 mmol, 4 equiv) in Et₃N (0.45 mL) was added. The resulting brown solution was stirred for 1.5 hours. The reaction mixture was transferred into a separating funnel containing H₂O (10 mL) and NH₄Cl (saturated aqueous solution, 10 mL). The mixture was extracted with pentane (3 x 25 mL) and volatiles were removed *in vacuo* (Note: extraction with other solvents, such as Et₂O or EtOAc led to lower yields). The resulting organic residue was transferred to a MW vial and Pd(dba)₂ (4.3 mg, 0.0075 mmol, 0.05 equiv) and P(2-furyl)₃ (3.5 mg, 0.015 mmol, 0.1 equiv) were added to the vial before sealing it. The reaction vessel was flushed with Ar, and toluene (3 mL), aqueous 3 M KOH (0.3 mL, 0.9 mmol, 6 equiv) and 3-bromopyridine (58 µL, 0.6 mmol, 4 equiv) were added. The resulting biphasic red mixture was stirred at room temperature for 10 minutes, while it became yellow. Then, the vial was placed in an oil bath at 110 °C and stirred for 16 hours. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 7:3 to 1:1), affording pure **65** as a pale yellow oil (20 mg, 58% yield, d.r. >20:1). (*R,R*)-**65** was obtained with a 98.0:2.0 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 10.9$ min, $\tau_{\text{minor}} = 13.2$ min.

Appearance: pale yellow oil.

TLC R_f = 0.4 (EtOAc/Petroleum Ether 1:1).

$[\alpha]_{20}^D = -271.9$ ($c = 0.47$, CHCl₃).

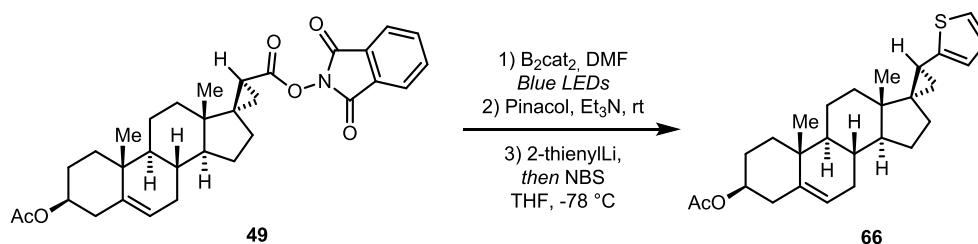
¹H NMR (400 MHz, CDCl₃) δ = 8.47 (d, $J = 2.2$ Hz, 1H), 8.45 (dd, $J = 4.8, 1.6$ Hz, 1H), 7.37 (dt, $J = 7.9, 2.0$ Hz, 1H), 7.22 (ddd, $J = 7.9, 4.8, 0.9$ Hz, 1H), 7.08 (dt, $J = 10.2, 8.4$ Hz, 1H), 6.93 (ddd, $J = 11.5, 7.5, 2.3$ Hz, 1H), 6.89 – 6.84 (m, 1H), 2.15 (ddd, $J = 8.7, 6.0, 4.6$ Hz, 1H), 2.11 (ddd, $J = 8.8, 6.1, 4.6$ Hz, 1H), 1.50 – 1.42 (m, 2H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 150.5 (dd, $J = 248.0, 12.8$ Hz, C_F), 149.0 (dd, $J = 246.2, 12.6$ Hz, C_F), 148.4 (CH), 147.6 (CH), 138.9 (dd, $J = 5.6, 3.8$ Hz, C_q), 137.4 (C_q), 132.8 (CH), 123.5 (CH), 122.0 (dd, $J = 6.0, 3.4$ Hz, CH), 117.3 (d, $J = 17.3$ Hz, CH), 114.8 (d, $J = 17.6$ Hz), 27.0 (CH), 25.4 (CH), 17.9 (CH₂).

¹⁹F NMR (377 MHz, CDCl₃) δ = -137.9 (d, $^3J_{\text{FF}} = 21.2$ Hz), -141.6 (d, $^3J_{\text{FF}} = 21.2$ Hz) ppm.

HRMS (ESI-TOF) calc'd for [C₁₄H₁₁F₂N+H]⁺: 232.0932, found: 232.0944.

Synthesis of the arylcyclopropane derived from androsterone (**66**)



This procedure has been modified from the original protocol developed by Aggarwal.^[5] An 8 mL vial was charged with a stirring bar, redox-active ester **49** (106 mg, 0.2 mmol, 1.0 equiv) and 2,2'-bibenzo[*d*][1,3,2]dioxaborole (B_2cat_2 , 71.0 mg, 0.30 mmol, 1.5 equiv), and degassed DMF (2.0 mL, 0.1 M) was added. Then, Ar was flushed to displace the air in the vial. (*Note: According to the original procedure, it is very important to purge the vial headspace with Ar or N_2 prior to initiating the photoinduced borylation reaction*). The vial was capped and the mixture was stirred under blue LED lights during 14 hours. After this time, the lights were removed, the solution was allowed to cool to room temperature and a solution of 2,3-dimethylbutane-2,3-diol (pinacol, 94.5 mg, 0.80 mmol, 4 equiv) in Et_3N (0.70 mL) was added. The resulting brown solution was stirred for 1.5 hours. The reaction mixture was transferred into a separating funnel containing H_2O (15 mL) and NH_4Cl (saturated aqueous solution, 15 mL). The mixture was extracted with pentane (3 x 40 mL) and volatiles were removed *in vacuo*. The crude material was dissolved in THF. Concurrently, following Aggarwal's procedure,^[23] thiophene (19.2 μL , 0.24 mmol, 1.2 equiv) was dissolved in THF (1 mL) in an 8 mL vial under Ar. The colorless solution was cooled to -78°C and after 10 minutes, *n*-BuLi (0.92 μL , 0.24 mmol, 1.2 equiv, 2.6 M in hexanes) was added dropwise. After stirring at 0°C for 30 minutes the mixture was cooled to -78°C . Then, the THF (0.8 mL) solution of the crude cyclopropylboronate **56** was added dropwise. After 1 hour, a fresh solution *N*-bromosuccinimide (NBS, 0.48 mL, 0.24 mmol, 1.2 equiv, 0.5 M in THF) was added. After 1 hour, sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (1.5 mL) was added and the reaction was allowed to reach room temperature. Extraction with ethyl acetate (3 x 30 mL), washing with brine (50 mL) and drying over anh. MgSO_4 afforded crude cyclopropane **66**, mixed with a 15% of cyclopropylboronate **57**. The crude product was purified by silica gel chromatography (petroleum ether/ Et_2O 98:2), affording pure (–)-**66** (45 mg, 55%, d.r. 9:1).

Appearance: white solid.

m.p.: 170.3 – 172.5 $^\circ\text{C}$.

TLC R_f = 0.4 (petroleum ether/ Et_2O 98:2).

$[\alpha]_{20}^D = -69.3$ ($c = 0.55$, CHCl_3).

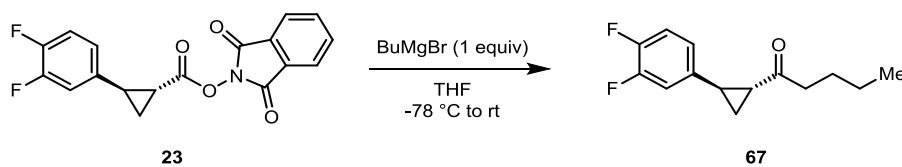
¹H NMR (500 MHz, CDCl₃) δ = 7.05 (dd, J = 5.1, 1.2 Hz, 1H), 6.90 (dd, J = 5.1, 3.5 Hz, 1H), 6.68 (dt, J = 3.5, 1.1 Hz, 1H), 5.40 – 5.37 (m, 1H), 4.61 (dtd, J = 11.5, 6.4, 3.1 Hz, 1H), 2.37 – 2.27 (m, 2H), 2.04 – 1.99 (m, 4H), 1.95 (ddd, J = 9.2, 6.0, 1.0 Hz, 1H), 1.91 – 1.84 (m, 2H), 1.82 – 1.71 (m, 2H), 1.64 – 1.56 (m, 3H), 1.51 (dd, J = 10.6, 5.1 Hz, 1H), 1.45 (dd, J = 12.9, 3.9 Hz, 1H), 1.37 – 1.11 (m, 6H), 1.04 – 0.96 (m, 5H), 0.86 (s, 3H), 0.64 (dd, J = 6.0, 4.8 Hz, 1H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 170.7 (C_q), 146.1 (C_q), 139.8 (C_q), 126.8 (CH), 123.7 (CH), 122.7 (CH), 122.4 (CH), 74.1 (CH), 55.4 (CH), 50.4 (CH), 41.5 (C_q), 40.1 (C_q), 38.3 (CH₂), 37.2 (CH₂), 36.9 (C_q), 33.5 (CH₂), 32.6 (CH), 32.0 (CH₂), 29.8 (CH₂), 27.9 (CH₂), 25.0 (CH₂), 21.6 (CH₃), 20.6 (CH₂), 19.7 (CH₂), 19.5 (CH₃), 17.9 (CH), 16.9 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₂₇H₃₆O₂S+Na]⁺: 447.2328; found: 447.2321.

2.3.6. Synthesis of cyclopropyl ketones

Synthesis of 1-((1*R*,2*R*)-2-(3,4-difluorophenyl)cyclopropyl)pentan-1-one (**67**)



Redox-active ester **23** (103 mg, 0.3 mmol, 1.0 equiv.) was charged in a vial equipped with a PTFE-coated stir bar, and sealed with a pierceable septum screw cap. The atmosphere was exchanged with Ar, and 3.0 mL of dry THF were charged via syringe (final concentration 0.1 M). The solution was placed in an acetone-dry ice bath and butylmagnesium bromide solution (BuMgBr, 1.12 M, 270 μ L, 1.0 equiv.) was added via a Hamilton syringe dropwise over a period of 5 seconds. Once addition was complete, the vial was removed from the cold bath and let warm to room temperature. After 1 hour, 2 mL of water were added, and the mixture was extracted with 3 $\times$ 2 mL portions of diethyl ether. The organic extracts were collected, dried over Na₂SO₄ and filtered through a Pasteur pipette packed with silica gel, and the resulting filtrate was dried *in vacuo*. The crude product was purified by silica gel chromatography (petroleum ether/Et₂O 9:1), affording pure **67** as a clear oil (33 mg, 46% yield, d.r. >20:1). Compound (*S,S*)-**67** was obtained with a 98.6:1.4 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 4.2 min, τ_{minor} = 4.4 min.

Appearance: clear oil.

$[\alpha]_{20}^D$ = +253.1 (c = 0.433, CHCl₃)

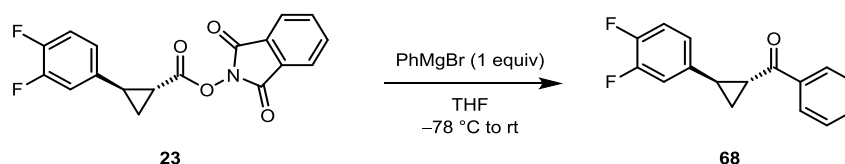
¹H NMR (400 MHz, CDCl₃) δ = 7.06 (dt, J = 10.1, 8.3 Hz, 1H), 6.90 – 6.79 (m, 2H), 2.59 (t, J = 7.4 Hz, 2H), 2.45 (ddd, J = 9.1, 6.5, 4.0 Hz, 1H), 2.13 (ddd, J = 8.2, 5.3, 4.0 Hz, 1H), 1.67 – 1.56 (m, 3H), 1.39 – 1.30 (m, 2H), 1.27 (ddd, J = 8.2, 6.4, 4.3 Hz, 1H), 0.91 (t, J = 7.3 Hz, 3H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 208.8 (C_q), 150.5 (dd, J = 248.0, 12.9 Hz, C_F), 149.2 (dd, J = 246.9, 12.7 Hz, C_F), 137.7 (dd, J = 5.9, 3.7 Hz, C_q), 122.4 (dd, J = 6.1, 3.5 Hz, CH), 117.3 (d, J = 17.3 Hz, CH), 115.0 (d, J = 17.7 Hz, CH), 44.0 (CH₂), 32.1 (CH), 27.7 (d, J = 1.7 Hz, CH), 26.2 (CH₂), 22.5 (CH₂), 18.9 (CH₂), 14.0 (CH₃) ppm.

¹⁹F NMR (377 MHz, CDCl₃) δ = –137.7 (d, $^3J_{\text{FF}}$ = 21.1 Hz), –141.0 (d, $^3J_{\text{FF}}$ = 21.6 Hz) ppm.

HRMS (ESI-TOF) calc'd for [C₁₄H₁₆F₂O + H]⁺: 239.1242; found: 239.1279.

Synthesis of phenyl((1R,2R)-2-(p-tolyl)cyclopropyl)methanone (68)



Redox-active ester **23** (103 mg, 0.3 mmol, 1.0 equiv.) was charged in a vial equipped with a PTFE-coated stir bar, and sealed with a pierceable septum screw cap. The atmosphere was exchanged with Ar, and 3.0 mL of dry THF were charged via syringe (final concentration 0.1 M). The solution was placed in an acetone-dry ice bath and butylmagnesium bromide solution (3.0 M, 100 μ L, 1.0 equiv) was added via a Hamilton syringe dropwise over a period of 5 seconds. Once addition was complete, the vial was removed from the cold bath and let warm to room temperature. After 1 hour, 2 mL of water were added, and the mixture was extracted with 3 $\times$ 2 mL portions of diethyl ether. The organic extracts were collected, dried over Na₂SO₄ and filtered through a Pasteur pipette packed with silica gel, and the resulting filtrate was dried *in vacuo*. The crude product was purified by silica gel chromatography (petroleum ether/Et₂O 9:1), affording pure **68** as a clear oil (46 mg, 62% yield, d.r. >20:1). Compound (*R,R*)-**68** was obtained with a 98.0:2.0 enantiomeric ratio determined by HPLC using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 6.3 min, τ_{minor} = 5.5 min.

Appearance: clear oil.

$[\alpha]_{25.2}^{\text{D}}$ = –161.8 (c = 0.152, CHCl₃)

¹H NMR (400 MHz, CDCl₃) δ = 8.05 – 7.93 (m, 2H), 7.64 – 7.54 (m, 1H), 7.48 (dd, J = 8.3, 6.9 Hz, 2H), 7.09 (dt, J = 10.1, 8.3 Hz, 1H), 7.02 – 6.86 (m, 2H), 2.85 (ddd, J = 8.2, 5.3, 4.0

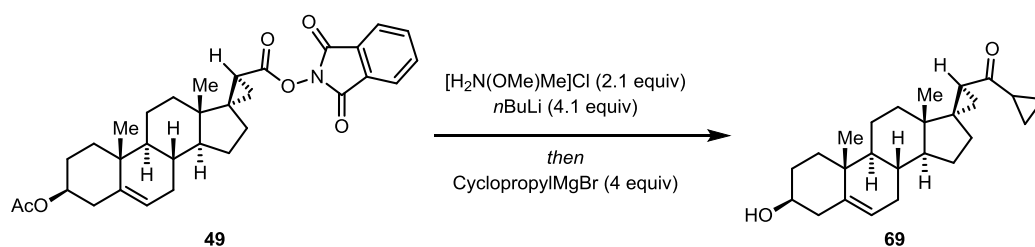
Hz, 1H), 2.67 (ddd, $J = 8.9, 6.5, 4.0$ Hz, 1H), 1.90 (ddd, $J = 9.0, 5.3, 4.3$ Hz, 1H), 1.49 (ddd, $J = 8.2, 6.5, 4.3$ Hz, 1H) ppm.

^{13}C NMR (101 MHz, CDCl_3) $\delta = 198.1$ (C_q), 150.5 (dd, $J = 248.3$ Hz, 12.9 Hz, C_F), 149.3 (dd, $J = 247.1$ Hz, 12.7 Hz, C_F), 137.7 (dd, $J = 5.9$ Hz, 3.8 Hz, C_q), 137.6 (C_q), 133.3 (CH), 128.8 (CH), 128.2 (CH), 122.6 (dd, $J = 6.2$ Hz, 3.4 Hz, CH), 117.4 (d, $J = 17.3$ Hz, CH), 115.2 (d, $J = 17.6$ Hz, CH), 29.2 (CH), 28.8 (d, $J = 1.5$ Hz, CH), 19.3 (CH_2) ppm.

^{19}F NMR (376 MHz, CDCl_3) $\delta = -137.6$ (d, $^3J_{\text{FF}} = 21.1$ Hz), -140.7 (d, $^3J_{\text{FF}} = 21.1$ Hz), ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{16}\text{H}_{12}\text{F}_2\text{O} + \text{Na}]^+$: 281.0748; found: 281.0727.

Synthesis of the cyclopropylketone derived from androsterone (**69**)



Freshly titrated butyllithium (1.9 equiv. relative to the ammonium salt, 550 μL , 1.46 mmol) was added dropwise at 0 $^\circ\text{C}$ to a suspension of finely powdered *N,O*-dimethylhydroxylammonium chloride (73.2 mg, 0.75 mmol, 2.1 equiv.) in 12 mL of dry THF, and the resulting mixture was stirred vigorously for 60 minutes at 0 $^\circ\text{C}$. To this solution, a solution of **49** (133 mg, 0.25 mmol, 1.0 equiv.) in dry THF (10 mL) was added dropwise at RT. Formation of the Weinreb amide was confirmed by TLC analysis. At this point, the reaction mixture was placed in an ice bath and cyclopropylmagnesium bromide (1.65 mL, 1.43 mmol, 4.0 equiv.) was added dropwise. Once complete consumption of the Weinreb amide was observed by TLC, the reaction mixture was quenched with 10 mL of sat. NH_4Cl . The mixture was extracted with 3×20 mL of diethyl ether. The organic extracts were collected, dried over Na_2SO_4 and filtered through a Pasteur pipette packed with silica gel, and the resulting filtrate was concentrated *in vacuo*. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 4:1), affording pure (+)-**69** as a white solid (60 mg, 46% yield, d.r.>20:1)

Appearance: white solid.

m.p.: 161.0 – 164.2 $^\circ\text{C}$

$[\alpha]_{25}^{\text{D}}$ = +62.8 ($c = 0.6$, CHCl_3)

¹H NMR (500 MHz, CDCl₃) δ = 5.38 (dt, J = 5.4, 2.1 Hz, 1H), 3.54 (tt, J = 11.2, 4.6 Hz, 1H), 2.40 – 2.18 (m, 2H), 2.12 – 1.96 (m, 3H), 1.93 – 1.71 (m, 4H), 1.70 – 1.39 (m, 8H), 1.35 – 1.05 (m, 7H), 1.04 (s, 3H), 1.03 – 0.93 (m, 2H), 0.87 (s, 3H), 0.86 – 0.80 (m, 2H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 209.3 (C_q), 140.9 (C_q), 121.7 (CH), 71.9 (CH), 54.7 (CH), 50.4 (CH), 45.6 (C_q), 42.4 (CH₂), 41.9 (C_q), 37.4 (CH₂), 36.8 (C_q), 33.4 (CH₂), 32.8 (CH), 31.9 (CH₂), 31.8 (CH₂), 30.2 (CH), 29.4 (CH₂), 24.8 (CH₂), 21.8 (CH), 20.7 (CH₂), 20.5 (CH₂), 19.6 (CH₃), 17.6 (CH₃), 10.3 (CH₂), 10.0 (CH₂) ppm.

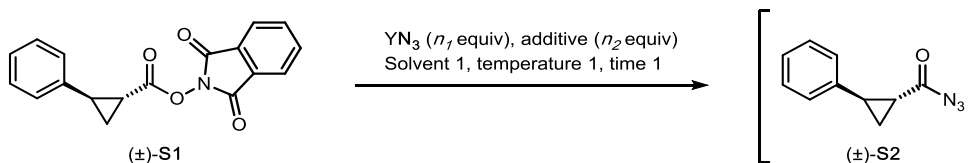
HRMS (ESI-TOF) calc'd for [C₂₅H₃₆O₂+Na]⁺: 391.2608, found: 391.2599.

2.3.7. Synthesis of aminocyclopropanes by Curtius rearrangement

Optimization of the formation of acylazide S2 intermediate from N-hydroxyphthalimide ester S1

A 2.5 mL screw-cap vial was charged with activated ester **S1** (1 equiv). The solid was dissolved in *solvent 1* [0.1 M] and an azide source Y-N₃ (n_1 equiv) was added solid or as a solution in deionized water [3:1 *solvent 1*/H₂O ratio]. An *additive* (n_2 equiv) was added in several entries. The vial was sealed with a screw-cap and the mixture stirred vigorously at *temperature 1* for *time 1* hours (see **table S1** for details).

If a crude NMR was measured at this stage, the mixture was partitioned between deionized water (10 mL) and EtOAc (5 mL) and the separated aqueous layer re-extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated. 1,3,5-Trimethoxybenzene (known amount) was added to the crude mixture which was fully dissolved in CDCl₃ and placed in an NMR tube. The CH signal α to the carbonyl was used as reference and integrated against the internal standard ArCH signal.

Table S1: Optimization of the reaction conditions for the formation of acylacide **S2**:

Entry	Y-N ₃ (n_1 equiv)	Additive (n_2 equiv)	Solvent 1	Temp. 1	Time 1 (h)	S2 ^a (%) / Unreacted S1 ^a (%)
1	NaN ₃ (3)	–	Acetone/H ₂ O	rt	5	29 / 66
2	TMSN ₃ (6)	–	Et ₂ O	rt	24	<5% conv. (insoluble)
3	TMSN ₃ (6)	–	EtOAc	rt	5	36 / 60
4	DPPN ₃ (3)	Et ₃ N	PhCH ₃	rt	24	30 / 70
5	DPPN ₃ (2)	–	PhCH ₃	rt	24	0 / 100
6	DPPN ₃ (3)	Imid.	PhCH ₃	rt	24	50 / 50
7	NaN ₃ (3)	TBSCl	Acetone/H ₂ O	rt	5	90 / 8
8	NaN ₃ (3)	HCl _{aq.} 1M	Acetone	rt	3-16	91 / 5
9	NaN ₃ (3)	HCl _{aq.} 1M	Acetone	rt	3-16	91 / 5
10	NaN ₃ (4)	HCl _{aq.} 1M	Acetone	rt	16	90-93 / 4-6

^a Yields and remaining amount of starting material were determined by crude ¹H NMR against 1,3,5-trimethoxybenzene as internal standard.

Study of the Curtius rearrangement of model *N*-hydroxyphthalimide ester **S1**

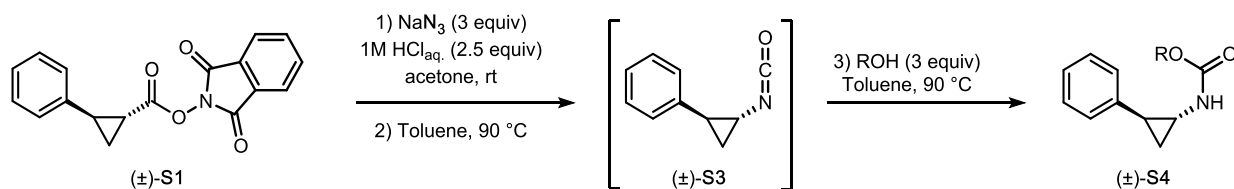
A 2.5 mL screw-cap vial was charged with activated ester **S1** (1 equiv). The solid was dissolved in acetone [0.1 M] and an solid NaN₃ (3 equiv) was added followed by addition of 1 M aqueous HCl (2.5 equiv). The vial was sealed with a screw-cap and the mixture stirred vigorously at room temperature for 16 hours. The crude mixture was then filtered through a short pad of silica gel eluting with heptane/EtOAc 95:5, the relevant fractions combined and concentrated *in vacuo*. The resulting oil was dissolved in toluene and transferred to a dry MW vial equipped with a magnetic stir bar, under nitrogen. The solution was heated at 90 °C for 2 hours then allowed to cool to room temperature.

If a crude NMR was acquired at this stage: the solvent was removed *in vacuo*, the residue dissolved in CDCl₃, 1,3,5-trimethoxybenzene (known amount) was added to the solution, which was homogenized and placed in an NMR tube. The CH signal α to the nitrogen was used as reference and integrated against the internal standard ArCH signal.

If the crude isocyanate was trapped in a one-pot procedure: to the crude isocyanate solution in toluene, was added alcohol ROH (3 equiv), the MW vial was sealed (with a MW cap), and the solution heated at 90 °C for 16 hours. The resulting solution was concentrated under vacuum and the crude mixture dissolved in CDCl₃, 1,3,5-trimethoxybenzene (known amount) was added to the solution, which was homogenized and placed in an NMR tube. The CH signal α

to the nitrogen was used as reference and integrated against the internal standard ArCH signal. (Note: the final carbamate is rotameric, all signals are broad in $CDCl_3$ at 25 °C).

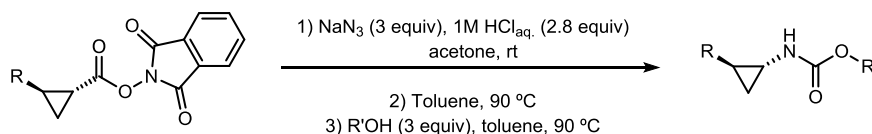
Table S2: Trapping of isocyanate **S3** with different alcohols:



Entry	S3 ³ (%) / unreacted S1 ^a (%)	ROH	S4 ^a
1	85 / 6	—	—
2	—	BnOH	75–80 (78) ^b
3	—	FmOH ^c	60–65 (10) ^d
4	—	TMSEtOH ^e	>70

^a Yields and remaining amount of starting material were determined by crude NMR against 1,3,5-trimethoxybenzene as internal standard; ^b Isolated yield after purification by column chromatography on silica gel; ^c FmOH = 9-fluorenemethanol, 2 equivalents were used in this case; ^d unreacted **S1**; ^e TMSEtOH = 2-(trimethylsilyl)ethanol.

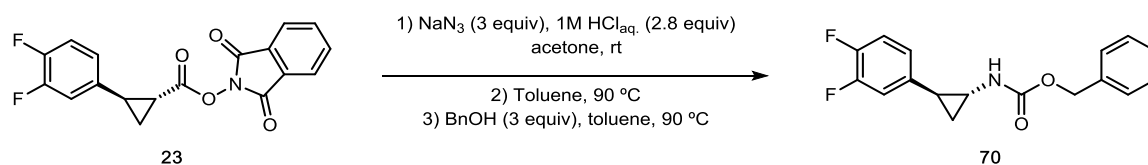
General procedure G for the synthesis of aminocyclopanes:



A 2.5 mL screw-cap vial was charged with a redox-active ester (1 equiv) and sodium azide (NaN_3 , 3 equiv) and a stir bar was added. The solids were then suspended in acetone (0.09–0.12M solution of substrate) and a 1M aqueous solution of HCl (2.8 equiv) was added in one portion. The vial was sealed with a screw-cap and the mixture stirred vigorously at room temperature for 5 hours (monitoring by TLC). [Note: all solids should dissolve within seconds or first couple of minutes; the solution should then turn pale yellow to darker yellow/orange, indicating the release of *N*-hydroxyphthalimide (water soluble)]. The crude solution was then loaded on a short pad of silica gel (usually 4–5 cm length, 2 cm pad diameter) and eluted with heptane/EtOAc 9:1. The relevant fractions (usually first 3–5 fractions) were combined, concentrated *in vacuo* and the crude acylazide transferred to a 7 mL MW vial (using CH_2Cl_2 as solvent and removing the volatiles under a stream of nitrogen). The crude intermediate was dissolved in anhydrous toluene (0.075–0.15M solution) and the solution stirred and heated at 90 °C for 2 hours (TLC monitoring) and allowed to cool to room temperature. An alcohol (3 equiv) was then added to the solution which was further stirred and heated at 90 °C for 16 hours then allowed to cool to room temperature. (Note: If the alcohol used is not volatile

(benzyl alcohol, fluorenamethanol,...) and since it usually co-elutes with the carbamate product, its excess can be easily removed by treatment of this crude solution with triethylamine (5 equiv), a crystal of DMAP, and acetic anhydride (4 equiv), stirring at room temperature for 2 hours). Purification by column chromatography on silica gel eluting with heptane/EtOAc 9:1 to 4:1 afforded the pure carbamate of the aminocyclopropane.

Synthesis of benzyl ((1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl)carbamate (70**)**



General procedure G was applied using **23** (0.175 mmol, 60 mg, 1.0 equiv), NaN₃ (0.52 mmol, 34.1 mg, 3.0 equiv), acetone (1.8 mL), 1M aq. HCl (0.49 mmol, 0.49 mL, 2.8 equiv) then anhydrous toluene (2 mL) and benzyl alcohol (0.52 mmol, 55 μ L, 3 equiv). The crude mixture thus obtained was treated with triethylamine (0.87 mmol, 122 μ L, 5 equiv), a crystal of DMAP and acetic anhydride (0.70 mmol, 66 μ L, 4 equiv) for 2h. The crude product was purified by silica gel chromatography (heptane/EtOAc 95:5 to 4:1), affording pure **70** as a colorless solid (42 mg, 79% yield, >30:1 d.r.). Compound (*R,S*)-**70** was obtained with a 98.3:1.7 enantiomeric ratio determined by SFC using a YMC SA (IA) column [150 $\times$ 4.6 mm, 3 μ m particle size – 5% EtOH/CO₂, 120 bars, 3.5 mL/min, 40 $^{\circ}$ C]: τ_{major} = 3.5 min, τ_{minor} = 4.0 min.

Appearance: colorless solid

TLC R_f = 0.38 (Heptane/EtOAc 7:3).

$[\alpha]_{20}^D$ = –62.0 (c = 0.98, CHCl₃).

m.p.: 75.8 $^{\circ}$ C - 76.4 $^{\circ}$ C

¹H NMR (500 MHz, CDCl₃) δ = 7.45 – 7.27 (m, 5H), 7.13 – 6.55 (br m, 3H), 5.35 – 4.86 (br m, 3H), 2.69 (br s, 1H), 2.06 (br s, 1H), 1.16 (app. br t, J = 6.7 Hz, 2H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 156.9 (C_q), 150.3 (dd, J = 247.7, 12.8 Hz, C_F), 149.1 (dd, J = 246.2, 12.7 Hz, C_F), 137.5 (broad, C_q), 136.3 (C_q), 128.7 (2 $\times$ CH), 128.4 (CH), 128.3 (broad, 2 $\times$ CH), 122.9 (br, CH), 117.1 (d, J = 17.1 Hz, CH), 115.9 (d, J = 17.4 Hz, CH), 67.0 (CH₂), 32.7 (CH), 24.7 (CH), 15.8 (CH₂) ppm.

¹⁹F NMR (471 MHz, CDCl₃) δ = –138.19 (br d with shoulder, $^3J_{\text{FF}}$ = 20.8 Hz), –141.59 (d, $^3J_{\text{FF}}$ = 21.3 Hz) ppm.

¹H NMR (500 MHz, CD₃CN) δ = 7.43 – 7.26 (m, 5H), 7.23 – 6.75 (m, 3H), 6.00 (br s, NH_{maj} rot), 5.69 (br s, NH_{min} rot), 5.18 – 5.01 (br m, 2H), 2.70 – 2.59 (br m, 1H), 2.01 (ddd, J = 9.5, 6.4, 3.2 Hz, 1H), 1.23 – 1.10 (m, 2H) ppm.

¹³C NMR (126 MHz, CD₃CN) δ = 157.8 (C_q), 150.9 (dd, J = 245.0, 12.7 Hz, C_F), 149.5 (dd, J = 243.3, 12.7 Hz, C_F), 139.9 (br, C_q), 138.2 (C_q), 129.4 (2 $\times$ CH), 128.9 (CH), 128.7 (2 $\times$ CH), 123.8 (dd, J = 6.1, 3.3 Hz, CH), 117.9 (d, J = 17.2 Hz, CH), 115.9 (d, J = 17.6 Hz, CH), 66.9 (CH₂), 34.0 (CH), 24.8 (CH), 16.1 (CH₂) ppm.

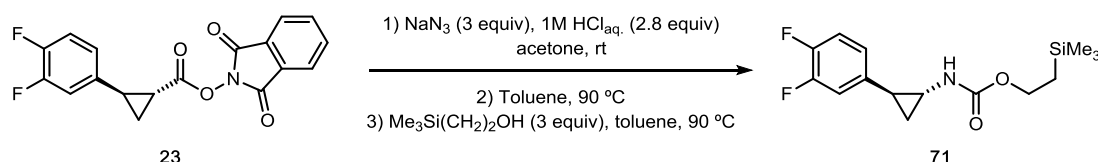
¹⁹F NMR (471 MHz, CD₃CN) δ = -140.53 (d, $^3J_{\text{FF}}$ = 20.8 Hz), -144.24 (br d, $^3J_{\text{FF}}$ = 20.7 Hz) ppm.

¹H NMR (600 MHz, CD₃CN, 323 K) δ = 7.43 – 7.28 (m, 5H), 7.13 (q, J = 8.9 Hz, 1H), 7.08 – 6.85 (br m, 2H), 5.90 (br s, NH), 5.14 – 5.04 (br m, 2H), 2.66 (ddd, J = 7.4, 4.4, 2.1 Hz, 1H), 2.03 (ddd, J = 9.5, 6.4, 3.2 Hz, 1H), 1.20 (ddd, J = 9.6, 5.9, 4.5 Hz, 1H), 1.17 – 1.11 (m, 1H) ppm.

¹³C NMR (151 MHz, CD₃CN, 323 K) δ = 157.9 (C_q), 151.1 (dd, J = 245.0, 12.8 Hz, C_F), 149.7 (dd, J = 243.4, 12.7 Hz, C_F), 140.0 (m, C_q), 138.4 (C_q), 129.5 (2 $\times$ CH), 129.0 (CH), 128.8 (2 $\times$ CH), 124.0 (dd, J = 6.2, 3.4 Hz, CH), 118.1 (d, J = 17.3 Hz, CH), 116.2 (d, J = 17.6 Hz, CH), 67.2 (CH₂), 34.2 (CH), 25.1 (CH), 16.2 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₇H₁₅F₂NO₂ + H]⁺ 304.1144; found 304.1127.

Synthesis of 2-(trimethylsilyl)ethyl ((1R,2S)-2-(3,4-difluorophenyl)cyclopropyl)carbamate (71)



General procedure G was applied using **23** (0.15 mmol, 51.5 mg, 1.0 equiv), NaN₃ (0.45 mmol, 29.3 mg, 3.0 equiv), acetone (1.5 mL), 1M aq. HCl (0.42 mmol, 0.42 mL, 2.8 equiv) then anhydrous toluene (2 mL) and 2-(trimethylsilyl)ethanol (0.45 mmol, 65 μ L, 3 equiv). The crude product was purified by silica gel chromatography (heptane/EtOAc 95:5 to 4:1), affording pure **71** as a pale yellow oil (41 mg, 87% yield, >30:1 d.r.). Compound (*R,S*)-**71** was obtained with a 97.8:2.2 enantiomeric ratio determined by SFC using a Lux C4 column [150 $\times$ 4.6 mm, 3 μ m particle size – 5% EtOH/CO₂, 120 bars, 3.5 mL/min, 40 °C]: τ_{major} = 1.3 min, τ_{minor} = 1.7 min.

Appearance: pale yellow oil

TLC R_f = 0.51 (Heptane/EtOAc 7:3).

$[\alpha]_{20}^D = -52.8$ ($c = 0.95$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) $\delta = 7.04$ (q, $J = 8.7$ Hz, 1H), 7.01 – 6.94 (br m, 1H), 6.91 (br s, 1H), 4.96 (br s, NH), 4.29 – 4.07 (br m, 2H), 2.65 (br s, 1H), 2.05 (app. br s, 1H), 1.15 (app. dd, $J = 8.5, 4.7$ Hz, 2H), 1.06 – 0.92 (br m, 2H), 0.03 (s, 9H) ppm.

^{13}C NMR (126 MHz, CDCl_3) $\delta = 157.4$ (C_q), 150.3 (dd, $J = 247.6, 12.8$ Hz, C_F), 149.1 (dd, $J = 246.1, 12.7$ Hz, C_F), 137.6 (dd, $J = 5.9, 3.7$ Hz, C_q), 123.0 (br, CH), 117.1 (d, $J = 17.2$ Hz, CH), 115.9 (d, $J = 17.2$ Hz, CH), 63.4 (CH_2), 32.6 (CH), 24.8 (CH), 17.9 (CH_2), 15.8 (CH_2), –1.4 (3 x CH_3) ppm.

^{19}F NMR (471 MHz, CDCl_3) $\delta = -138.29$ (d, $^3J_{\text{FF}} = 21.3$ Hz), –141.69 (br d with shoulder, $^3J_{\text{FF}} = 20.0$ Hz) ppm.

^1H NMR (500 MHz, CD_3CN) $\delta = 7.19$ – 7.11 (m, 1H), 7.02 (ddd, $J = 12.0, 7.7, 2.0$ Hz, 1H), 6.98 – 6.90 (br m, 1H), 5.80 (br s, $\text{NH}_{\text{maj rot}}$), 5.53 (br s, $\text{NH}_{\text{min rot}}$), 4.17 – 4.05 (m broad, 2H), 2.65 – 2.56 (br m, 1H), 1.98 (ddd, $J = 9.4, 6.4, 3.2$ Hz, 1H), 1.17 (dt, $J = 9.6, 5.2$ Hz, 1H), 1.12 (app. q, $J = 6.3$ Hz, 1H), 0.99 – 0.91 (m, 2H), 0.02 (s, 9H) ppm.

^{13}C NMR (126 MHz, CD_3CN) $\delta = 158.0$ (C_q), 150.9 (dd, $J = 244.9, 12.8$ Hz, C_F), 149.4 (dd, $J = 243.2, 12.7$ Hz, C_F), 140.0 (m broad, C_q), 123.7 (dd, $J = 6.1, 3.3$ Hz, CH), 117.9 (d, $J = 17.2$ Hz, CH), 115.9 (d, $J = 17.6$ Hz, CH), 63.3 (CH_2), 34.0 (CH), 24.9 (CH), 18.3 (CH_2), 16.1 (CH_2), –1.5 (3 x CH_3) ppm.

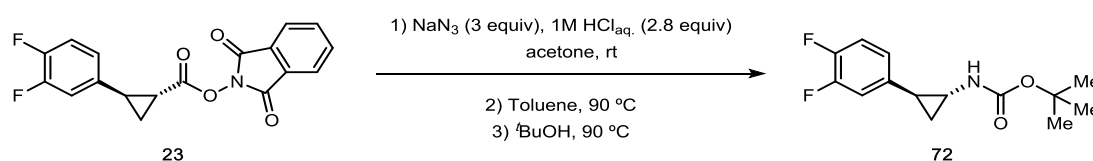
^{19}F NMR (471 MHz, CD_3CN) $\delta = -140.55$ (br d with shoulder, $^3J_{\text{FF}} = 15.9$ Hz), –144.28 (br d, $^3J_{\text{FF}} = 19.6$ Hz) ppm.

^1H NMR (600 MHz, CD_3CN , 323K) $\delta = 7.18$ – 7.11 (m, 1H), 7.04 (ddd, $J = 12.0, 7.7, 2.1$ Hz, 1H), 6.96 (dq, $J = 6.1, 1.7$ Hz, 1H), 5.68 (br s, NH), 4.13 (app. dd, $J = 9.0, 7.4$ Hz, 2H), 2.62 (ddd, $J = 7.5, 3.1, 1.4$ Hz, 1H), 2.00 (ddd, $J = 9.5, 6.4, 3.2$ Hz, 1H), 1.20 – 1.15 (m, 1H), 1.15 – 1.10 (m, 1H), 1.00 – 0.93 (m, 2H), 0.03 (s, 9H) ppm.

^{13}C NMR (151 MHz, CD_3CN , 323 K) $\delta = 158.1$ (C_q), 151.1 (dd, $J = 245.0, 12.8$ Hz, C_F), 149.6 (dd, $J = 243.4, 12.7$ Hz, C_F), 140.2 (dd, $J = 5.9, 3.7$ Hz, C_q), 123.9 (dd, $J = 6.2, 3.4$ Hz, CH), 118.0 (d, $J = 17.5$ Hz, CH), 116.2 (d, $J = 17.6$ Hz, CH), 63.5 (CH_2), 34.1 (CH), 25.1 (br s, CH), 18.5 (CH_2), 16.2 (CH_2), –1.3 (3 x CH_3) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{15}\text{H}_{21}\text{F}_2\text{NO}_2\text{Si} + \text{NH}_4]^+$ 331.1648; found 331.1644.

Synthesis of tert-butyl ((1R,2S)-2-(3,4-difluorophenyl)cyclopropyl)carbamate (72)



A modification of general procedure G was applied using **23** (0.175 mmol, 60.0 mg, 1.0 equiv), NaN₃ (0.525 mmol, 34.1 mg, 3.0 equiv), acetone (1.9 mL), 1M aq. HCl (0.48 mmol, 0.48 mL, ~2.8 equiv). After filtration on silica gel of the reaction mixture and concentration of the solvents, the crude carboxyl azide was transferred to a MW vial (removing the volatiles under a stream of nitrogen), dissolved in anhydrous toluene (0.5 mL) and heated at 90 °C for 2 hours under nitrogen. High grade anhydrous *tert*-butanol (1.5 mL) was then added, the MW vial was sealed and the resulting solution heated at 90 °C for 24 hours. The crude mixture thus obtained was concentrated *in vacuo* and the resulting crude was purified by silica gel chromatography (heptane/EtOAc 95:5 to 4:1), affording pure **72** as a colorless solid (32.8 mg, 70% yield, >30:1 d.r.). Compound (*R,S*)-**72** was obtained with a 98.5:1.5 enantiomeric ratio determined by SFC using a Whelk-O1 column [150×4.6 mm, 3 μm particle size – 5% *i*PrOH/CO₂, 120 bars, 3.5 mL/min, 40 °C]: τ_{major} = 1.8 min, τ_{minor} = 2.1 min.

Appearance: colorless solid

m.p.: 110.8 °C - 111.8 °C

TLC R_f = 0.45 (Heptane/EtOAc 7:3).

[α]₂₀^D = –63.2 (*c* = 1.10, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.03 (dt, *J* = 10.2, 8.4 Hz, 1H), 7.00 – 6.92 (m, 1H), 6.89 (br s, 1H), 4.84 (br s, 1H), 2.69 – 2.59 (m, 1H), 2.07 – 1.96 (m, 1H), 1.45 (s, 9H), 1.18 – 1.07 (m, 2H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 156.4 (C_q), 150.3 (dd, *J* = 247.5, 12.8 Hz, C_F), 149.0 (dd, *J* = 245.9, 12.7 Hz, C_F), 137.9 (dd, *J* = 5.7, 3.7 Hz, C_q), 122.8 (br s, CH), 117.1 (d, *J* = 17.1 Hz, CH), 115.8 (br d, *J* = 17.7 Hz, CH), 80.0 (C_q), 32.5 (br, CH), 28.5 (CH₃), 24.7 (br, CH), 16.0 (CH₂) ppm.

¹⁹F NMR (471 MHz, CDCl₃) δ = –138.33 (d, ³*J*_{FF} = 21.1 Hz), –141.84 (br d, ³*J*_{FF} = 20.7 Hz) ppm.

¹H NMR (500 MHz, CD₃CN) δ = 7.15 (dt, *J* = 10.8, 8.5 Hz, 1H), 7.02 (ddd, *J* = 12.2, 7.7, 2.2 Hz, 1H), 6.94 (dq, *J* = 6.2, 2.0 Hz, 1H), 5.63 (br s, NH_{maj} rot), 5.34 (br s, NH_{min} rot), 2.63 – 2.51 (m, 1H), 1.96 (ddt, *J* = 9.5, 6.3, 3.2 Hz, 1H), 1.40 (s, 9H), 1.15 (ddd, *J* = 9.5, 5.8, 4.6 Hz, 1H), 1.10 (dt, *J* = 7.6, 6.1 Hz, 1H) ppm.

¹³C NMR (126 MHz, CD₃CN) δ = 157.2 (C_q), 150.9 (dd, *J* = 244.7, 12.8 Hz, C_F), 149.4 (dd, *J* = 243.1, 12.7 Hz, C_F), 140.2 (dd, *J* = 6.2, 3.6 Hz, C_q), 123.7 (dd, *J* = 5.8, 3.2 Hz, CH), 117.9 (d, *J* = 17.2 Hz, CH), 115.8 (d, *J* = 17.6 Hz, CH), 79.6 (C_q), 33.9 (CH), 28.6 (CH₃), 24.9 (CH), 16.2 (CH₂) ppm.

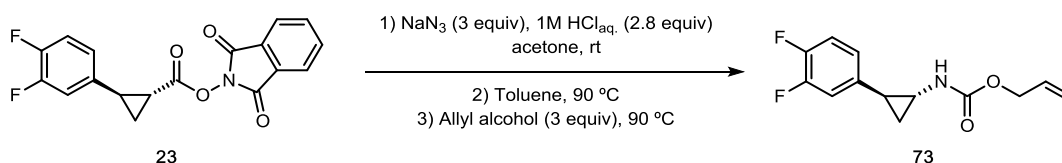
¹⁹F NMR (471 MHz, CD₃CN) δ = -140.64 (br d, $^3J_{\text{FF}}$ = 19.8 Hz, F¹ major rotamer), -140.77 (br s, F¹ minor rotamer), -144.42 (br d with shoulder, $^3J_{\text{FF}}$ = 20.1 Hz, F²) ppm.

¹H NMR (600 MHz, CD₃CN, 323 K) δ = 7.17 (dt, J = 10.8, 8.5 Hz, 1H), 7.05 (ddd, J = 12.1, 7.7, 2.2, 1H), 7.00 – 6.95 (m, 1H), 5.53 (br s, NH), 2.61 (ddt, J = 6.0, 4.5, 3.0 Hz, 1H), 1.99 (ddt, J = 9.1, 6.1, 3.0 Hz, 1H), 1.43 (s, 9H), 1.17 (ddd, J = 9.5, 5.8, 4.6 Hz, 1H), 1.12 (dt, J = 7.6, 6.1 Hz, 1H) ppm.

¹³C NMR (151 MHz, CD₃CN, 323 K) δ = 157.4 (C_q), 151.1 (dd, J = 244.9, 12.8 Hz, C_F), 149.6 (dd, J = 243.2, 12.7 Hz, C_F), 140.4 (dd, J = 6.1, 3.6 Hz, C_q), 123.9 (dd, J = 6.2, 3.3 Hz, CH), 118.0 (d, J = 17.4 Hz, CH), 116.1 (d, J = 17.6 Hz, CH), 79.8 (C_q), 34.1 (CH), 28.7 (CH₃), 25.2 (CH), 16.3 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₄H₁₇F₂NO₂ + H]⁺ 270.1300; found 270.1302.

Synthesis of allyl ((1R,2S)-2-(3,4-difluorophenyl)cyclopropyl)carbamate (73)



General procedure G was applied using **23** (0.15 mmol, 52 mg, 1.0 equiv), NaN₃ (0.45 mmol, 29.5 mg, 3.0 equiv), acetone (1.5 mL), 1M aq. HCl (0.42 mmol, 0.42 mL, 2.8 equiv) then anhydrous toluene (2 mL) and allyl alcohol (0.45 mmol, 31 μ L, 3 equiv). The crude product was purified by silica gel chromatography (heptane/EtOAc 9:1 to 4:1), affording pure **73** as a colorless solid (30 mg, 78% yield, >30:1 d.r.). Compound (*R,S*)-**73** was obtained with a 98.1:1.9 enantiomeric ratio determined by SFC using a Whelk-O1 column [150×4.6 mm, 3 μ m particle size – 5% EtOH/CO₂, 120 bars, 3.5 mL/min, 40 °C]: τ_{major} = 2.3 min, τ_{minor} = 2.7 min.

Appearance: colorless solid

m.p.: 72.9 °C - 73.5 °C

TLC R_f = 0.36 (Heptane/EtOAc 7:3).

$[\alpha]_{20}^{\text{D}}$ = -65.7 (c = 1.03, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ = 7.09 – 6.81 (m, 3H), 5.92 (dtt, J = 16.3, 10.9, 5.6 Hz, 1H), 5.34 – 5.27 (m, 1H), 5.25 – 5.20 (m, 1H), 5.06 (br s with shoulder, NH), 4.59 (app. br s, 2H), 2.72 – 2.63 (m, 1H), 2.11 – 2.01 (m, 1H), 1.21 – 1.12 (m, 2H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 156.8 (C_q), 150.3 (dd, J = 247.7, 12.8 Hz, C_F), 149.1 (dd, J = 246.2, 12.7 Hz, C_F), 137.5 (dd, J = 5.7, 3.8 Hz, C_q), 132.8 (CH), 123.0 (br, CH), 118.1

(CH₂), 117.1 (d, *J* = 17.2 Hz, CH), 115.9 (d, *J* = 17.4 Hz, CH), 65.8 (CH₂), 32.6 (CH), 24.8 (CH), 15.8 (CH₂) ppm.

¹⁹F NMR (471 MHz, CDCl₃) δ = −138.23 (br d with shoulder, ³*J*_{FF} = 20.7 Hz), −144.60 (d, ³*J*_{FF} = 21.3 Hz) ppm.

¹H NMR (500 MHz, CD₃CN) δ = 7.15 (dt, *J* = 10.8, 8.5 Hz, 1H), 7.03 (ddd, *J* = 12.1, 7.7, 2.1 Hz, 1H), 6.99 – 6.91 (m, 1H), 5.92 (ddt, *J* = 17.2, 10.6, 5.4 Hz, 1H + NH_{maj} rot), 5.63 (br s, NH_{min} rot), 5.28 (d, *J* = 17.2 Hz, 1H), 5.18 (d, *J* = 10.4 Hz, 1H), 4.51 (app. d, *J* = 4.0 Hz, 2H), 2.63 (ddt, *J* = 5.9, 4.5, 3.0 Hz, 1H), 2.01 (ddd, *J* = 9.3, 6.4, 3.1 Hz, 1H), 1.22 – 1.10 (m, 2H) ppm.

¹³C NMR (126 MHz, CD₃CN) δ = 157.6 (C_q), 150.9 (dd, *J* = 244.9, 12.8 Hz, C_F), 149.5 (dd, *J* = 243.3, 12.7 Hz, C_F), 140.0 (br, C_q), 134.5 (CH), 123.8 (dd, *J* = 6.2, 3.3 Hz, CH), 118.0 (d, *J* = 17.2 Hz, CH), 117.5 (br, CH₂), 115.9 (d, *J* = 17.6 Hz, CH), 65.8 (CH₂), 34.0 (CH), 24.8 (CH), 16.1 (CH₂) ppm.

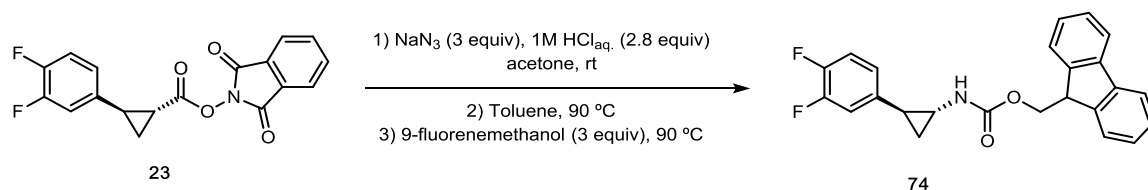
¹⁹F NMR (471 MHz, CD₃CN) δ = −140.60 (br d, ³*J*_{FF} = 20.7 Hz), −144.30 (d, ³*J*_{FF} = 20.9 Hz) ppm.

¹H NMR (600 MHz, CD₃CN, 323K) δ = 7.15 (dt, *J* = 10.8, 8.5 Hz, 1H), 7.04 (ddd, *J* = 12.1, 7.7, 2.2 Hz, 1H), 6.97 (app. dq, *J* = 6.3, 2.0 Hz, 1H), 5.94 (ddt, *J* = 17.2, 10.7, 5.4 Hz, 1H), 5.84 (br s, NH), 5.29 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.18 (dq, *J* = 10.6, 1.3 Hz, 1H), 4.53 (app. d, *J* = 5.2 Hz, 2H), 2.65 (ddt, *J* = 5.9, 4.5, 3.0 Hz, 1H), 2.03 (ddd, *J* = 9.5, 6.4, 3.2 Hz, 1H), 1.22 – 1.17 (m, 1H), 1.15 (dt, *J* = 7.5, 6.2 Hz, 1H) ppm.

¹³C NMR (151 MHz, CD₃CN, 323K) δ = 157.7 (C_q), 151.1 (dd, *J* = 245.0, 12.8 Hz, C_F), 149.7 (dd, *J* = 243.4, 12.7 Hz, C_F), 140.1 (dd, *J* = 6.0, 3.6 Hz, C_q), 134.6 (CH), 124.0 (dd, *J* = 6.2, 3.4 Hz, CH), 118.1 (d, *J* = 17.3 Hz, CH), 117.6 (br, CH₂), 116.2 (d, *J* = 17.7 Hz, CH), 66.0 (CH₂), 34.1 (CH), 25.1 (CH), 16.2 (CH₂) ppm.

HRMS (ESI-TOF) calc'd for [C₁₃H₁₃F₂NO₂ + H]⁺ 254.0987; found 254.0967.

Synthesis of (9H-fluoren-9-yl)methyl ((1R,2S)-2-(3,4-difluorophenyl)cyclopropyl)carbamate (74)



General procedure G was applied using **23** (0.19 mmol, 65 mg, 1.0 equiv), NaN₃ (0.57 mmol, 37 mg, 3.0 equiv), acetone (1.9 mL), 1M aq. HCl (0.53 mmol, 0.53 mL, 2.8 equiv) then

anhydrous toluene (2 mL) and 9-fluorene-methanol (0.57 mmol, 111 mg, 3 equiv). The crude mixture thus obtained was treated with triethylamine (0.80 mmol, 111 μ L, 4.2 equiv), a crystal of DMAP and acetic anhydride (0.76 mmol, 71 μ L, 4 equiv) for 1.5 h. The crude product was purified by silica gel chromatography (heptane/EtOAc 95:5 to 3:1), affording pure **74** as a colorless solid (57 mg, 77% yield, >30:1 d.r.). Compound (*R,S*)-**74** was obtained with a 97.9:2.1 enantiomeric ratio determined by SFC using a Lux A1 (AD) column [150 $\times$ 4.6 mm, 3 μ m particle size – 30% EtOH/CO₂, 120 bars, 3.5 mL/min, 40 $^{\circ}$ C]: τ_{major} = 1.9 min, τ_{minor} = 2.5 min.

Appearance: colorless solid

m.p.: 161.8 – 162.6 $^{\circ}$ C

TLC R_f = 0.34 (Heptane/EtOAc 7:3).

$[\alpha]_{20}^D$ = -49.0 (c = 1.00, CHCl₃).

^1H NMR (500 MHz, CDCl₃) δ = 7.82 – 7.67 (br m, 2H), 7.58 (br s, 2H), 7.45 – 7.15 (br m, 4H), 7.11 – 6.65 (br m, 3H), 5.09 (br s, NH_{maj rot}), 4.95 (br s, NH_{min rot}), 4.46 (br s, 2H), 4.22 (t, J = 6.7 Hz, 1H), 2.72 – 2.65 (m, 1H), 2.13 – 1.92 (br m, 1H), 1.16 (br s, 2H) ppm.

^{13}C NMR (126 MHz, CDCl₃) δ = 156.9 (C_q), 150.3 (dd, J = 247.7, 12.8 Hz, C_F), 149.1 (dd, J = 246.2, 12.7 Hz, C_F), 144.0 (br, C_q), 143.9 (br, C_q), 141.47 (C_q), 141.45 (C_q), 137.5 (br, C_q), 127.9 (2 $\times$ CH), 127.2 (2 $\times$ CH), 125.1 (2 $\times$ CH), 122.9 (br, CH), 120.1 (2 $\times$ CH), 117.2 (d, J = 17.2 Hz, CH), 115.9 (d, J = 15.6 Hz, CH), 66.8 (CH₂), 47.4 (CH), 32.6 (CH), 24.7 (CH), 15.8 (CH₂) ppm.

^{19}F NMR (471 MHz, CDCl₃) δ = -137.82 (br s, F¹ minor rotamer), -138.15 (br d, $^3J_{\text{FF}}$ = 20.7 Hz, F¹ major rotamer), -141.55 (d, $^3J_{\text{FF}}$ = 21.2 Hz, F²) ppm.

^1H NMR (500 MHz, CD₃CN) δ = 7.82 (app. br d, J = 6.2 Hz, 2H), 7.64 (app. br s, 2H), 7.50 – 7.22 (m, 4H), 7.14 (q, J = 8.7 Hz, 1H), 7.08 – 6.80 (br m, 2H), 6.02 (br s, NH_{maj rot}), 5.60 (br s, NH_{min rot}), 4.48 – 4.29 (br m, 2H), 4.21 (t, J = 6.8 Hz, 1H), 2.62 (ddt, J = 5.9, 4.5, 3.0 Hz, 1H), 1.98 (ddd, J = 9.4, 6.4, 3.1 Hz, 1H), 1.23 – 1.00 (m, 2H) ppm.

^{13}C NMR (126 MHz, CD₃CN) δ = 157.7 (C_q), 150.9 (dd, J = 244.8, 12.8 Hz, C_F), 149.5 (dd, J = 243.2, 12.6 Hz, C_F), 145.2 (C_q), 145.1 (br s, C_q), 142.1 (C_q), 142.1 (br s, C_q), 140.0 (dd, J = 6.2, 3.6 Hz, C_q), 128.7 (2 $\times$ CH), 128.1 (2 $\times$ CH), 126.1 (2 $\times$ CH), 123.7 (br s, CH), 121.0 (2 $\times$ CH), 118.0 (d, J = 17.2 Hz, CH), 115.8 (d, J = 17.0 Hz, CH), 66.9 (CH₂–O), 48.1 (CH), 34.0 (CH), 24.8 (CH), 16.1 (CH₂) ppm.

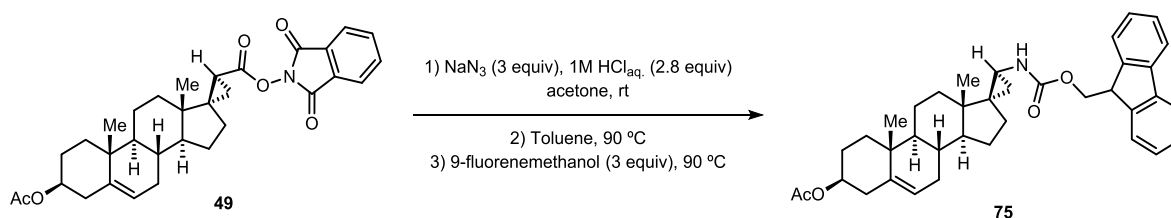
^{19}F NMR (471 MHz, CD₃CN) δ = -140.55 (d, $^3J_{\text{FF}}$ = 20.9 Hz, F¹), -144.26 (br d, $^3J_{\text{FF}}$ = 20.6 Hz, F² major rotamer), -144.50 (br s, F² minor rotamer) ppm.

^1H NMR (600 MHz, CD_3CN , 323 K) δ = 7.82 (app. br d, J = 7.4 Hz, 2H), 7.69 – 7.57 (m, 2H), 7.41 (app. t, J = 7.4 Hz, 2H), 7.37 – 7.26 (m, 2H), 7.14 (dt, J = 10.6, 8.6 Hz, 1H), 7.07 – 6.87 (m, 2H), 5.91 (br s, NH), 4.46 – 4.32 (br m, 2H), 4.23 (t, J = 6.8 Hz, 1H), 2.63 (ddd, J = 7.4, 4.4, 2.1 Hz, 1H), 2.00 (ddd, J = 9.4, 6.3, 3.2 Hz, 1H), 1.22 – 1.05 (m, 2H) ppm.

^{13}C NMR (151 MHz, CD_3CN , 323 K) δ = 157.8 (C_q), 151.1 (dd, J = 245.0, 12.8 Hz, C_F), 149.7 (dd, J = 243.3, 12.7 Hz, C_F), 145.4 (C_q), 145.3 (C_q), 142.3 (C_q), 142.3 (C_q), 140.1 (dd, J = 6.1, 3.6 Hz, C_q), 128.8 ($2 \times \text{CH}$), 128.2 ($2 \times \text{CH}$), 126.2 ($2 \times \text{CH}$), 123.9 (br s, CH), 121.1 ($2 \times \text{CH}$), 118.1 (d, J = 17.6 Hz, CH), 116.1 (d, J = 17.3 Hz, CH), 67.2 (CH_2), 48.4 (CH), 34.1 (CH), 25.1 (CH), 16.3 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{24}\text{H}_{19}\text{F}_2\text{NO}_2 + \text{H}]^+$ 392.1457; found 392.1440.

Synthesis of cyclopropylamine derived from androsterone (**75**)



A modification of general procedure G was applied using **49** (0.094 mmol, 50.0 mg, 1.0 equiv), NaN_3 (0.492 mmol, 32.0 mg, 5.2 equiv), acetone/EtOAc 1:1 (2.0 mL), 1M aq. HCl (0.325 mmol, 325 μL , ~ 3.5 equiv). The biphasic mixture was stirred vigorously at room temperature for 66 hours, whereupon additional NaN_3 (0.046 mmol, 3.0 mg, 0.5 equiv) was added and the biphasic mixture stirred for further 26 hours. After filtration on silica gel of the reaction mixture (washing with Hept/EtOAc 95:5 to 4:1), the relevant fractions were concentrated, the crude carboxyl azide was transferred to a MW vial (removing the volatiles under a stream of nitrogen), dissolved in anhydrous toluene (0.7 mL) and heated at 90 °C for 2.5 hours under nitrogen. 9-Fluorenemethanol (0.282 mmol, 55.4 mg, 3.0 equiv) was then added, the MW vial was sealed and the resulting solution heated at 90 °C for 22 hours then allowed to cool to room temperature. The crude solution thus obtained was diluted with dichloromethane (0.7 mL), treated with triethylamine (0.423 mmol, 59 μL , 4.5 equiv), a crystal of DMAP and acetic anhydride (0.376 mmol, 35 μL , 4 equiv) for 1.5 h. The crude product was purified by silica gel chromatography (heptane/EtOAc 95:5 to 4:1), affording pure (–)-**75** as a colorless solid (26.0 mg, 48% yield, dr >20:1). (*Note*: unreacted starting activated **49** ester (19 mg, 38%) was also recovered during the first filtration on silica $\rightarrow$ reaction yield: 77% brsm).

Appearance: colorless solid

m.p.: 192.5 °C (decomp.)

TLC R_f = 0.41 (Heptane/EtOAc 7:3).

$[\alpha]_{20}^D = -31.7$ ($c = 1.10$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ = 7.76 (d, $J = 7.5$ Hz, 2H), 7.72 – 7.54 (br m, 2H), 7.40 (t, $J = 7.4$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 2H), 5.39 (d, $J = 4.9$ Hz, 1H), 4.82 (br s, $\text{NH}_{\text{maj rot}}$), 4.74 – 4.48 (br m, $1\text{H}_{\text{maj rot}} + 2\text{H}_{\text{min rot}}$), 4.48 – 4.35 (br m, $2\text{H}_{\text{maj rot}} + 1\text{H}_{\text{min rot}}$), 4.33 – 4.17 (br m, 1H), 2.53 – 2.39 (m, 1H), 2.38 – 2.26 (m, 2H), 2.10 – 1.92 (m, 5H), 1.91 – 1.75 (m, 3H), 1.66 – 1.20 (m, 9H), 1.19 – 0.81 (m, 10H), 0.18 (s, 1H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 170.7 (C_q), 157.3 (C_q), 144.14 (C_q), 144.07 (C_q), 141.5 ($2 \times \text{C}_q$), 139.8 (C_q), 127.8 ($2 \times \text{CH}$), 127.14 (CH), 127.13 (CH), 125.2 ($2 \times \text{CH}$), 122.6 (CH), 120.1 ($2 \times \text{CH}$), 74.0 (CH), 66.5 (CH_2), 55.6 (CH), 50.3 (CH), 47.4 (CH), 40.9 (C_q), 38.2 (CH_2), 37.5 (C_q), 37.1 (CH_2), 36.8 (C_q), 33.9 (br, CH_2), 32.4 (CH), 32.0 (CH_2), 29.8 (CH_2), 29.1 (CH_2), 27.9 (CH_2), 24.9 (CH_2), 21.6 (CH_3), 20.6 (CH_2), 19.5 (CH_3), 18.6 (br, CH), 16.7 (CH_3) ppm.

^1H NMR (500 MHz, CD_3CN) δ = 7.82 (d, $J = 7.5$ Hz, 2H), 7.69 – 7.62 (m, 2H), 7.41 (t, $J = 7.5$ Hz, 2H), 7.32 (td, $J = 7.5, 0.9$ Hz, 2H), 5.65 (br s, $\text{NH}_{\text{maj rot}}$), 5.38 (d, $J = 4.0$ Hz, 1H), 5.17 (br s, $\text{NH}_{\text{min rot}}$), 4.57 – 4.15 (m, 4H), 2.38 (br s, $1\text{H}_{\text{maj rot}}$), 2.29 (app. d, $J = 7.7$ Hz, $2\text{H} + 1\text{H}_{\text{min rot}}$), 2.07 – 1.95 (m, 5H), 1.90 – 1.70 (m, 3H), 1.64 – 1.17 (m, 9H), 1.16 – 0.79 (m, 10H), 0.19 (br s, 1H) ppm.

^{13}C NMR (126 MHz, CD_3CN) δ = 171.1 (C_q), 157.9 (C_q), 145.3 (br, C_q), 145.2 (C_q), 142.1 (br, $2 \times \text{C}_q$), 141.0 (C_q), 128.6 ($2 \times \text{CH}$), 128.04 (CH), 128.03 (CH), 126.1 (br with shoulder, $2 \times \text{CH}$), 123.2 (CH), 120.9 ($2 \times \text{CH}$), 74.6 (CH), 66.7 (CH_2), 56.5 (CH), 51.1 (CH), 48.2 (CH), 41.5 (C_q), 38.9 (CH_2), 38.1 (C_q), 37.8 (CH_2), 37.5 (C_q), 34.7 (br, CH_2), 33.1 (CH), 32.6 (CH_2), 29.8 (CH), 29.5 (CH_2), 28.5 (CH_2), 25.4 (CH_2), 21.5 (CH_3), 21.3 (CH_2), 19.7 (CH_3), 18.1 (br, CH), 17.1 (CH_3) ppm.

^1H NMR (400 MHz, CD_3CN , 323 K) δ = 7.82 (d, $J = 7.5$ Hz, 2H), 7.66 (d, $J = 7.5$ Hz, 2H), 7.41 (t, $J = 7.4$ Hz, 2H), 7.36 – 7.30 (m, 2H), 5.47 (br s, NH), 5.39 (d, $J = 4.7$ Hz, 1H), 4.50 (ddt, $J = 16.3, 8.3, 4.5$ Hz, 1H), 4.45 – 4.28 (m, 2H), 4.23 (t, $J = 6.7$, 1H), 2.39 (br s, 1H), 2.31 (d, $J = 7.8$ Hz, 2H), 2.10 – 1.72 (m, 8H), 1.68 – 1.22 (m, 9H), 1.18 – 0.75 (m, 10H), 0.19 (br s, 1H) ppm.

^{13}C NMR (101 MHz, CD_3CN , 323 K) δ = 171.2 (C_q), 158.1 (C_q), 145.53 (C_q), 145.45 (C_q), 142.4 (br, $2 \times \text{C}_q$), 141.3 (C_q), 128.8 ($2 \times \text{CH}$), 128.20 (CH), 128.19 (CH), 126.3 ($2 \times \text{CH}$), 123.3 (CH), 121.1 ($2 \times \text{CH}$), 74.9 (H), 67.0 (CH_2), 56.8 (CH), 51.5 (CH), 48.5 (CH), 41.8 (C_q), 39.1 (CH_2), 38.4 (C_q), 38.1 (CH_2), 37.8 (C_q), 35.0 (CH_2), 33.4 (CH), 32.9 (CH_2), 30.2

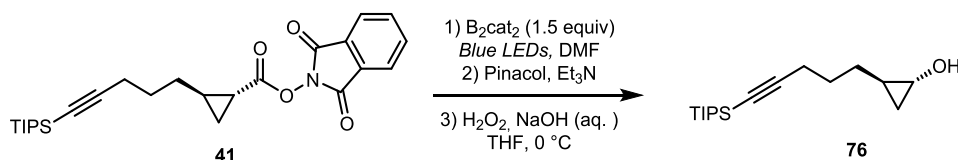
(CH), 29.9 (CH₂), 28.8 (CH₂), 25.6 (CH₂), 21.6 (CH₃), 21.5 (CH₂), 19.9 (CH₃), 18.5 (br, CH), 17.2 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₃₈H₄₅NO₄+Na]⁺ 602.3241; found 602.3244.

2.4. Synthetic applications of redox-active cyclopropanes

2.4.1. Synthesis of grazoprevir® fragment

Synthesis of (1*R*,2*R*)-2-(5-(triisopropylsilyl)pent-4-yn-1-yl)cyclopropan-1-ol (**76**)



General procedure F was applied using **41** (68.0 mg, 0.15 mmol, 1.0 equiv, dr >20:1) and B_2cat_2 (B_2cat_2 , 54 mg, 0.23 mmol, 1.5 equiv, dr >20:1) in DMF (1.5 mL) for 16 hours. Then, pinacol (71 mg, 0.6 mmol, 4 equiv) dissolved in Et_3N (0.45 mL). Extraction with pentane afforded the crude cyclopropylboronate intermediate, which was oxidized according to general procedure F (see above). Crude **76** (d.r. 8.6:1) was purified by silica gel chromatography (Petroleum Ether/ Et_2O 9:1), affording pure (*R,R*)-**76** as a colorless oil (25.2 mg, 60% yield, d.r. >20:1). Optical purity of compound (*R,R*)-**76** was determined by HPLC after benzylation (see below).

Appearance: colorless oil.

TLC R_f = 0.35 (Petroleum Ether/ Et_2O 9:1).

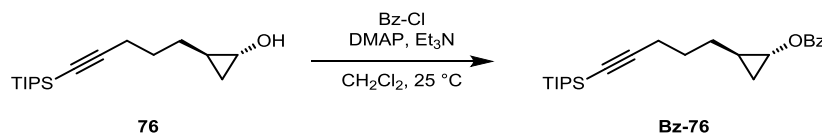
$[\alpha]_{20}^D = -20.4$ ($c = 1.0$, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ = 3.22 (dt, $J = 6.4, 2.6$ Hz, 1H), 2.29 (t, $J = 7.0$ Hz, 2H), 1.93 (br s, 1H), 1.62 (p, $J = 7.2$ Hz, 2H), 1.42 – 1.33 (m, 1H), 1.27 – 1.21 (m, 1H), 1.09 – 0.98 (m, 21H), 0.93 – 0.88 (m, 1H), 0.70 (ddd, $J = 9.9, 5.6, 2.9$ Hz, 1H), 0.33 (dd, $J = 12.0, 6.0$ Hz, 1H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ = 109.1 (C_q), 80.5 (C_q), 52.8 (CH), 30.7 (CH_2), 28.4 (CH_2), 20.5 (CH), 19.7 (CH_2), 18.8 (CH_3), 14.6 (CH_2), 11.5 (CH) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{17}\text{H}_{32}\text{OSi}+\text{Na}]^+$: 303.2115; found: 303.2118.

Synthesis of (1*R*,2*R*)-2-(5-(triisopropylsilyl)pent-4-yn-1-yl)cyclopropyl benzoate (**Bz-76**)



Cyclopropanol **76** (28 mg, 0.1 mmol, 1.0 equiv) was reacted with benzoyl chloride (BzCl , 24 μL , 0.2 mmol, 2.0 equiv), triethylamine (41 μL , 0.3 mmol, 3.0 equiv) and 4-dimethylaminopyridine (DMAP, 6 mg, 0.05 mmol, 0.5 equiv) in CH_2Cl_2 (1.0 mL) for 1 hour. After quenching with H_2O (15 mL), the mixture was extracted with Et_2O (3 x 25 mL).

Combined organic layers were washed with brine (50 mL) and dried over MgSO₄. Solvent was removed by rotatory evaporation and crude cyclopropyl benzoate **Bz-76** was purified by silica gel chromatography (Pentane/Et₂O 98:2), affording pure compound **Bz-76** as a colorless oil (36 mg, 94% yield, d.r. >20:1). (*R,R*)-**Bz-76** was obtained with a 95.4:4.6 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (99.5:0.5), 1.0 mL/min]: $\tau_{\text{major}} = 5.4$ min, $\tau_{\text{minor}} = 5.9$ min.

Appearance: colorless oil.

TLC $R_f = 0.51$ (Pentane/Et₂O 95:5).

$[\alpha]_{20}^D = +3.8$ ($c = 0.1$, CHCl₃).

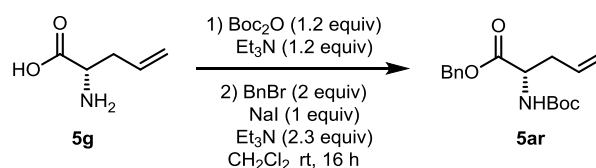
¹H NMR (400 MHz, CDCl₃) $\delta = 8.03 - 7.95$ (m, 2H), 7.59 – 7.50 (m, 1H), 7.47 – 7.38 (m, 2H), 4.06 (dt, $J = 6.7, 2.8$ Hz, 1H), 2.34 (t, $J = 6.9$ Hz, 2H), 1.78 – 1.63 (m, 2H), 1.58 – 1.49 (m, 1H), 1.49 – 1.37 (m, 1H), 1.23 – 1.13 (m, 1H), 1.11 – 0.99 (m, 22H), 0.67 (dd, $J = 13.0, 6.5$ Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) $\delta = 167.5$ (C_q), 133.1 (CH), 130.2 (C_q), 129.7 (CH), 128.5 (CH), 108.9 (C_q), 80.7 (C_q), 54.9 (CH), 30.4 (CH₂), 28.0 (CH₂), 19.7 (CH₂), 18.8 (CH₃), 18.3 (CH), 12.4 (CH₂), 11.5 (CH) ppm. (*Note: the multiplicity was assigned by analogy with the corresponding cyclopropanol, due to missing crosspeaks in the edited HSQC*).

HRMS (ESI-TOF) calc'd for [C₂₄H₃₆O₂Si+Na]⁺: 407.2377; found: 407.2378.

2.4.2. Synthesis of (+)-belactosin A fragment

Synthesis of protected (*S*)-allylglycine (**5ar**)



Under argon atmosphere, a flask was loaded with **5g** (1 g, 8.69 mmol, 1 equiv) and di-*tert*-butyl dicarbonate (2.39 mL, 10.42 mmol, 1.2 equiv) were dissolved in dry CH₂Cl₂ (17 mL). Triethylamine (1.5 mL, 10.42 mmol, 1.2 equiv) were added and the mixture was stirred at room temperature for 8 hours. Once the reaction was done, the volatiles were removed under vacuum. To the crude product, NaI (1.3 g, 8.69 mmol, 1 equiv) was added and the mixture was dissolved in dry CH₂Cl₂ (15 mL). To the resulting suspension, benzyl bromide (2 mL, 17.37 mmol, 2 equiv) and triethylamine (2.78 mL, 19.98 mmol, 2.3 equiv) were added and the reaction was stirred overnight. After the reaction was complete, the mixture was washed with water (2 x 5 mL), the organic phase dried over anhydrous Na₂SO₄ and concentrated under

vacuum. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 9:1), affording pure **5ar** as a colorless oil (1.86 g, 70% yield). NMR data of **77** are in agreement with literature values.^[24]

Appearance: colorless oil.

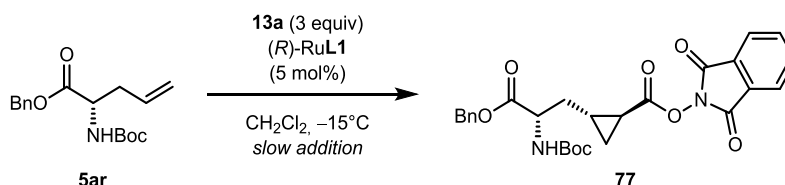
TLC R_f = 0.73 (Petroleum Ether/EtOAc 7:3)

$[\alpha]_{20}^D = -8.5$ ($c = 1.0$, CHCl_3).

^1H NMR (400 MHz, CDCl_3) δ = 7.41 – 7.29 (m, 5H), 5.65 (ddt, $J = 16.0, 11.4, 7.2$ Hz, 1H), 5.26 – 4.99 (m, 4H), 4.42 (q, $J = 6.5$ Hz, 1H), 2.61 – 2.37 (m, 2H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ = 172.0 (C_q), 155.3 (C_q), 135.5 (C_q), 132.3 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 119.3 (CH), 80.0 (C_q), 67.2 (CH_2), 53.1 (CH), 36.9 (CH_2), 28.4 (CH_3).

Synthesis of cyclopropane derived from (S)-allylglycine (77)



Under argon atmosphere, a 20 mL microwave vial equipped with a PTFE coated magnetic stirring bar, was loaded with **5ar** (122 mg, 0.4 mmol) and **(R)-RuL1(CH₃CN)₄PF₆** (12.65 mg, 0.020 mmol) and to it, dry degassed CH_2Cl_2 (2 mL) was added. The mixture was cooled to -15°C and a 0.2 M solution of **13a** (6 mL, 1.200 mmol) in dry degassed CH_2Cl_2 was slowly added over the course of 24 hours using a syringe pump. Once the addition was complete, the reaction was monitored by TLC (petroleum ether/EtOAc 7:3) to check for complete consumption of the starting materials, then the solvent was removed under vacuum. The crude product was purified by silica gel chromatography (petroleum ether/EtOAc 7:3), affording pure (+)-**77** as a white solid (200 mg, 98% yield). The diastereomeric ratio was determined by HPLC chromatography using a Chiralpak-IA column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: 84.3:13.3:0.2:2.2

Appearance: white solid.

m.p.: 72.6 $^\circ\text{C}$ - 75.1 $^\circ\text{C}$

TLC R_f = 0.37 (petroleum ether/EtOAc 7:3)

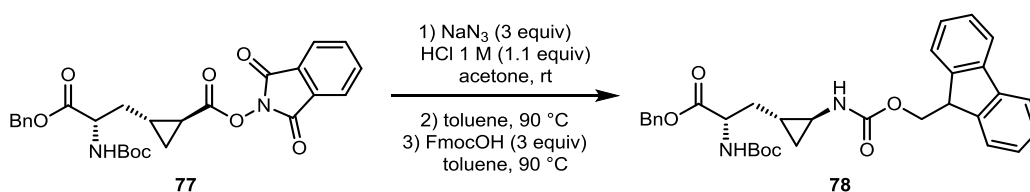
$[\alpha]_{20}^D = +64.8$ ($c = 1.0$, CHCl_3).

¹H NMR (400 MHz, CDCl₃) δ = 7.91 – 7.84 (m, 2H), 7.80 – 7.74 (m, 2H), 7.41 – 7.28 (m, 5H), 5.37 (d, J = 7.9 Hz, 1H), 5.25 – 5.19 (m, 2H), 4.54 – 4.43 (m, 1H), 2.22 – 2.12 (m, 1H), 1.76 – 1.55 (m, 3H), 1.44 (s, 9H), 0.97 – 0.75 (m, 2H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 171.7 (C_q), 170.1 (C_q), 162.0 (C_q), 155.2 (C_q), 135.3 (C_q), 134.8 (CH), 129.1 (C_q), 128.8 (CH), 128.7 (CH), 128.7 (CH), 124.1 (CH), 80.2 (C_q), 67.5 (CH₂), 53.4 (CH), 35.6 (CH₂), 28.4 (CH₃), 20.9 (CH), 17.0 (CH₂), 16.6 (CH) ppm.

HRMS (ESI-TOF) calc'd for [C₂₇H₂₈N₂O₈+Na]⁺: 531.1738; found: 531.1739.

Synthesis of cyclopropylamine derived from (*S*)-allylglycine (**78**)



A 4 mL screw cap vial equipped with a PTFE coated magnetic stirring bar was loaded with **77** (102 mg, 0.2 mmol, 1 equiv) and sodium azide (39 mg, 0.6 mmol, 3 equiv). The reagents were then dissolved in acetone (2 mL) and to it 1M aq. HCl (240 μ L, 0.24 mmol, 1.2 equiv) was added, then the mixture was stirred at room temperature overnight. Once the reaction was complete, monitoring by TLC (petroleum ether/EtOAc 9:1), the crude acyl azide intermediate was purified by silica gel chromatography (petroleum ether/EtOAc 9:1). The purified acyl azide was dried azeotropically with toluene and then transferred in a 4 mL screw-cap vial loaded with a PTFE coated magnetic stirring bar. Dry toluene (1.5 mL) was added and the mixture heated at 90°C for 3 hours, followed by the addition of (9H-fluoren-9-yl)methanol (118 mg, 0.6 mmol, 3 equiv). The reaction mixture was stirred at 90°C for 16 hours, then the solvent was removed under vacuum. The crude product was purified by silica gel chromatography (CH₂Cl₂/EtOAc 99:1), affording pure (–)-**78** as a white solid (72.3 mg, 65%). The NMR data are in agreement with the reported literature³⁶.

Appearance: white solid.

m.p.: 51.2 °C - 53.1 °C

TLC R_f = 0.25 (CH₂Cl₂/EtOAc 99:1)

$[\alpha]_{20}^D$ = –1.40 (c = 1.0, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ = 7.76 (d, J = 7.5 Hz, 2H), 7.58 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.37 – 7.27 (m, 8H), 6.59 (d, J = 9.0 Hz, 1H), 5.16 (d, J = 13.4 Hz, 2H), 4.56 (bs, 1H), 4.44 (bdd, J = 10.6, 7.0 Hz, 1H), 4.36 (bt, J = 8.8 Hz, 1H), 4.20 (bt, J = 6.7 Hz, 1H),

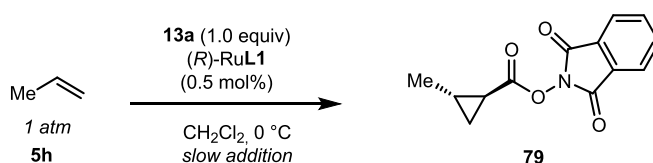
2.33 (s, 1H), 2.15 – 2.03 (m, 1H), 1.46 (s, 10H), 0.87 – 0.75 (m, 1H), 0.75 – 0.62 (s, 1H), 0.60 – 0.45 (d, $J = 6.7$ Hz, 1H) ppm.

^{13}C NMR (126 MHz, CDCl_3) $\delta = 172.2$ (C_q), 157.4 (C_q), 144.1 (C_q), 144.0 (C_q), 141.4 (C_q), 135.6 (C_q), 128.7 (CH), 128.4 (CH), 128.3 (CH), 127.8 (CH), 127.1 (CH), 125.2 (CH), 120.1 (CH), 79.7 (C_q), 67.1 (CH_2), 66.8 (CH_2), 53.5 (CH), 47.3 (CH), 35.1 (CH_2), 29.6 (CH), 28.5 (CH_3), 17.2 (CH), 12.8 (CH_2) ppm.

HRMS (ESI-TOF) calc'd for $[\text{C}_{33}\text{H}_{36}\text{N}_2\text{O}_6 + \text{Na}]^+$: 579.2466; found: 579.2465.

2.4.3. Enantioselective cyclopropanation-borylation of propene towards (–)-spongidepsin.

Synthesis of 1,3-dioxoisindolin-2-yl (1*S*,2*S*)-2-methylcyclopropane-1-carboxylate (**79**)



A 100 mL round bottom flask was charged with $(R)\text{-RuL1}(\text{CH}_3\text{CN})_4\text{PF}_6$ (0.008 mmol, 5.1 mg, 0.001 equiv) and CH_2Cl_2 (45 mL) under Ar. The yellow solution was placed in an ice/water bath at $0\text{ }^\circ\text{C}$ and stirred for 10 minutes. Then, a plastic balloon, equipped with a plastic syringe, was filled with propene and a long needle was attached to the syringe. Then, propene was bubbled through the solution using a needle as a vent for 5 minutes (The balloon was refilled once, in total around 3 grams of propene were taken from the can). After this time, the vent was removed –leaving the flask under static propene atmosphere - and a solution of **13a** (43.3 mL mmol, 8.65 mmol, 1.0 equiv, 0.2 M in CH_2Cl_2) was added over 2 hours using a syringe pump.

One hour after the addition was completed, TLC analysis (petroleum ether/EtOAc 4:1) showed a mixture of starting material **13a** and desired cyclopropane **79**. Then, additional $(R)\text{-RuL1}(\text{CH}_3\text{CN})_4\text{PF}_6$ (0.035 mmol, 21.8 mg, 0.004 equiv) was added in one portion. After 30 minutes, all the starting material **13a** was consumed. The septum was removed and the mixture was allowed to stirred at room temperature for 1 hour, in order to release the remaining propene in solution. The solvent was removed under vacuum and the crude reaction mixture was passed through a pad of silica gel eluting with CH_2Cl_2 . Pure **79** was obtained without further purification (2.05 g, 97%, 6:1 dr). Compound (*S,S*)-**79** was obtained with a 96.7:3.3 enantiomeric ratio determined by HPLC using a Chiralpak-ID column [*i*-hexane/*i*-PrOH (80:20), 1.0 mL/min]: $\tau_{\text{major}} = 16.8$ min, $\tau_{\text{minor}} = 21.4$ min. (*S,S*)-**79** Can be

further purified by crystallization from CH₂Cl₂/petroleum ether obtaining white crystals in 20:1 dr and 98.4:1.6 er.

Appearance: white solid.

m.p.: 70.2 °C - 71.8 °C

TLC R_f = 0.6 (petroleum ether/EtOAc 7:3).

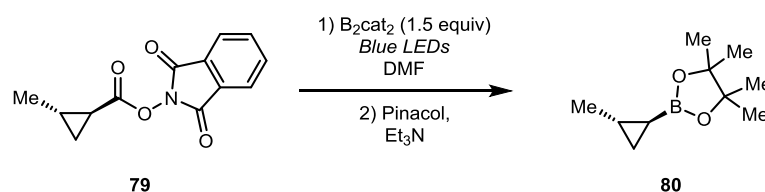
[α]₂₀^D = +96.42 (c = 0.95, CHCl₃).

¹H NMR (400 MHz, CDCl₃) δ = 7.88 – 7.82 (m, 2H), 7.78 – 7.72 (m, 2H), 1.71 – 1.59 (m, 2H), 1.39 (dt, J = 8.8, 4.6 Hz, 1H), 1.20 (d, J = 5.7 Hz, 3H), 0.98 (ddd, J = 8.3, 6.9, 4.4 Hz, 1H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 170.6 (C), 162.1 (C), 134.8 (CH), 129.0 (C), 124.0 (CH), 19.9 (CH), 18.9 (CH₂), 18.2 (CH), 17.8 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₁₃H₁₁NO₄+Na]⁺ 268.0586; found 268.0572.

*Synthesis of 4,4,5,5-tetramethyl-2-((1S,2S)-2-methylcyclopropyl)-1,3,2-dioxaborolane (**80**)*



General procedure E was applied using **79** (98 mg, 0.4 mmol, 1.0 equiv, dr 20:1) and B₂cat₂ (143 mg, 0.6 mmol, 1.5 equiv) in DMF (4.0 mL) for 6 hours. The crude product was purified by silica gel chromatography (Petroleum Ether/Et₂O 95:5), affording pure (*S,S*)-**80** as a colorless oil (37 mg, 51% yield, d.r. 6.4:1). Characterization data are consistent with values reported in the literature.^[25]

Appearance: Colorless oil.

TLC R_f = 0.70 (Petroleum Ether/Et₂O 98:2).

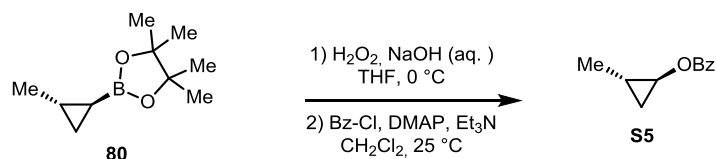
[α]₂₀^D = +32.8 (c = 0.83, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ = 1.20 (s, 12 H), 1.06 (d, J = 5.8 Hz, 3H), 0.96 – 0.90 (m, 1H), 0.66 (ddd, J = 7.7, 6.0, 3.2 Hz, 1H), 0.34 (ddd, J = 9.3, 5.2, 3.2 Hz, 1H), -0.47 (dt, J = 9.3, 5.7 Hz, 1H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 82.9 (C_q), 24.9 (CH₃), 20.1 (CH₃), 12.7 (CH₂), 12.5 (CH), 1.9 (CH) ppm.

MS (200 °C, 70 eV, m/e): 83 (M⁺-C₄H₈O₂B, 100), 125 (M⁺-C₃H₅O, 50), 85 (M⁺-C₃H₆O, 50).

The optical purity for **S5** was determined after oxidation and benzylation of the cyclopropanol, following the procedure described for compound **76**:



(*S,S*)-**S5** was obtained with a 95.9:4.1 enantiomeric ratio determined by HPLC using Chiralpak-AS-H column [*i*-hexane, 0.5 mL/min]: $\tau_{\text{major}} = 21.2$ min, $\tau_{\text{minor}} = 19.0$ min. Characterization data are in agreement with the values reported in the literature.^[25]

Appearance: Colorless oil.

TLC $R_f = 0.37$ (Petroleum Ether/Et₂O 98:2).

$[\alpha]_{20}^D = -68.0$ ($c = 0.1$, CHCl₃).

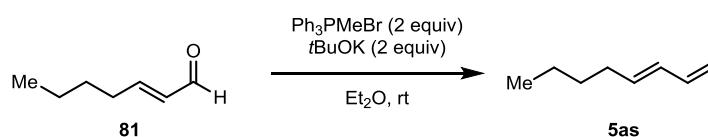
¹H NMR (500 MHz, CDCl₃) $\delta = 8.01 - 7.96$ (m, 2H), 7.58 – 7.50 (m, 1H), 7.45 – 7.35 (m, 2H), 4.06 – 3.94 (m, 1H), 1.19 – 1.14 (m, 1H), 1.12 (d, $J = 5.7$ Hz, 3H), 0.96 (ddd, $J = 9.6$, 6.2, 3.0 Hz, 1H), 0.61 (q, $J = 6.3$ Hz, 1H) ppm.

¹³C NMR (126 MHz, CDCl₃) $\delta = 167.6$ (C_q), 133.1 (CH), 130.3 (C_q), 129.6 (CH), 128.5 (CH), 56.0 (CH), 16.4 (CH₃), 13.5 (CH₂), 13.1 (CH) ppm.

MS (200 °C, 70 eV, m/e): 105 ($M^+ - C_4H_7O$, 100), 77 ($M^+ - C_5H_7O_2$, 33).

2.4.4. Total Synthesis of (–)-dictyopterene A

Synthesis of (E)-octa-1,3-diene (5as)



Adapted from Ritter and co-workers.^[16]

A two-necked flask under argon atmosphere was charged with methyltriphenylphosphonium bromide (9.55 g, 26.7 mmol) and Et₂O (30 mL). To it was added potassium 2-methylpropan-2-olate (3.00 g, 26.7 mmol) and the mixture was stirred at room temperature. After 2 hours, the mixture turned to a deep yellow colour and (*E*)-hept-2-enal **81** (1.750 mL, 13.37 mmol) was added slowly. The mixture quickly turned to a white suspension and was stirred overnight. The day after, the mixture was poured directly over a column of SiO₂ packed with pentane and eluted with pure pentane to afford pure **5as** as a colorless oil (1.054 g, 72%).

(Note: the final product is volatile). NMR data of **5as** are in agreement with the literature values.^[26]

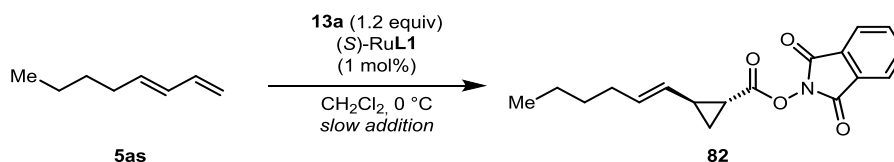
Appearance: colorless oil.

TLC R_f = 0.98 (Petroleum Ether)

¹H NMR (400 MHz, CDCl₃) δ = 6.31 (dt, J = 17.0, 10.2 Hz, 1H), 6.05 (dd, J = 15.2, 10.4 Hz, 1H), 5.71 (dt, J = 14.7, 7.7 Hz, 1H), 5.08 (ddd, J = 17.0, 1.7, 0.8 Hz, 1H), 4.95 (ddd, J = 10.1, 1.7, 0.8 Hz, 1H), 2.09 (q, J = 8.5, 7.7 Hz, 2H), 1.43 – 1.28 (m, 4H), 0.90 (t, J = 6.6 Hz, 3H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 137.5 (CH), 135.6 (CH), 131.1 (CH), 114.6 (CH₂), 32.4 (CH₂), 31.5 (CH₂), 22.4 (CH₂), 14.1 (CH₂) ppm.

Synthesis of 1,3-dioxoisindolin-2-yl (1*R*,2*S*)-2-((*E*)-hex-1-en-1-yl)cyclopropane-1-carboxylate (**82**)



General procedure A was applied using **13a** (0.48 mmol, 1.6 mL, 1.2 equiv), olefin **5as**^[26a] (0.1 mmol, 44 mg, 1.0 equiv) and (*S*)-**RuL1**(CH₃CN)₄PF₆ (0.001 mmol, 2.5 mg, 0.01 equiv). The crude product was purified by silica gel chromatography (Petroleum Ether/EtOAc 4:1), affording pure **82** as a pale yellow oil (119 mg, 95% yield, d.r. 7:1). Compound (*R,R*)-**82** was obtained with a 96.4:3.6 enantiomeric ratio determined by HPLC using a Chiralpak-IC column [*i*-hexane/*i*-PrOH (90:10), 1.0 mL/min]: τ_{major} = 11.7 min, τ_{minor} = 10.2 min (*major diastereoisomer*); τ_{major} = 11.7 min, τ_{minor} = 10.2 min (*minor diastereoisomer*).

Appearance: pale yellow oil.

TLC R_f = 0.48 (Petroleum Ether/EtOAc 4:1).

$[\alpha]_{20}^D = -209.2$ (c = 1.0, CHCl₃).

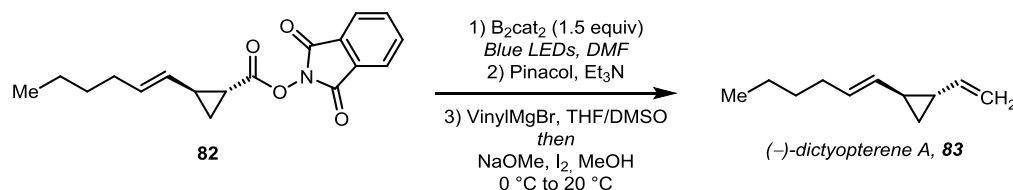
¹H NMR (400 MHz, CDCl₃) δ = 7.91 – 7.85 (m, 2H), 7.81 – 7.76 (m, 2H), 5.78 (dt, J = 15.4, 6.8 Hz, 1H_{minor}), 5.69 (dt, J = 15.3, 6.9 Hz, 1H_{major}), 5.42 – 5.31 (m, 1H_{minor}), 5.09 (ddt, J = 15.3, 8.0, 1.5 Hz, 1H_{major}), 2.27 – 2.17 (m, 1H_{major} + 1H_{minor}), 2.06 – 1.97 (m, 2H_{major} + 2H_{minor}), 1.89 (ddd, J = 8.6, 5.0, 3.9 Hz, 1H_{major}), 1.55 (dt, J = 9.4, 4.9 Hz, 1H_{major}), 1.49 – 1.42 (m, 1H_{minor}), 1.43 – 1.28 (m, 4H_{major} + 4H_{minor}), 1.24 (ddd, J = 8.3, 6.8, 4.7 Hz, 1H_{major}), 0.96 – 0.83 (m, 3H_{major} + 3H_{minor}) ppm.

¹³C NMR (101 MHz, CDCl₃) δ = 170.1 (C_q), 168.5 (C_{minor}), 162.2 (C_q), 135.2 (C_{minor}), 134.8 (CH), 134.8 (C_{minor}), 133.4 (CH), 129.1 (C_{minor}), 129.1 (C_q), 128.1 (CH), 124.6 (C_{minor}), 124.1

(CH), 124.0 (C_{minor}), 32.4 (C_{minor}), 32.2 (CH₂), 31.6 (C_{minor}), 31.5 (CH₂), 29.8 (C_{minor}), 27.3 (CH), 26.3 (C_{minor}), 22.3 (CH₂), 22.3 (C_{minor}), 18.9 (CH), 17.8 (C_{minor}), 17.5 (CH₂), 16.0 (C_{minor}), 14.1 (CH₃) ppm.

HRMS (ESI-TOF) calc'd for [C₁₈H₁₉NNaO₄]⁺; found: 336.1209.

Synthesis of (–)-dictyopterene A (**83**)



General procedure E was applied using **82** (63 mg, 0.2 mmol, 1.0 equiv, dr 7:1) and B₂cat₂ (71 mg, 0.3 mmol, 1.5 equiv) in DMF (2 mL) for 14 hours. After transesterification to the pinacol boronate and extraction with pentane, the crude cyclopropylboronate was transferred to a vial, and the solvent was removed.

Then, following an adapted literature procedure,^[27] crude cyclopropylboronate was dissolved in a v/v 1:1 mixture of THF/DMSO (1.5 mL in total) under Ar. The solution was placed in an ice/water bath and stirred for 10 minutes. A solution of vinylMgBr (0.32 mL, 0.95 M in THF, 0.3 mmol, 1.5 equiv) was added dropwise, after 10 minutes, the reaction mixture was stirred at room temperature for 30 minutes. After this, the vial was placed in an ice/water bath and a solution of NaOMe (0.33 mL, 3 M in MeOH, 1 mmol, 5 equiv) was added, followed by dropwise addition of a I₂ solution (0.48 mL, 0.5 M in MeOH, 0.24 mmol, 1.2 equiv). The mixture was stirred for 30 minutes at 0 °C, and then quenched with sat. aq. Na₂S₂O₃. To this mixture, water was added and the resulting mixture was extracted with pentane (2 x 15 mL). The combined organic phase was dried over anh. Na₂SO₄ and the solvent was partially removed by rotatory evaporation. (*Note: the final product is volatile*).

Crude ¹H NMR analysis evidenced a 52% yield, using 1,1,2,2-tetrachloroethane as internal standard.^[28] The crude product was purified by silica gel chromatography using pentane as the eluent. The yield after the column was also determined by internal standard, as we observed an important decrease in yield if pentane was fully removed. For this reason, in the reported NMR spectra, both internal standard and pentane can be observed. Compound (–)-**83** was obtained with a 95.5:4.5 enantiomeric ratio determined by GC-MS using a Hydrodex-B6-TBDM column, 70 °C isothermal, τ_{major} = 31.5 min, τ_{minor} = 31.0 min.

TLC R_f = 0.85 (pentane)

[α]₂₀^D = –36.5 (c = 0.4, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ = 5.49 (dt, *J* = 15.2, 6.8 Hz, 1H), 5.44 – 5.34 (m, 1H), 5.10 – 4.97 (m, 2H), 4.86 (dd, *J* = 10.3, 1.7 Hz, 1H), 2.02 – 1.90 (m, 2H), 1.43 – 1.35 (m, 2H), 1.34 – 1.29 (m, 4H), 0.94 – 0.85 (m, 3H), 0.82 – 0.72 (m, 2H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ = 141.0 (CH), 131.7 (CH), 129.3 (CH), 112.0 (CH₂), 32.3 (CH₂), 31.9 (CH₂), 24.4 (CH), 23.7 (CH), 22.4 (CH₂), 14.9 (CH₂), 14.1 (CH₃) ppm.

MS (200 °C, 70 eV, m/e): 79 (M-C₅H₁₁, 100%), 77 (62%), 91 (41%).

2.5. Optimization studies

An 8 mL screw-cap vial under argon atmosphere, equipped with a PTFE coated magnetic stirring bar, was loaded with **5a** (12.0 mg, 0.1 mmol, 1.0 equiv), the indicated catalyst (0.001 mmol, 0.01 equiv unless stated otherwise; see **Table S3**) and dry CH₂Cl₂ (0.6 mL). Using a syringe pump, **13a** (1.2 mmol, 1.2 mL, 1.2 equiv) was added to the stirring solution over the course of 40 minutes. The reaction was stirred at the specified temperature until all the starting material was consumed, monitoring by TLC (petroleum ether/EtOAc 4:1). Once the reaction was complete, the solvent was removed and the crude mixture was analyzed by ¹H NMR using 1,1,2,2-tetrachloroethane as an internal standard. For *entry* 7, the crude was filtered through a short pad of silica to remove the copper catalyst before ¹H NMR analysis.

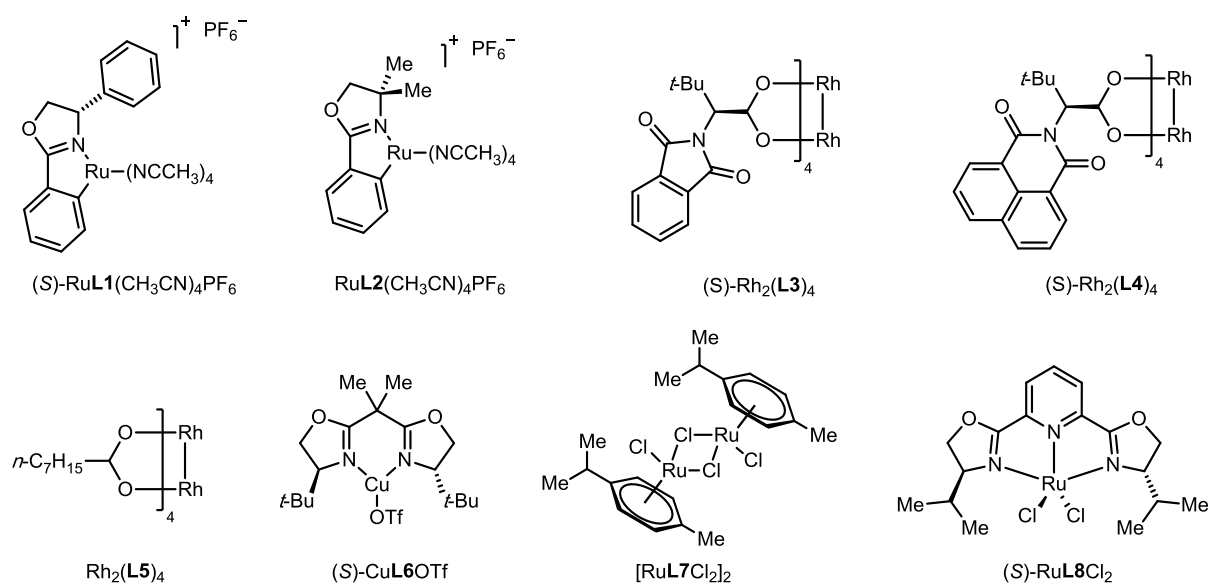
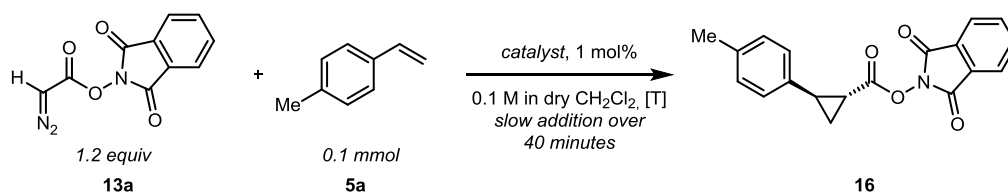


Figure S1: Some relevant catalysts included in this screening.

Table S3: Catalyst screening and temperature optimization.

Entry	Catalyst	T [°C]	Time after addition (h)	Yield ^a (%)	dr (<i>trans</i> : <i>cis</i>)	<i>ee</i> _{trans} (%)	<i>ee</i> _{cis} (%)
1	Pd(OAc) ₂	rt	2	69	4.5:1	-	-
2	Rh ₂ (OAc) ₄	rt	-	69	2:1	-	-
3	Rh ₂ (L5) ₄	rt	-	69	2:1	-	-
4	(<i>S</i>)-Rh ₂ (L3) ₄	rt	-	72	1:1.3	6	-4
5	(<i>S</i>)-Rh ₂ (L4) ₄	rt	-	82	1:1	19	7
6	(<i>S</i>)-Cu L6 ^b	rt	18	49	4:1	88	73
7	(<i>S</i>)-Cu L6 ^{b,c}	rt	-	54	5.3:1	90	73
8	[Ru L7 Cl ₂] ₂	rt	3	50	8:1	-	-
9	(<i>S</i>)-Ru L8 Cl ₂ ^d	rt	48 ^f	63	20:1	82	-
10	Ru L2 ^e	0	-	98	>20:1	-	-
11	(<i>S</i>)-Ru L1	rt	-	92	>20:1	94	-
12	(<i>S</i>)-Ru L1	0	-	98	>20:1	94	-
13	(<i>R</i>)-Ru L1	-10	-	98	>20:1	-96	-
14	(<i>R</i>)-Ru L1	-20	-	97	>20:1	-96	-
15	(<i>S</i>)-Ru L1	-30	-	97	>20:1	96	-

^a Yield was determined by ¹H NMR using 1,1,2,2-tetrachloroethane as an internal standard. ^b The catalyst was generated *in situ* by stirring (CuOTf)₂·PhH with 1.1 eq of the ligand in dichloromethane for 30 minutes.^[29] ^c: Catalyst loading 10 mol%. ^d The catalyst was generated *in situ* by stirring [Ru**L7**Cl₂]₂ with 2 equiv of the ligand in dichloromethane for 30 minutes.^[30] ^e The reaction was performed using 1 equiv of **13a** and 5 equiv of **5a**. ^f The reaction did not reach full conversion.

2.6. Competition Experiments

Starting Materials

NHPI-DA (**13a**) was prepared as described in **Section 2.1.1**. Compounds **15a**, **15b**, **15c** were purchased from commercial sources. Compounds **15d**,^[31] **15e**^[32] and **15f**^[33] were prepared adapting procedures reported in the literature.

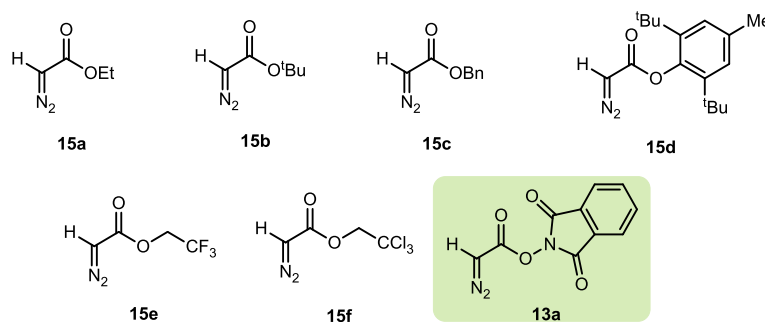


Figure S2: Diazocompounds used in the competition experiments.

Experimental details

An 8 mL vial was charged with the corresponding alkene **5** (0.4 mL, 0.2 mmol, 1.0 equiv, 0.5 M in CH₂Cl₂ stock solution), (**S**)-**RuL1**(CH₃CN)₄PF₆ (0.2 mL, 0.002 mmol, 0.01 equiv, 0.01 M in CH₂Cl₂ stock solution) and CH₂Cl₂ (0.4 mL). The resulting solution was placed in an ice-water bath and stirred for 10 minutes under Ar. Concurrently, a 0.2 M solution of the corresponding diazocompound (**13a**, **15a-f**) in CH₂Cl₂ was prepared in a volumetric flask under Ar. Then, 1 mL of this diazocompound solution (0.2 mmol, 1.0 equiv) was added to the solution containing the alkene in one portion (1-2 seconds). Intense bubbling was observed. The reaction was monitored by TLC until the diazocompound was consumed and it was then concentrated (not fully to minimize the loss of volatile products) and analyzed by ¹H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

In general, the reactions were complete after 30 minutes, except when **15d** was used, which took 3 hours to reach completion at room temperature. The mass balance (cyclopropanation + dimerization products) was >90% in all cases, except for **15d**. These reactions gave different side-products that could not be characterized, due to unstability on silica gel.

As a reference for the integration, reported spectroscopic data for compounds **16'b**,^[34] **16'a**,^[34] **16'c**^[35] and **17'a**^[36] were followed. The rest were assigned by analogy. When possible, the diastereomeric ratio (dr) was also quantified using ¹H NMR spectroscopy (our data is consistent with all the major diastereoisomers being *trans*).

Results of the competition experiments

The results of the competition experiments are reported in the following tables, and are grouped depending on the reacted olefin. These results are present in the **Scheme 2C** of the main manuscript.

Table S4: Single-shot experiments of different diazo-acetates with 4-methylstyrene (**5a**).

Entry	R	Yield 18 , 18'a-f ^a (%)	d.r. ^a	Yield 21 ^a (%)
1	<i>t</i> -Bu, 15b	26	7.5:1	68
2	Ethyl, 15a	36	7.6:1	61
3	Bn, 15c	48	6.4:1	53
4	BHT, 15d	61	>10:1	10
5	CH ₂ CF ₃ , 15e	66	4.8:1	30
6	CH ₂ CCl ₃ , 15f	78	7.0:1	17
7	Phthalimide, 13a	99	>20:1	<5

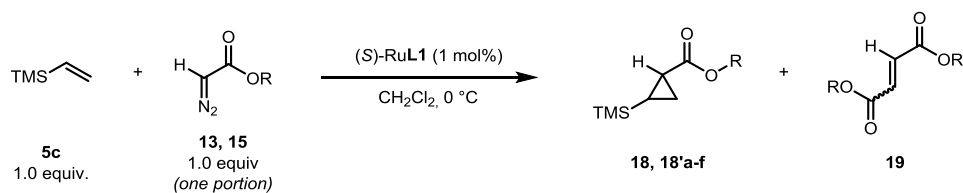
^a Yield and d.r. determined by ¹H NMR, using 1,1,2,2-tetrachloroethane as internal standard.

Table S5: Single-shot experiments of different diazo-acetates with 1-hexene (**5b**).

Entry	R	Yield 19 , 19'a-f ^a (%)	d.r. ^a	Yield 21 ^a (%)
1	<i>t</i> -Bu, 15b	5	nd	89
2	Ethyl, 15a	8	nd	87
3	Bn, 15c	7	nd	84
4	BHT, 15d	<10	nd	10
5	CH ₂ CF ₃ , 15e	23	8:1	72
6	CH ₂ CCl ₃ , 15f	26	8:1	69
7	Phthalimide, 13a	72	8.6:1	22

^a Yield and d.r. determined by ¹H NMR, using 1,1,2,2-tetrachloroethane as internal standard. nd = not determined.

Table S6: Single-shot experiments of different diazo-acetates with vinyltrimethylsilane (**5c**).



Entry	R	Yield 20 , 20'a-f ^a (%)	d.r. ^a	Yield 21 ^a (%)
1	<i>t</i> -Bu, 15b	<5	nd	92
2	Ethyl, 15a	<5	nd	98
3	Bn, 15c	<5	nd	90
4	BHT, 15d	<5	nd	9
5	CH ₂ CF ₃ , 15e	7	nd	86
6	CH ₂ CCl ₃ , 15f	9	nd	82
7	Phthalimide, 13a	41	>10 : 1	>22*

^a Yield and d.r. determined by ¹H NMR, using 1,1,2,2-tetrachloroethane as internal standard. nd = not determined. * Not quantified due to insolubility.

3. Crystallographic data

Crystallographic data for compound 13a:

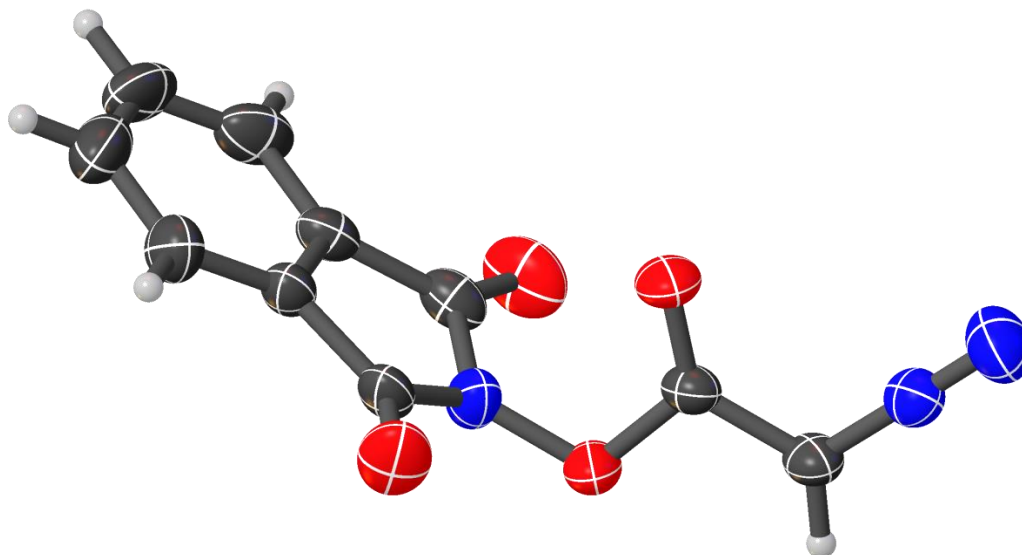


Figure S3 – Structure of compound **13a**. Complete crystallographic data for compound **13a** has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with deposition number 1851523.

Crystal Data for $\text{C}_{10}\text{H}_5\text{N}_3\text{O}_4$ ($M = 231.17$ g/mol): monoclinic, space group $P2_1$ (no. 4), $a = 6.7499(6)$ Å, $b = 5.0850(3)$ Å, $c = 14.8437(11)$ Å, $\beta = 92.656(3)^\circ$, $V = 508.94(7)$ Å³, $Z = 2$, $T = 295.3$ K, $\mu(\text{MoK}\alpha) = 0.121$ mm⁻¹, $D_{\text{calc}} = 1.509$ g/cm³, 12835 reflections measured ($5.494^\circ \leq 2\theta \leq 71.406^\circ$), 4642 unique ($R_{\text{int}} = 0.0734$, $R_{\text{sigma}} = 0.0898$) which were used in all calculations. The final R_1 was 0.0872 ($I > 2\sigma(I)$) and wR_2 was 0.2096 (all data).

Crystallographic data for compound 22:

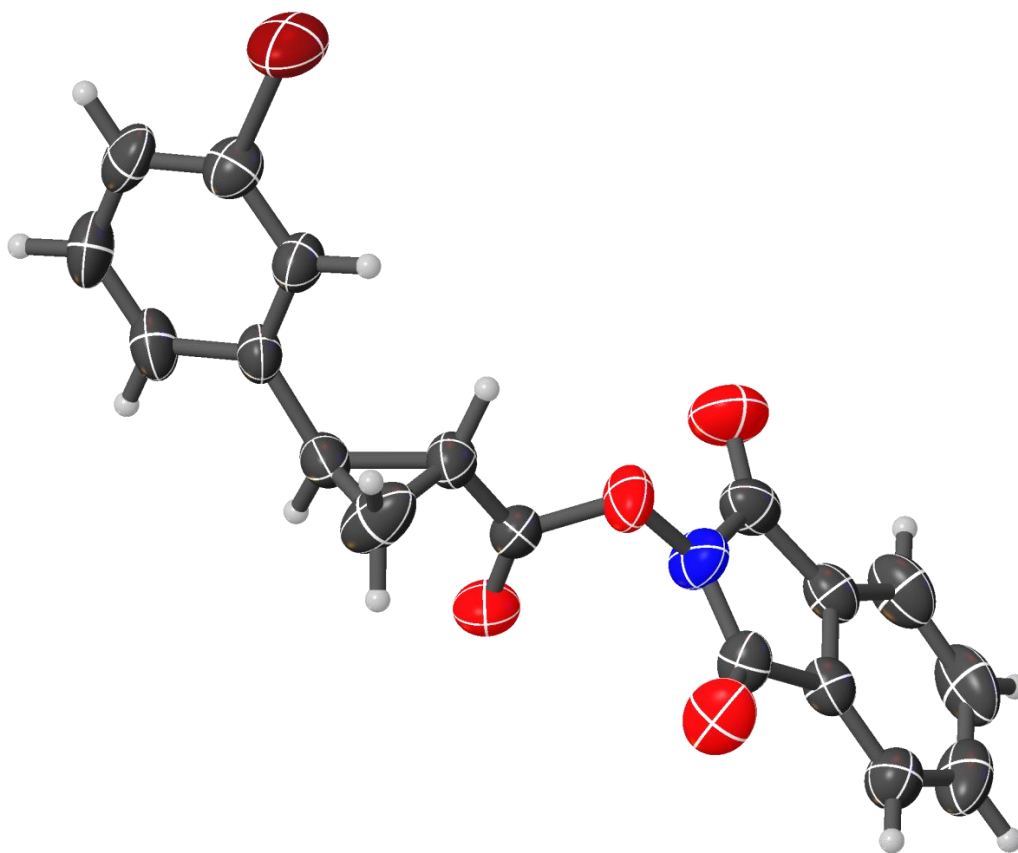


Figure S4 – Structure of compound 22. Complete crystallographic data for compound 22 has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with deposition number 1851521.

Crystal Data for $C_{18}H_{12}BrNO_4$ ($M = 386.20$ g/mol): triclinic, space group P1 (no. 1), $a = 7.9401(3)$ Å, $b = 8.4127(3)$ Å, $c = 12.8633(5)$ Å, $\alpha = 103.660(3)^\circ$, $\beta = 91.909(3)^\circ$, $\gamma = 101.726(3)^\circ$, $V = 814.52(6)$ Å³, $Z = 2$, $T = 293(2)$ K, $\mu(\text{MoK}\alpha) = 2.545$ mm⁻¹, $D_{\text{calc}} = 1.575$ g/cm³, 21169 reflections measured ($6.486^\circ \leq 2\theta \leq 56.638^\circ$), 7372 unique ($R_{\text{int}} = 0.0218$, $R_{\text{sigma}} = 0.0265$) which were used in all calculations. The final R_1 was 0.0423 ($I > 2\sigma(I)$) and wR_2 was 0.1099 (all data) and the Flack parameter was 0.008(10).

Crystallographic data for compound 32:

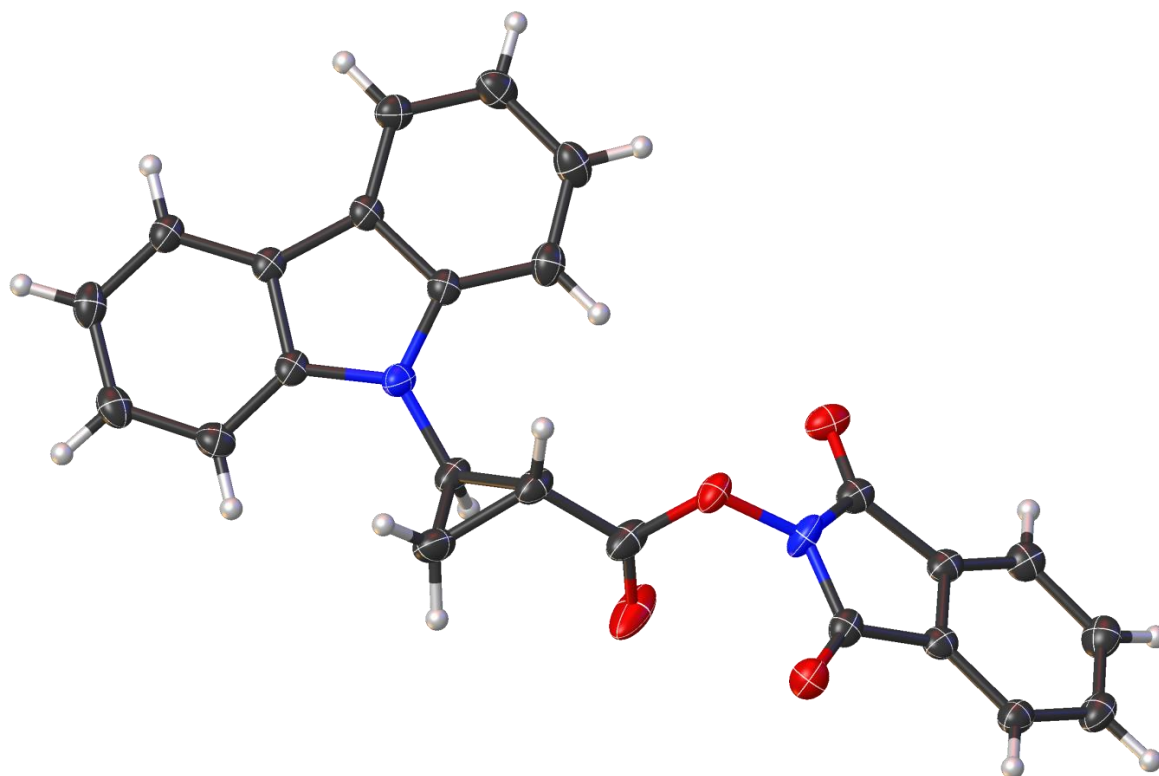


Figure S5 – Structure of compound **32**. Complete crystallographic data for compound **32** has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with deposition number 1851524.

Crystal Data for $C_{24}H_{16}N_2O_4$ ($M = 396.39$ g/mol): monoclinic, space group $P2_1$ (no. 4), $a = 7.59831(16)$ Å, $b = 8.98089(19)$ Å, $c = 14.2368(3)$ Å, $\beta = 102.795(2)^\circ$, $V = 947.39(3)$ Å³, $Z = 2$, $T = 100$ K, $\mu(\text{CuK}\alpha) = 0.787$ mm⁻¹, $D_{\text{calc}} = 1.390$ g/cm³, 18473 reflections measured ($6.366^\circ \leq 2\theta \leq 134.706^\circ$), 3365 unique ($R_{\text{int}} = 0.0713$, $R_{\text{sigma}} = 0.0392$) which were used in all calculations. The final R_1 was 0.0376 ($I > 2\sigma(I)$) and wR_2 was 0.0967 (all data) and the Flack parameter was $-0.07(13)$.

Crystallographic data for compound **41**:

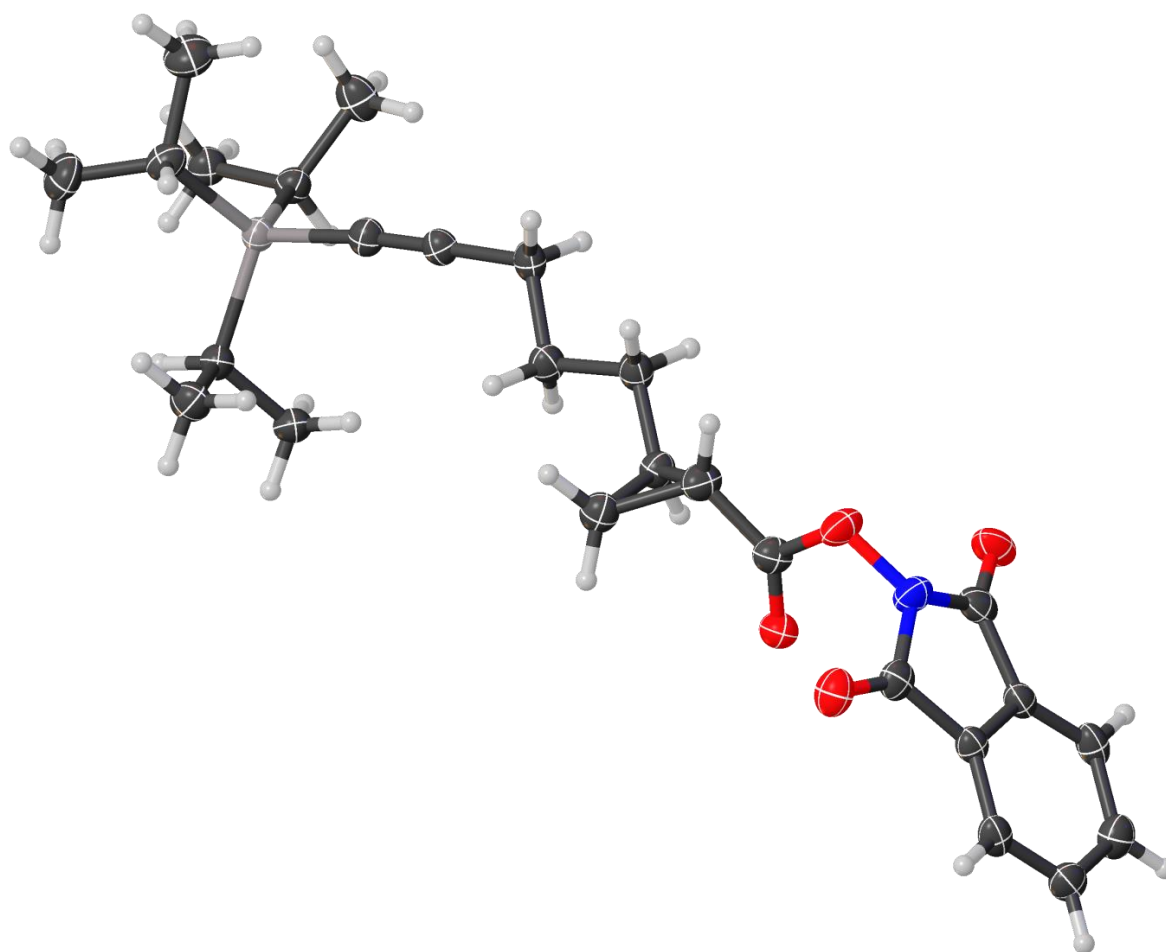


Figure S6 – Structure of compound **41**. Complete crystallographic data for compound **41** has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with deposition number 1851525.

Crystal Data for $C_{26}H_{35}NO_4Si$ ($M = 453.64$ g/mol): monoclinic, space group $P2_1$ (no. 4), $a = 8.3518(4)$ Å, $b = 13.9551(6)$ Å, $c = 11.4966(6)$ Å, $\beta = 108.025(6)^\circ$, $V = 1274.18(12)$ Å³, $Z = 2$, $T = 100$ K, $\mu(\text{CuK}\alpha) = 1.055$ mm⁻¹, $D_{\text{calc}} = 1.182$ g/cm³, 35096 reflections measured ($8.088^\circ \leq 2\theta \leq 135.802^\circ$), 4541 unique ($R_{\text{int}} = 0.0960$, $R_{\text{sigma}} = 0.0526$) which were used in all calculations. The final R_1 was 0.0423 ($I > 2\sigma(I)$) and wR_2 was 0.1023 (all data) and the Flack parameter was $-0.01(3)$.

Crystallographic data for compound **49**:

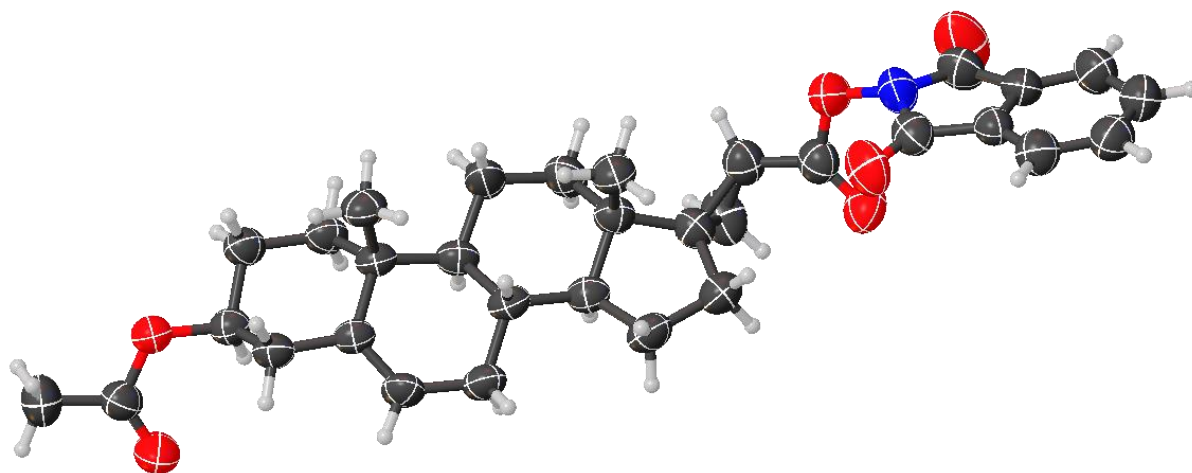
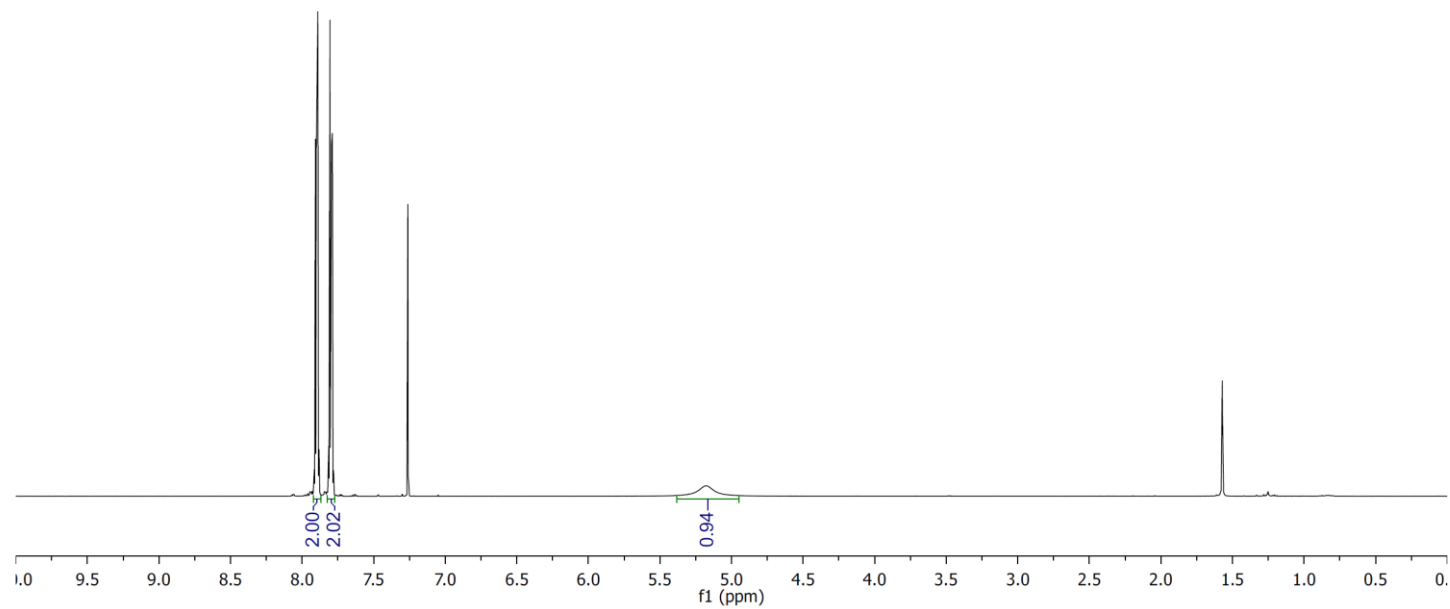
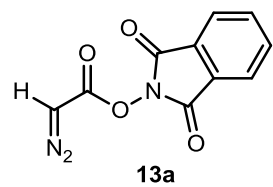


Figure S7 – Structure of compound **49**. Complete crystallographic data for compound **49** has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with deposition number 1851522.

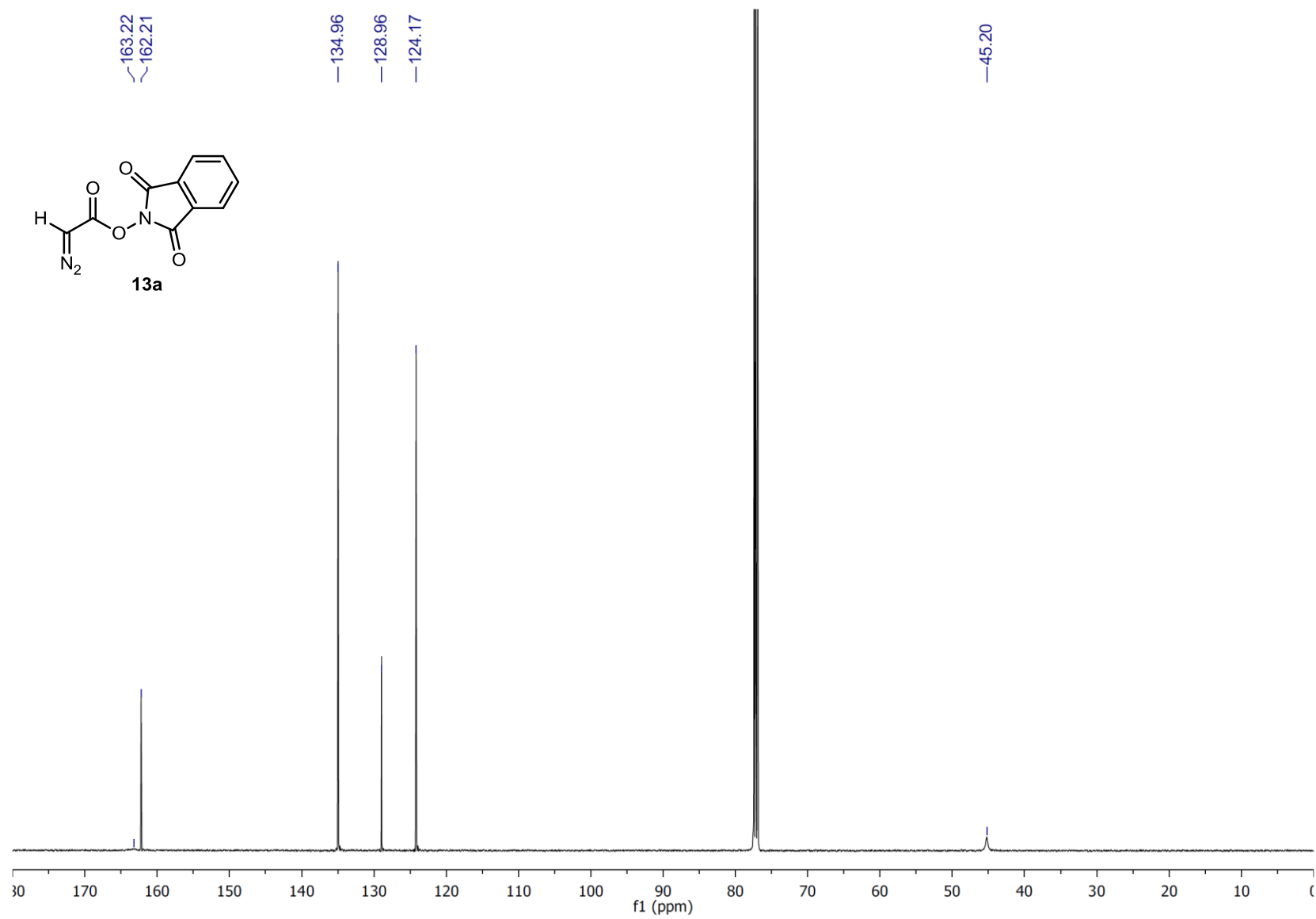
Crystal Data for $C_{32}H_{37}NO_6$ ($M = 531.62$ g/mol): monoclinic, space group $P2_1$ (no. 4), $a = 9.3510(2)$ Å, $b = 27.4980(8)$ Å, $c = 11.2933(3)$ Å, $\beta = 98.356(3)^\circ$, $V = 2873.06(14)$ Å³, $Z = 4$, $T = 293(2)$ K, $\mu(\text{MoK}\alpha) = 0.084$ mm⁻¹, $D_{\text{calc}} = 1.229$ g/cm³, 39392 reflections measured ($6.792^\circ \leq 2\theta \leq 55.882^\circ$), 11820 unique ($R_{\text{int}} = 0.0523$, $R_{\text{sigma}} = 0.0626$) which were used in all calculations. The final R_1 was 0.0564 ($I > 2\sigma(I)$) and wR_2 was 0.1127 (all data).

4. NMR spectra of synthesized compounds

^1H NMR (500 MHz, CDCl_3) for compound **13a**



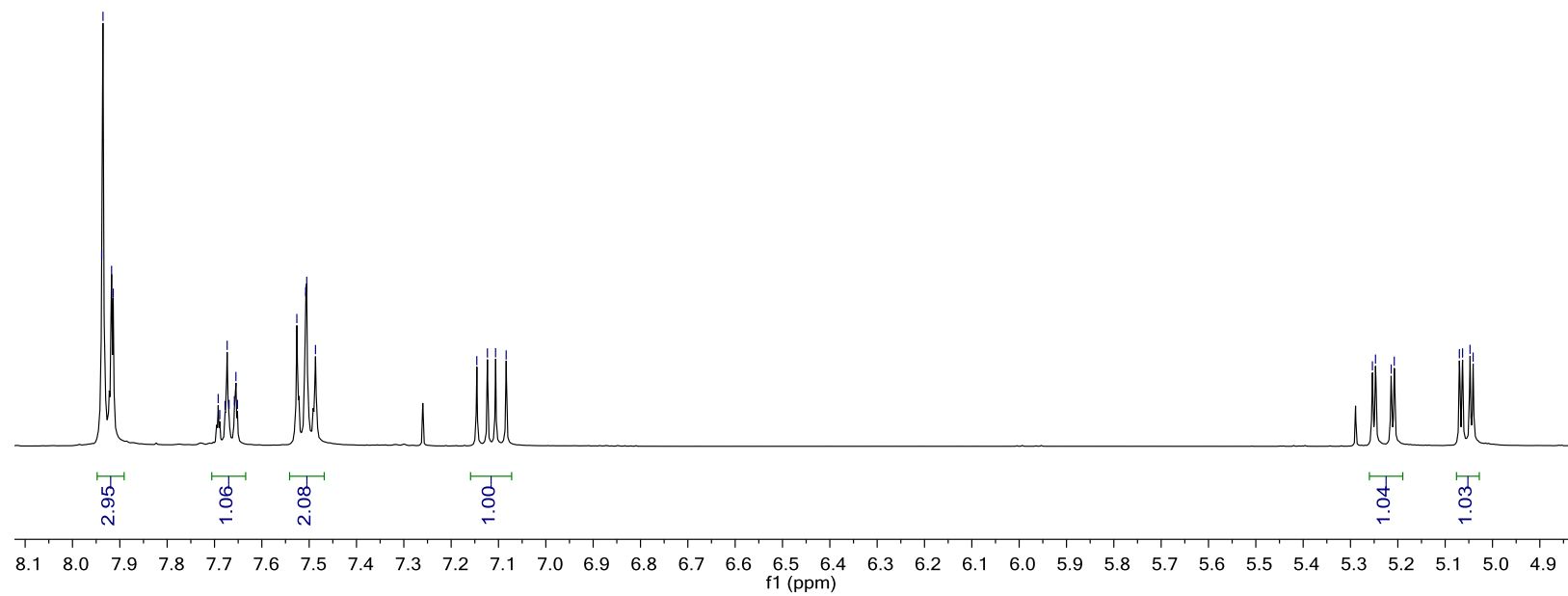
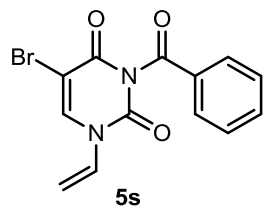
^{13}C NMR (126 MHz, CDCl_3) for compound **13a**



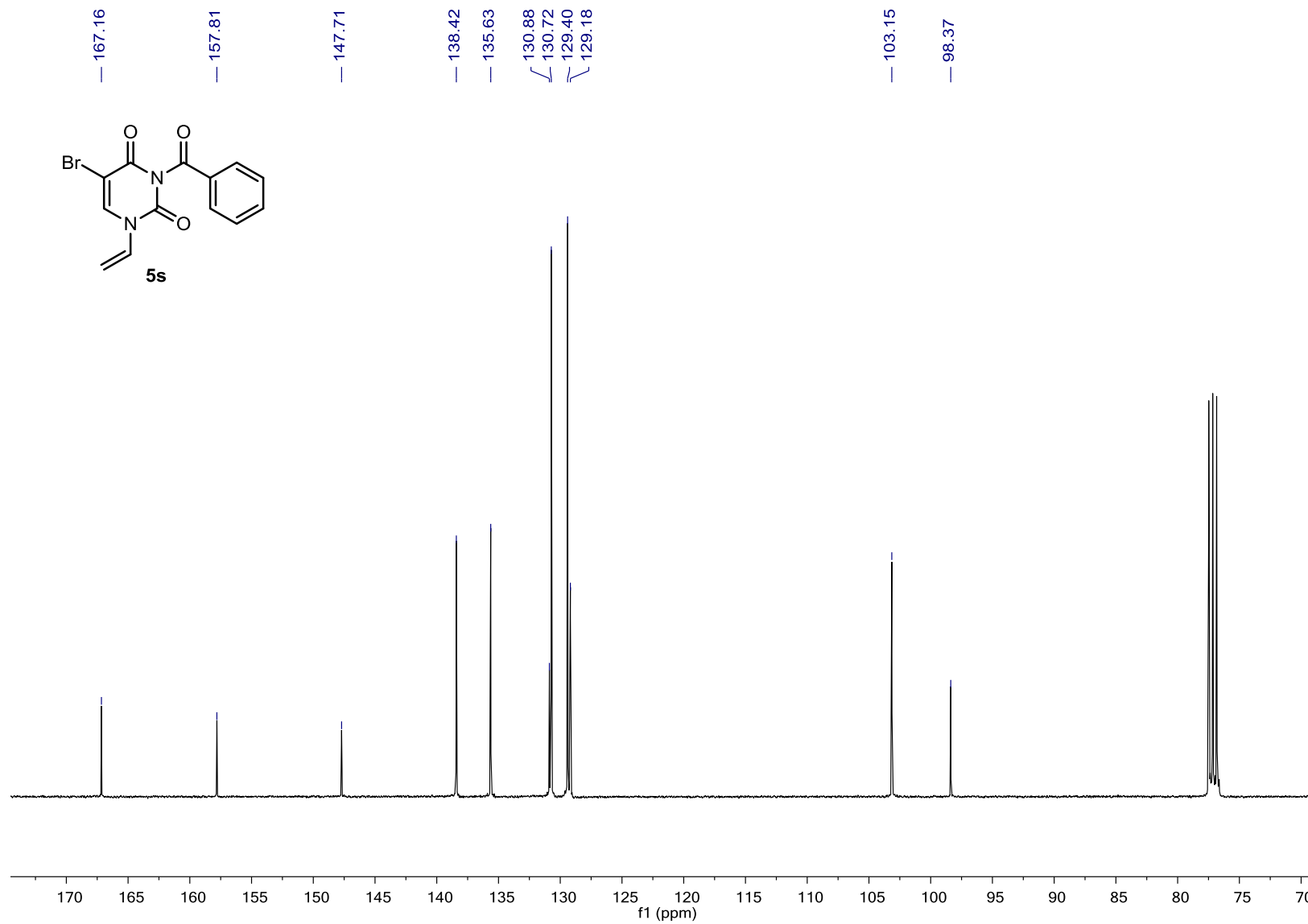
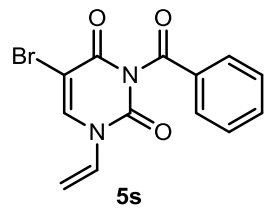
^1H NMR (400 MHz, CDCl_3) for compound **5s**

7.94
7.94
7.92
7.91
7.69
7.69
7.68
7.67
7.67
7.66
7.65
7.65
7.53
7.51
7.51
7.49
7.15
7.12
7.11
7.08

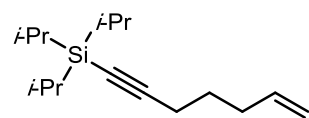
5.25
5.25
5.21
5.21
5.07
5.06
5.05
5.04



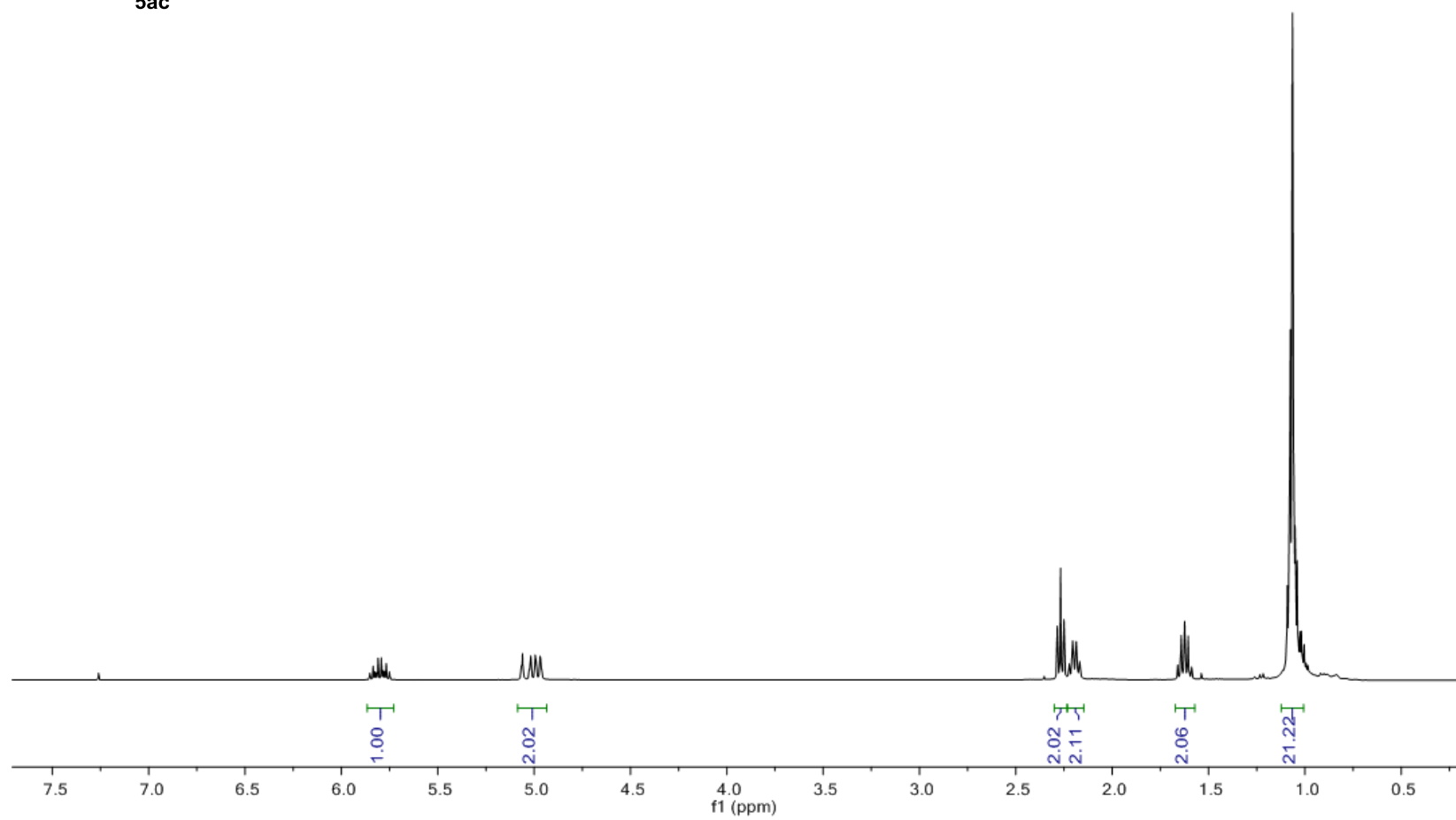
¹³C NMR (101 MHz, CDCl₃) for compound **5s**



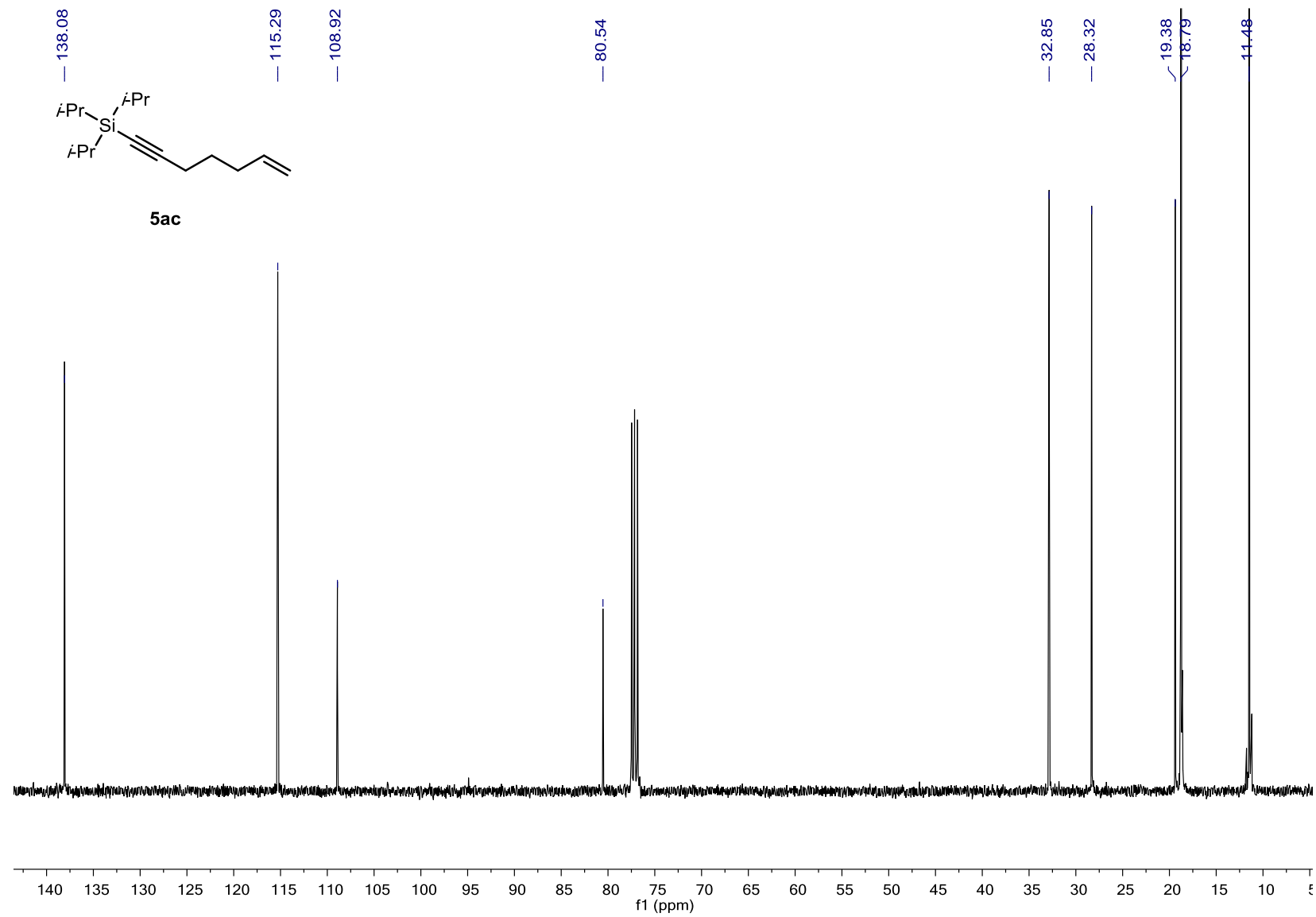
^1H NMR (400 MHz, CDCl_3) for compound **5ac**



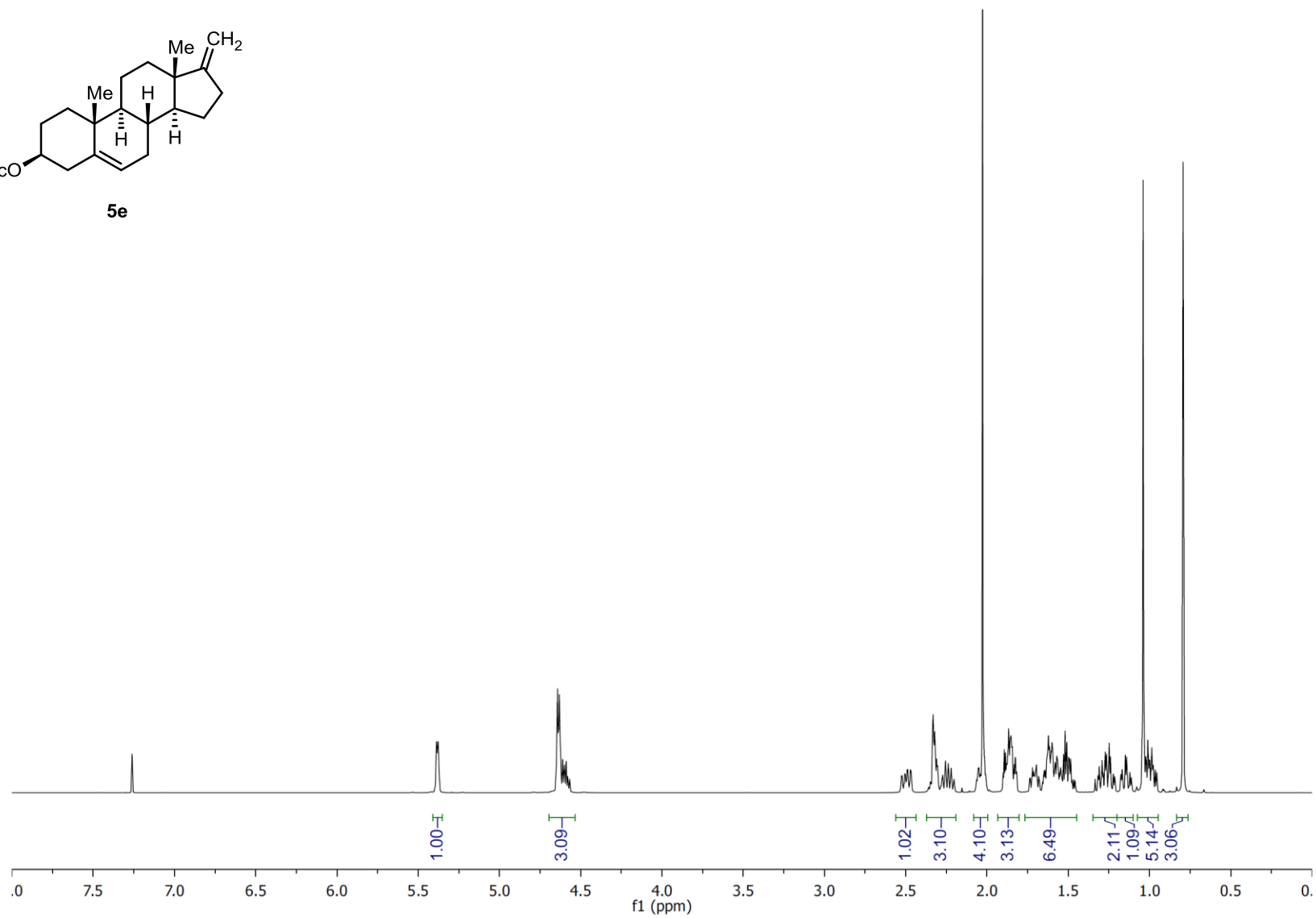
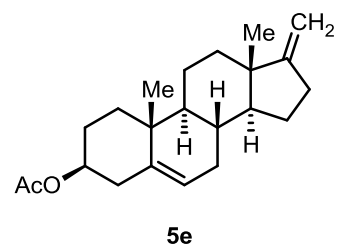
5ac



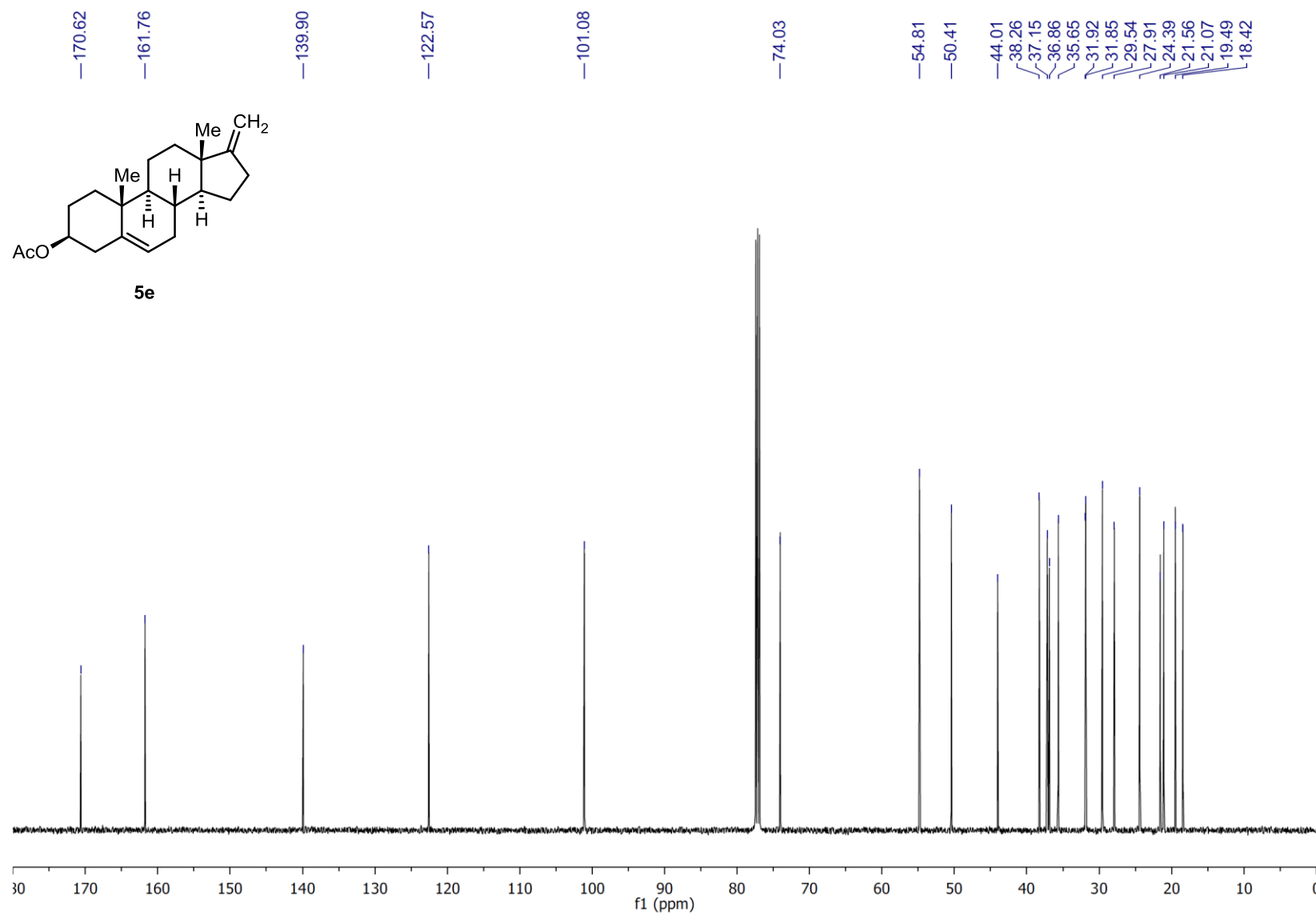
^{13}C NMR (101 MHz, CDCl_3) for compound **5ac**



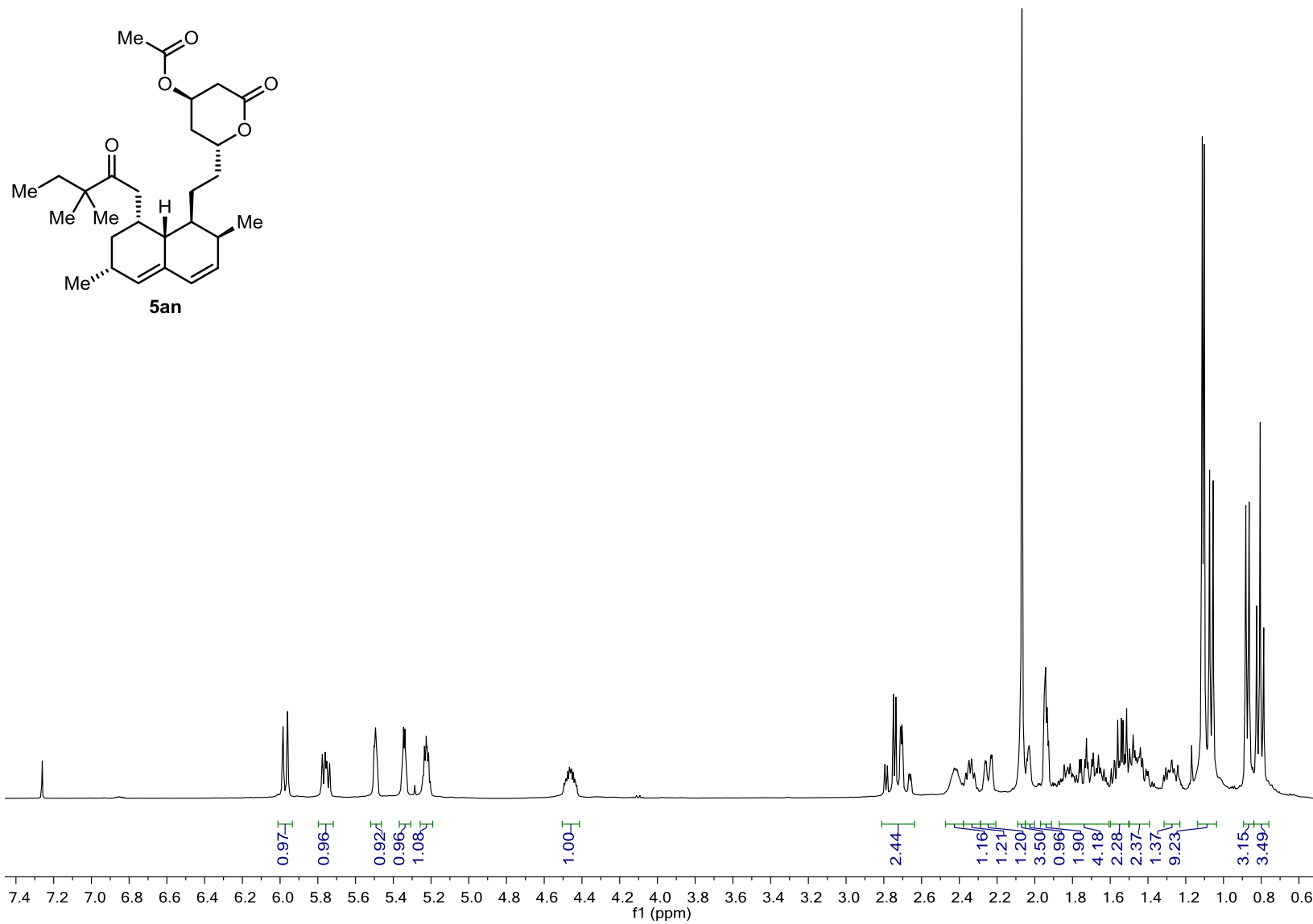
^1H NMR (500 MHz, CDCl_3) for compound **5e**



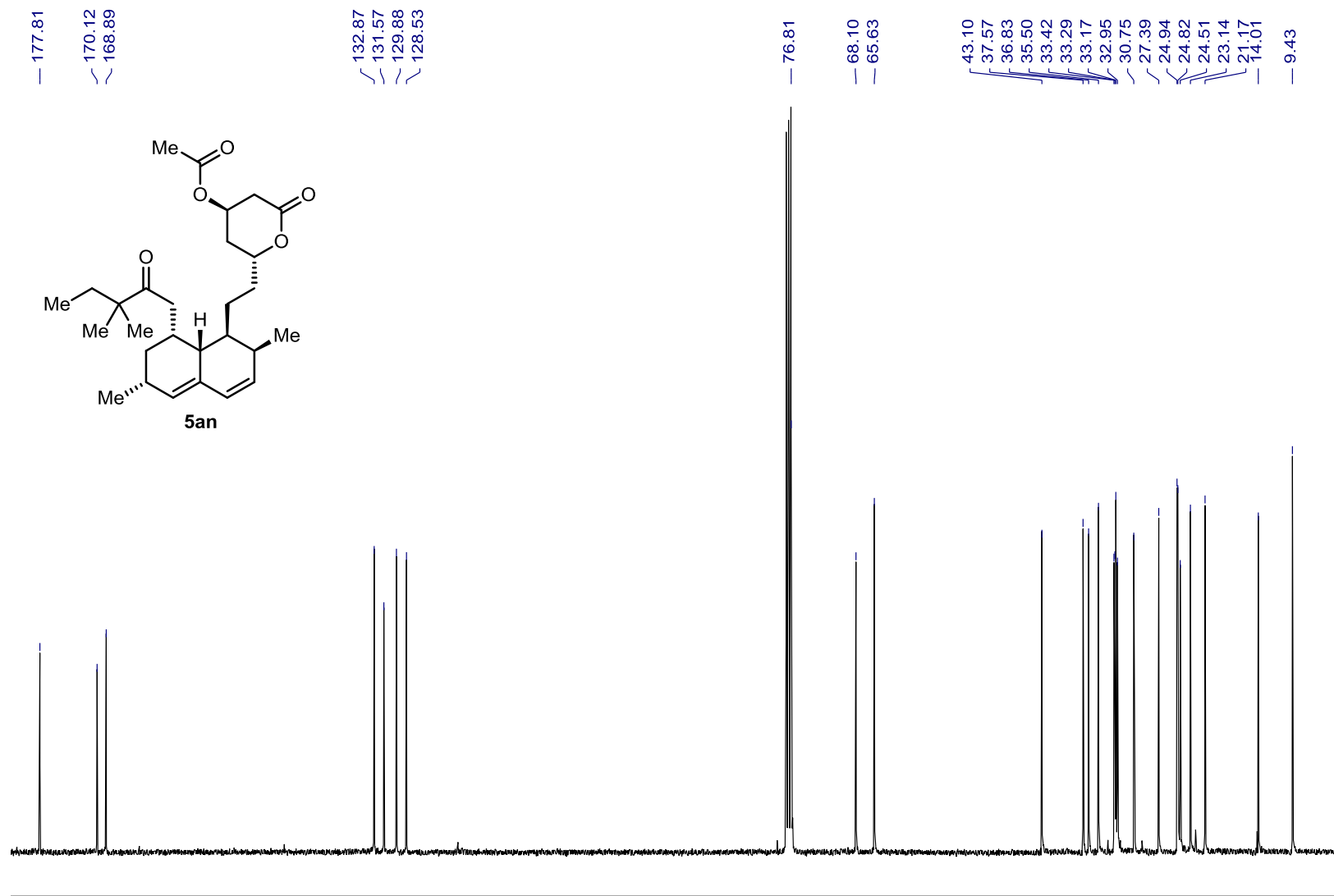
^{13}C NMR (126 MHz, CDCl_3) for compound **5e**



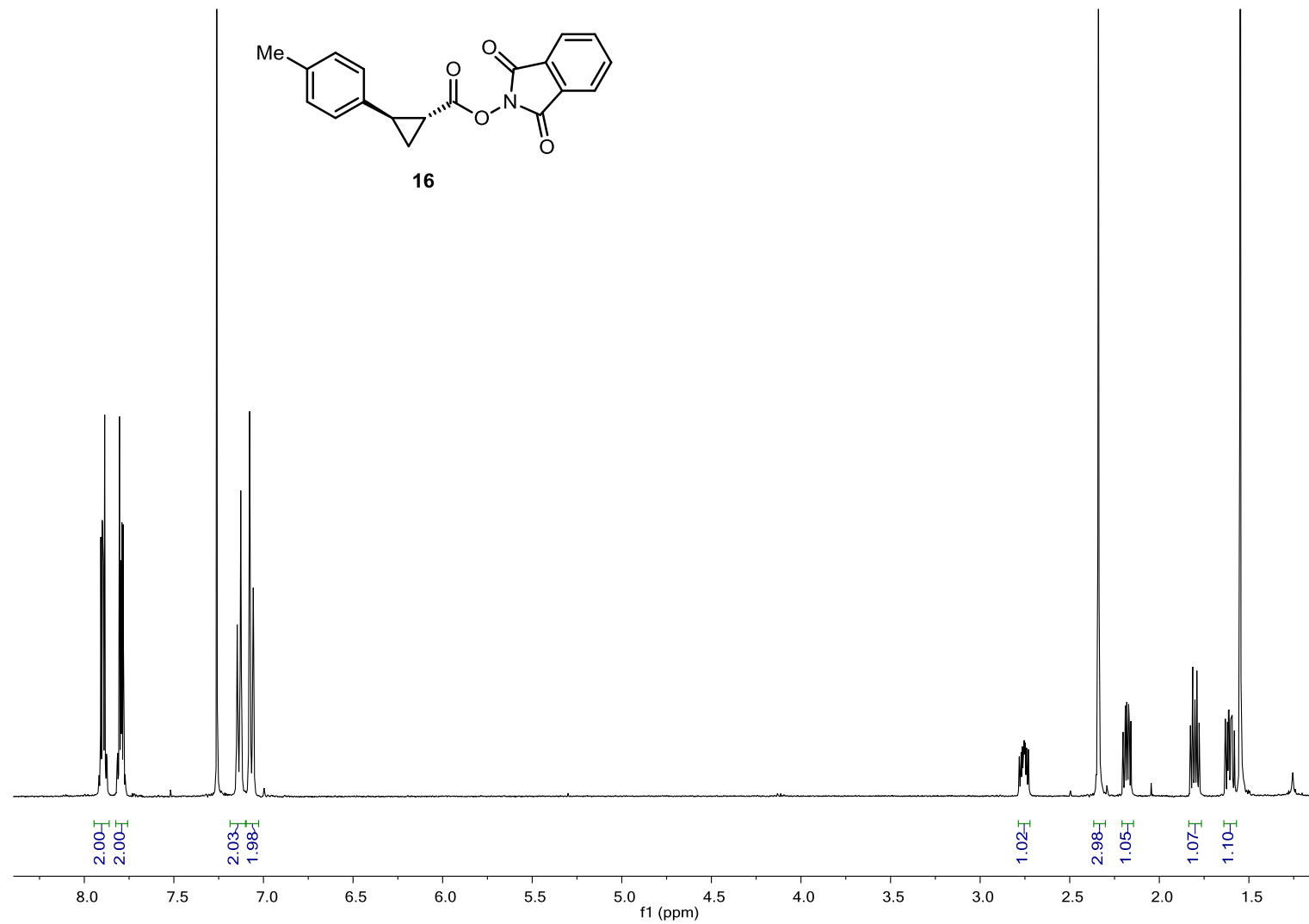
^1H NMR (400 MHz, CDCl_3) for compound **5an**



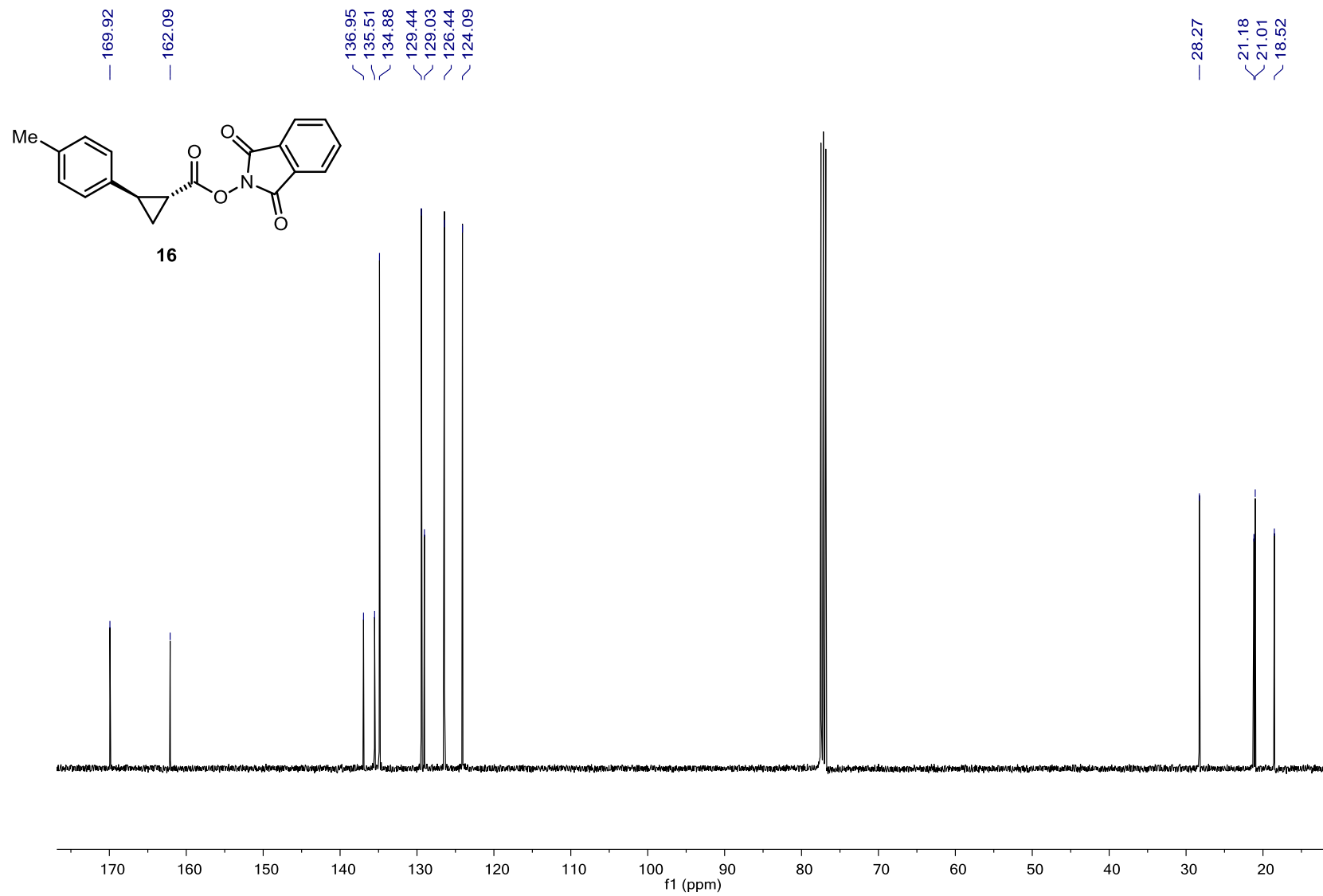
^{13}C NMR (101 MHz, CDCl_3) for compound **5an**



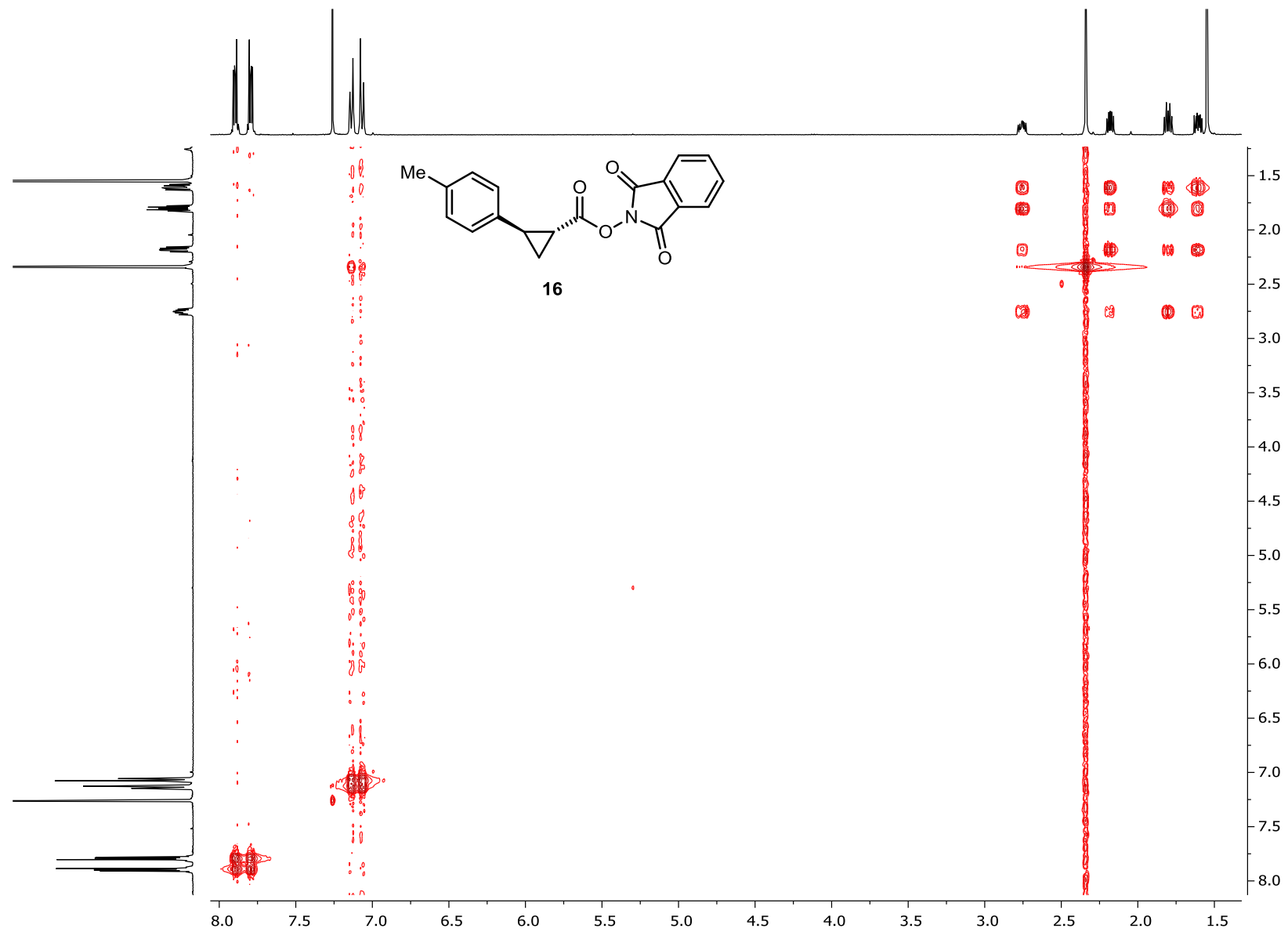
^1H NMR (400 MHz, CDCl_3) for compound **16**



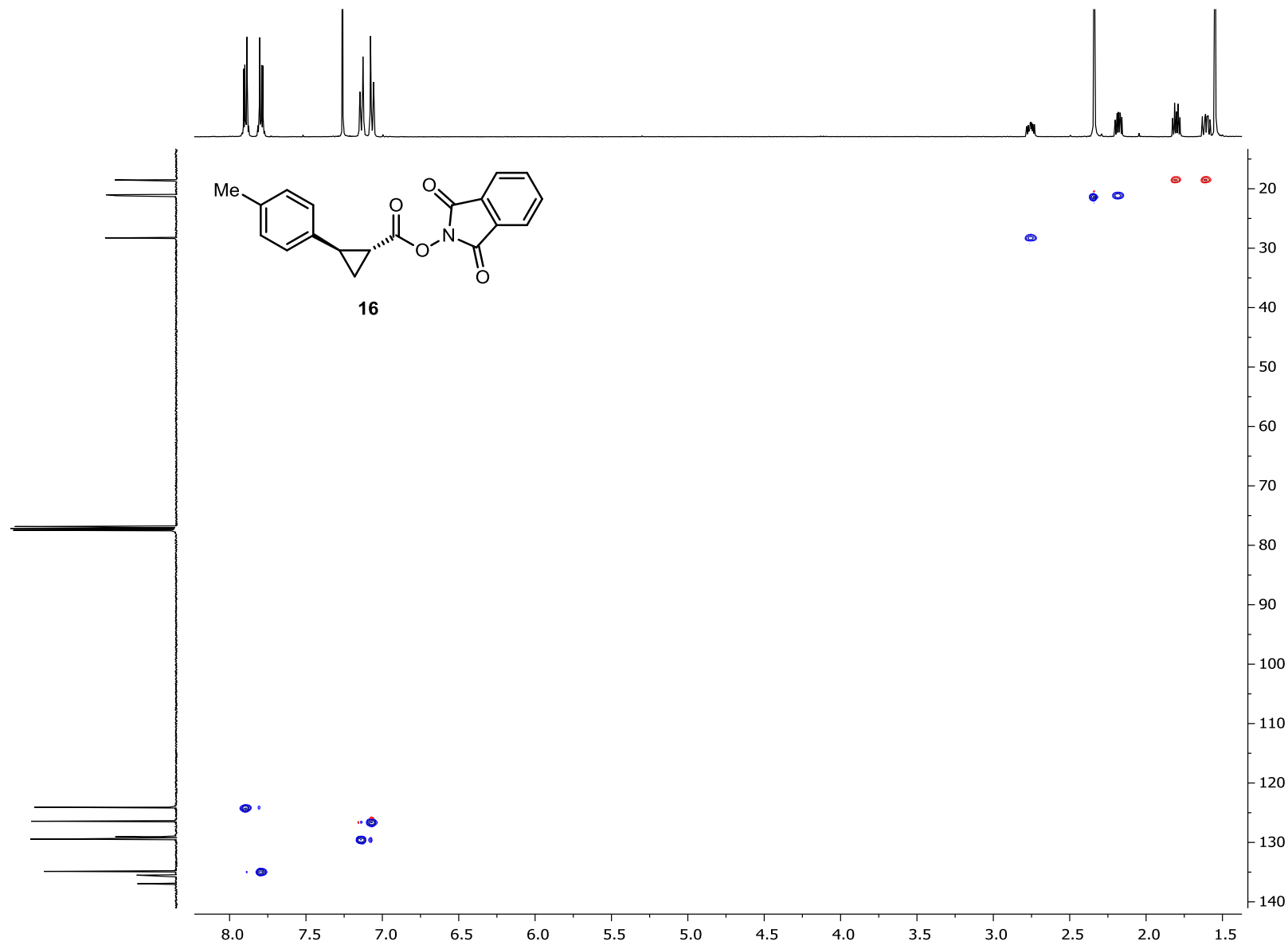
^{13}C NMR (101 MHz, CDCl_3) for compound **16**



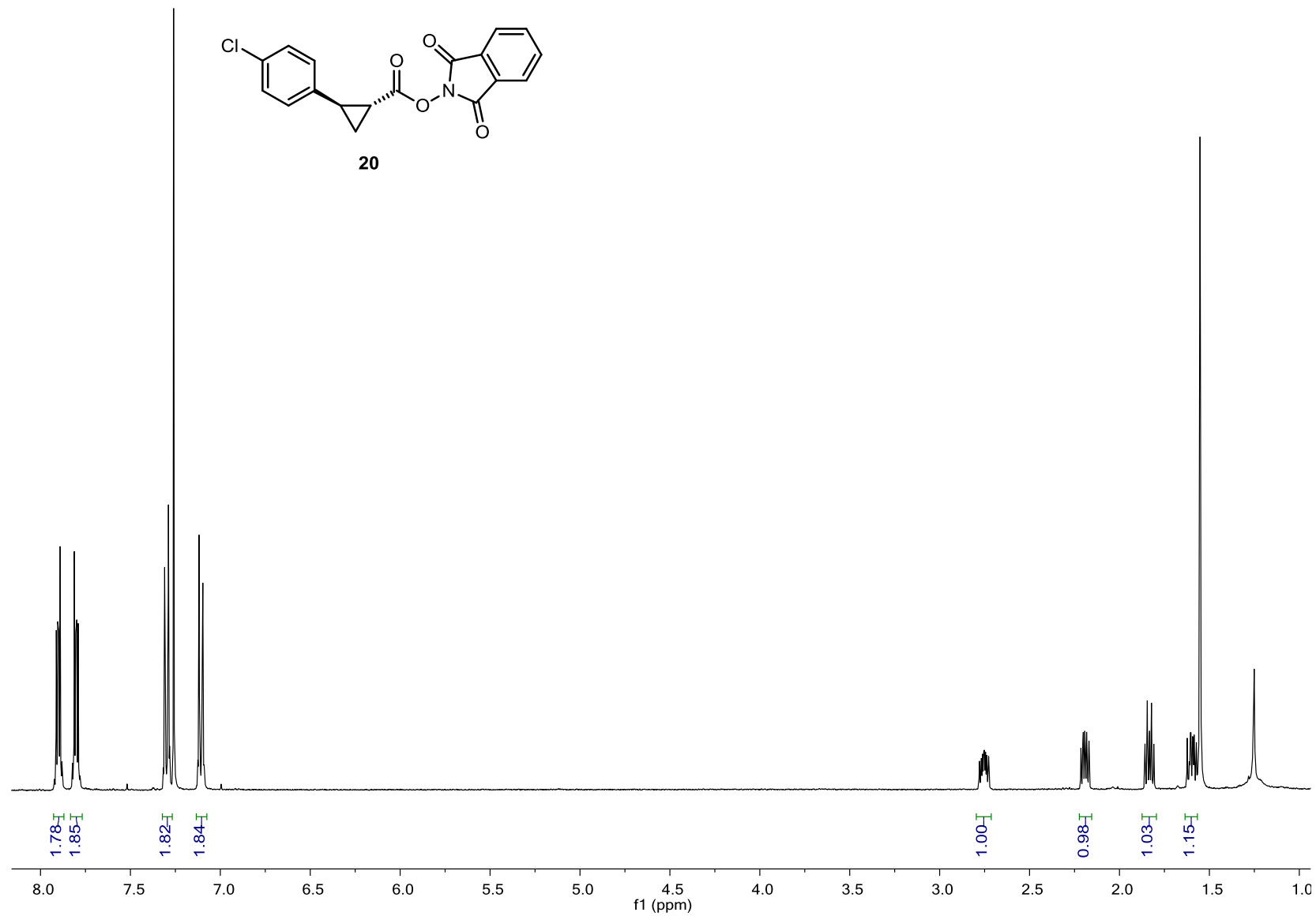
COSY NMR (400 MHz, CDCl₃) for compound **16**



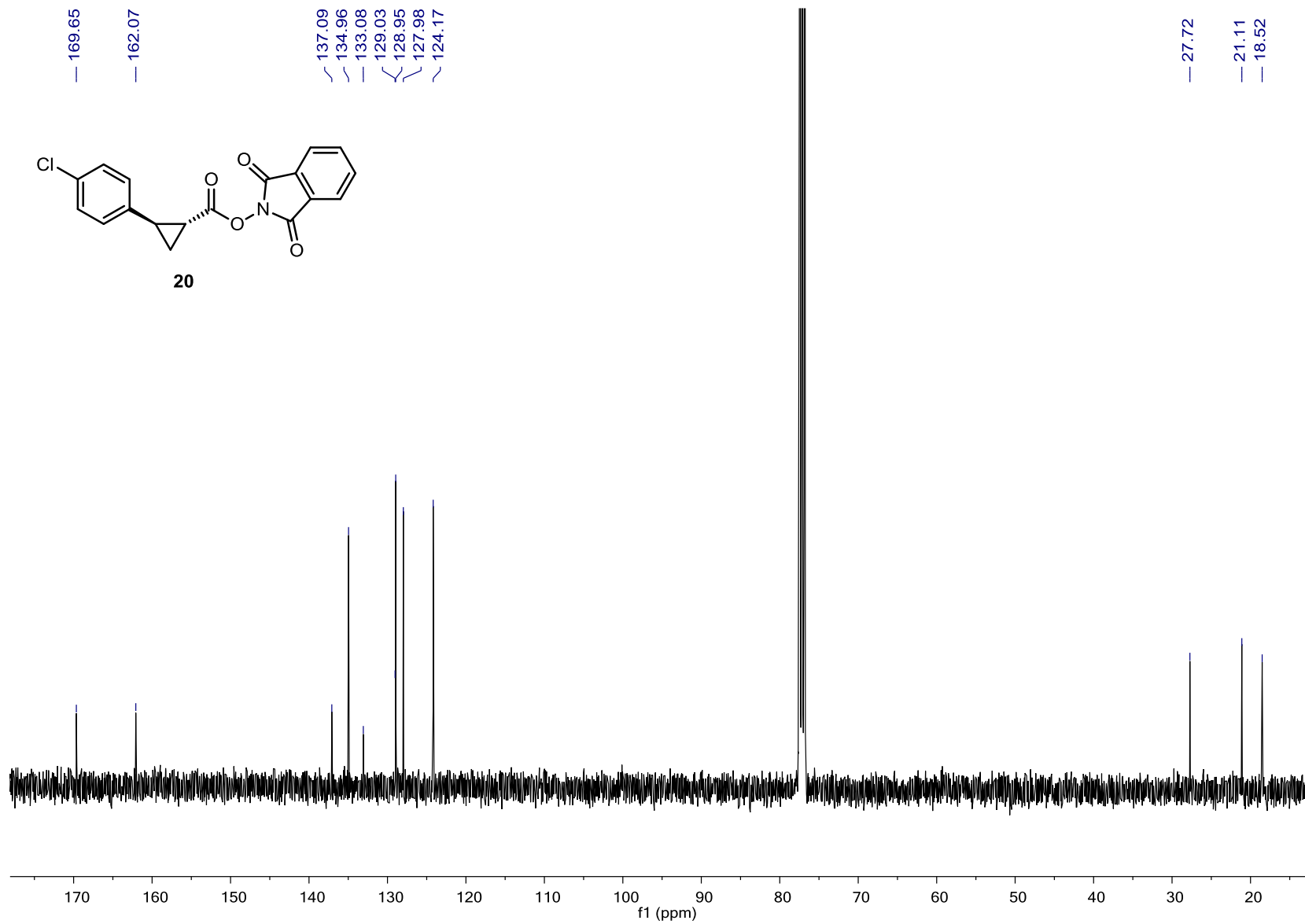
HSQC NMR (400 MHz, CDCl₃) for compound **16**



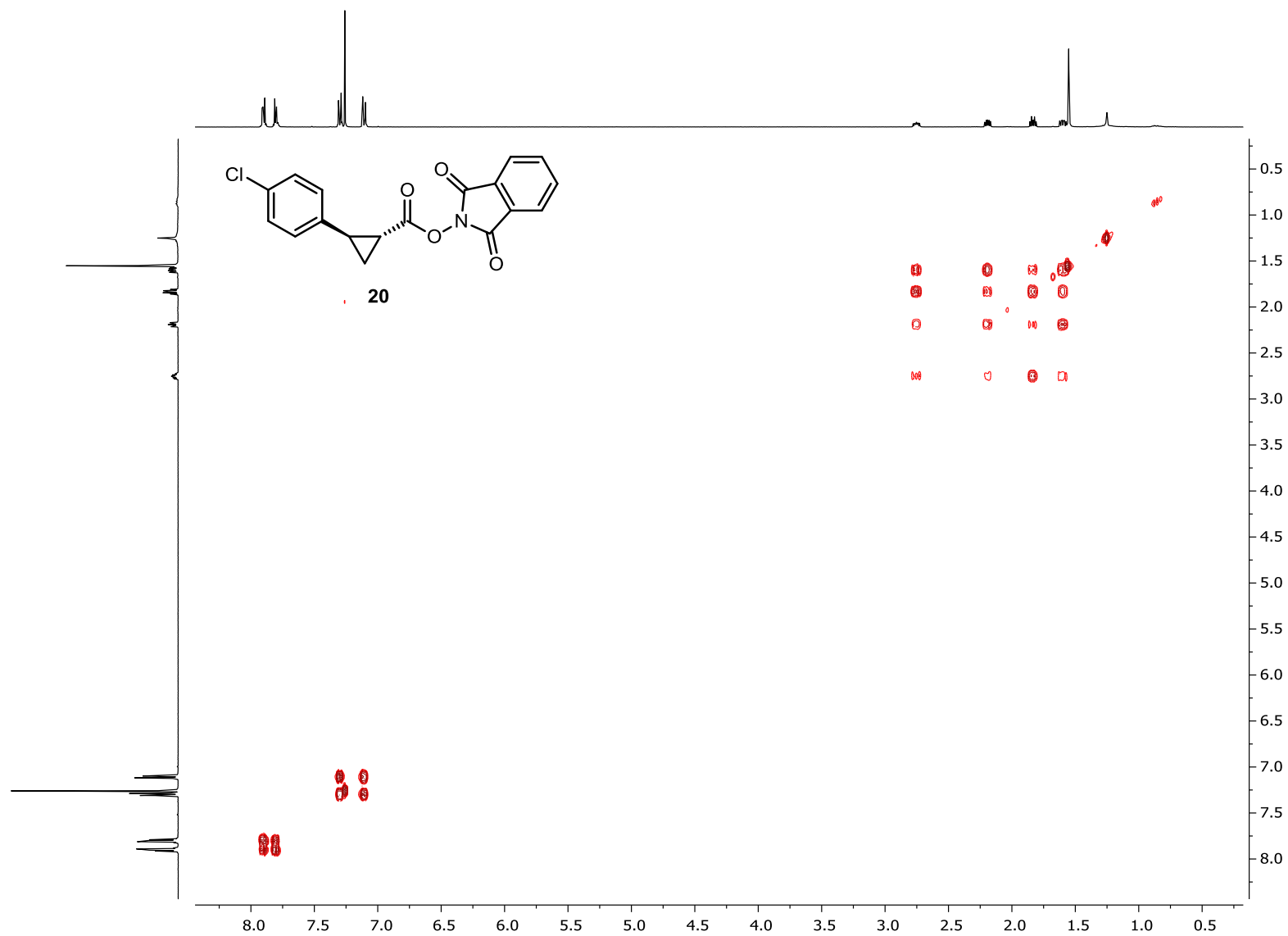
^1H NMR (400 MHz, CDCl_3) for compound **20**



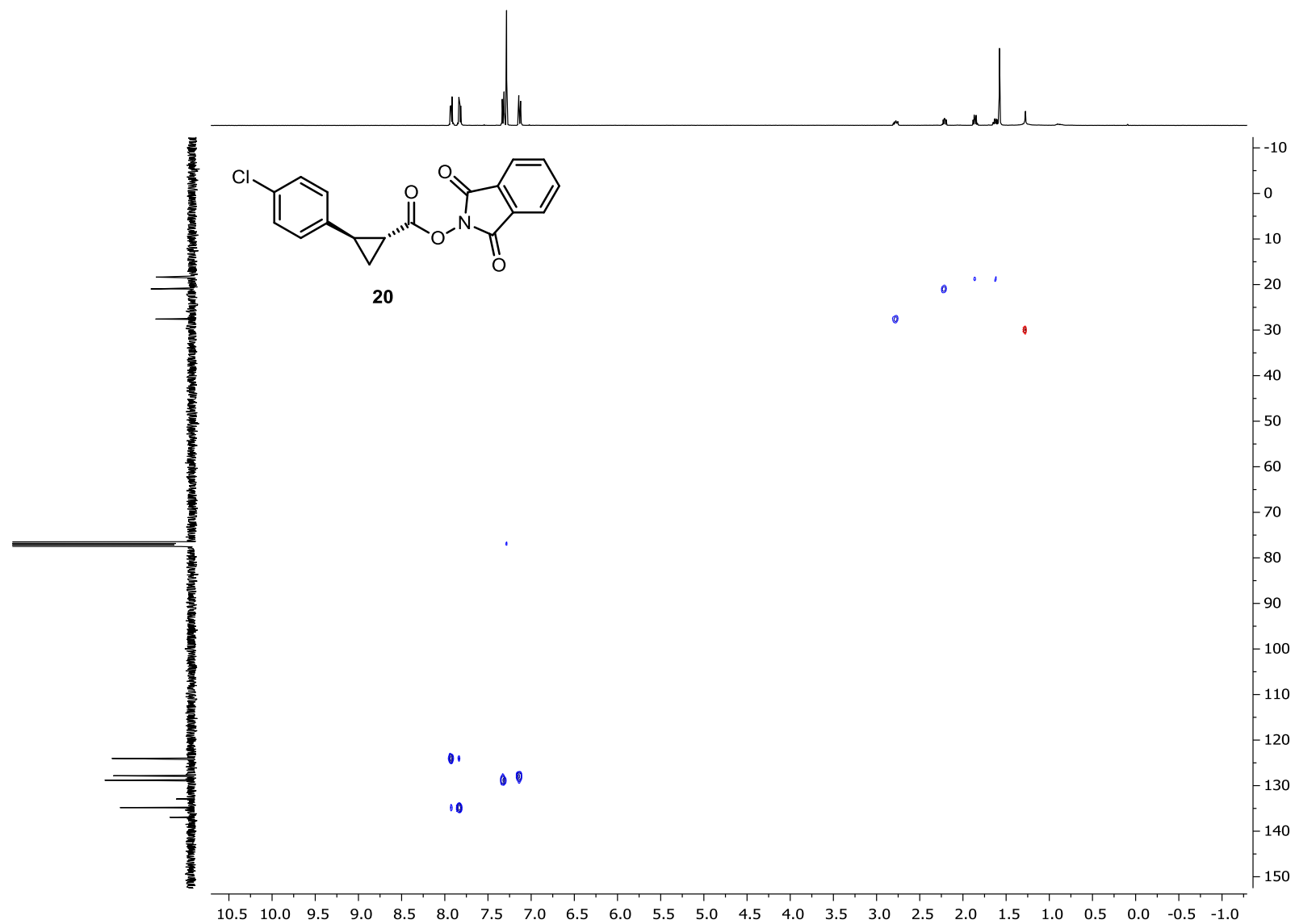
^{13}C NMR (101 MHz, CDCl_3) for compound **20**



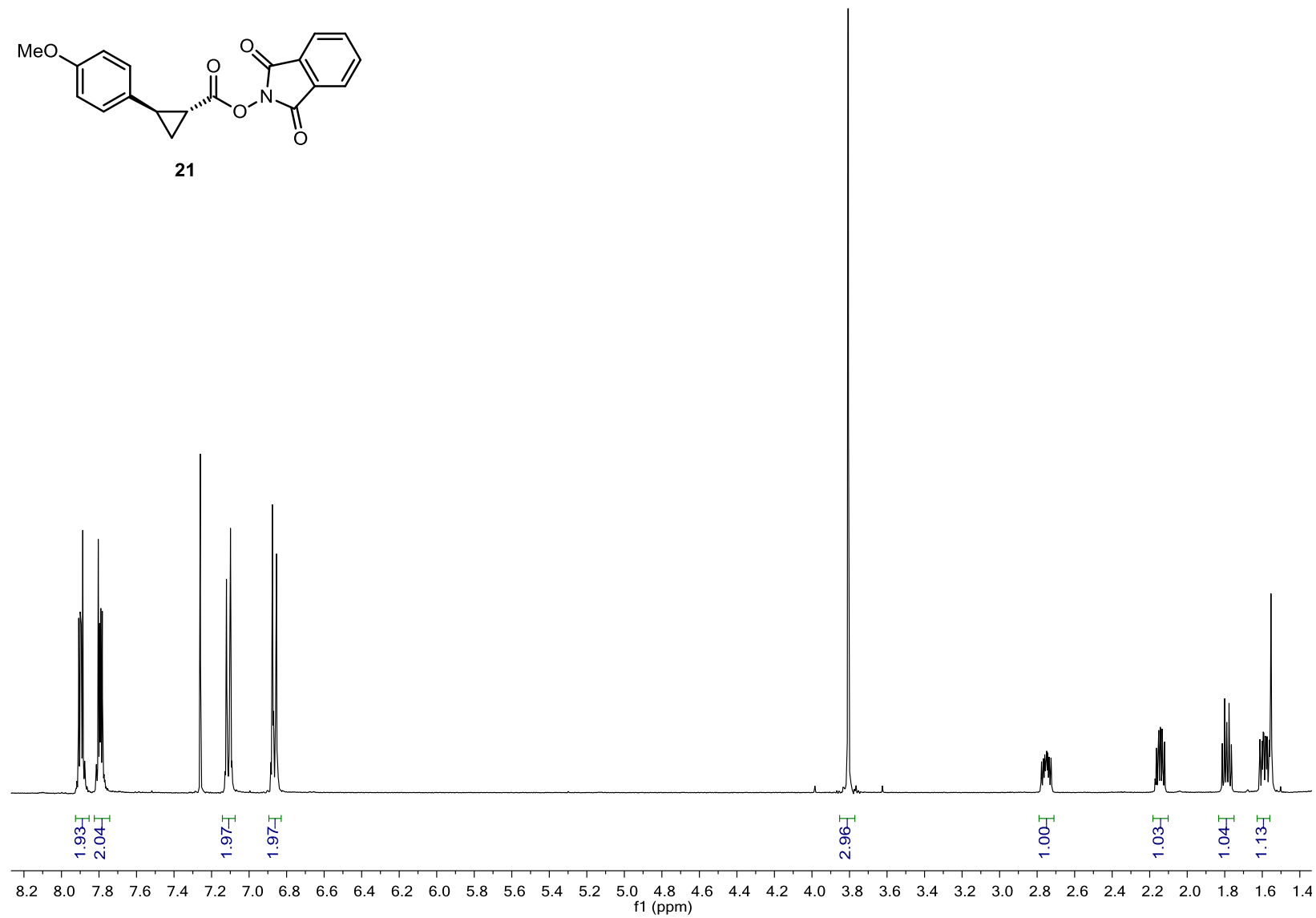
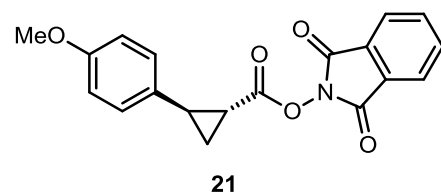
COSY NMR (400 MHz, CDCl₃) for compound **20**



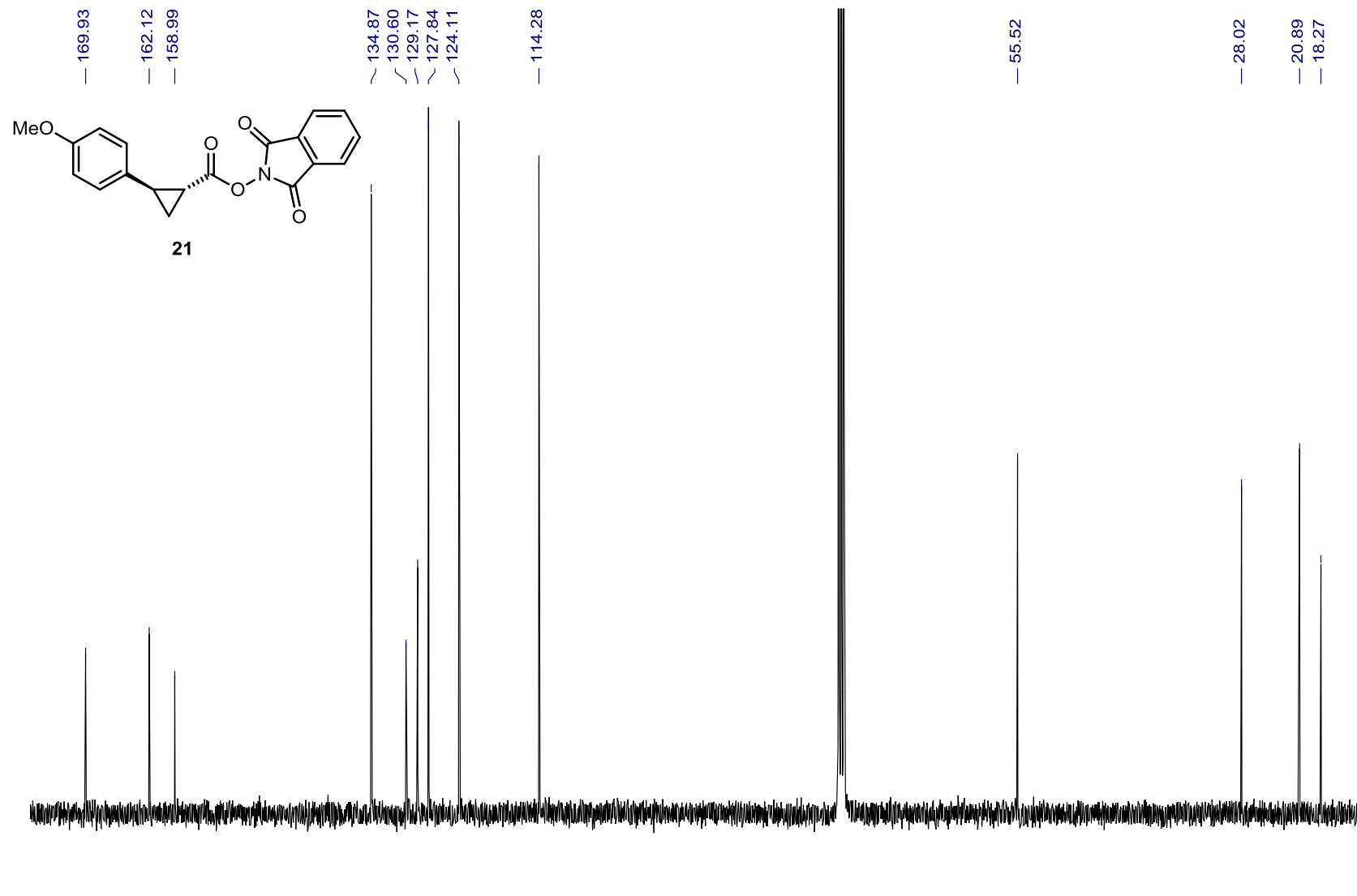
HSQC NMR (400 MHz, CDCl_3) for compound **20**



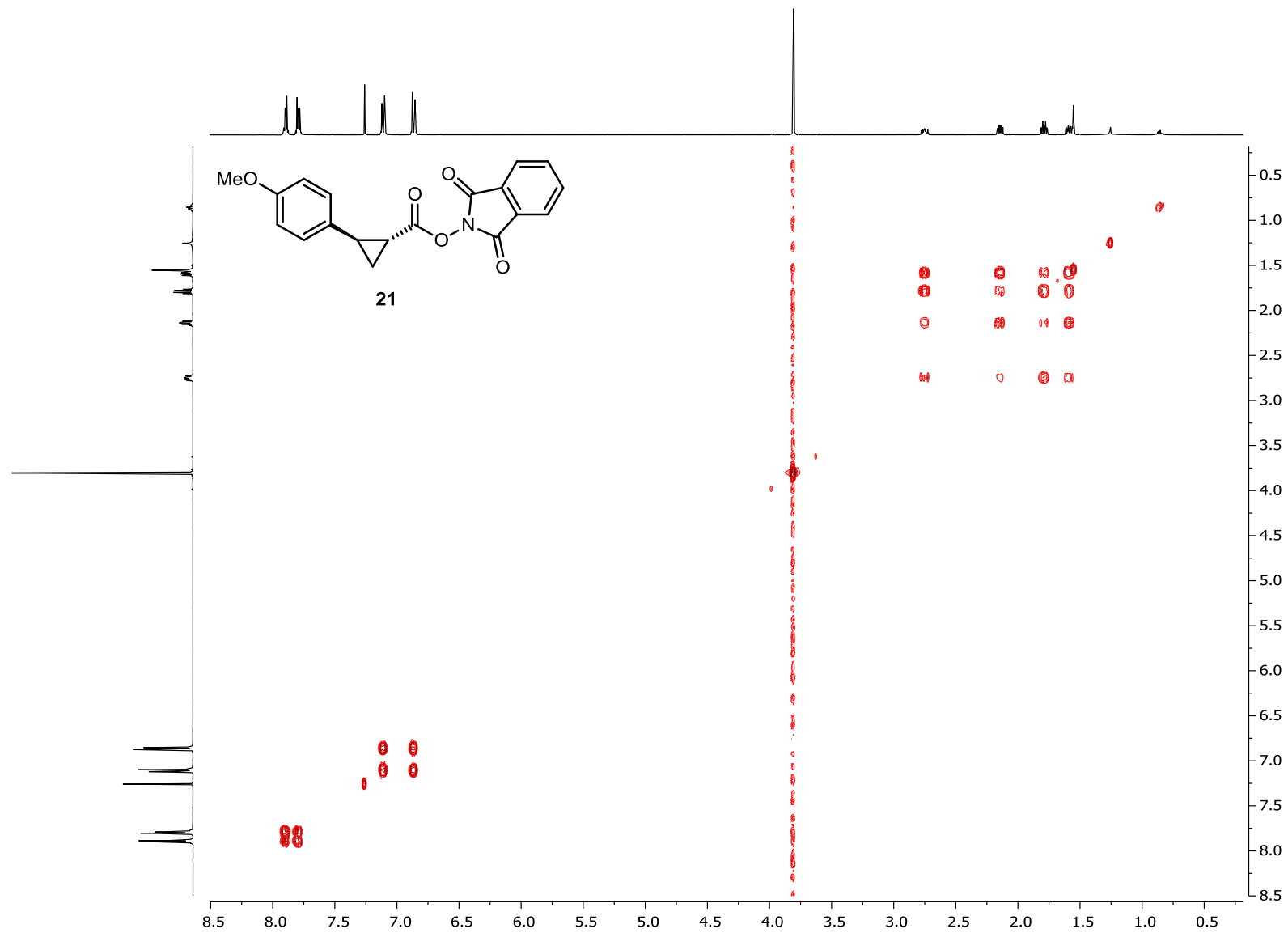
^1H NMR (400 MHz, CDCl_3) for compound **21**



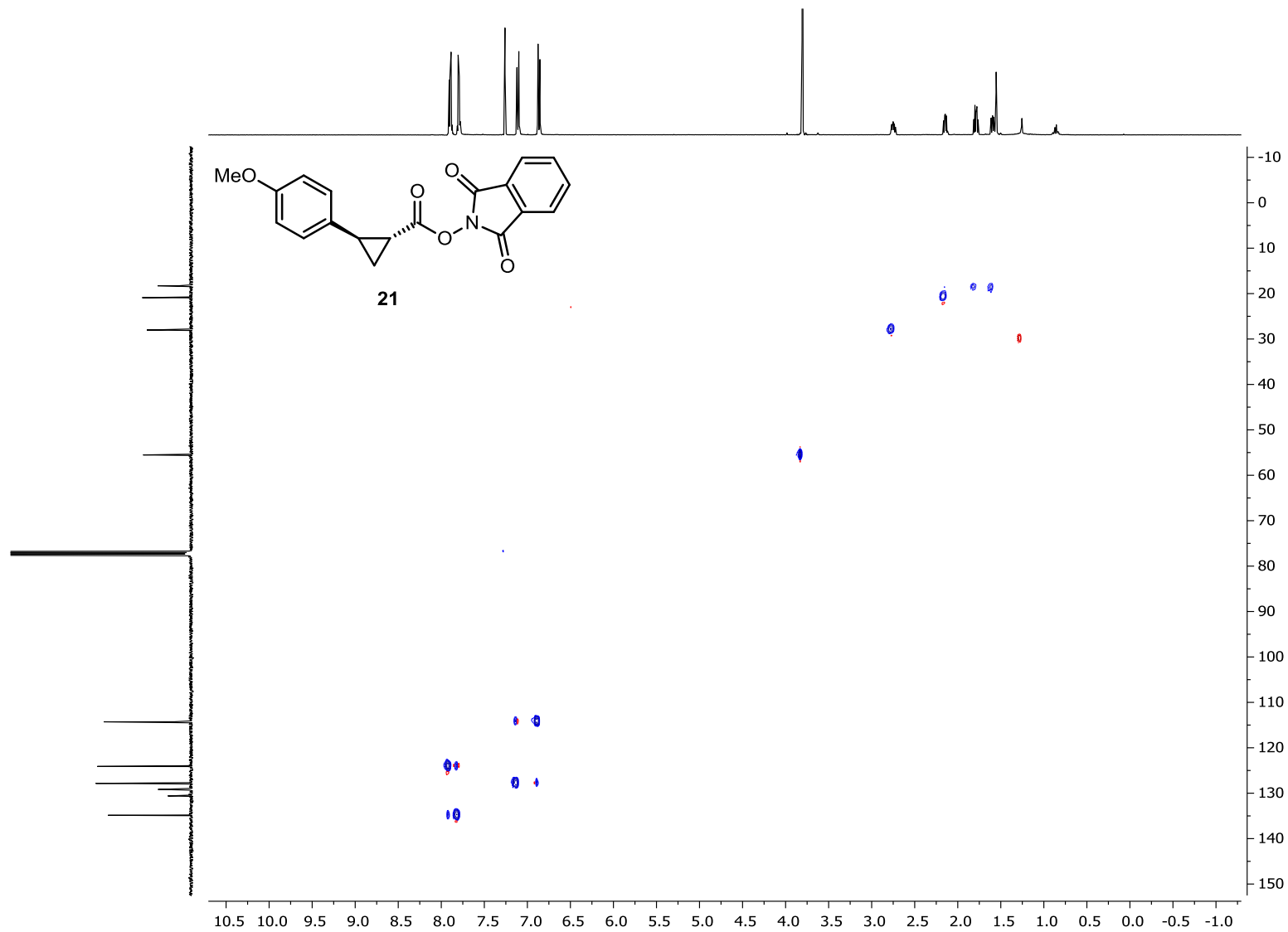
^{13}C NMR (101 MHz, CDCl_3) for compound **21**



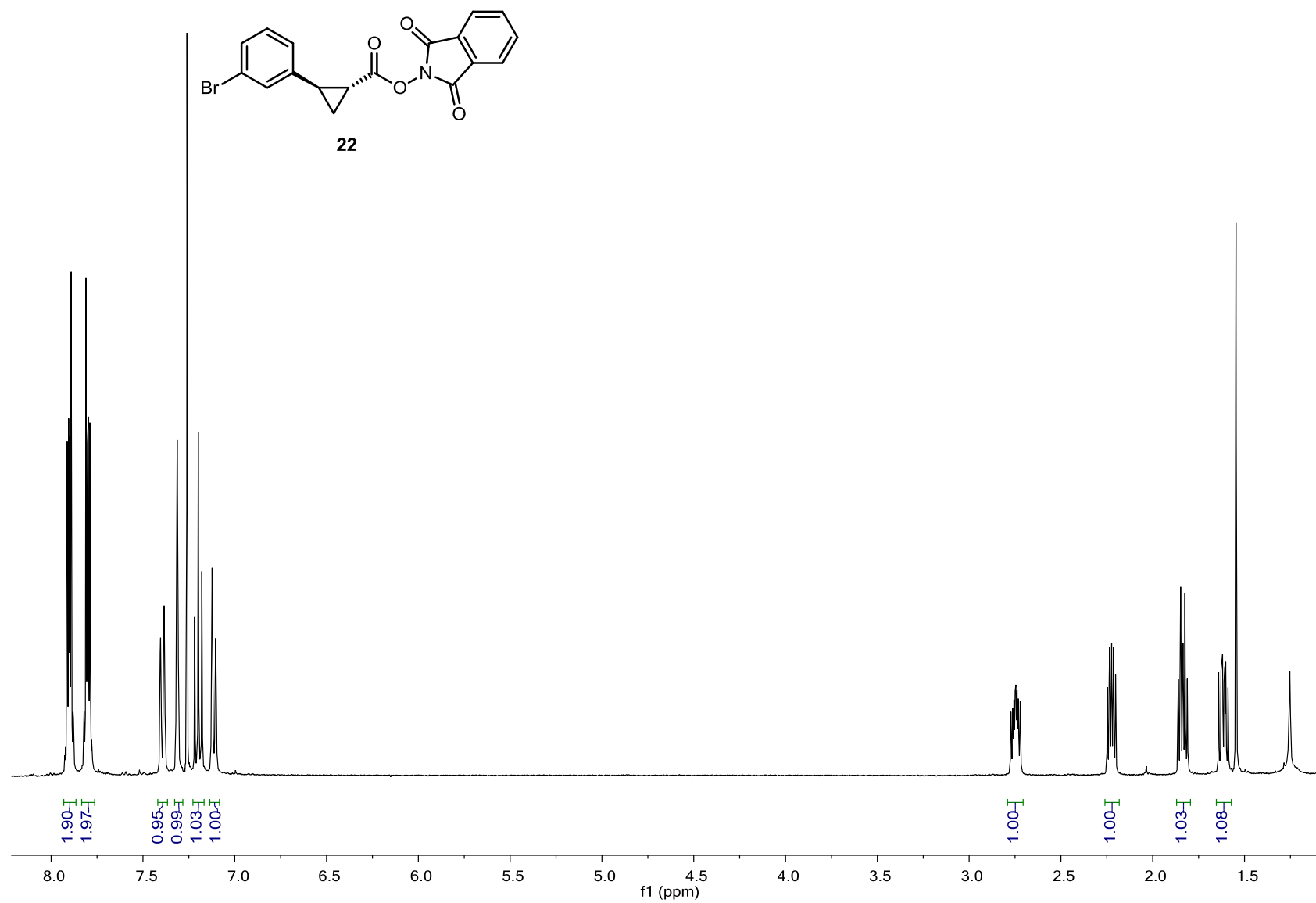
COSY NMR (400 MHz, CDCl₃) for compound 21



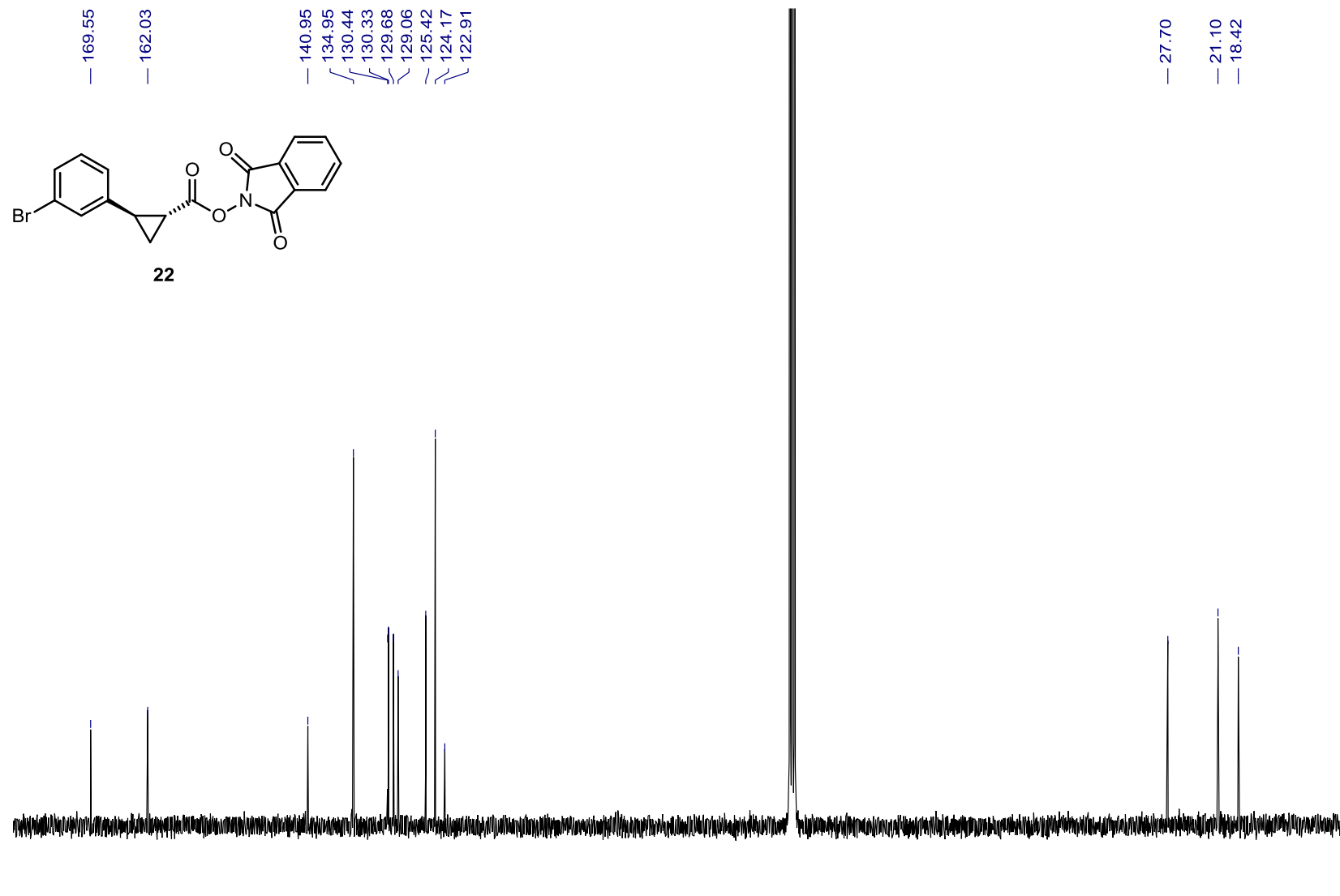
HSQC NMR (400 MHz, CDCl₃) for compound **21**



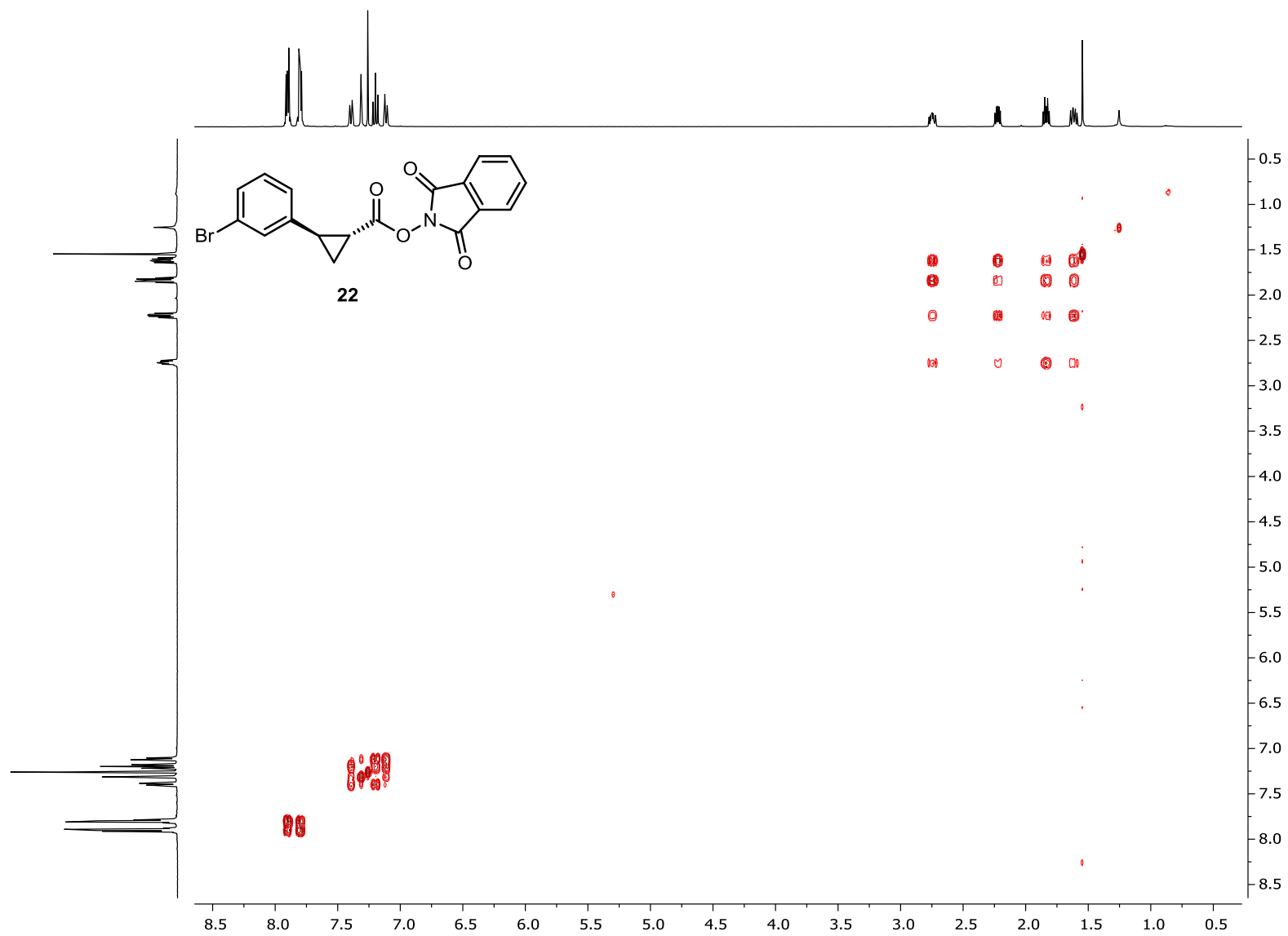
^1H NMR (400 MHz, CDCl_3) for compound 22



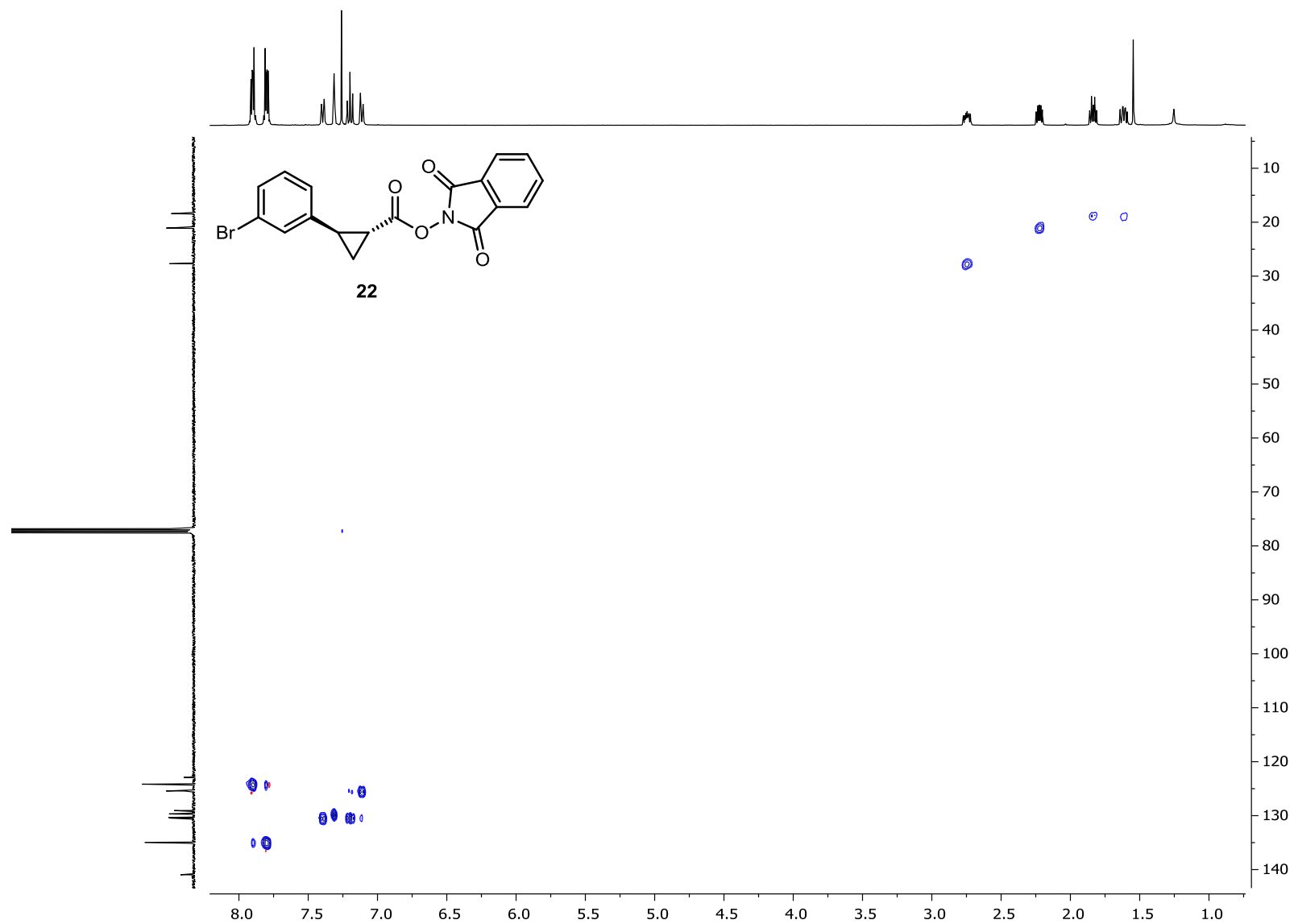
^{13}C NMR (101 MHz, CDCl_3) for compound **22**



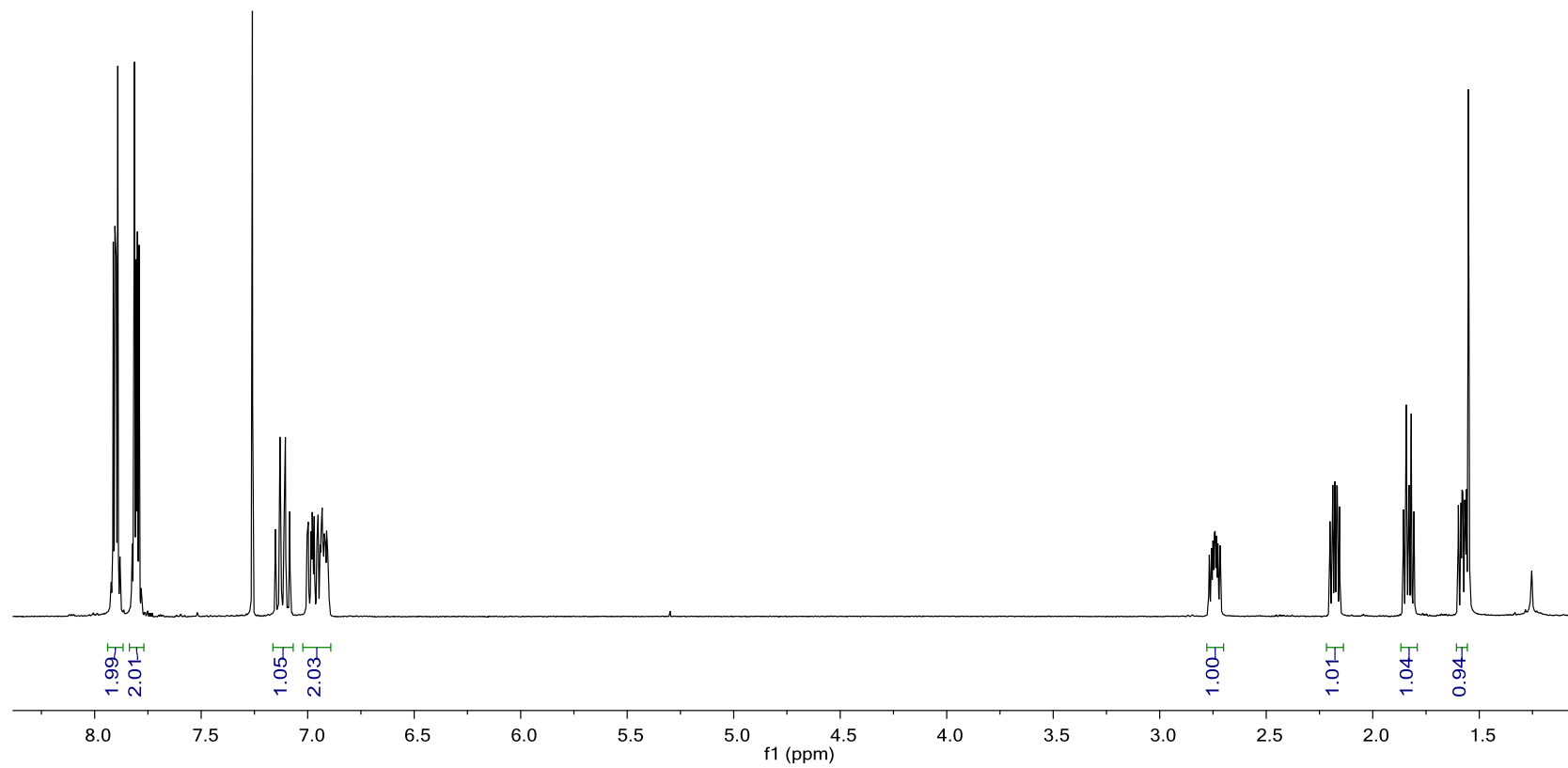
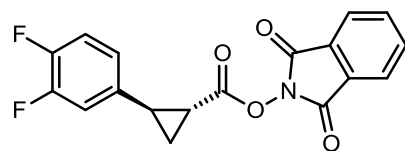
COSY NMR (400 MHz, CDCl₃) for compound 22



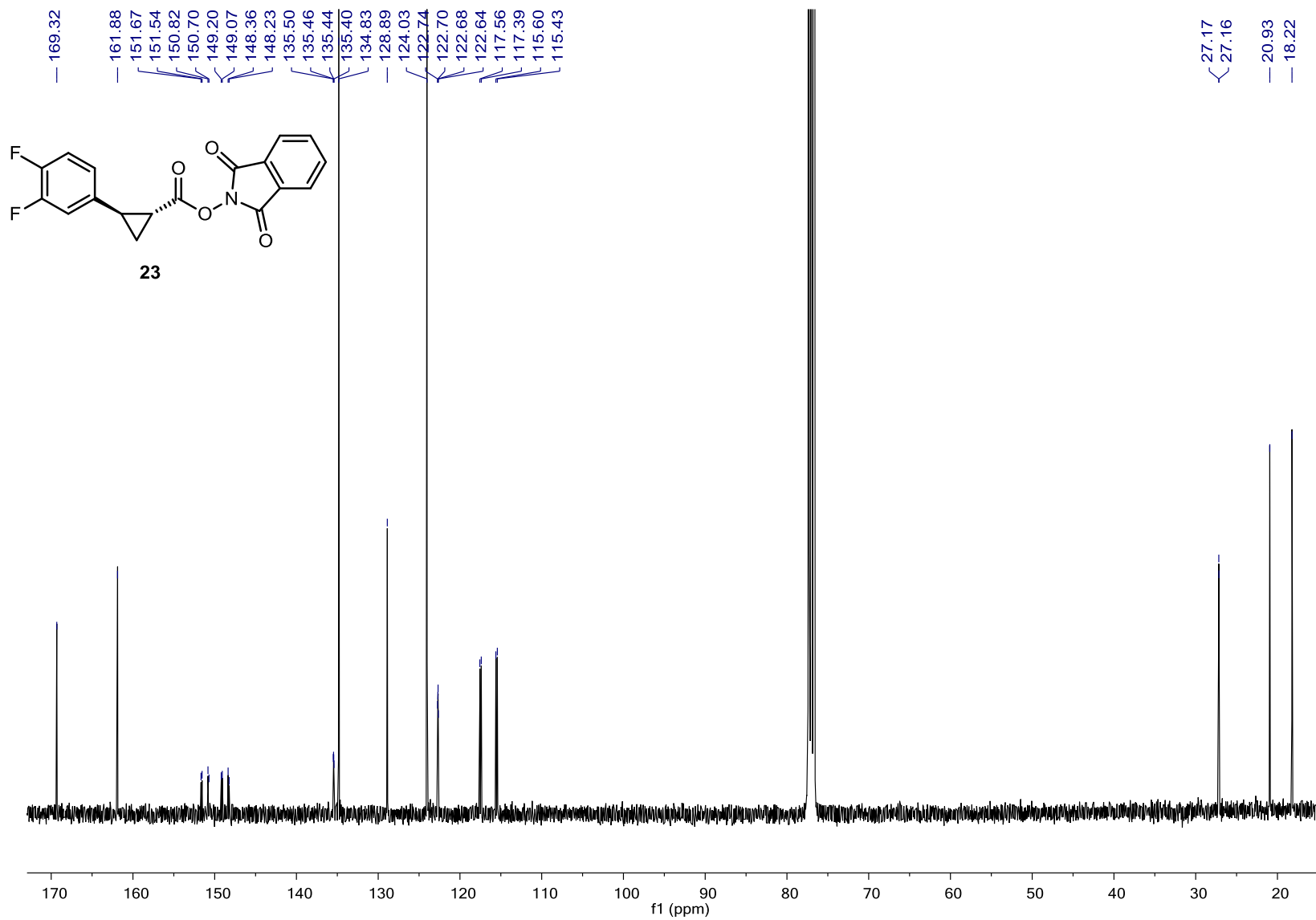
HSQC NMR (400 MHz, CDCl₃) for compound 22



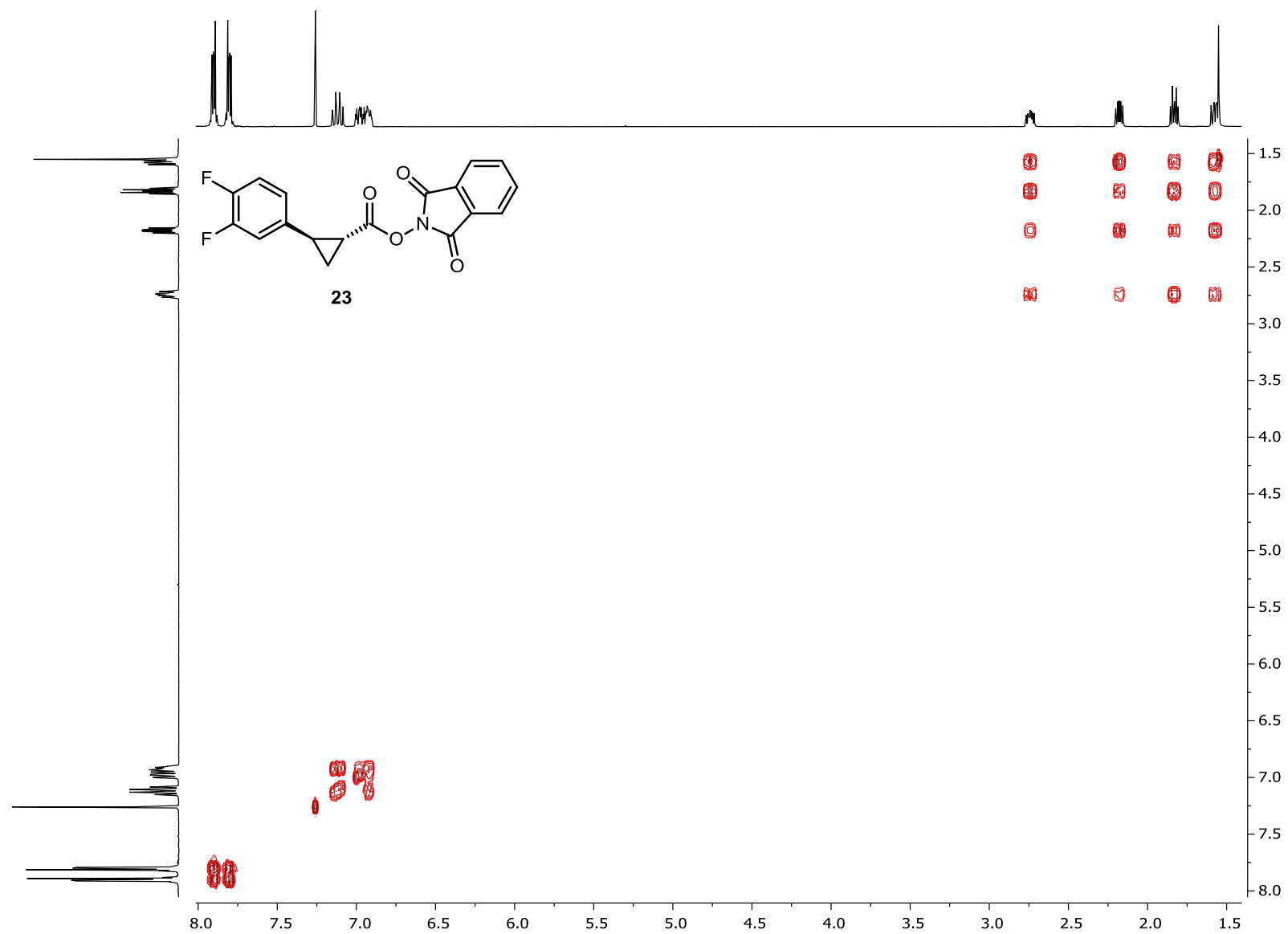
^1H NMR (400 MHz, CDCl_3) for compound **23**



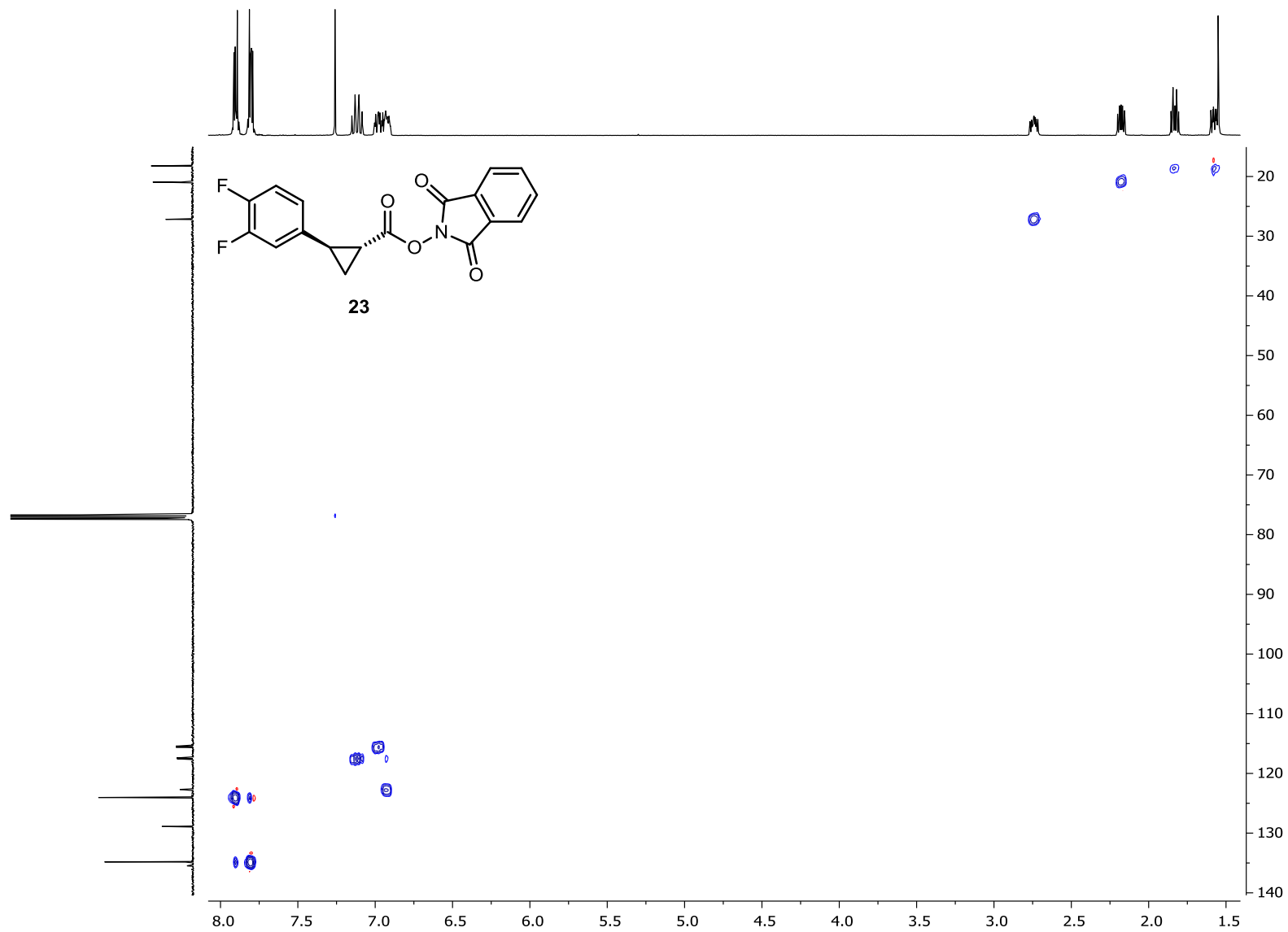
^{13}C NMR (101 MHz, CDCl_3) for compound **23**



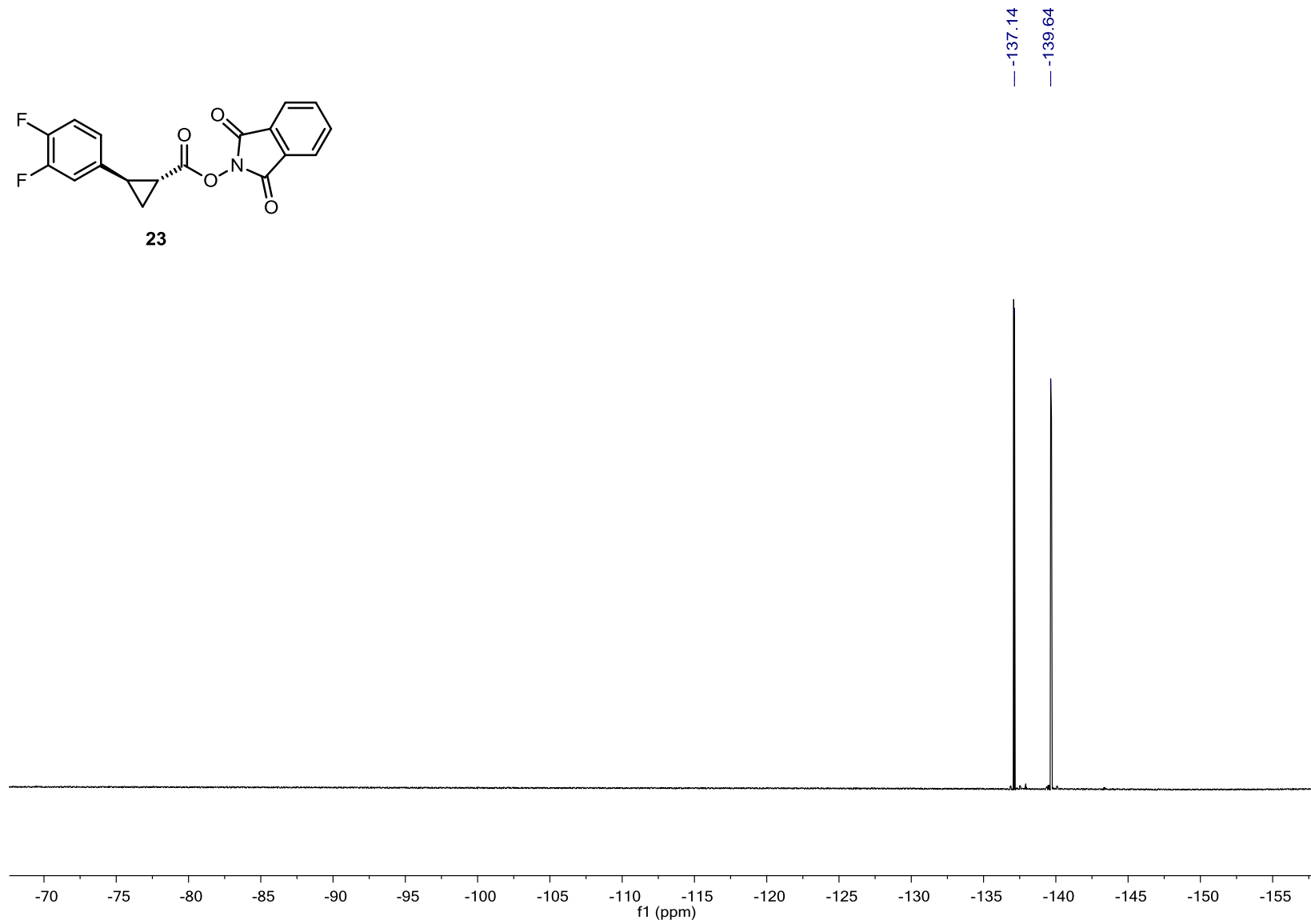
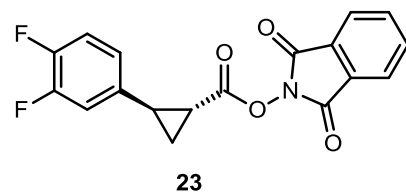
COSY NMR (400 MHz, CDCl₃) for compound 23



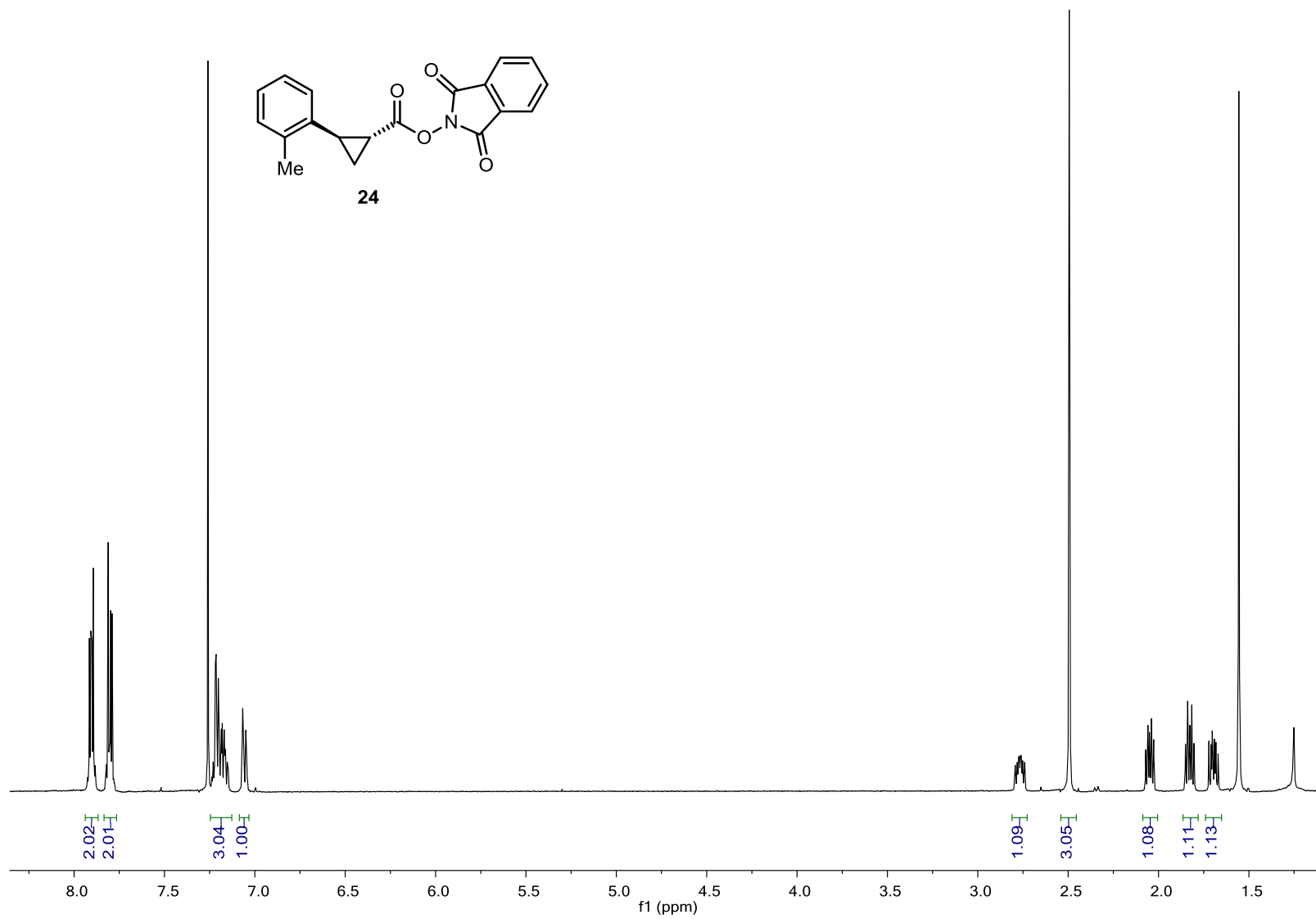
HSQC NMR (400 MHz, CDCl₃) for compound **23**



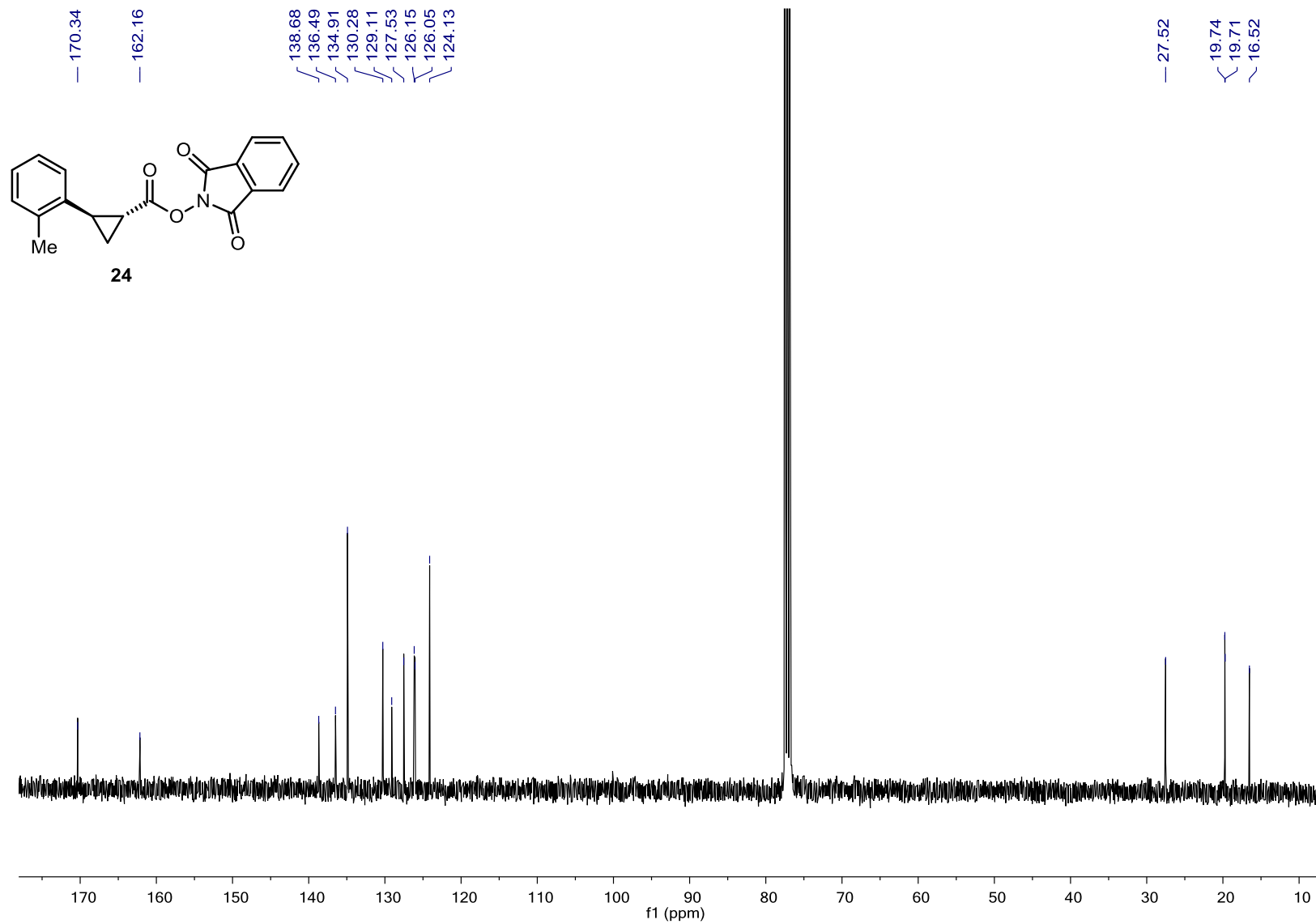
^{19}F NMR (377 MHz, CDCl_3) for compound **23**



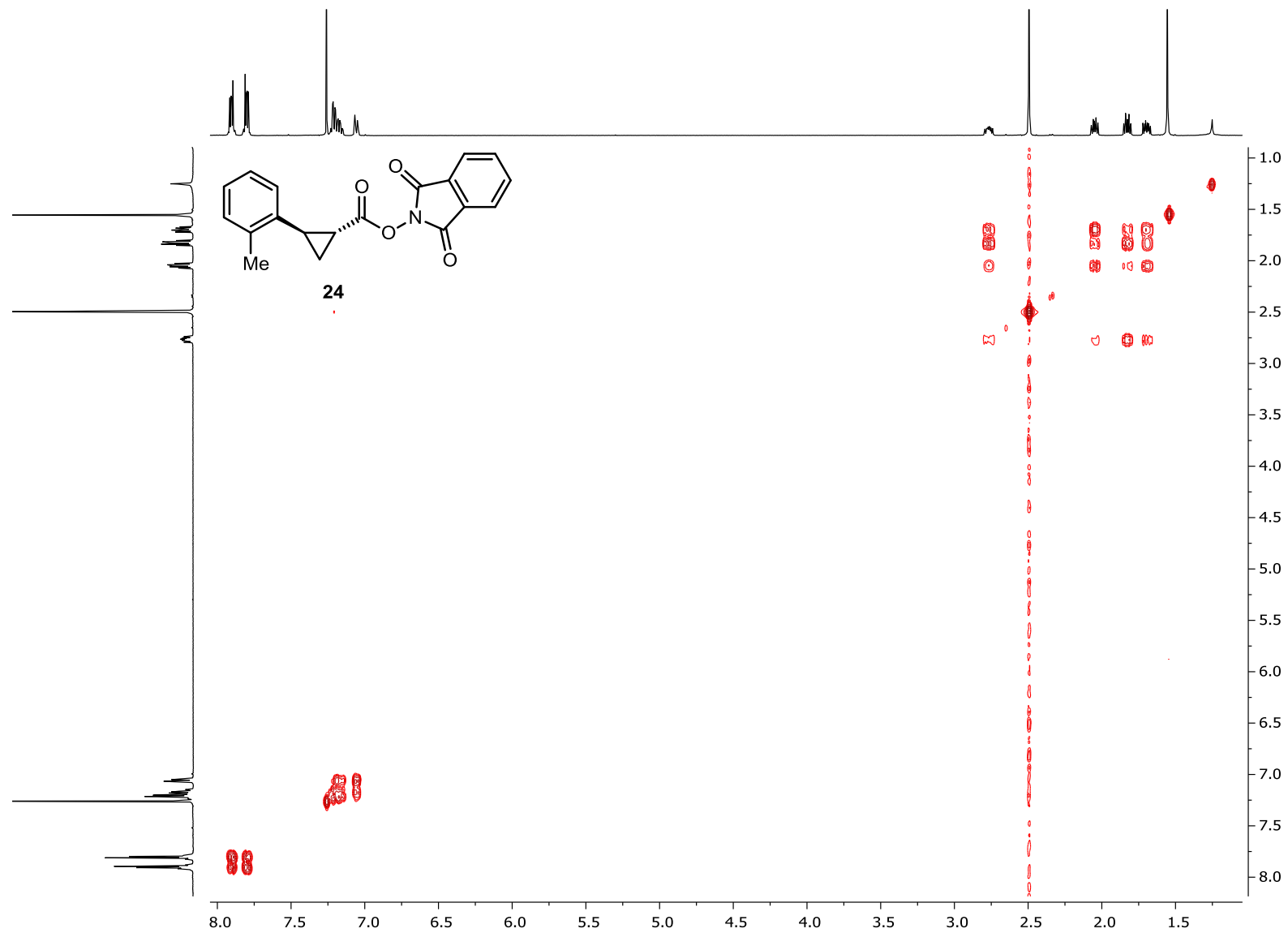
^1H NMR (400 MHz, CDCl_3) for compound **24**



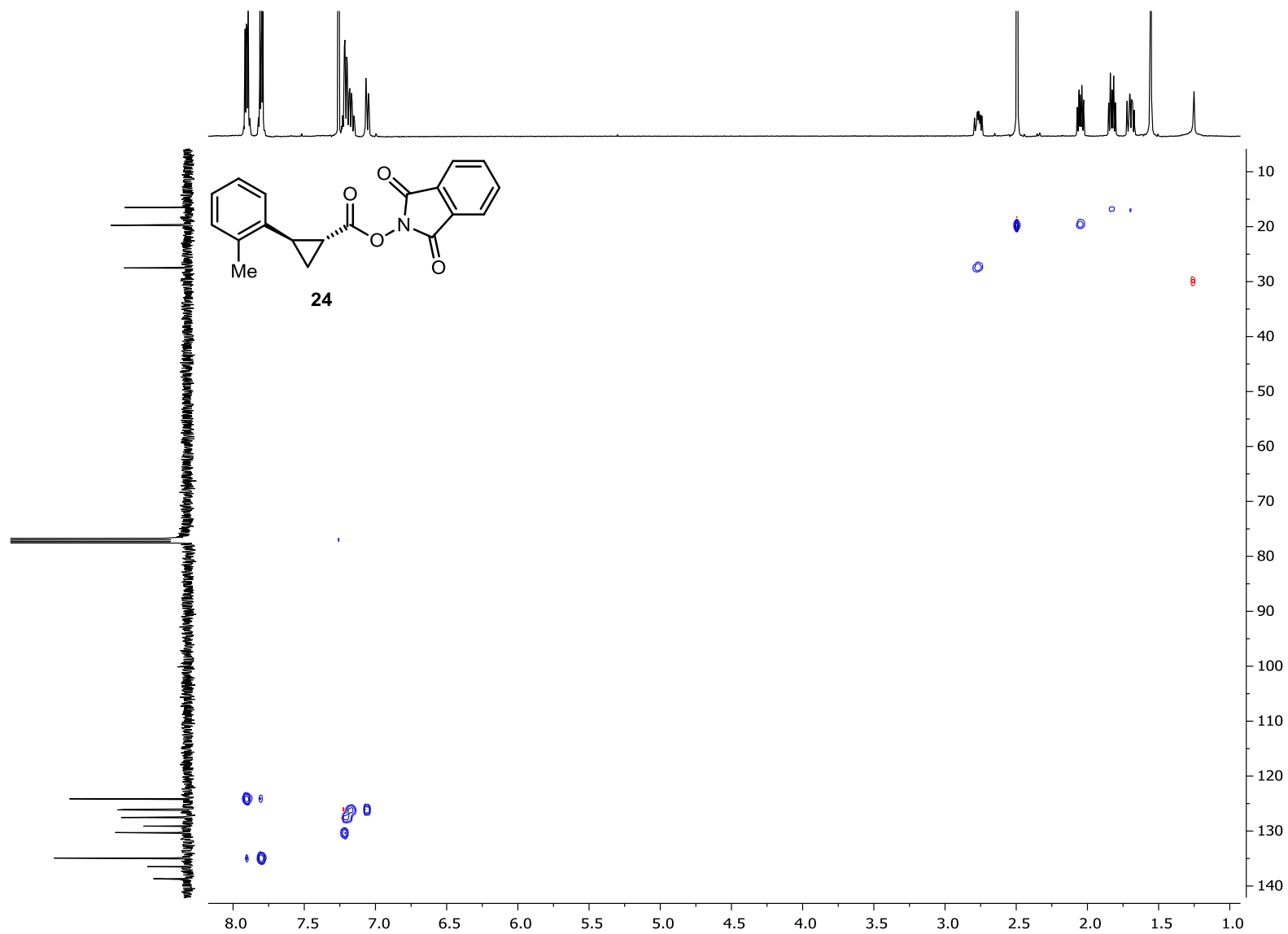
^{13}C NMR (101 MHz, CDCl_3) for compound **24**



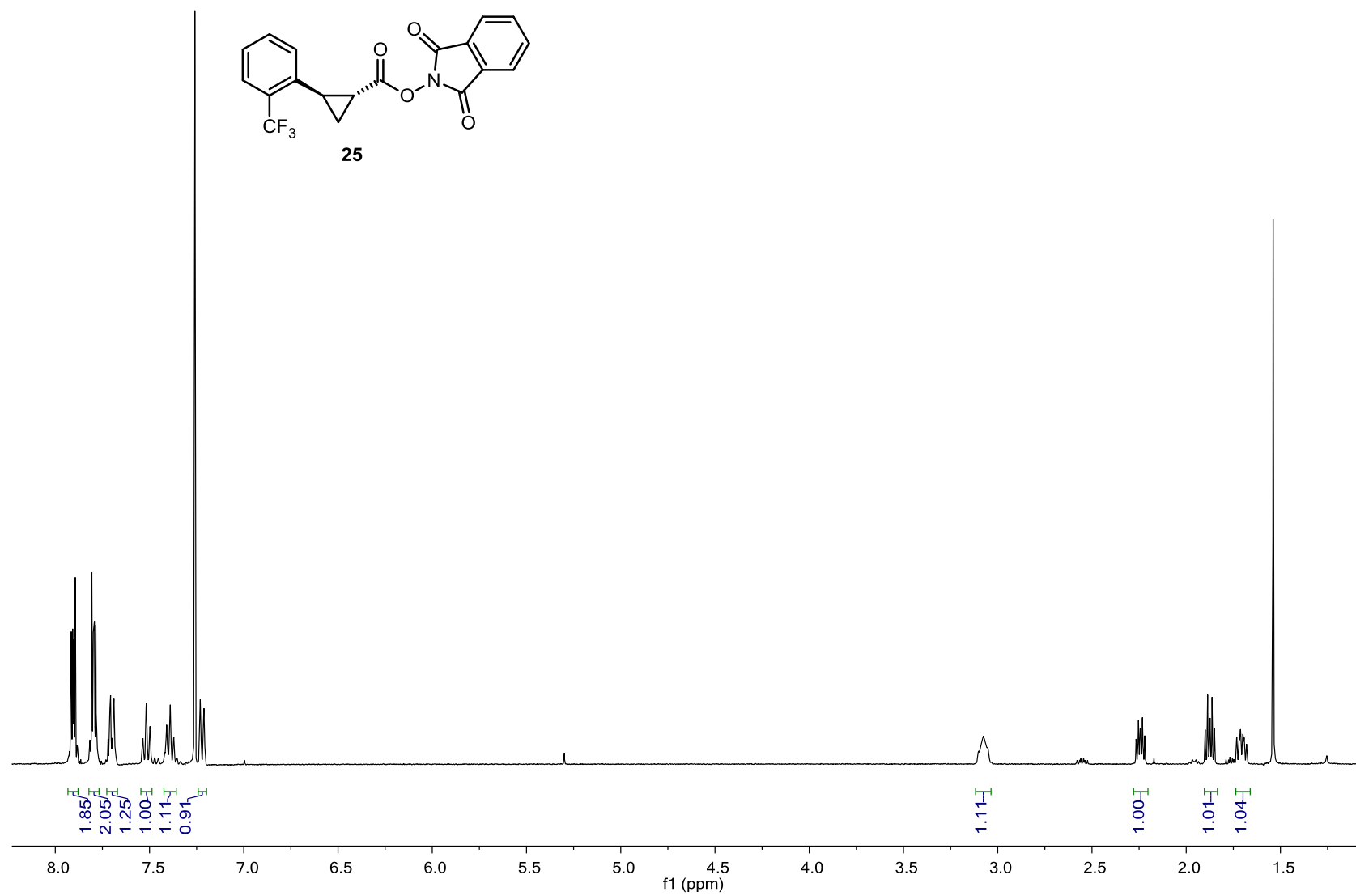
COSY NMR (400 MHz, CDCl₃) for compound **24**



HSQC NMR (400 MHz, CDCl₃) for compound **24**

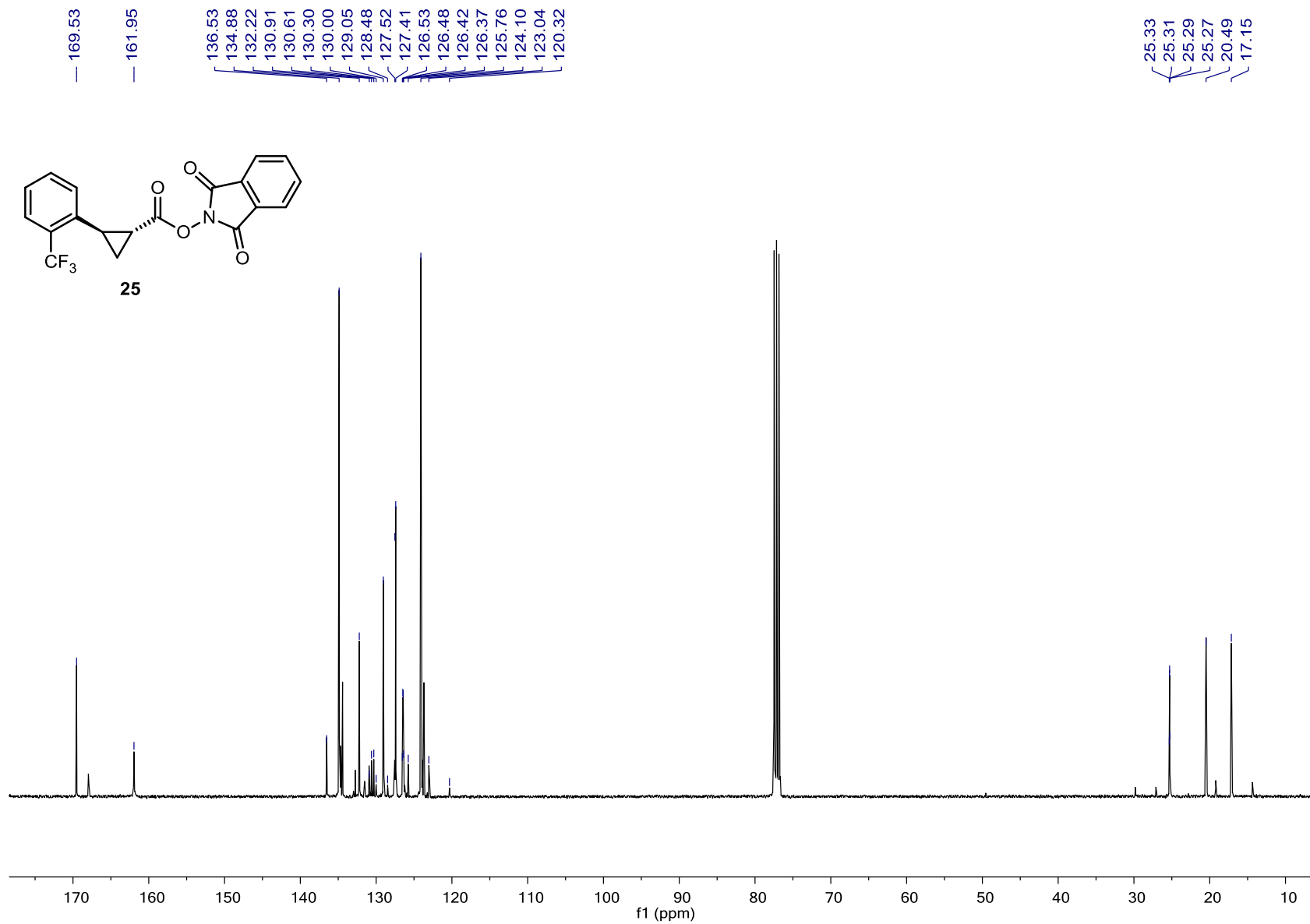


^1H NMR (400 MHz, CDCl_3) for compound 25



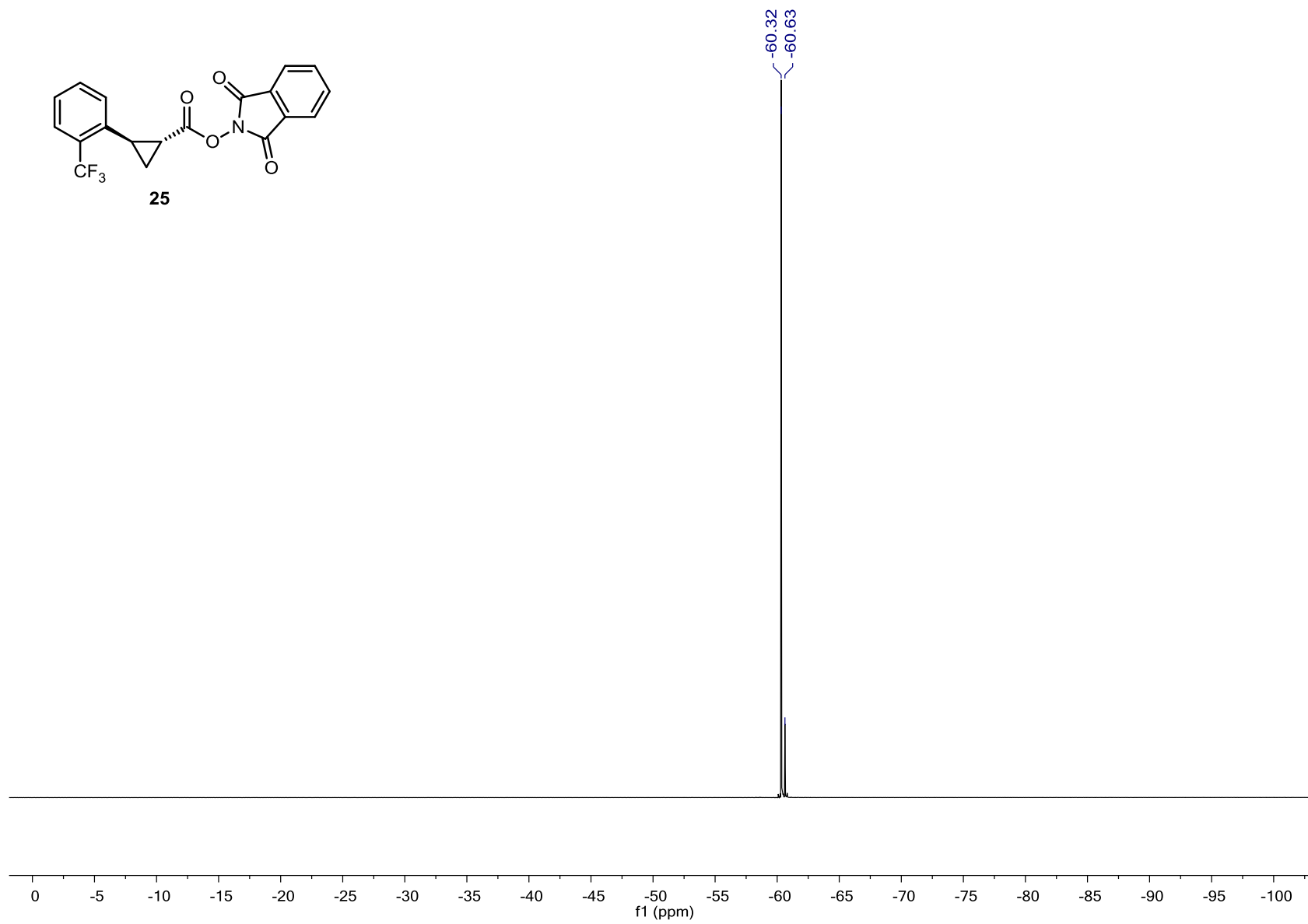
S139

^{13}C NMR (101 MHz, CDCl_3) for compound **25**



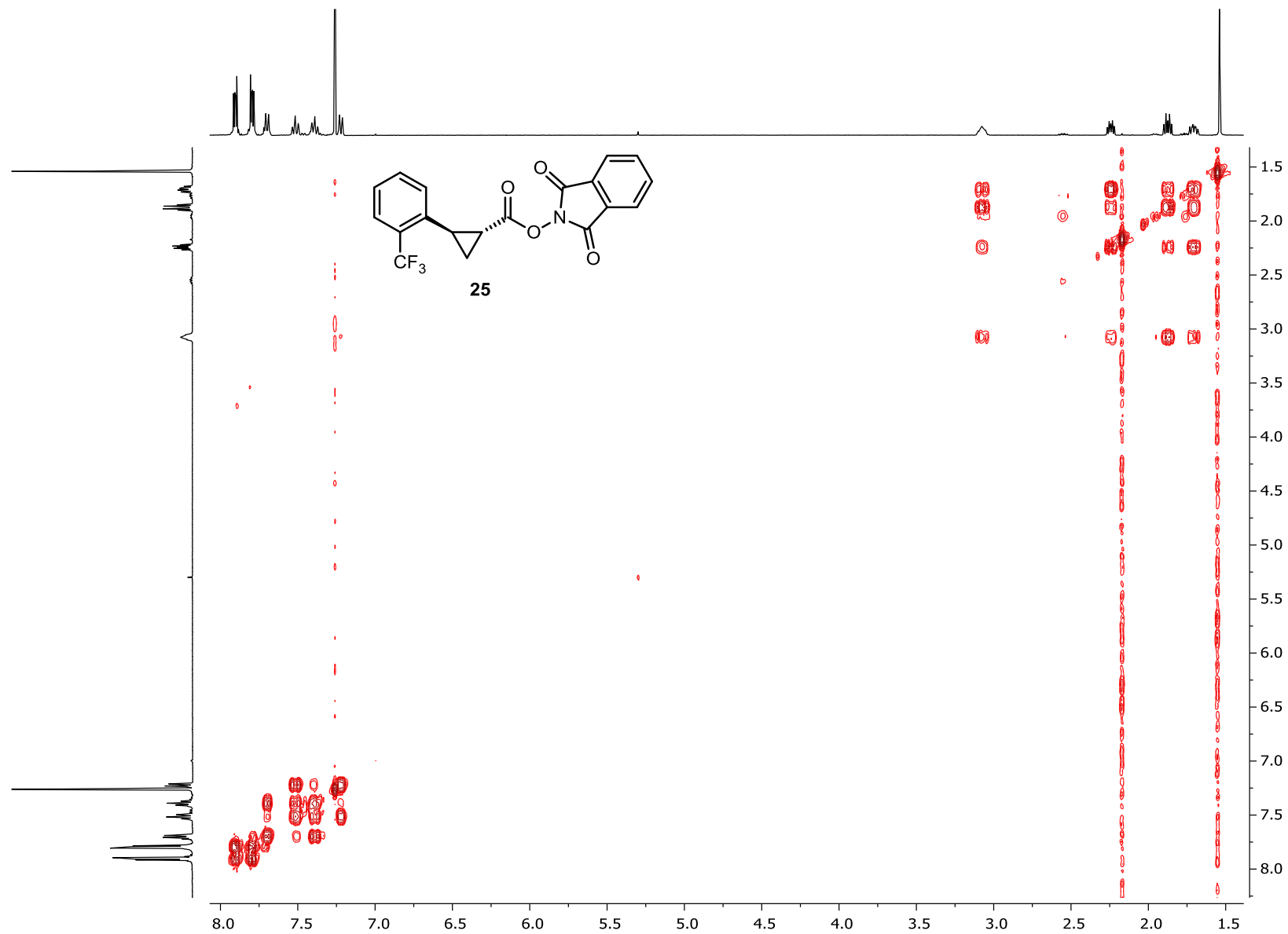
S140

^{19}F NMR (377 MHz, CDCl_3) for compound **25**



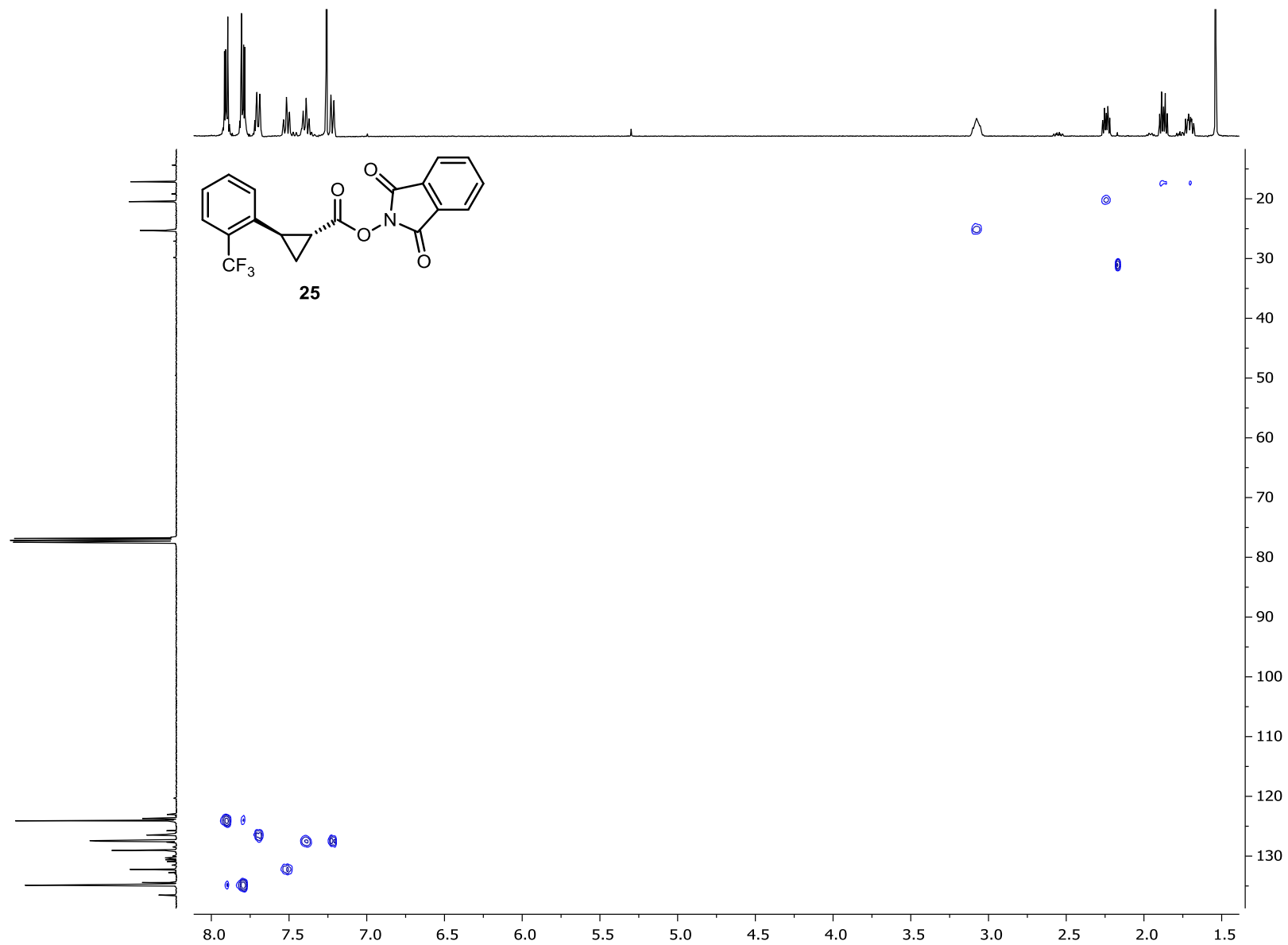
S141

COSY NMR (400 MHz, CDCl₃) for compound 25



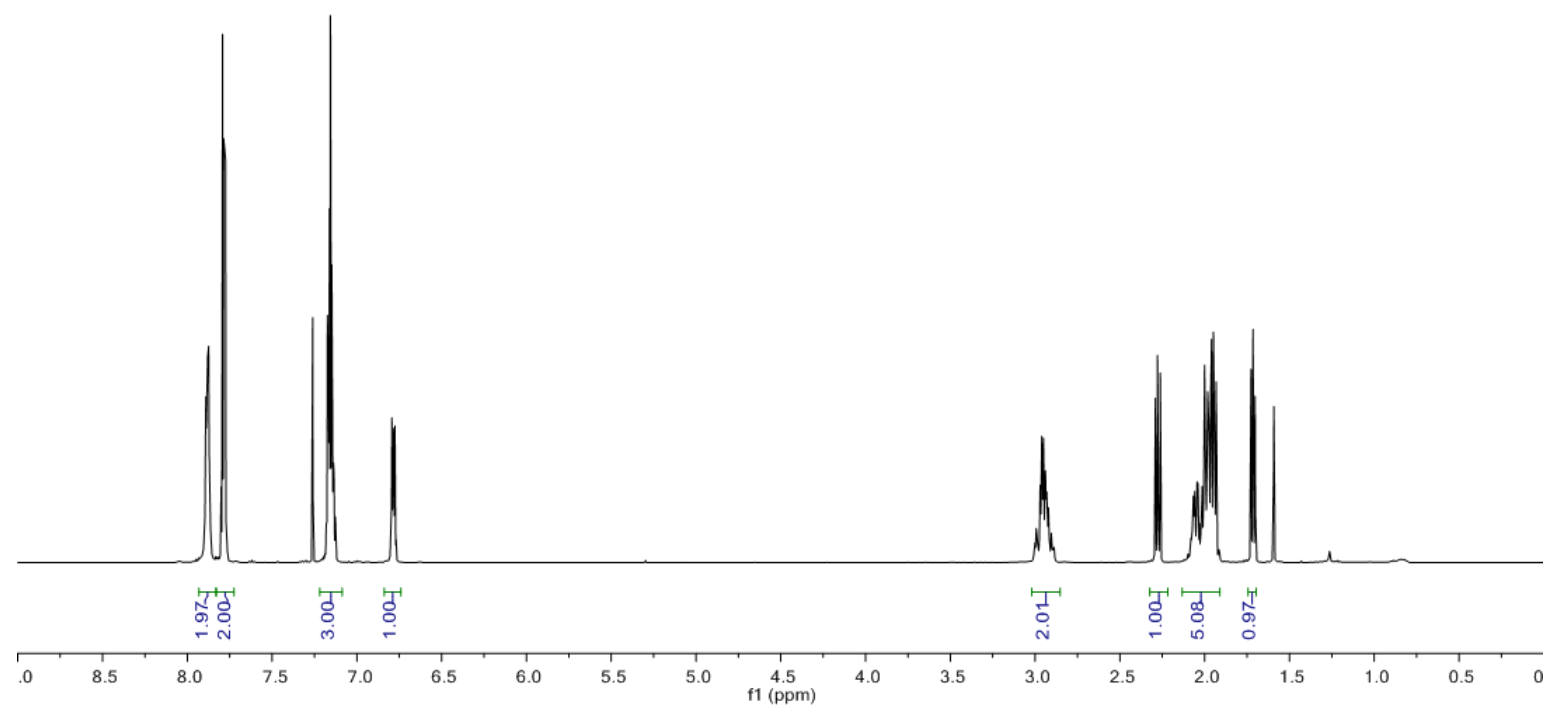
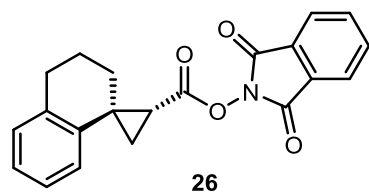
S142

HSQC NMR (400 MHz, CDCl₃) for compound **25**



S143

^1H NMR (500 MHz, CDCl_3) for compound **26**

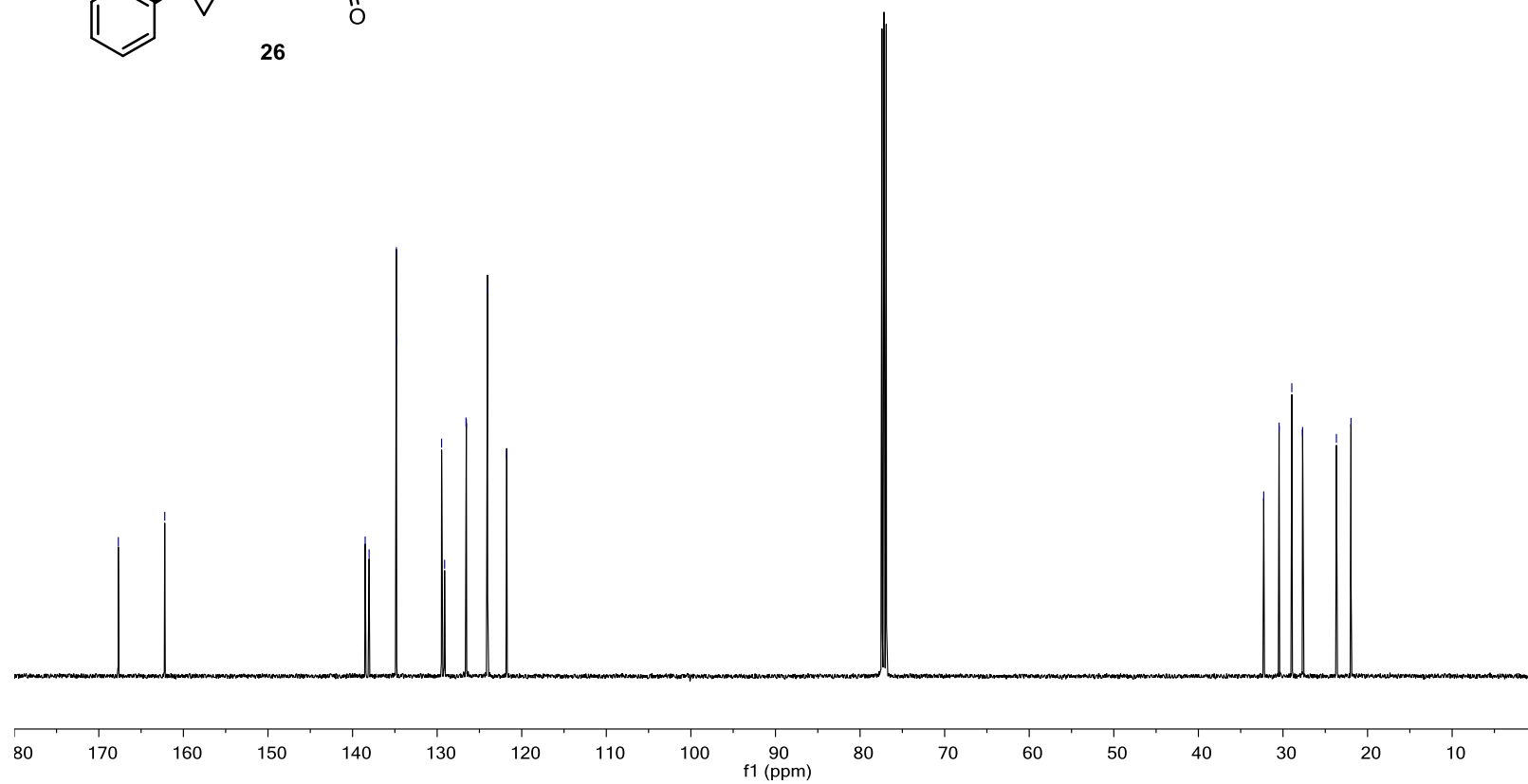
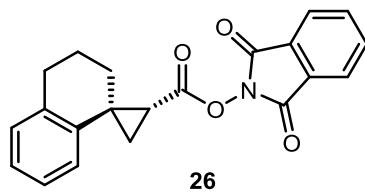


^{13}C NMR (126 MHz, CDCl_3) for compound **26**

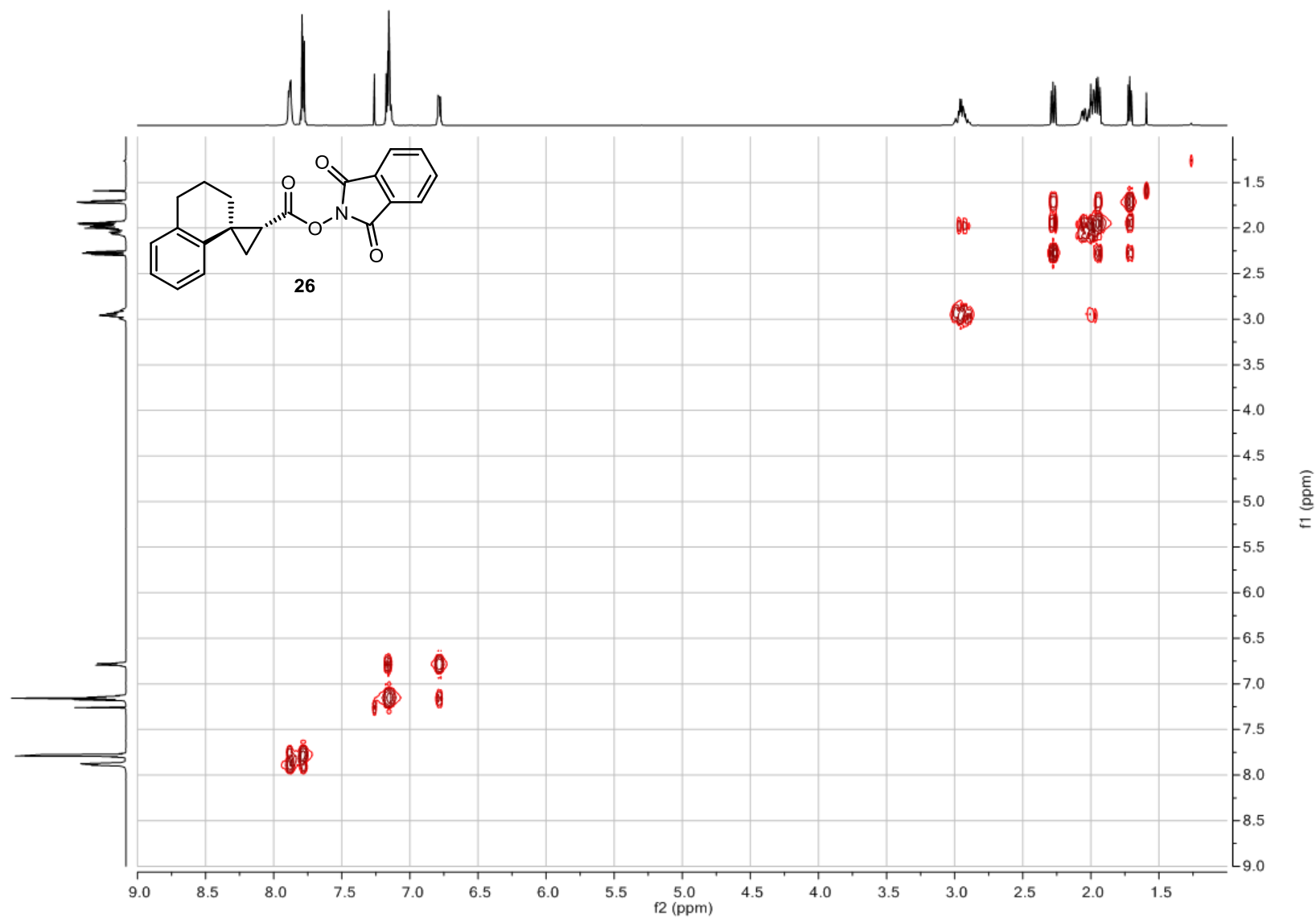
— 167.69
— 162.20

138.51
138.05
134.82
134.81
129.47
129.12
126.58
126.55
124.04
121.78

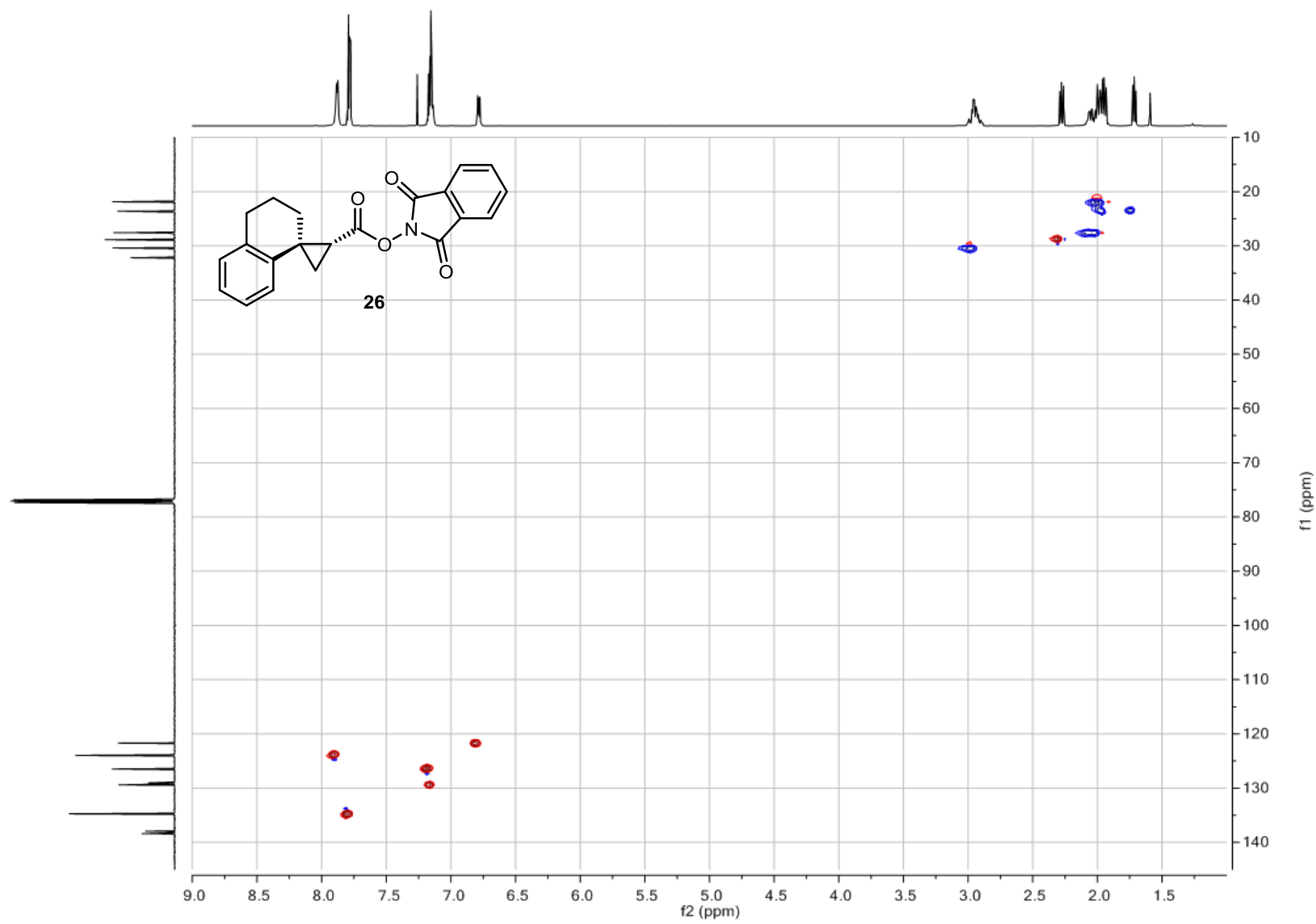
32.27
30.46
28.96
27.68
23.68
21.96



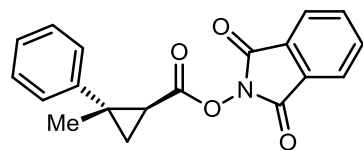
COSY NMR (500 MHz, CDCl₃) for compound 26



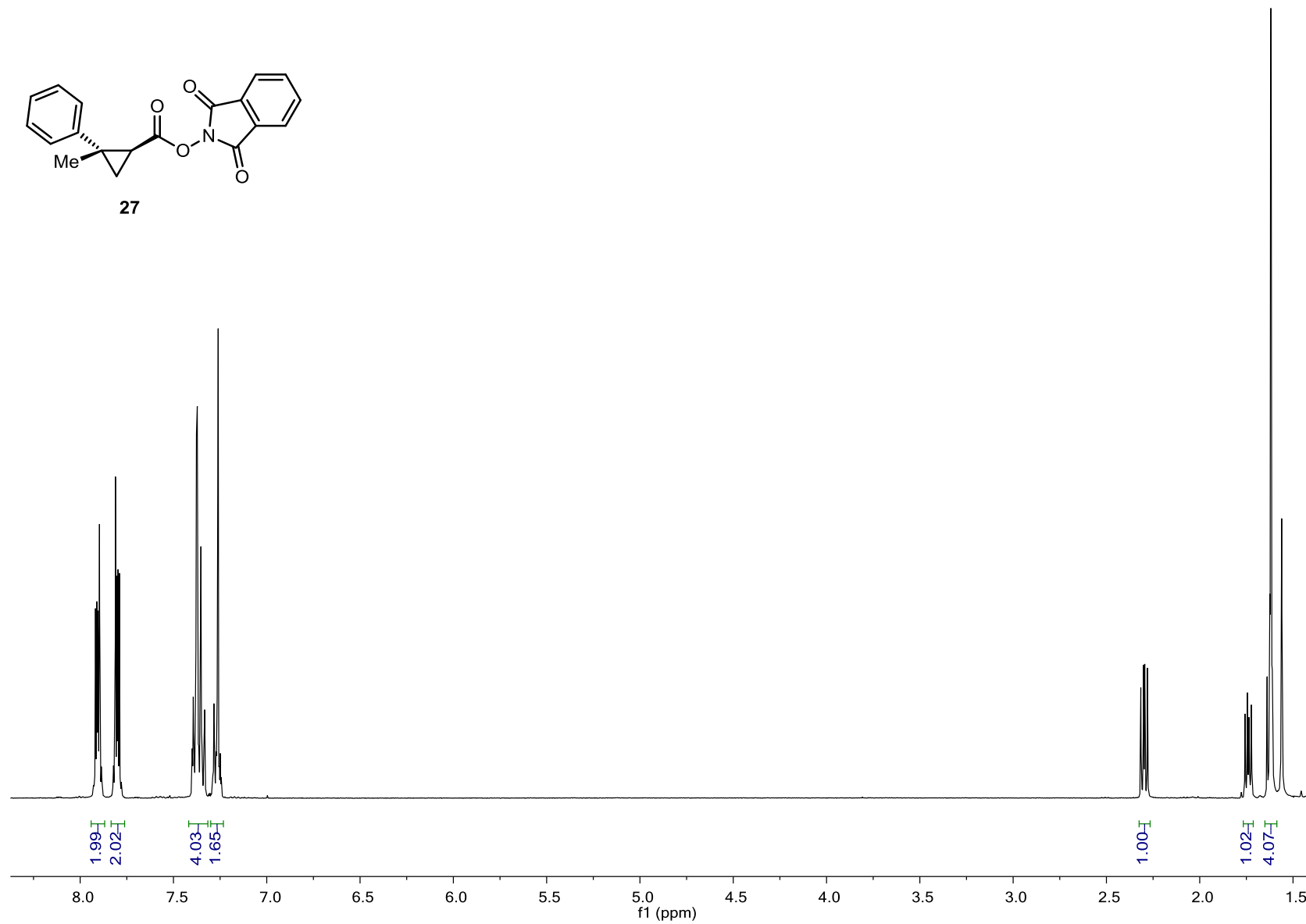
HSQC NMR (500 MHz, CDCl₃) for compound **26**



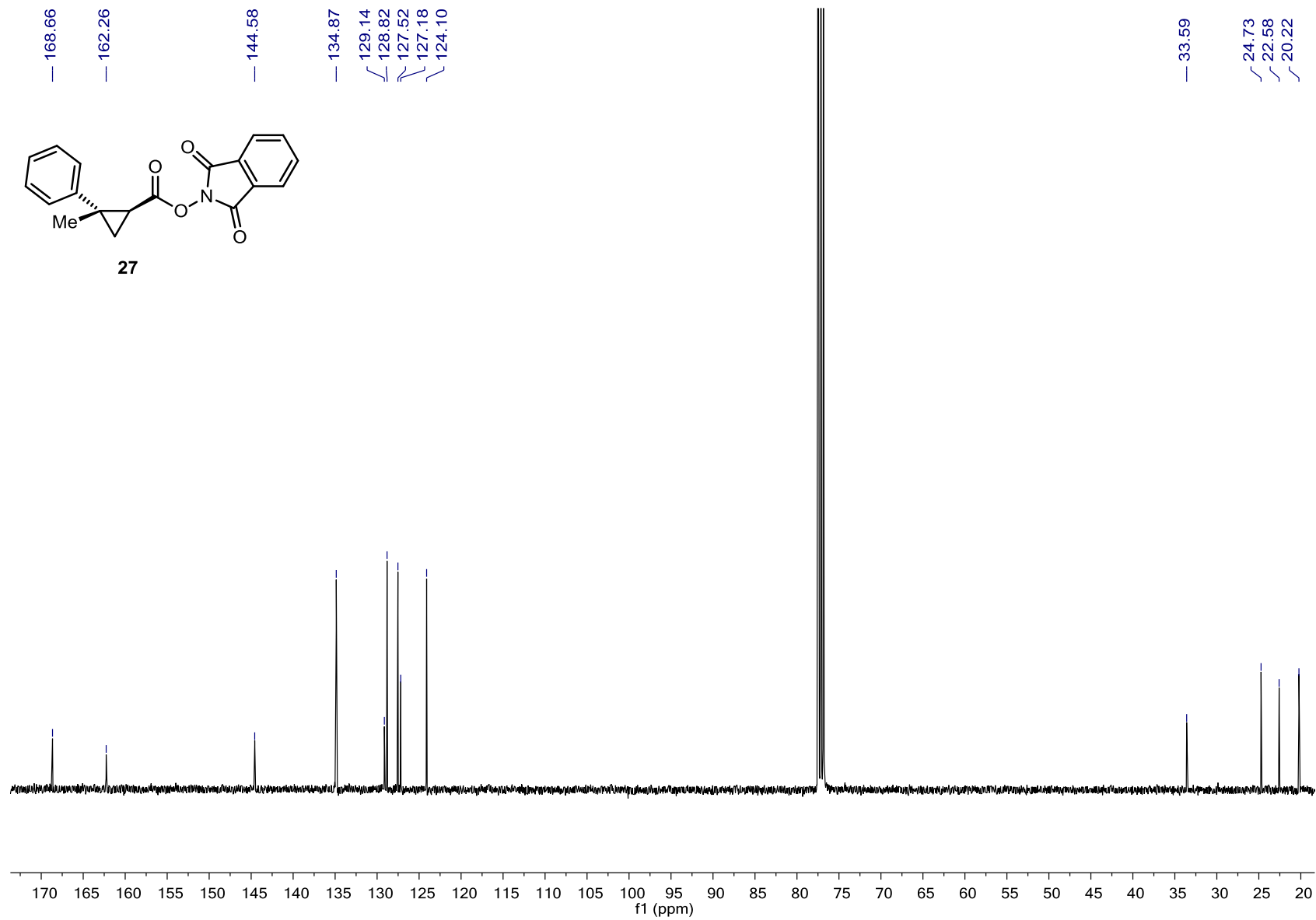
^1H NMR (400 MHz, CDCl_3) for compound **27**



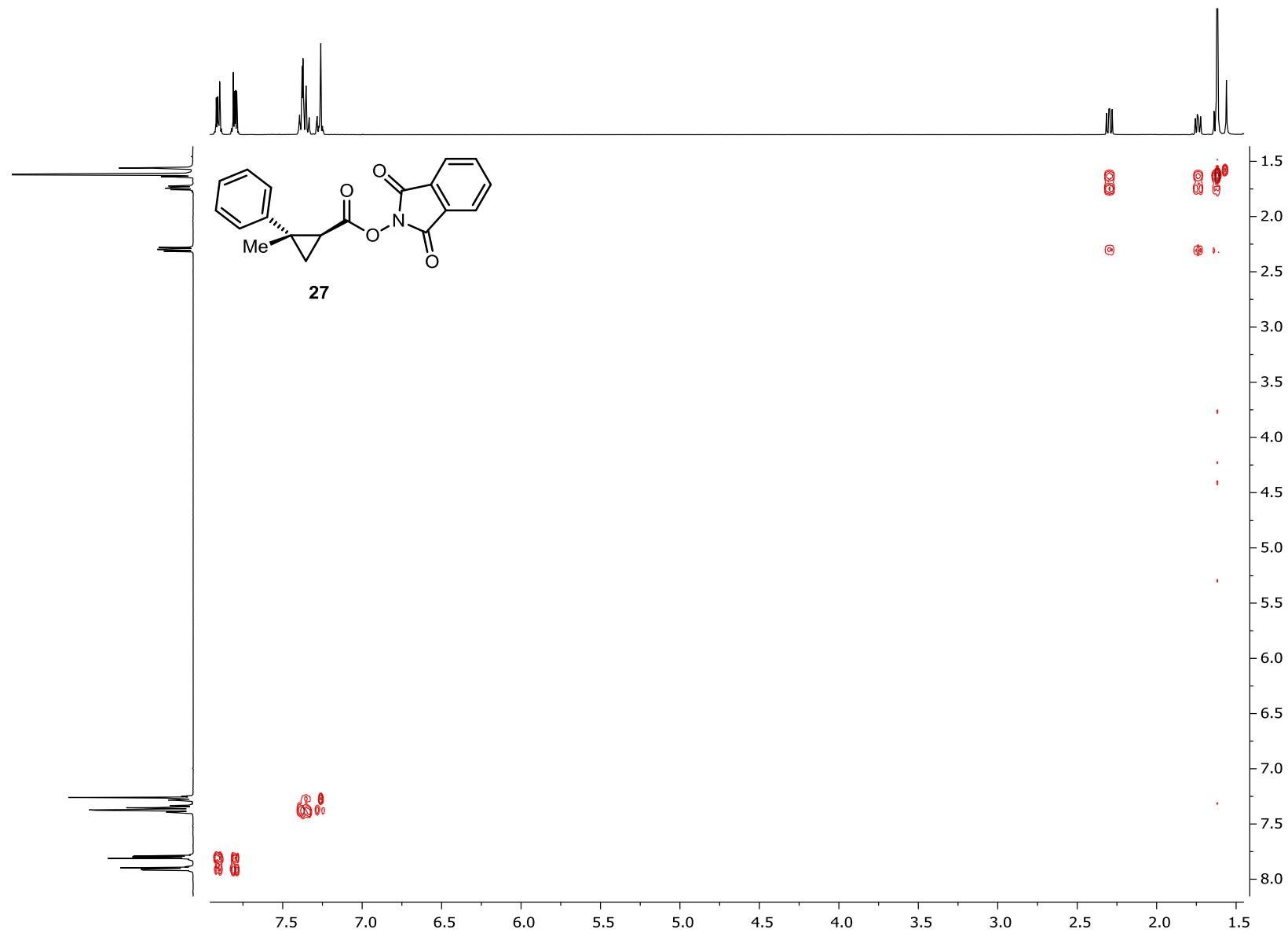
27



^{13}C NMR (101 MHz, CDCl_3) for compound **27**

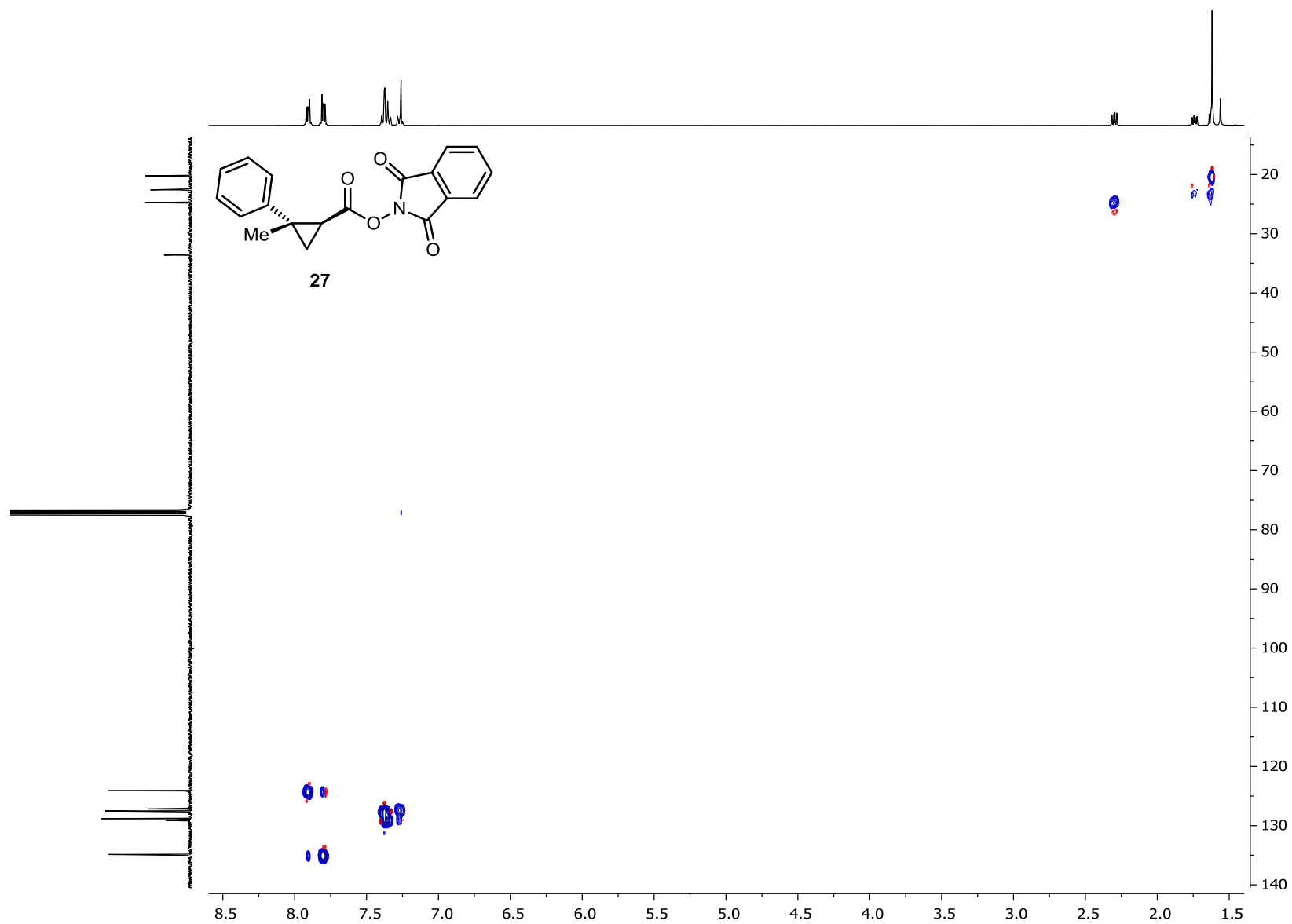


COSY NMR (400 MHz, CDCl₃) for compound 27



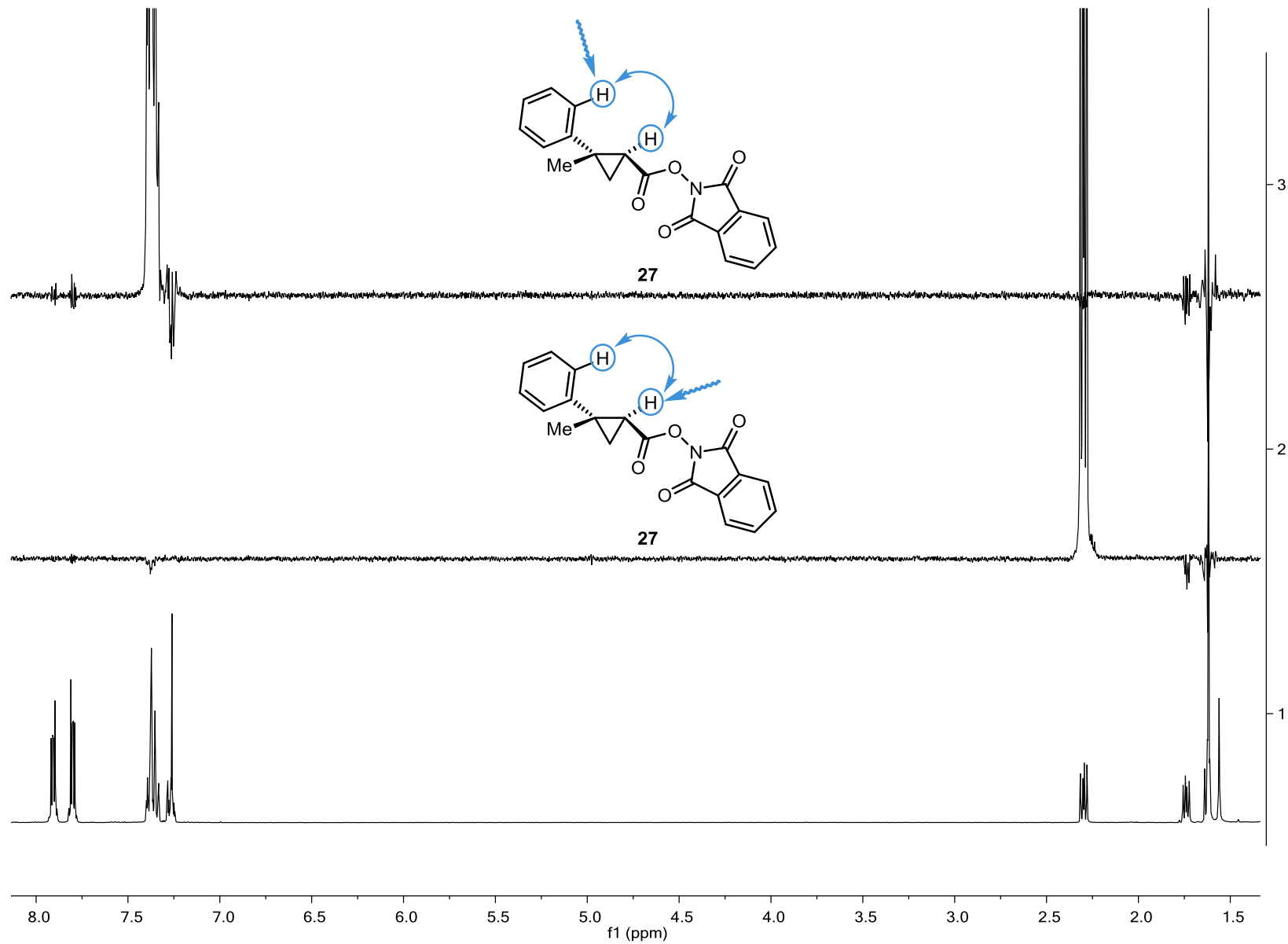
S150

HSQC NMR (400 MHz, CDCl₃) for compound **27**



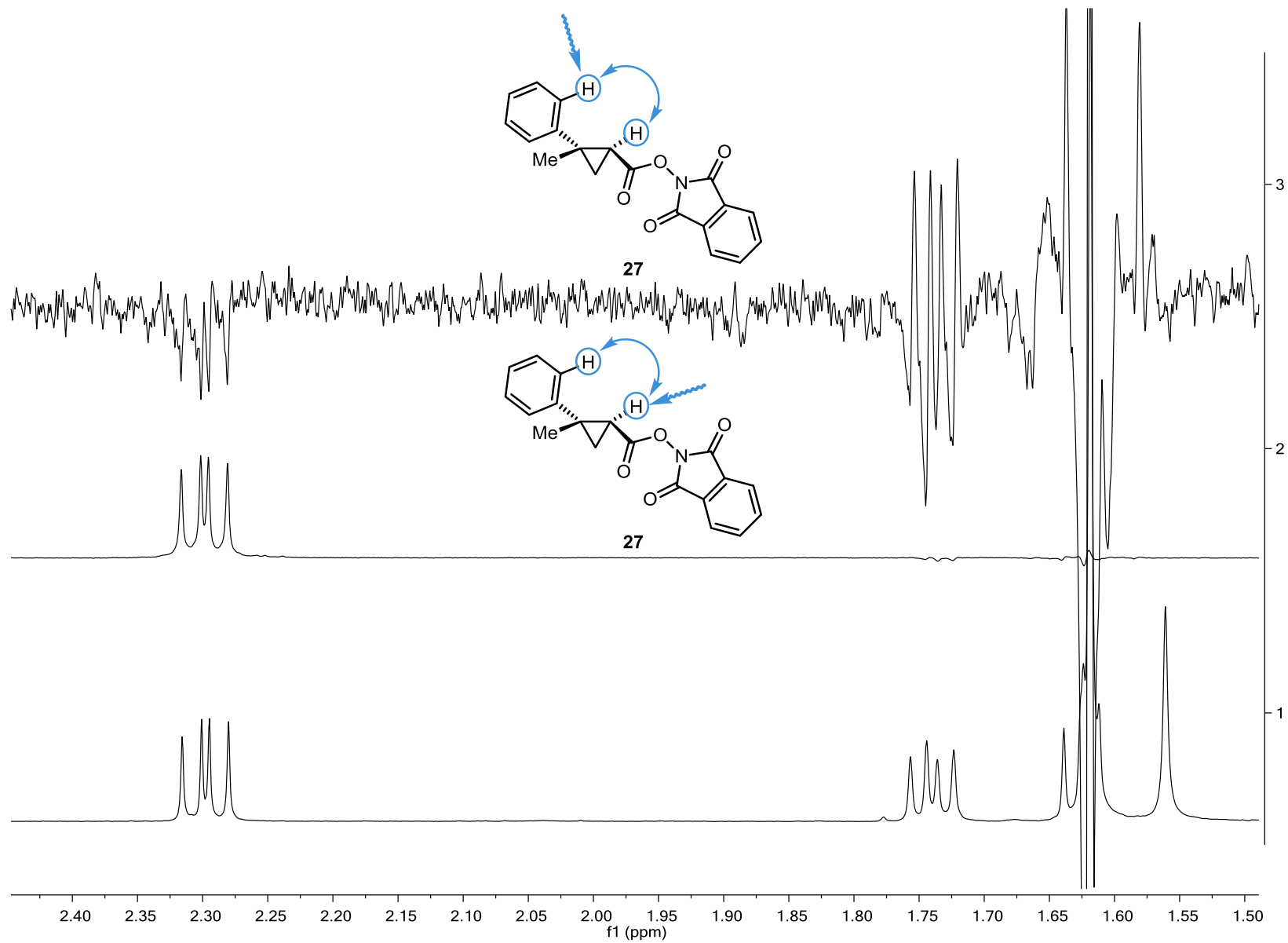
S151

1D NOESY NMR (400 MHz, CDCl₃) for compound 27

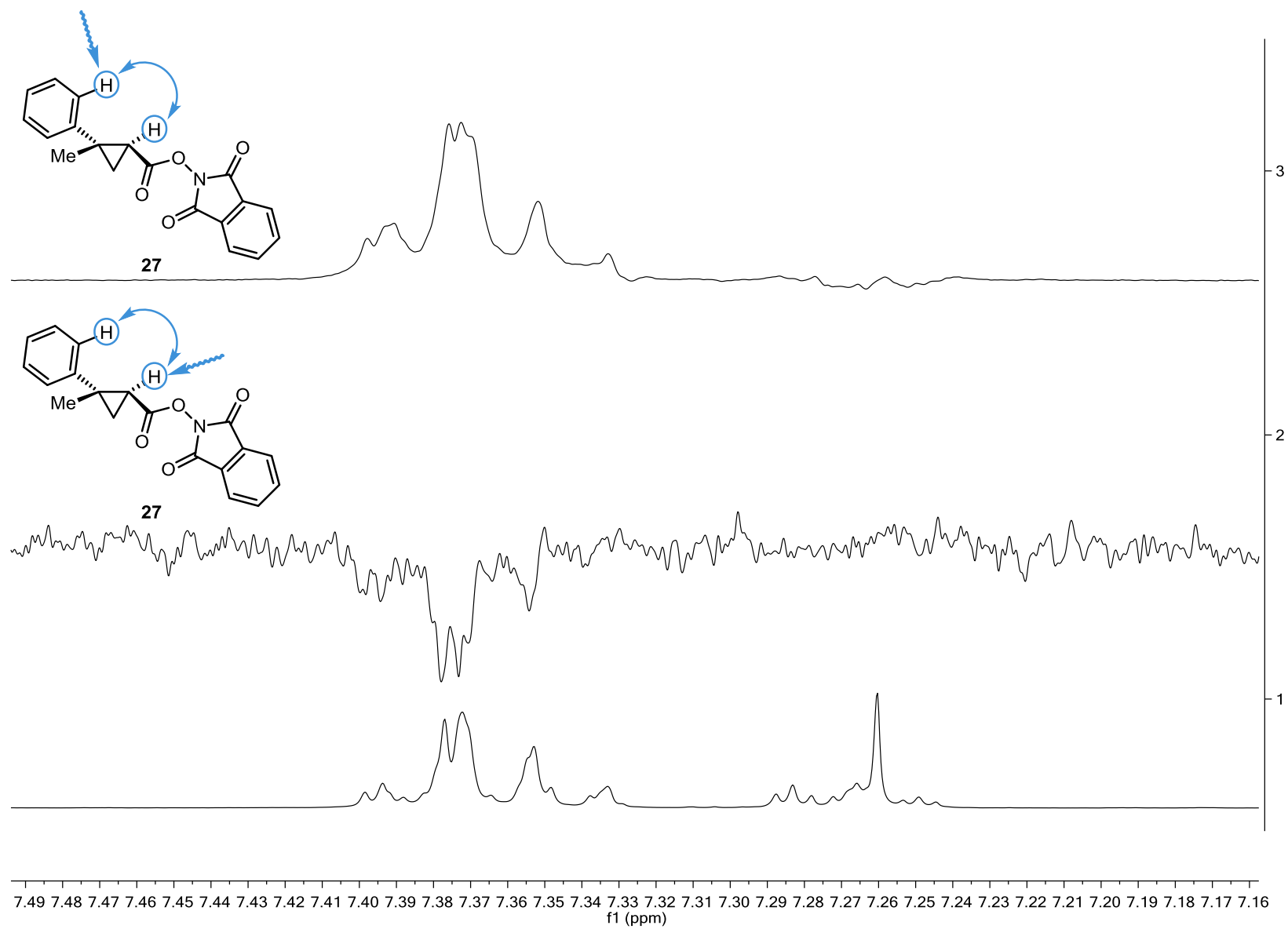


S152

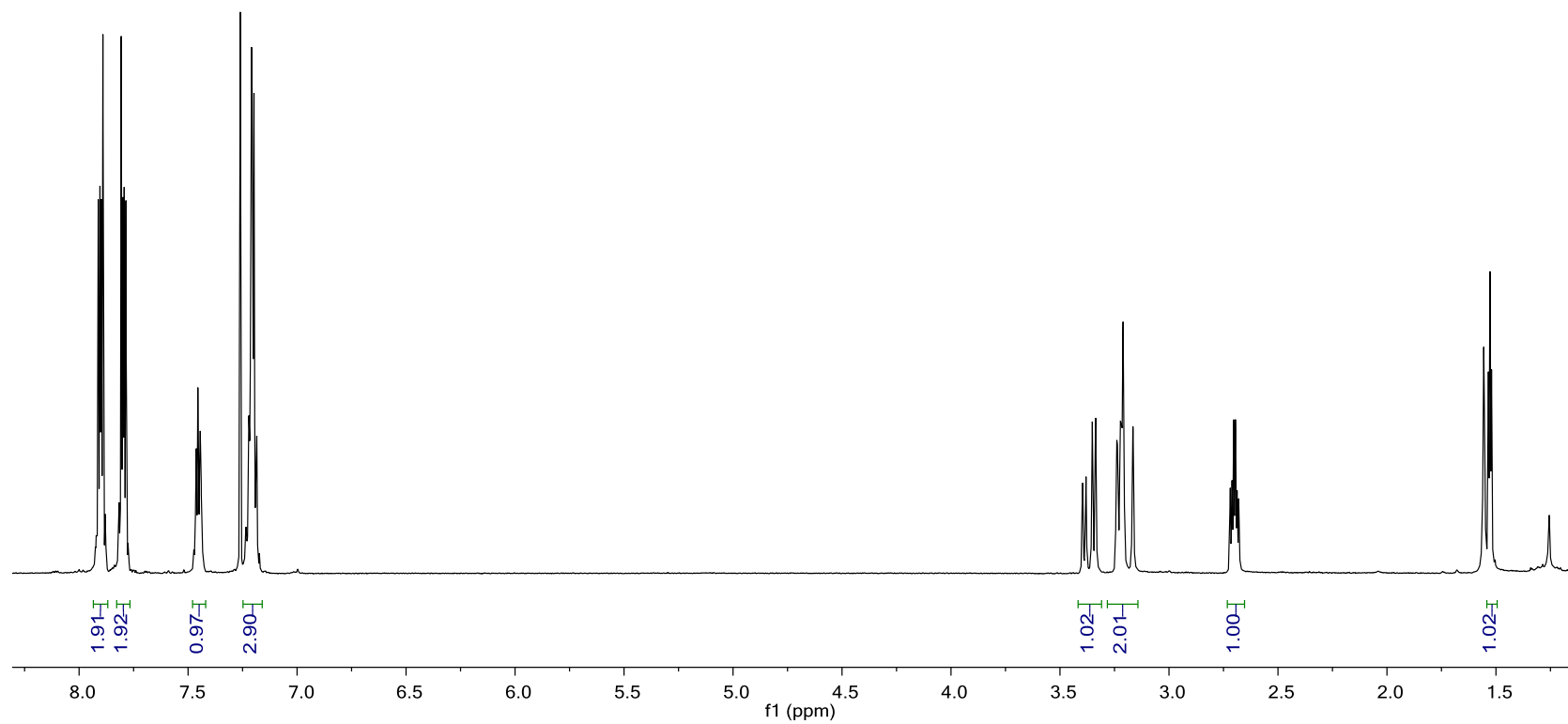
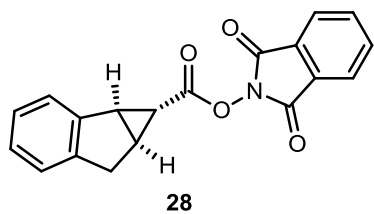
1D NOESY NMR expansion (400 MHz, CDCl₃) for compound **27**



1D NOESY expansion NMR (400 MHz, CDCl₃) for compound **27**

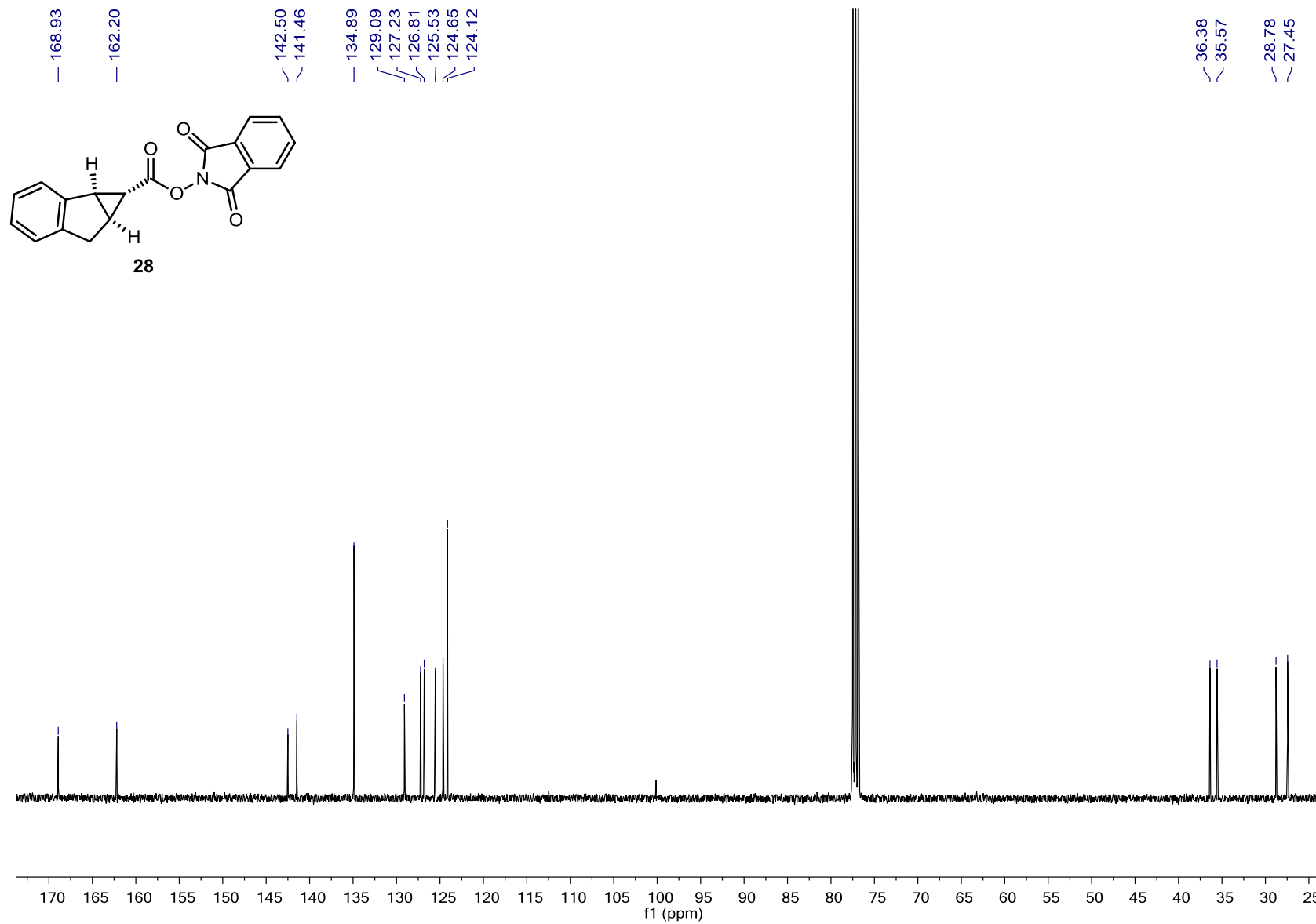


^1H NMR (400 MHz, CDCl_3) for compound **28**

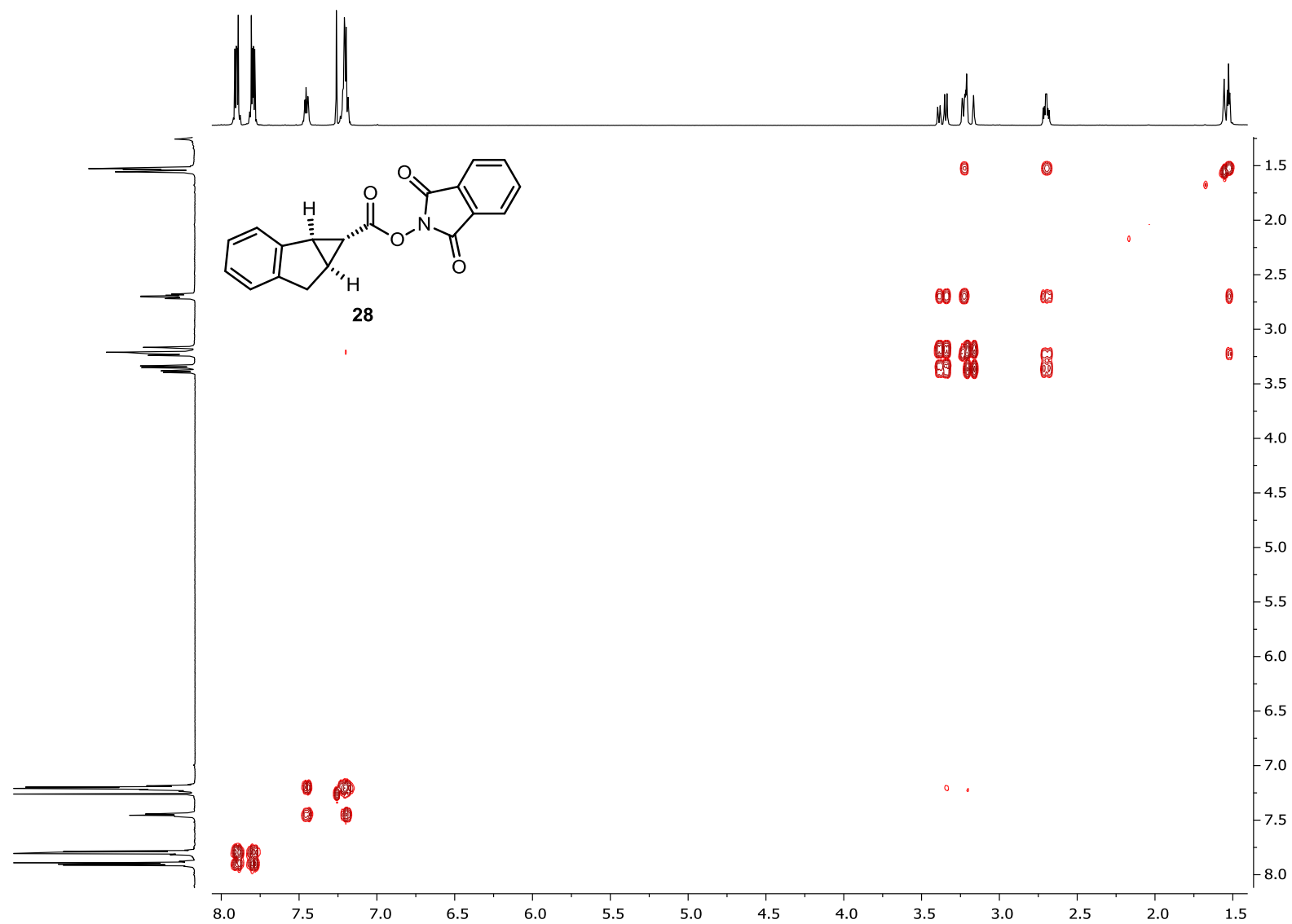


S155

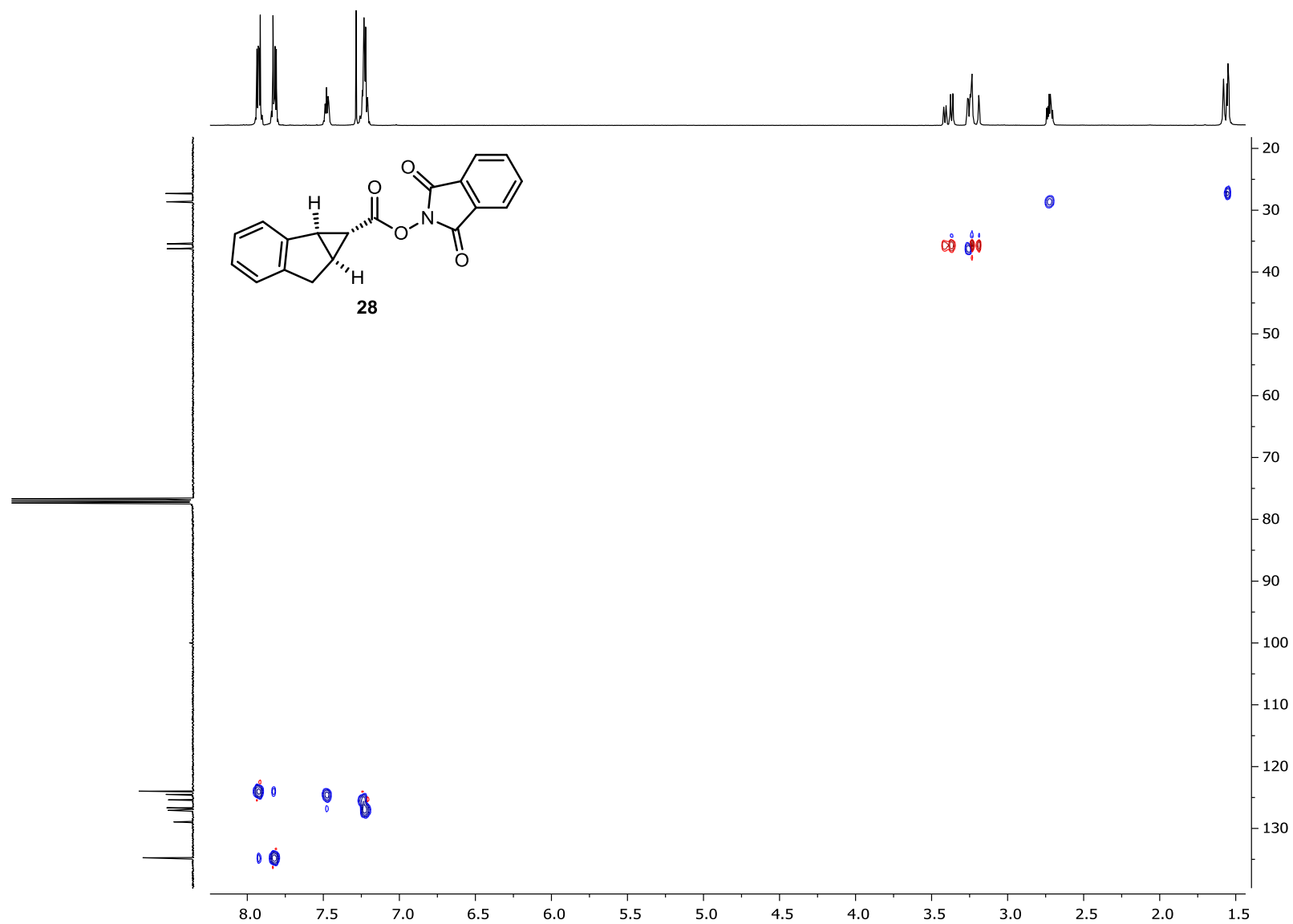
^{13}C NMR (101 MHz, CDCl_3) for compound **28**



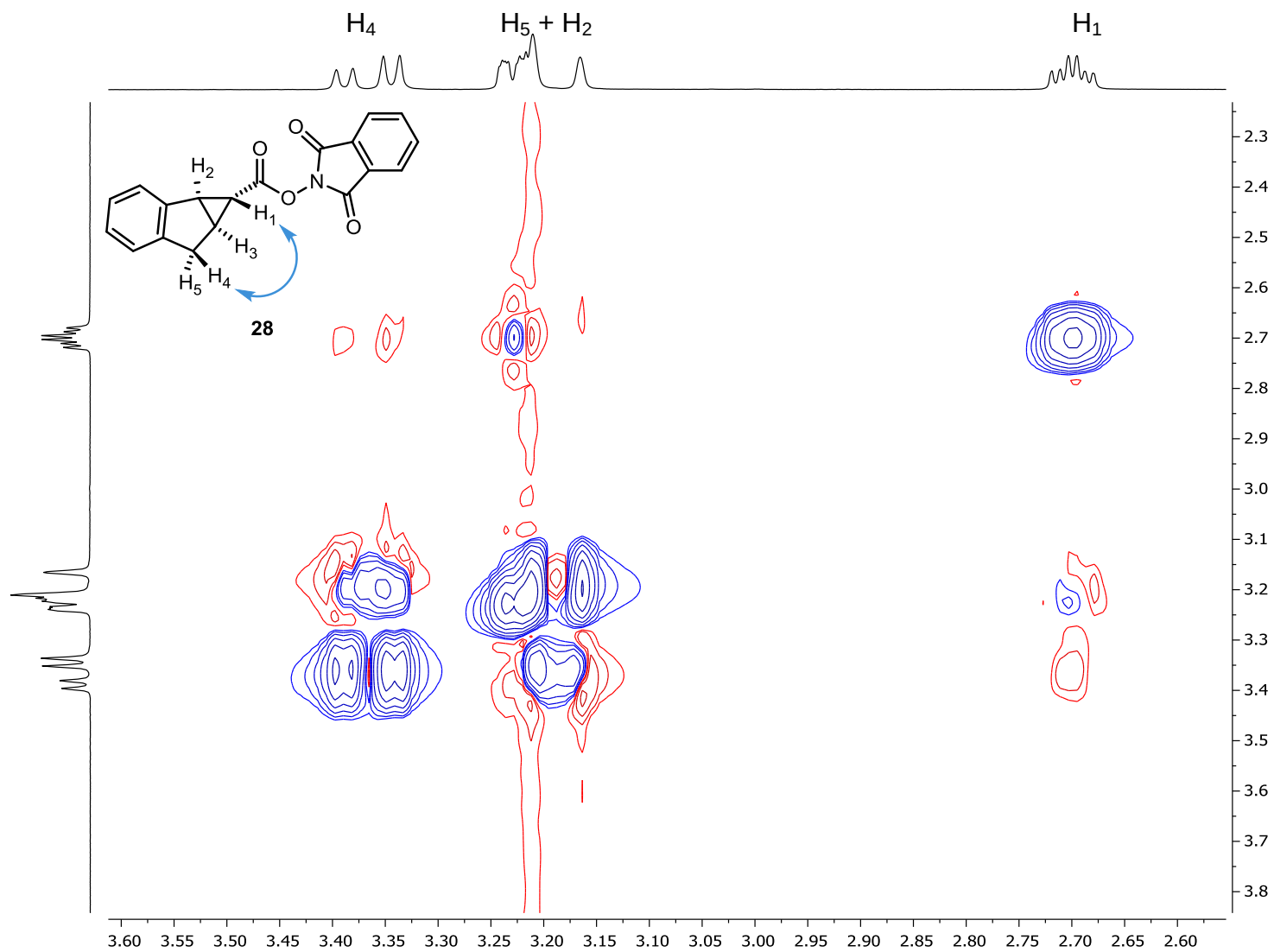
COSY NMR (400 MHz, CDCl₃) for compound **28**



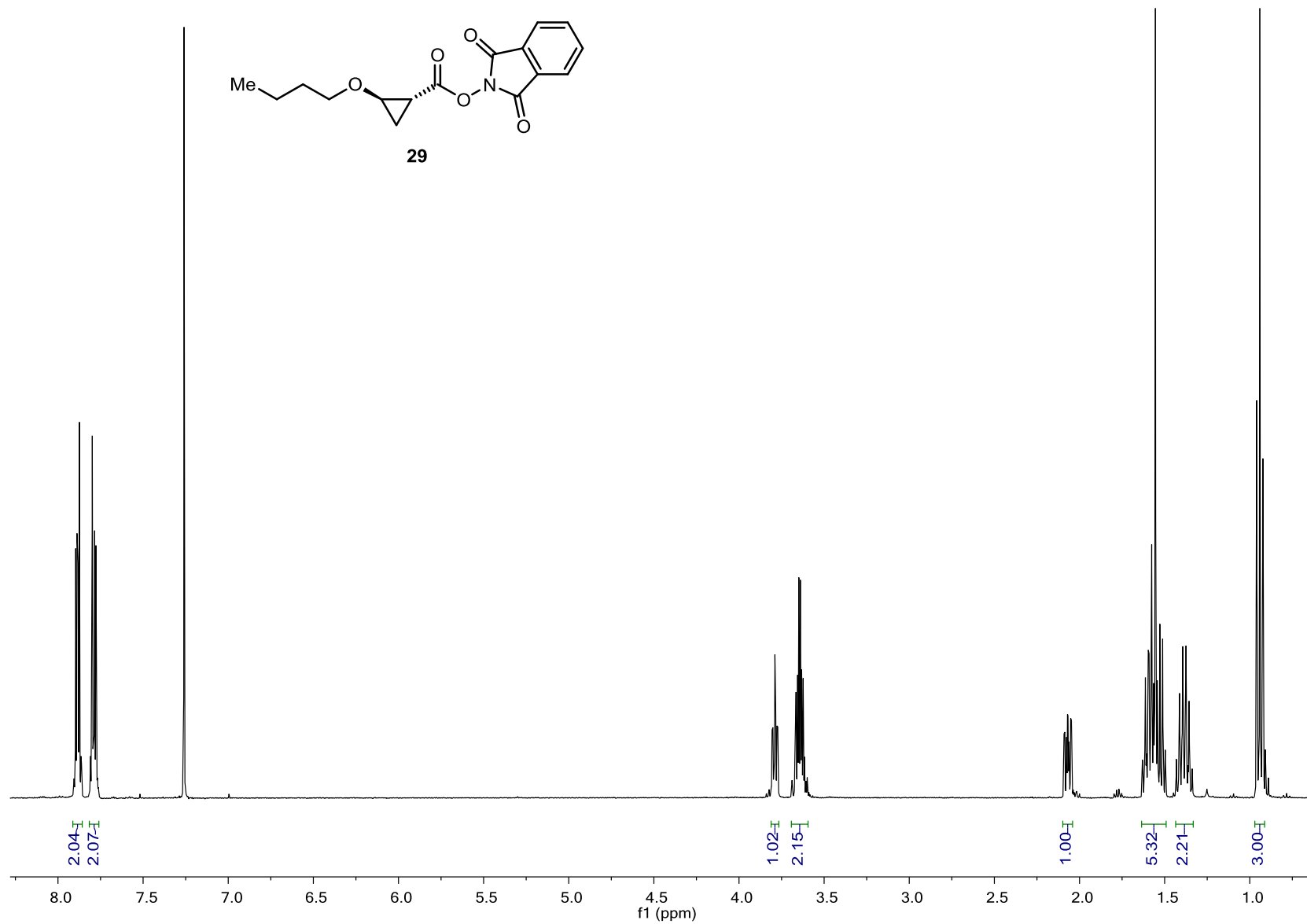
HSQC NMR (400 MHz, CDCl₃) for compound **28**



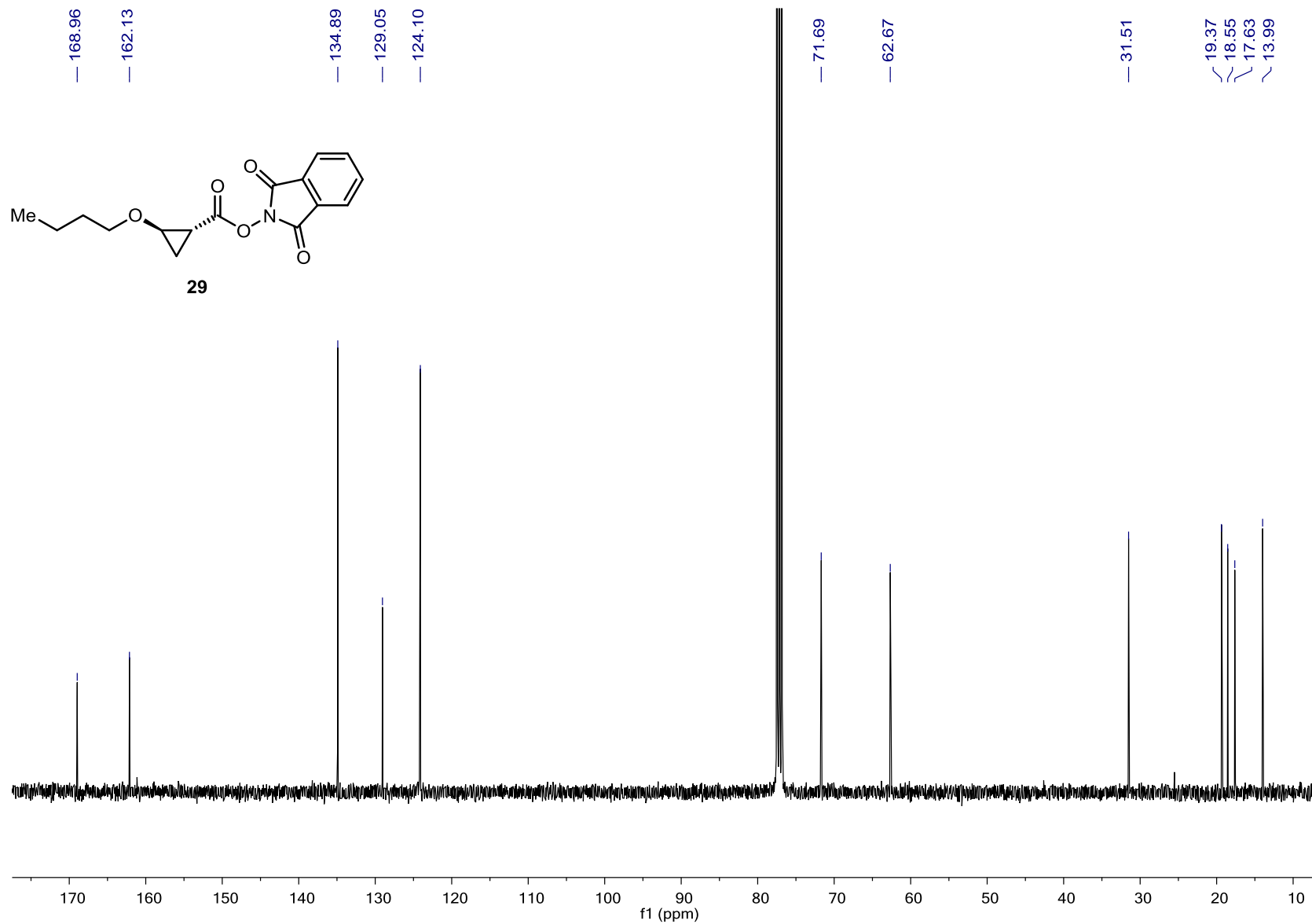
NOESY NMR (400 MHz, CDCl₃) for compound **28**



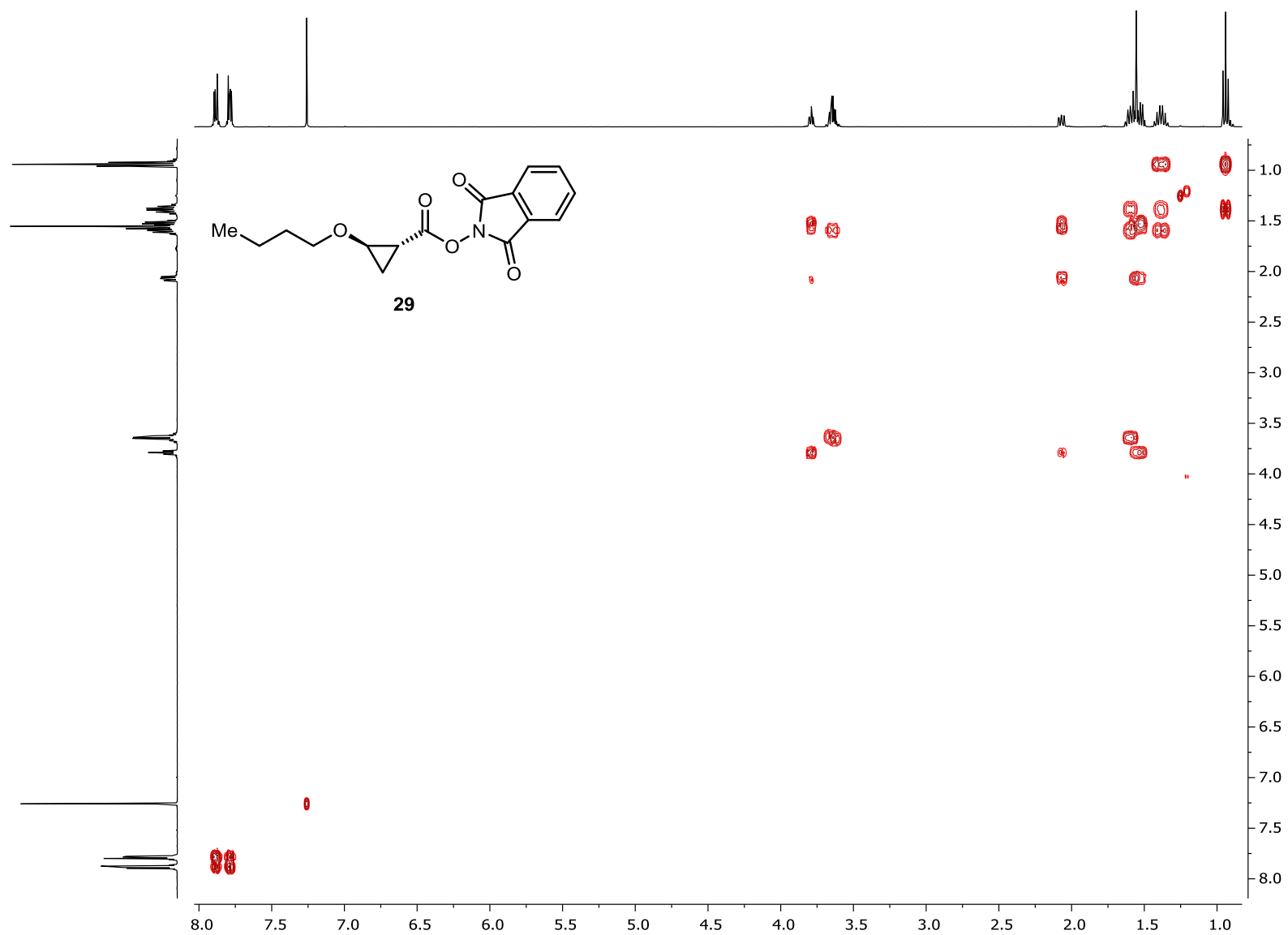
^1H NMR (400 MHz, CDCl_3) for compound **29**



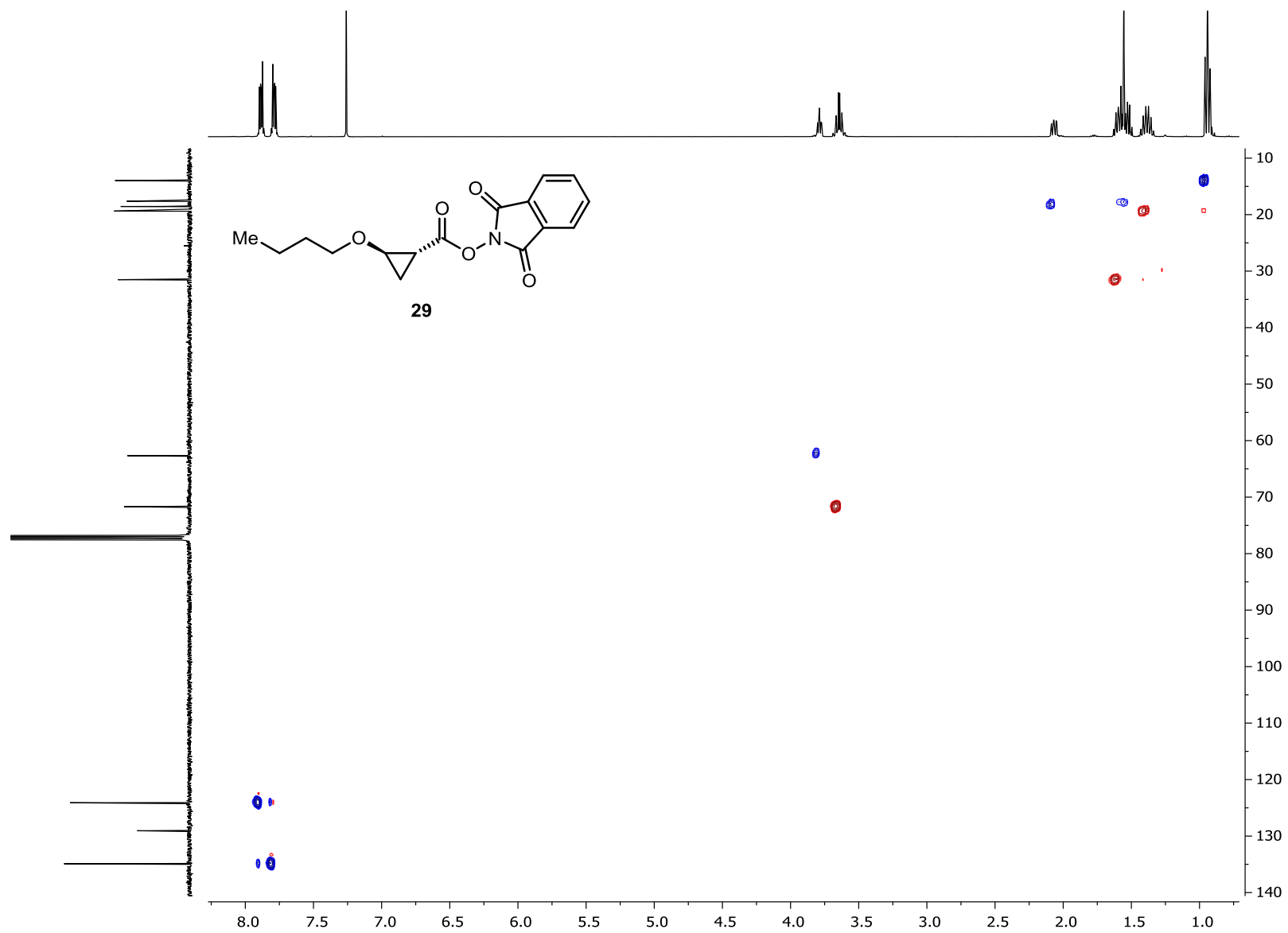
^{13}C NMR (101 MHz, CDCl_3) for compound **29**



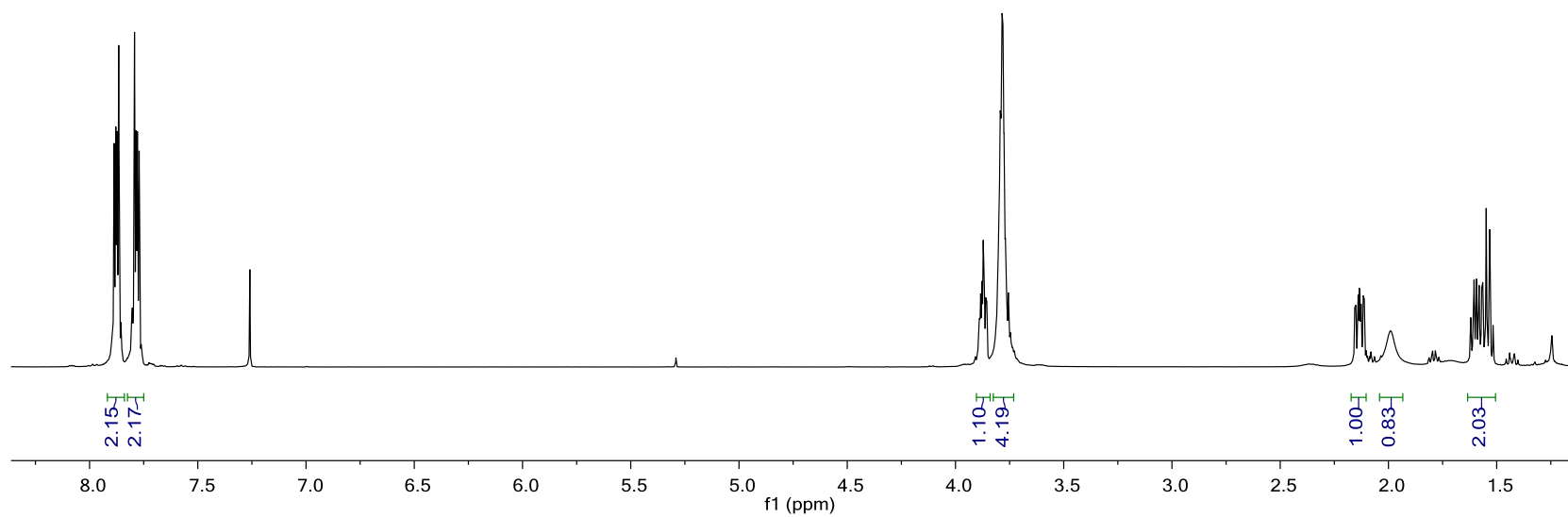
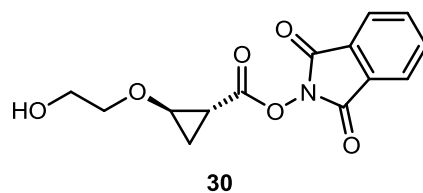
COSY NMR (400 MHz, CDCl₃) for compound 29



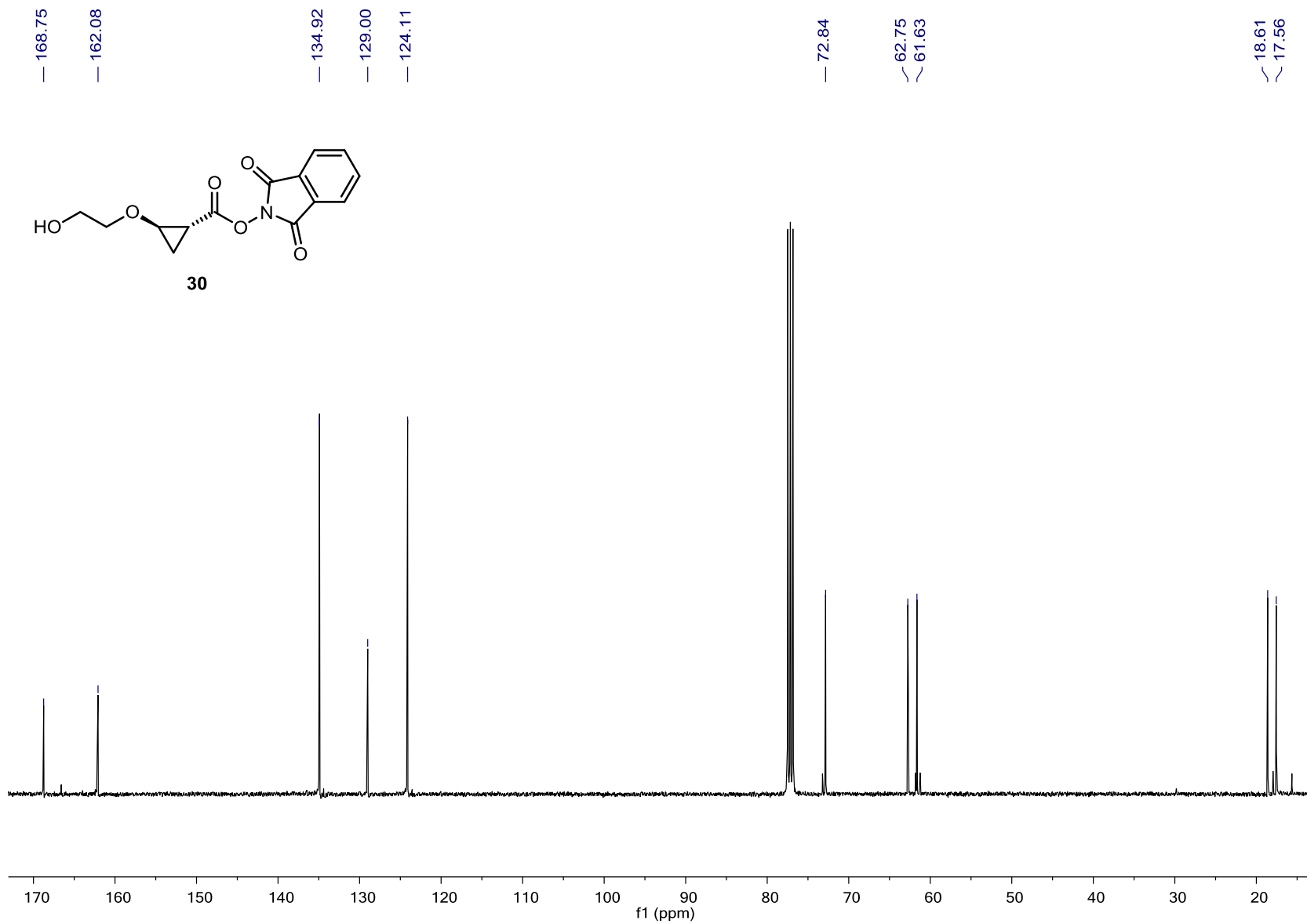
HSQC NMR (400 MHz, CDCl₃) for compound **29**



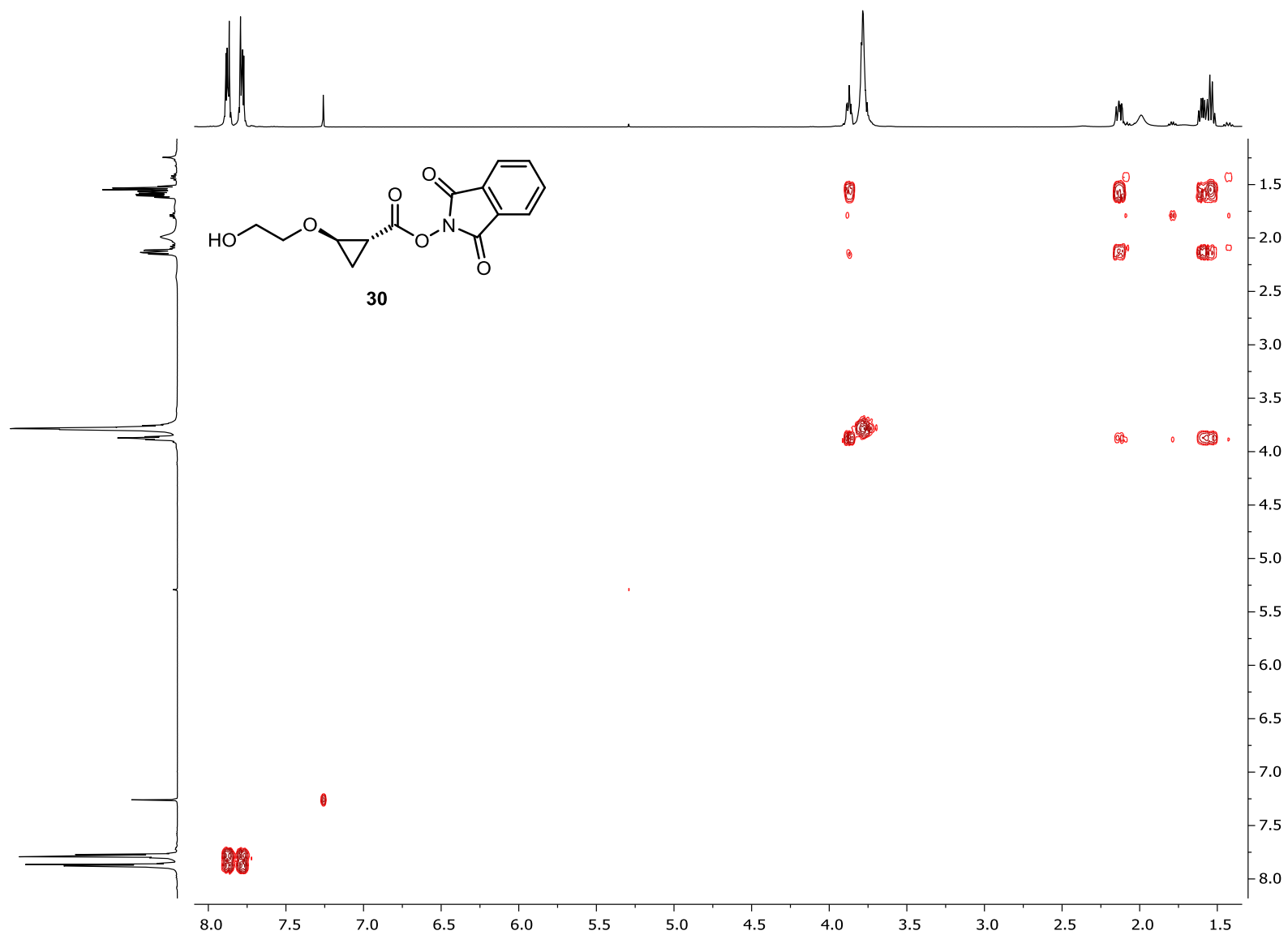
^1H NMR (400 MHz, CDCl_3) for compound **30**



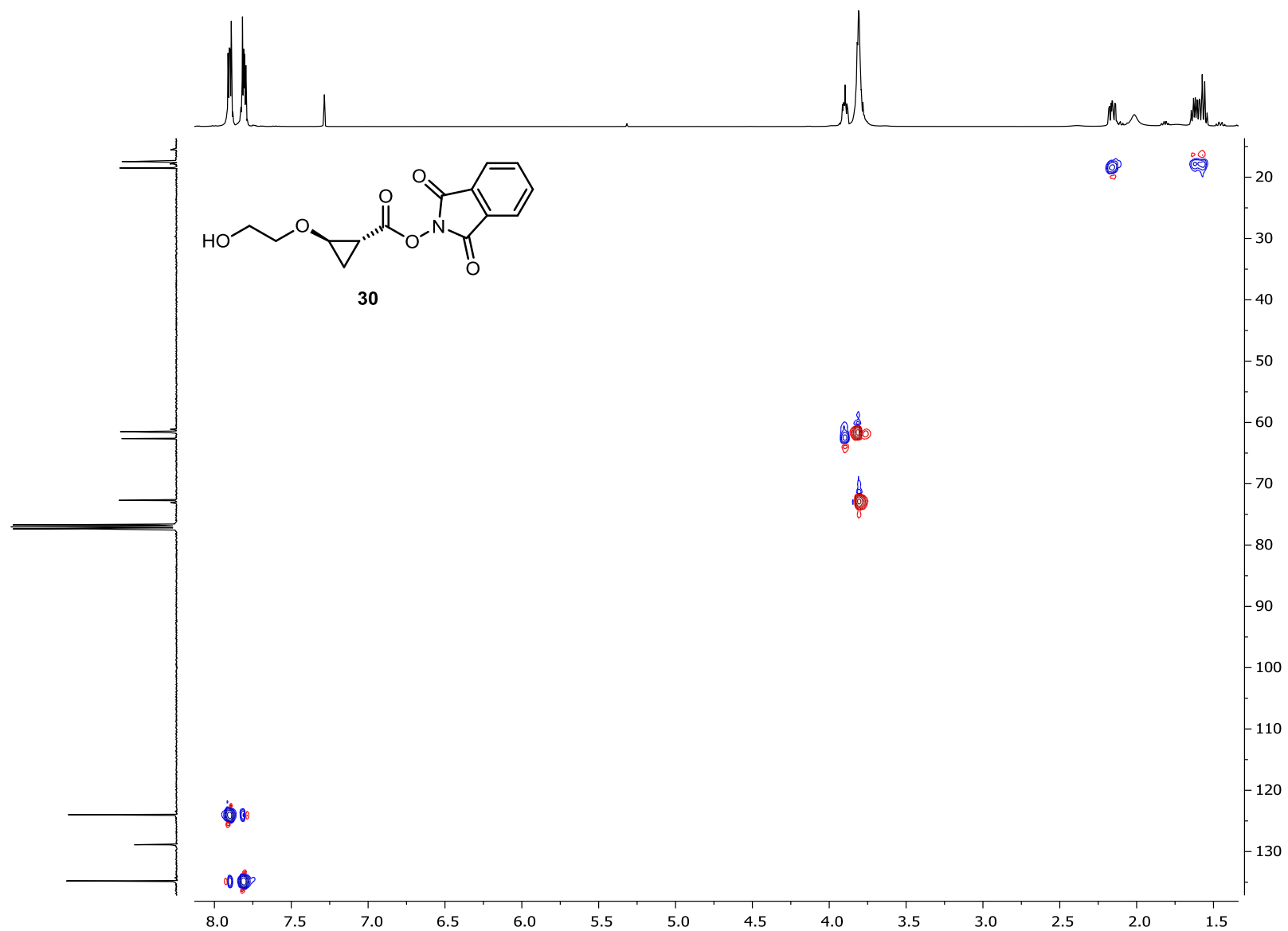
^{13}C NMR (101 MHz, CDCl_3) for compound **30**



COSY NMR (400 MHz, CDCl₃) for compound 30

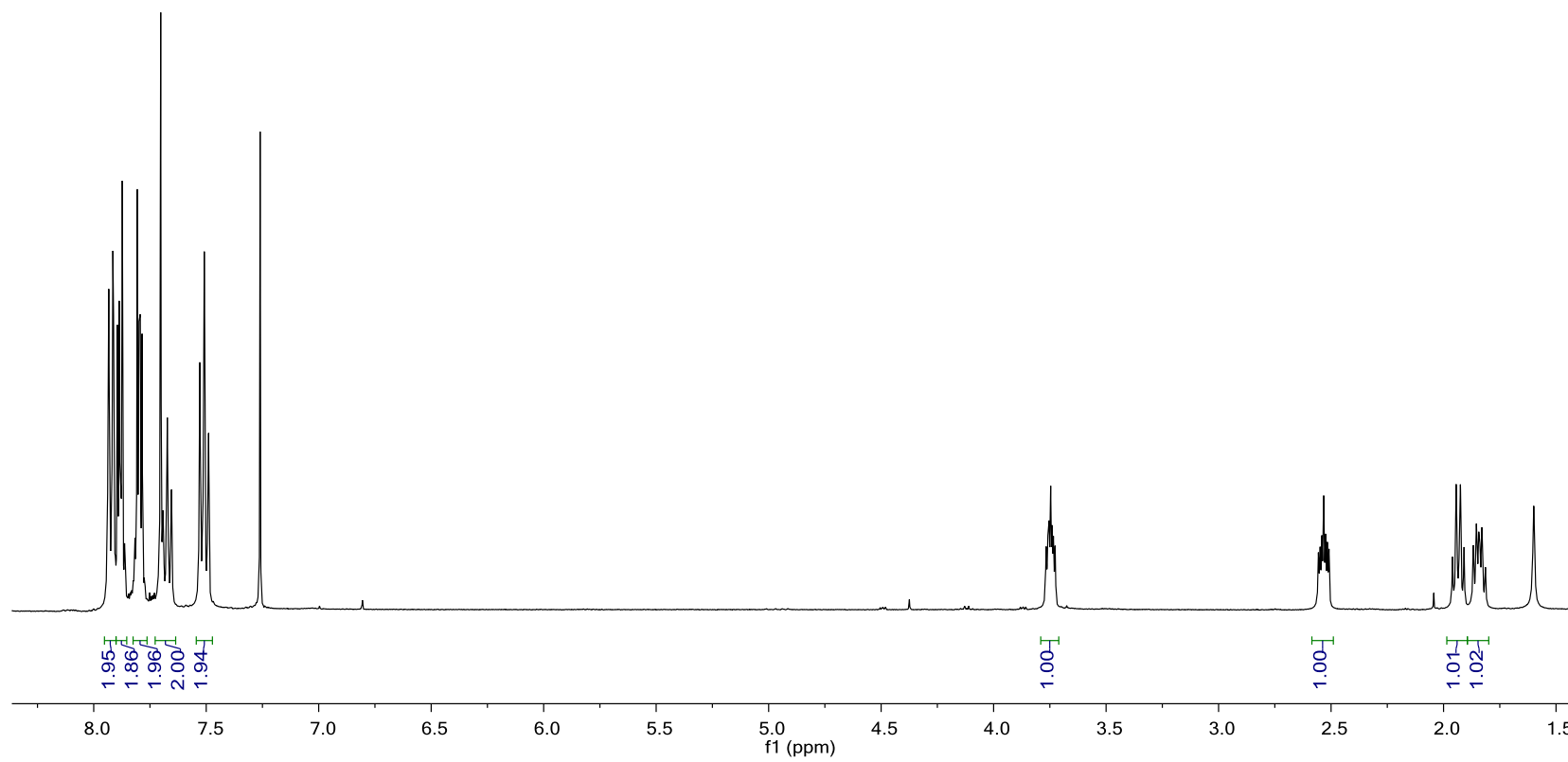
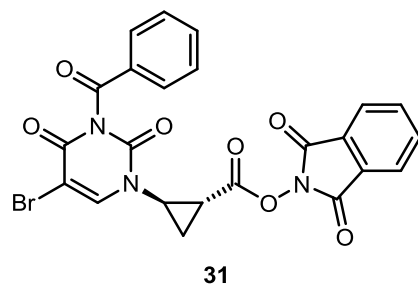


HSQC NMR (400 MHz, CDCl₃) for compound **30**

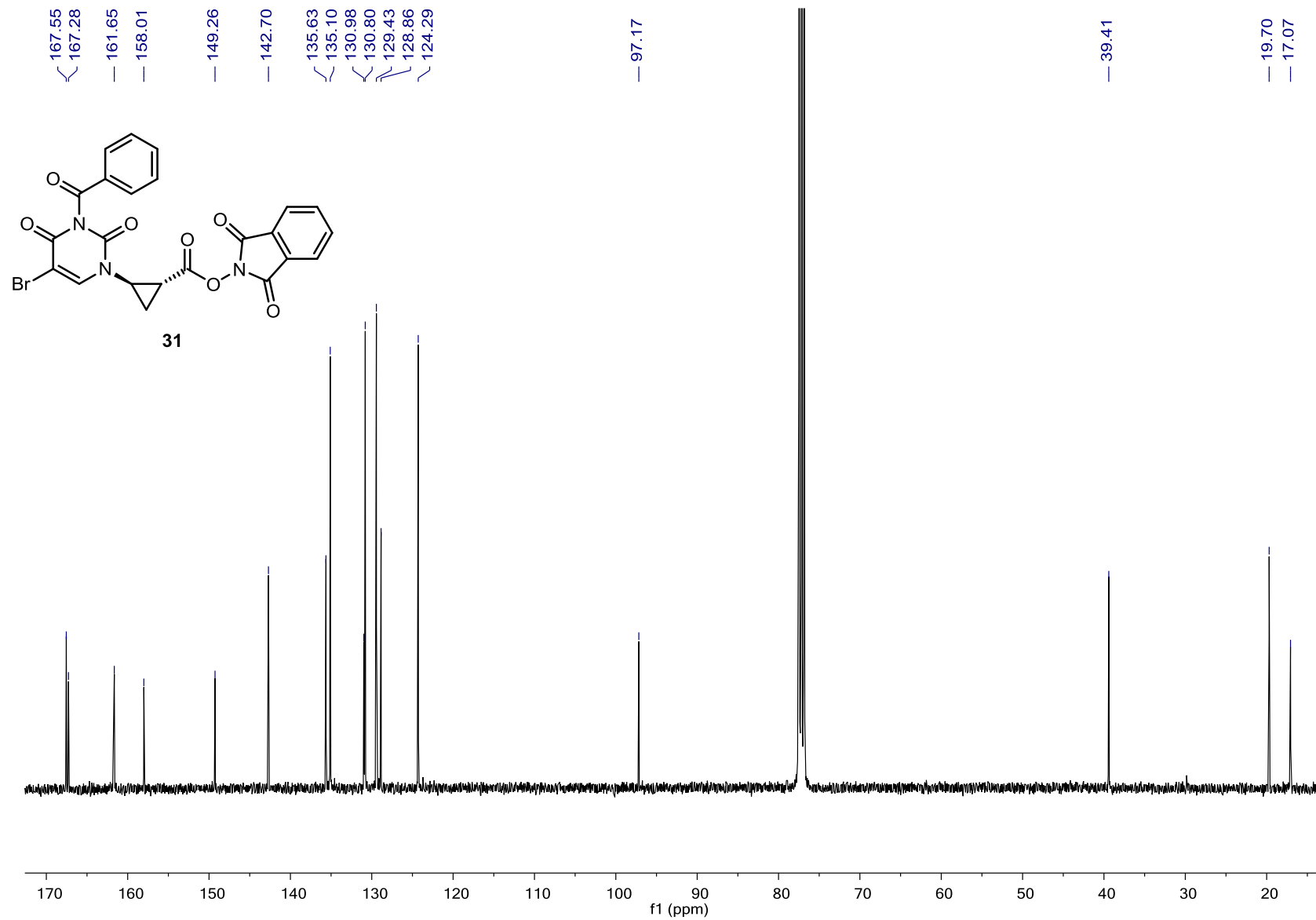


S167

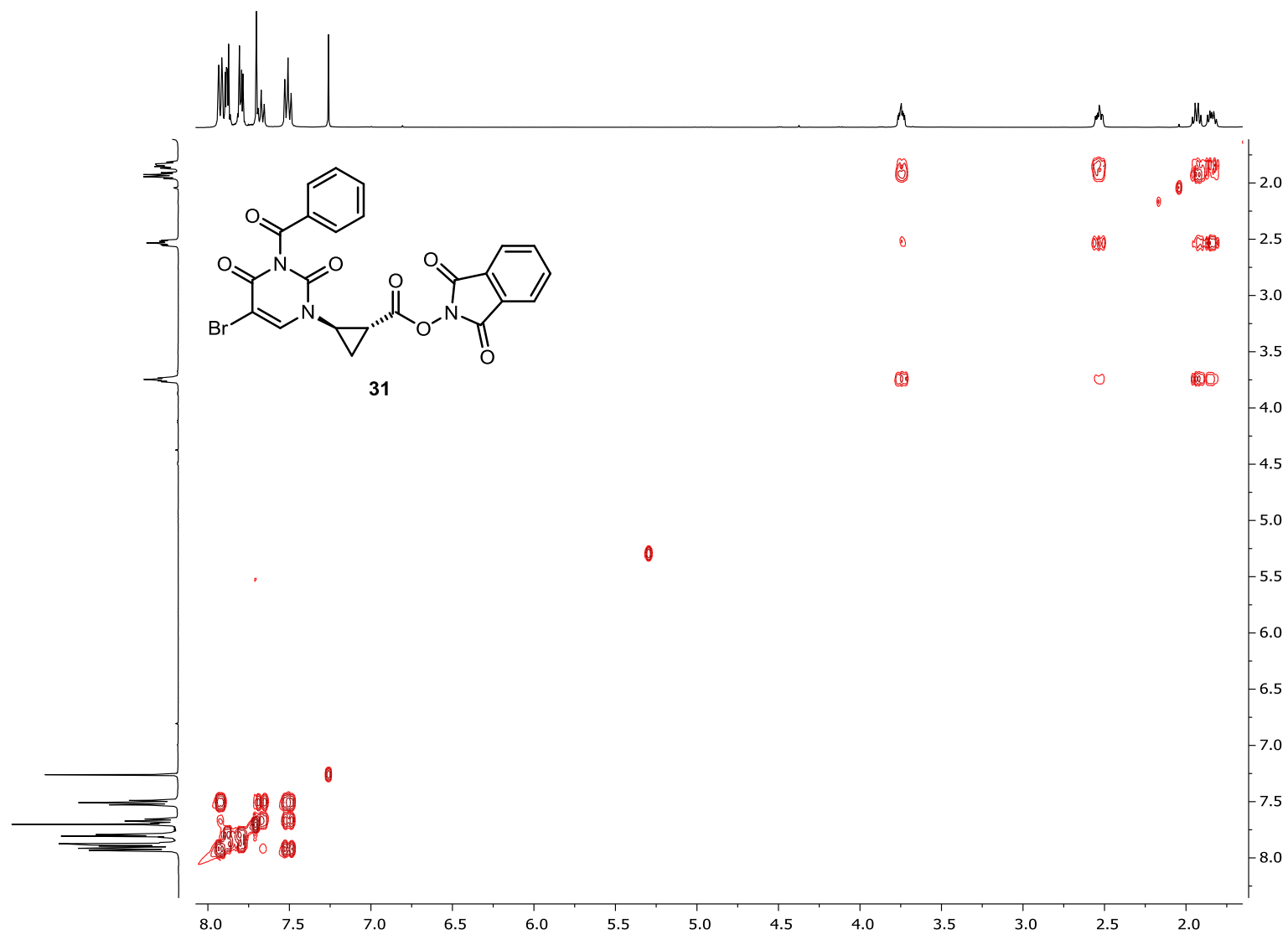
^1H NMR (400 MHz, CDCl_3) for compound **31**



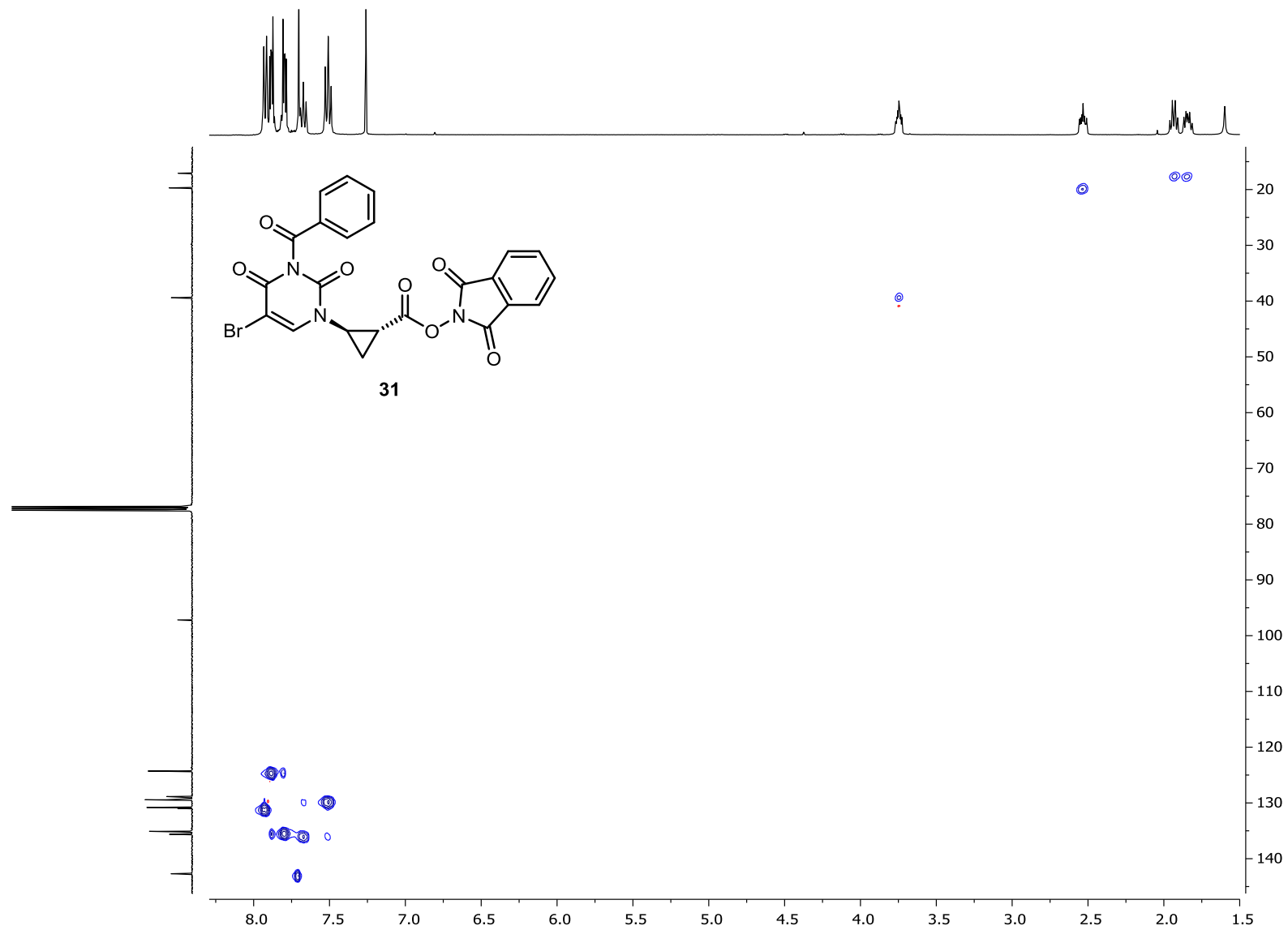
^{13}C NMR (101 MHz, CDCl_3) for compound **31**



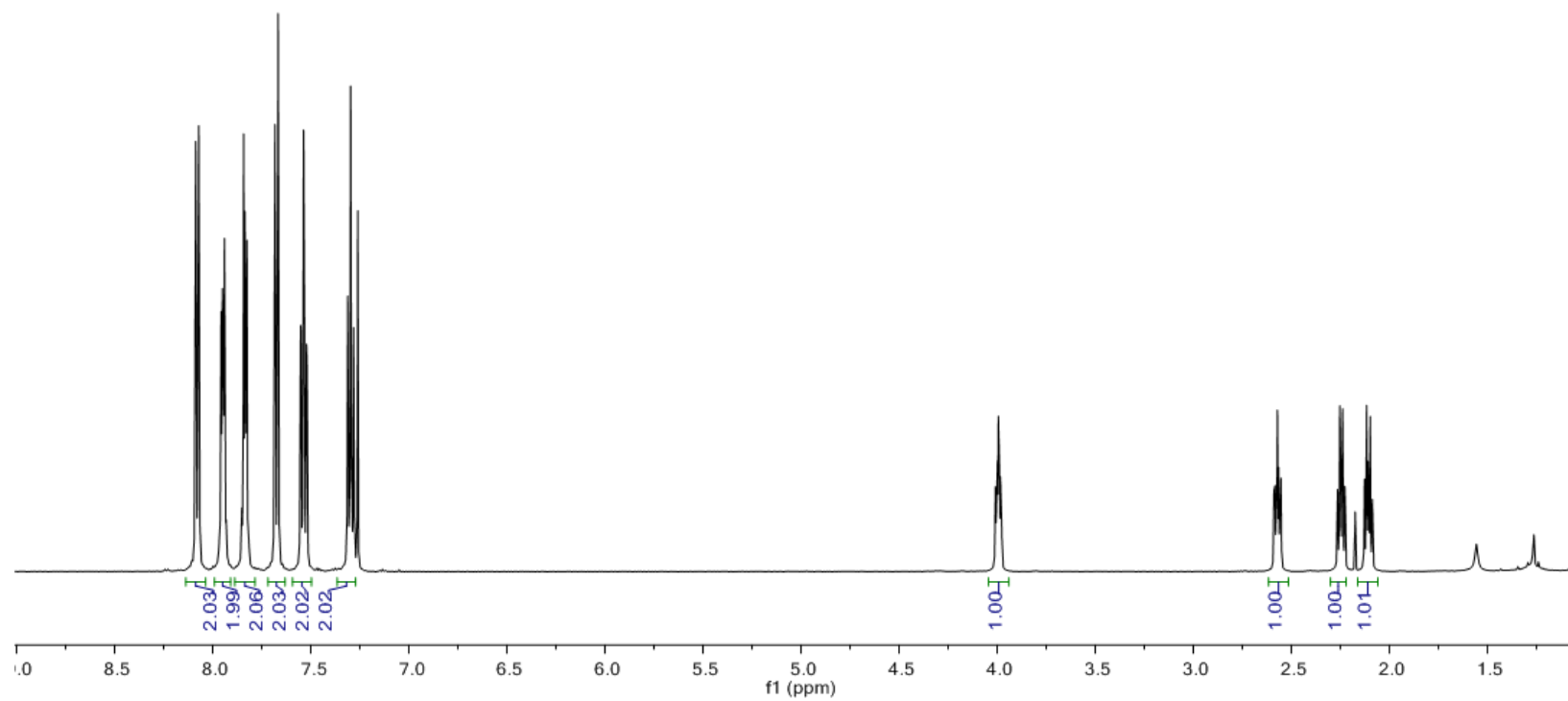
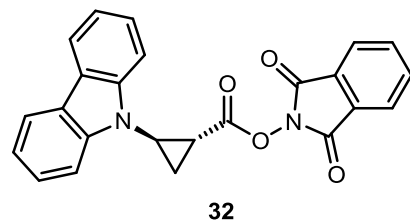
COSY NMR (400 MHz, CDCl₃) for compound 31



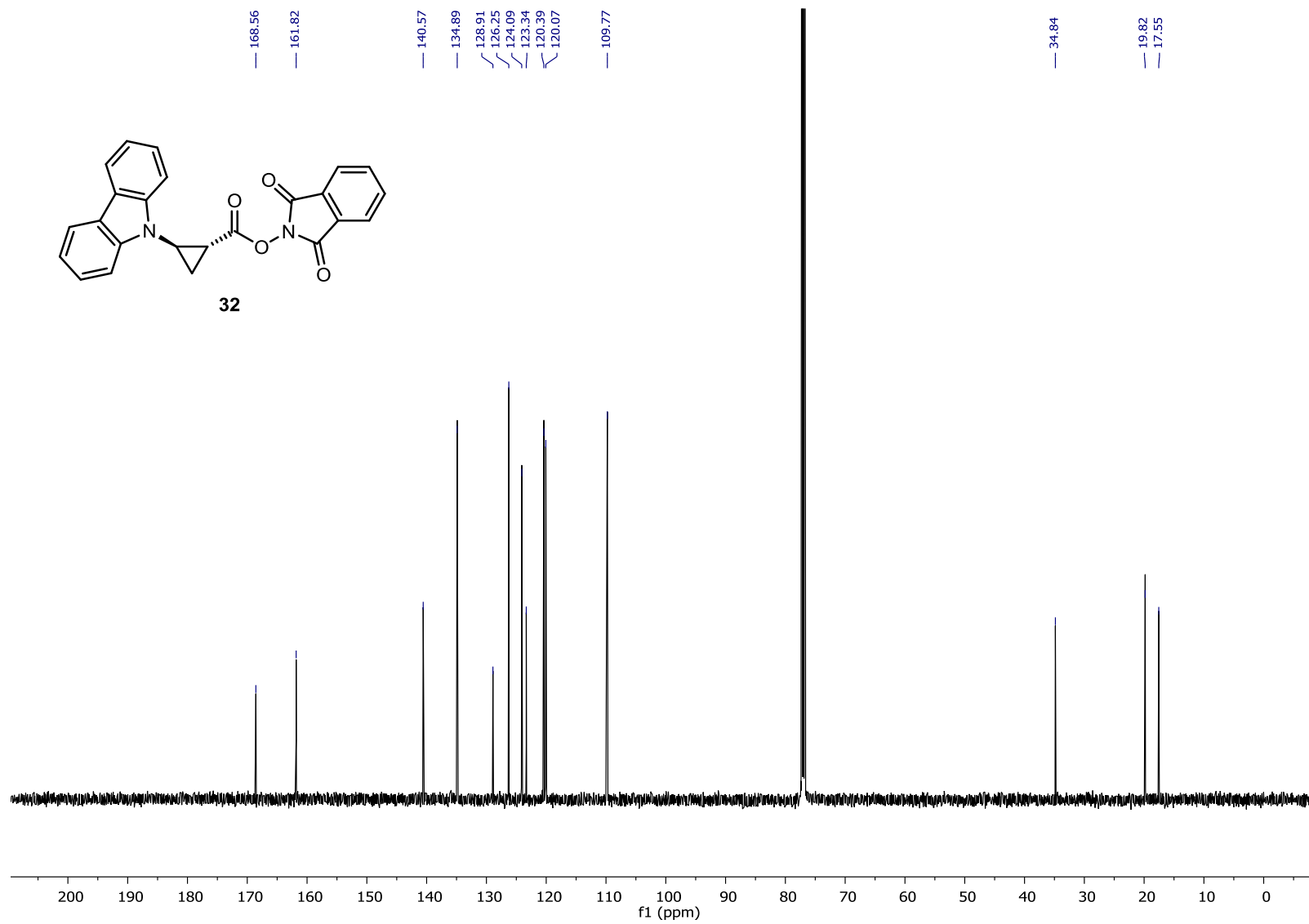
HSQC NMR (400 MHz, CDCl₃) for compound **31**



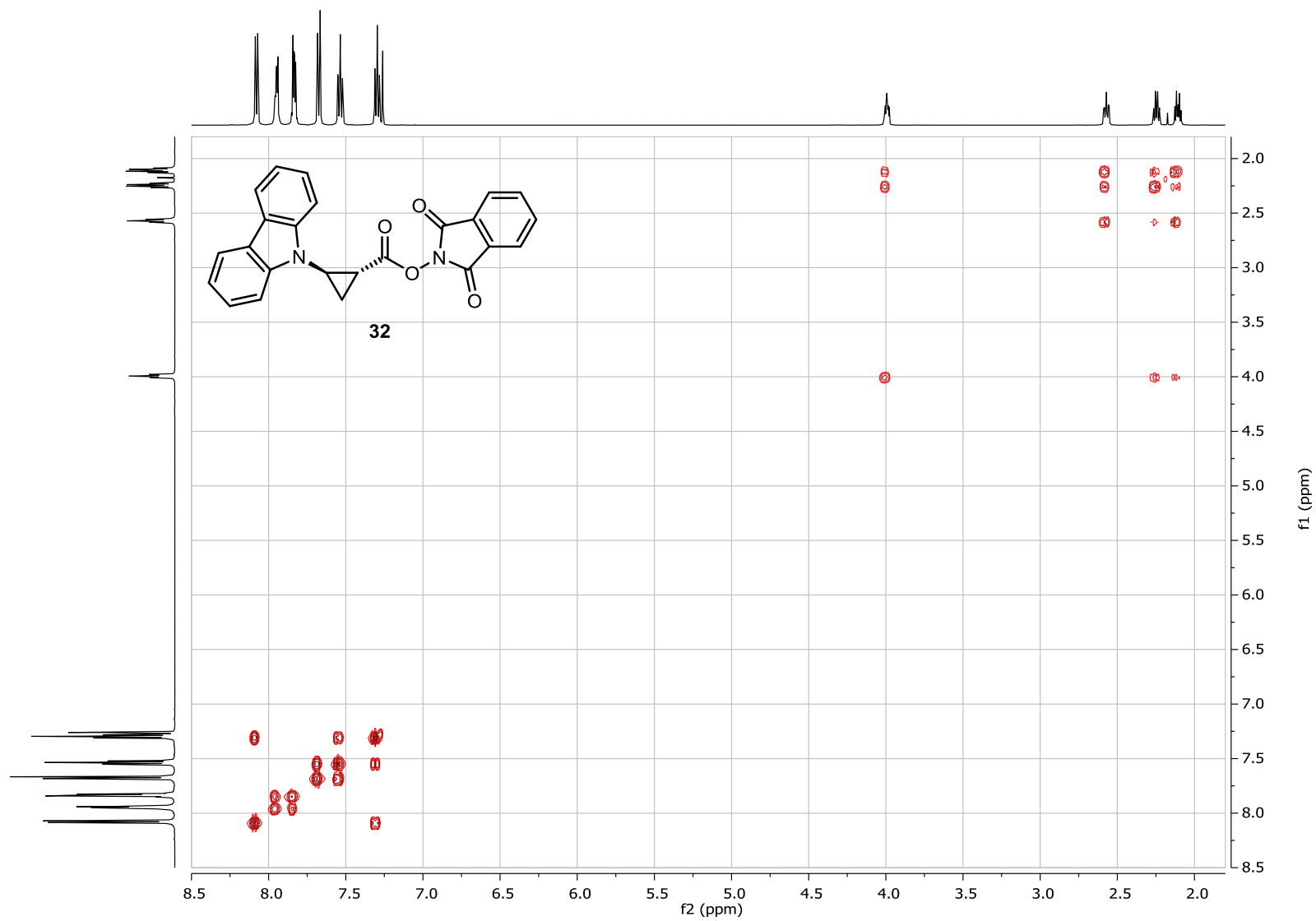
^1H NMR (500 MHz, CDCl_3) for compound **32**



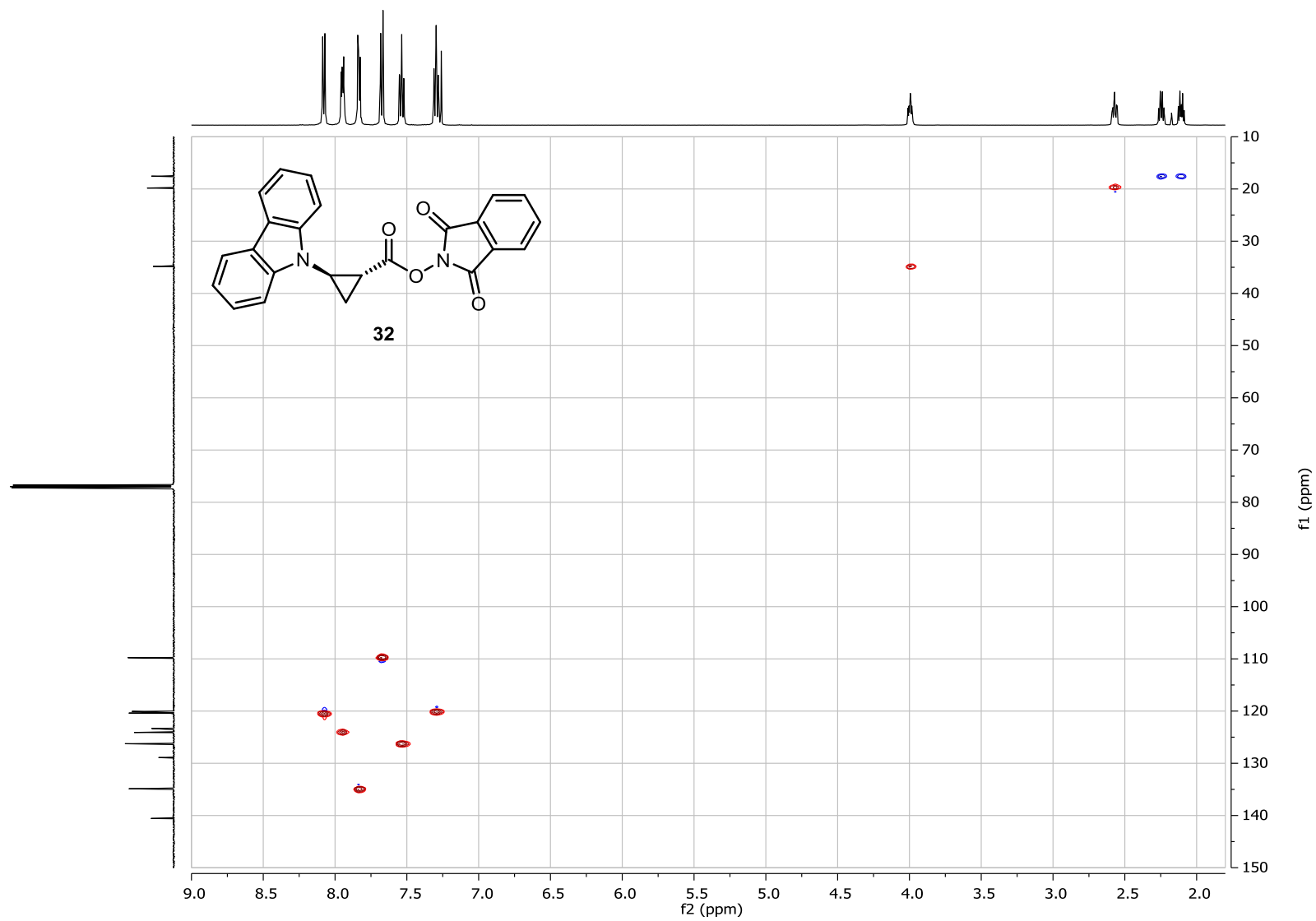
^{13}C NMR (126 MHz, CDCl_3) for compound **32**



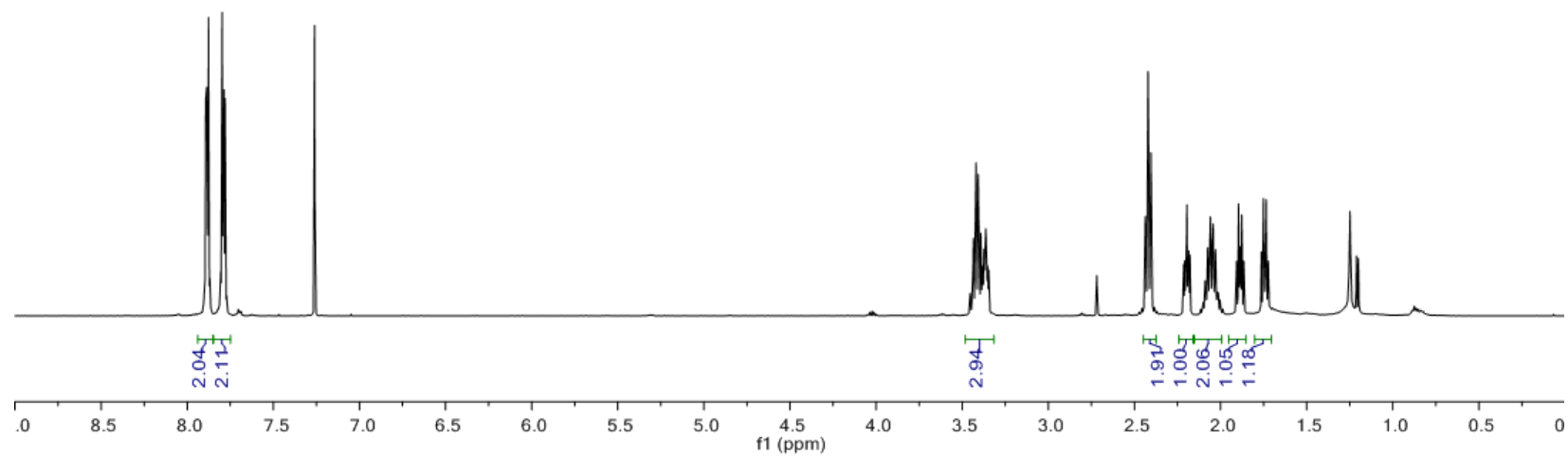
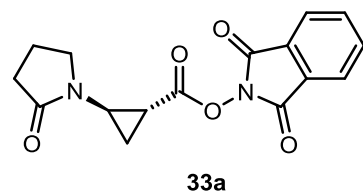
COSY NMR (500 MHz, CDCl₃) for compound **32**



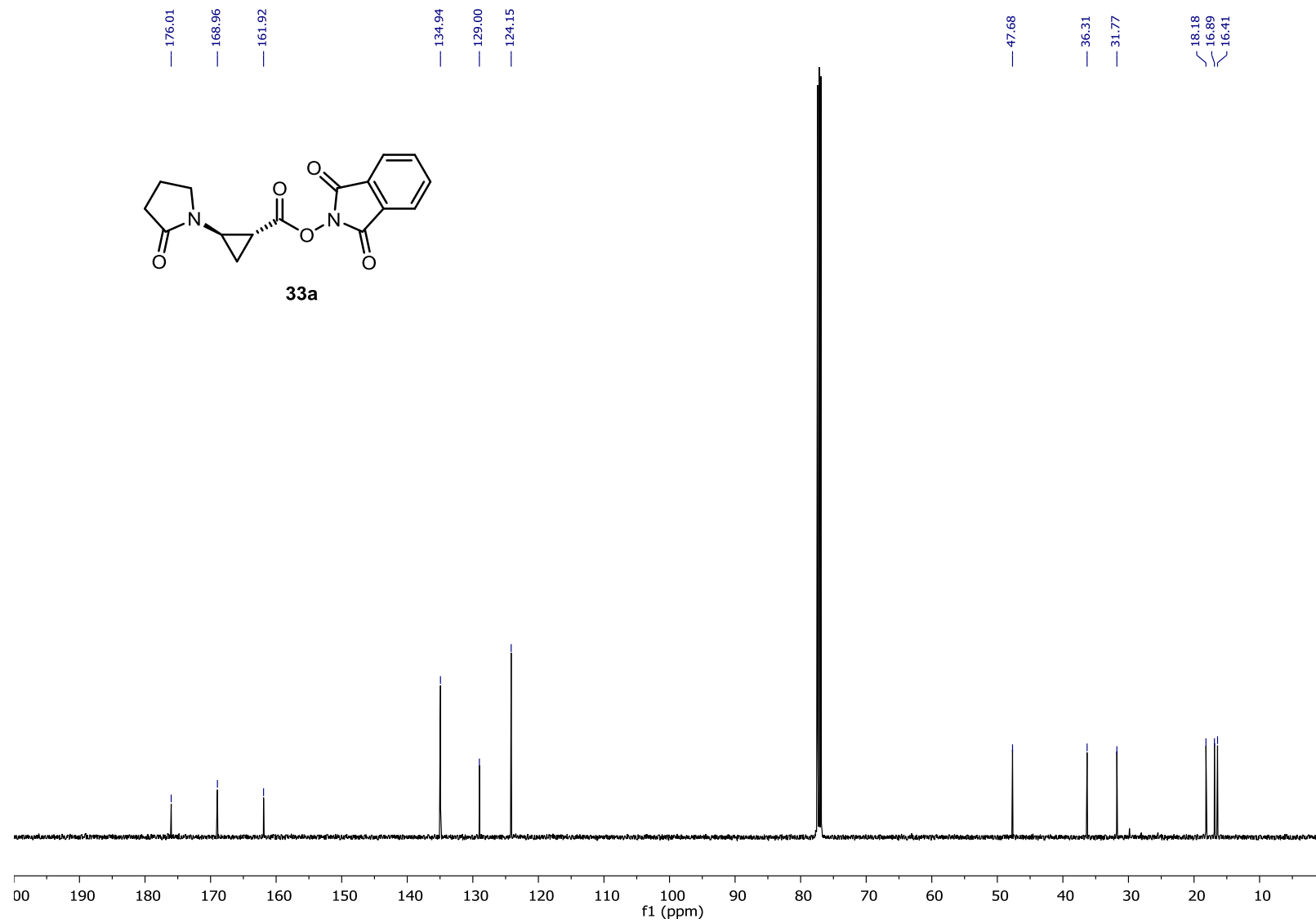
HSQC NMR (500 MHz, CDCl₃) for compound **32**



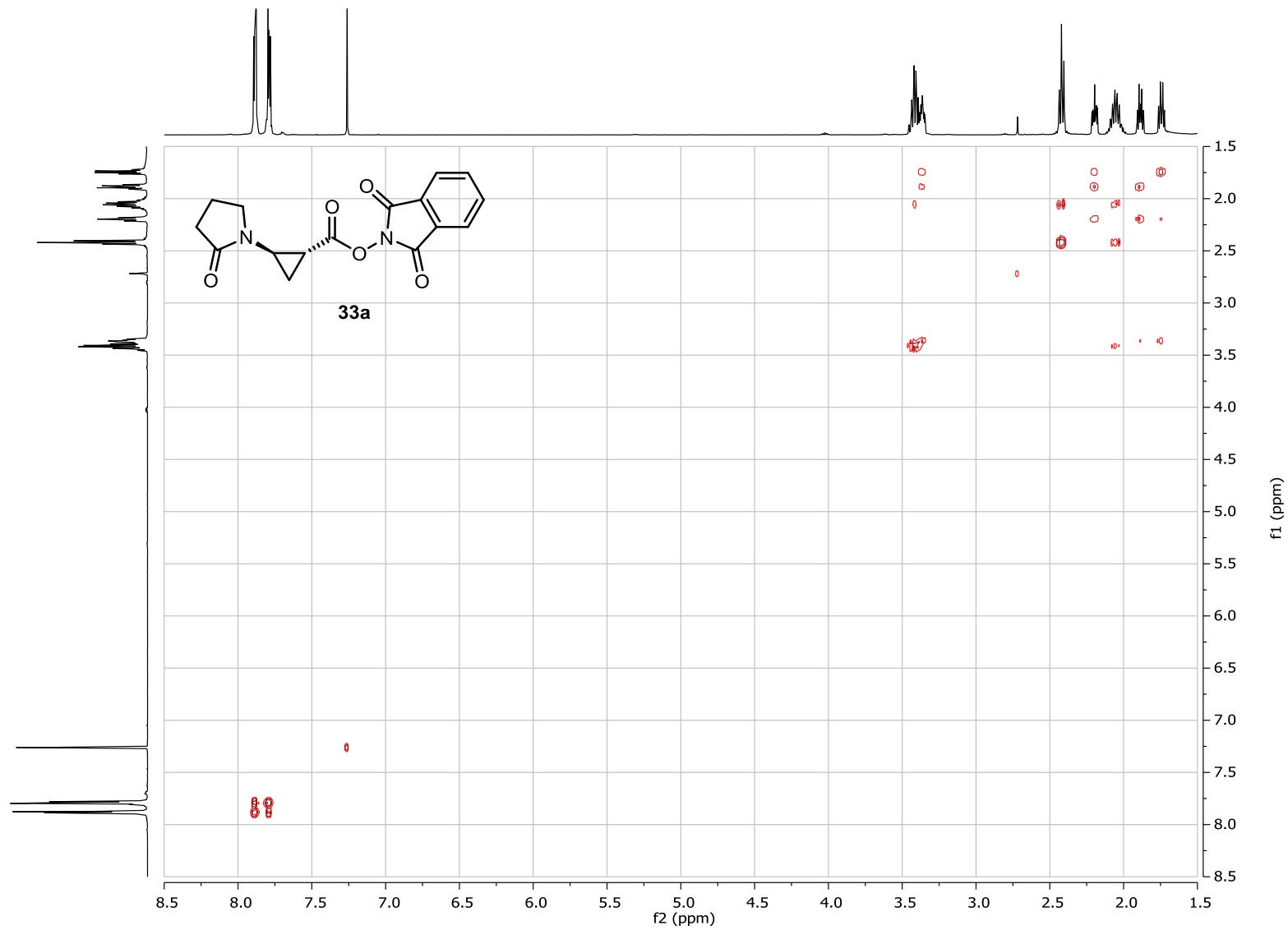
^1H NMR (500 MHz, CDCl_3) for compound **33a**



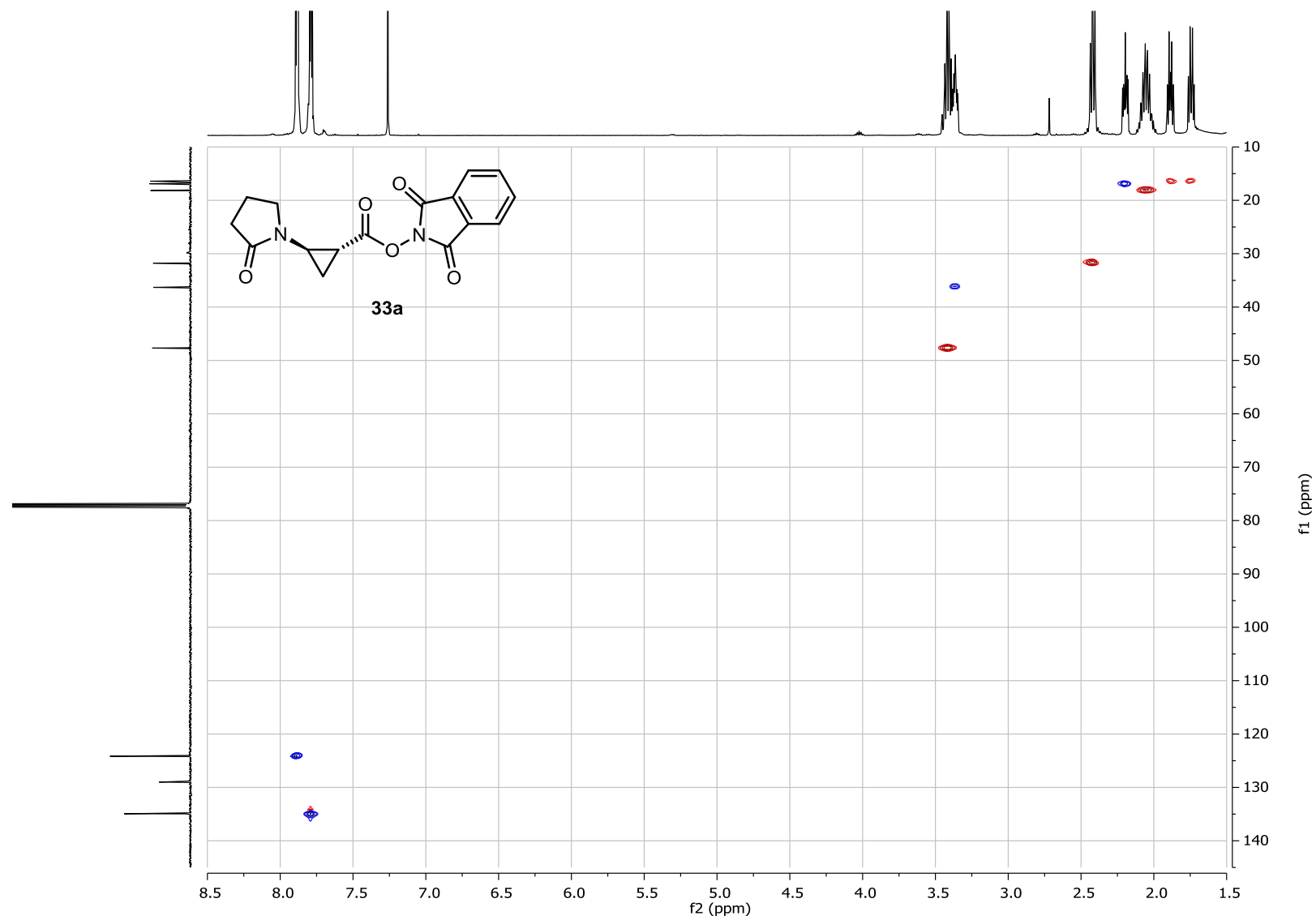
^{13}C NMR (126 MHz, CDCl_3) for compound **33a**



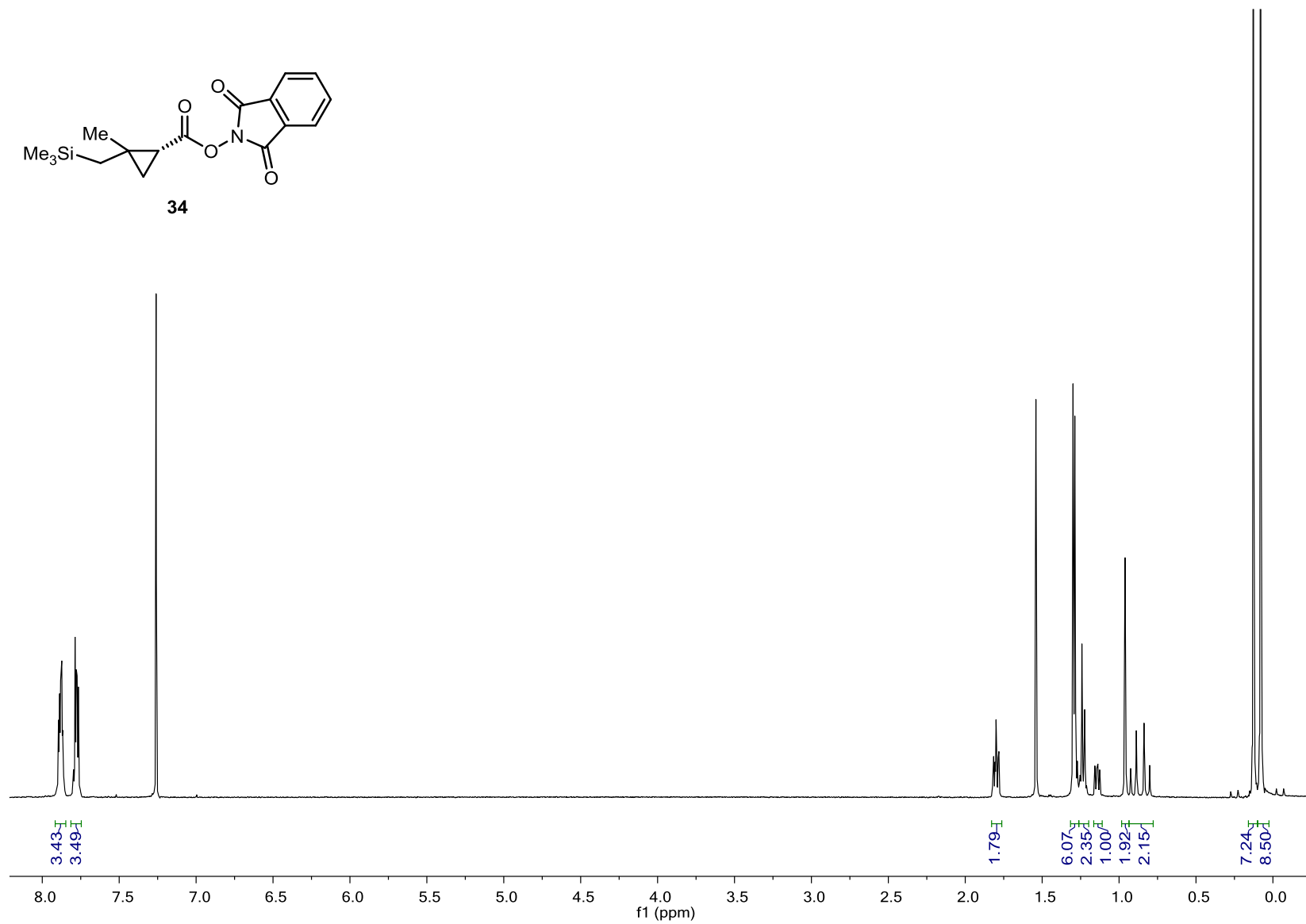
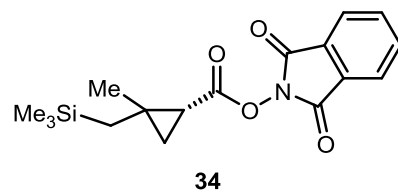
COSY NMR (500 MHz, CDCl₃) for compound **33a**



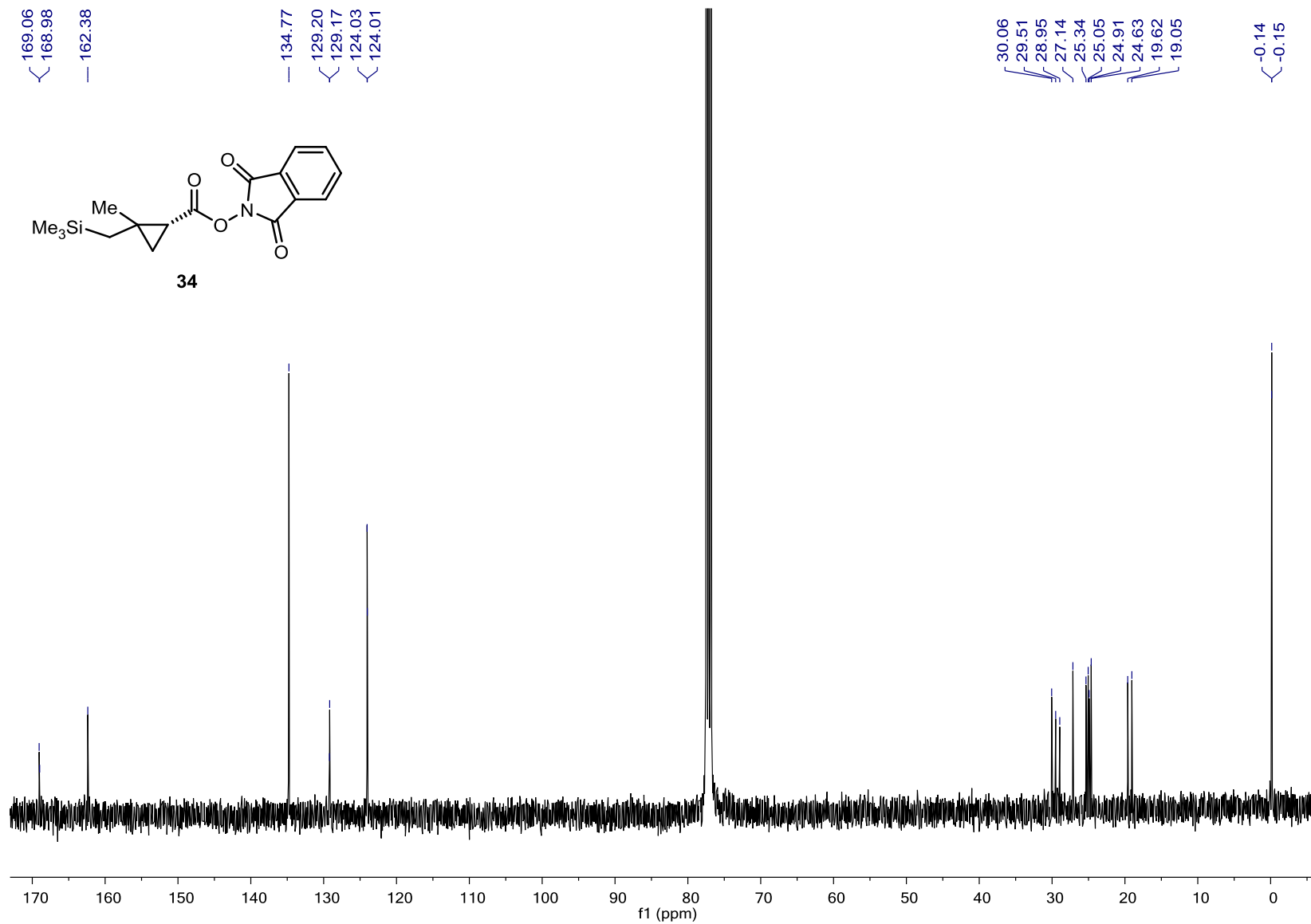
HSQC NMR (500 MHz, CDCl₃) for compound **33a**



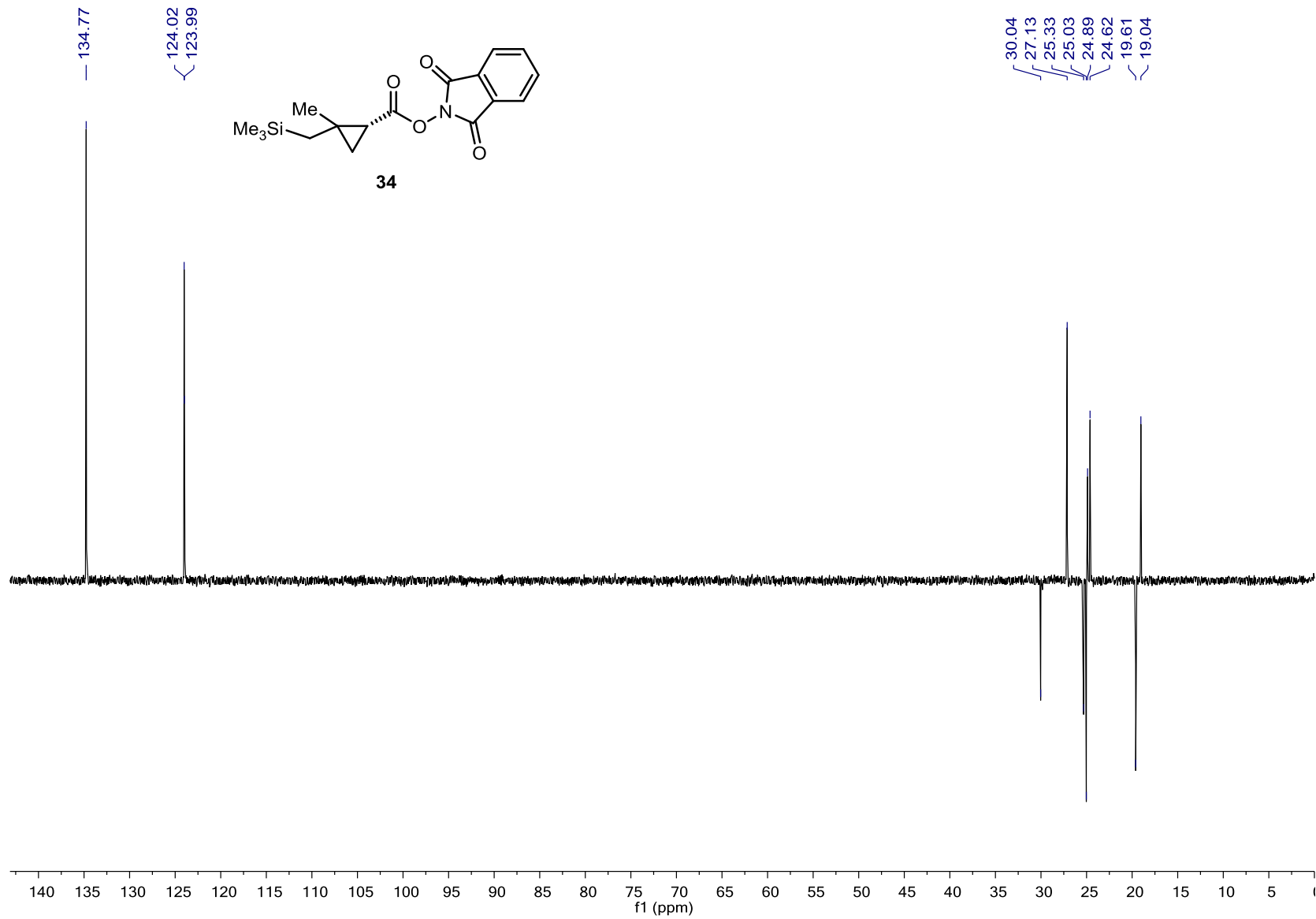
^1H NMR (400 MHz, CDCl_3) for compound **34**



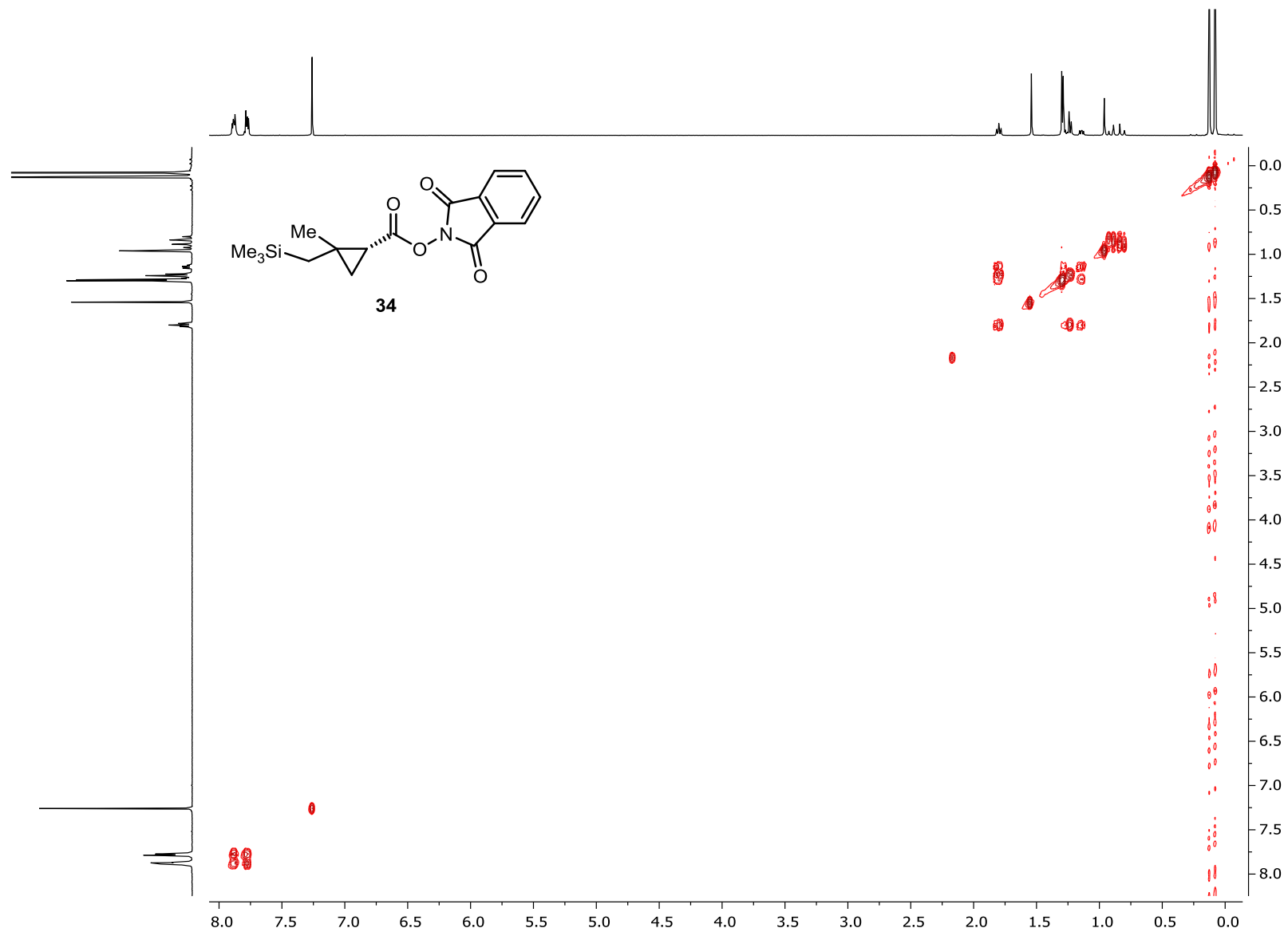
^{13}C NMR (101 MHz, CDCl_3) for compound **34**



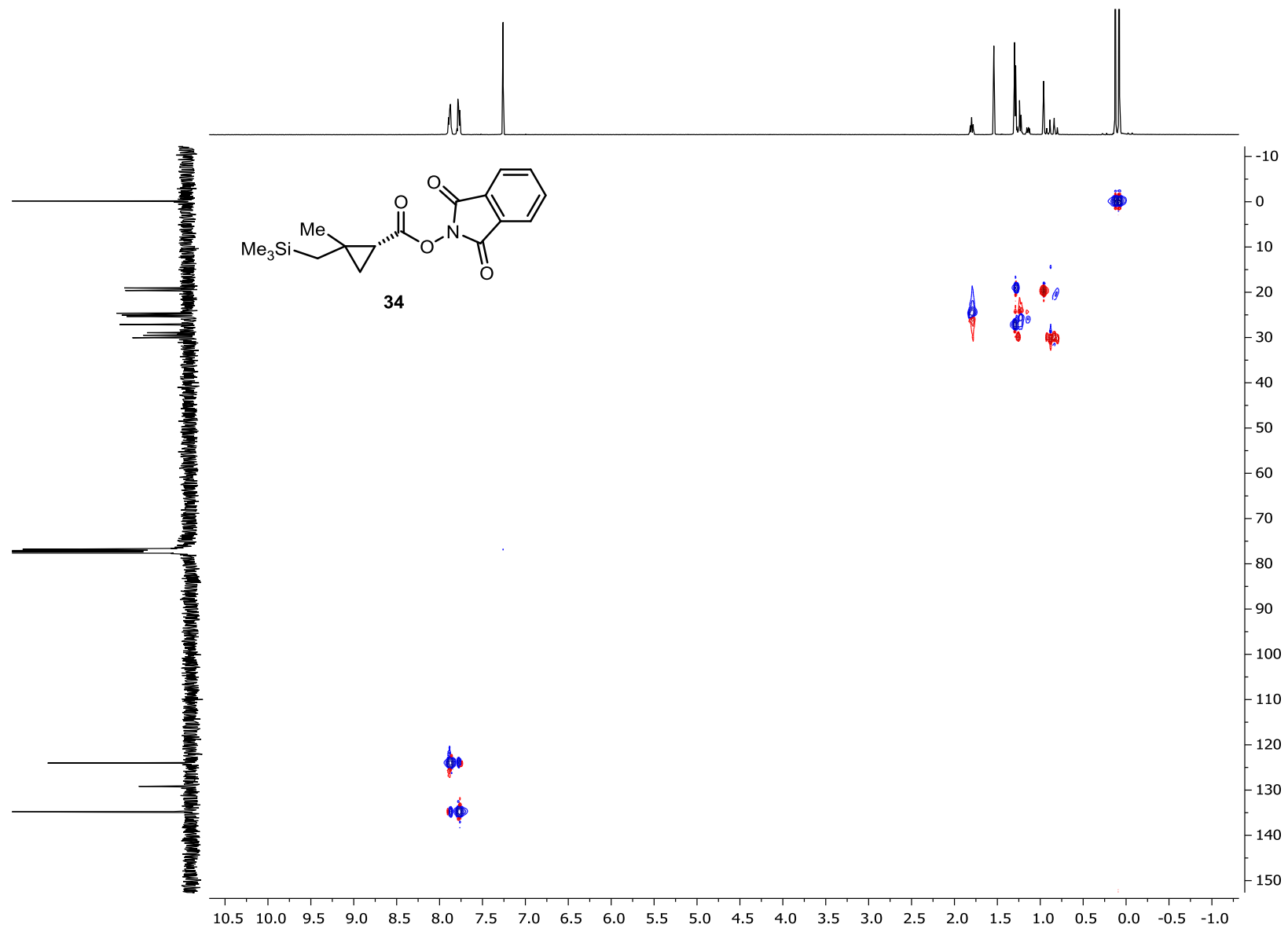
DEPT 135° NMR (101 MHz, CDCl₃) for compound **34**



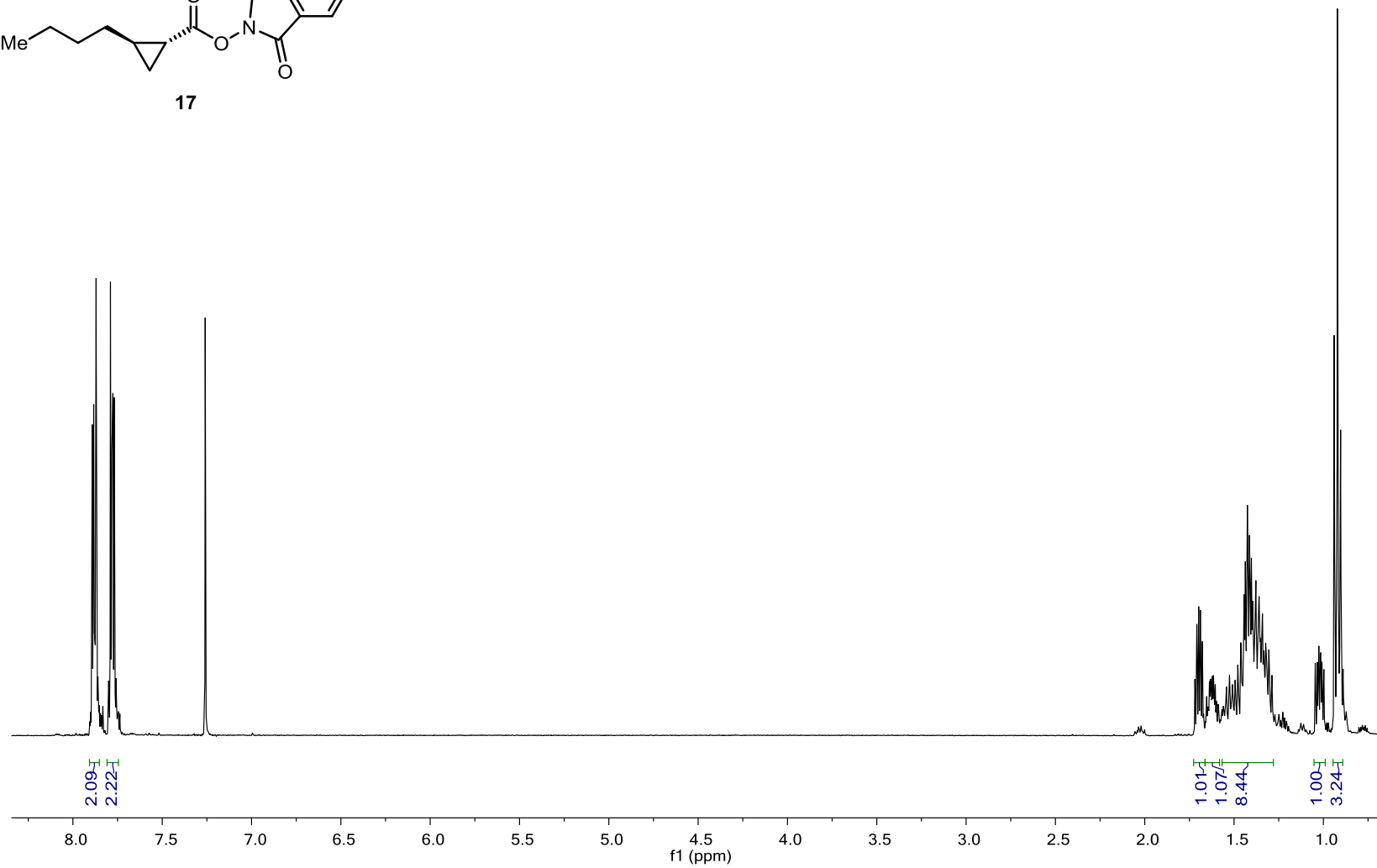
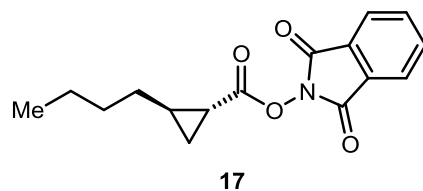
COSY NMR (400 MHz, CDCl₃) for compound **34**



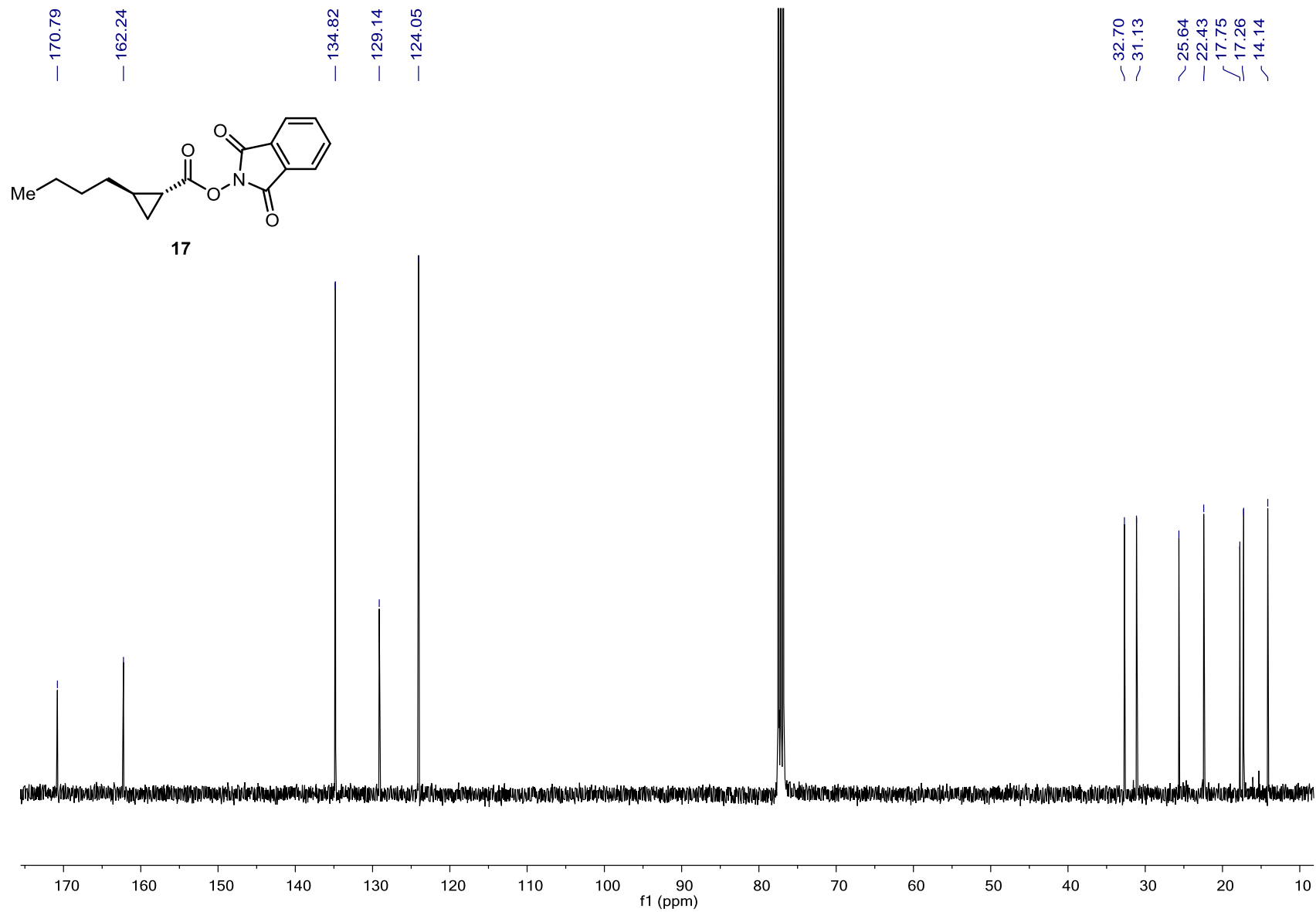
HSQC NMR (400 MHz, CDCl₃) for compound **34**



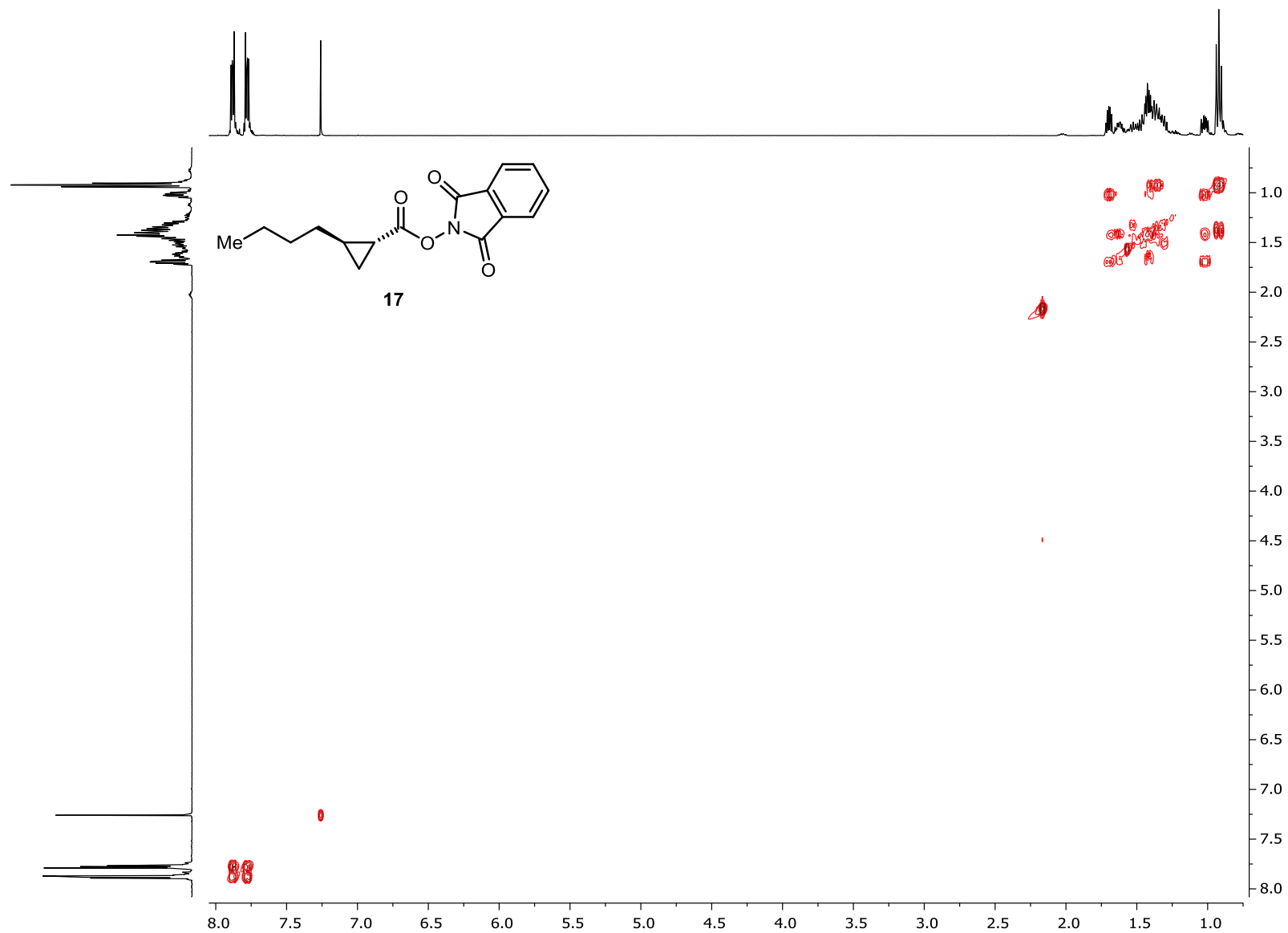
^1H NMR (400 MHz, CDCl_3) for compound **17**



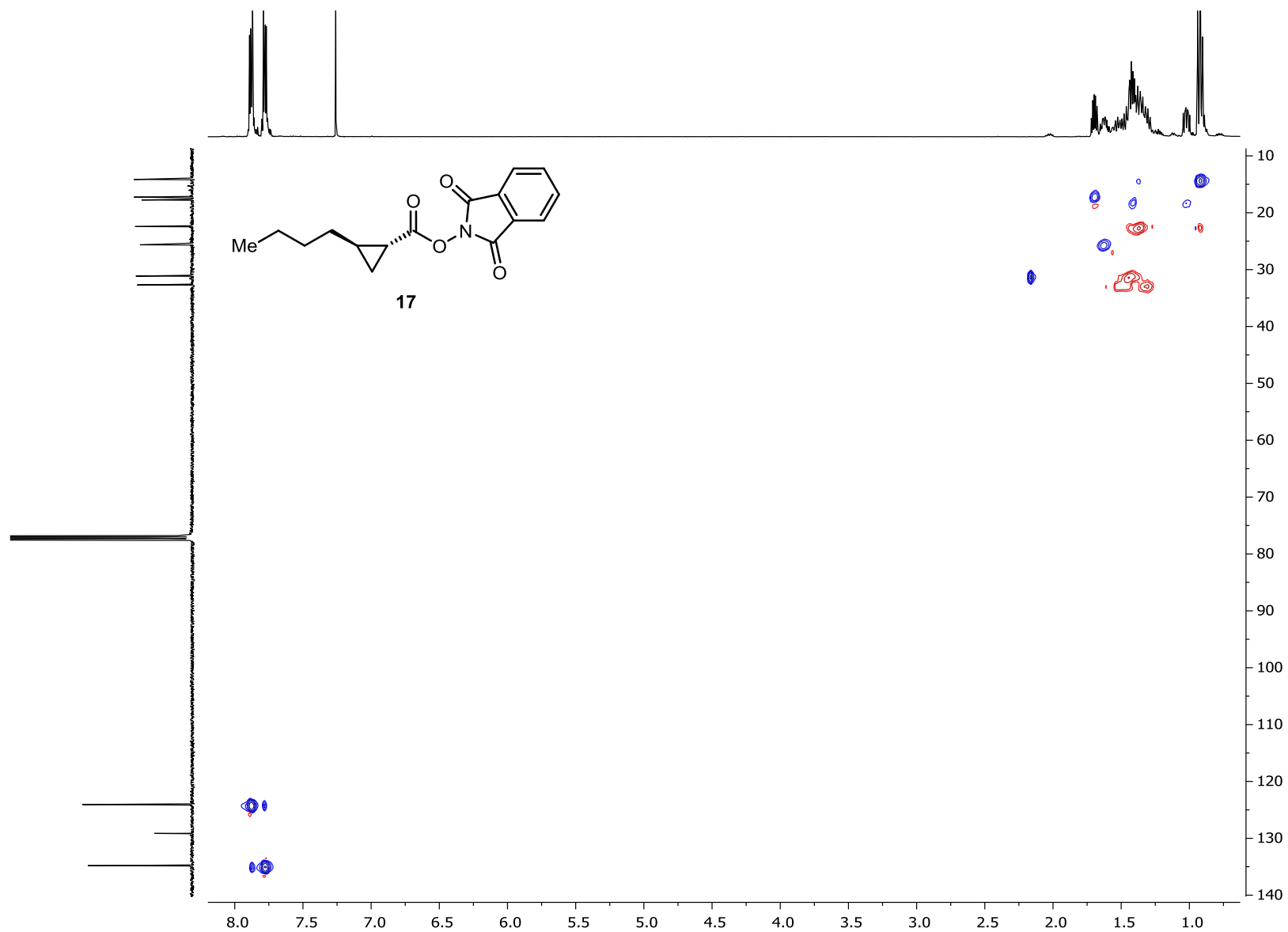
^{13}C NMR (101 MHz, CDCl_3) for compound **17**



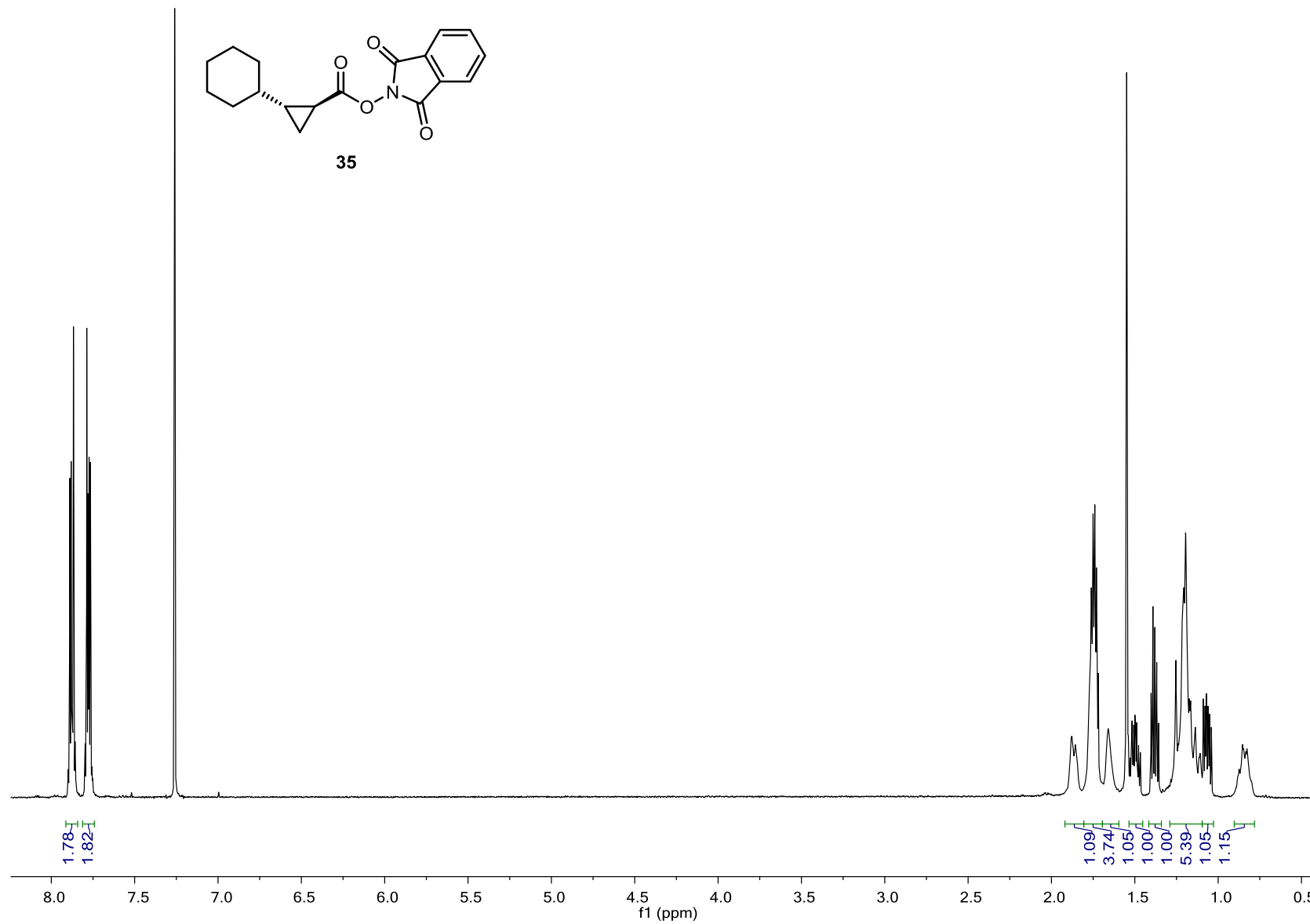
COSY NMR (400 MHz, CDCl₃) for compound **17**



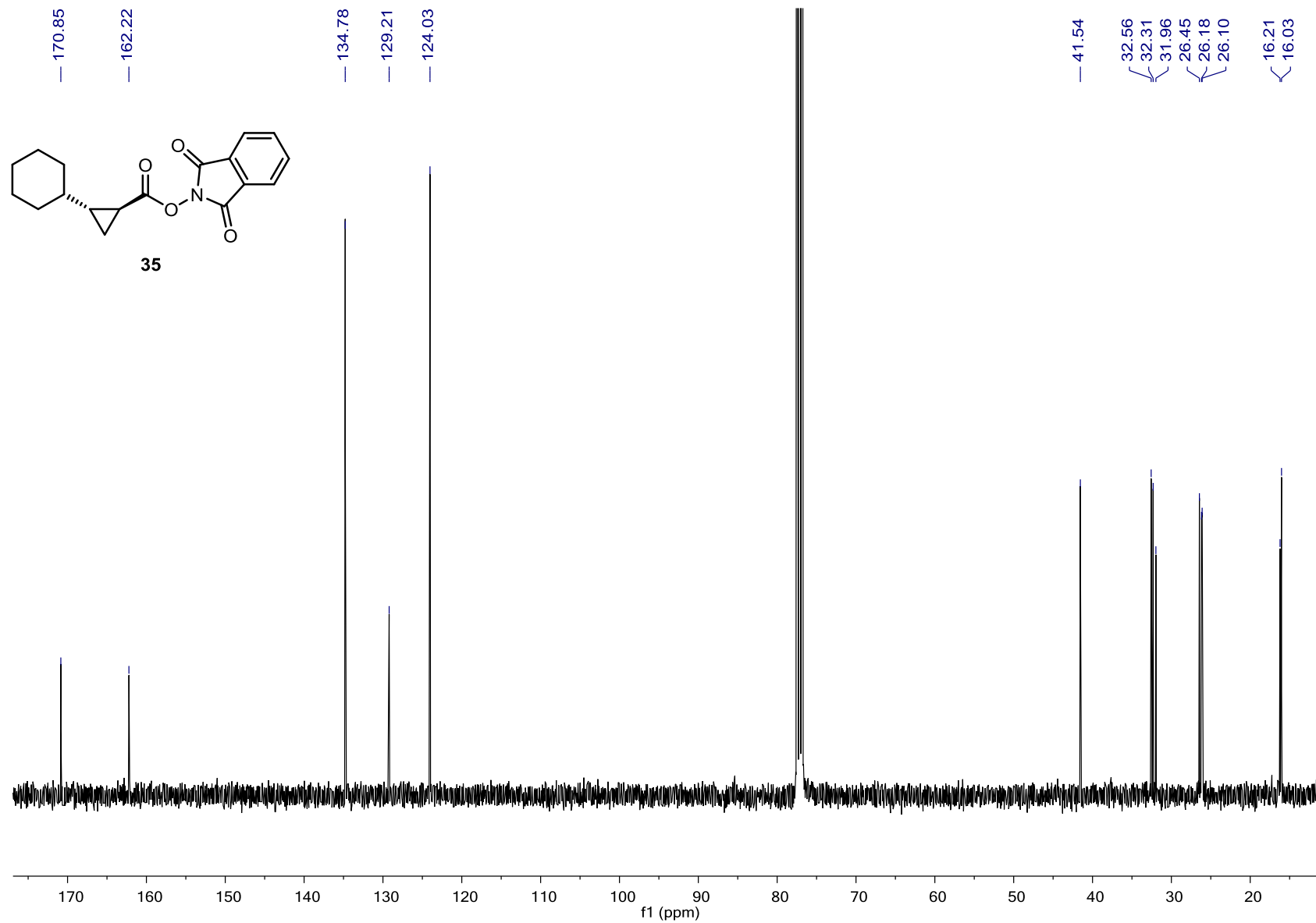
HSQC NMR (400 MHz, CDCl₃) for compound **17**



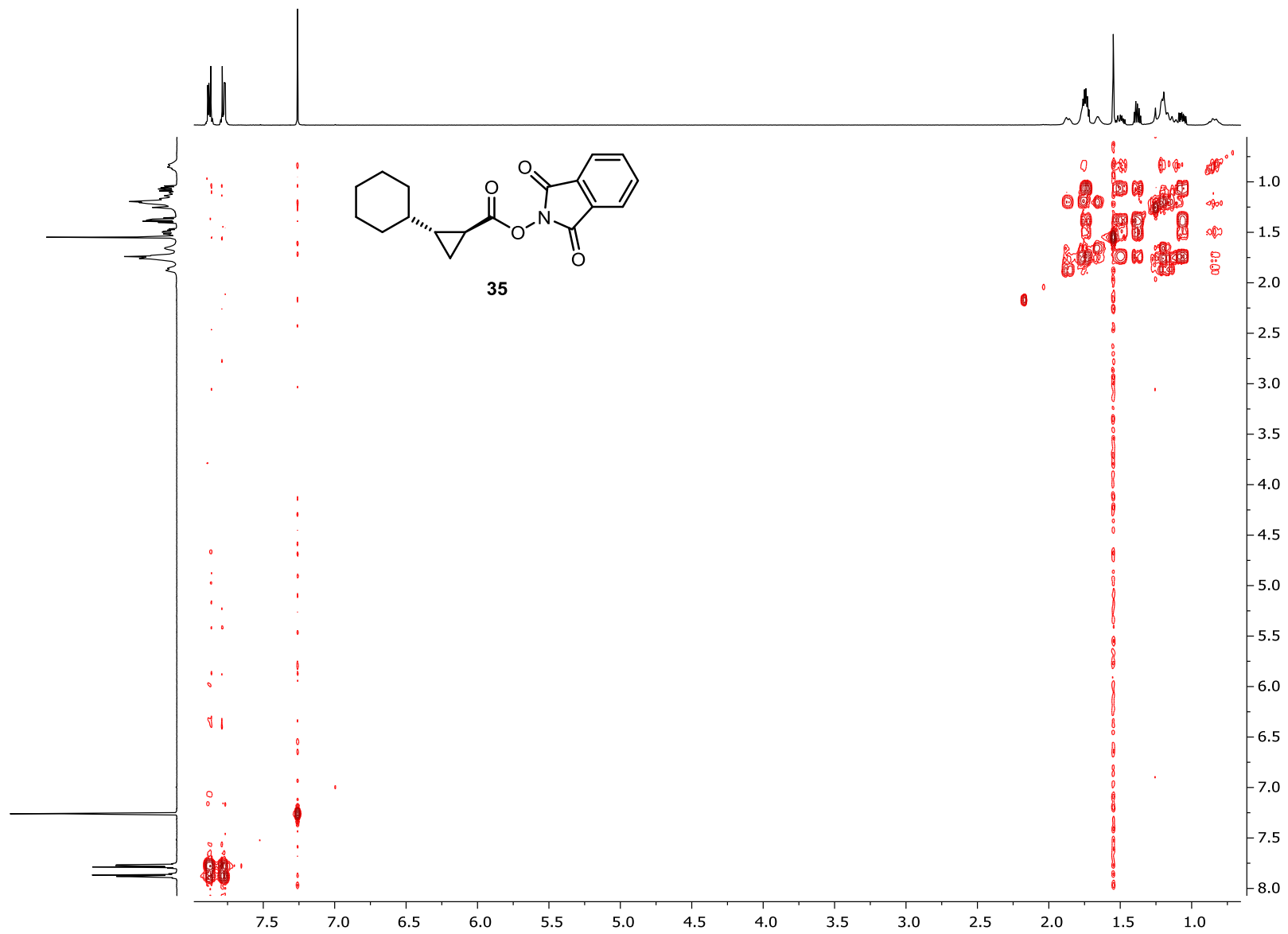
^1H NMR (400 MHz, CDCl_3) for compound 35



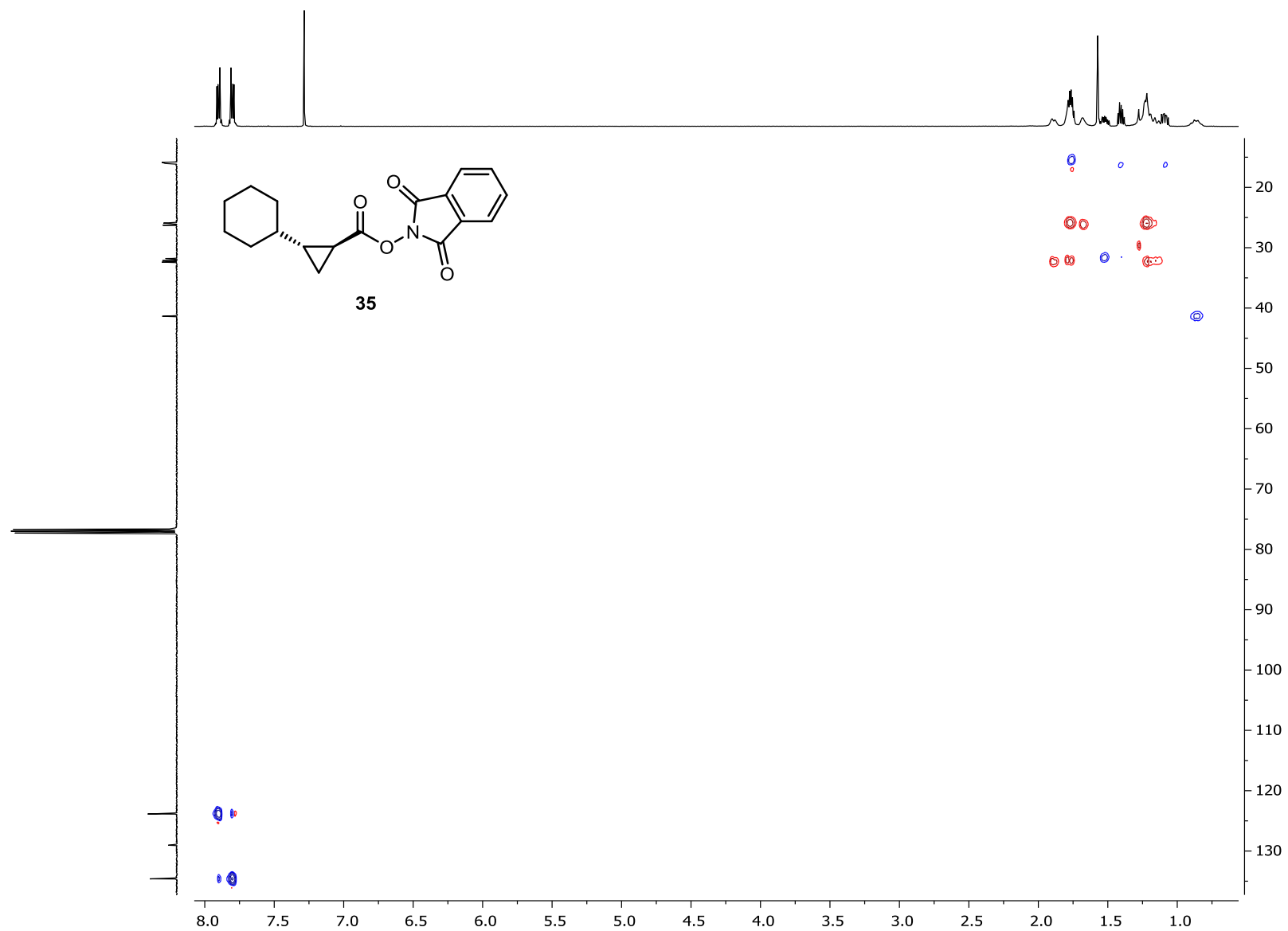
^{13}C NMR (101 MHz, CDCl_3) for compound **35**



COSY NMR (400 MHz, CDCl₃) for compound **35**

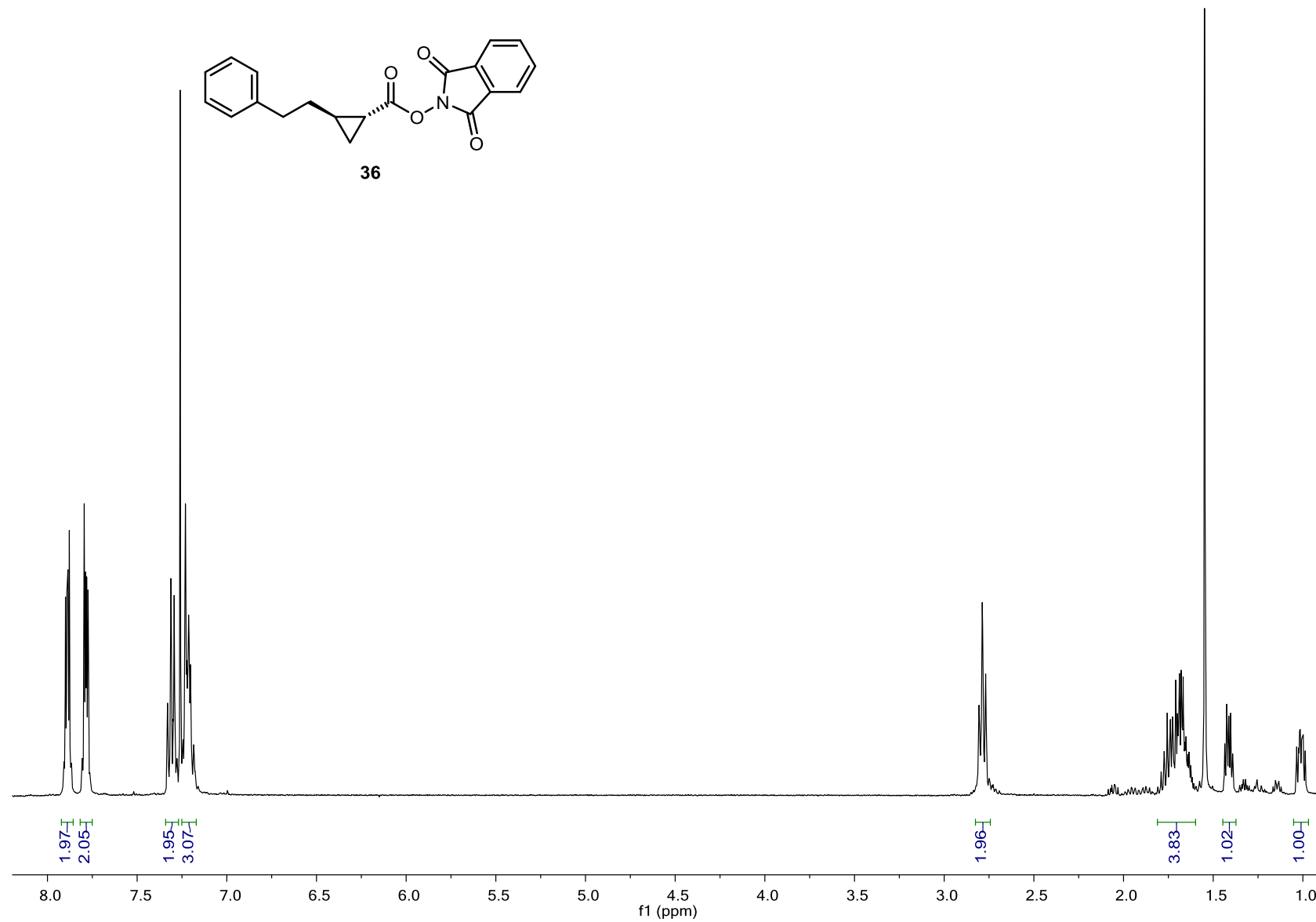


HSQC NMR (400 MHz, CDCl₃) for compound **35**

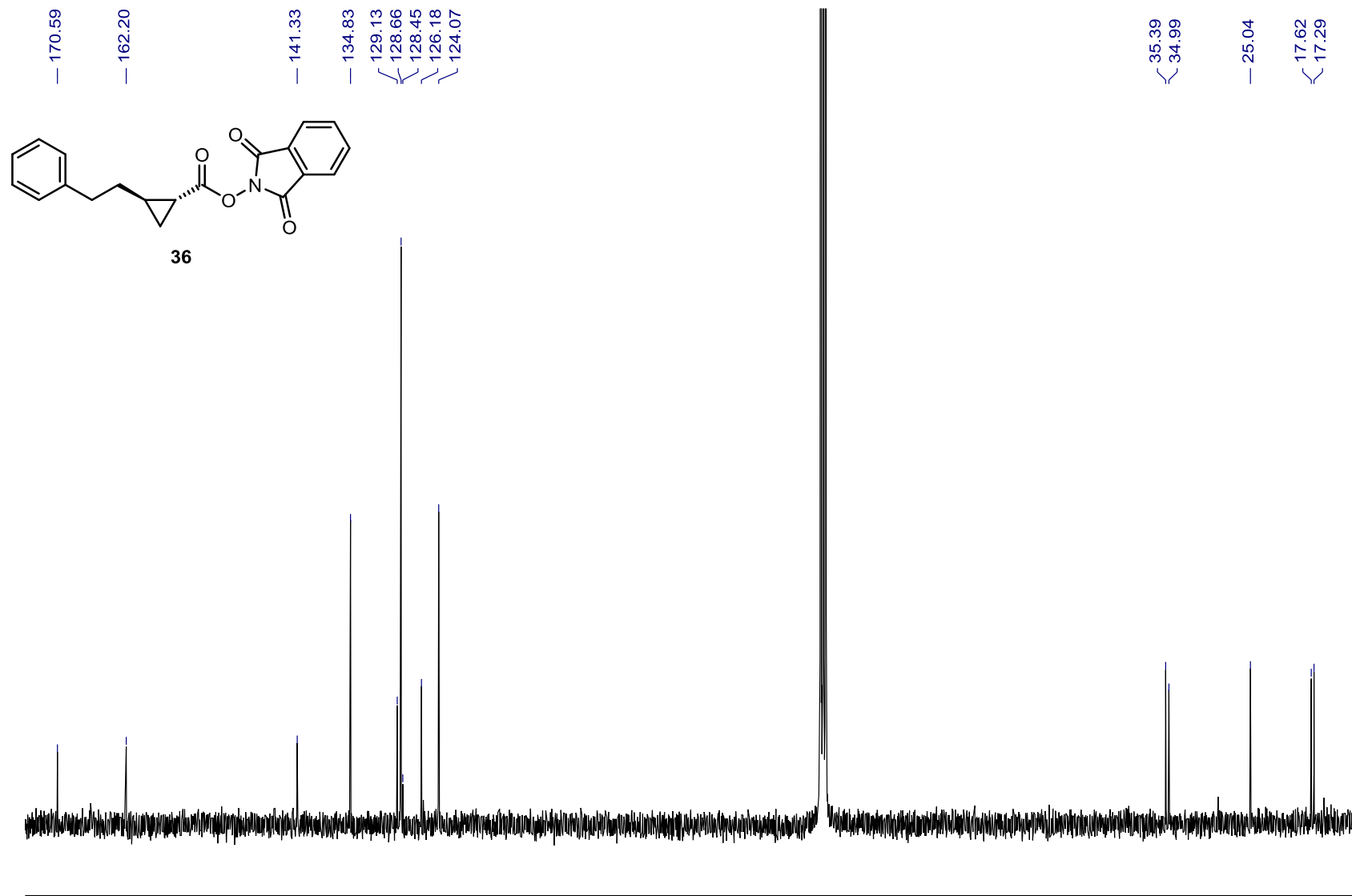


S192

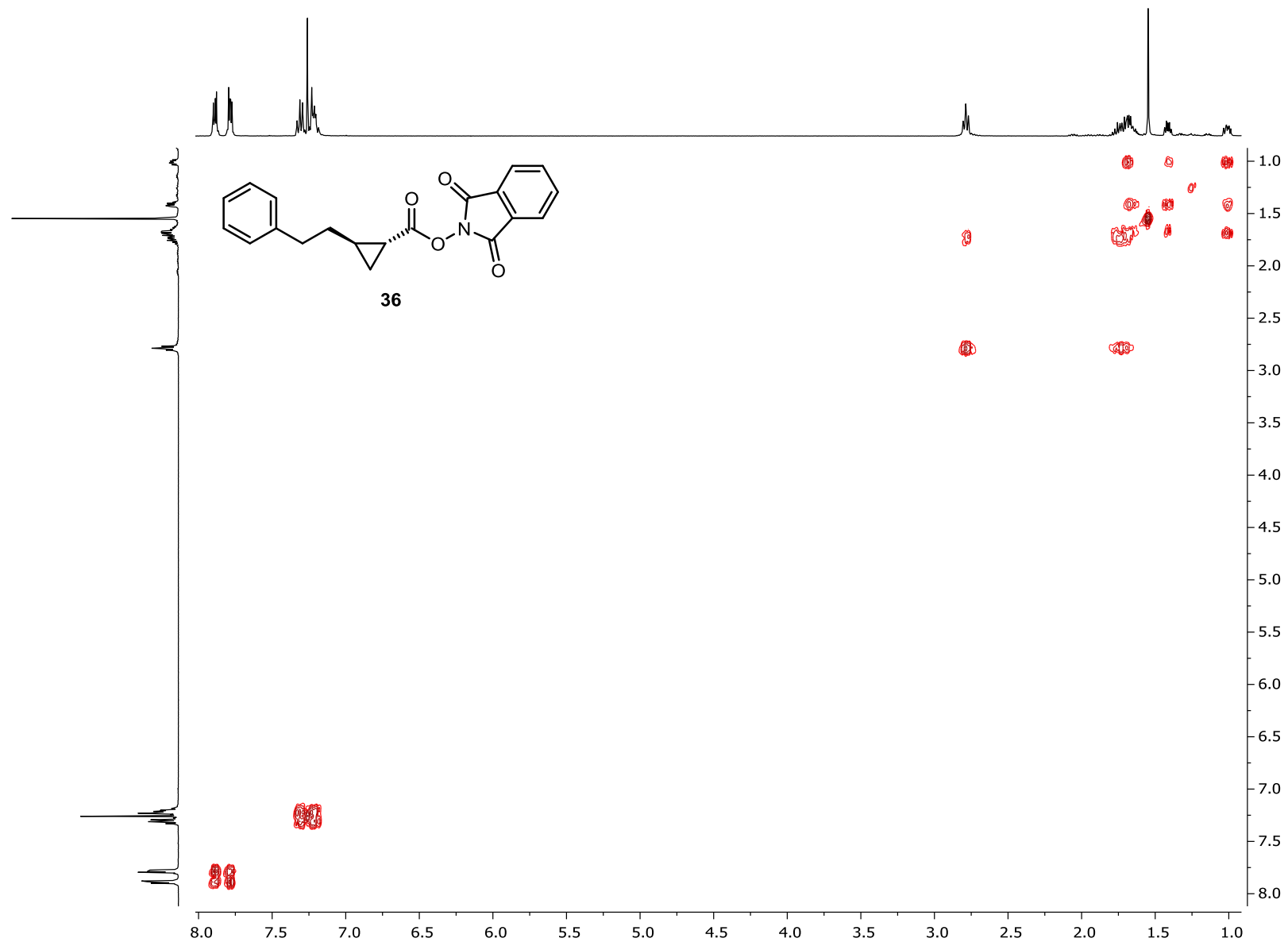
^1H NMR (400 MHz, CDCl_3) for compound **36**



^{13}C NMR (101 MHz, CDCl_3) for compound **36**

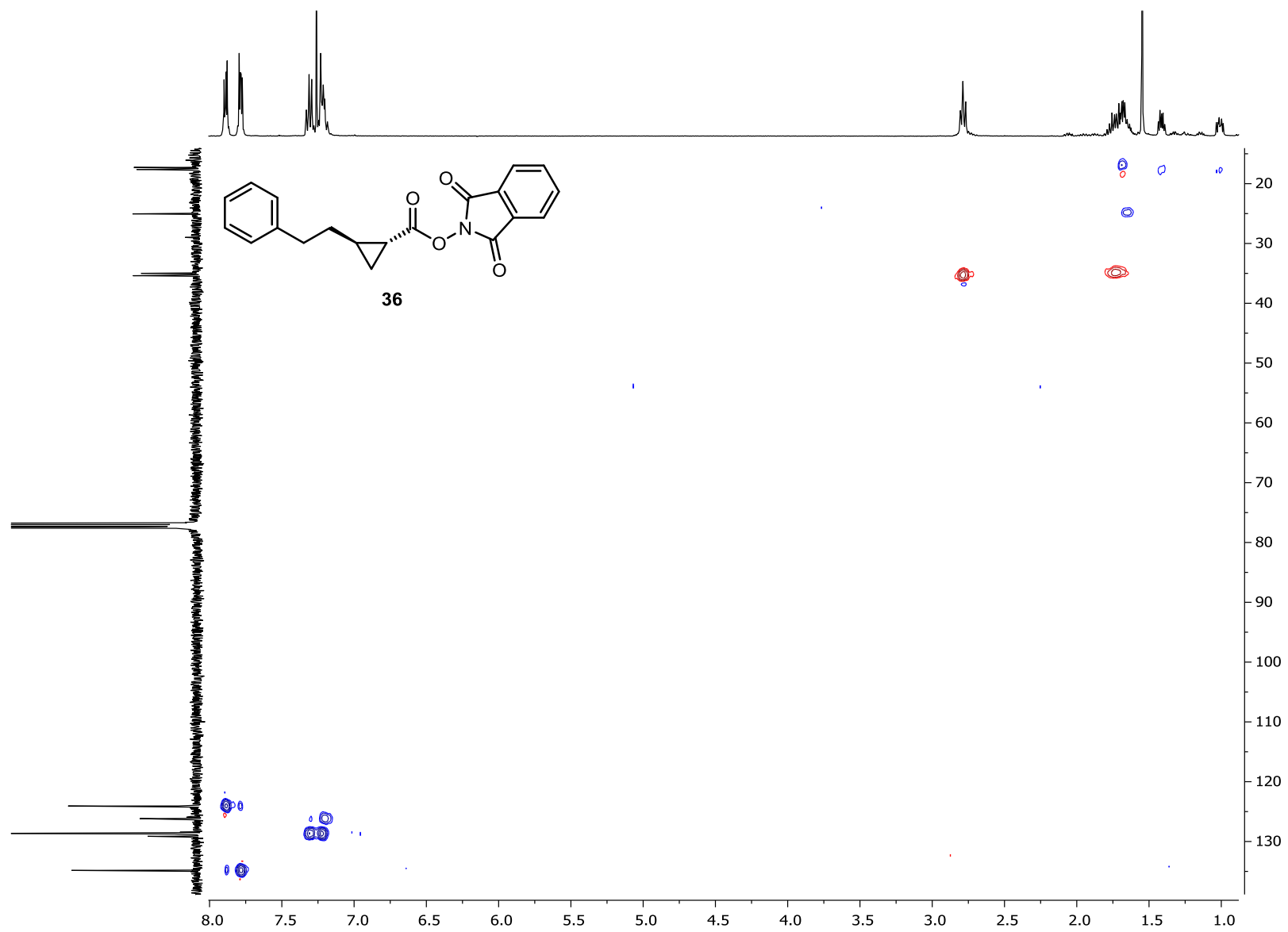


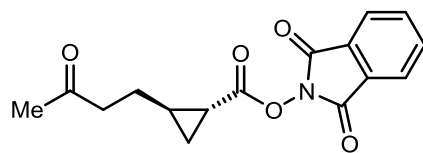
COSY NMR (400 MHz, CDCl₃) for compound **36**



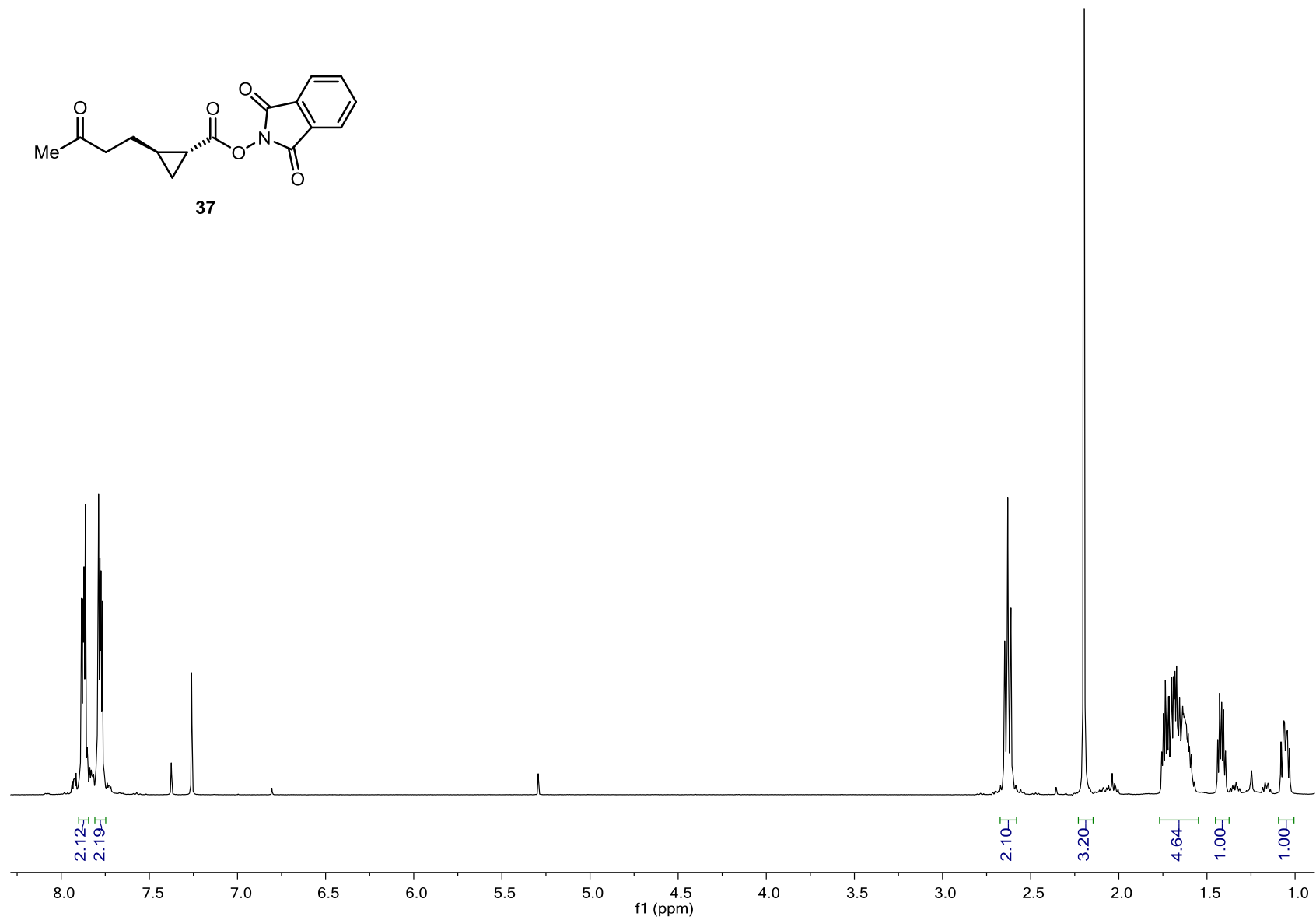
S195

HSQC NMR (400 MHz, CDCl₃) for compound **36**



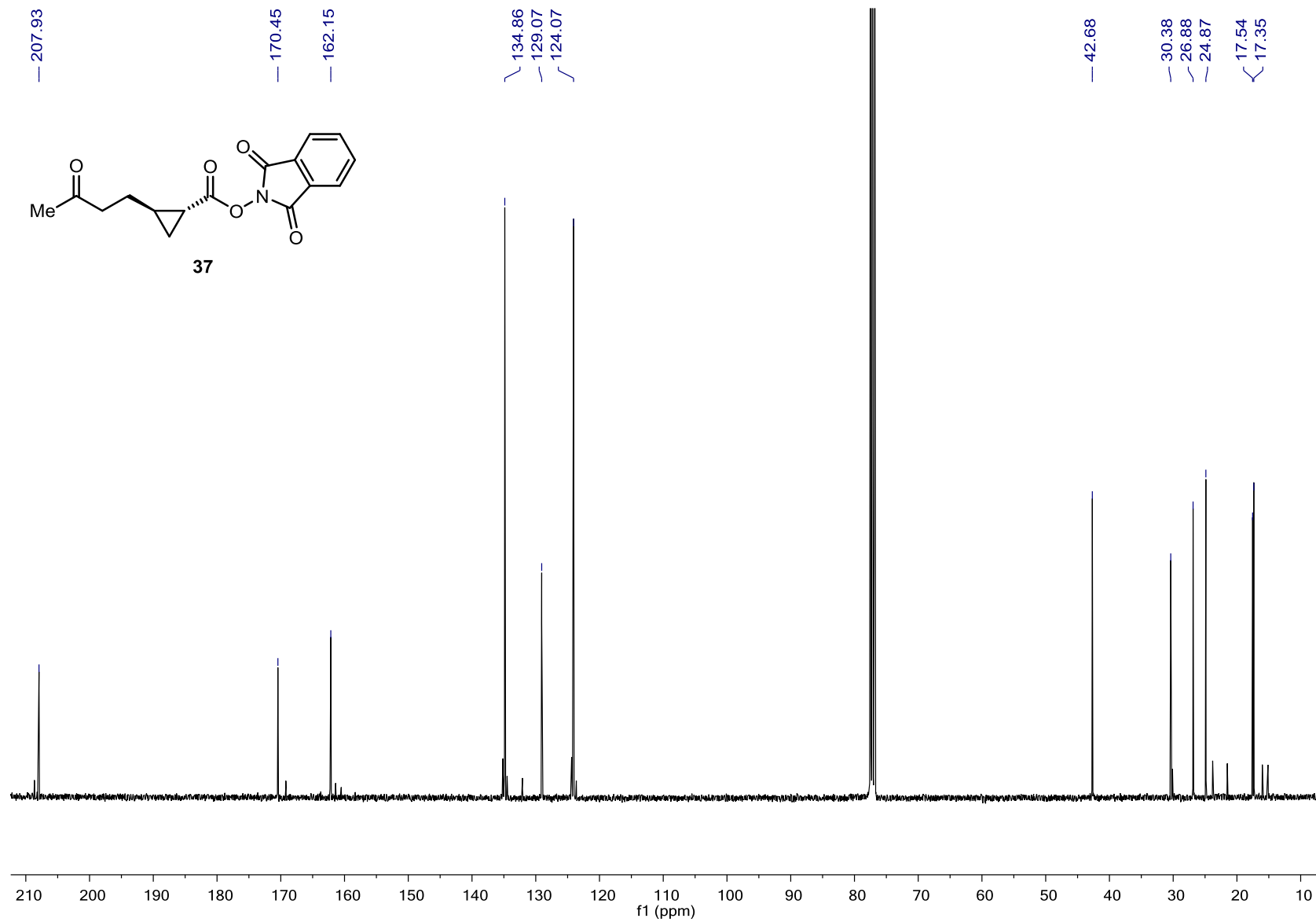
^1H NMR (400 MHz, CDCl_3) for compound **37**

37

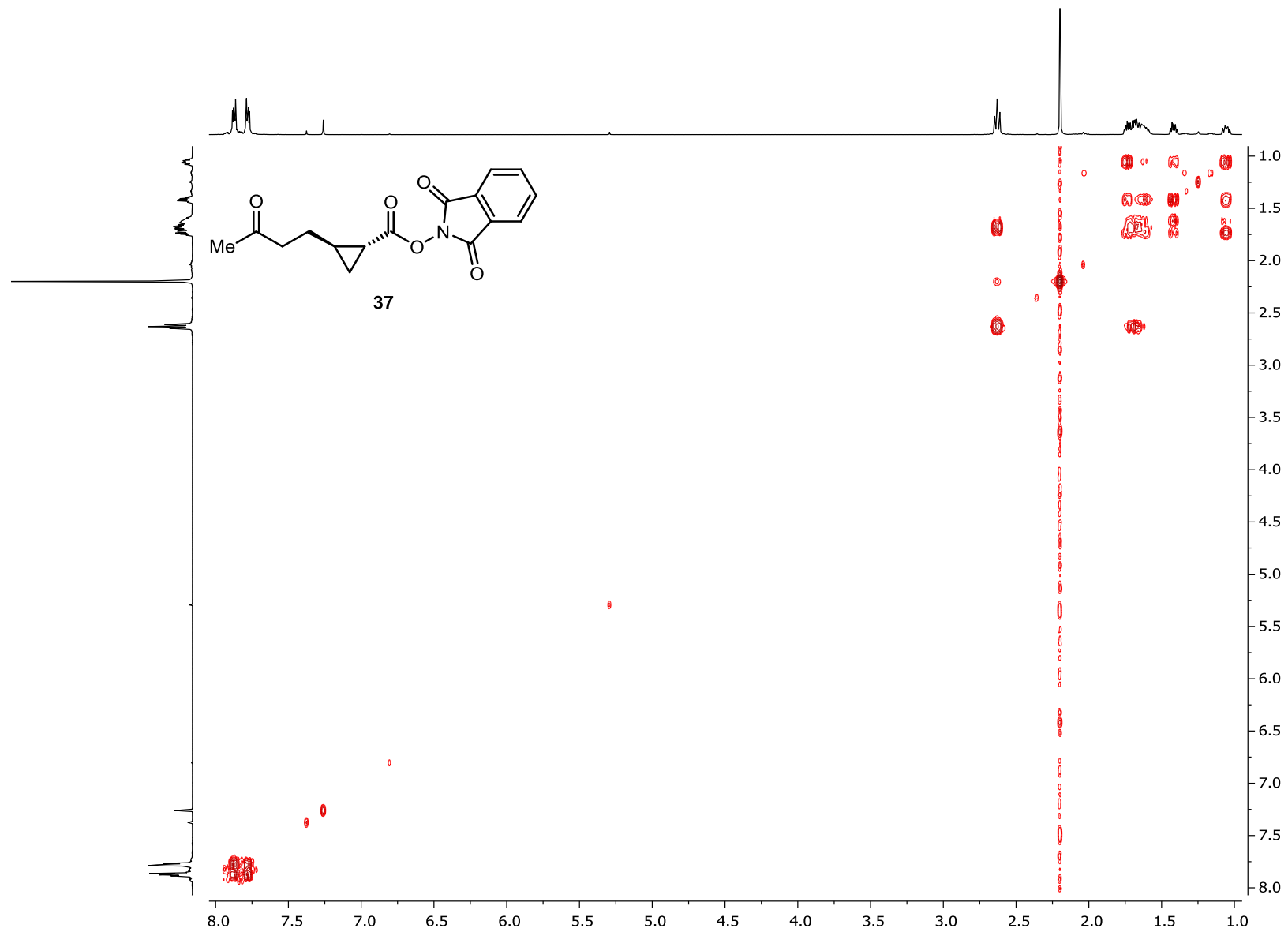


S197

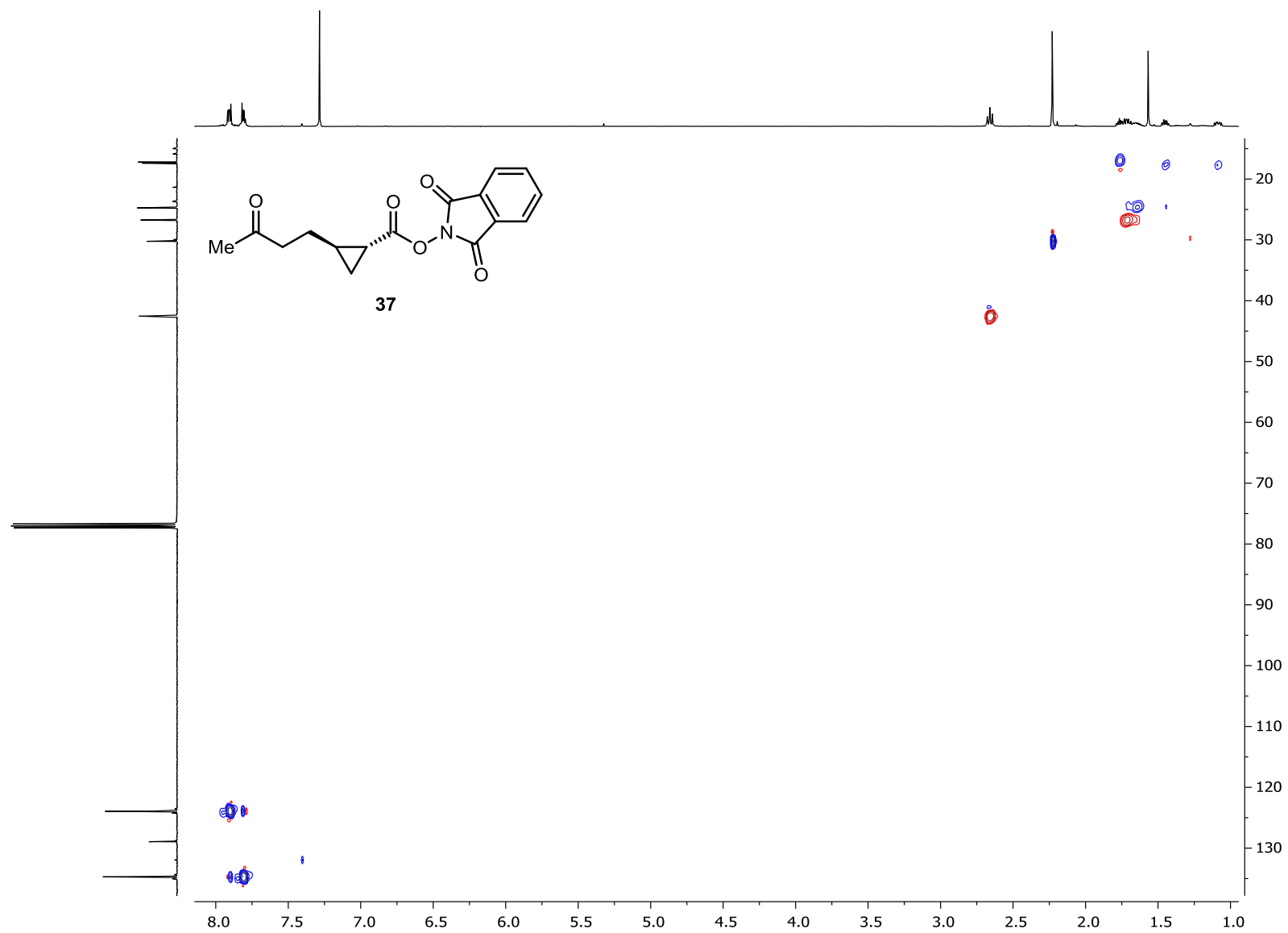
^{13}C NMR (101 MHz, CDCl_3) for compound **37**



COSY NMR (400 MHz, CDCl₃) for compound **37**

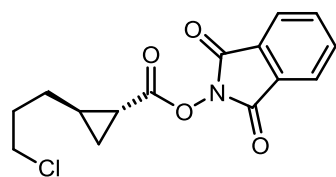


HSQC NMR (400 MHz, CDCl₃) for compound **37**

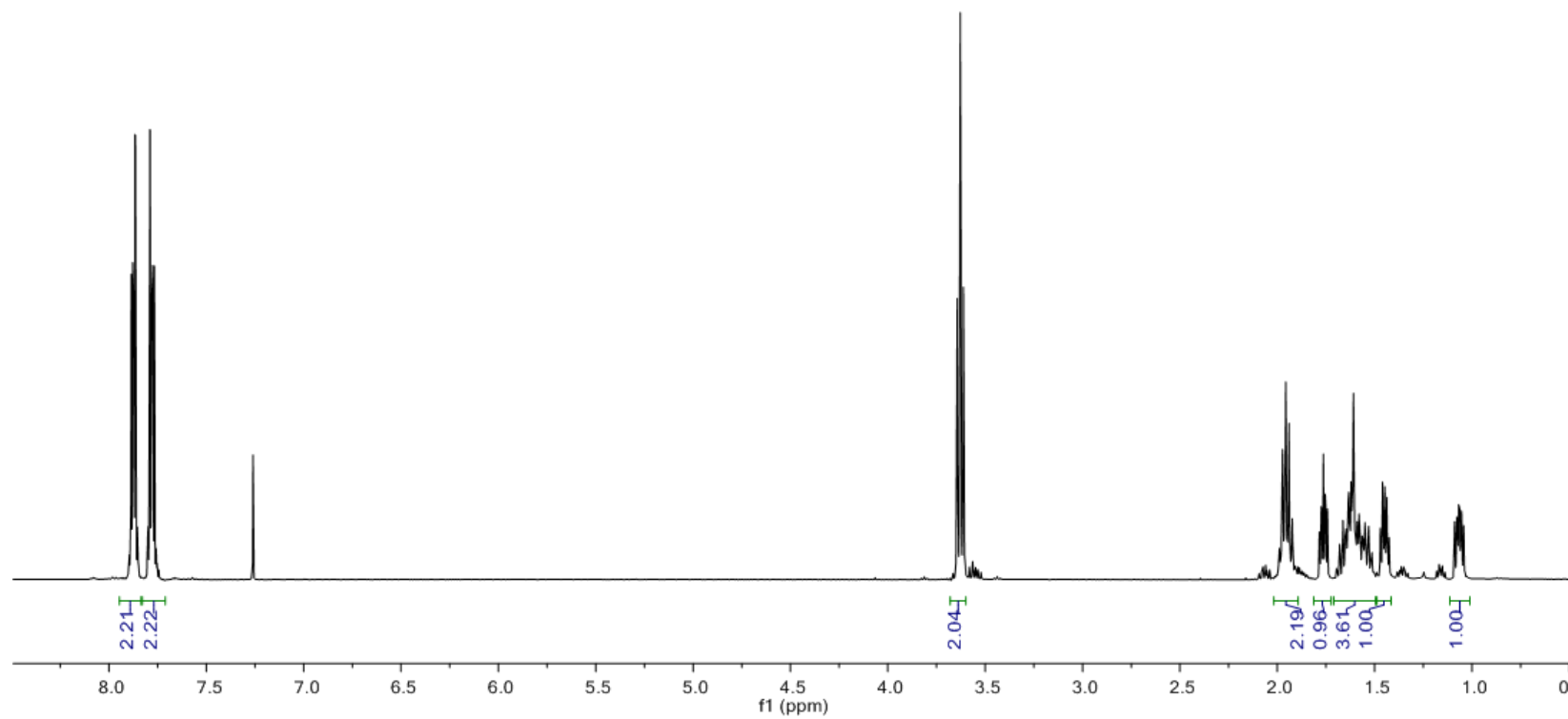


S200

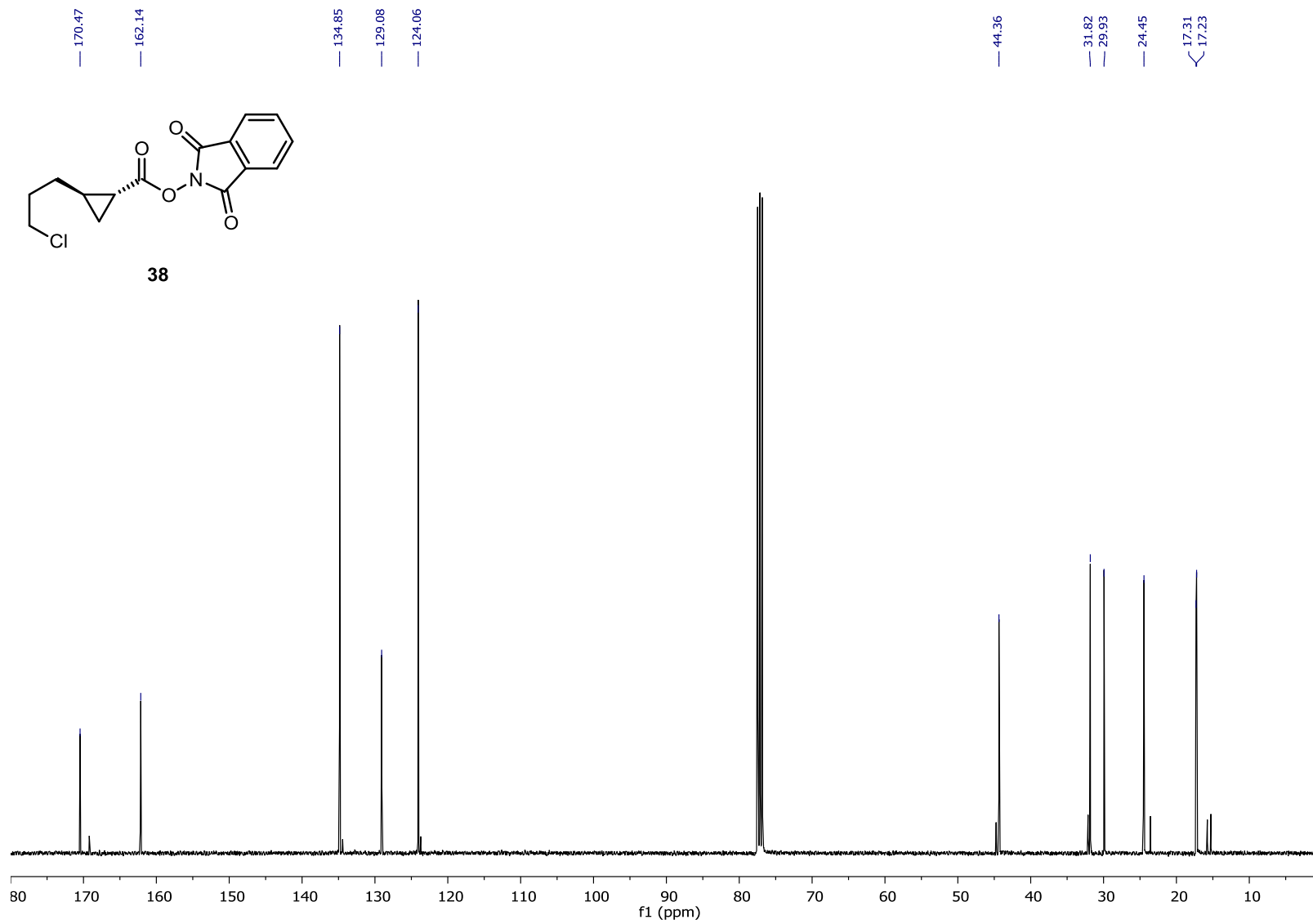
^1H NMR (400 MHz, CDCl_3) for compound **38**



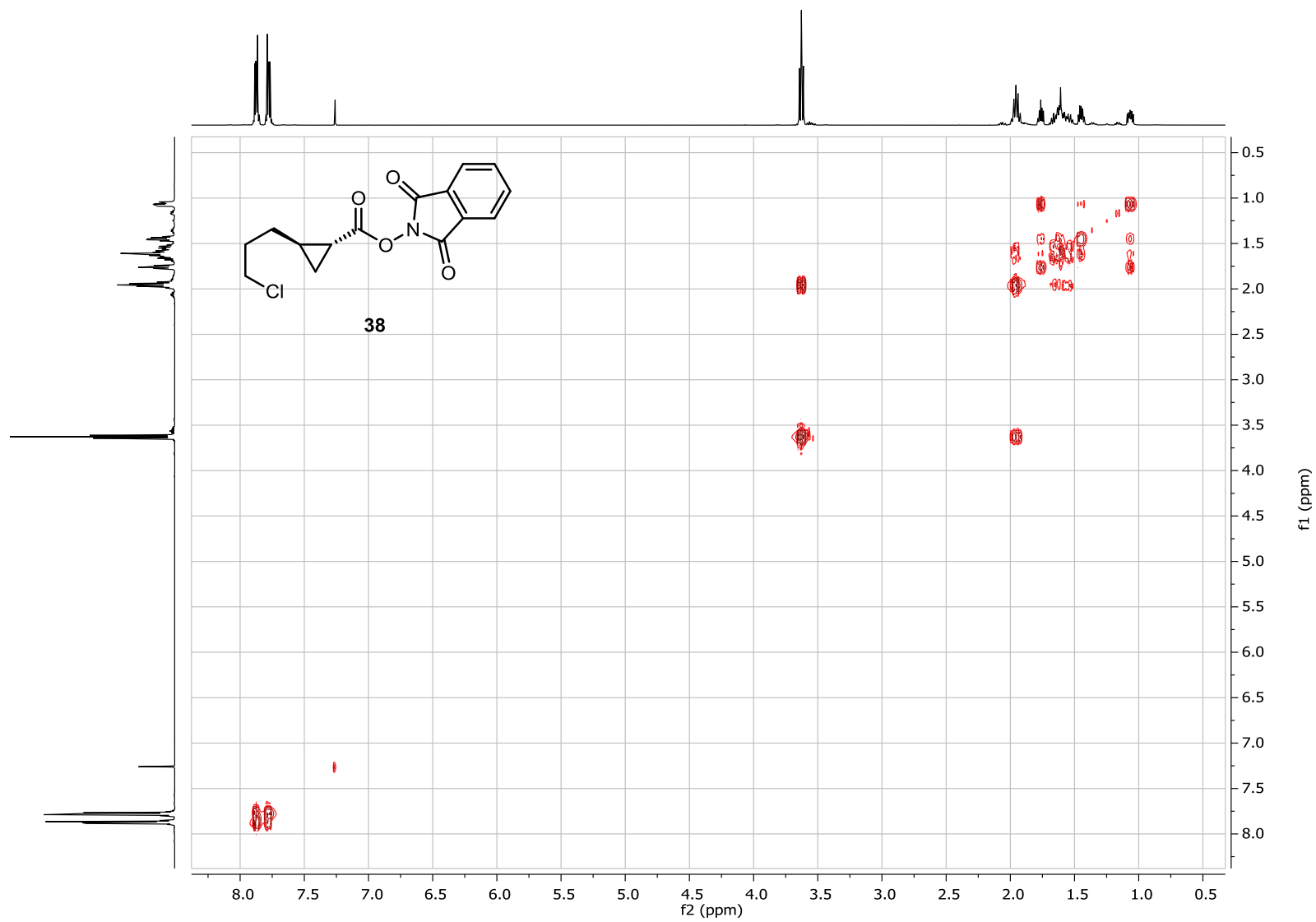
38



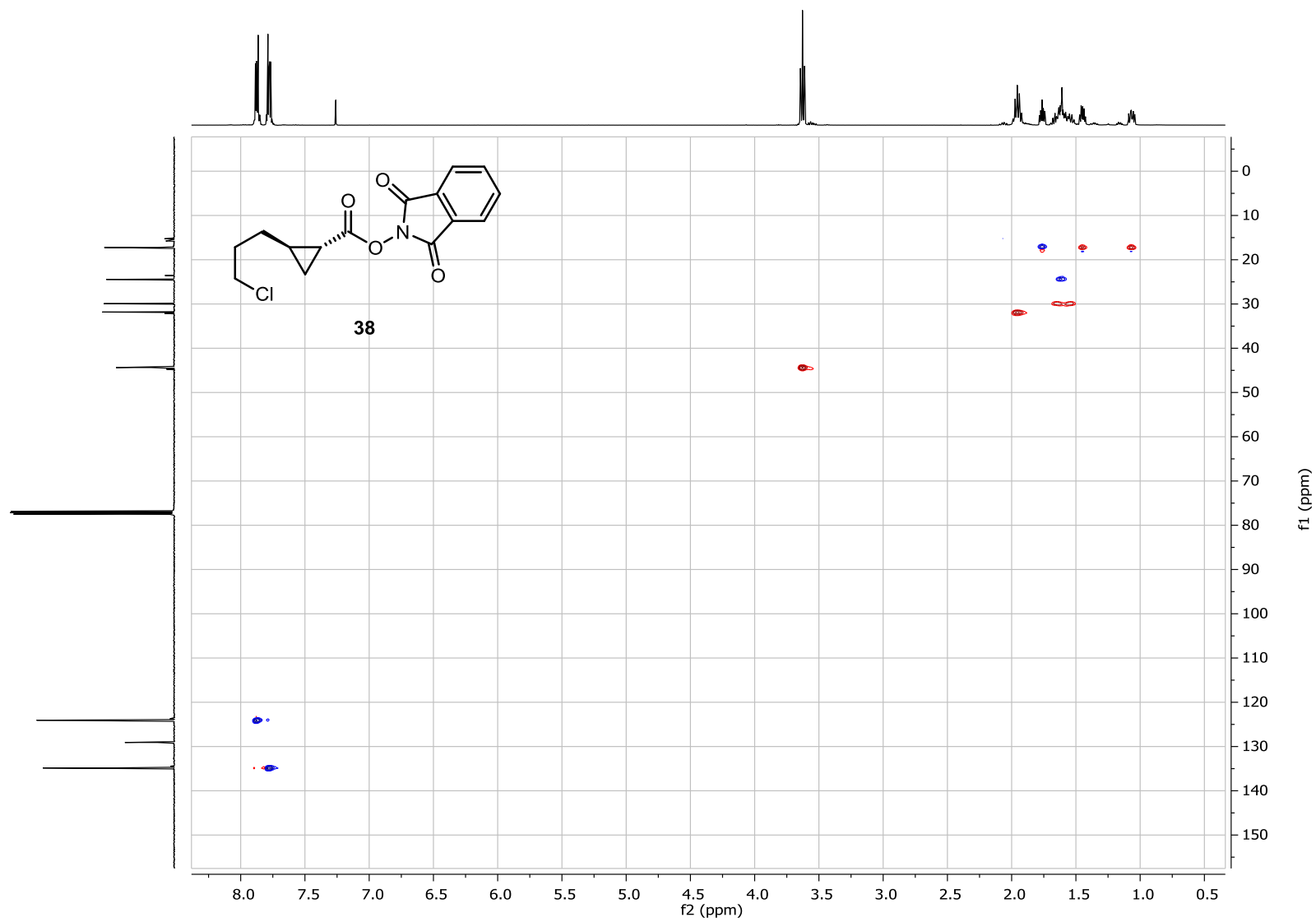
^{13}C NMR (101 MHz, CDCl_3) for compound **38**



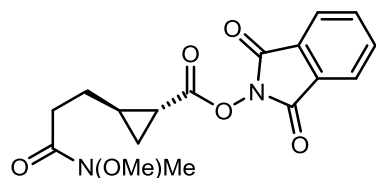
COSY NMR (400 MHz, CDCl₃) for compound 38



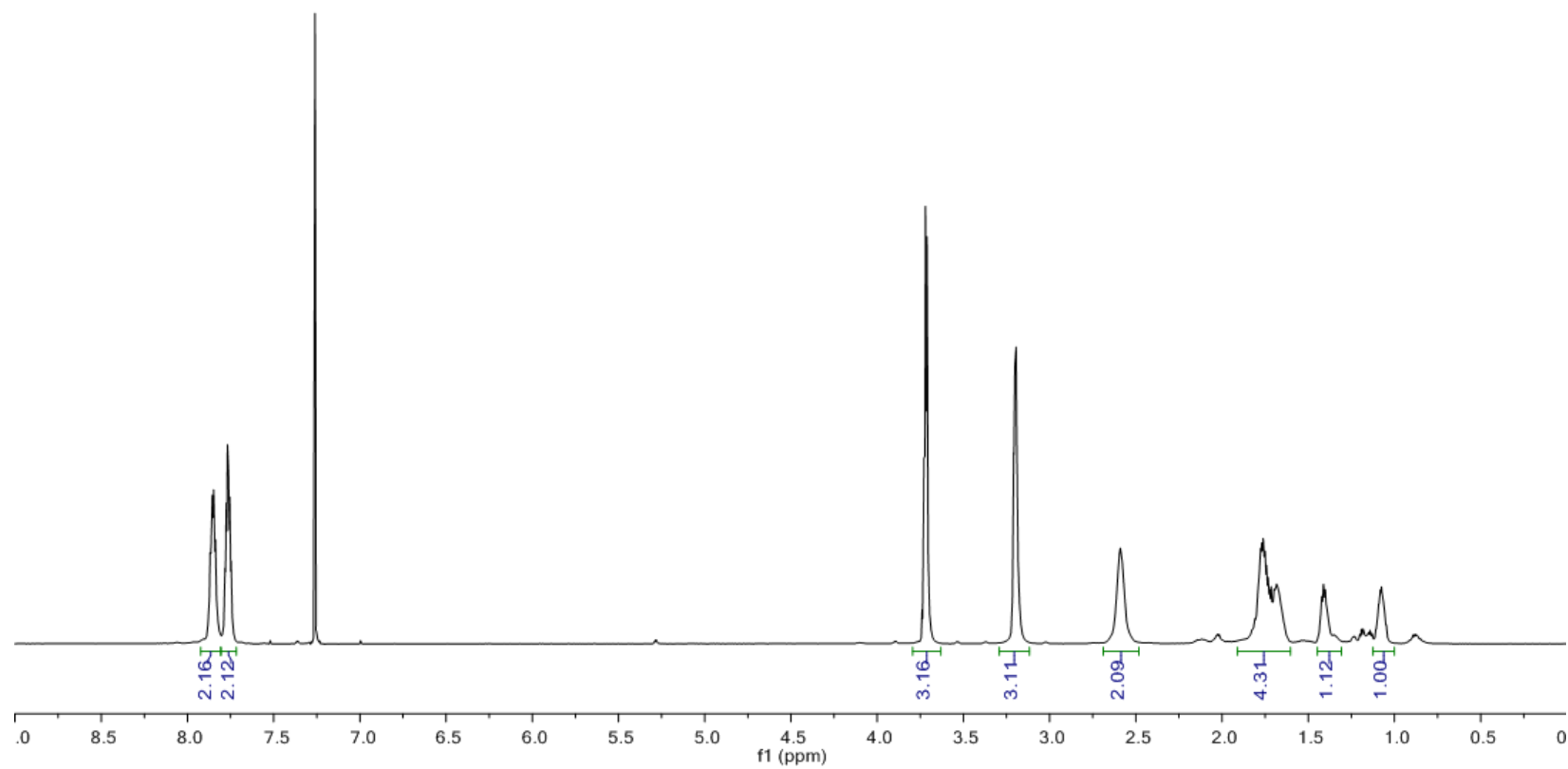
HSQC NMR (400 MHz, CDCl_3) for compound **38**



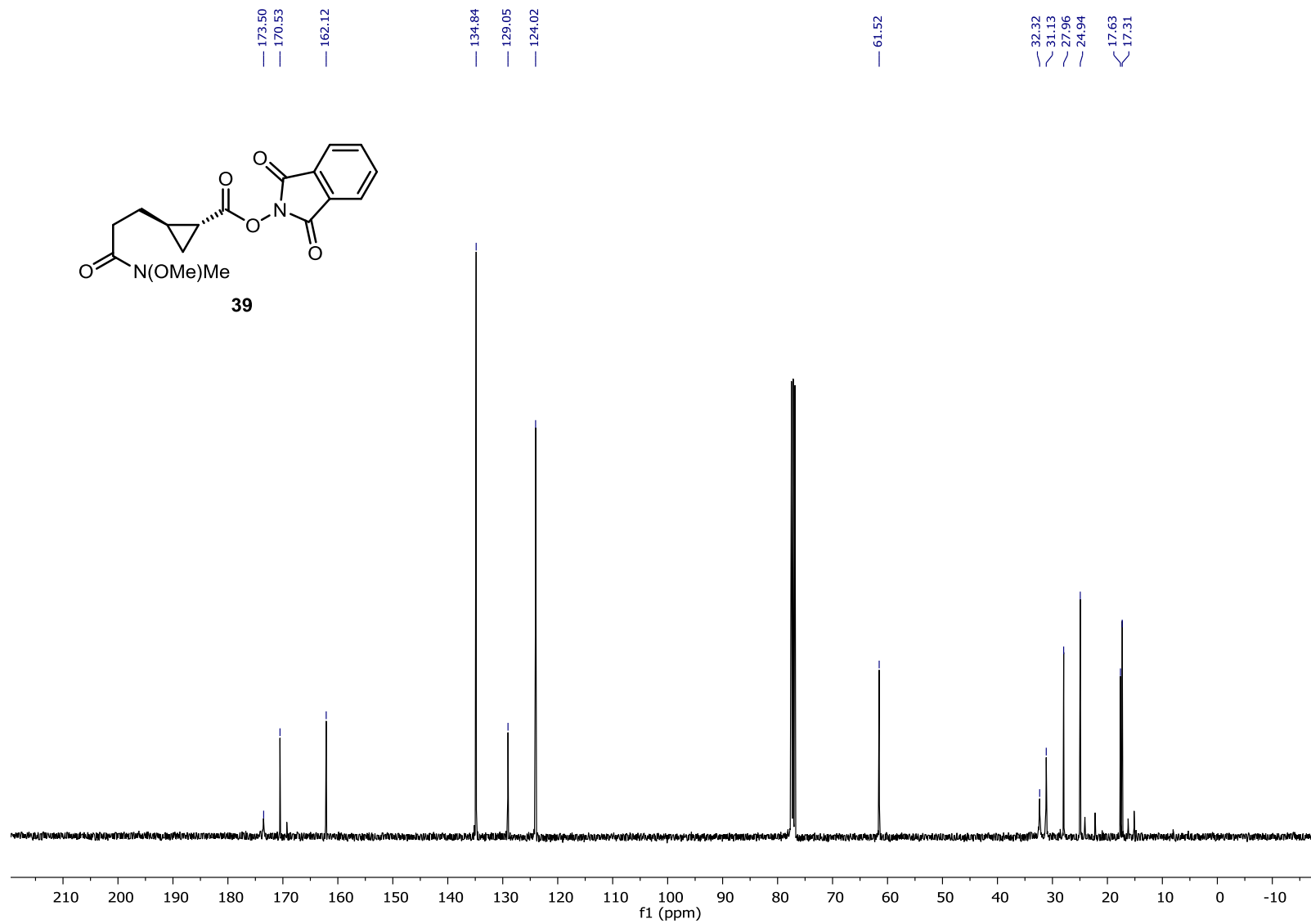
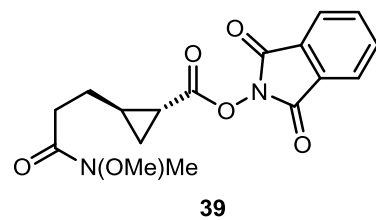
^1H NMR (400 MHz, CDCl_3) for compound **39**



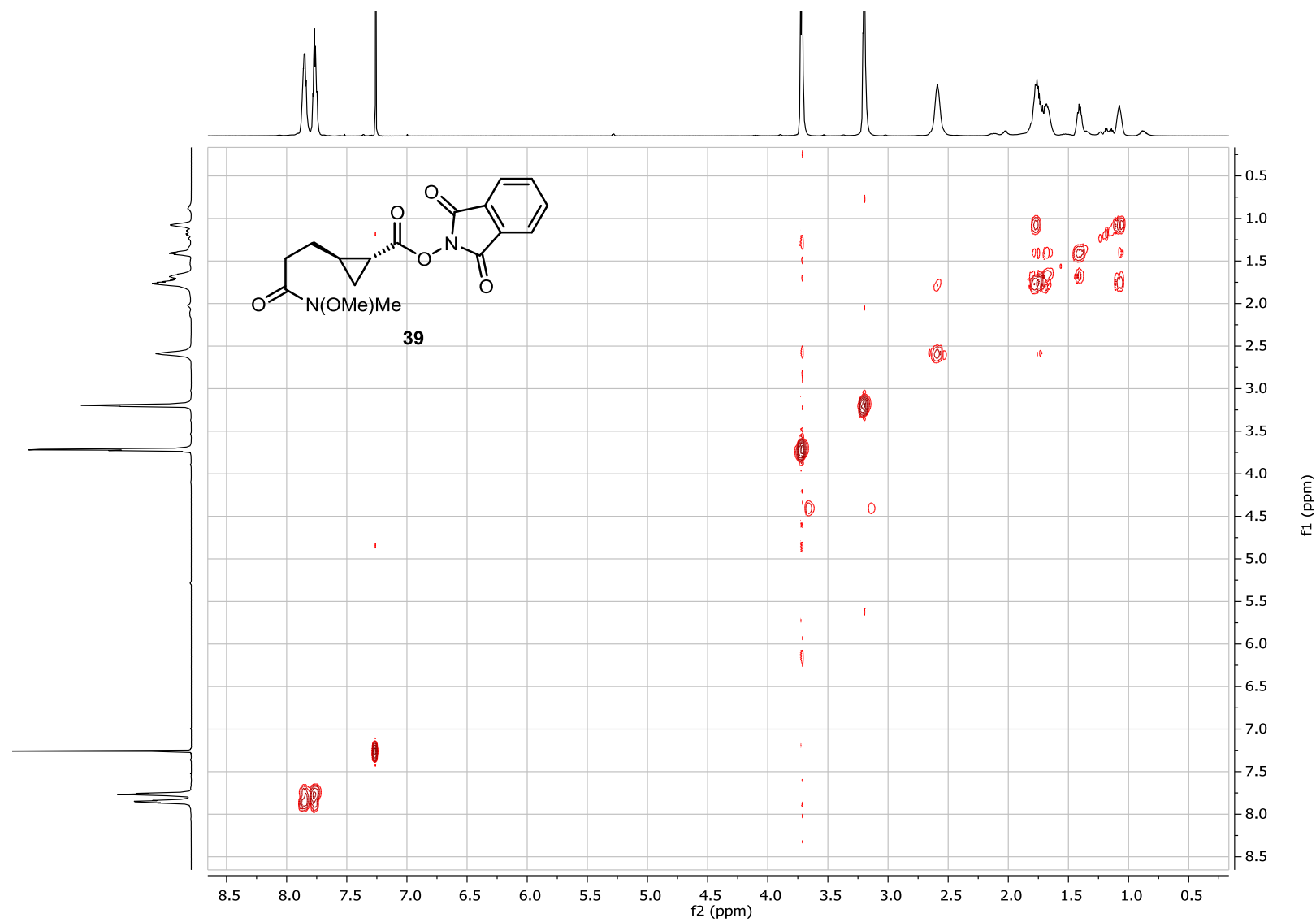
39



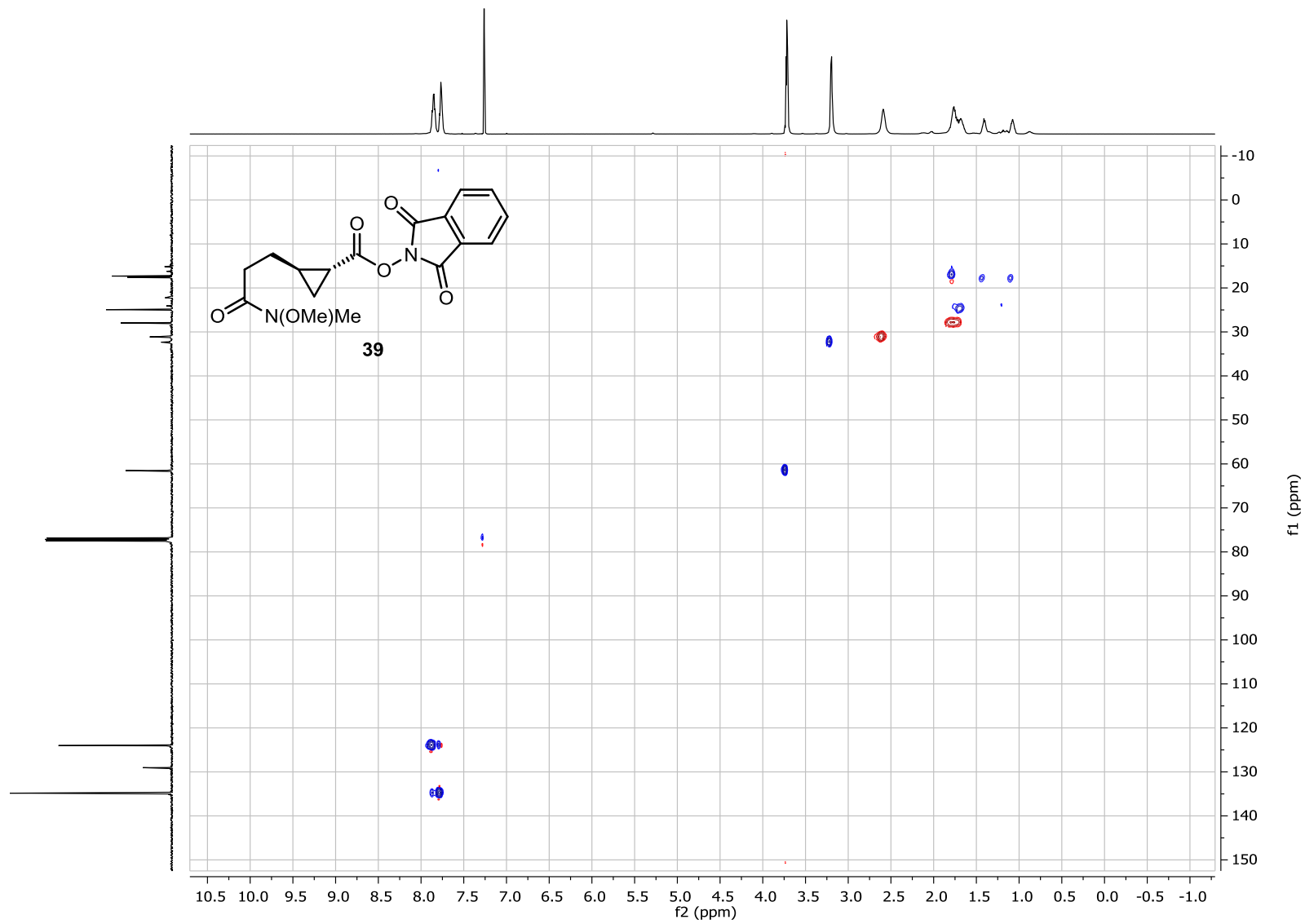
^{13}C NMR (101 MHz, CDCl_3) for compound **39**



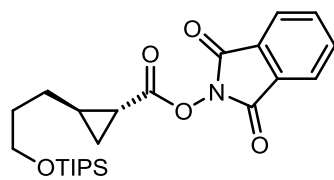
COSY NMR (400 MHz, CDCl_3) for compound **39**



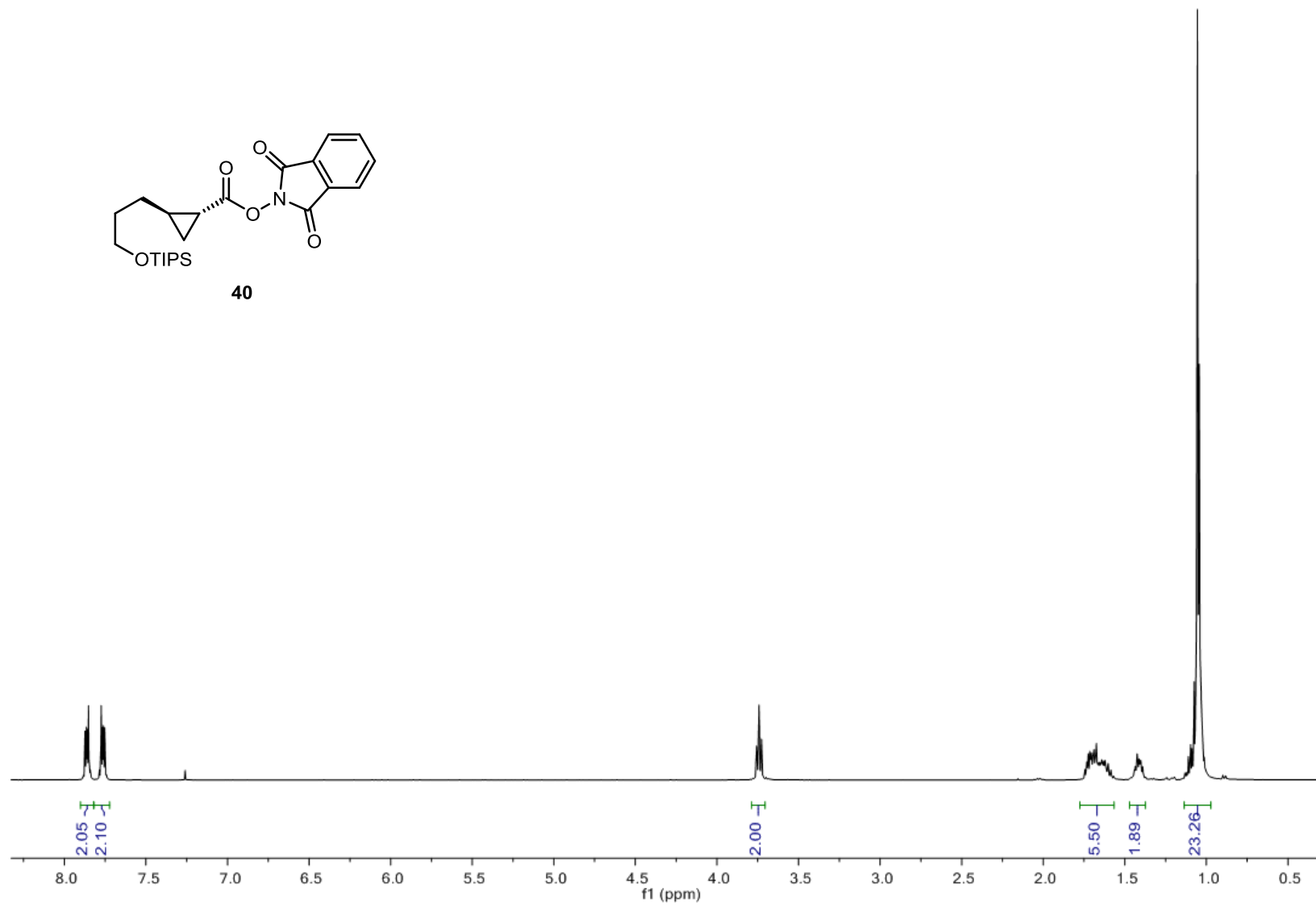
HSQC NMR (400 MHz, CDCl₃) for compound **39**



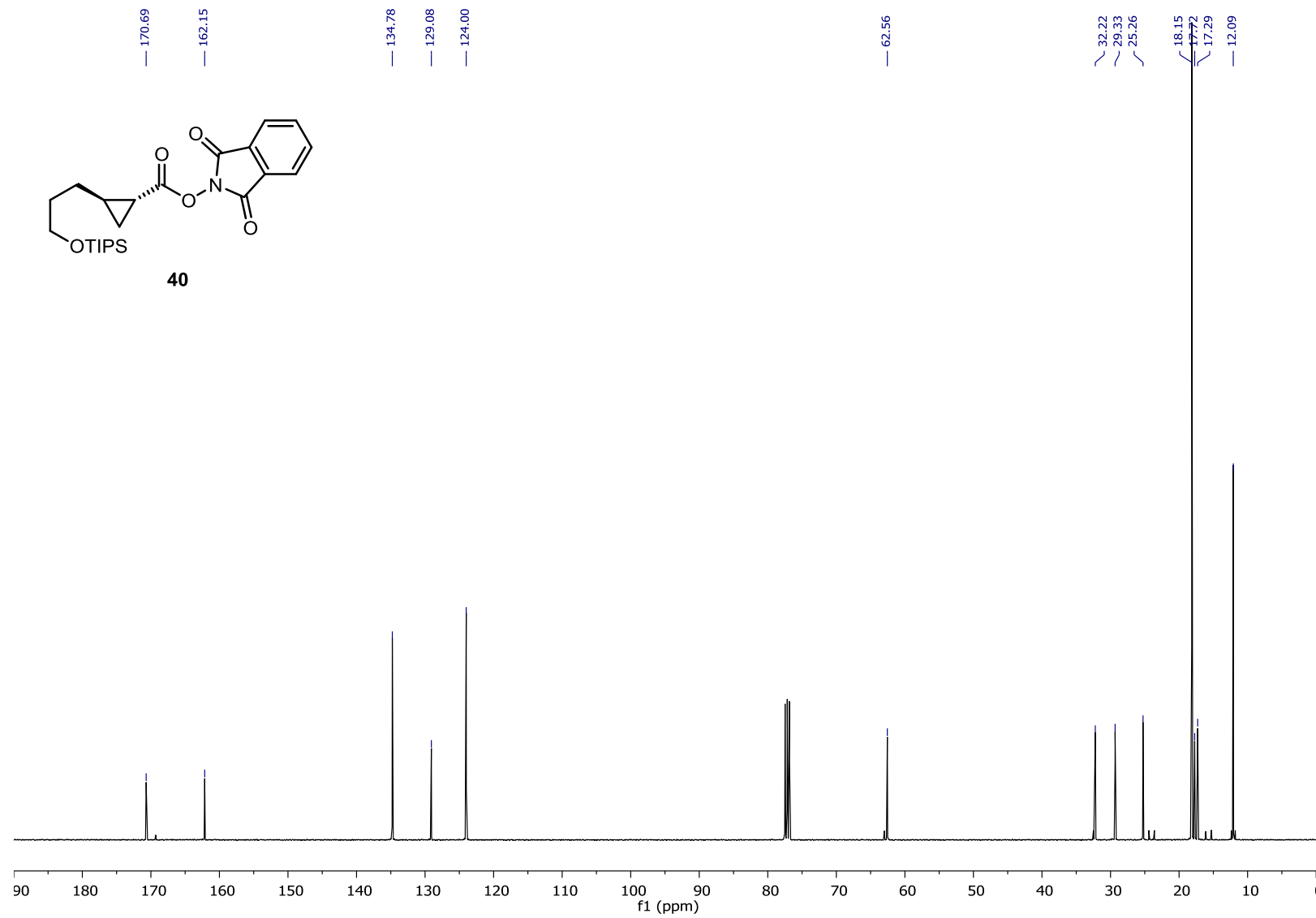
^1H NMR (400 MHz, CDCl_3) for compound **40**



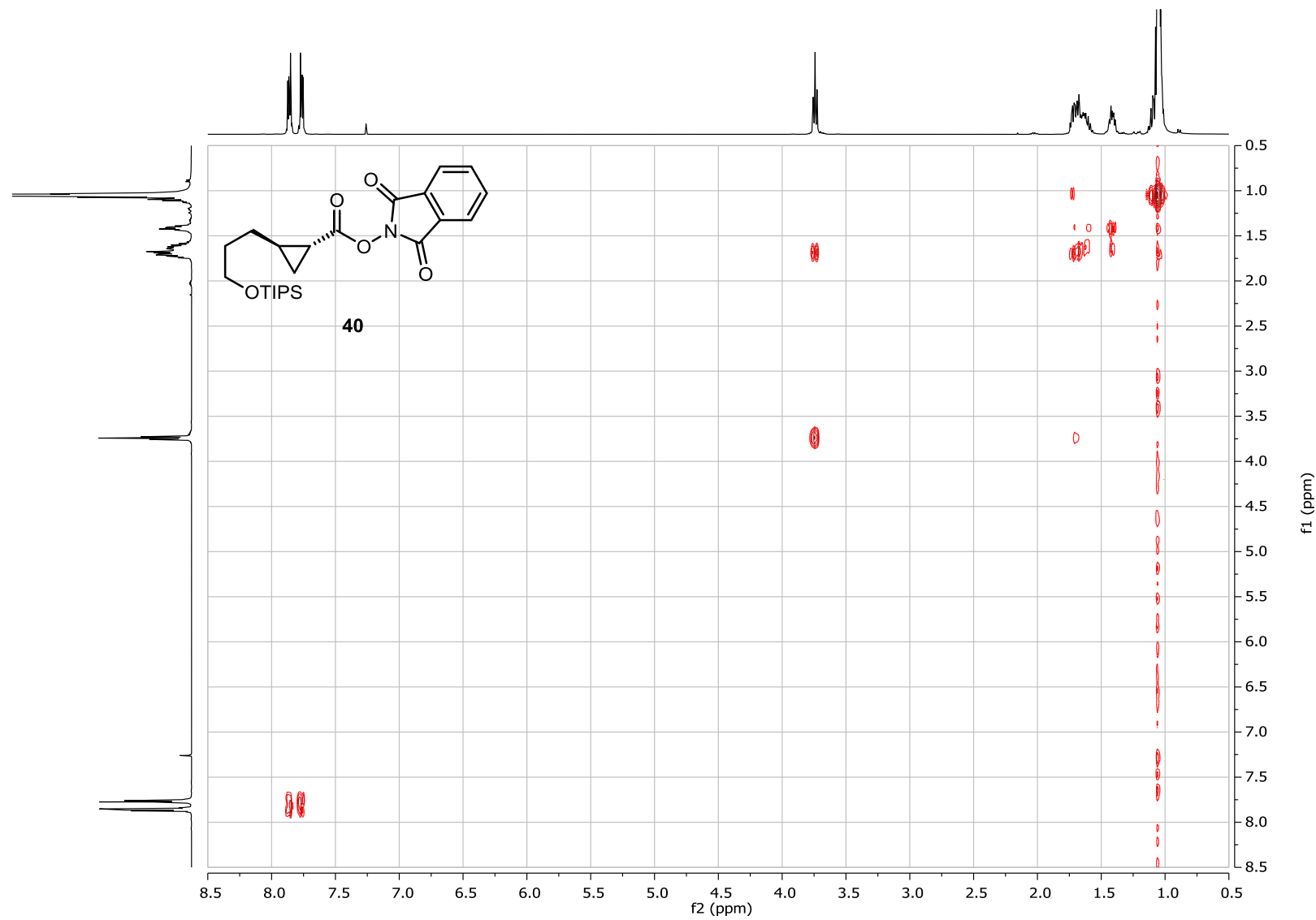
40



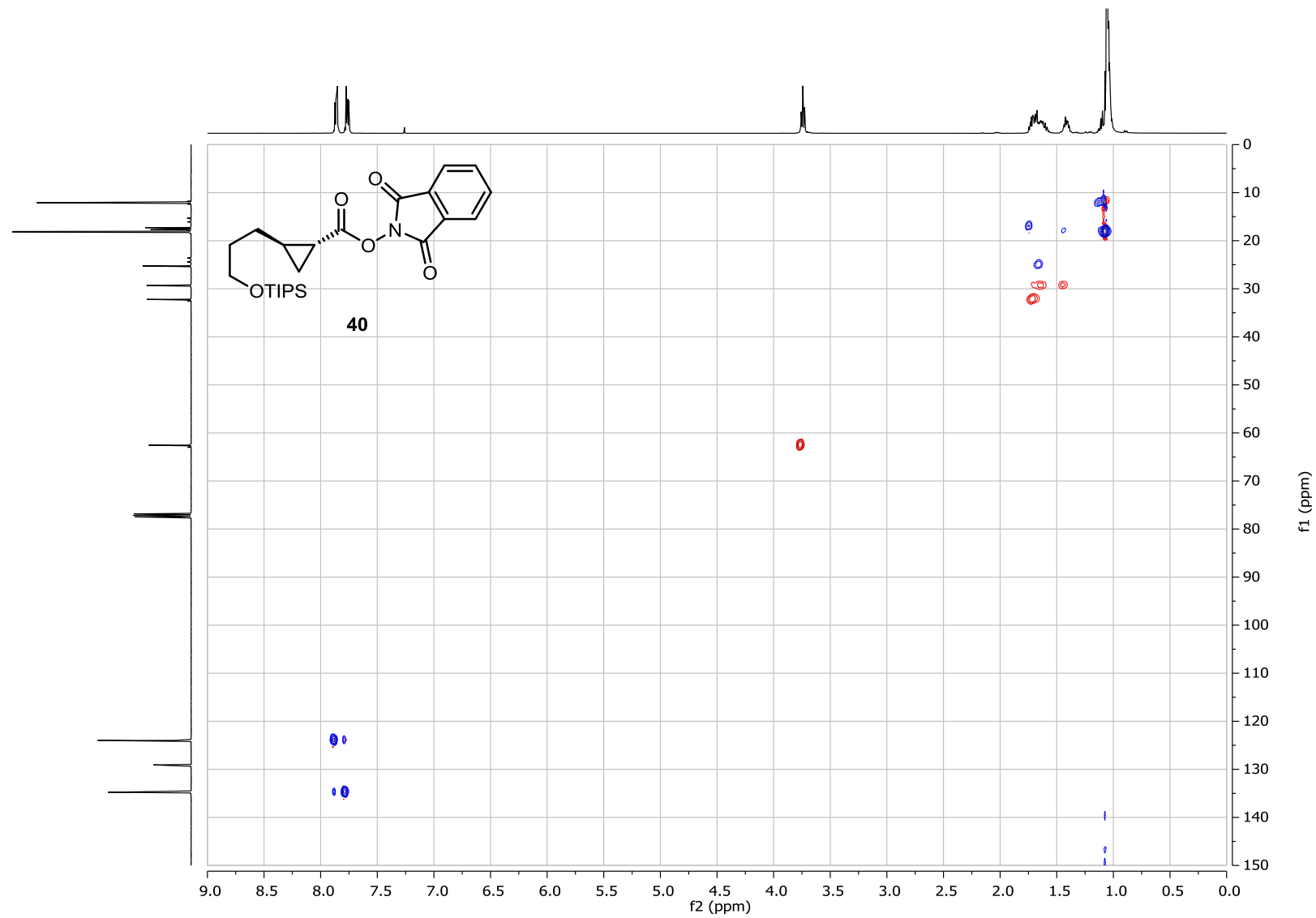
^{13}C NMR (101 MHz, CDCl_3) for compound **40**



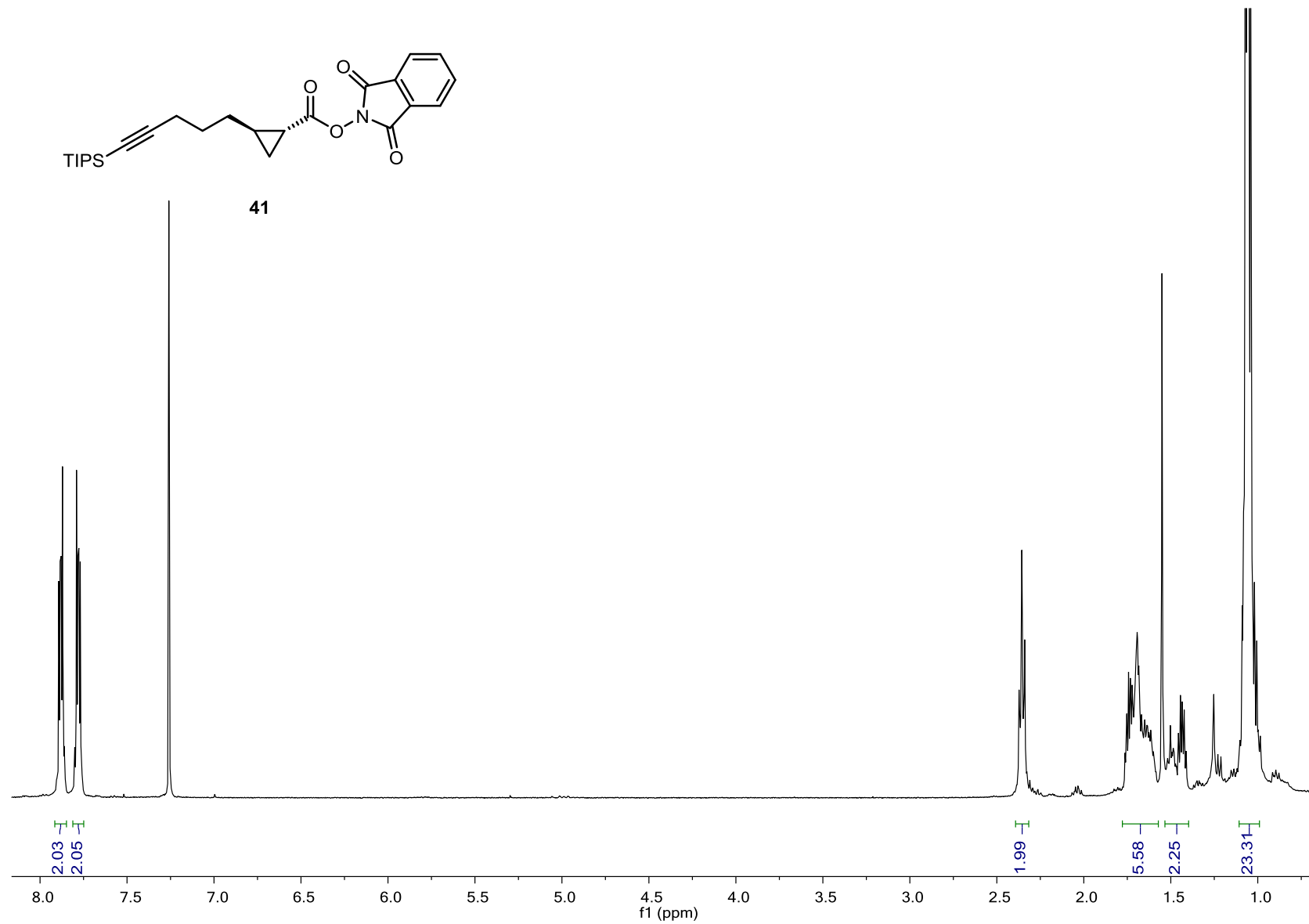
COSY NMR (400 MHz, CDCl_3) for compound **40**



HSQC NMR (400 MHz, CDCl₃) for compound **40**

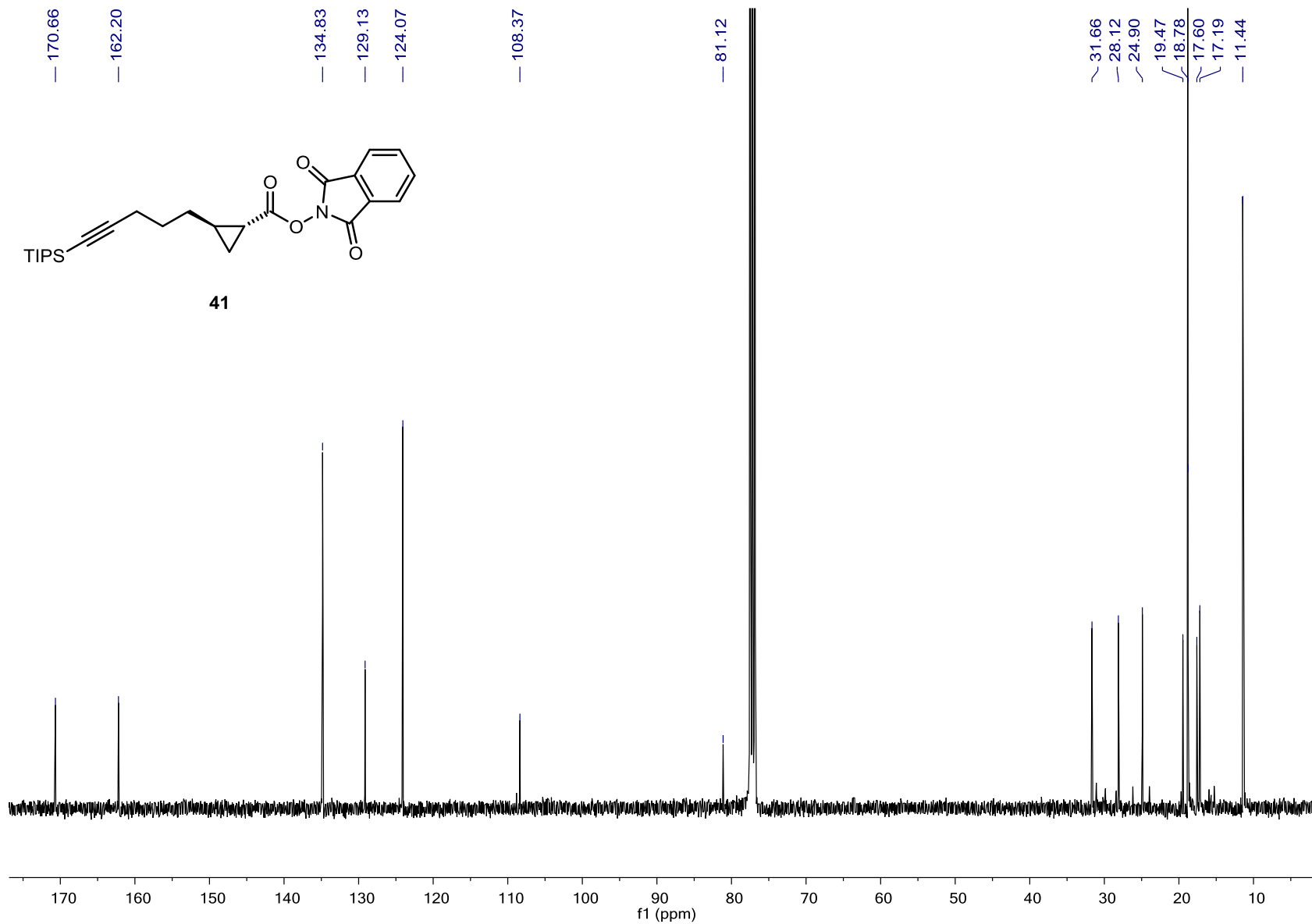


^1H NMR (400 MHz, CDCl_3) for compound **41**

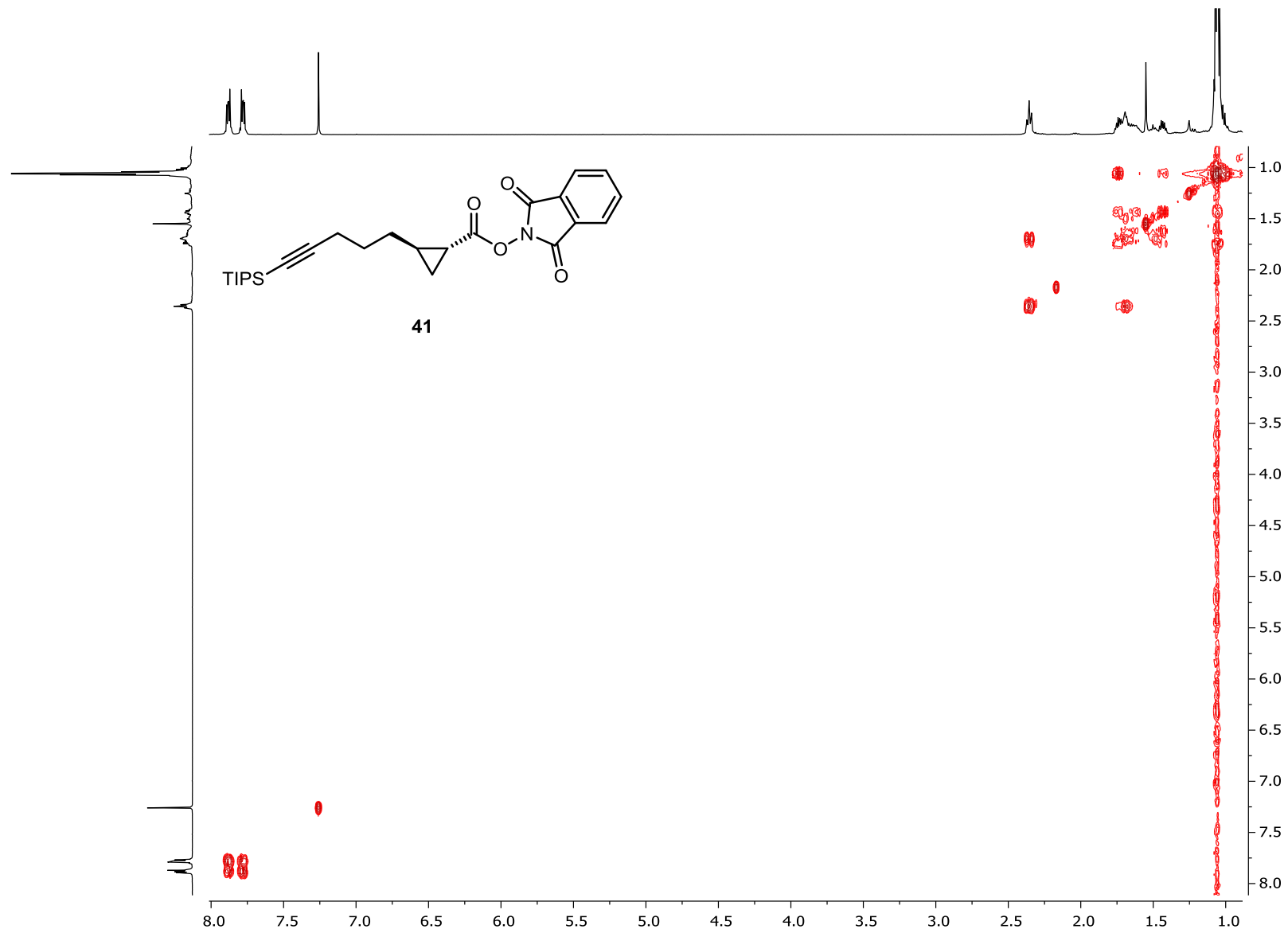


S213

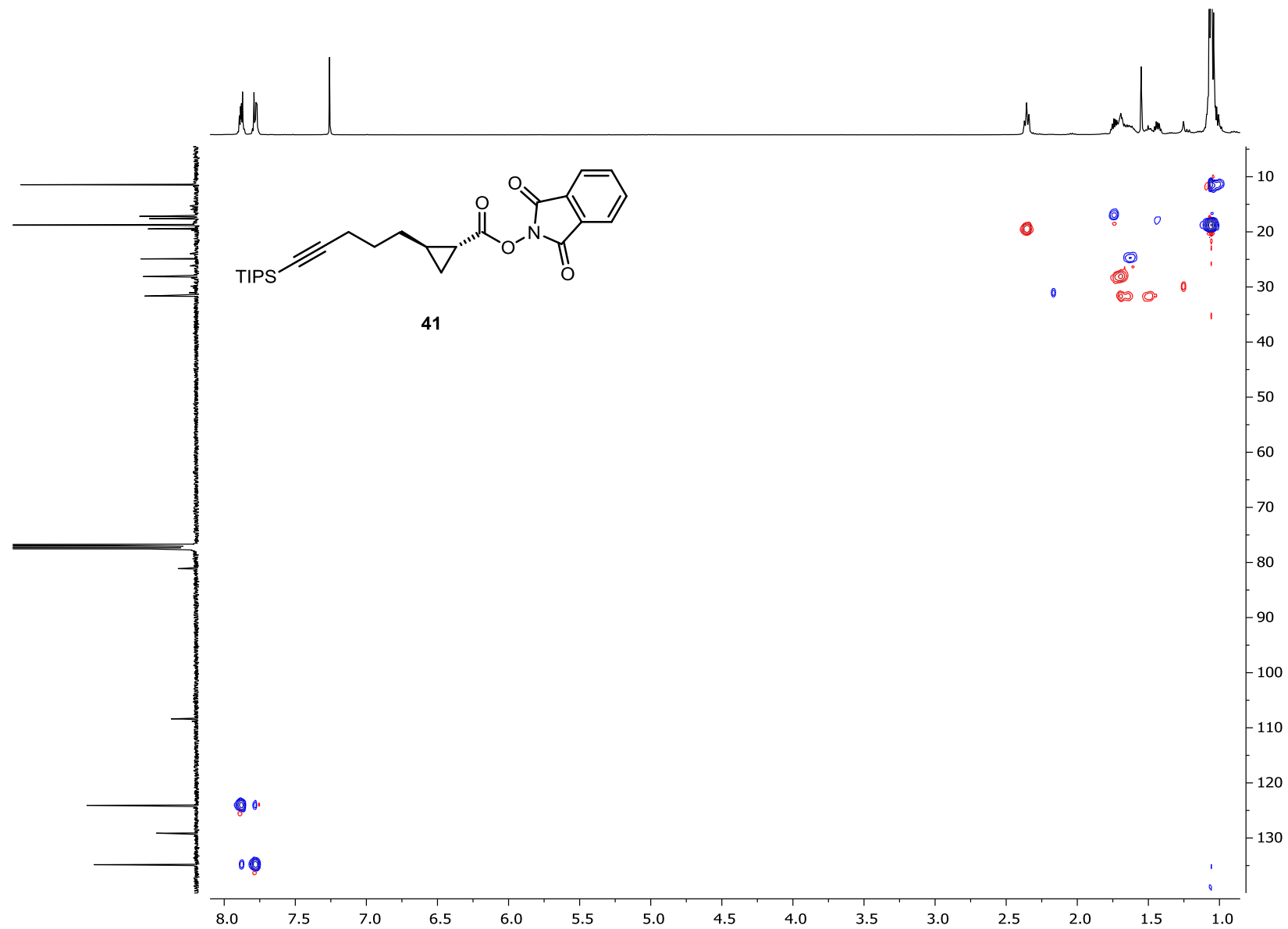
^{13}C NMR (101 MHz, CDCl_3) for compound **41**



COSY NMR (400 MHz, CDCl₃) for compound **41**

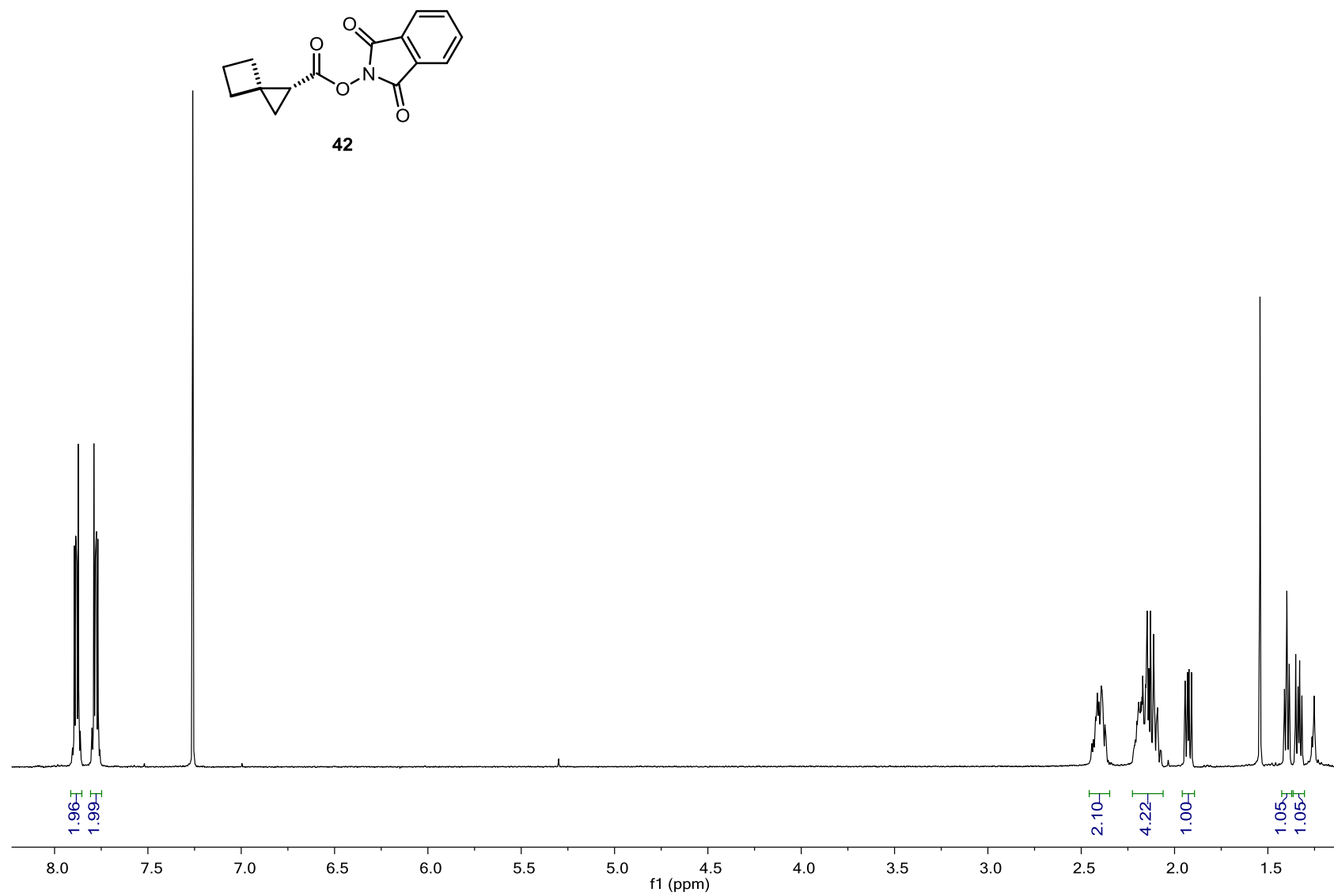


HSQC NMR (400 MHz, CDCl₃) for compound **41**



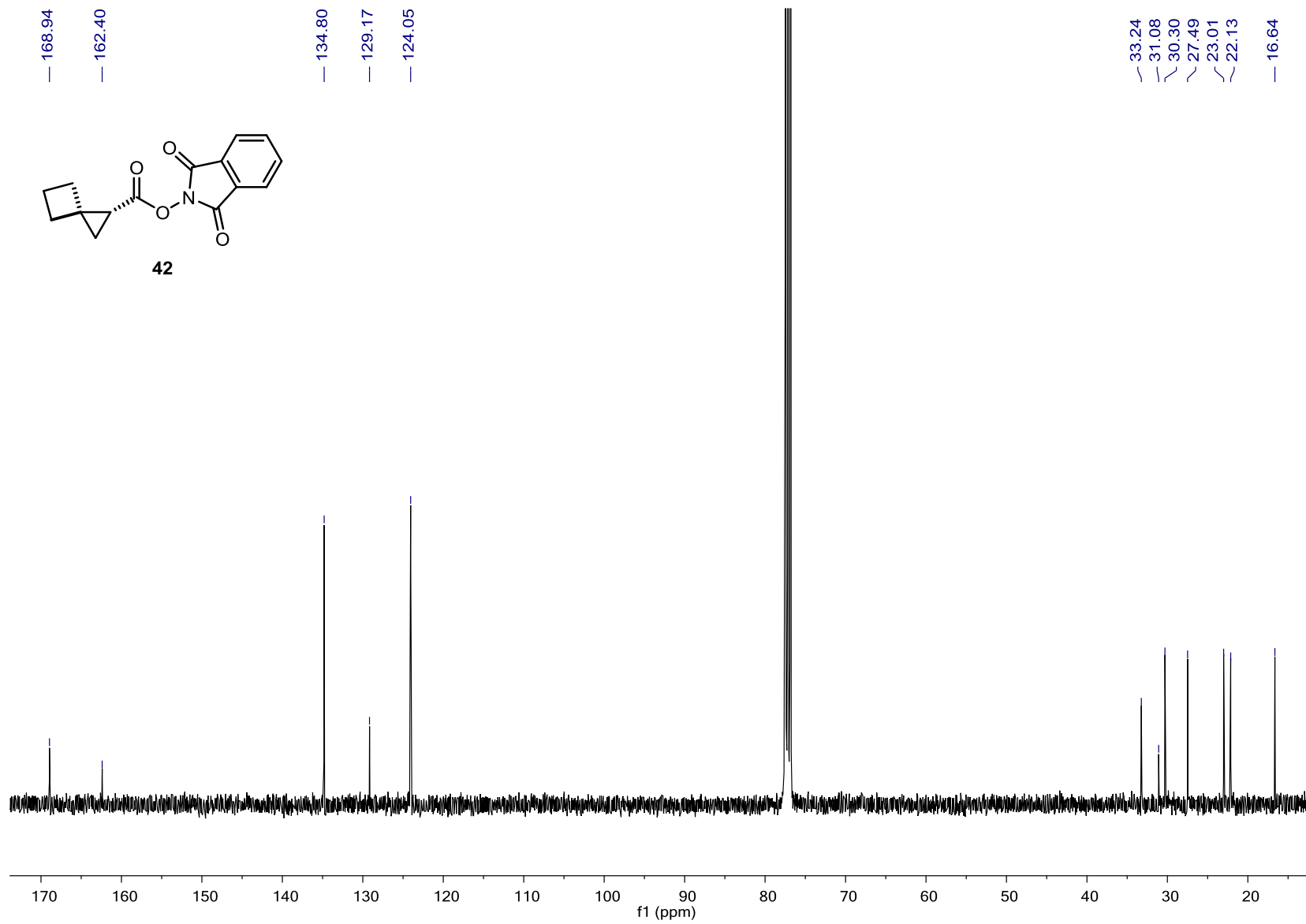
S216

^1H NMR (400 MHz, CDCl_3) for compound **42**

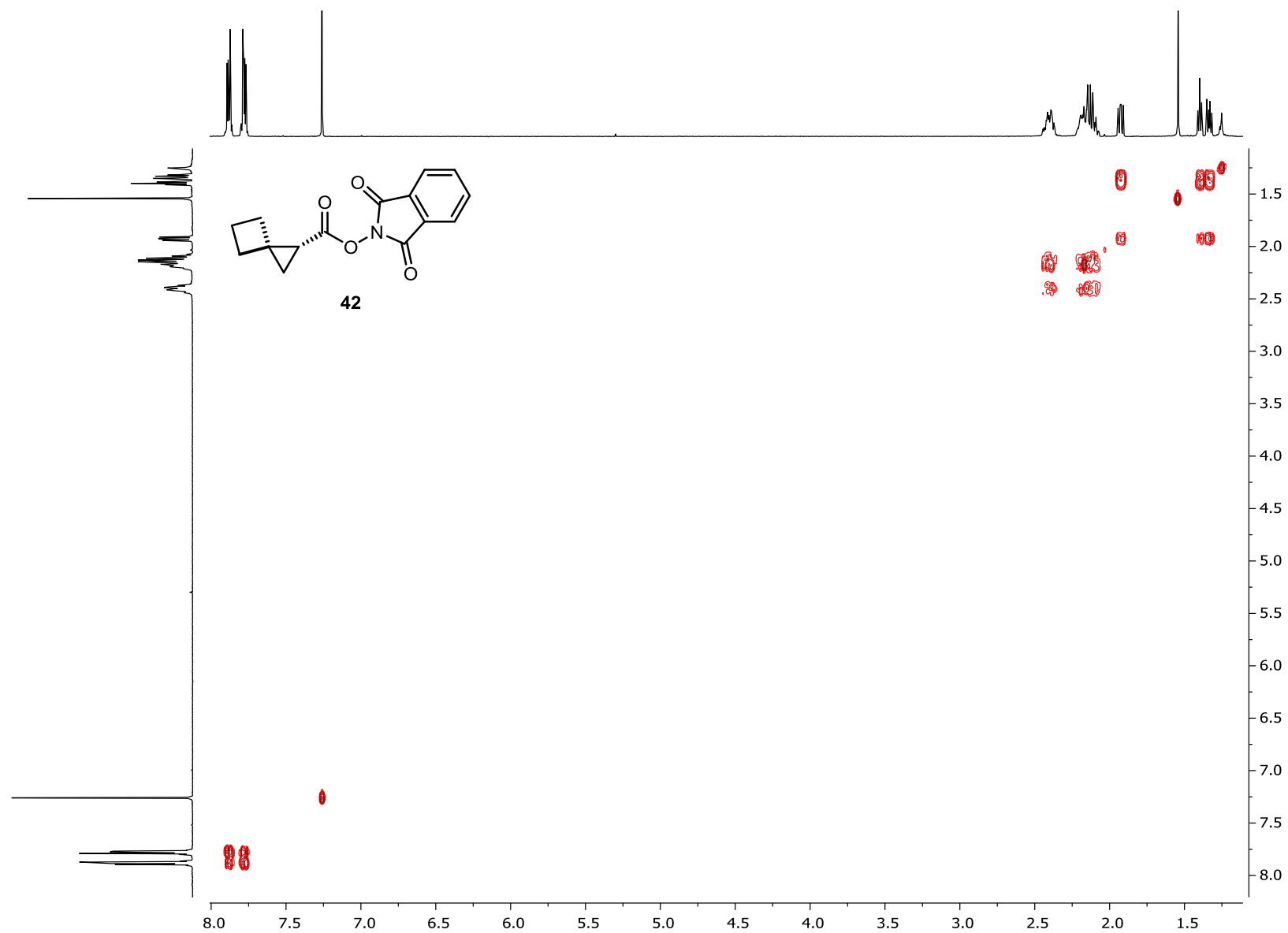


S217

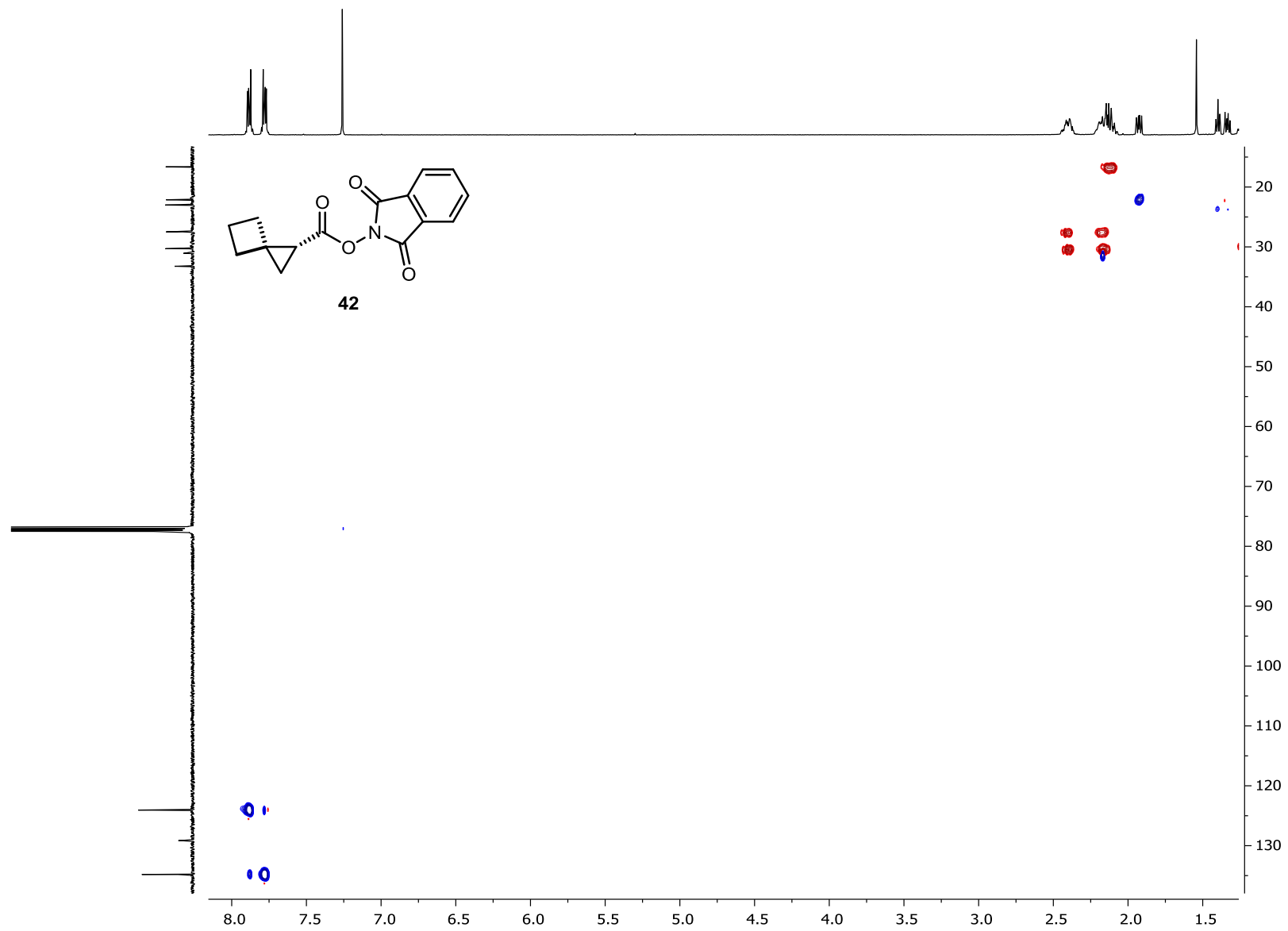
^{13}C NMR (101 MHz, CDCl_3) for compound **42**



COSY NMR (400 MHz, CDCl₃) for compound 42

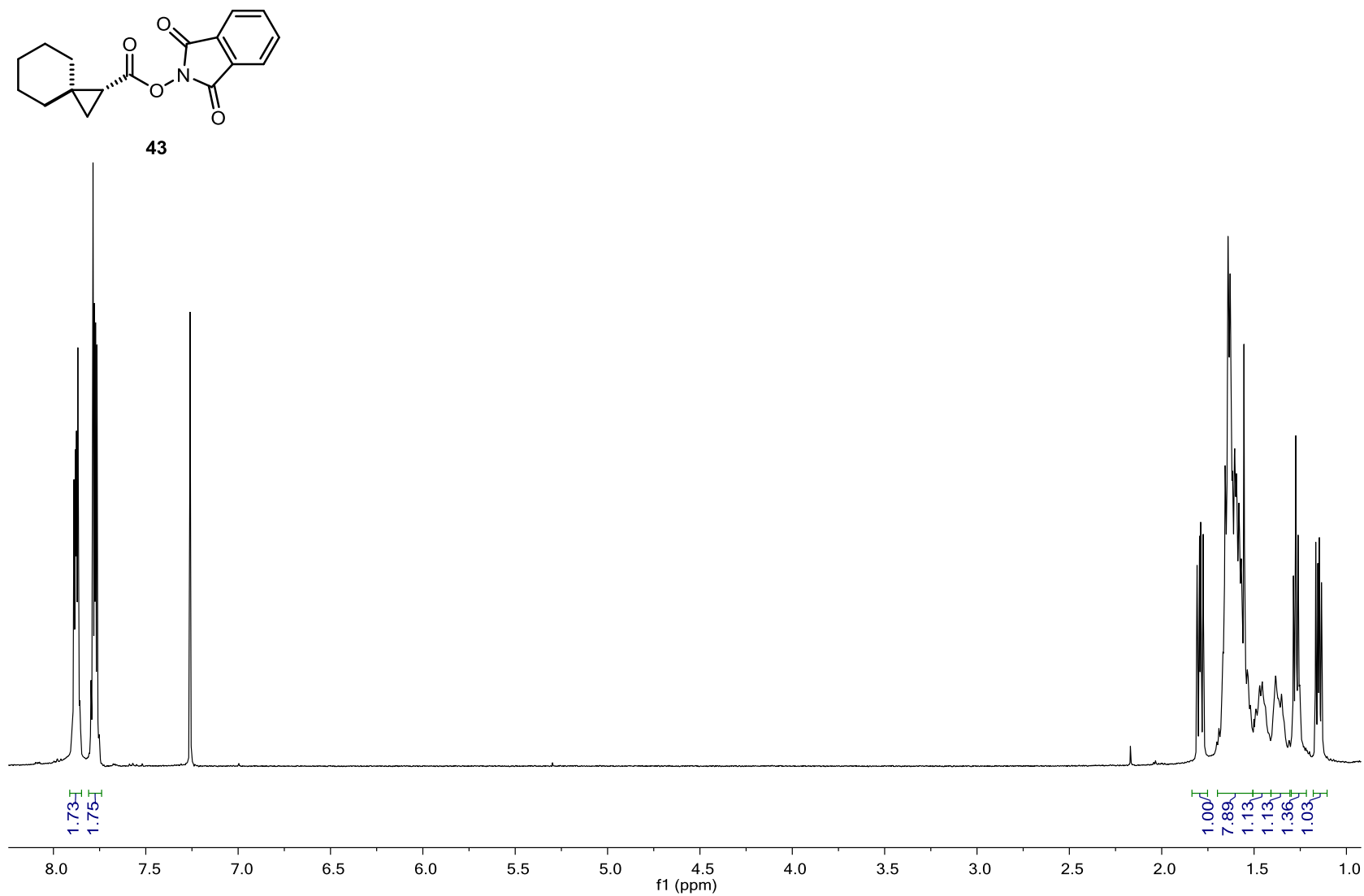


HSQC NMR (400 MHz, CDCl₃) for compound **42**



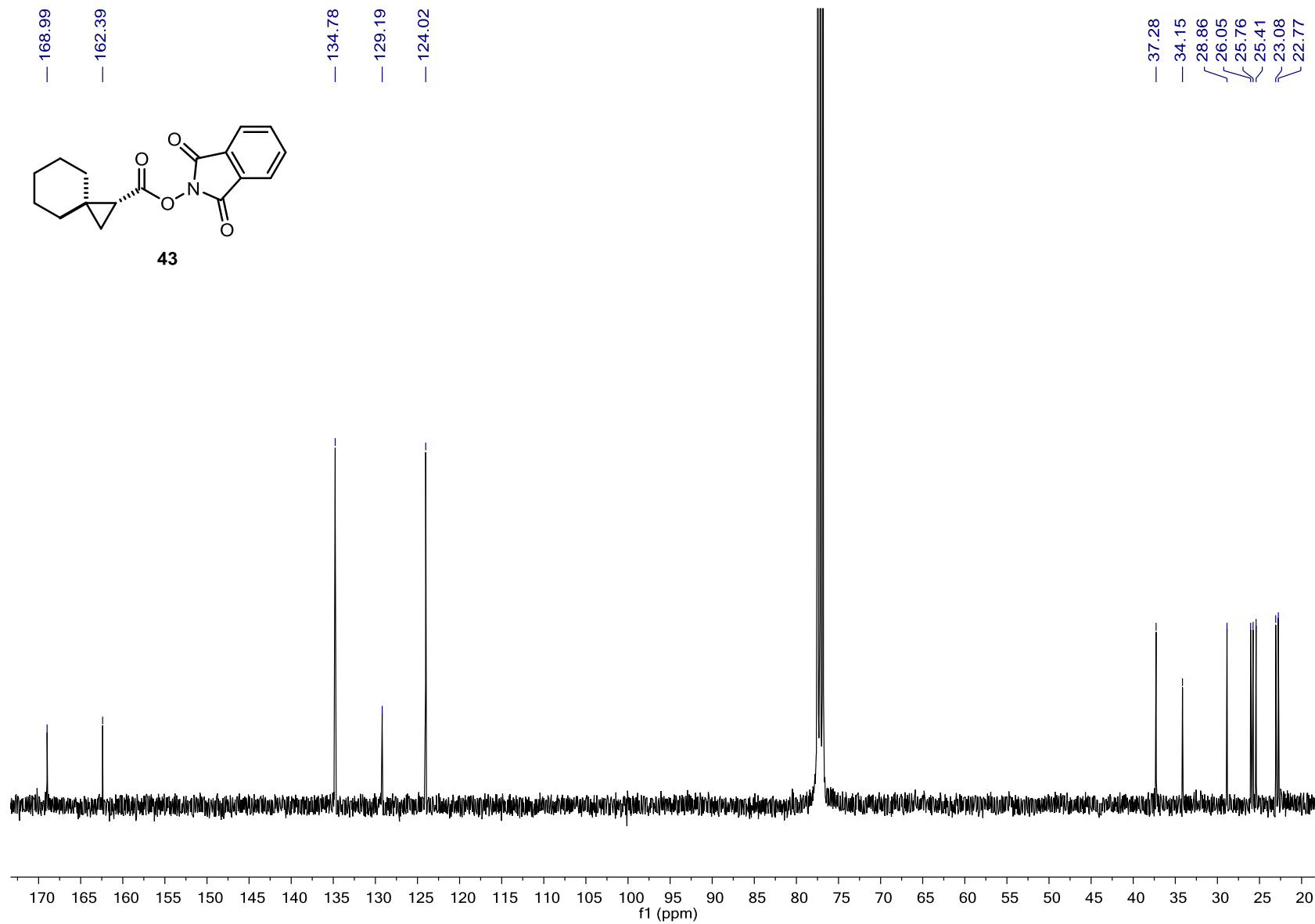
S220

^1H NMR (400 MHz, CDCl_3) for compound **43**

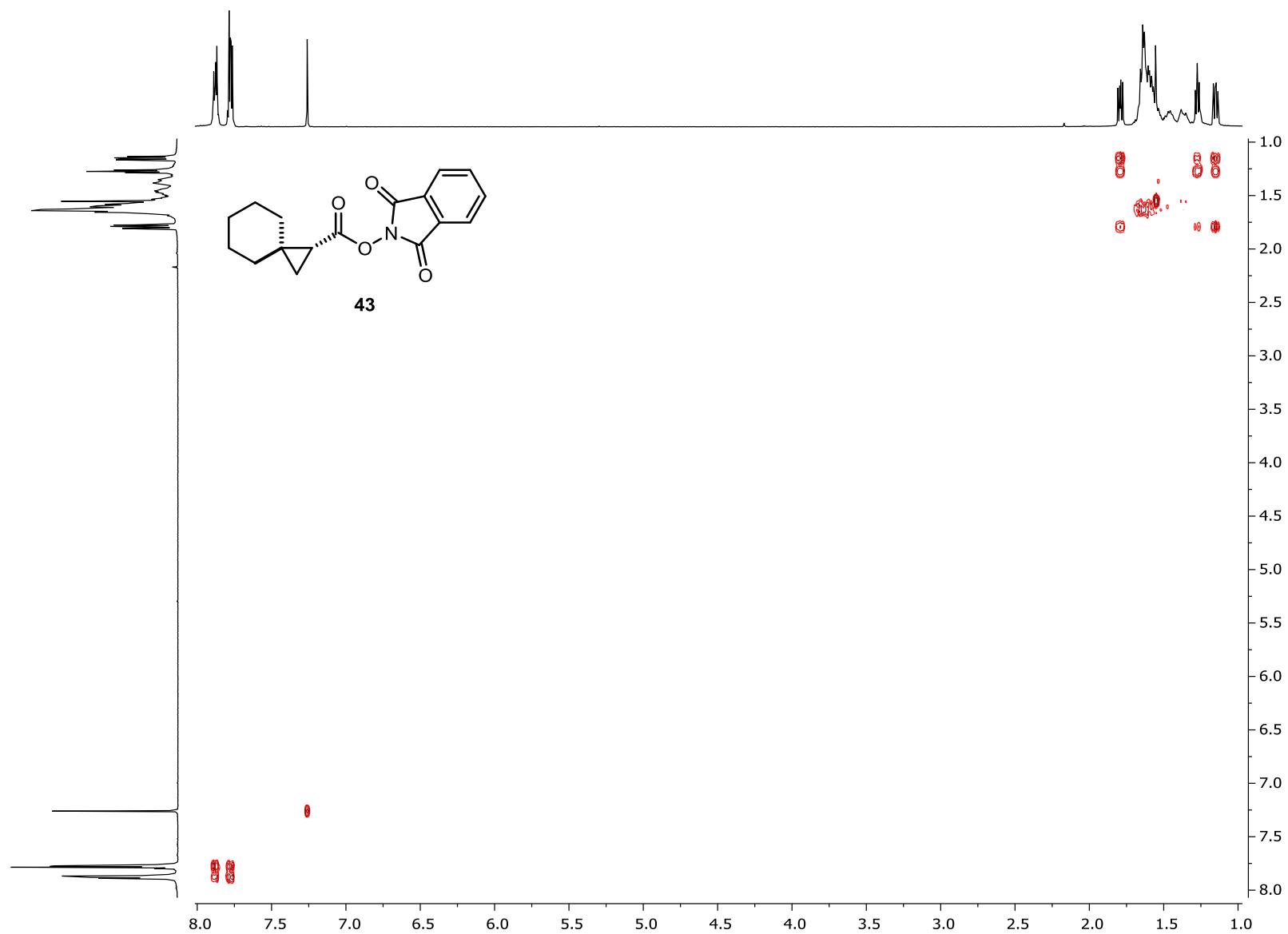


S221

^{13}C NMR (101 MHz, CDCl_3) for compound **43**

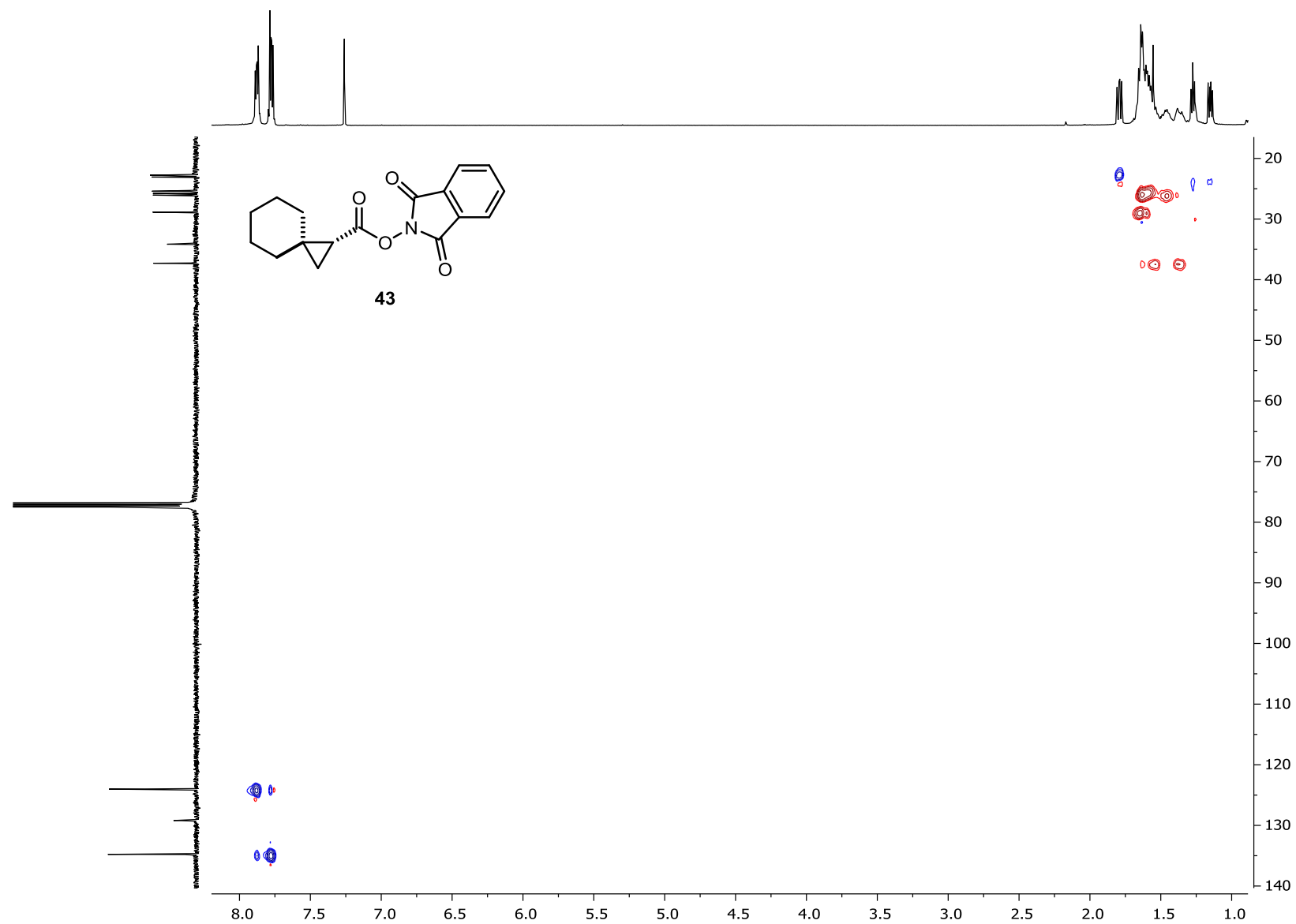


COSY NMR (400 MHz, CDCl₃) for compound **43**

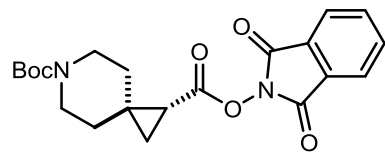


S223

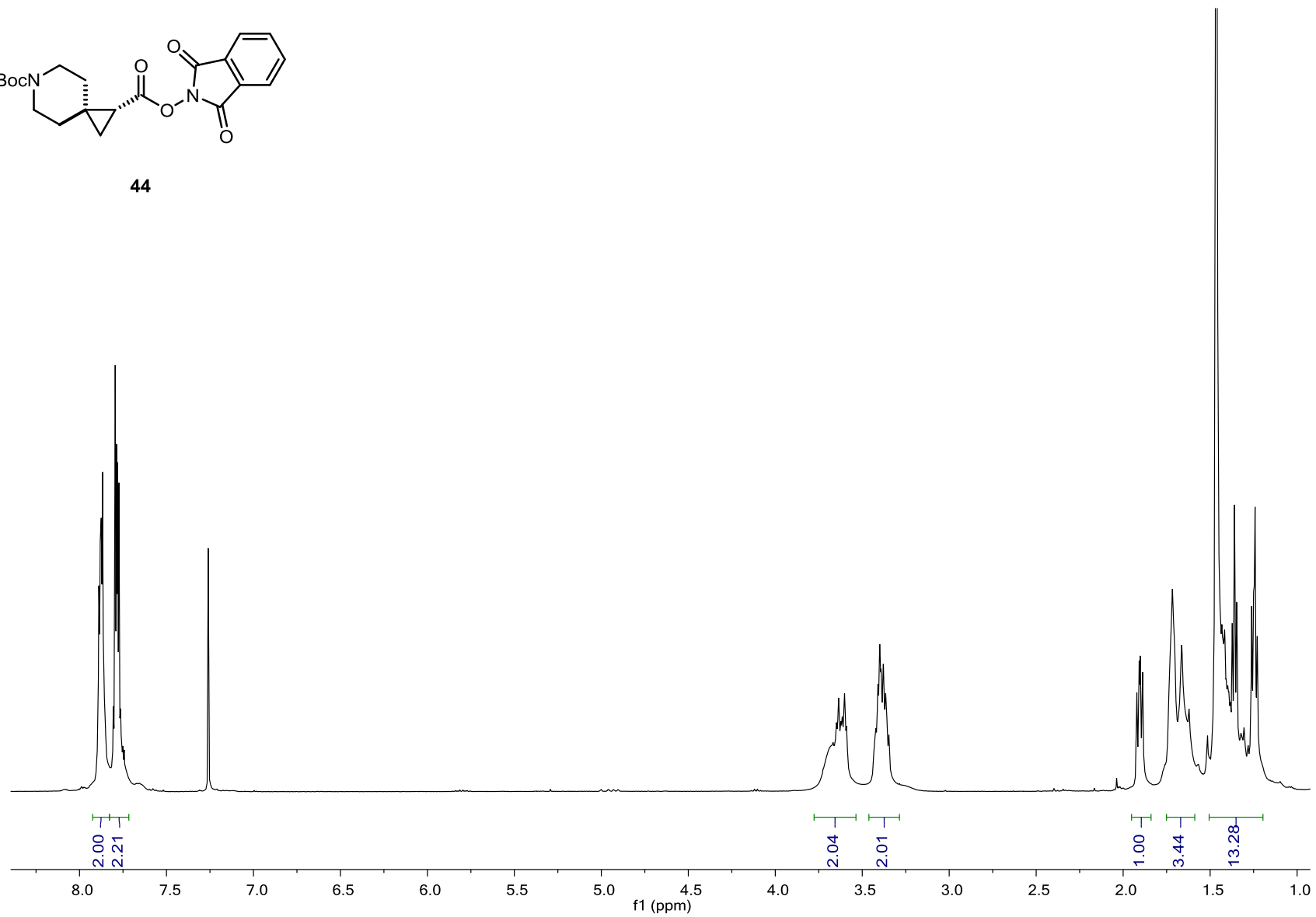
HSQC NMR (400 MHz, CDCl₃) for compound **43**



^1H NMR (400 MHz, CDCl_3) for compound **44**

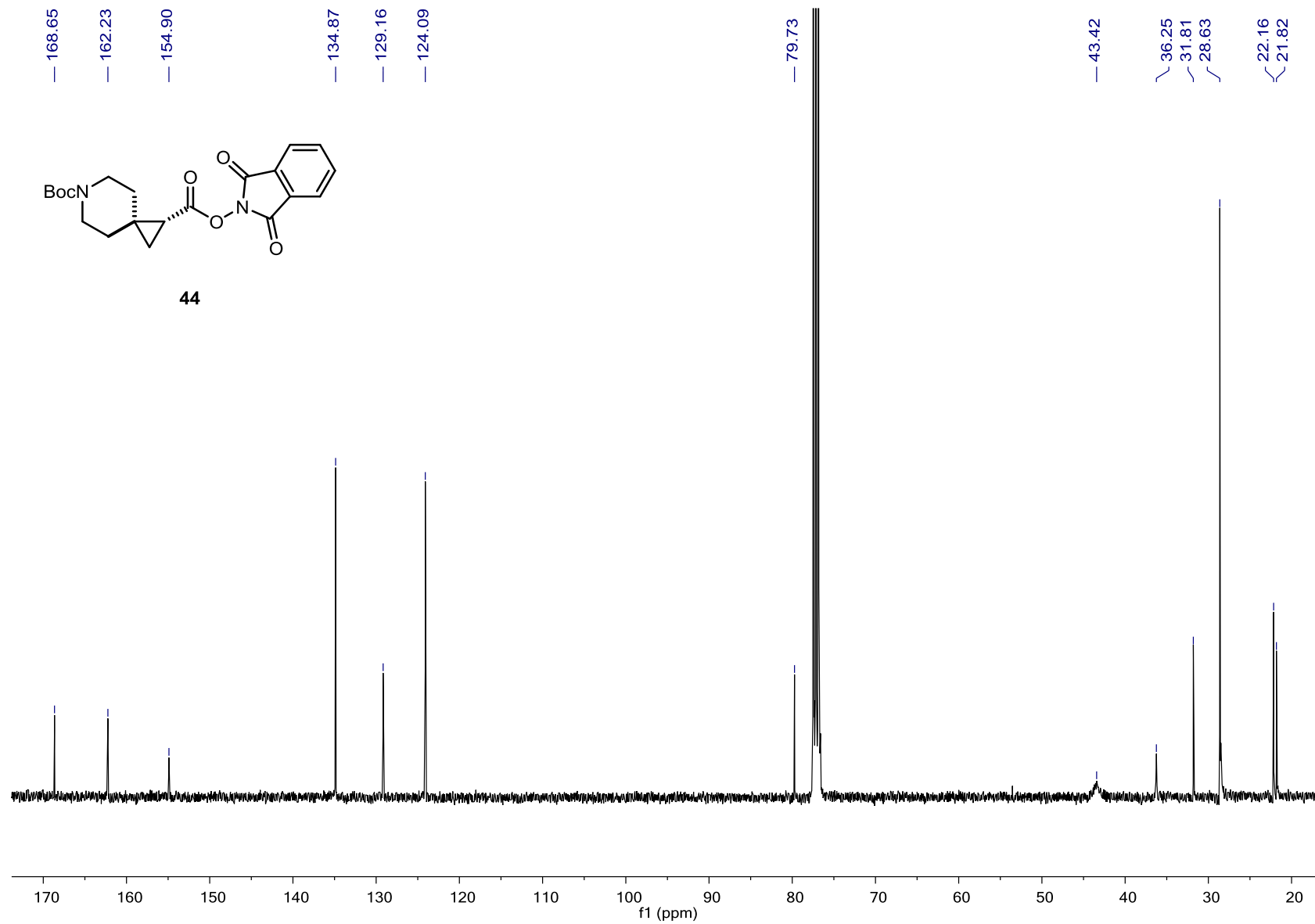


44

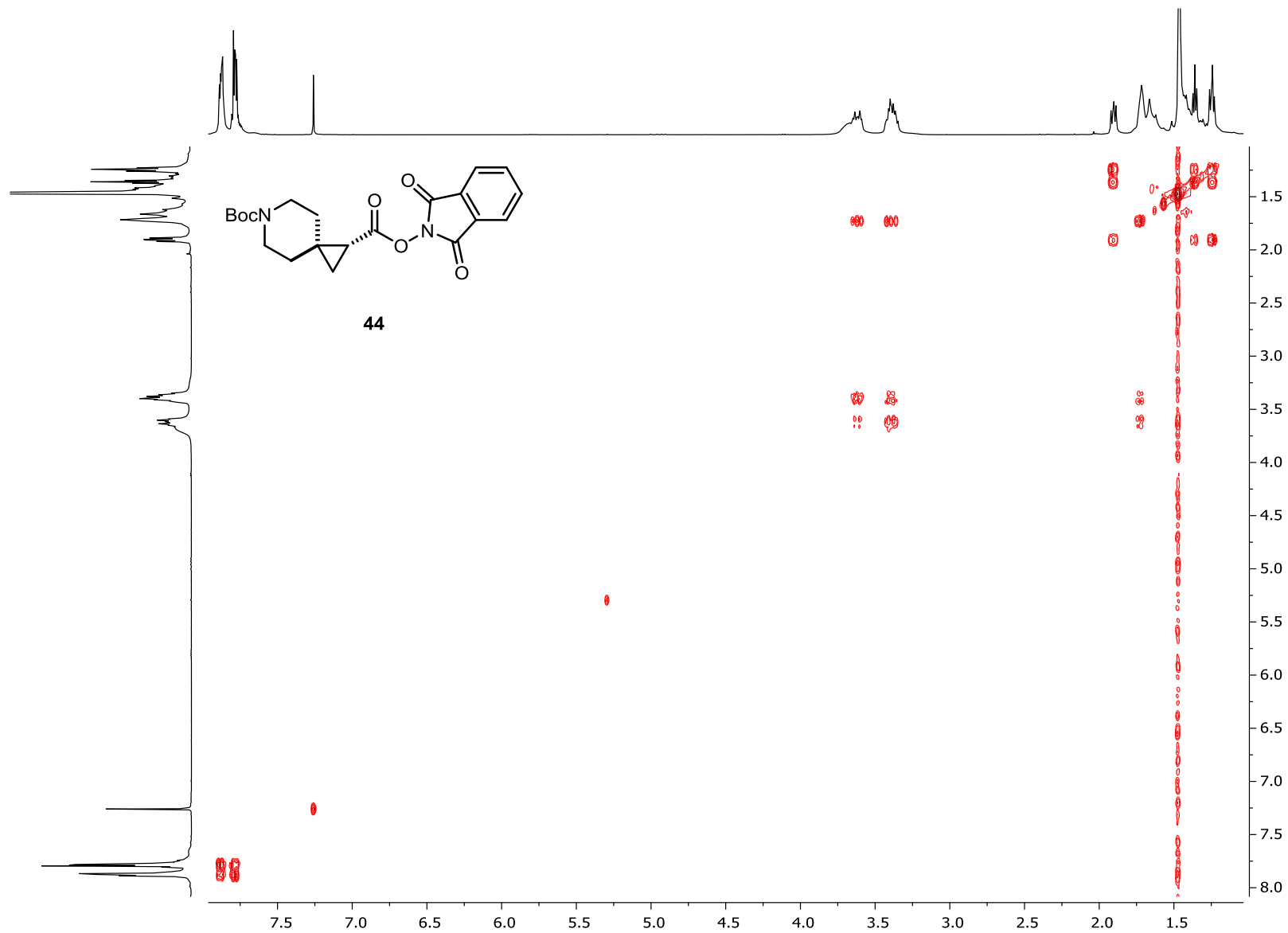


S225

^{13}C NMR (101 MHz, CDCl_3) for compound **44**

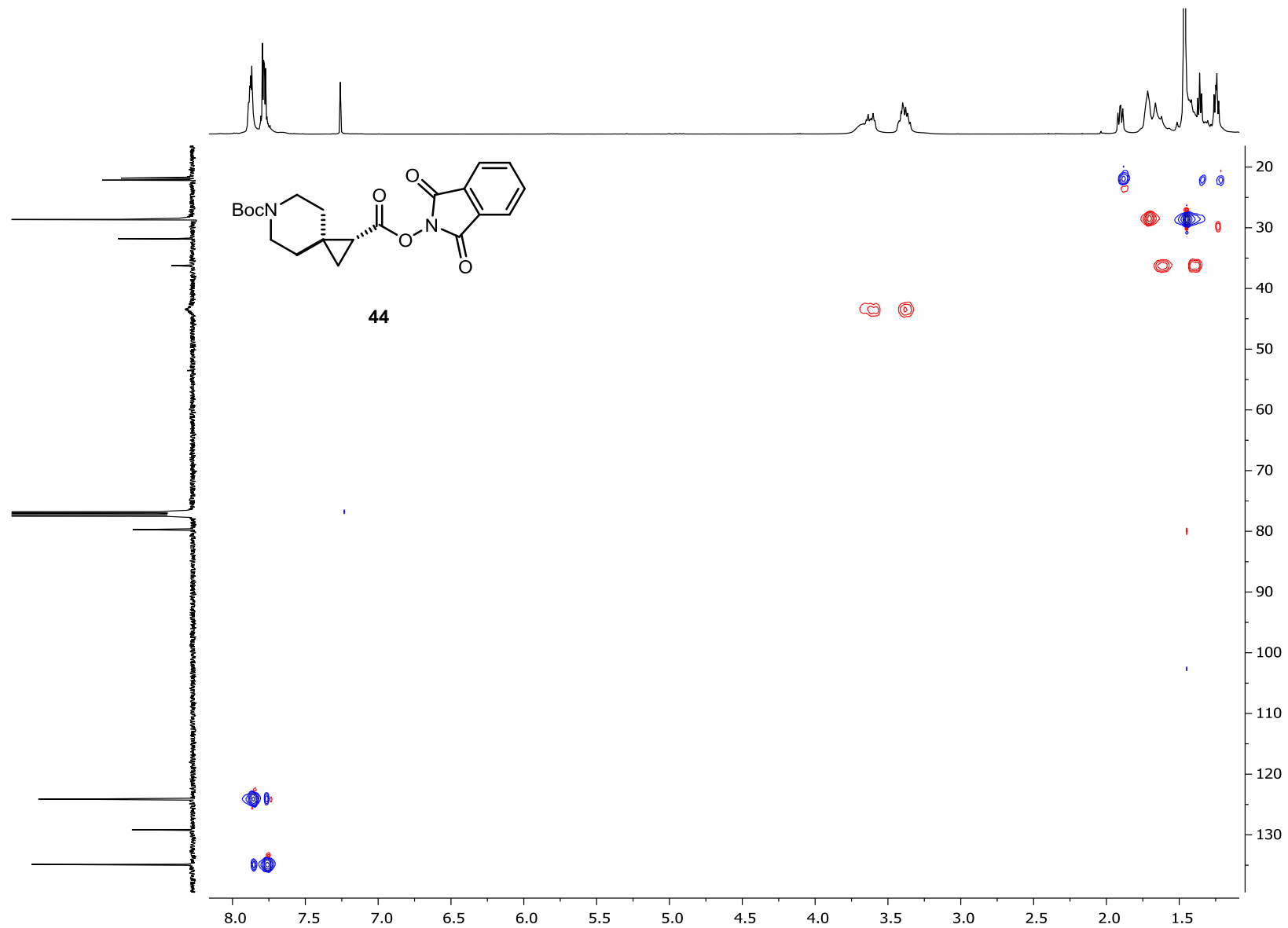


COSY NMR (400 MHz, $CDCl_3$) for compound **44**



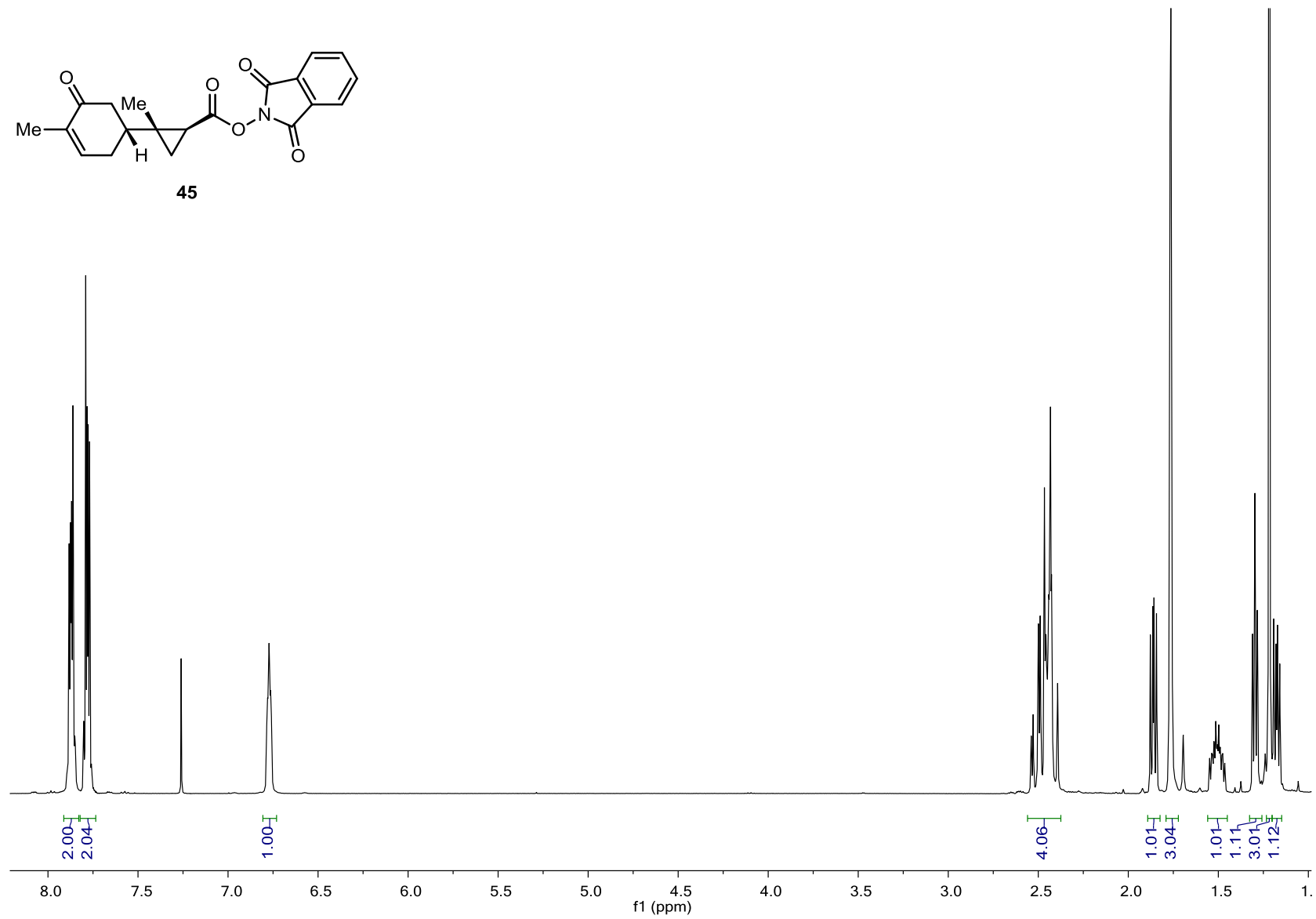
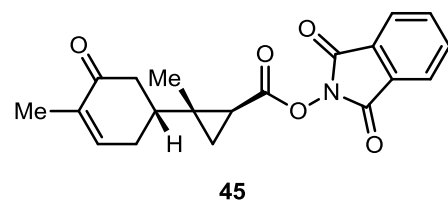
S227

HSQC NMR (400 MHz, CDCl₃) for compound **44**

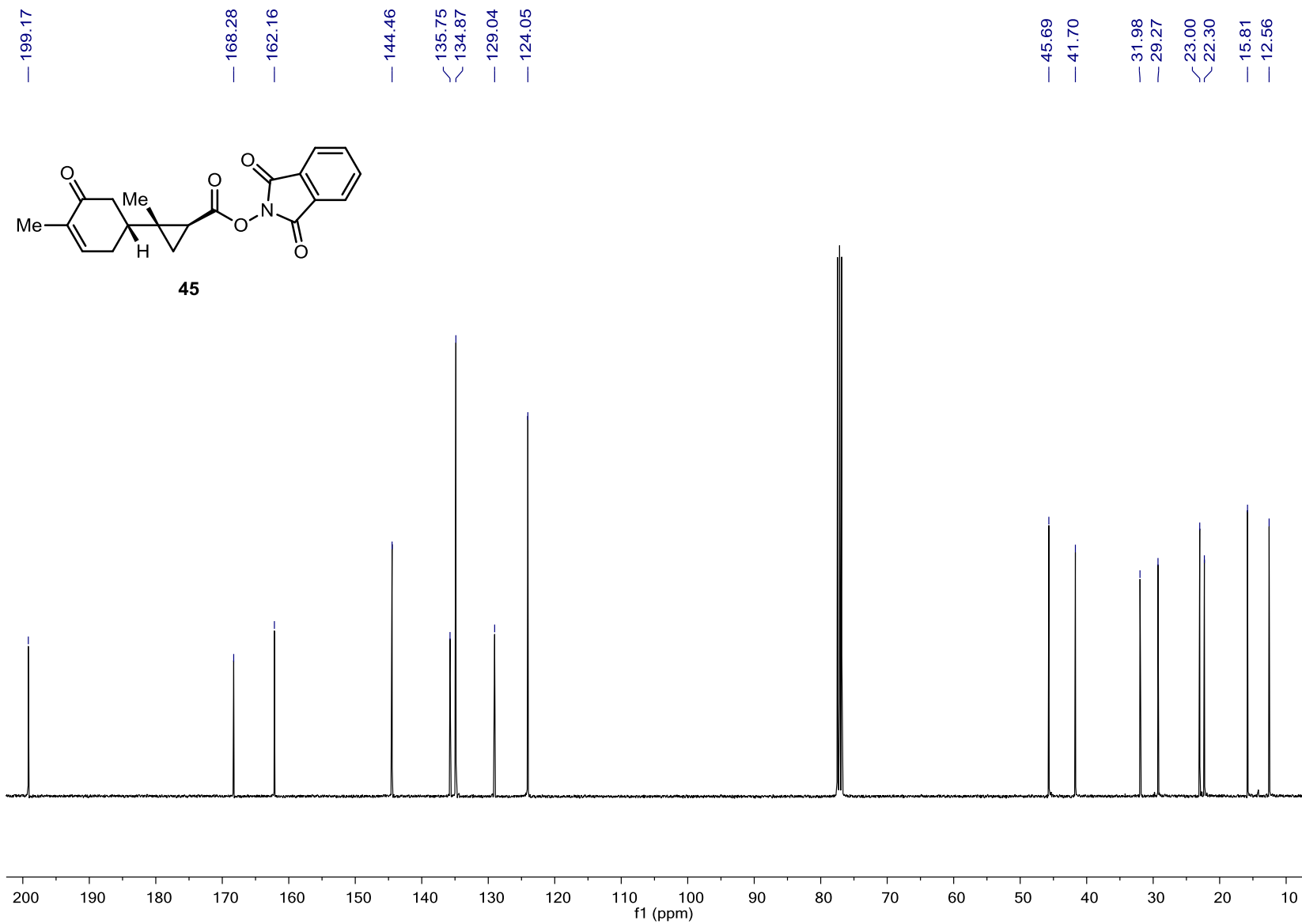


S228

^1H NMR (400 MHz, CDCl_3) for compound **45**

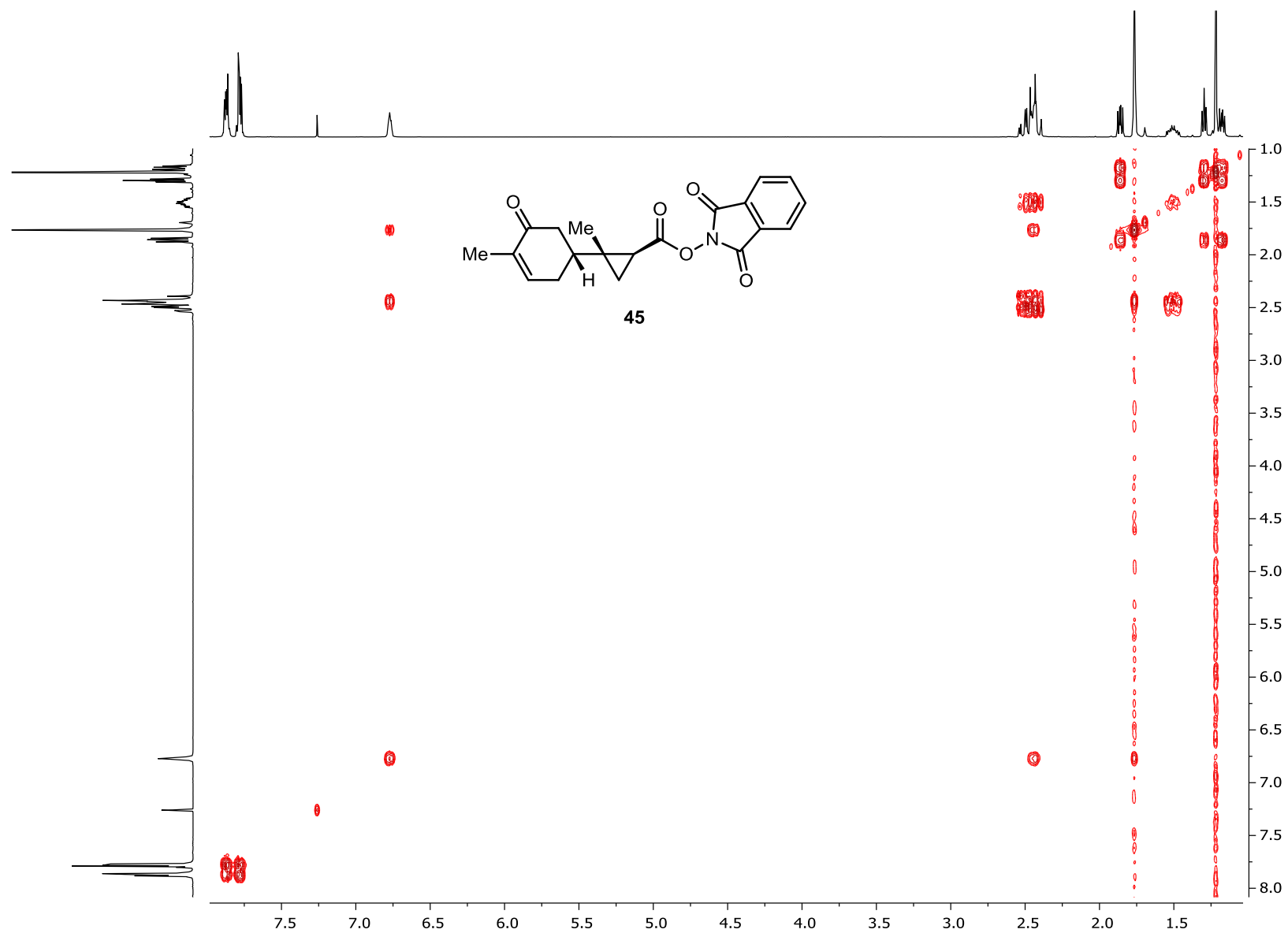


^{13}C NMR (101 MHz, CDCl_3) for compound **45**



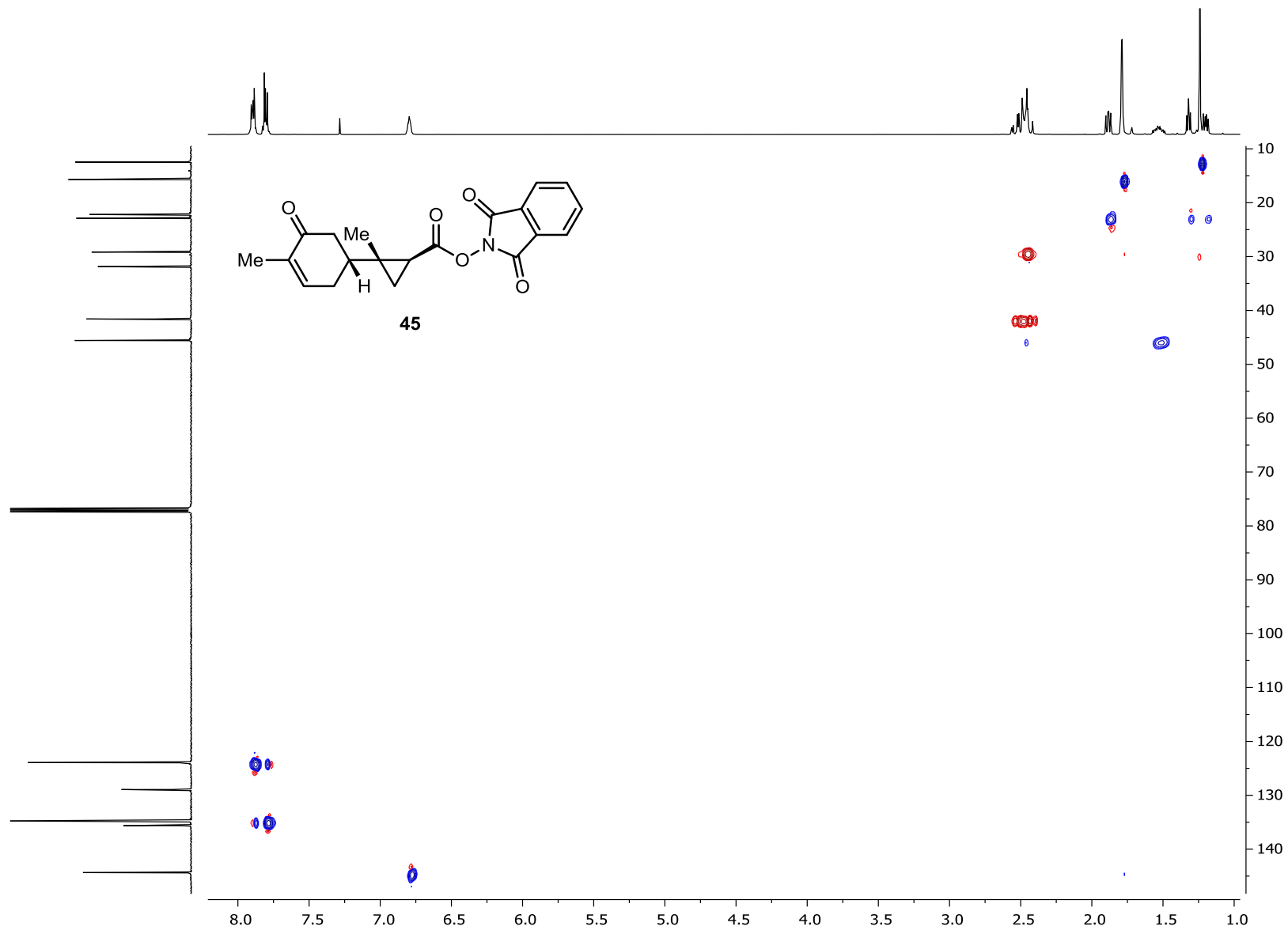
S230

COSY NMR (400 MHz, CDCl₃) for compound **45**



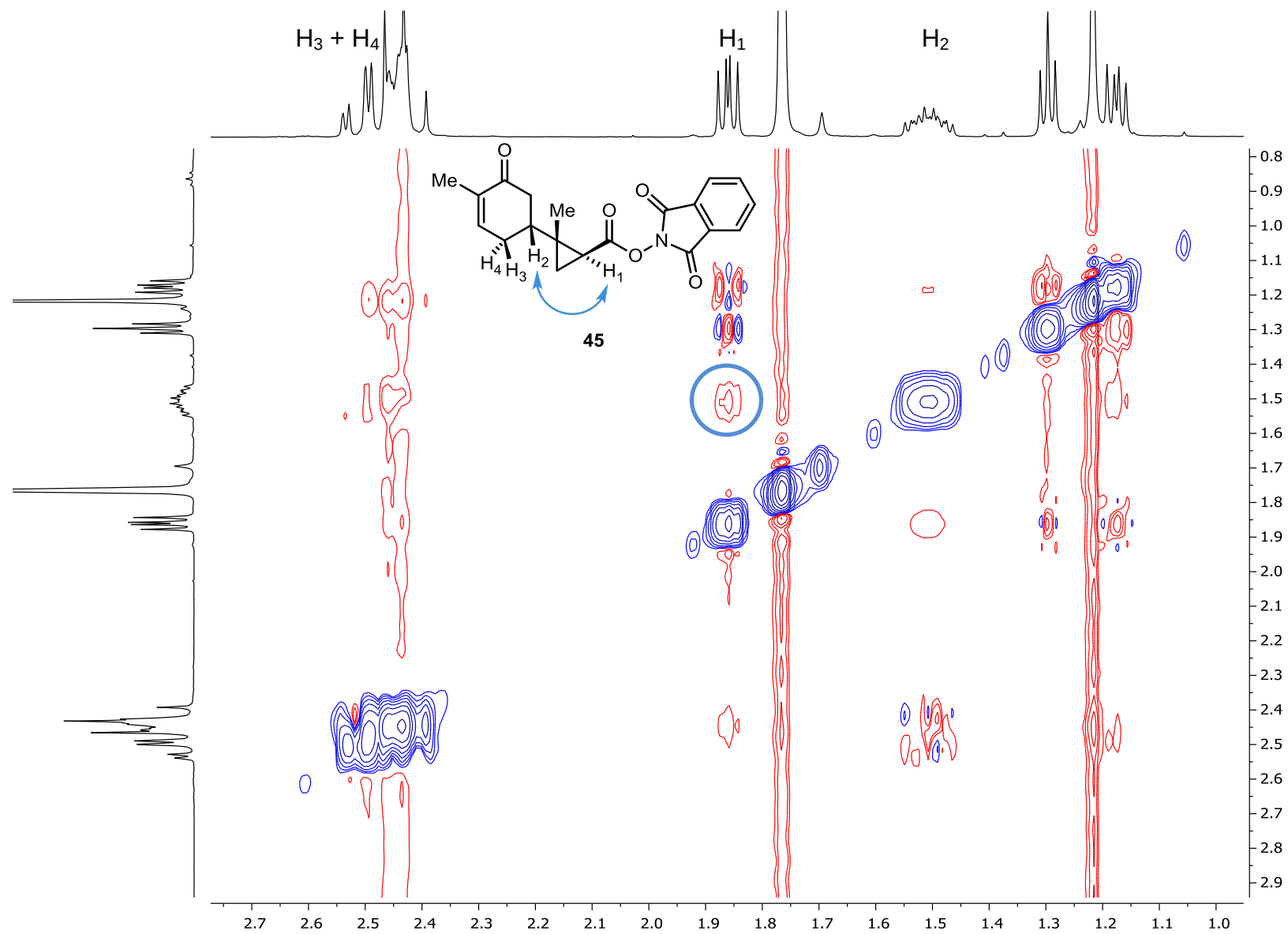
S231

HSQC NMR (400 MHz, CDCl₃) for compound **45**



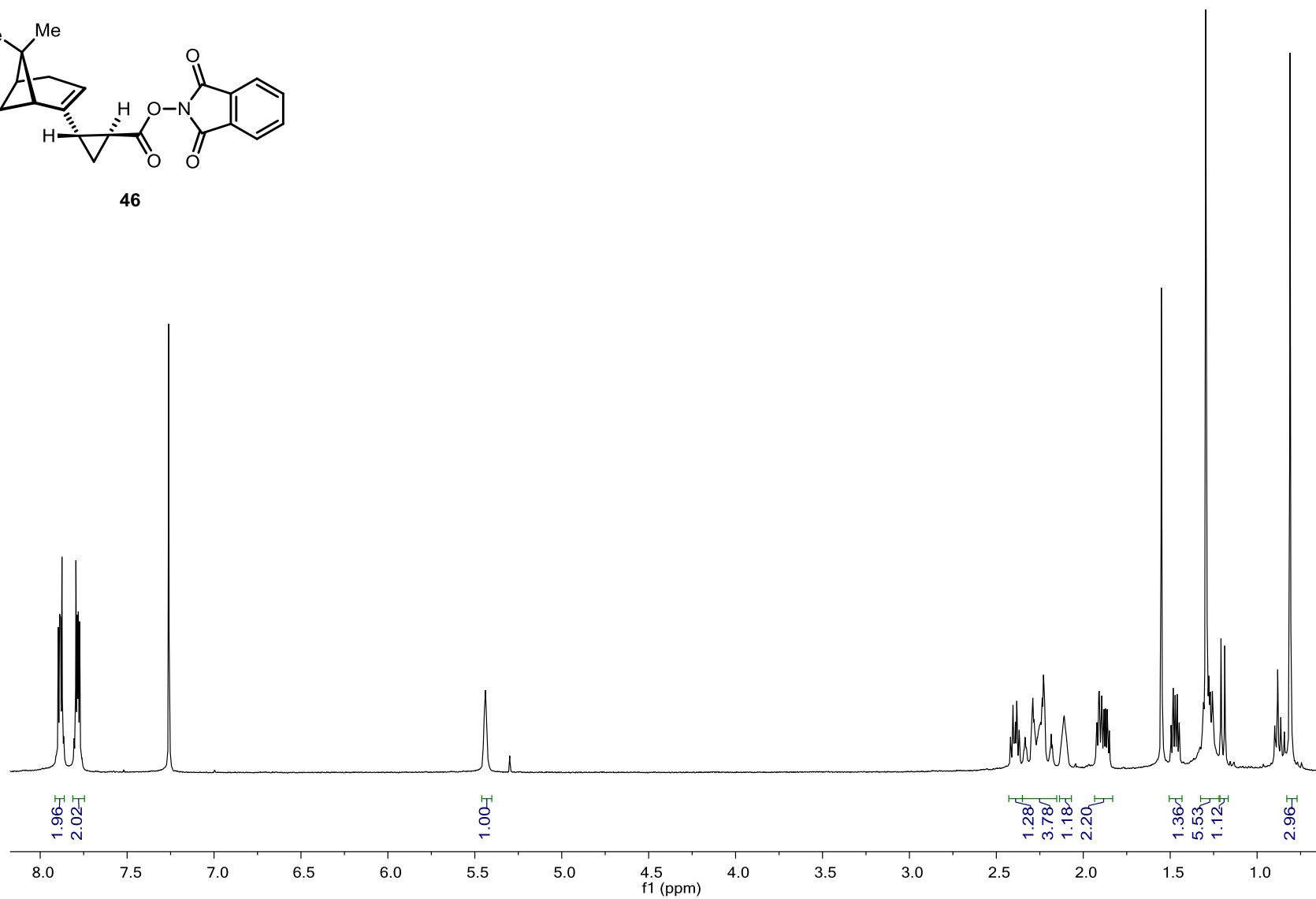
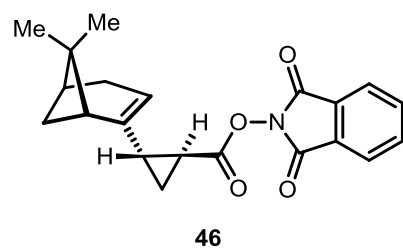
S232

NOESY NMR (400 MHz, CDCl₃) for compound **45**



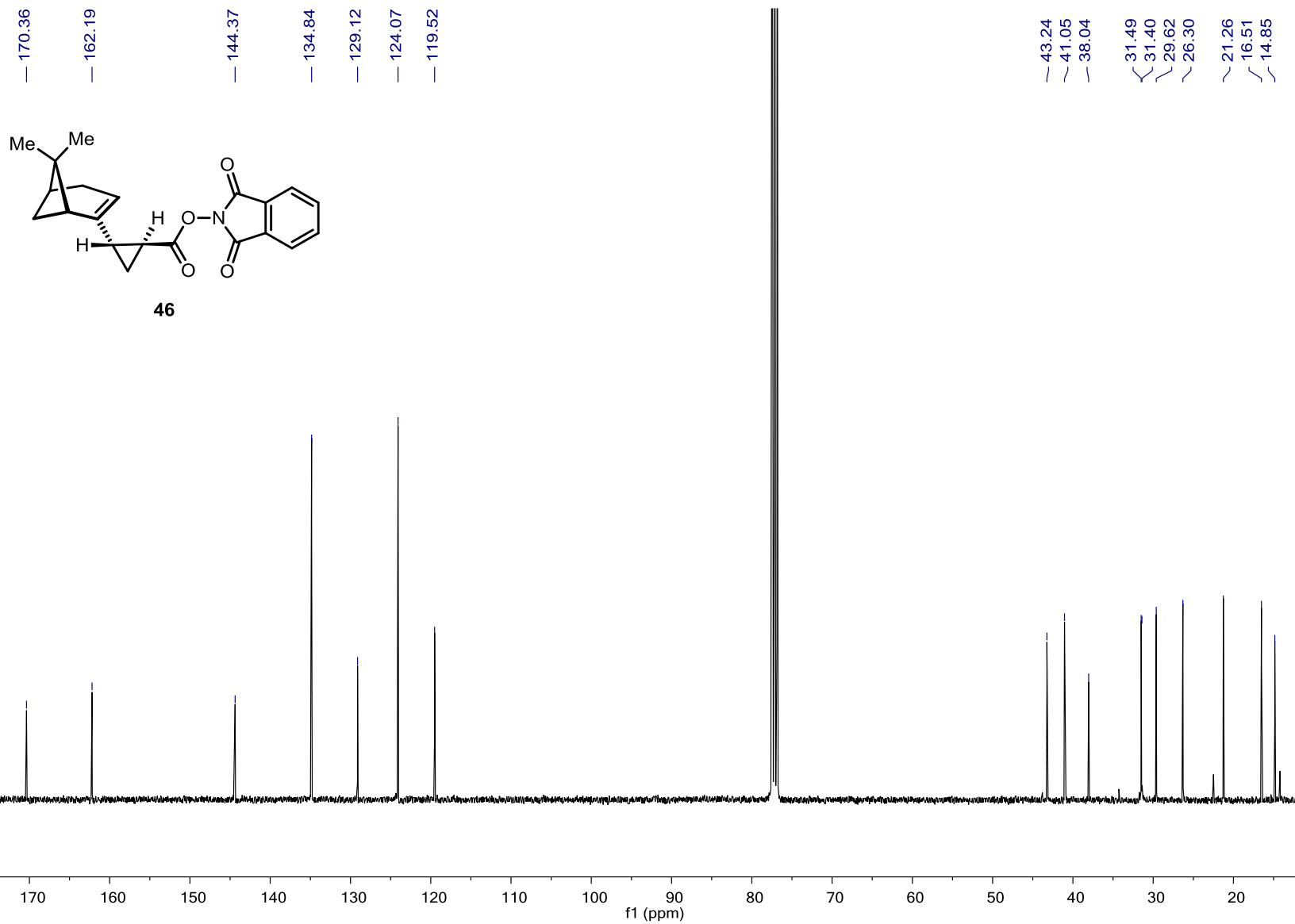
S233

^1H NMR (400 MHz, CDCl_3) for compound **46**

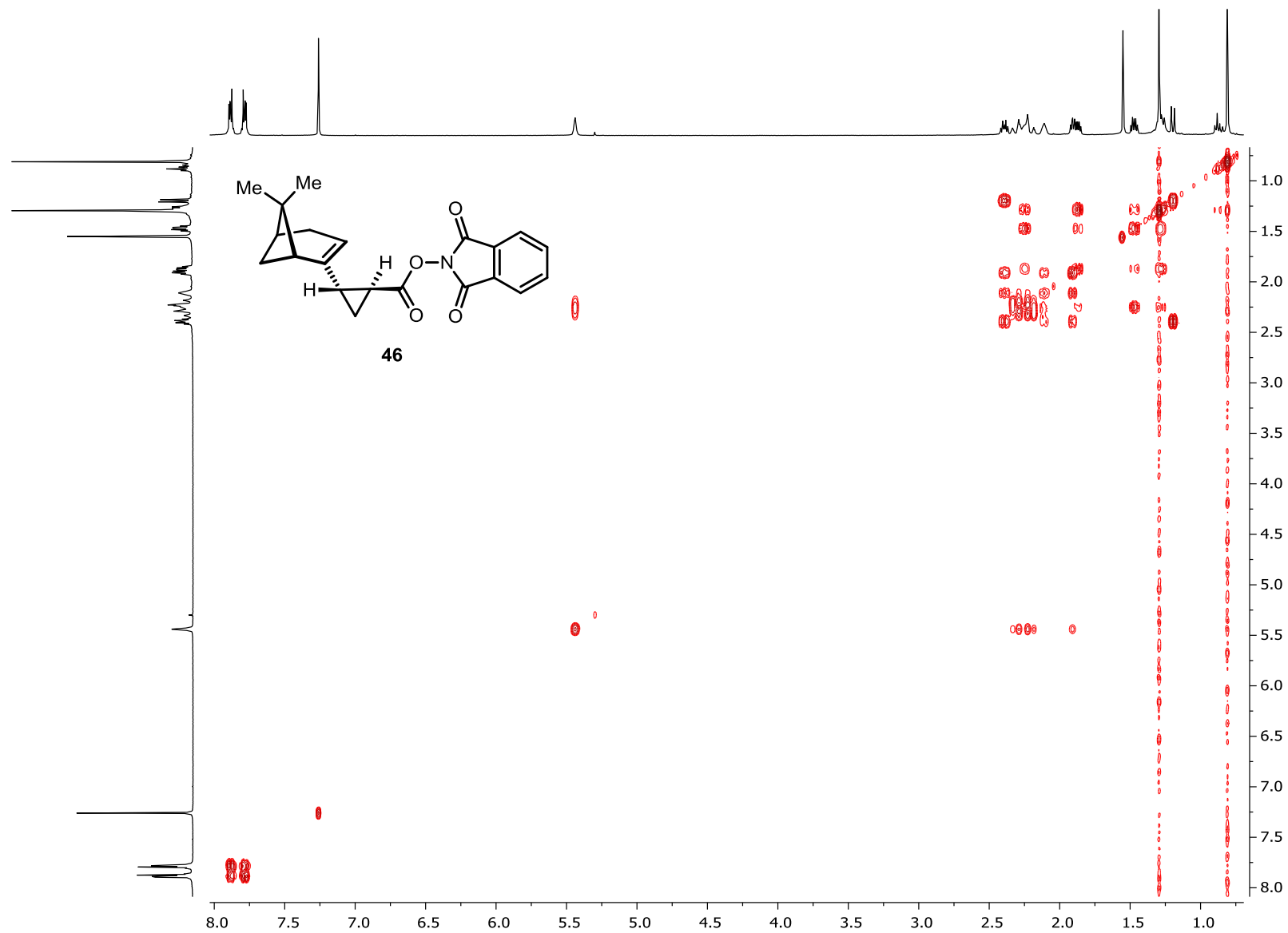


S234

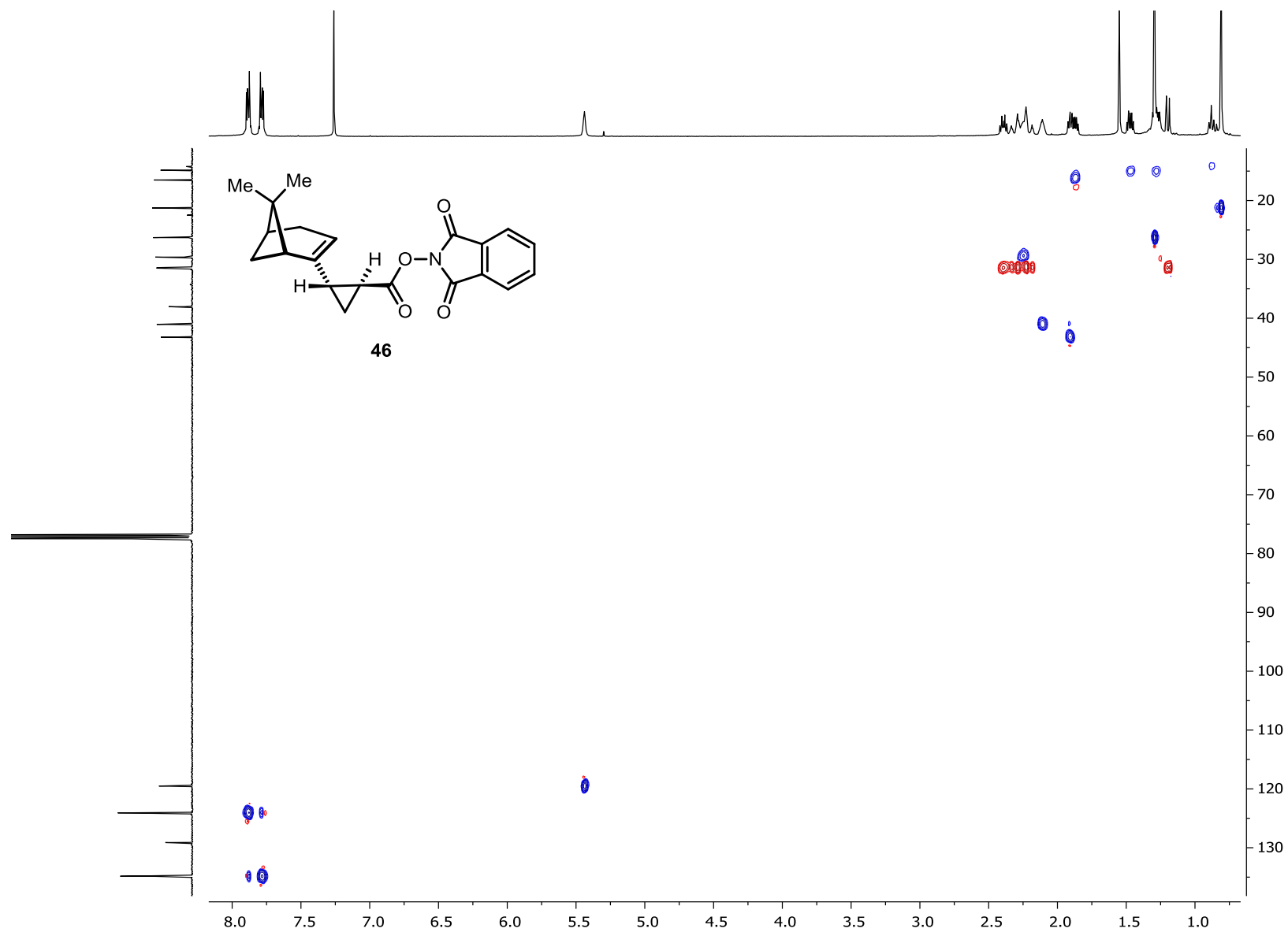
^{13}C NMR (101 MHz, CDCl_3) for compound **46**



COSY NMR (400 MHz, $CDCl_3$) for compound **46**

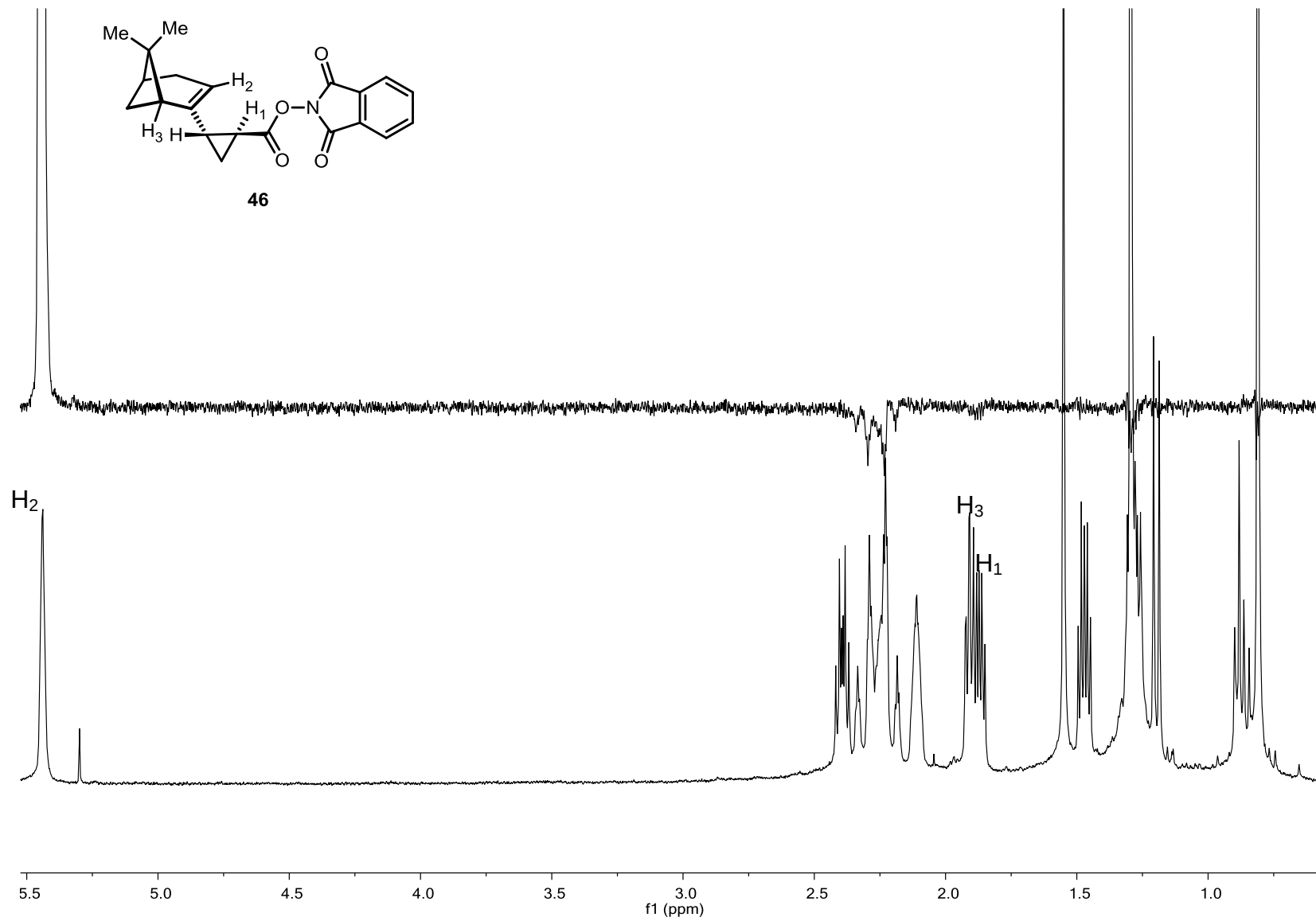


HSQC NMR (400 MHz, CDCl₃) for compound **46**

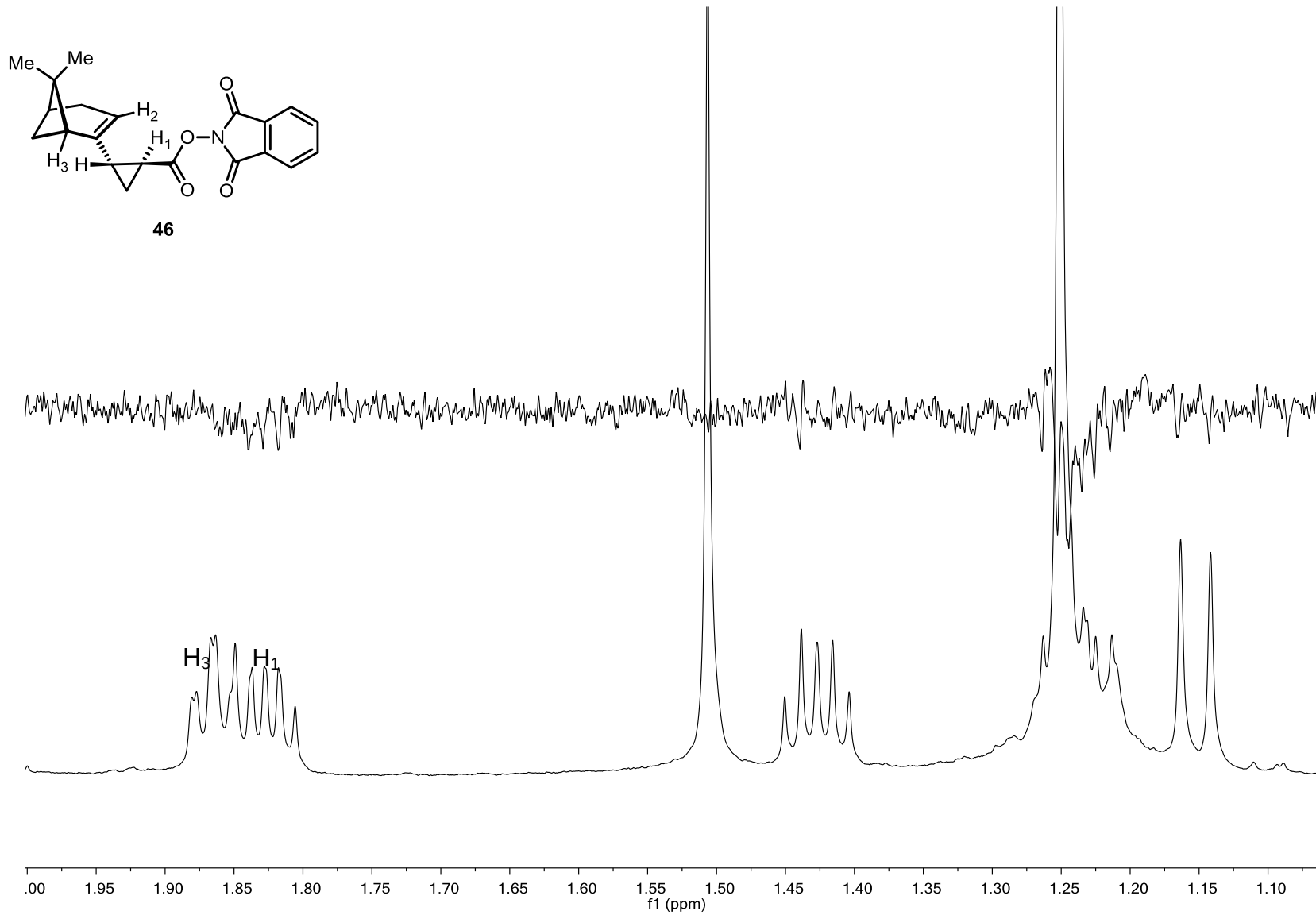


S237

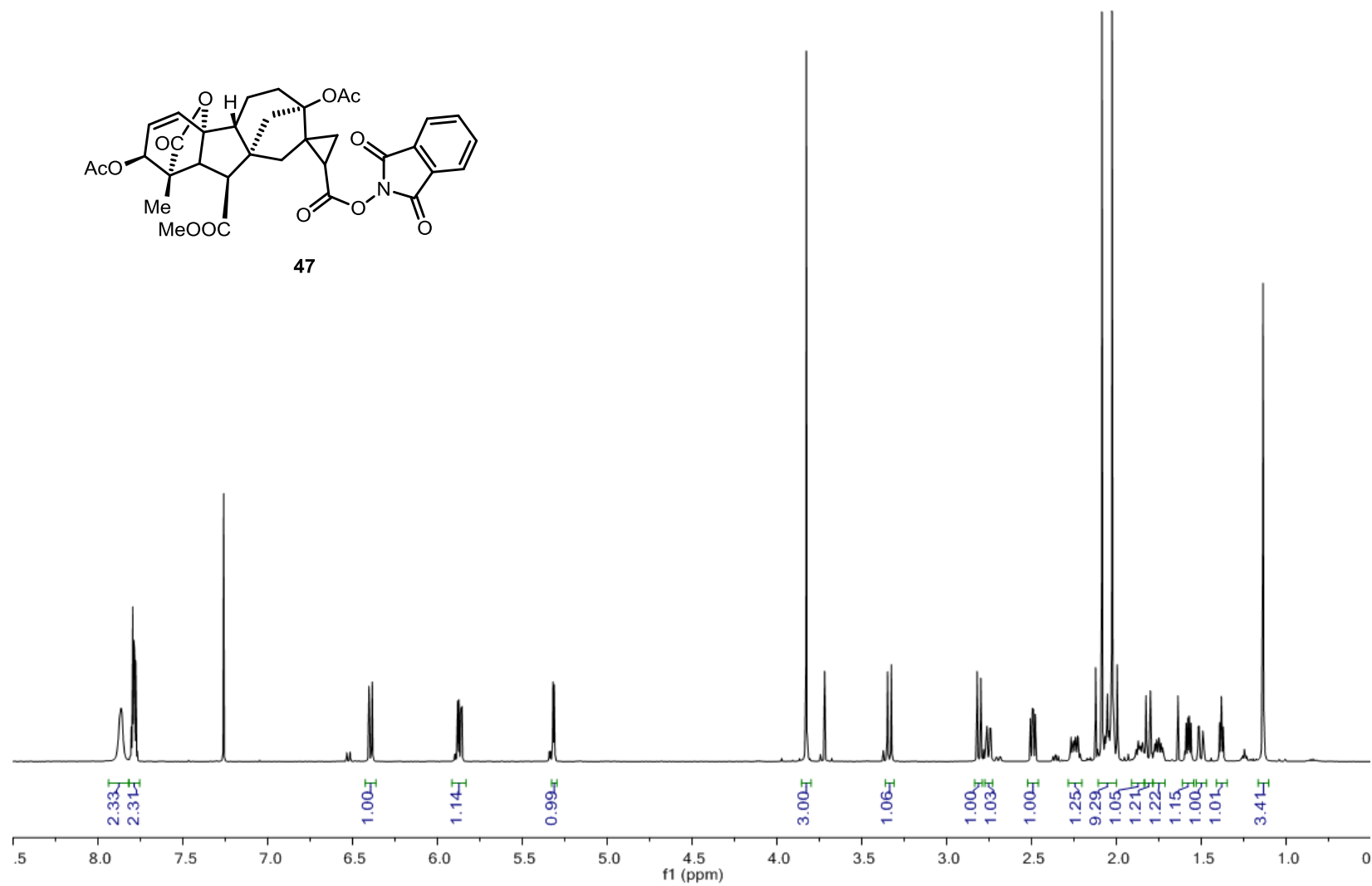
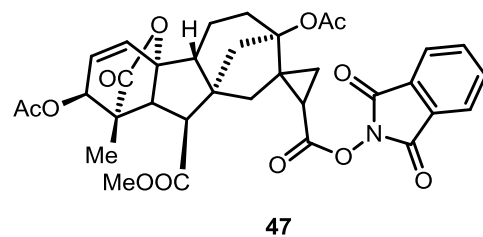
1D NOESY NMR (400 MHz, $CDCl_3$) for compound **46**



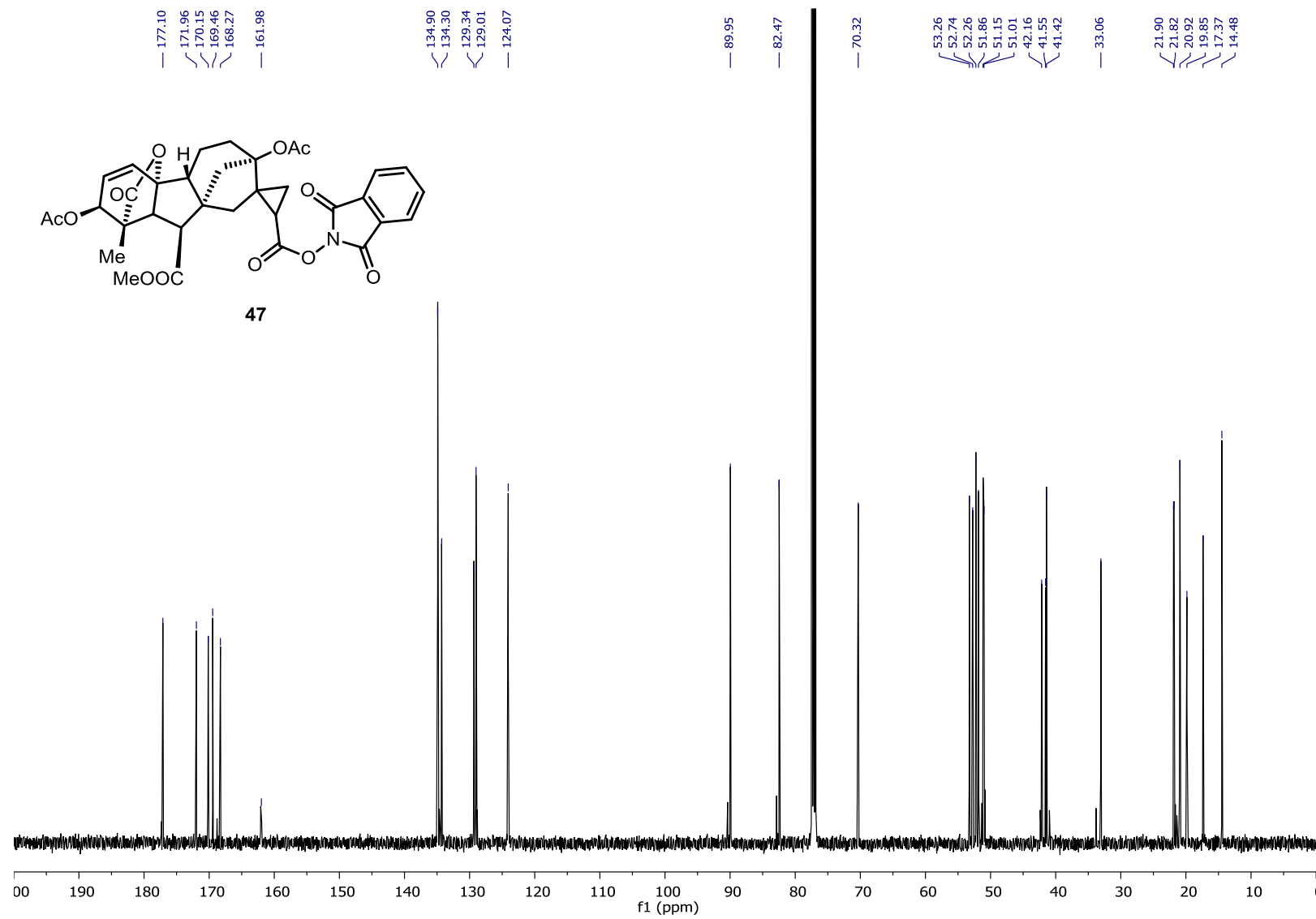
1D NOESY (expansion) NMR (400 MHz, CDCl_3) for compound **46**



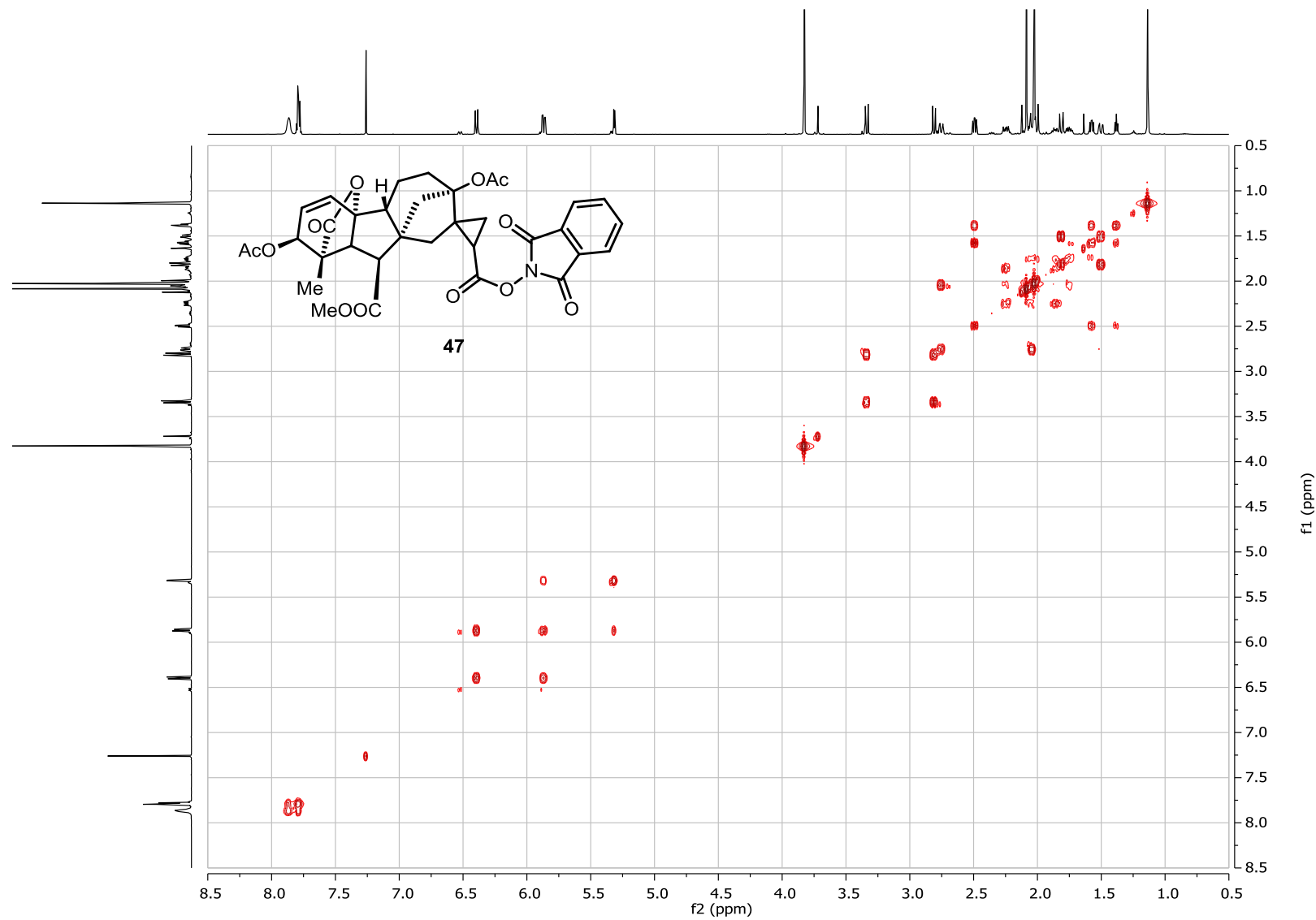
^1H NMR (500 MHz, CDCl_3) for compound **47**



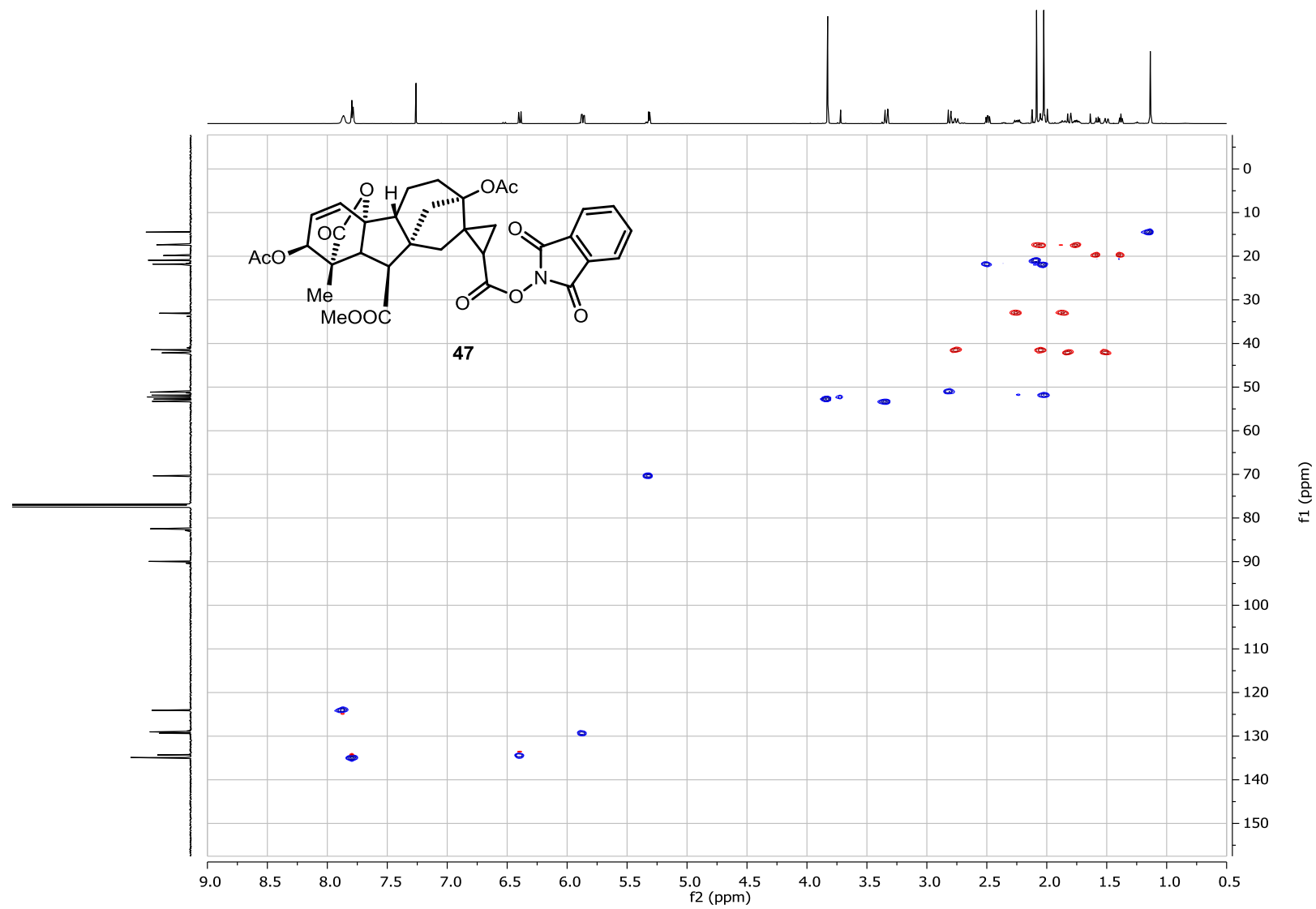
^{13}C NMR (126 MHz, CDCl_3) for compound **47**



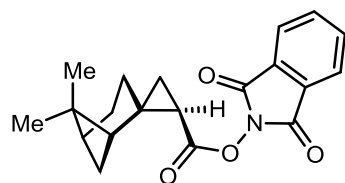
COSY NMR (500 MHz, CDCl₃) for compound **47**



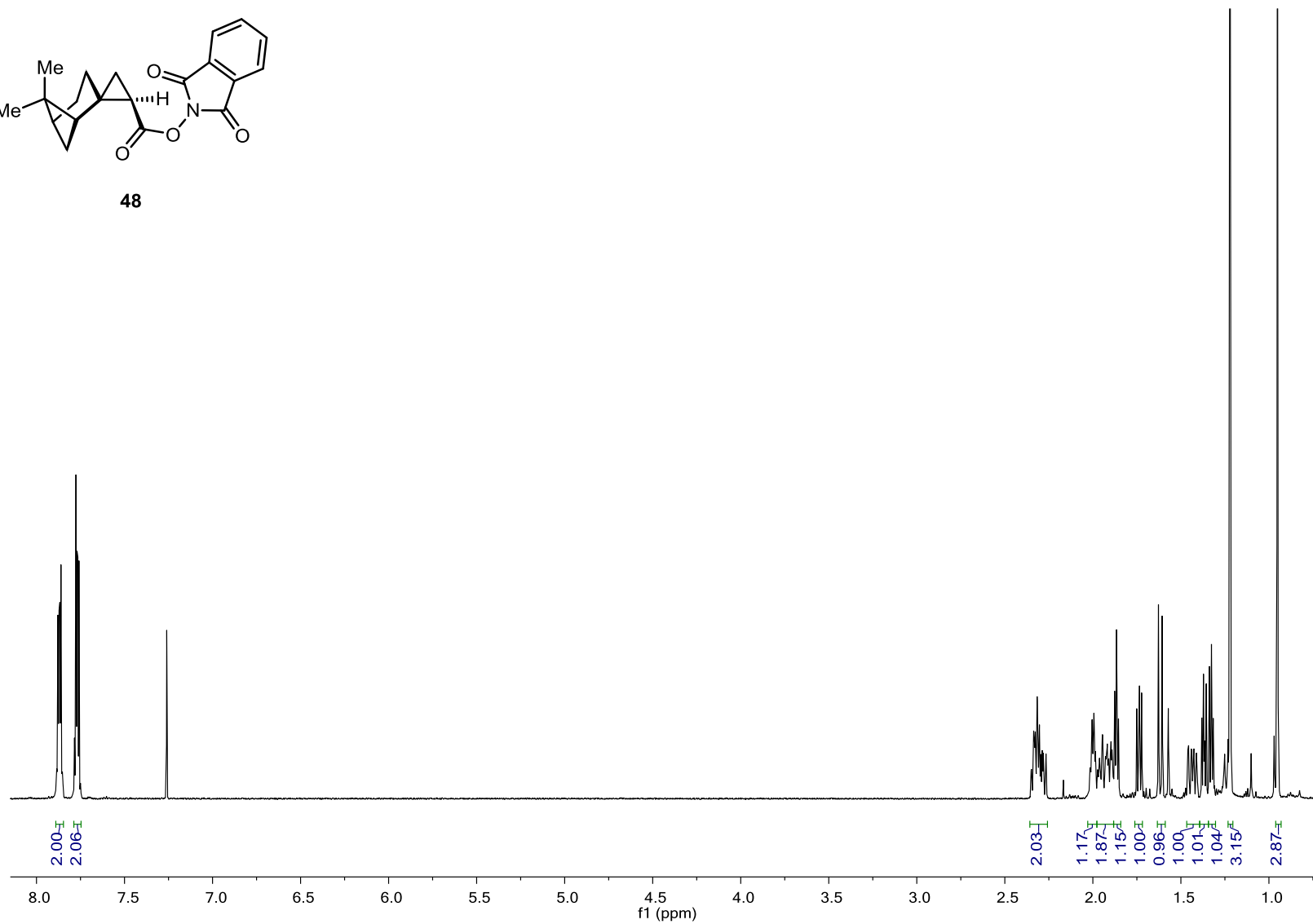
HSQC NMR (500 MHz, CDCl₃) for compound **47**



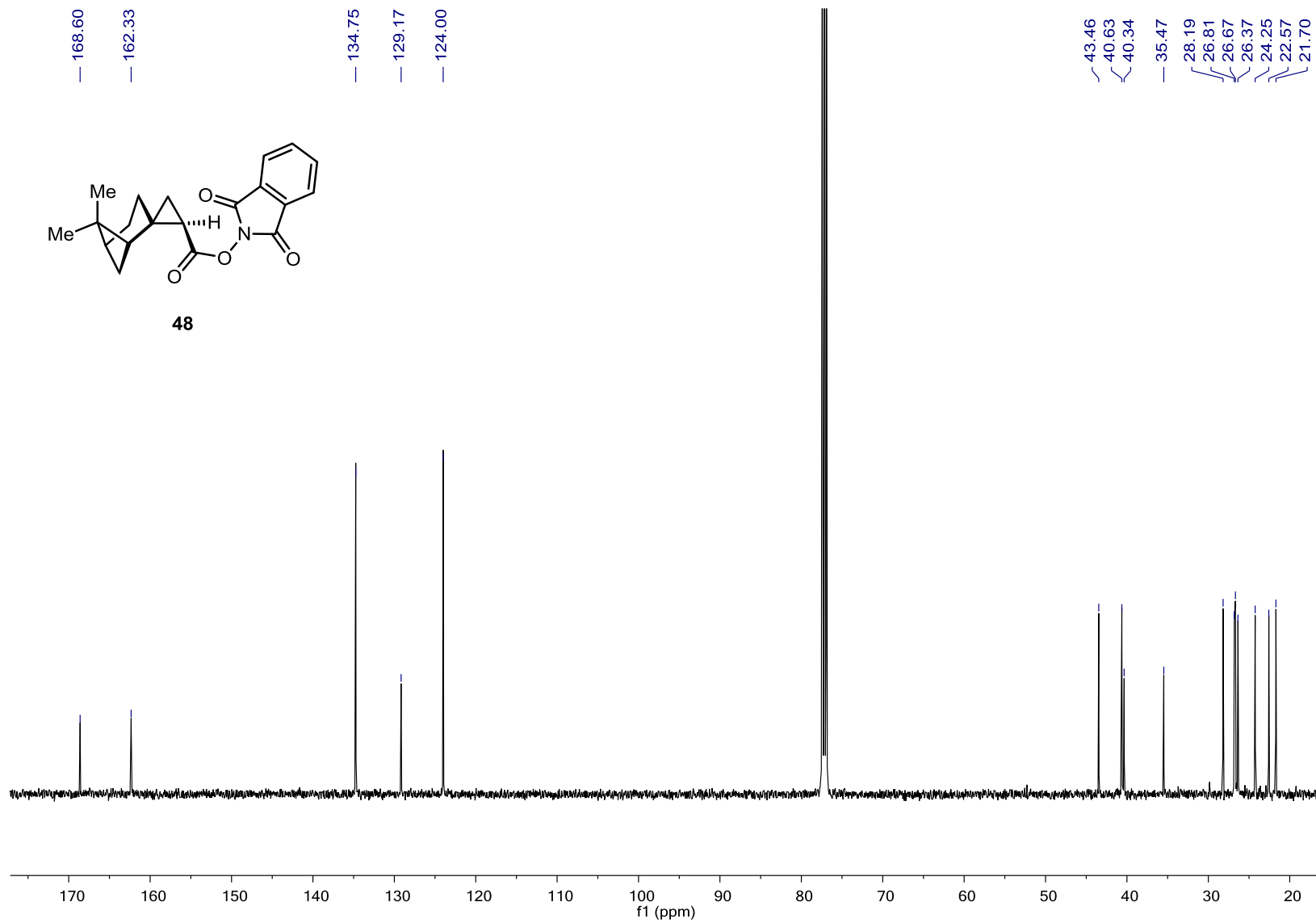
^1H NMR (500 MHz, CDCl_3) for compound **48**



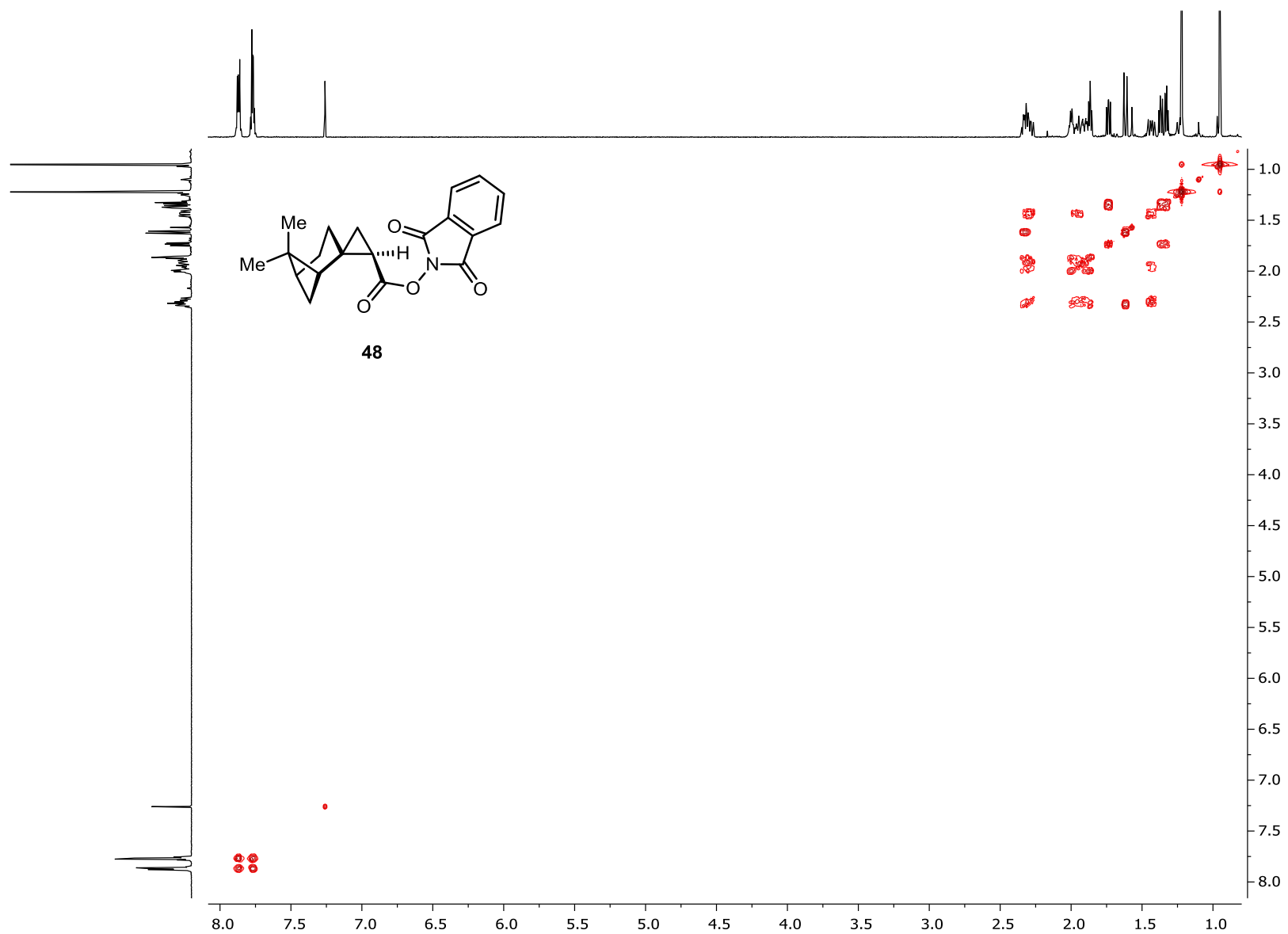
48



^{13}C NMR (126 MHz, CDCl_3) for compound **48**

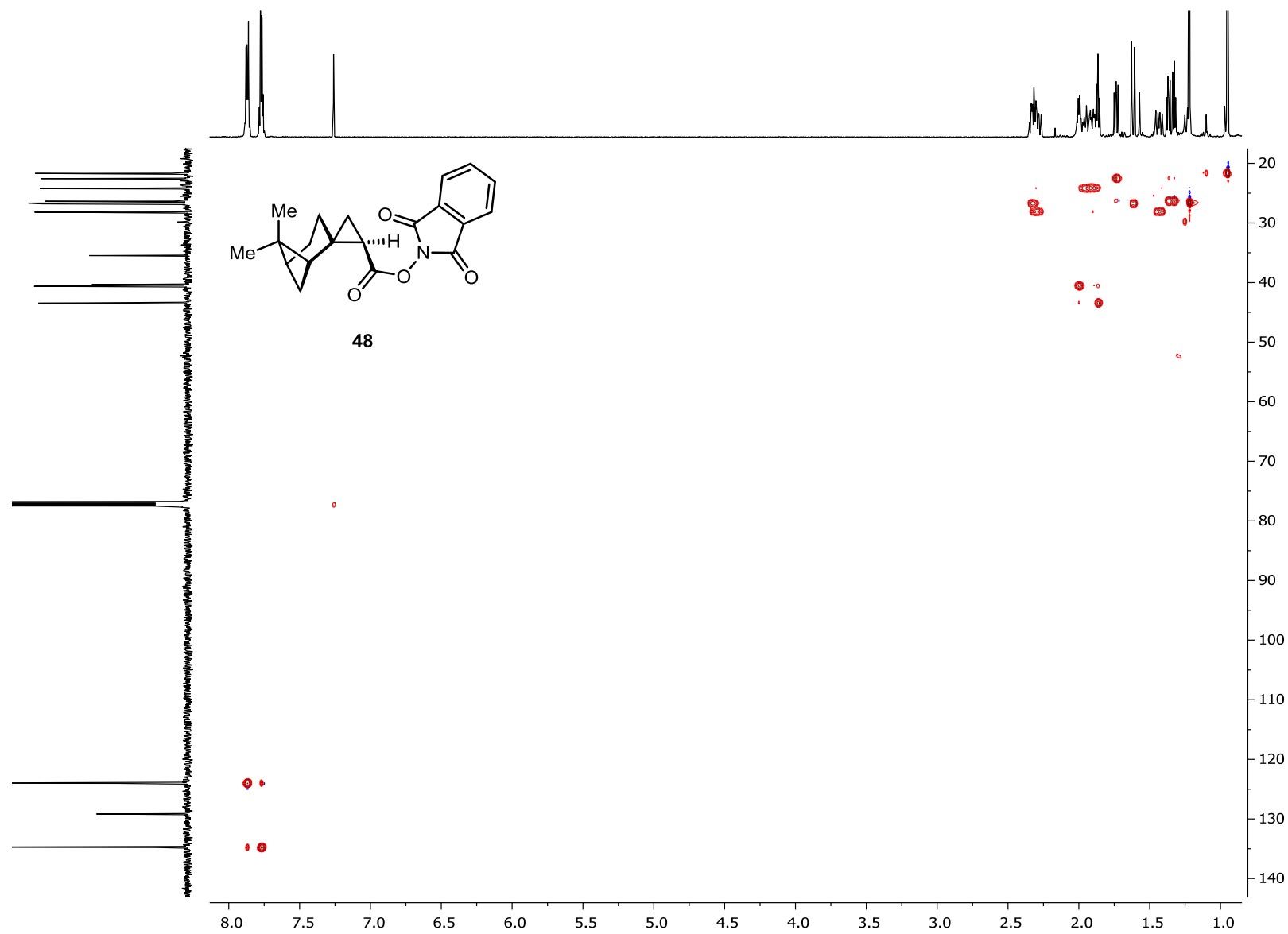


COSY NMR (500 MHz, CDCl₃) for compound 48



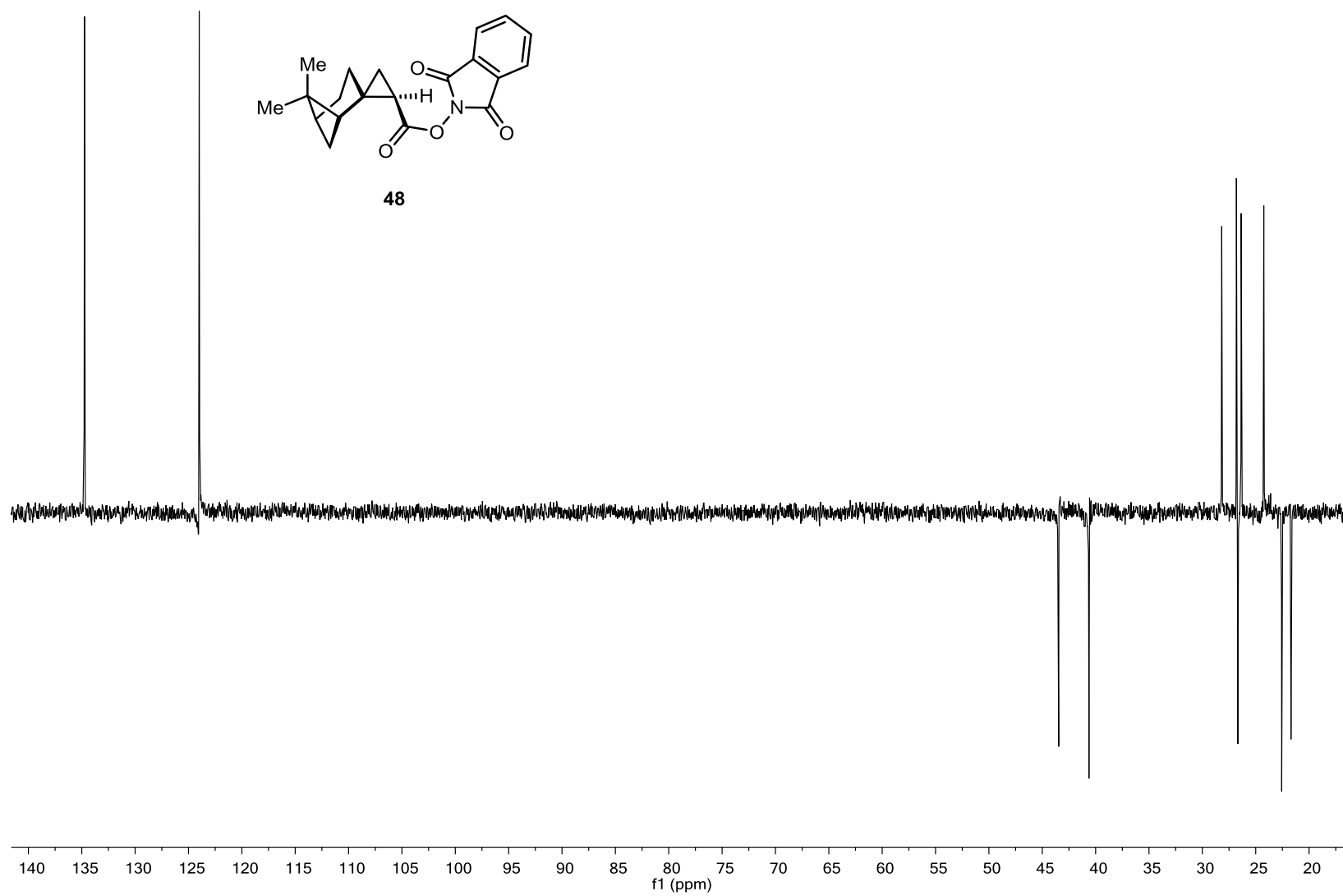
S246

HSQC NMR (500 MHz, CDCl₃) for compound **48**

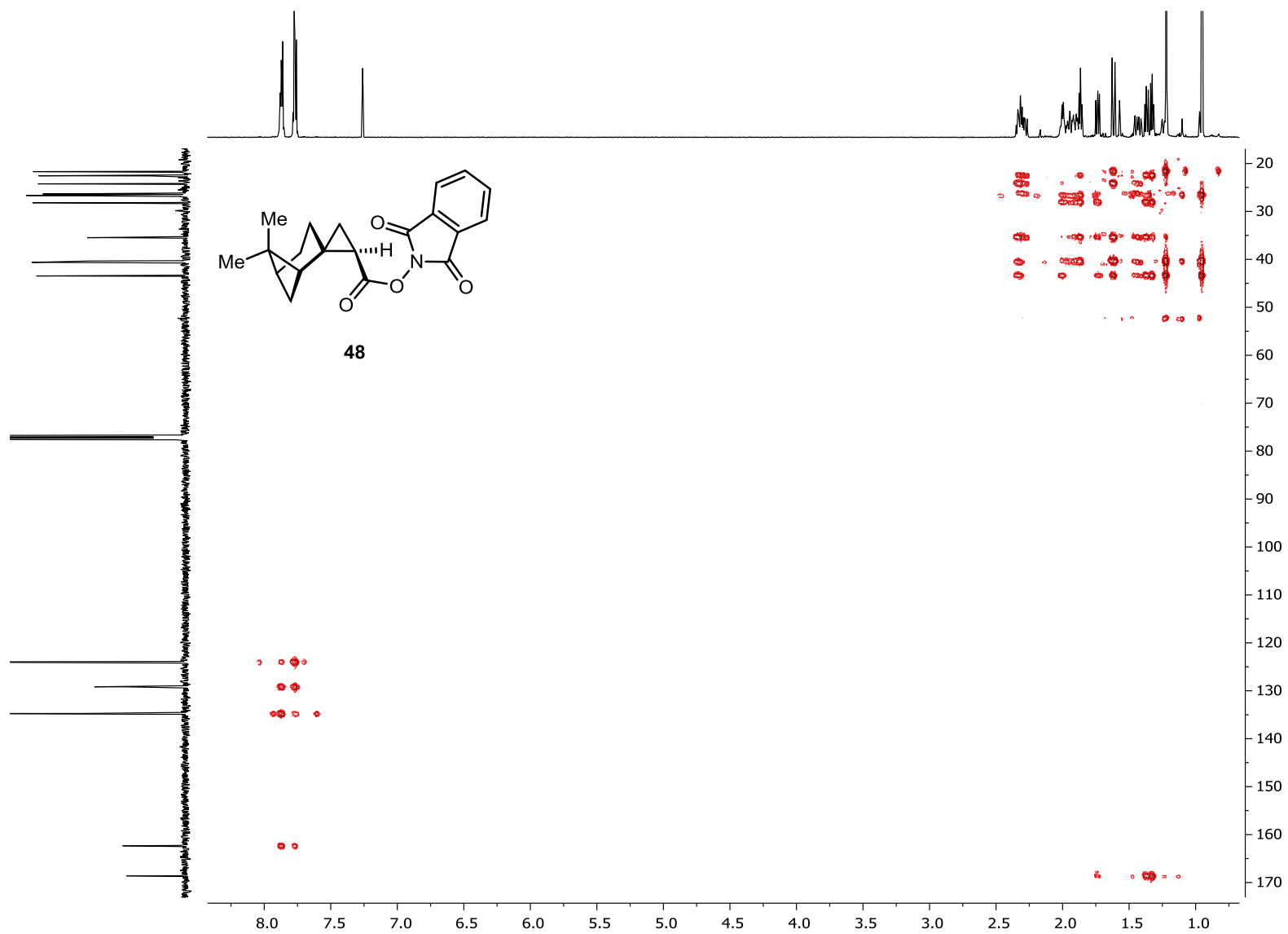


S247

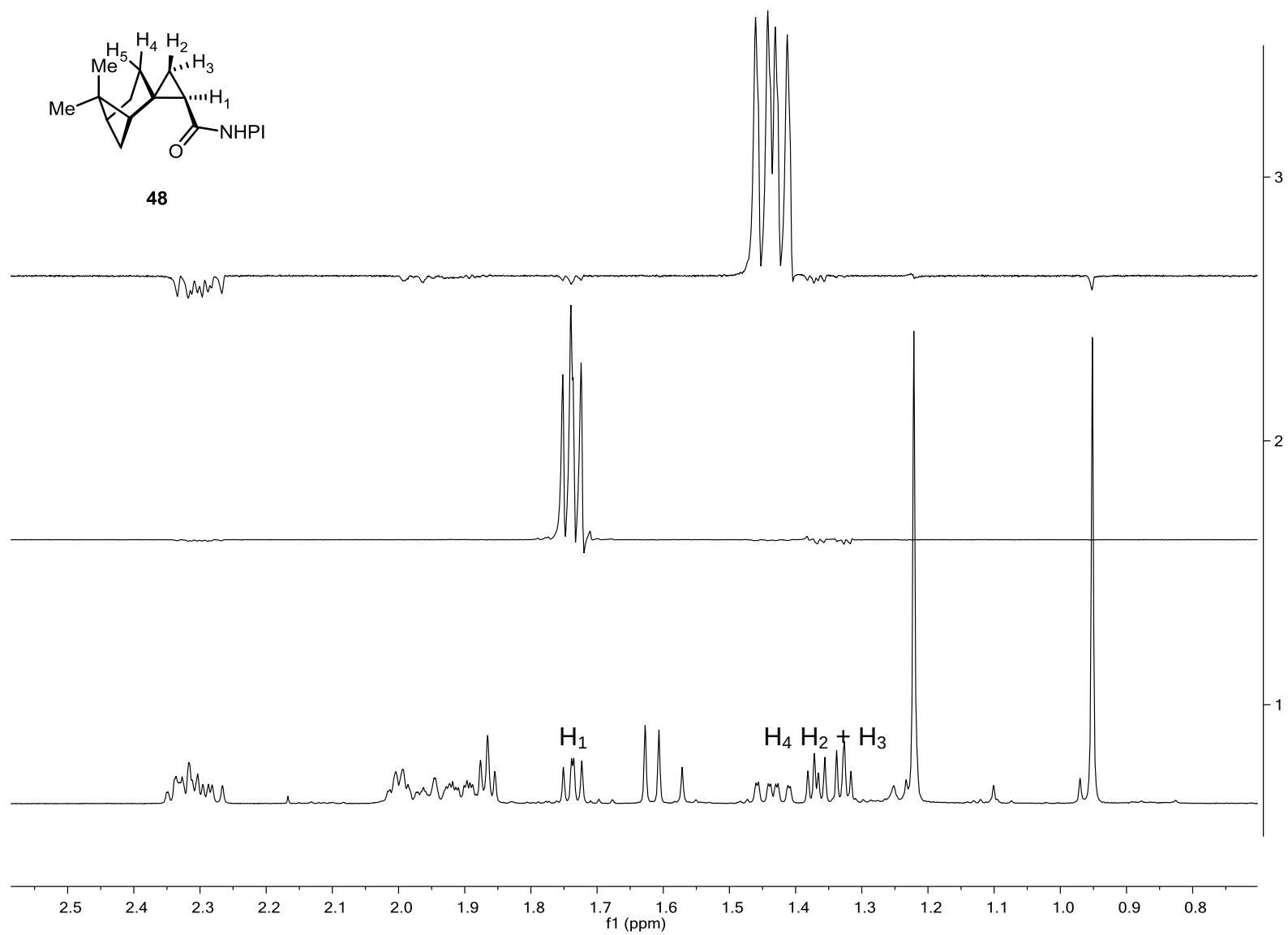
DEPT 135° NMR (500 MHz, CDCl₃) for compound **48**



HMBC NMR (500 MHz, CDCl₃) for compound **48**

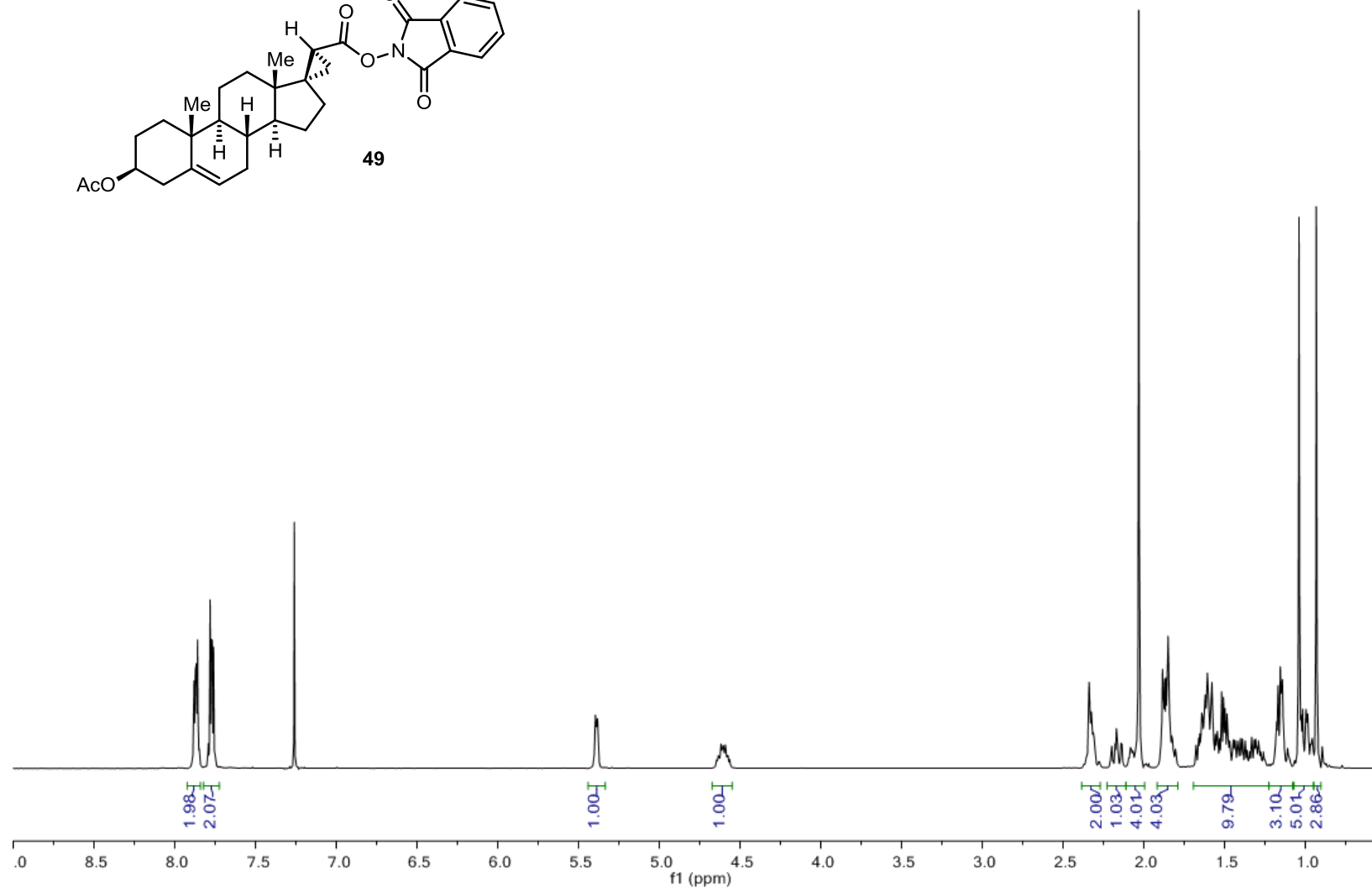
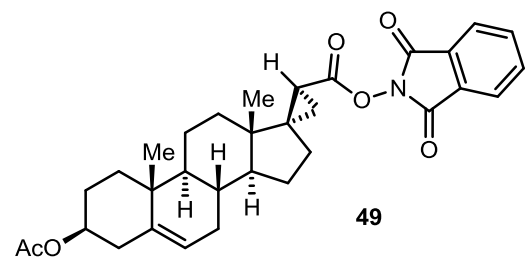


1D-NOESY NMR (500 MHz, CDCl₃) for compound **48**

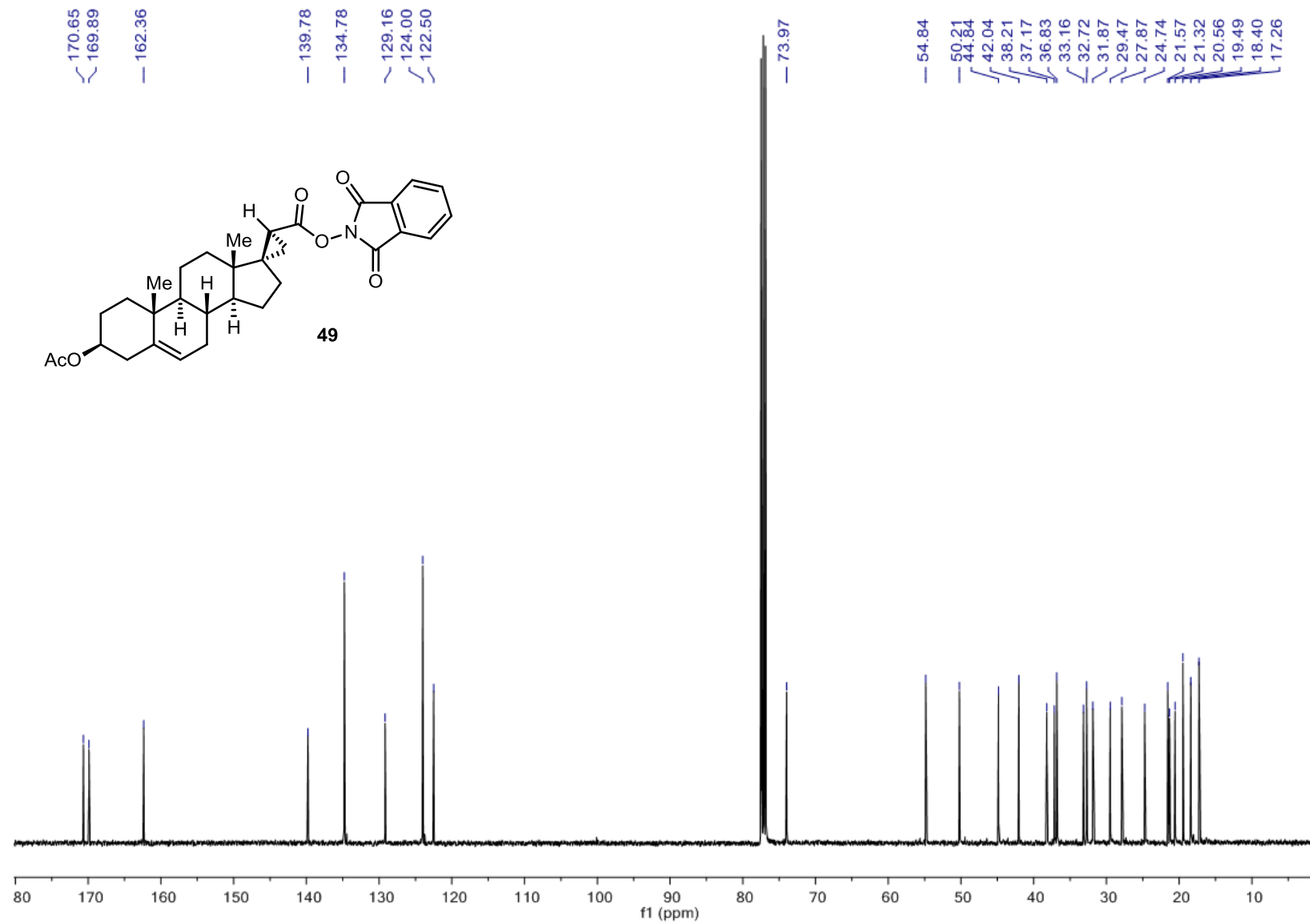


S250

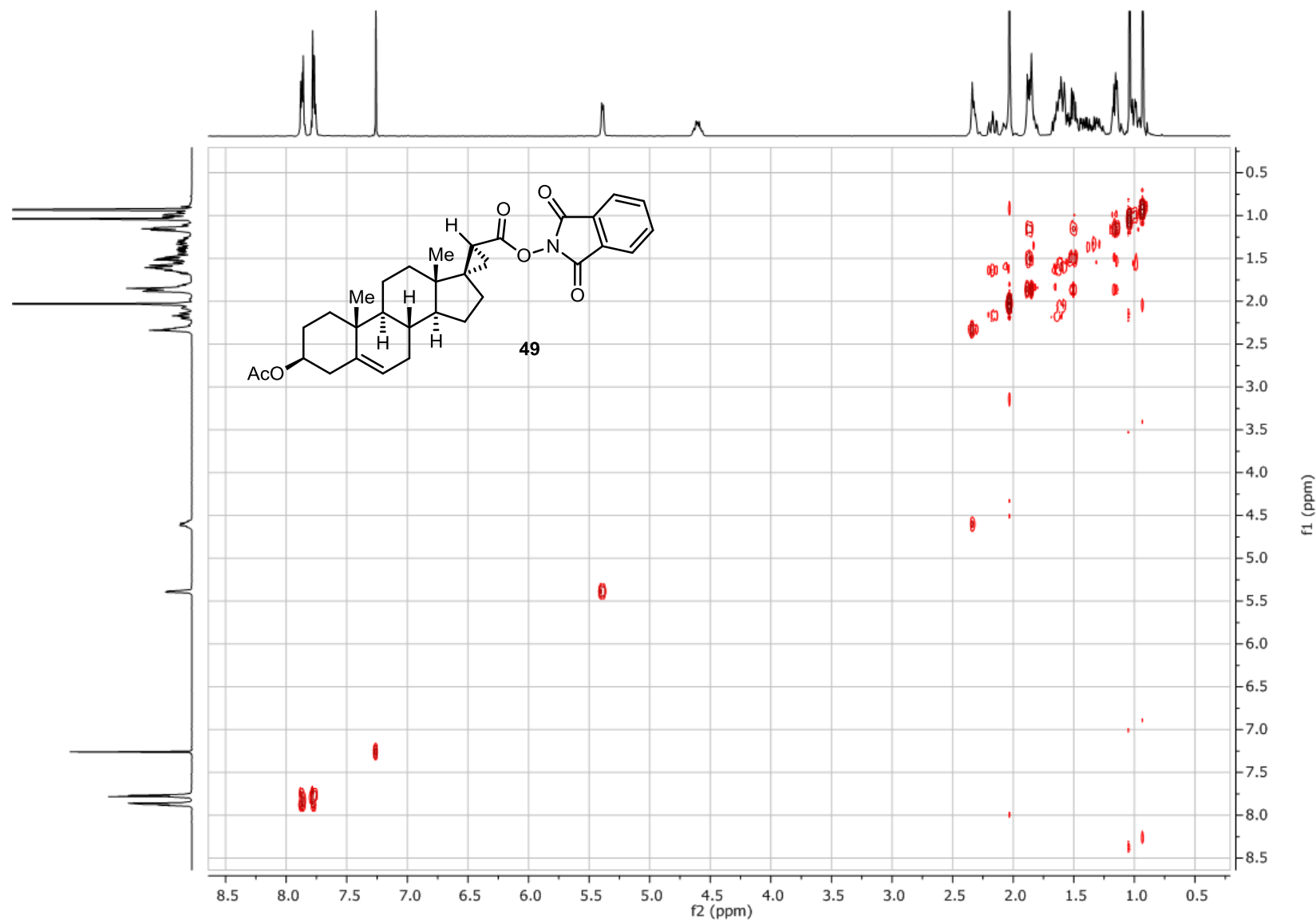
^1H NMR (400 MHz, CDCl_3) for compound **49**



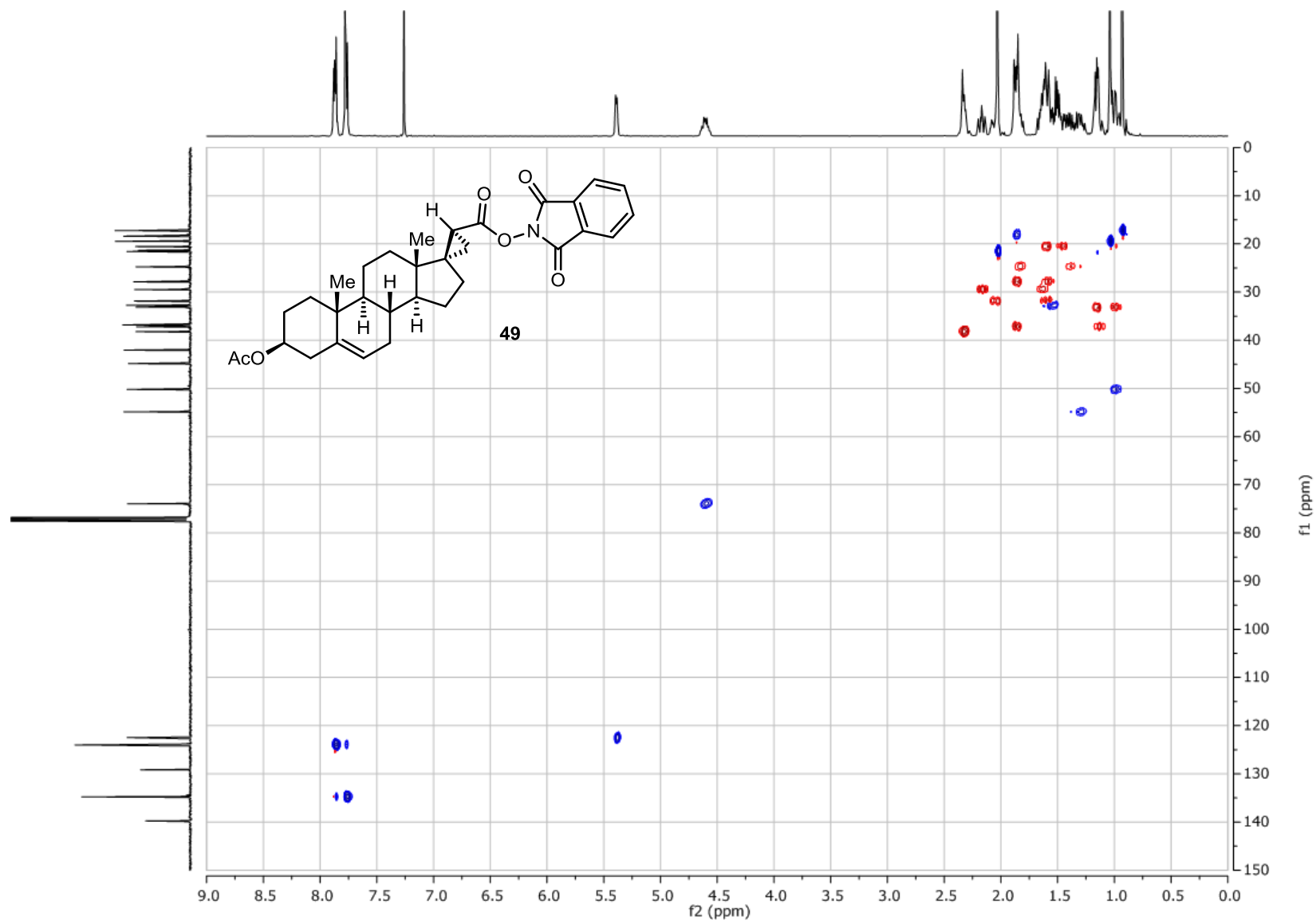
^{13}C NMR (101 MHz, CDCl_3) for compound **49**



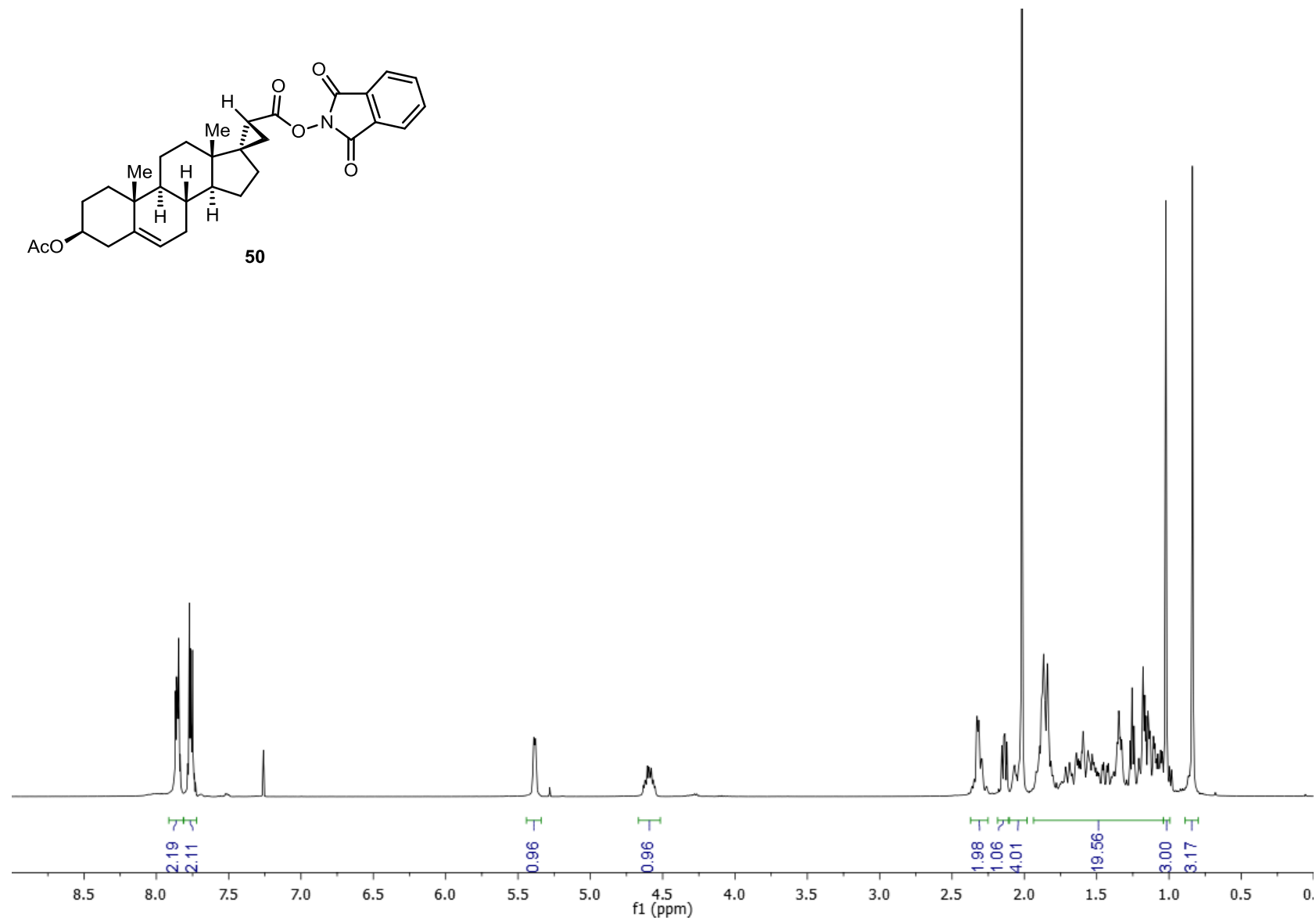
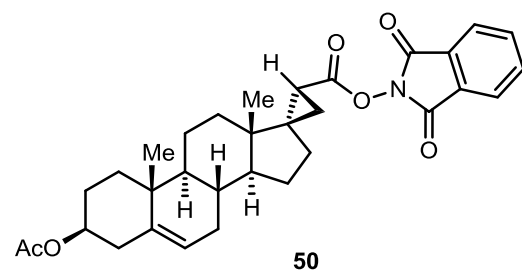
COSY NMR (400 MHz, CDCl_3) for compound **49**



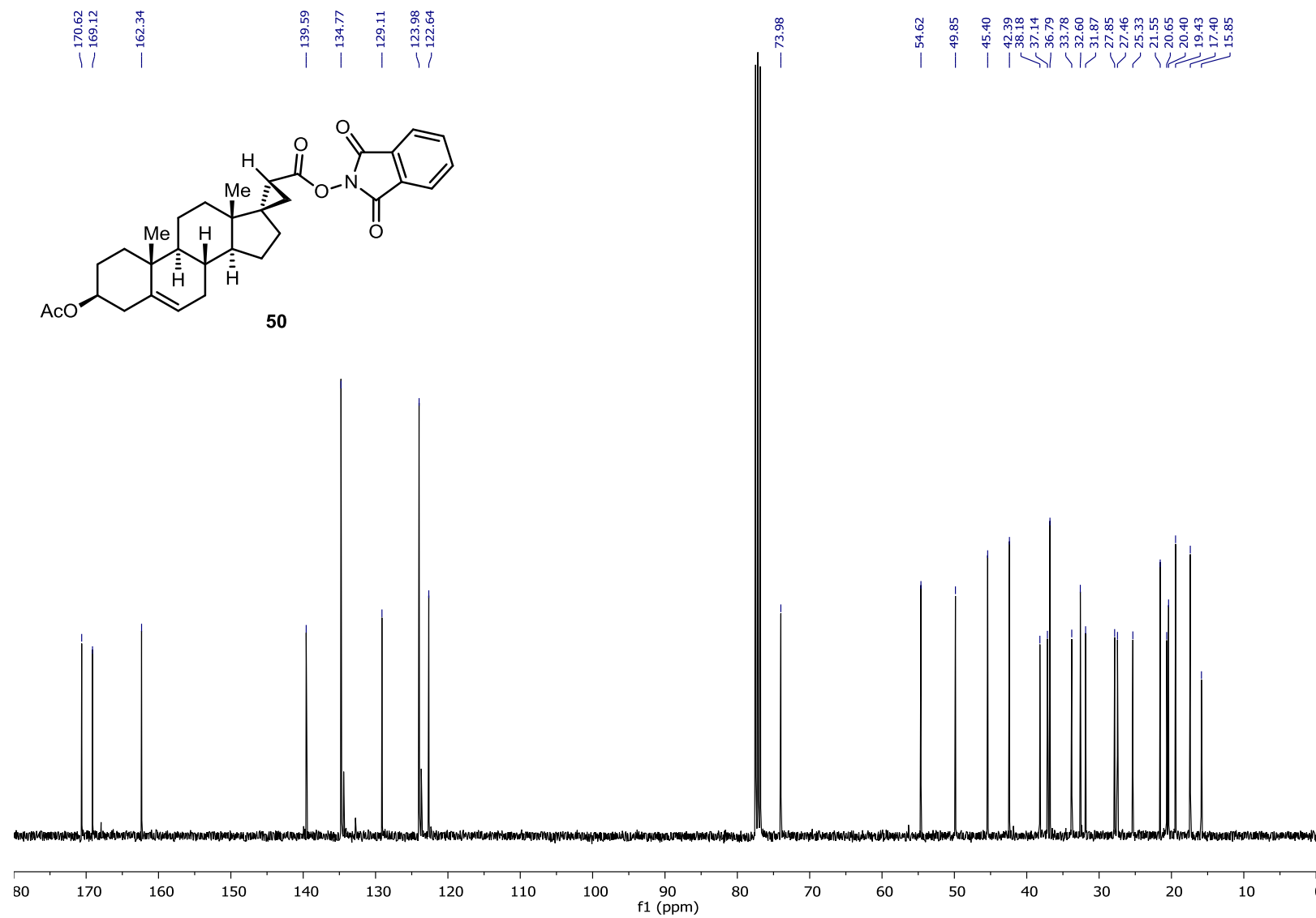
HSQC NMR (400 MHz, CDCl₃) for compound **49**



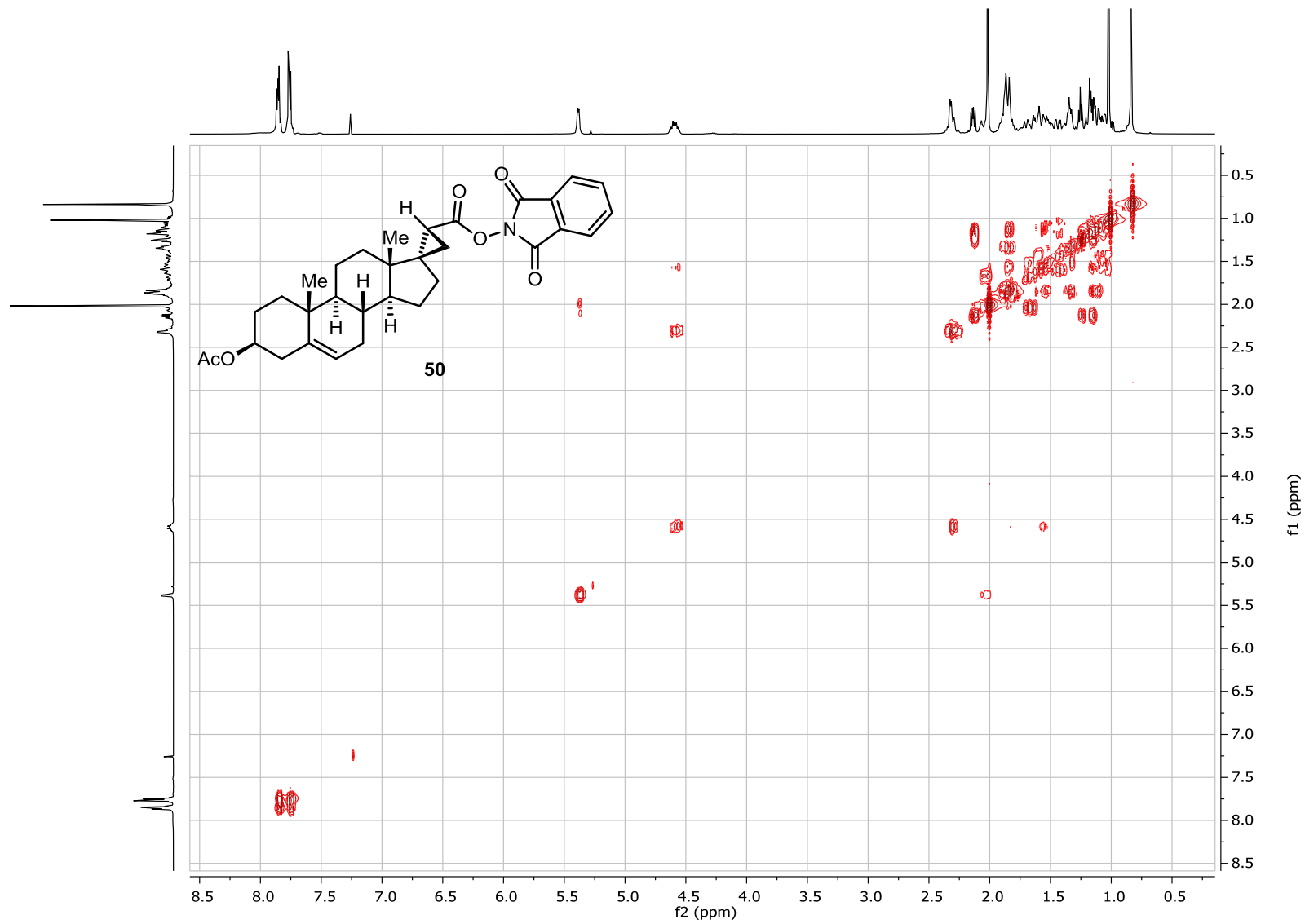
^1H NMR (400 MHz, CDCl_3) for compound **50**



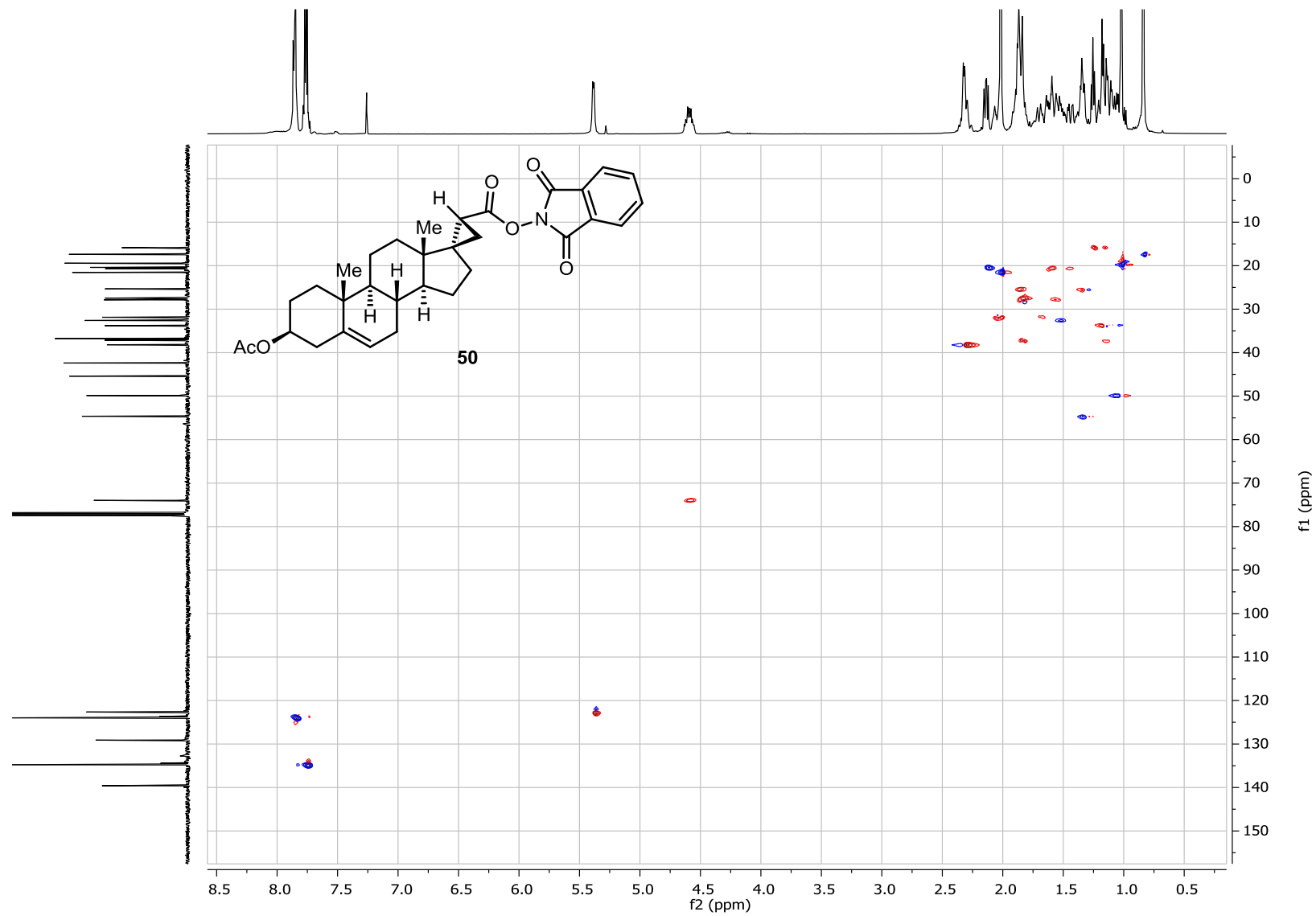
^{13}C NMR (101 MHz, CDCl_3) for compound **50**



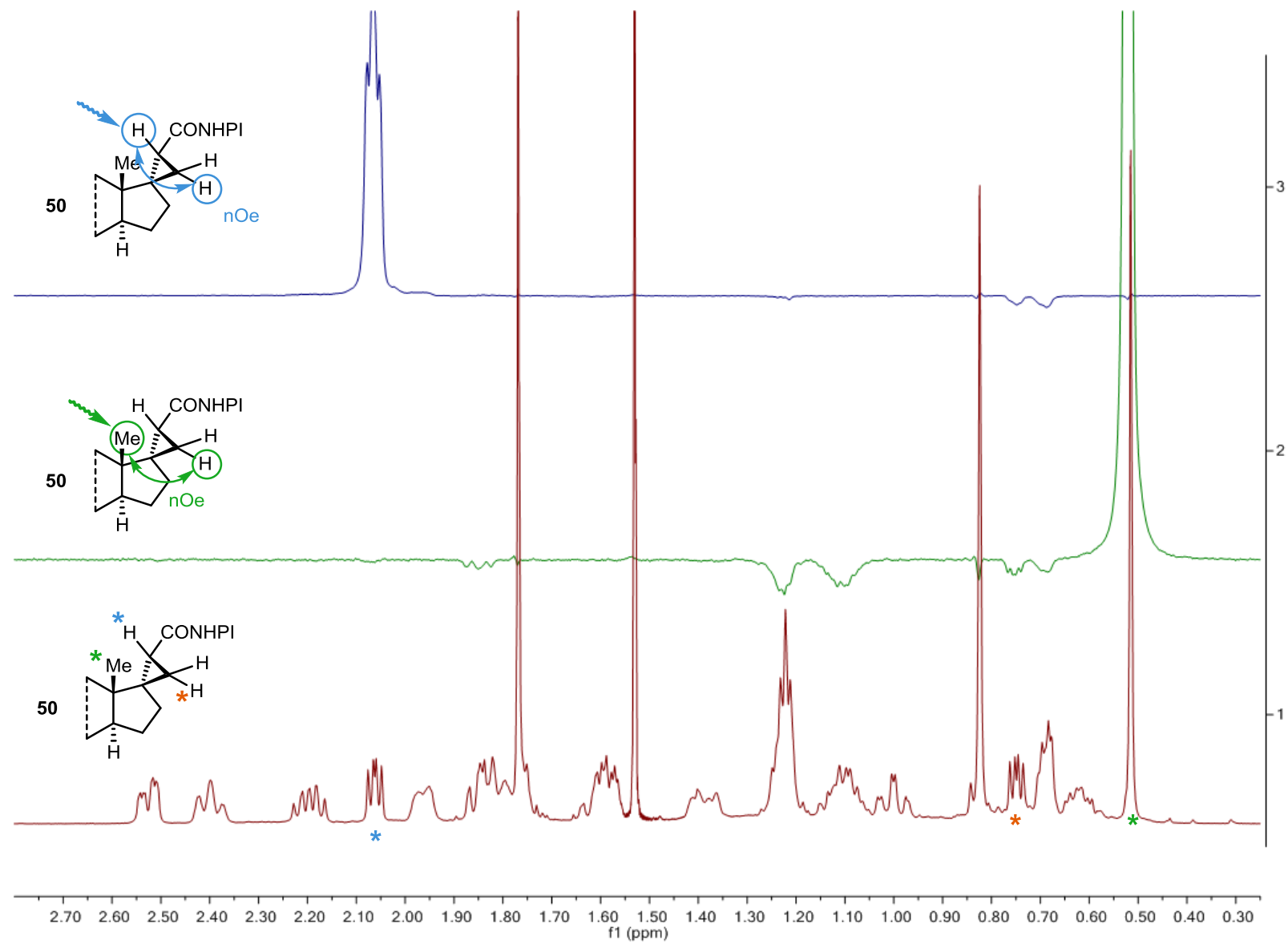
COSY NMR (400 MHz, CDCl₃) for compound **50**



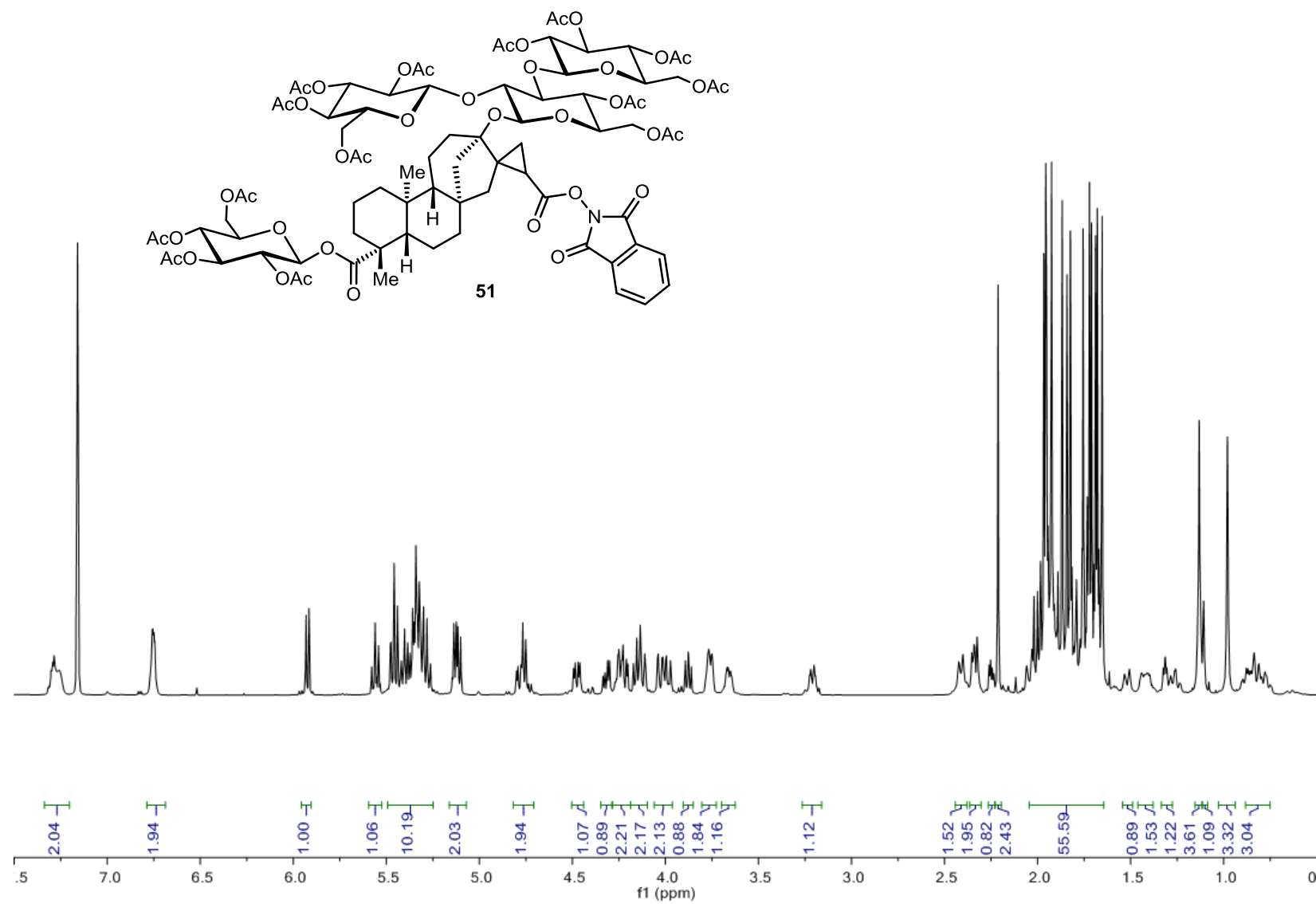
HSQC NMR (400 MHz, CDCl₃) for compound **50**



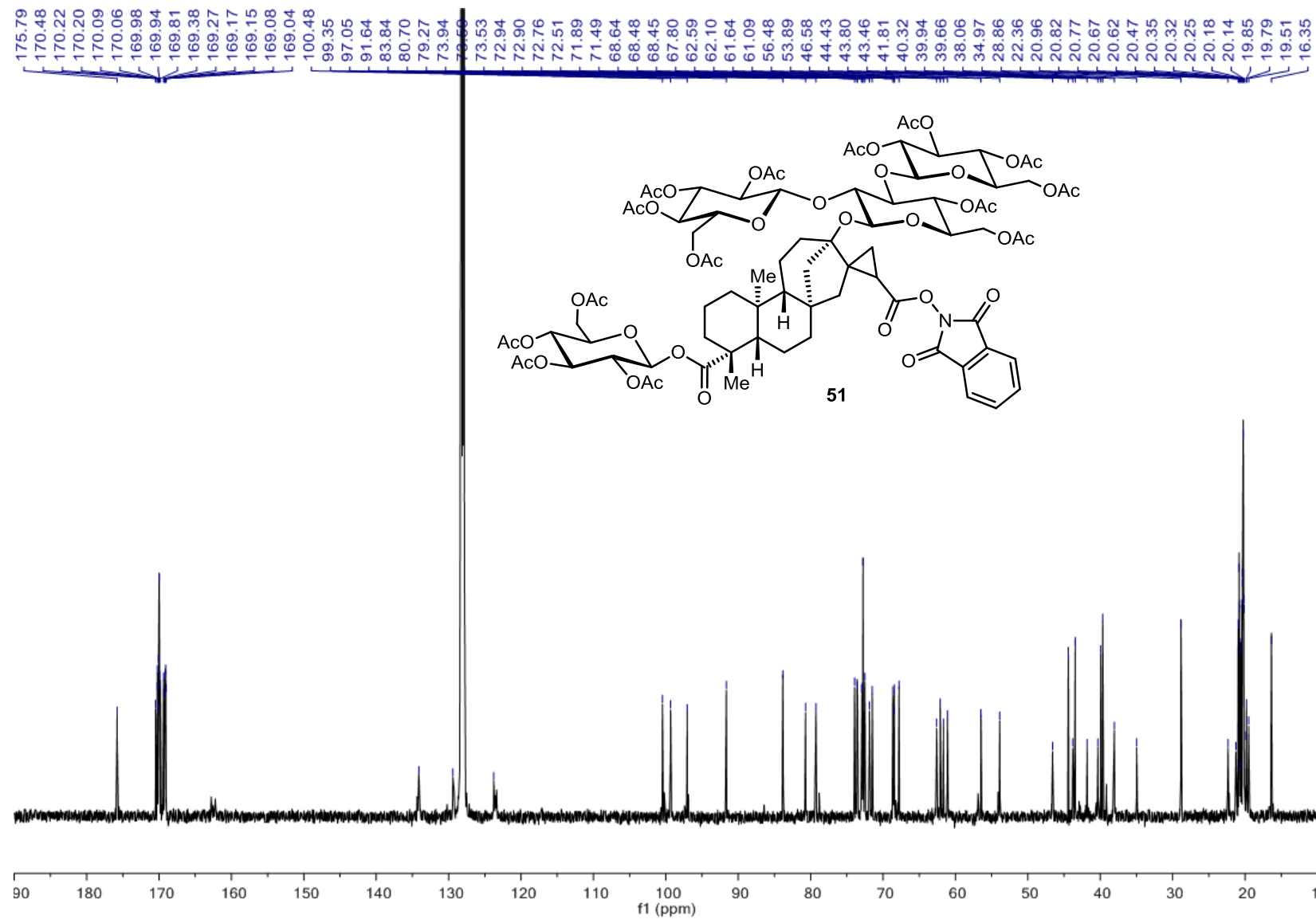
Selective *n*Oe NMR (500 MHz, C_6D_6 , 0 °C) for compound **50**



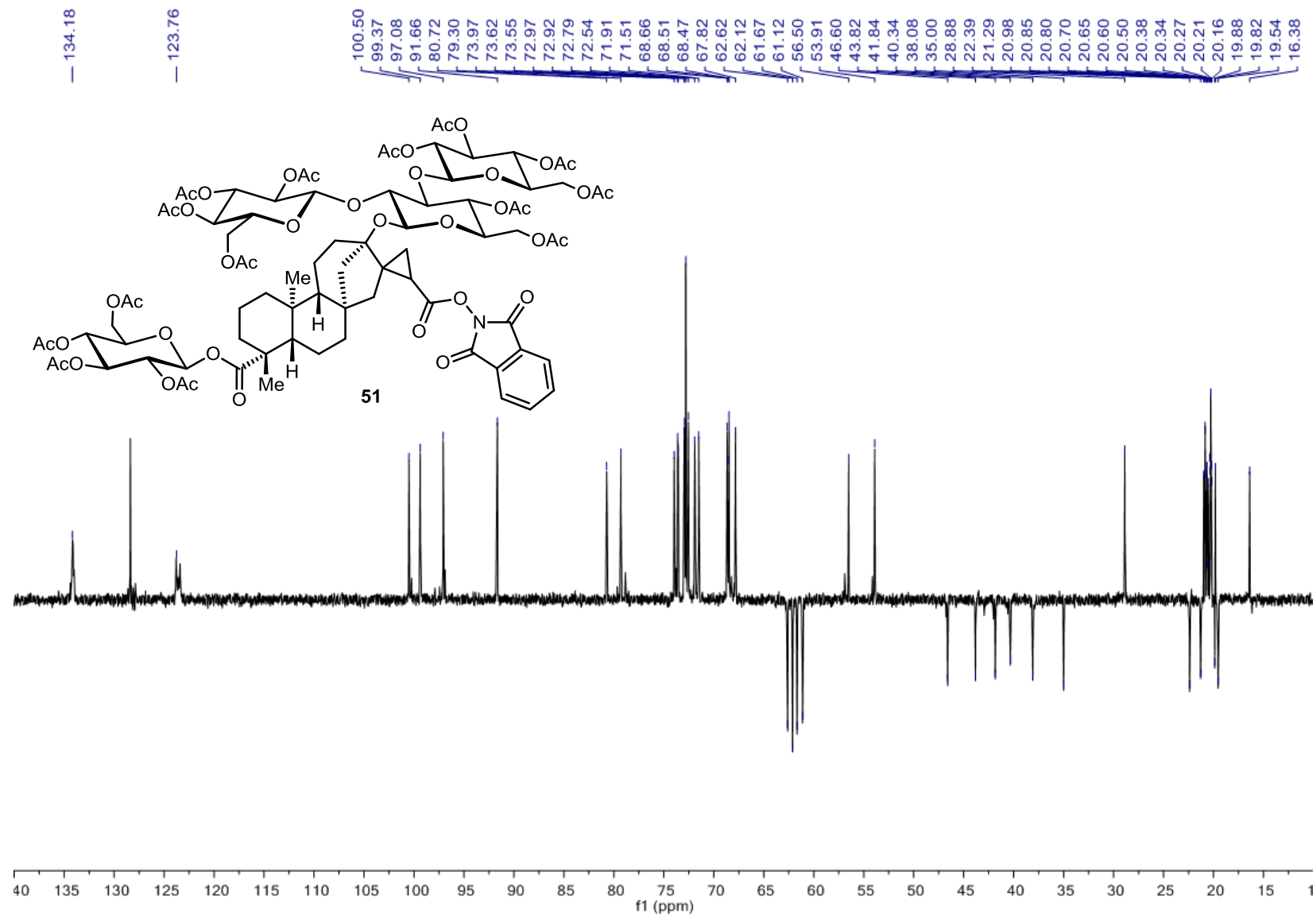
^1H NMR (500 MHz, C_6D_6) for compound **51**



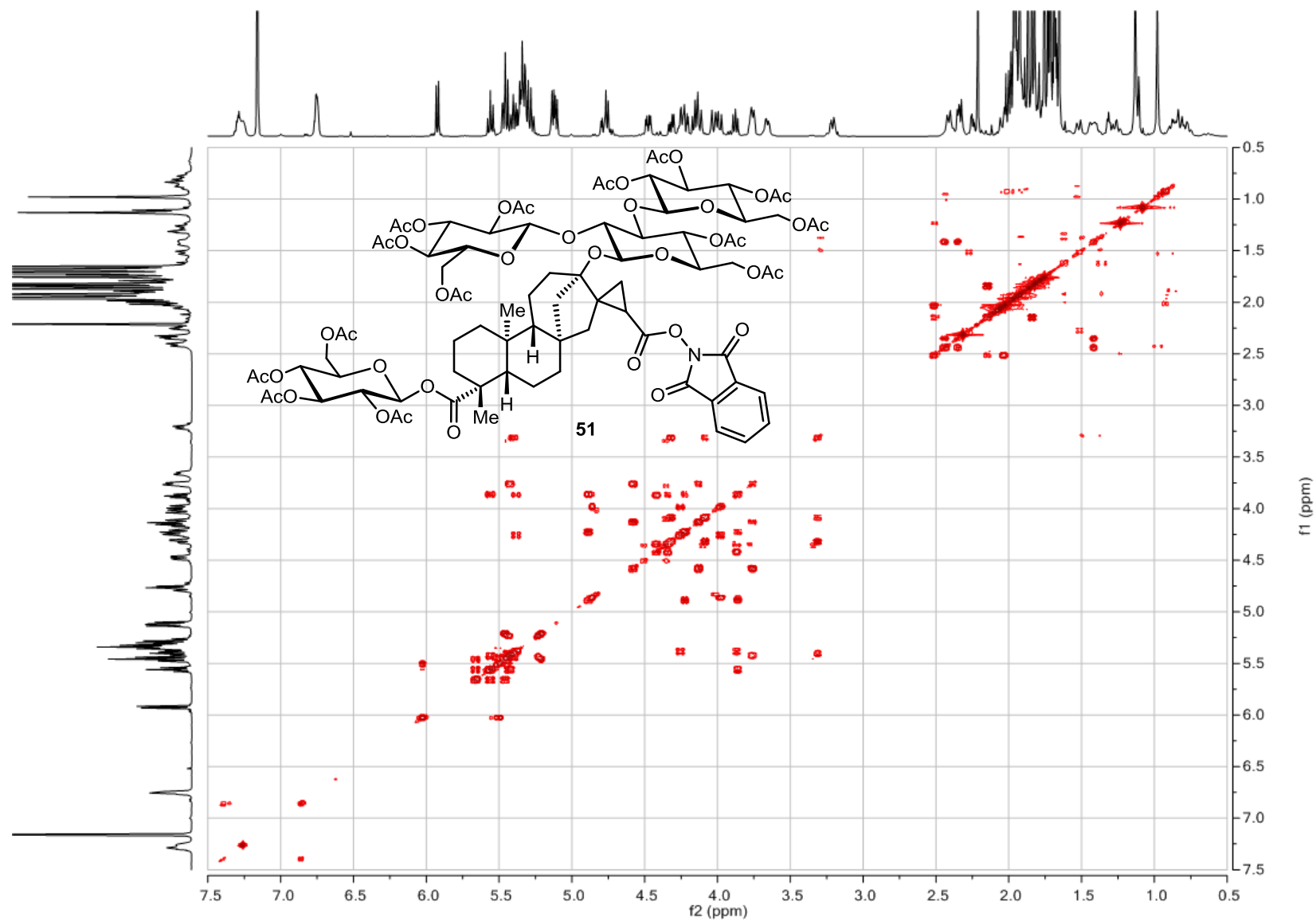
^{13}C NMR (126 MHz, C_6D_6) for compound **51**



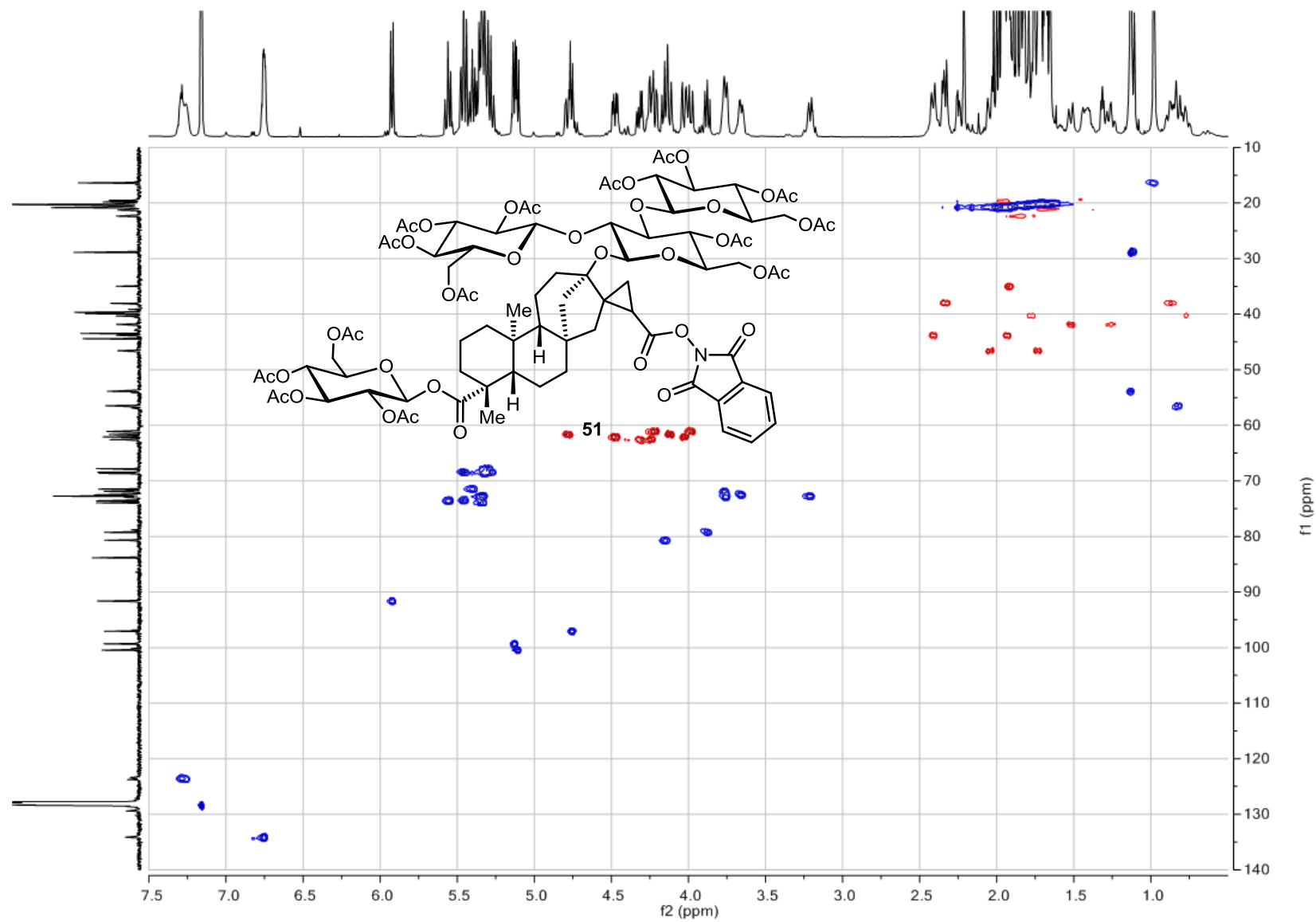
DEPT 135° NMR (126 MHz, C₆D₆) for compound **51**



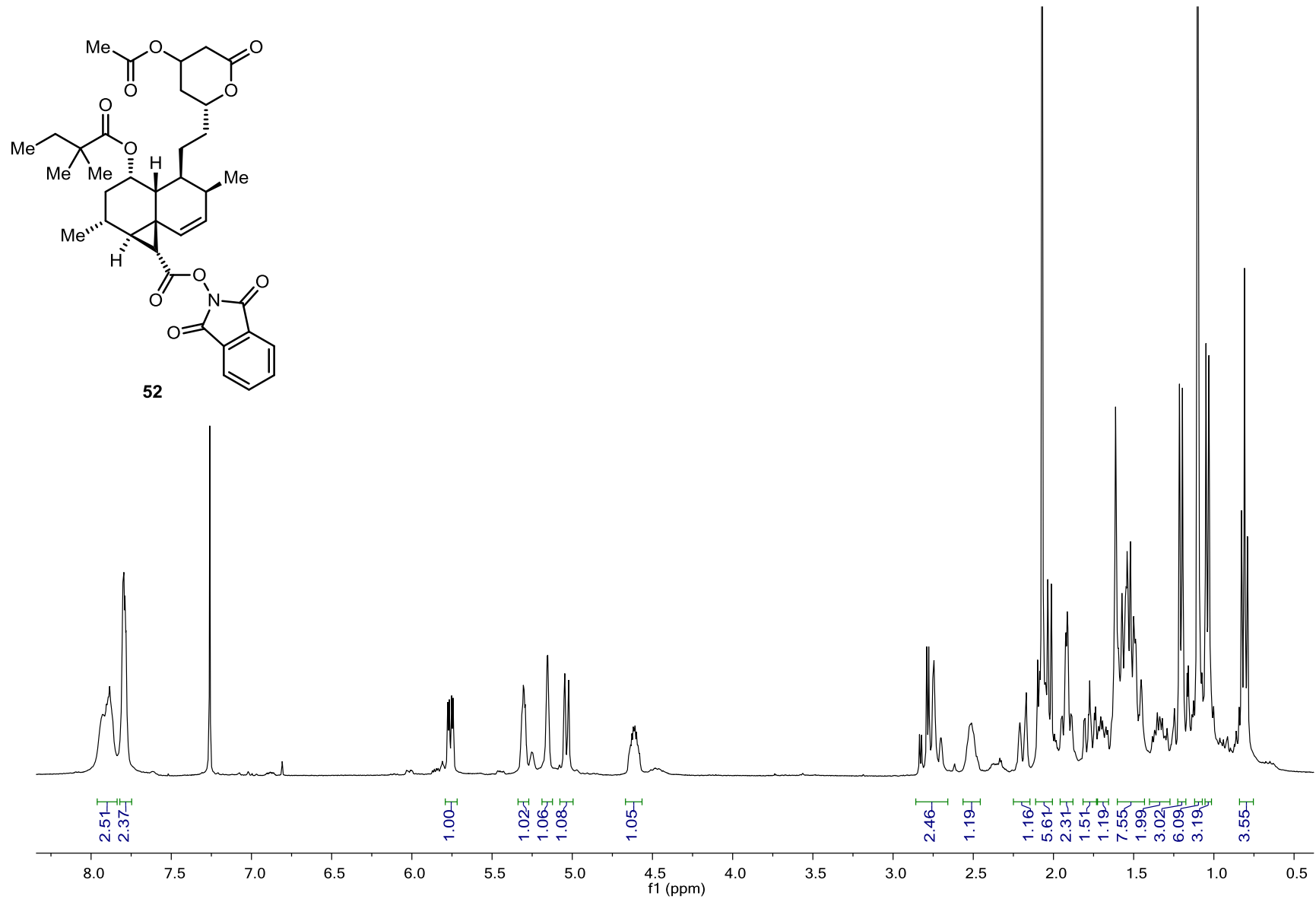
COSY NMR (500 MHz, C_6D_6) for compound **51**



HSQC NMR (500 MHz, C₆D₆) for compound **51**

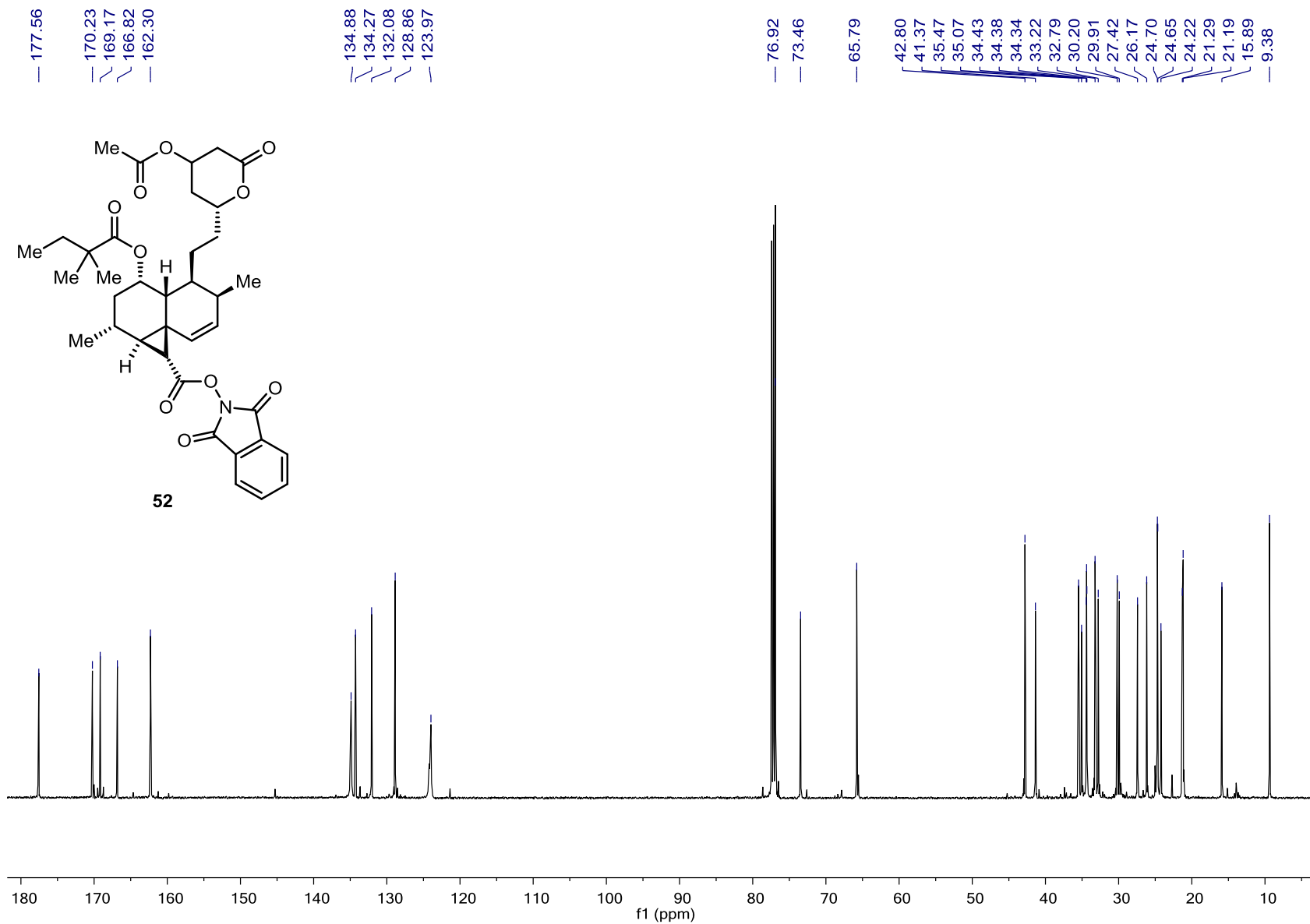


^1H NMR (400 MHz, CDCl_3) for compound **52**

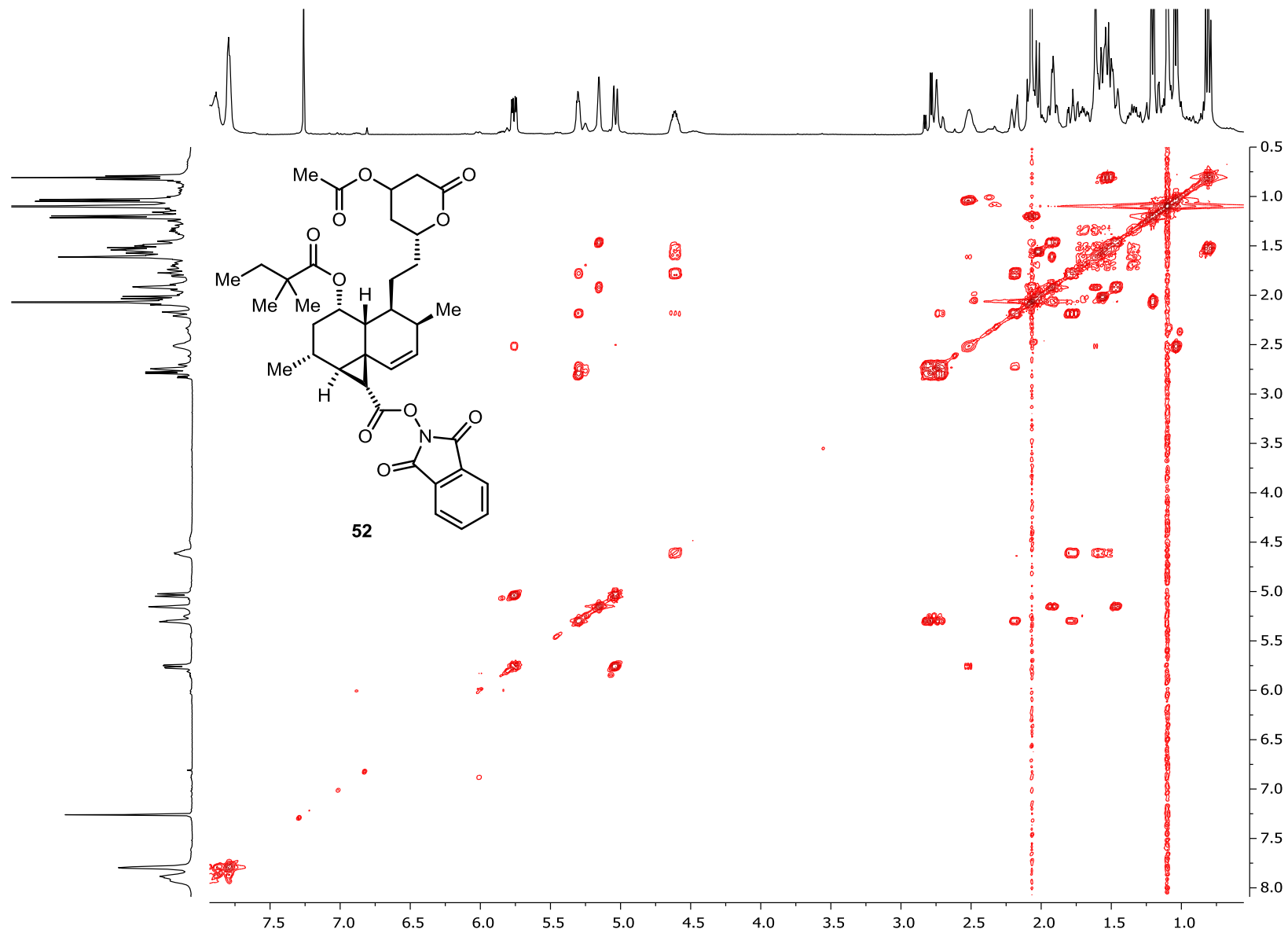


S265

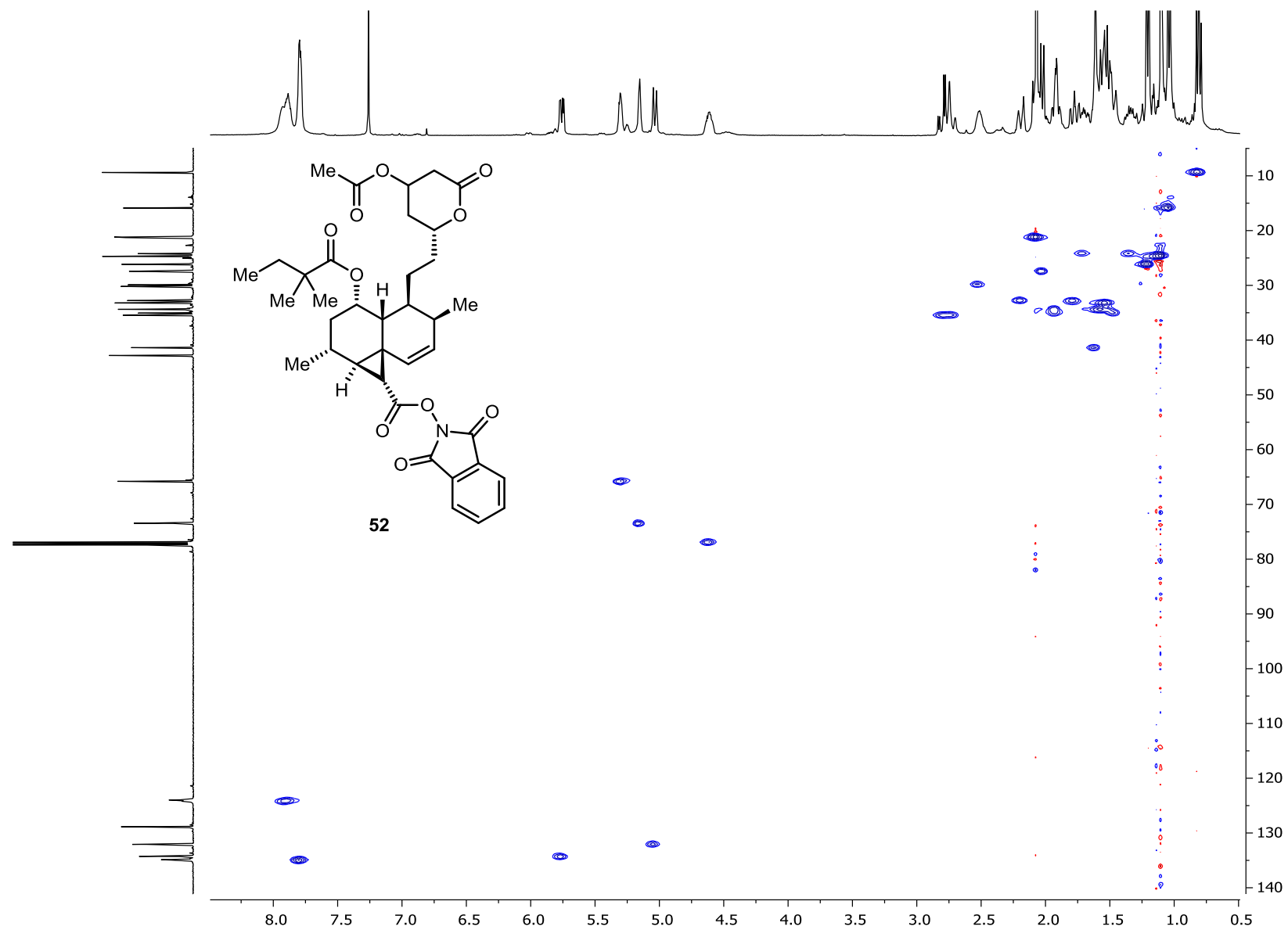
^{13}C NMR (101 MHz, CDCl_3) for compound **52**



COSY NMR (400 MHz, CDCl₃) for compound 52

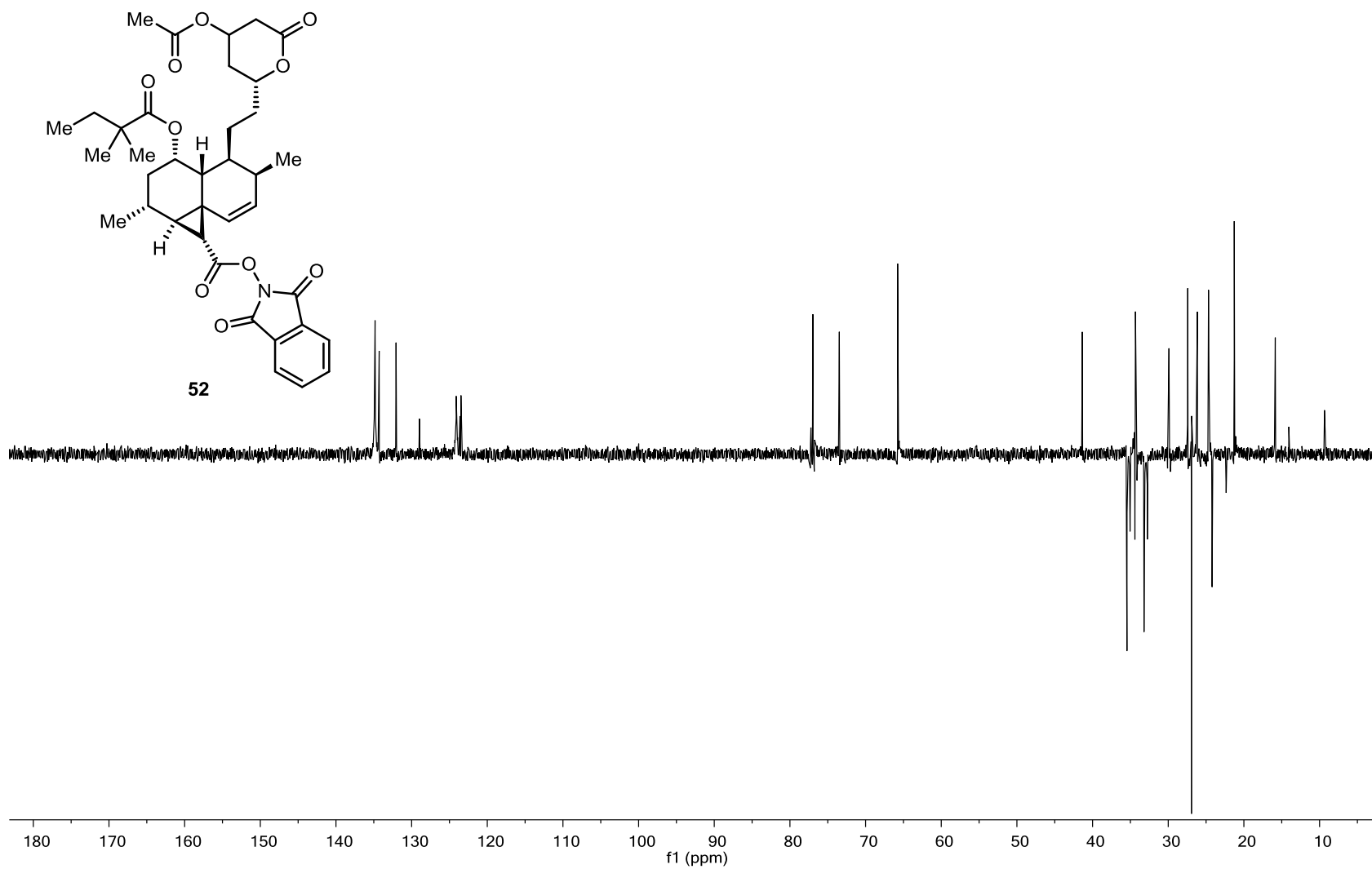


HSQC NMR (400 MHz, CDCl₃) for compound 52



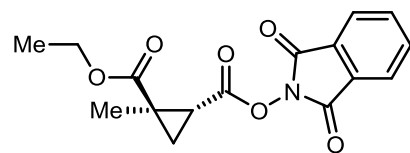
S268

DEPT 135° NMR (400 MHz, CDCl₃) for compound 52

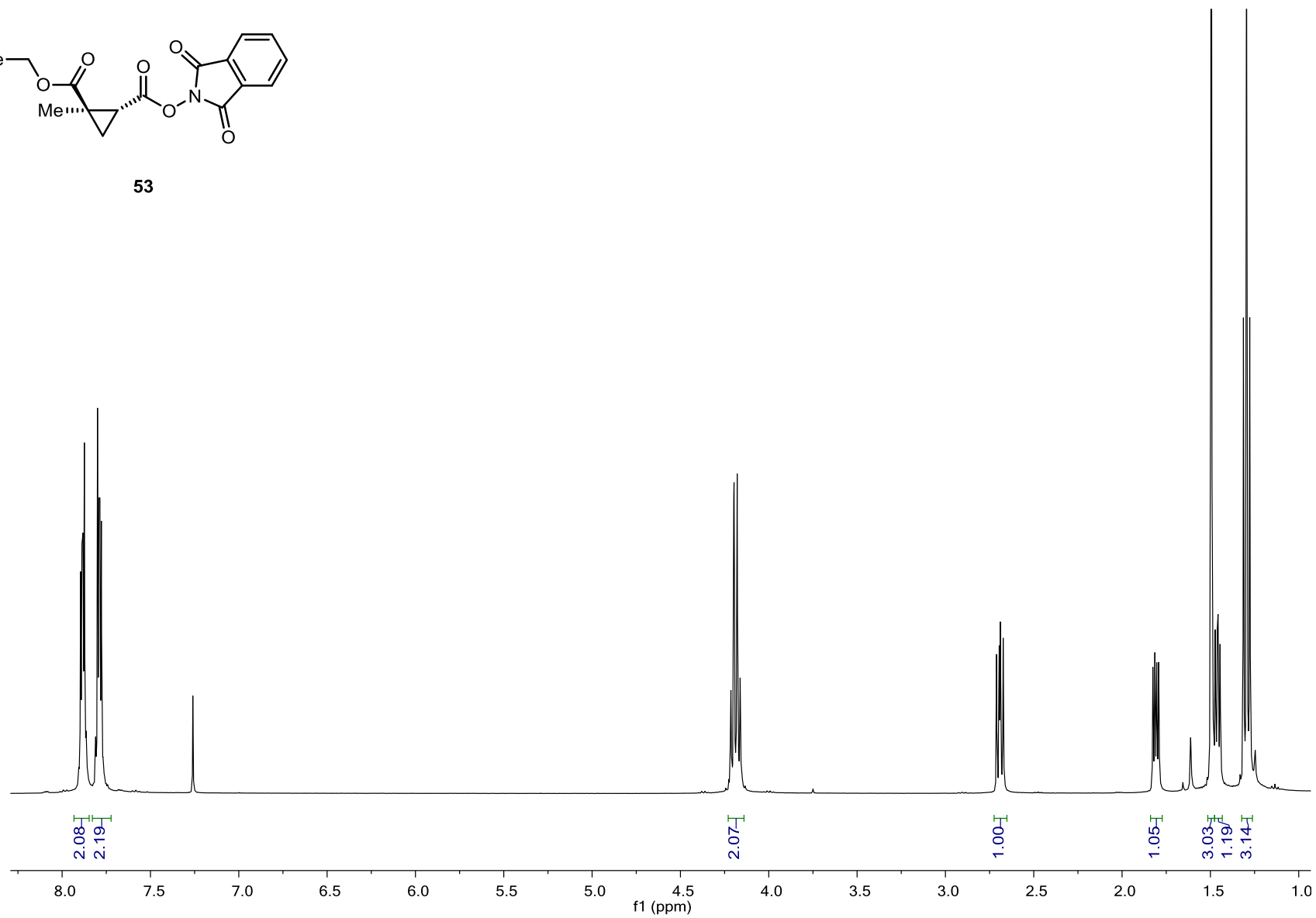


S269

^1H NMR (400 MHz, CDCl_3) for compound 53

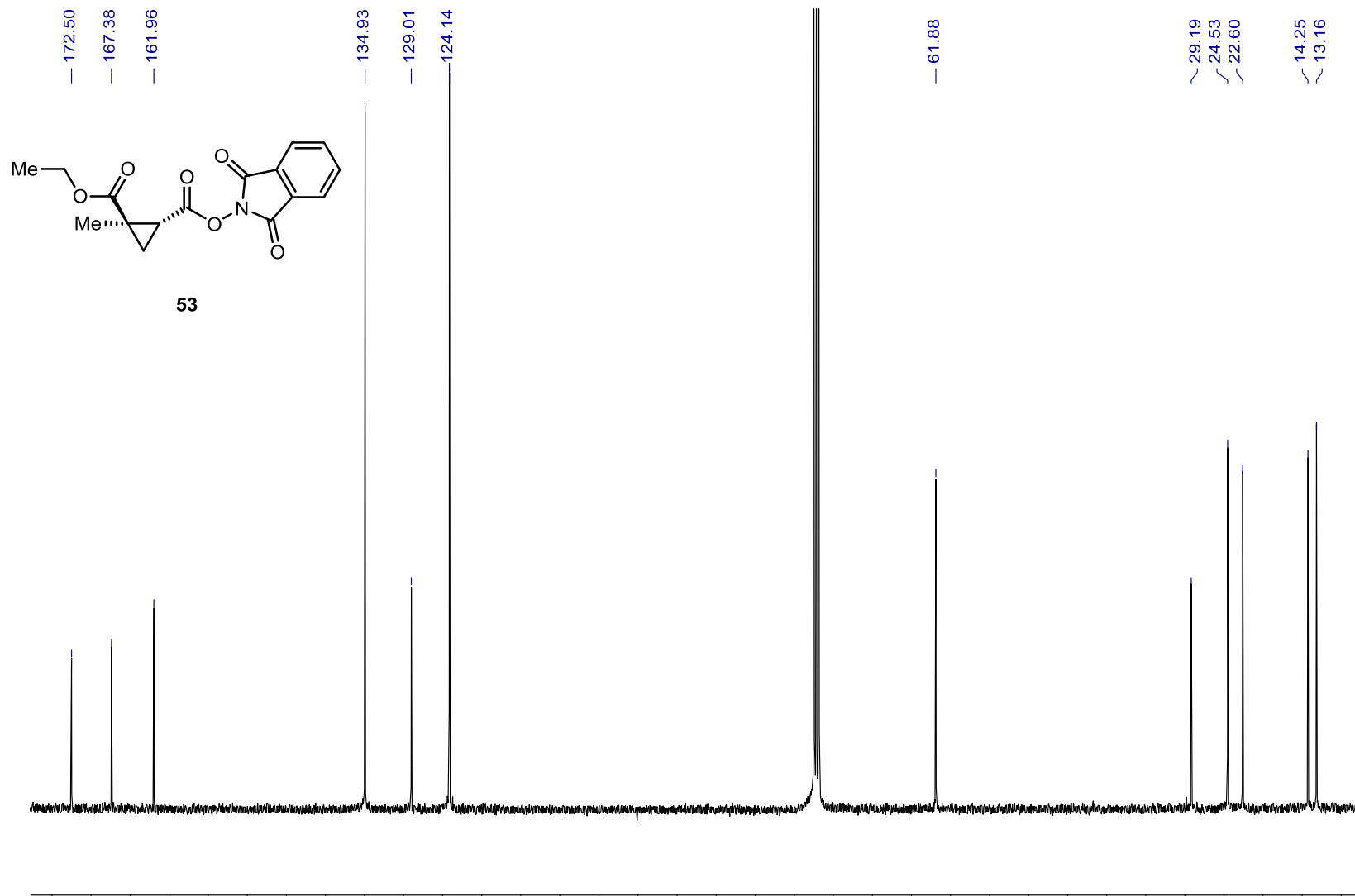


53

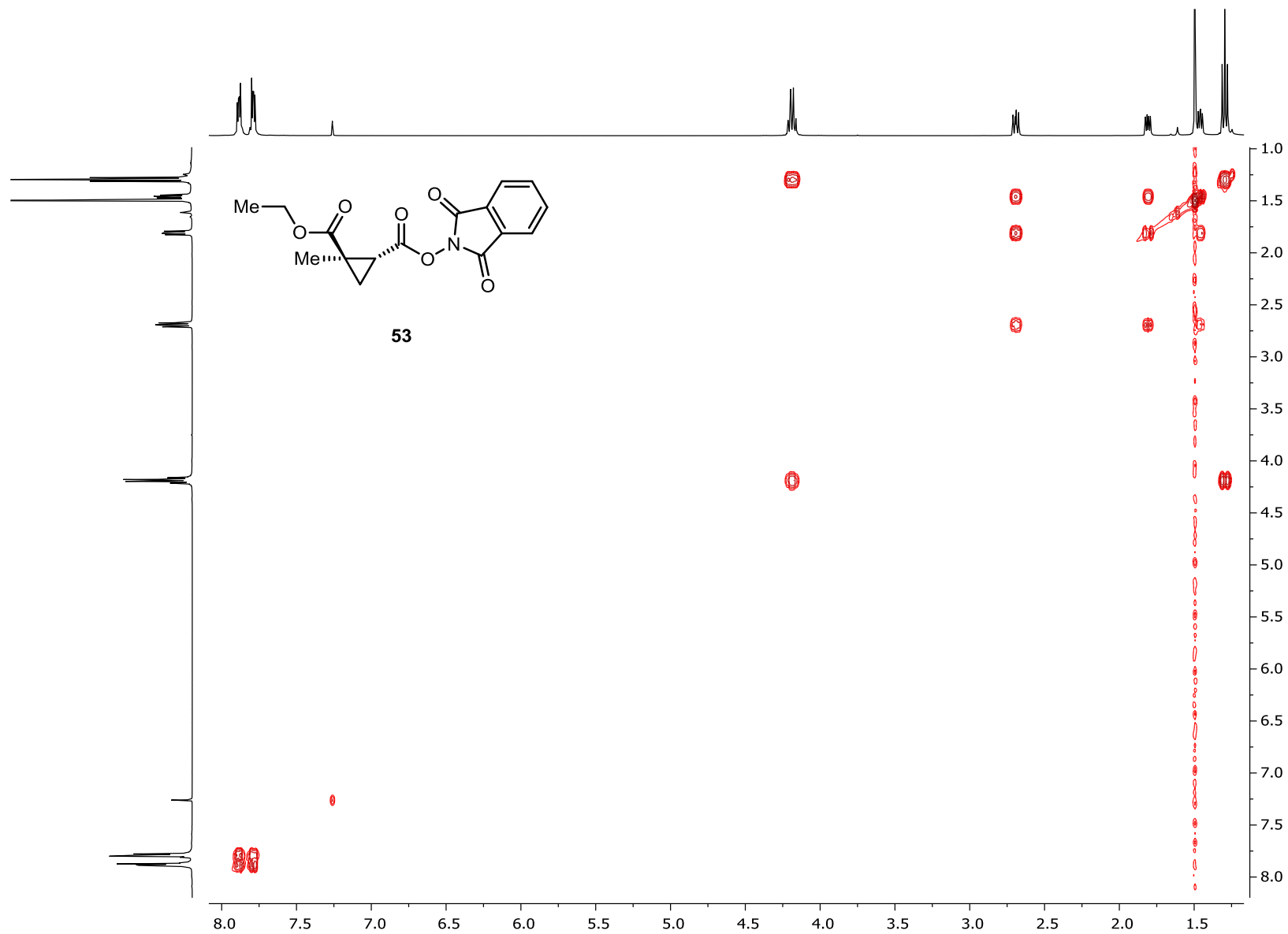


S270

^{13}C NMR (101 MHz, CDCl_3) for compound **53**

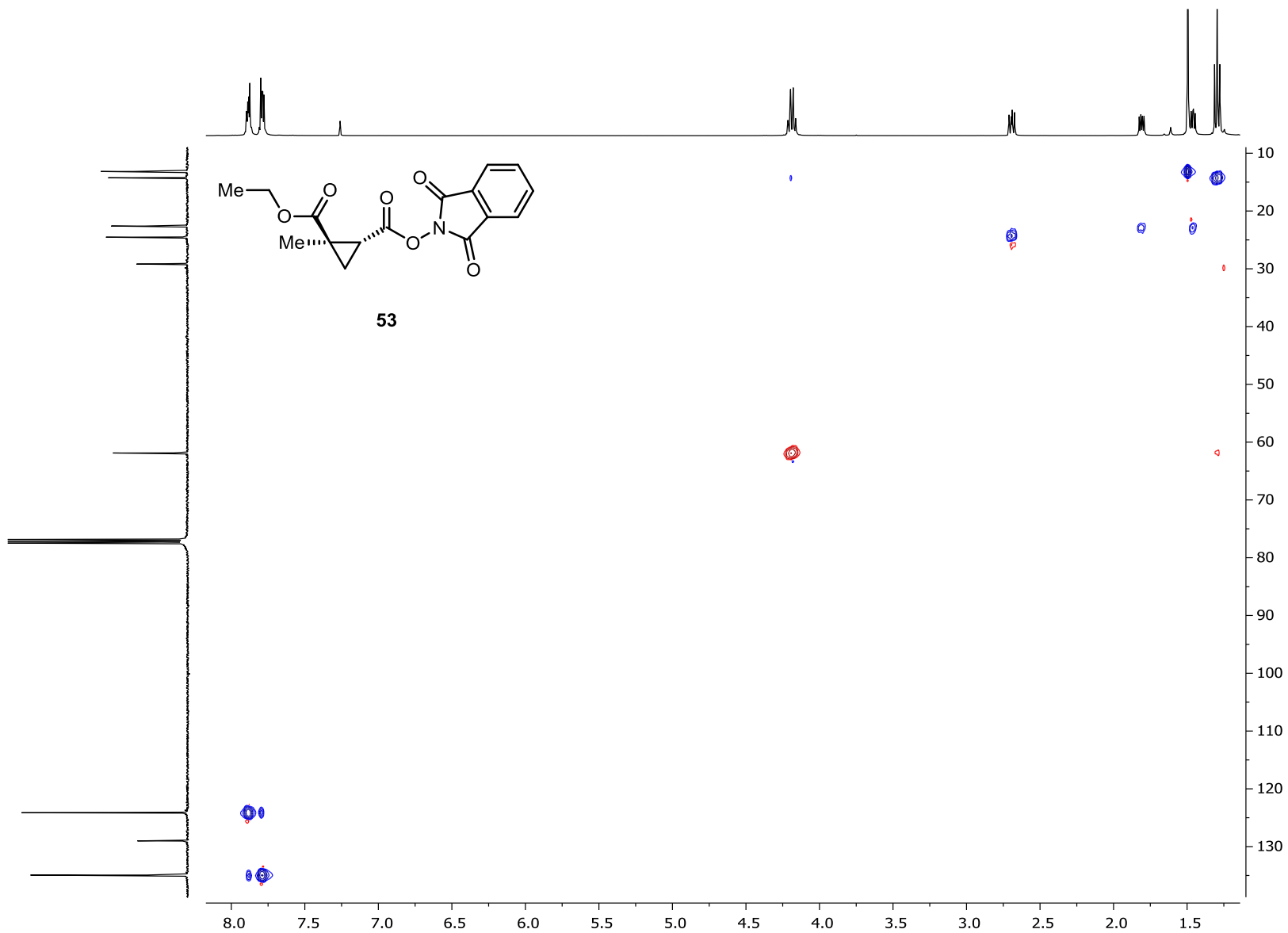


COSY NMR (400 MHz, CDCl₃) for compound 53



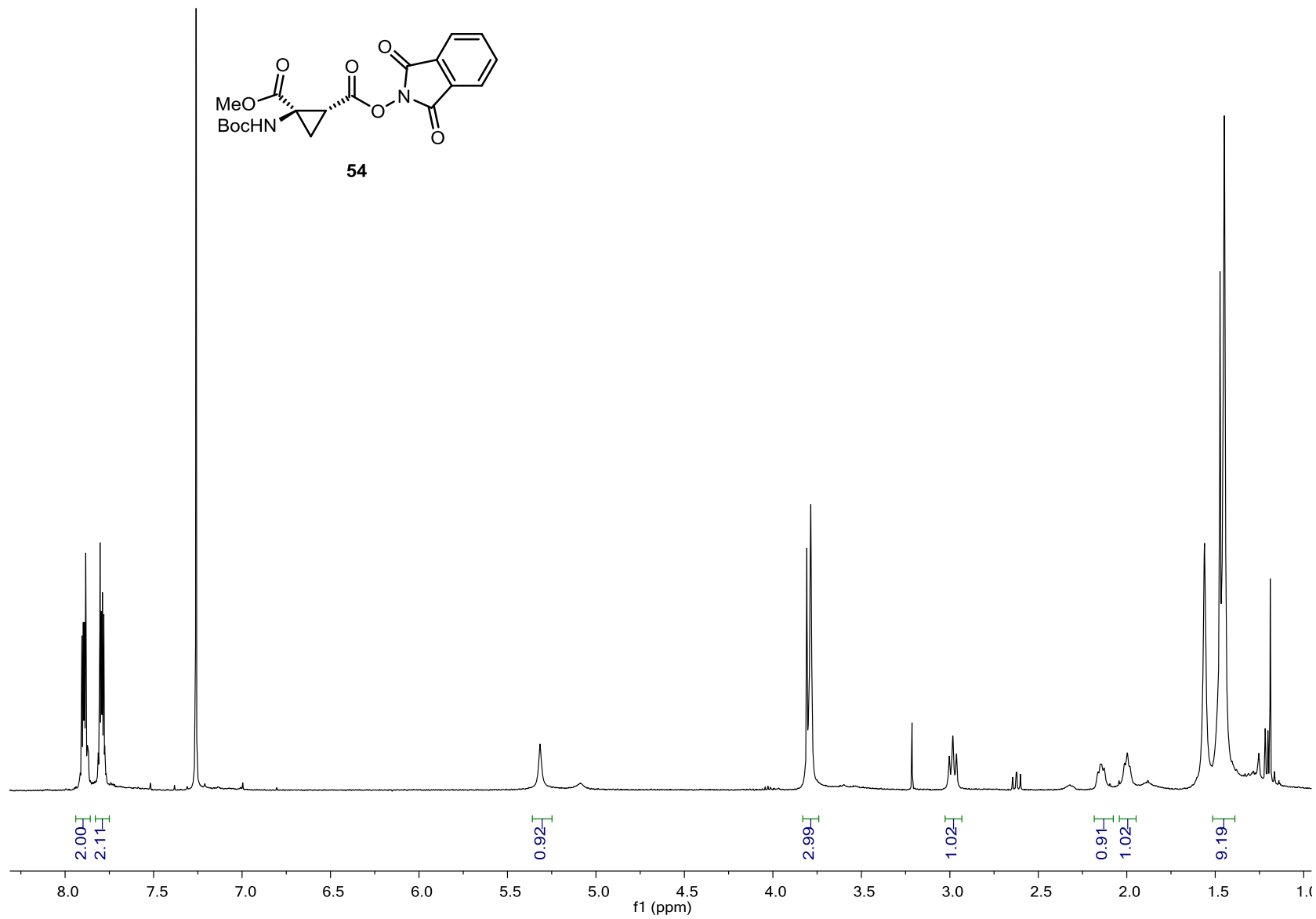
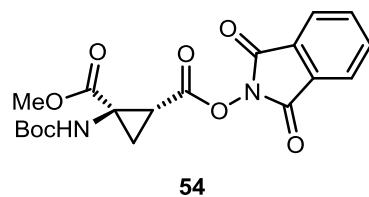
S272

HSQC NMR (400 MHz, CDCl₃) for compound **53**

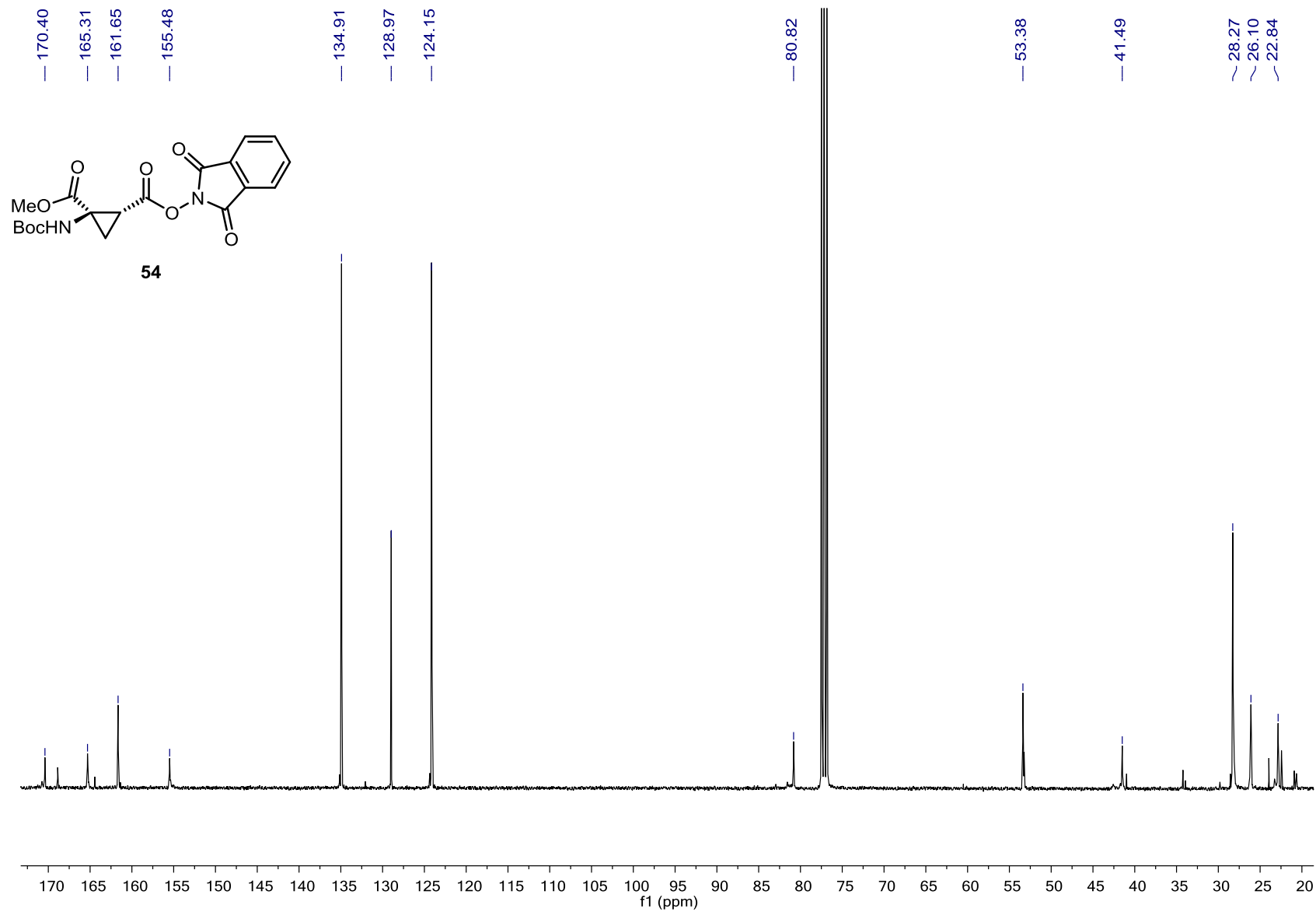


S273

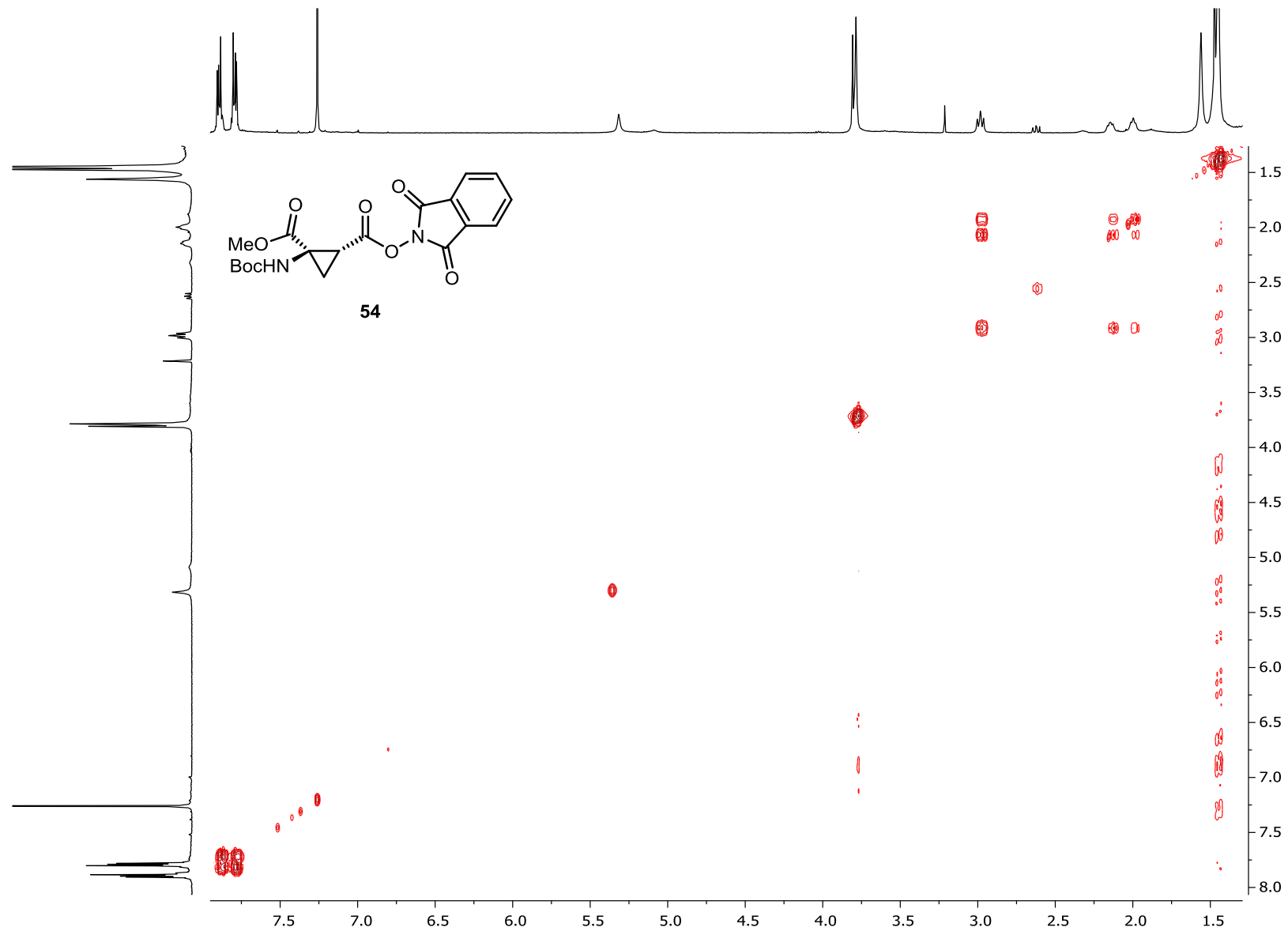
^1H NMR (400 MHz, CDCl_3) for compound **54**



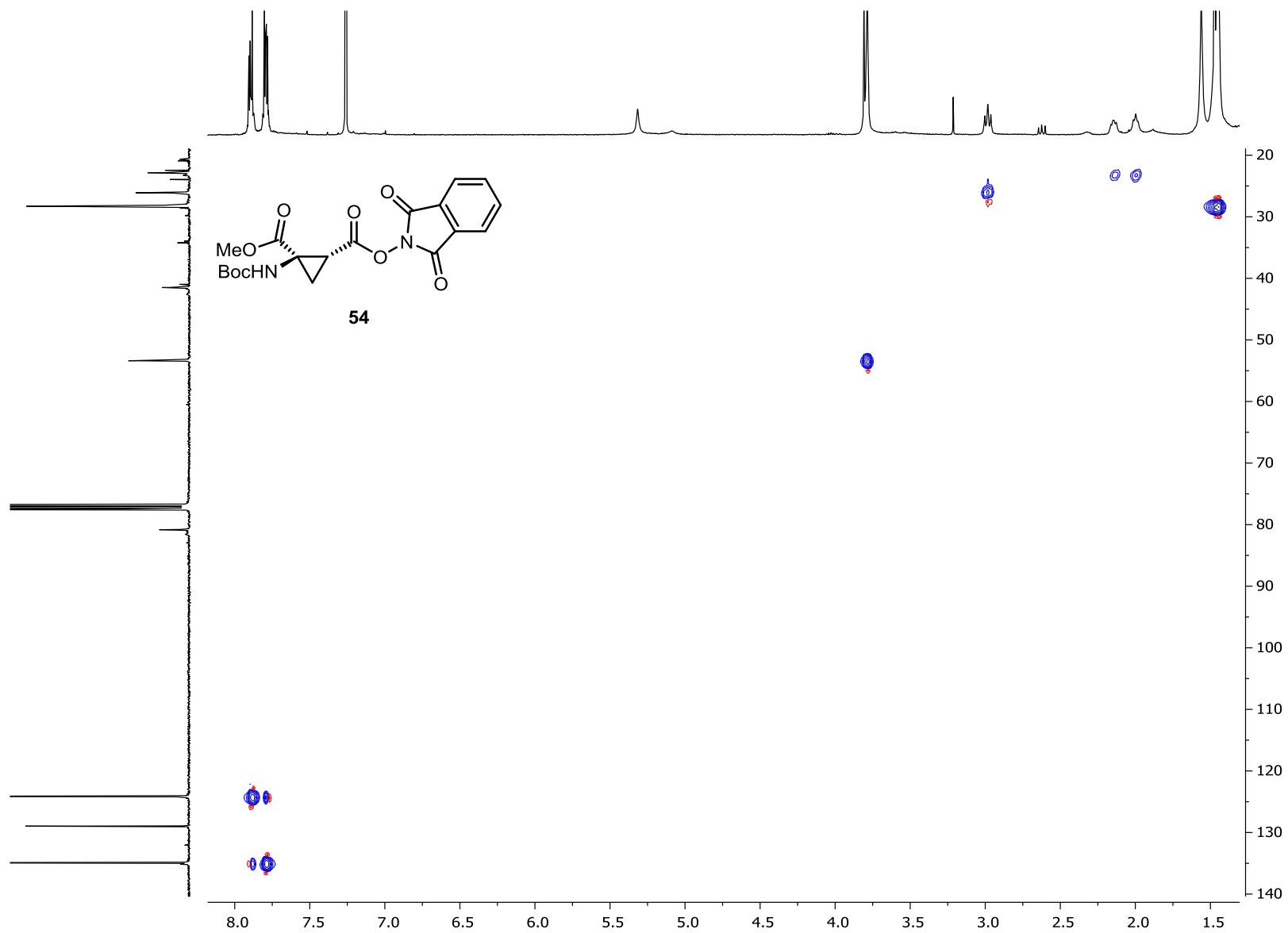
^{13}C NMR (101 MHz, CDCl_3) for compound **54**



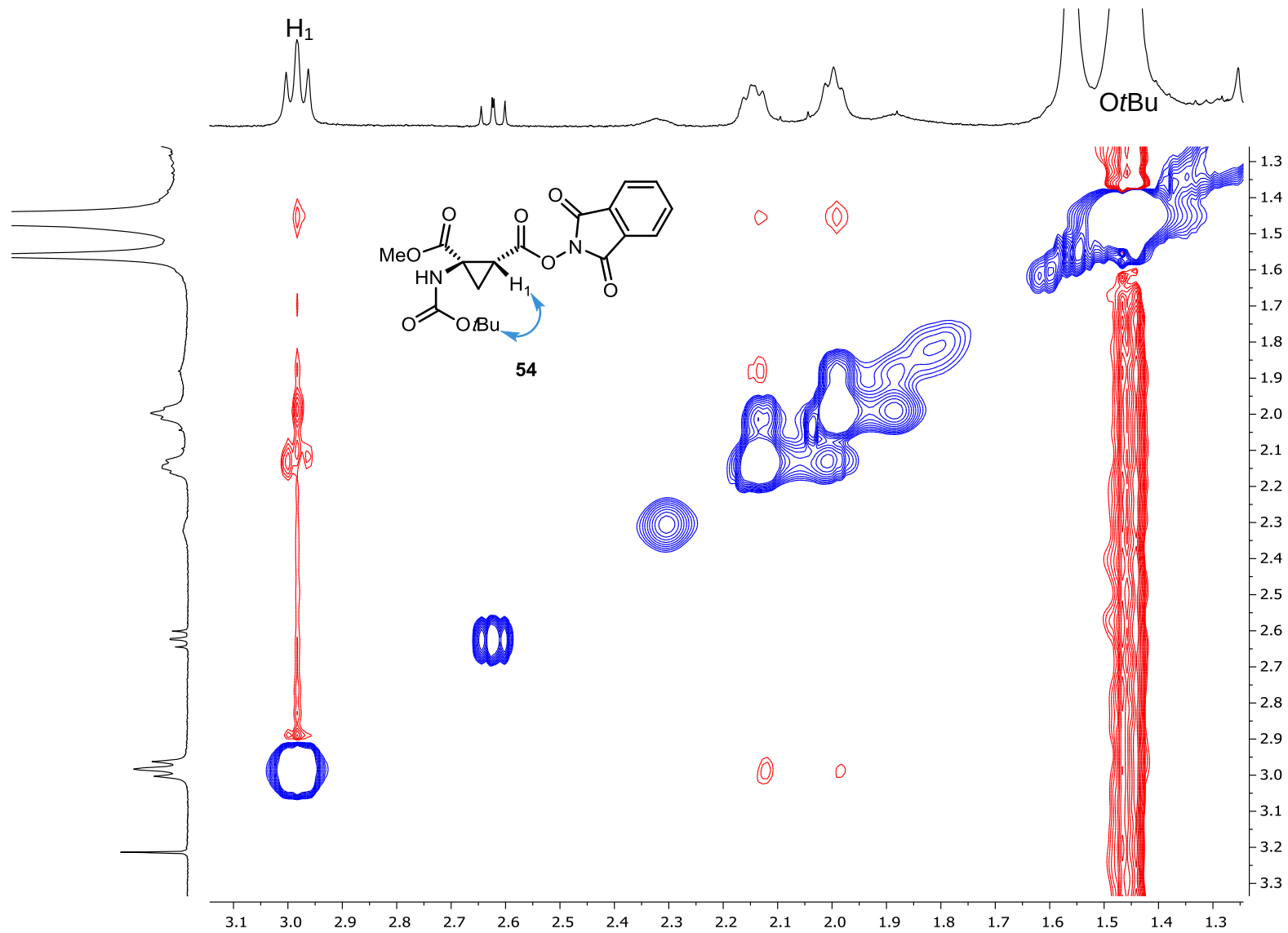
COSY NMR (400 MHz, CDCl₃) for compound **54**



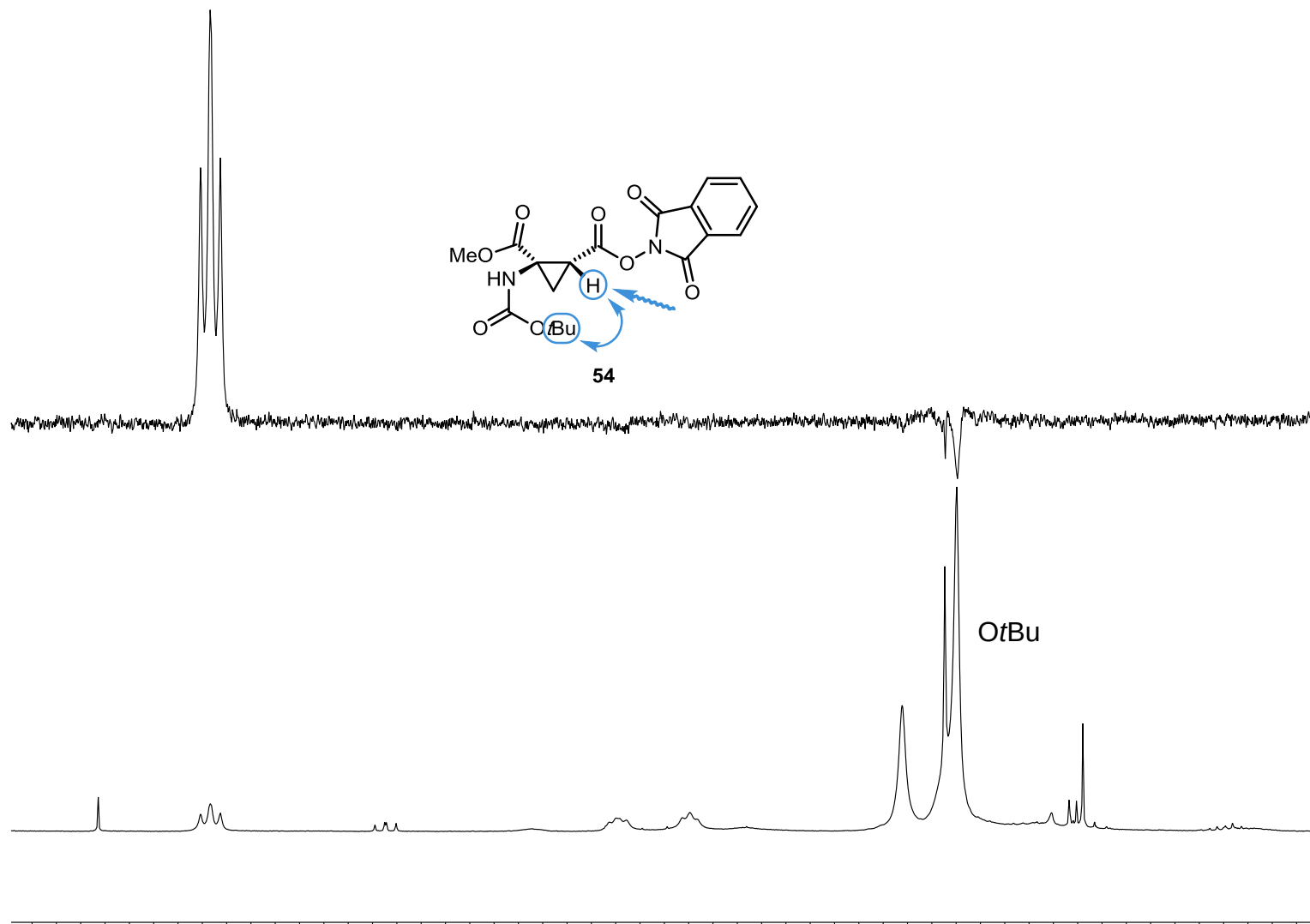
HSQC NMR (400 MHz, CDCl₃) for compound **54**



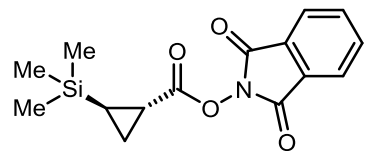
NOESY NMR (400 MHz, CDCl₃) for compound **54**



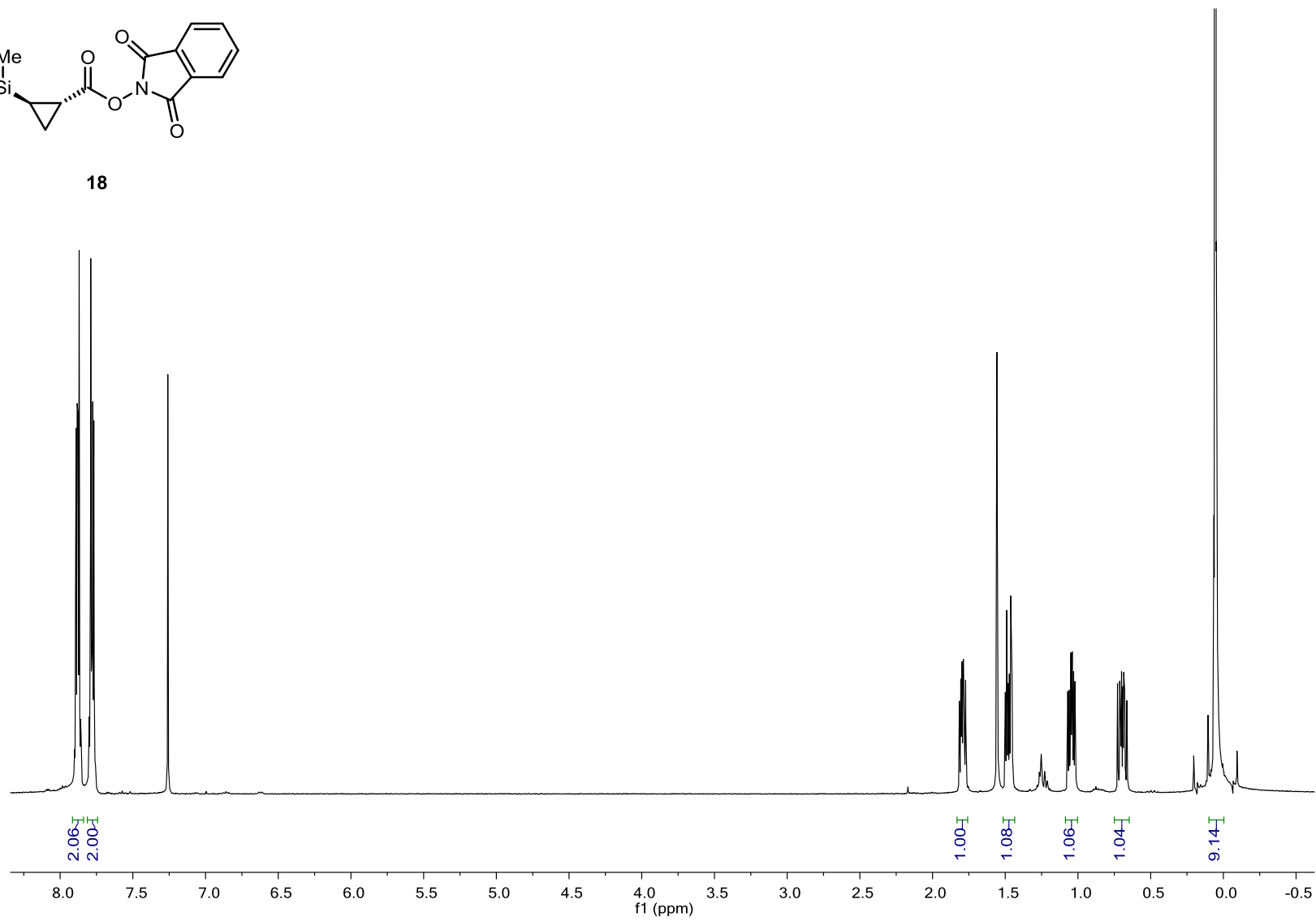
1D NOESY NMR (400 MHz, CDCl_3) for compound **54**



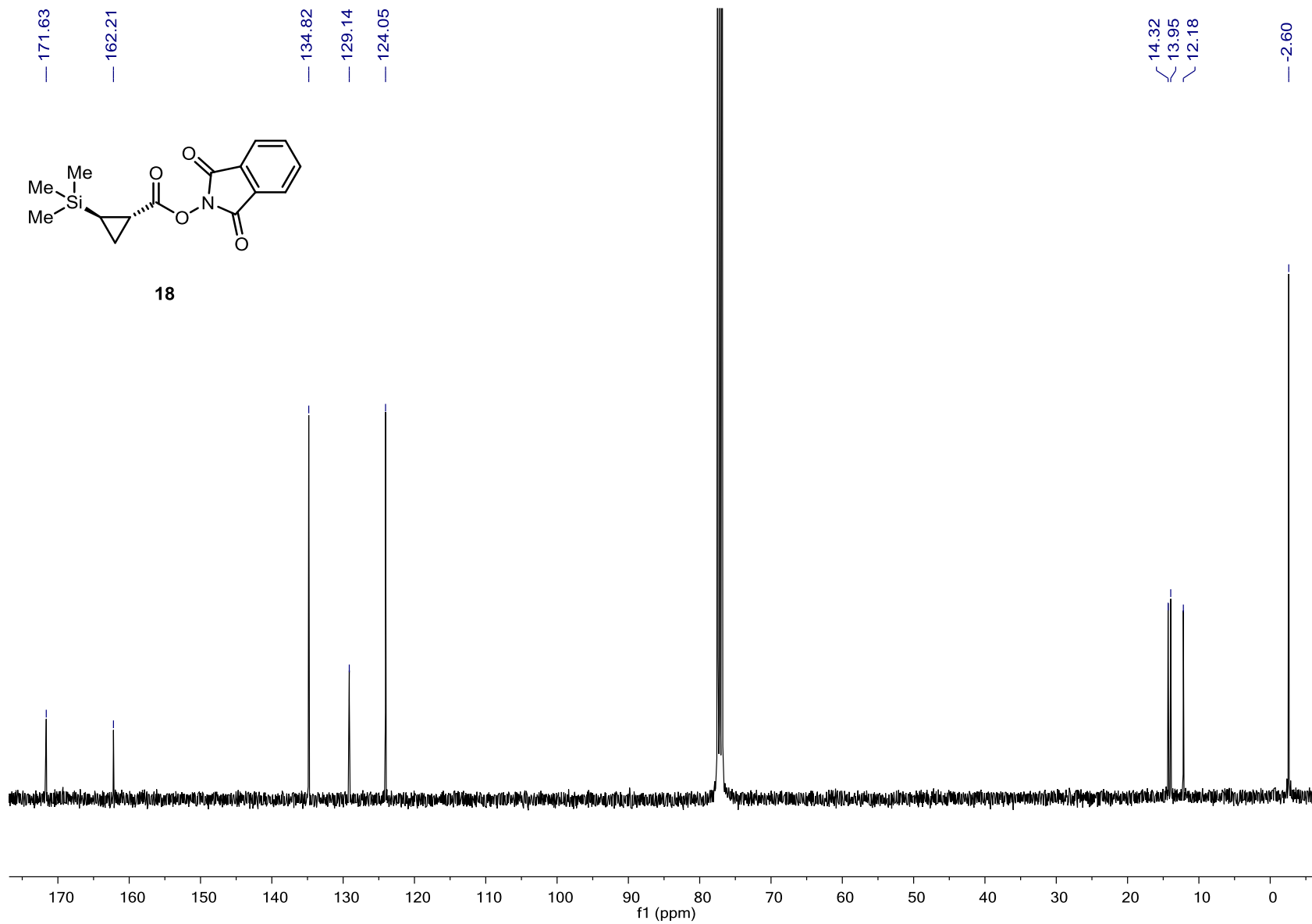
^1H NMR (400 MHz, CDCl_3) for compound **18**



18

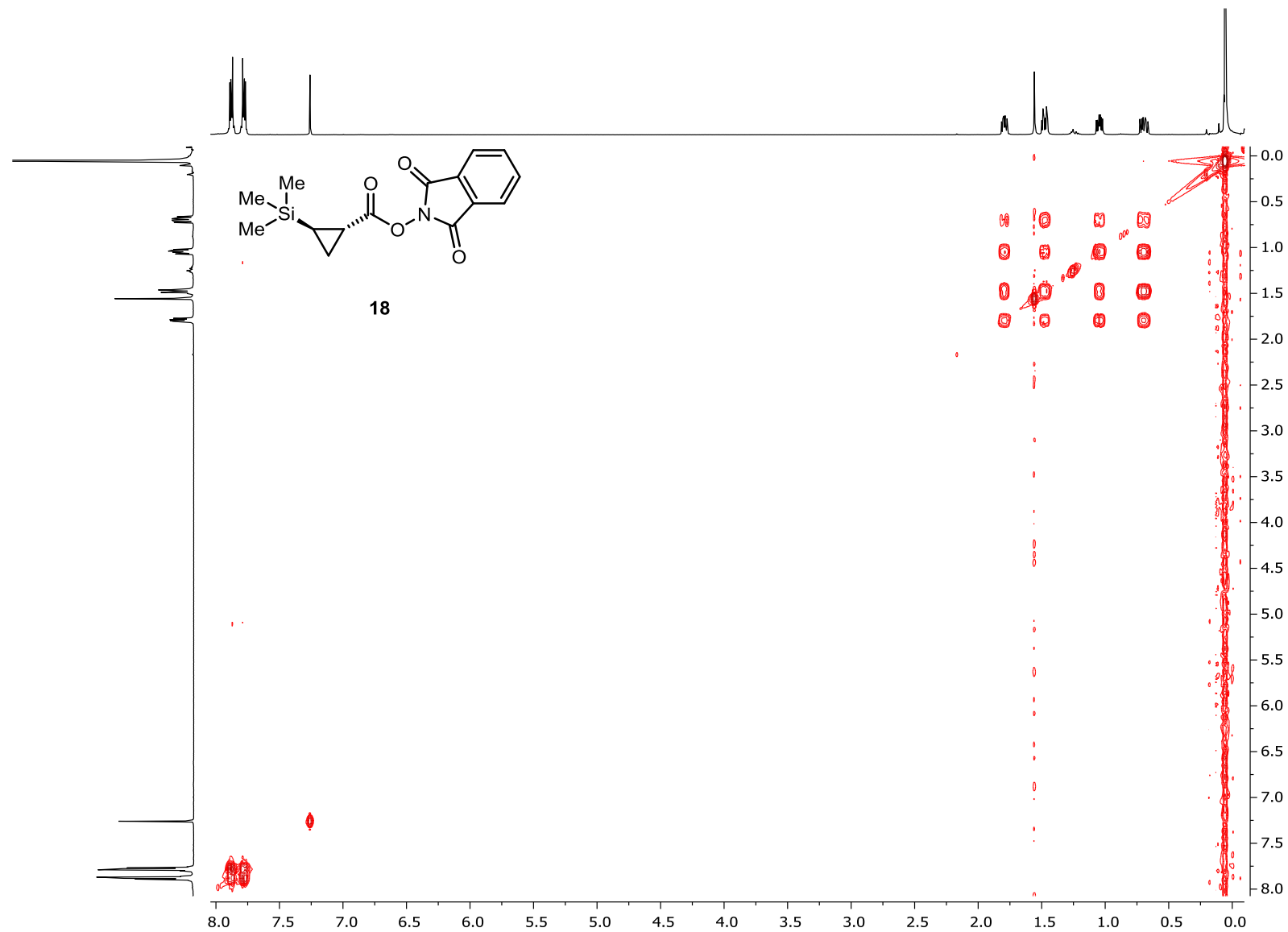


^{13}C NMR (101 MHz, CDCl_3) for compound **18**

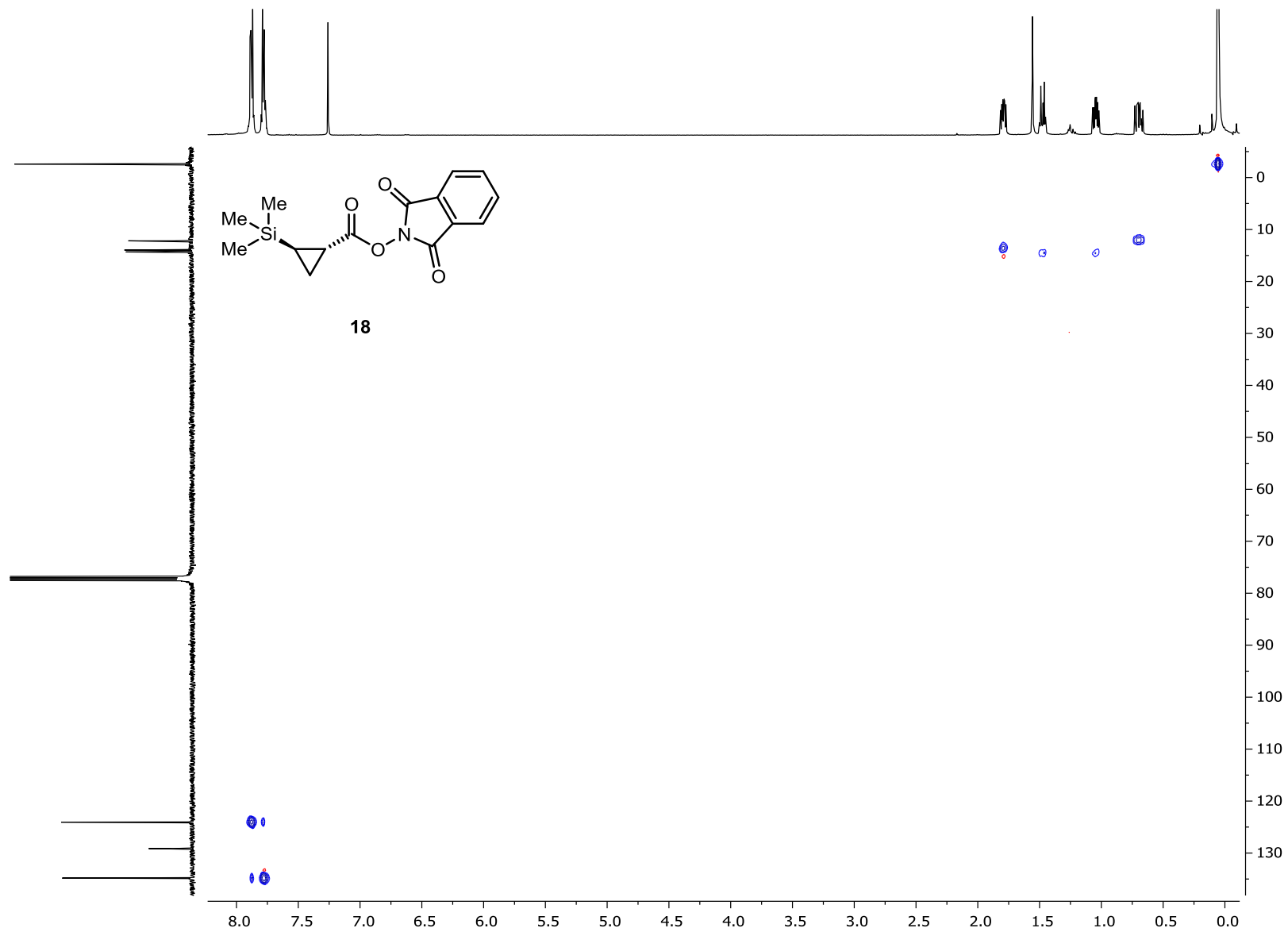


S281

COSY NMR (400 MHz, CDCl₃) for compound **18**

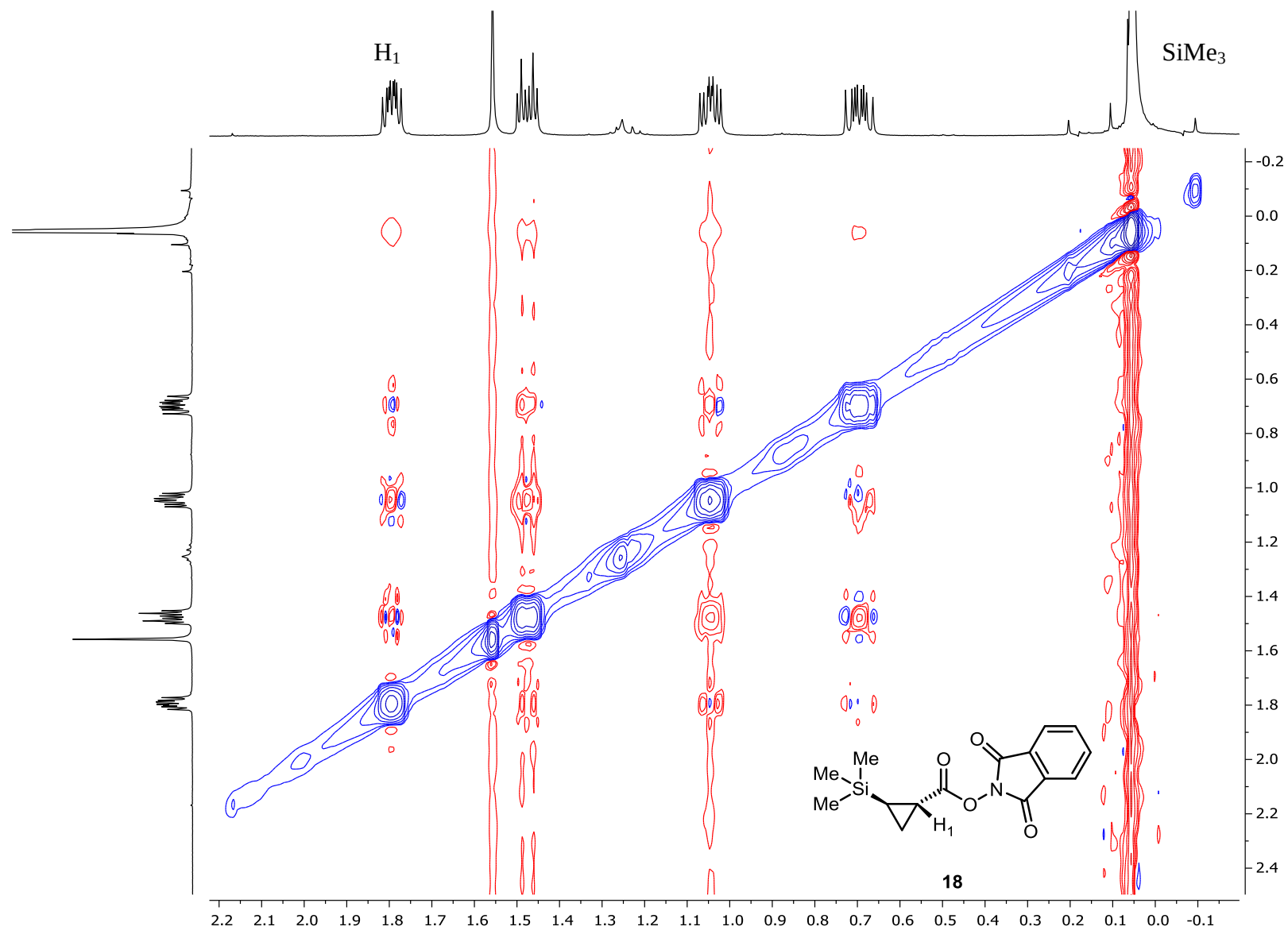


HSQC NMR (400 MHz, CDCl₃) for compound **18**

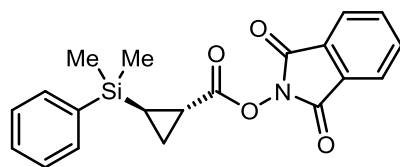


S283

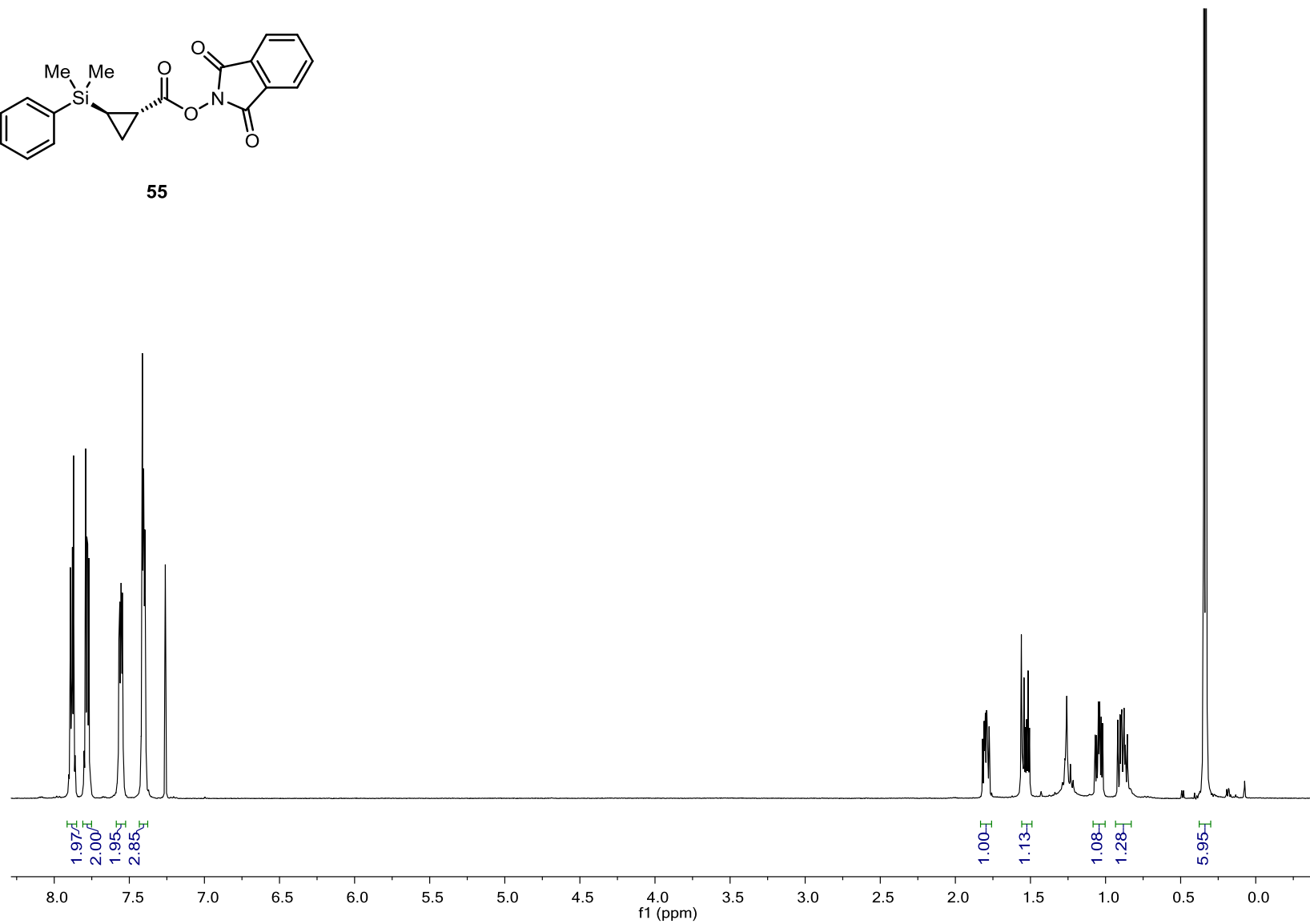
NOESY NMR (400 MHz, CDCl₃) for compound **18**



^1H NMR (400 MHz, CDCl_3) for compound 55

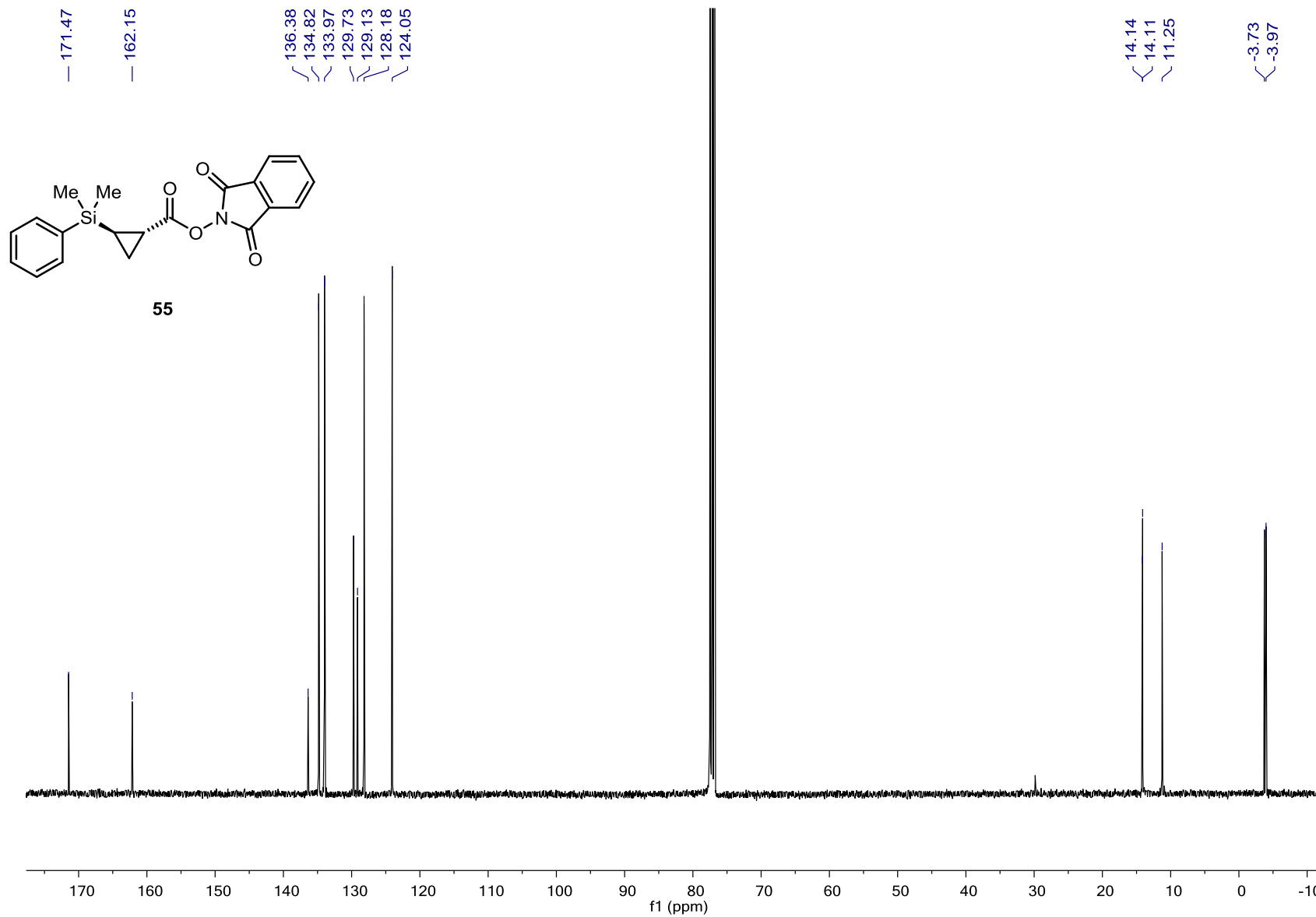


55



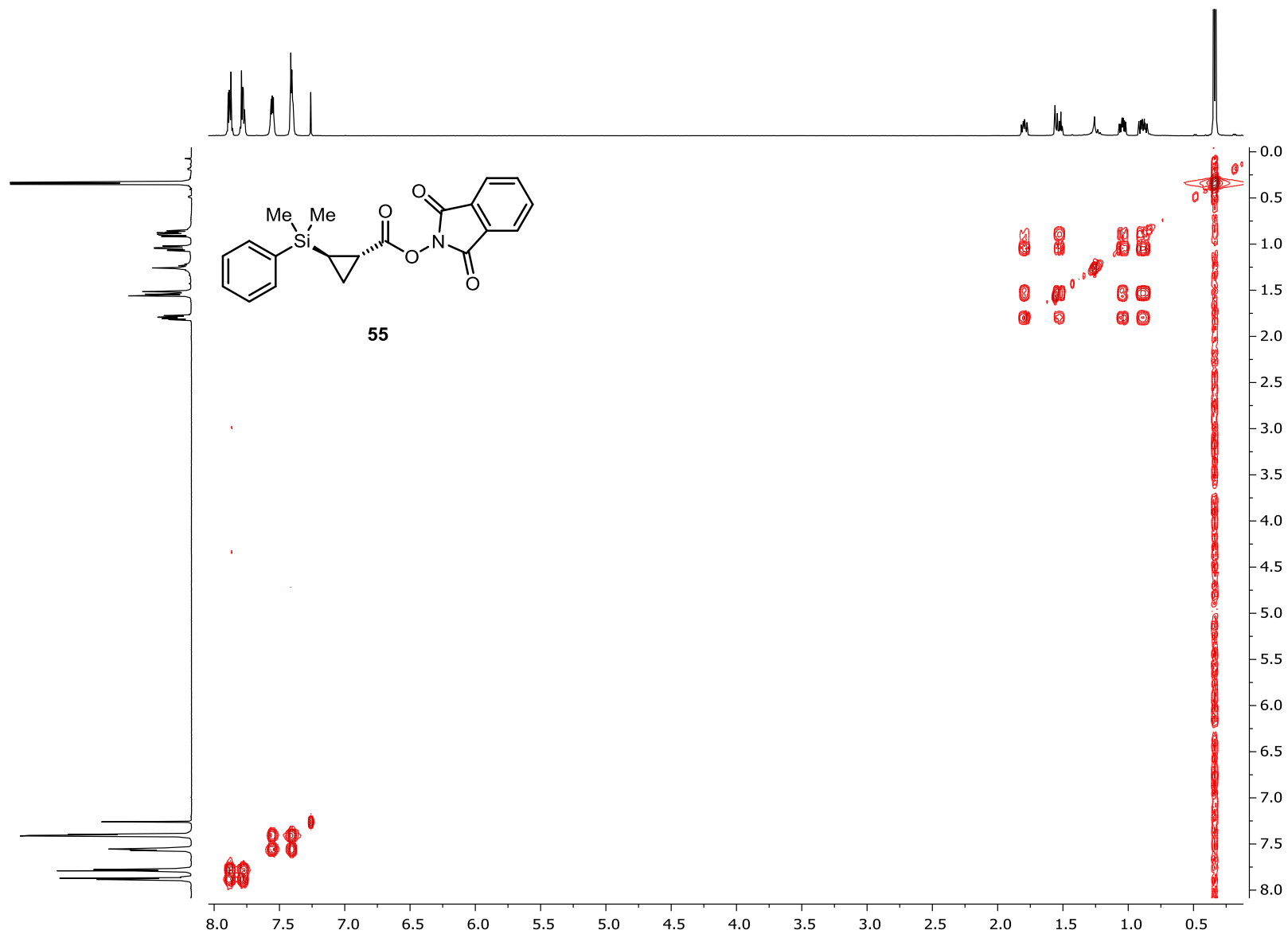
S285

^{13}C NMR (101 MHz, CDCl_3) for compound **55**

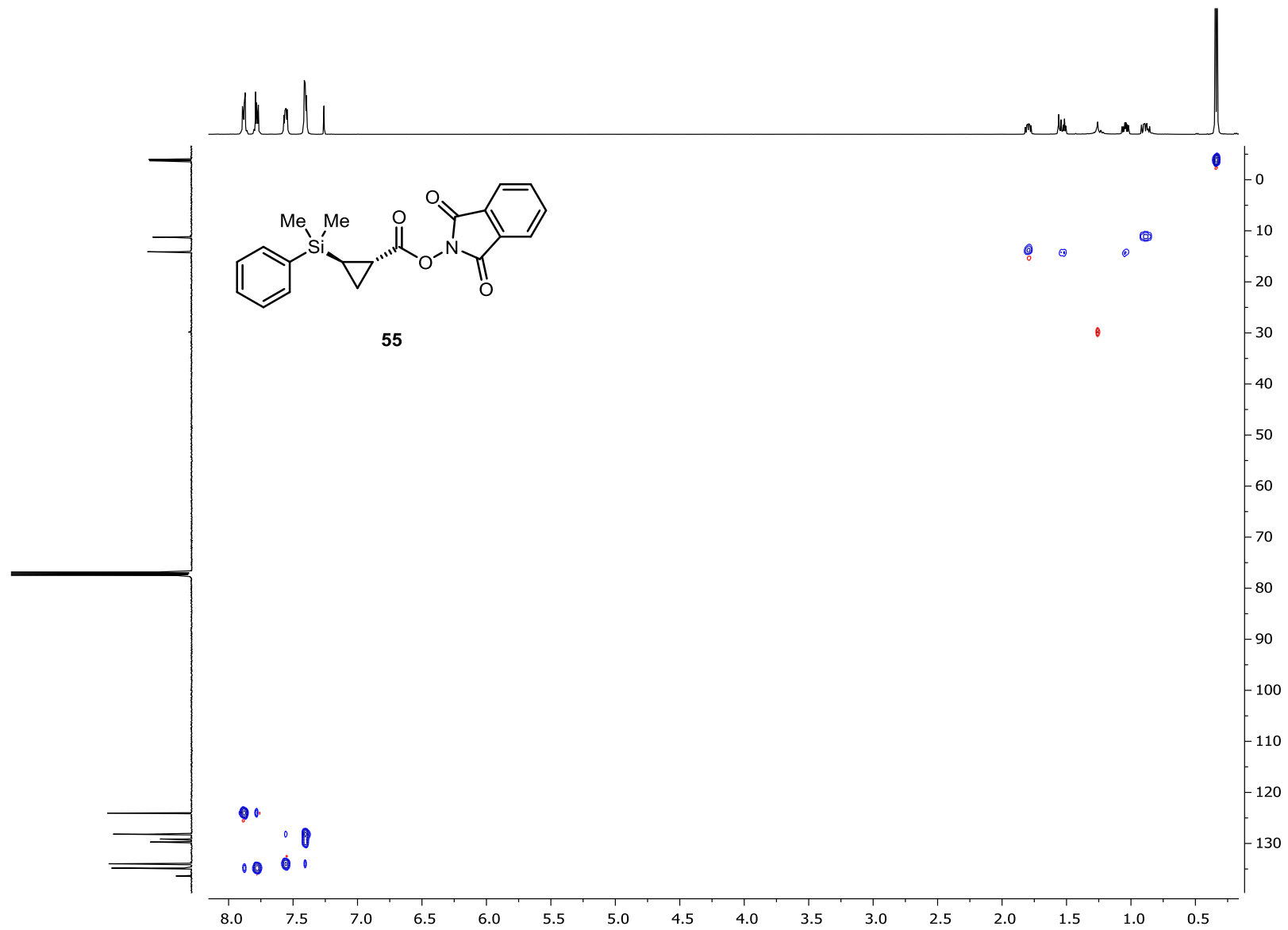


S286

COSY NMR (400 MHz, CDCl₃) for compound 55

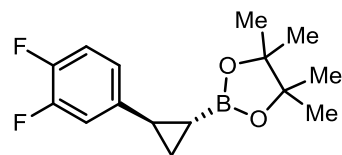


HSQC NMR (400 MHz, CDCl₃) for compound 55

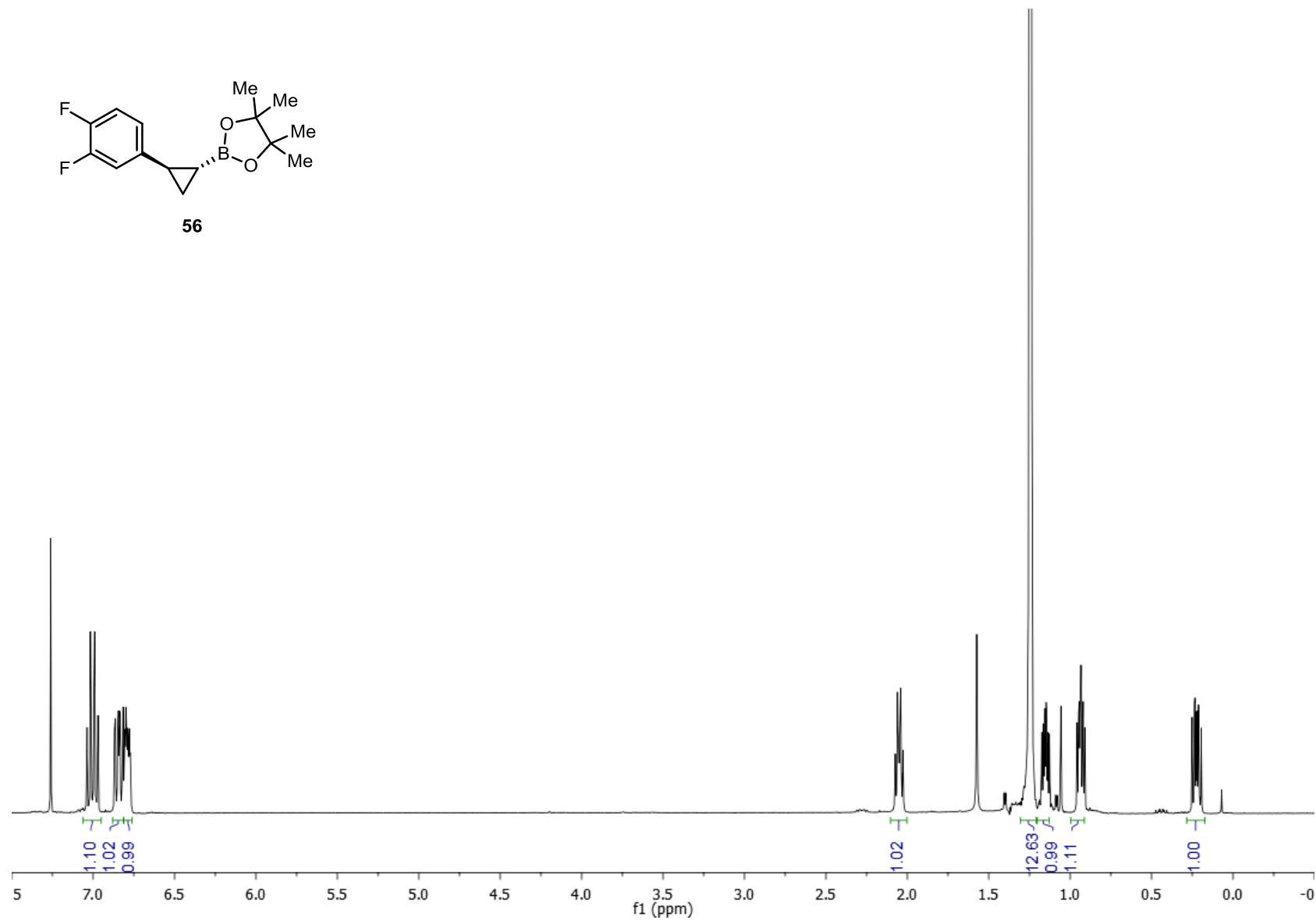


S288

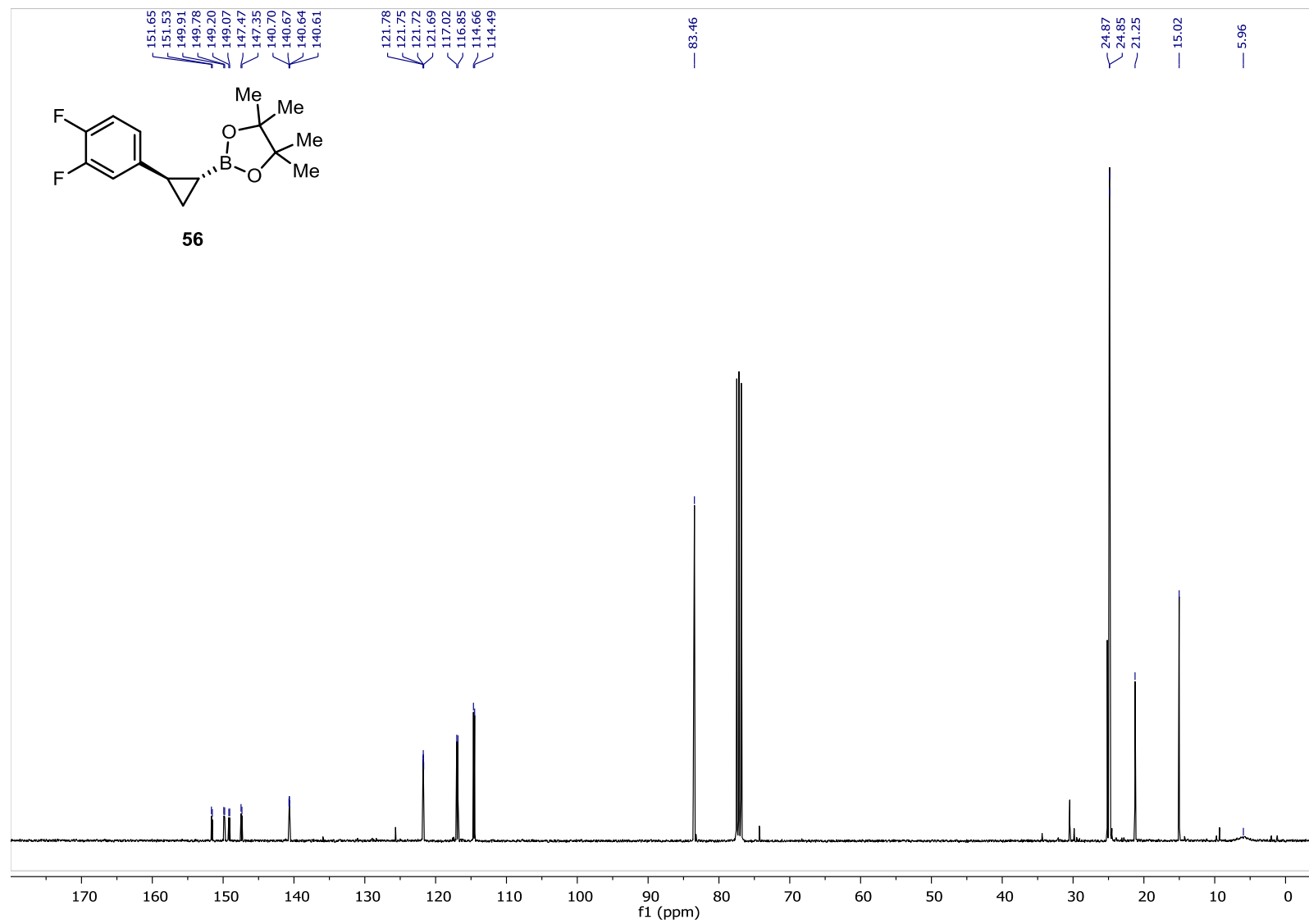
^1H NMR (400 MHz, CDCl_3) for compound **56**



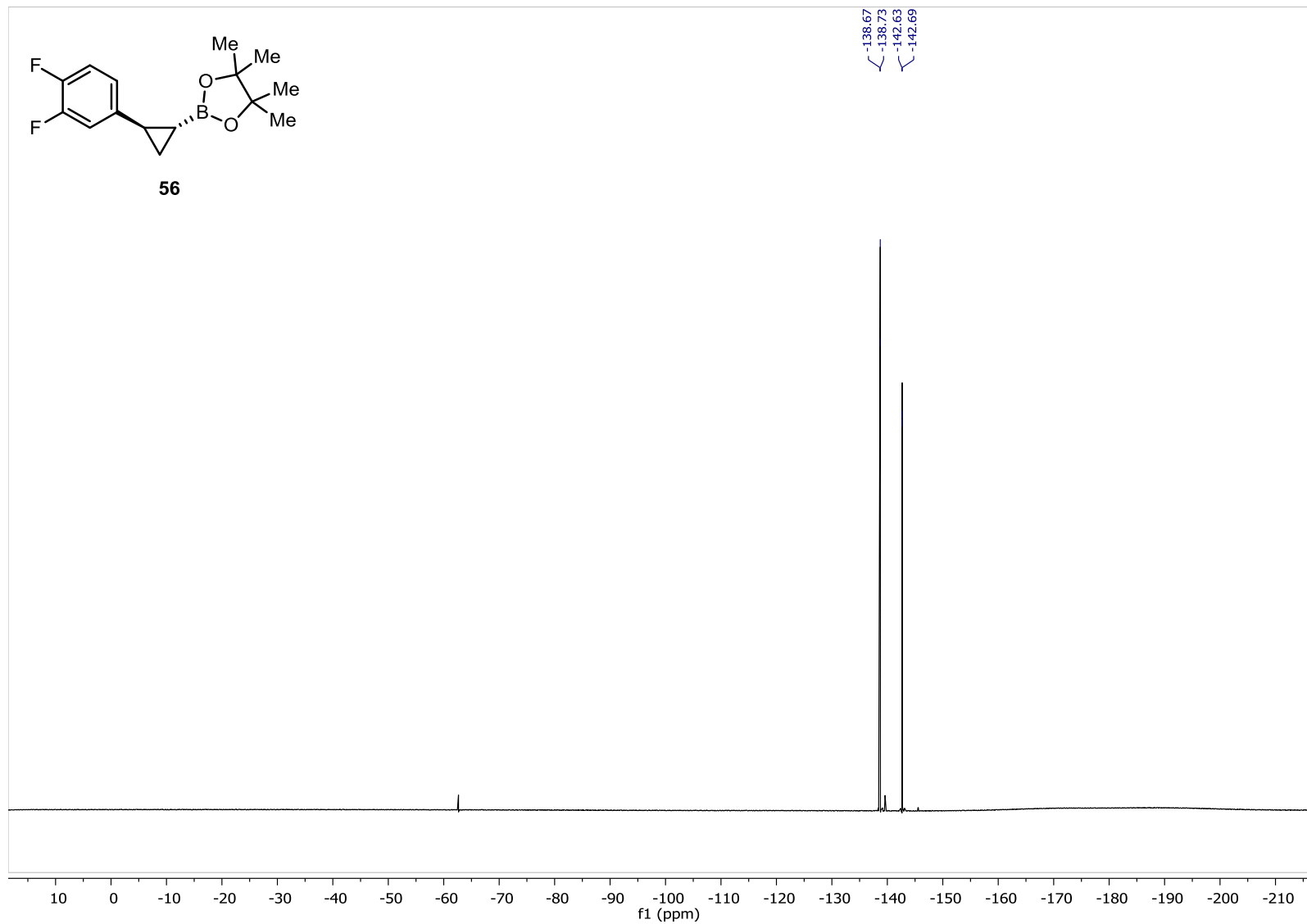
56



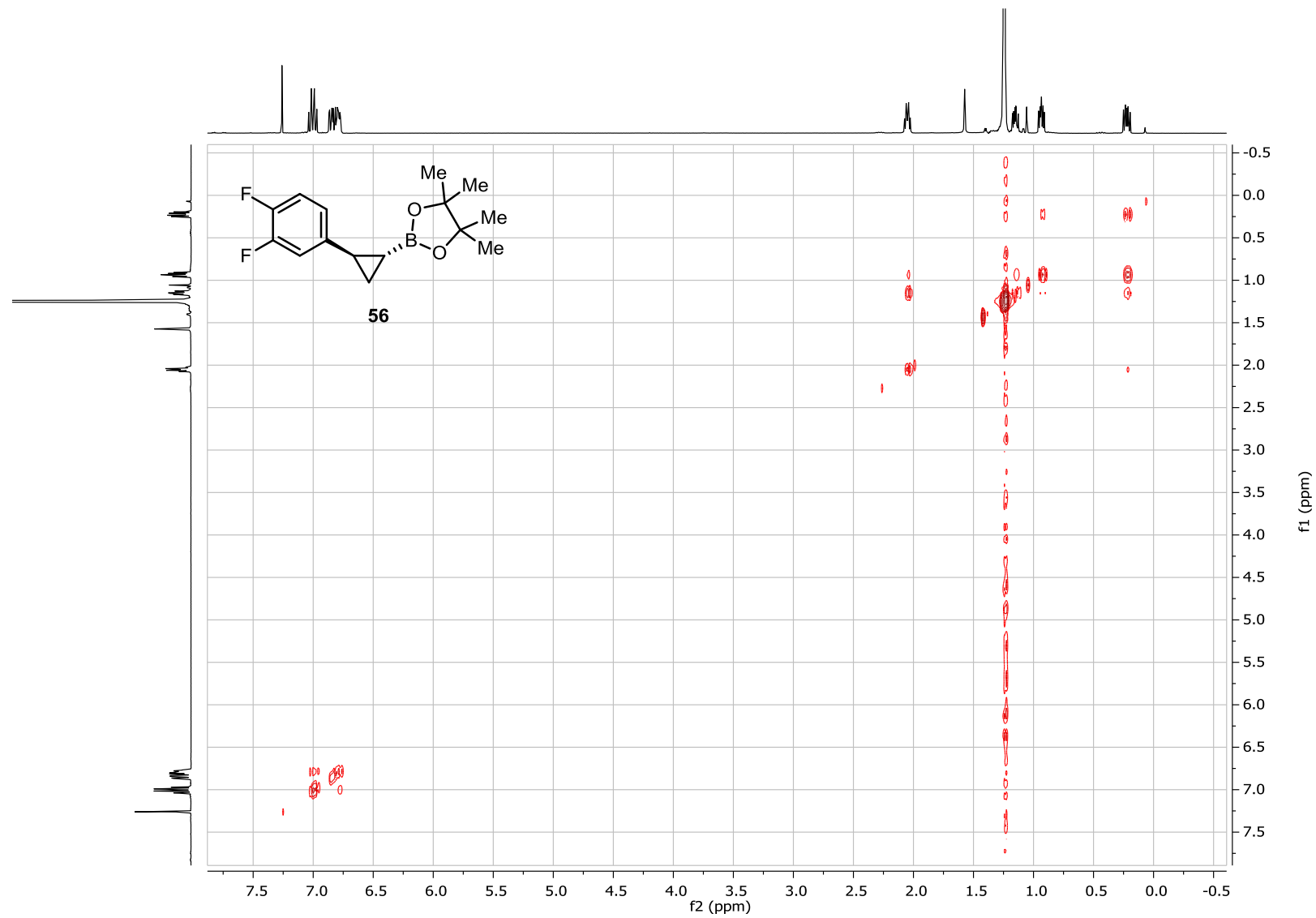
^{13}C NMR (101 MHz, CDCl_3) for compound **56**



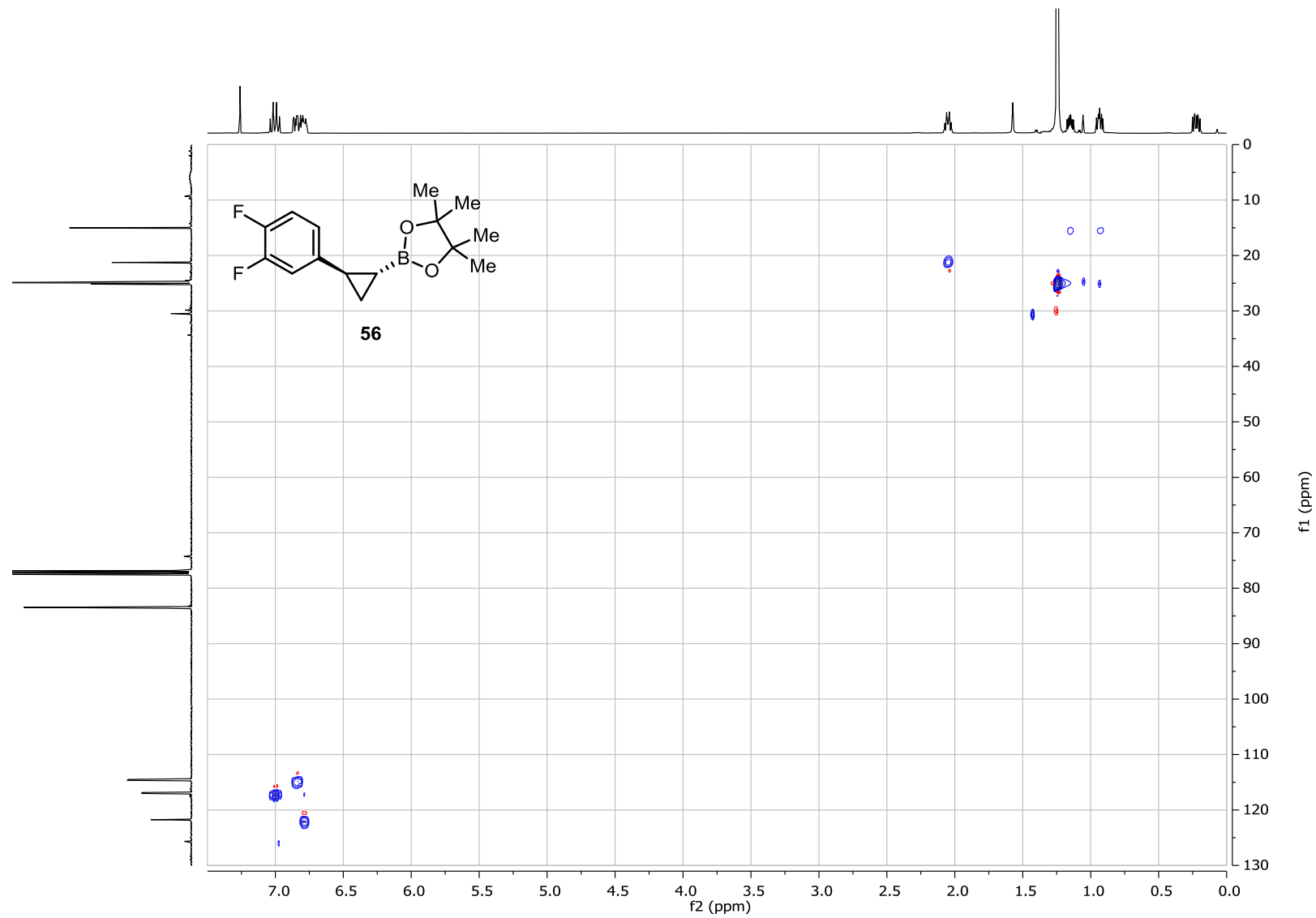
^{19}F NMR (377 MHz, CDCl_3) for compound **56**



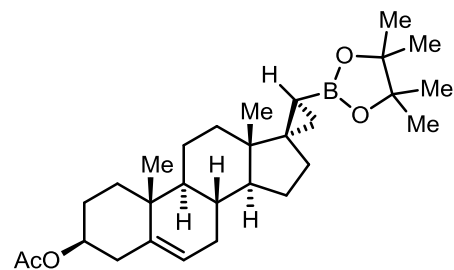
COSY NMR (400 MHz, CDCl₃) for compound **56**



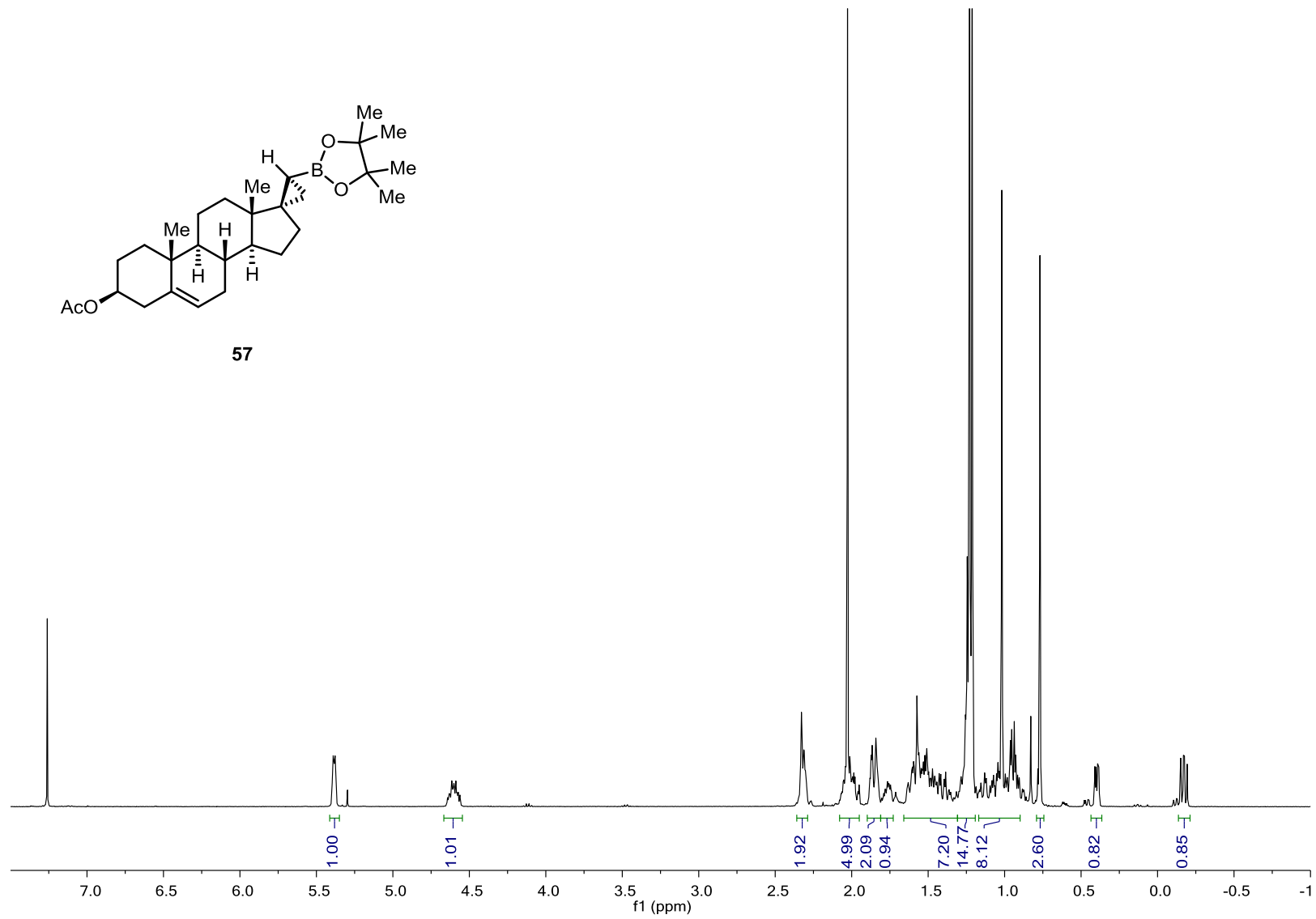
HSQC NMR (400 MHz, CDCl₃) for compound **56**



^1H NMR (400 MHz, CDCl_3) for compound **57**

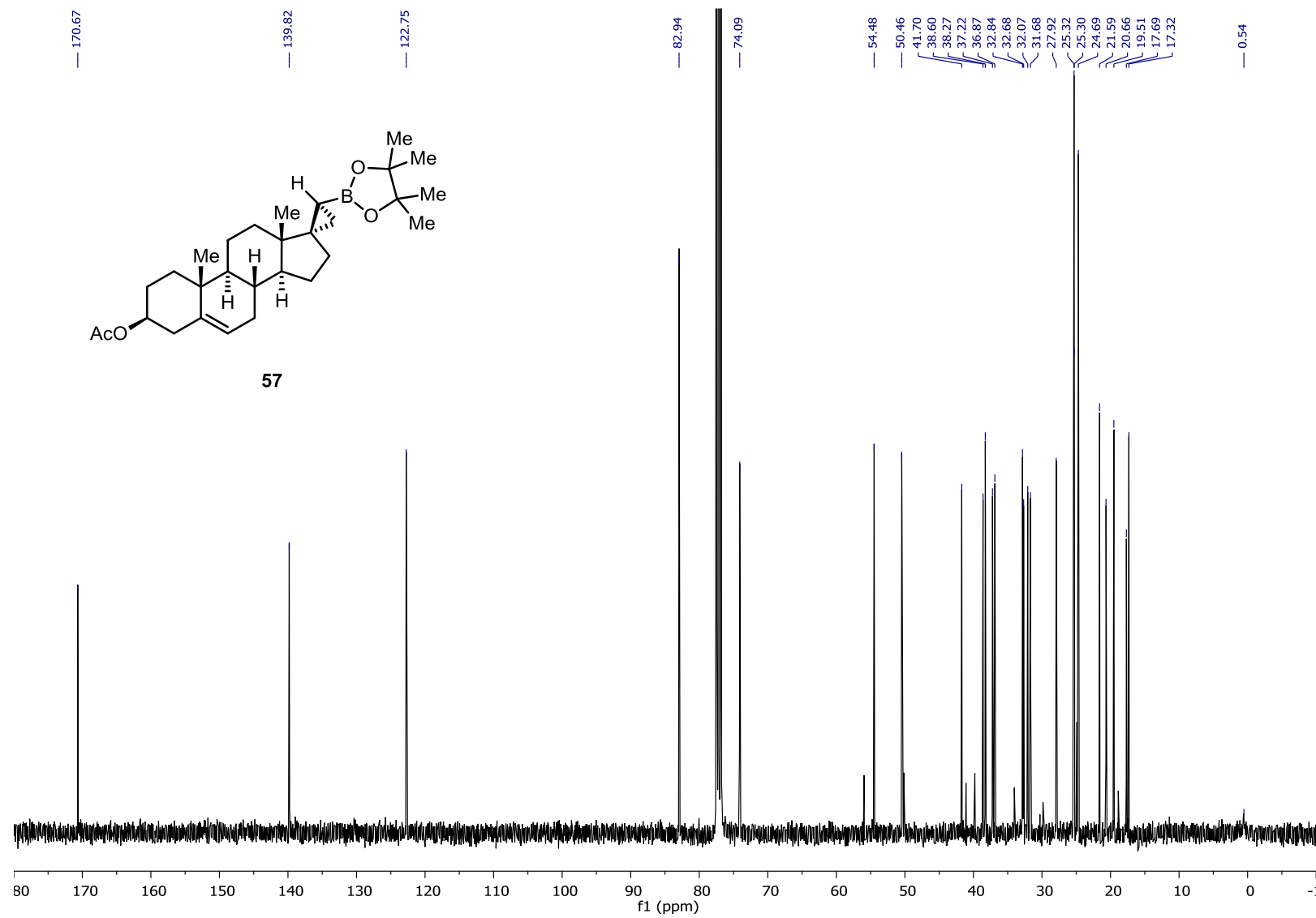


57

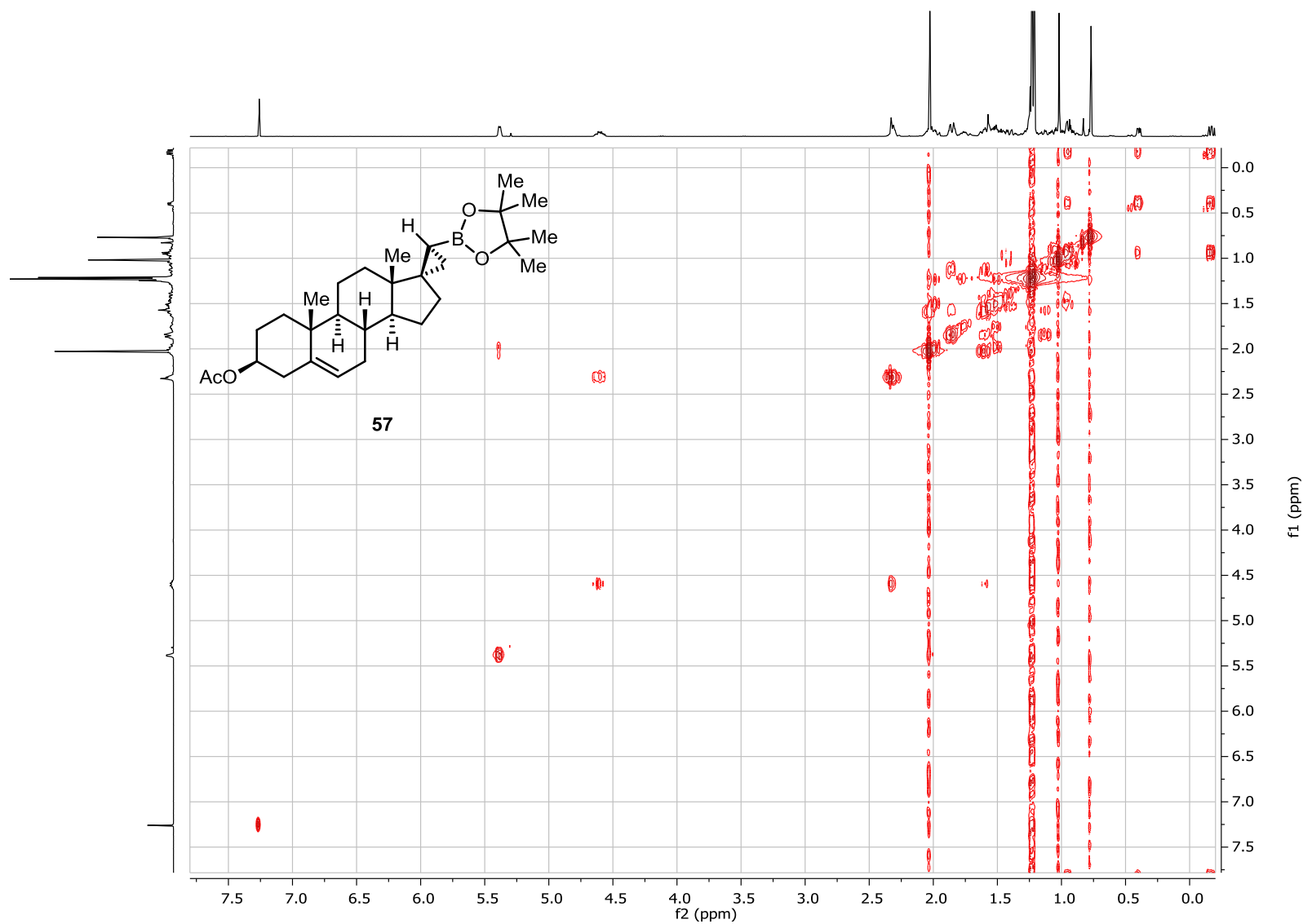


S294

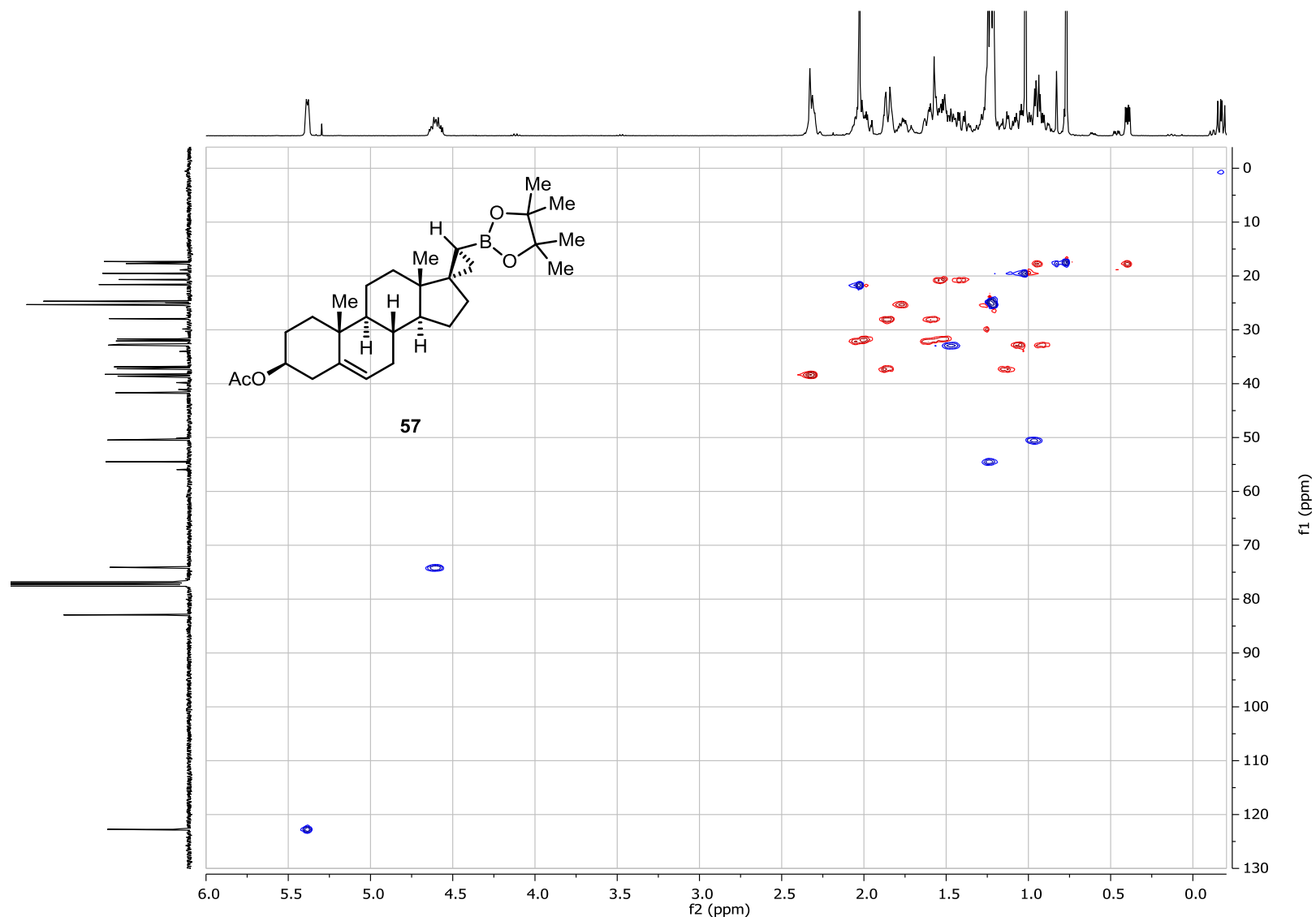
^{13}C NMR (101 MHz, CDCl_3) for compound **57**



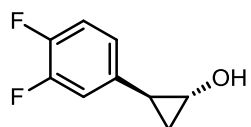
COSY NMR (400 MHz, CDCl_3) for compound **57**



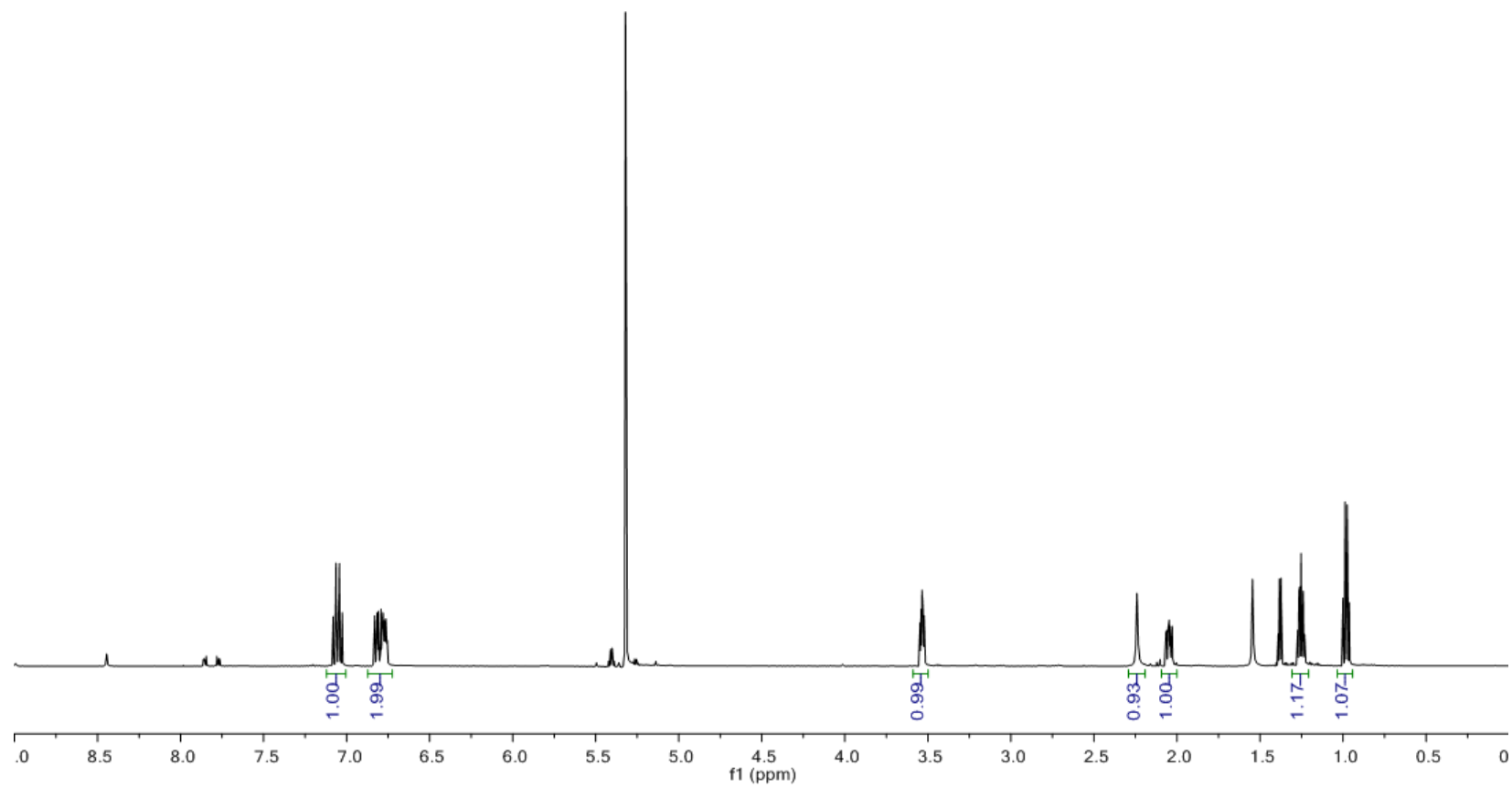
HSQC NMR (400 MHz, CDCl₃) for compound 57



^1H NMR (500 MHz, CD_2Cl_2) for compound **58**



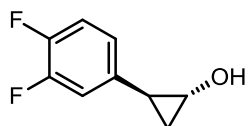
58



^{13}C NMR (126 MHz, CD_2Cl_2) for compound **58**

151.73
151.63
150.12
150.02
149.77
149.67
148.18
148.07
139.33
139.30
139.28
139.26

122.48
122.45
122.43
122.40
117.51
117.37
115.10
114.96

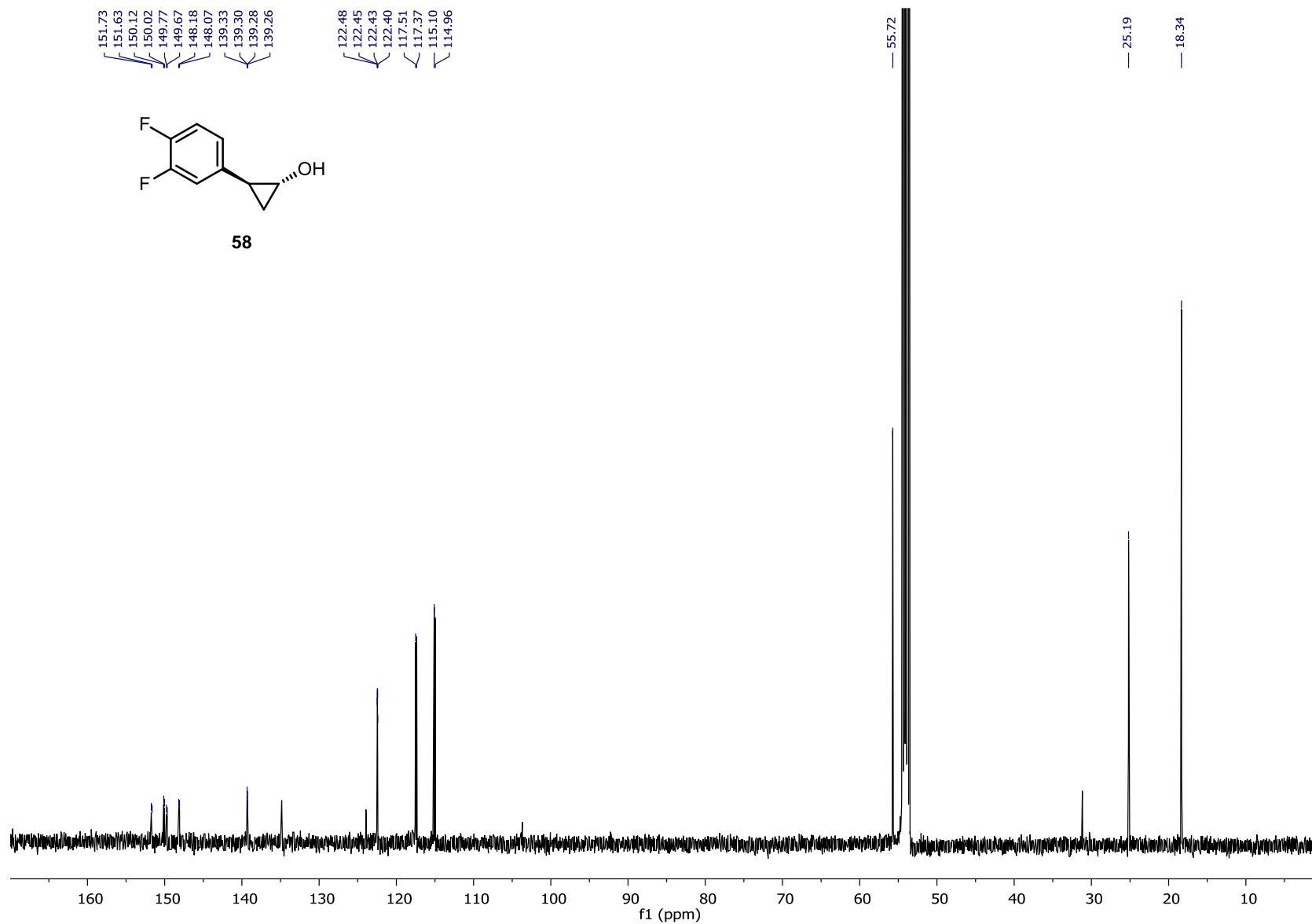


58

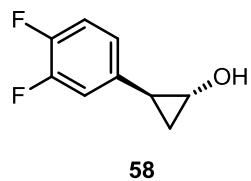
55.72

25.19

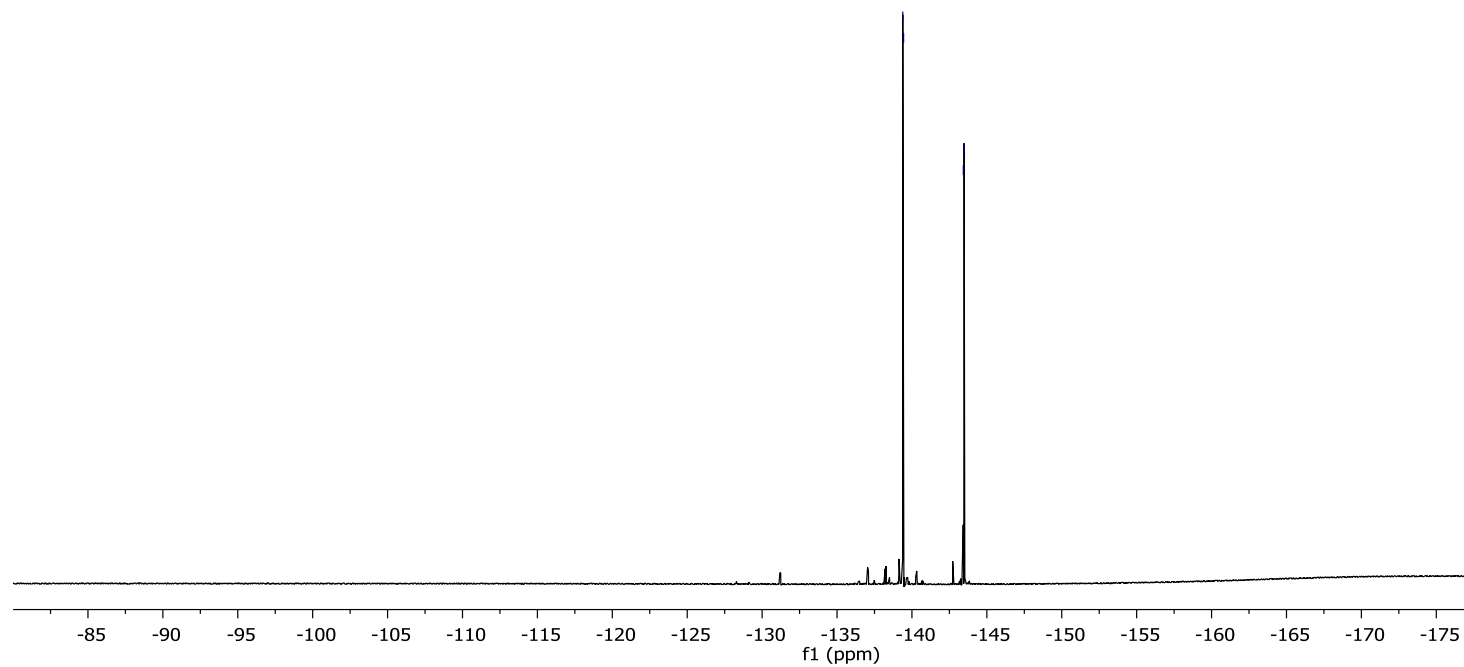
18.34



^{19}F NMR (377 MHz, CD_2Cl_2) for compound **58**

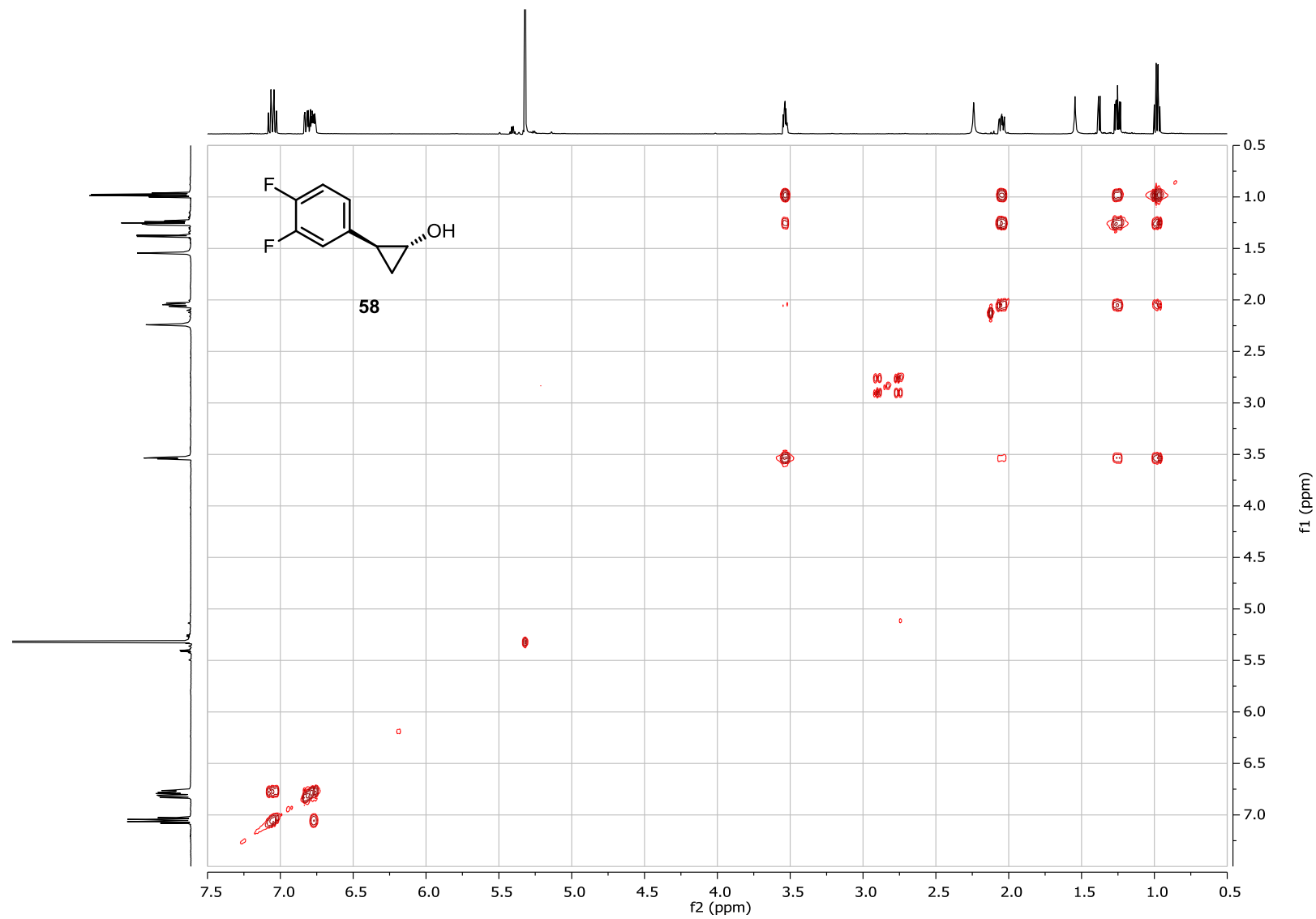


-139.39
-139.44
-143.43
-143.48



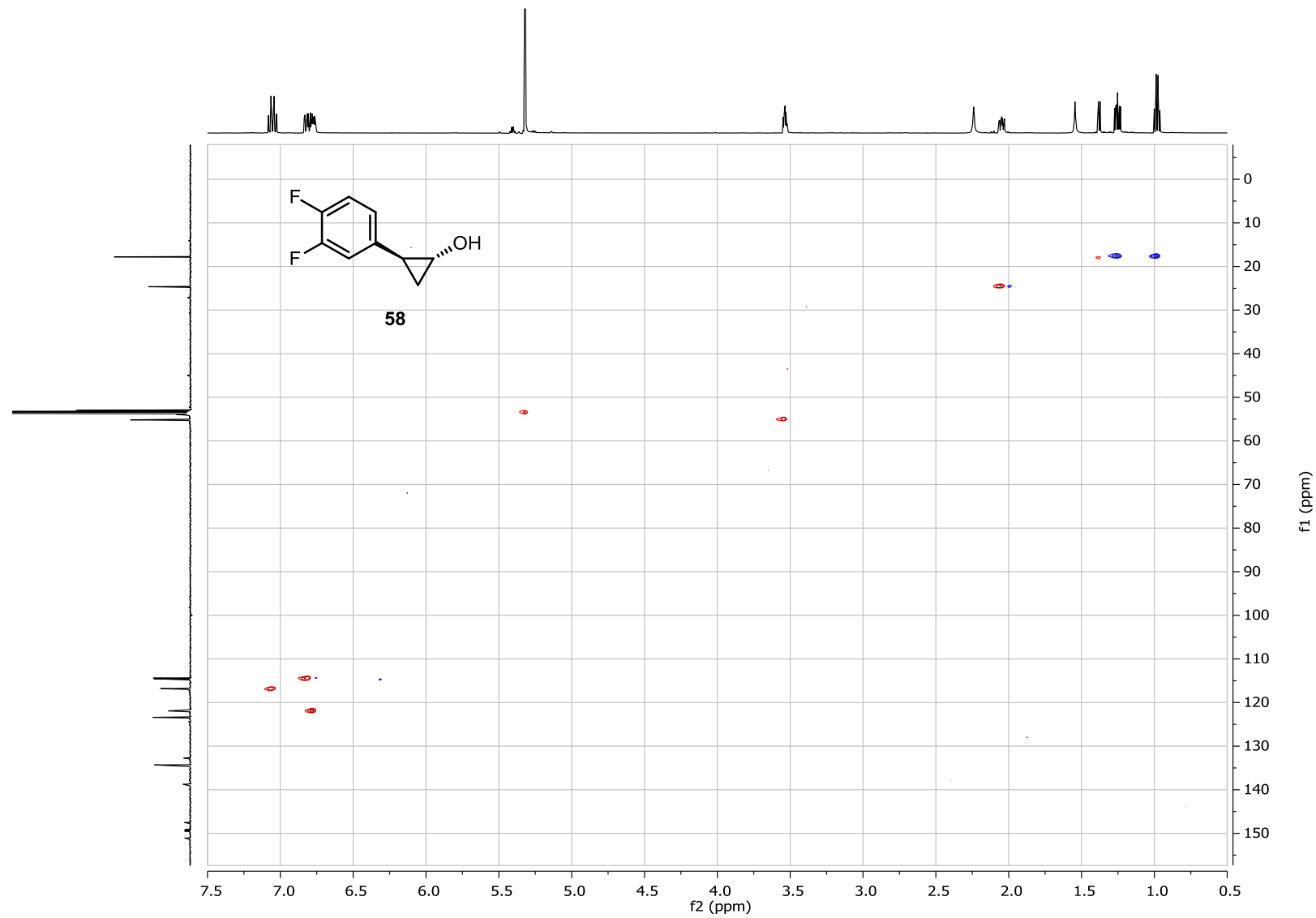
S300

COSY NMR (500 MHz, CD_2Cl_2) for compound **58**

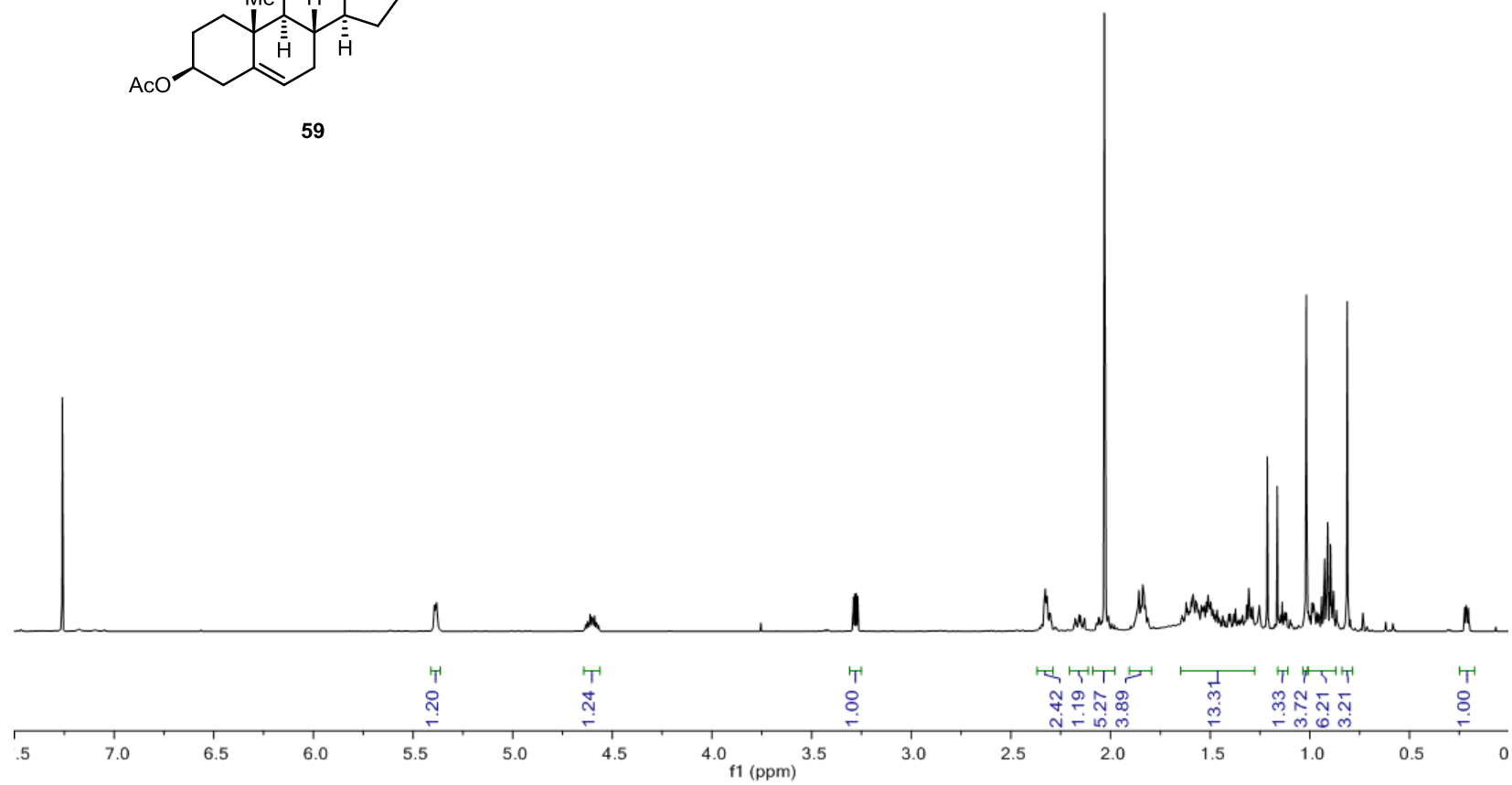
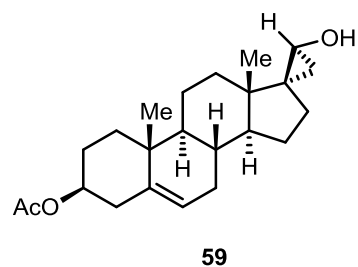


S301

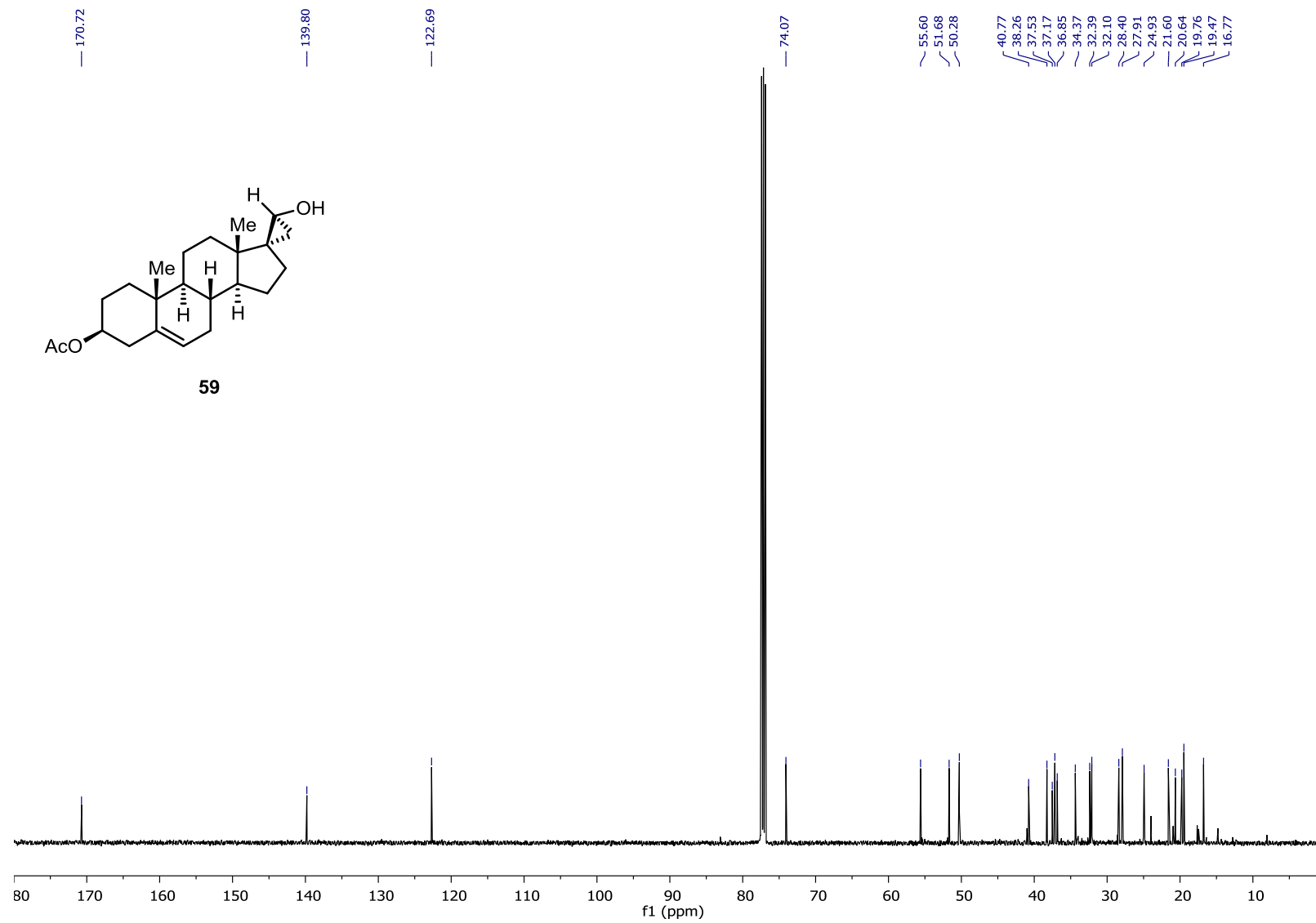
HSQC NMR (500 MHz, CD₂Cl₂) for compound **58**



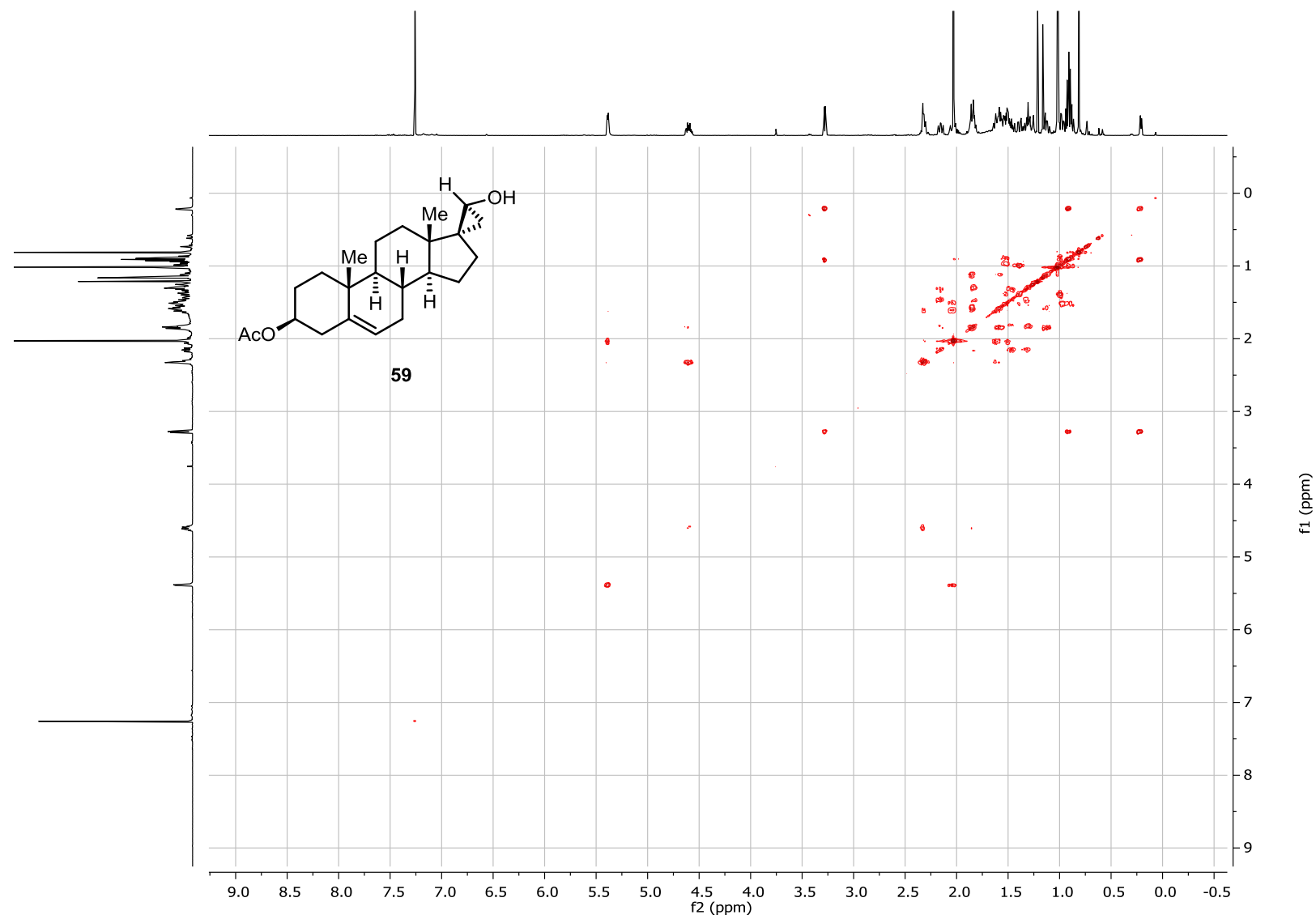
^1H NMR (500 MHz, CDCl_3) for compound **59**



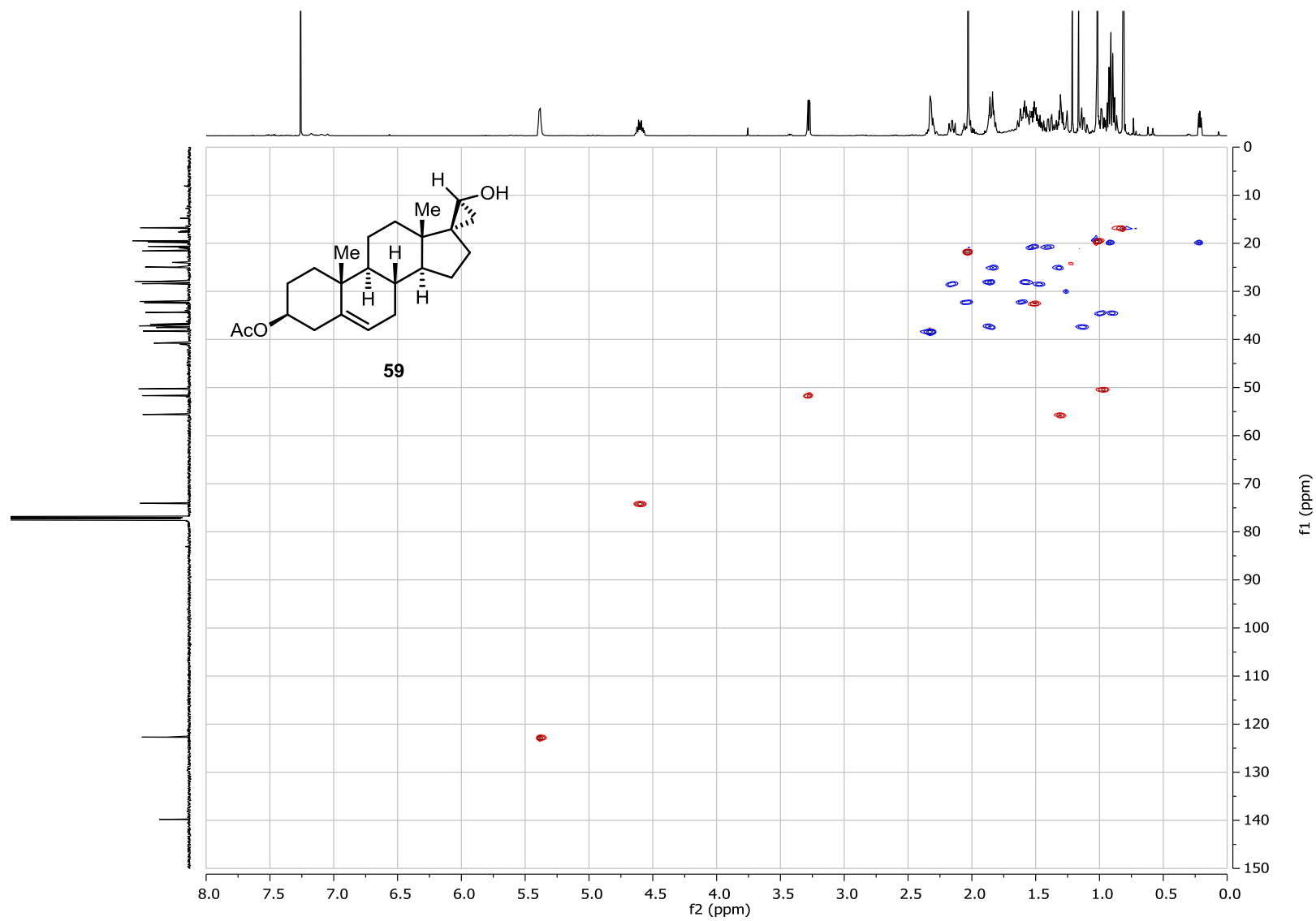
^{13}C NMR (126 MHz, CDCl_3) for compound **59**



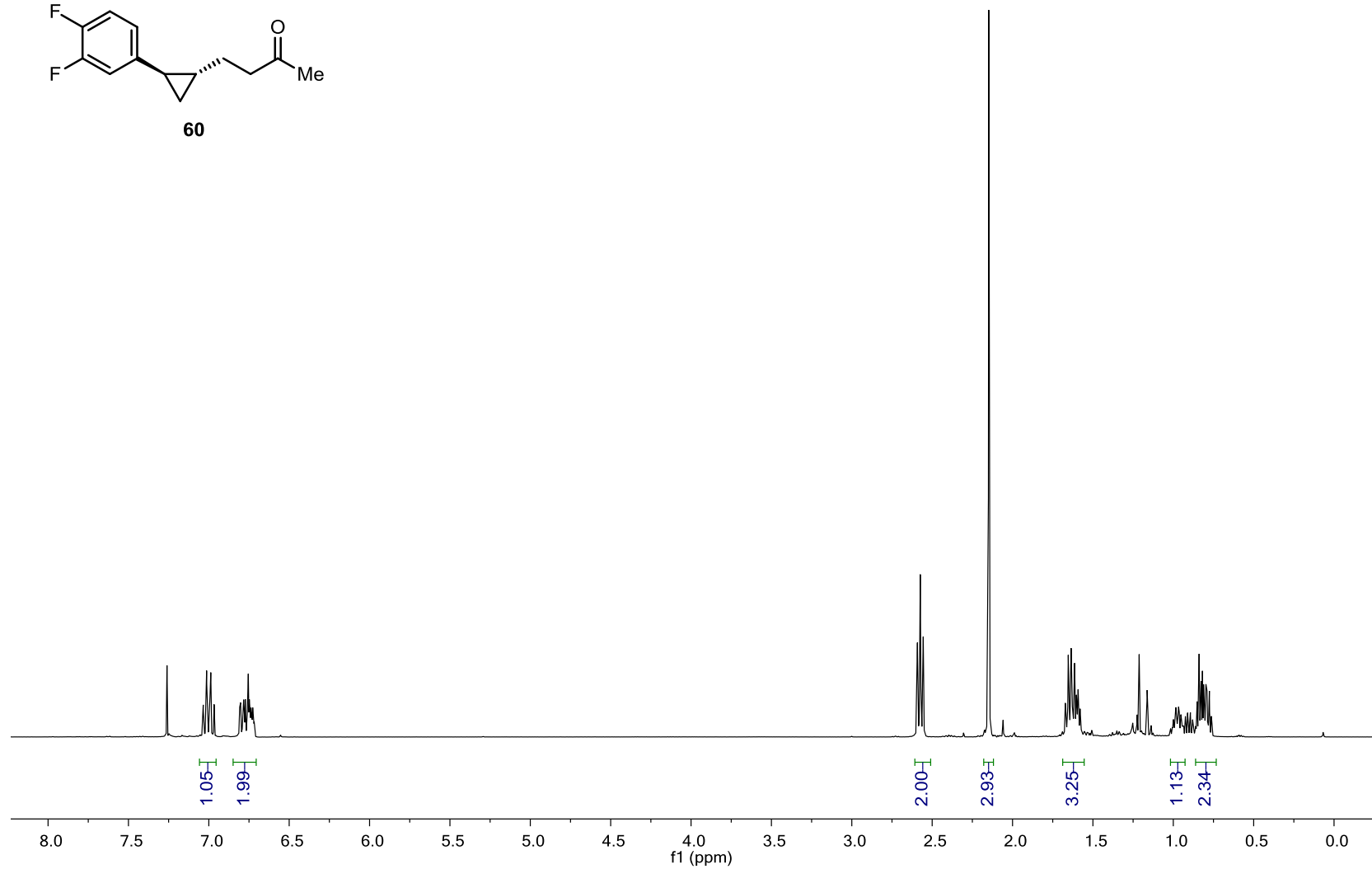
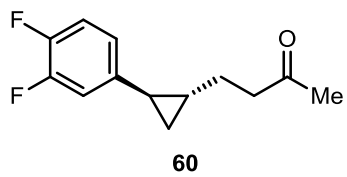
COSY NMR (500 MHz, CDCl₃) for compound 59



HSQC NMR (500 MHz, CDCl_3) for compound **59**

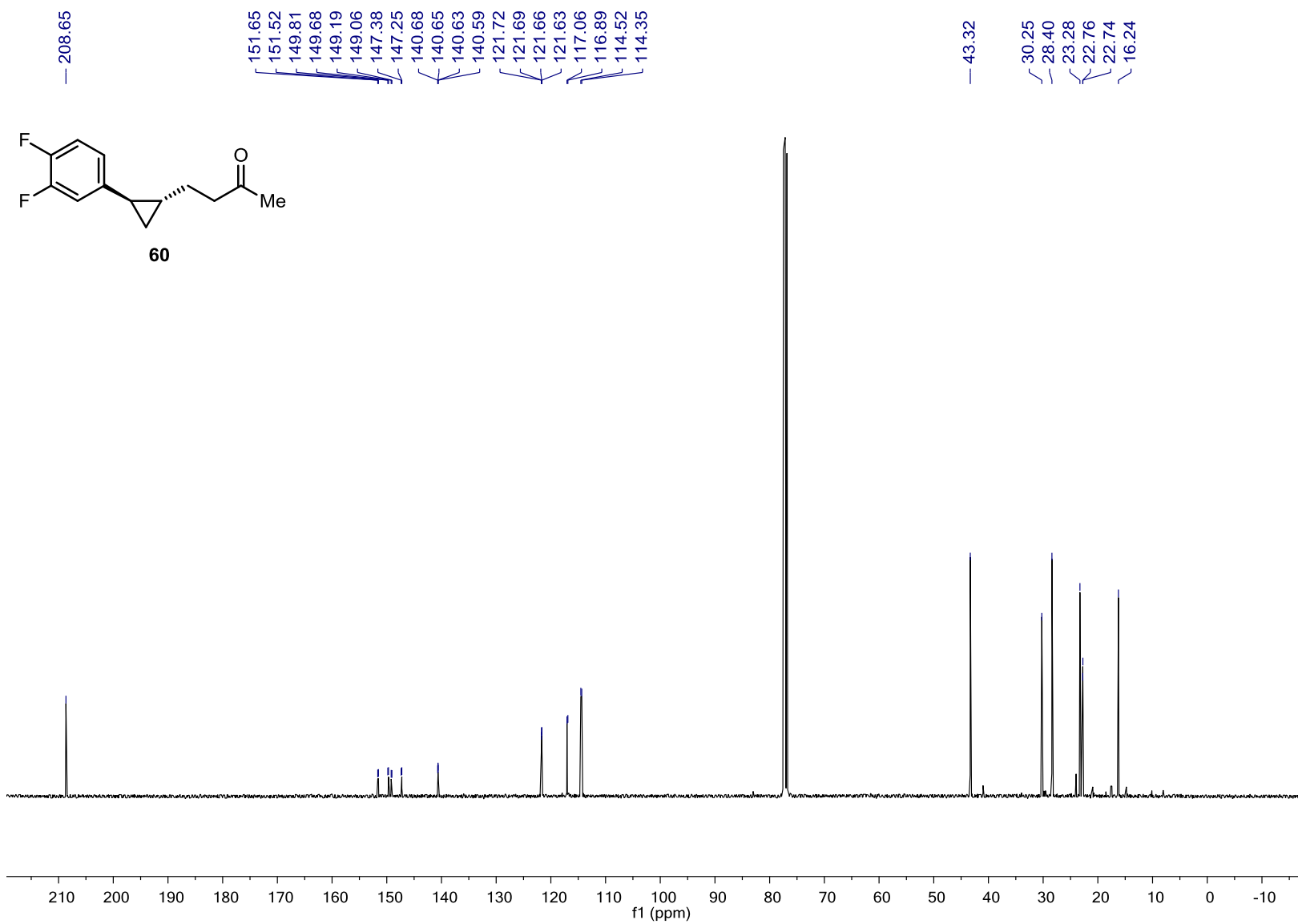


^1H NMR (400 MHz, CDCl_3) for compound **60**

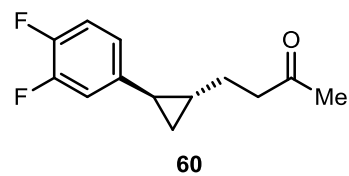


S307

^{13}C NMR (101 MHz, CDCl_3) for compound **60**

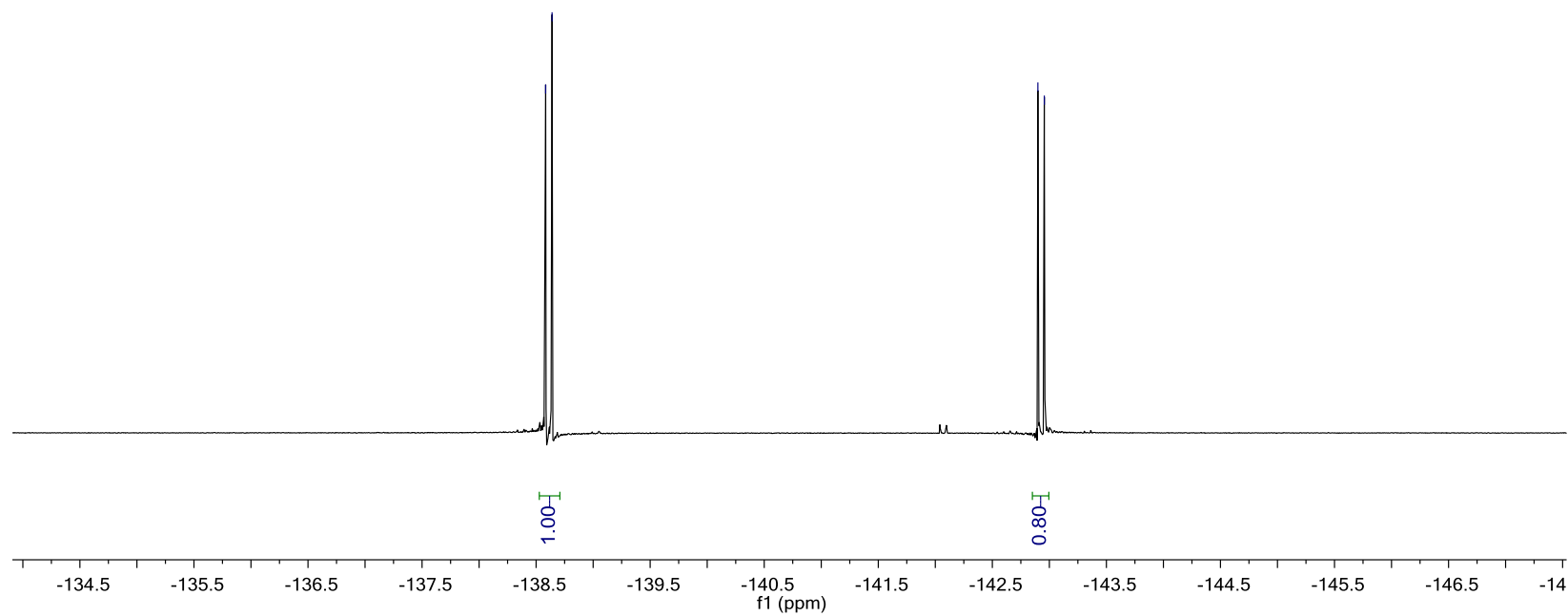


^{19}F NMR (376MHz, CDCl_3) for compound **60**

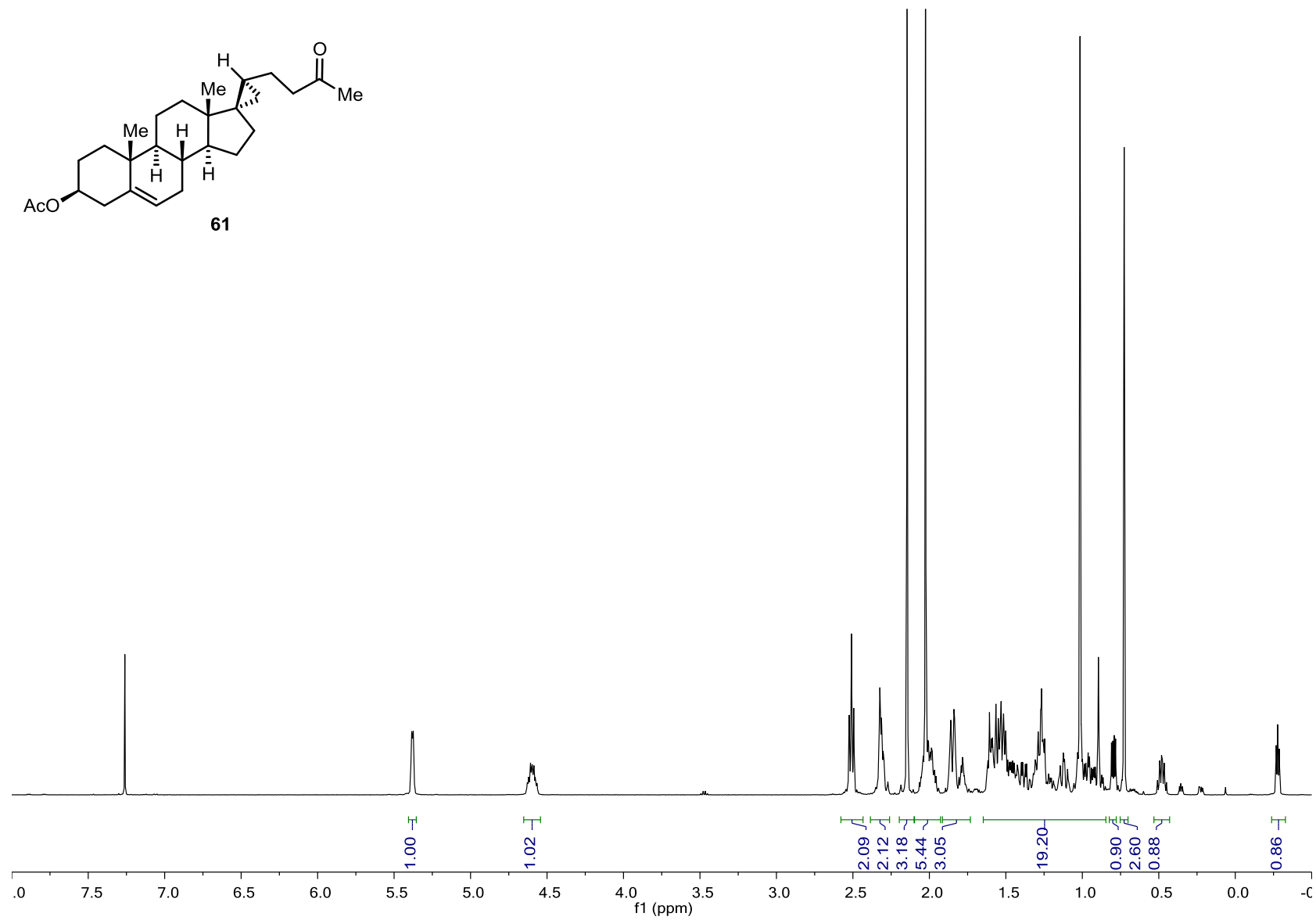
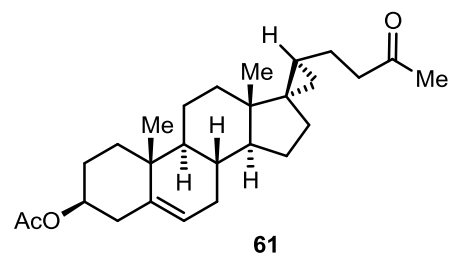


-138.58
-138.64

-142.90
-142.96

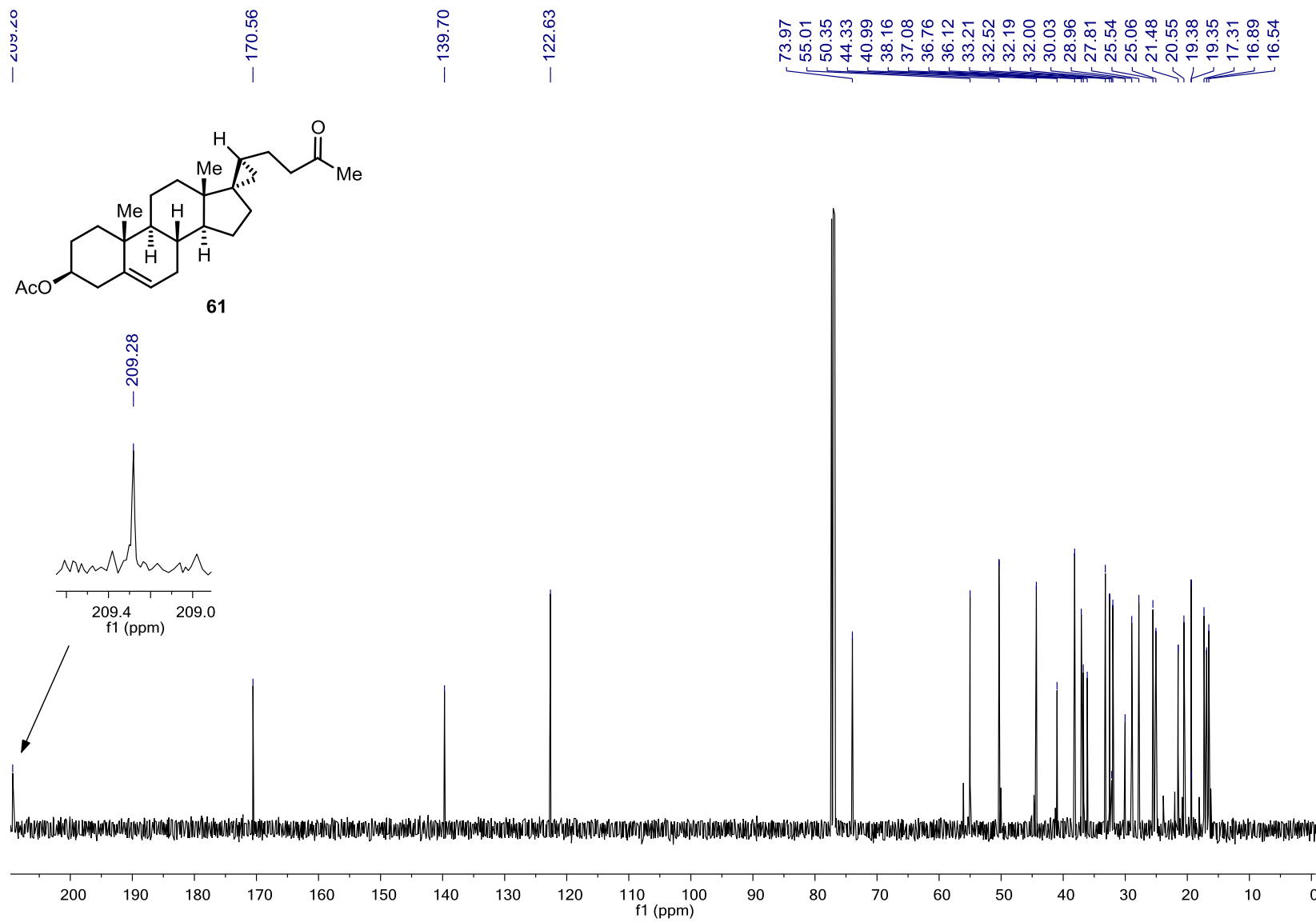


^1H NMR (500 MHz, CDCl_3) for compound **61**

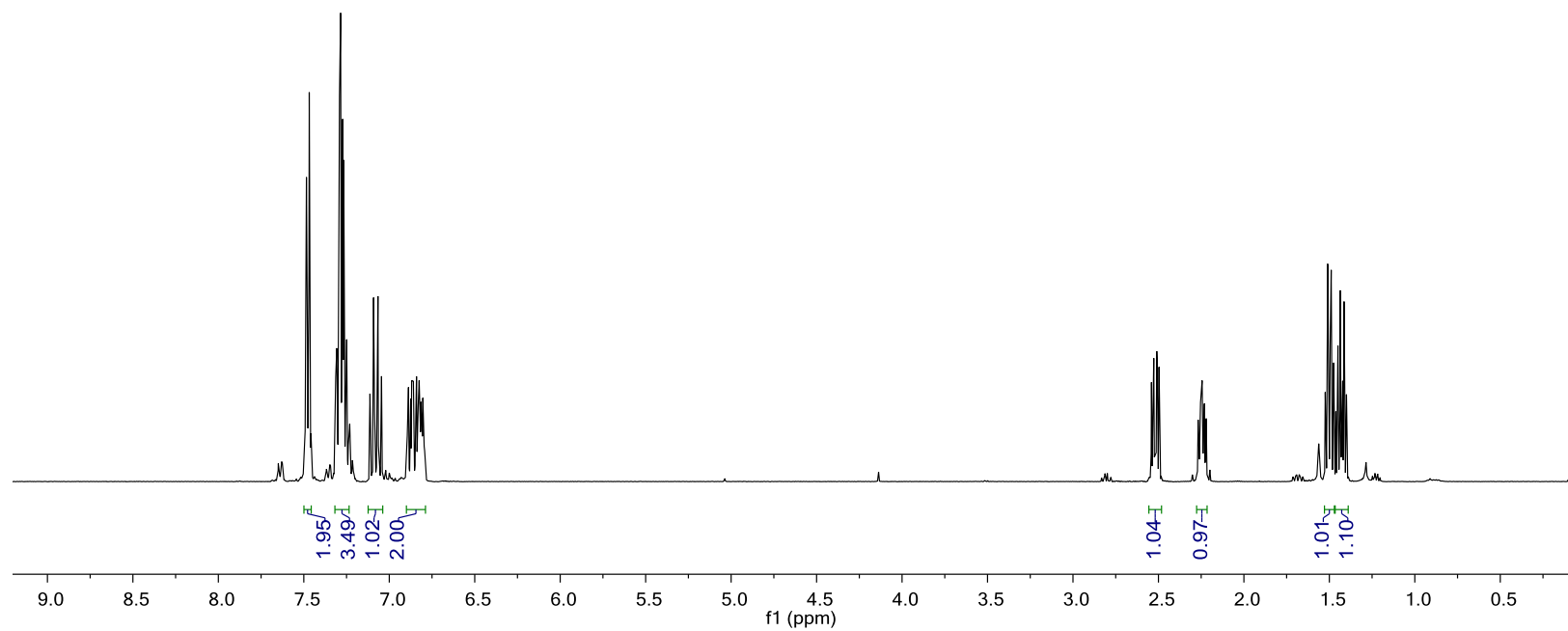
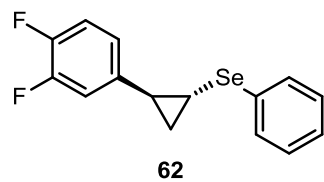


S310

^{13}C NMR (126 MHz, CDCl_3) for compound **61**



^1H NMR (400 MHz, CDCl_3) for compound **62**

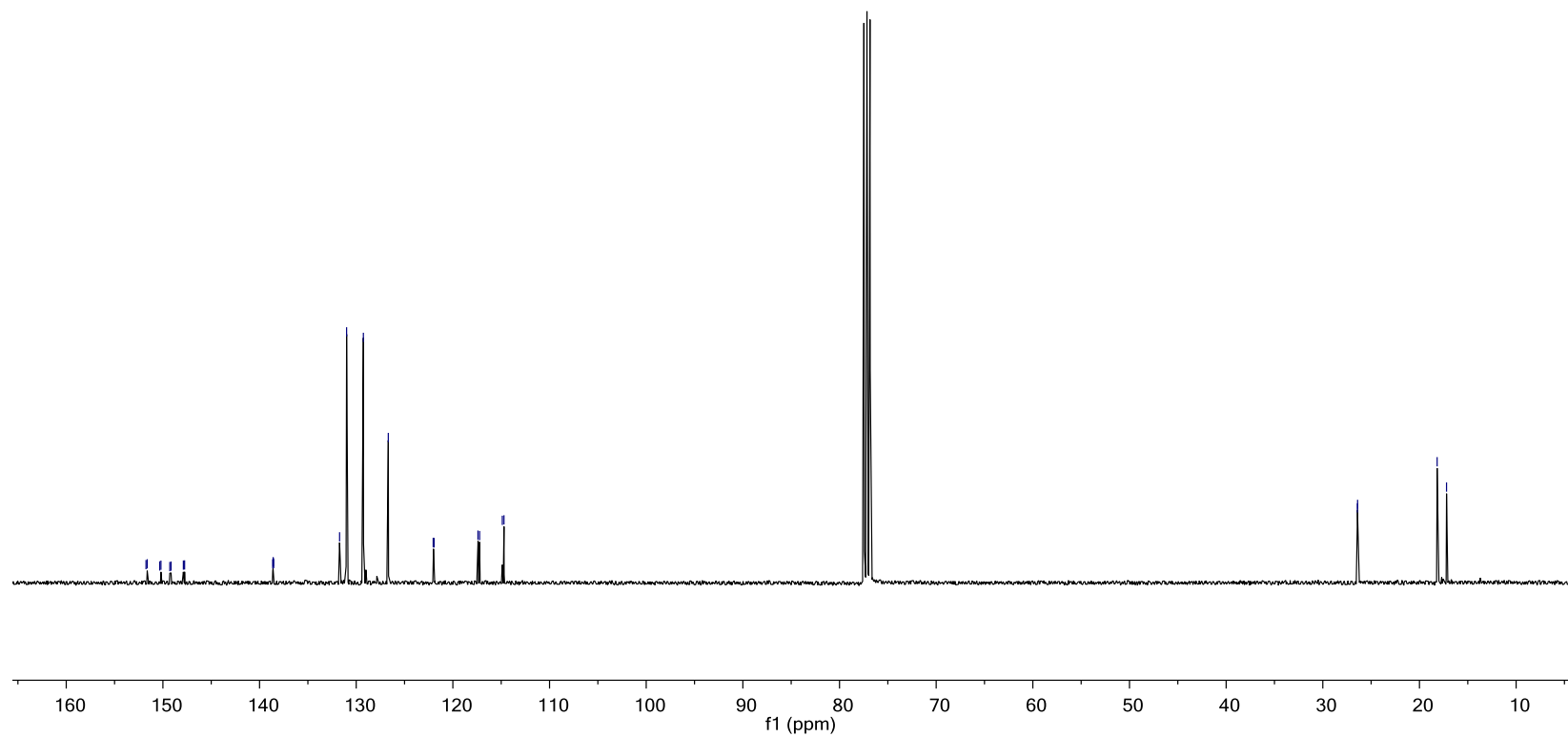
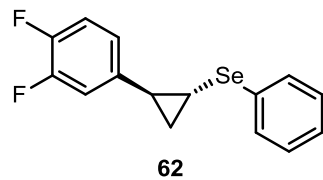


^{13}C NMR (101 MHz, CDCl_3) for compound **62**

151.75
151.62
150.33
150.20
149.29
149.16
147.88
147.75
138.64
138.60
138.58
138.54
131.72
130.99
129.26
126.68
122.04
122.00
121.98
121.94
117.40
117.23
114.89
114.71

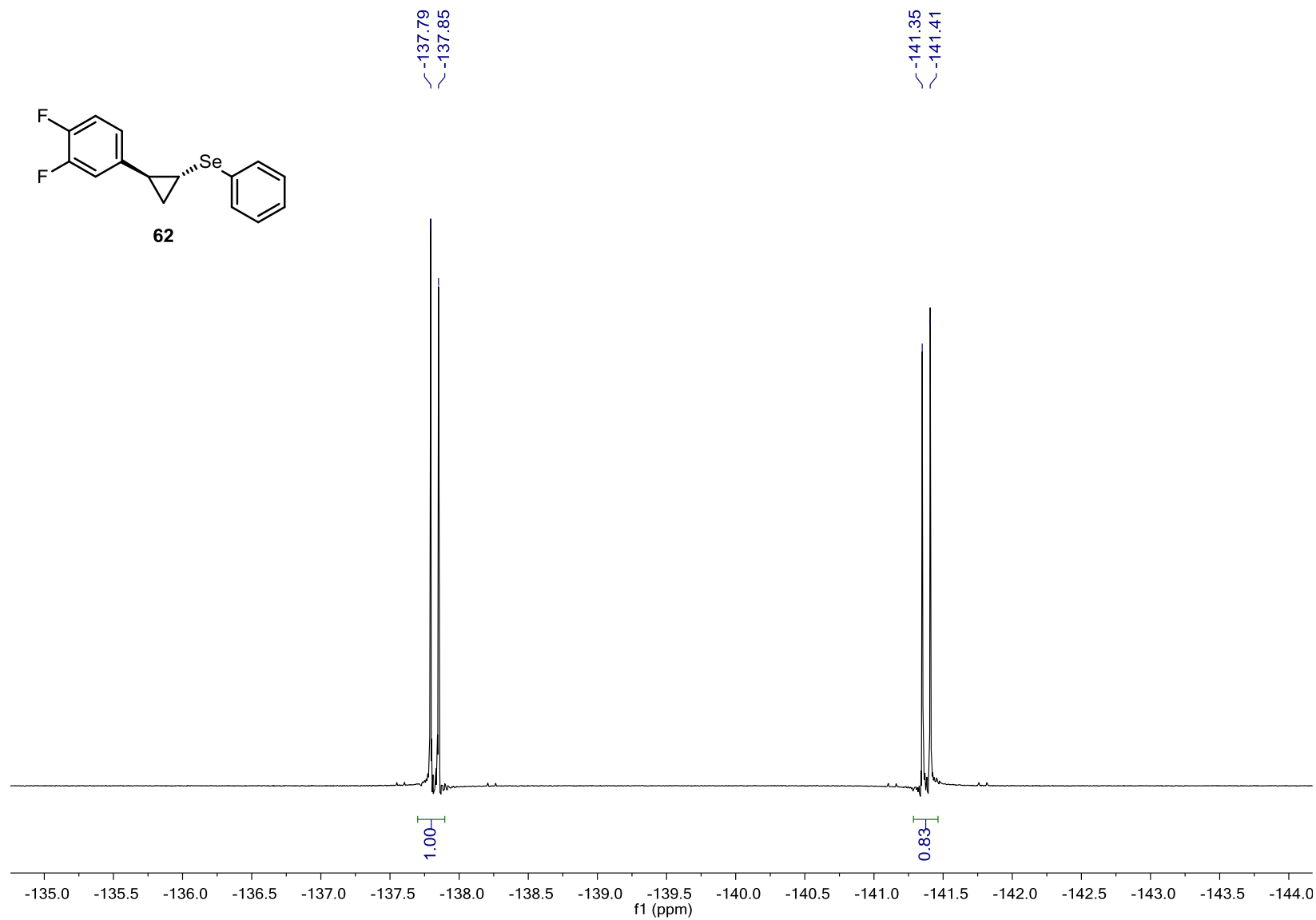
26.42
26.40

18.17
17.20

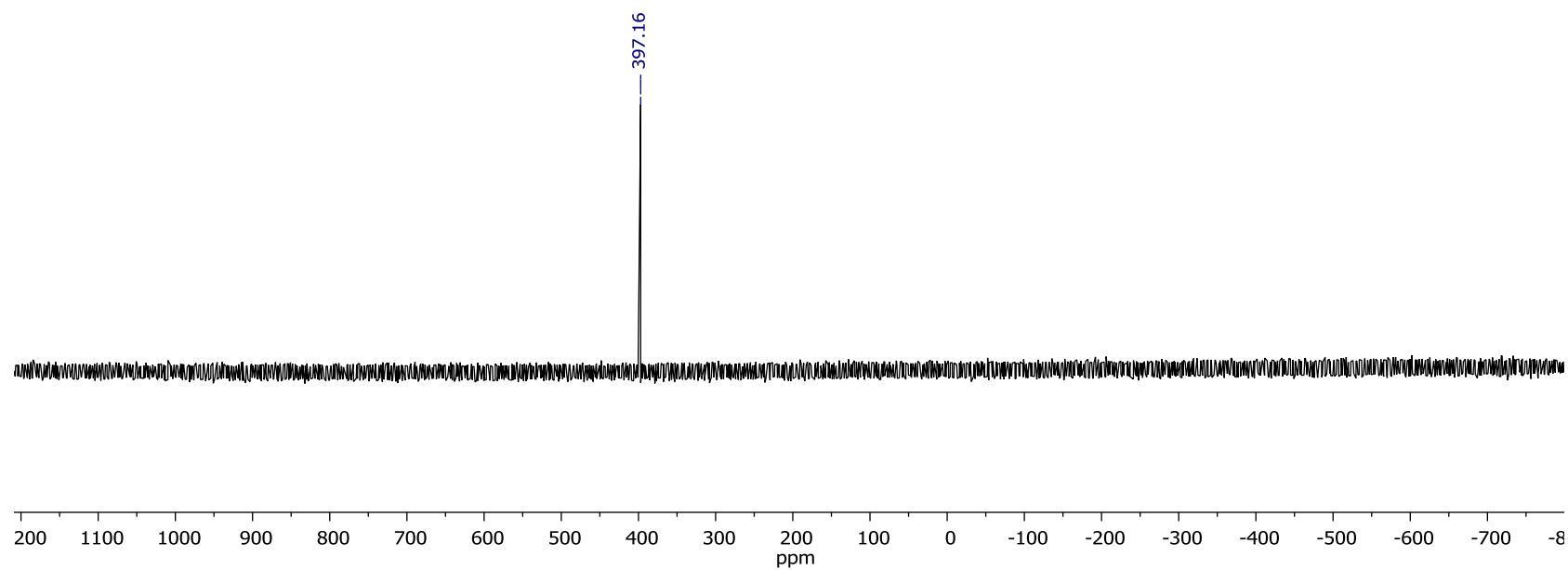
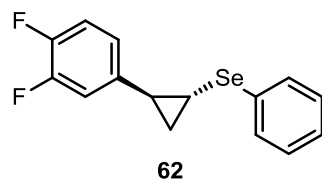


S313

^{19}F NMR (376MHz, CDCl_3) for compound **62**

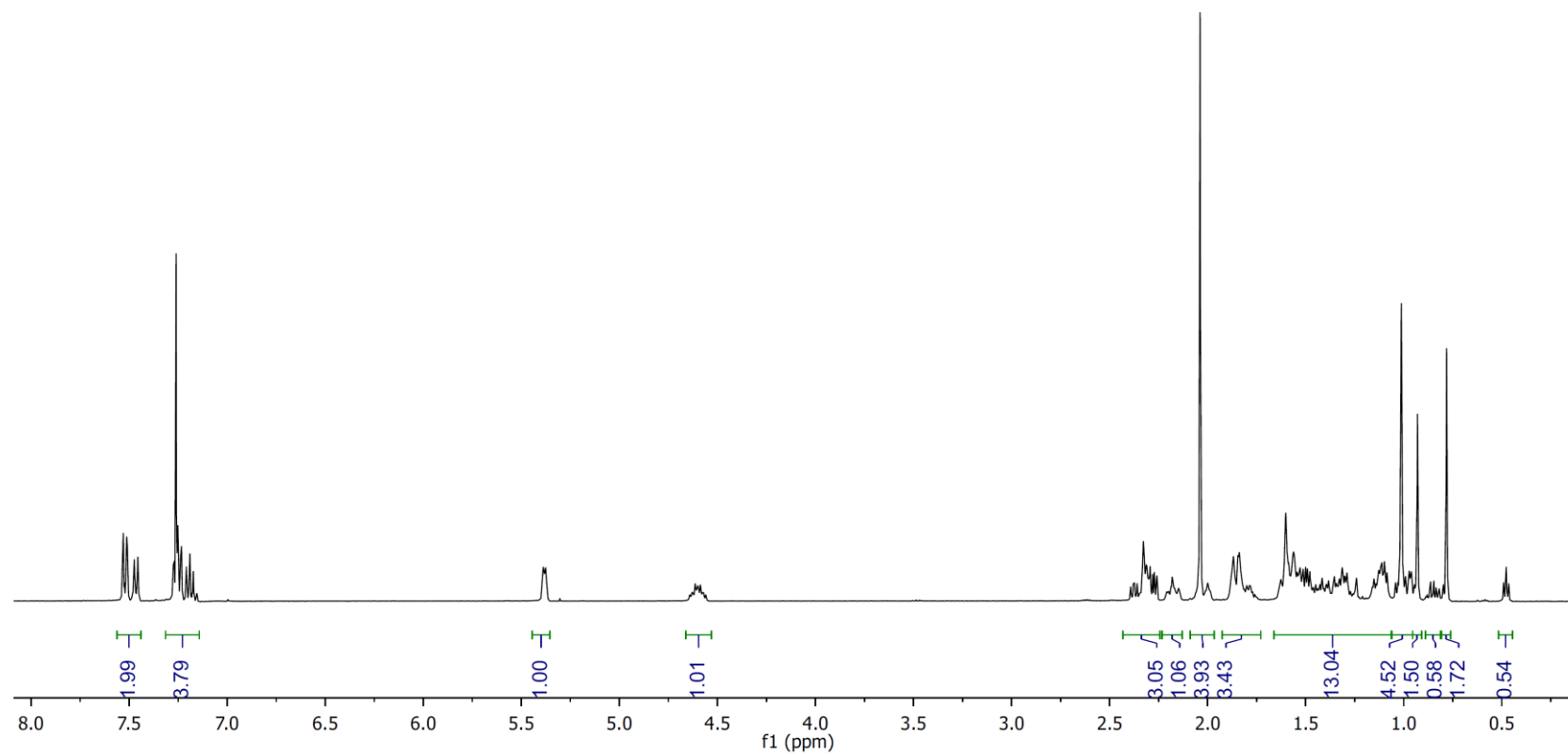
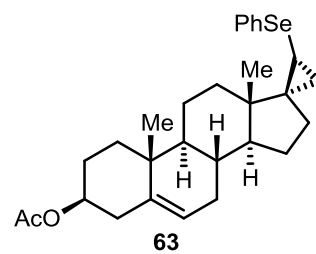


^{77}Se NMR (95MHz, CDCl_3) for compound **62**



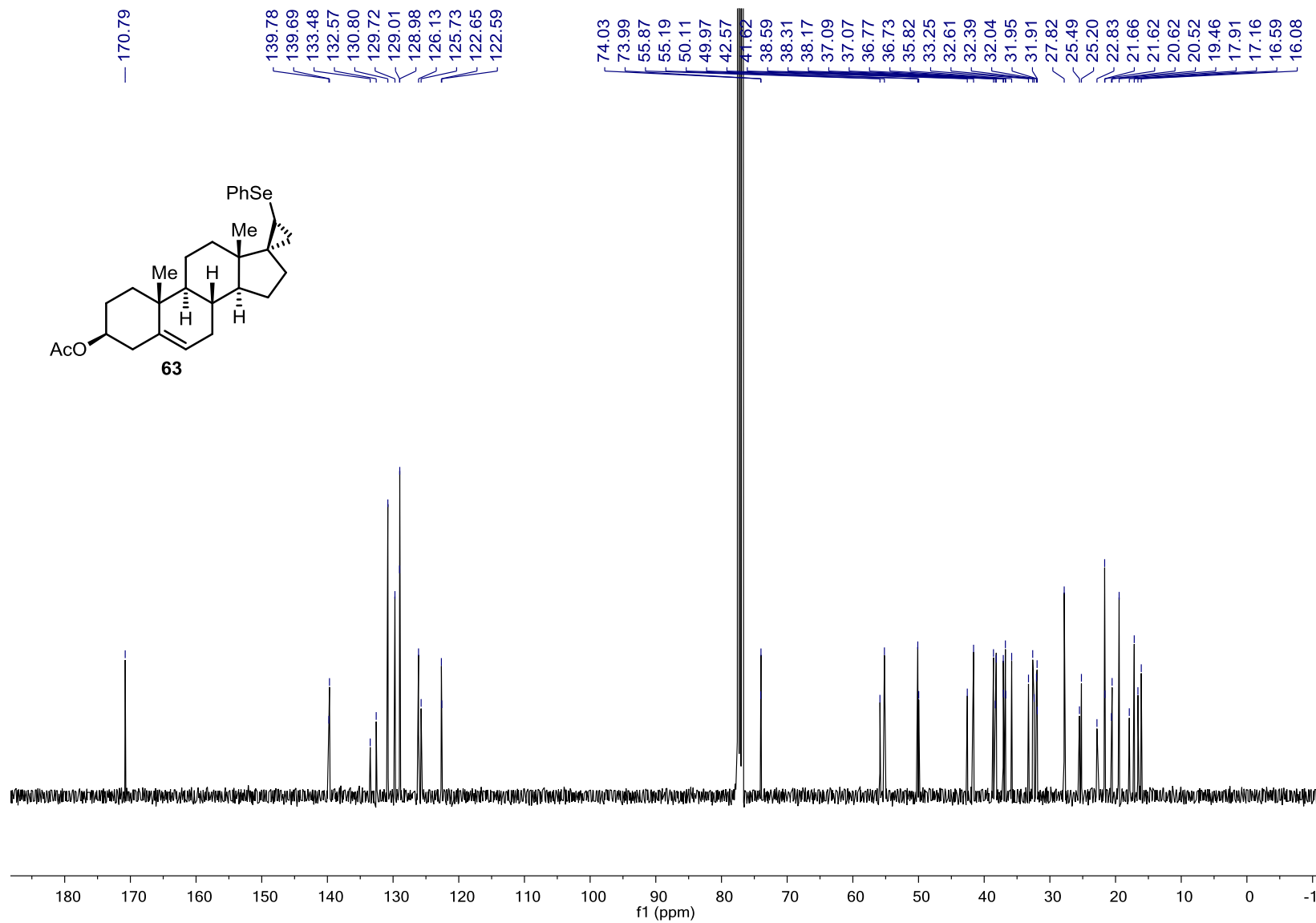
S315

^1H NMR (400 MHz, CDCl_3) for compound **63**

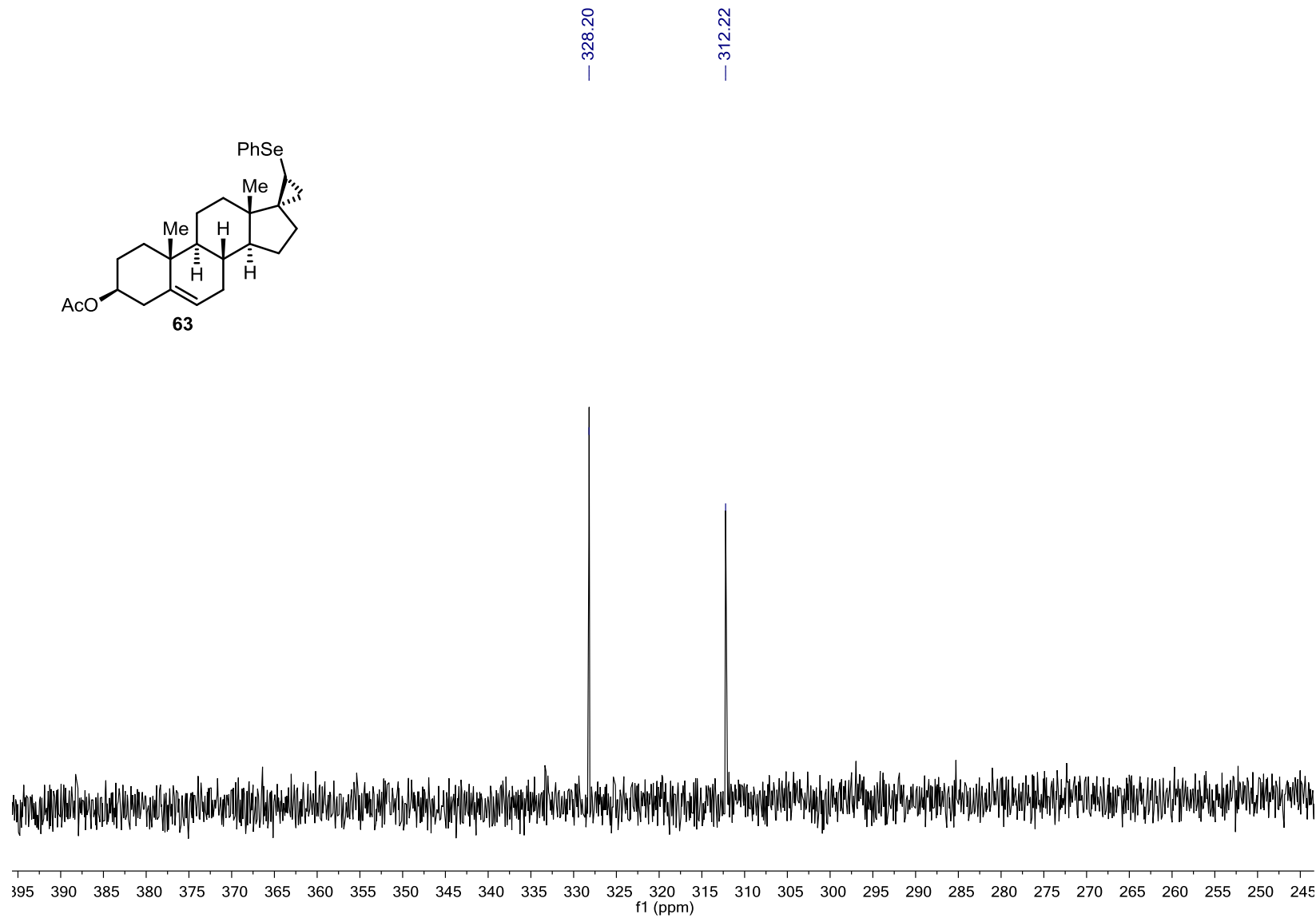
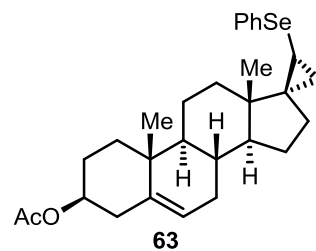


S316

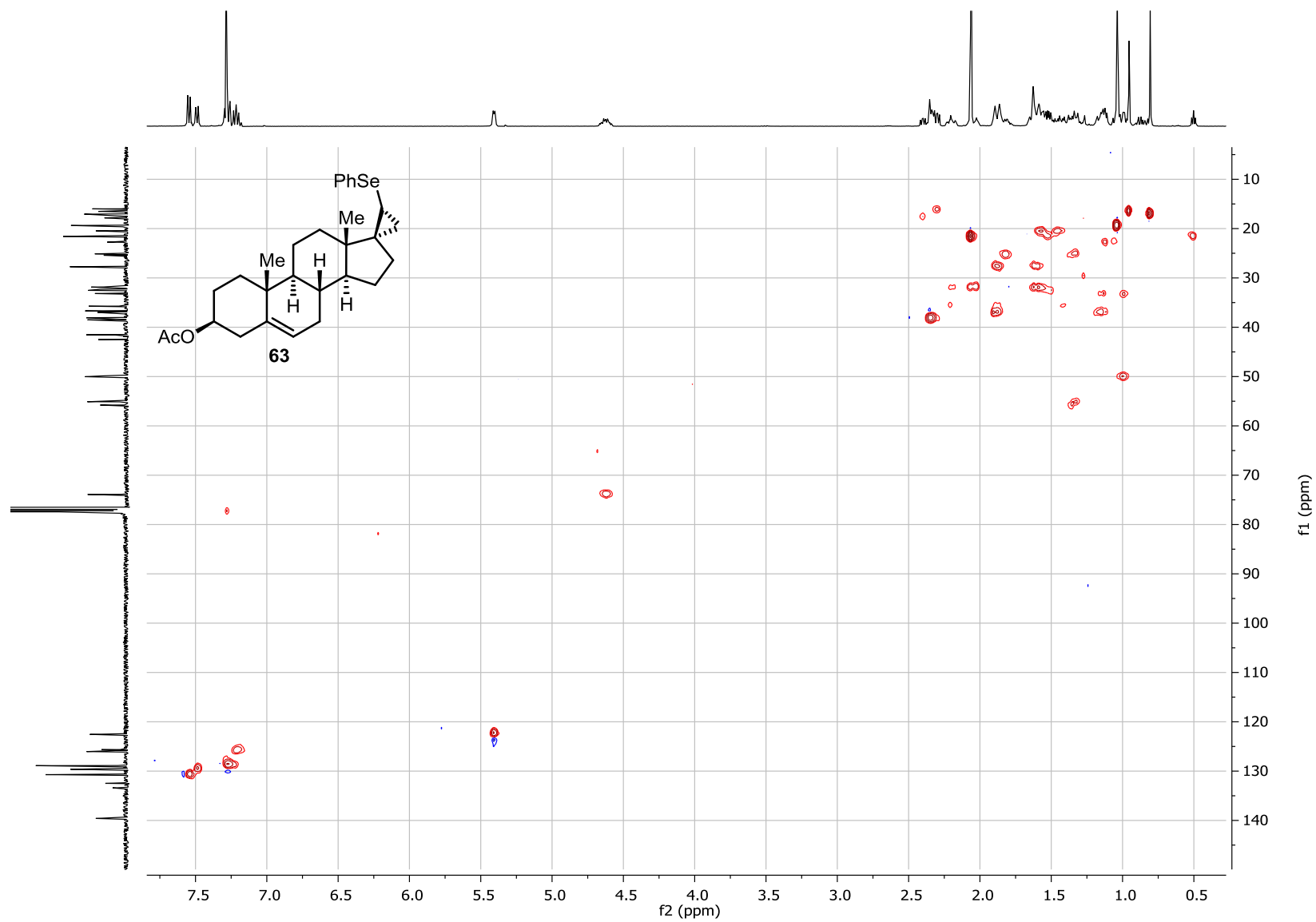
^{13}C NMR (101 MHz, CDCl_3) for compound **63**



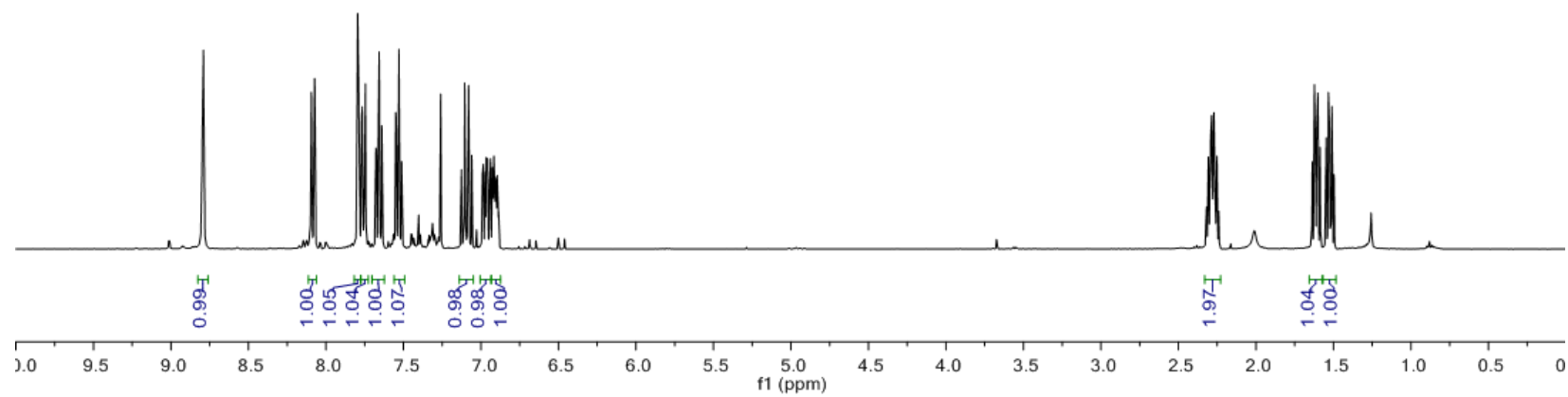
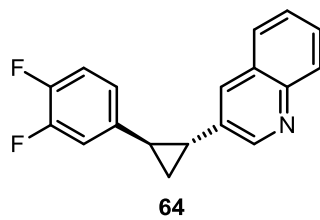
^{77}Se NMR (95MHz, CDCl_3) for compound **63**



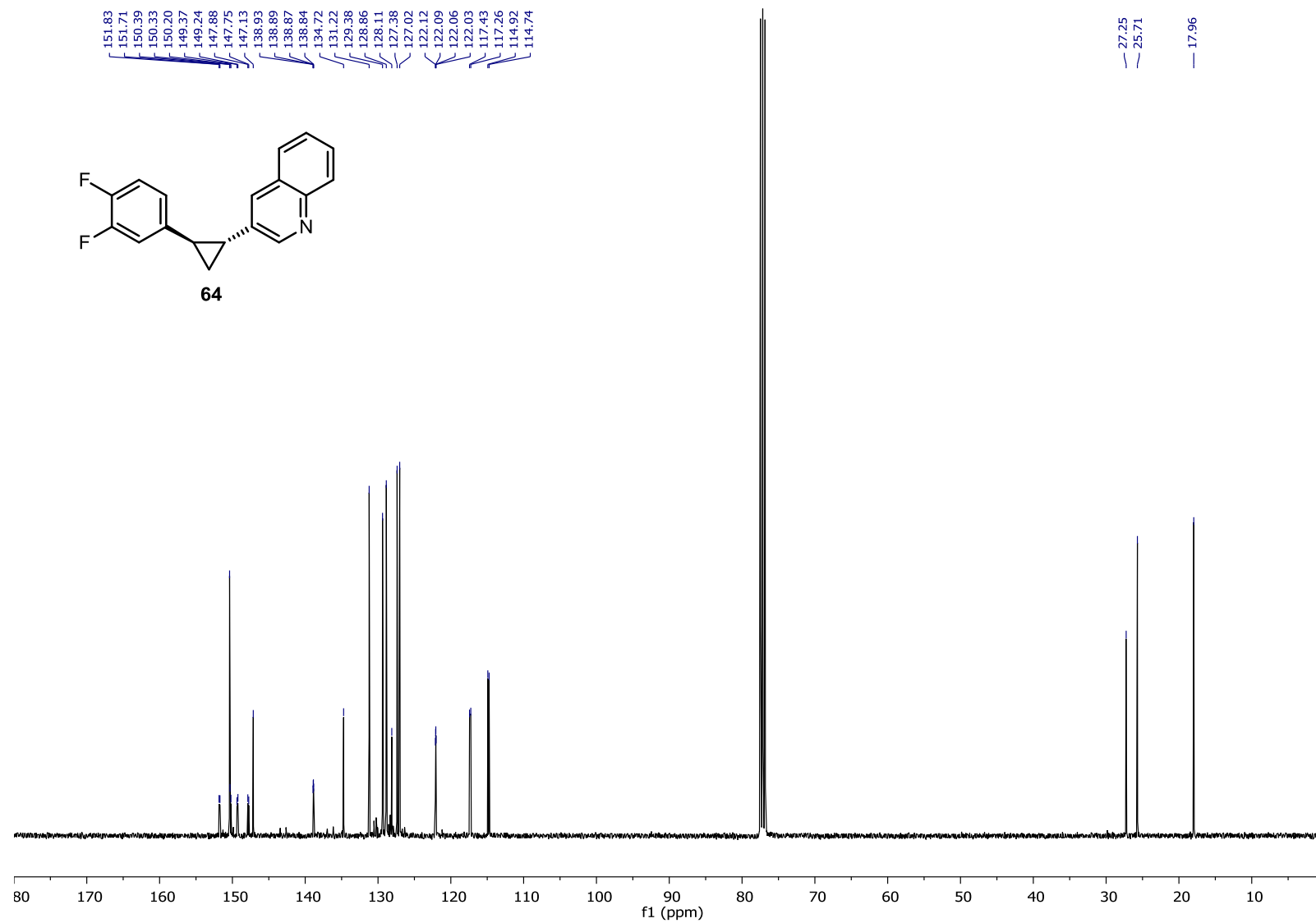
HSQC NMR (400 MHz, CDCl₃) for compound **63**



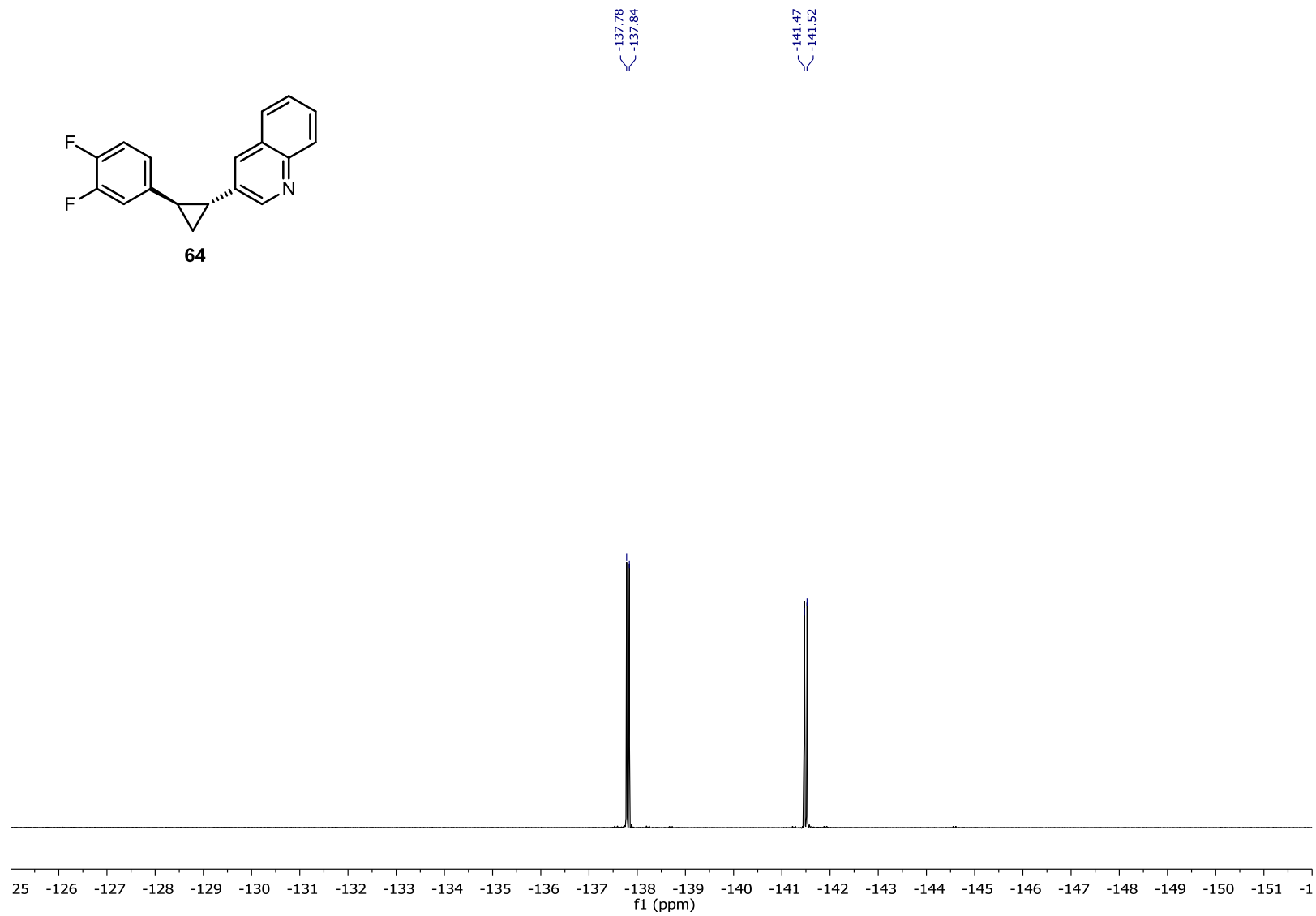
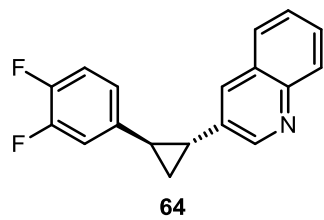
^1H NMR (400 MHz, CDCl_3) for compound **64**



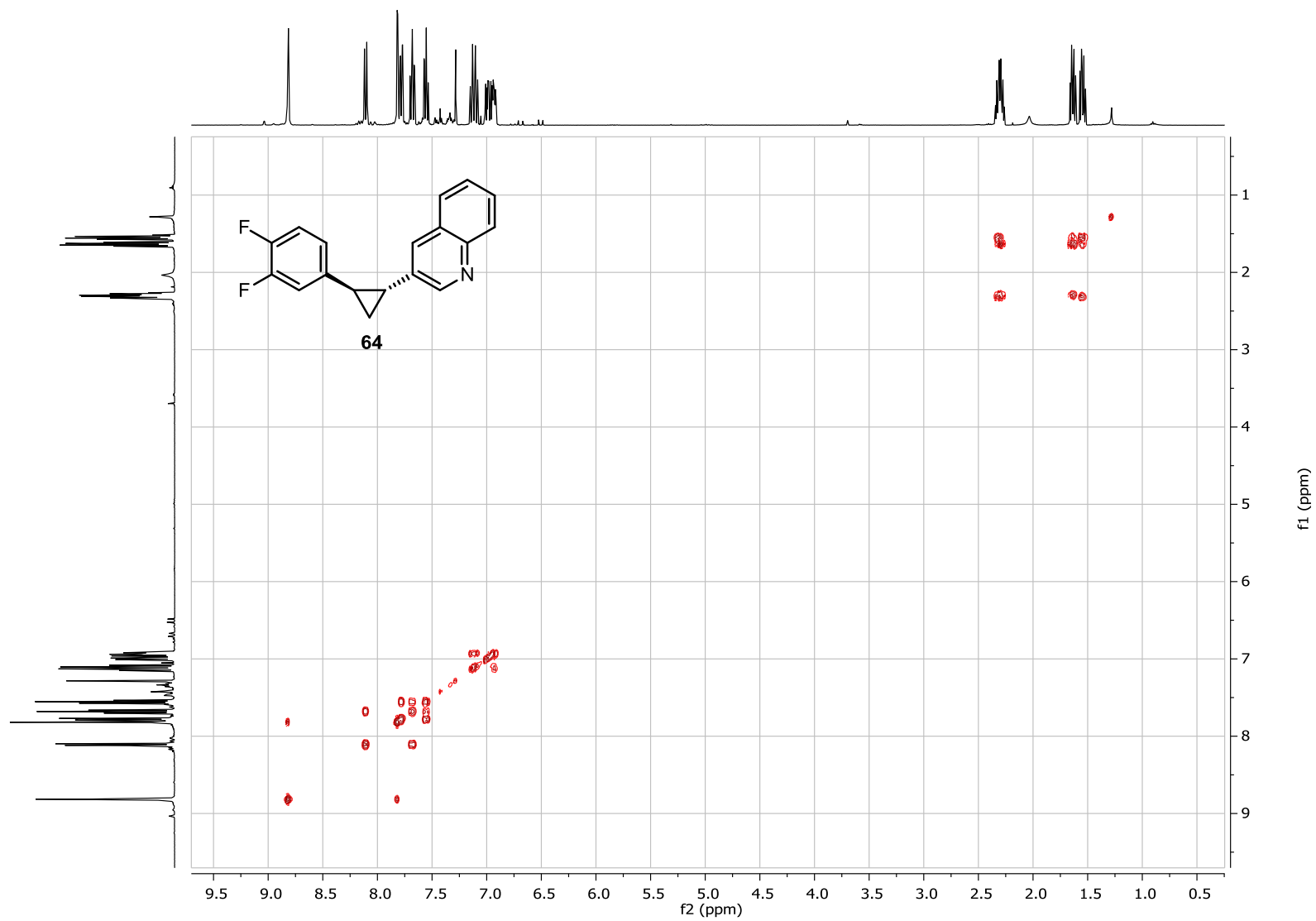
^{13}C NMR (101 MHz, CDCl_3) for compound **64**



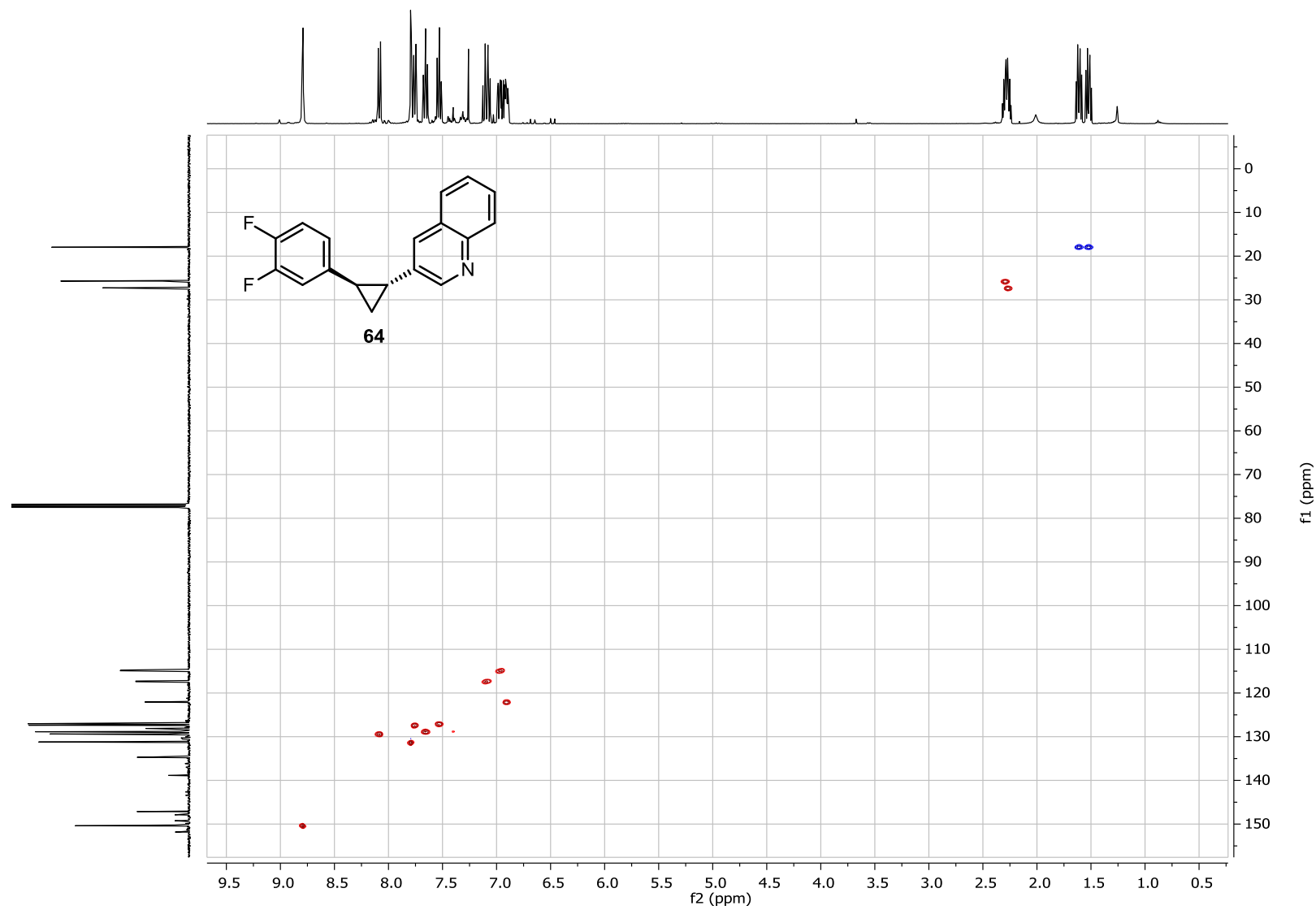
^{19}F NMR (376MHz, CDCl_3) for compound **64**



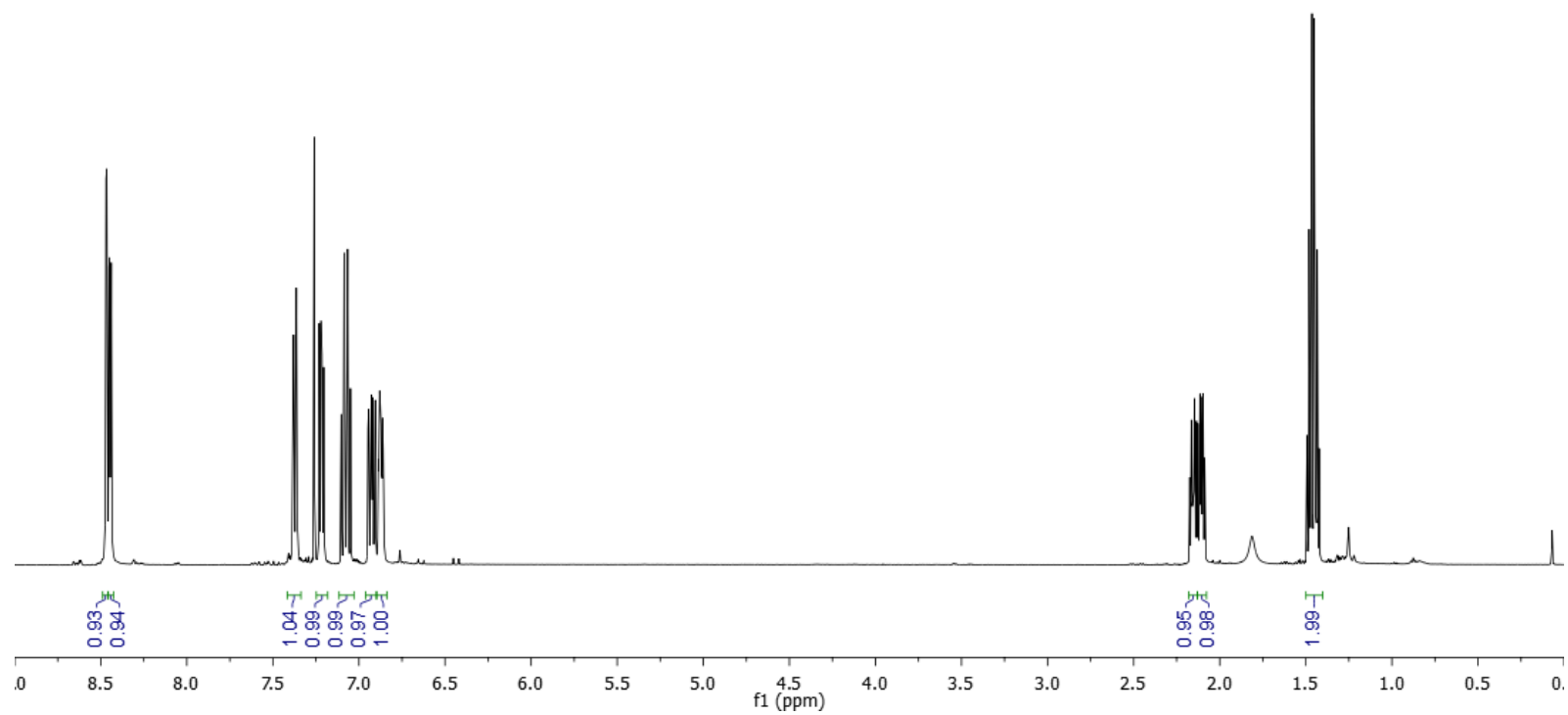
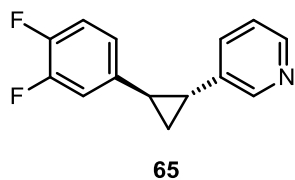
COSY NMR (400 MHz, CDCl₃) for compound **64**



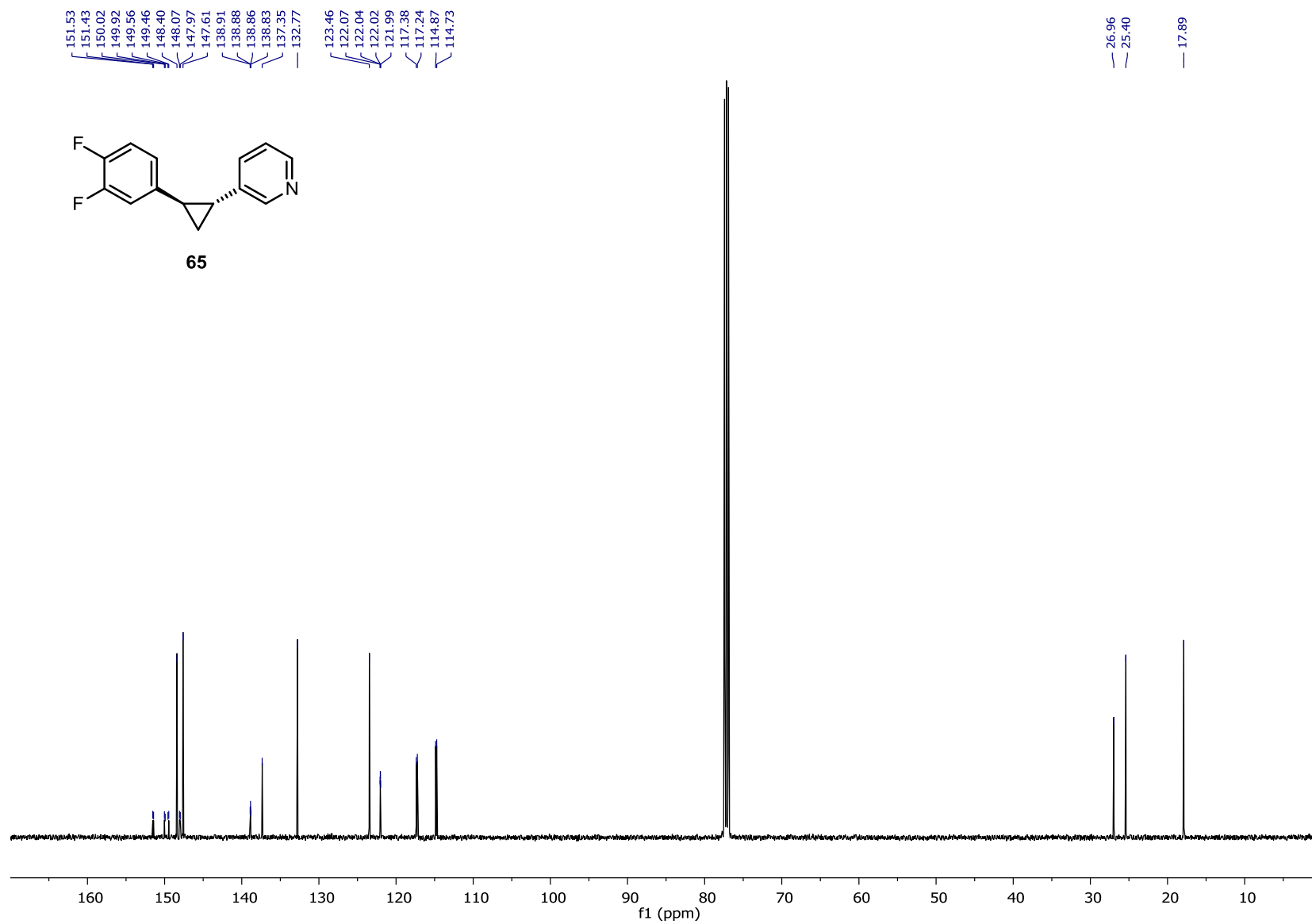
HSQC NMR (400 MHz, CDCl₃) for compound **64**



^1H NMR (500 MHz, CDCl_3) for compound **65**

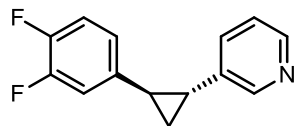


^{13}C NMR (126 MHz, CDCl_3) for compound **65**



S326

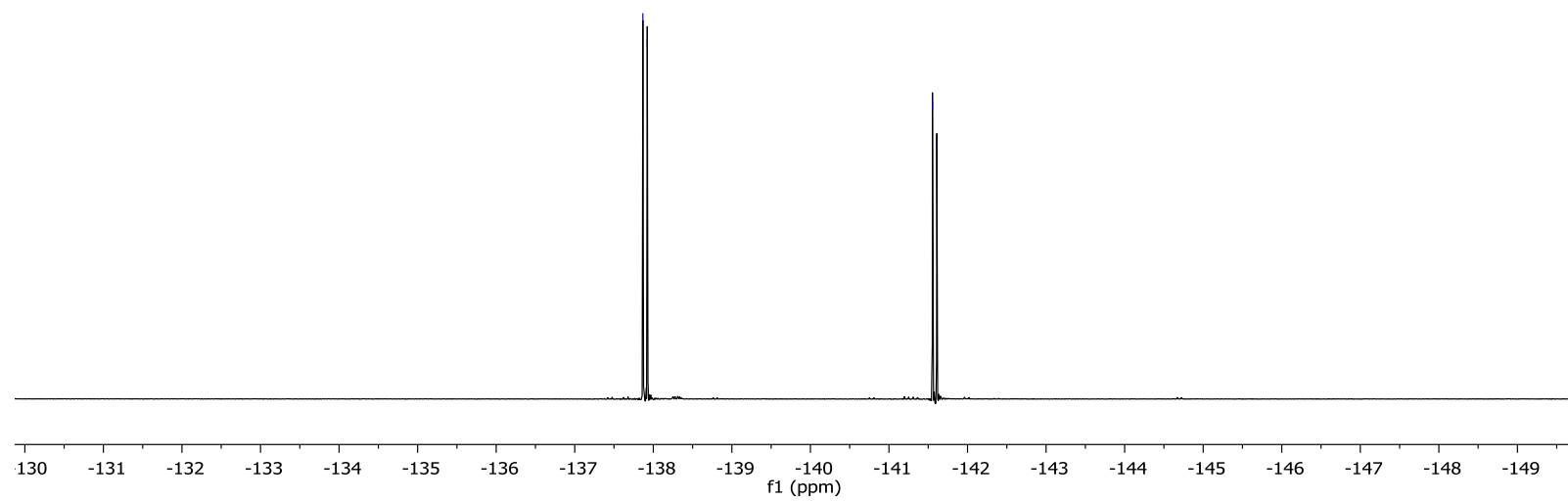
^{19}F NMR (376 MHz, CDCl_3) for compound **65**



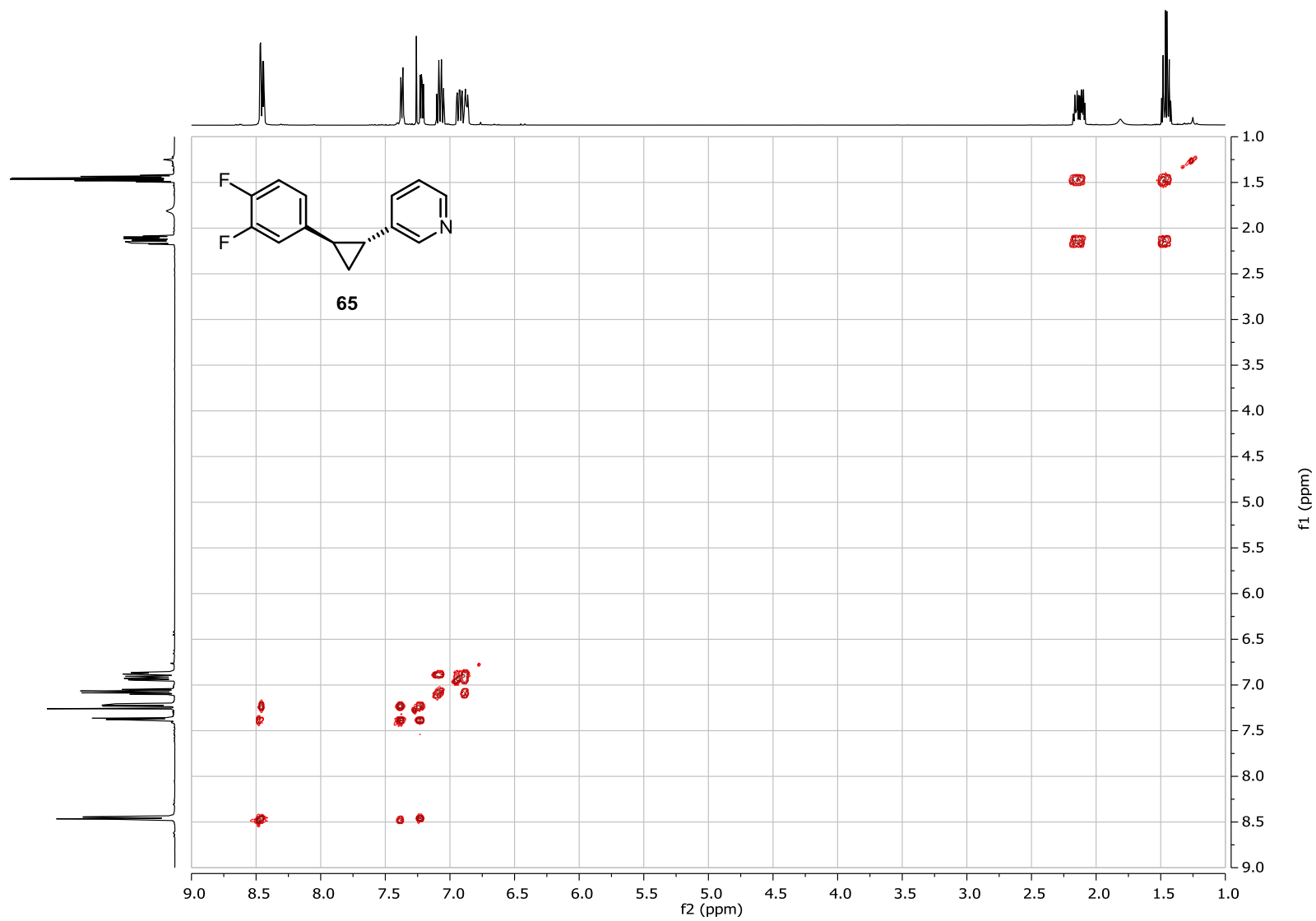
65

-137.87
-137.92

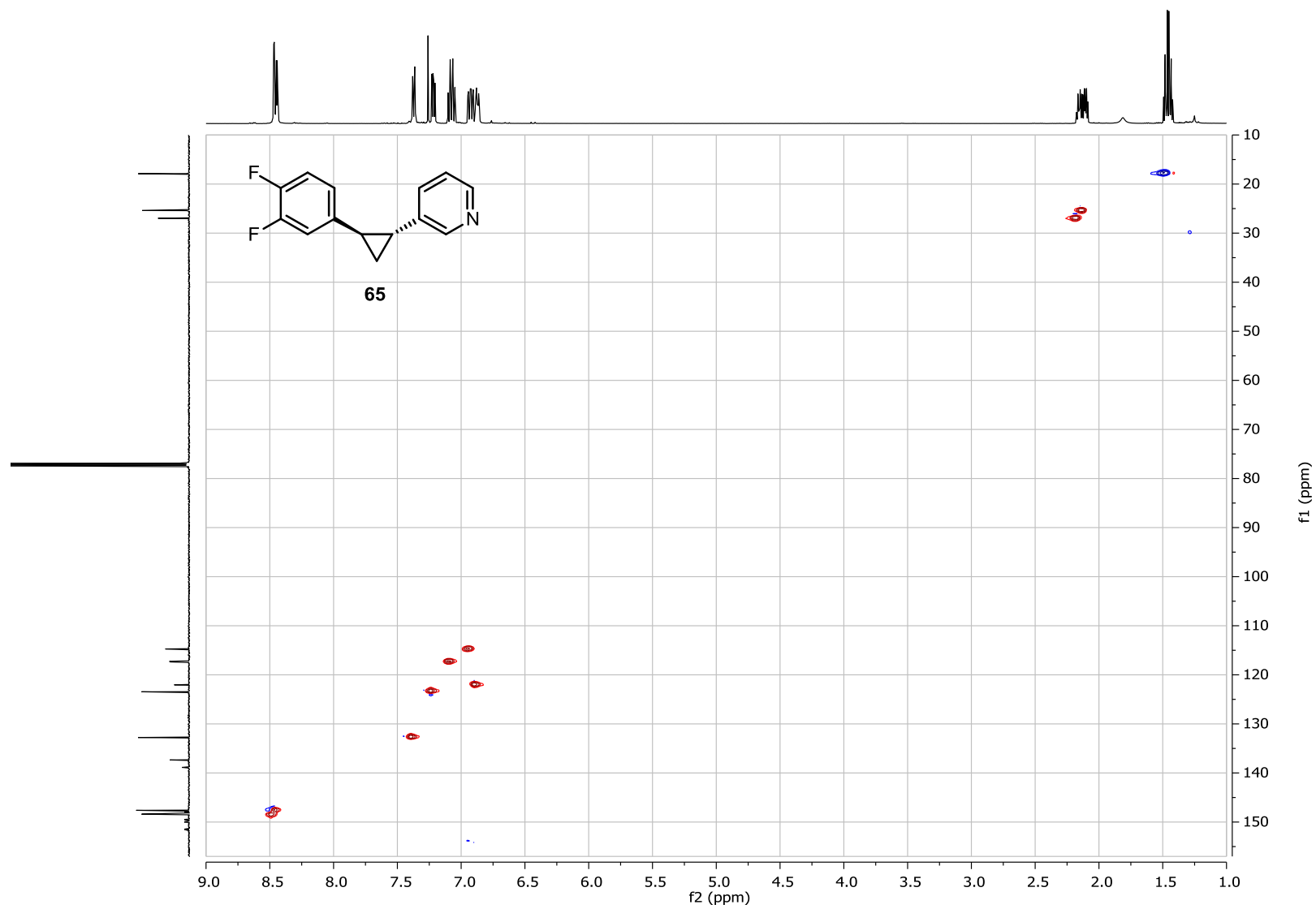
-141.55
-141.61



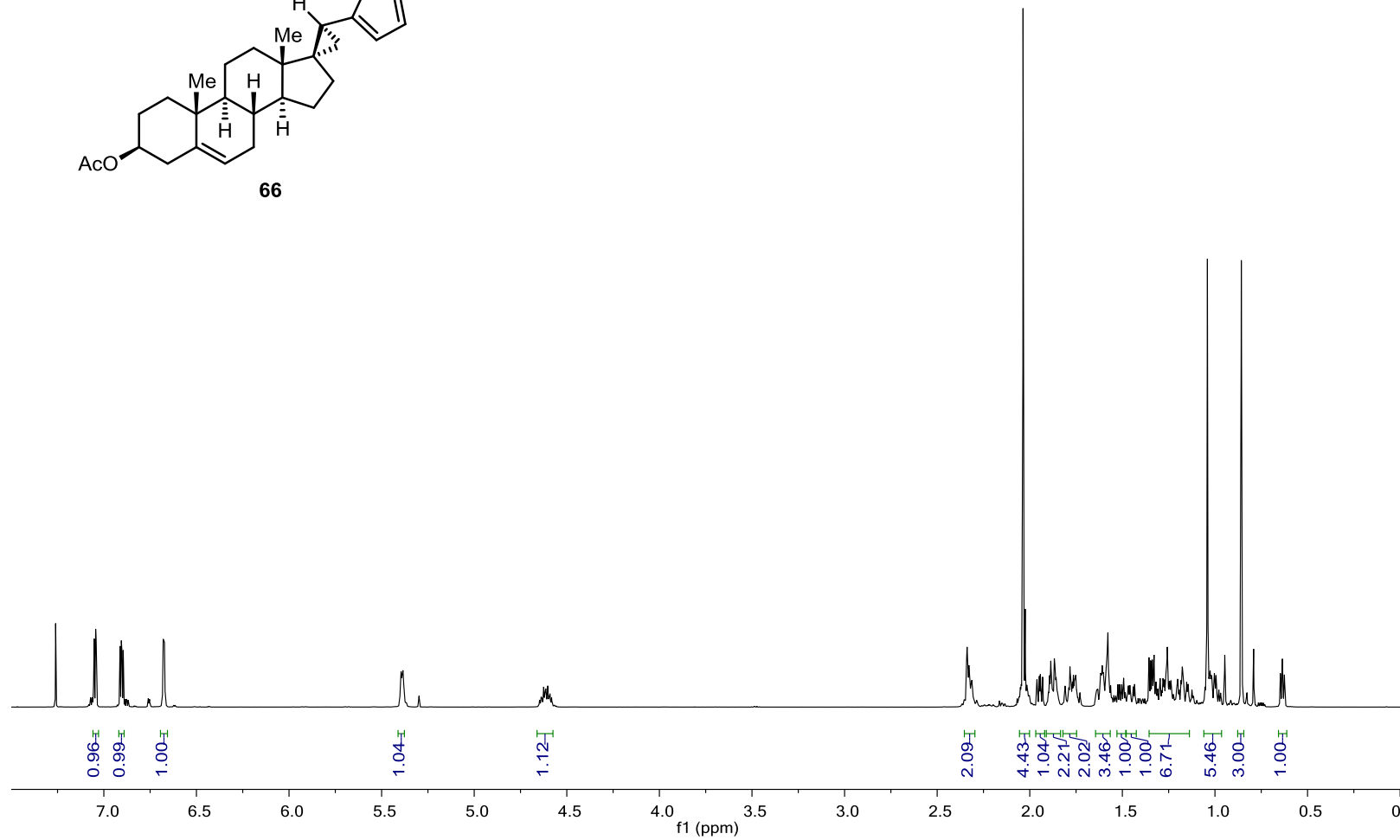
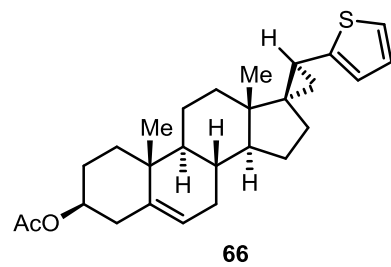
COSY NMR (500 MHz, CDCl₃) for compound 65



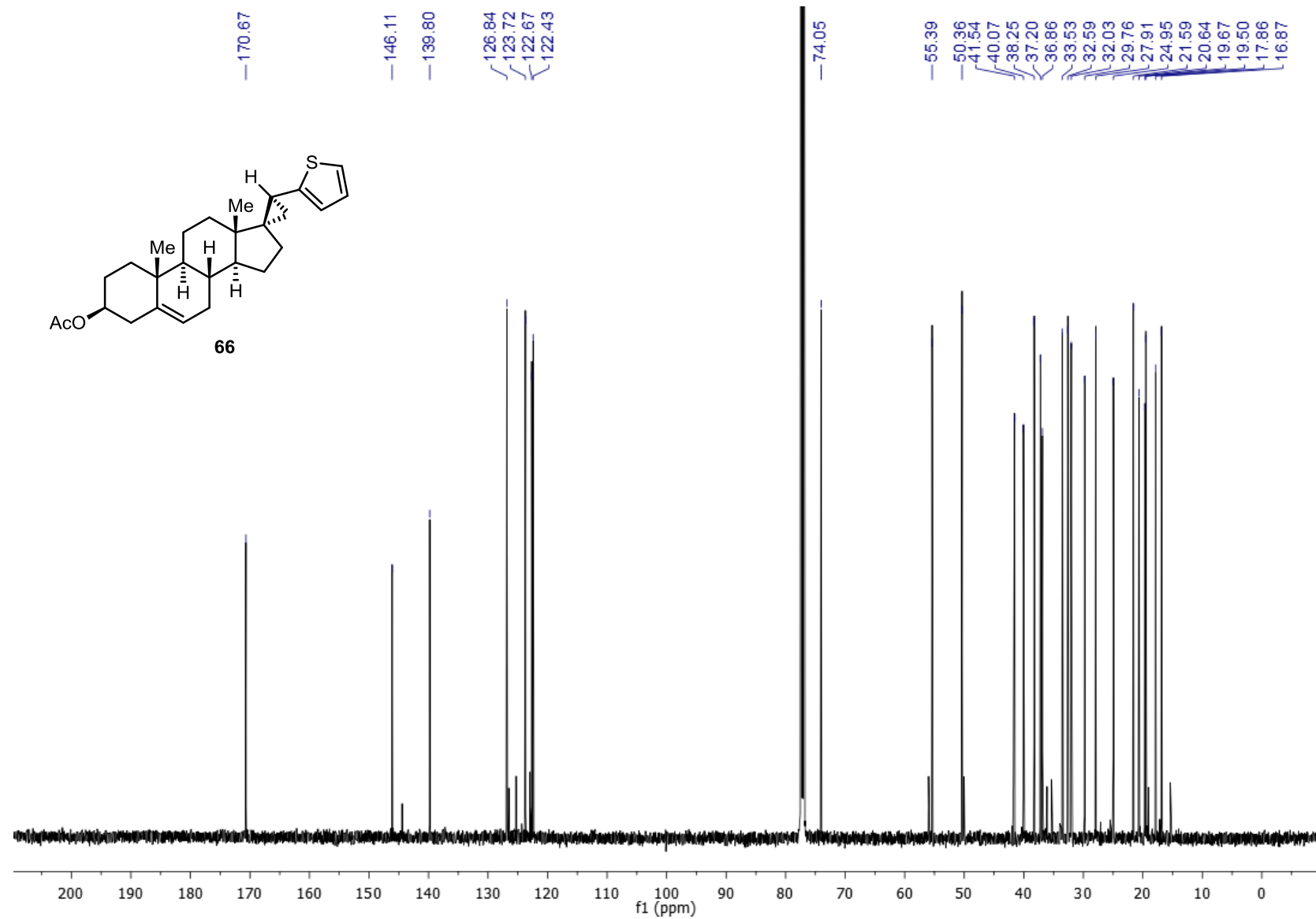
HSQC NMR (500 MHz, CDCl₃) for compound **65**



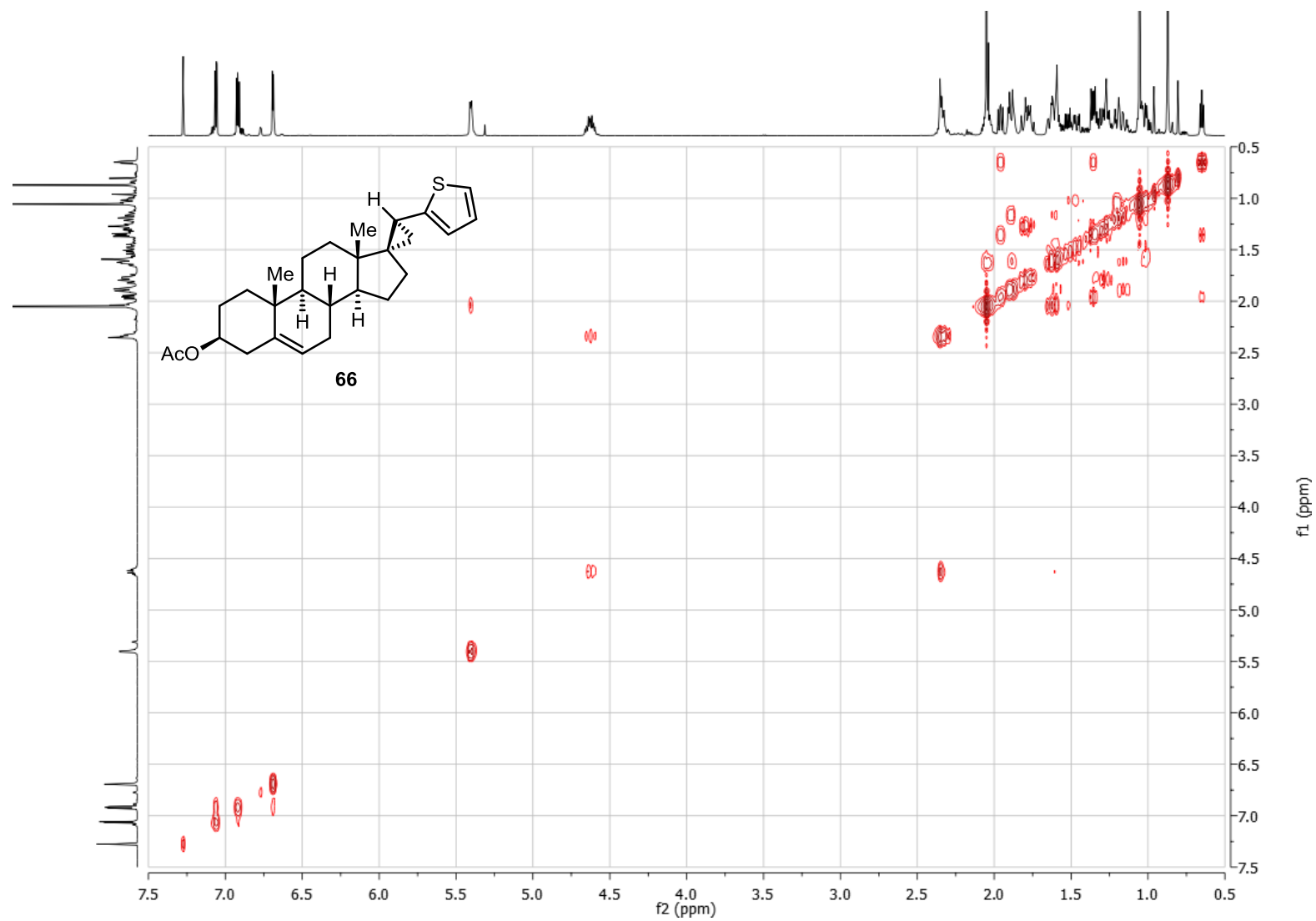
^1H NMR (500 MHz, CDCl_3) for compound **66**



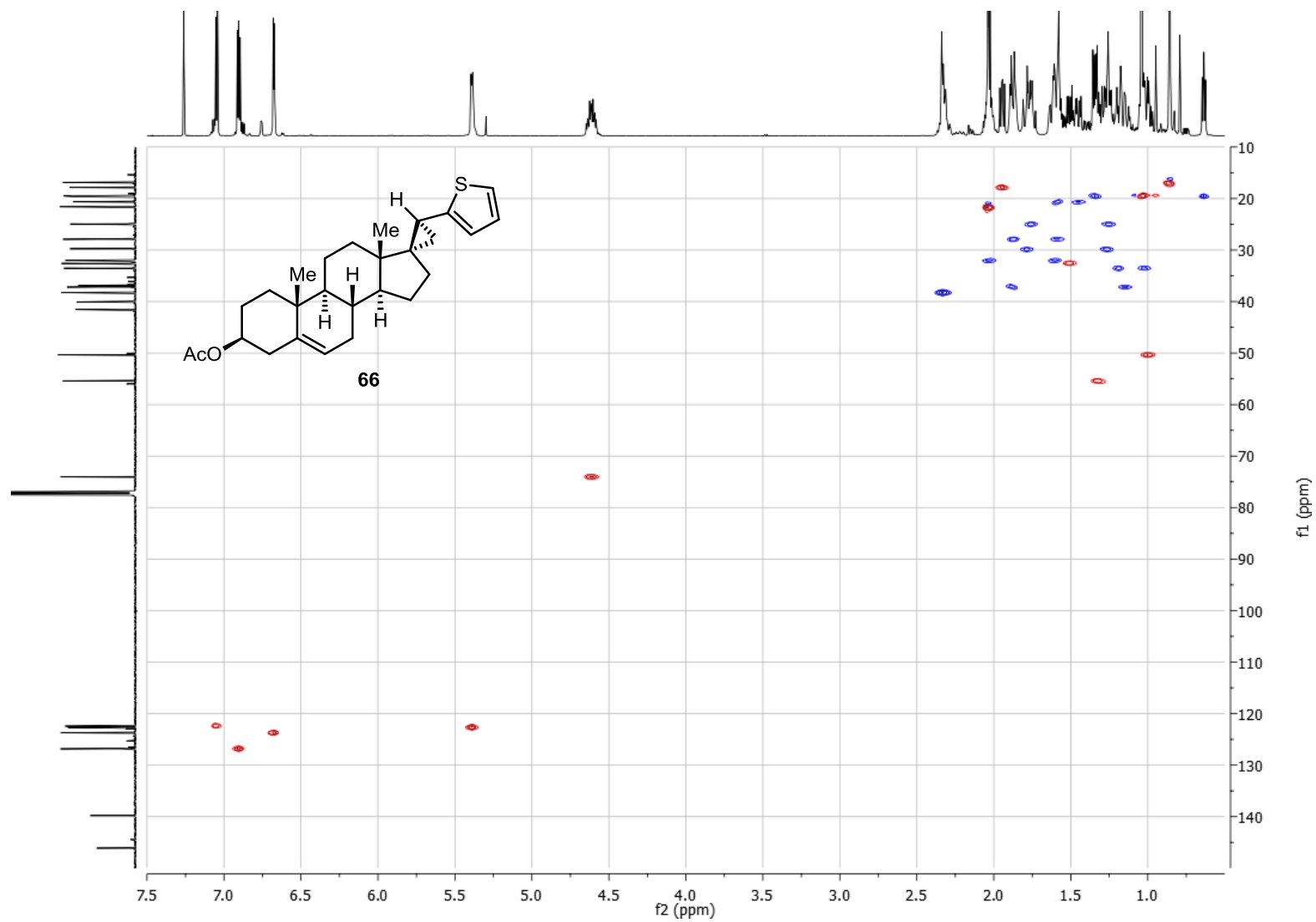
^{13}C NMR (126 MHz, CDCl_3) for compound **66**



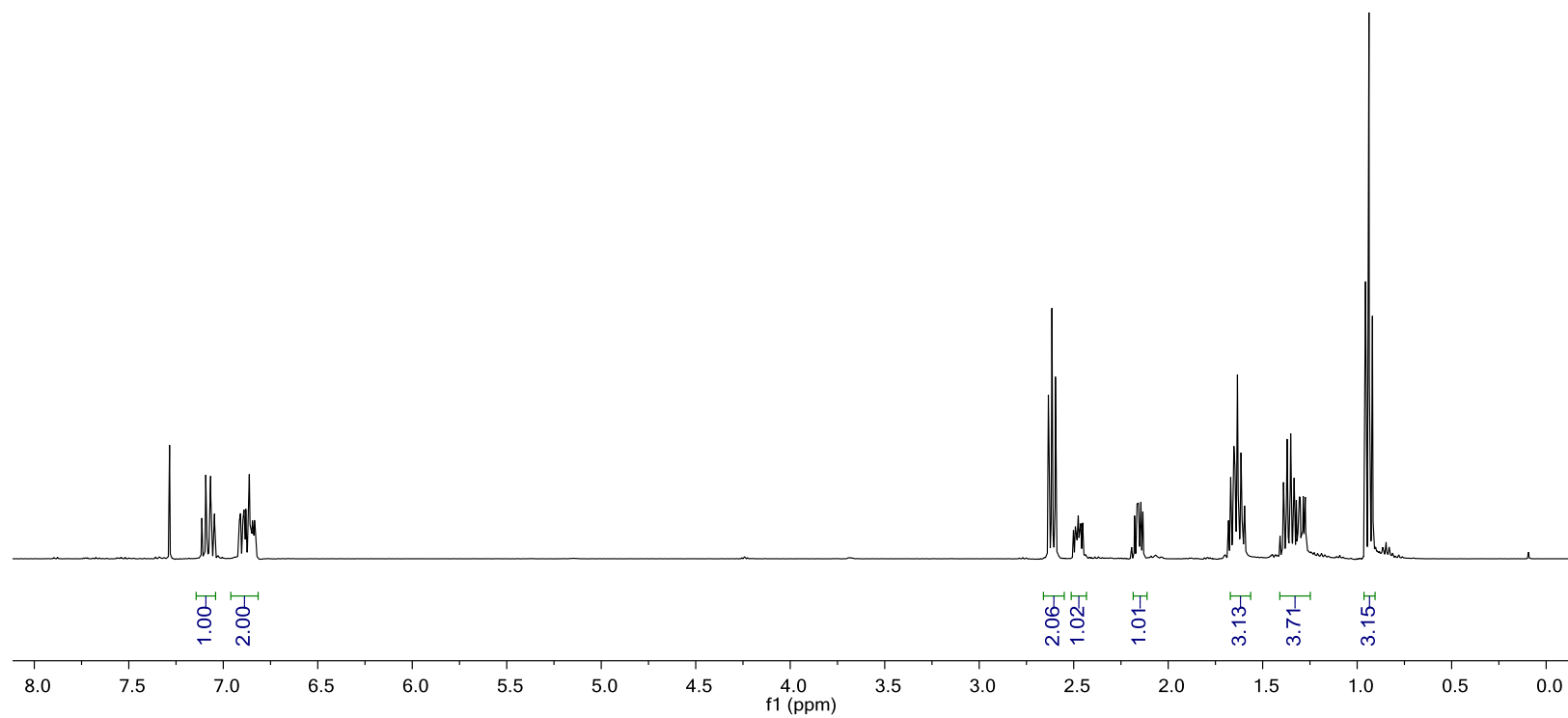
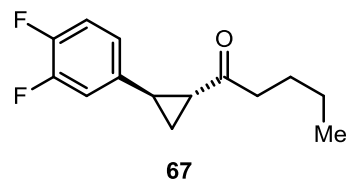
COSY NMR (500 MHz, CDCl₃) for compound 66



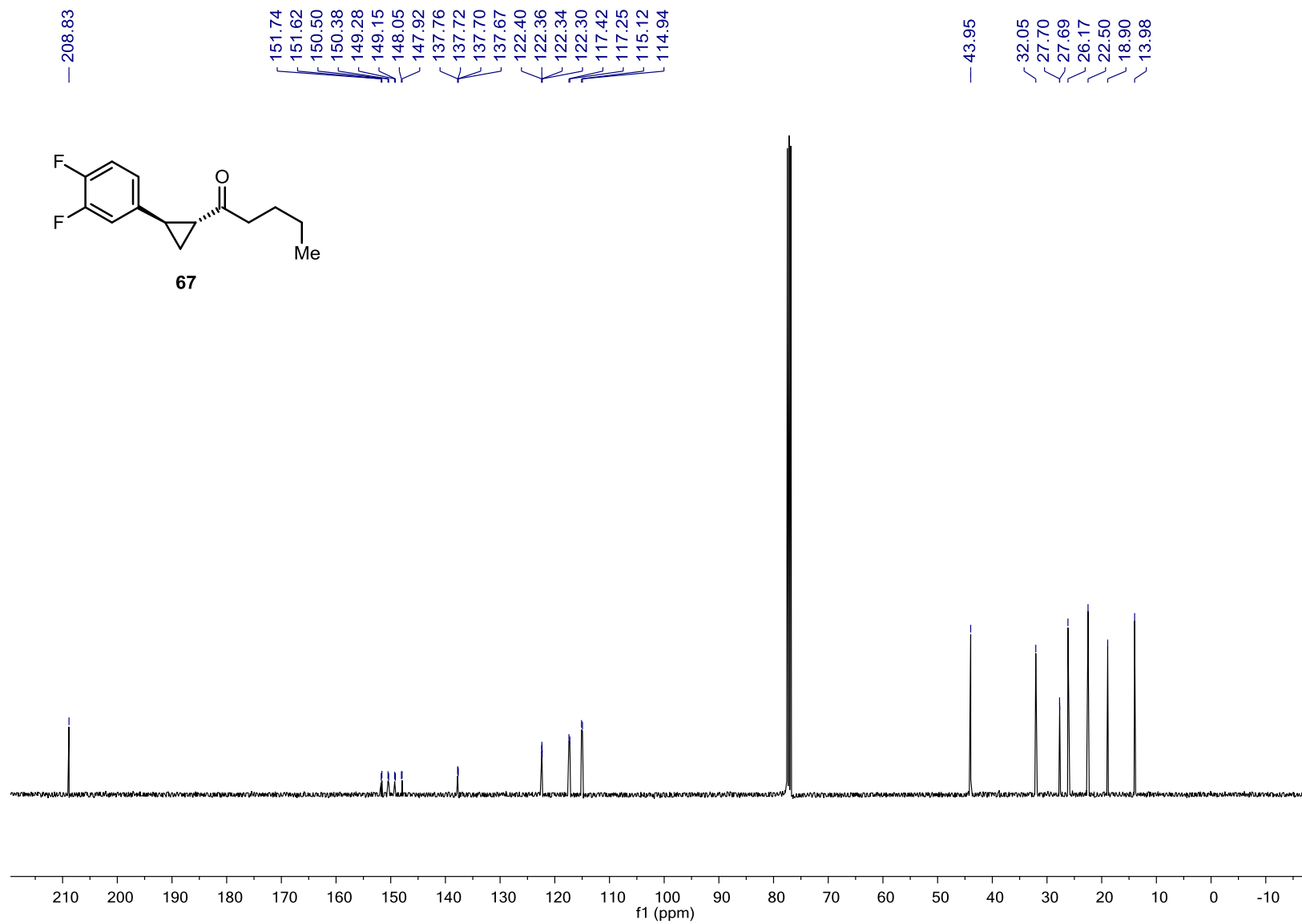
HSQC NMR (500 MHz, CDCl_3) for compound **66**



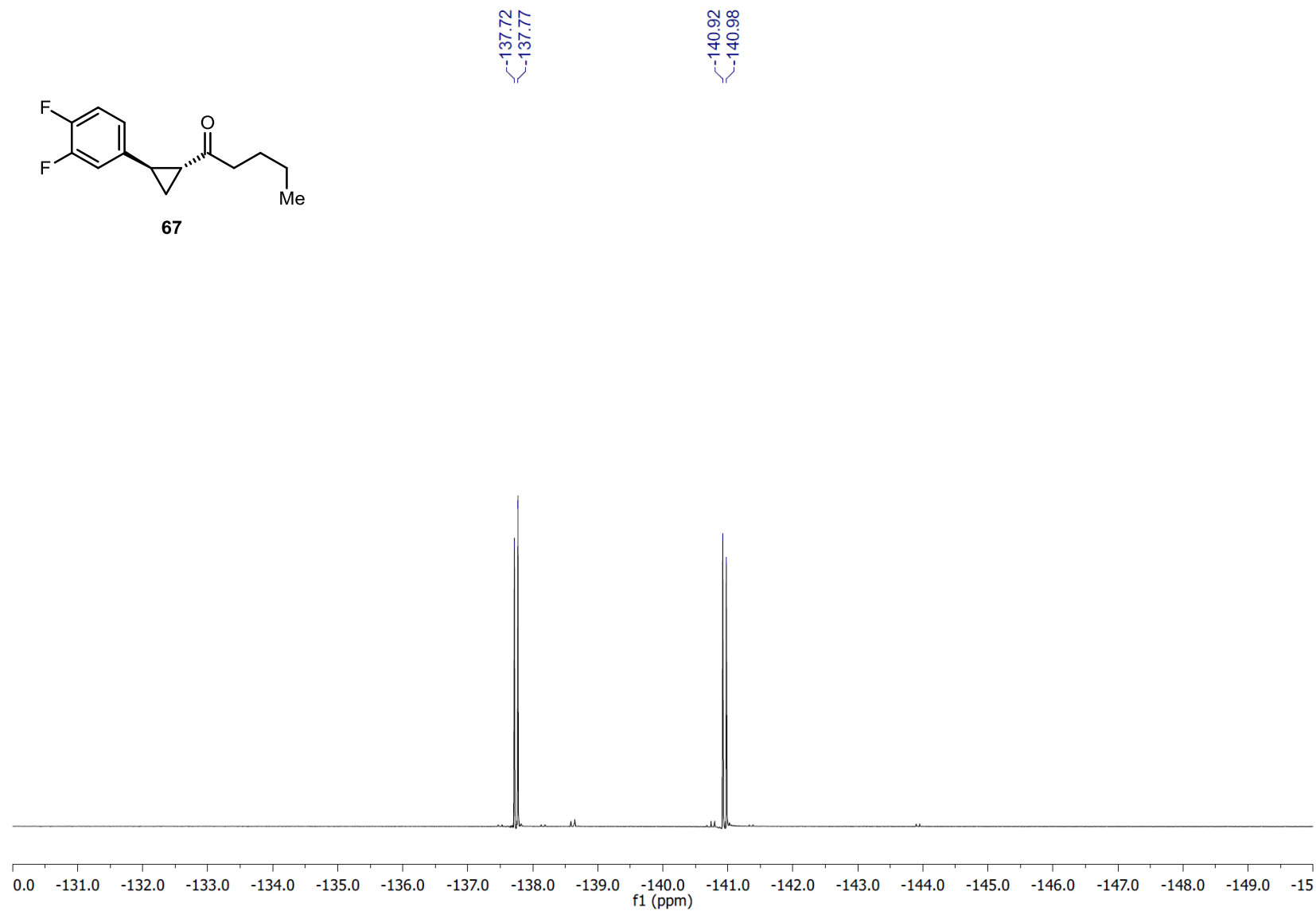
^1H NMR (400 MHz, CDCl_3) for compound **67**



^{13}C NMR (101 MHz, CDCl_3) for compound **67**

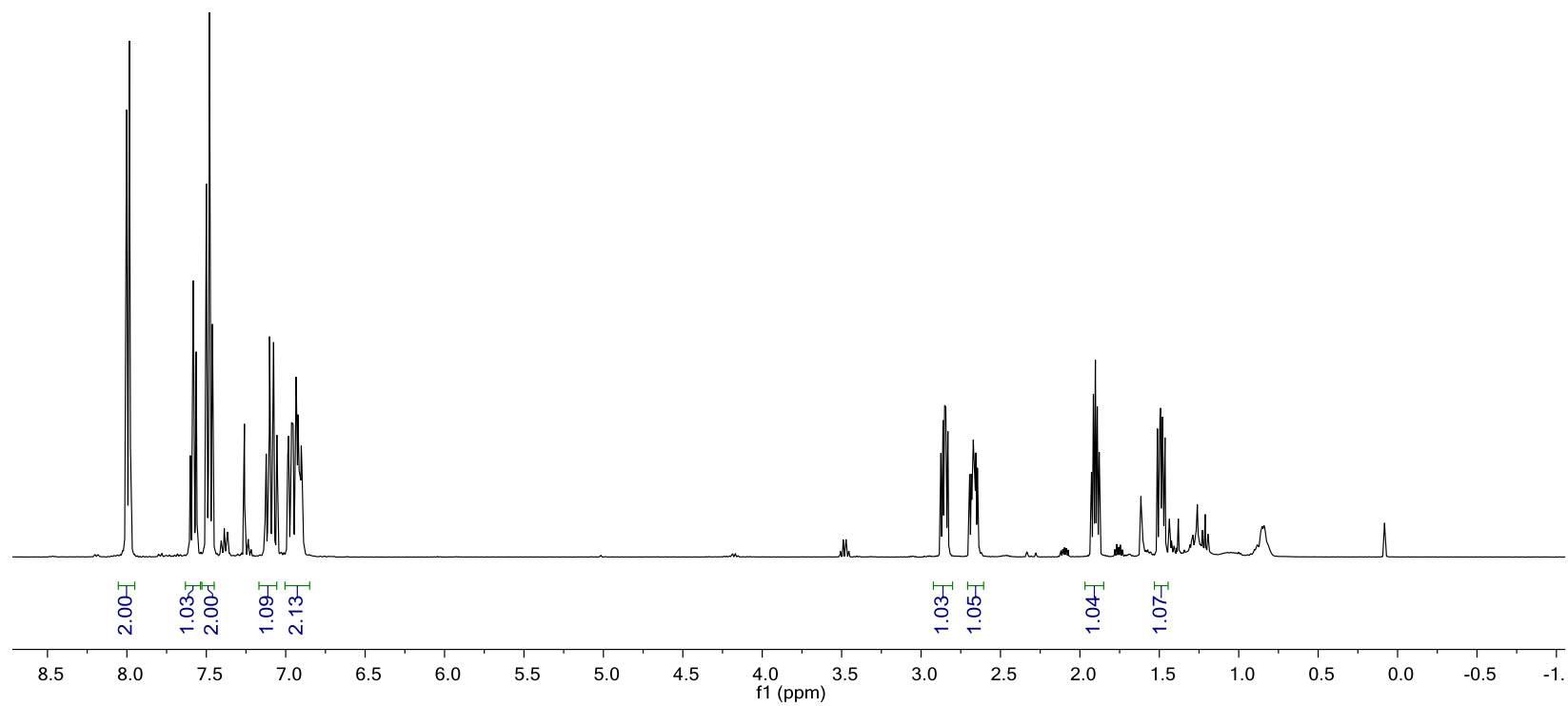
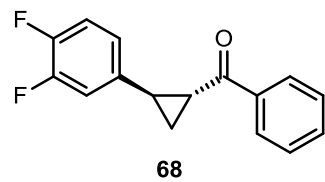


^{19}F NMR (376MHz, CDCl_3) for compound **67**

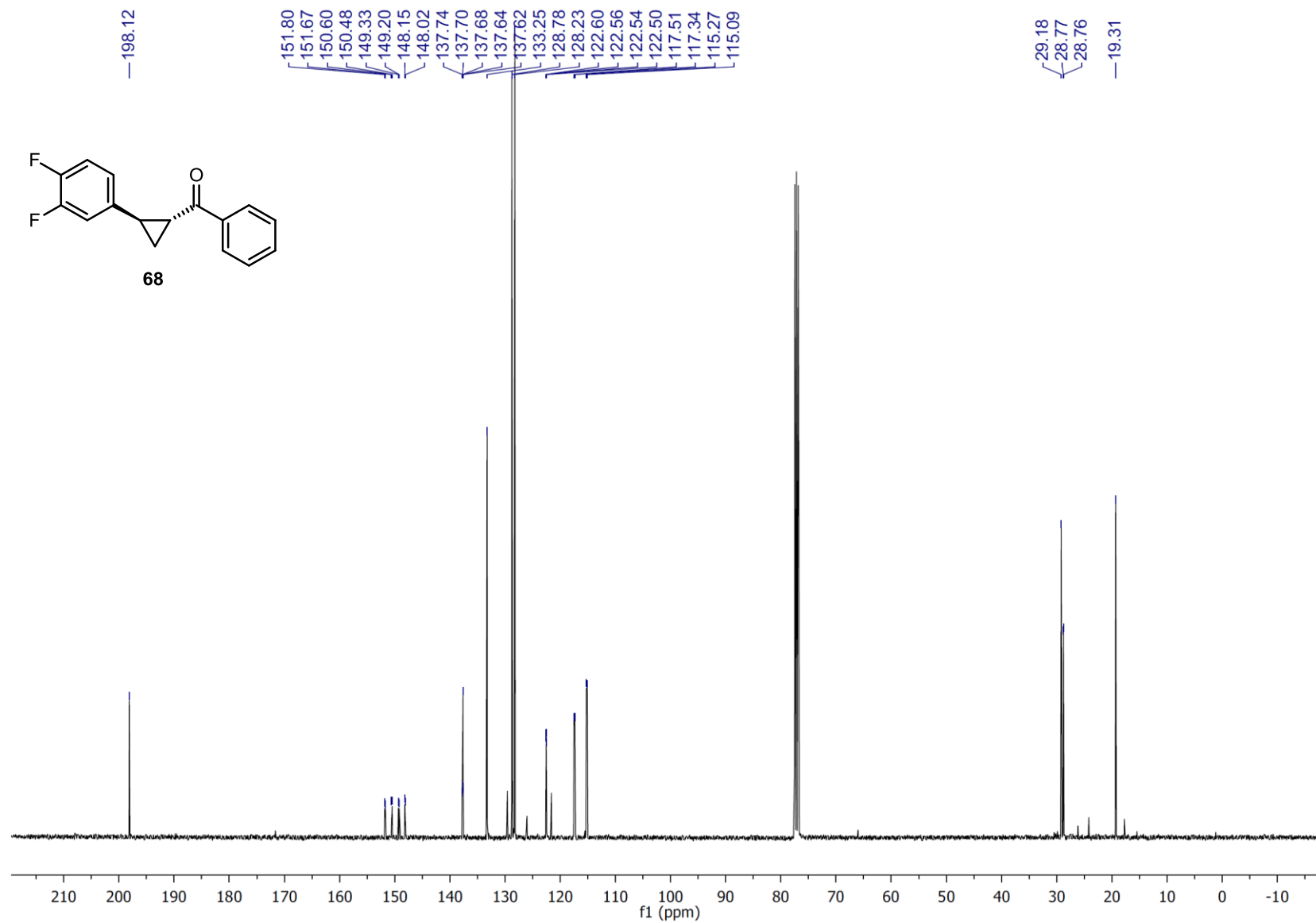


S336

^1H NMR (400 MHz, CDCl_3) for compound **68**

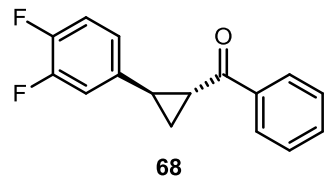


^{13}C NMR (101 MHz, CDCl_3) for compound **68**



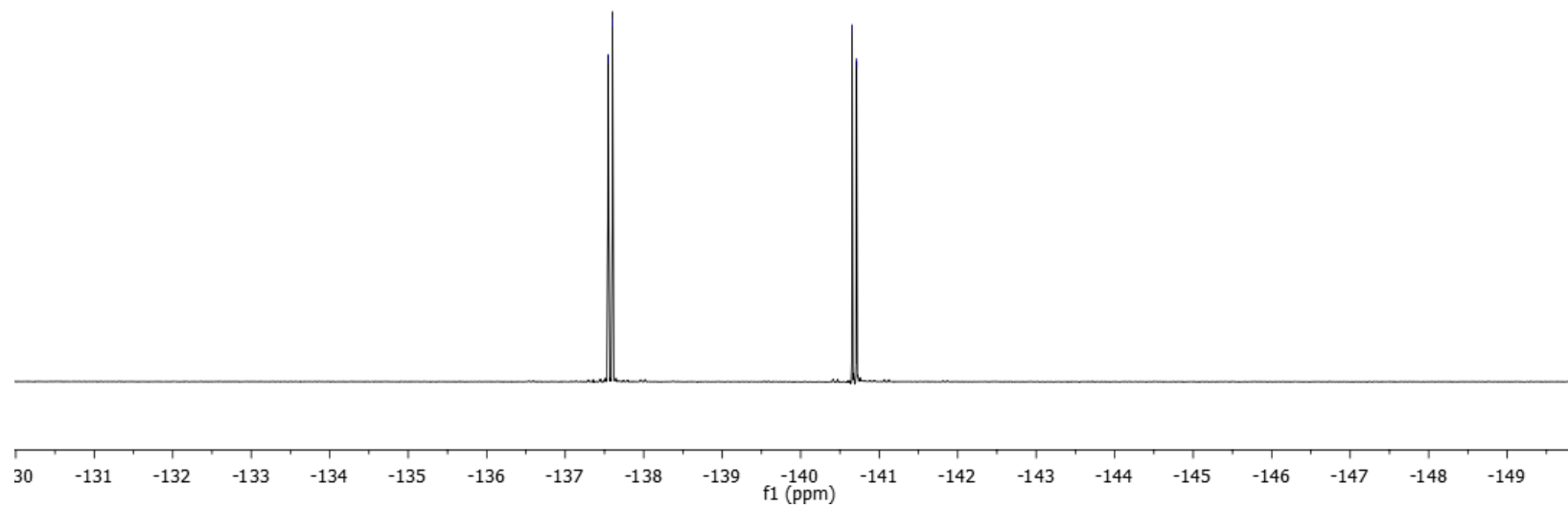
S338

^{19}F NMR (376MHz, CDCl_3) for compound **68**

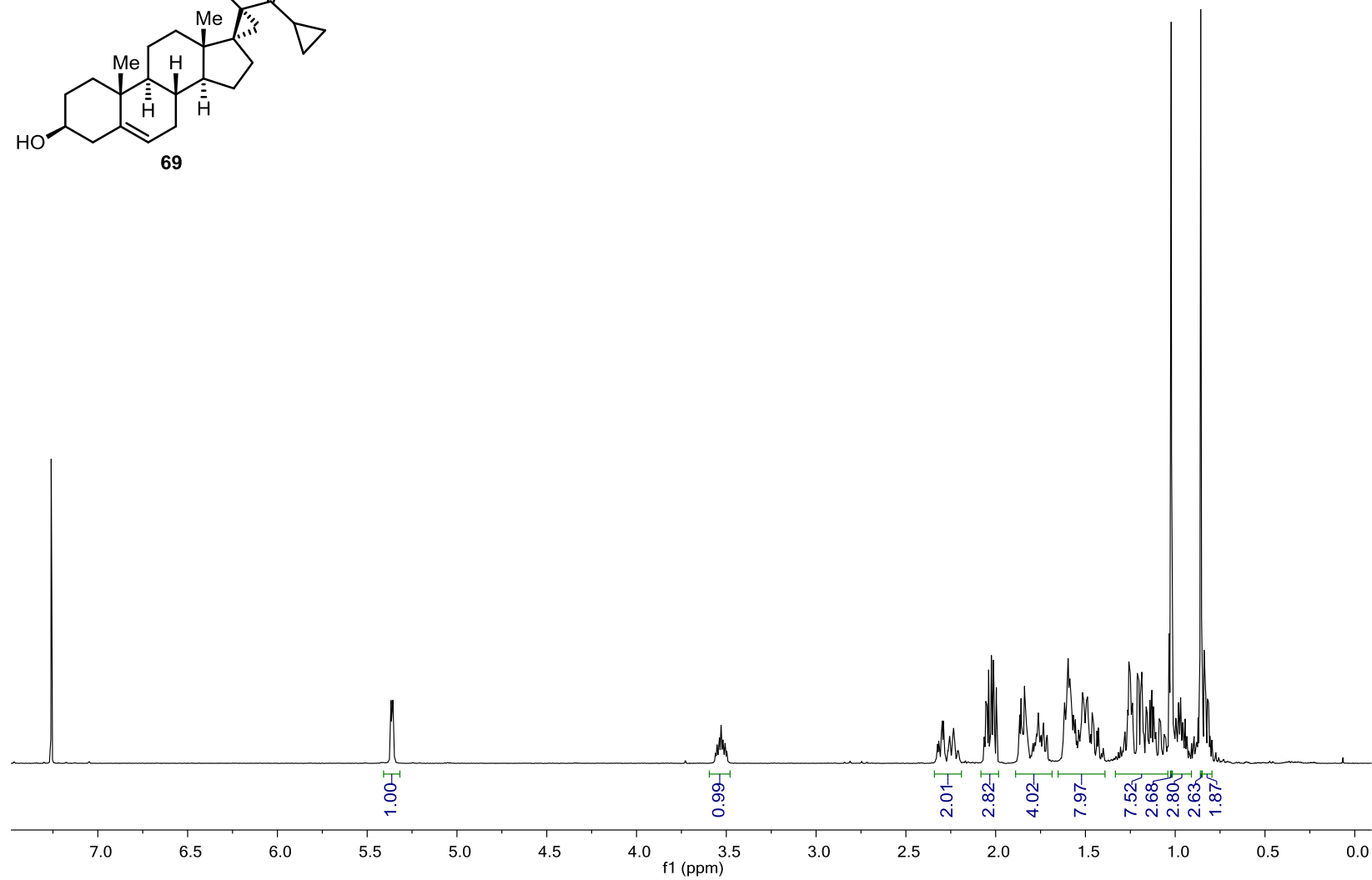
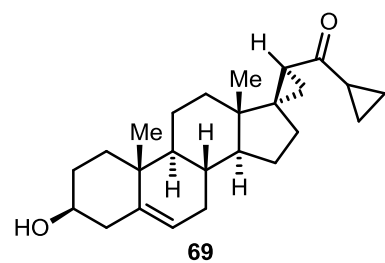


137.55
137.60

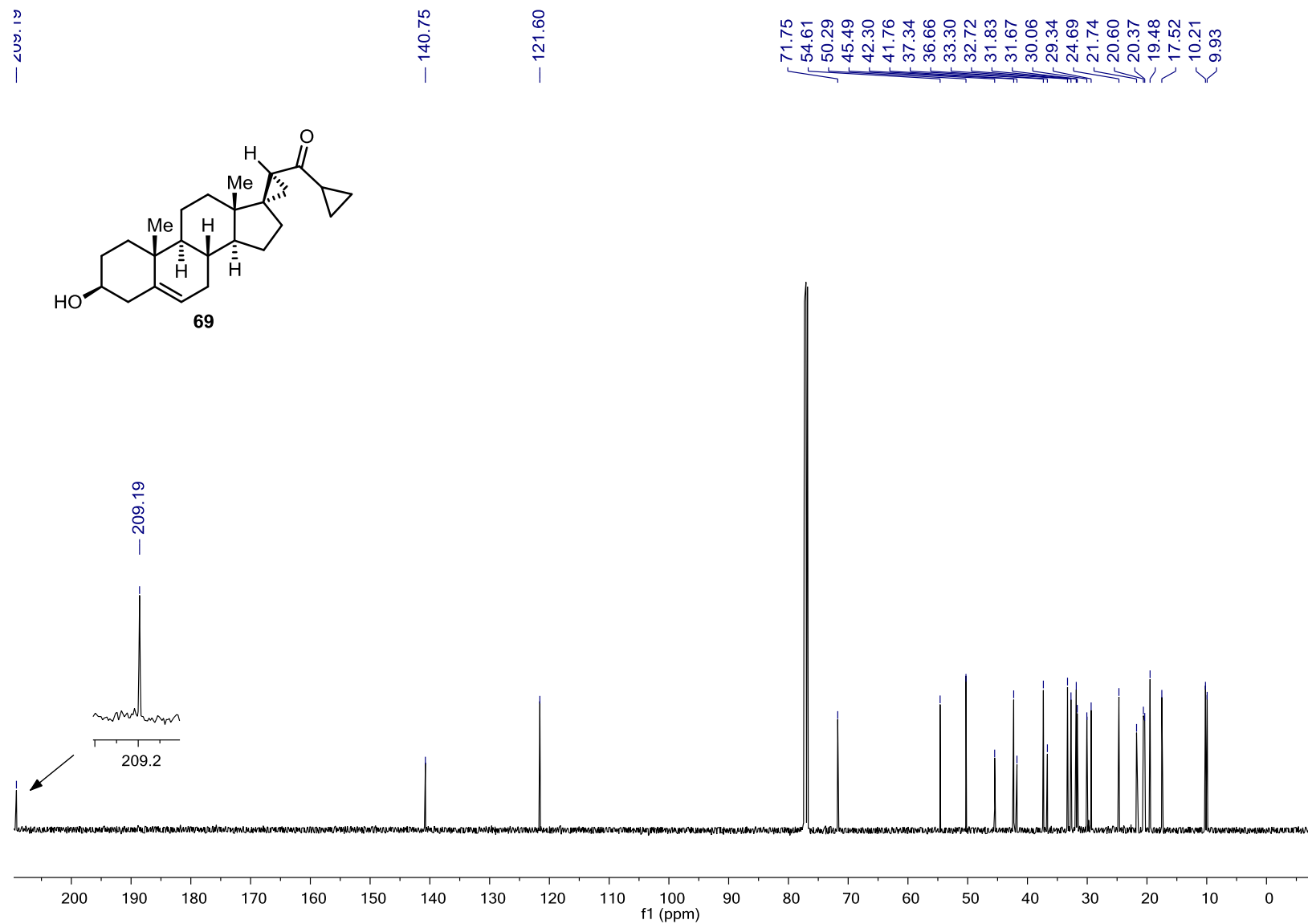
140.66
140.71



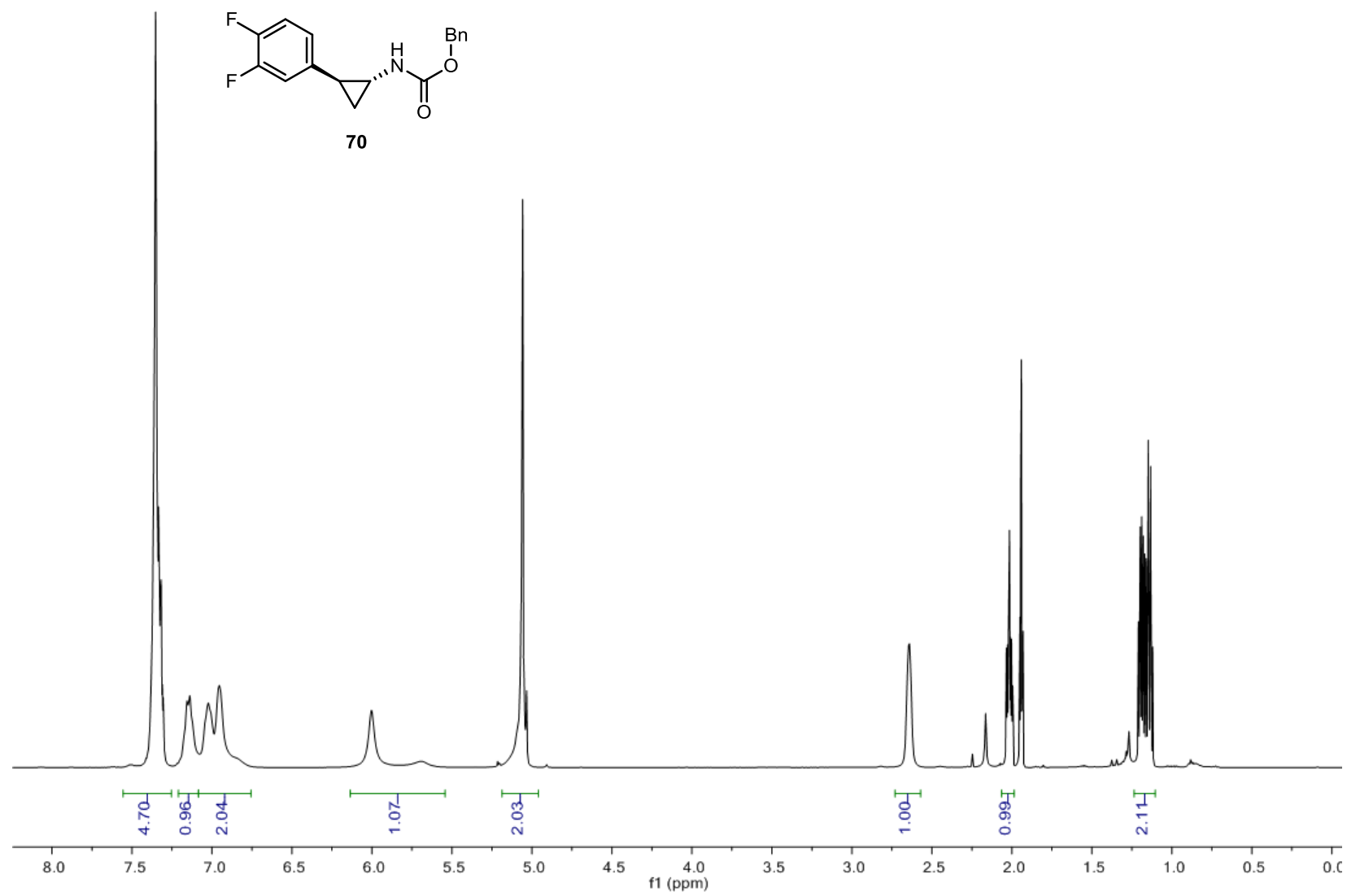
^1H NMR (500 MHz, CDCl_3) for compound **69**



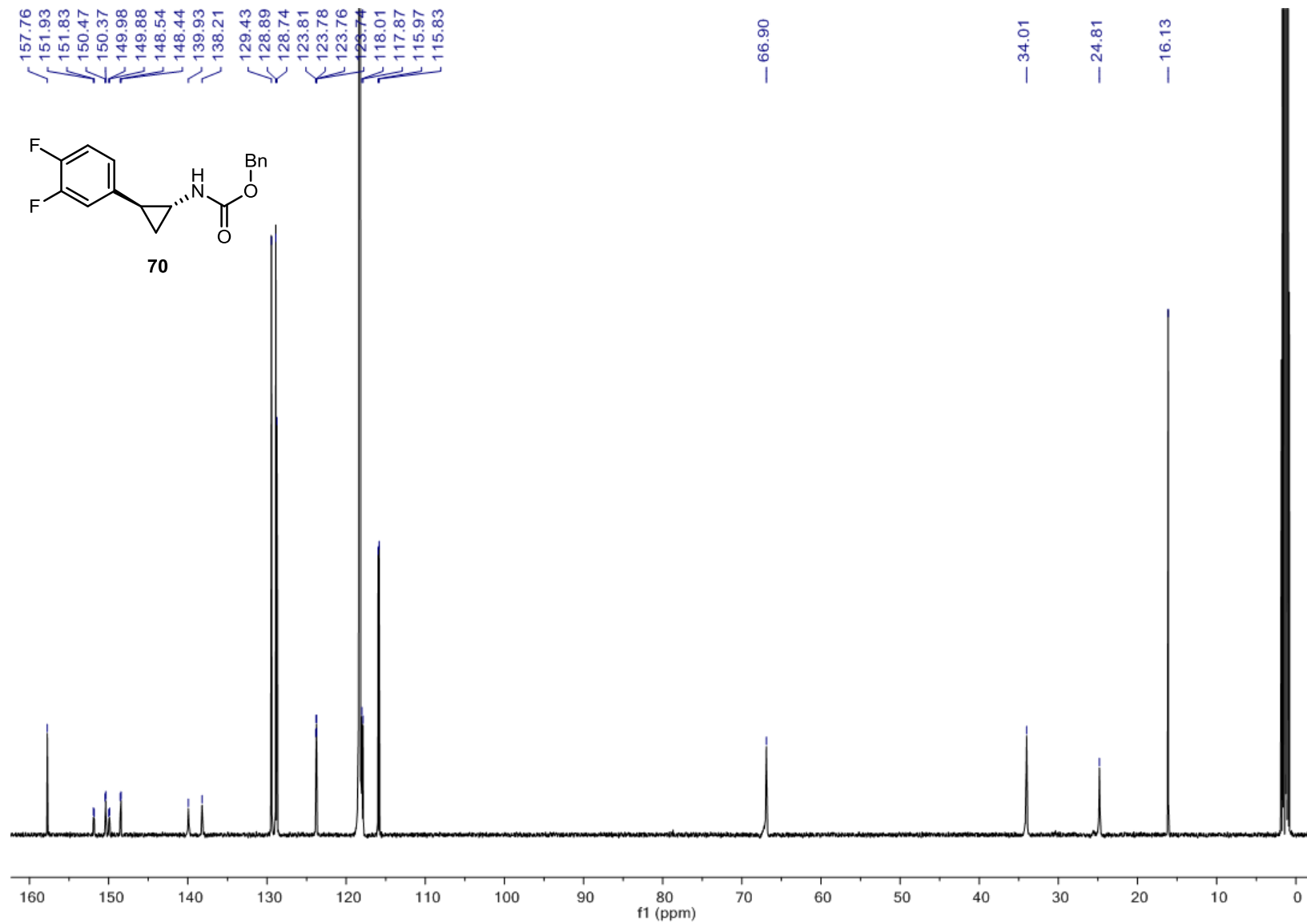
^{13}C NMR (126 MHz, CDCl_3) for compound **69**



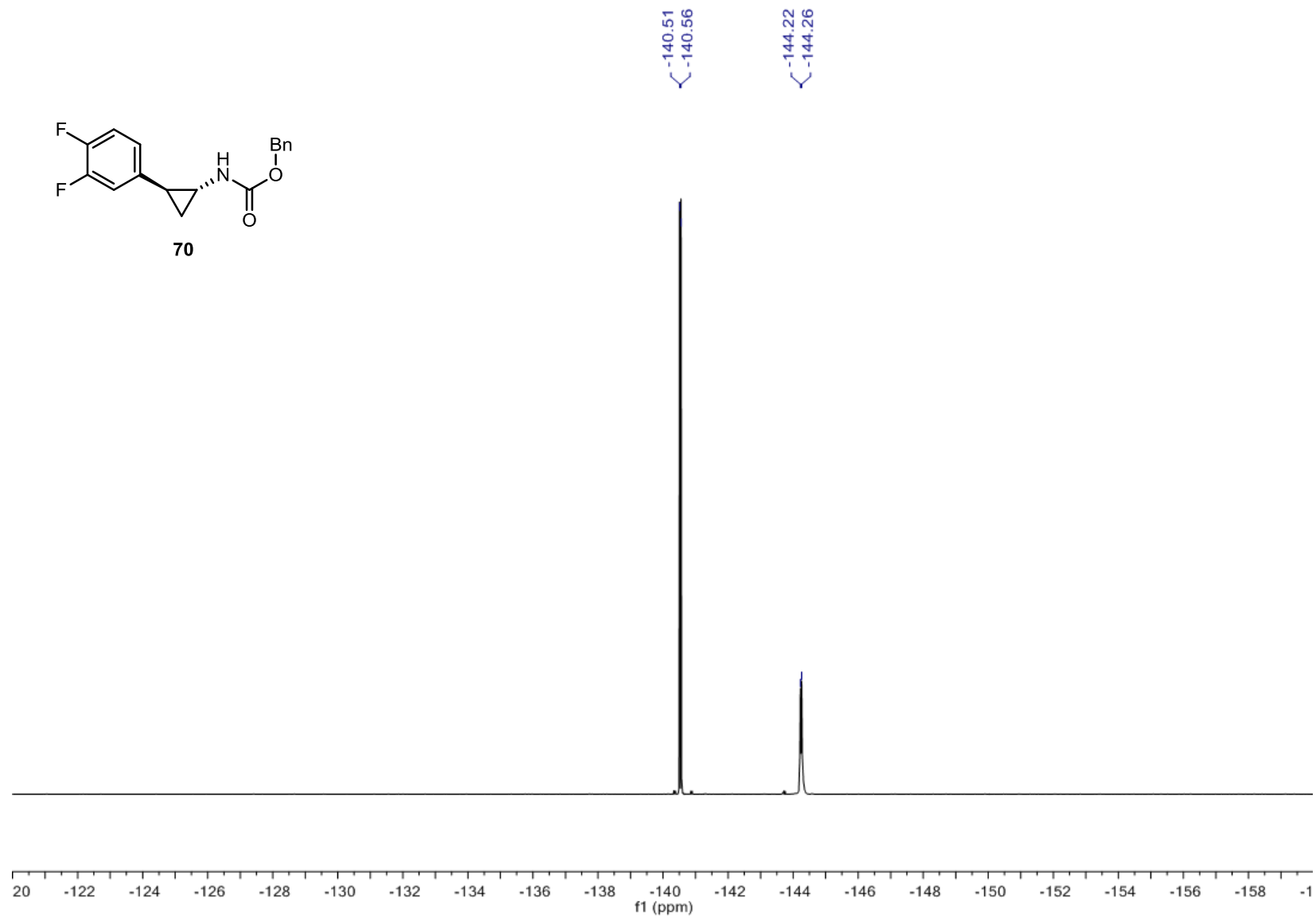
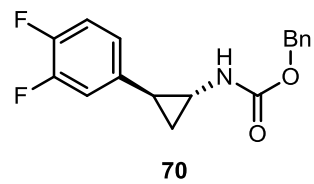
^1H NMR (500 MHz, CD_3CN) for compound **70**



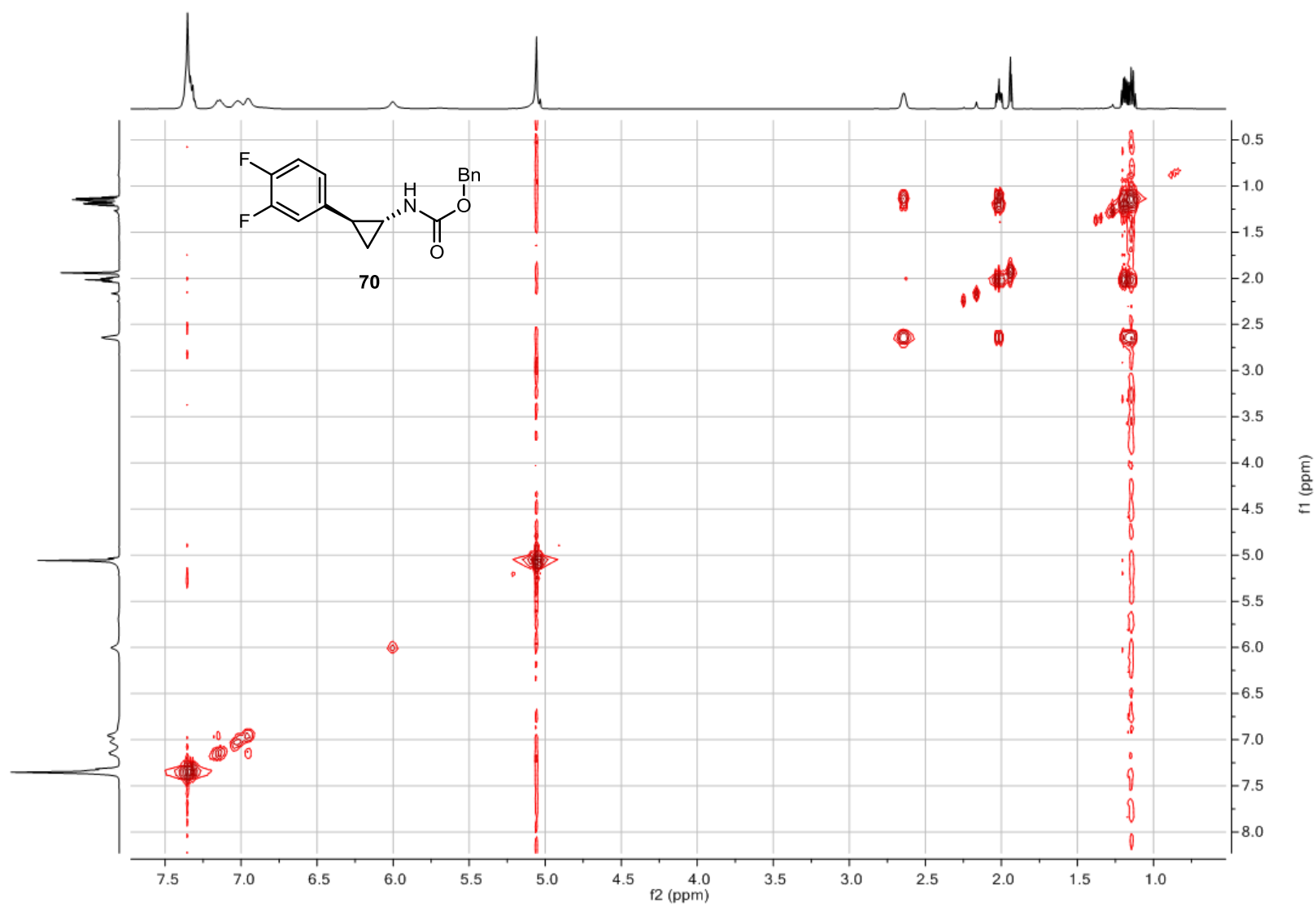
^{13}C NMR (126 MHz, CD_3CN) for compound **70**



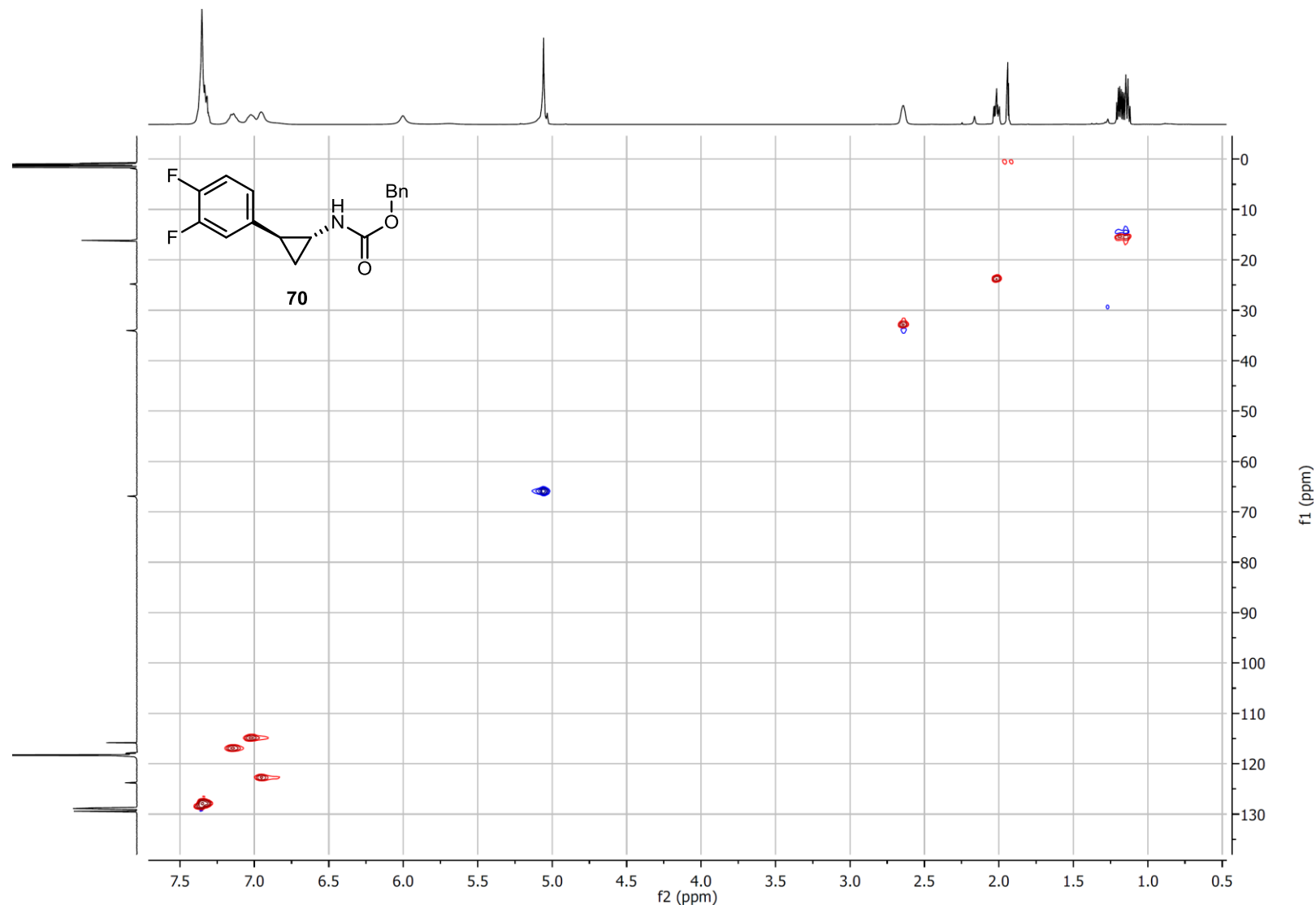
^{19}F NMR (376 MHz, CD_3CN) for compound **70**



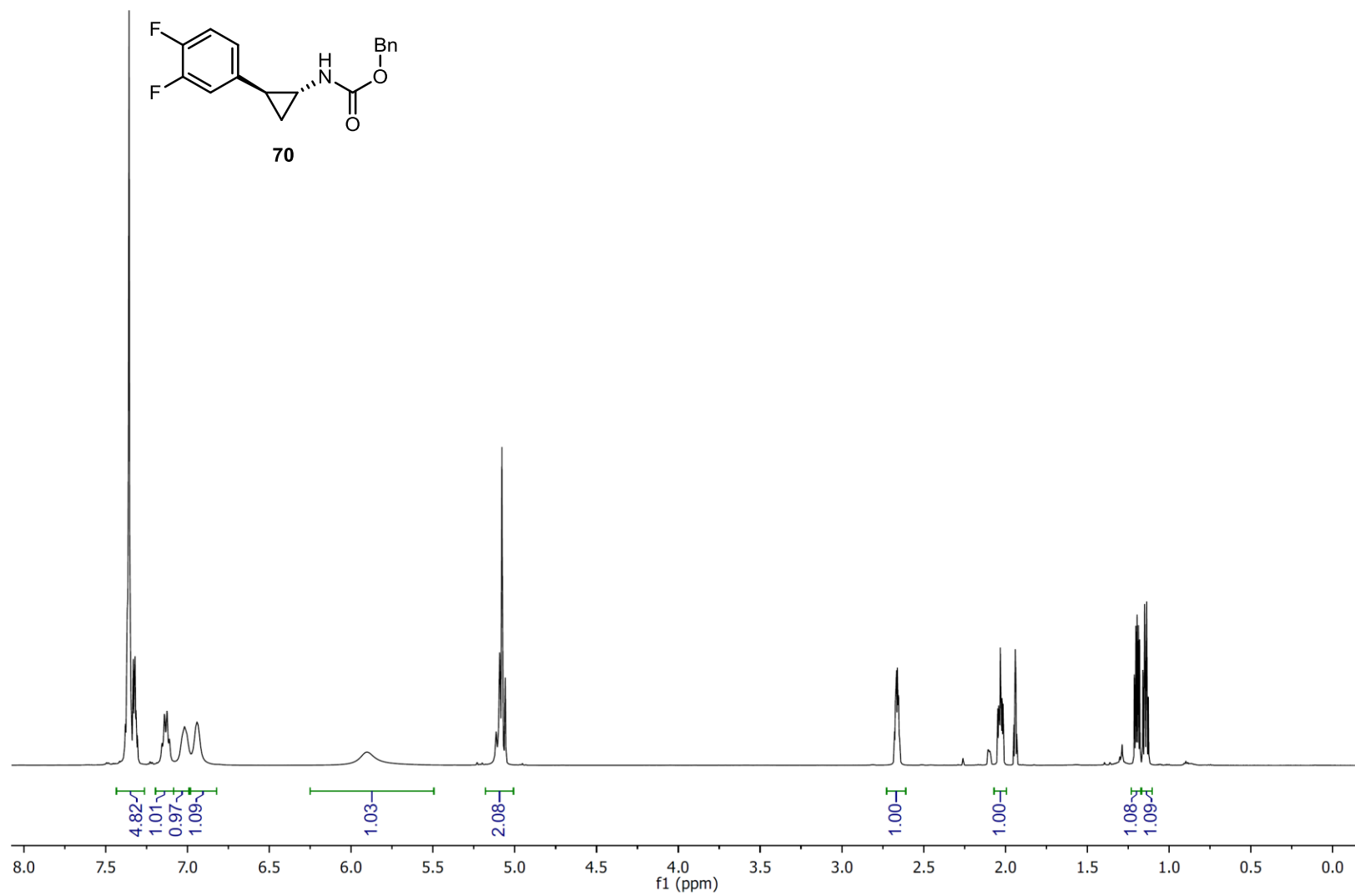
COSY NMR (500 MHz, CD₃CN) for compound **70**



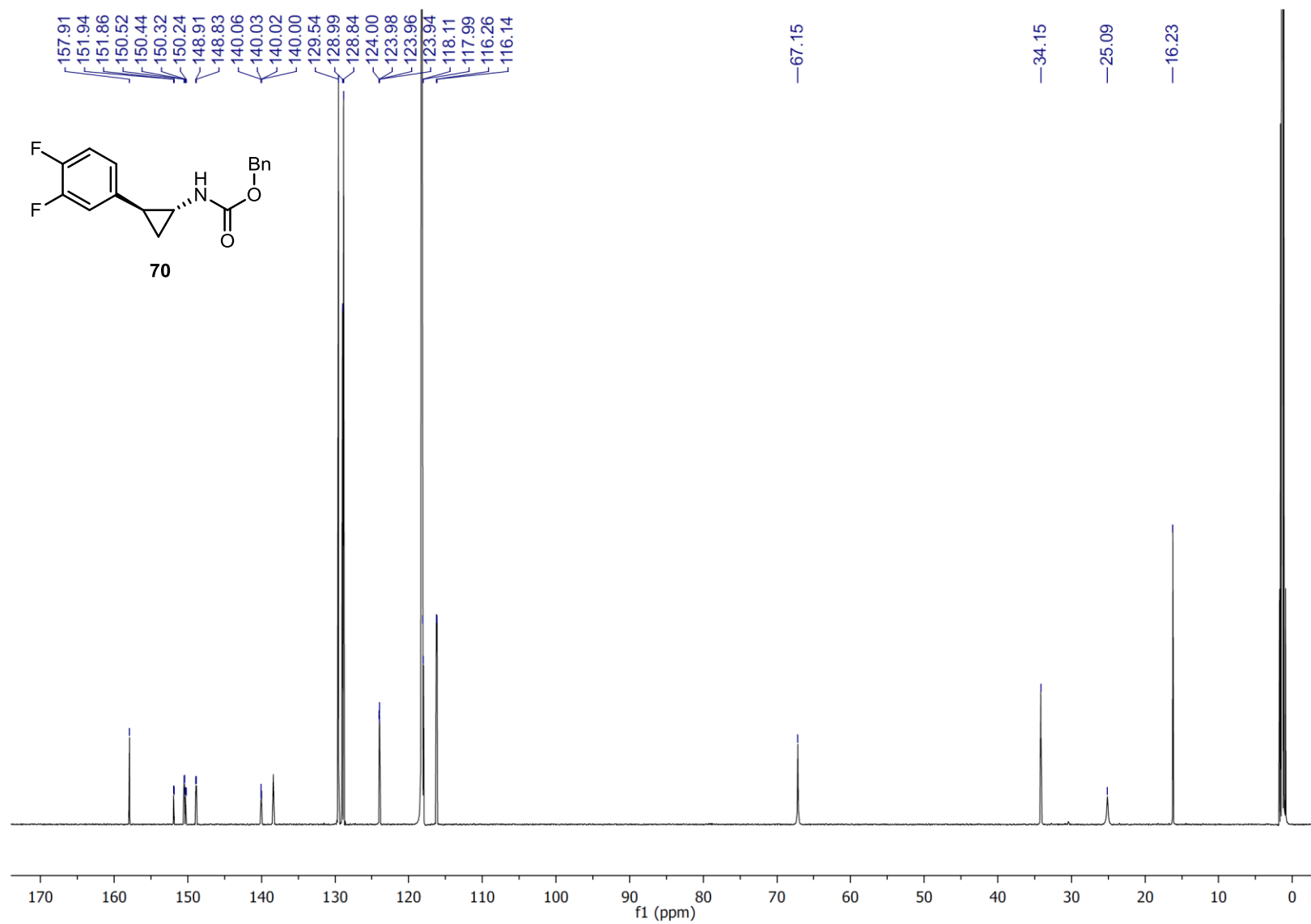
HSQC NMR (500 MHz, CD₃CN) for compound **70**



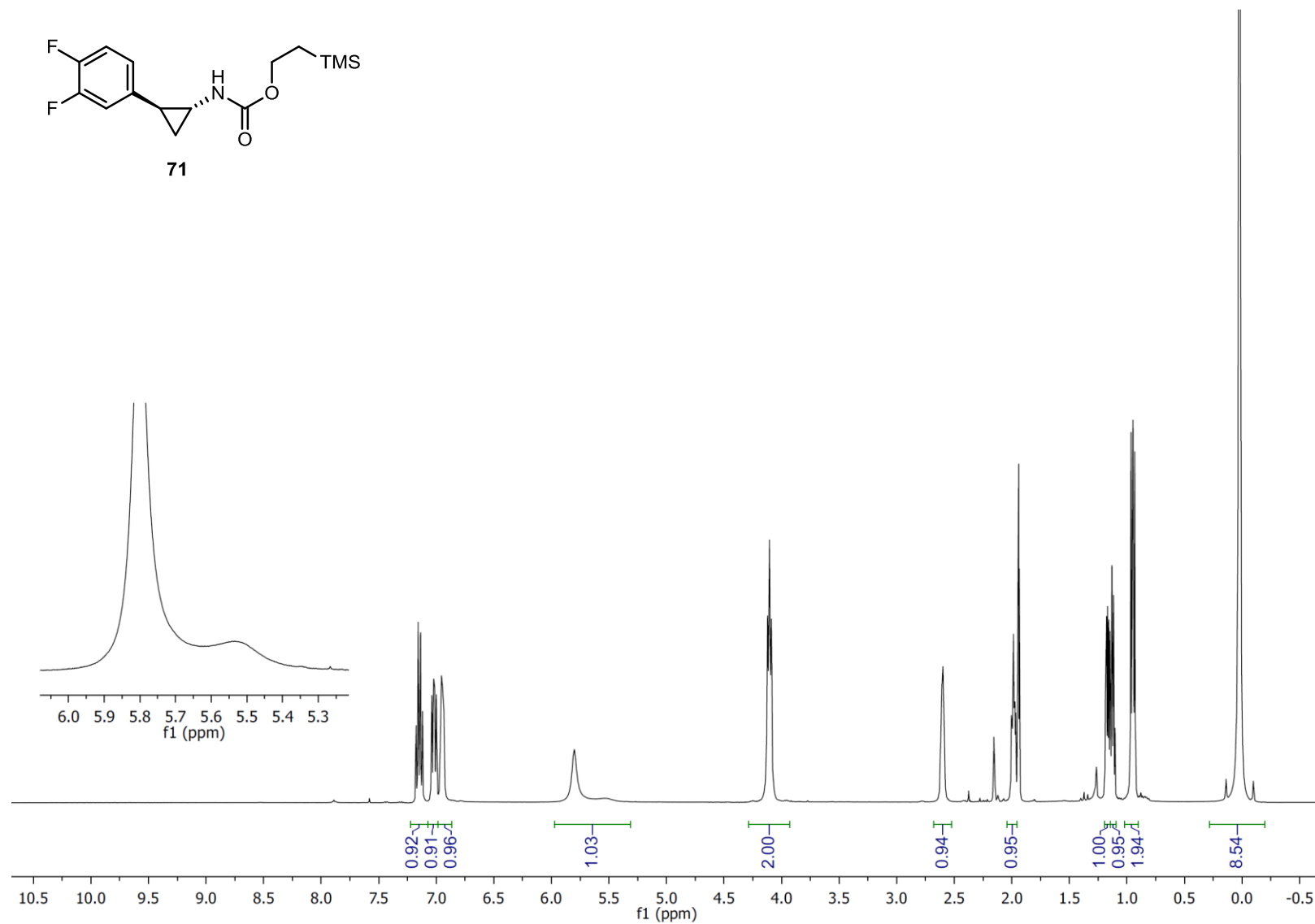
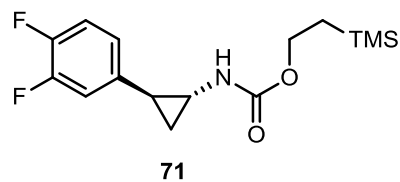
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **70**



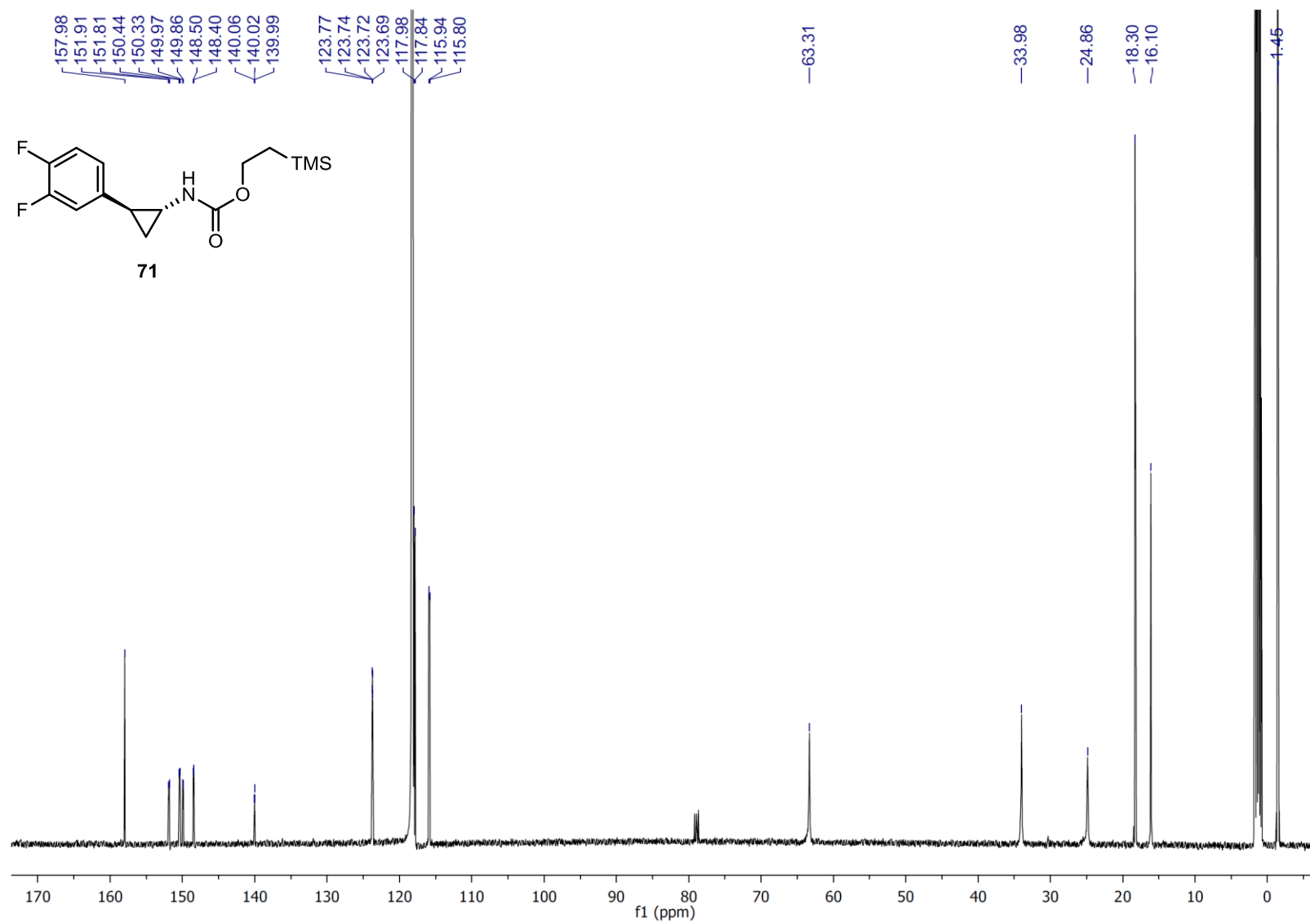
^{13}C NMR (150 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **70**



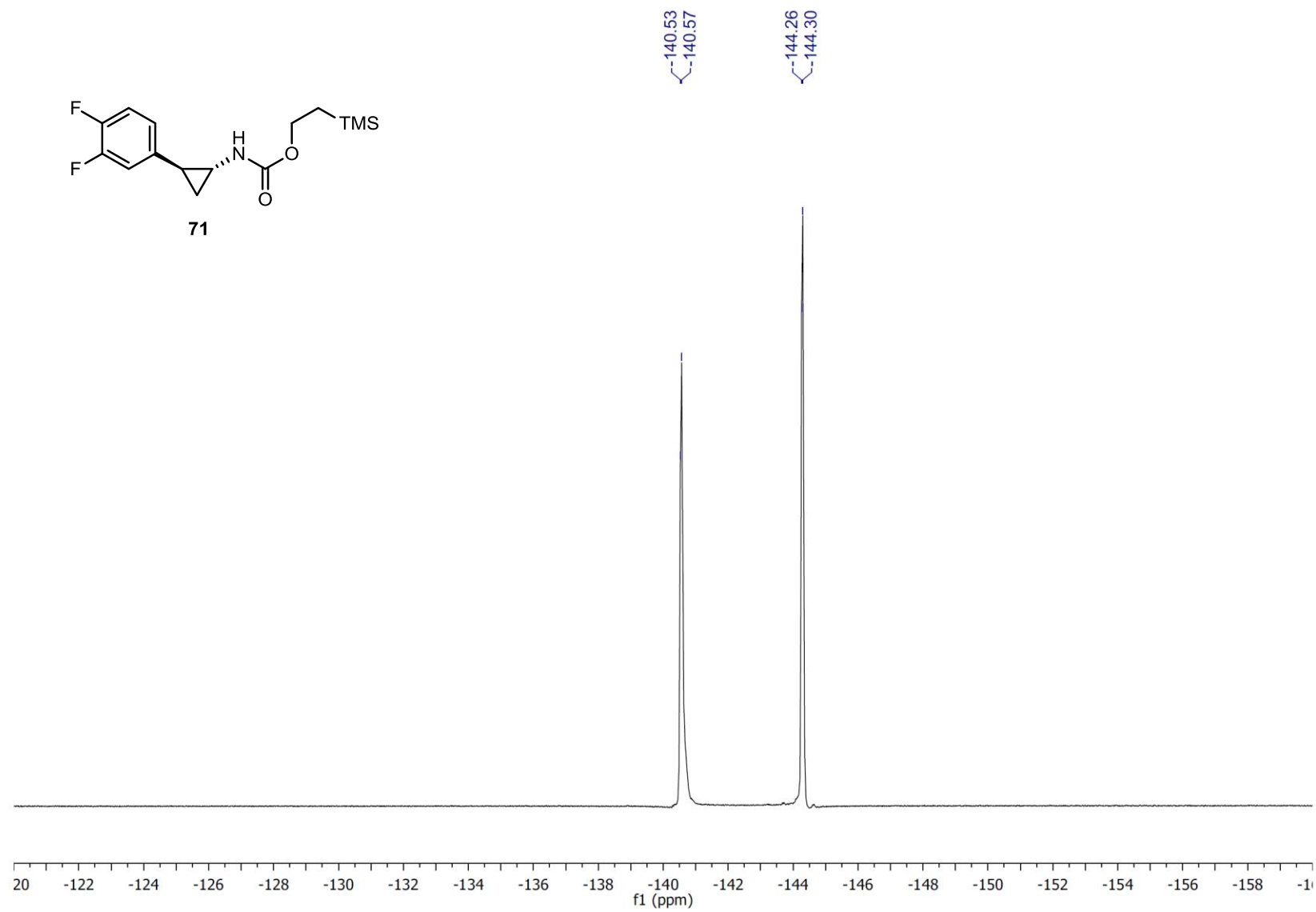
^1H NMR (500 MHz, CD_3CN) for compound **71**



^{13}C NMR (126 MHz, CD_3CN) for compound **71**

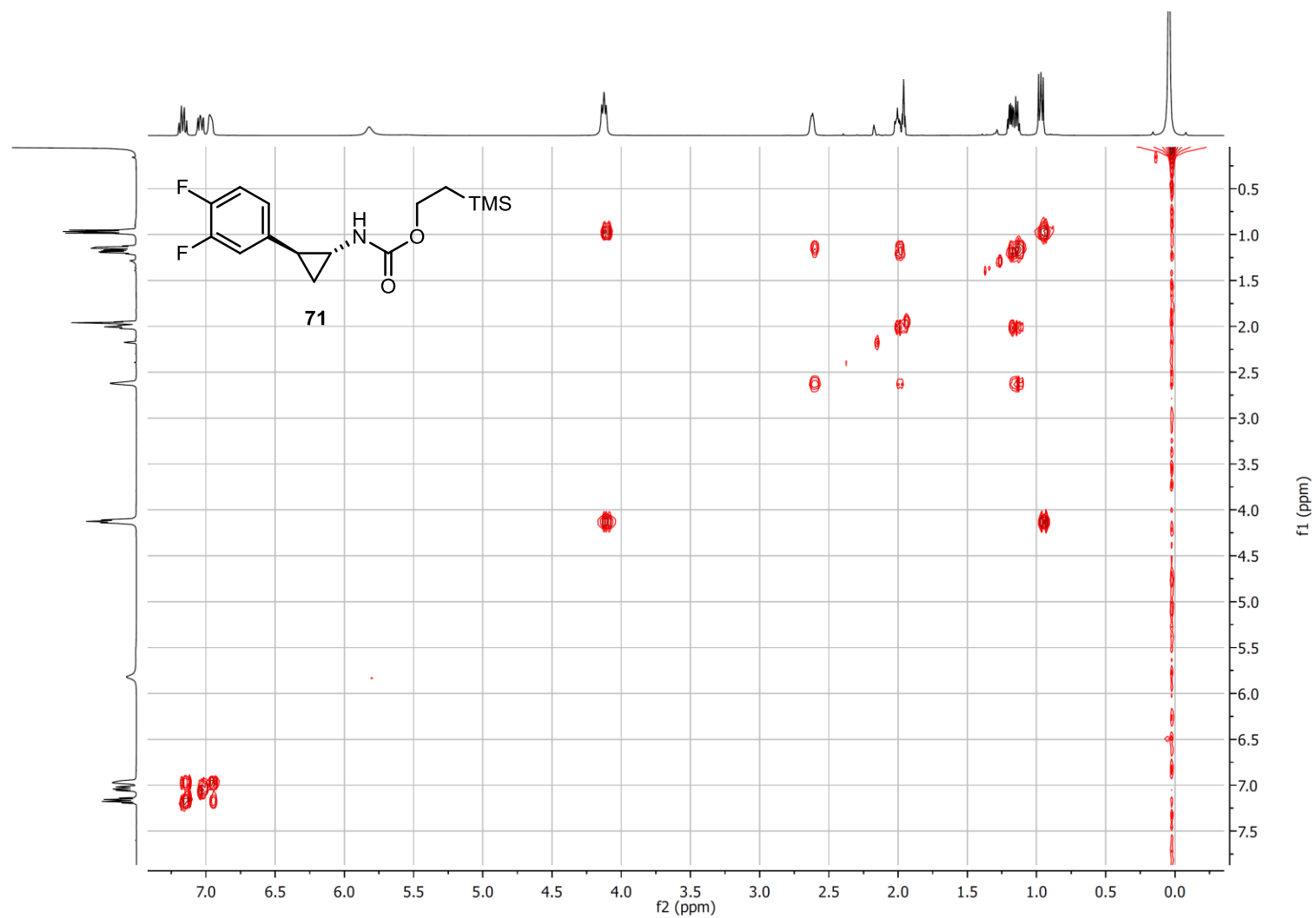


^{19}F NMR (376 MHz, CD_3CN) for compound **71**

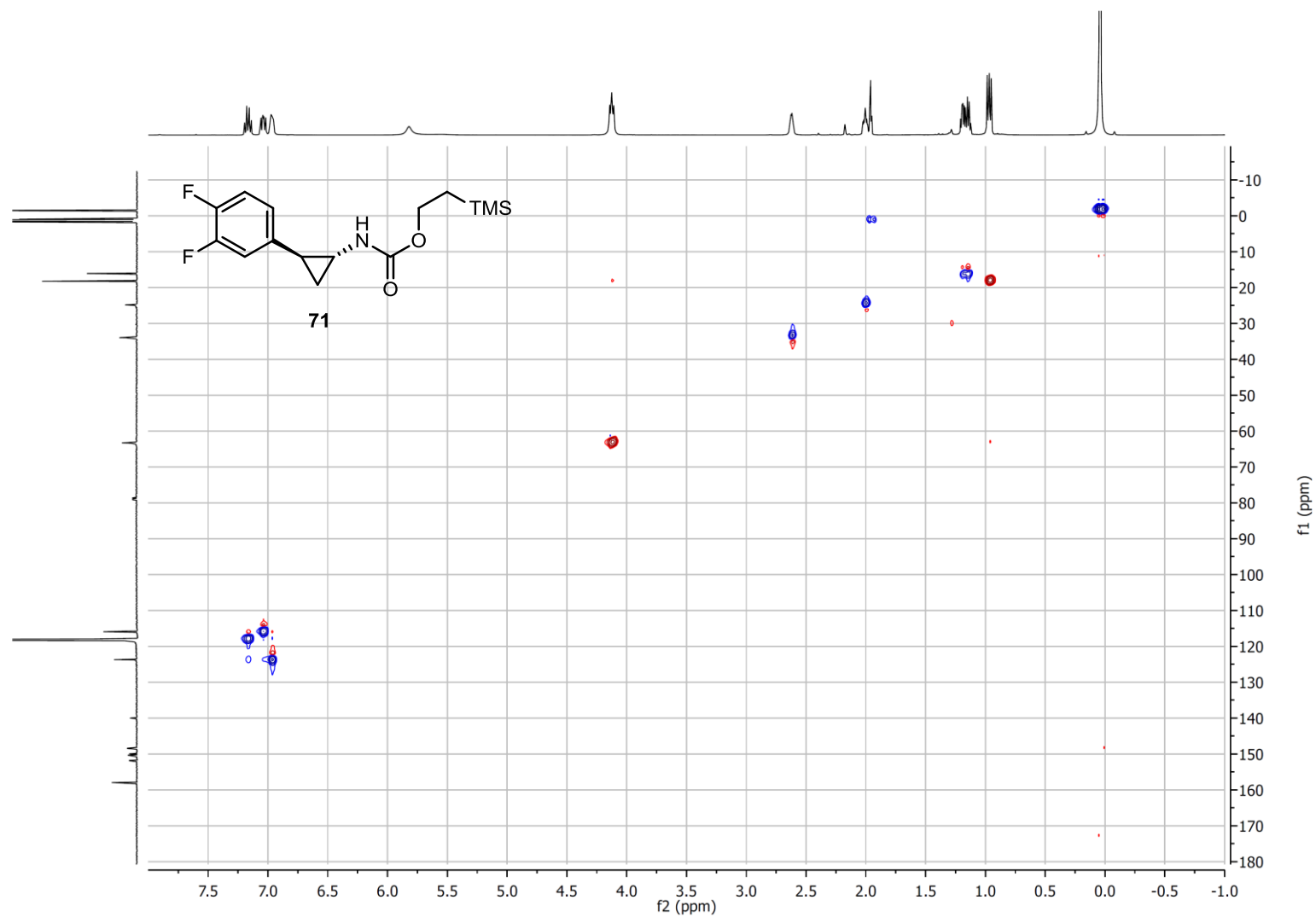


S351

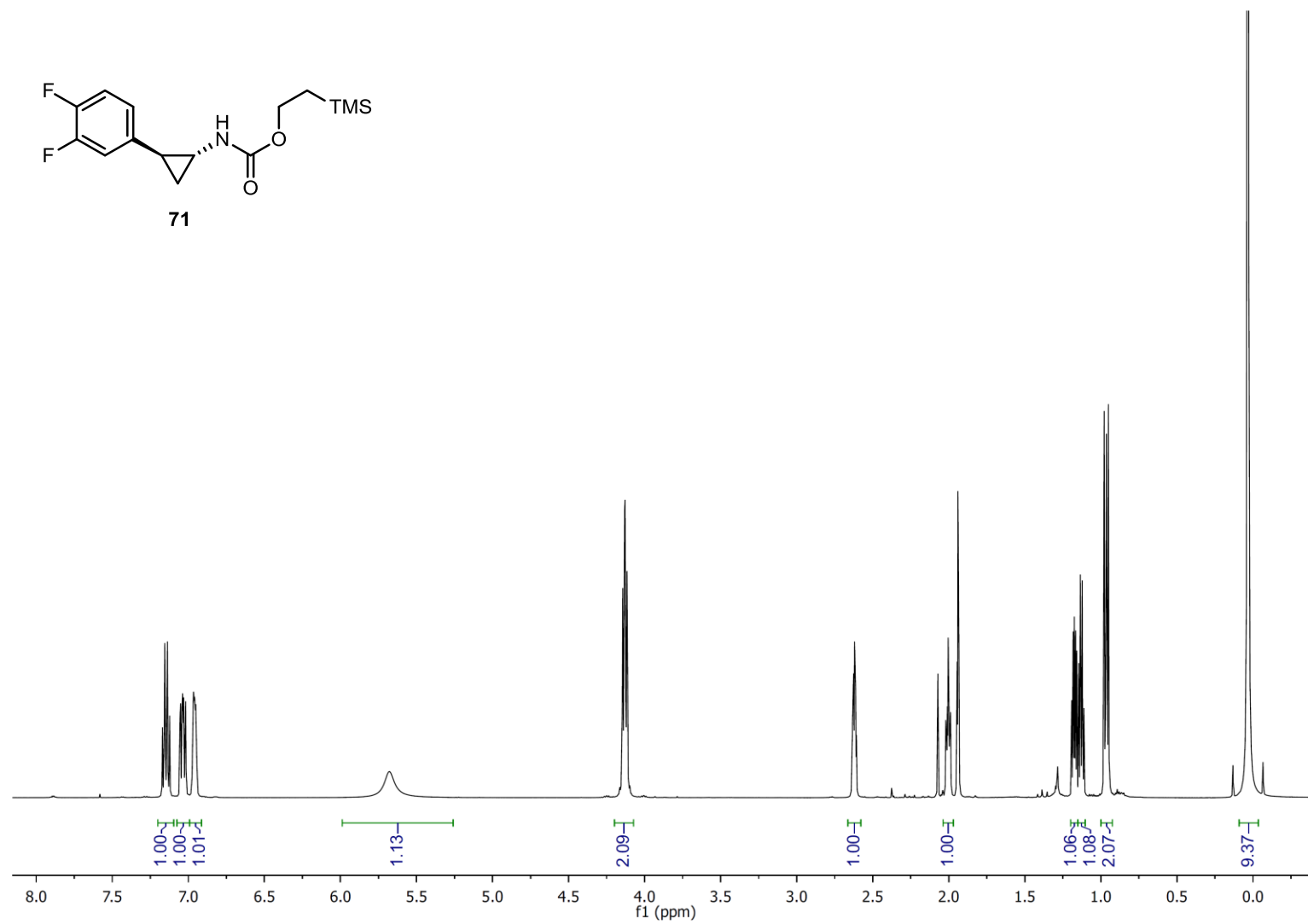
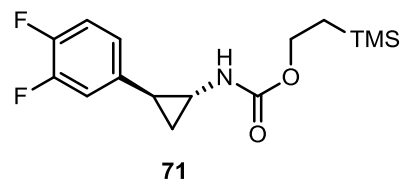
COSY NMR (500 MHz, CD₃CN) for compound **71**



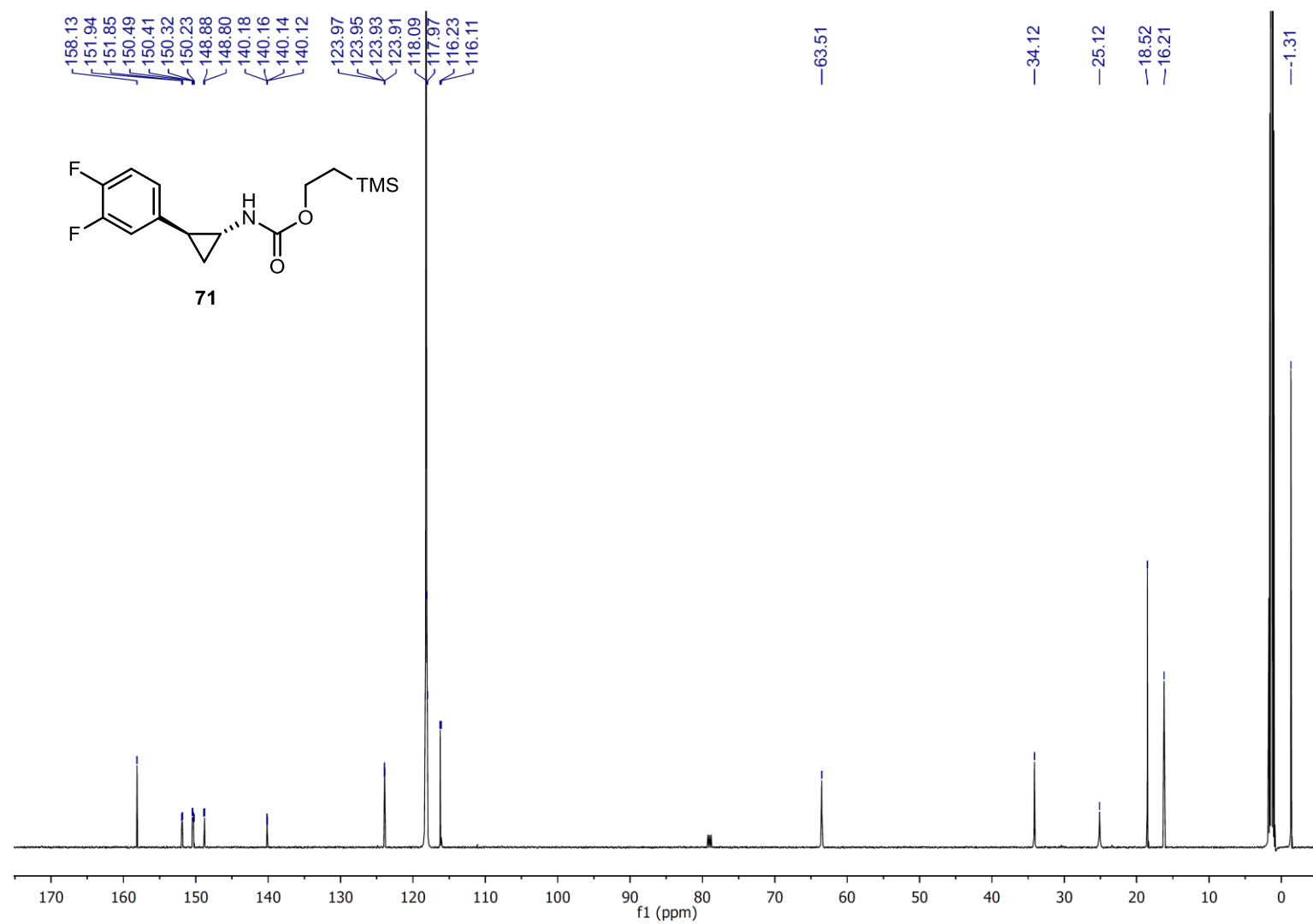
HSQC NMR (500 MHz, CD₃CN) for compound **71**



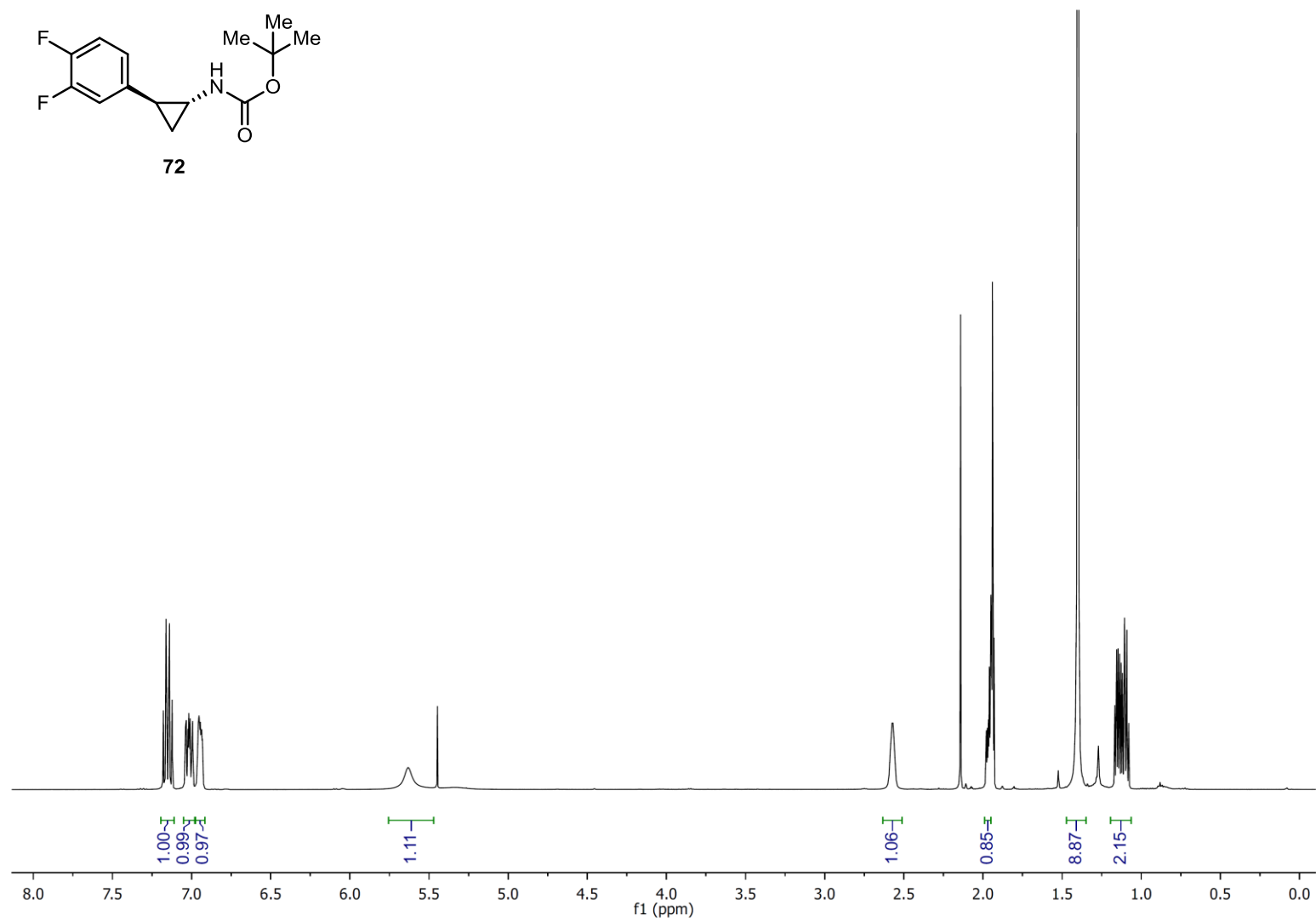
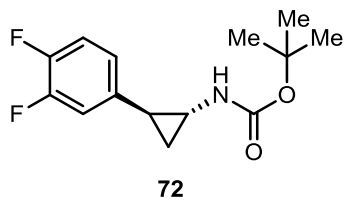
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **71**



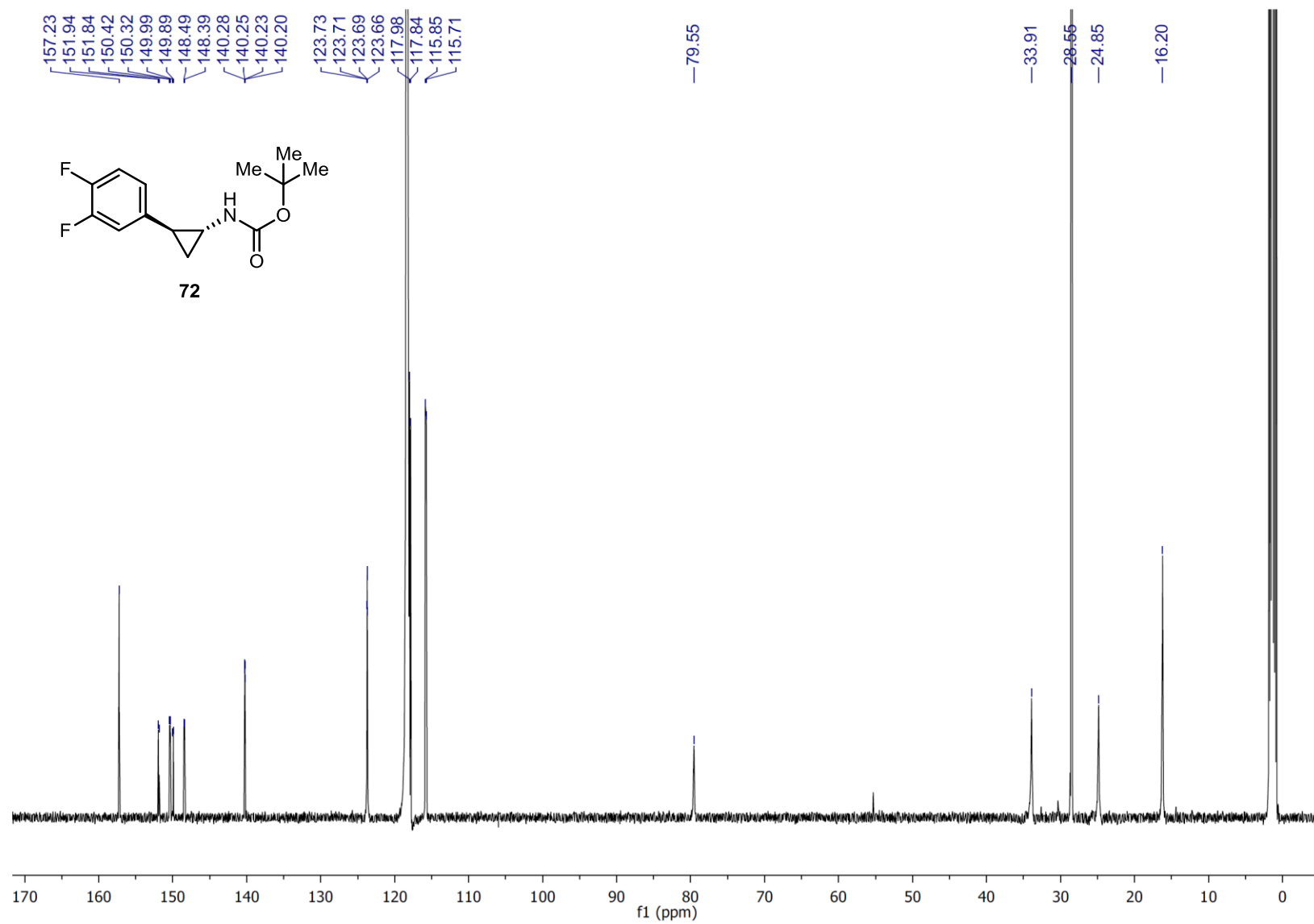
^{13}C NMR (150 MHz, CD_3CN , 50 °C) for compound **71**



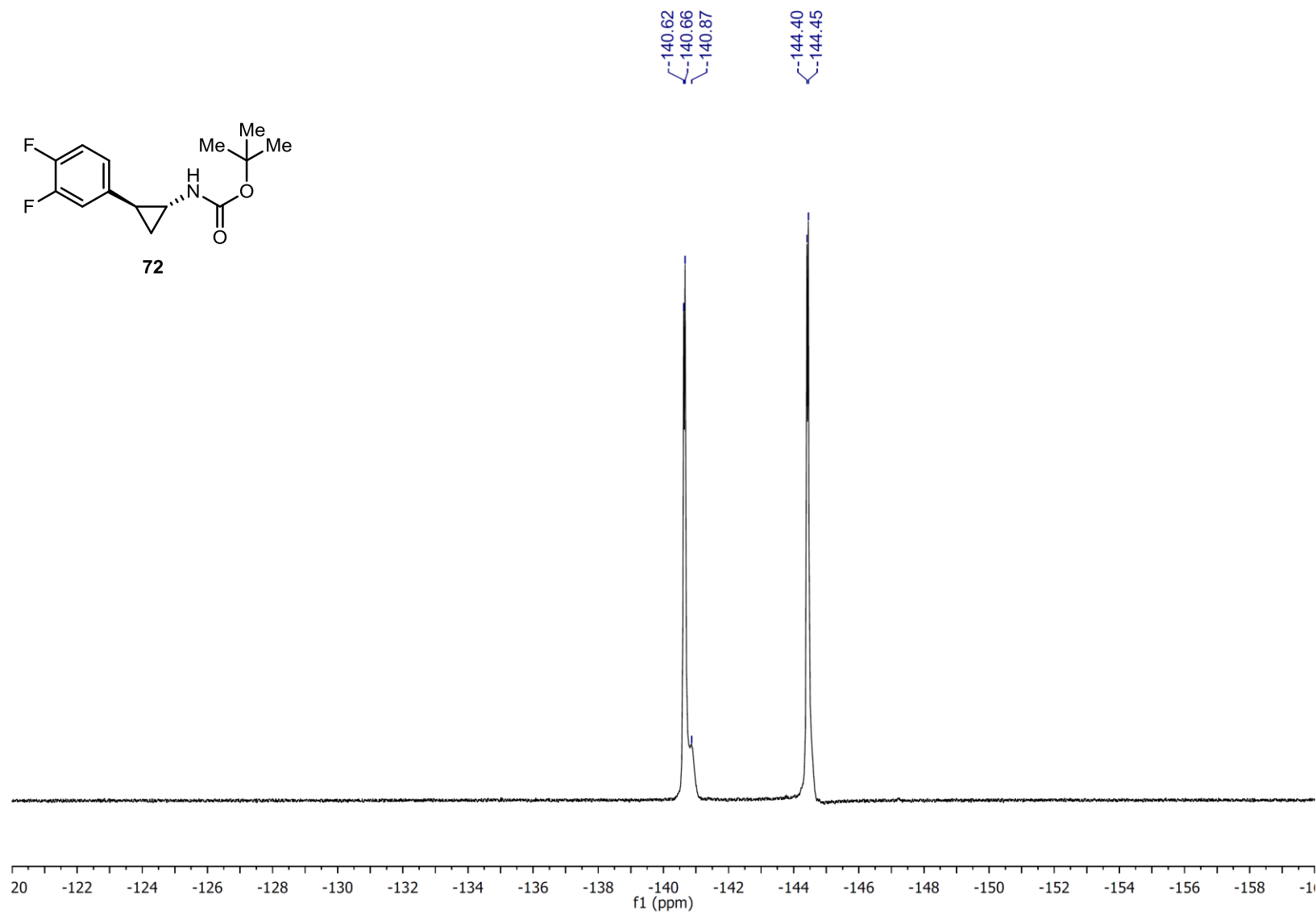
^1H NMR (500 MHz, CD_3CN) for compound **72**



^{13}C NMR (126 MHz, CD_3CN) for compound **72**

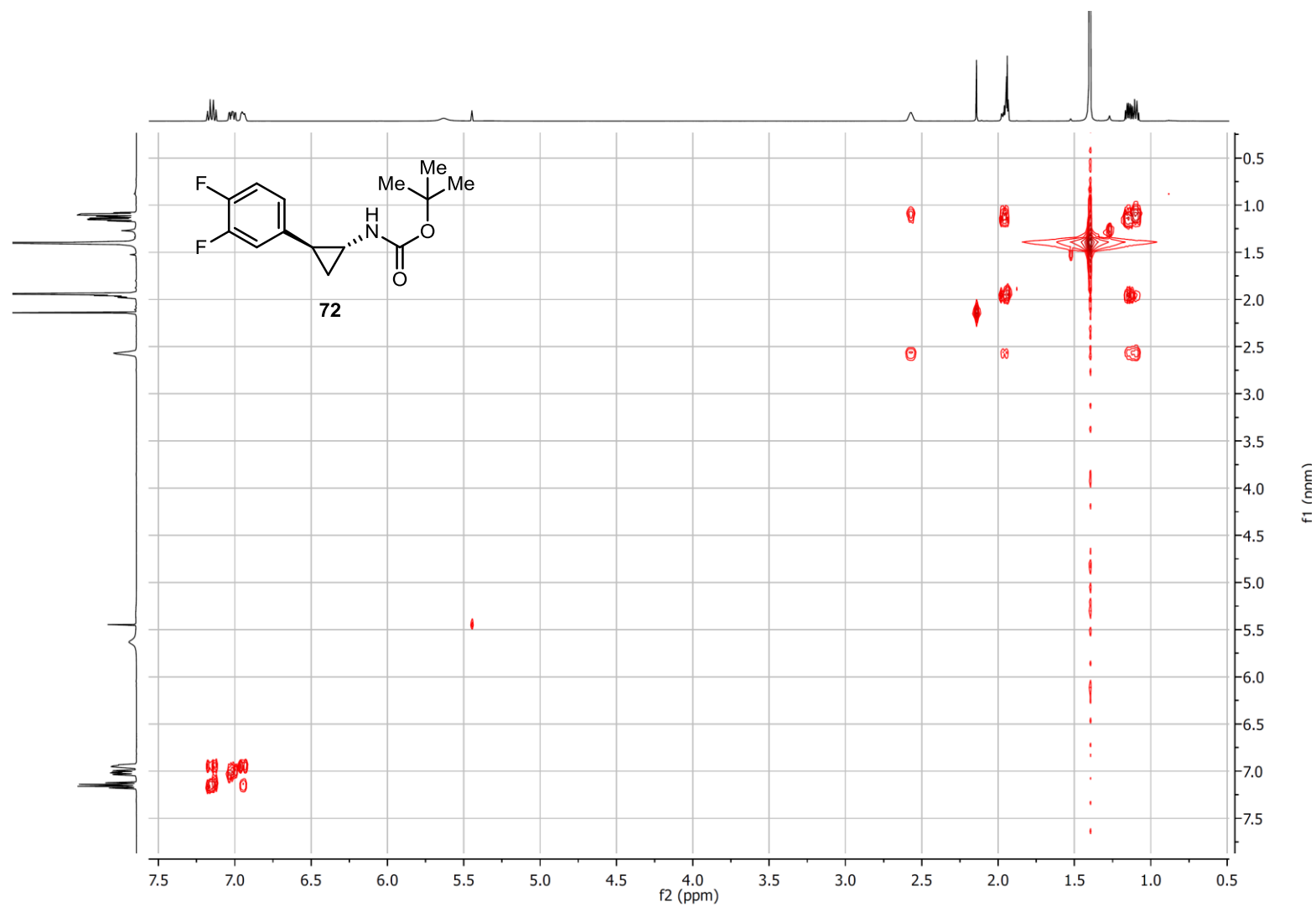


^{19}F NMR (376 MHz, CD_3CN) for compound **72**

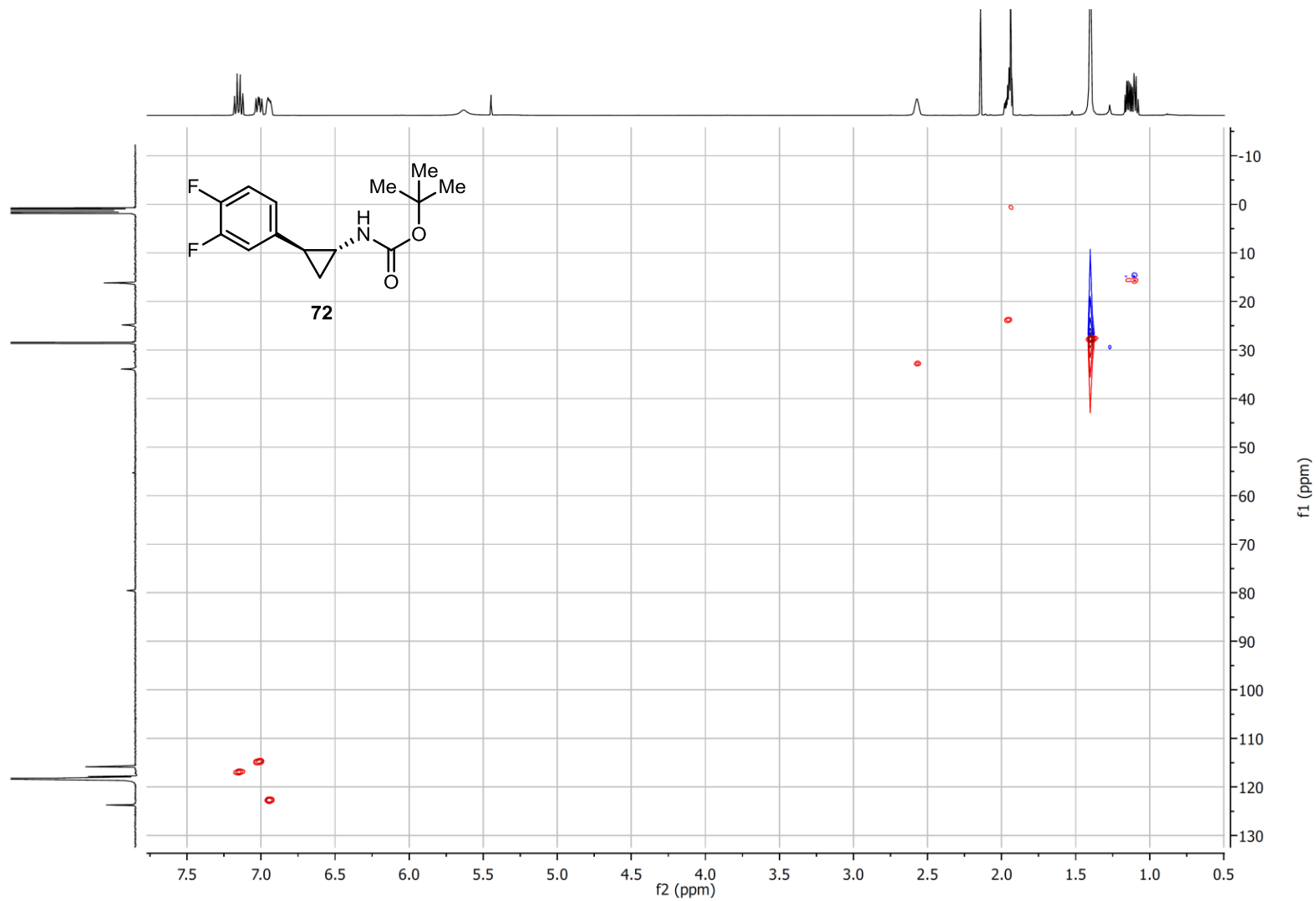


S358

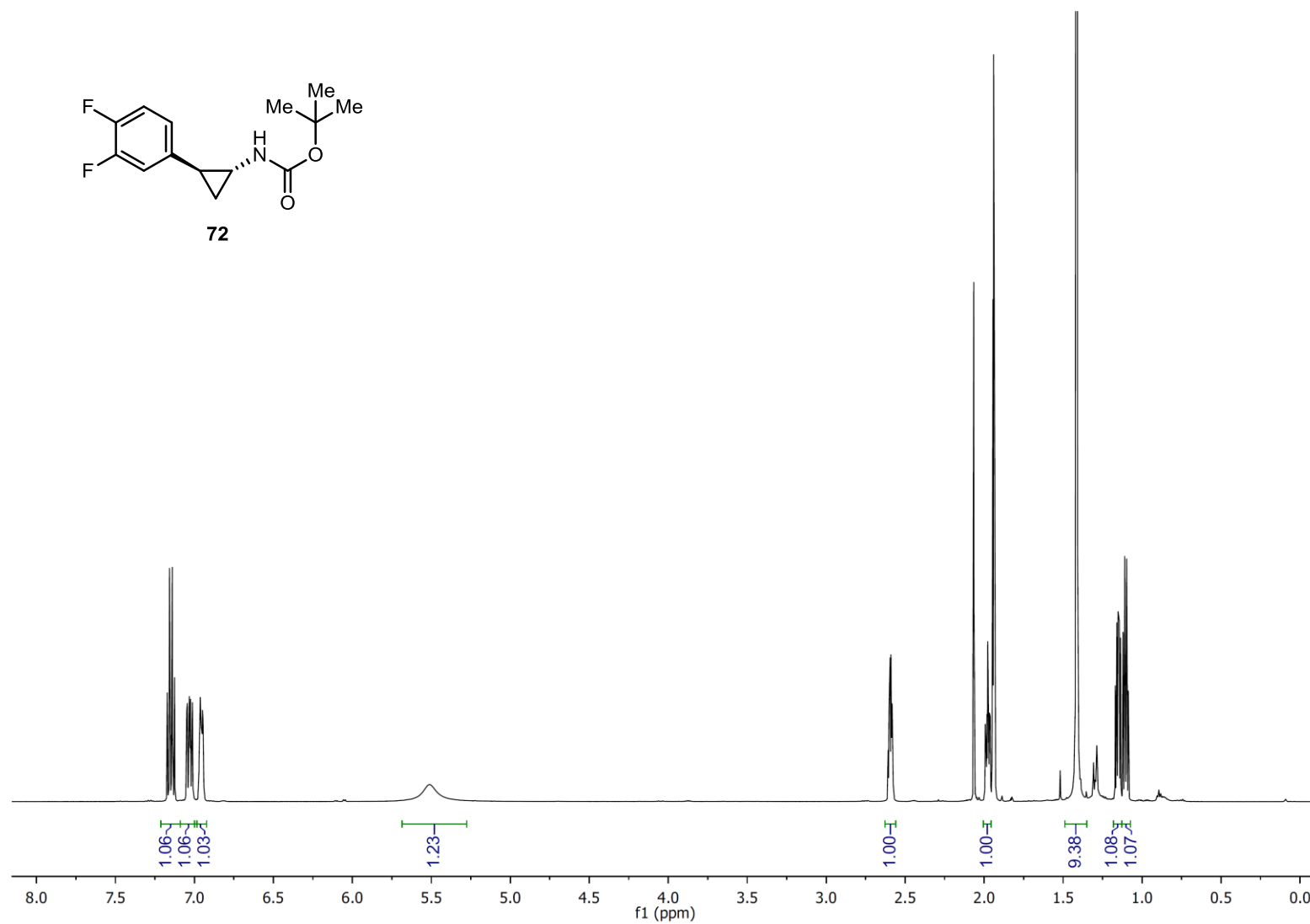
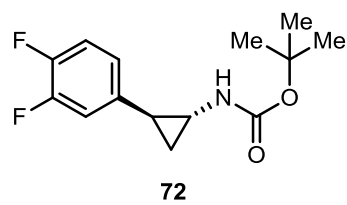
COSY NMR (500 MHz, CD₃CN) for compound 72



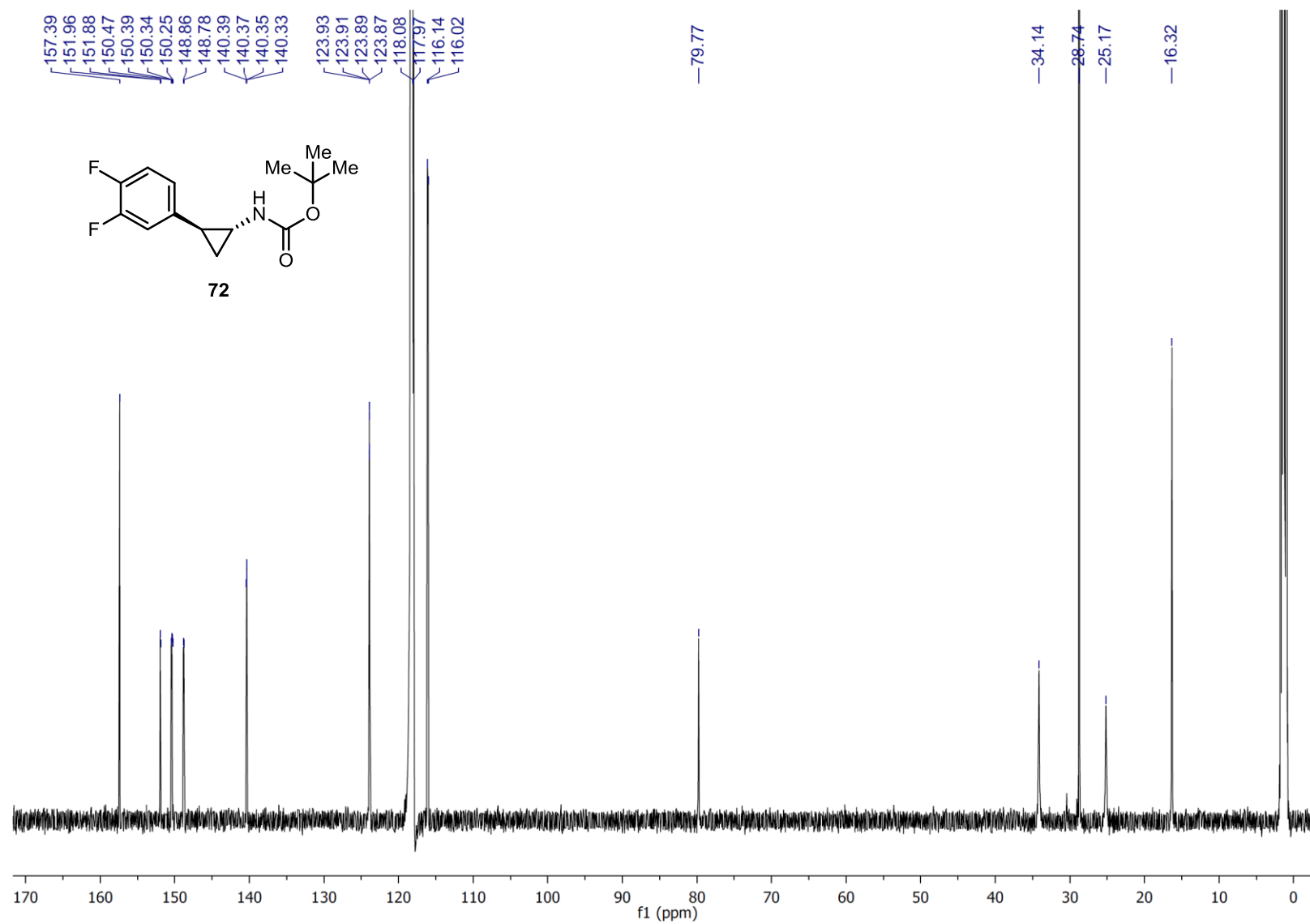
HSQC NMR (500 MHz, CD₃CN) for compound 72



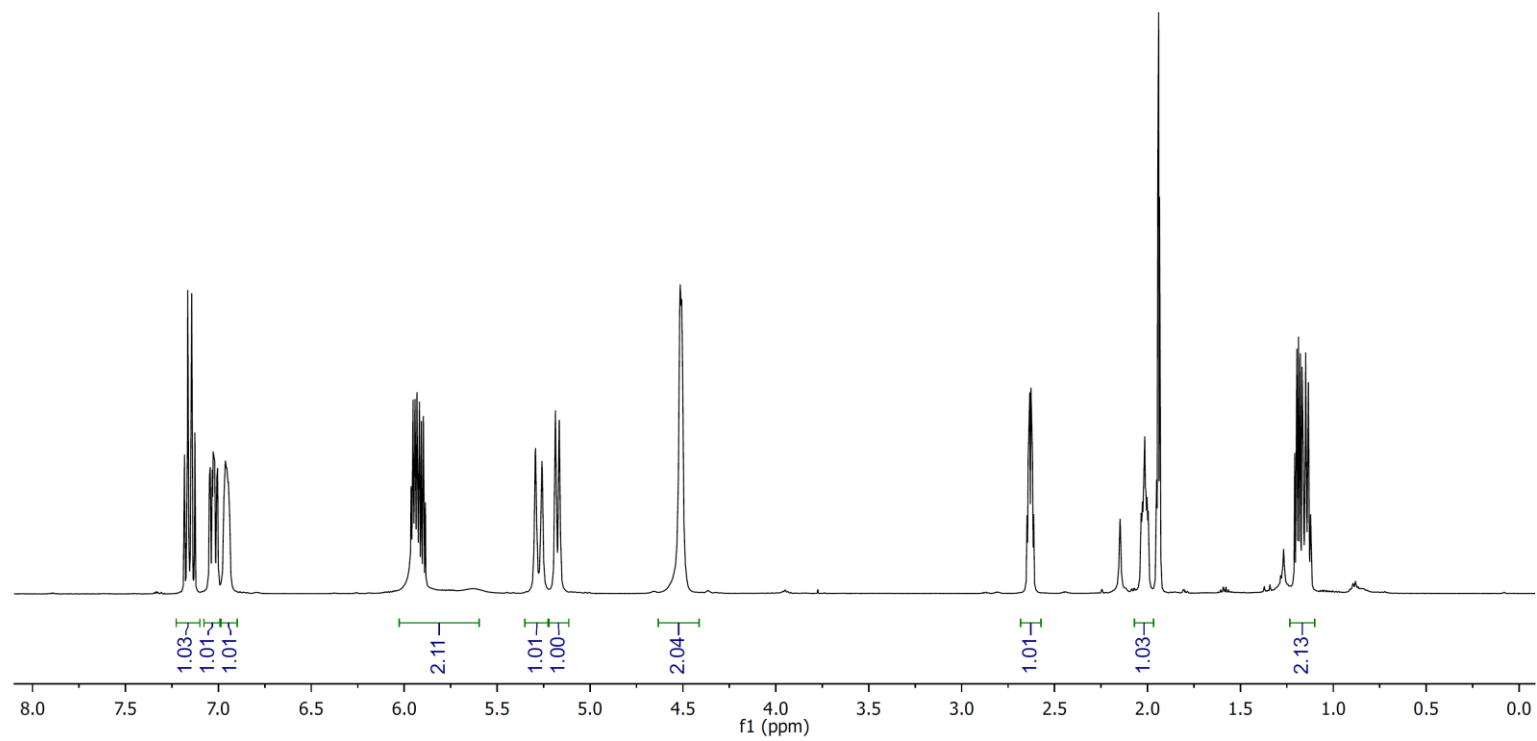
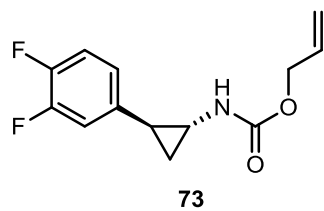
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **72**



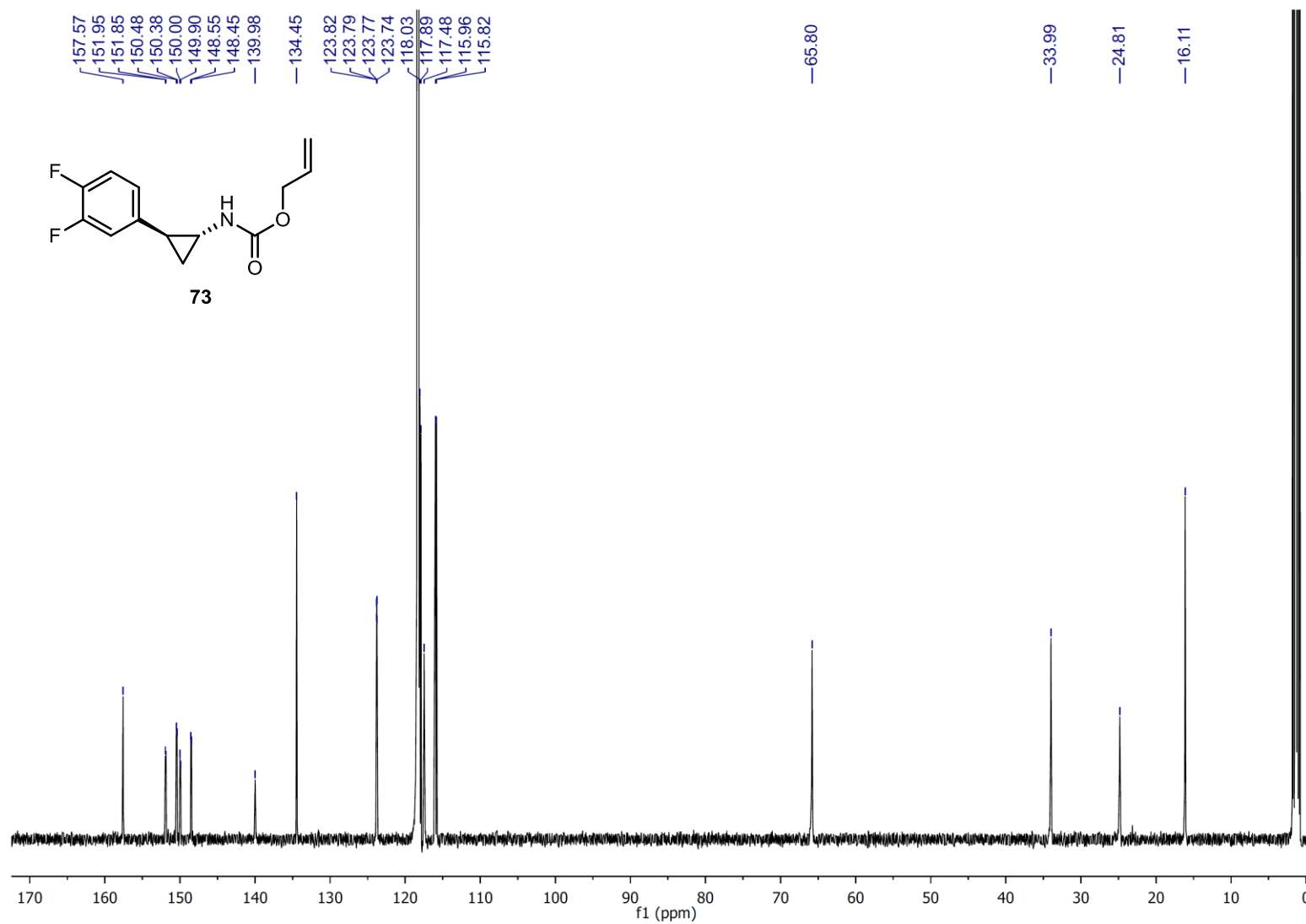
^{13}C NMR (150 MHz, CD_3CN , 50 °C) for compound **72**



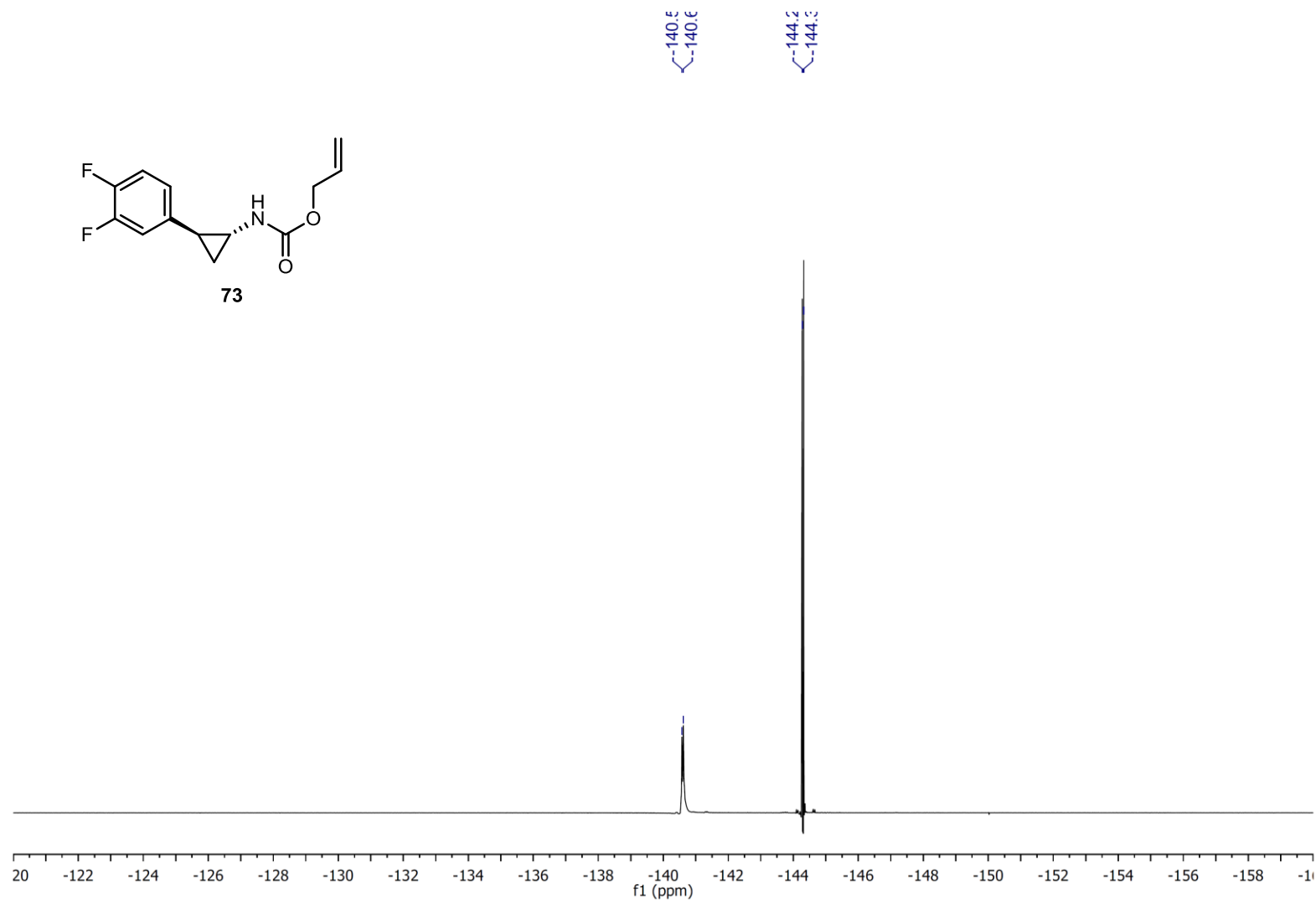
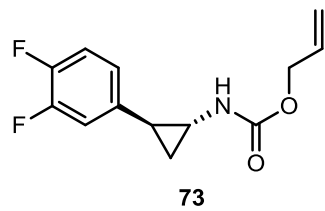
^1H NMR (500 MHz, CD_3CN) for compound **73**



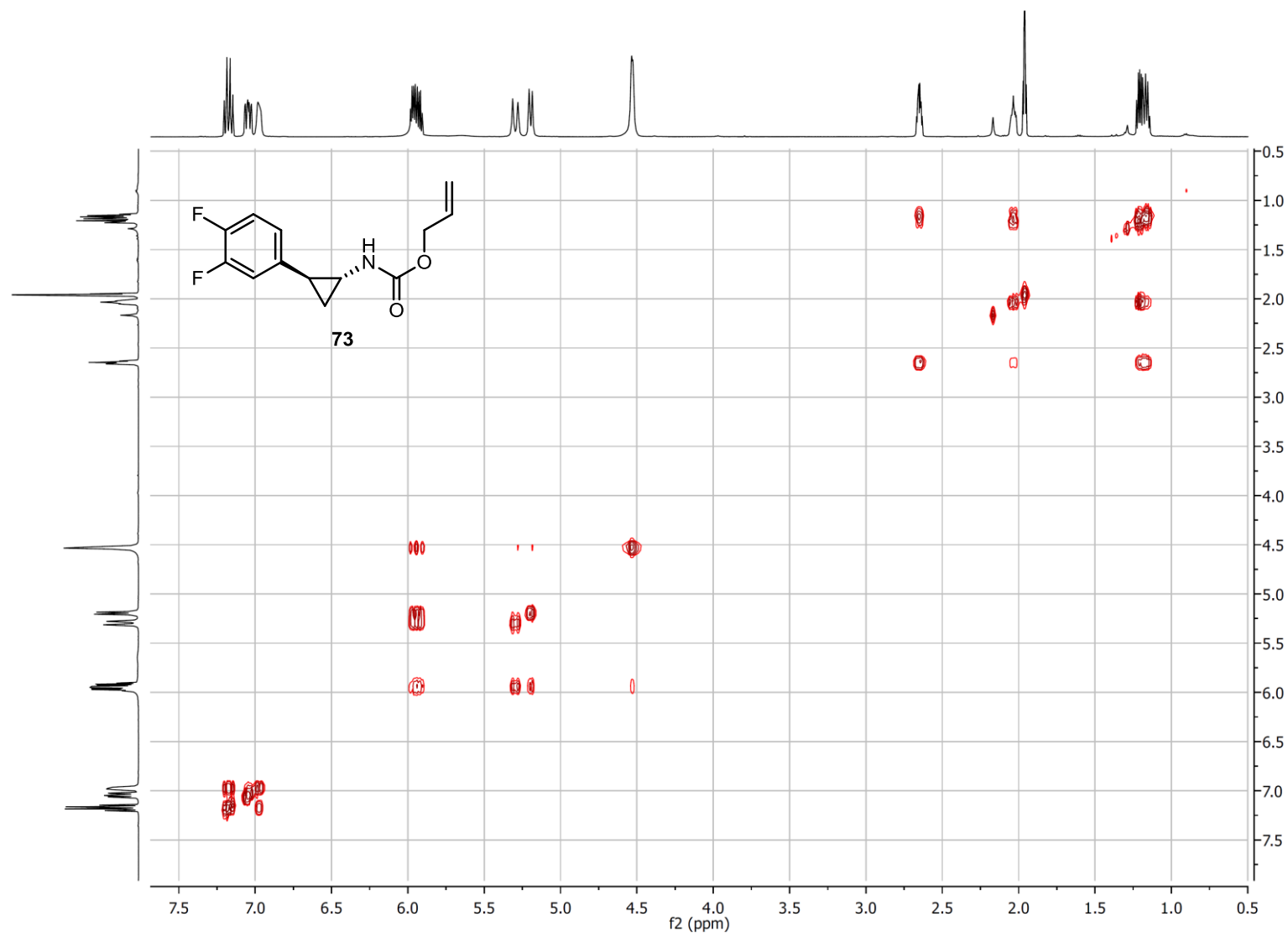
^{13}C NMR (126 MHz, CD_3CN) for compound **73**



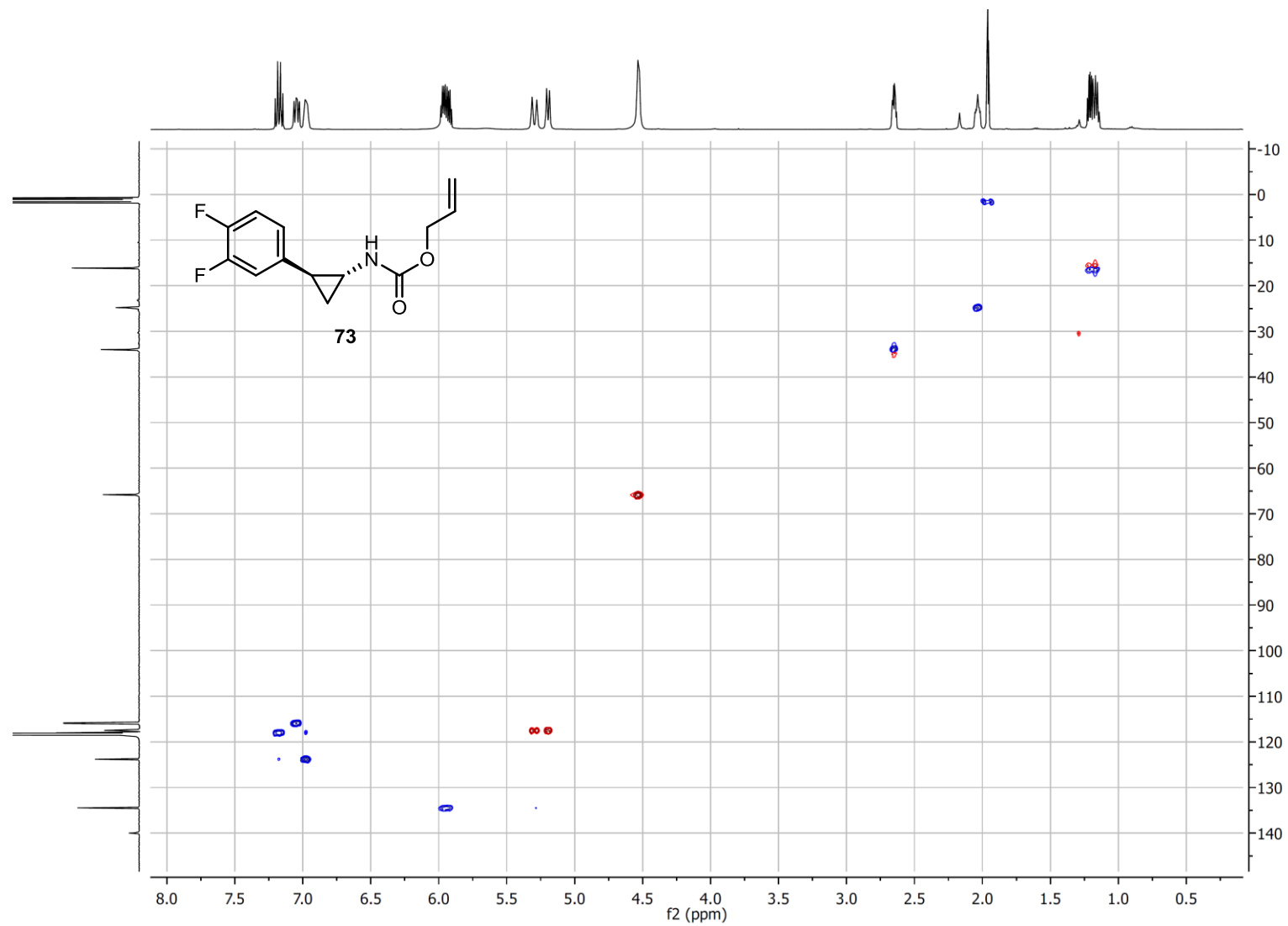
^{19}F NMR (376 MHz, CD_3CN) for compound **73**



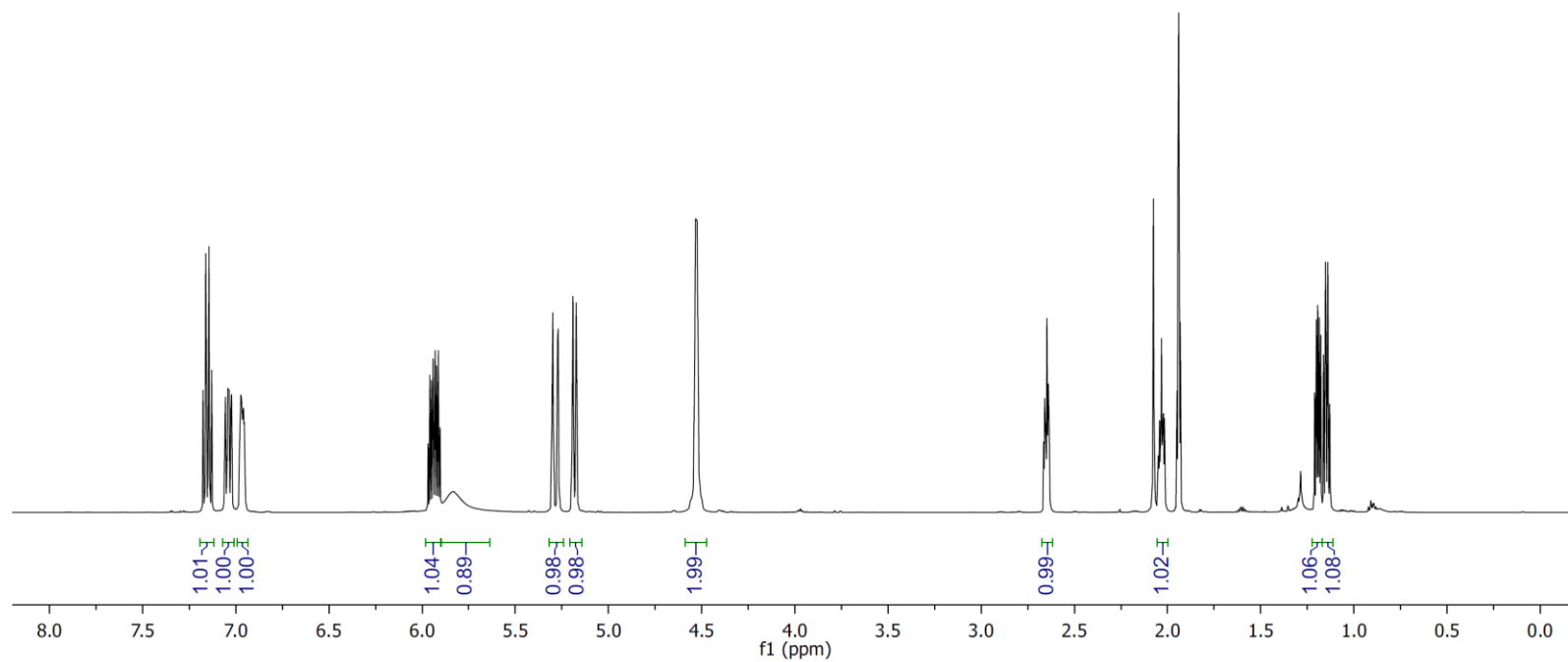
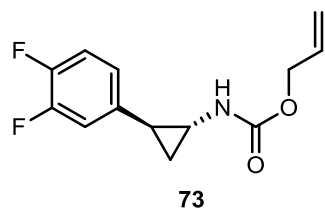
COSY NMR (500 MHz, CD₃CN) for compound **73**



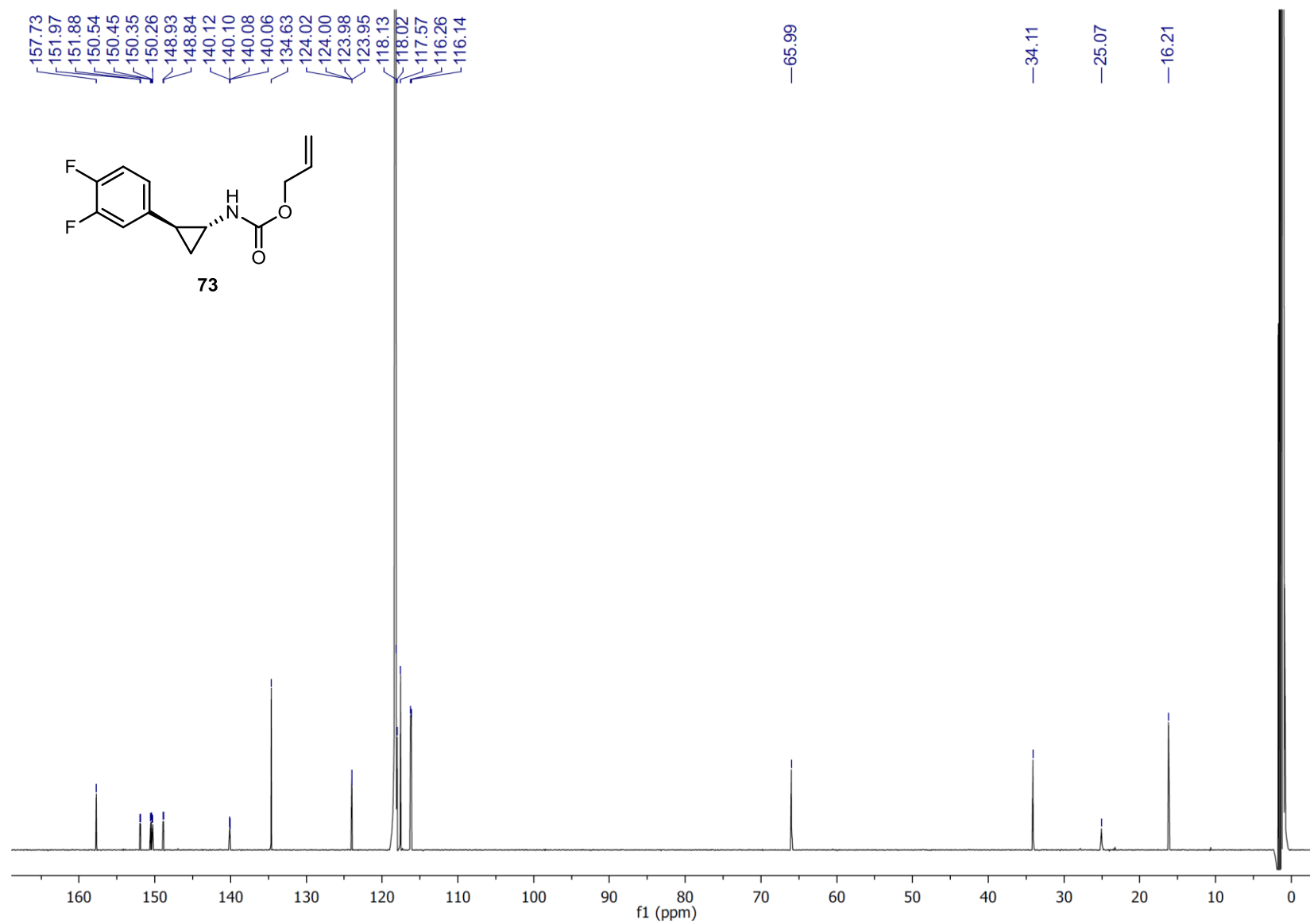
HSQC NMR (500 MHz, CD₃CN) for compound 73



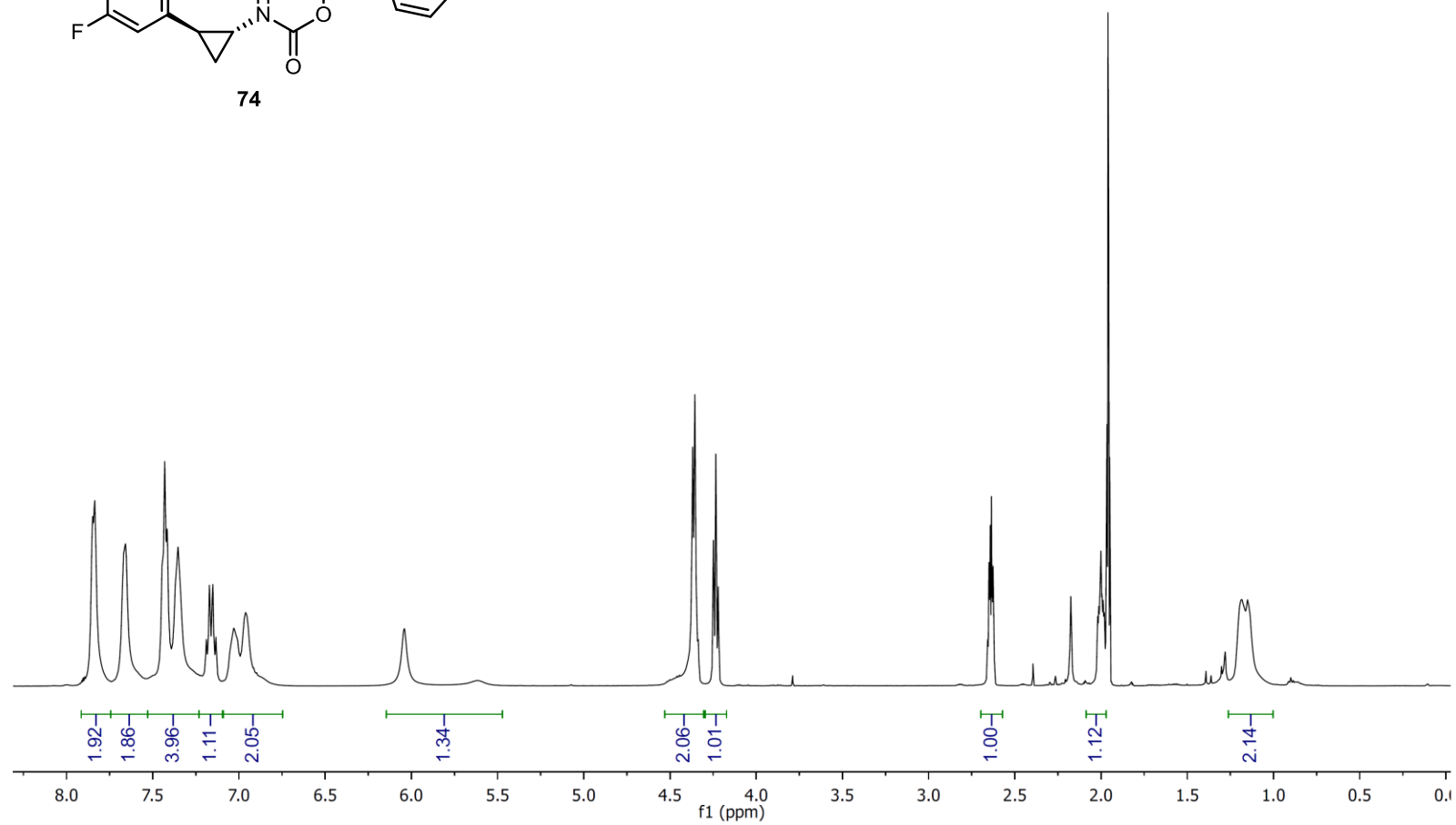
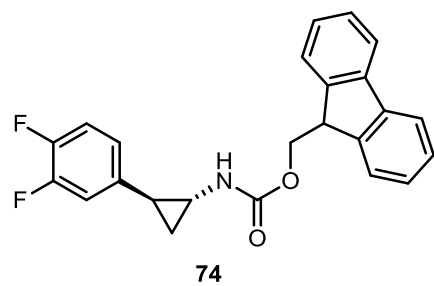
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **73**



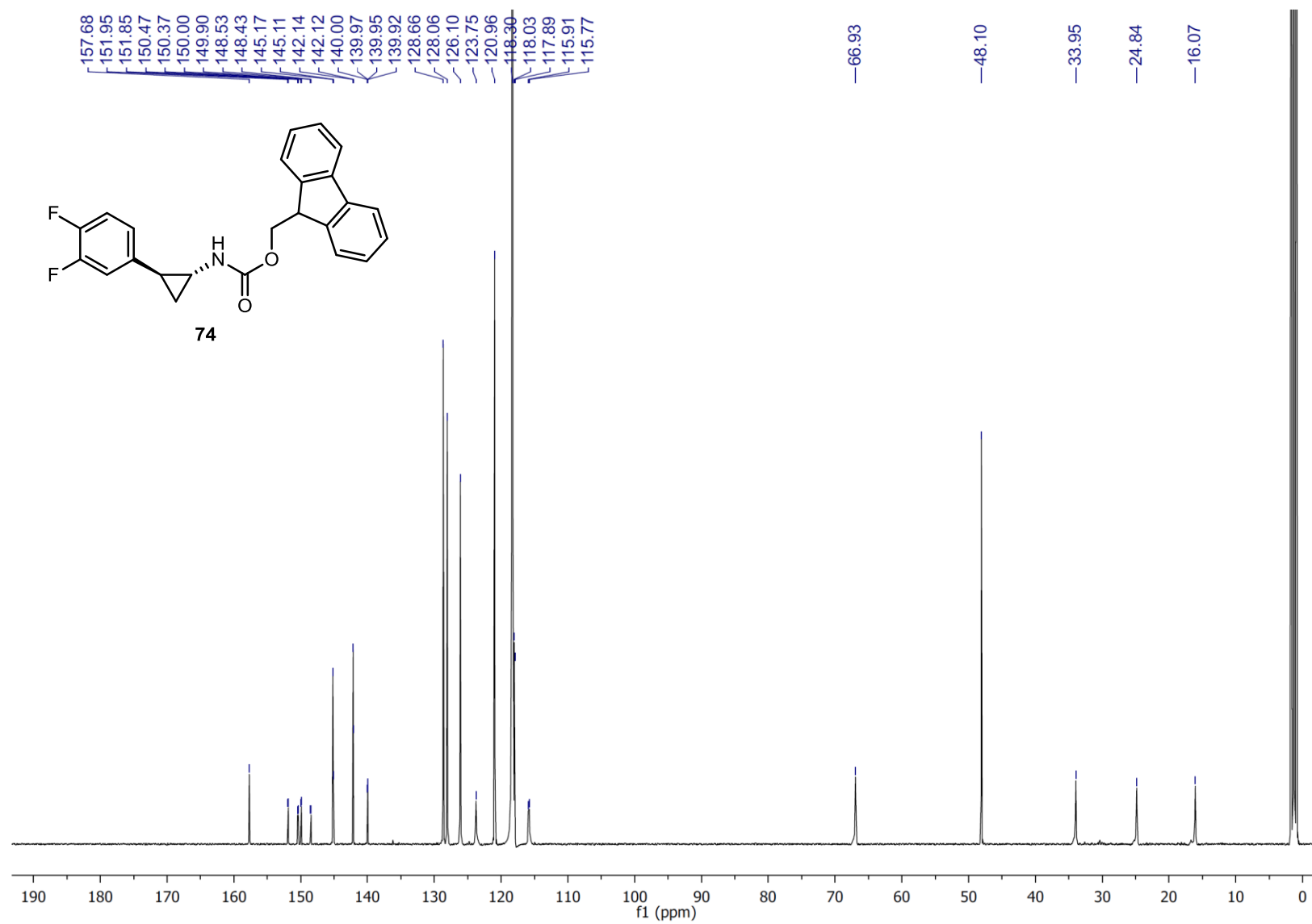
^{13}C NMR (150 MHz, CD_3CN , 50 °C) for compound **73**



^1H NMR (500 MHz, CD_3CN) for compound **74**

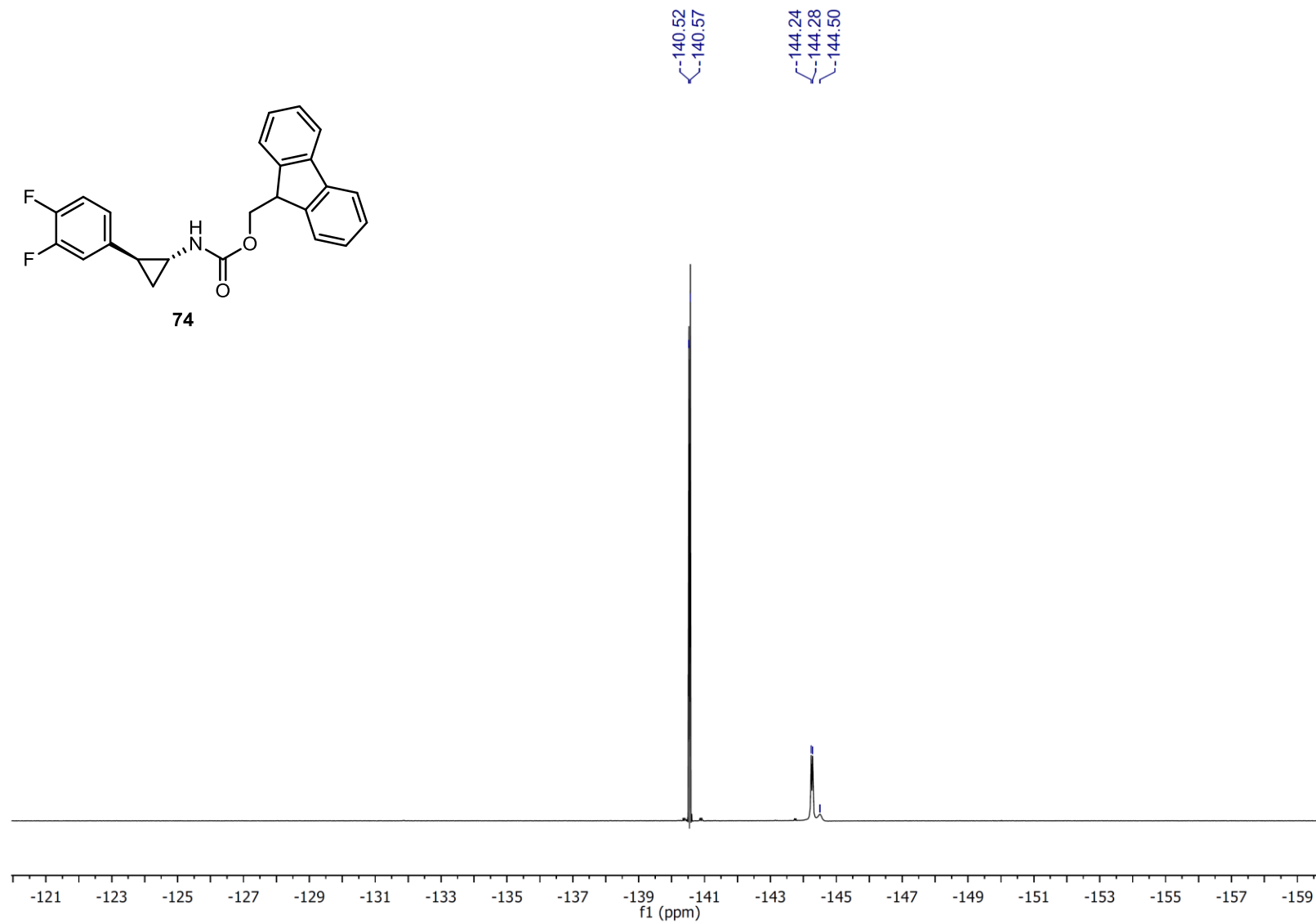


^{13}C NMR (126 MHz, CD_3CN) for compound **74**

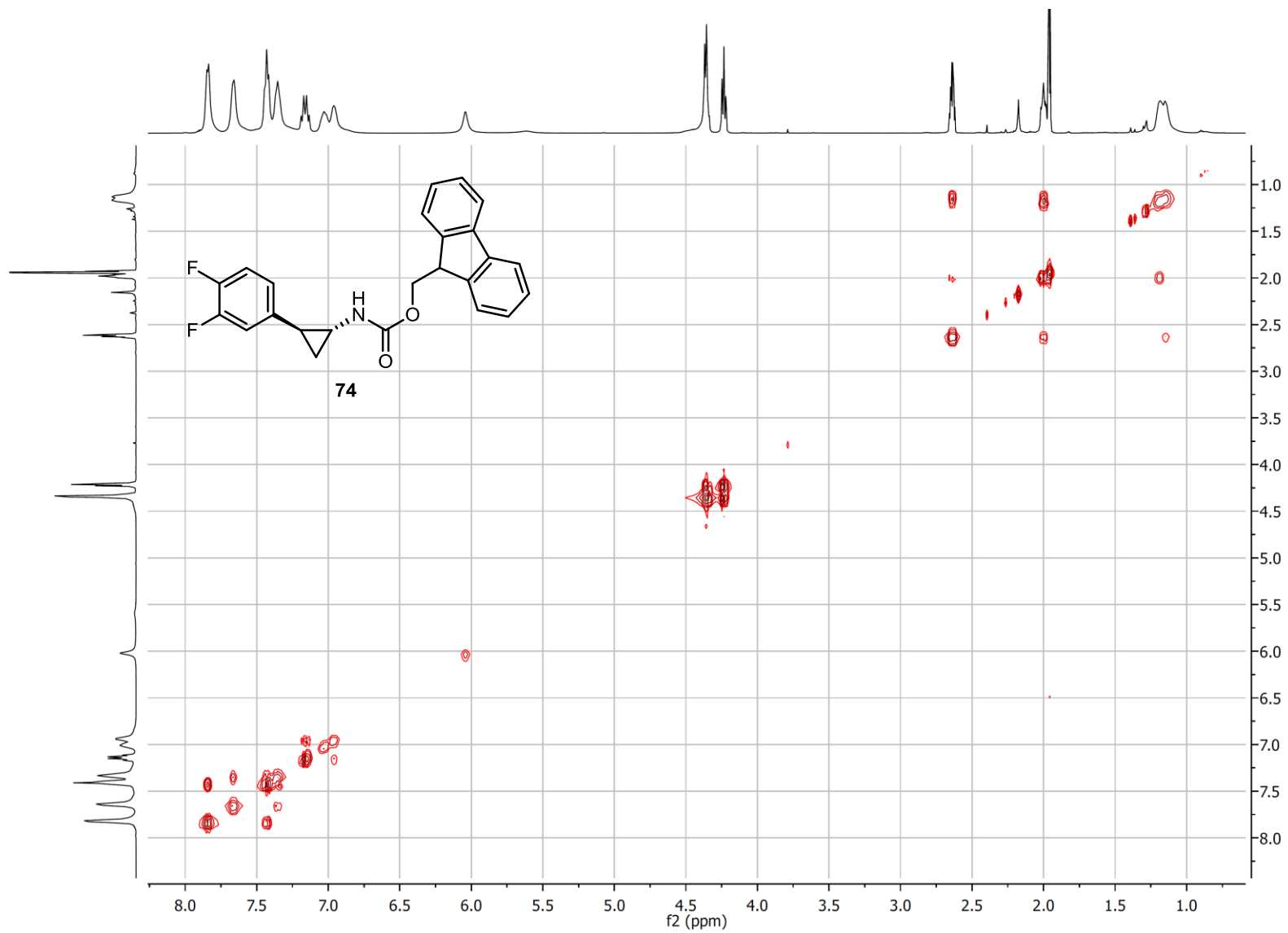


S371

^{19}F NMR (376 MHz, CD_3CN) for compound **74**

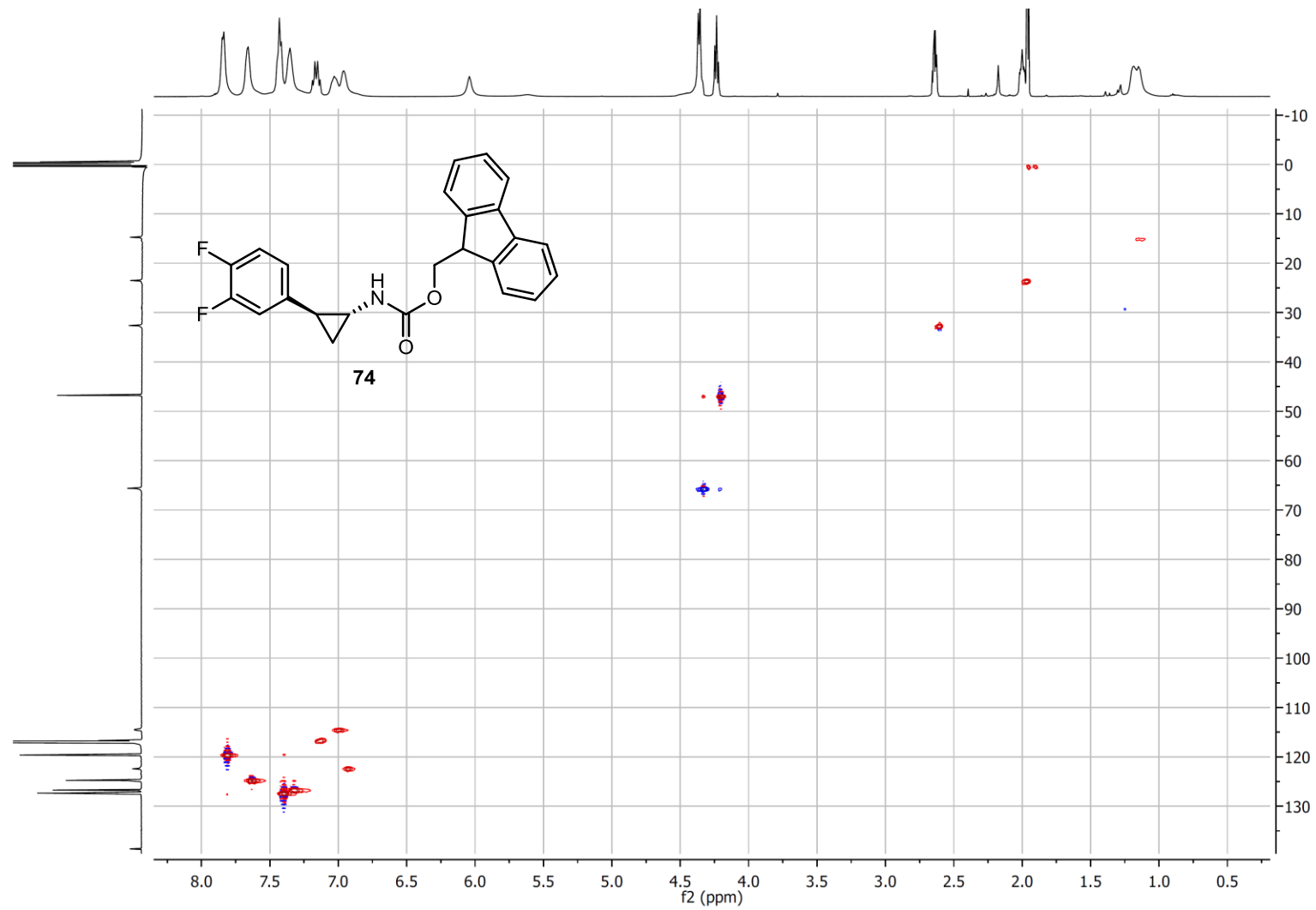


COSY NMR (500 MHz, CD₃CN) for compound **74**

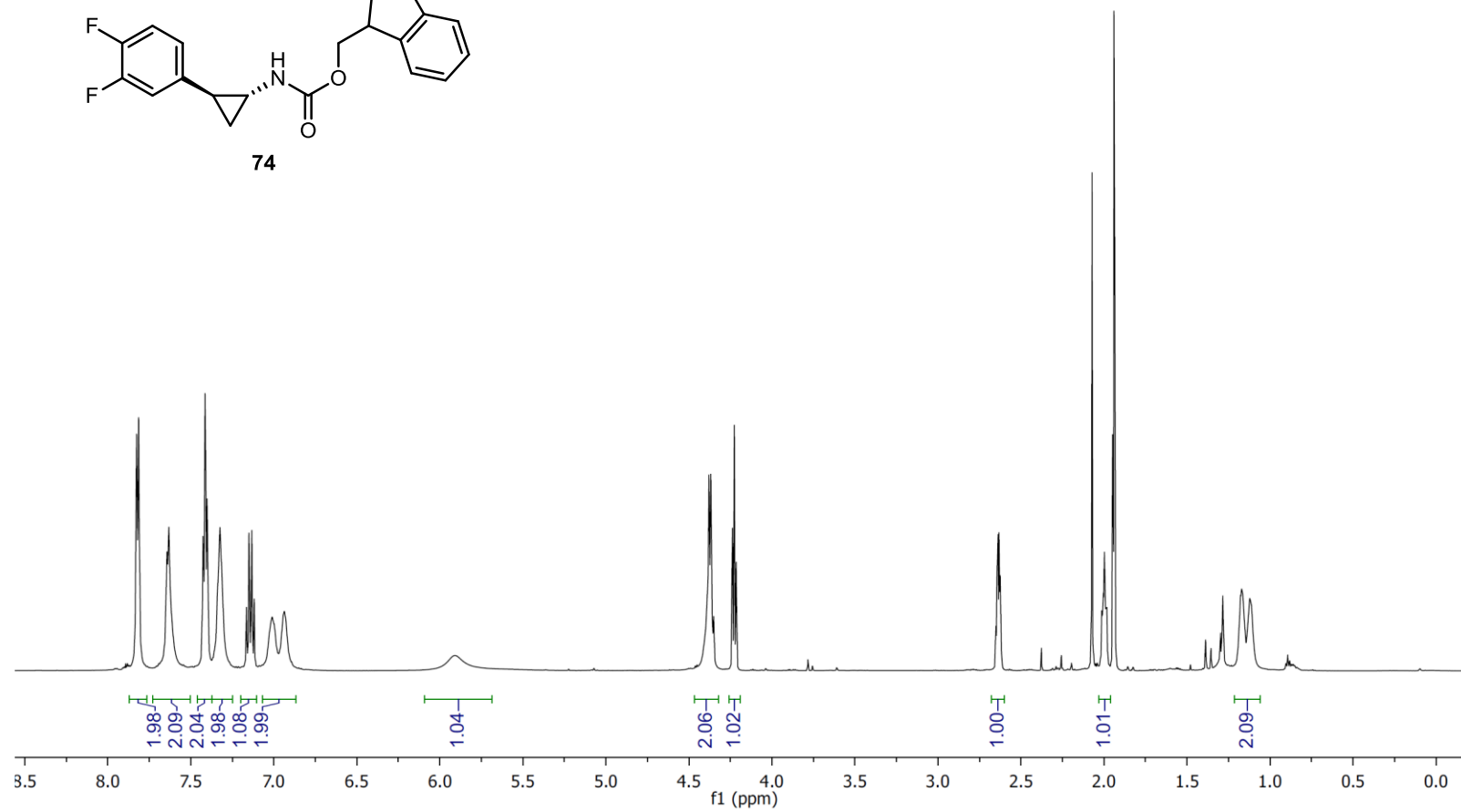
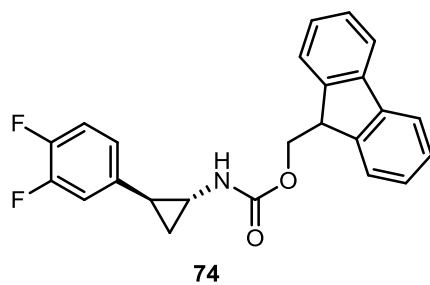


S373

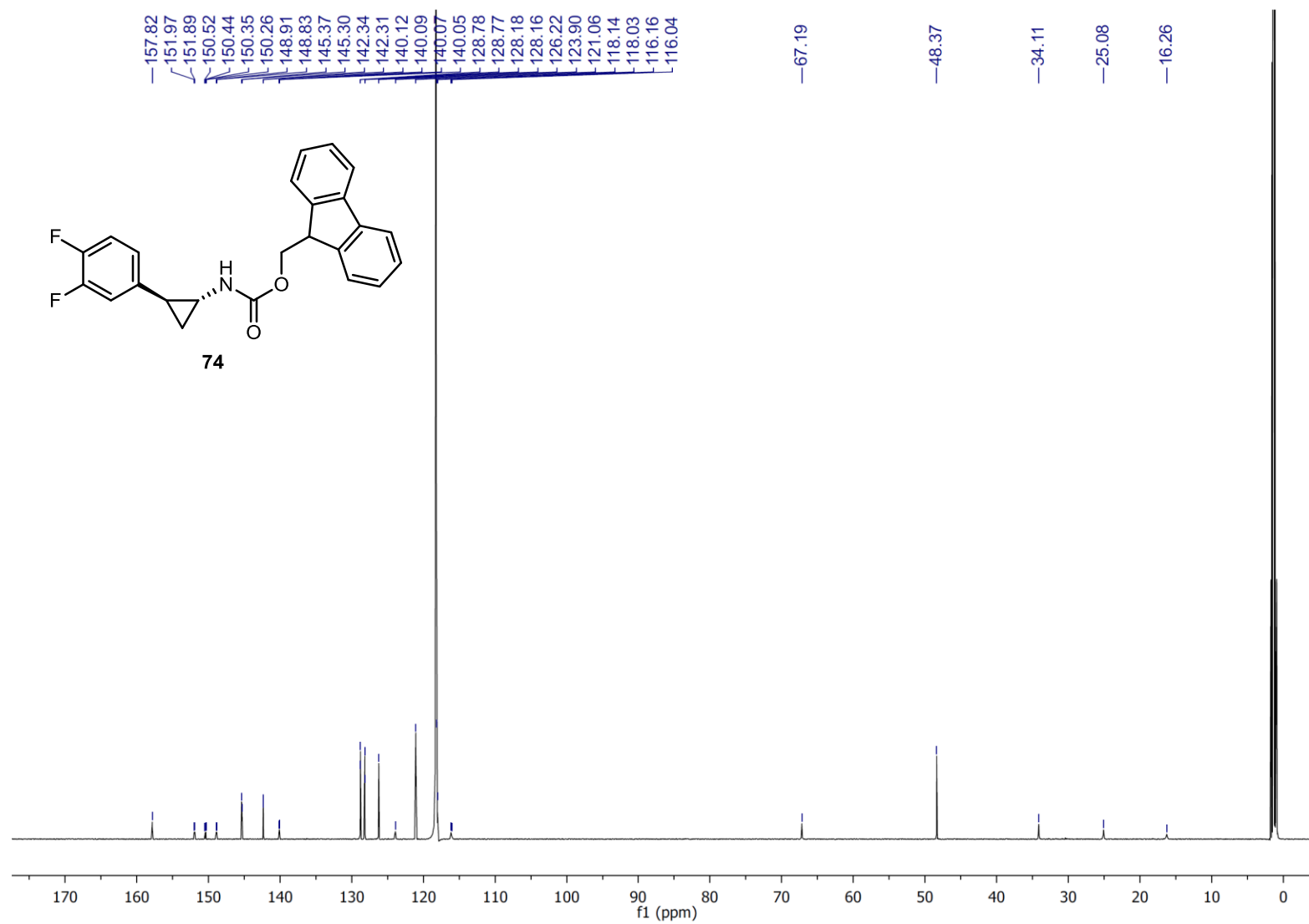
HSQC NMR (500 MHz, CD₃CN) for compound **74**



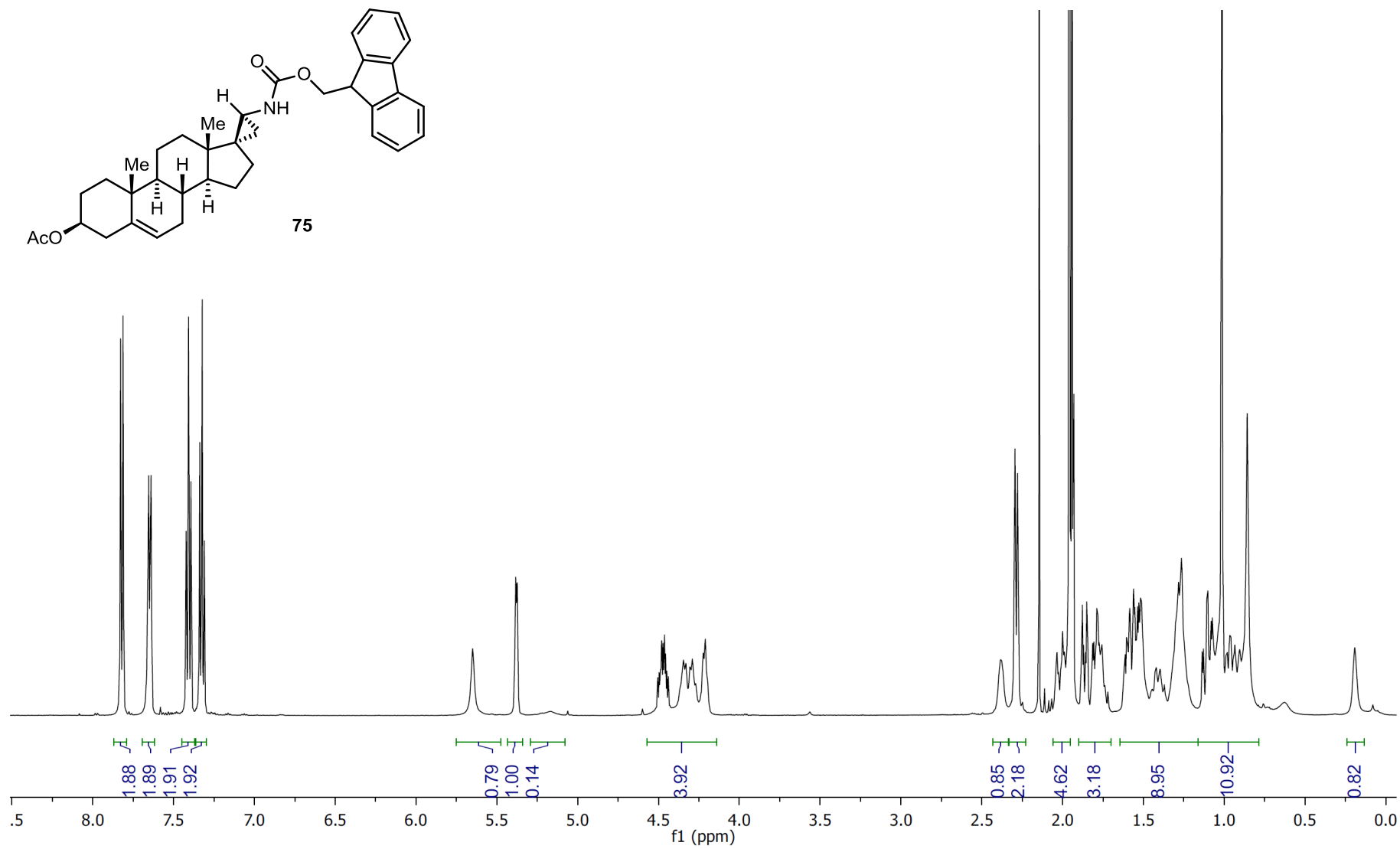
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **74**



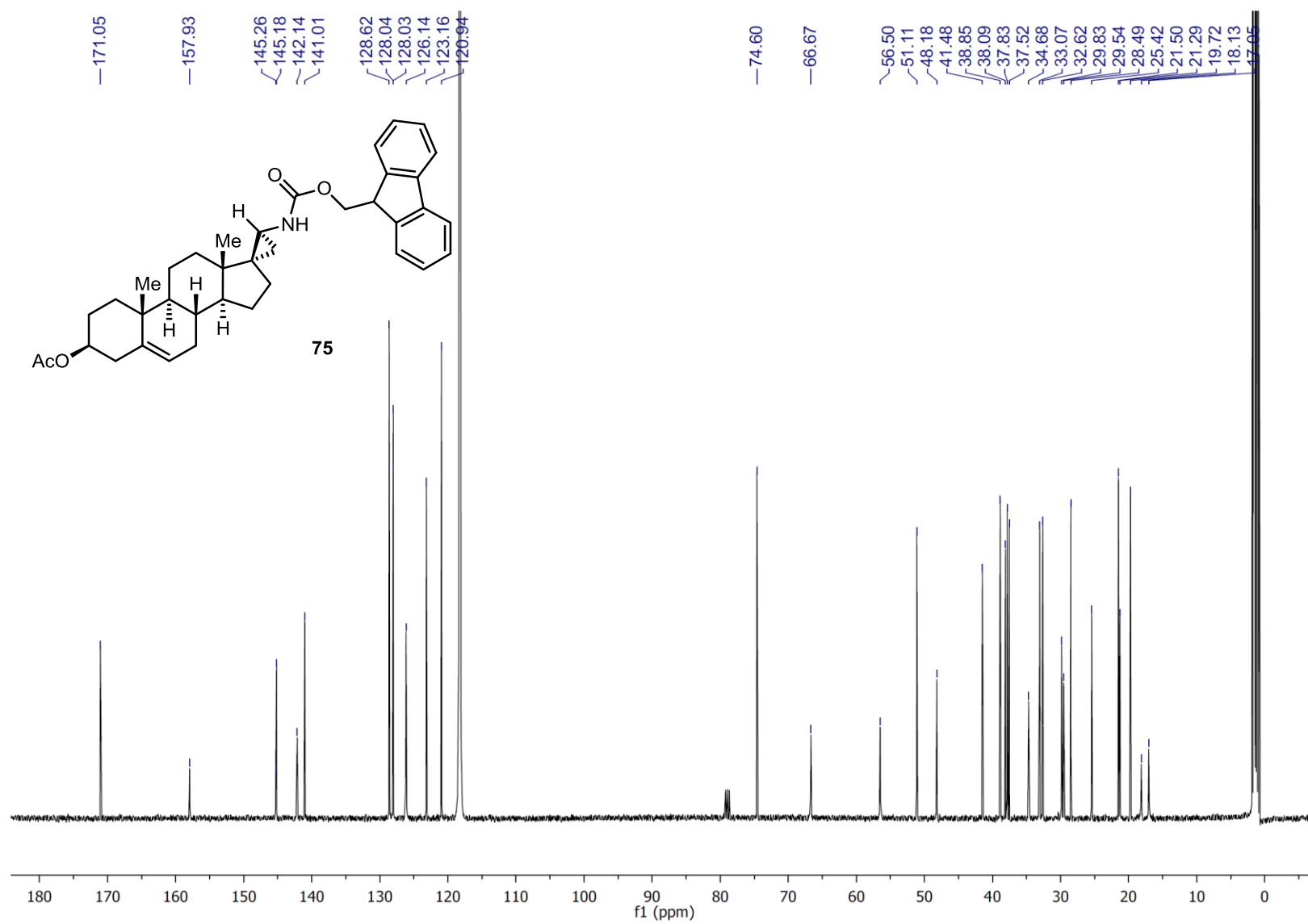
^{13}C NMR (150 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound **74**



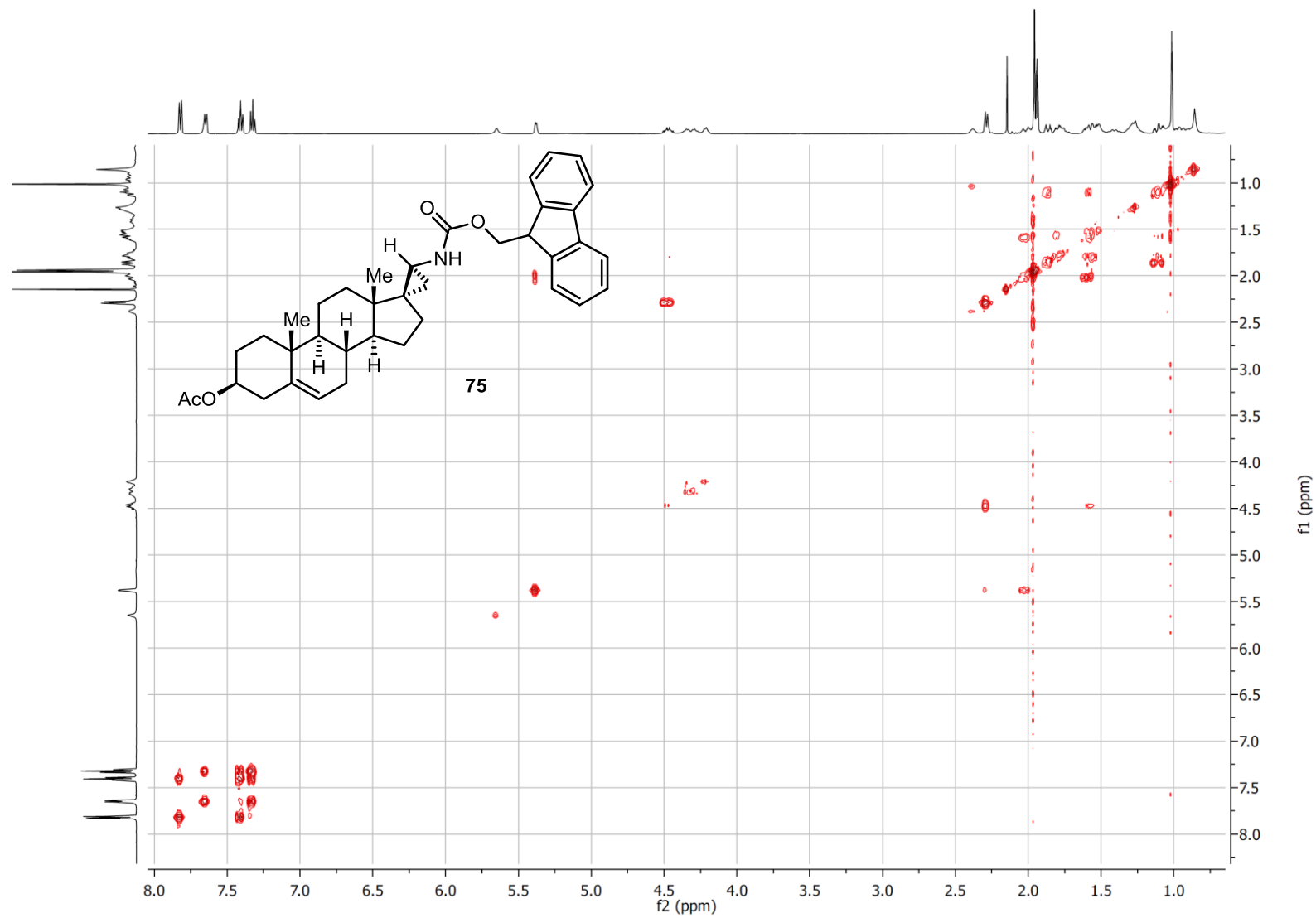
^1H NMR (500 MHz, CD_3CN) for compound 75



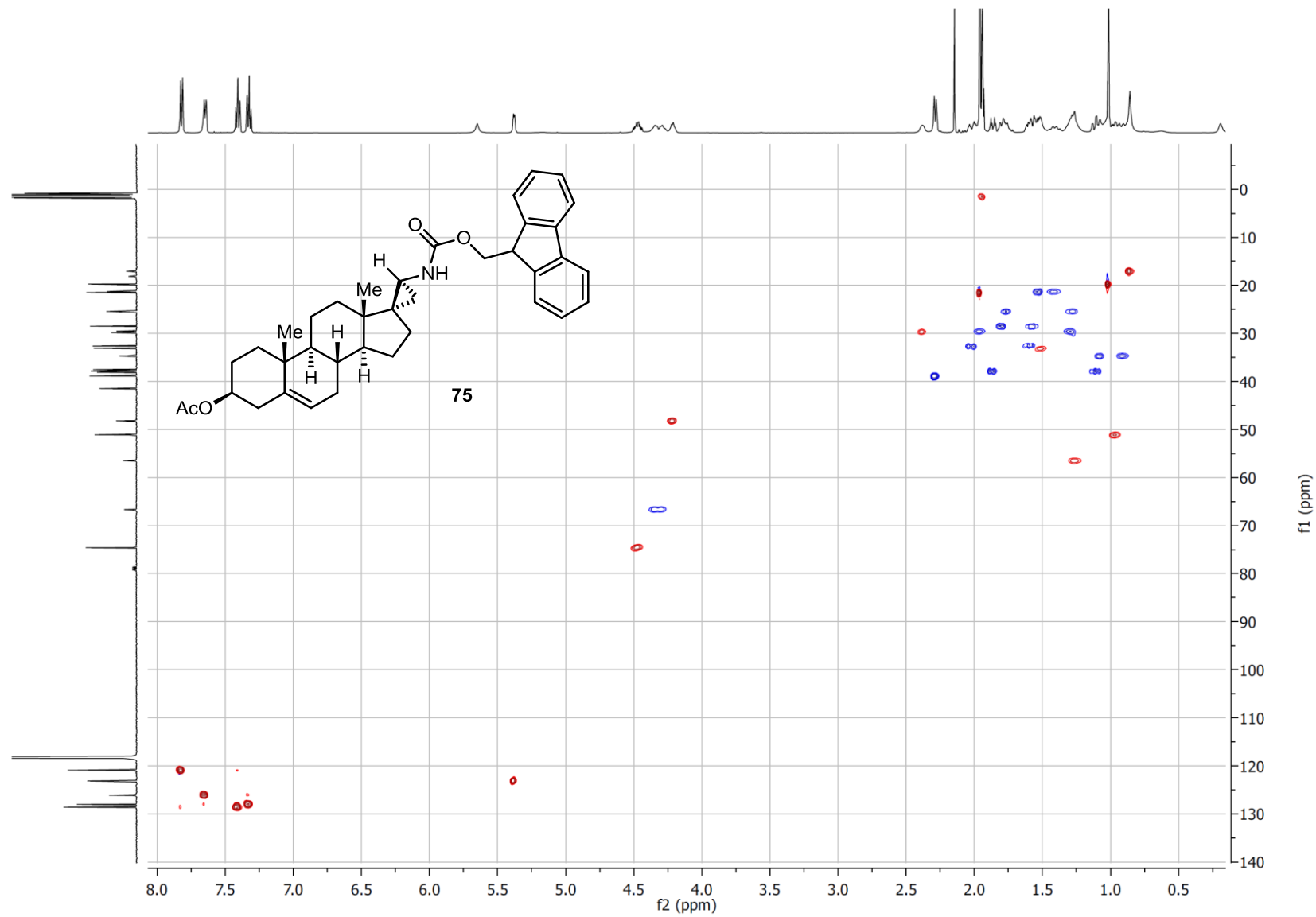
^{13}C NMR (126 MHz, CD_3CN) for compound 75



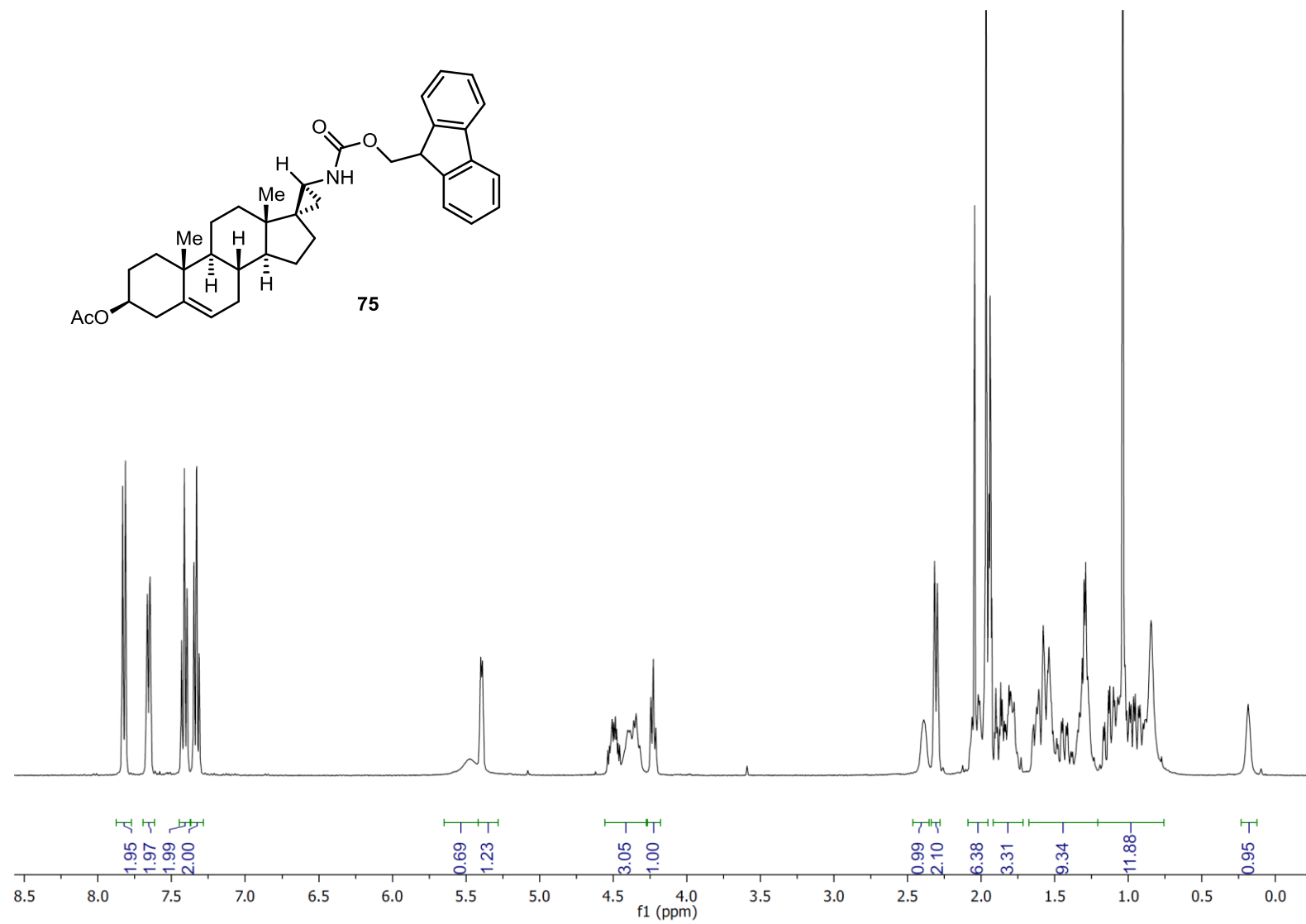
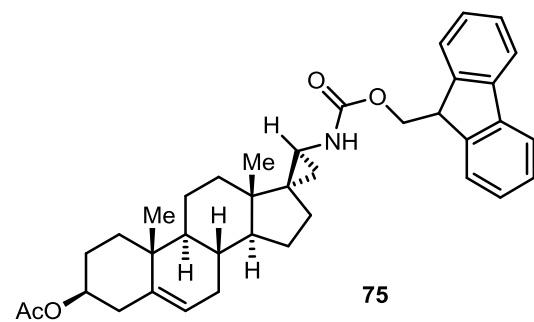
COSY NMR (500 MHz, CD₃CN) for compound 75



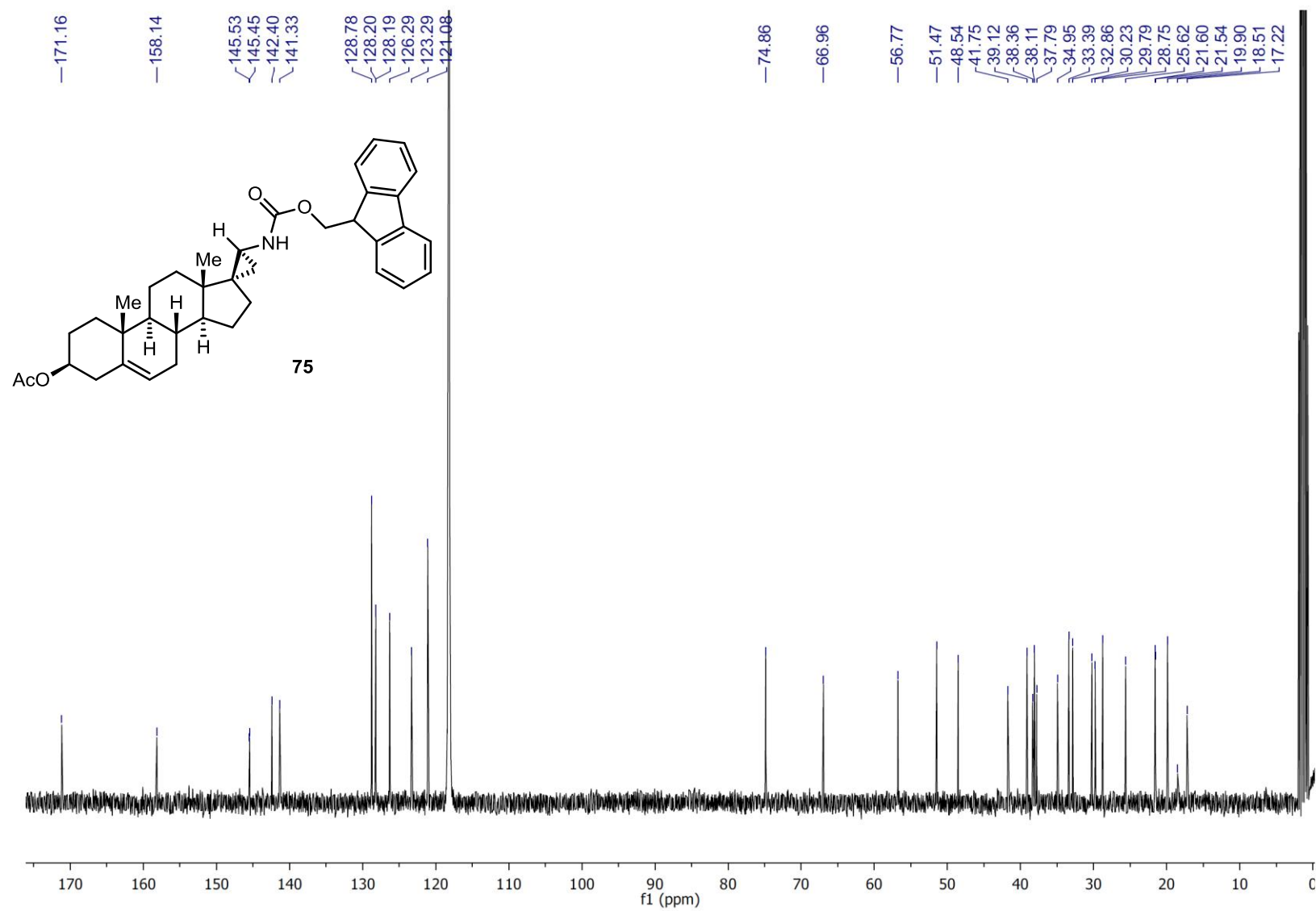
HSQC NMR (500 MHz, CD₃CN) for compound 75



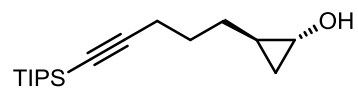
^1H NMR (600 MHz, CD_3CN , 50 $^\circ\text{C}$) for compound 75



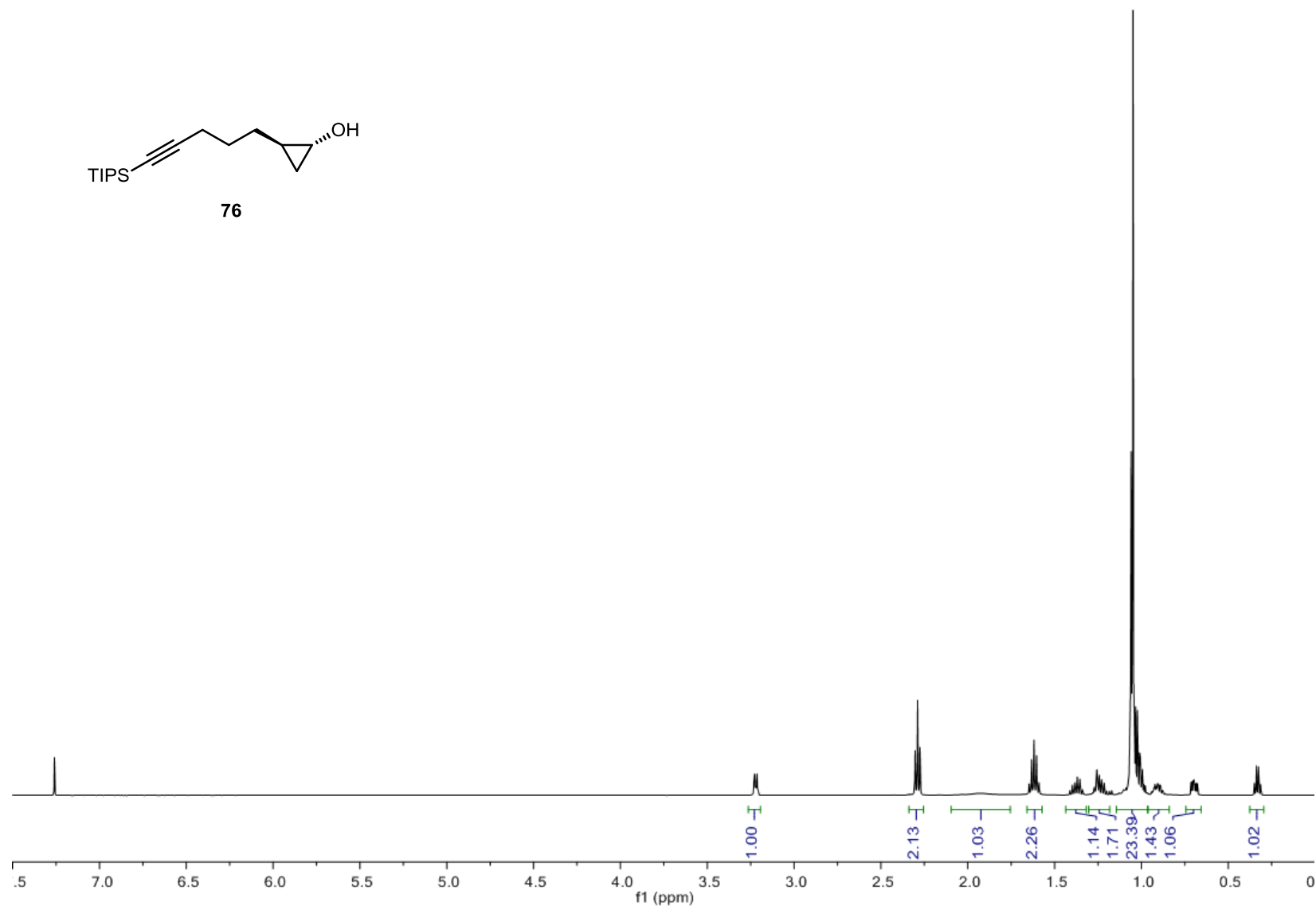
^{13}C NMR (150 MHz, CD_3CN , 50 °C) for compound **75**



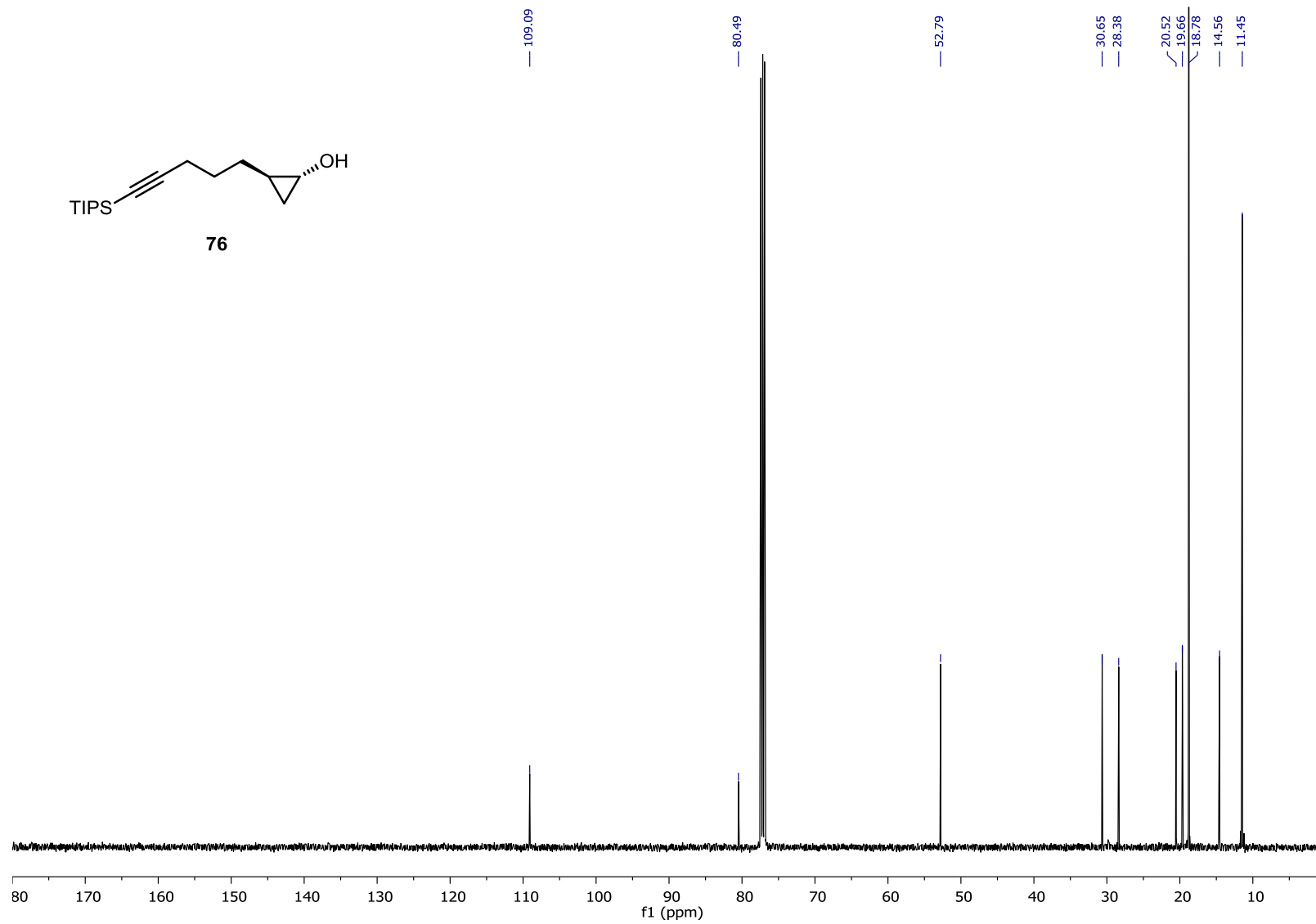
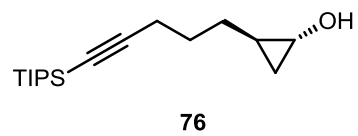
^1H NMR (500 MHz, CDCl_3) for compound **76**



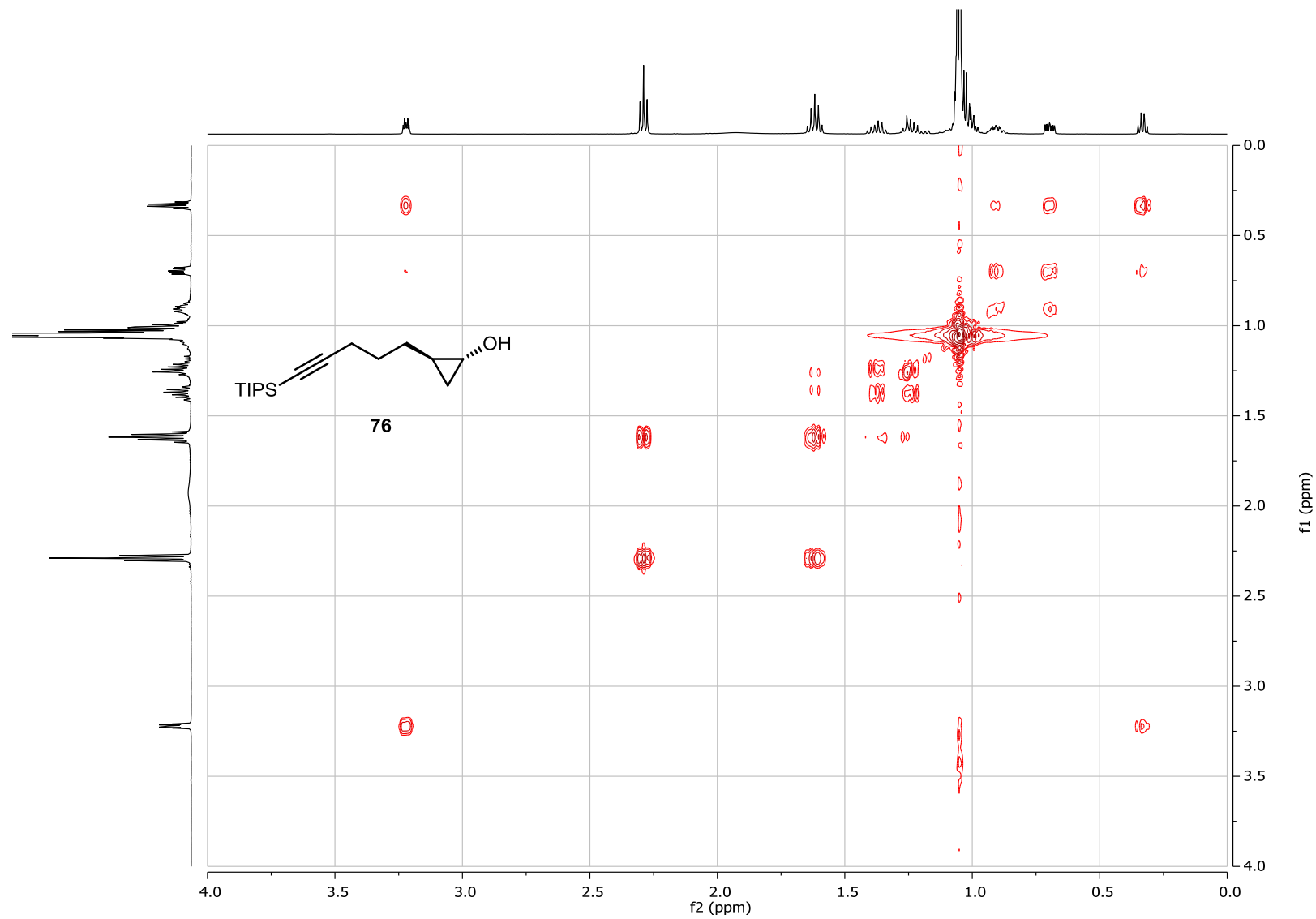
76



^{13}C NMR (126 MHz, CDCl_3) for compound **76**

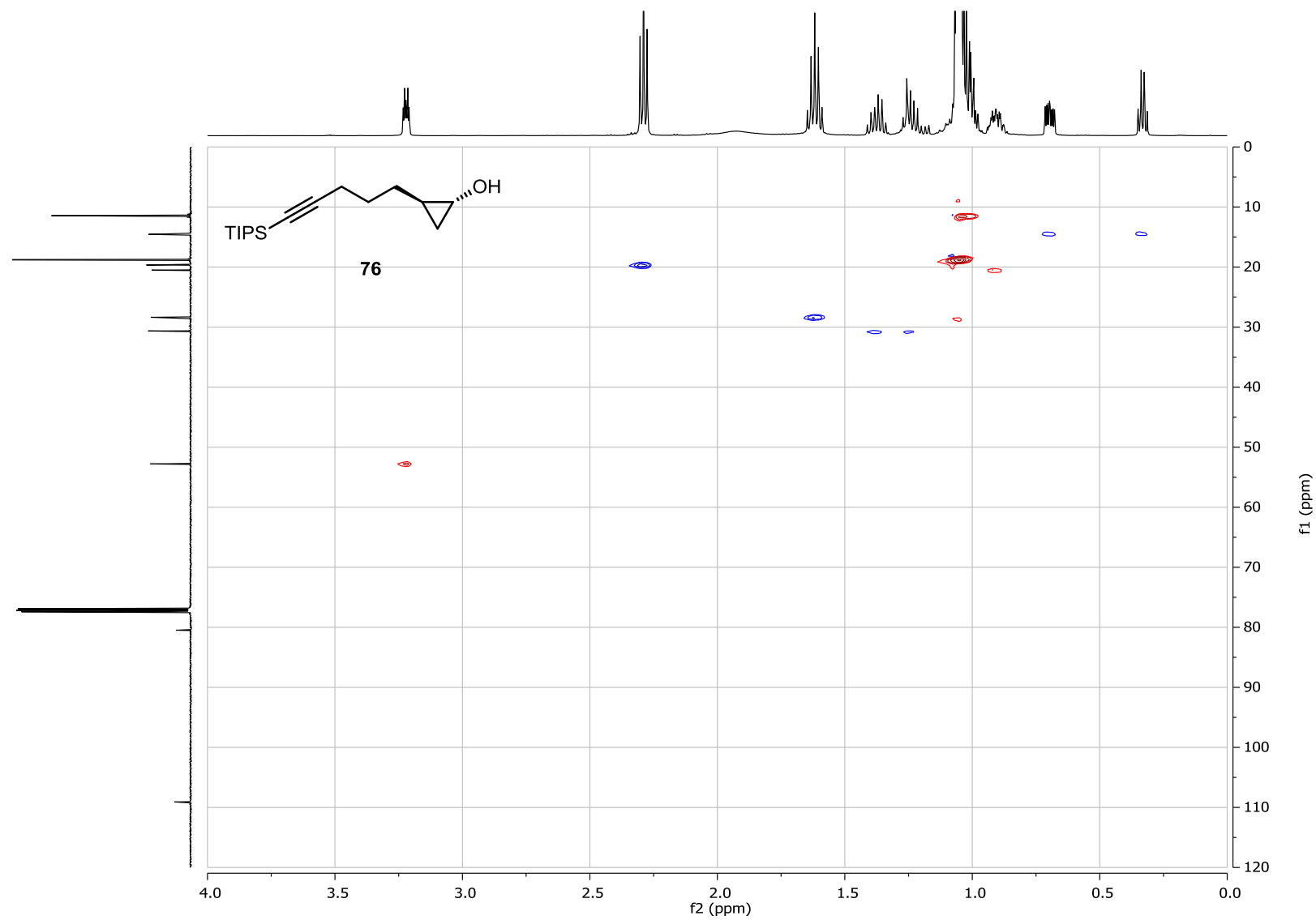


COSY NMR (500 MHz, CDCl_3) for compound **76**



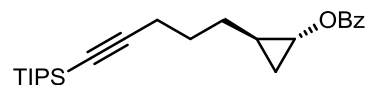
S385

HSQC NMR (500 MHz, CDCl_3) for compound **76**

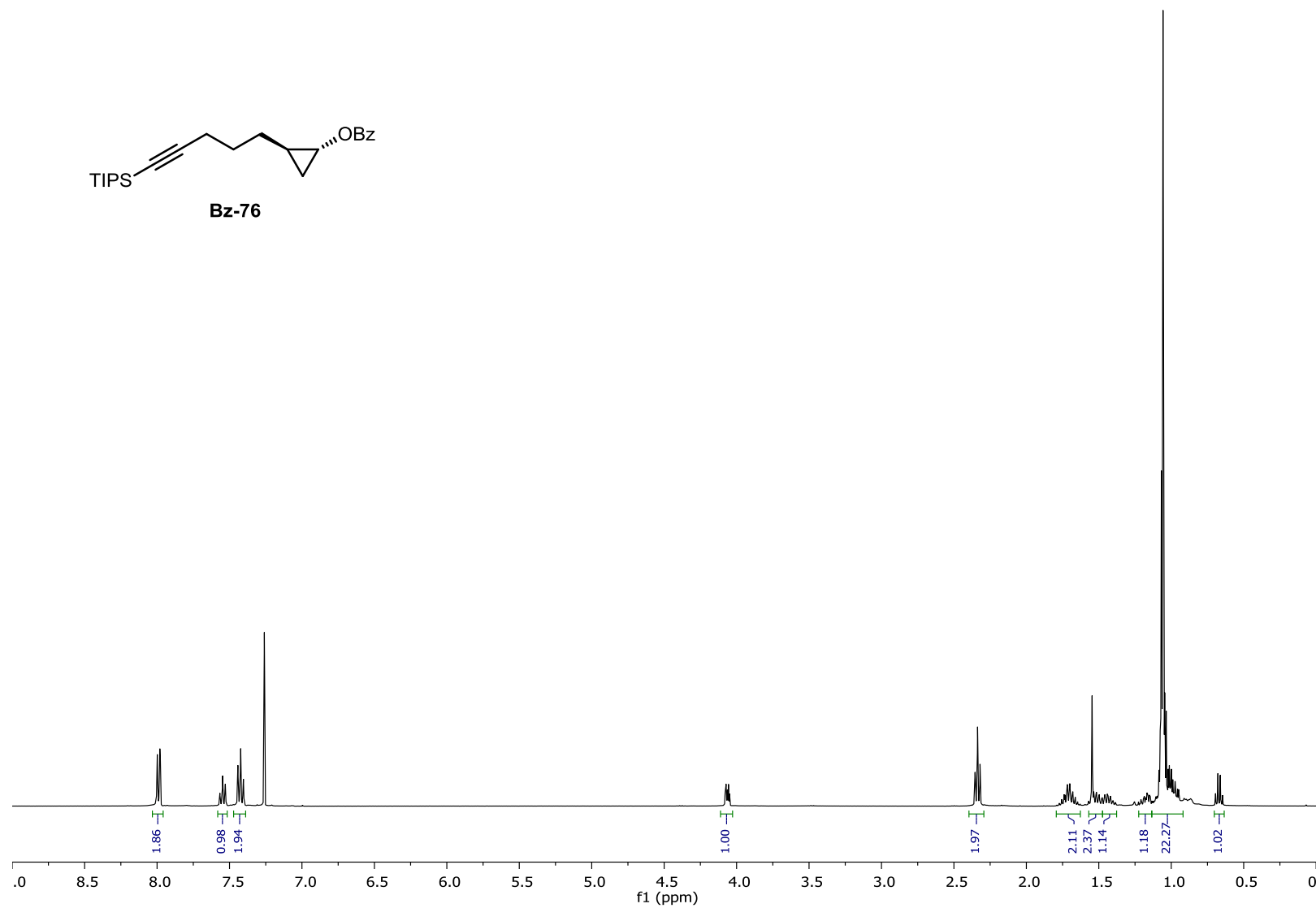


S386

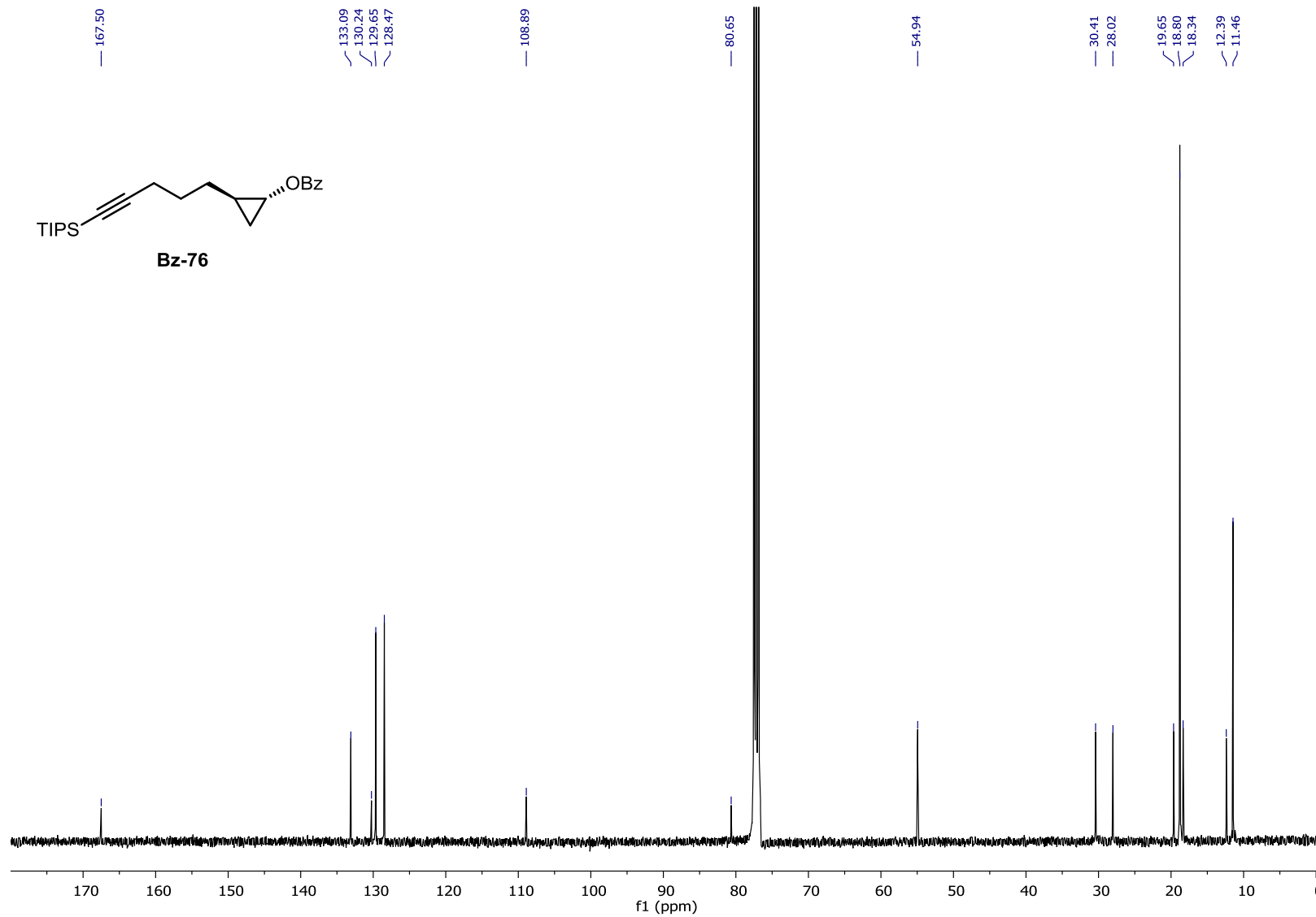
^1H NMR (500 MHz, CDCl_3) for compound **Bz-76**



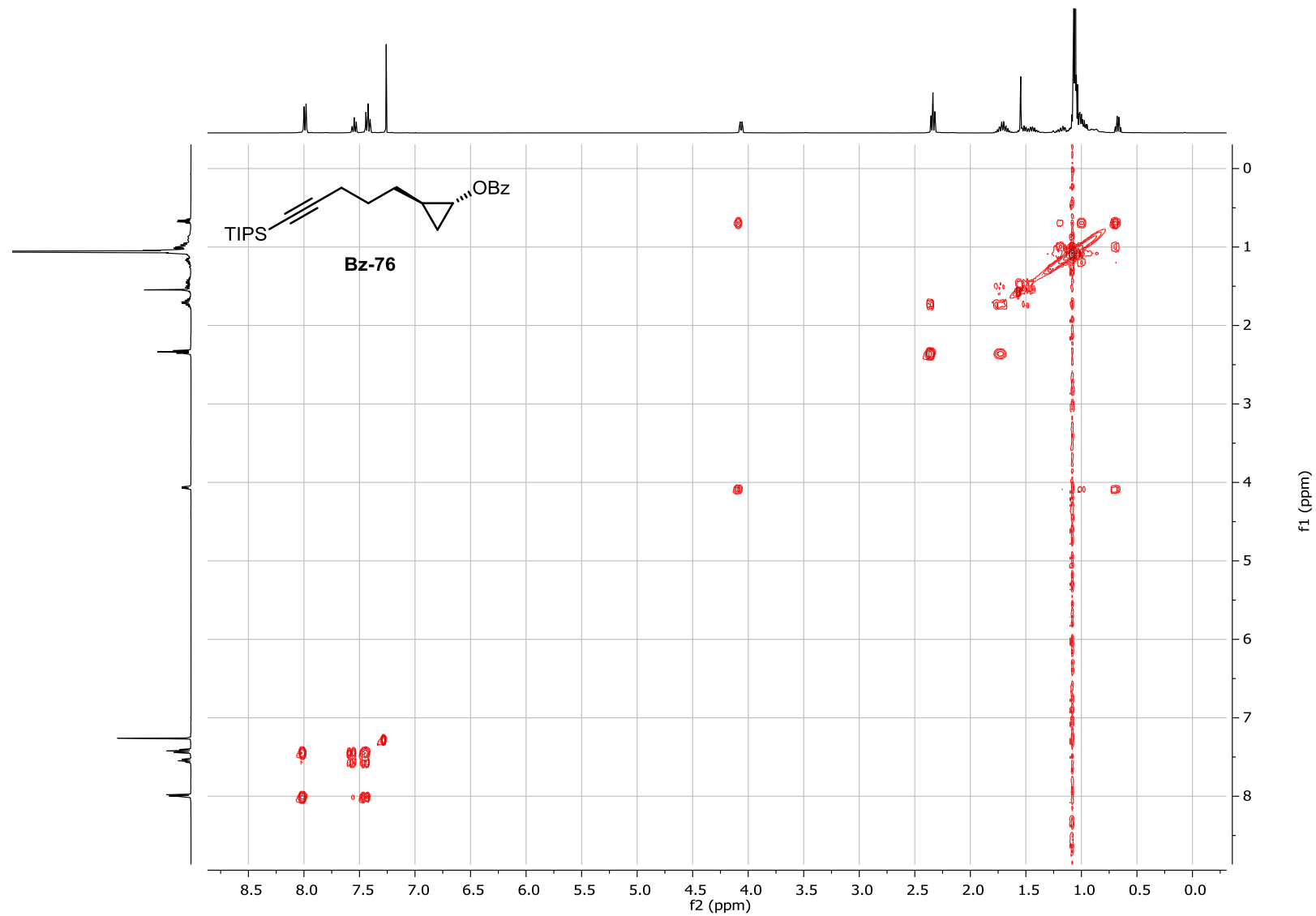
Bz-76



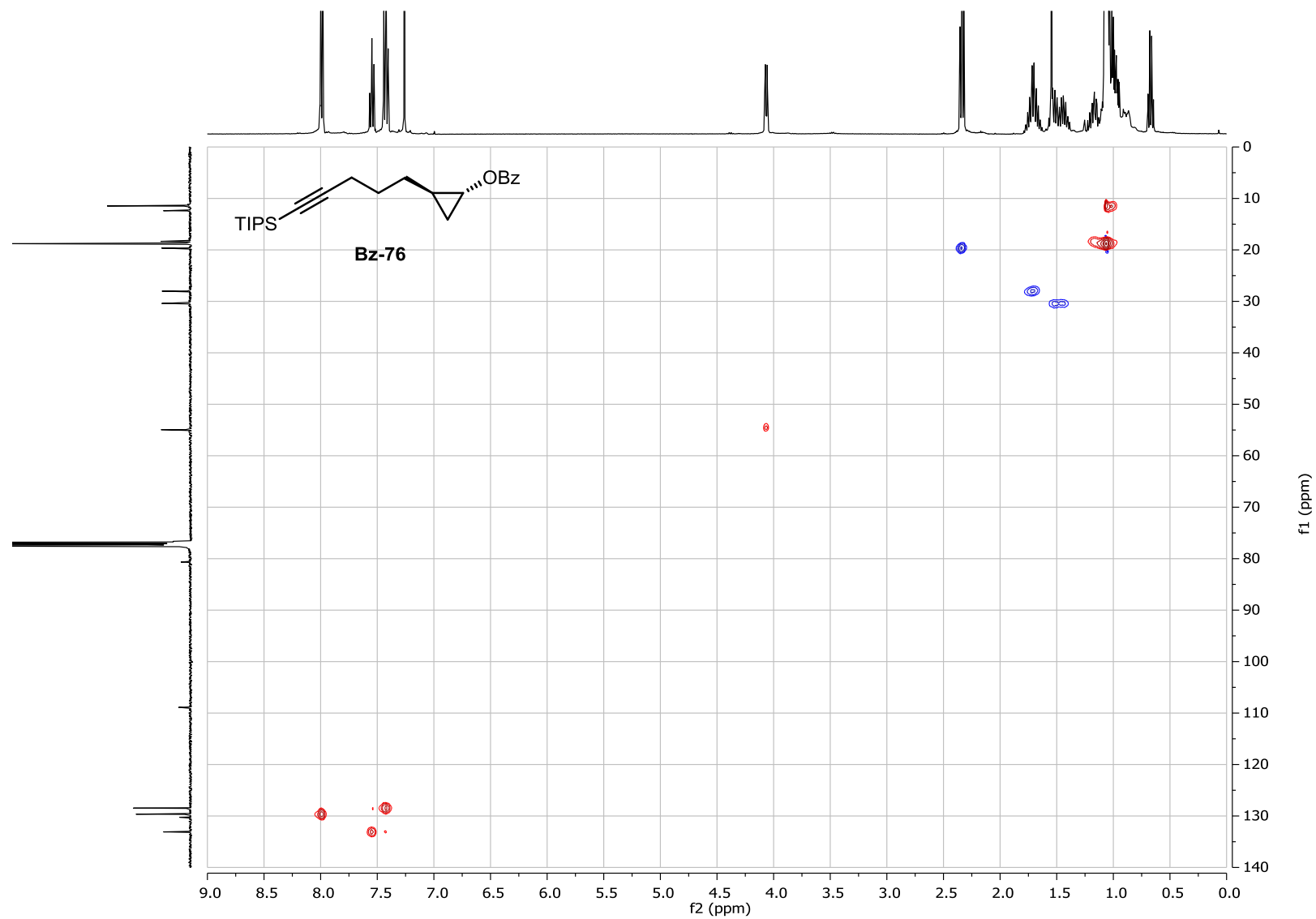
^{13}C NMR (126 MHz, CDCl_3) for compound **Bz-76**



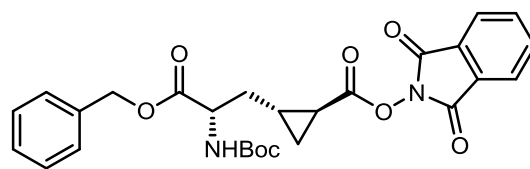
COSY NMR (500 MHz, CDCl_3) for compound **Bz-76**



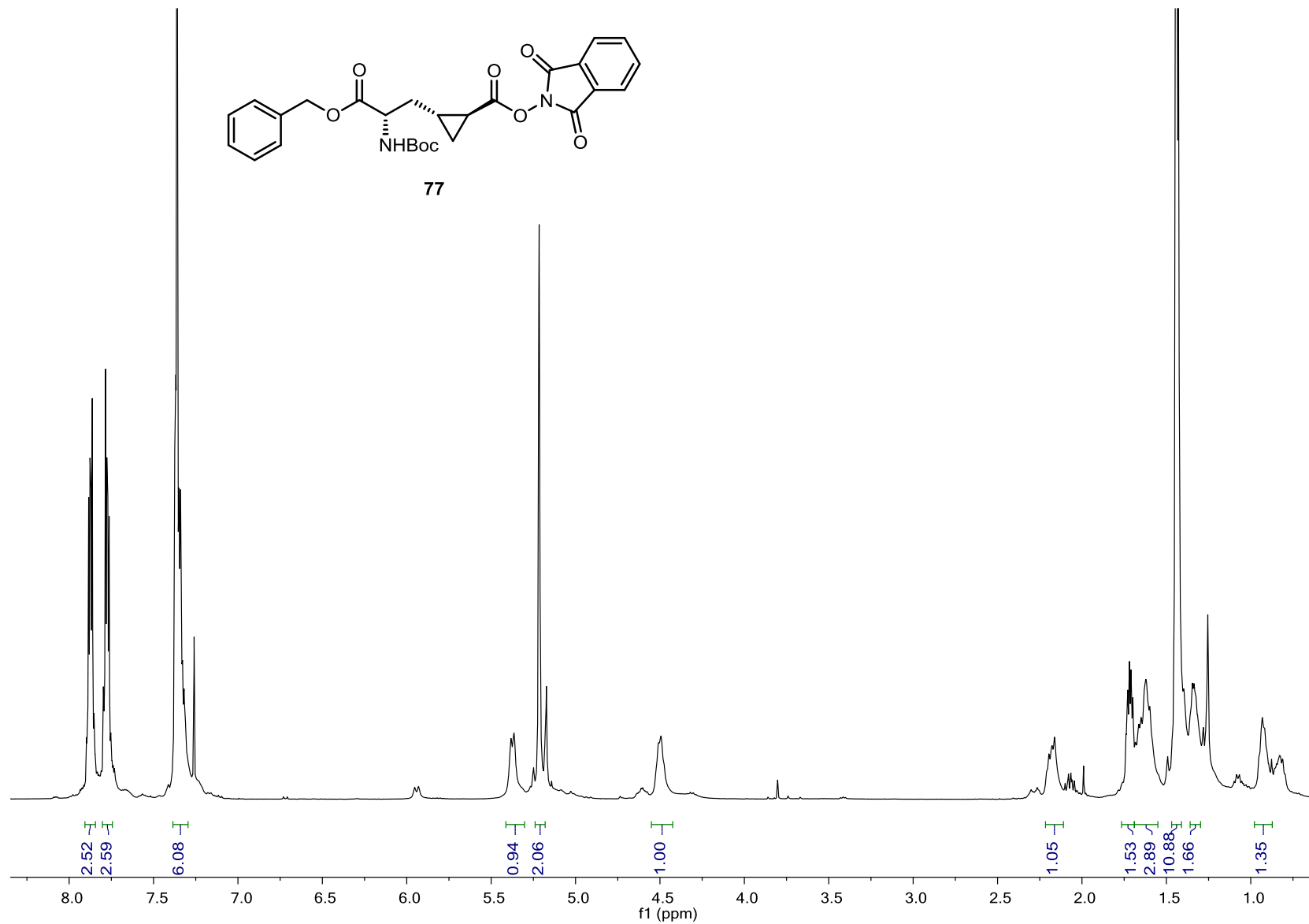
HSQC NMR (500 MHz, CDCl₃) for compound **Bz-76**



^1H NMR (400 MHz, CDCl_3) for compound 77

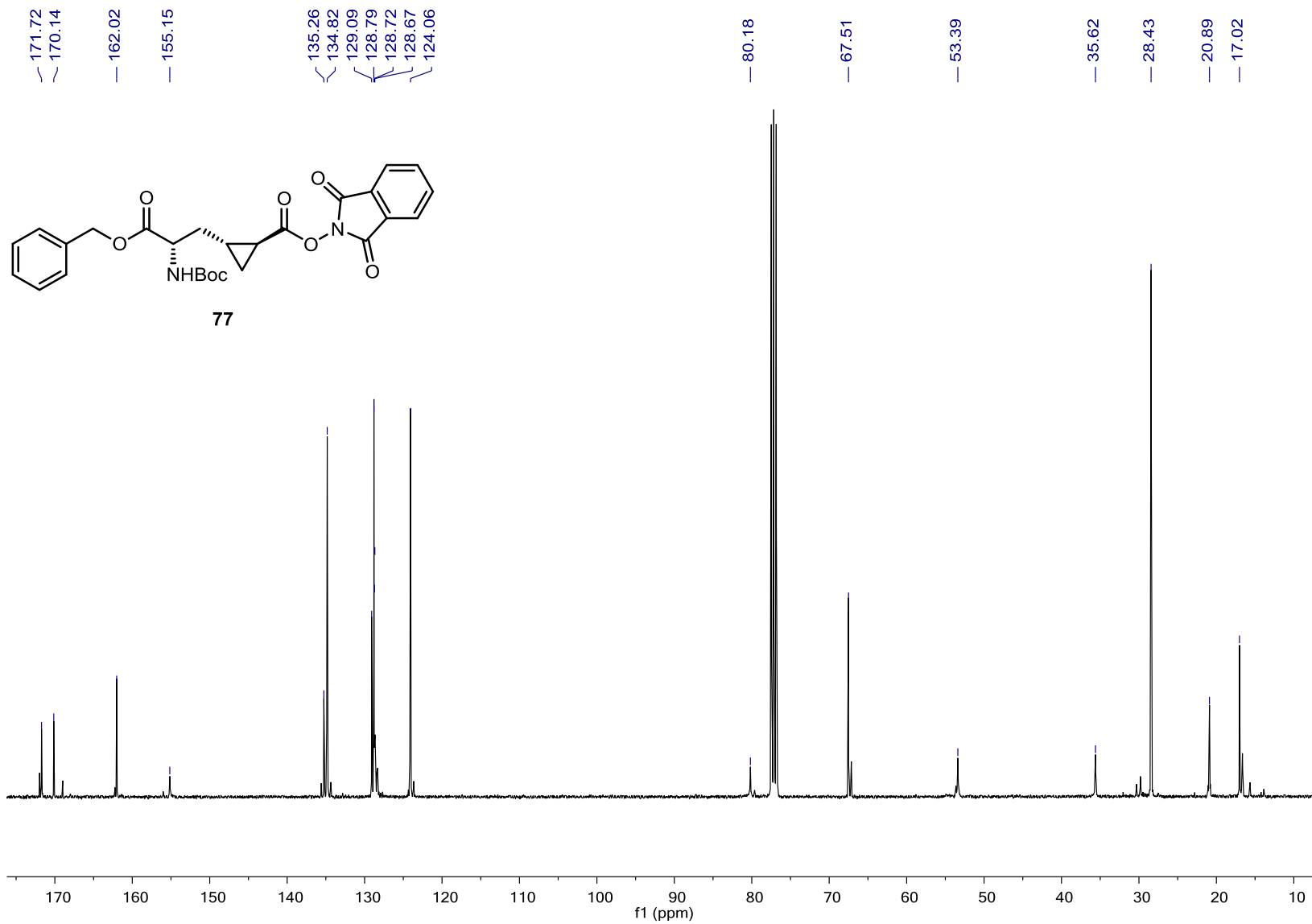


77

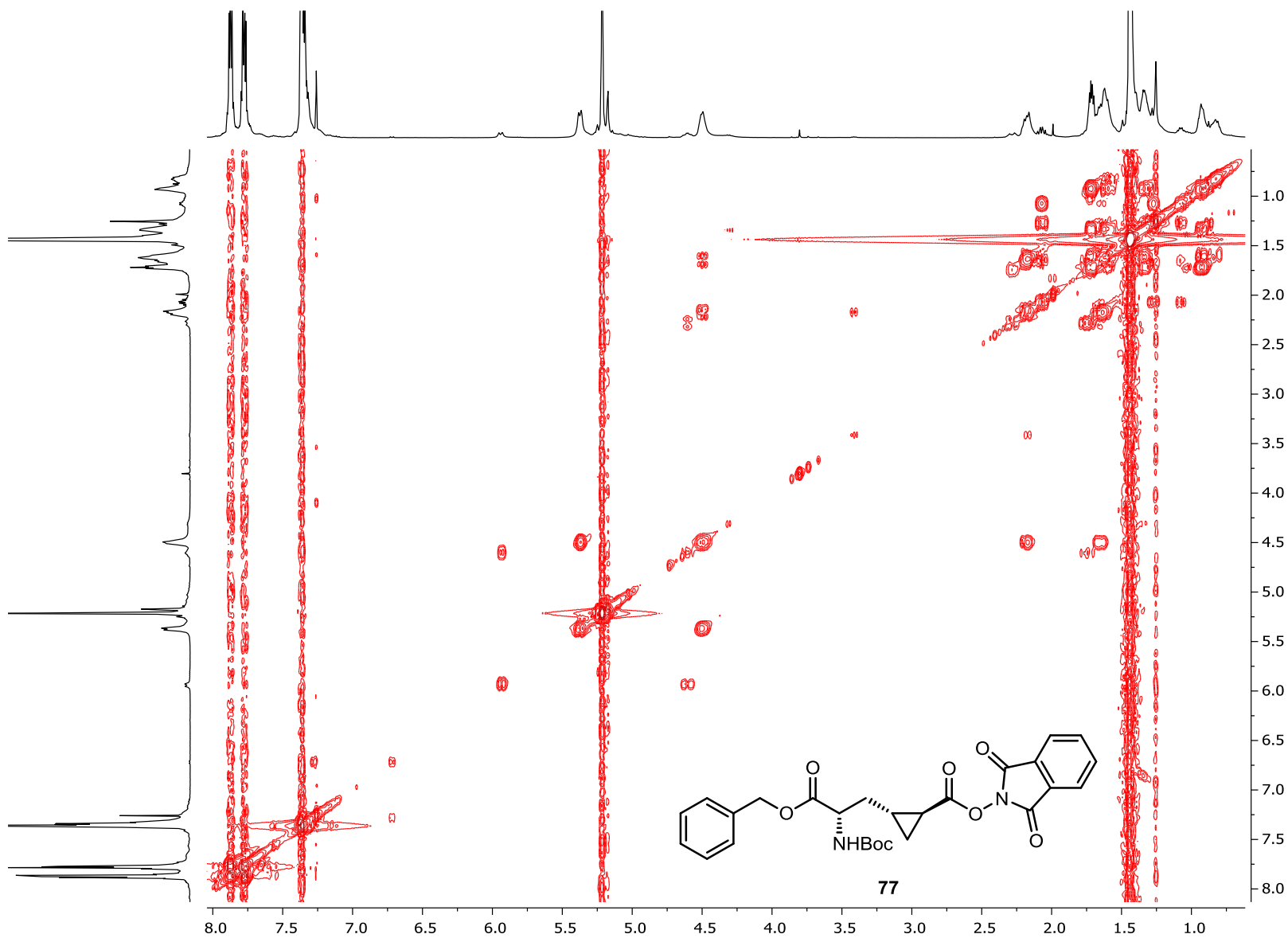


S391

^{13}C NMR (101 MHz, CDCl_3) for compound **77**

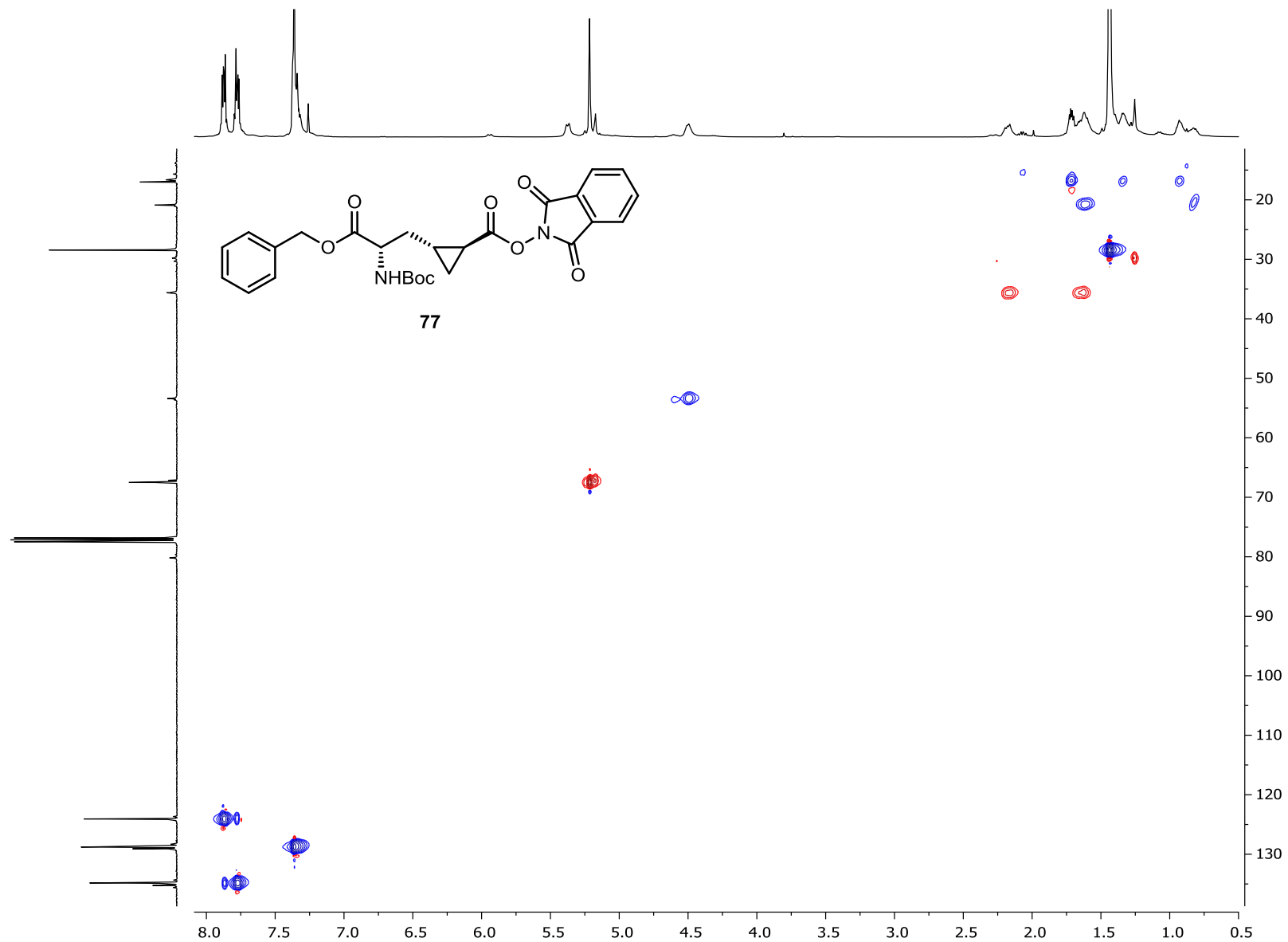


COSY NMR (400 MHz, CDCl₃) for compound 77



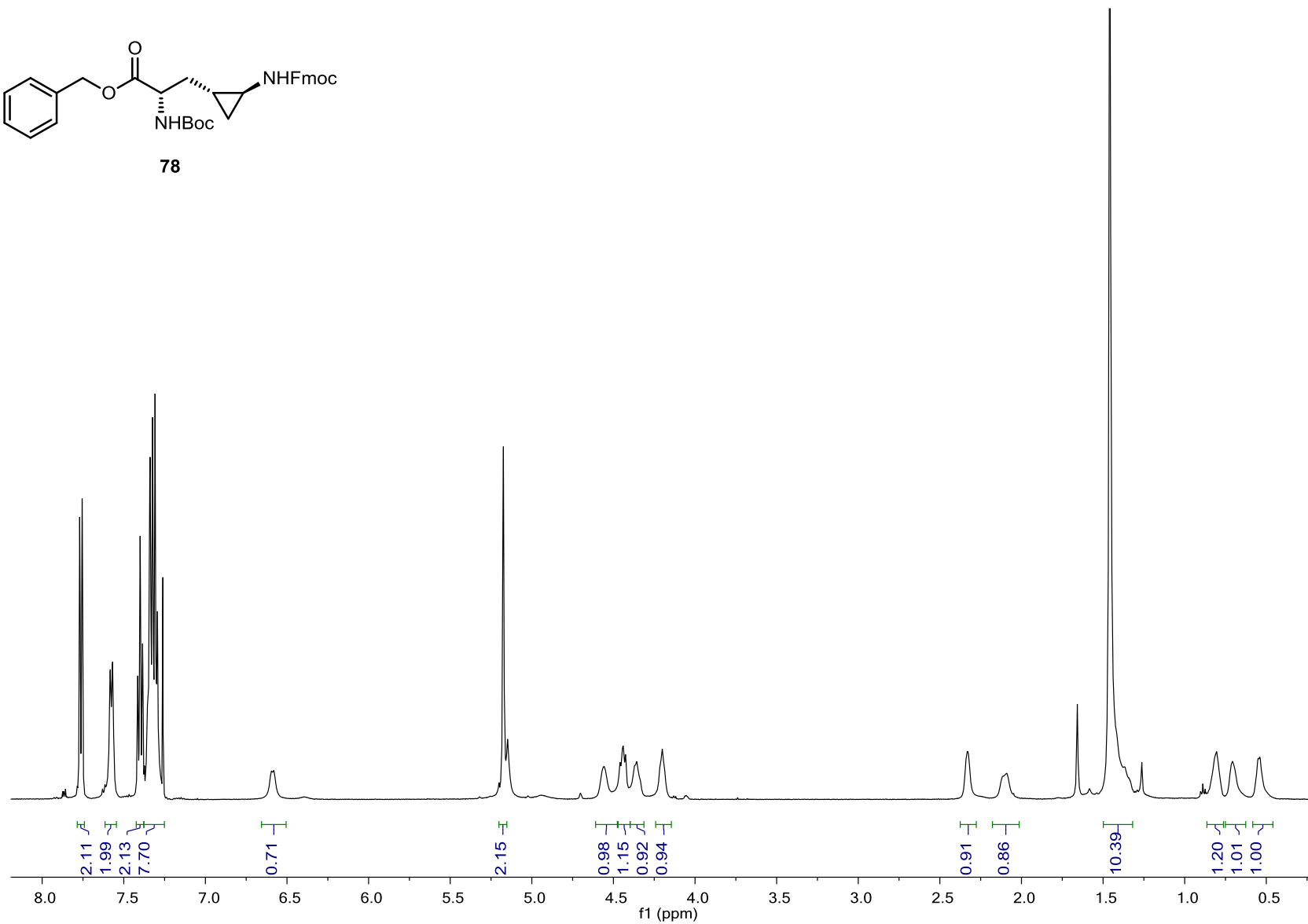
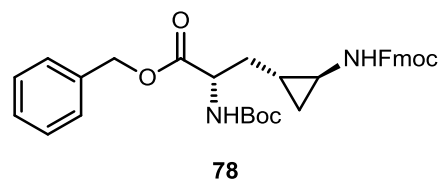
S393

HSQC NMR (400 MHz, CDCl₃) for compound **77**



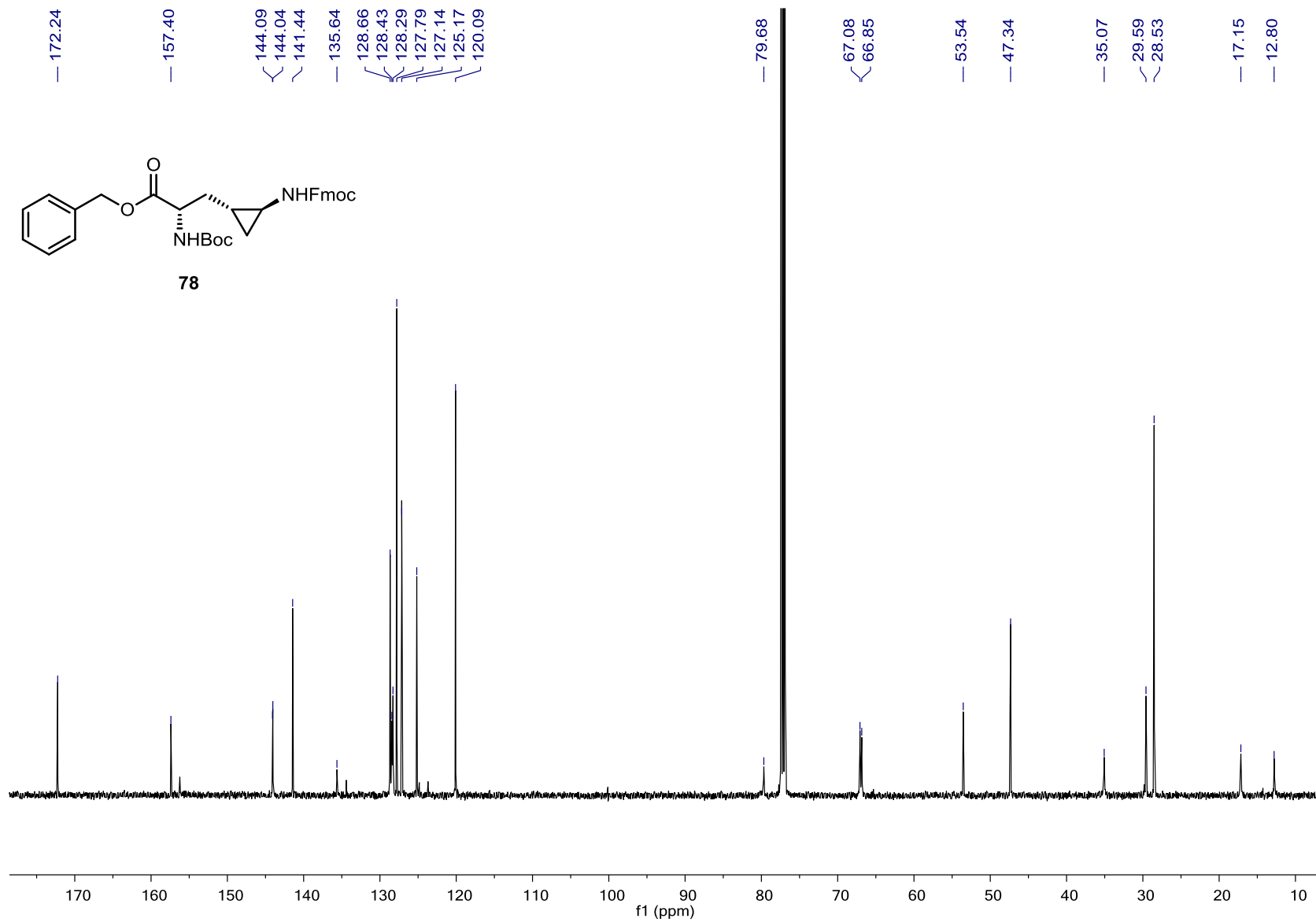
S394

^1H NMR (500 MHz, CDCl_3) for compound **78**

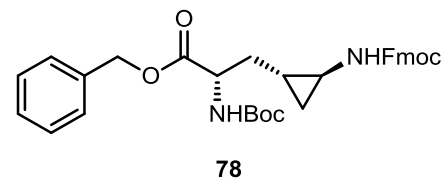
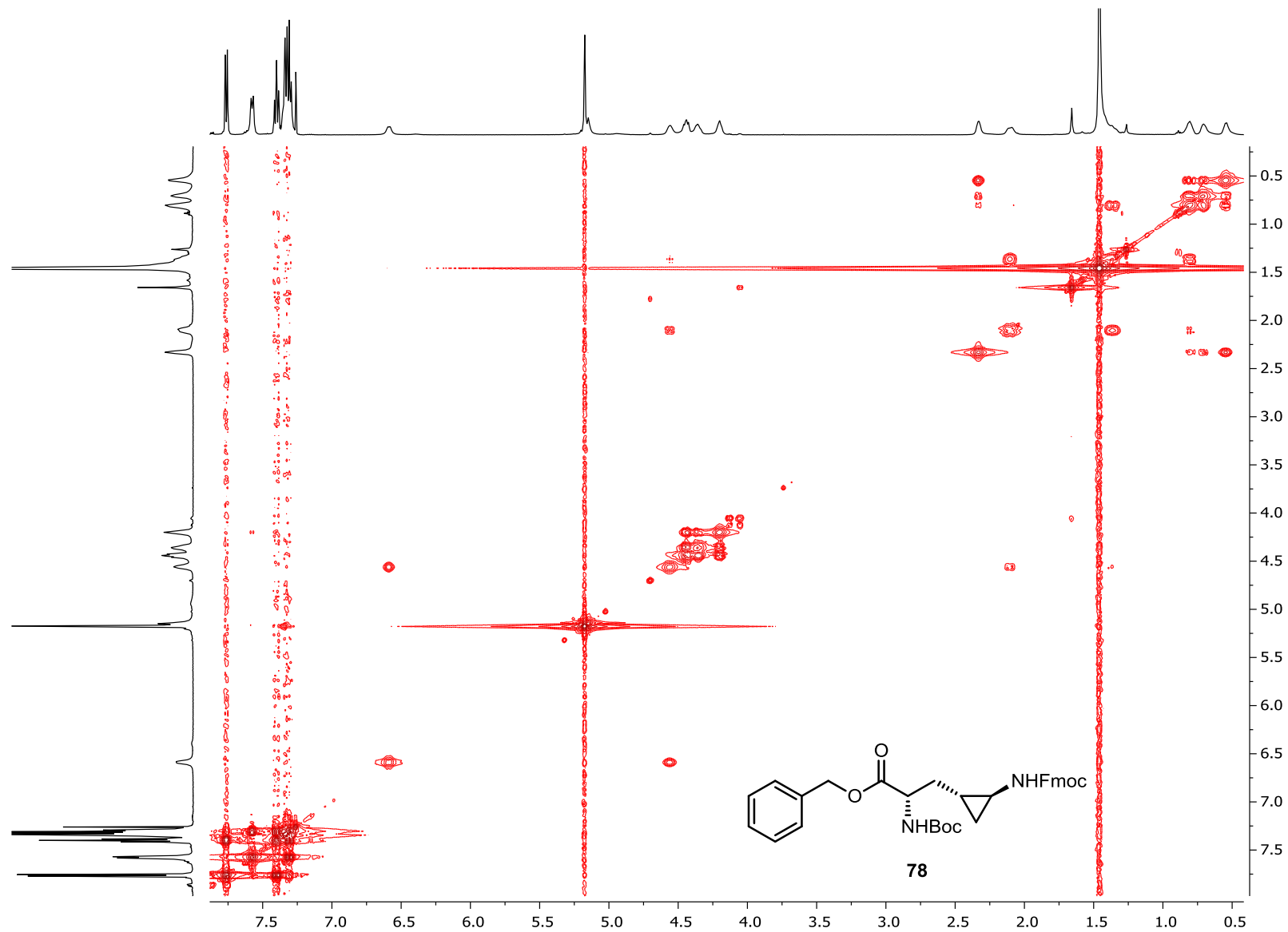


S395

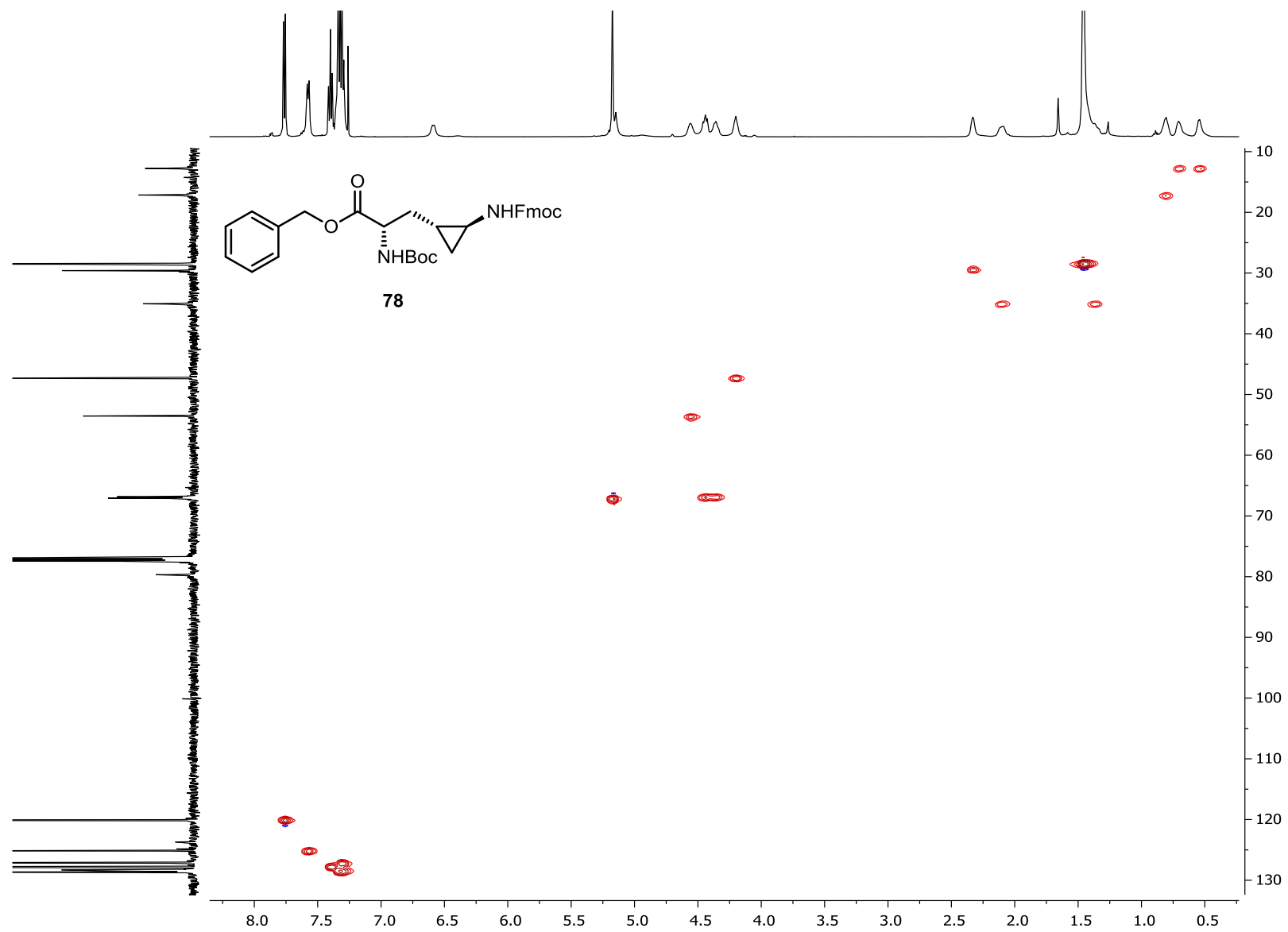
^{13}C NMR (126 MHz, CDCl_3) for compound **78**



COSY NMR (500 MHz, CDCl₃) for compound 78

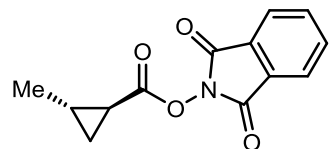


HSQC NMR (500 MHz, CDCl₃) for compound **78**

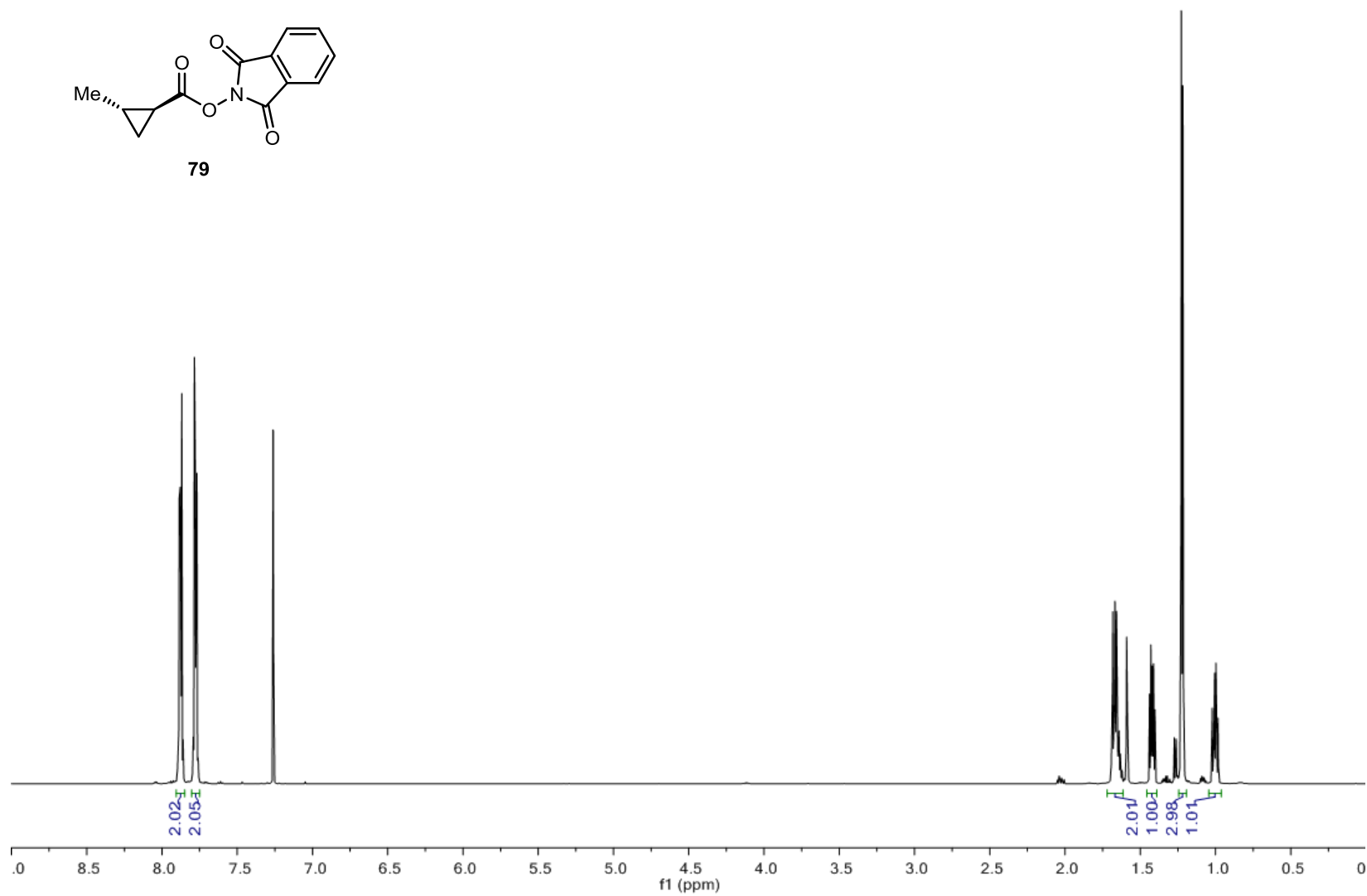


S398

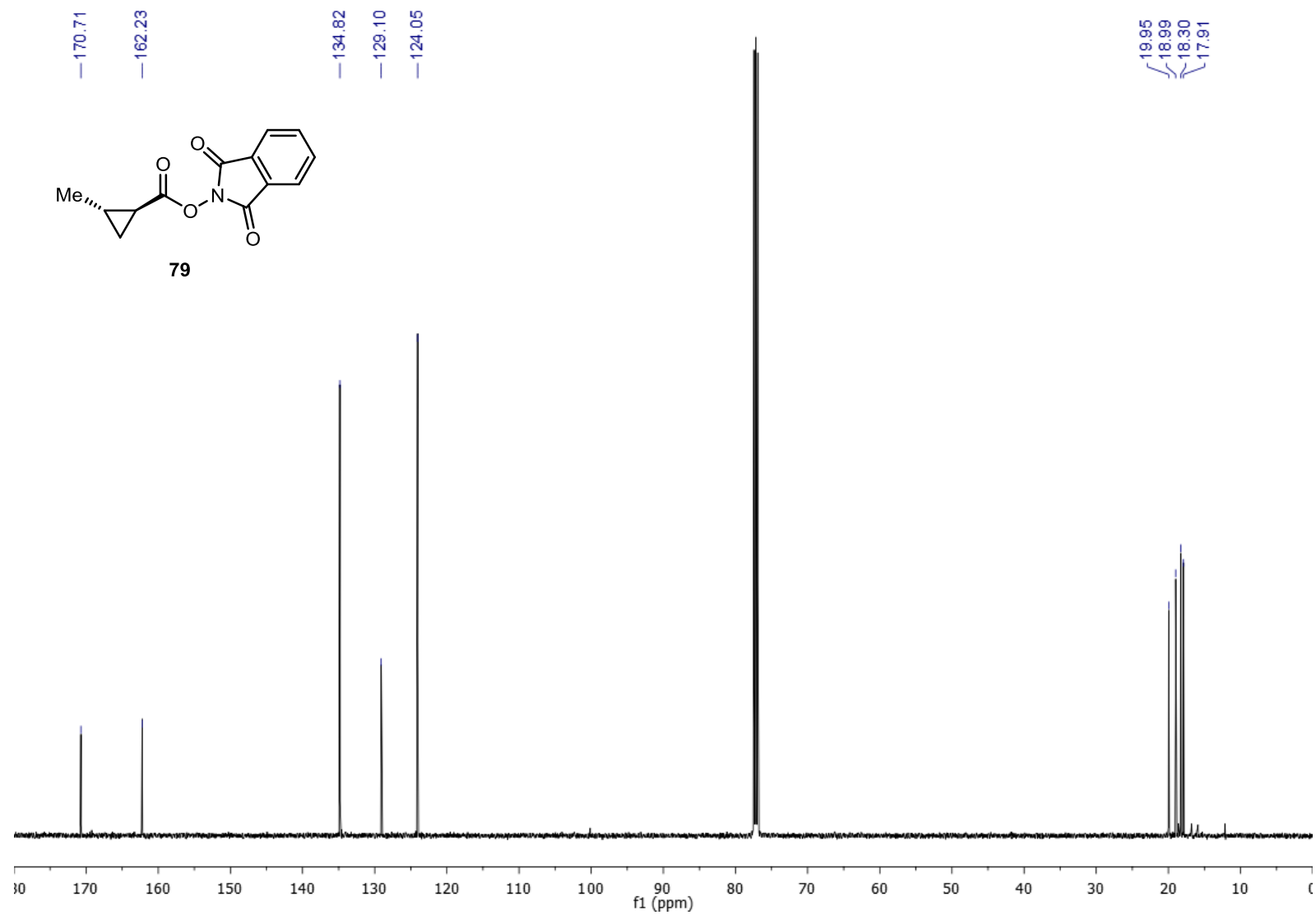
^1H NMR (500 MHz, CDCl_3) for compound **79**



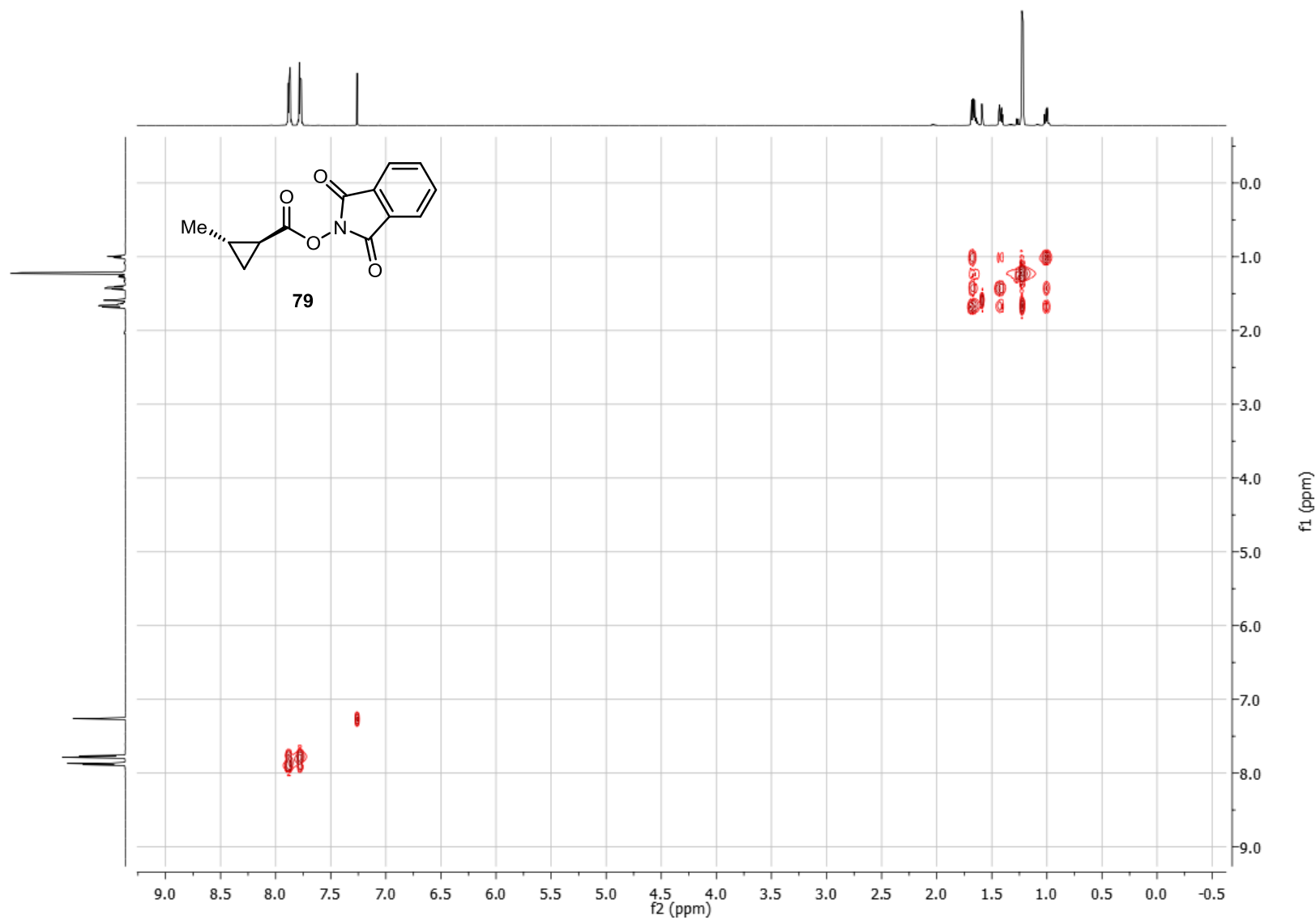
79



^{13}C NMR (126 MHz, CDCl_3) for compound **79**

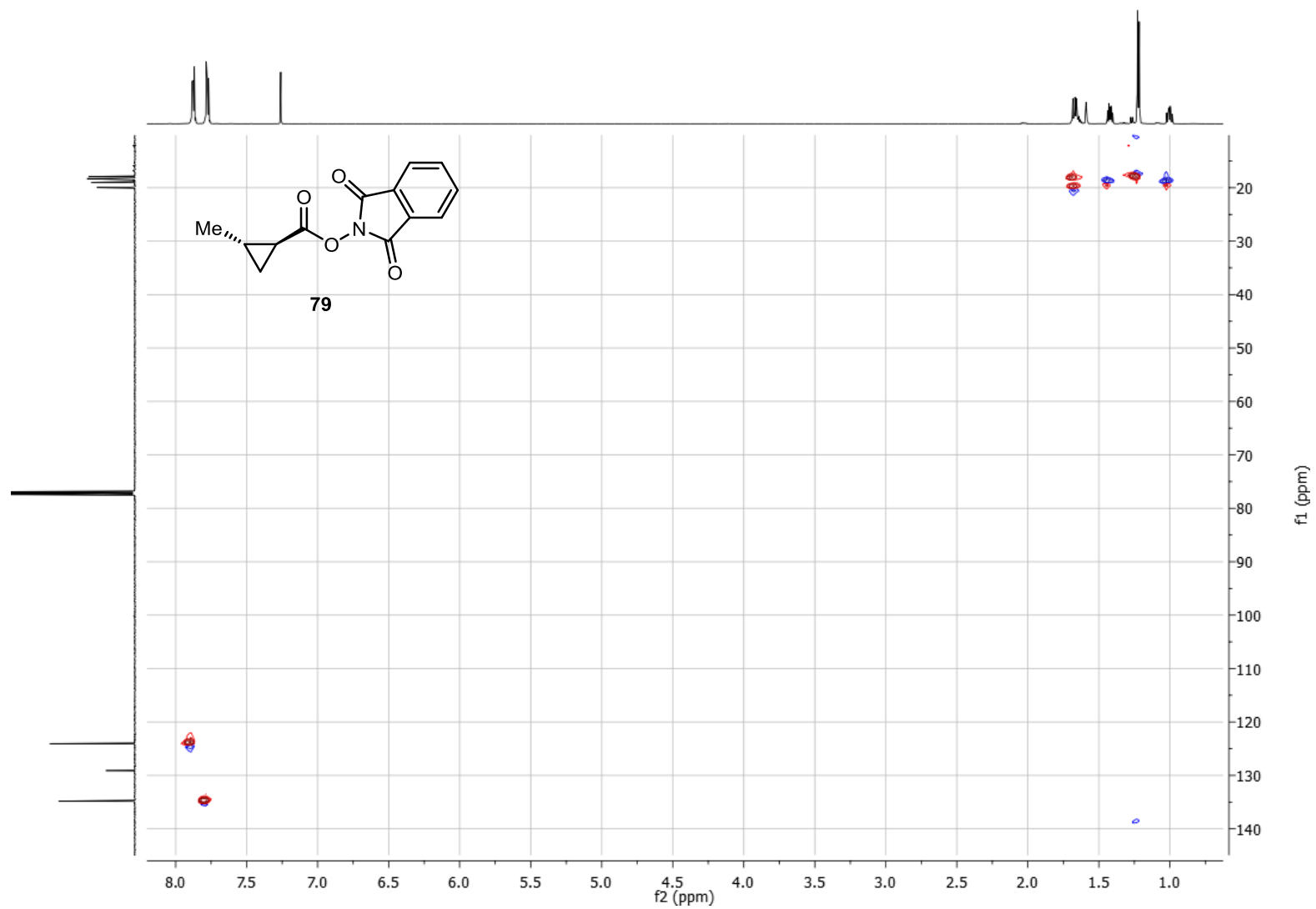


COSY NMR (500 MHz, CDCl₃) for compound 79

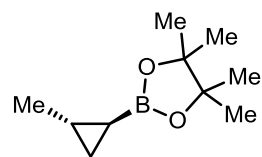


S401

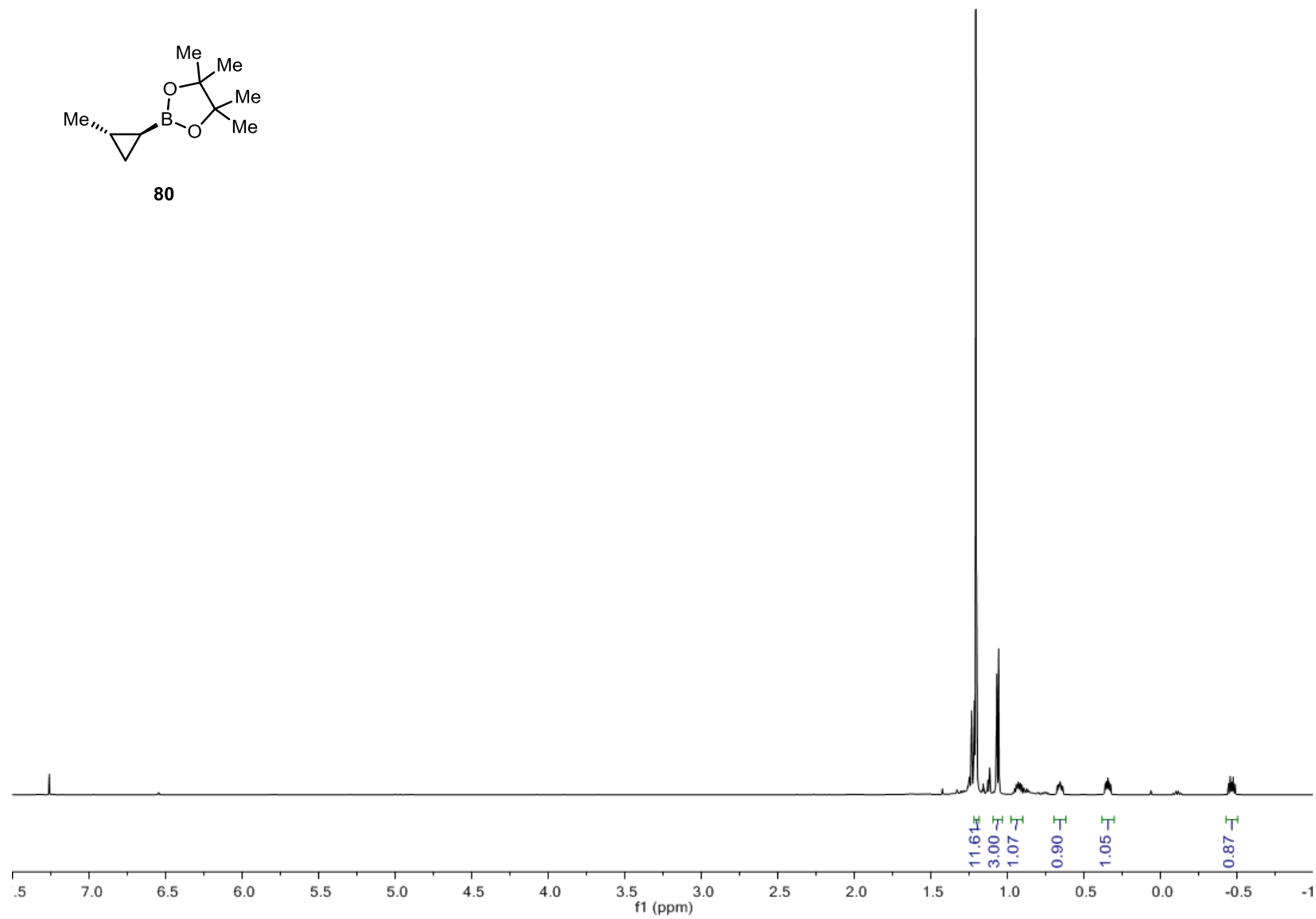
HSQC NMR (500 MHz, CDCl₃) for compound **79**



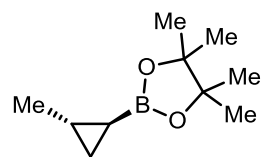
^1H NMR (500 MHz, CDCl_3) for compound **80**



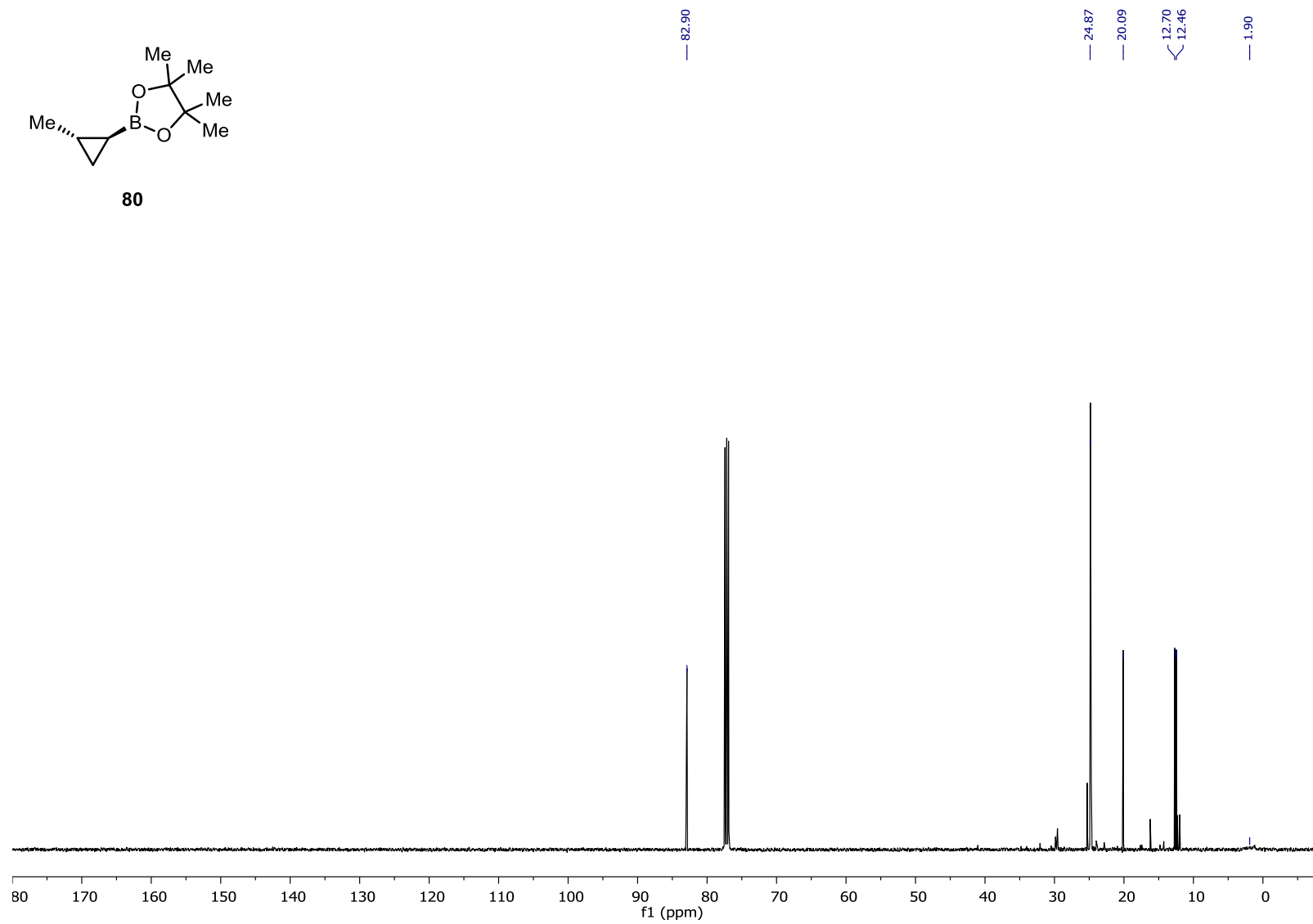
80



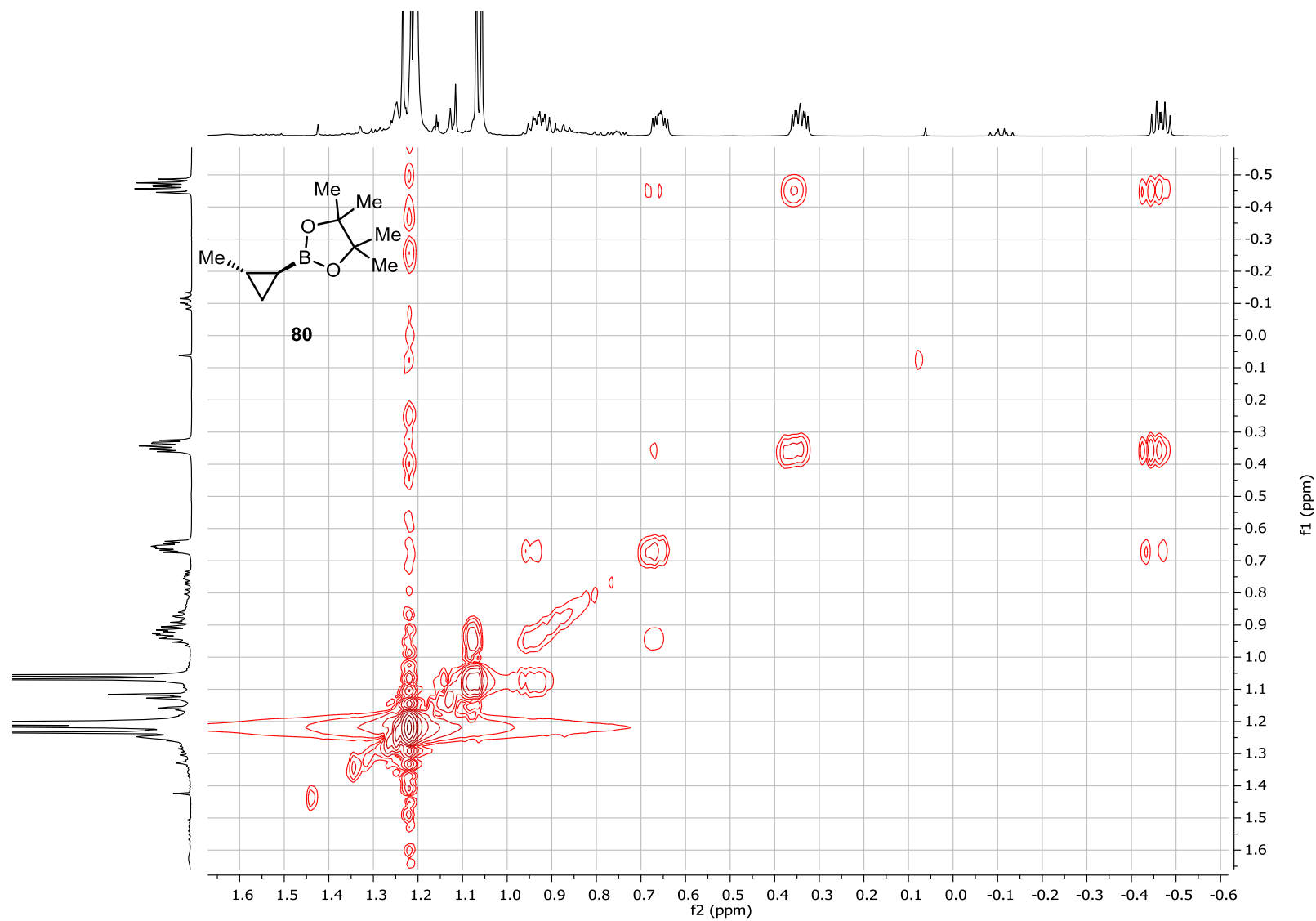
^{13}C NMR (126 MHz, CDCl_3) for compound **80**



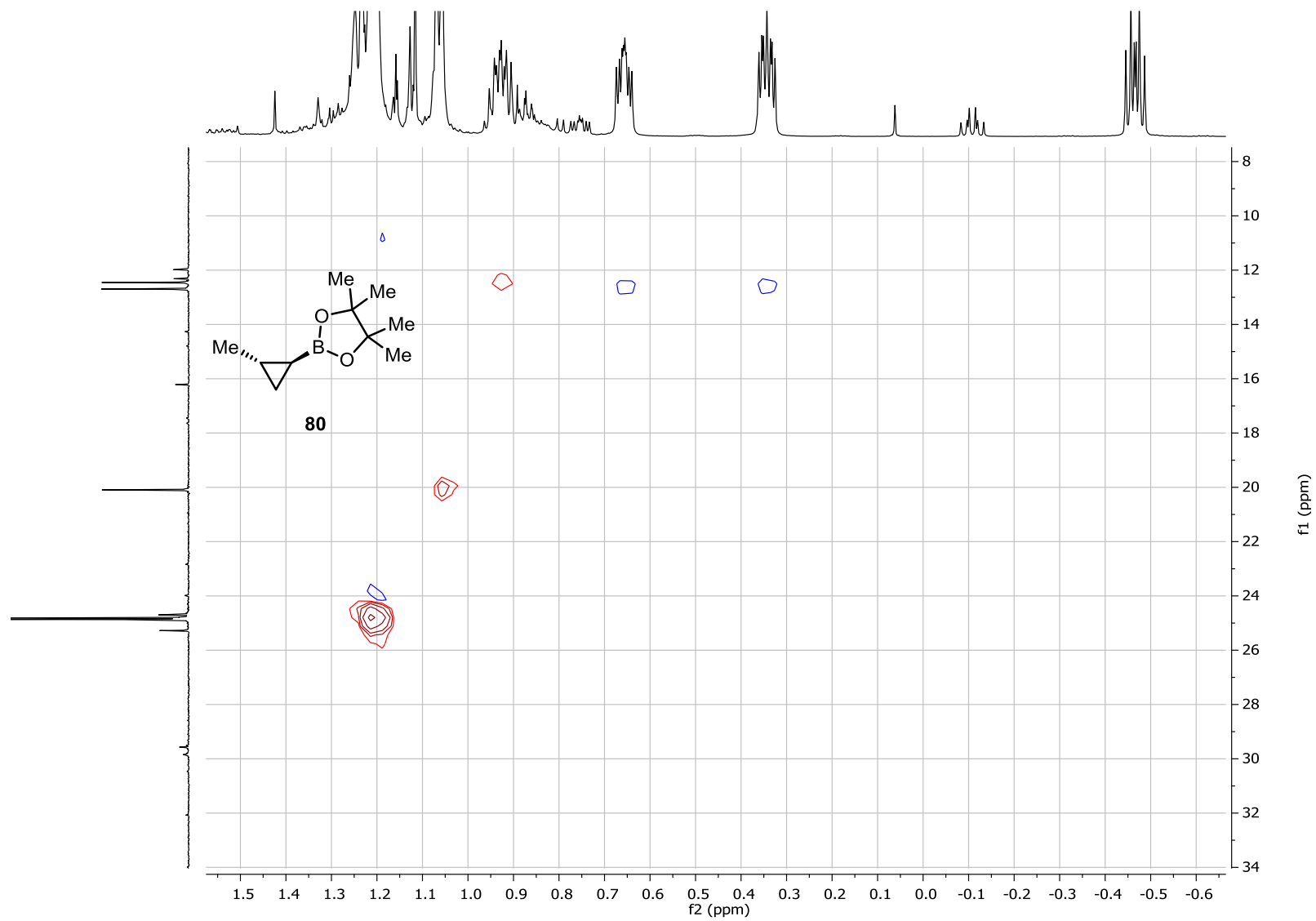
80



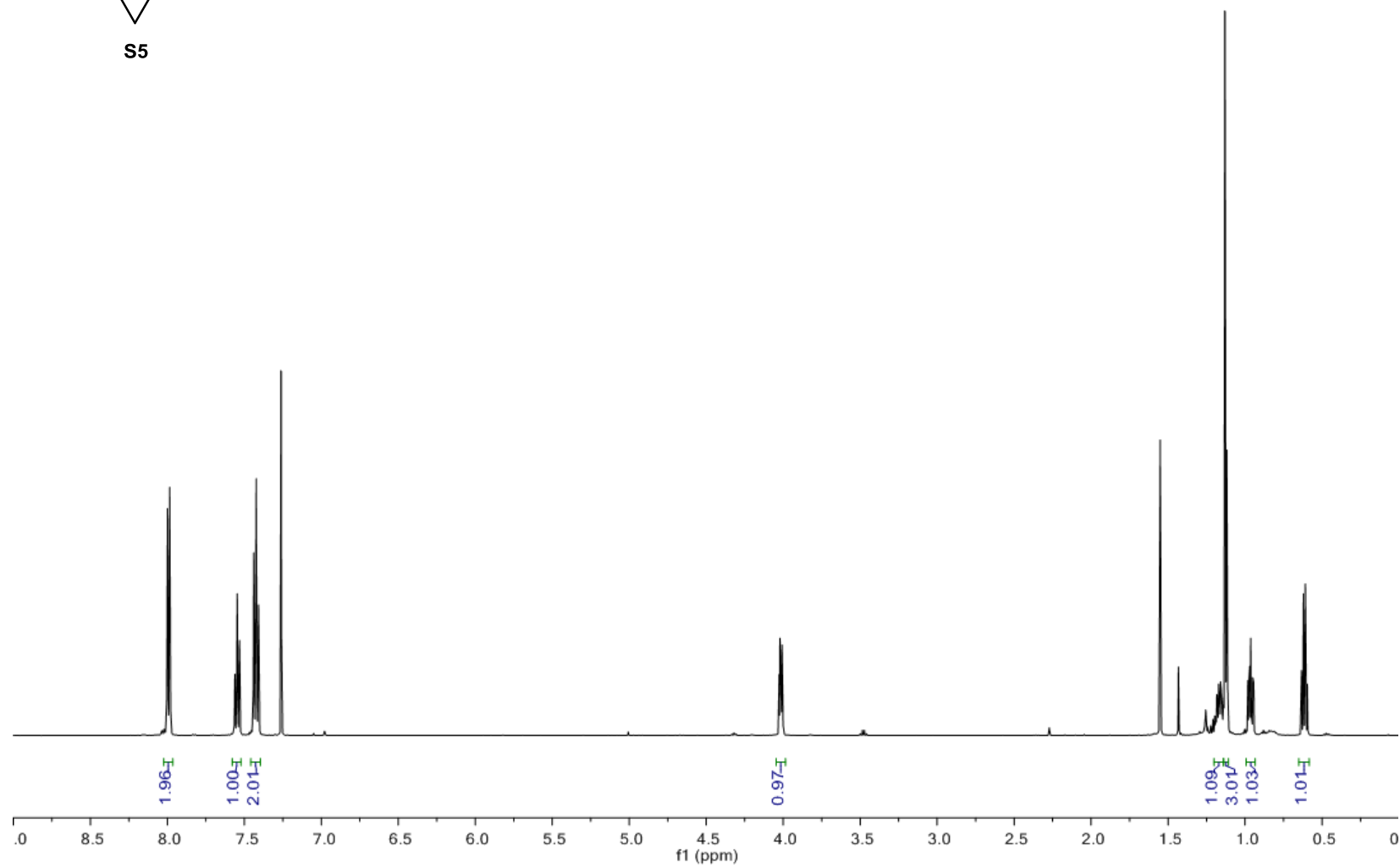
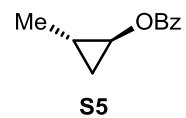
COSY NMR (500 MHz, CDCl_3) for compound **80**



HSQC NMR (500 MHz, CDCl₃) for compound **80**

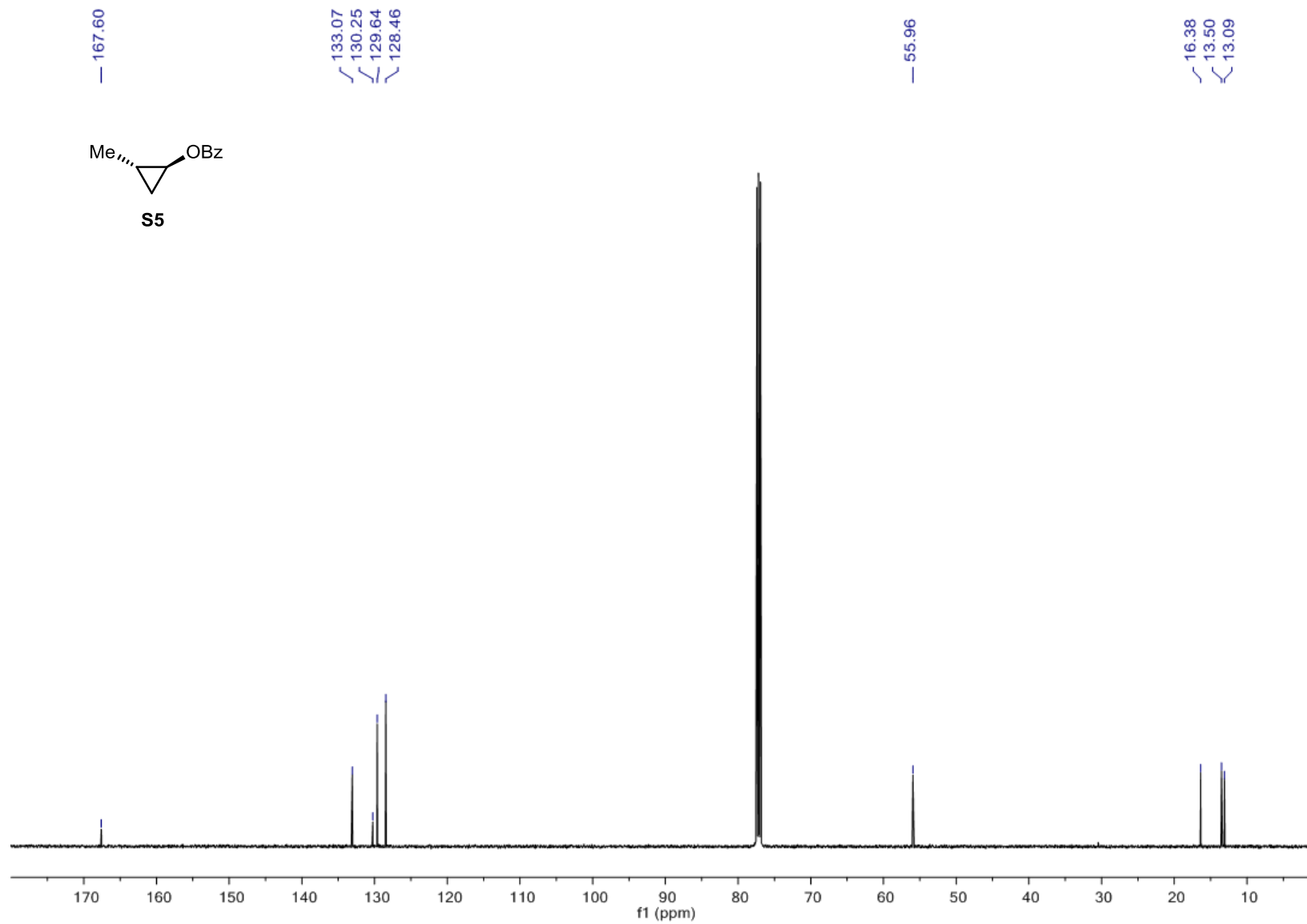


^1H NMR (500 MHz, CDCl_3) for compound **S5**



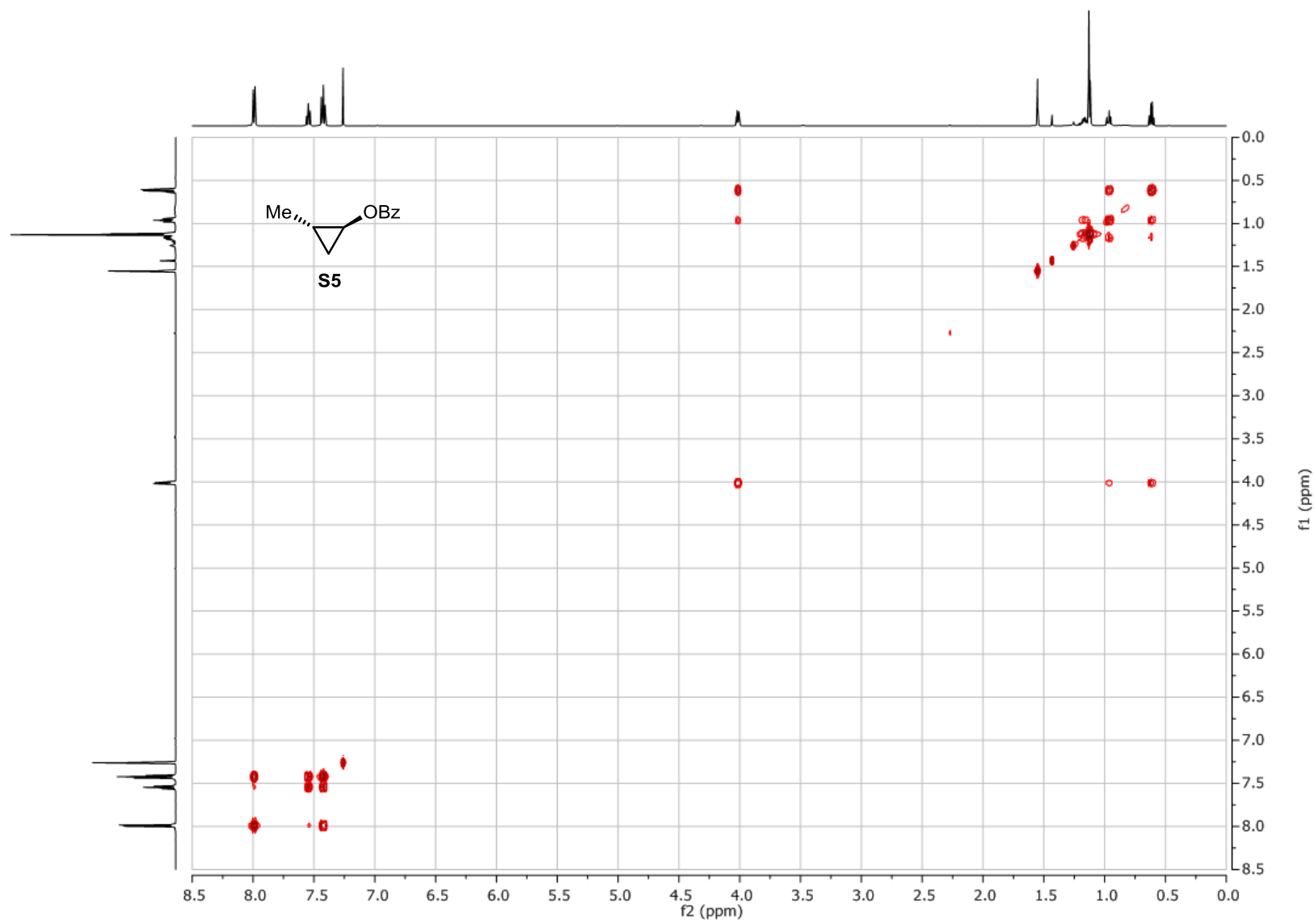
S407

^{13}C NMR (126 MHz, CDCl_3) for compound **S5**



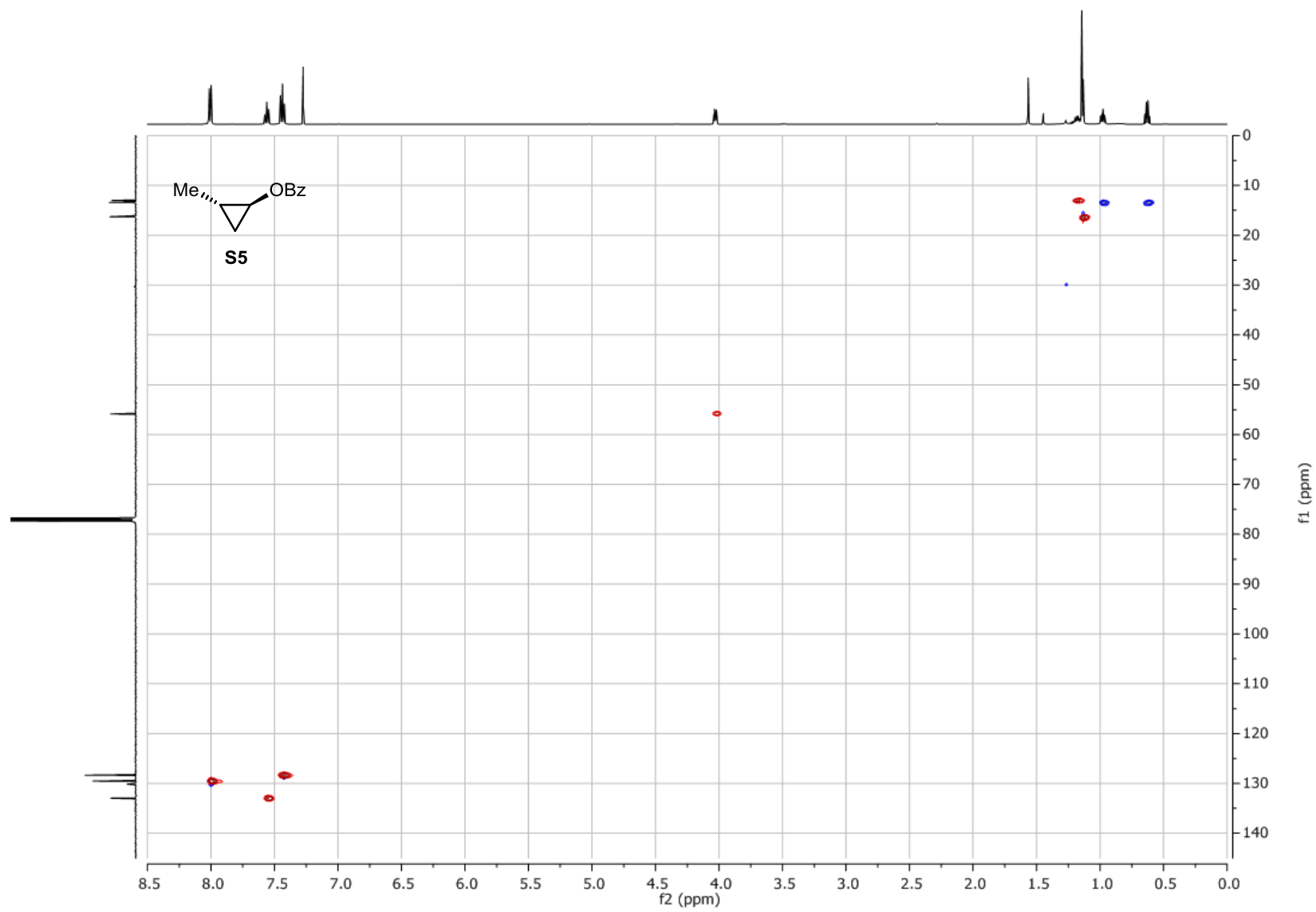
S408

COSY NMR (500 MHz, CDCl_3) for compound **S5**



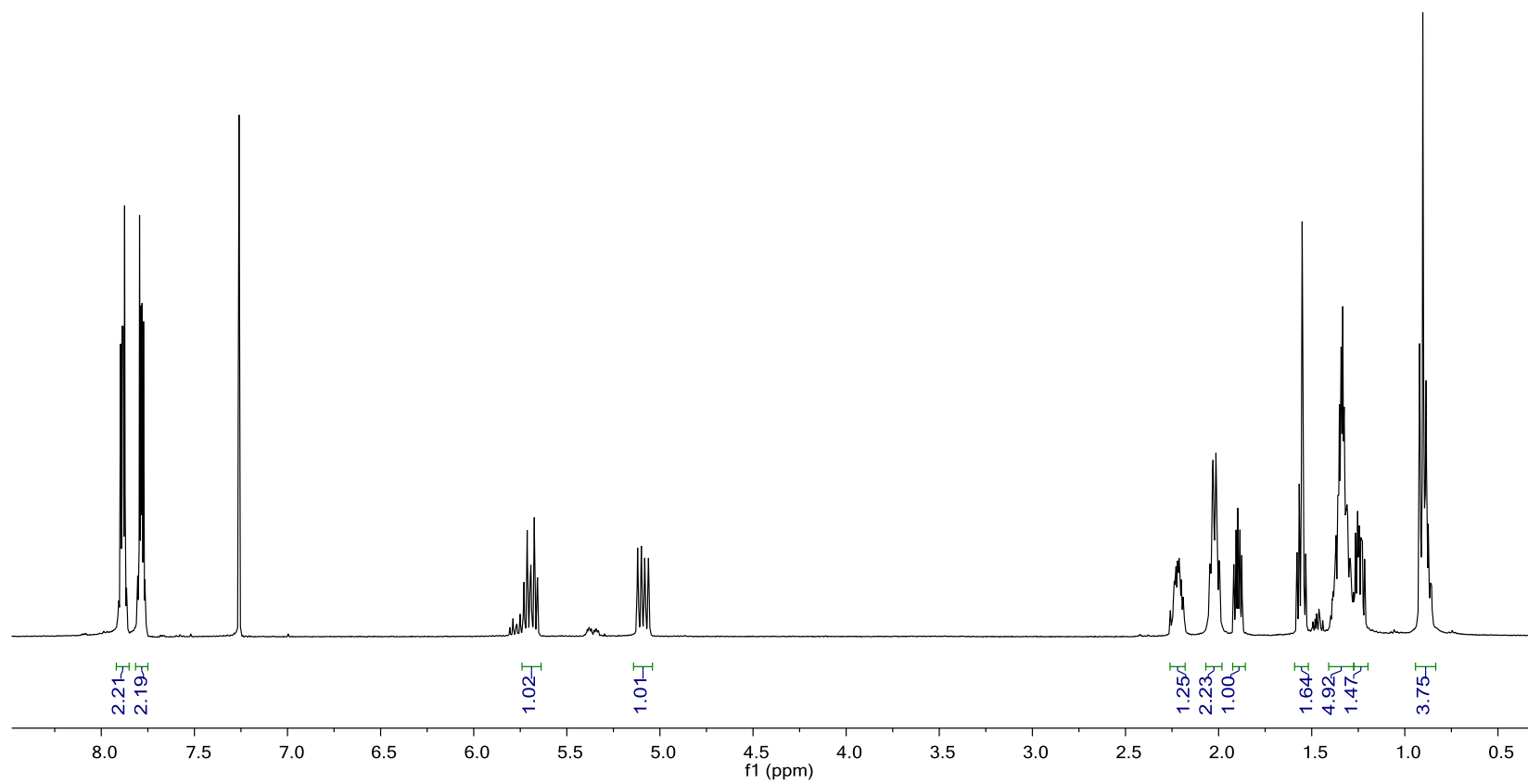
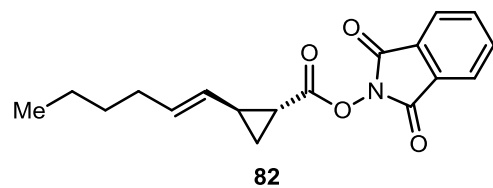
S409

HSQC NMR (500 MHz, CDCl₃) for compound S5



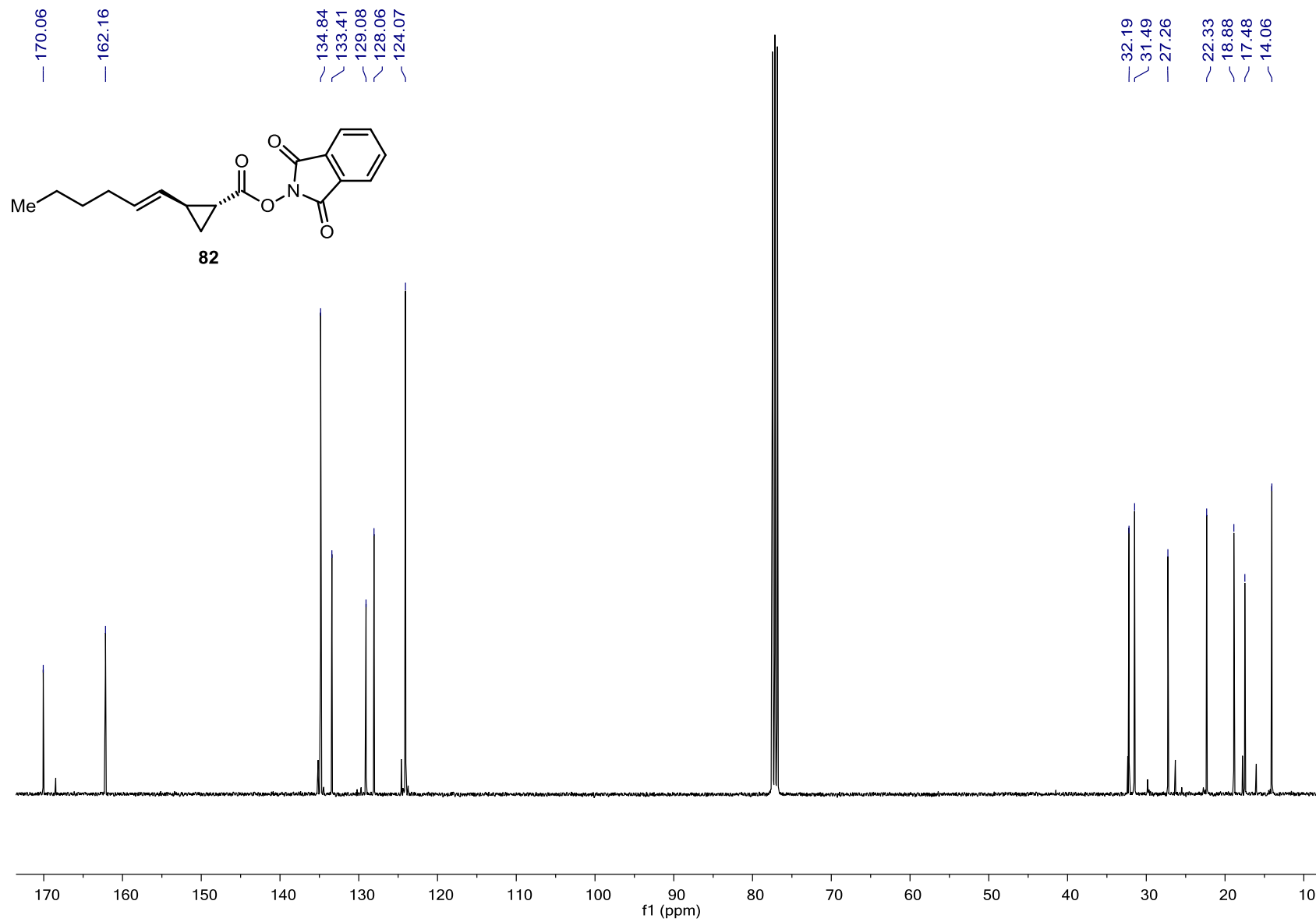
S410

^1H NMR (400 MHz, CDCl_3) for compound **82**



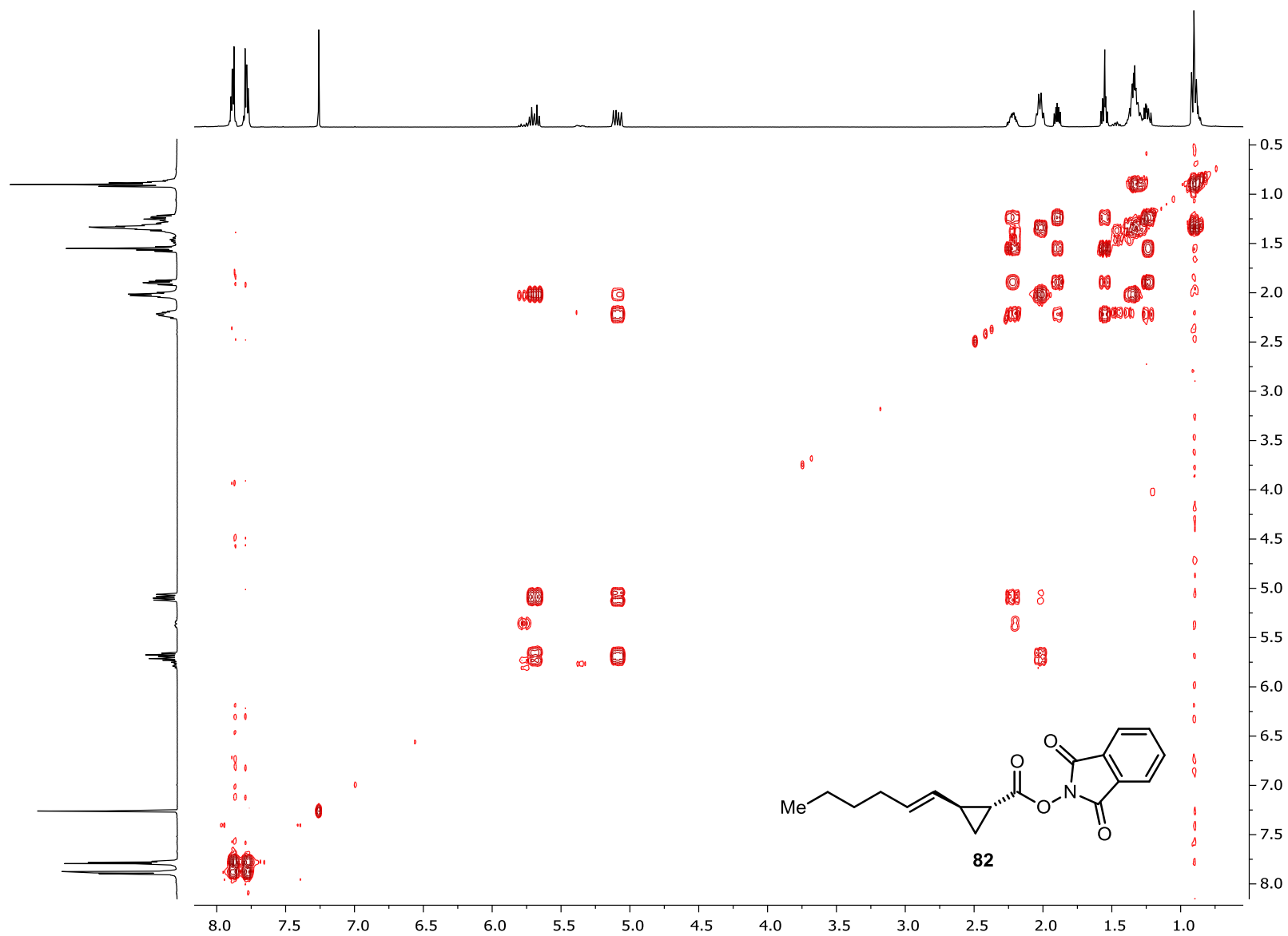
S411

^{13}C NMR (101 MHz, CDCl_3) for compound **82**



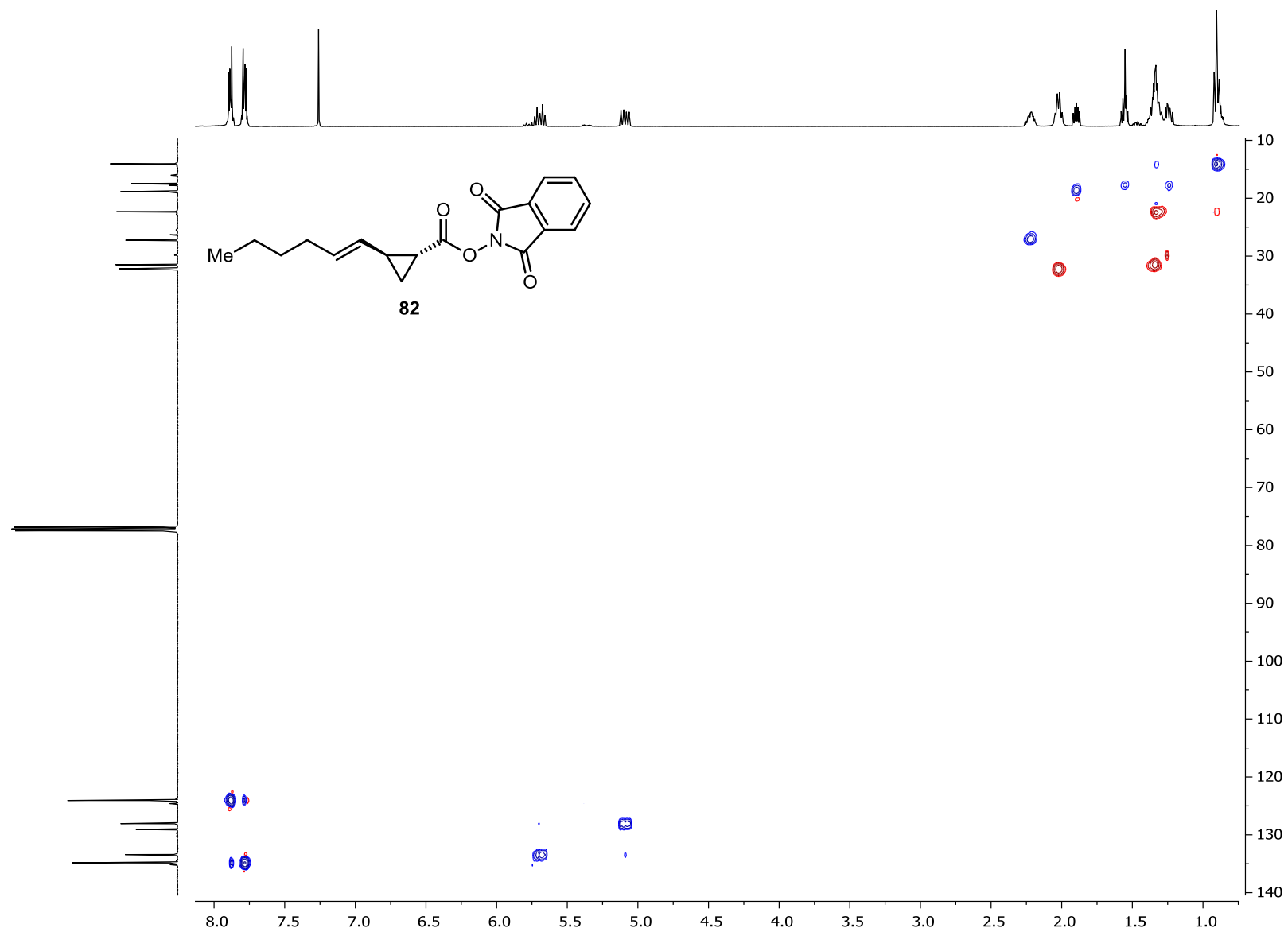
S412

COSY NMR (400 MHz, $CDCl_3$) for compound **82**



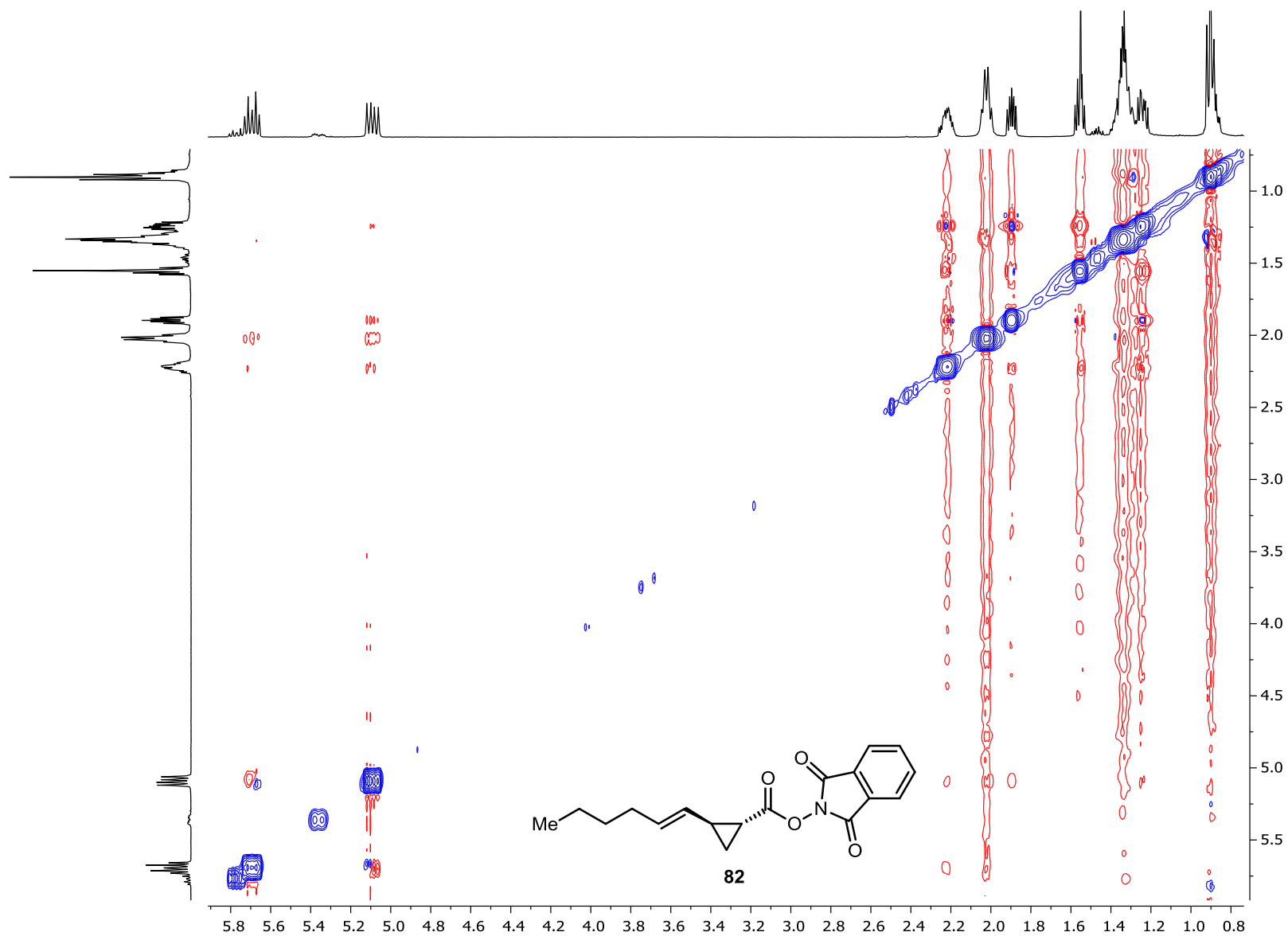
S413

HSQC NMR (400 MHz, CDCl₃) for compound **82**

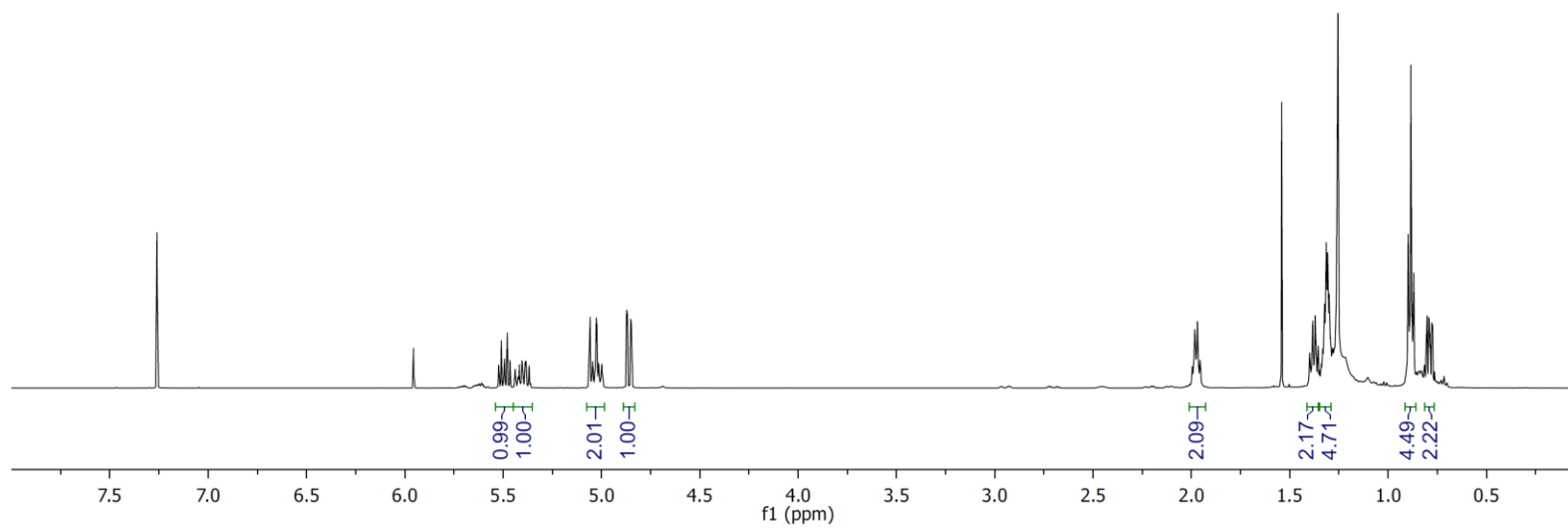
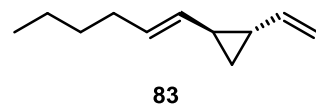


S414

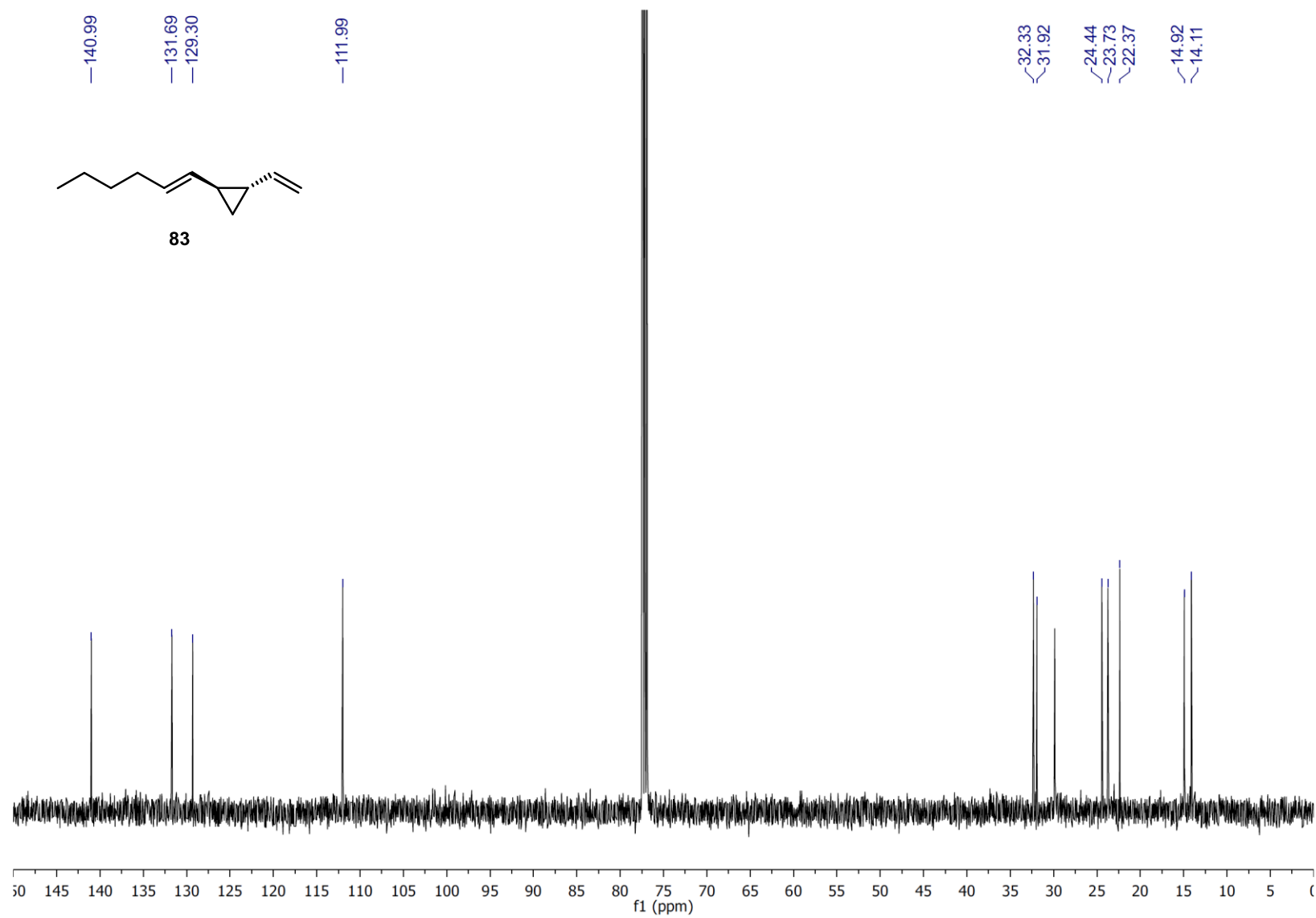
NOESY NMR (400 MHz, CDCl₃) for compound **82**



^1H NMR (500 MHz, CDCl_3) for compound **83**



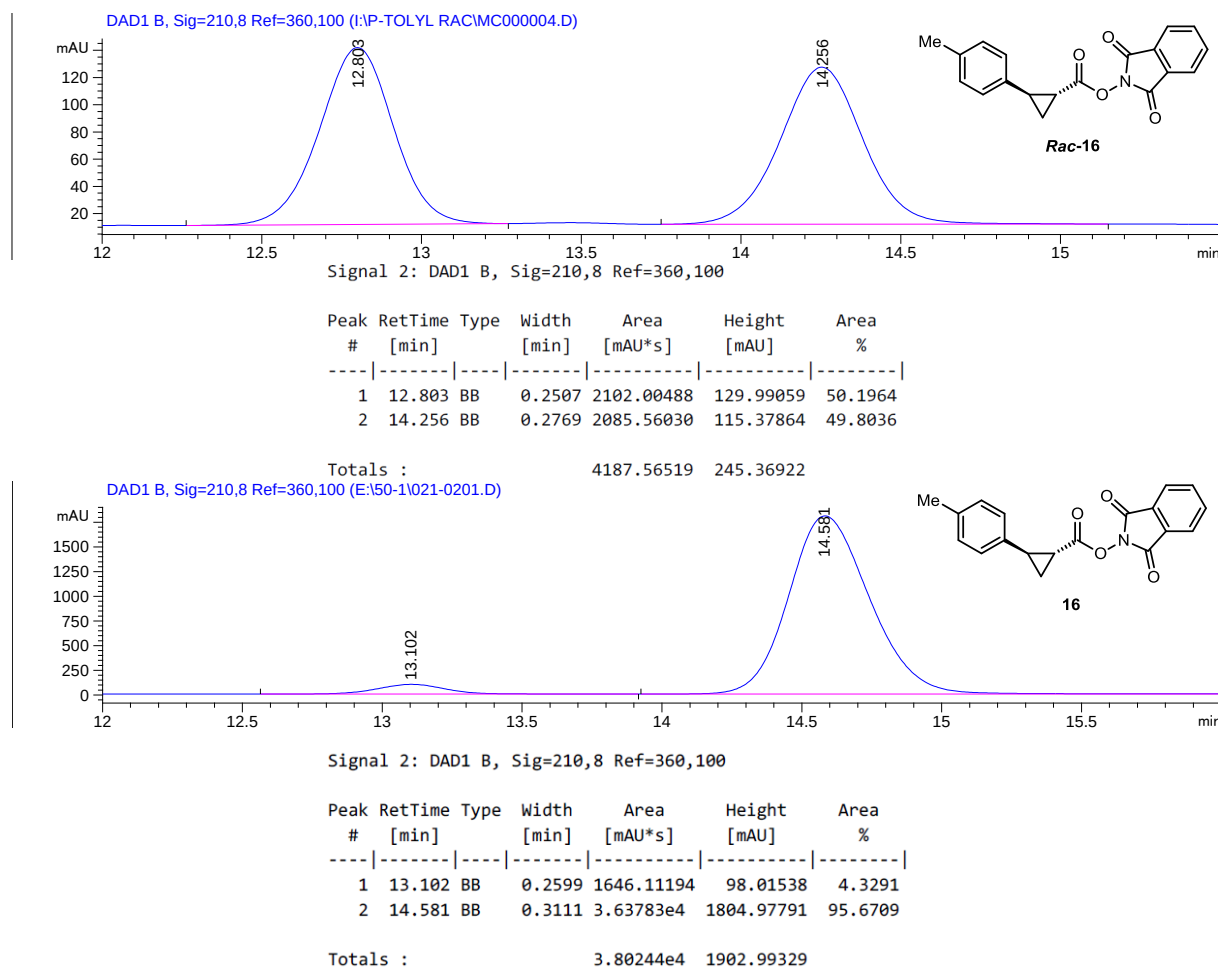
^{13}C NMR (126 MHz, CDCl_3) for compound **83**



S417

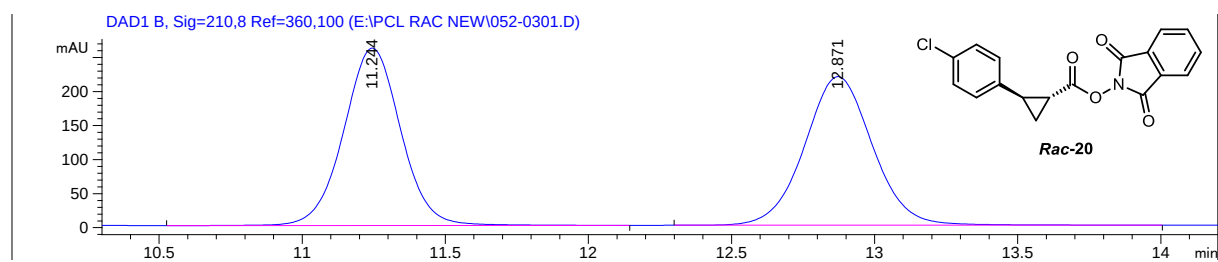
5. Chromatography data of enantioenriched compounds

HPLC traces for compound **16**:



Analysis Conditions: Daicel Chiralpak-IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

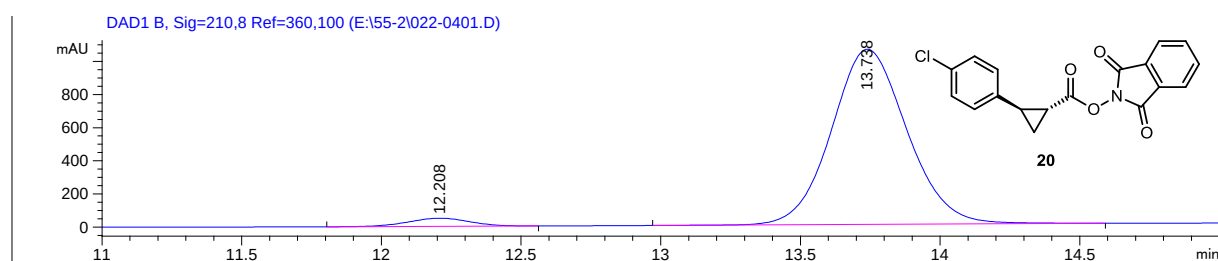
HPLC traces for compound **20**:



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.244	BB	0.2140	3621.10376	260.81006	50.0800
2	12.871	BB	0.2549	3609.53052	218.27570	49.9200

Totals : 7230.63428 479.08575



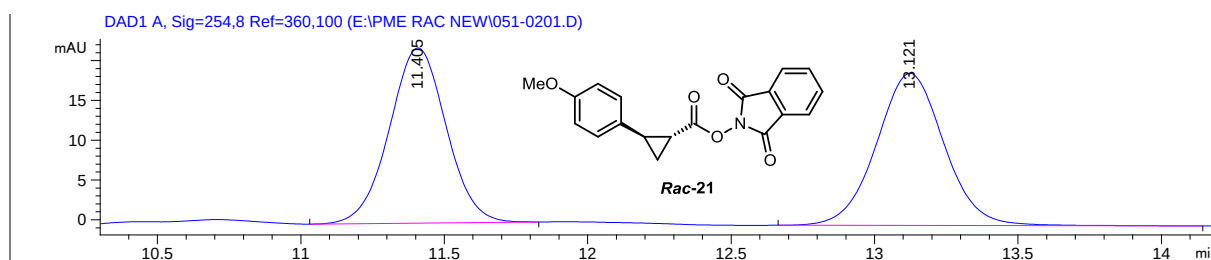
Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.208	BB	0.2397	757.78711	49.19143	3.6703
2	13.738	BB	0.2893	1.98884e4	1058.25220	96.3297

Totals : 2.06462e4 1107.44362

Analysis Conditions: Daicel Chiralpak-IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

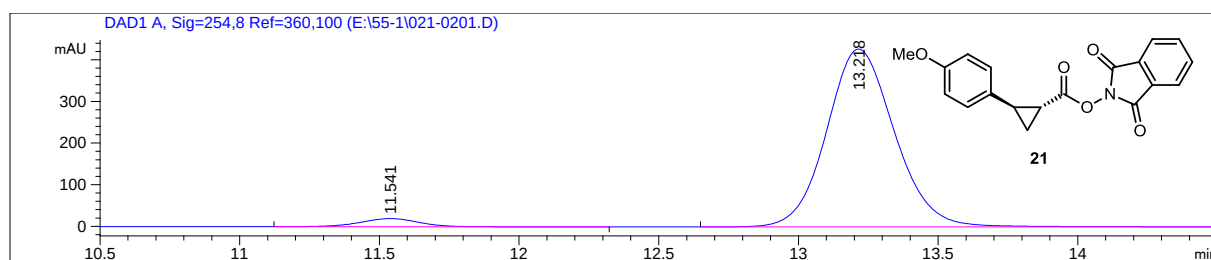
HPLC traces for compound **21**:



Signal 1: DAD1 A, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.405	BB	0.2128	303.35641	22.01353	49.2291
2	13.121	BB	0.2509	312.85715	19.11605	50.7709

Totals : 616.21356 41.12958



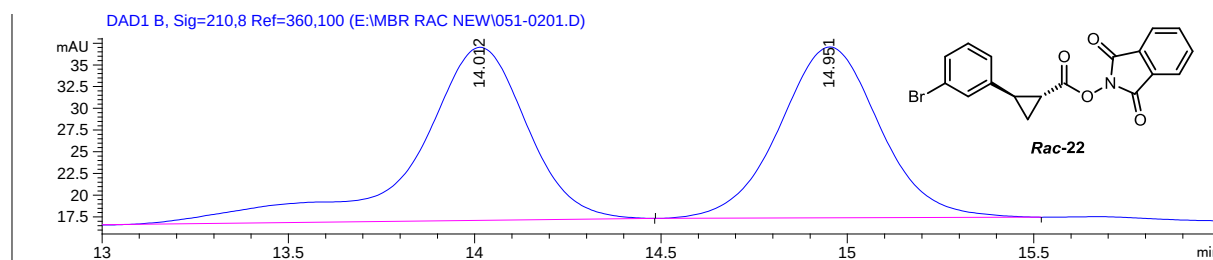
Signal 1: DAD1 A, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.541	BB	0.2252	289.32904	19.71210	3.8454
2	13.218	BB	0.2616	7234.76270	427.12933	96.1546

Totals : 7524.09174 446.84143

Analysis Conditions: Daicel Chiralpak-IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 254 nm.

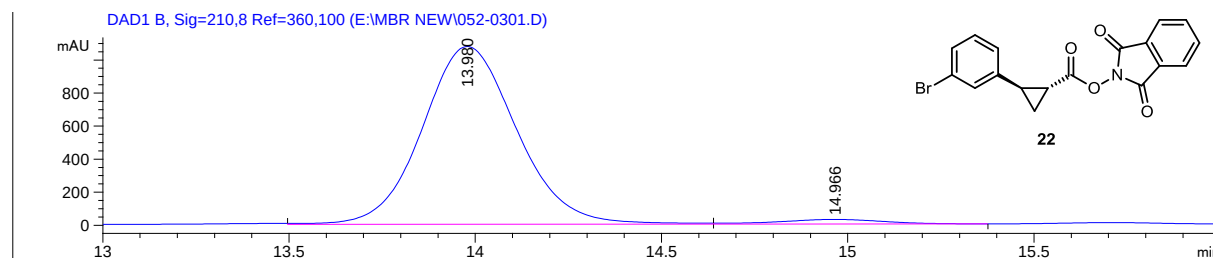
HPLC traces for compound 22:



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.012	BB	0.3086	417.93417	19.93743	53.1550
2	14.951	BB	0.2884	368.32166	19.67557	46.8450

Totals : 786.25583 39.61300



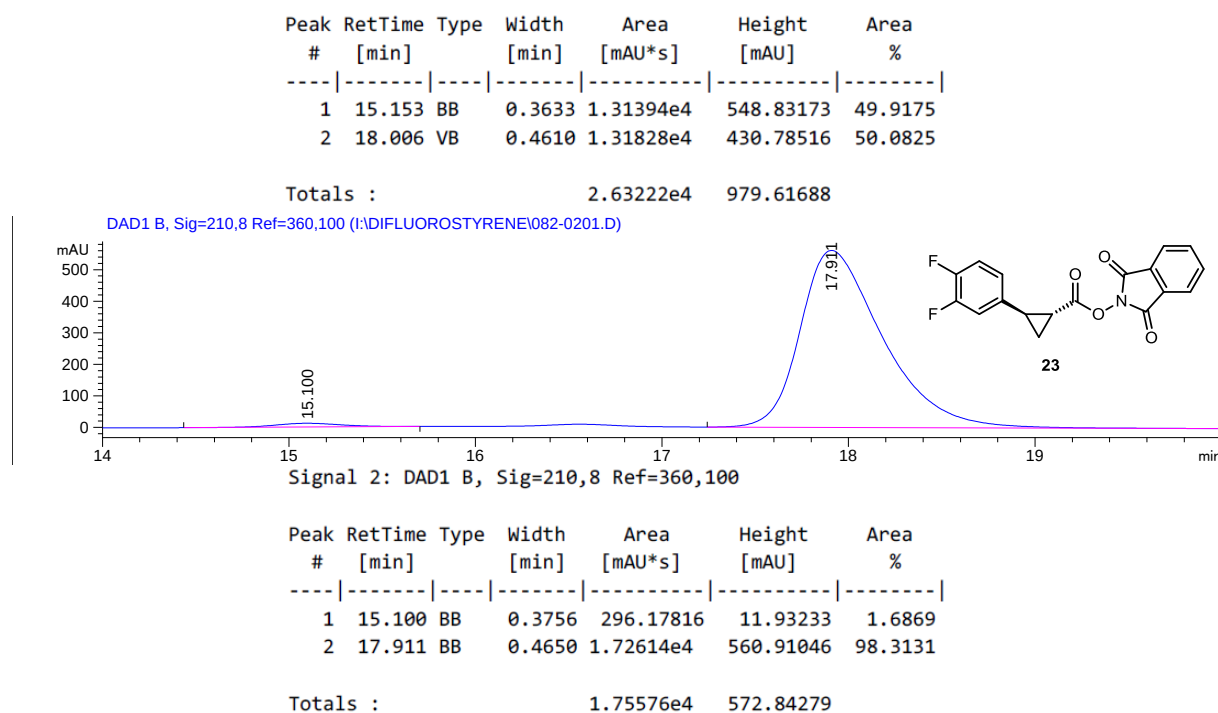
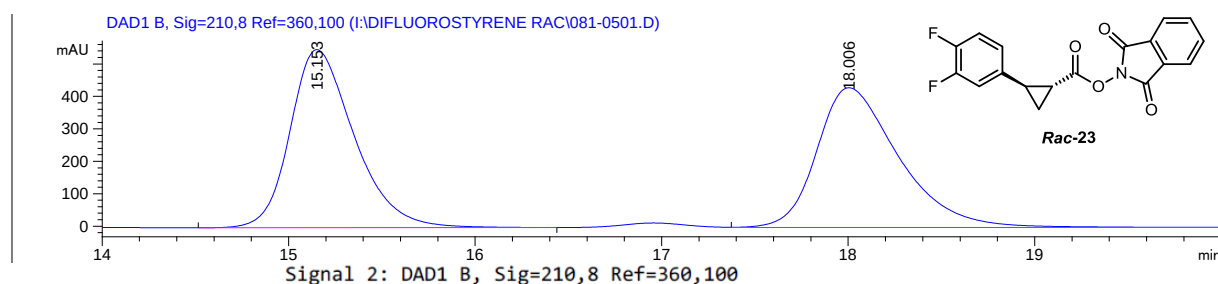
Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.980	VV	0.2721	1.90072e4	1076.15576	97.3113
2	14.966	VB	0.2886	525.16101	27.52468	2.6887

Totals : 1.95324e4 1103.68044

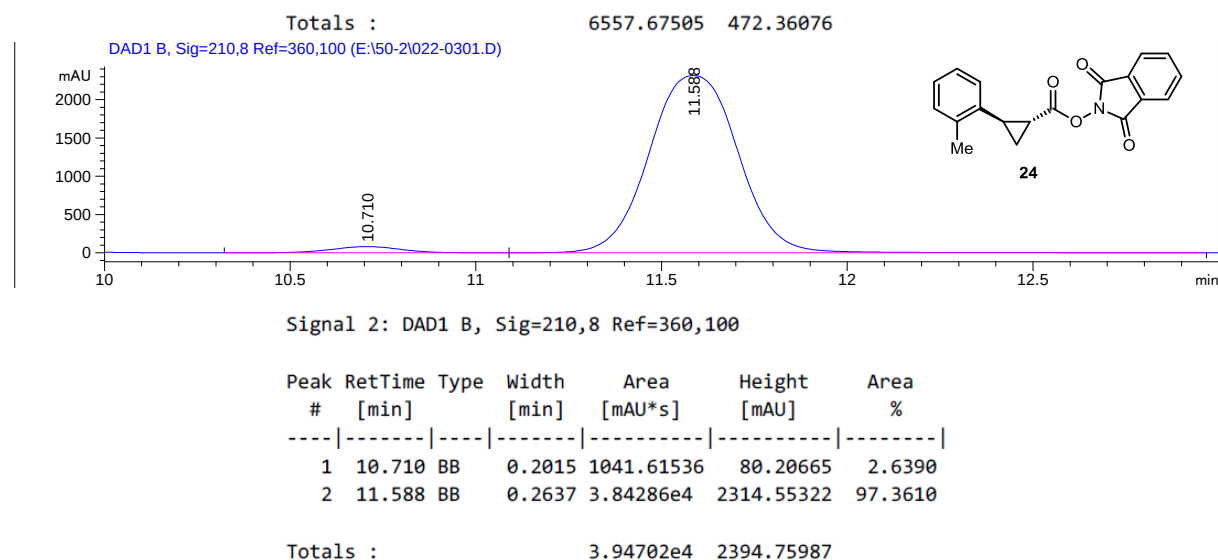
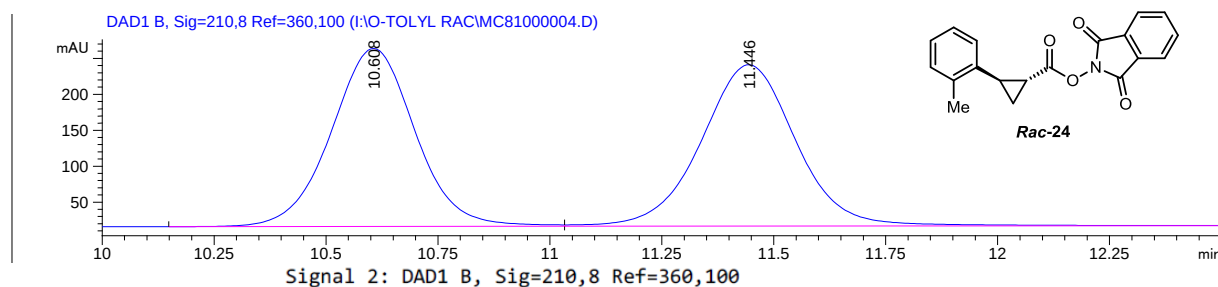
Analysis Conditions: Daicel Chiralpak-IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **23**:



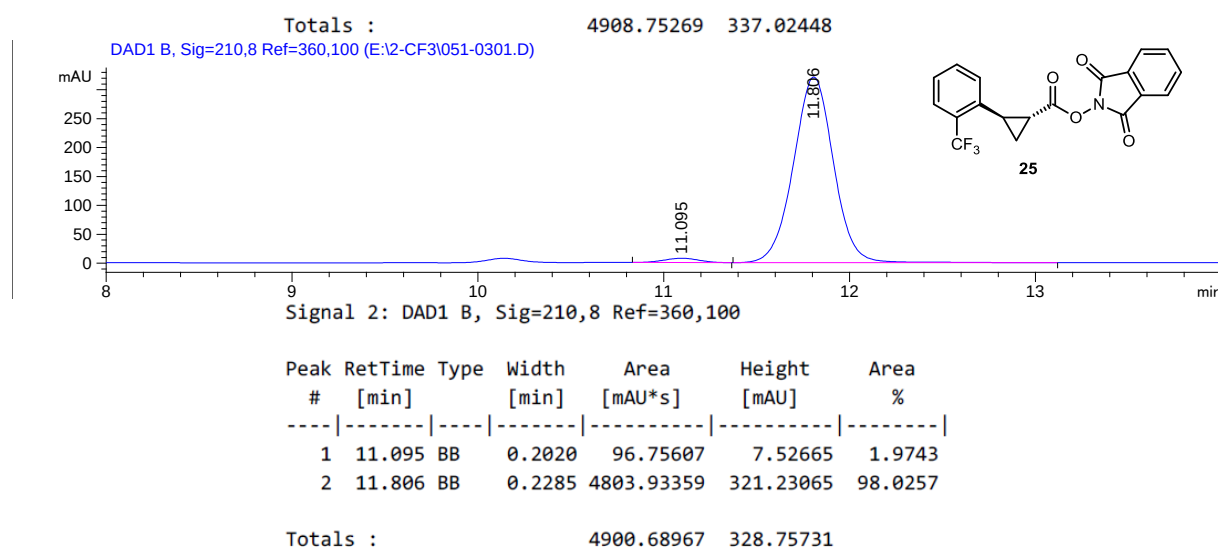
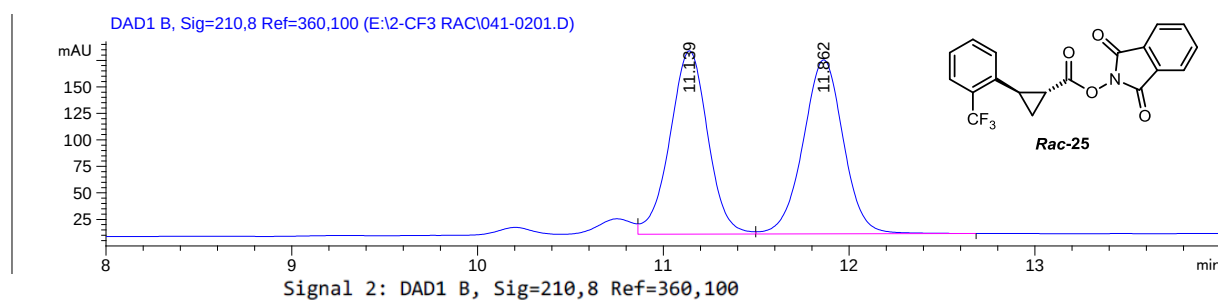
Analysis Conditions: Daicel Chiralpak- ID column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **24**:



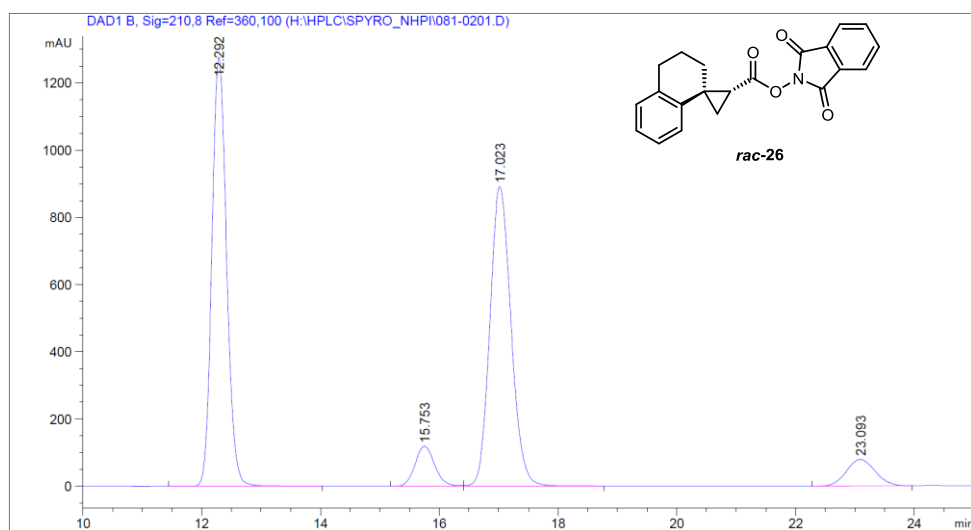
Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound 25:



Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

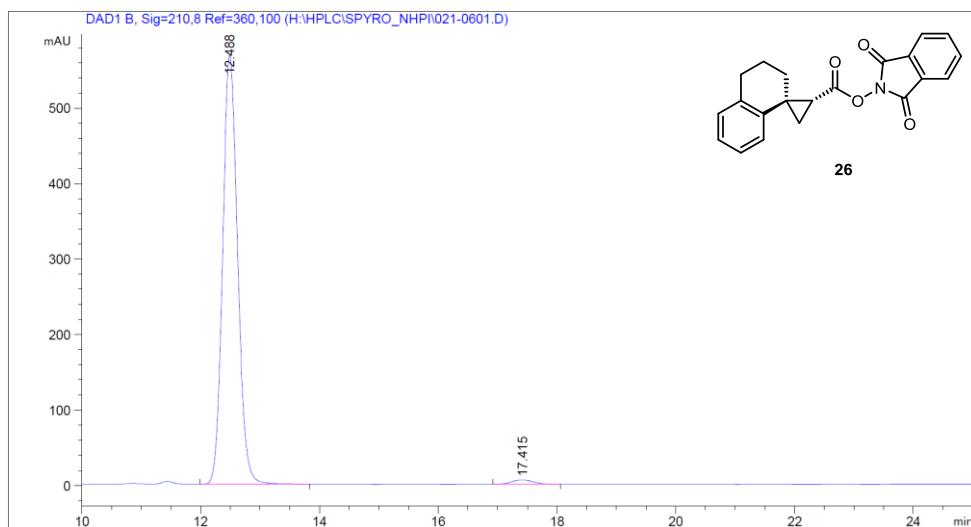
HPLC traces for compound **26**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.292	BB	0.2684	2.19235e4	1276.22351	44.4311
2	15.753	BV	0.3571	2735.18604	118.59876	5.5433
3	17.023	VB	0.3826	2.20295e4	890.53656	44.6459
4	23.093	BB	0.5215	2654.51050	79.10724	5.3798

Totals : 4.93426e4 2364.46607



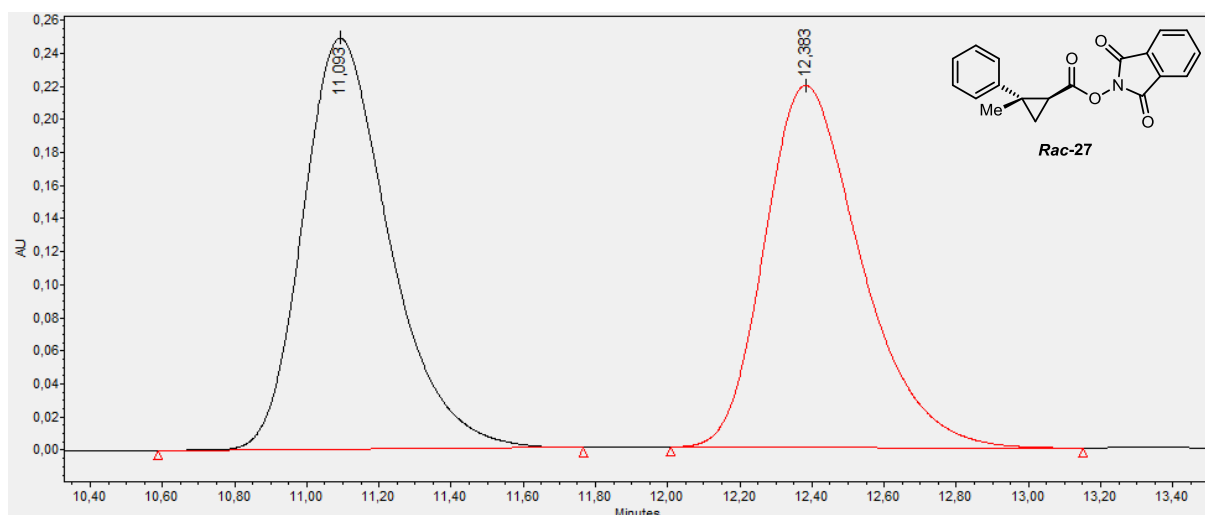
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.488	BB	0.2716	9908.42383	567.77106	98.5578
2	17.415	BB	0.3933	144.99188	5.65083	1.4422

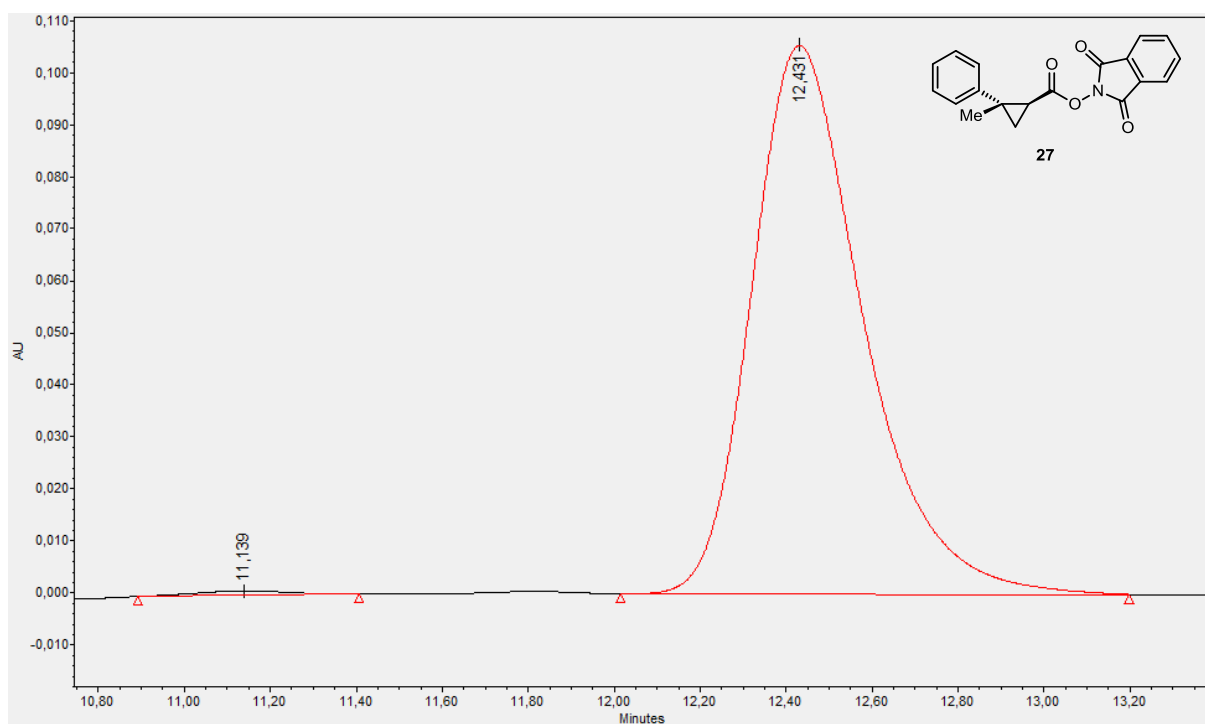
Totals : 1.00534e4 573.42188

Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 90:10 *i*-hexane:*i*-PrOH, flow rate 1.00 mL/min, λ = 210 nm.

HPLC traces for compound 27:



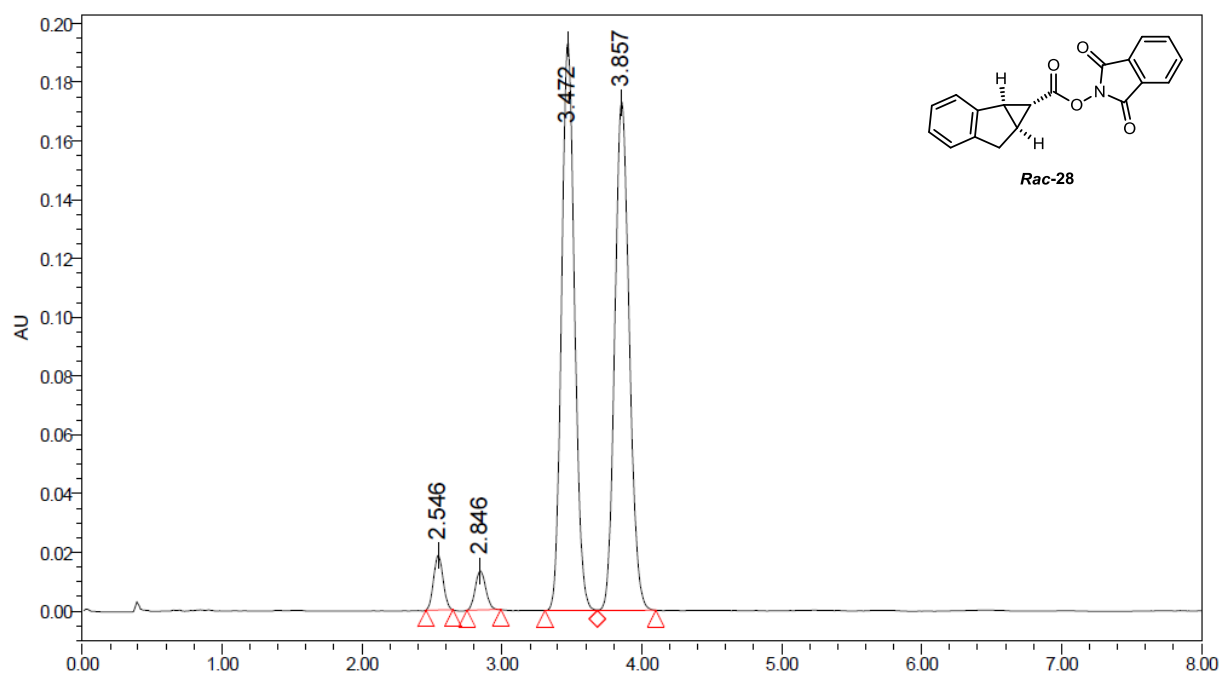
Peak #	RetTime [min]	Type	Area [μV*s]	Height [μV]	Area %
1	11.093	BB	4151561	248703	50.53
2	12.383	BB	4064863	218938	49.47



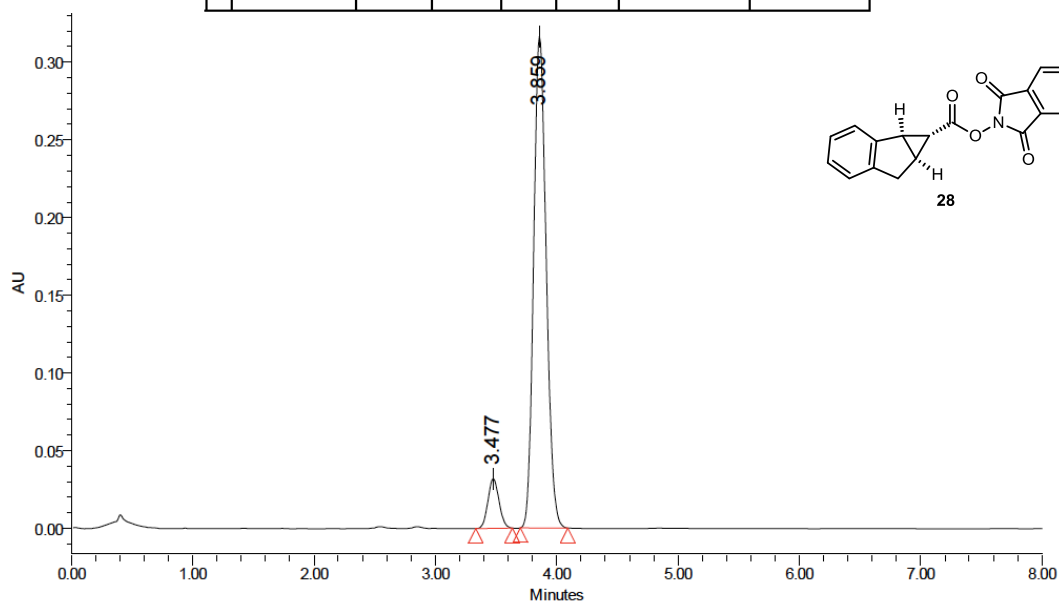
Peak #	RetTime [min]	Type	Area [μV*s]	Height [μV]	Area %
1	11.139	BB	11422	816	0.60
2	12.431	BB	1902392	105377	99.40

Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ: 210 nm.

HPLC traces for compound **28**:



	Retention Time	Area	% Area	K	N	USP Resolution	Width @ 50%
1	2.546	88132	3.32	0.000	6407.2		7.477002e-002
2	2.846	69303	2.61	0.118	6708.0	2.213	8.184075e-002
3	3.472	1251545	47.10	0.364	6577.6	3.962	1.003330e-001
4	3.857	1248057	46.97	0.515	6526.6	2.089	1.118403e-001

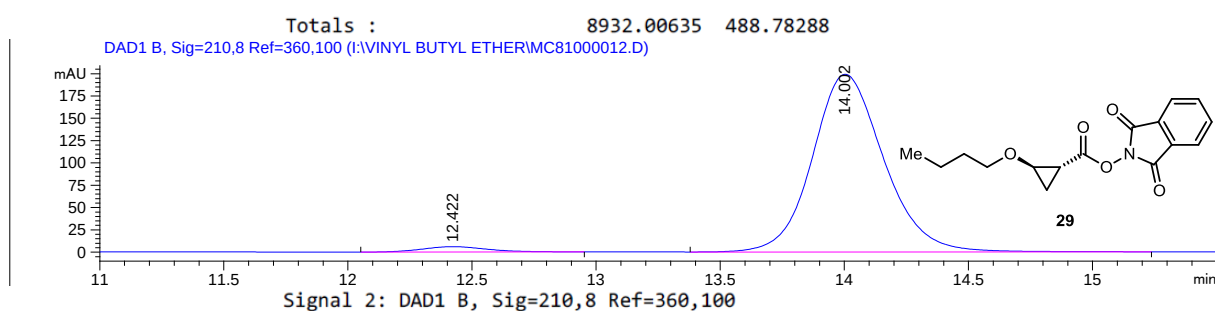
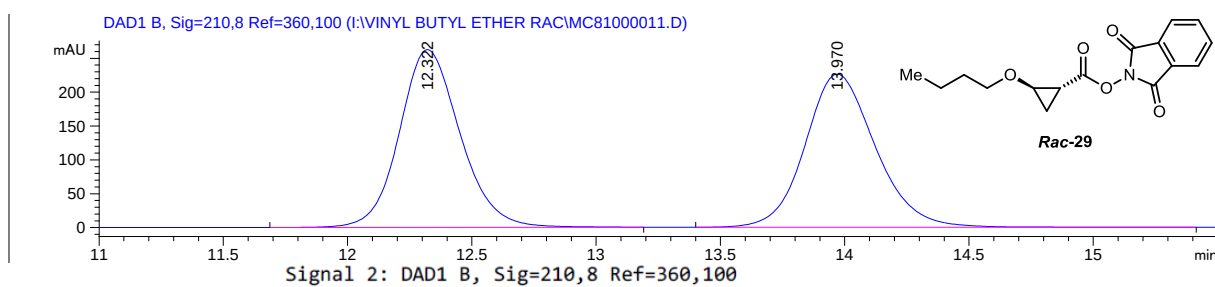


	Retention Time	Area	% Area	K	N	USP Resolution
1	3.477	202609	8.19	0.000	6816.1	
2	3.859	2271613	91.81	0.110	6551.0	2.087

ee = 83.6

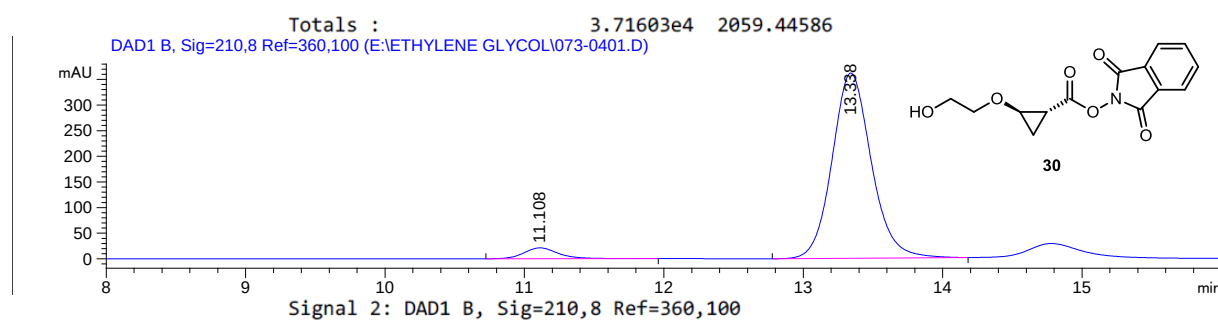
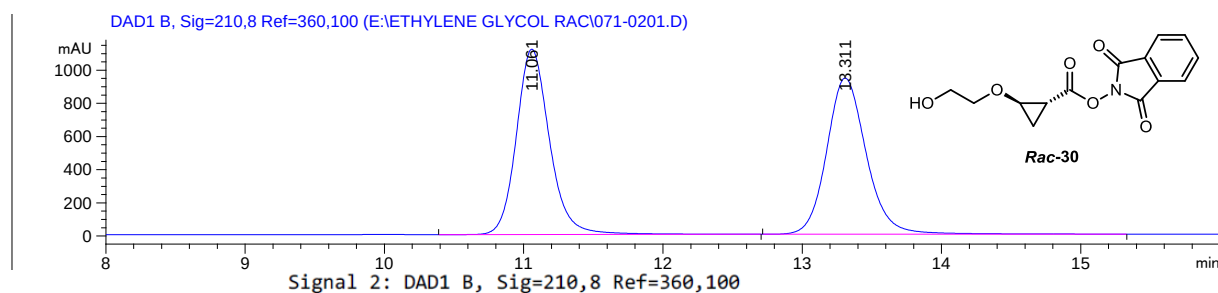
Analysis Conditions: Daicel LUX A1 column (0.46cm internal diameter x 15cm), temperature 40°C, eluent 90:10 CO₂:EtOH, 120 bar, flow rate 3.5 mL/min, λ : 230 nm.

HPLC traces for compound 29:



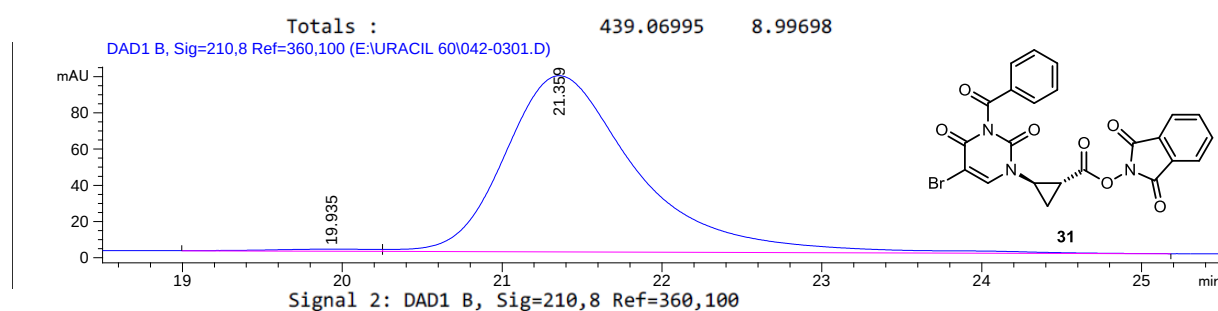
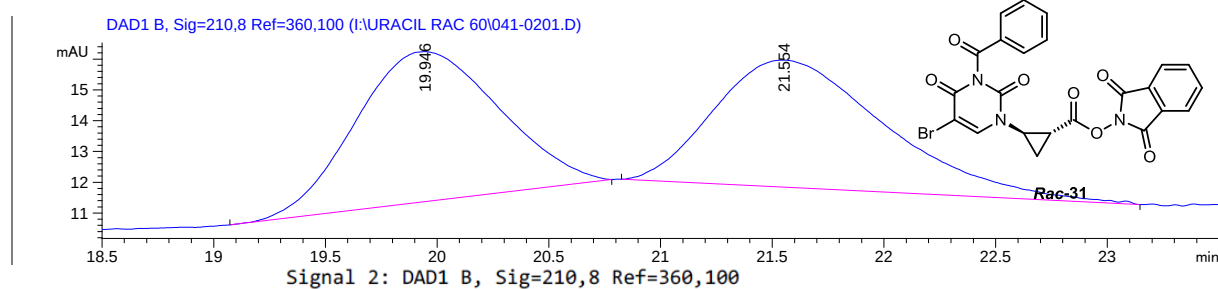
Analysis Conditions: Daicel Chiralpak- ID column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **30**:



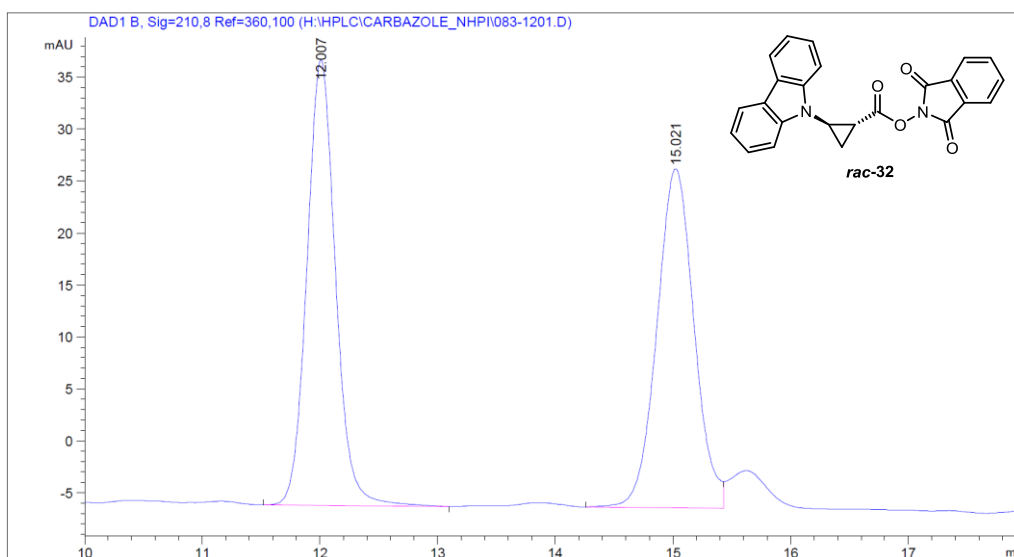
Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **31**:



Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 60:40 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

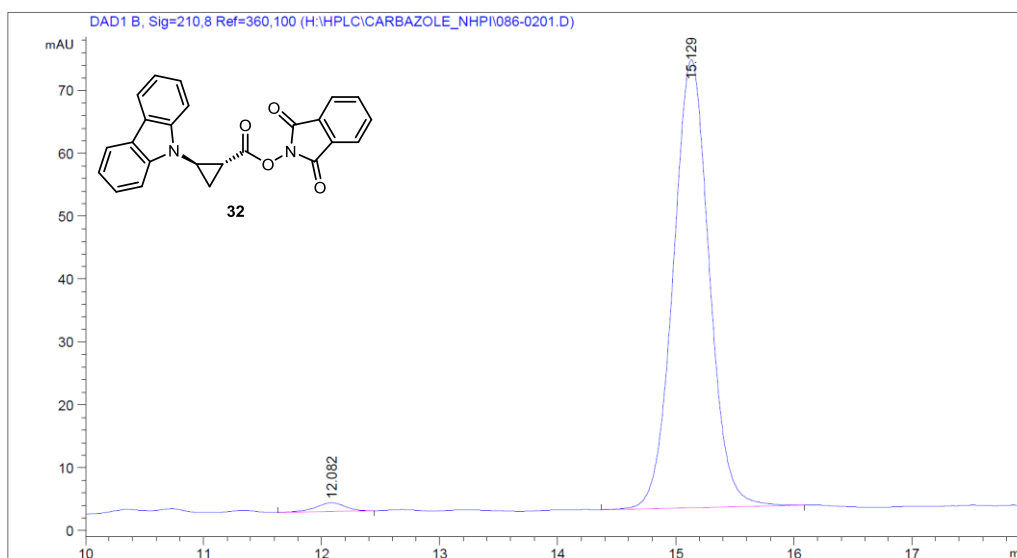
HPLC traces for compound **32**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.007	BB	0.2591	724.13770	42.87294	50.2826
2	15.021	BV	0.3399	715.99841	32.63739	49.7174

Totals : 1440.13611 75.51033



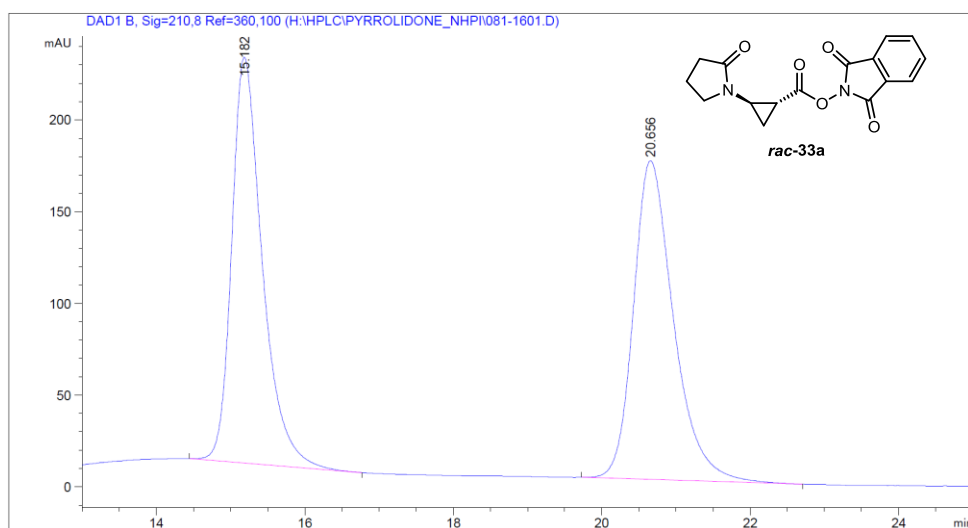
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.082	BB	0.2599	24.34274	1.40691	1.5899
2	15.129	BB	0.3267	1506.71411	71.25117	98.4101

Totals : 1531.05685 72.65808

Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i*-PrOH, flow rate 1.00 mL/min, λ = 210 nm.

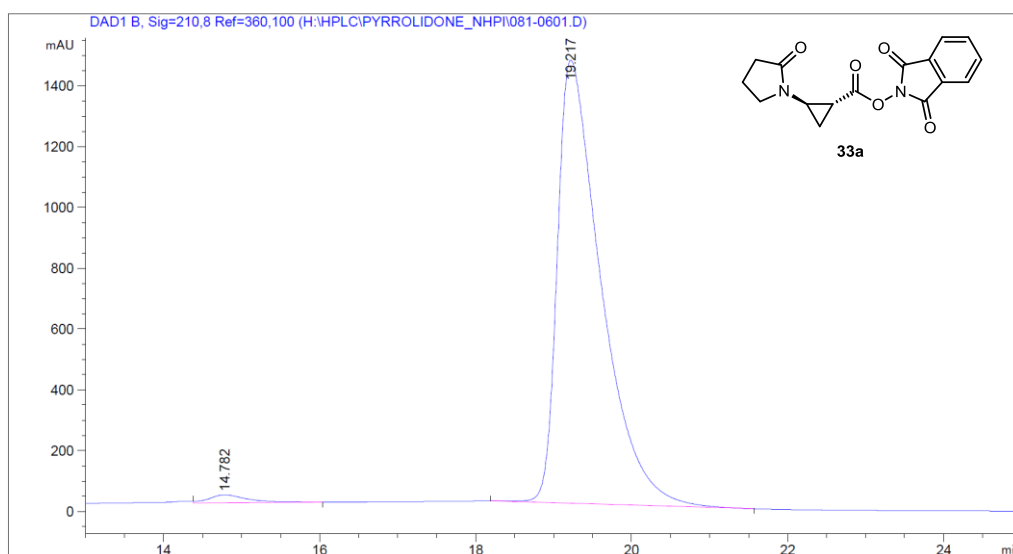
HPLC traces for compound **33a**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.182	BB	0.4287	6343.40723	221.08267	49.2768
2	20.656	BB	0.5644	6529.61523	173.75891	50.7232

Totals : 1.28730e4 394.84158



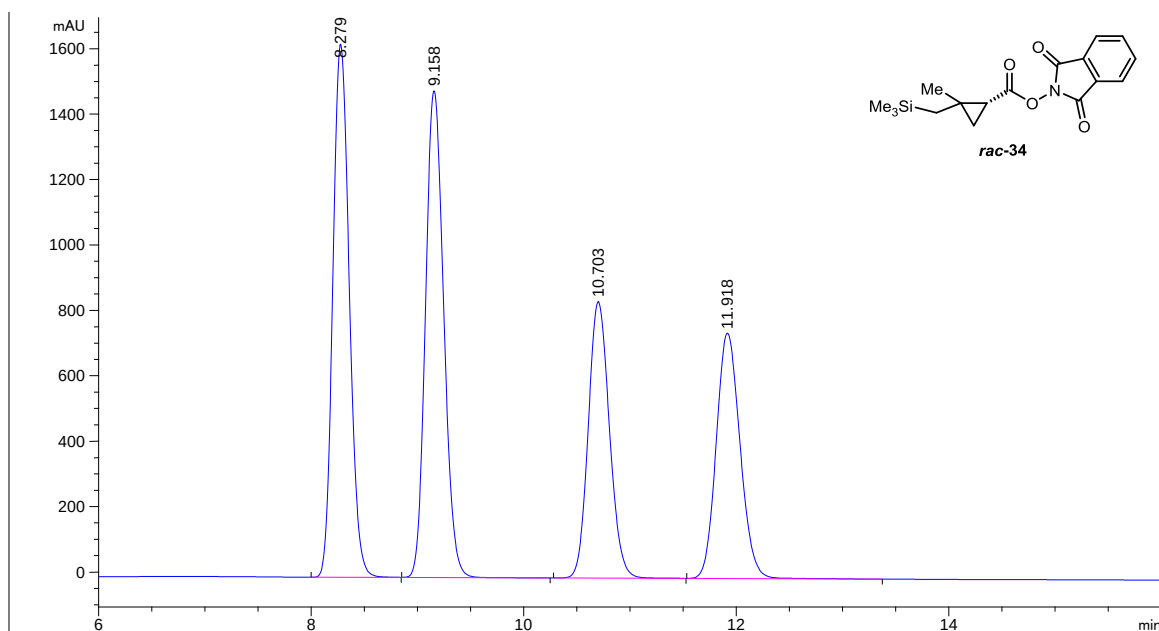
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.782	VB	0.4857	852.90265	25.66370	1.4795
2	19.217	BB	0.5725	5.67945e4	1457.83276	98.5205

Totals : 5.76474e4 1483.49646

Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 70:30 *i*-hexane:*i*-PrOH, flow rate 1.00 mL/min, λ = 210 nm.

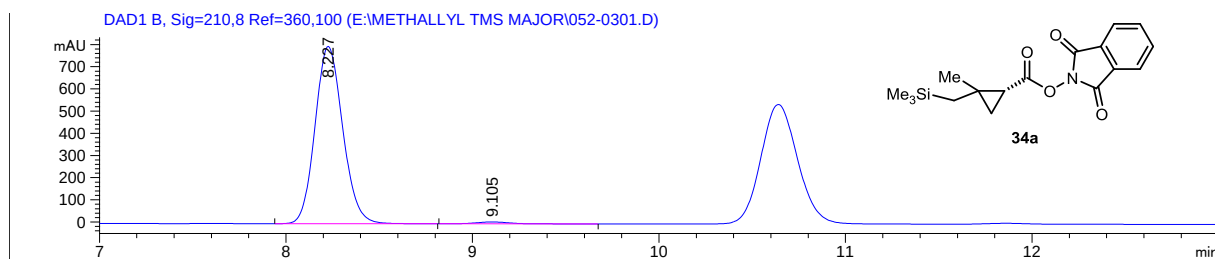
HPLC traces for compound **34**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.279	BB	0.1689	1.74638e4	1630.87280	29.8602
2	9.158	BB	0.1865	1.76752e4	1488.52917	30.2215
3	10.703	BB	0.2147	1.16518e4	845.67969	19.9225
4	11.918	BB	0.2418	1.16946e4	750.51648	19.9958

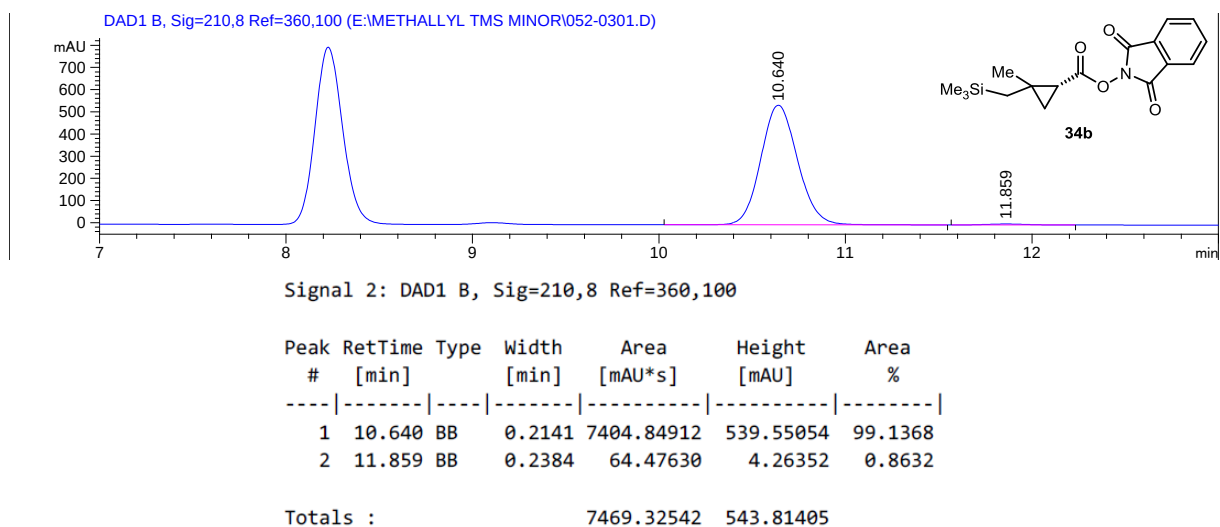
Totals : 5.84854e4 4715.59814



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

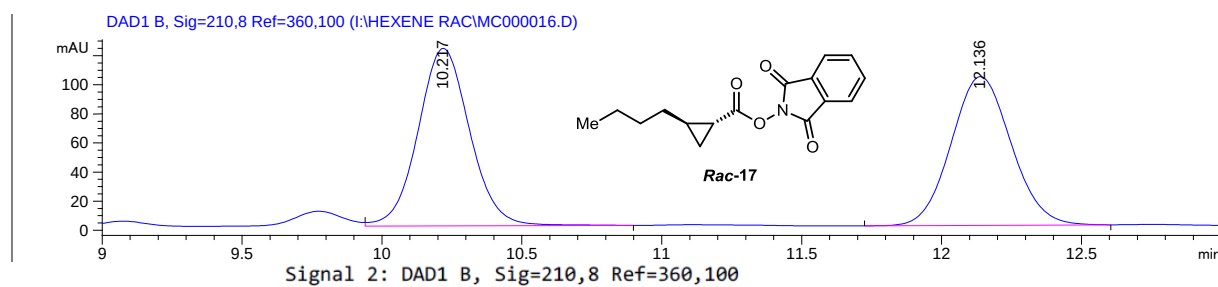
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.227	BB	0.1602	8234.27246	799.32410	98.7818
2	9.105	BB	0.1872	101.54457	8.39185	1.2182

Totals : 8335.81703 807.71594



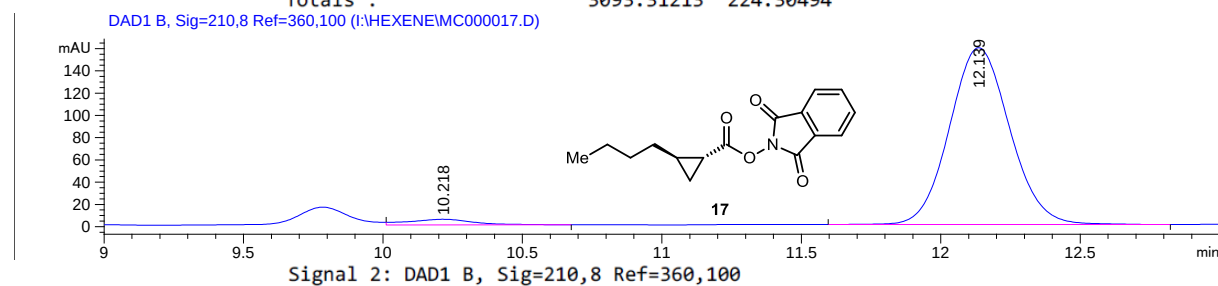
Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 95:5 *i*-hexane:*i*-PrOH, flow rate 1.00 mL/min, λ = 210 nm.

HPLC traces for compound **17**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.217	VB	0.1977	1565.58948	122.02603	50.6121
2	12.136	BB	0.2323	1527.72266	102.27891	49.3879

Totals : 3093.31213 224.30494

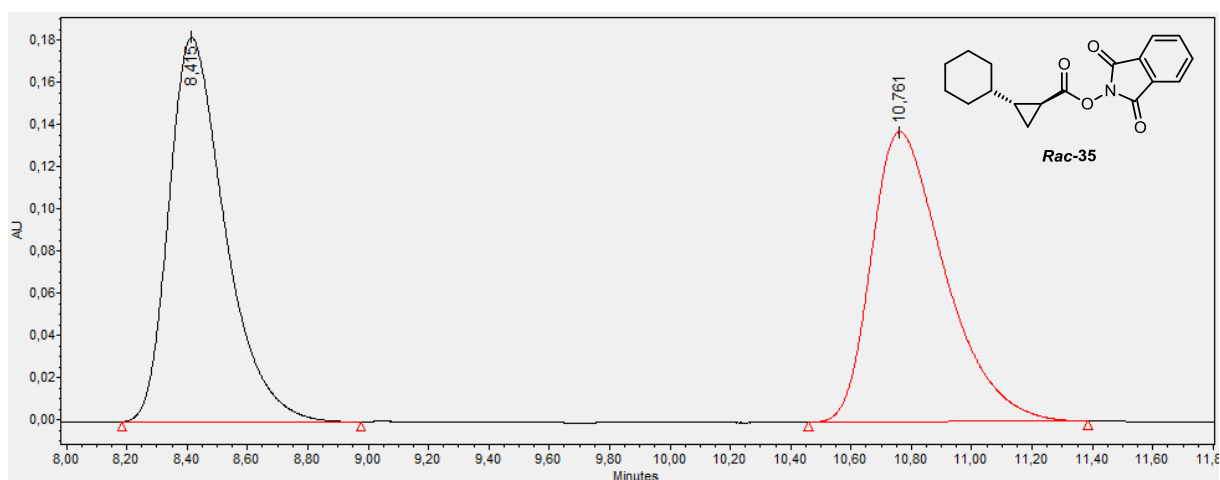


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.218	VB	0.2318	81.19734	5.04364	3.2871
2	12.139	BB	0.2334	2389.00977	158.94249	96.7129

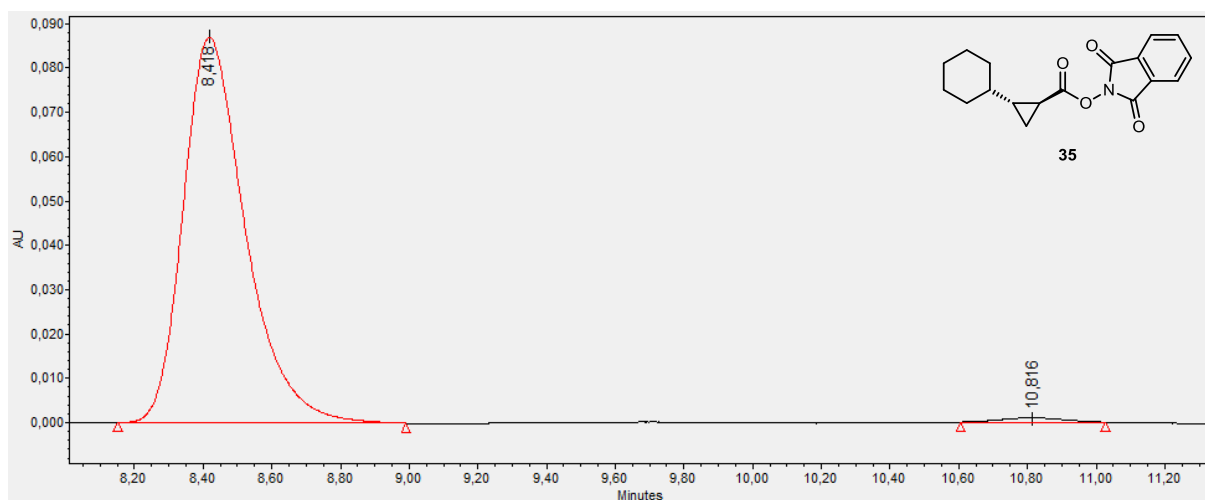
Totals : 2470.20711 163.98613

Analysis Conditions: Daicel Chiralpak- IC column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound 35:



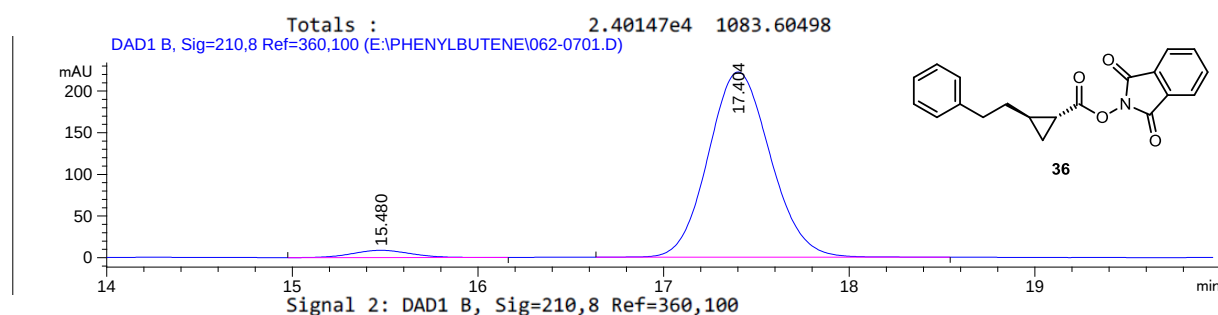
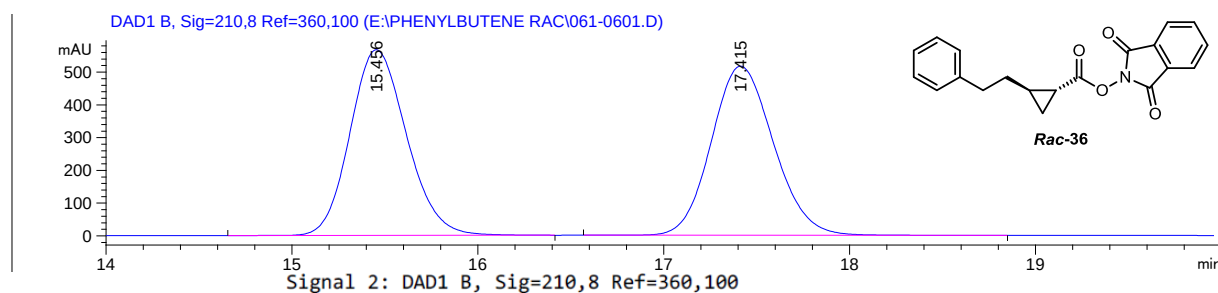
Peak #	RetTime [min]	Type	Area [$\mu\text{V}\cdot\text{s}$]	Height [μV]	Area %
1	8.415	BB	2349059	182263	50.12
2	10.761	BB	2338009	137635	49.88



Peak #	RetTime [min]	Type	Area [$\mu\text{V}\cdot\text{s}$]	Height [μV]	Area %
1	8.418	BB	1096650	87008	98.90
2	10.816	BB	12190	973	1.10

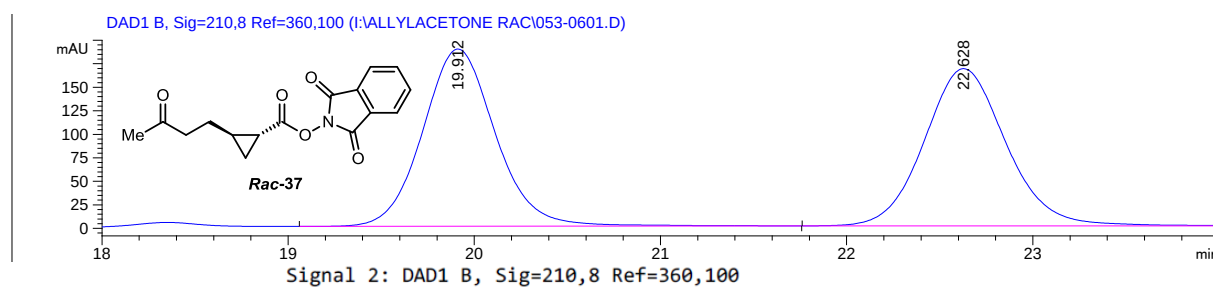
Analysis Conditions: Daicel Chiralpak- IC column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 254 nm.

HPLC traces for compound **36**:



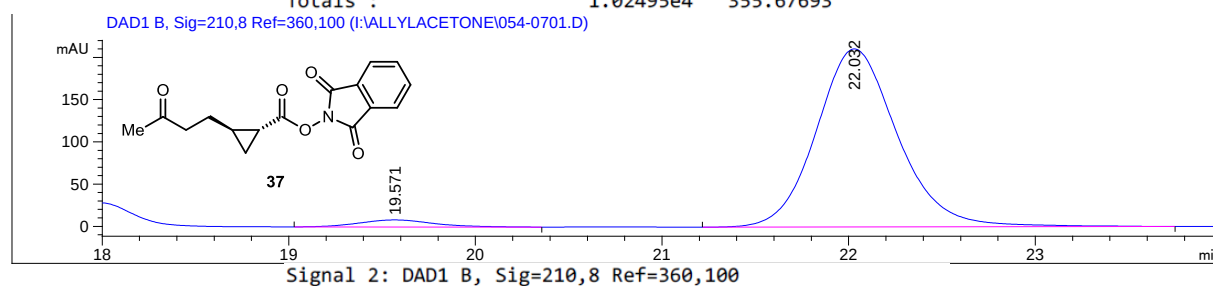
Analysis Conditions: Daicel Chiralpak- IC column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **37**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.912	BB	0.4166	5113.89307	188.45009	49.8942
2	22.628	BB	0.4683	5135.58887	167.22684	50.1058

Totals : 1.02495e4 355.67693

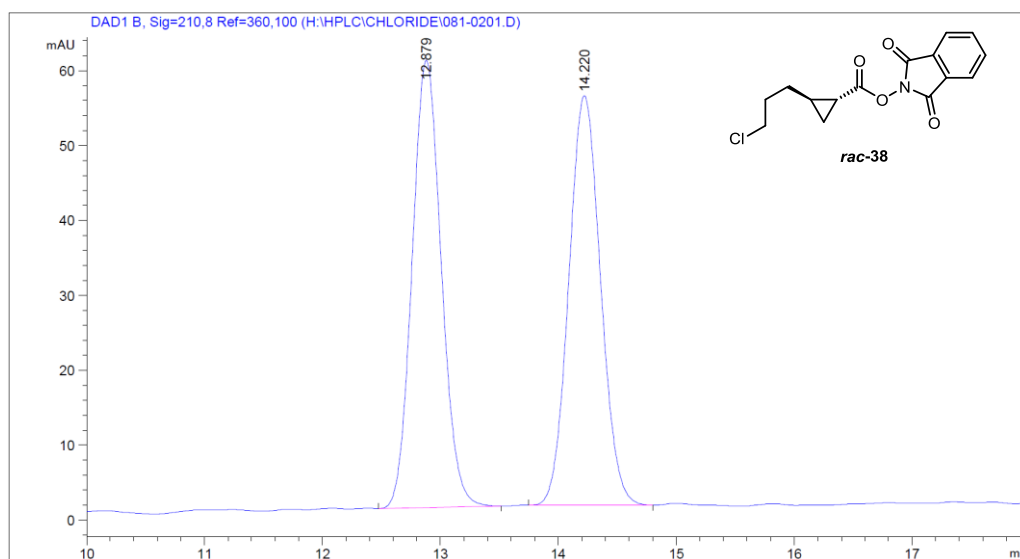


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.571	BB	0.4075	231.98184	8.36638	3.5023
2	22.032	BB	0.4617	6391.70361	210.80794	96.4977

Totals : 6623.68546 219.17432

Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

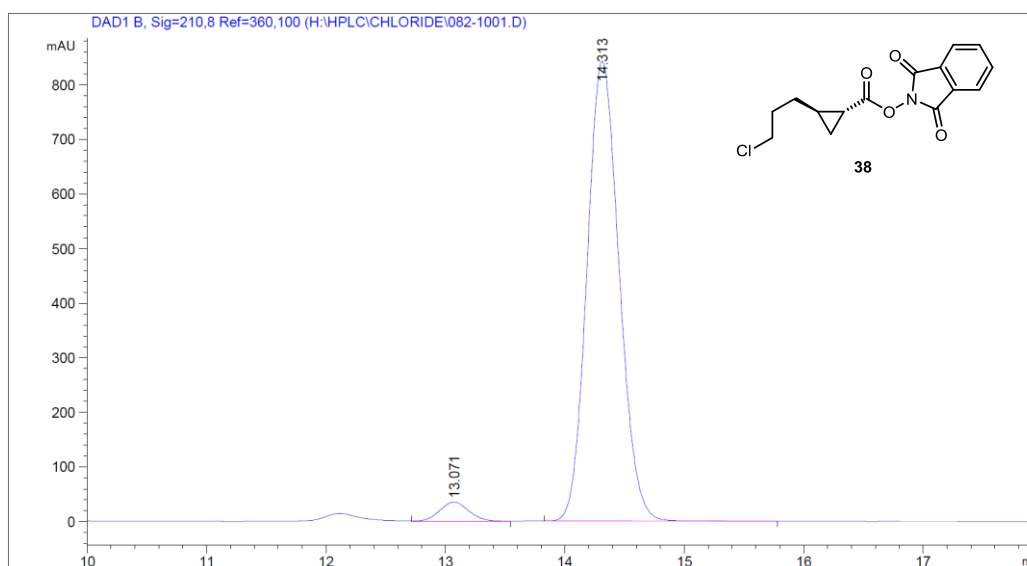
HPLC traces for compound **38**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.879	BB	0.2660	1023.77795	59.71968	50.0549
2	14.220	BB	0.2901	1021.53320	54.65379	49.9451

Totals : 2045.31116 114.37347



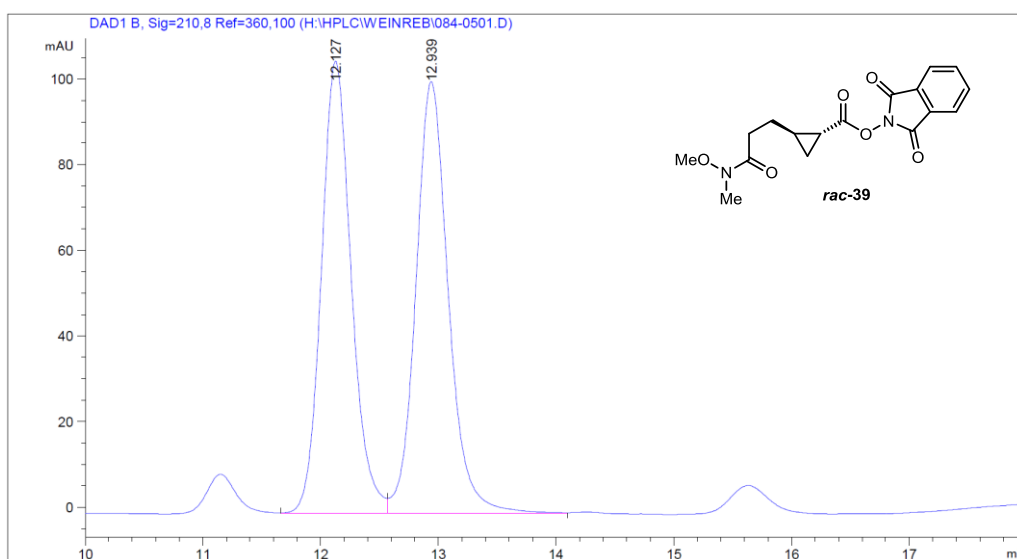
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.071	VB	0.2645	593.94049	34.90332	3.6400
2	14.313	BB	0.2917	1.57232e4	842.68188	96.3600

Totals : 1.63171e4 877.58521

Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i*-PrOH, flow rate 1.0 mL/min, λ = 210 nm.

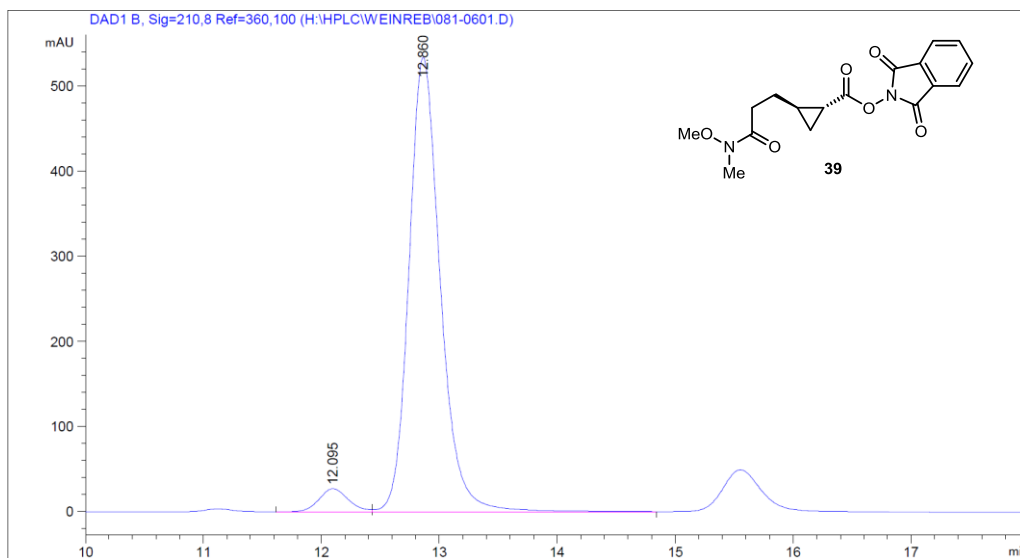
HPLC traces for compound **39**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.127	BV	0.2693	1856.52026	105.48479	49.1003
2	12.939	VB	0.2909	1924.55945	100.72237	50.8997

Totals : 3781.07971 206.20716



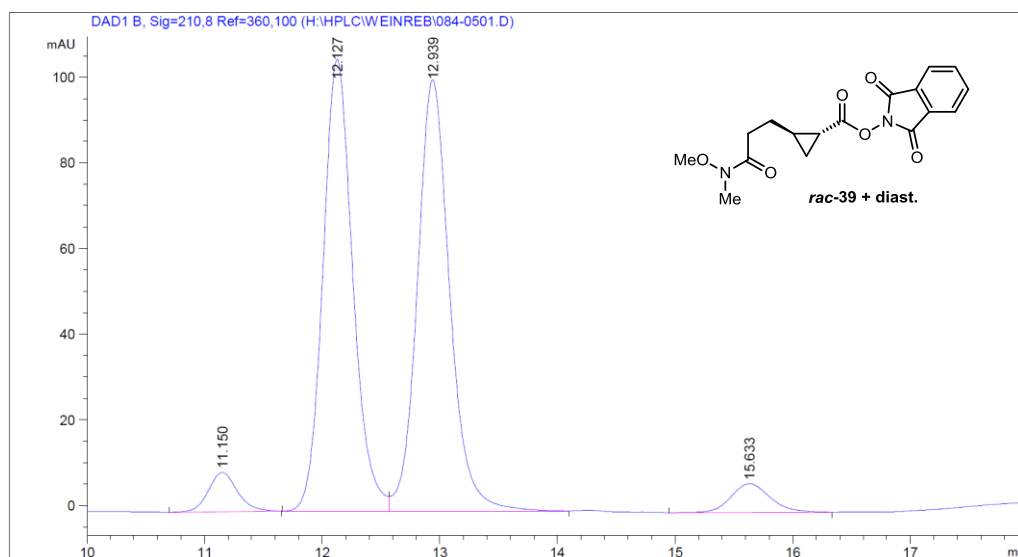
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.095	BV	0.2663	471.08200	27.16418	4.5637
2	12.860	VB	0.2813	9851.34277	533.81787	95.4363

Totals : 1.03224e4 560.98205

Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i*-PrOH, flow rate 1.0 mL/min, λ = 210 nm.

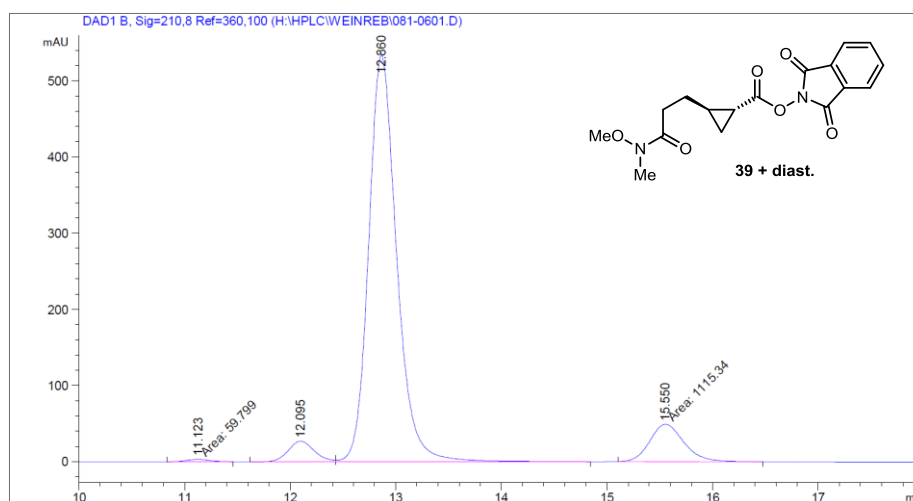
HPLC traces for compound **39** (dr determination):



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.150	BB	0.2602	157.90494	9.20229	3.8559
2	12.127	BV	0.2693	1856.52026	105.48479	45.3349
3	12.939	VB	0.2909	1924.55945	100.72237	46.9964
4	15.633	BB	0.3587	156.13971	6.72825	3.8128

Totals : 4095.12436 222.13769



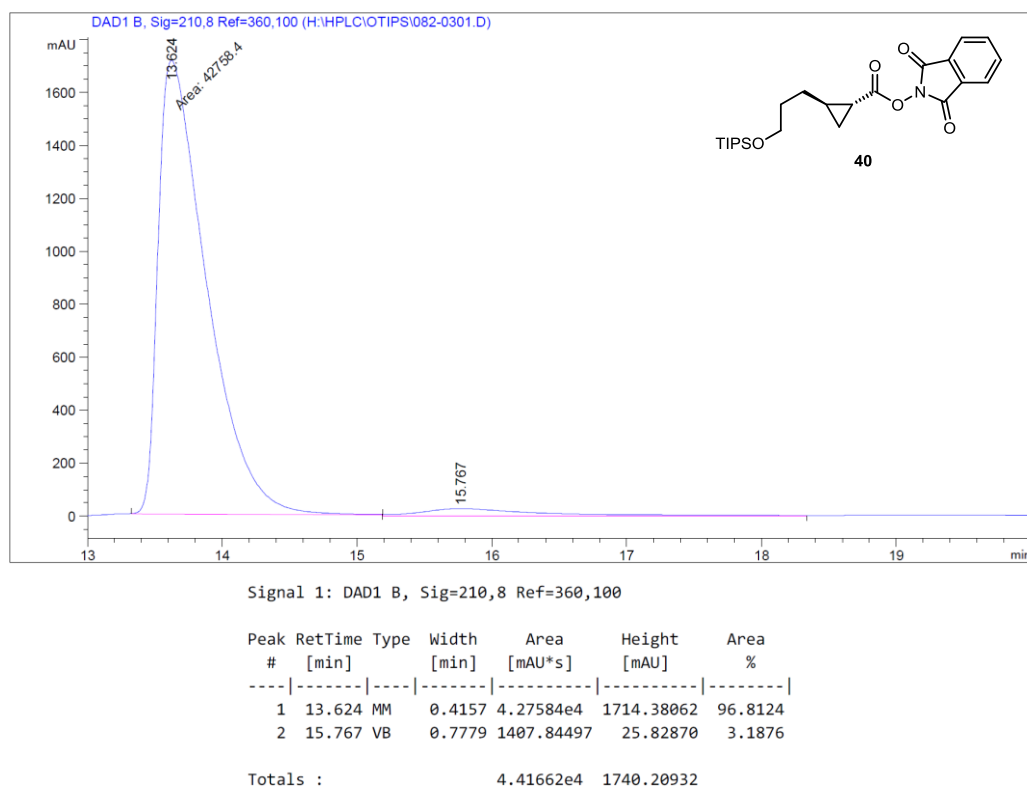
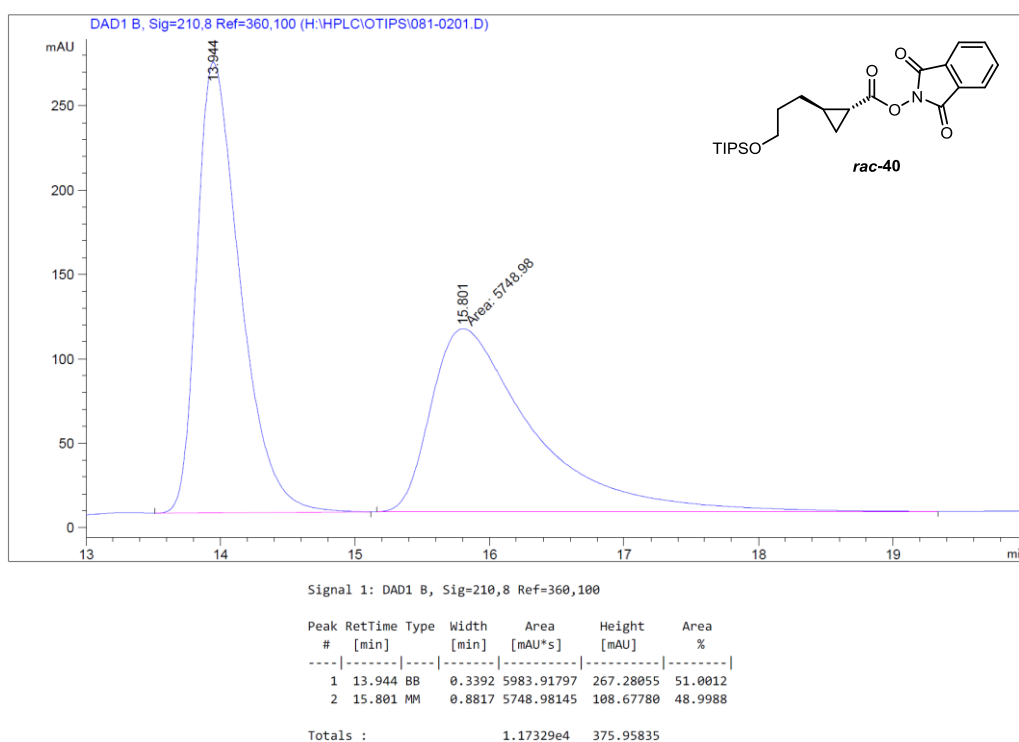
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.123	MM	0.2848	59.79895	3.49979	0.5201
2	12.095	BV	0.2663	471.08200	27.16418	4.0972
3	12.860	VB	0.2813	9851.34277	533.81787	85.6820
4	15.550	MM	0.3794	1115.33679	48.99632	9.7006

Totals : 1.14976e4 613.47817

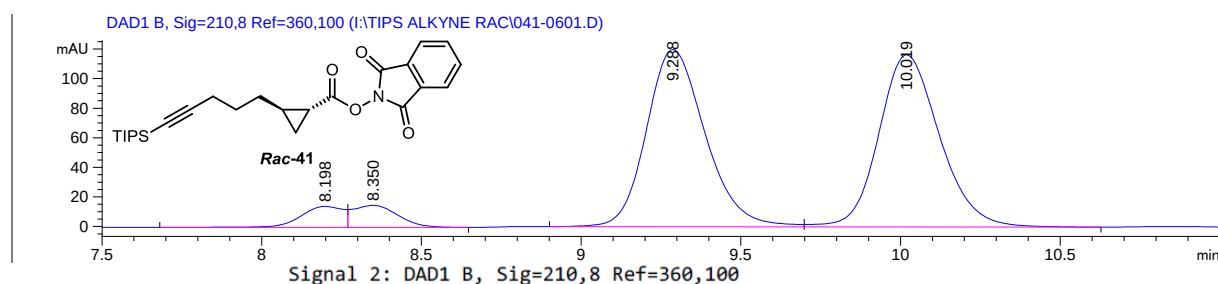
Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i*-PrOH, flow rate 1.0 mL/min, λ = 210 nm.

HPLC traces for compound 40:



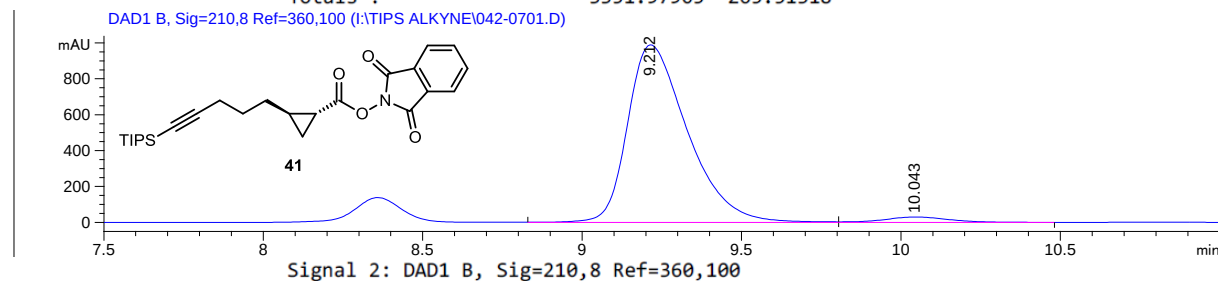
Analysis Conditions: Daicel Chiralpak IF column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 98:2 *i*-hexane:*i*-PrOH, flow rate 1.0 mL/min, λ = 210 nm.

HPLC traces for compound **41**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.198	BV	0.1374	130.64110	14.19488	3.8974
2	8.350	VB	0.1453	144.64252	14.89162	4.3151
3	9.288	BV	0.1973	1534.61255	119.93047	45.7823
4	10.019	VB	0.2044	1542.08289	116.49622	46.0051

Totals : 3351.97905 265.51318

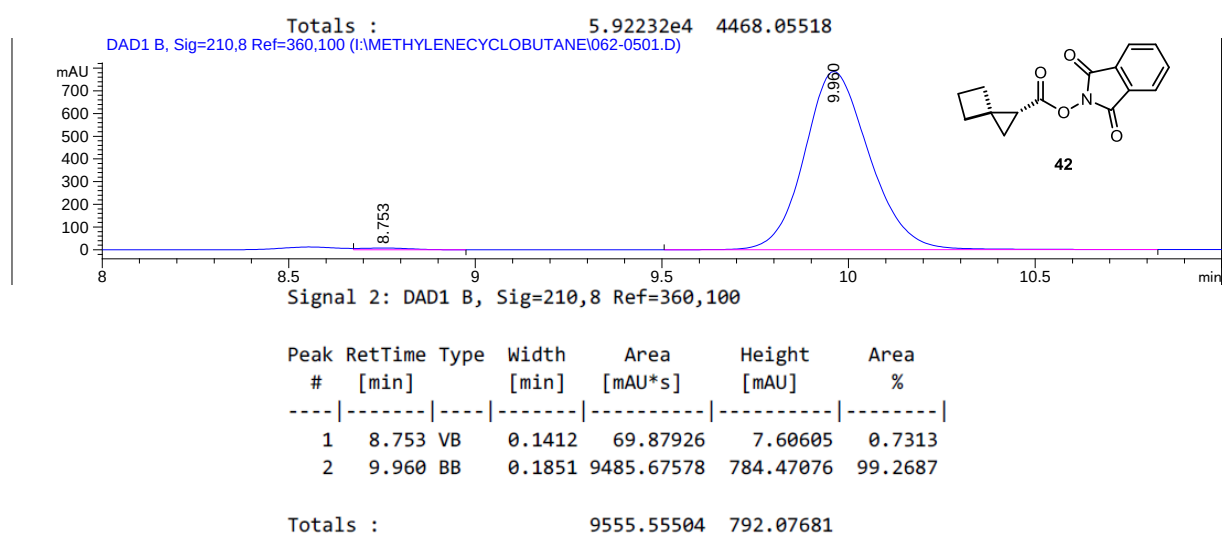
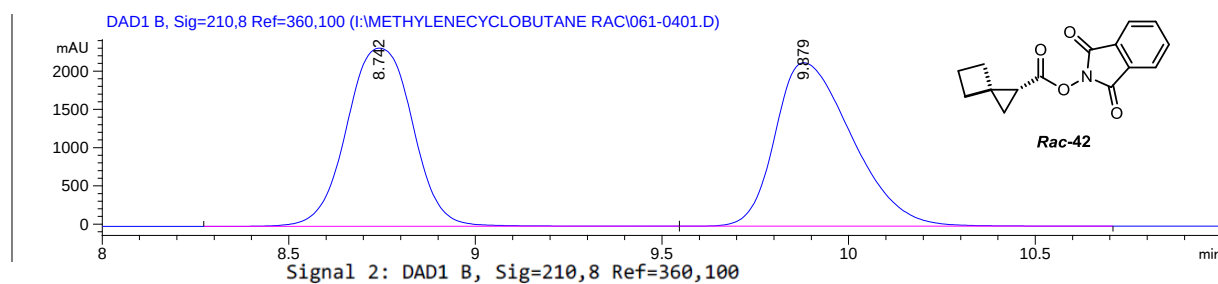


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.212	VV	0.1982	1.29086e4	989.41754	96.9098
2	10.043	VB	0.2104	411.62485	29.93841	3.0902

Totals : 1.33202e4 1019.35595

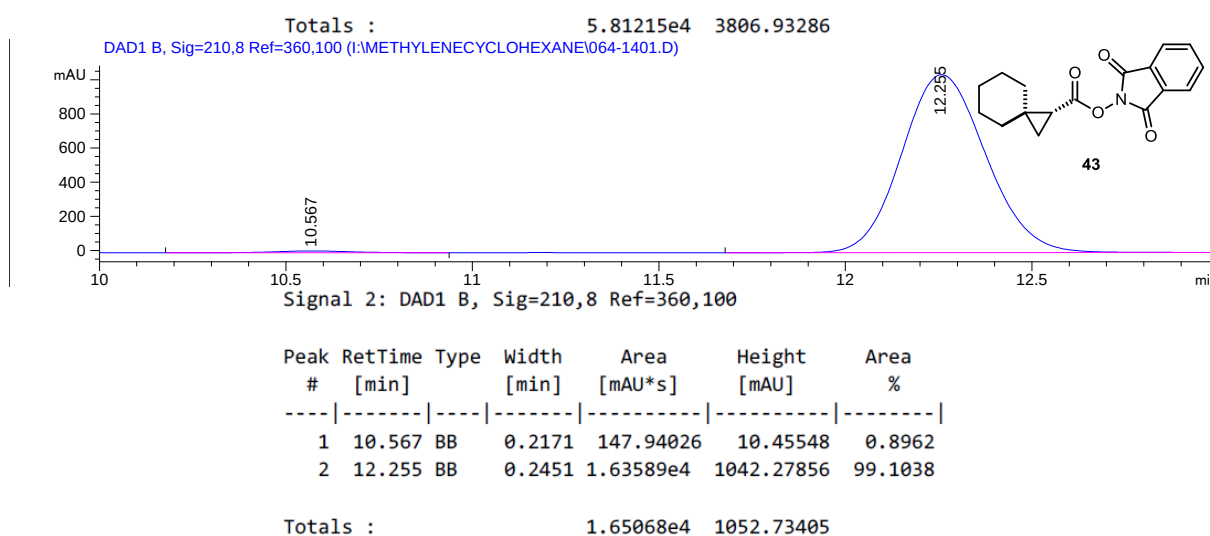
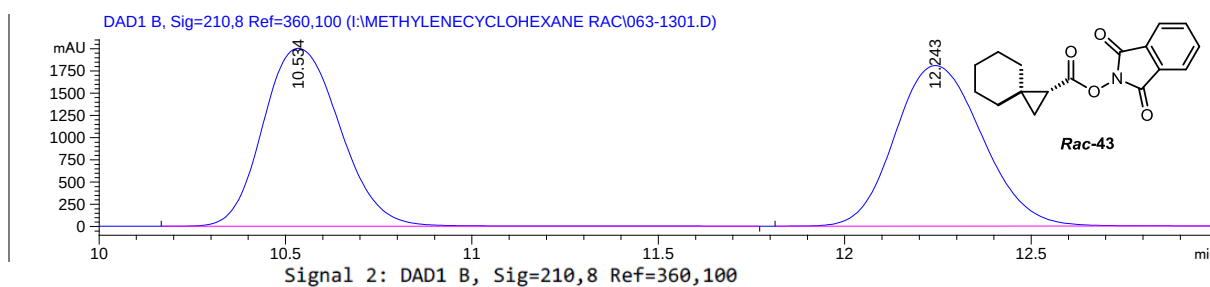
Analysis Conditions: Daicel Chiralpak- IF column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 95:15 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **42**:



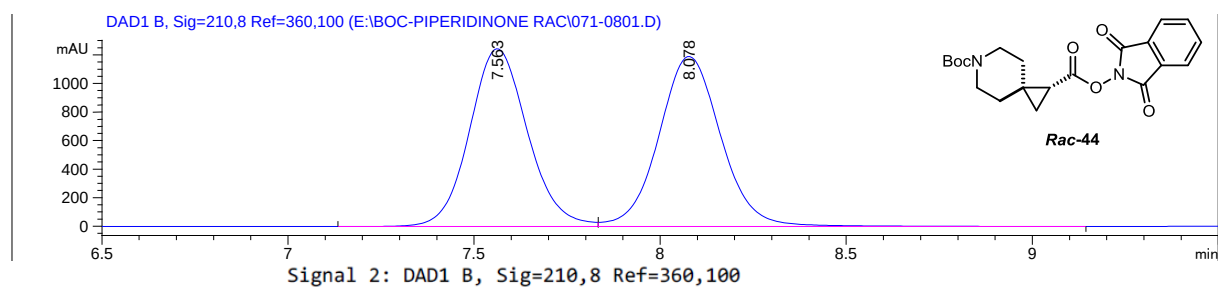
Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **43**:



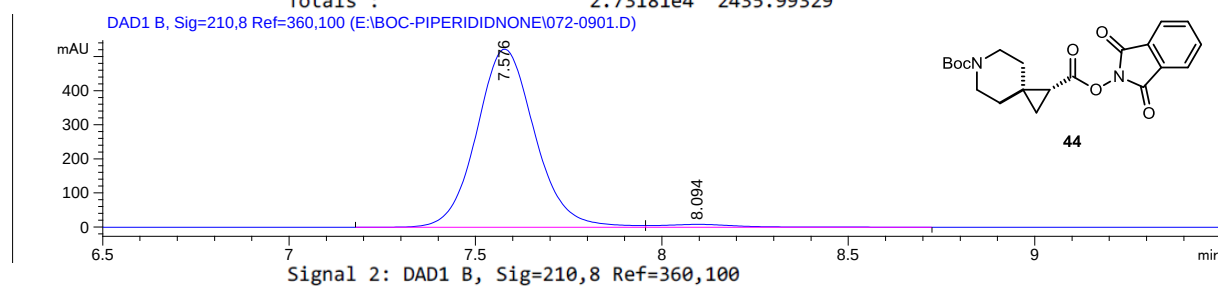
Analysis Conditions: Daicel Chiralpak- IC column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **44**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.563	BV	0.1665	1.35005e4	1244.95337	49.4198
2	8.078	VB	0.1793	1.38176e4	1191.03992	50.5802

Totals : 2.73181e4 2435.99329

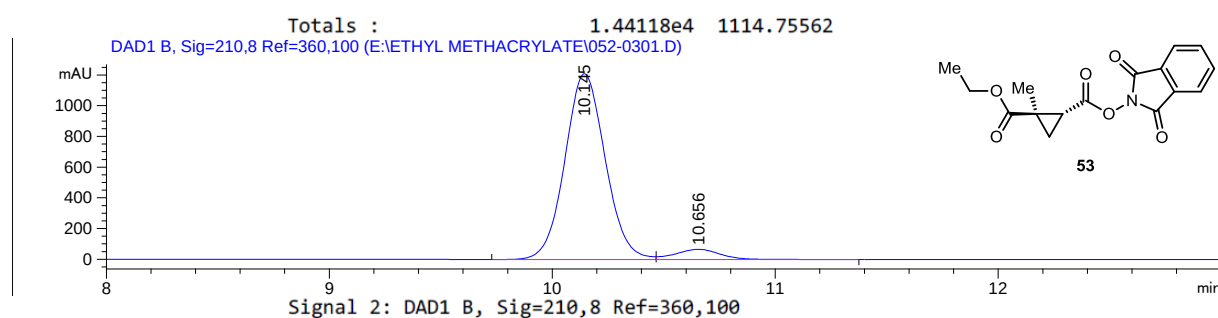
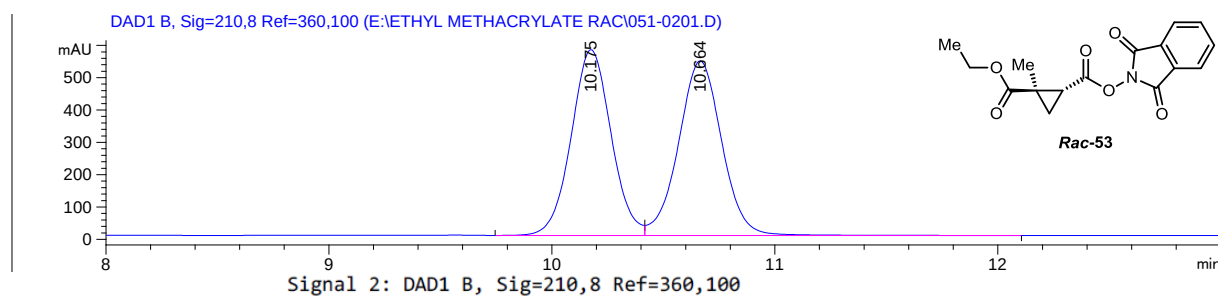


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.576	BV	0.1667	5677.94580	522.65442	97.9870
2	8.094	VB	0.2051	116.64380	8.34119	2.0130

Totals : 5794.58960 530.99561

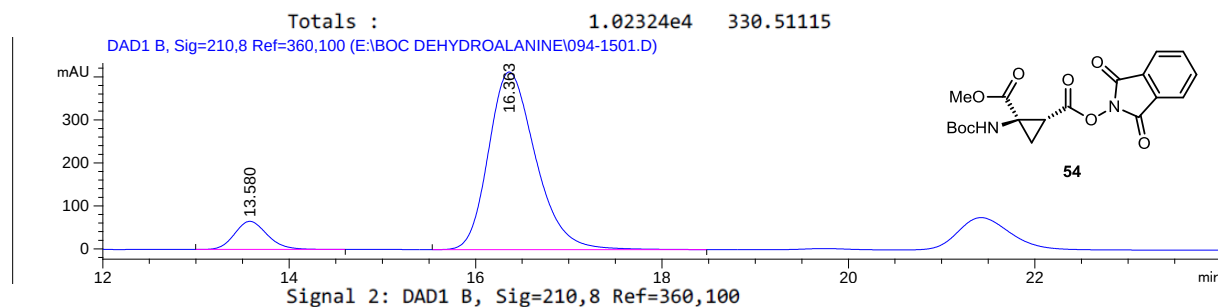
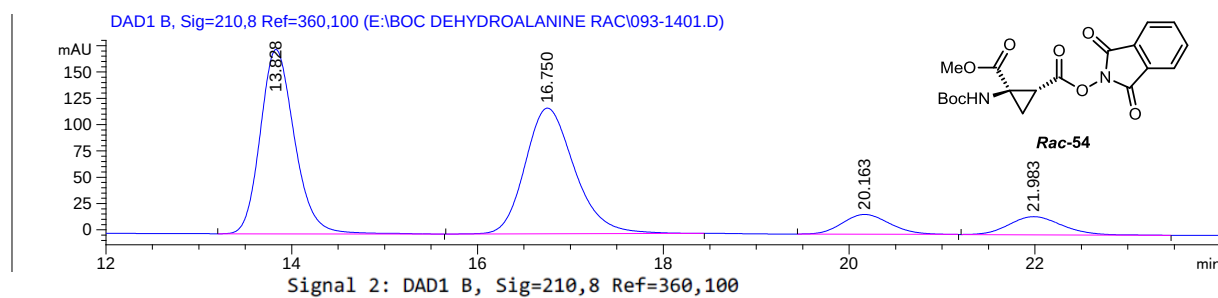
Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **53**:



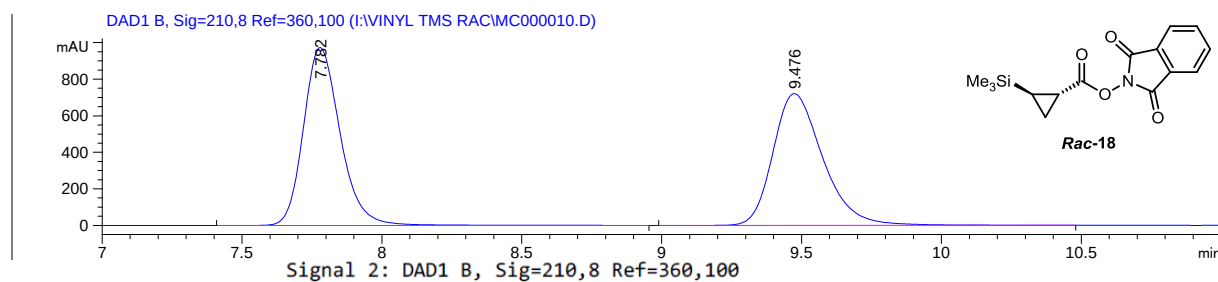
Analysis Conditions: Daicel Chiralpak- IA column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **54**:

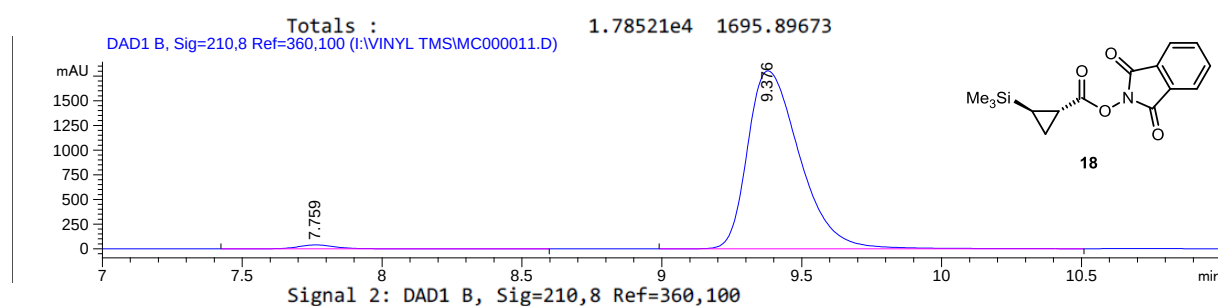


Analysis Conditions: Daicel Chiralpak- IB column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 80:20 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound **18**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.782	BB	0.1407	8916.19824	974.64636	49.9447
2	9.476	BB	0.1905	8935.94141	721.25037	50.0553

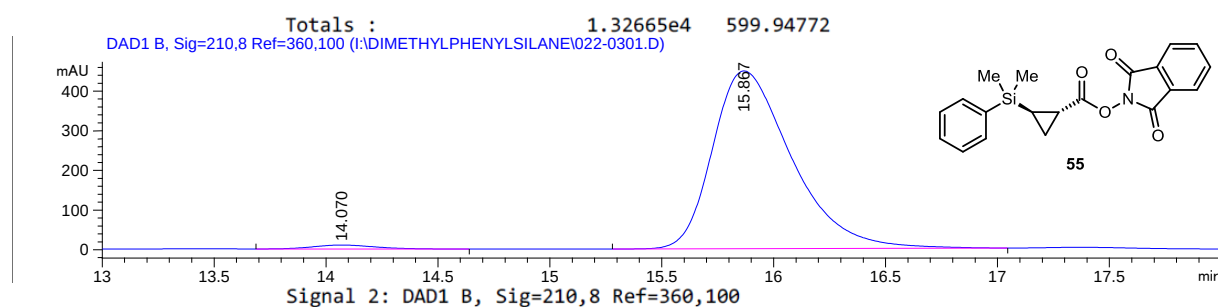
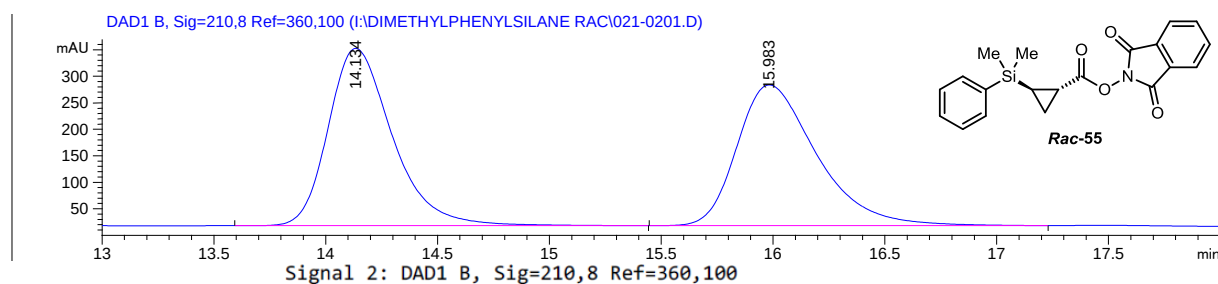


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.759	BB	0.1446	376.36920	39.71611	1.5909
2	9.376	BB	0.2006	2.32810e4	1803.95483	98.4091

Totals : 2.36574e4 1843.67094

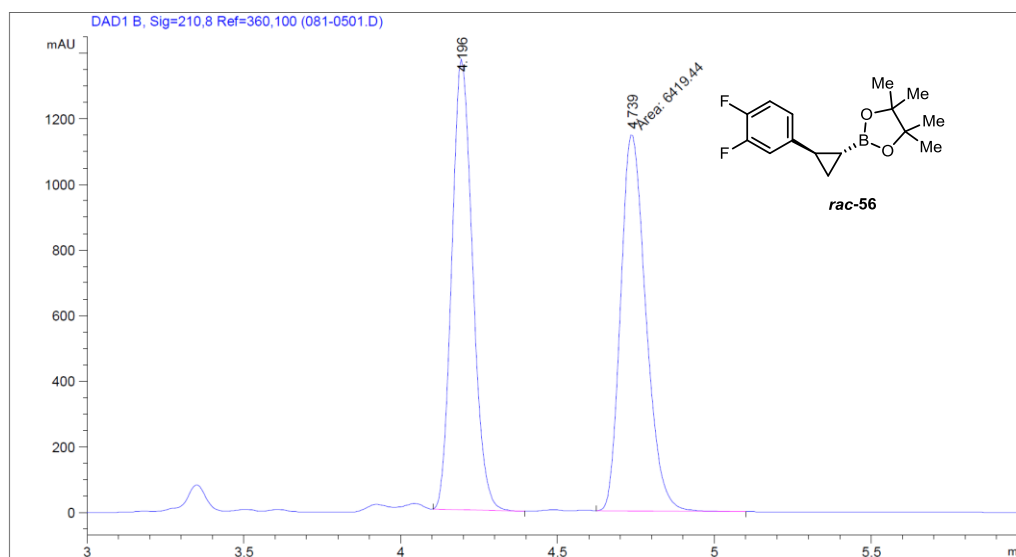
Analysis Conditions: Daicel Chiralpak- IF column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

HPLC traces for compound 55:



Analysis Conditions: Daicel Chiralpak- IF column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 95:5 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

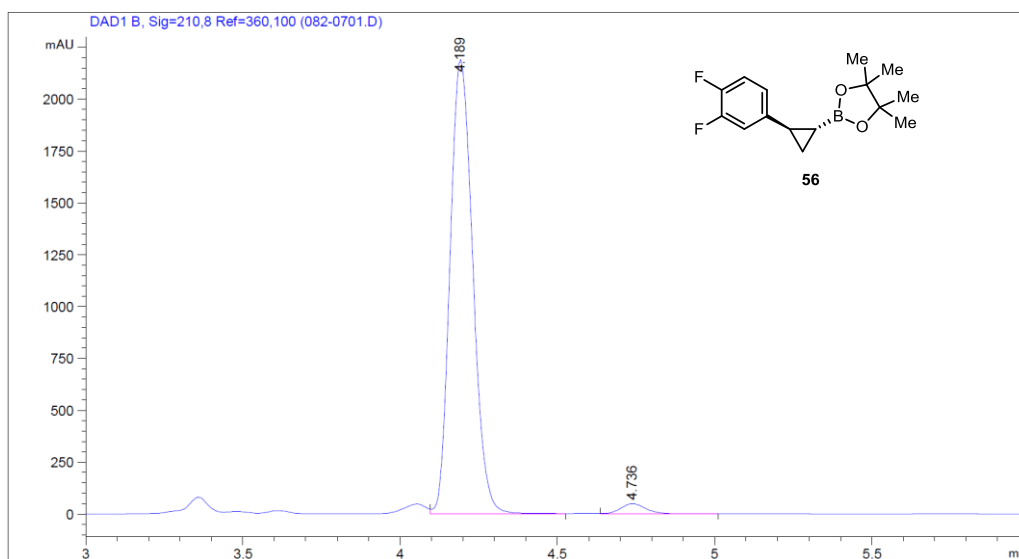
HPLC traces for compound **56**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.196	BB	0.0717	6322.65527	1373.54028	49.6202
2	4.739	MM	0.0929	6419.43604	1151.62012	50.3798

Totals : 1.27421e4 2525.16040



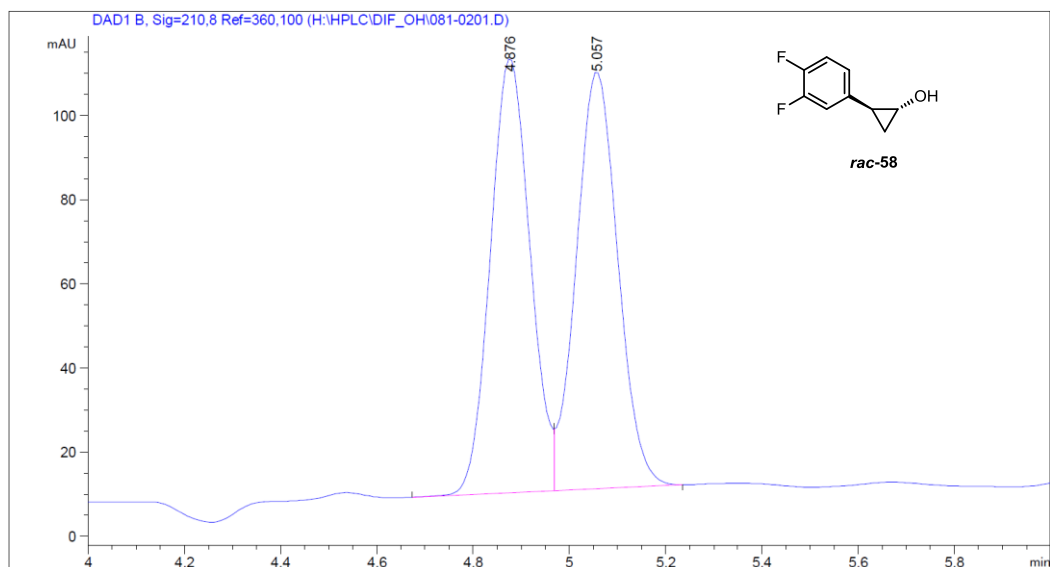
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.189	VB	0.0803	1.09376e4	2190.10815	97.6848
2	4.736	VB	0.0853	259.22772	47.75568	2.3152

Totals : 1.11969e4 2237.86383

Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 99.5:0.5 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, $\lambda = 210$ nm.

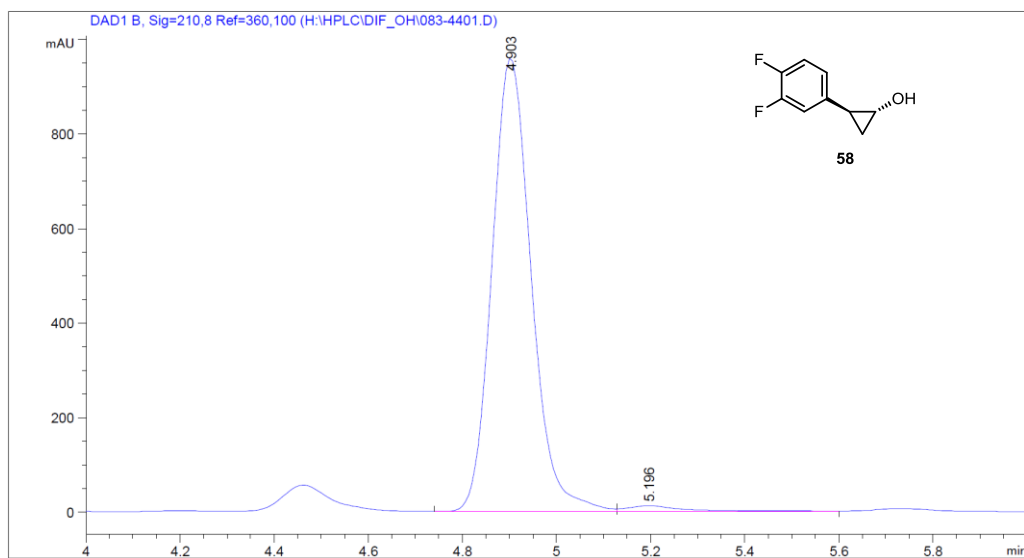
HPLC traces for compound **58**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.876	BV	0.0909	592.21167	103.34051	49.7869
2	5.057	VB	0.0943	597.28027	99.18047	50.2131

Totals : 1189.49194 202.52098



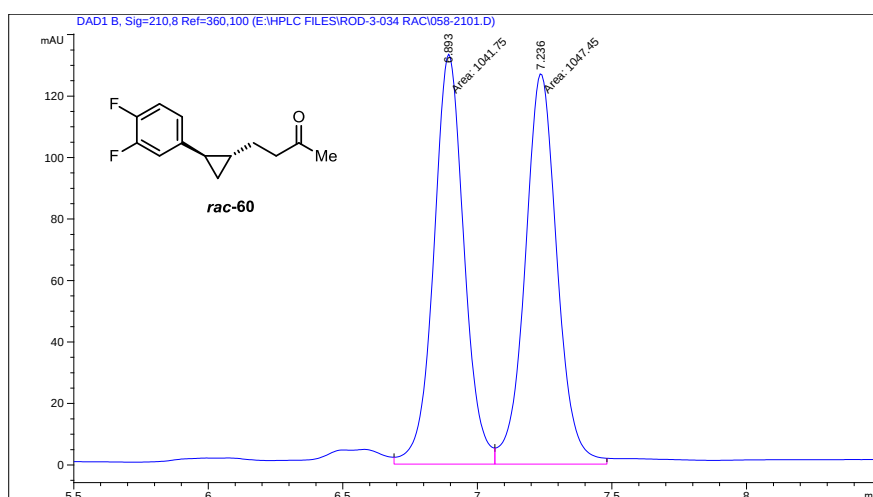
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.903	BV	0.0894	5545.88037	959.75226	98.2949
2	5.196	VB	0.1126	96.20422	12.11654	1.7051

Totals : 5642.08459 971.86880

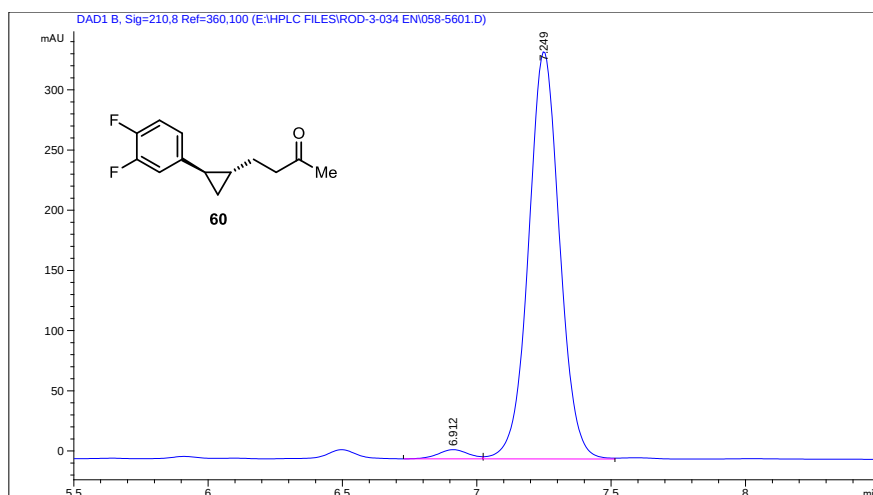
Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 90:10 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, λ = 210 nm.

HPLC traces for compound **60**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.893	MF	0.1301	1041.75183	133.44209	49.8635
2	7.236	FM	0.1373	1047.45435	127.16975	50.1365
Totals :		2089.20618	260.61184			

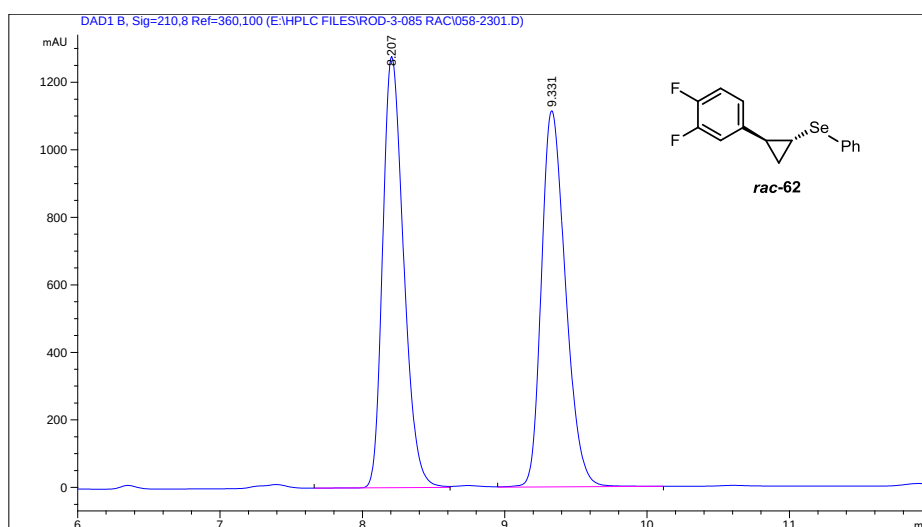


Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.912	BV	0.1189	59.78262	7.67224	2.1498
2	7.249	VV	0.1217	2721.03906	338.64072	97.8502
Totals :		2780.82168	346.31295			

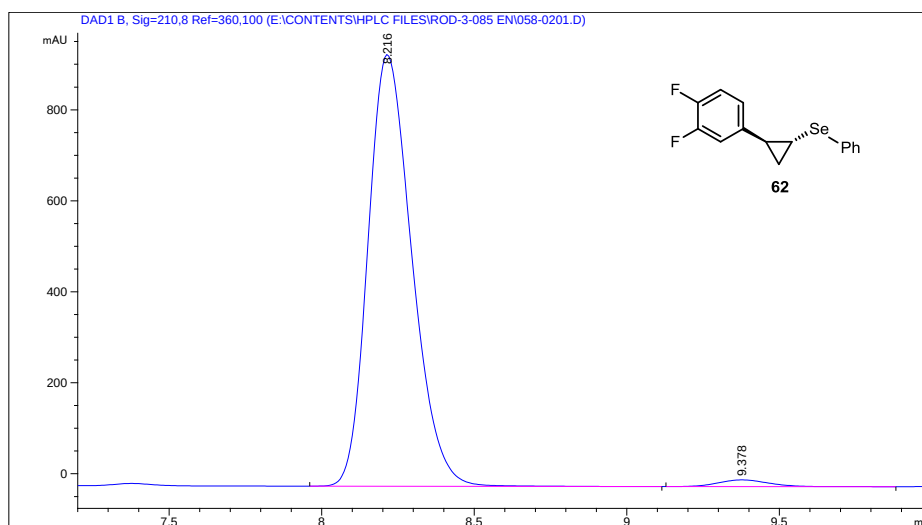
Analysis Conditions: Daicel Chiralpak ID column (0.46 cm internal diameter x 25 cm), temperature 25 °C, eluent 95.0:5.0 *i*-hexane:*i*-PrOH, flow rate 1.00 mL/min, λ = 210.8 nm.

HPLC traces for compound **62**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.207	BV	0.1592	1.30563e4	1277.38867	49.8750
2	9.331	VB	0.1834	1.31217e4	1114.51318	50.1250
Totals :		2.61780e4	2391.90186			

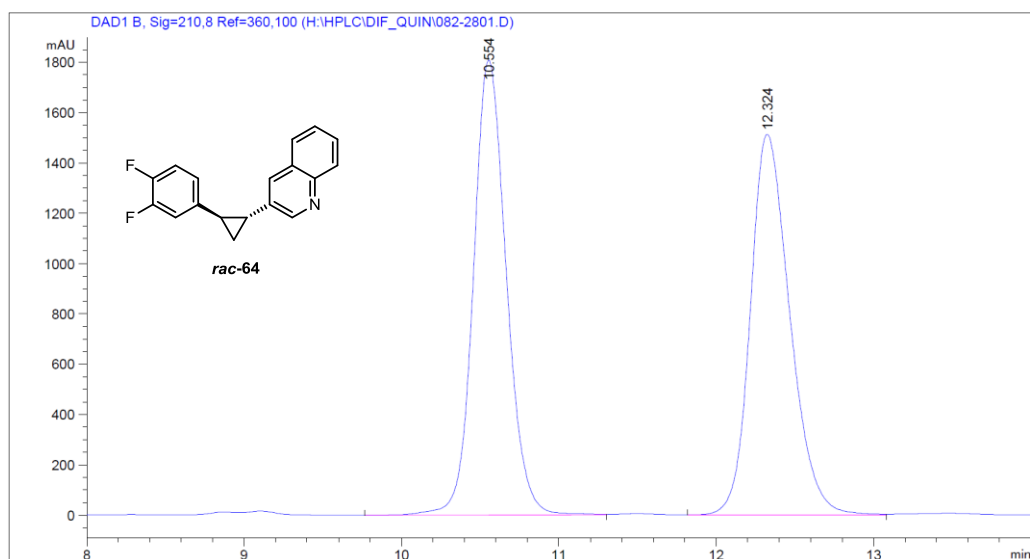


Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.216	BB	0.1546	9482.28125	948.81836	98.2597
2	9.378	BB	0.1770	167.94472	14.73244	1.7403
Totals :		9650.22597	963.55080			

Analysis Conditions: Daicel Chiralpak OJH column (0.46 cm internal diameter x 25 cm), temperature 25 °C, eluent 90.0:10.0 i-hexane:i PrOH, flow rate 1.00 mL/min, λ = 210.8 nm.

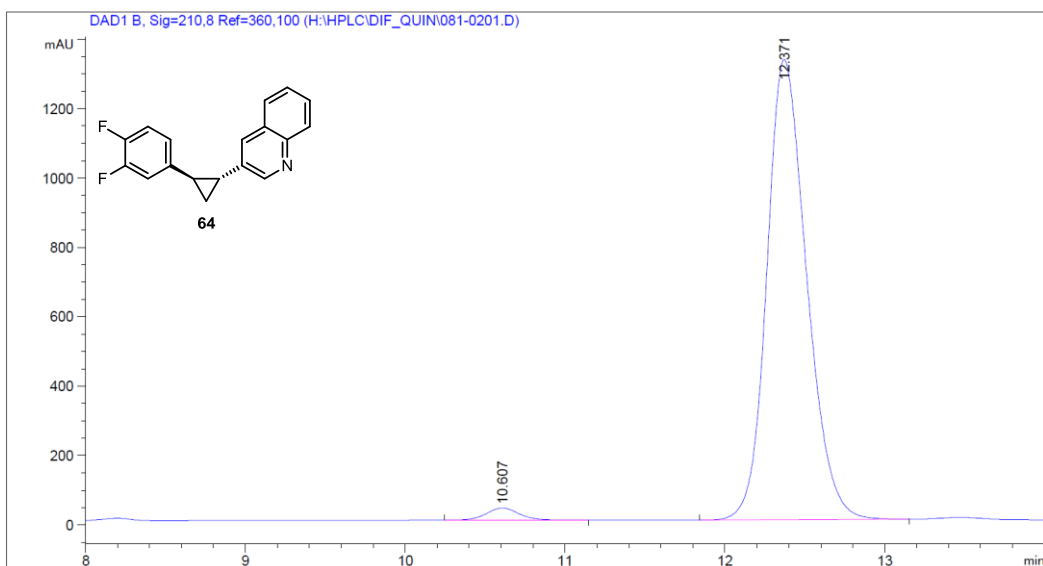
HPLC traces for compound **64**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.554	BV	0.2237	2.63000e4	1807.95520	49.9712
2	12.324	BV	0.2670	2.63303e4	1513.08972	50.0288

Totals : 5.26302e4 3321.04492



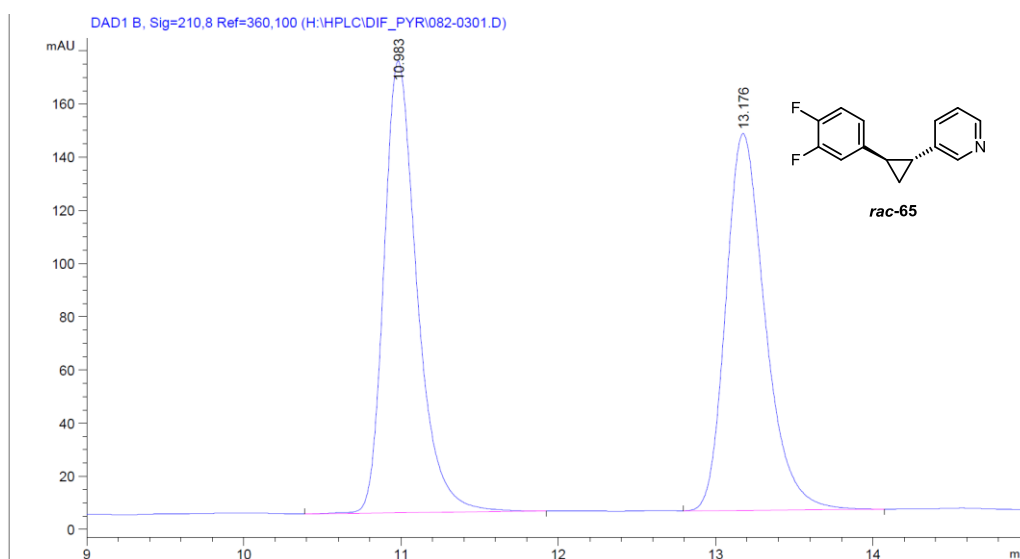
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.607	BB	0.2212	497.52750	34.72393	2.1226
2	12.371	BB	0.2658	2.29423e4	1326.60889	97.8774

Totals : 2.34398e4 1361.33281

Analysis Conditions: Daicel Chiralpak ID column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, λ = 210 nm.

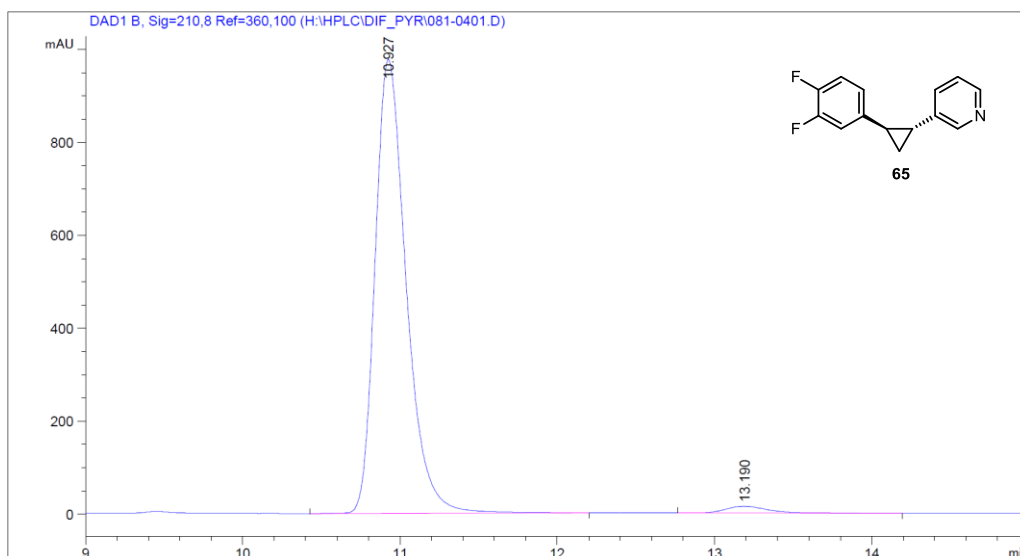
HPLC traces for compound **65**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.983	BB	0.2229	2489.47192	169.97118	50.2663
2	13.176	BB	0.2648	2463.09595	141.67099	49.7337

Totals : 4952.56787 311.64217



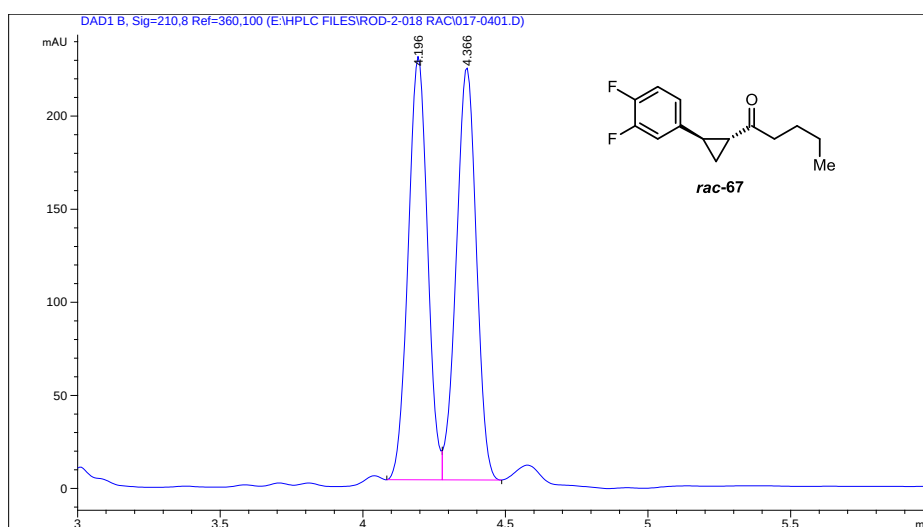
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.927	BB	0.2102	1.34235e4	977.64905	97.9864
2	13.190	BB	0.2833	275.84467	14.81104	2.0136

Totals : 1.36993e4 992.46009

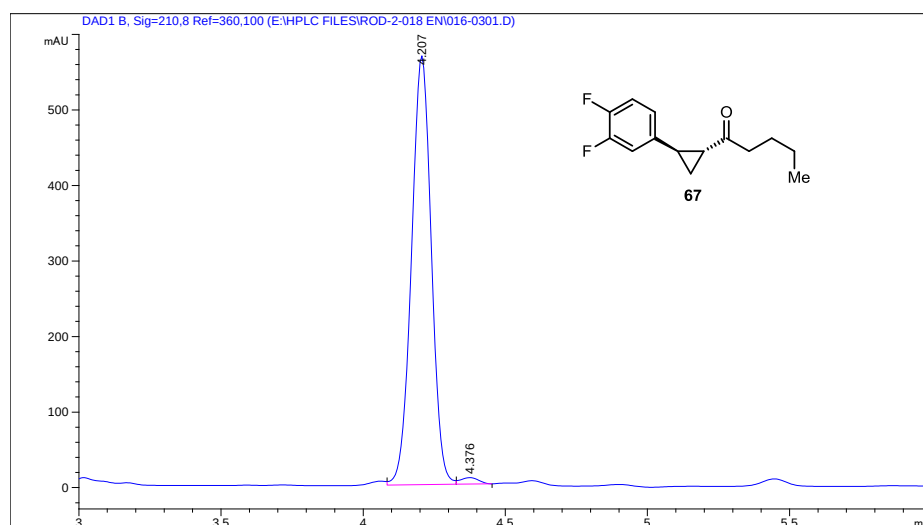
Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, λ = 210 nm.

HPLC traces for compound **67**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.207	BV	0.1592	1.30563e4	1277.38867	49.8750
2	9.331	VB	0.1834	1.31217e4	1114.51318	50.1250
Totals :		2.61780e4	2391.90186			

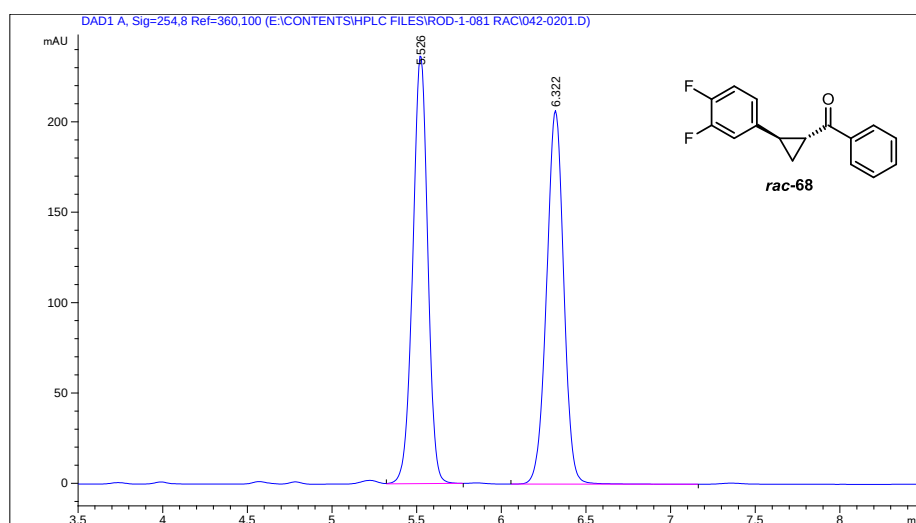


Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.207	VV	0.0744	2746.87720	567.85583	98.6367
2	4.376	VB	0.0692	37.96592	8.64301	1.3633
Totals :		2784.84311	576.49884			

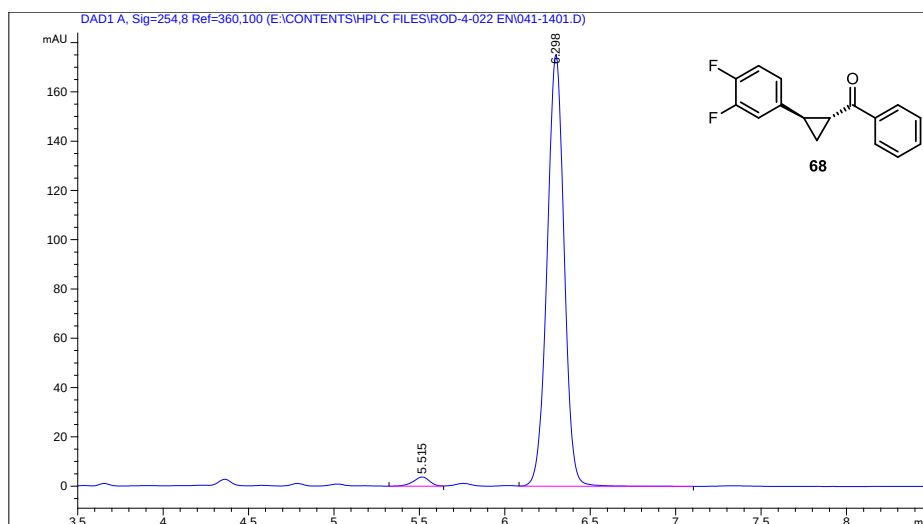
Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25 °C, eluent 90.0:10.0 i-hexane:i PrOH, flow rate 1.00 mL/min, λ = 210 nm.

HPLC traces for compound **68**:



Signal 1: DAD1 A, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.526	VB	0.0956	1455.95679	237.10577	50.0515
2	6.322	BB	0.1080	1452.95996	206.74487	49.9485
Totals :		2908.91675	443.85065			

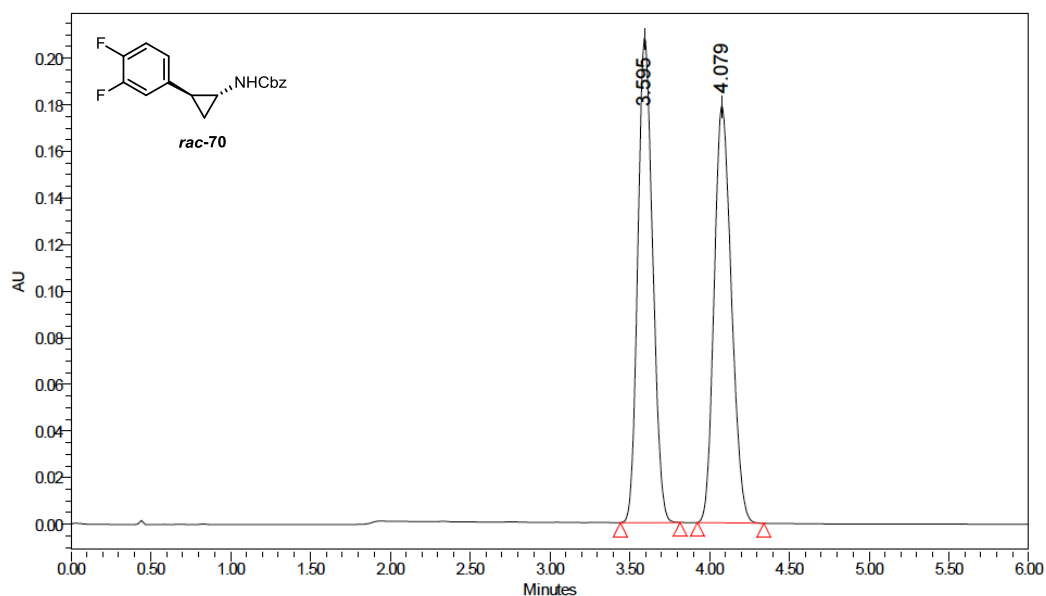


Signal 1: DAD1 A, Sig=254,8 Ref=360,100

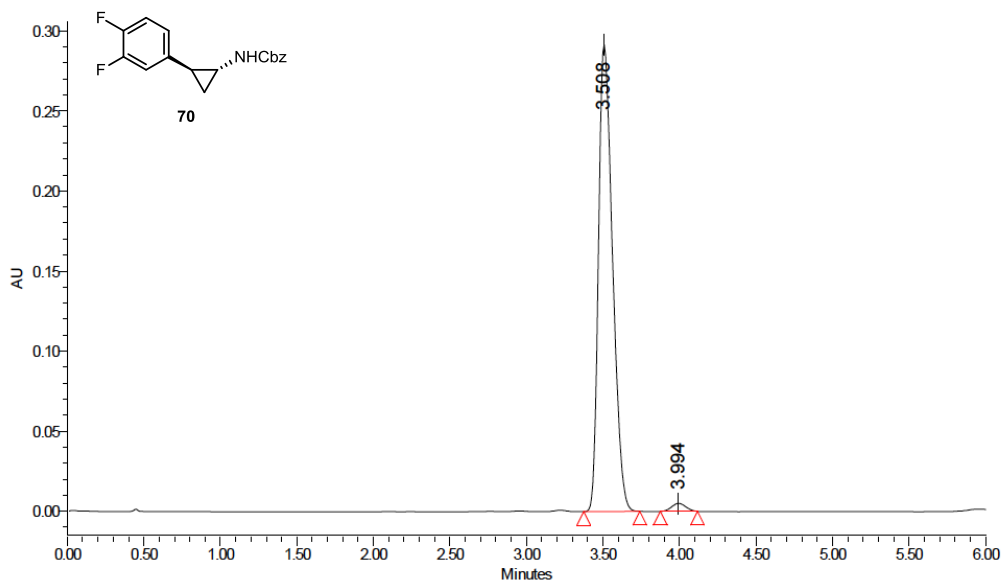
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.515	BV	0.1015	24.68592	3.71522	1.9971
2	6.298	VV	0.1066	1211.40955	175.32248	98.0029
Totals :		1236.09546	179.03770			

Analysis Conditions: Daicel Chiralpak IA column (0.46 cm internal diameter x 25 cm), temperature 25 °C, eluent 90.0:10.0 i-hexane:i PrOH, flow rate 1.00 mL/min, λ = 254.8 nm.

SFC traces for compound **70**:



	Retention Time	Area	% Area	K	N	USP Resolution	Width @ 50%
1	3.595	1350595	50.01	0.000	6771.9		1.018138e-001
2	4.079	1350145	49.99	0.135	6361.1	2.508	1.183135e-001

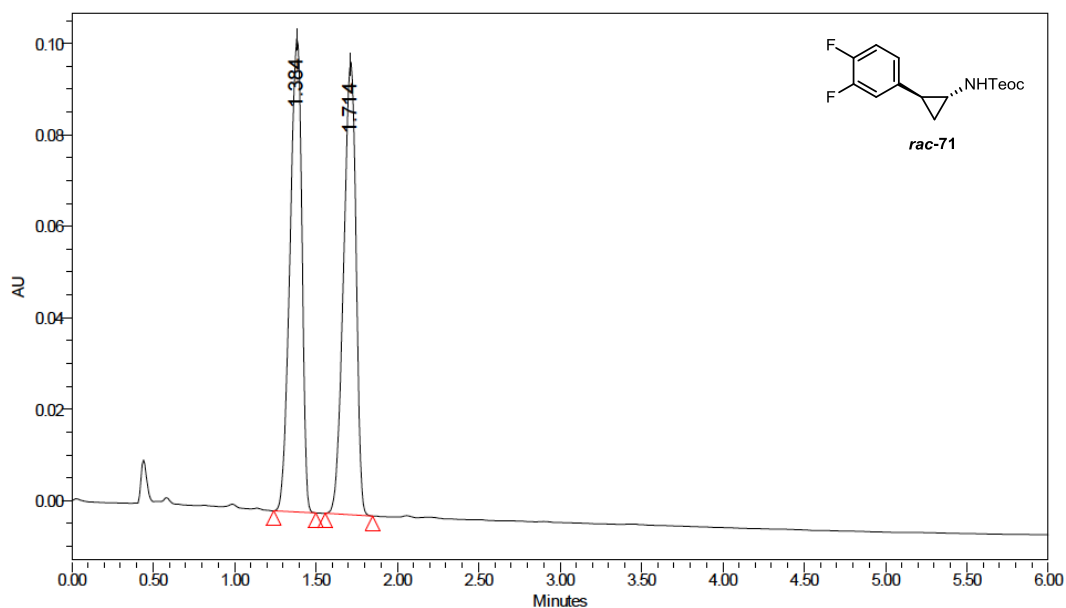


	Retention Time	Area	% Area	K	N	USP Resolution
1	3.508	1859770	98.30	0.000	6637.4	
2	3.994	32233	1.70	0.139	8196.1	2.753

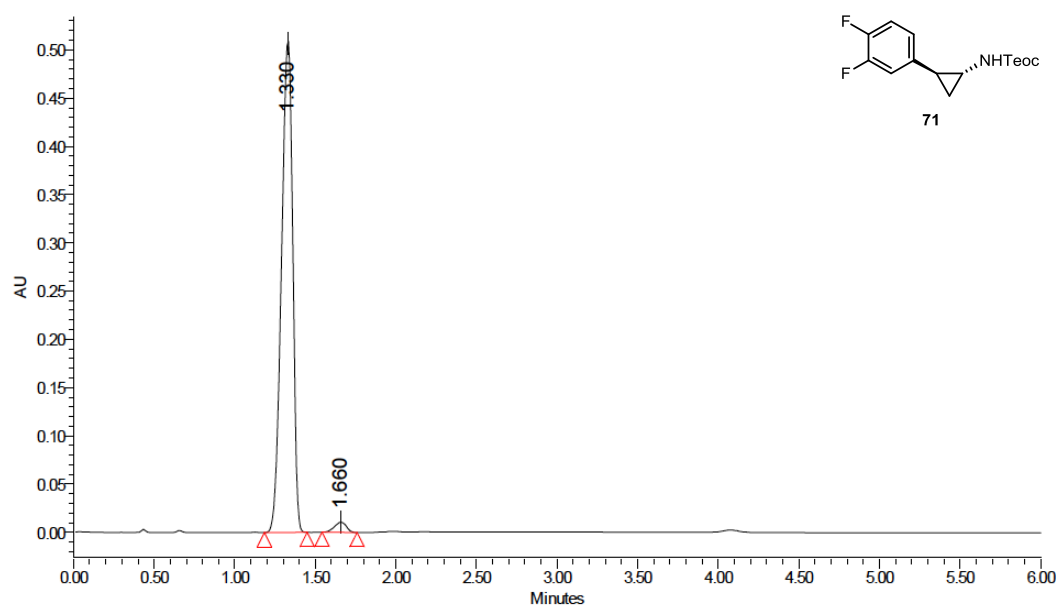
ee = 96.6

Analysis Conditions: YMC SA (IA) column (150 mm × 4.6 mm, 3Å particle size), temperature 40 °C, pressure 120 bars, eluent 95:5 scCO₂:EtOH, flow rate 3.50 mL/min, λ = 220 nm.

SFC traces for compound **71**:



	Retention Time	Area	% Area	K	N	USP Resolution	Width @ 50%
1	1.384	525768	49.94	0.000	1641.2		8.139272e-002
2	1.714	526961	50.06	0.238	2303.7	2.347	8.441027e-002

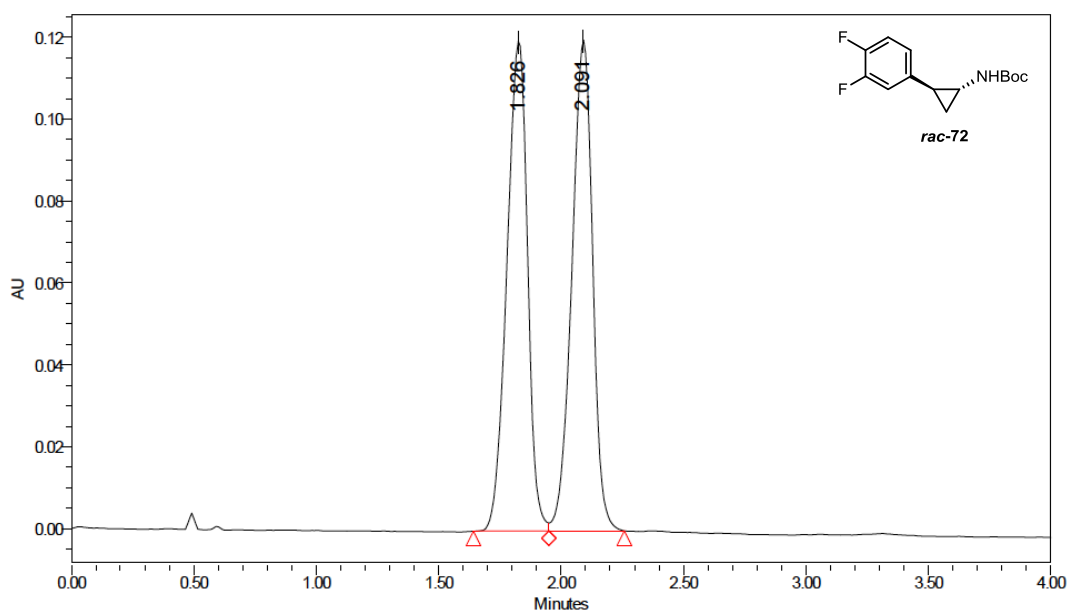


	Retention Time	Area	% Area	K	N	USP Resolution
1	1.330	2461655	97.84	0.000	1687.0	
2	1.660	54359	2.16	0.248	2262.9	2.447

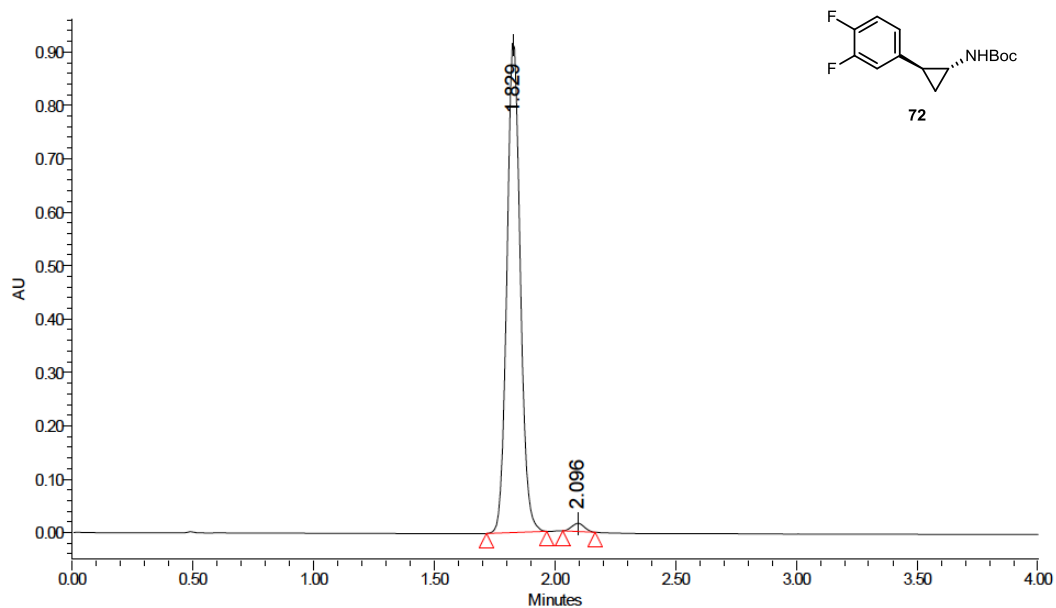
ee = 95.7

Analysis Conditions: Lux C4 column (150 mm × 4.6 mm, 3Å particle size), temperature 40 °C, pressure 120 bars, eluent 95:5 scCO₂:EtOH, flow rate 3.50 mL/min, λ = 230 nm.

SFC traces for compound 72:



	Retention Time	Area	% Area	K	N	USP Resolution	Width @ 50%
1	1.826	700871	49.85	0.000	2245.7		9.118497e-002
2	2.091	705081	50.15	0.145	2923.0	1.685	9.065000e-002

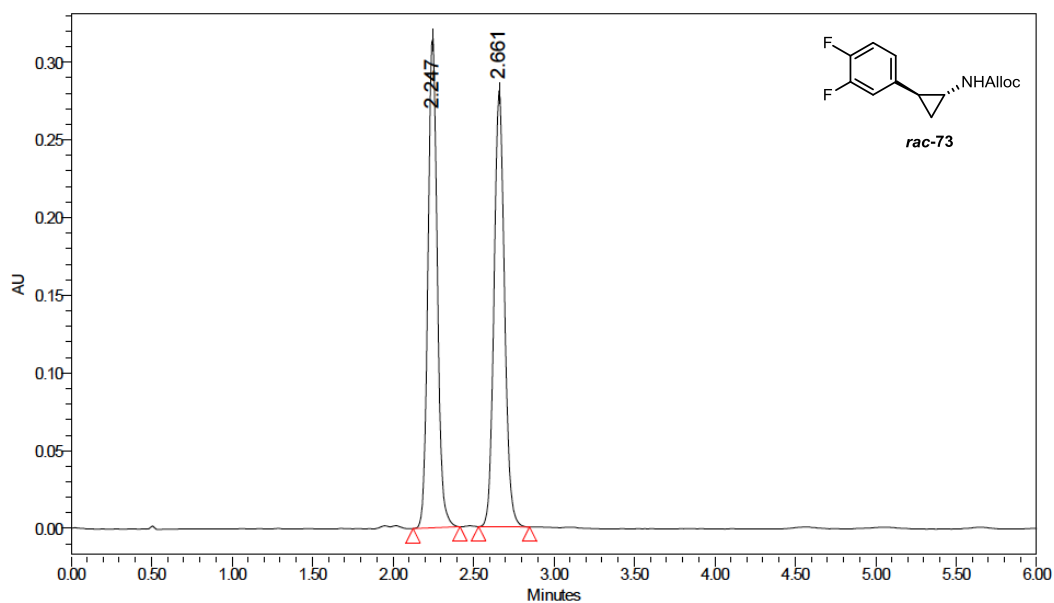


	Retention Time	Area	% Area	K	N	USP Resolution
1	1.829	3544081	98.49	0.000	5304.0	
2	2.096	54453	1.51	0.146	7337.4	2.632

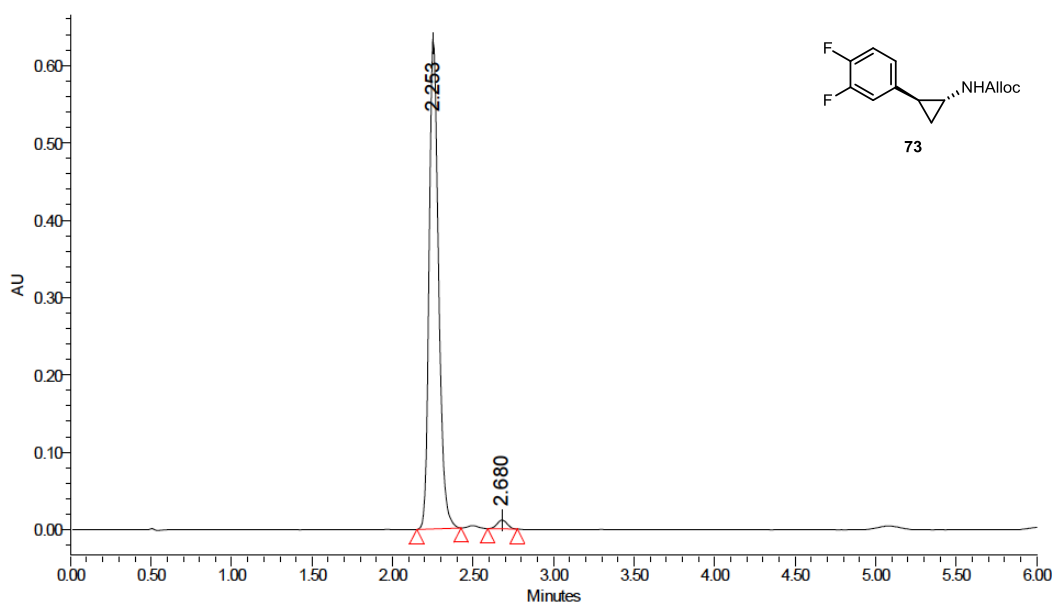
ee = 97.0

Analysis Conditions: (S,S)-Whelk-O1 column (150 mm × 4.6 mm, 3Å particle size), temperature 40 °C, pressure 120 bars, eluent 95:5 scCO₂:i-PrOH, flow rate 3.50 mL/min, λ = 220 nm.

SFC traces for compound 73:



	Retention Time	Area	% Area	K	N	USP Resolution	Width @ 50%
1	2.247	1272798	50.04	0.000	7450.3		6.133362e-002
2	2.661	1270887	49.96	0.184	8029.3	3.646	6.904967e-002

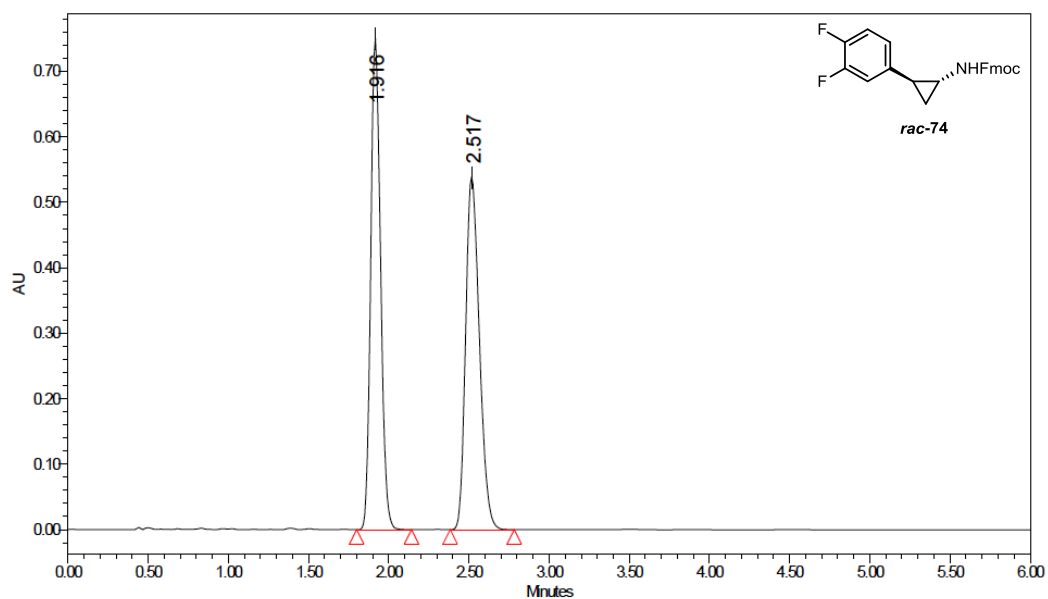


	Retention Time	Area	% Area	K	N	USP Resolution
1	2.253	2579875	98.13	0.000	7233.6	
2	2.680	49225	1.87	0.189	8476.3	3.764

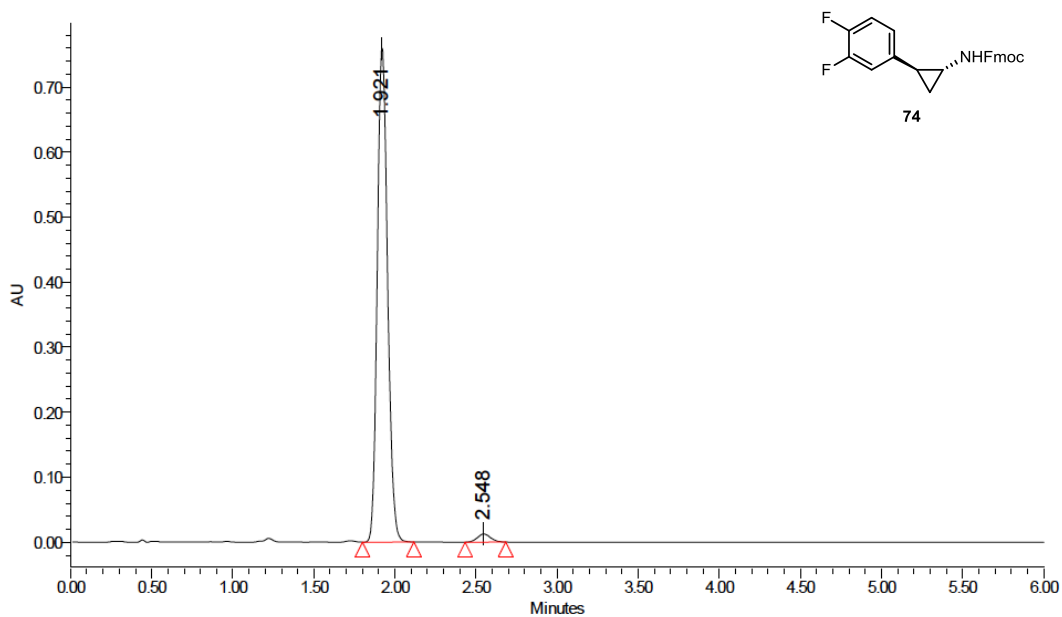
ee = 96.3

Analysis Conditions: (S,S)-Whelk-O1 column (150 mm × 4.6 mm, 3Å particle size), temperature 40 °C, pressure 120 bars, eluent 95:5 scCO₂:EtOH, flow rate 3.50 mL/min, λ = 230 nm.

SFC traces for compound **74**:



	Retention Time	Area	%Area	k'	N	USP Resolution	Width @50%
1	1.916	3196739	49.90	0.000	4605.0		6.585838e-002
2	2.517	3209635	50.10	0.314	4023.1	4.354	9.276896e-002

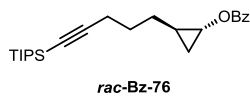
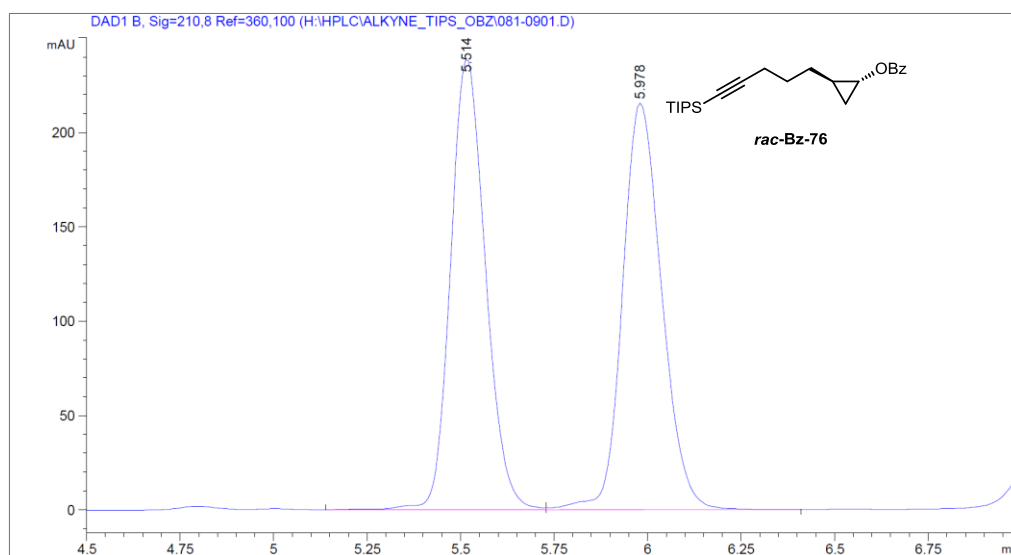


	Retention Time	Area	%Area	k'	N	USP Resolution
1	1.921	3358548	97.91	0.000	4317.4	
2	2.548	71521	2.09	0.326	4397.6	4.565

ee = 95.8

Analysis Conditions: Lux A1 (AD) column (150 mm × 4.6 mm, 3Å particle size), temperature 40 °C, pressure 120 bars, eluent 70:30 scCO₂:EtOH, flow rate 3.50 mL/min, λ = 254 nm.

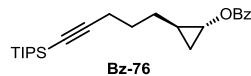
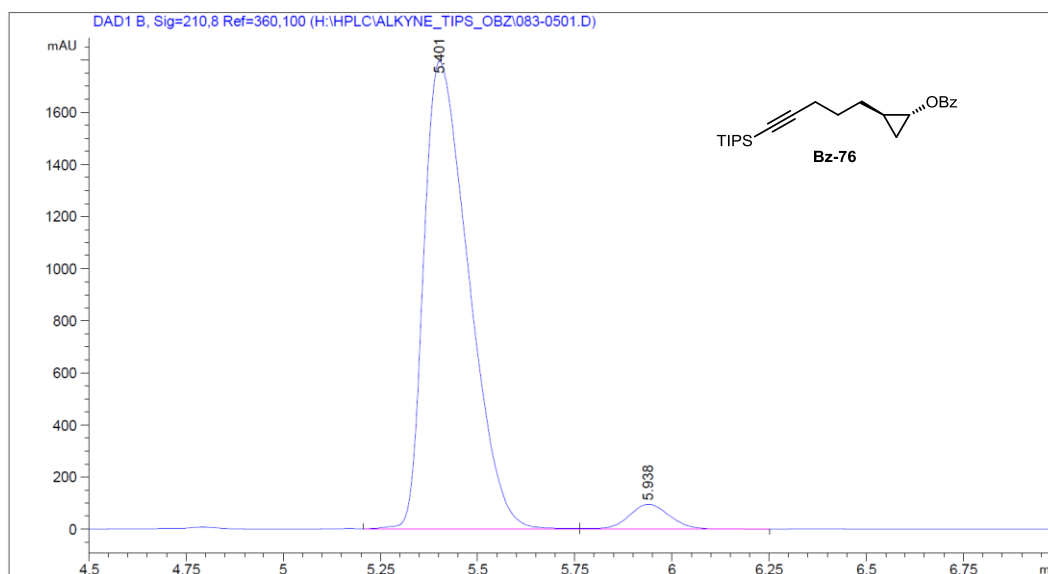
HPLC traces for compound **Bz-76**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.514	BV	0.0997	1550.22144	238.83098	49.6922
2	5.978	VB	0.1130	1569.42847	215.41148	50.3078

Totals : 3119.64990 454.24246



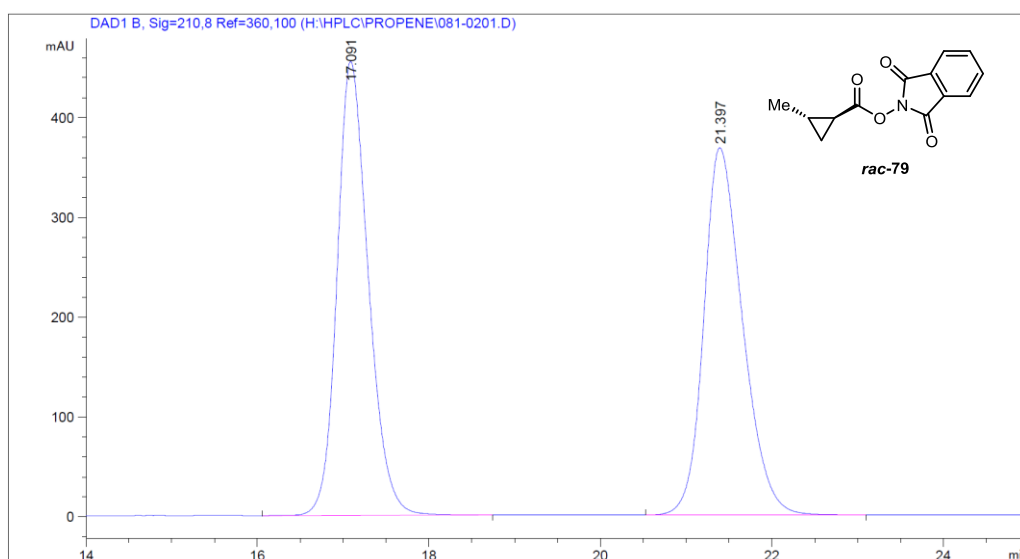
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.401	VV	0.1251	1.43463e4	1798.59119	95.4338
2	5.938	VB	0.1103	686.42438	95.04737	4.5662

Totals : 1.50327e4 1893.63856

Analysis Conditions: Daicel Chiralpak IC column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 99.5:0.5 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, λ = 210 nm.

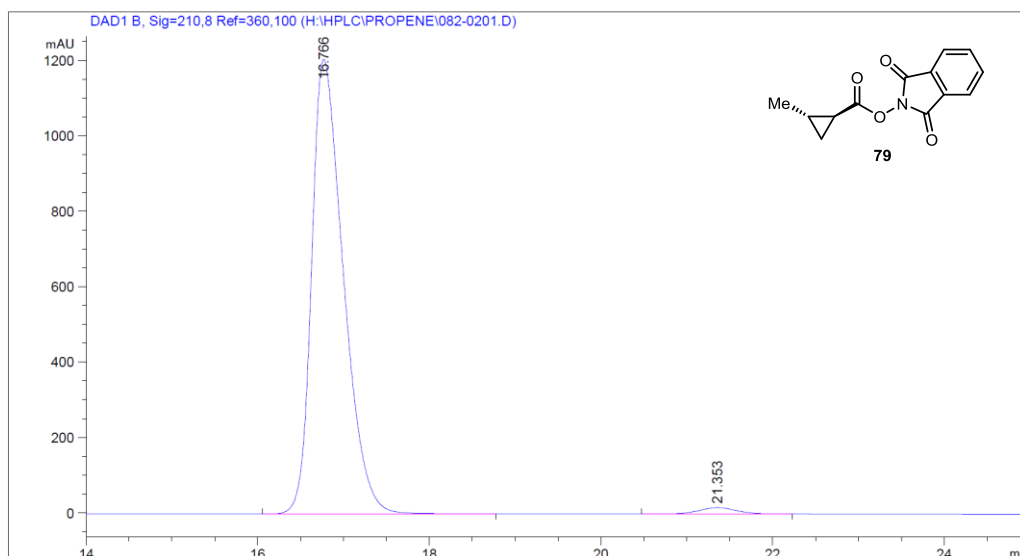
HPLC traces for compound **79**:



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.091	BB	0.3877	1.15278e4	454.86255	49.9291
2	21.397	BB	0.4787	1.15605e4	367.78223	50.0709

Totals : 2.30883e4 822.64478



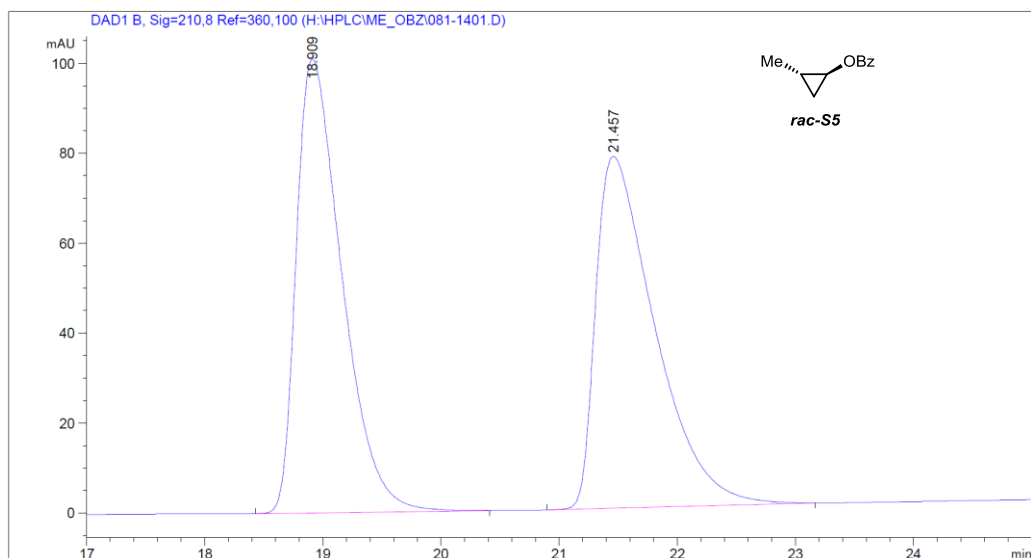
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.766	BB	0.3884	3.08534e4	1206.27197	98.3581
2	21.353	BB	0.4607	515.04126	17.13285	1.6419

Totals : 3.13684e4 1223.40483

Analysis Conditions: Daicel Chiralpak ID column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent 80:20 *i*-hexane:*i* PrOH, flow rate 1.00 mL/min, λ = 210 nm.

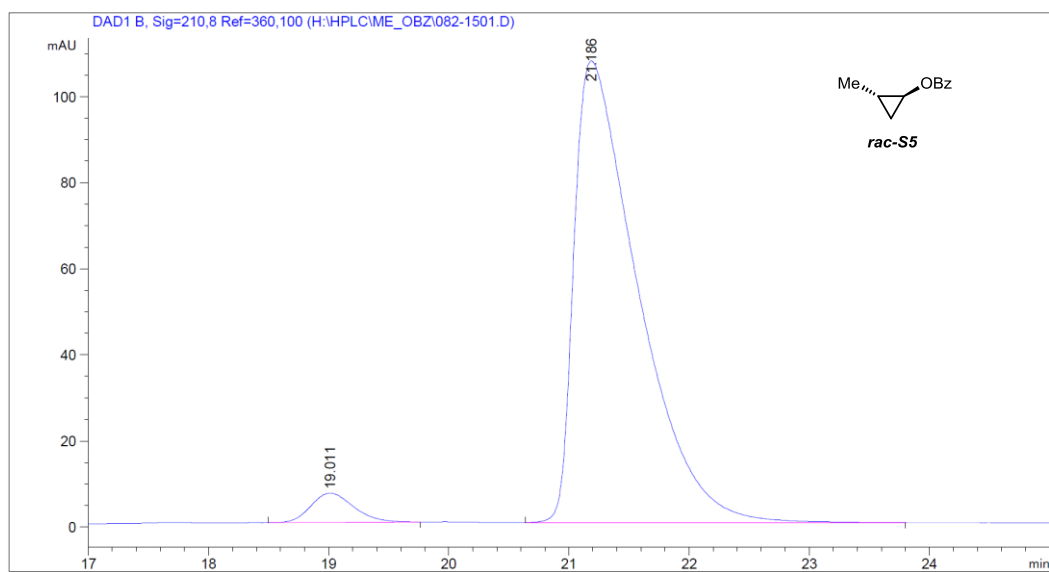
HPLC traces for compound **S5**



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.909	BB	0.4109	2706.91260	100.93965	49.8746
2	21.457	BB	0.5176	2720.52051	78.25485	50.1254

Totals : 5427.43311 179.19450



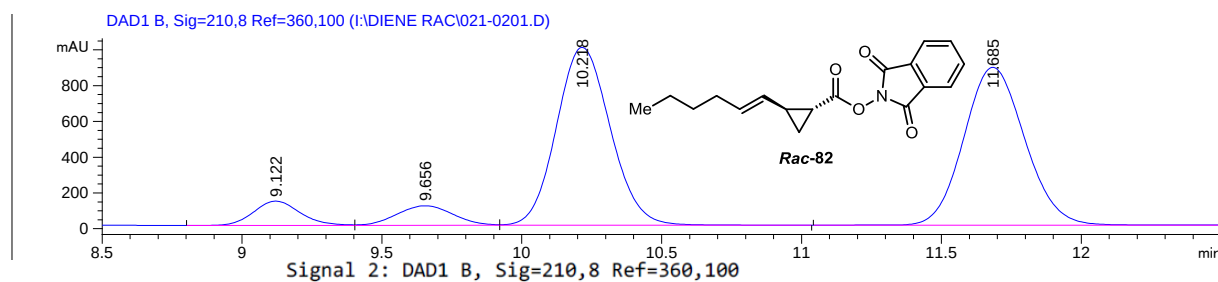
Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.011	BB	0.3781	168.38000	6.81767	4.0843
2	21.186	BB	0.5440	3954.24780	107.27836	95.9157

Totals : 4122.62781 114.09603

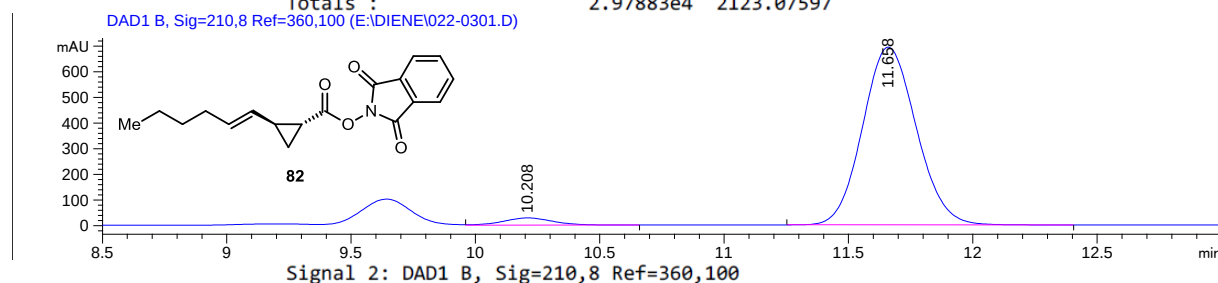
Analysis Conditions: Daicel Chiralpak AS-H column (0.46 cm internal diameter x 25 cm), temperature 25°C, eluent *i*-hexane, flow rate 0.5 mL/min, λ = 210 nm.

HPLC traces for compound **82**:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.122	BV	0.1764	1566.79883	136.03677	5.2598
2	9.656	VV	0.2204	1523.33313	109.45454	5.1139
3	10.218	VB	0.2084	1.33386e4	995.17572	44.7781
4	11.685	BB	0.2366	1.33595e4	882.40894	44.8483

Totals : 2.97883e4 2123.07597

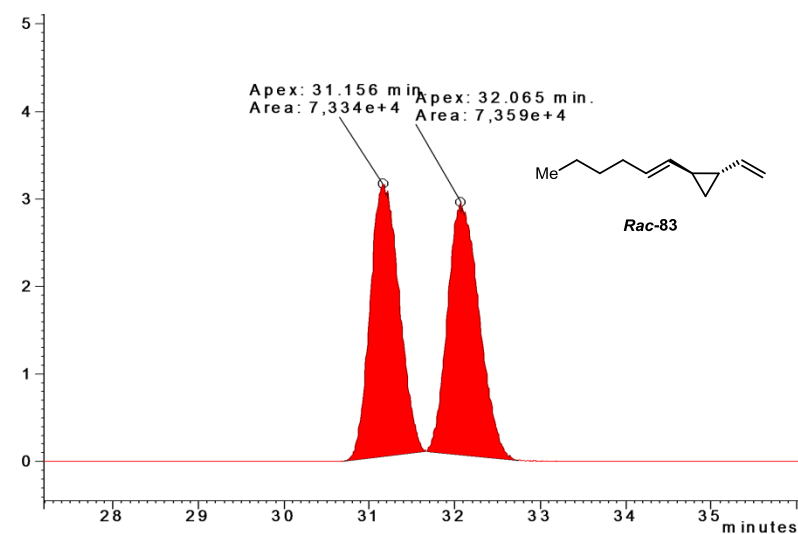


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.208	VB	0.2130	385.99384	27.97613	3.5759
2	11.658	BB	0.2332	1.04083e4	693.15558	96.4241

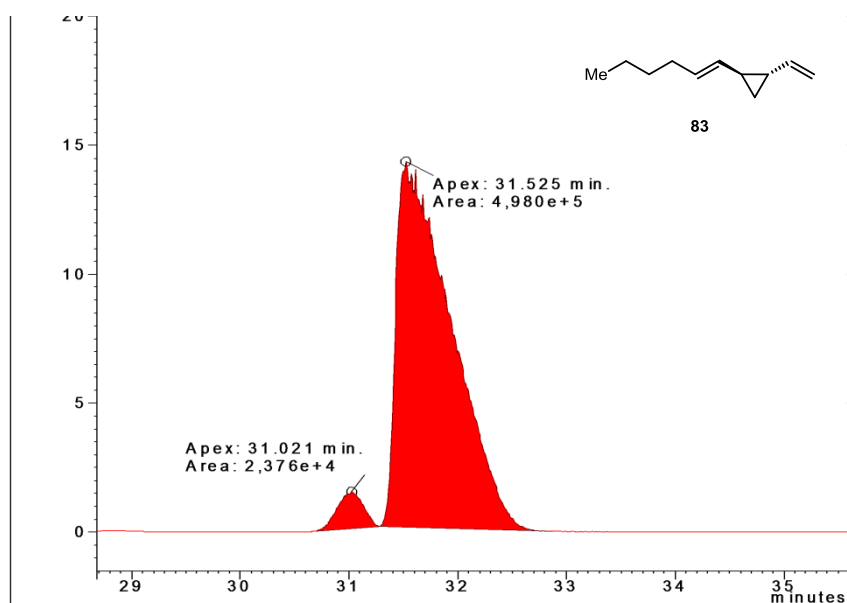
Totals : 1.07943e4 721.13170

Analysis Conditions: Daicel Chiralpak- IC column (0.46cm internal diameter x 25cm), temperature 25°C, eluent 90:10 iHexane:iPrOH, flow rate 1 mL/min, λ : 210 nm.

GC traces for compound **83**:



Peak	RetTime (min)	Area (TIC)	Area (%)
1	31.16	73340	49.9
2	32.07	73590	50.1



Peak	RetTime (min)	Area (TIC)	Area (%)
1	31.02	23760	4.5
2	31.53	498000	95.5

Analysis Conditions: Hydrodex-B6-TBDM column, 70 °C isothermal, $\tau_{\text{major}} = 31.5$ min, $\tau_{\text{minor}} = 31.0$ min.

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