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Supporting Information

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Enantioselective Protonations Catalyzed by Chiral Bicyclic Guanidine

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Supporting Information

General Information and Acknowledgements

General procedures and methods

Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in 4 mL vials with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile reagents/compounds was removed in high *vacuo* by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ~30 mmHg and heated with a water bath at 33°C using Heidolph or Büchi rotary evaporator with Eyela A-3S aspirator. The condenser was cooled with running water at 0°C. Suction filtration was conducted using Hirch Funnel.

ACE sealed tubes were used for reactions that required heating unless otherwise stated. Reactions requiring temperatures up to −60°C were stirred in Thermo Neslab CB-80 cryobath using Cryotrol temperature controller. Reactions requiring temperatures up to −40°C were stirred in either Thermo Neslab CB-60 with Cryotrol temperature controller or Eyela PSL-1400 with digital temperature controller cryobaths. HPLC grade isopropanol was used as the bath medium. Reactions requiring temperatures up to −78°C were stirred in either ether/dry ice or acetone/dry ice baths. Reactions requiring temperatures up to −116°C were stirred in ether/liquid nitrogen slush bath in a Dewar apparatus. Temperature was maintained by adding additional liquid nitrogen whenever necessary so that solid ether was always present.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated plates, Merck 60 F_{254}. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining with iodine, $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 60 (0.040 mm - 0.063 mm, Merck). Columns were packed as slurry of silica gel in hexane and equilibrated with the appropriate solvent/solvent mixture prior to use. The analyte was loaded neat or as a concentrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentations

Proton nuclear magnetic resonance (^{1}H NMR), carbon NMR (^{13}C NMR), phosphorous NMR (^{31}P NMR) and fluorine NMR (^{19}F NMR) spectra were recorded in $CDCl_3$ otherwise stated. ^{1}H (500.1331 MHz), ^{13}C (125.7710 MHz) with complete proton decoupling and ^{31}P (202.4462 MHz) with complete proton decoupling NMR were performed on a 500 MHz Bruker AMX NMR spectrometer. ^{19}F NMR (282.3761

MHz) was performed on a 300 MHz Bruker ACF NMR spectrometer. ^{1}H-^{1}H 2D Correlation (COSY) and ^{1}H Nuclear Overhauser Effect (NOESY) NMR were performed on a 500 MHz Bruker AMX NMR spectrometer. Chemical shifts were reported as δ in units of parts per million (ppm) downfield from tetramethylsilane (δ 0.00), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *quintet*, *sextet*, *septet*, *m* (multiplets), *dd* (doublet of doublets), *ddd* (doublet of doublet of doublets), *dt* (doublet of triplets), *dq* (doublet of quartets), *dm* (doublet of multiplets), and *br* (broad). Coupling constants (*J*) were recorded in Hertz (Hz). The number of proton atoms (*n*) for a given resonance was indicated by *n*H. The number of carbon atoms (*n*) for a given resonance was indicated by *n*C. The number of fluorine atoms (*n*) for a given resonance was indicated by *n*F.

High resolution Fast Atom Bombardment (FAB) mass spectra were performed by Mdm Wong Lai Kwai and Mdm Lai Hui Ngee from the Chemical and Molecular Analysis Centre (CMAC) of the National University of Singapore. They were obtained on a Finnigan/MAT 95XL-T spectrometer. High resolution Electrospray Ionization (ESI) mass spectra were obtained on a Shimadzu LCMS-IT-TOF spectrometer including an SPD-M20A prominence PDA detector, CBM-20A prominence communication bus module, CTO-20A prominence column oven, SIL-20AC prominence auto sampler, DGU-20A3 prominence degasser and LC-20AD prominence liquid chromatograph. Shimadzu Formula Predictor Software was used to process the data. MS and HRMS were reported in units of mass of charge ratio (m/z). Mass samples were dissolved in CH_3CN (HPLC Grade) unless otherwise stated. Infrared spectra (IR) were recorded by dissolving samples in $CHCl_3$ and spread as a thin film on NaCl cells unless otherwise stated. BIO-RAD Excalibur FTS3000 FTIR spectrometer was used to record the IR spectra. Optical rotations were recorded on a Jasco DIP-1000 polarimeter with a sodium lamp of wavelength 589 nm and reported as follows; $[\alpha]_{\lambda}^{T^{\circ}C}$ (c = g/100 mL, solvent). Melting points were determined on a BÜCHI B-540 melting point apparatus.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis on Shimadzu HPLC units, including an SPD-20A prominence UV/VIS detector, CBM-20A prominence communication bus module, CTO-20A prominence column oven, SIL-20AC prominence auto sampler, DGU-20A3 prominence degasser and two LC-20AD prominence liquid chromatographs. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Single crystal X-Ray diffraction studies were obtained on a Bruker-AXS Smart Apex CCD single-crystal diffractometer.

Materials

All commercial reagents were purchased from Sigma-Aldrich, Fluka, Alfa Aesar, Merck, TCI, Acros and Matrix of the highest purity grade. They were used without further purification unless specified. Deuterium oxide of 99.96% purity in ampoules was purchased from Cambridge Isotope Laboratories. All solvents used, mainly hexane (Hex), ethyl acetate (EtOAc), and dichloromethane (DCM), were distilled. Anhydrous DCM and MeCN were distilled from CaH_2. Anhydrous THF, Et_2O and toluene were distilled from Na/benzophenone. Saturated solutions of sodium chloride, sodium bicarbonate, and sodium carbonate were prepared from the respective solids. All compounds synthesized were stored in fridge and light-sensitive compounds were protected with aluminium foil. Catalyst **1** was synthesized previously by our group.[1]

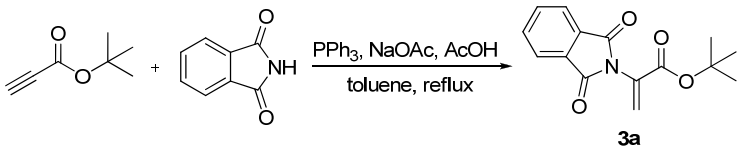
Acknowledgements

We will like to thank Dr Koh Lip Lin, Ms Tan Geok Kheng and Ms Woo Su Fen from the Chemical and Molecular Analysis Centre (CMAC) of the National University of Singapore for solving the X-Ray crystal structures.

[1] W. Ye, D. Leow, S. L. M. Goh, C.-T. Tan, C.-H. Chian, C.-H. Tan, *Tetrahedron Lett.* **2006**, *47*, 1007–1010.

Syntheses and Characterizations of Starting Materials

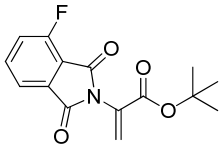
Representative procedure for synthesis of 2-phthalimidoacrylates[2]



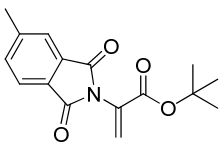
3a

A solution of phthalimide (441 mg, 3.00 mmol, 1.00 equiv), triphenylphosphine (78.7 mg, 0.300 mmol, 0.10 equiv.), and sodium acetate (123 mg, 1.50 mmol, 0.50 equiv.) in 3.00 mL of toluene was refluxed for 10 min. Subsequently, acetic acid (172 μL, 3.00 mmol, 1.00 equiv.) and *tert*-butyl propiolate (412 μL, 3.00 mmol, 1.00 equiv.) were added at RT. The reaction was refluxed for 18 h after which it was directly purified by flash chromatography to yield phthalimide **3a**.

***tert*-Butyl 2-phthalimidoacrylate** (**3a**) Yellow solid; R_f (Hex/EtOAc = 2/1): 0.33; mp: 91.1–91.4°C; 90% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.44 (*s*, 9H), 5.87 (*s*, 1H), 6.53 (*s*, 1H), 7.71–7.74 (*m*, 2H), 7.83–7.87 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz, $CDCl_3$): δ 27.7, 82.6, 123.7, 126.5, 130.5, 131.7, 134.3, 161.1, 166.4 ppm; IR (film): 3680, 3480, 2982, 2935, 2256, 1790, 1767, 1724, 1641, 1610, 1470, 1388, 1370, 1299, 1258, 1213, 1145, 1106, 1087, 909, 888, 848, 731, 680, 650 cm^{-1}; HRMS (FAB): $C_{15}H_{16}O_4N_1^+$ ([M+H]$^+$), Calc. 274.1074, Found 274.1072.

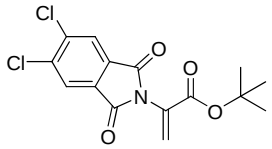


***tert*-Butyl 2-(3-fluoro-phthalimido)acrylate** (**3b**) Pale yellow solid; R_f (Hex/EtOAc = 4/1): 0.39; 83% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.47 (*s*, 9H), 5.90 (*s*, 1H), 6.57 (*s*, 1H), 7.39–7.43 (*m*, 1H), 7.71–7.78 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz, $CDCl_3$): δ 27.7, 82.9, 117.67 (*d*, $J_{C\text{-}F}$ = 11.9 Hz), 119.98 (*d*, $J_{C\text{-}F}$ = 3.7 Hz), 122.6, 122.8, 127.1, 133.9, 136.97 (*d*, $J_{C\text{-}F}$ = 7.3 Hz), 157.84 (*d*, $J_{C\text{-}F}$ = 266.7 Hz), 160.9, 165.3 (*m*) ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ −36.04 (*dd*, $J_{C\text{-}F}$ = 9.3, 3.1 Hz) ppm; IR (film): 3020, 1788, 1727, 1642, 1526, 1484, 1389, 1300, 1216, 1148, 929, 759, 669 cm^{-1}; HRMS (FAB): $C_{15}H_{15}O_4N_1F_1^+$ ([M+H]$^+$), Calc. 292.0980, Found 292.0984.



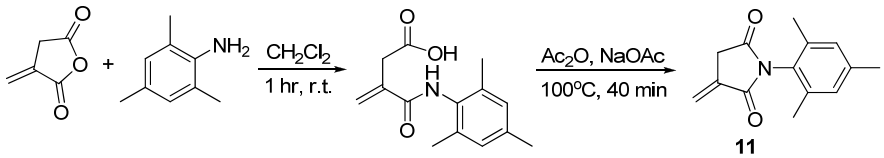
[2] B. M. Trost, G. R. Dake, *J. Am. Chem. Soc.* **1997**, *119*, 7595–7596.

***tert*-Butyl 2-(4-methyl-phthalimido)acrylate** (**3c**) Pale yellow solid; R_f (Hex/EtOAc = 4/1): 0.28; 85% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.46 (*s*, 9H), 2.51 (*s*, 3H), 5.87 (*s*, 1H), 6.54 (*s*, 1H), 7.53 (*d*, *J* = 7.6 Hz, 1H), 7.68 (*s*, 1H), 7.76 (*d*, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz, $CDCl_3$): δ 22.0, 27.8, 82.6, 123.7, 124.2, 126.4, 129.2, 130.6, 132.2, 134.9, 145.7, 161.2, 166.5, 166.7 ppm; IR (film): 2982, 1781, 1724, 1643, 1392, 1370, 1300, 1153, 1102, 907, 736, 650 cm^{-1}; HRMS (FAB): $C_{16}H_{18}O_4N_1^+$ ([M+H]$^+$), Calc. 288.1230, Found 288.1221.



***tert*-Butyl 2-(4,5-dichloro-phthalimido)acrylate** (**3d**) Yellow solid; R_f (Hex/EtOAc = 4/1): 0.43; 81% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.47 (*s*, 9H), 5.90 (*s*, 1H), 6.58 (*s*, 1H), 7.98 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz, $CDCl_3$): δ 27.8, 83.0, 125.8, 127.1, 130.3, 130.9, 139.4, 160.8, 164.5 ppm; IR (film): 2982, 2255, 1788, 1725, 1386, 1323, 1149, 909, 732 cm^{-1}; HRMS (FAB): $C_{15}H_{14}O_4N_1{}^{35}Cl_2^+$ ([M+H]$^+$), Calc. 342.0294, Found 342.0285.

Representative procedure for synthesis of itaconimides[3]

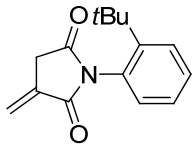


Itaconic anhydride (1.121 g, 10.00 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (8.00 mL) in a 25 mL round-bottomed flask with stirring. When all the itaconic anhydride was dissolved, the 2,4,6-trimethylaniline (1.352 g, 10.00 mmol, 1.00 equiv.) was added dropwise and the mixture stirred over an hour. The solvent was removed in vacuo. Acetic anhydride (3.30 mL, 35 mmol, 3.5 equiv.) and NaOAc (328 mg, 4 mmol, 0.40 equiv.) were added to the round-bottomed flask equipped with a glass stopper. The reaction mixture was refluxed for 40 minutes. The crude reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (3 × 40 mL). The organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed and purification of the crude product by flash column chromatography yielded the product **11**.

***N*-2,4,6-Trimethylphenyl itaconimide** (**11**) Pale yellow solid; R_f (Hex/EtOAc = 2/1): 0.63; mp: 120.1–120.6°C; 49% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.07 (*s*, 6H), 2.31 (*s*, 3H), 3.55 (*t*, *J* = 1.9 Hz, 2H), 5.74 (*t*, *J* = 1.9 Hz, 1H), 6.47 (*t*, *J* = 2.5 Hz, 1H), 6.98 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.7,

[3] M. P. Cava, A. A. Deana, K. Muth, M. J. Mitchell, *Org Syn. Coll.* **Vol V.**, 944–944.

21.0, 34.0, 121.4, 127.5, 129.3, 133.2, 135.2, 139.4, 168.4, 172.7 ppm; IR (film): 3155, 2931, 2531, 2404, 2255, 1714, 1481, 1379, 1266, 1161, 1028, 908, 732, 650, 584 cm^{-1}; HRMS (FAB): $C_{14}H_{16}O_2N_1^+$ ($[M+H]^+$), Calc. 230.1176, Found 230.1168.



Itconimide **14** exists as a pair of atropisomers. They can be separated by chiral HPLC analysis.

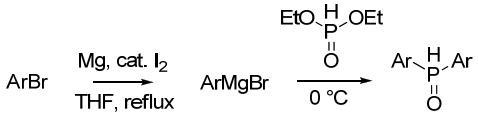
***N*-2-*tert*-Butylphenyl itaconimide** (**14**) Pale yellow solid; R_f (Hex/EtOAc = 2/1): 0.25; mp: 137.0–137.4°C; 51% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.30 (*s*, 9H), 3.51 (*t*, *J* = 2.5 Hz, 2H), 5.74 (*t*, *J* = 1.9 Hz, 1H), 6.47 (*t*, *J* = 2.5 Hz, 1H), 6.89 (*dd*, *J* = 8.2, 1.9 Hz, 1H), 7.30 (*dt*, *J* = 8.2, 1.9 Hz, 1H), 7.39–7.43 (*m*, 1H), 7.60 (*dd*, *J* = 8.2, 1.3 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 31.5, 34.2, 35.5, 121.6, 127.3, 128.8, 129.7, 130.1, 130.5, 133.2, 148.0, 169.8, 174.0 ppm; IR (film): 2967, 2521, 2255, 1896, 1714, 1483, 1380, 1265, 1156, 908, 731, 650 cm^{-1}; HRMS (FAB): $C_{15}H_{18}O_2N_1^+$ ($[M+H]^+$), Calc. 244.1332, Found 244.1332. HPLC analysis: Chiralcel OF (Hex/IPA = 80/20, 1.0 mL/min, 214 nm, 23°C) 13.2, 34.9 min.

Representative procedure for synthesis of benzhydryl mercaptan[4]

Benzhydryl mercaptan **2k** was prepared from the literature protocol.[4] Data was consistent with the literature.

Representative procedure for synthesis of secondary phosphine oxides[5]

Secondary phosphine oxides **10e** and **10h** were prepared from the literature protocol.[5] Secondary phosphine oxides **10a**, **10c** and **10d** were previously prepared by our group.[6] Data for all previously reported secondary phosphine oxides were consistent with the literature.



Arylbromide [Ar = 1-(2-Me-naphthyl)-] (780 μL, 5.00 mmol, 1.65 equiv.) was added dropwise to magnesium turnings (243 mg, 10.00 mmol, 3.30 equiv.) and catalytic iodine in THF (6.0 mL). The heat evolved by the reaction mixture was used to maintain it at reflux. Another 780 μL of arylbromide (5.00 mmol, 1.65 equiv.) was added dropwise to the reaction mixture to maintain the heat. The mixture was

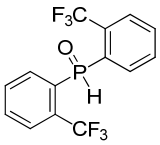
[4] T. Nishio, *J. Chem. Soc., Perkin Trans. 1* **1993**, 1113–1117.

[5] C. A. Busacca, J. C. Lorenz, N. Grinberg, N. Haddad, M. Hrapchak, B. Latli, H. Lee, P. Sabila, A. Saha, M. Sarvestani, S. Shen, R. Varsolona, X. Wei, C. H. Senanayake, *Org. Lett.* **2005**, *7*, 4277–4280.

[6] X. Fu, Z. Jiang, C.-H. Tan, *Chem. Commun.* **2007**, *47*, 5058–5060.

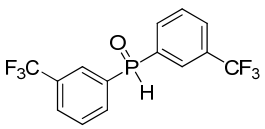
refluxed for until most of the magnesium turnings had reacted. Diethyl phosphite (386 μL, 3.00 mmol, 1.00 equiv.) was then added dropwise at 0°C. The reaction mixture was warmed up slowly to RT and stirred for an additional 2 hours. Once the reaction was completed, saturated aqueous NH_4Cl was added until no further precipitate was observed. The mixture was then concentrated in vacuo and extracted with CH_2Cl_2 (3 x 20 mL). The organic layer was washed with brine and dried over Na_2SO_4. It was concentrated in vacuo and purified by flash column chromatography. The product collected after FC was further re-crystallized from EtOAc to yield the pure secondary phosphine oxide product **10b**.

Bis-(2-Me-naphth-1-yl)-phosphine oxide (**10b**) White solid; R_f (Hex/EtOAc = 1/1): 0.24; mp: 149.3–149.6°C; 74% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.45 (*s*, 6H), 7.20–7.22 (*m*, 2H), 7.41–7.46 (*m*, 4H), 7.80 (*d*, J = 7.6 Hz, 2H), 7.86 (*d*, J = 8.9 Hz, 2H), 8.86–8.88 (*m*, 2H), 9.25 (*d*, $J_{P\text{-}H}$ = 484.3 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 21.2 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 124.5 (*d*, $J_{C\text{-}P}$ = 9.2 Hz), 125.1, 125.5, 125.9, 127.4, 128.8, 129.6 (*d*, $J_{C\text{-}P}$ = 11.9 Hz), 132.0 (*d*, $J_{C\text{-}P}$ = 9.2 Hz), 132.7 (*d*, $J_{C\text{-}P}$ = 2.8 Hz), 134.0 (*d*, $J_{C\text{-}P}$ = 10.1 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 10.4 ppm; IR (film): 3052, 2972, 2365, 2229, 1927, 1619, 1594, 1557, 1508, 1450, 1423, 1354, 1322, 1179, 1026, 997, 972, 909, 817, 776, 732, 660, 645 cm^{-1}; HRMS (FAB): $C_{22}H_{20}O_1P_1^+$ ([M+H]$^+$), Calc. 331.1246, Found 331.1248.



The product collected after FC was re-crystallized from Hex/methyl *tert*-butyl ether (MTBE) to obtain pure phosphine oxide **10f**.

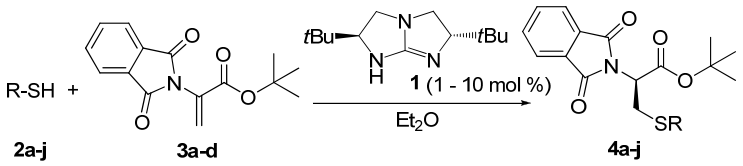
Bis-[(2-trifluoromethyl)phenyl]-phosphine oxide (**10f**) Brown crystals; R_f (Hex/EtOAc = 1/2): 0.32; mp: 120.1–120.4°C; 86% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 7.68–7.73 (*m*, 4H), 7.78–7.82 (*m*, 2H), 7.94–7.99 (*m*, 2H), 8.56 (*dm*, $J_{P\text{-}H}$ = 536.5 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 122.5 (*dq*, $J_{C\text{-}P}$ = 275, 2.7 Hz), 127.0 (*d*, $J_{C\text{-}P}$ = 4.6 Hz), 129.4 (*d*, $J_{C\text{-}P}$ = 96.2 Hz), 131.5 (*dd*, $J_{C\text{-}P}$ = 33.0, 7.3 Hz), 132.0 (*d*, $J_{C\text{-}P}$ = 11.0 Hz), 132.7 (*d*, $J_{C\text{-}P}$ = 2.8 Hz), 134.4 (*d*, $J_{C\text{-}P}$ = 7.3 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 10.06 (*septet*, 7.4 Hz) ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 18.47 (*dd*, J = 8.2, 3.1 Hz) ppm; IR (film): 3156, 3069, 2892, 2618, 2417, 2241, 1960, 1835, 1724, 1587, 1443, 1311, 1183, 1131, 1044, 911, 733 cm^{-1}; HRMS (FAB): $C_{14}H_{10}O_1F_6P_1^+$ ([M+H]$^+$), Calc. 339.0368, Found 339.0370.



The product was purified by FC.

Bis-[(3-trifluoromethyl)phenyl]-phosphine oxide (**10g**) Yellow solid; R_f (Hex/EtOAc = 1/2): 0.43; mp: 50.3–50.7°C; 60% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 7.64–7.67 (*m*, 2H), 7.83–7.88 (*m*, 4H), 7.99 (*d*, *J* = 13.9 Hz, 2H), 8.16 (*d*, J_{P-H} = 493.1 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 123.3 (*q*, J_{C-P} = 274 Hz), 126.5–127.6 (*m*), 129.66–129.71 (*m*), 129.82, 131.73 (*dq*, J_{C-P} = 33.0, 12.8 Hz), 131.96 (*d*, J_{C-P} = 11.5 Hz), 133.78 (*d*, J_{C-P} = 11.5 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 18.5 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 12.96 ppm; IR (film): 3155, 3069, 2902, 2359, 2341, 2253, 1607, 1426, 1382, 1328, 1279, 1174, 1139, 1074, 948, 908, 803, 733, 651, 527 cm^{-1}; HRMS (ESI): $C_{14}H_{10}O_1F_6P_1^+$ ($[M+H]^+$), Calc. 339.0373, Found 339.0374.

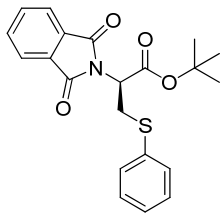
Representative Procedure for Enantioselective Protonation Reaction of *tert*-Butyl 2-Phthalimidoacrylates 3 with Aromatic Thiols 2 Catalyzed by Chiral Bicyclic Guanidine 1



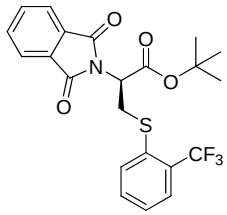
Thiophenol **2j** (R = 4-aminophenyl) (13.8 mg, 0.110 mmol, 1.10 equiv.) and catalyst **1** (0.22 mg, 0.0010 mmol, 0.010 equiv.) in Et_2O (1.00 mL) were stirred in a 4 mL sample vial at −116°C Et_2O/liquid N_2 slush bath.[7] After being stirred for 10 min, phthalimidoacrylate **3a** (27.3 mg, 0.100 mmol, 1.00 equiv.) was added as solid and stirred for 4 h at −116°C (phthalimidoacrylate **3a** was added at −78°C for reactions conducted at −50°C). The reaction was monitored by TLC. 80% conversion was achieved after 4 h. Dry ice was then added to the ether bath and the temperature was allowed to warm to −78°C gradually. After another 2.5 h of stirring, the reaction was completed. It was filtered through a short plug of silica gel to remove catalyst. The solvent was removed in vacuo. The crude product was purified by gradient elution (Hex/EtOAc = 19/1 to 2/1) to afford product **4j** as bright yellow crystals. For reactions involving thiols with lower boiling points, the crude mixtures obtained after filtering were subjected to high vacuum to remove the excess thiols to obtain the products.

(*S*)-*tert*-Butyl 3-(4-aminophenylthio)-2-phthalimidopropanoate (**4j**) Bright yellow crystals; R_f (Hex/EtOAc = 1/1): 0.30; mp: 156.3–156.8°C; 82% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.39 (*s*, 9H), 3.49 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.51–3.69 (*br*, 2H), 3.67 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.85 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 6.53 (*d*, *J* = 8.2 Hz, 2H), 7.22 (*d*, *J* = 8.2 Hz, 2H), 7.69–7.72 (*m*, 2H), 7.79–7.82 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 35.4, 53.0, 83.0, 115.9, 121.9, 123.3, 131.8, 134.0, 134.8, 145.5, 167.1, 167.6 ppm; IR (film): 3478, 3396, 3209, 3155, 2983, 2934, 2254, 1777, 1716, 1620, 1598, 1530, 1496, 1470, 1391, 1371, 1276, 1155, 1099, 1013, 991, 908, 854, 841, 825, 790, 732, 650 cm^{-1}; HRMS (FAB): $C_{21}H_{22}O_4N_2{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 398.1295, Found 398.1310, 100% rel., $C_{17}H_{15}O_4N_2{}^{32}S_1{}^+$ ([M-C(CH$_3$)$_3$+H]$^+$), Calc. 343.0740, Found 343.0751, 49% rel.; $[\alpha]_D^{29}$: +158.9 (c 3.0, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 50/50, 1.0 mL/min, 214 nm, 23°C) 12.4 (major), 23.7 min, 90% *ee*.

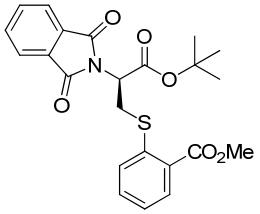
[7] R. E. Rondeau, *J. Chem. Eng. Data* **1966**, *11*, 124–124.



(*S*)-*tert*-Butyl 3-(phenylthio)-2-phthalimidopropanoate (**4a**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.23; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.41 (*s*, 9H), 3.67 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.79 (*dd*, *J* = 15.1, 11.4 Hz, 1H), 4.91 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 7.04 (*t*, *J* = 7.6 Hz, 1H), 7.14 (*t*, *J* = 7.6 Hz, 2H), 7.33–7.35 (*m*, 2H), 7.67–7.70 (*m*, 2H), 7.76–7.78 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 33.6, 53.0, 83.2, 123.3, 126.9, 128.9, 131.1, 131.7, 133.9, 134.1, 166.8, 167.4 ppm; IR (film): 3020, 1718, 1478, 1391, 1216, 1155, 929, 757, 669 cm^{-1}; HRMS (ESI): $C_{21}H_{21}O_4N_1S_1^+$ ([M+H]$^+$), Calc. 384.1270, Found 384.1270, 100% rel., $C_{17}H_{13}O_4N_1S_1^+$ ([M-C$(CH_3)_3$+H]$^+$), Calc. 328.0644, Found 328.0619, 60% rel.; $[\alpha]_D^{25}$: +53.2 (c 3.6, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 17.7 (major), 23.1 min, 90% *ee*.

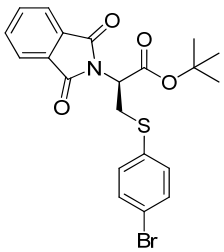


(*S*)-*tert*-Butyl 3-(2-trifluoromethyl-phenylthio)-2-phthalimidopropanoate (**4b**) White solid; mp: 100.1–100.5°C; R_f (Hex/EtOAc = 4/1): 0.27; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.42 (*s*, 9H), 3.83 (*d*, *J* = 8.2 Hz, 2H), 4.92 (*t*, *J* = 7.6 Hz, 1H), 7.26 (*t*, *J* = 7.6 Hz, 1H), 7.46 (*t*, *J* = 7.6 Hz, 1H), 7.57–7.59 (*m*, 2H), 7.71–7.73 (*m*, 2H), 7.80–7.84 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 33.3, 51.9, 83.5, 122.4, 123.4, 124.6, 126.6, 126.9–127.1 (*m*), 131.7, 131.95, 132.04, 134.1 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 15.32 ppm; IR (film): 2983, 2934, 2255, 1778, 1719, 1594, 1573, 1470, 1441, 1390, 1313, 1260, 1173, 1154, 1136, 1117, 1100, 1035, 991, 908, 876, 841, 732, 650, 531 cm^{-1}; HRMS (FAB): $C_{22}H_{21}O_4N_1F_3{}^{32}S_1^+$ ([M+H]$^+$), Calc. 452.1138, Found 452.1160, 25% rel., $C_{18}H_{13}O_4N_1F_3{}^{32}S_1^+$ ([M-C$(CH_3)_3$+H]$^+$), Calc. 396.0512, Found 396.0527, 100% rel.; $[\alpha]_D^{27}$: +59.9 (c 4.4, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 97/3, 0.5 mL/min, 214 nm, 23°C) 43.3 (major), 51.4 min, 93% *ee*.

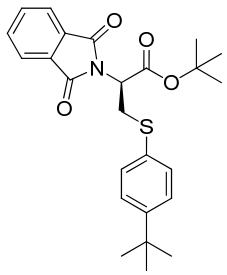


0.50 mL of ether was used instead of 1.00 mL.

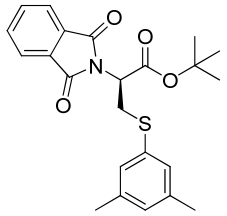
(*S*)-*tert*-Butyl 3-(methyl benzoate-2-thio)-2-phthalimidopropanoate (**4c**) Yellow liquid; R_f (Hex/EtOAc = 4/1): 0.13; 98% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.43 (*s*, 9H), 3.77–3.84 (*m*, 5H), 4.98 (*dd*, *J* = 9.5, 5.0 Hz, 1H), 7.09–7.12 (*m*, 1H), 7.39–7.44 (*m*, 2H), 7.68–7.71 (*m*, 2H), 7.77–7.81 (*m*, 3H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.7, 31.7, 52.0, 83.3, 123.4, 124.8, 127.2, 129.4, 131.1, 131.7, 132.2, 134.0, 138.6, 166.6, 166.8, 167.3 ppm; IR (film): 2985, 2256, 1778, 1717, 1640, 1470, 1436, 1391, 1256, 1155, 912, 734, 650 cm^{-1}; HRMS (FAB): $C_{23}H_{24}O_6N_1{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 442.1319, Found 442.1309, 42% rel., $C_{19}H_{16}O_6N_1{}^{32}S_1{}^+$ ($[M\text{-}C(CH_3)_3+H]^+$), Calc. 386.0693, Found 386.0697, 100% rel.; $[\alpha]_D^{24}$: +33.8 (c 4.2, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 14.4 (major), 16.1 min, 90% *ee*.



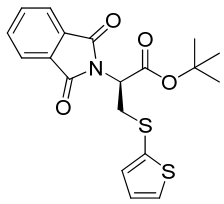
(*S*)-*tert*-Butyl 3-(4-bromo-phenylthio)-2-phthalimidopropanoate (**4d**) White solid; mp: 106.2–106.6°C; R_f (Hex/EtOAc = 4/1): 0.30; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.41 (*s*, 9H), 3.62 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.78 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.89 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 7.17–7.22 (*m*, 4H), 7.69–7.72 (*m*, 2H), 7.75–7.79 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 33.6, 53.1, 83.3, 121.1, 123.3, 131.5, 131.9, 132.8, 133.2, 134.1, 166.6, 167.4 ppm; IR (film): 3155, 2983, 2934, 2254, 1777, 1717, 1474, 1416, 1391, 1371, 1306, 1258, 1155, 1092, 1070, 1010, 992, 908, 856, 842, 816, 733, 650, 530 cm^{-1}; HRMS (FAB): $C_{21}H_{20}O_4N_1{}^{79}Br_1{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 461.0291, Found 461.0294, 85% rel., $C_{21}H_{20}O_4N_1{}^{81}Br_1{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 463.0270, Found 463.0286, 100% rel.; $[\alpha]_D^{26}$: +43.1 (c 4.3, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 0.5 mL/min, 214 nm, 23°C) 43.4 (major), 55.1 min, 90% *ee*.



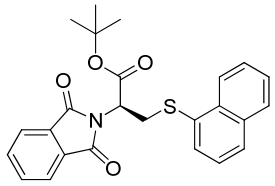
(*S*)-*tert*-Butyl 3-(4-*tert*-butyl-phenylthio)-2-phthalimidopropanoate (**4e**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.43; 92% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.18 (*s*, 9H), 1.40 (*s*, 9H), 3.62 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.78 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.93 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 7.13–7.16 (*m*, 2H), 7.26–7.28 (*m*, 2H), 7.67–7.69 (*m*, 2H), 7.75–7.78 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 31.1, 33.9, 34.3, 53.5, 83.1, 123.3, 125.9, 130.5, 131.3, 131.7, 133.9, 150.3, 166.9, 167.4 ppm; IR (film): 2967, 2936, 2906, 2871, 2256, 1778, 1721, 1613, 1593, 1489, 1470, 1391, 1371, 1303, 1257, 1155, 1120, 1099, 1013, 991, 945, 910, 875, 841, 829, 791, 734, 649, 556, 530 cm^{-1}; HRMS (FAB): $C_{25}H_{29}O_4N_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 439.1812, Found 439.1812, 92% rel., $C_{21}H_{22}O_4N_1{}^{32}S_1{}^+$ ([M-C(CH$_3$)$_3$+H]$^+$), Calc. 384.1264, Found 384.1260, 100% rel.; $[\alpha]_D^{25}$: +41.2 (c 4.1, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 97/3, 0.5 mL/min, 214 nm, 23°C) 53.2 (major), 66.6 min, 93% *ee*.



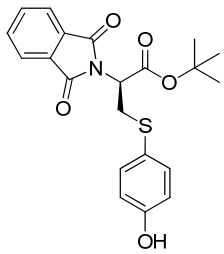
(*S*)-*tert*-Butyl 3-(3,5-dimethyl-phenylthio)-2-phthalimidopropanoate (**4f**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.36; 98% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.41 (*s*, 9H), 2.10 (*s*, 6H), 3.59 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.83 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.94 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 6.50 (*s*, 1H), 6.91 (*s*, 2H), 7.66–7.68 (*m*, 2H), 7.71–7.74 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 20.9, 27.8, 33.1, 53.7, 83.1, 123.0, 128.5, 128.9, 131.6, 133.4, 133.7, 138.4, 166.9, 167.3 ppm; IR (film): 2981, 2921, 2861, 2256, 1777, 1719, 1600, 1581, 1469, 1390, 1370, 1257, 1155, 1100, 992, 947, 875, 844, 732, 687, 649 cm^{-1}; HRMS (FAB): $C_{23}H_{25}O_4N_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 411.1499, Found 411.1513, 85% rel., $C_{19}H_{18}O_4N_1{}^{32}S_1{}^+$ ([M-C(CH$_3$)$_3$+H]$^+$), Calc. 356.0951, Found 356.0951, 100% rel.; $[\alpha]_D^{28}$: +28.5 (c 4.0, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 1.0 mL/min, 254 nm, 23°C) 20.7 (major), 27.4 min, 94% *ee*.



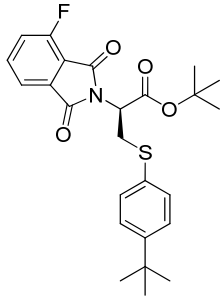
(*S*)-*tert*-Butyl 3-(thiophen-2-ylthio)-2-phthalimidopropanoate (**4g**) Light yellow liquid; R_f (Hex/EtOAc = 4/1): 0.32; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.39 (*s*, 9H), 3.54 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.65 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.91 (*dd*, *J* = 11.4, 4.4 Hz, 1H), 6.87–6.88 (*m*, 1H), 7.14 (*dd*, *J* = 3.8, 1.3 Hz, 1H), 7.29 (*dd*, *J* = 5.7, 1.3 Hz, 1H), 7.72–7.75 (*m*, 2H), 7.84–7.87 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 37.7, 52.6, 83.2, 123.5, 127.5, 130.2, 131.8, 132.3, 134.1, 135.2, 166.8, 167.6 ppm; IR (film): 2982, 1777, 1717, 1470, 1391, 1371, 1258, 1155, 1099, 908, 733, 650 cm^{-1}; HRMS (ESI): $C_{19}H_{19}N_1O_4S_2^+$ ($[M+H]^+$), Calc. 390.0834, Found 390.0842, 45% rel., $C_{15}H_{11}N_1O_4S_2^+$ ($[M\text{-}C(CH_3)_3+H]^+$), Calc. 334.0208, Found 334.0166, 100% rel.; $[\alpha]_D^{25}$: +115.8 (c 3.9, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 15.5 (major), 18.7 min, 91% *ee*.



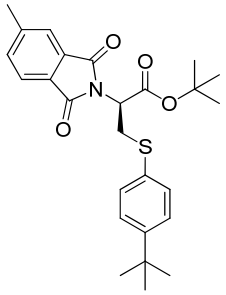
(*S*)-*tert*-Butyl 3-(naphthalen-1-ylthio)-2-phthalimidopropanoate (**4h**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.29; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.38 (*s*, 9H), 3.72 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.92 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.95 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 7.30 (*t*, *J* = 7.6 Hz, 1H), 7.40–7.43 (*m*, 1H), 7.46–7.49 (*m*, 1H), 7.59–7.68 (*m*, 7H), 8.36 (*d*, *J* = 8.2 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 33.8, 53.2, 83.1, 123.2, 125.4, 125.4, 126.1, 126.6, 128.3, 128.4, 131.2, 131.3, 131.5, 133.4, 133.8, 133.9, 166.9, 167.3 ppm; IR (film): 3477, 3058, 2981, 2934, 2256, 1777, 1717, 1504, 1470, 1390, 1304, 1257, 1155, 1100, 946, 909, 875, 842, 800, 772, 733, 649, 530 cm^{-1}; HRMS (FAB): $C_{25}H_{23}O_4N_1{}^{32}S_1^+$ ($[M+H]^+$), Calc. 433.1342, Found 433.1360, 100% rel., $C_{21}H_{16}O_4N_1{}^{32}S_1^+$ ($[M\text{-}C(CH_3)_3+H]^+$), Calc. 378.0795, Found 378.0797, 88% rel.; $[\alpha]_D^{28}$: +64.7 (c 5.0, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 25.7 (major), 35.1 min, 89% *ee*.



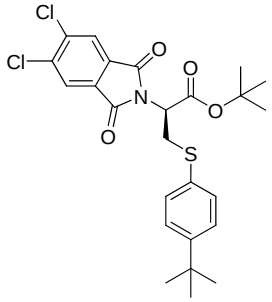
(*S*)-*tert*-Butyl 3-(4-hydroxyphenylthio)-2-phthalimidopropanoate (**4i**) Molten white solid; R_f (Hex/EtOAc = 1/1): 0.25; 97% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.40 (*s*, 9H), 3.54 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.70 (*dd*, *J* = 14.5, 12.0 Hz, 1H), 4.87 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 6.31 (*br*, 1H), 6.66 (*d*, *J* = 8.2 Hz, 2H), 7.27 (*d*, *J* = 8.2 Hz, 2H), 7.69–7.71 (*m*, 2H), 7.79–7.82 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 35.2, 53.1, 83.4, 116.1, 123.5, 123.8, 131.6, 134.2, 134.8, 156.1, 167.1, 167.9 ppm; IR (film): 3597, 3156, 2983, 2254, 1776, 1716, 1495, 1392, 1260, 1155, 1099, 909, 734, 650 cm^{-1}; HRMS (FAB): $C_{21}H_{21}O_5N_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 399.1135, Found 399.1151, 100% rel., $C_{17}H_{14}O_5N_1{}^{32}S_1{}^+$ ([M-C(CH$_3$)$_3$+H]$^+$), Calc. 344.0587, Found 344.0584, 81% rel.; $[\alpha]_D^{23}$: +93.0 (c 3.3, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 90/10, 1.0 mL/min, 214 nm, 23°C) 9.2 (major), 11.6 min, 84% *ee*.



(*S*)-*tert*-Butyl 3-(4-*tert*-butyl-phenylthio)-2-(3-fluoro-phthalimido)propanoate (**4k**) Pale yellow liquid; R_f (Hex/EtOAc = 4/1): 0.33; 99% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.19 (*s*, 9H), 1.42 (*s*, 9H), 3.60 (*dd*, *J* = 15.1, 3.8 Hz, 1H), 3.79 (*dd*, *J* = 15.1, 12.0 Hz, 1H), 4.92 (*dd*, *J* = 12.0, 3.8 Hz, 1H), 7.15–7.17 (*m*, 2H), 7.27–7.34 (*m*, 3H), 7.59 (*d*, *J* = 6.9 Hz, 1H), 7.66–7.70 (*m*, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 31.1, 33.7, 34.4, 53.7, 83.3, 117.4, 117.5, 119.46, 119.49, 122.3, 122.4, 125.9, 126.1, 127.7, 129.6, 130.4, 131.4, 133.9, 136.45, 136.50, 150.4, 156.4, 158.5, 164.0, 166.21, 166.24, 166.58 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ −36.74 (*q*, *J* = 4.1 Hz, 1F) ppm; IR (film): 2968, 2360, 2341, 2255, 1779, 1722, 1483, 1391, 1371, 1262, 1155, 1103, 908, 731, 650 cm^{-1}; HRMS (FAB): $C_{25}H_{28}O_4N_1F_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 457.1718, Found 457.1700, 83% rel., $C_{21}H_{21}O_4N_1F_1{}^{32}S_1{}^+$ ([M-C(CH$_3$)$_3$+H]$^+$), Calc. 402.1170, Found 402.1162, 100% rel.; $[\alpha]_D^{25}$: +41.6 (c 4.4, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 0.5 mL/min, 214 nm, 23°C) 33.8 (major), 39.4 min, 92% *ee*.

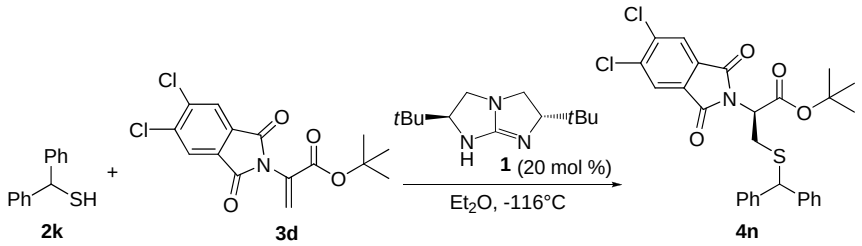


(*S*)-*tert*-Butyl 3-(4-*tert*-butyl-phenylthio)-2-(4-methyl-phthalimido)propanoate (**4l**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.35; 98% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.18 (*s*, 9H), 1.40 (*s*, 9H), 2.47 (*s*, 3H), 3.61 (*dd*, *J* = 15.1, 3.8 Hz, 1H), 3.77 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.91 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 7.13–7.16 (*m*, 2H), 7.26–7.28 (*m*, 2H), 7.46 (*d*, *J* = 7.6 Hz, 1H), 7.56 (*s*, 1H), 7.65 (*d*, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 21.9, 27.8, 31.1, 33.9, 34.3, 53.4, 83.0, 123.2, 123.8, 125.8, 129.1, 130.6, 131.3, 132.1, 134.5, 145.2, 150.2, 167.0, 167.5, 167.6 ppm; IR (film): 2967, 2254, 1775, 1717, 1387, 1258, 1156, 1104, 909, 735, 650 cm^{-1}; HRMS (FAB): $C_{26}H_{31}O_4N_1{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 453.1968, Found 453.1964; $[\alpha]_D^{26}$: +52.1 (c 4.4, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 17.5 (major), 23.5 min, 92% *ee*.



(*S*)-*tert*-Butyl 3-(4-*tert*-butyl-phenylthio)-2-(4,5-dichloro-phthalimido)propanoate (**4m**) Yellow liquid; R_f (Hex/EtOAc = 4/1): 0.55; 95% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.17 (*s*, 9H), 1.40 (*s*, 9H), 3.57 (*dd*, *J* = 14.5, 3.8 Hz, 1H), 3.78 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.91 (*dd*, *J* = 12.0, 3.8 Hz, 1H), 7.12 (*d*, *J* = 8.2 Hz, 2H), 7.23 (*d*, *J* = 8.2 Hz, 2H), 7.81 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 31.1, 33.4, 34.3, 54.2, 83.4, 125.3, 125.9, 130.2, 130.7, 131.3, 138.9, 150.5, 165.4, 166.4 ppm; IR (film): 2969, 2254, 1785, 1723, 1604, 1385, 1259, 1155, 1099, 907, 736, 651 cm^{-1}; HRMS (FAB): $C_{25}H_{27}O_4N_1{}^{35}Cl_2{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 507.1032, Found 507.1040; $[\alpha]_D^{25}$: +32.8 (c 4.2, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 95/5, 0.5 mL/min, 214 nm, 23°C) 18.0 (major), 22.8 min, 92% *ee*.

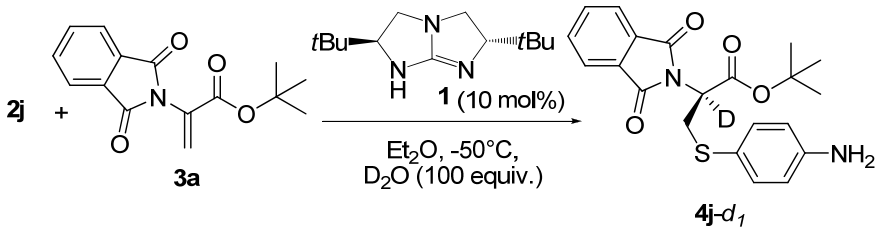
Procedure for Enantioselective Protonation Reaction of Phthalimidoacrylate 3d with Alkyl Thiol 2k Catalyzed by Chiral Bicyclic Guanidine 1



Benzhydryl mercaptan **2k** (22.0 mg, 0.110 mmol, 1.10 equiv.) and catalyst **1** (4.46 mg, 0.020 mmol, 0.200 equiv.) in Et_2O (1.00 mL) were pre-stirred in a 4 mL sample vial at −116°C Et_2O/liquid N_2 slush bath for 10 min.[7] Phthalimidoacrylate **3d** (34.2 mg, 0.100 mmol, 1.00 equiv.) was divided into five portions and added to the reaction mixture at 5 min intervals. After the last portion was added, it was stirred for a further 5 min at −116°C. Dry ice was then added to the ether bath and the temperature was allowed to warm to −78°C gradually over 1 h. After another 0.5 h of stirring at −78°C, the reaction was completed. It was filtered through a short plug of silica gel to remove catalyst. The solvent was removed in vacuo. The crude product was purified by gradient elution (Hex/EtOAc = 19/1 to 9/1) to afford product **4n** as pale yellow powder.

(*S*)-*tert*-Butyl 3-(benzhydrylthio)-2-(4,5-dichloro-phthalimido)propanoate (**4n**) Pale yellow powder; R_f (Hex/EtOAc = 9/1): 0.22; mp: 115.0–115.3°C; 96% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.37 (*s*, 9H), 3.12 (*dd*, *J* = 14.5, 4.4 Hz, 1H), 3.27 (*dd*, *J* = 14.5, 11.4 Hz, 1H), 4.86 (*dd*, *J* = 11.4, 4.4 Hz, 1H), 5.24 (*s*, 1H), 7.17–7.34 (*m*, 8H), 7.47 (*d*, *J* = 7.6 Hz, 2H), 7.95 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 31.1, 52.2, 53.4, 83.3, 125.6, 127.3, 127.4, 128.1, 128.4, 128.5, 128.7, 130.9, 139.1, 140.1, 140.7, 165.6, 166.4 ppm; IR (film): 2981, 2254, 1781, 1721, 1603, 1384, 1258, 1154, 907, 732, 650 cm^{-1}; HRMS (FAB): $C_{28}H_{26}O_4N_1{}^{35}Cl_2{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 542.0954, Found 542.0940; $[\alpha]_D^{23}$: +73.7 (c 1.9, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 0.5 mL/min, 214 nm, 23°C) 11.5 (major), 12.8 min, 91% *ee*.

Procedure for Enantioselective Deuteration Reaction of *tert*-Butyl 2-Phthalimidoacrylate 3a with Thiol 2j Catalyzed by Chiral Bicyclic Guanidine 1

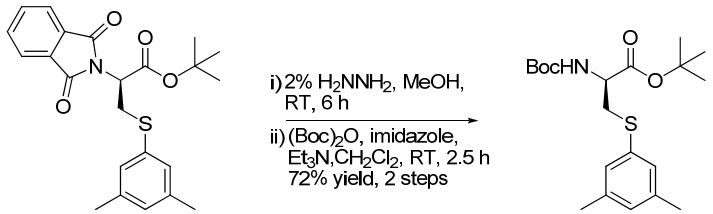


Thiophenol **2j** (R = 4-aminophenyl) (13.8 mg, 0.110 mmol, 1.10 equiv.), D_2O (181 μL, 10.0 mmol, 100 equiv.) and catalyst **1** (2.23 mg, 0.0100 mmol) in Et_2O (1.00 mL) were stirred in a flame-dried 4.0 mL sample vial fitted with rubber septum under N_2 atmosphere. After being stirred for 30 min at RT, the rubber septum was changed to screw-cap. The vial was then submerged in −78°C cryobath and stirred for 10 min. Phthalimidoacrylate **3a** (27.3 mg, 0.100 mmol, 1.00 equiv.) was added as solid at −78°C and stirred for 1 h at −50°C. The reaction was monitored by TLC. After reaction was completed, it was filtered through silica gel to remove catalyst. The solvent was removed in vacuo. The crude product was purified by gradient elution (Hex/EtOAc = 19/1 to 2/1) to afford product **4j**-d_1 as bright yellow crystals. Deuteration level was determined by ^{1}H NMR integration with respect to the peak at 6.48 ppm.

(*S*)-*tert*-Butyl 3-(4-aminophenylthio)-2-phthalimidopropanoate-2-d_1 (**4j**-d_1) Bright yellow crystals; R_f (Hex/EtOAc = 1/1): 0.30; mp: 163.3–163.8°C; 90% yield; 97% deuteration; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.39 (*s*, 9H), 3.47 (*d*, *J* = 14.5, 1H), 3.64–3.67 (*br*, 2H), 3.66 (*d*, *J* = 14.5, 1H), 4.85 (*dd*, *J* = 11.4, 3.8 Hz, 3.1%), 6.53 (*d*, *J* = 8.2 Hz, 2H), 7.22 (*d*, *J* = 8.8 Hz, 2H), 7.69–7.72 (*m*, 2H), 7.79–7.82 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.8, 35.4, 52.77 (*d*, *J* = 22.0 Hz, 1C), 83.0, 115.4, 121.0, 123.3, 131.8, 133.9, 135.0, 146.5, 167.1, 167.6 ppm; IR (film): 3464, 3379, 3020, 2979, 2935, 2401, 2361, 2342, 1778, 1715, 1621, 1598, 1497, 1469, 1391, 1371, 1257, 1216, 1177, 1157, 1103, 1057, 921, 871, 834, 822, 756, 668, 626 cm^{-1}; HRMS (ESI): $C_{21}H_{22}{}^2HO_4N_2{}^{32}S_1{}^+$ ($[M+H]^+$), Calc. 400.1441, Found 400.1441, 24% rel., $C_{17}H_{14}{}^2H O_4N_2{}^{32}S_1{}^+$ ($[M\text{-}C(CH_3)_3+H]^+$), Calc. 344.0815, Found 344.0822, 100% rel.; $[\alpha]_D^{29}$: +136.9 (c 2.8, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 50/50, 1.0 mL/min, 214 nm, 23°C) 10.7 (major), 18.5 min, 91% *ee*.

Procedures for Chemoselective Removal of Various Protecting Groups from Cysteine Derivatives 4

Chemoselective removal of *N*-phthalimide protecting group



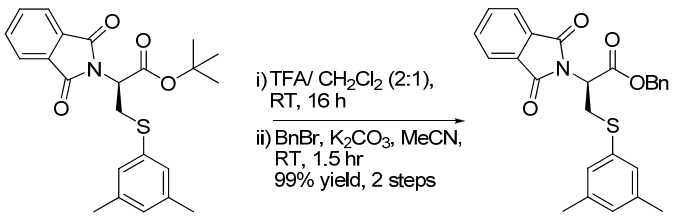
4f, 92% *ee* **5**, 90% *ee*

To a solution of cysteine derivative **4f** (30.0 mg, 0.070 mmol, 1.00 equiv.) in MeOH (2.0 mL) was added 2% H_2NNH_2 in MeOH (0.25 mL, 0.168 mmol, 2.40 equiv.) dropwise at ambient temperature. The mixture was stirred at RT for 6 h. The solvent was then removed in vacuo. It was taken up with EtOAc (5 mL) and washed with 6% K_2CO_3 (5 mL) solution. The organic layer was dried and evaporated. This crude reaction mixture was used for the next step without any further purification.

To a solution of above obtained product (1.0 equiv.) in CH_2Cl_2 (2.0 mL) was added $(Boc)_2O$ (17 mg, 0.080 mmol, 1.1 equiv.), imidazole (0.7 mg, 0.010 mmol, 0.1 equiv.) and Et_3N (2 drops) at 0°C. The mixture was stirred at RT for 2.5 h. Removal of solvent followed by flash chromatography yielded product **5**.

(*S*)-*tert*-Butyl 2-(tert-butoxycarbonylamino)-3-(3,5-dimethylphenylthio)propanoate (**5**) Colorless liquid; R_f (Hex/EtOAc = 4/1): 0.49; 72% yield (two steps); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.40 (*s*, 9H), 1.44 (*s*, 9H), 2.27 (*s*, 6H), 3.29 (*dd*, *J* = 13.2, 5.0 Hz, 1H), 3.38 (*dd*, *J* = 13.2, 3.8 Hz, 1H), 4.44 (*br*, 1H), 5.26 (*d*, *J* = 6.9 Hz, 1H), 6.82 (*s*, 1H), 7.02 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 21.1, 27.9, 28.2, 37.2, 54.1, 79.7, 82.5, 128.0, 128.5, 135.1, 138.6, 155.0, 169.7 ppm; IR (film): 3019, 2115, 1702, 1647, 1500, 1216, 1154, 1047, 846, 774 cm^{-1}; HRMS (FAB): $C_{20}H_{31}O_4N_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 381.1968, Found 381.1970; $[\alpha]_D^{25}$: −26.5 (c 1.6, $CHCl_3$); HPLC analysis: Chiralcel IA (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 6.5 (major), 7.8 min, 90% *ee*.

Chemoselective removal of *tert*-butyl ester protecting group



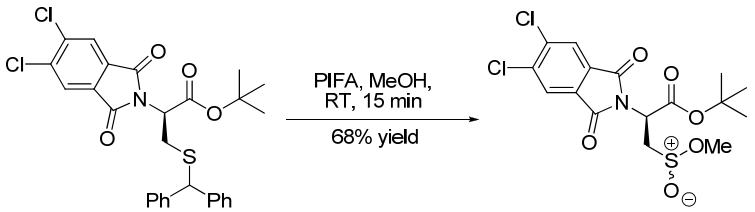
4f, 94% *ee* **6**, 90% *ee*

Cysteine derivative **4f** (15.0 mg, 0.040 mmol, 1.00 equiv.) was dissolved in TFA/CH_2Cl_2 (2:1, 0.90 mL) at RT. The mixture was stirred at RT for 16 h. The solvent was then removed in vacuo.

This crude reaction mixture was dissolved in CH_3CN (1.0 mL) and treated with solid K_2CO_3 (14.0 mg, 0.100 mmol, 2.50 equiv.) and benzyl bromide (8.0 mg, 0.048 mmol, 1.20 equiv.). The reaction mixture was stirred at RT for 1.5 h. Removal of solvent followed by flash chromatography yielded product **6**.

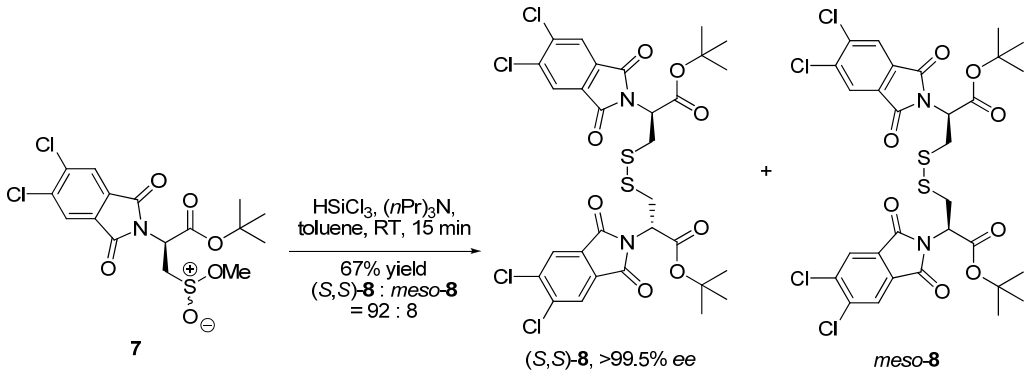
(*S*)-Benzyl 3-(3,5-dimethyl-phenylthio)-2-phthalimidopropanoate (**6**) White solid; R_f (Hex/EtOAc = 4/1): 0.38; mp: 92.2–92.5°C; 99% yield (two steps); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.11 (*s*, 6H), 3.65 (*dd*, *J* = 15.1, 3.8 Hz, 1H), 3.88 (*dd*, *J* = 15.1, 11.4 Hz, 1H), 5.08 (*dd*, *J* = 11.4, 3.8 Hz, 1H), 5.17 (*dd*, *J* = 15.1, 12.0 Hz, 2H), 6.53 (*s*, 1H), 6.91 (*s*, 2H), 7.25–7.32 (*m*, 5H), 7.67–7.69 (*m*, 2H), 7.72–7.75 (*m*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 20.9, 33.2, 53.0, 67.7, 123.1, 128.1, 128.4, 128.5, 128.7, 129.0, 131.5, 133.1, 133.9, 135.0 138.5, 167.2, 167.9 ppm; IR (film): 3172, 2110, 1716, 1644, 1388, 1232, 1176, 1099, 912, 733 cm^{-1}; HRMS (FAB): $C_{26}H_{24}O_4N_1{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 446.1421, Found 446.1425; $[\alpha]_D^{24}$: 14.9 (c 1.6, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 12.1, 15.5 (major) min, 90% *ee*.

Chemoselective removal of *S*-benzhydryl protecting group



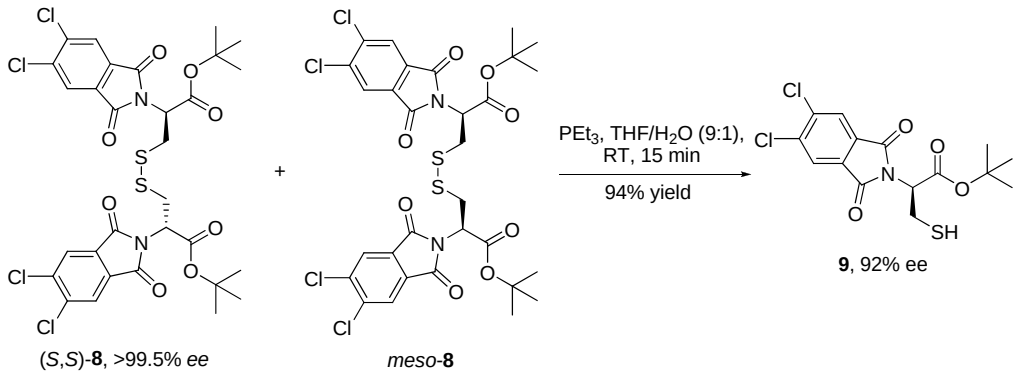
To a solution of cysteine derivative **4n** (27.1 mg, 0.050 mmol, 1.00 equiv.) in MeOH (2.00 mL) was added [bis(trifluoroacetoxy)iodo]benzene (PIFA) (45.1 mg, 0.105 mmol, 2.10 equiv.) as a solid at RT. The mixture was stirred at RT for 15 min. Removal of solvent followed by flash chromatography yielded product **7** as a mixture of diastereomers (*d.r.* = 54.3 : 45.7) as determined from NMR.

(*2S*)-*tert*-Butyl 3-(methoxysulfinyl)-2-(4,5-dichloro-phthalimido)propanoate (**7**) Light yellow liquid; R_f (Hex/EtOAc = 4/1): 0.19; 68% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.42 (*s*, 9H), 3.44–3.62 (*m*, 2H), 3.71 (*s*, 1.63H), 3.73 (*s*, 1.37H), 5.25–5.31 (*m*, 1H), 7.94 (two *s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.7, 46.7, 47.1, 54.7, 54.88, 54.94, 55.1, 84.26, 84.31, 125.7, 130.74, 130.76, 139.4, 165.14, 165.20, 165.85, 165.92 ppm; IR (film): 2984, 2254, 1784, 1726, 1383, 1258, 1153, 988, 909, 735, 650 cm^{-1}; HRMS (FAB): $C_{16}H_{18}O_6N_1{}^{35}Cl_2{}^{32}S_1{}^+$ ([M+H]$^+$), Calc. 422.0226, Found 422.0219.



Sulfinate **7** (14.3 mg, 0.034 mmol, 1.00 equiv.) was dissolved in toluene (0.30 mL) and trichlorosilane (20.0 μL, 0.198 mmol, 5.80 equiv.) was added to it at RT. After stirring for 5 min, $(n\text{Pr})_3\text{N}$ (6.7 μL, 0.036 mmol, 1.05 equiv.) was added dropwise to the reaction. The mixture was stirred at RT for 15 min. H_2O (2.0 mL) was added to quench the reaction. Subsequently, it was extracted with EtOAc (3 × 2 mL). The combined organic layer was dried over Na_2SO_4. Removal of solvent followed by flash chromatography yielded product **8** as a mixture of diastereomers (*S*,*S*)-**8** : *meso*-**8** = 91.9 : 8.1 as determined from HPLC analysis.[8]

***N,N'*-di-(4,5-dichloro-phthaloyl)-D,D-cystine di-*tert*-butyl ester** (**8**) Molten white solid; R_f (Hex/EtOAc = 4/1): 0.45; 67% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.43 (*s*, 9H), 3.41 (*dd*, *J* = 14.5, 10.7 Hz, 1H), 3.46 (*dd*, *J* = 14.5, 5.0 Hz, 1H), 5.09 (*dd*, *J* = 10.7, 4.4 Hz, 1H), 7.90 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 27.9, 36.3, 52.2, 83.8, 125.7, 130.8, 139.2, 166.6, 166.5 ppm; IR (film): 3159, 2254, 1782, 1724, 1602, 1384, 1261, 1154, 1098, 1014, 907, 733, 651 cm^{-1}; HRMS (FAB): $C_{30}H_{28}O_8N_2{}^{35}Cl_4{}^{32}S_2{}^+$ ([M+H]$^+$), Calc. 748.0036, Found 748.0013, 61% rel., $C_{30}H_{28}O_8N_2{}^{35}Cl_3{}^{37}Cl_1{}^{32}S_2{}^+$ ([M+H]$^+$), Calc. 750.0006, Found 750.0026, 100% rel.; $[\alpha]_D^{23}$: 197.6 (c 0.5, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 1.0 mL/min, 214 nm, 23°C) 10.7 (major), 12.9 (*meso*), 17.9 min, >99.5% *ee*.



Cystine derivative **8** (mixture of diastereomers, 3.5 mg, 0.0047 mmol, 1.00 equiv.) was dissolved in THF/H_2O (9:1, 0.10 mL). Triethyl phosphine (1.0 M in THF, 18.5 μL, 0.0186 mmol, 4.00 equiv.) was added

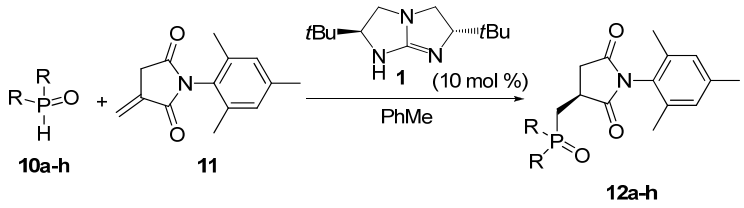
[8] T. H. Chan, J. P. Montillier, W. F. Van Horn, D. N. Harpp, *J. Am. Chem. Soc.* **1970**, *92*, 7224–7225.

to it at RT. The mixture was stirred at RT for 15 min. The solvent was then removed in vacuo. EtOAc (2.0 mL) was added and washed three times with H_2O (1.0 mL). The combined aqueous layer was extracted with EtOAc (1.0 mL). The combined organic layer was dried over Na_2SO_4. Removal of solvent followed by flash chromatography yielded product **9**.[9]

***N*-(4,5-dichloro-phthaloyl)-D-cysteine *tert*-butyl ester** (**9**) Molten white solid; R_f (Hex/EtOAc = 4/1): 0.47; 94% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.43 (*s*, 9H), 3.24 (*dd*, *J* = 14.5, 10.5 Hz, 1H), 3.26–3.31 (*m*, 1H), 4.79 (*dd*, *J* = 10.8, 5.2 Hz, 1H), 7.96 (*s*, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 23.7, 27.8 56.1, 83.6, 125.7, 128.8, 130.8, 130.9, 139.3, 165.7, 166.1 ppm; IR (film): 3019, 2360, 2342, 1782, 1724, 1384, 1260, 1216, 1154, 1113, 768, 669 cm^{-1}; HRMS (ESI): $C_{15}H_{15}O_4N_1{}^{32}S_1{}^{35}Cl_2{}^+$ ($[M+H]^+$), Calc. 376.0177, Found 376.0178, 100% rel., $C_{11}H_7O_4N_1{}^{32}S_1{}^{35}Cl_2{}^+$ ($[M\text{-}C(CH_3)_3+H]^+$), Calc. 319.9551, Found 319.9565, 98% rel.; $[\alpha]_D^{22}$: −7.3 (c 0.32, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 0.5 mL/min, 214 nm, 23°C) 16.8 (major), 19.5 min, 92% *ee*.

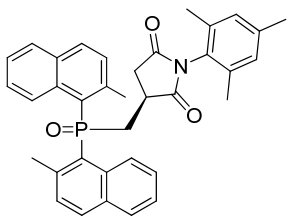
[9] L. Käsbeck, H. Kessler, *Liebigs Ann./Recueil* **1997**, 165–167.

Representative Procedure for Enantioselective Protonation Reaction of Itaconimide 11 with Secondary Phosphine Oxides 10 Catalyzed by Chiral Bicyclic Guanidine 1

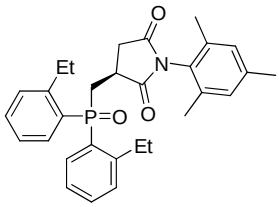


Bis-naphth-1-yl-phosphine oxide **10a** (Ar = naphtha-1-yl) (30.2 mg, 0.100 mmol, 1.00 equiv.) was sonicated in toluene (1.00 mL) in a 4 mL sample vial for 5 mins for it to dissolve well. Catalyst **1** (2.23 mg, 0.0100 mmol, 0.100 equiv.) was added and the vial was submerged in cryobath at 0°C. After being stirred for 10 min, itaconimide **11** (25.2 mg, 0.110 mmol, 1.10 equiv.) was added as solid and stirred for 2 hours. The reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was loaded onto silica gel column and purified by gradient elution (Hex/EtOAc = 9/1 to 1/2) to afford product **12a** as white solid.

(*S*)-3-{[Bis(naphthalen-1-yl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12a**) White solid; R_f (Hex/EtOAc = 1/2): 0.30; mp: 127.0–128.0°C; 95% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.02 (*s*, 3H), 2.28 (*s*, 3H), 2.70–2.80 (*m*, 2H), 2.95 (*dd*, J = 18.9, 9.5 Hz, 1H), 3.44–3.51 (*m*, 1H), 3.64 (*ddd*, J = 15.1, 10.7, 1.9 Hz, 1H), 6.93 (*s*, 2H), 7.47–7.56 (*m*, 5H), 7.59 (*dt*, J = 8.2, 2.6 Hz, 1H), 7.91 (*d*, 7.0 Hz, 2H), 8.01–8.12 (*m*, 4H), 8.65 (*dd*, J = 31.5, 8.2 Hz, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.6, 21.0, 32.2 (*d*, $J_{C\text{-}P}$ = 72.4 Hz), 35.7 (*d*, $J_{C\text{-}P}$ = 2.8 Hz), 124.7 (*dd*, $J_{C\text{-}P}$ = 13.8, 4.6 Hz), 126.0 (*dd*, $J_{C\text{-}P}$ = 42.2, 5.5 Hz), 126.7 (*d*, $J_{C\text{-}P}$ = 12.8 Hz), 127.4, 127.7 (*d*, $J_{C\text{-}P}$ = 8.3 Hz), 128.4, 129.0 (*d*, $J_{C\text{-}P}$ = 41.2 Hz), 129.3, 129.5 (*d*, $J_{C\text{-}P}$ = 65.0 Hz), 132.0 (*dd*, $J_{C\text{-}P}$ = 10.1, 12.8 Hz), 133.0 (*dd*, $J_{C\text{-}P}$ = 55.9, 8.3 Hz), 133.7 (*dd*, $J_{C\text{-}P}$ = 6.4, 2.8 Hz), 134.0 (*dd*, $J_{C\text{-}P}$ = 12.8, 9.2 Hz), 135.1 (*d*, $J_{C\text{-}P}$ = 9.2 Hz), 139.4, 174.86, 178.07 ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 34.8 ppm; IR (film): 3155, 3054, 2927, 2555, 2404, 2251, 1958, 1711, 1602, 1484, 1381, 1188, 909, 733 cm^{-1}; HRMS (FAB): $C_{34}H_{31}O_3N_1P_1^+$ ([M+H]$^+$), Calc. 532.2036, Found 532.2031; $[\alpha]_D^{26}$: +12.8 (c 3.2, $CHCl_3$); HPLC analysis: Chiralpak IA (Hex/IPA = 87/13, 1.3 mL/min, 214 nm, 23°C), 38.9, 42.2 (major) min, 98% *ee*.



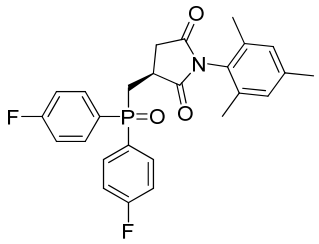
(*S*)-3-{[Bis(2-methylnaphthalen-1-yl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12b**) White solid; R_f (Hex/EtOAc = 1/2): 0.49; mp: 107.3–107.9°C; 93% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.97 (*s*, 6H), 2.27 (*s*, 3H), 2.42 (*s*, 3H), 2.65 (*br*, 4H), 2.79 (*dd*, *J* = 22.7, 12.6 Hz, 1H), 2.84 (*dd*, *J* = 18.3, 8.8 Hz, 1H), 3.37 (*br*, 1H), 3.73 (*t*, *J* = 11.3 Hz, 1H), 6.91 (*s*, 2H), 7.23 (*dd*, *J* = 8.2, 3.8 Hz, 1H), 7.27–7.32 (*m*, 2H), 7.41 (*t*, 7.6 Hz, 1H), 7.45–7.48 (*m*, 2H), 7.81–7.85 (*m*, 2H), 7.89 (*dd*, *J* = 8.2, 4.4 Hz, 2H), 8.41 (*br*, 1H), 8.79–8.81 (*m*, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.63, 17.67, 21.0, 23.26–23.47 (*m*), 35.4, 36.5, 37.74 (*d*, $J_{C\text{-}P}$ = 68.7 Hz), 125.37–125.51 (*m*), 125.64 (*d*, $J_{C\text{-}P}$ = 14.7 Hz), 127.0, 127.32 (*d*, $J_{C\text{-}P}$ = 7.3 Hz), 128.96 (*d*, $J_{C\text{-}P}$ = 9.2 Hz), 129.26 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 130.04–130.68 (*m*, 2C), 132.34 (*dd*, $J_{C\text{-}P}$ = 72.9, 36.4 Hz), 132.69, 133.60 (*dd*, $J_{C\text{-}P}$ = 93.5, 10.1 Hz), 135.12 (*d*, $J_{C\text{-}P}$ = 11.0 Hz), 139.31, 141.67 (*d*, $J_{C\text{-}P}$ = 9.8 Hz), 175.04, 178.21 (*d*, $J_{C\text{-}P}$ = 17.4 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 37.97 (*br*) ppm; IR (film): 3668, 3017, 2984, 2925, 2401, 1779, 1711, 1612, 1597, 1508, 1487, 1444, 1421, 1379, 1305, 1181, 1027, 989, 925, 868, 820, 752, 666, 638, 562 cm^{-1}; HRMS (ESI): $C_{36}H_{35}O_3N_1P_1^+$ ($[M+H]^+$), Calc. 560.2355, Found 560.2355; $[\alpha]_D^{28}$: +25.6 (c 1.2, $CHCl_3$); HPLC analysis: Chiralpak IB (Hex/IPA = 90/10, 1.0 mL/min, 214 nm, 23°C), 52.3, 65.0 (major) min, 87% *ee*.



0.40 mL of toluene was used instead of 1.00 mL.

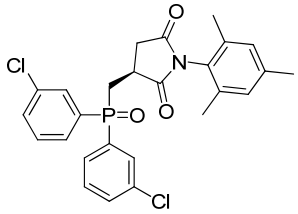
(*S*)-3-{[Bis(2-ethylphenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12c**) White solid; R_f (Hex/EtOAc = 1/2): 0.59; mp: 68.2–68.9°C; 94% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 0.91–0.95 (*m*, 6H), 2.02 (*d*, *J* = 8.2 Hz, 3H), 2.04 (*d*, *J* = 4.4 Hz, 3H), 2.28 (*s*, 3H), 2.45–2.53 (*m*, 1H), 2.72–2.83 (*m*, 5H), 3.03 (*dd*, *J* = 18.9, 9.5 Hz, 1H), 3.26–3.32 (*m*, 1H), 3.39 (*ddd*, *J* = 14.5, 9.5, 1.9 Hz, 1H), 6.94 (*d*, *J* = 3.1 Hz, 2H), 7.29–7.38 (*m*, 4H), 7.48–7.53 (*m*, 2H), 7.76 (*dd*, *J* = 12.6, 7.6 Hz, 1H), 7.88 (*dd*, *J* = 12.6, 7.6 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 15.01, 15.2, 17.6, 21.0, 26.85 (*d*, $J_{C\text{-}P}$ = 4.6 Hz), 31.5, 32.0, 35.43 (*d*, $J_{C\text{-}P}$ = 2.8 Hz), 35.7, 125.97 (*dd*, $J_{C\text{-}P}$ = 11.9, 2.8 Hz), 127.4, 129.32 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 130.41 (*dd*, $J_{C\text{-}P}$ = 11.0, 7.3 Hz), 131.34 (*d*, $J_{C\text{-}P}$ = 11.0 Hz), 131.74 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 132.45 (*t*, $J_{C\text{-}P}$ = 2.8 Hz), 135.14 (*d*, $J_{C\text{-}P}$ = 17.4 Hz), 139.4, 148.0 (*dd*, $J_{C\text{-}P}$ = 51.3, 9.2 Hz), 174.9, 178.31 (*d*, $J_{C\text{-}P}$ = 17.4 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 32.4 ppm; IR (film): 3063, 2973, 2931, 2875, 2253, 2232, 1780, 1711, 1634, 1611, 1594, 1487, 1475, 1440, 1379, 1305, 1291, 1192, 1139, 1092, 912, 870, 853, 742, 691, 648 cm^{-1}; HRMS (FAB): $C_{30}H_{35}O_3N_1P_1^+$ ($[M+H]^+$), Calc. 488.2349, Found 488.2353; $[\alpha]_D^{28}$: +18.3 (c 3.2, $CHCl_3$); HPLC analysis:

Chiralpak ADH + Chiralpak IA (Hex/IPA = 80/20, 1.0 mL/min, 214 nm, 23°C), 30.1 (major), 36.9 min, 92% *ee*.



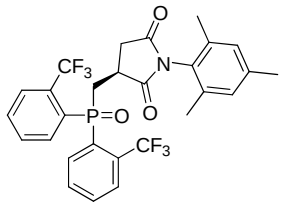
0.40 mL of toluene was used instead of 1.00 mL.

(*S*)-3-{[Bis(4-fluorophenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12d**) White solid; R_f (Hex/EtOAc = 1/2): 0.49; mp: 57.2–57.6°C; 79% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.02 (*s*, 3H), 2.28 (*s*, 3H), 2.34–2.42 (*m*, 1H), 2.87 (*dd*, J = 18.9, 5.7 Hz, 1H), 3.07 (*dd*, J = 18.9, 9.5 Hz, 1H), 3.17–3.26 (*m*, 2H), 6.94 (*s*, 2H), 7.19–7.24 (*m*, 4H), 7.75–7.85 (*m*, 4H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.60, 17.62, 21.0, 31.67 (*d*, $J_{C\text{-}P}$ = 72.4 Hz), 35.16 (*d*, $J_{C\text{-}P}$ = 3.7 Hz), 35.3, 116.37–116.79 (*m*, 2C), 127.3, 129.37 (*d*, $J_{C\text{-}P}$ = 8.3 Hz), 133.08 (*t*, $J_{C\text{-}P}$ = 9.2 Hz), 133.42 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 135.99 (*d*, $J_{C\text{-}P}$ = 9.2 Hz), 139.5, 174.4, 177.78 (*d*, $J_{C\text{-}P}$ = 17.4 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 29.7 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ -29.38–-29.23 (*m*, 1F) ppm; IR (film): 2934, 2341, 2249, 1712, 1594, 1497, 1384, 1191, 1113, 1047, 909, 833, 732 cm^{-1}; HRMS (FAB): $C_{26}H_{25}O_3N_1F_2P_1^+$ ($[M+H]^+$), Calc. 468.1535, Found 468.1523; $[\alpha]_D^{25}$: +13.4 (c 2.9, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 40/60, 1.0 mL/min, 214 nm, 23°C), 33.1 (major), 63.0 min, 91% *ee*.

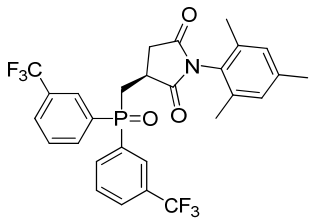


(*S*)-3-{[Bis(3-chlorophenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12e**) White solid; R_f (Hex/EtOAc = 1/2): 0.21; mp: 65.1–65.5°C; 95% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.03 (*s*, 3H), 2.29 (*s*, 3H), 2.37–2.44 (*m*, 1H), 2.86 (*dd*, J = 18.9, 6.3 Hz, 1H), 3.09 (*dd*, J = 18.9, 9.5 Hz, 1H), 3.19–3.31 (*m*, 2H), 6.94 (*s*, 2H), 7.45–7.52 (*m*, 2H), 7.55–7.59 (*m*, 2H), 7.63–7.71 (*m*, 2H), 7.80 (*dd*, J = 25.9, 12.0 Hz, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.66, 17.68, 21.1, 31.26 (*d*, $J_{C\text{-}P}$ = 73.3 Hz), 35.21 (*d*, $J_{C\text{-}P}$ = 35.8 Hz), 56.8, 128.58 (*dd*, $J_{C\text{-}P}$ = 28.4, 9.1 Hz), 129.41 (*d*, $J_{C\text{-}P}$ = 7.3 Hz), 130.47 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 130.67 (*d*, $J_{C\text{-}P}$ = 13.7 Hz), 130.86 (*d*, $J_{C\text{-}P}$ = 10.1 Hz), 132.86 (*dd*, $J_{C\text{-}P}$ = 11.9, 2.8 Hz), 135.13 (*d*, $J_{C\text{-}P}$ = 6.4 Hz), 135.78 (*dd*, $J_{C\text{-}P}$ = 22.0, 14.7 Hz), 139.6, 174.4, 177.59 (*d*, $J_{C\text{-}P}$ = 17.4 Hz) ppm; ^{31}P NMR

(202.44 MHz, $CDCl_3$): δ 28.8 ppm; IR (film): 3166, 3022, 2922, 1780, 1707, 1610, 1566, 1487, 1469, 1380, 1305, 1192, 1135, 1078, 988, 926, 870, 835, 756, 712, 687, 667, 639, 563 cm^{-1}; HRMS (ESI): $C_{26}H_{25}O_3N_1P_1Cl_2^+$ ($[M+H]^+$), Calc. 500.0949, Found 500.0950; $[\alpha]_D^{25}$: +8.9 (c 4.2, $CHCl_3$); HPLC analysis: Chiralpak IA + Chiralpak ADH (Hex/IPA = 80/20, 1.0 mL/min, 214 nm, 23°C), 32.3 (major), 53.2 min, 92% *ee*.

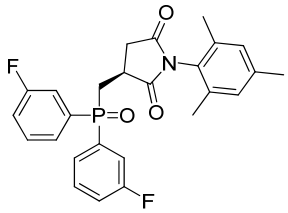


(*S*)-3-{[Bis(2-trifluoromethylphenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12f**) White solid; R_f (Hex/EtOAc = 1/1): 0.23; mp 197.8–198.5°C; 89% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.03 (*s*, 3H), 2.28 (*s*, 3H), 2.56–2.64 (*m*, 1H), 2.75 (*dd*, *J* = 18.9, 6.3 Hz, 1H), 2.97 (*dd*, *J* = 18.3, 8.8 Hz, 1H), 3.25–3.33 (*m*, 1H), 3.52–3.57 (*m*, 1H), 6.94 (*d*, *J* = 3.2 Hz, 2H), 7.70–7.85 (*m*, 6H), 8.25 (*dt*, *J* = 14.5, 7.6 Hz, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.58, 17.61, 21.0, 32.51 (*d*, $J_{C\text{-}P}$ = 78.8 Hz), 35.37 (*d*, $J_{C\text{-}P}$ = 2.7 Hz), 35.7, 123.38 (*dd*, $J_{C\text{-}P}$ = 271.3, 8.3 Hz), 127.3, 127.75–127.91 (*m*, 1C), 128.09–128.20 (*m*, 1C), 129.33 (*d*, $J_{C\text{-}P}$ = 7.3 Hz), 131.67–131.86 (*m*, 1C), 132.02, 132.53 (*dd*, $J_{C\text{-}P}$ = 9.2, 2.8 Hz), 134.14 (*dd*, $J_{C\text{-}P}$ = 14.7, 8.3 Hz), 135.12 (*d*, $J_{C\text{-}P}$ = 7.3 Hz), 139.46, 174.6, 177.63 (*d*, $J_{C\text{-}P}$ = 18.3 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 31.2 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 19.38 (*d*, *J* = 61.9 Hz) ppm; IR (film): 2925, 2253, 1712, 1475, 1381, 1311, 1184, 1130, 1039, 908, 731 cm^{-1}; HRMS (FAB) $C_{28}H_{25}O_3N_1F_6P_1^+$ ($[M+H]^+$) Calc. 568.1471, Found 568.1483; $[\alpha]_D^{27}$ +21.4 (c 4.0, $CHCl_3$); HPLC analysis Chiralpak IB (Hex/IPA = 70/30, 0.5 mL/min, 214 nm, 23°C) 19.8 (major), 23.0 min, 96% *ee*.



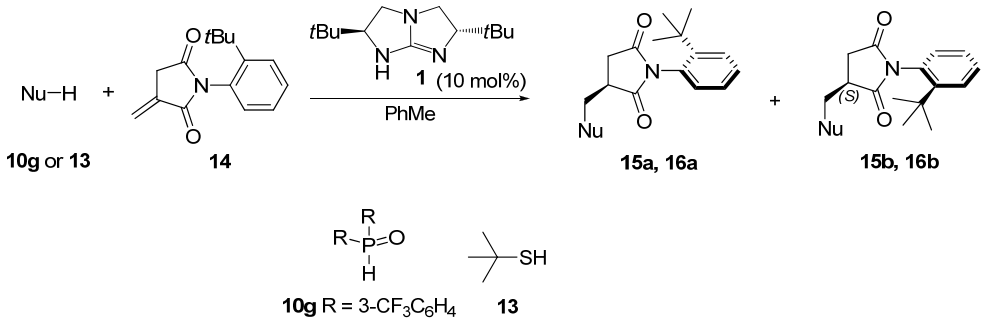
(*S*)-3-{[bis(3-trifluoromethylphenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12g**) White solid; R_f (Hex/EtOAc = 1/2): 0.48; mp 180.0–180.4°C; 93% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.02 (*s*, 3H), 2.29 (*s*, 3H), 2.45–2.53 (*m*, 1H), 2.90 (*dd*, *J* = 18.9, 5.7 Hz, 1H), 3.11 (*dd*, *J* = 18.9, 9.5 Hz, 1H), 3.24–3.33 (*m*, 2H), 6.94 (*s*, 2H), 7.66–7.74 (*m*, 2H), 7.85–7.89 (*m*, 2H), 7.95–8.04 (*m*, 2H), 8.13 (*dd*, *J* = 28.4, 11.4 Hz, 2H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.62, 17.64, 21.0, 31.25 (*d*, $J_{C\text{-}P}$ = 72.4 Hz), 35.03 (*d*, $J_{C\text{-}P}$ = 2.8 Hz), 35.4, 122.33 (*d*, $J_{C\text{-}P}$ = 272.2 Hz), 127.20, 127.35–127.46 (*m*, 1C), 127.80–127.91

(*m*, 1C), 129.40 (*d*, $J_{C\text{-}P}$ = 8.3 Hz), 129.43–129.57 (*m*, 1C), 129.87 (*dd*, $J_{C\text{-}P}$ = 17.4, 11.9 Hz), 131.69–132.21 (*m*, 1C), 133.74 (*dd*, $J_{C\text{-}P}$ = 26.6, 10.1 Hz), 135.11 (*d*, $J_{C\text{-}P}$ = 4.6 Hz), 139.59, 174.16, 177.41 (*d*, $J_{C\text{-}P}$ = 16.5 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 28.9 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 13.17 (*d*, *J* = 6.2 Hz) ppm; IR (film): 2981, 2925, 2870, 2254, 1783, 1714, 1607, 1486, 1454, 1423, 1380, 1327, 1278, 1195, 1175, 1140, 1090, 1075, 1049, 909, 803, 740, 731, 651 cm^{-1}; HRMS (ESI) $C_{28}H_{25}O_3N_1F_6P_1^+$ ($[M+H]^+$) Calc. 568.1476, Found 568.1475; $[\alpha]_D^{28}$ -8.1 (c 1.3, $CHCl_3$); HPLC analysis Chiralpak IA (Hex/IPA = 80/20, 1.0 mL/min, 214 nm, 23°C) 8.1, 9.6(major) min, 94% *ee*.



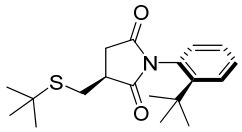
(*S*)-3-{[Bis(3-fluorophenyl)phosphoryl]methyl}-1-mesitylpyrrolidine-2,5-dione (**12h**) White solid; R_f (Hex/EtOAc = 1/2): 0.59; mp: 145.0–145.3°C; 88% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.00 (*s*, 3H), 2.02 (*s*, 3H), 2.28 (*s*, 3H), 2.38–2.45 (*m*, 1H), 2.87 (*dd*, *J* = 18.9, 5.7 Hz, 1H), 3.09 (*dd*, *J* = 18.9, 9.5 Hz, 1H), 3.19–3.32 (*m*, 2H), 6.94 (*s*, 2H), 7.28–7.31 (*m*, 2H), 7.48–7.62 (*m*, 6H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 17.62, 17.64, 21.0, 31.26 (*d*, $J_{C\text{-}P}$ = 72.4 Hz), 35.04 (*d*, $J_{C\text{-}P}$ = 3.7 Hz), 35.3, 117.45–118.07 (*m*), 119.74–120.02 (*m*), 126.09–126.45 (*m*), 127.19, 129.37 (*d*, $J_{C\text{-}P}$ = 8.3 Hz), 131.08–131.37 (*m*), 133.04–134.30 (*m*), 135.91 (*d*, $J_{C\text{-}P}$ = 7.3 Hz), 139.6, 162.75 (*dt*, $J_{C\text{-}P}$ = 252.0, 16.5 Hz), 174.4, 177.62 (*d*, $J_{C\text{-}P}$ = 17.4 Hz) ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 29.0 ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ -33.57 (*dm*, *J* = 38.1 Hz, 1F) ppm; IR (film): 2923, 2253, 1782, 1712, 1605, 1584, 1480, 1423, 1380, 1305, 1269, 1229, 1194, 1101, 908, 790, 733, 650 cm^{-1}; HRMS (ESI): $C_{26}H_{25}O_3N_1F_2P_1^+$ ($[M+H]^+$), Calc. 468.1540, Found 468.1539; $[\alpha]_D^{25}$: +13.0 (c 2.5, $CHCl_3$); HPLC analysis: Chiralpak IA (Hex/IPA = 80/20, 1.0 mL/min, 214 nm, 23°C), 13.8 (major), 18.0 min, 94% *ee*.

Procedures for Enantioselective Protonation Reaction of Axially Chiral Itaconimide 14 Catalyzed by Chiral Bicyclic Guanidine 1



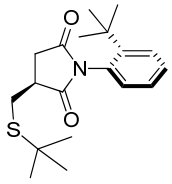
Bis-[(3-trifluoromethyl)phenyl]-phosphine oxide **10g** [Ar = (3- trifluoromethyl)phenyl] (33.8 mg, 0.100 mmol, 1.00 equiv.) was dissolved in toluene (1.00 mL) in a 4 mL sample vial. Catalyst **1** (2.23 mg, 0.0100 mmol, 0.100 equiv.) was added and the vial was submerged in cryobath at −50°C. After being stirred for 10 min, itaconimide **14** (26.8 mg, 0.110 mmol, 1.10 equiv.) was added as solid and stirred for 4 hours. The reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was loaded onto silica gel column and purified by gradient elution (Hex/EtOAc = 9/1 to 1/1) to afford inseparable products **15a**, **15b** as white solids in 1.1 (*syn*) :1 (*anti*) diastereomeric ratio (*d.r.*).

***syn/anti*-(*S*)-3-{Bis[3-(trifluoromethyl)phenyl]phosphoryl}methyl-1-(2-*tert*-butylphenyl)pyrrolidine-2,5-dione** (**15a, 15b**) White solid; R_f (Hex/EtOAc = 1/1): 0.20; 92% combined yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.27 (*s*, 9H, *anti*), 1.30 (*s*, 9H, *syn*), 2.44 (*dd*, *J* = 26.8, 12.9 Hz, 1H, *syn*), 2.65 (*dd*, *J* = 25.5, 10.4 Hz, 1H, *anti*), 2.79 (*dd*, *J* = 18.6, 5.7 Hz, 1H, *anti*), 2.89 (*dd*, *J* = 17.7, 4.7 Hz, 1H, *syn*), 3.07 (*dd*, *J* = 18.6, 9.5 Hz, 1H, *anti*), 3.16 (*dd*, *J* = 26.5, 9.5 Hz, 1H, *syn*), 3.18–3.24 (*m*, 1H, *syn*), 3.24–3.29 (*m*, 1H, *anti*), 3.32–3.34 (*m*, 1H, *anti*), 3.34–3.36 (*m*, 1H, *syn*), 6.79 (*d*, *J* = 7.6 Hz, 1H, *syn*), 6.86 (*d*, *J* = 7.6 Hz, 1H, *anti*), 7.27–7.30 (*m*, 2H), 7.39–7.42 (*m*, 2H), 7.57–7.60 (*m*, 2H), 7.70–7.75 (*m*, 4H), 7.88–7.91 (*m*, 4H), 7.96–8.06 (*m*, 4H), 8.09–8.20 (*m*, 4H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 30.3, 30.80, 30.84, 31.4, 31.5, 31.7, 35.1, 35.3, 35.4, 35.5, 35.8, 35.9, 120.1, 122.2, 124.4, 126.2, 126.3, 126.6, 127.38–127.27.49 (*m*), 127.61–127.69 (*m*), 127.89–127.97 (*m*), 128.75, 129.0, 129.42–129.52 (*m*), 129.76–129.99 (*m*), 130.15, 130.44, 130.57, 131.60–132.39 (*m*), 133.16, 133.20, 133.28, 133.55–134.06 (*m*), 147.88, 175.28, 175.57, 178.28, 178.41, 178.57, 178.70 ppm; ^{31}P NMR (202.44 MHz, $CDCl_3$): δ 28.7 (*anti*), 29.1 (*syn*) ppm; ^{19}F NMR (282.38 MHz, $CDCl_3$): δ 13.16 (*syn*), 13.19 (*anti*) ppm; IR (film): 2972, 2912, 2254, 1784, 1715, 1606, 1491, 1443, 1423, 1382, 1327, 1278, 1185, 1175, 1140, 1074, 909, 835, 803, 739 cm^{-1}; HRMS (ESI): $C_{29}H_{26}O_3N_1F_6P_1Na_1^+$ ([M+Na]$^+$), Calc. 604.1452, Found 604.1451; $[\alpha]_D^{29}$: -20.2 (c 1.3, $CHCl_3$); HPLC analysis: Chiralpak IB + Chiralcel ODH (Hex/IPA = 90/10, 1.0 mL/min, 214 nm, 23°C), 42.2 (*syn*), 47.8 (*syn*, major), 55.6 (*anti*, major), 75.5 min (*anti*, major), 53.1 (*syn*): 46.9 (*anti*) d.r., 79 (*syn*): >99 (*anti*) % *ee*.



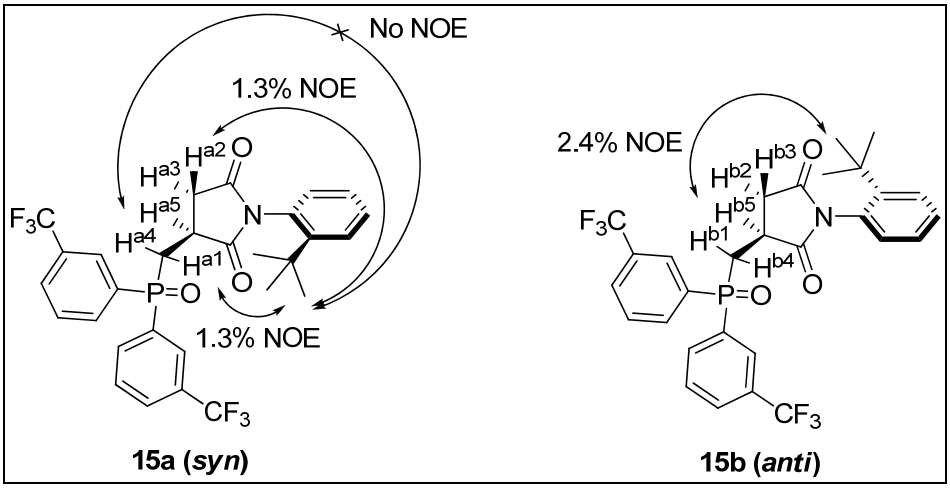
tert-Butyl thiol **13** (225 μL, 2.00 mmol, 20.0 equiv.) was dissolved in toluene (1.00 mL) in a 4 mL sample vial. Catalyst **1** (2.23 mg, 0.0100 mmol, 0.100 equiv.) was added and the vial was submerged in cryobath at −50°C. After being stirred for 10 min, itaconimide **14** (24.3 mg, 0.100 mmol, 1.00 equiv.) was added as solid and stirred for 30 hours. The reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was loaded onto silica gel column. It was purified by gradient elution (Hex/EtOAc = 30/1 to 7/1) to afford products **16a** and **16b** separately in 54 (*syn*):46 (*anti*) diastereomeric ratio (*d.r.*) with a combined yield of 97%.

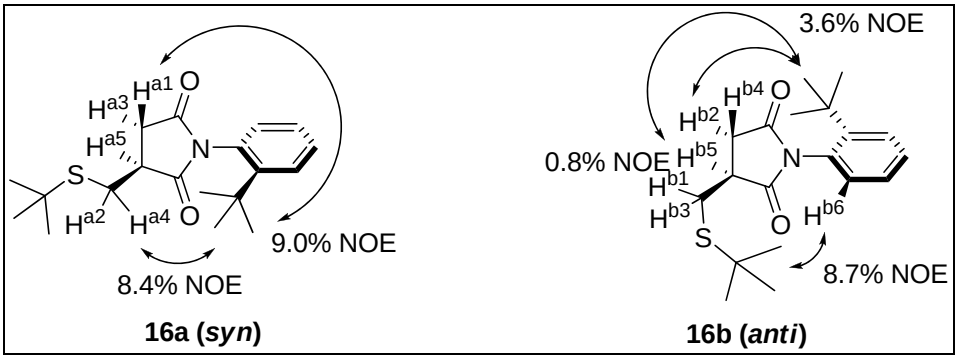
***syn*-(*S*)-1-(2-*tert*-Butylphenyl)-3-(*tert*-butylthiomethyl)pyrrolidine-2,5-dione** (**16a**) White solid; R_f (Hex/EtOAc = 4/1): 0.18; mp: 133.0–133.5°C; 52% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.32 (*s*, 9H), 1.36 (*s*, 9H), 2.79–2.85 (*m*, 2H), 2.99–3.04 (*m*, 1H), 3.17–3.24 (*m*, 2H), 6.82 (*dd*, *J* = 7.6, 1.3 Hz, 1H), 7.29 (*dt*, *J* = 7.6, 1.3 Hz, 1H), 7.37–7.40 (*m*, 1H), 7.58 (*dd*, *J* = 8.2, 1.9 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 29.0, 30.8, 31.7, 34.5, 35.6, 41.1, 42.9, 127.4, 128.7, 129.7, 130.5, 130.7, 148.2, 176.4, 178.1 ppm; IR (film): 2965, 2928, 2867, 2335, 2351, 1779, 1712, 1633, 1490, 1461, 1443, 1379, 1287, 1252, 1182, 1054, 909, 733, 650 cm^{-1}; HRMS (ESI): $C_{19}H_{28}O_2N_1S_1^+$ ([M+H]$^+$), Calc. 334.1841, Found 334.1834; $[\alpha]_D^{29}$: +37.9 (c 1.1, $CHCl_3$); HPLC analysis: Chiralpak IA (Hex/IPA = 90/10, 1.0 mL/min, 214 nm, 23°C), 12.9, 16.9 (major) min, 74% *ee*.



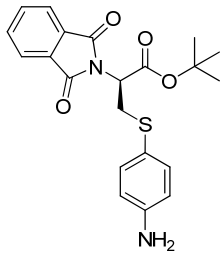
***anti*-(*S*)-1-(2-*tert*-Butylphenyl)-3-(*tert*-butylthiomethyl)pyrrolidine-2,5-dione** (**16b**) colorless liquid; R_f (Hex/EtOAc = 4/1): 0.28; 45% yield; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.30 (*s*, 9H), 1.35 (*s*, 9H), 2.83 (*dd*, *J* = 18.3, 4.4 Hz, 1H), 2.97 (*dd*, *J* = 12.6, 7.6 Hz, 1H), 3.01 (*dd*, *J* = 18.3, 8.8 Hz, 1H), 3.10 (*dd*, *J* = 12.0, 3.8 Hz, 1H), 3.22–3.27 (*m*, 1H), 6.92 (*dd*, *J* = 7.6, 1.3 Hz, 1H), 7.29 (*dt*, *J* = 7.6, 1.3 Hz, 1H), 7.38 (*dt*, *J* = 7.6, 1.3 Hz, 1H), 7.57 (*dd*, *J* = 7.6, 1.3 Hz, 1H) ppm; ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 29.2, 30.8, 31.6, 34.0, 35.5, 40.0, 42.8, 127.4, 128.7, 129.7, 130.5, 130.7, 147.9, 178.4, 178.6 ppm; IR (film): 2963, 2928, 2867, 2252, 1780, 1712, 1633, 1490, 1443, 1417, 1378, 1181, 912, 759, 731, 647, 628 cm^{-1}; HRMS (ESI): $C_{19}H_{28}O_2N_1S_1^+$ ([M+H]$^+$), Calc. 334.1841, Found 334.1842; $[\alpha]_D^{29}$: -2.6 (c 1.3, $CHCl_3$); HPLC analysis: Chiralcel OF (Hex/IPA = 90/10, 1.0 mL/min, 214 nm, 23°C), 11.8 (major), 18.3 min, 90% *ee*.

Determination of the Relative Configuration of Axially Chiral Imides 15 and 16 by ^{1}H-^{1}H 2D COSY NMR and ^{1}H NOESY NMR

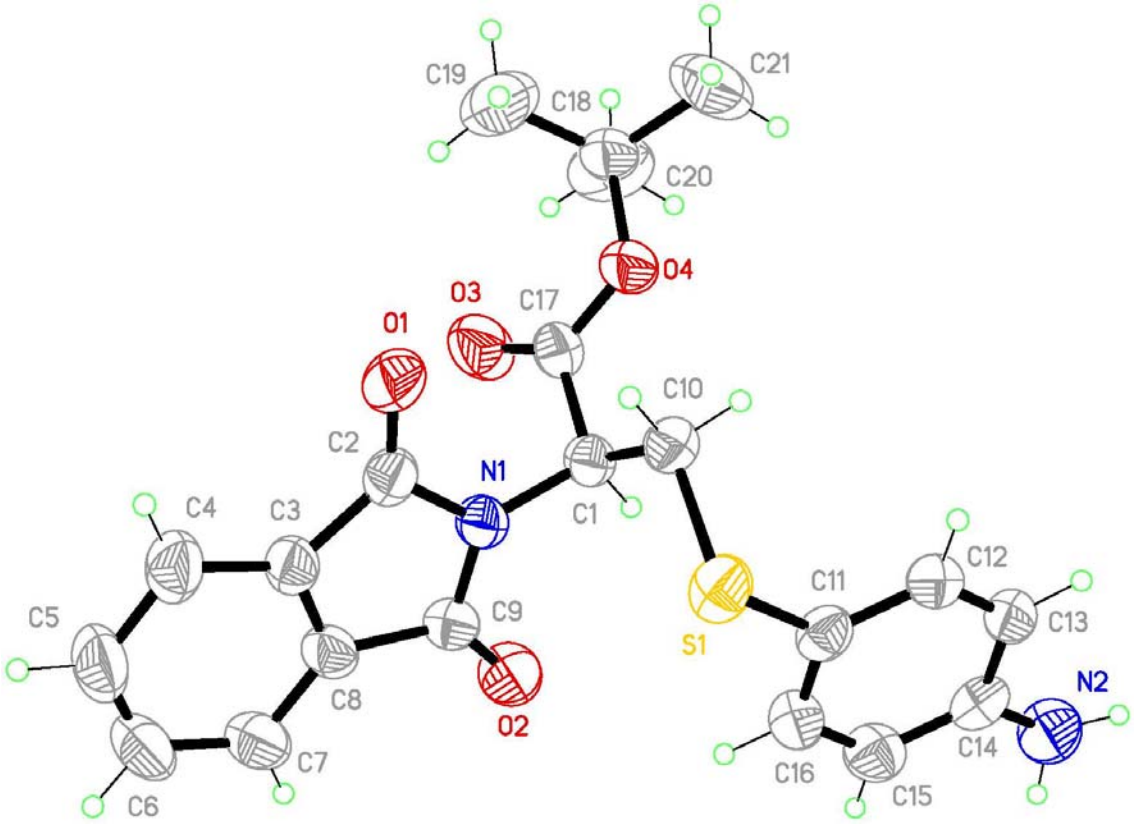




Determination of the Absolute Configuration of Chiral Cysteine Derivative 4j by X-Ray Crystallographic Analysis



Crystal of cysteine derivative **4j** was grown from Hex/DCM.



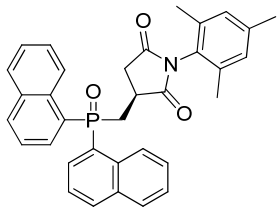
The crystal is monoclinic, space group P2(1). The asymmetric unit contains one molecule C21H22N2O4S1. The H atoms at N2 were located from difference map and refined without restraint. There are intermolecular H bonds between this NH2 and O's of neighboring molecules. Final R values are R1=0.048 and wR2=0.112 for 2-theta up to 55º. Flack value of x=-0.014 (0.072) indicates that the absolute structure as reported is correct.

Crystal data and structure refinement for 7579

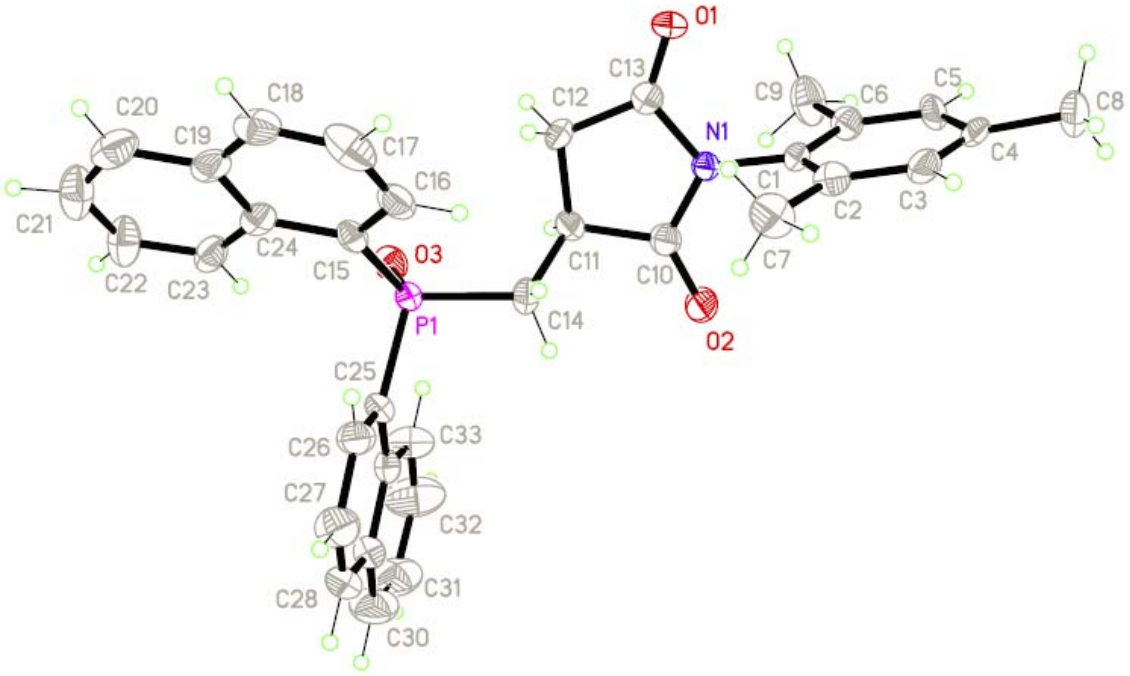
Identification code	7579
Empirical formula	C21 H22 N2 O4 S

Formula weight	398.47	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.162(4) Å	□= 90°.
	b = 6.378(2) Å	□= 103.913(7)°.
	c = 16.856(5) Å	□ = 90°.
Volume	1060.4(6) $Å^3$	
Z	2	
Density (calculated)	1.248 Mg/m^3	
Absorption coefficient	0.180 mm^{-1}	
F(000)	420	
Crystal size	0.16 x 0.08 x 0.02 mm^3	
Theta range for data collection	2.06 to 27.50°	
Index ranges	-13<=h<=13, -8<=k<=8, -21<=l<=21	
Reflections collected	13942	
Independent reflections	4877 [R(int) = 0.0335]	
Completeness to theta = 27.50°	99.9 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9964 and 0.9717	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4877 / 1 / 264	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0480, wR2 = 0.1068	
R indices (all data)	R1 = 0.0578, wR2 = 0.1112	
Absolute structure parameter	-0.01(7)	
Largest diff. peak and hole	0.292 and -0.160 $e.Å^{-3}$	

Determination of the Absolute Configuration of Chiral Imide 12a by X-Ray Crystallographic Analysis



Crystal of imide **12a** was grown from Hex/IPA.



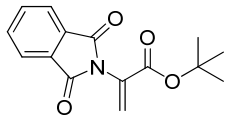
The crystal is monoclinic, space group P2(1). There is one molecule of the compound and half a hexane solvent molecule in the asymmetric. The structure is expected. Final R values are R1=0.0830 and wR2= 0.2187 for 2-theta max of 50 º. The Flack's parameter is x=0.0986 (esd 0.21). This indicates that the absolute as reported is correct.

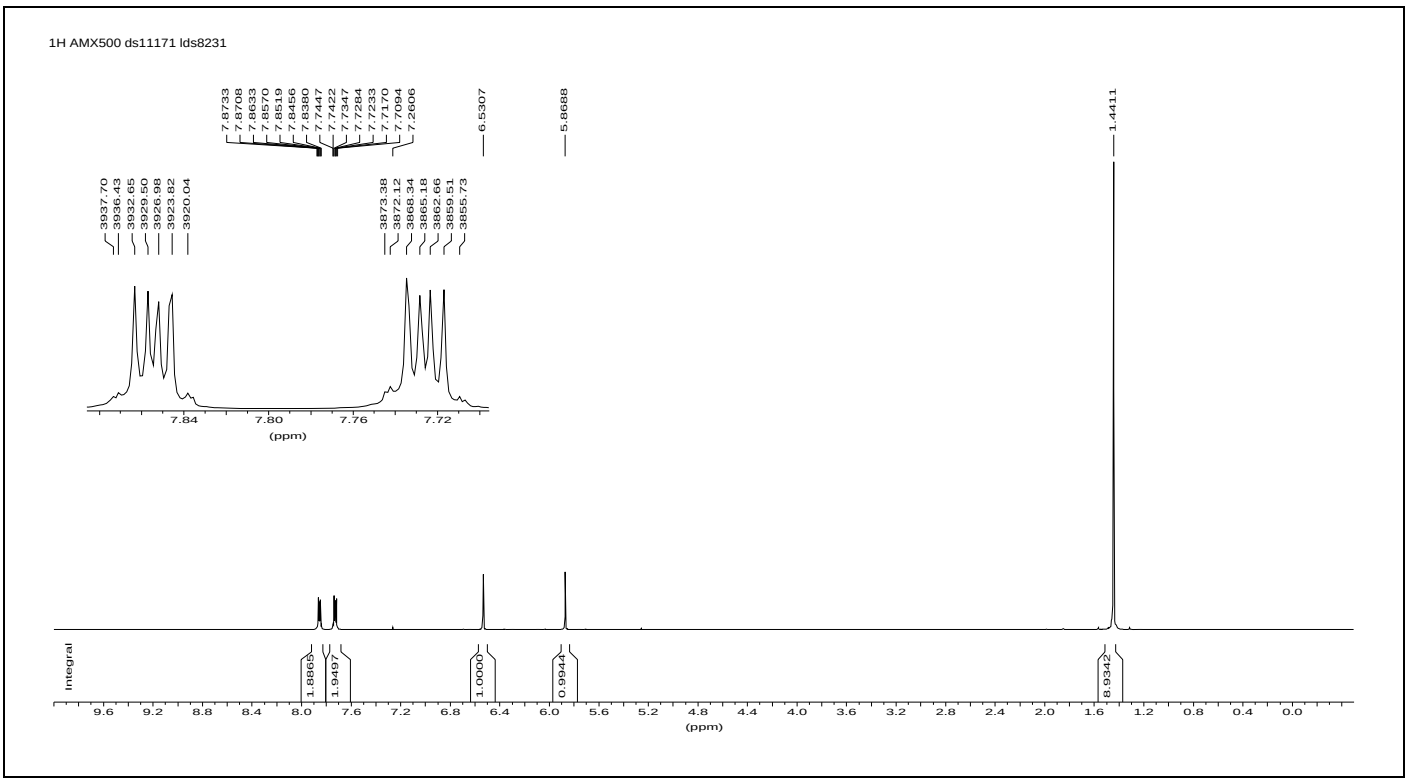
Crystal data and structure refinement for 7423

Identification code	7423
Empirical formula	C37 H37 N O3 P
Formula weight	574.65
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P2(1)	
Unit cell dimensions	a = 13.023(2) Å	□= 90°.
	b = 7.3527(11) Å	□= 103.977(3)°.
	c = 16.605(3) Å	□ = 90°.
Volume	1542.9(4) $Å^3$	
Z	2	
Density (calculated)	1.237 Mg/m^3	
Absorption coefficient	0.126 mm^{-1}	
F(000)	610	
Crystal size	0.60 x 0.12 x 0.06 mm^3	
Theta range for data collection	1.61 to 25.00°	
Index ranges	-15<=h<=15, -8<=k<=8, -19<=l<=19	
Reflections collected	15578	
Independent reflections	5428 [R(int) = 0.0495]	
Completeness to theta = 25.00°	99.8 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9925 and 0.9280	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5428 / 46 / 409	
Goodness-of-fit on F^2	1.183	
Final R indices [I>2sigma(I)]	R1 = 0.0830, wR2 = 0.2187	
R indices (all data)	R1 = 0.0867, wR2 = 0.2209	
Absolute structure parameter	0.1(2)	
Largest diff. peak and hole	0.865 and -0.327 $e.Å^{-3}$	

NMR Spectra

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7.7284
7.7233
7.7170
7.7094
7.2606
6.5307
5.8688
1.4411
3937.70
3936.43
3932.65
3929.50
3926.98
3923.82
3920.04
3873.38
3872.12
3868.34
3865.18
3862.66
3859.51
3855.73
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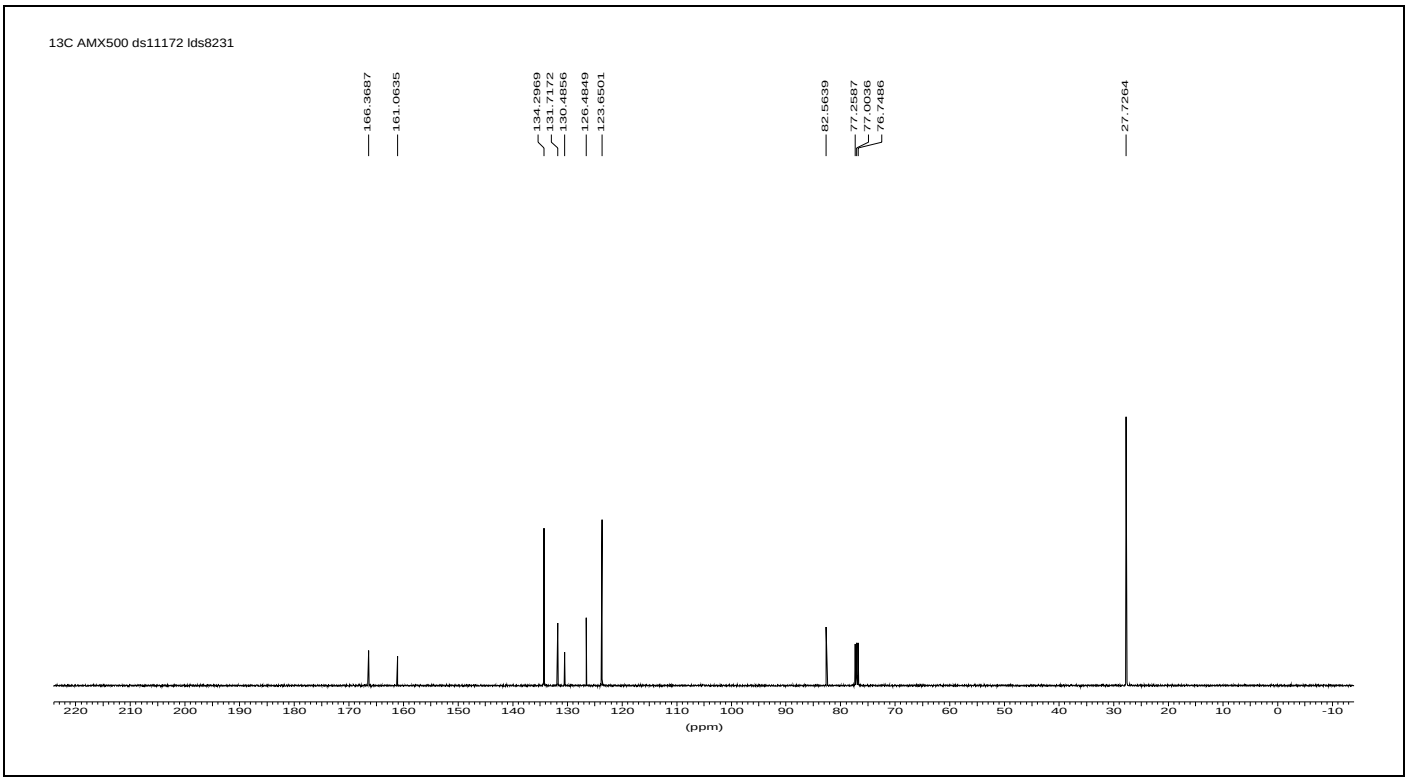
(ppm)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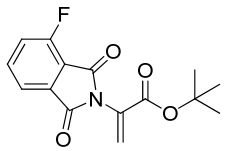
(ppm)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O
N
O
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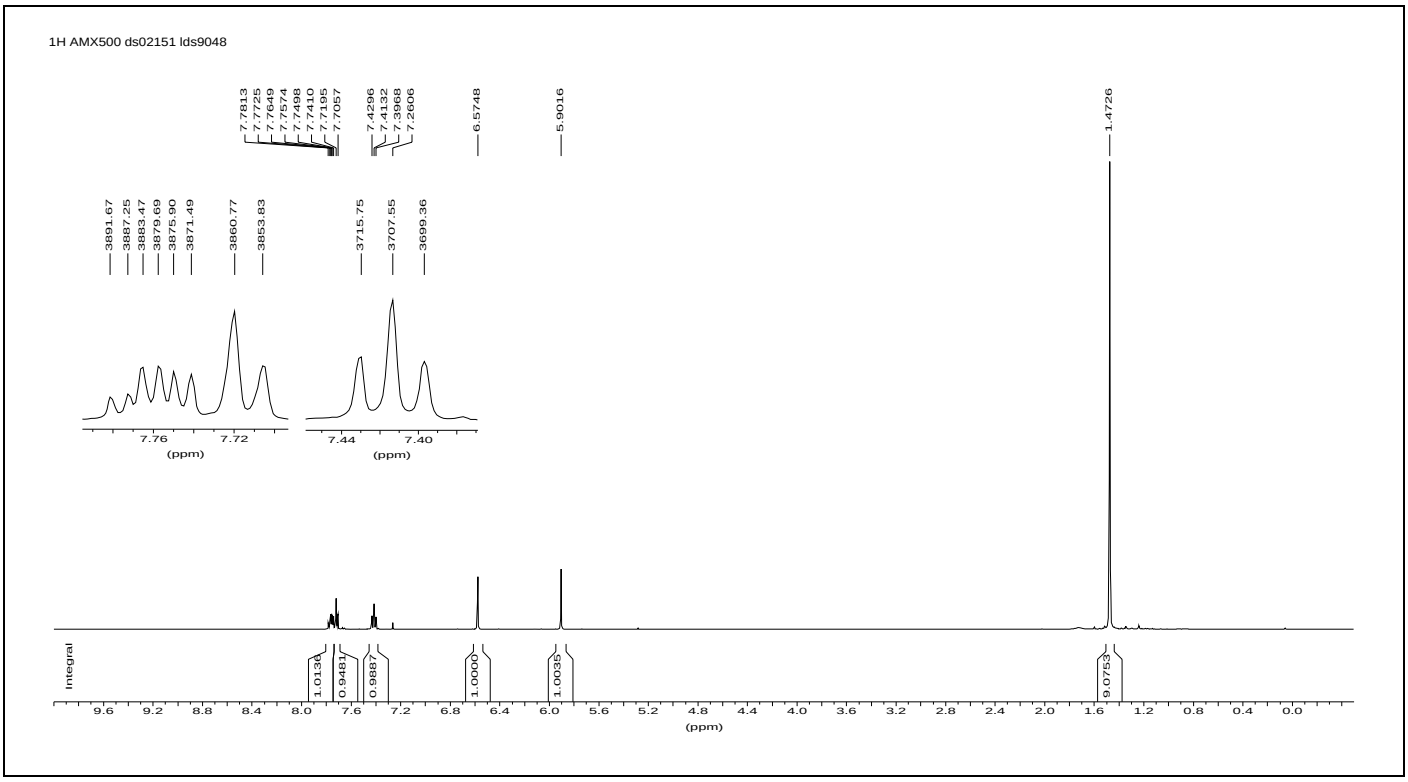
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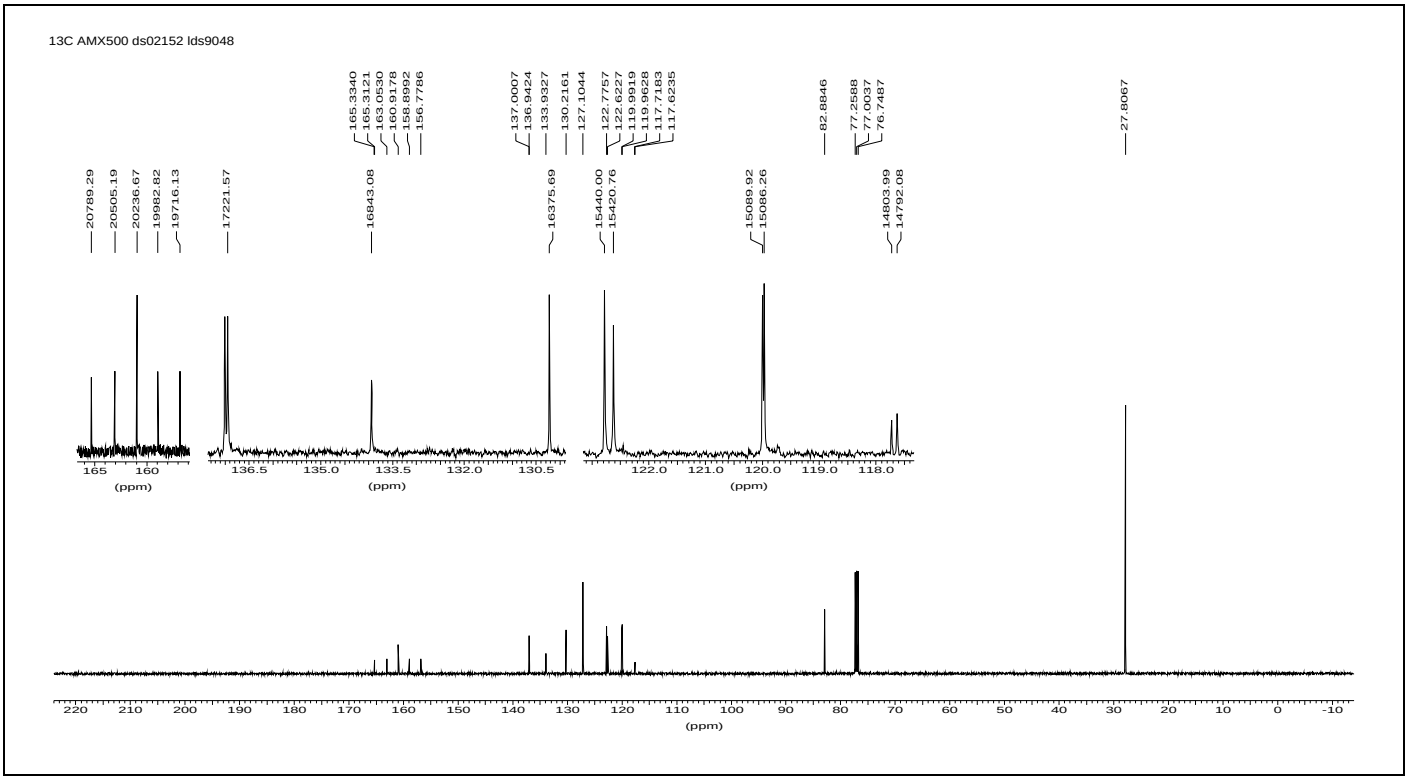
(ppm)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130.2161
127.1044
122.7757
122.6227
119.9919
119.9628
117.7183
117.6235
82.8846
77.2588
77.0037
76.7487
27.8067
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20505.19
20236.67
19982.82
19716.13
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15086.26
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14792.08
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160
(ppm)
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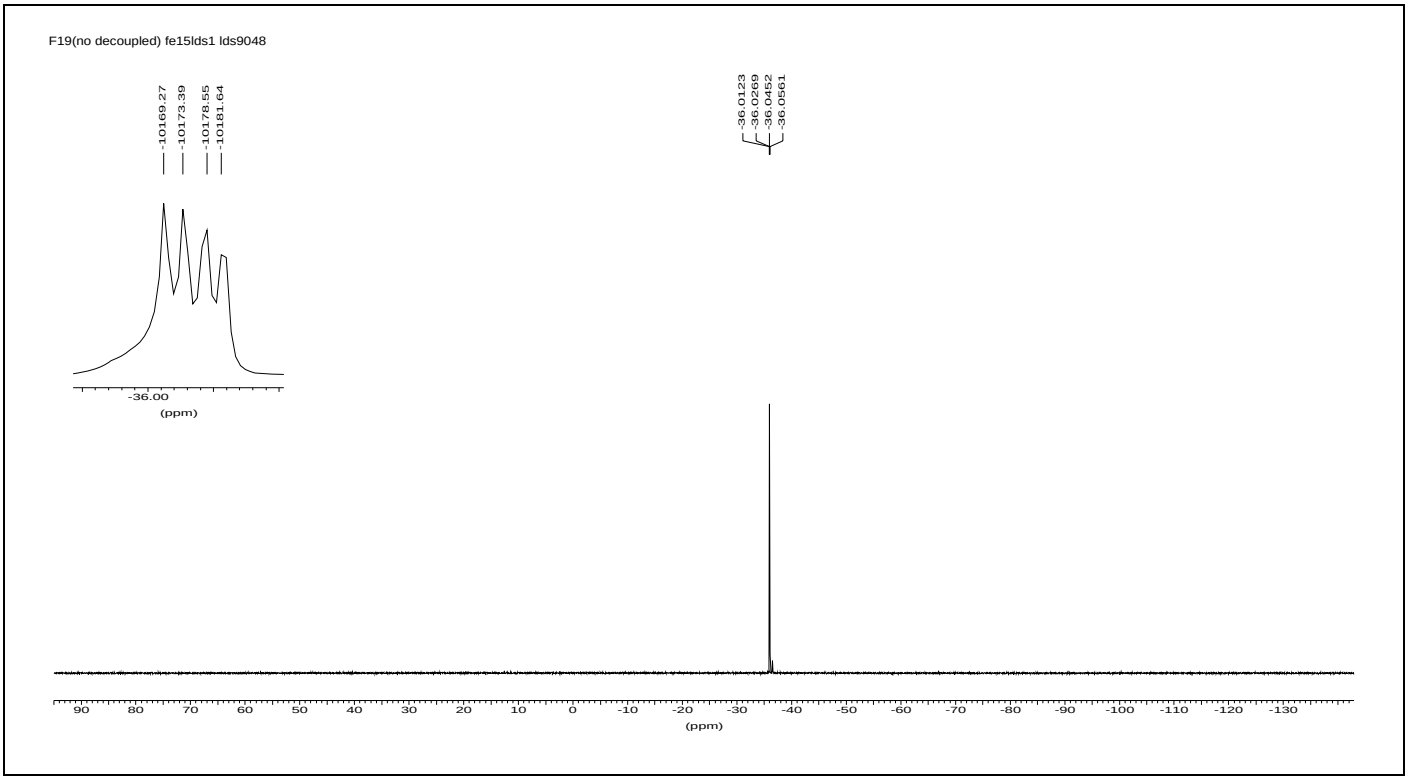
(ppm)
(ppm)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(ppm)
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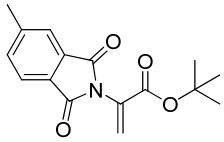
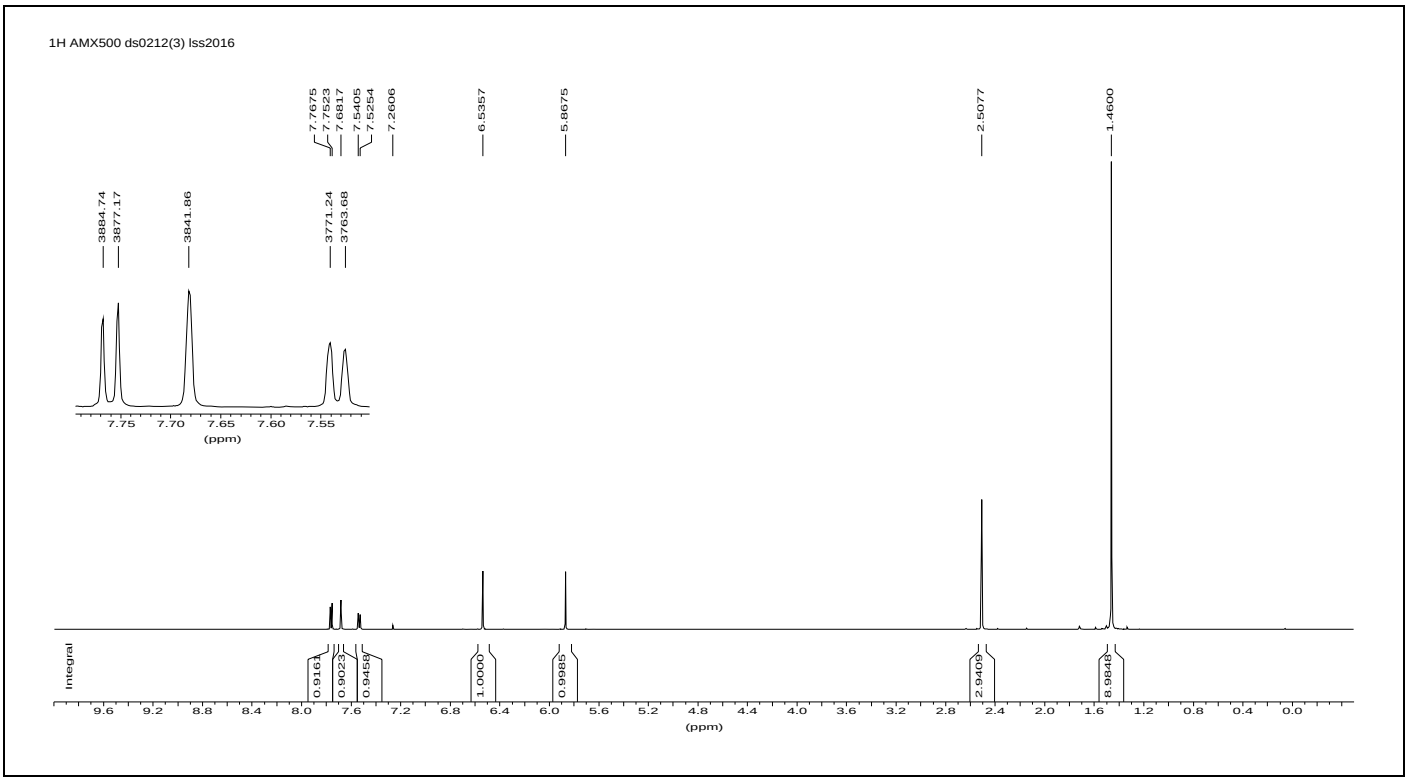
(ppm)

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2.5077
1.4600
3884.74
3877.17
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3771.24
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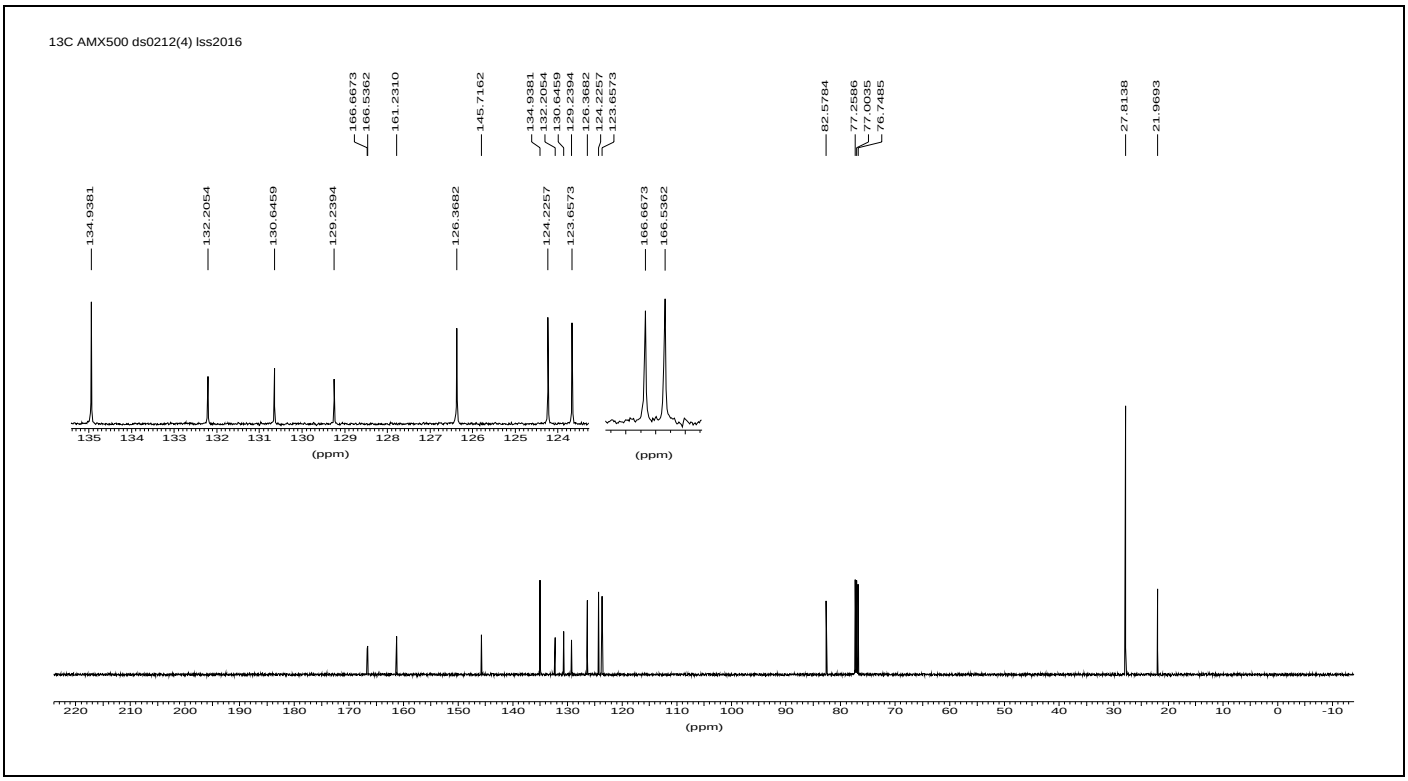
(ppm)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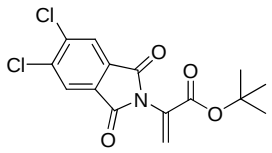
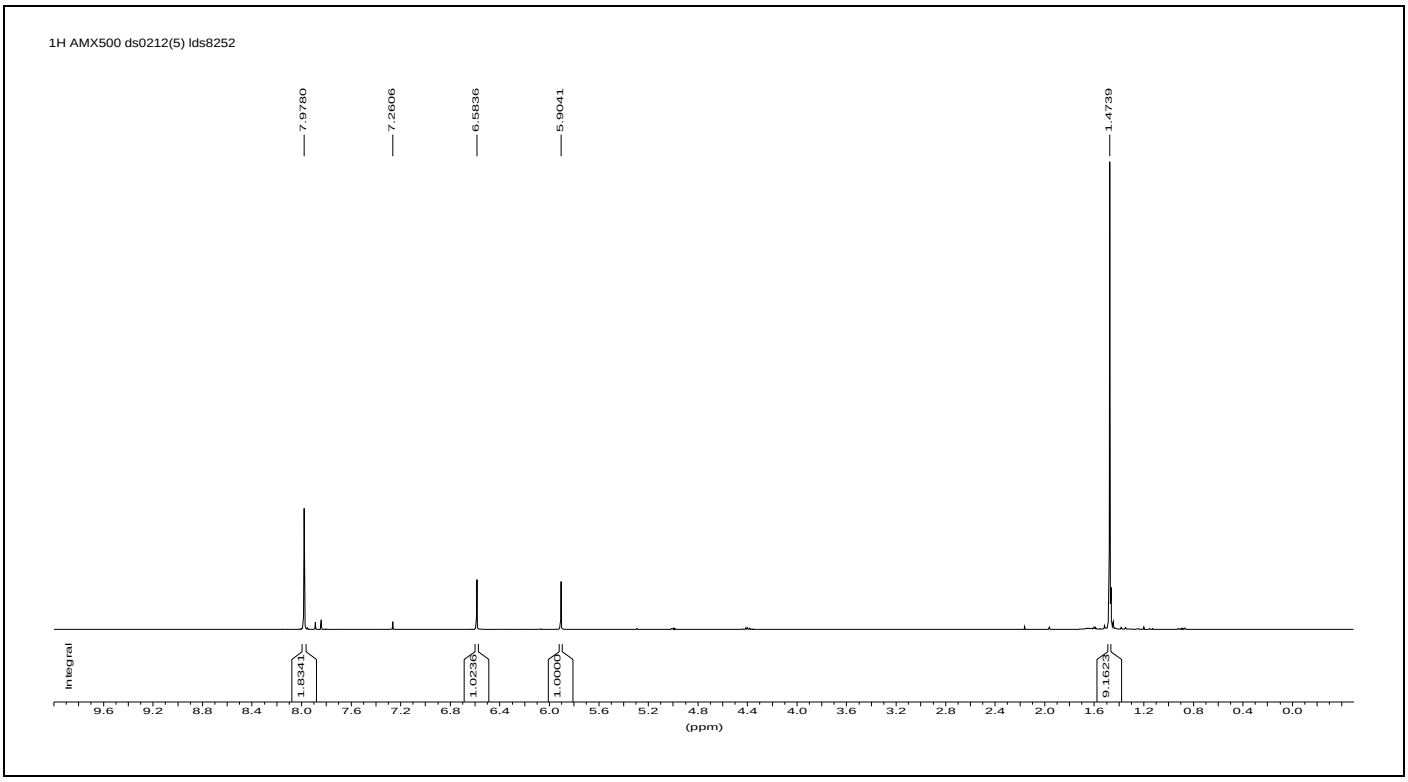
(ppm)
(ppm)
(ppm)


Cl
Cl
O
O
N
O
O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Integral
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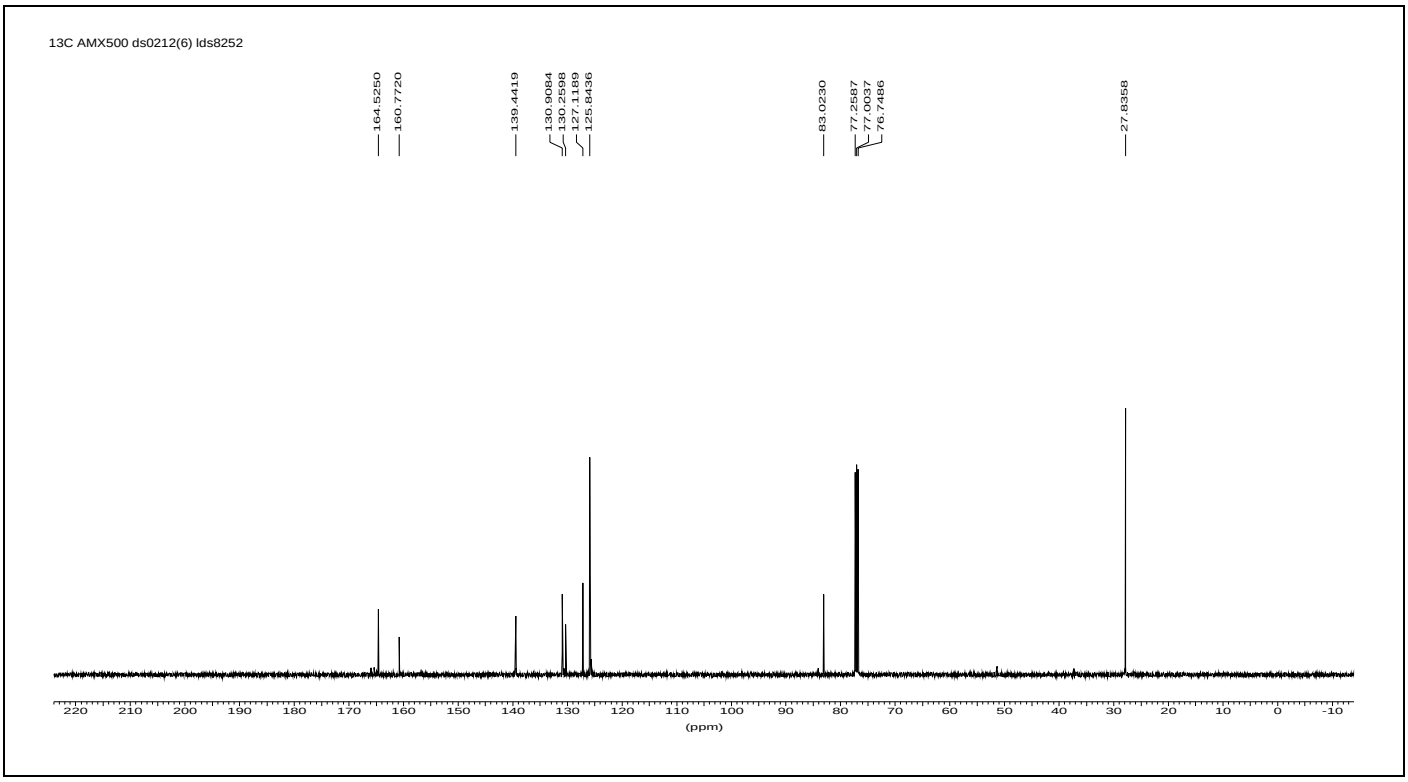
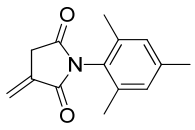
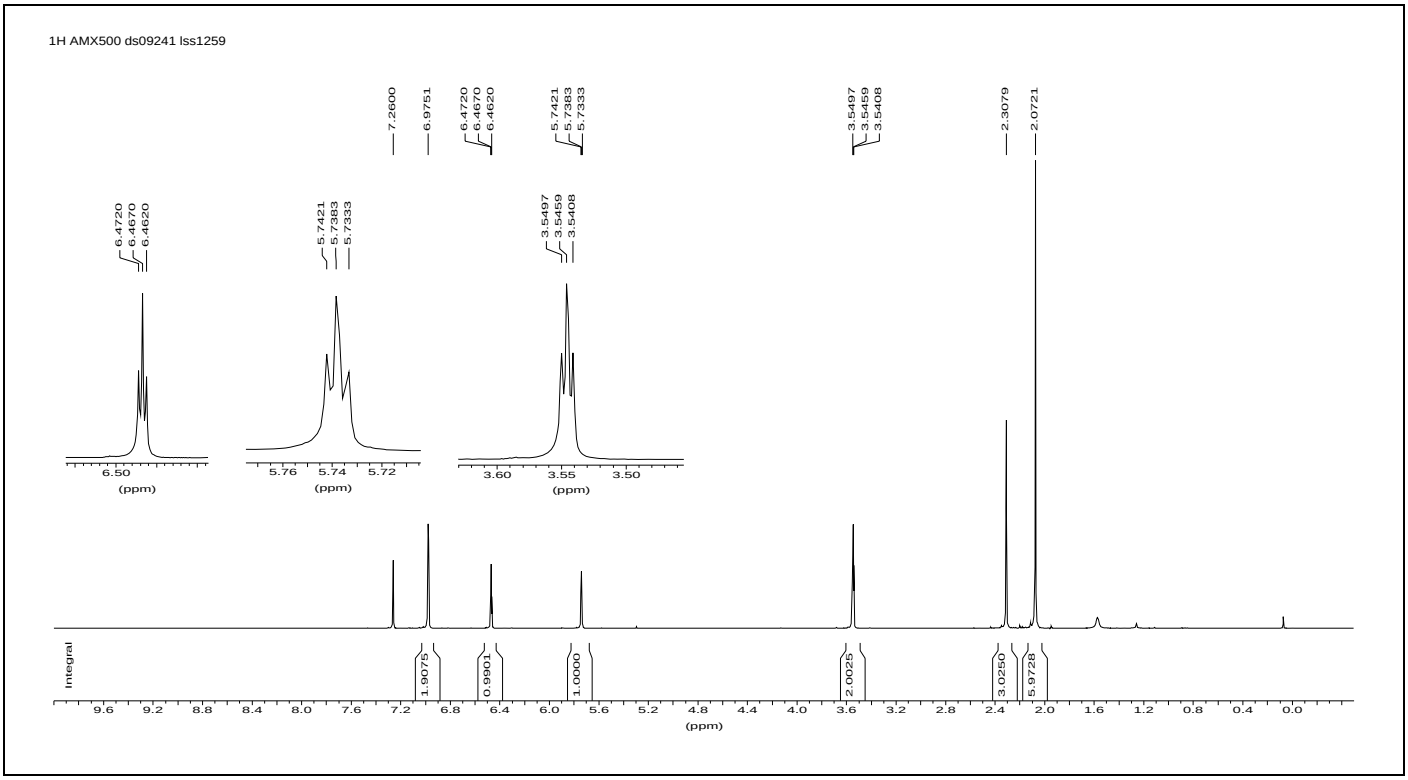
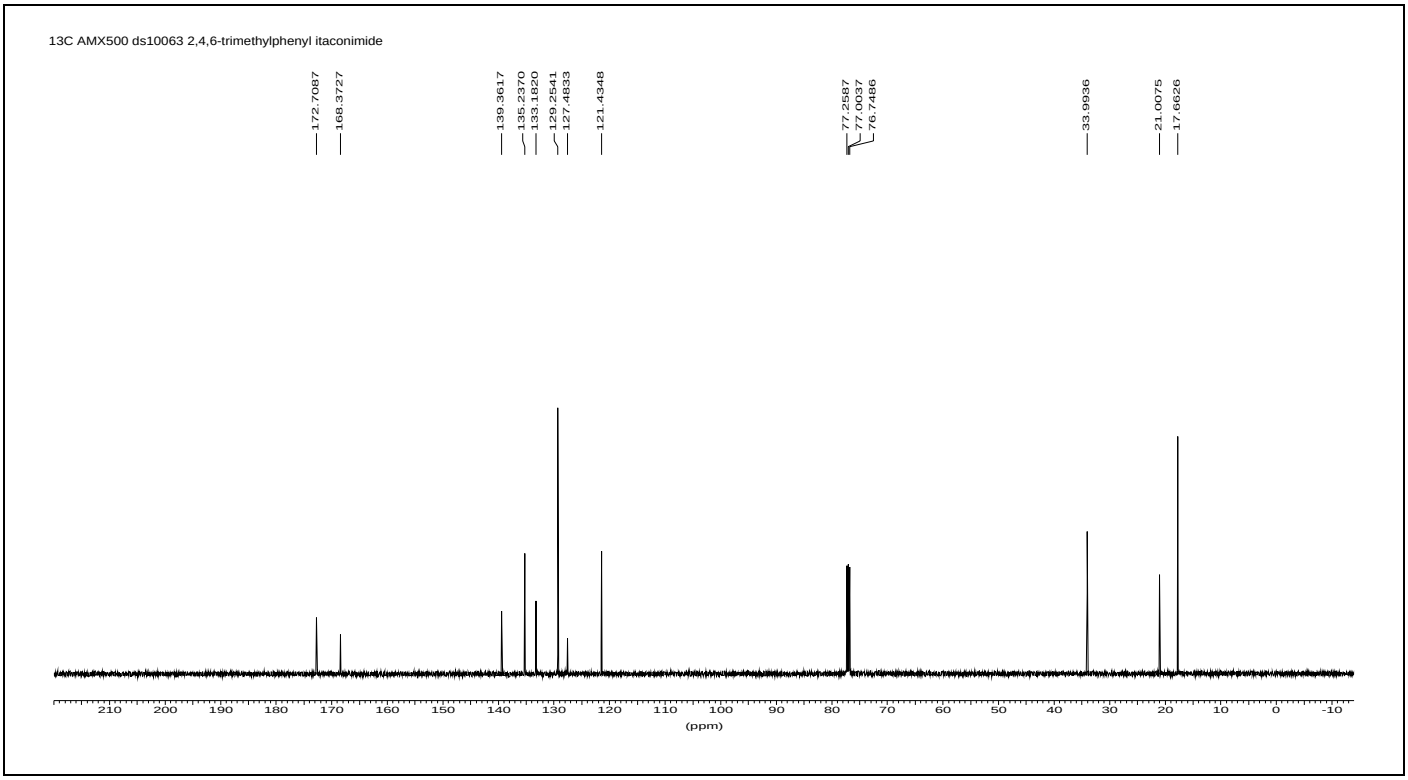
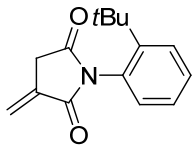
9.1623
(ppm)


13C AMX500 ds0212(6) lds8252
164.5250
160.7720
139.4419
130.9084
130.2598
127.1189
125.8436
83.0230
77.2587
77.0037
76.7486
27.8358
(ppm)

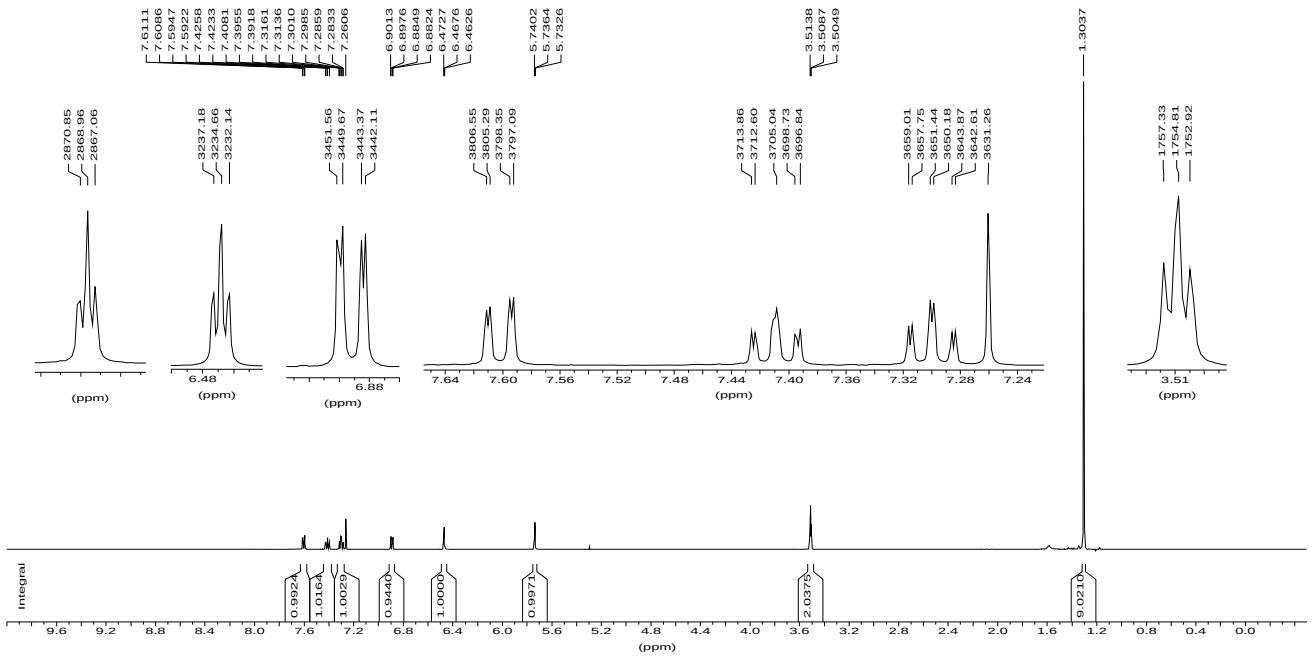



1H AMX500 ds09241 lss1259
7.2600
6.9751
6.4720
6.4670
6.4620
5.7421
5.7383
5.7333
3.5497
3.5459
3.5408
2.3079
2.0721
Integral
1.9075
0.9901
1.0000
2.0025
3.0250
5.9728
(ppm)

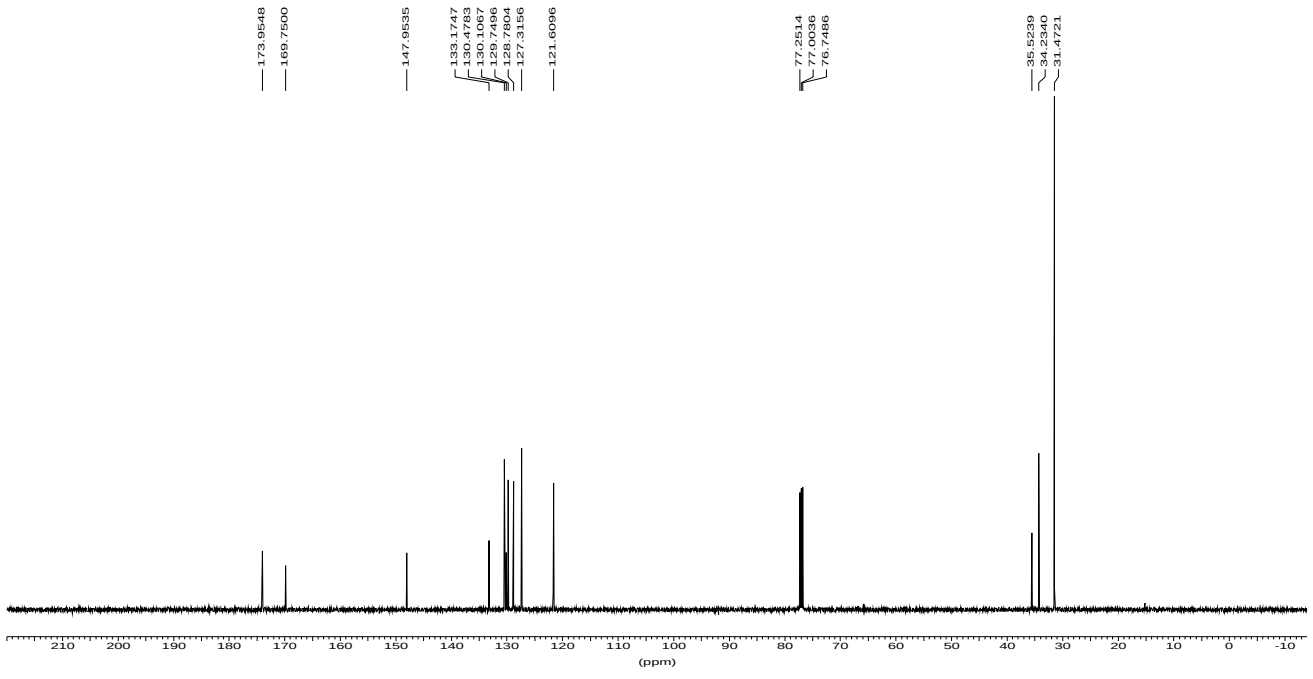

13C AMX500 ds10063 2,4,6-trimethylphenyl itaconimide
172.7087
168.3727
139.3617
135.2370
133.1820
129.2541
127.4833
121.4348
77.2587
77.0037
76.7486
33.9936
21.0075
17.6626
(ppm)

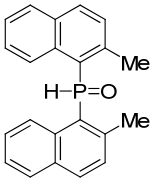


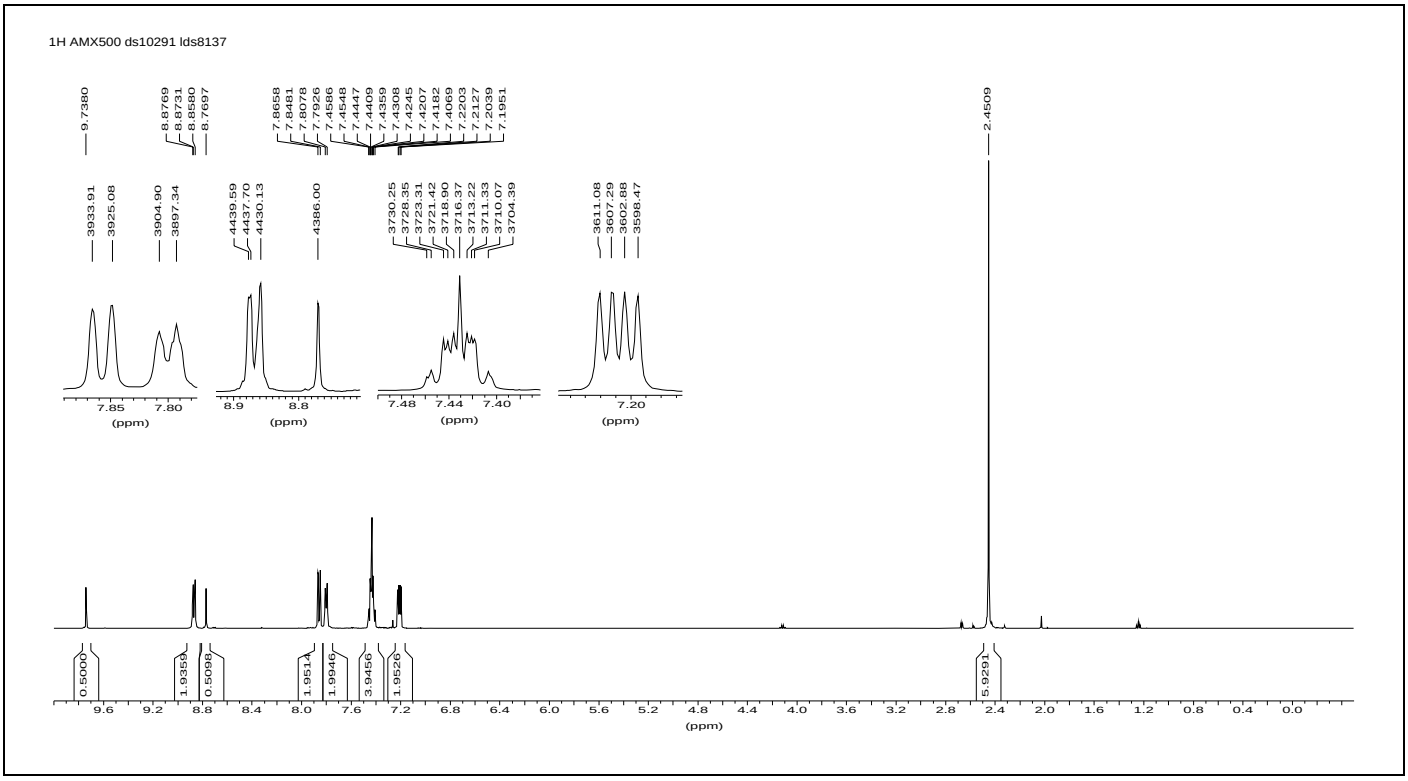
1H AMX500 ds09266 LSS2158

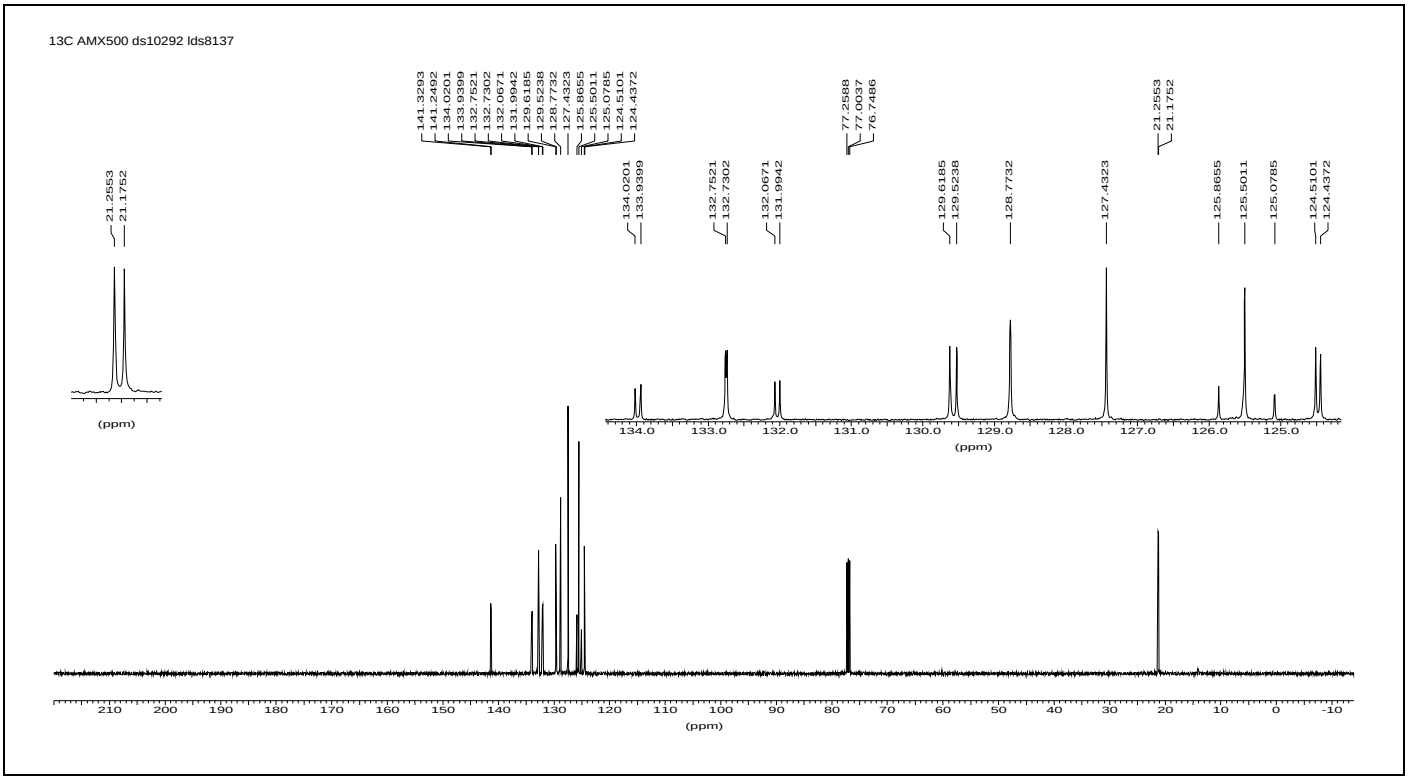


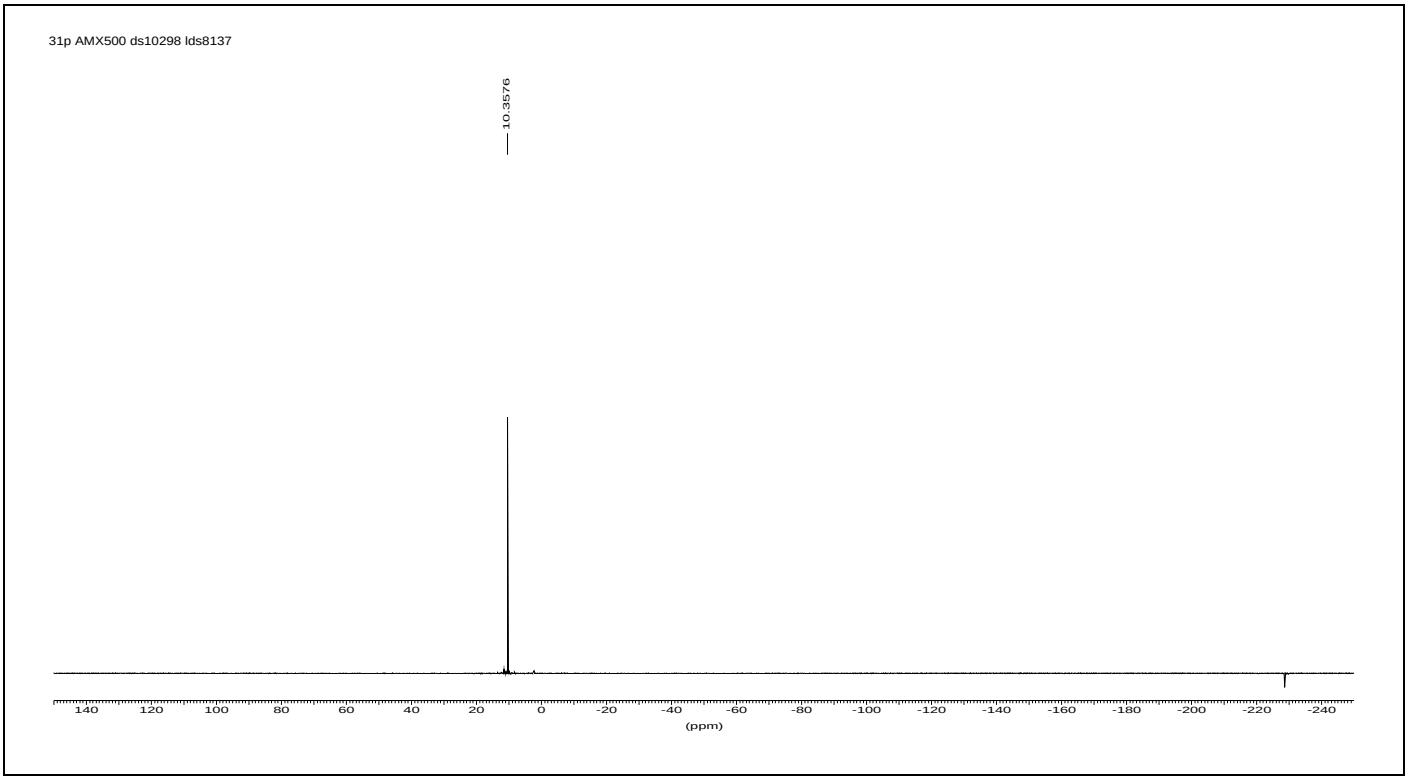
13C AMX500 ds10061 2-tert-butylphenyl itaconimide

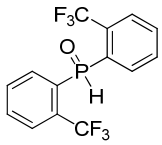



Me
H–P=O
Me

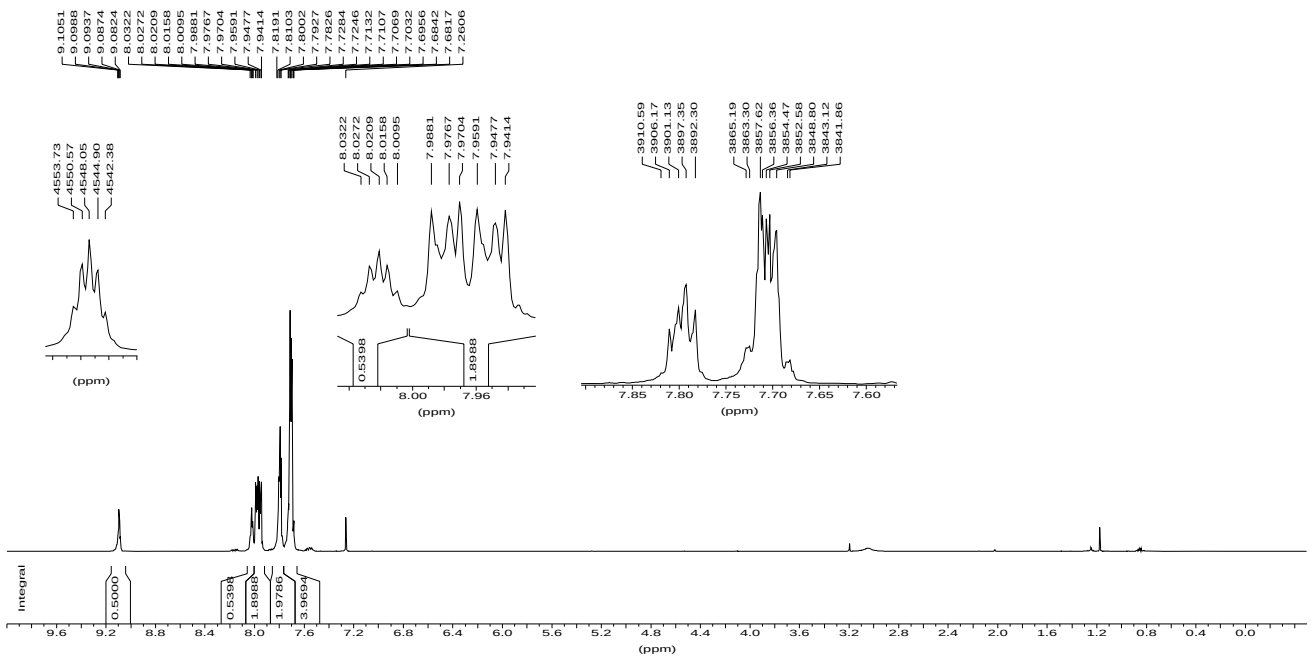

1H AMX500 ds10291 lds8137
9.7380
8.8769
8.8731
8.8580
8.7697
7.8658
7.8481
7.8078
7.7926
7.4586
7.4548
7.4447
7.4409
7.4359
7.4308
7.4245
7.4207
7.4182
7.4069
7.2203
7.2127
7.2039
7.1951
2.4509
3933.91
3925.08
3904.90
3897.34
4439.59
4437.70
4430.13
4386.00
3730.25
3728.35
3723.31
3721.42
3718.90
3716.37
3713.22
3711.33
3710.07
3704.39
3611.08
3607.29
3602.88
3598.47
0.5000
1.9359
0.5098
1.9514
1.9946
3.9456
1.9526
5.9291
(ppm)


13C AMX500 ds10292 lds8137
141.3393
141.2492
134.0201
133.9399
132.7521
132.7302
132.0671
131.9942
129.6185
129.5238
128.7732
127.4323
125.8655
125.5011
125.0785
124.5101
124.4372
77.2588
77.0037
76.7486
21.2553
21.1752
(ppm)

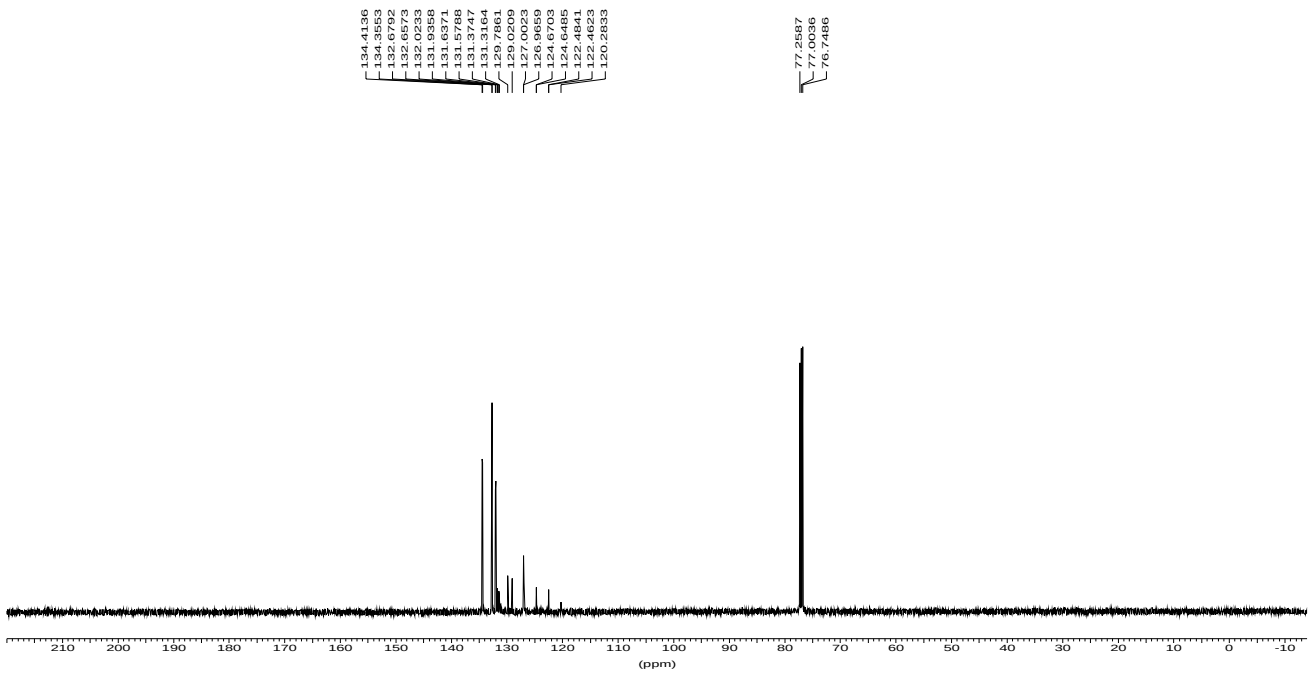

31p AMX500 ds10298 lds8137
10.3576
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
(ppm)



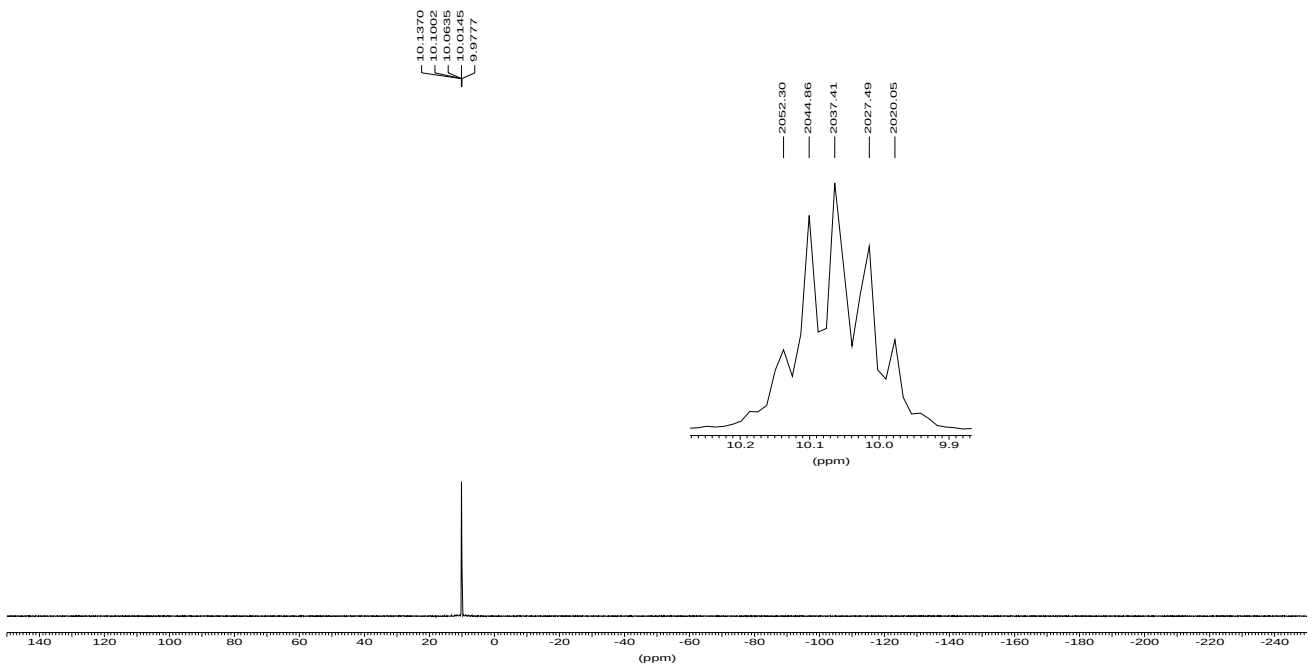
1H AMX500 ds10032 (2-CF3Ph)2P=OH



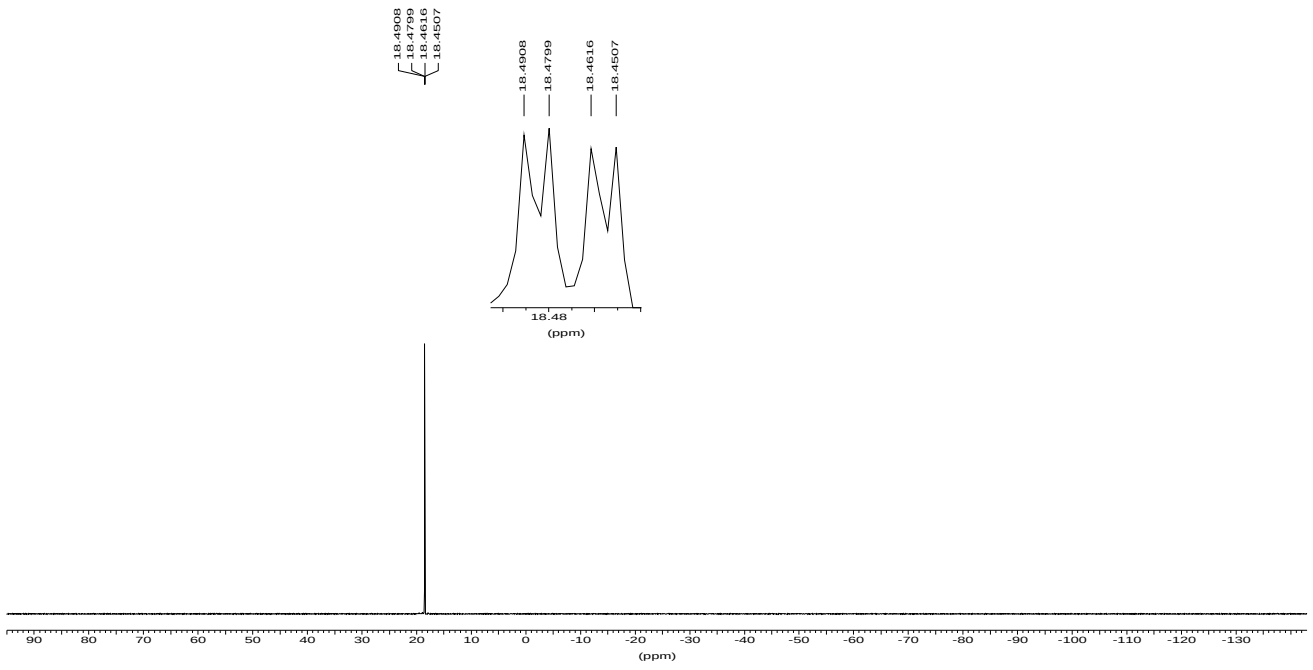
13C AMX500 ds10031 (2-CF3Ph)2P=OH

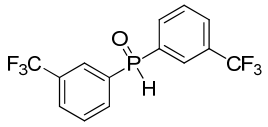


31p AMX500 ds1003(11) (2-CF3Ph)2P=OH

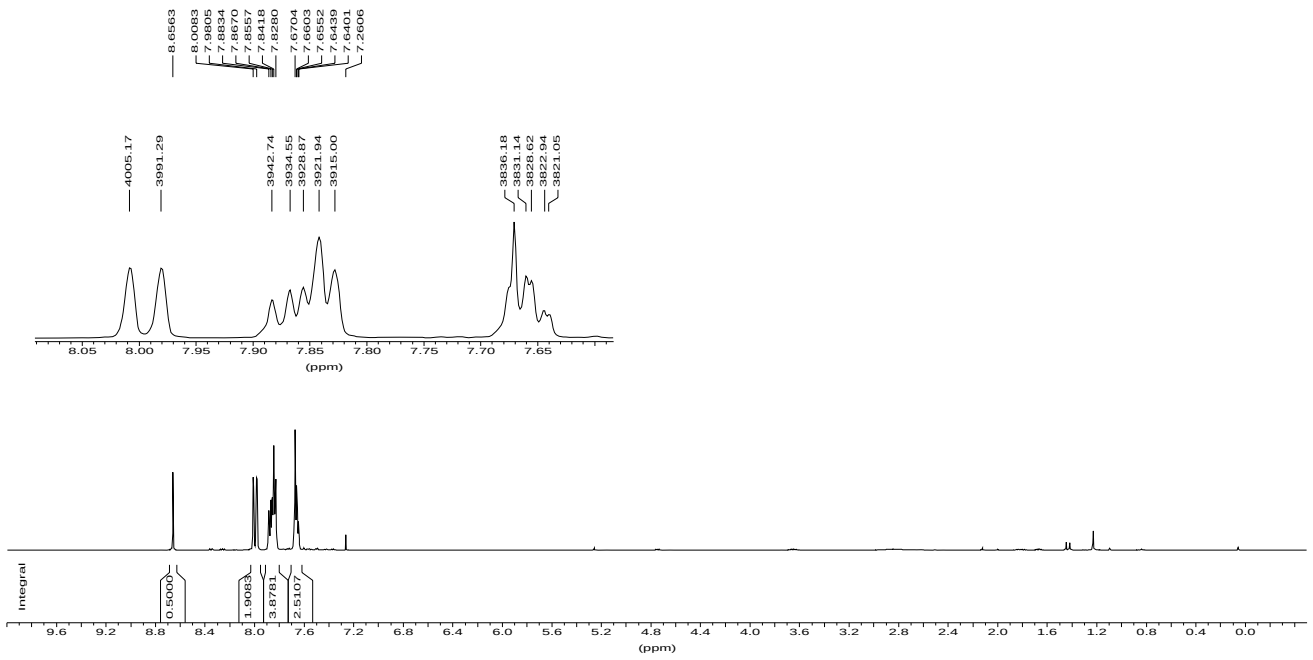


F19(no decoupled) oc03lds1 (2-CF3Ph)2P=O

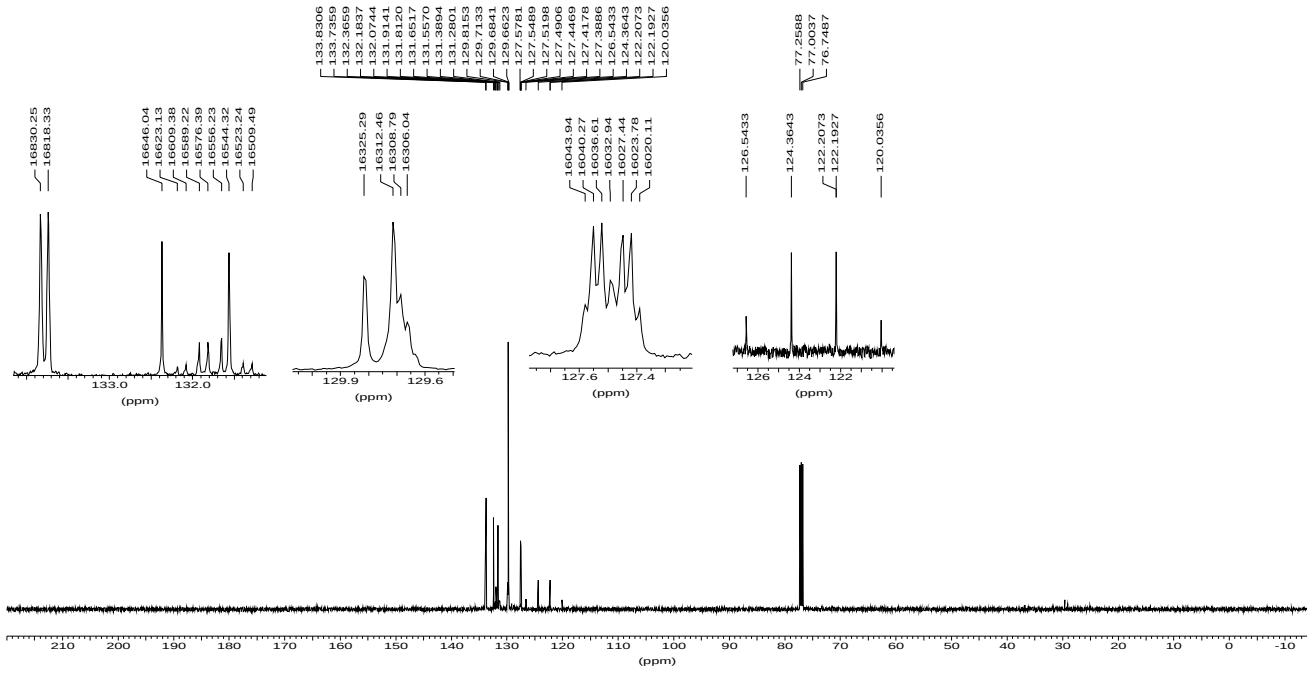




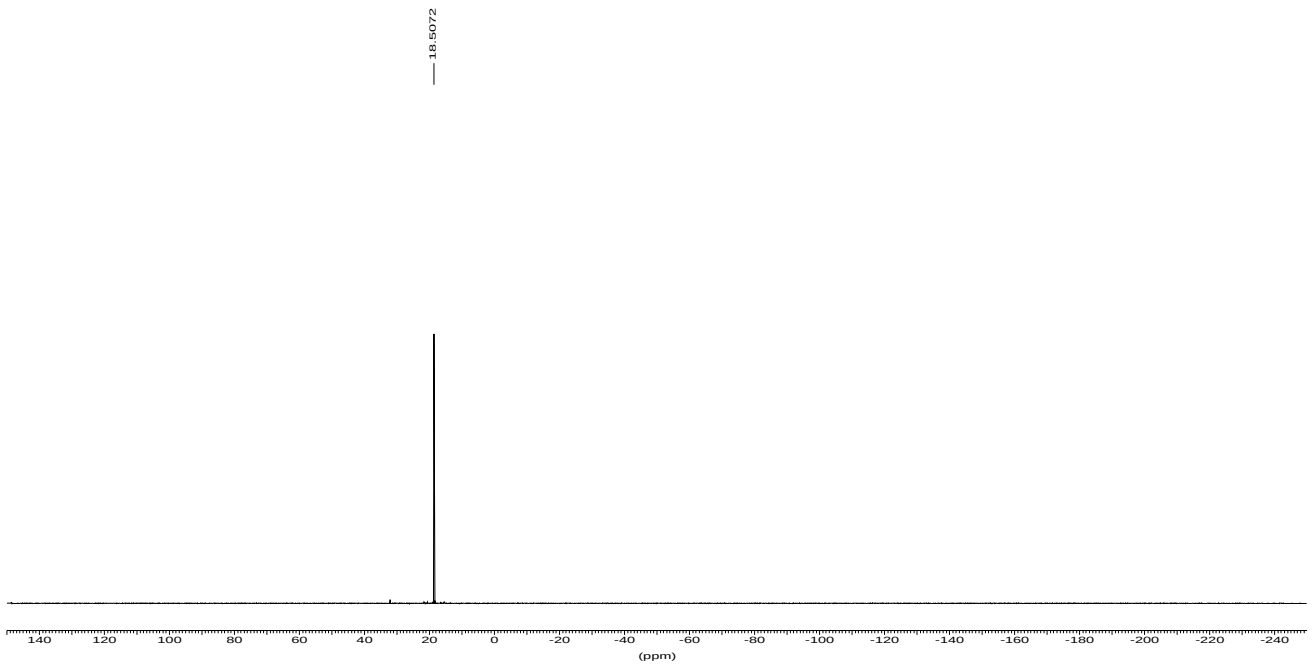
1H AMX500 ds11093 3-CF3P=O(H)



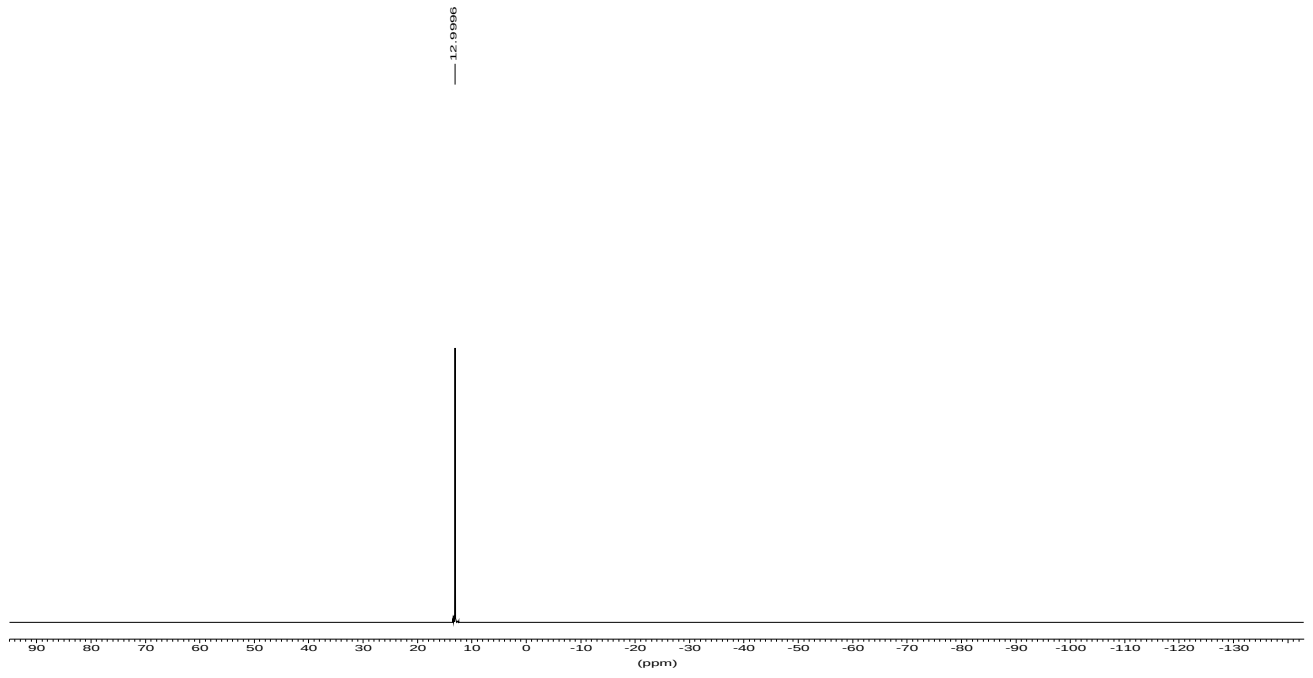
13C AMX500 ds11094 3-CF3P=O(H)

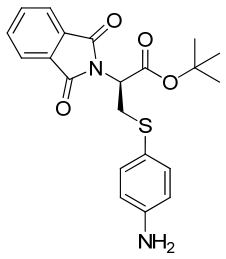


31p AMX500 ds11092 3-CF3P=O(H)

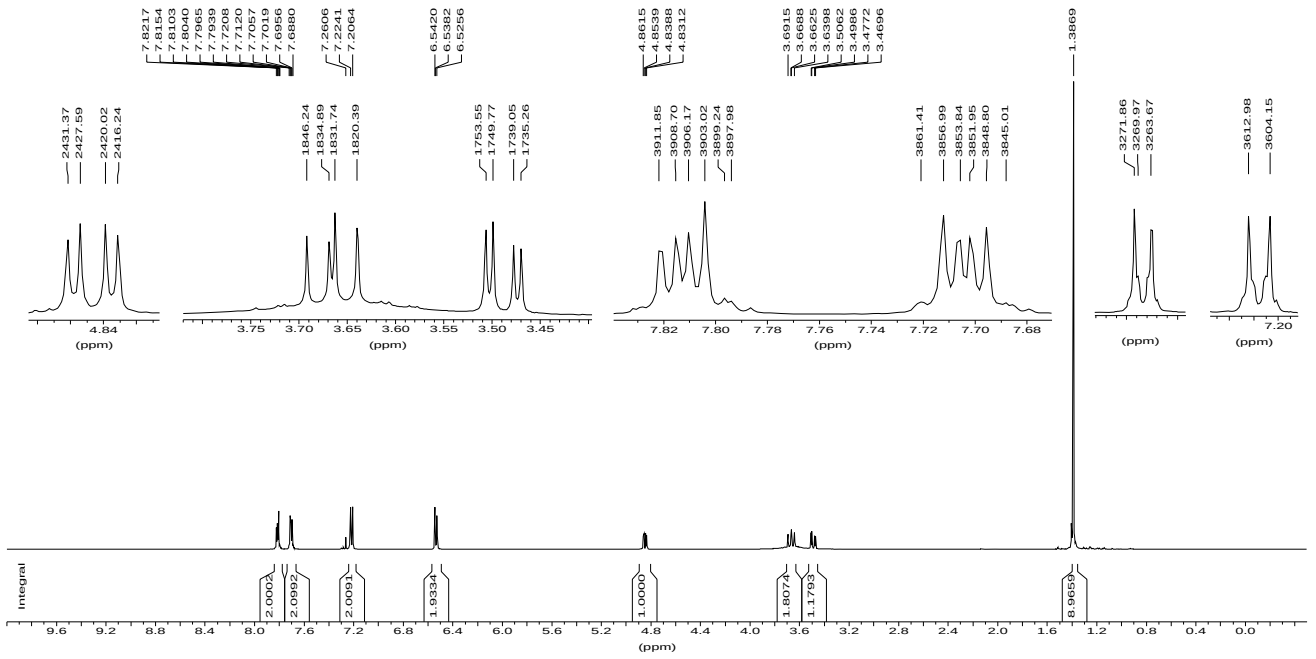


F19(no decoupled) nv26lds1 3-CF3POH

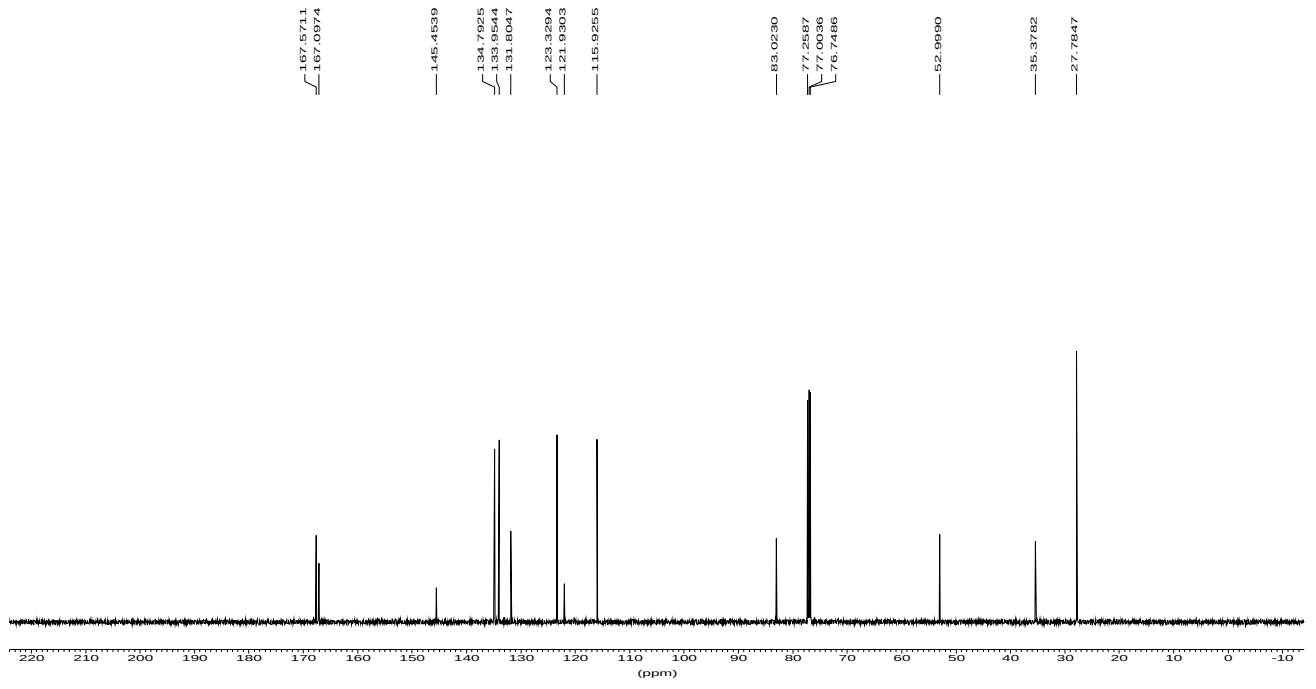


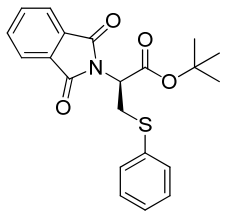


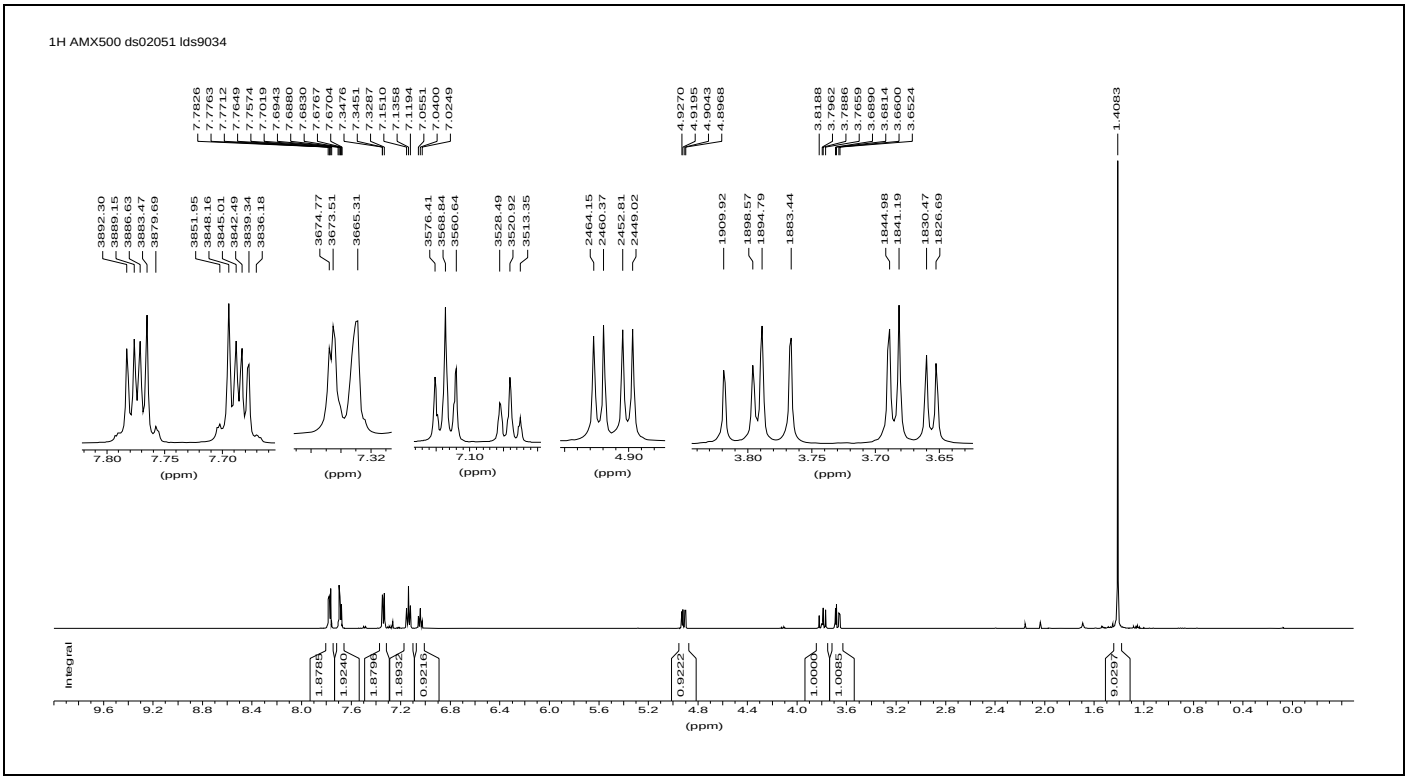
1H AMX500 ds11103 lds8235

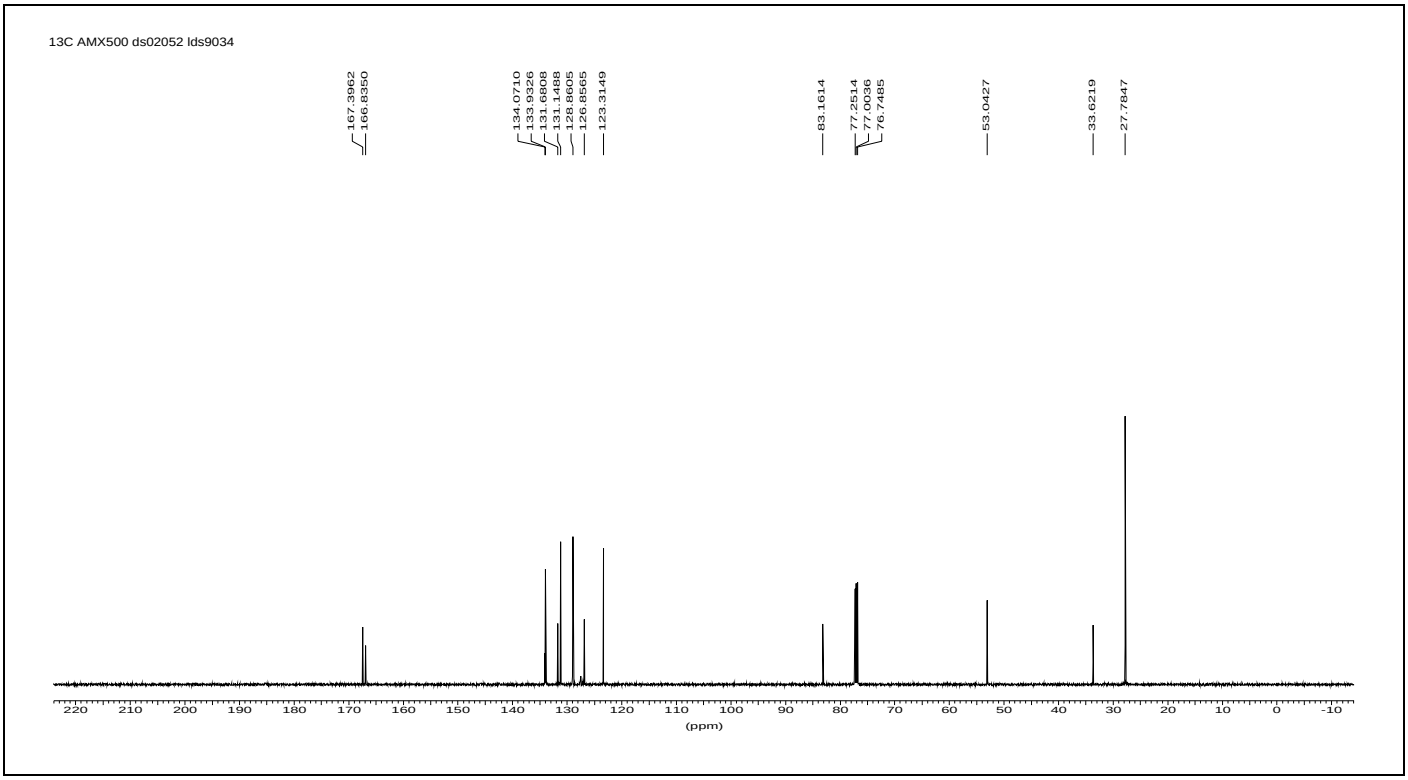


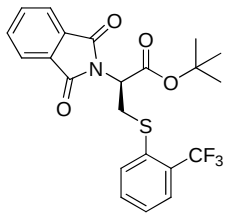
13C AMX500 ds11104 lds8235

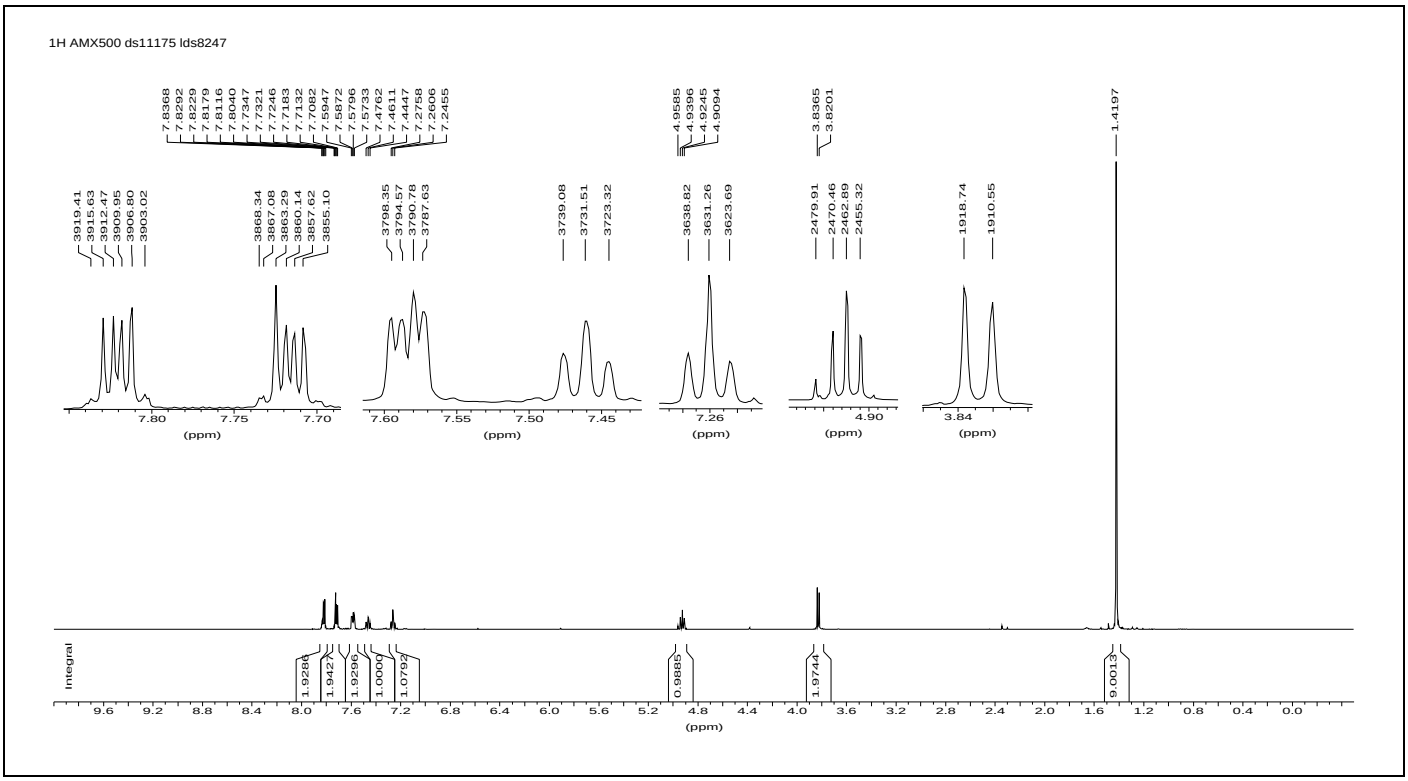


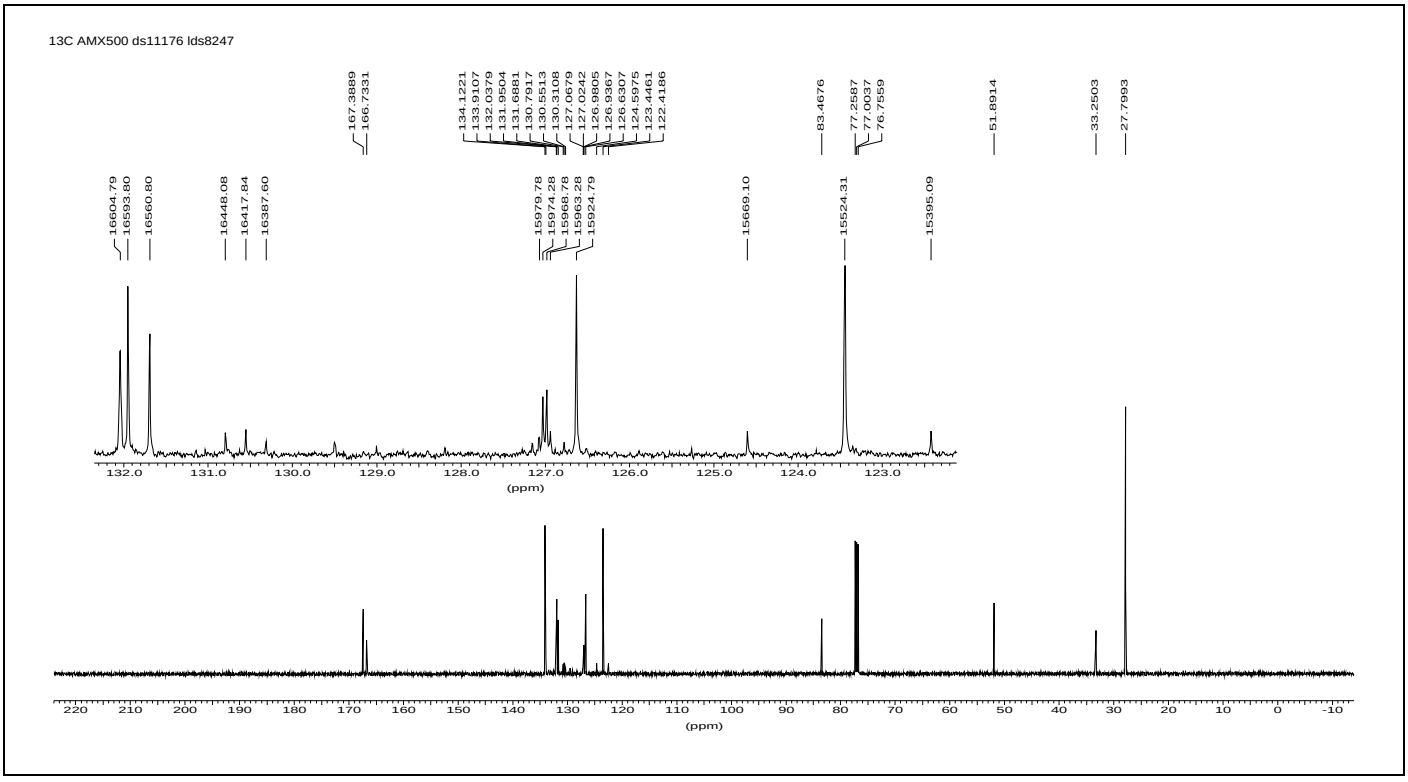


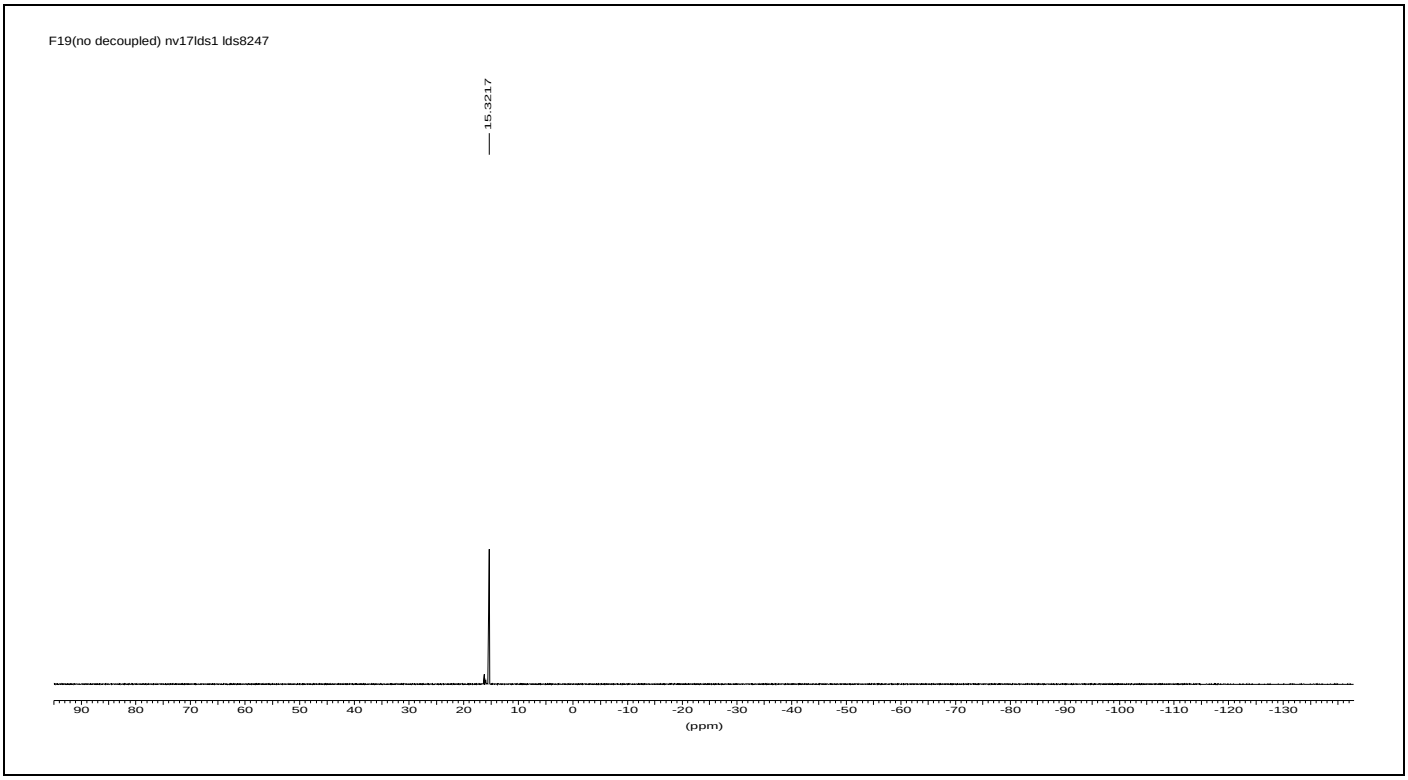

1H AMX500 ds02051 lds9034
7.7826
7.7763
7.7712
7.7649
7.7574
7.7019
7.6943
7.6880
7.6830
7.6767
7.6704
7.3476
7.3451
7.3287
7.1510
7.1358
7.1194
7.0551
7.0400
7.0249
4.9270
4.9195
4.9043
4.8968
3.8188
3.7962
3.7886
3.7659
3.6890
3.6814
3.6600
3.6524
1.4083
3892.30
3889.15
3886.63
3883.47
3879.69
3851.95
3848.16
3845.01
3842.49
3839.34
3836.18
3674.77
3673.51
3665.31
3576.41
3568.84
3560.64
3528.49
3520.92
3513.35
2464.15
2460.37
2452.81
2449.02
1909.92
1898.57
1894.79
1883.44
1844.98
1841.19
1830.47
1826.69
7.80
7.75
7.70
(ppm)
7.32
(ppm)
7.10
(ppm)
4.90
(ppm)
3.80
3.75
3.70
3.65
(ppm)
Integral
1.8788
1.9240
1.8799
1.8932
0.9216
0.9222
1.0000
1.0085
9.0297
(ppm)

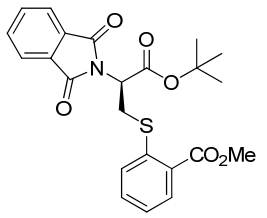

13C AMX500 ds02052 lds9034
167.3962
166.8350
134.0710
133.9326
131.6808
131.1488
128.8605
126.8565
123.3149
83.1614
77.2514
77.0036
76.7485
53.0427
33.6219
27.7847
(ppm)

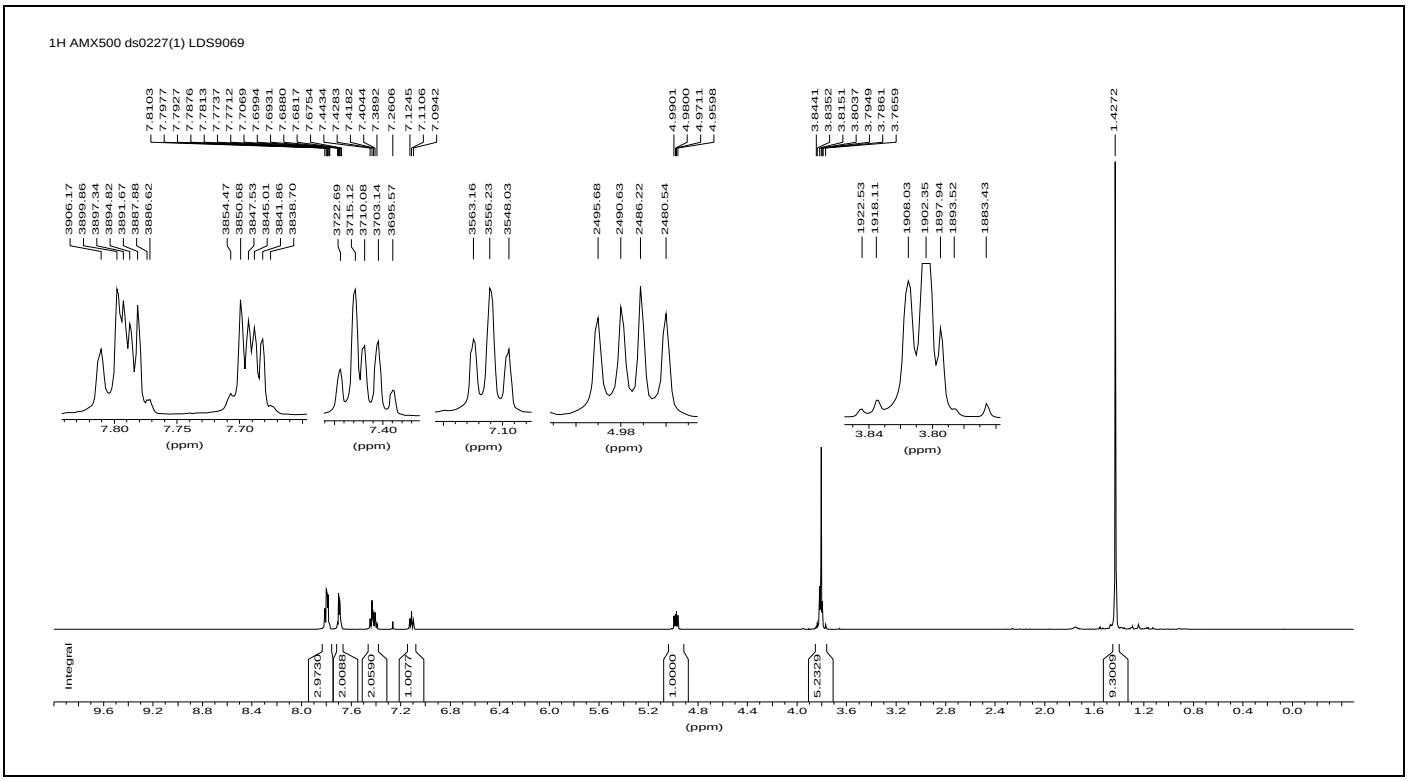

O
O
N
O
O
S
CF3

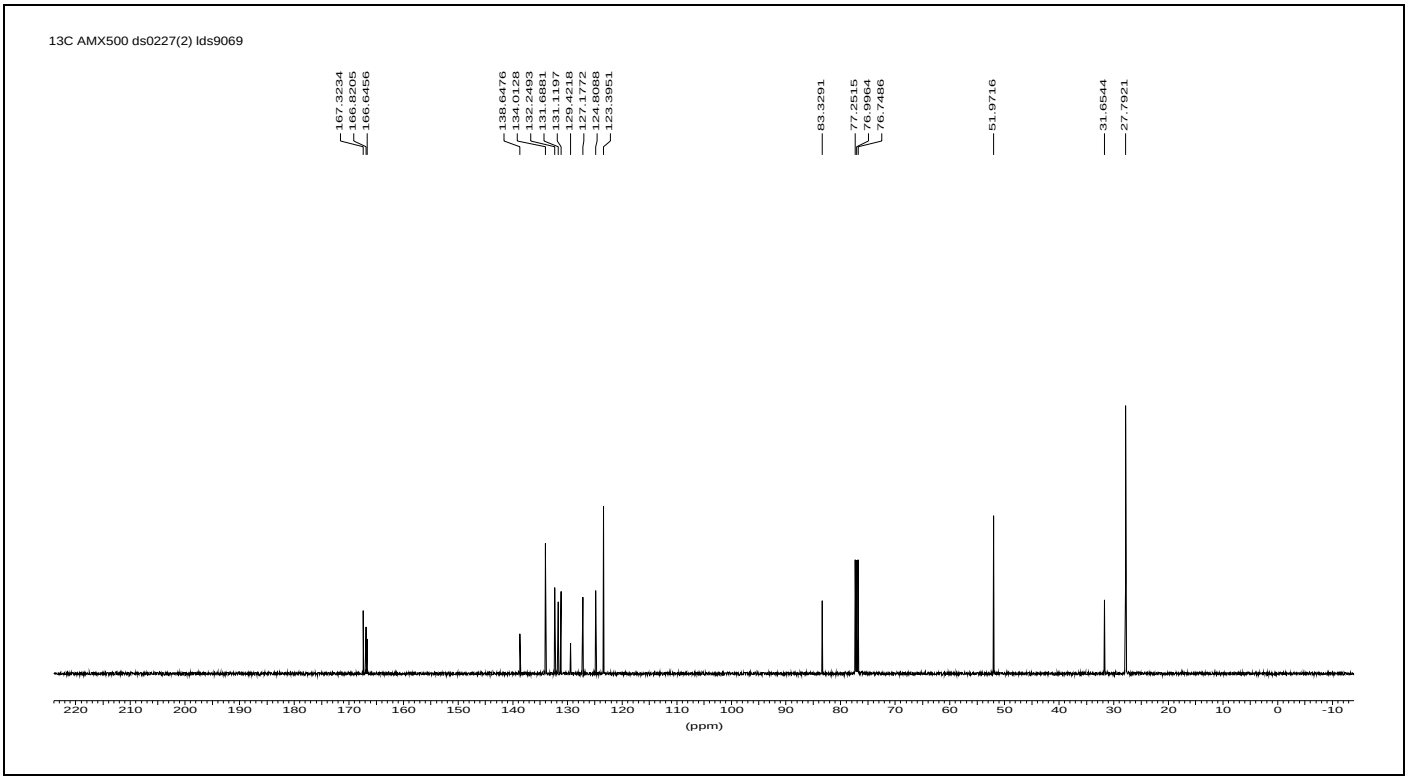

1H AMX500 ds11175 lds8247
7.8368
7.8292
7.8229
7.8179
7.8116
7.8040
7.7347
7.7321
7.7246
7.7183
7.7132
7.7082
7.5947
7.5872
7.5796
7.5733
7.4762
7.4711
7.4447
7.2758
7.2606
7.2455
4.9585
4.9396
4.9245
4.9094
3.8365
3.8201
1.4197
3919.41
3915.63
3912.47
3909.95
3906.80
3903.02
3868.34
3867.08
3863.29
3860.14
3857.62
3855.10
3798.35
3794.57
3790.78
3787.63
3739.08
3731.51
3723.32
3638.82
3631.26
3623.69
2479.91
2470.46
2462.89
2455.32
1918.74
1910.55
7.80
7.75
7.70
7.60
7.55
7.50
7.45
7.26
4.90
3.84
(ppm)
Integral
1.9288
1.9427
1.9296
1.0000
1.0792
0.9885
1.9744
9.0013
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0

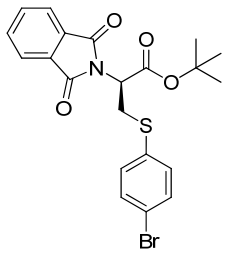

13C AMX500 ds11176 lds8247
167.3889
166.7331
134.1221
133.9107
132.0379
131.9504
131.6881
130.7917
130.5513
130.3108
127.0679
127.0242
126.9805
126.9367
126.6307
124.5975
123.4461
122.4186
83.4676
77.2587
77.0037
76.7559
51.8914
33.2503
27.7993
16604.79
16593.80
16560.80
16448.08
16417.84
16387.60
15979.78
15974.28
15968.78
15963.28
15924.79
15669.10
15524.31
15395.09
132.0
131.0
130.0
129.0
128.0
127.0
126.0
125.0
124.0
123.0
(ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

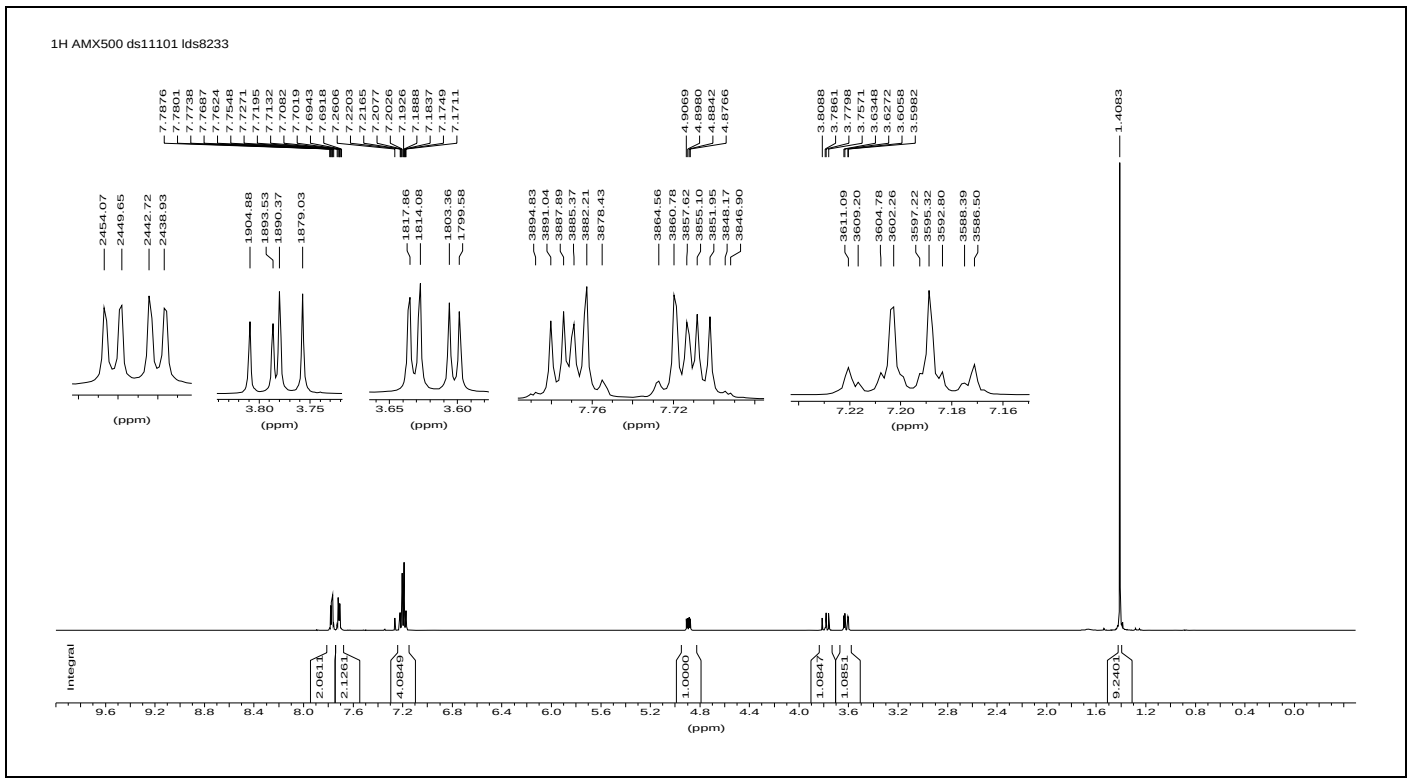

F19(no decoupled) nv17lds1 lds8247
15.3217
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130
(ppm)

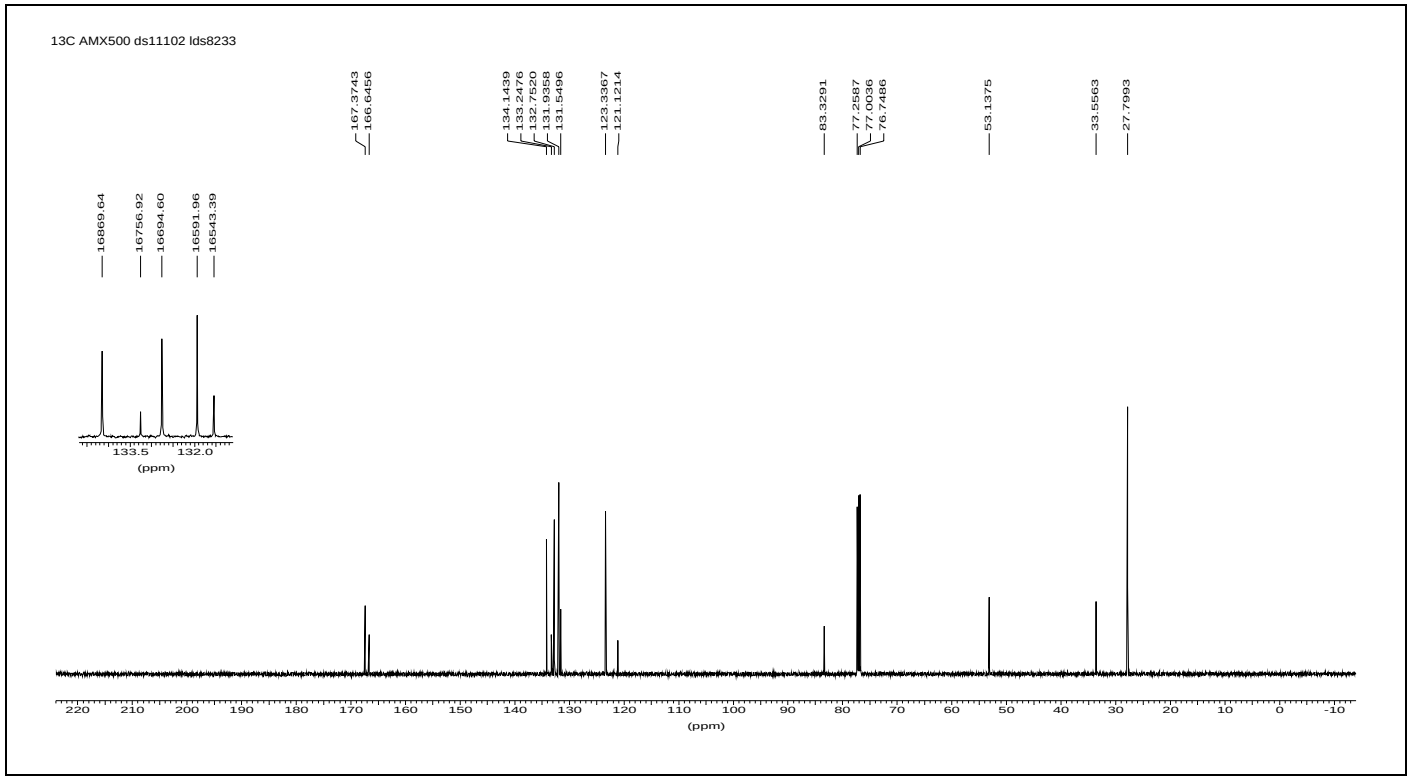

O
N
O
O
O
S
CO2Me

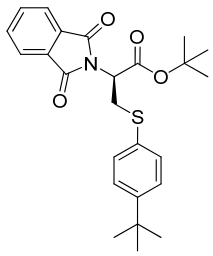

1H AMX500 ds0227(1) LDS9069
7.8103
7.7977
7.7927
7.7876
7.7813
7.7737
7.7712
7.7069
7.6994
7.6931
7.6880
7.6817
7.6754
7.4434
7.4283
7.4183
7.4044
7.3892
7.2606
7.1245
7.1106
7.0942
4.9901
4.9900
4.9711
4.9598
3.8441
3.8352
3.8151
3.8037
3.7949
3.7861
3.7659
1.4272
3906.17
3899.86
3897.34
3894.82
3891.67
3887.88
3886.62
3854.47
3850.68
3847.53
3845.01
3841.86
3838.70
3722.69
3715.12
3710.08
3703.14
3695.57
3563.16
3556.23
3548.03
2495.68
2490.63
2486.22
2480.54
1922.53
1918.11
1908.03
1902.35
1897.94
1893.52
1883.43
7.80
7.75
7.70
7.40
7.10
4.98
3.84
3.80
(ppm)
Integral
2.9730
2.0088
2.0590
1.0077
1.0000
5.2329
9.3009
(ppm)


13C AMX500 ds0227(2) lds9069
167.3234
166.8205
166.6456
138.6476
134.0126
132.2493
131.6881
131.1197
129.4218
127.1772
124.8088
123.3951
83.3291
77.2515
76.9964
76.7486
51.9716
31.6544
27.7921
(ppm)

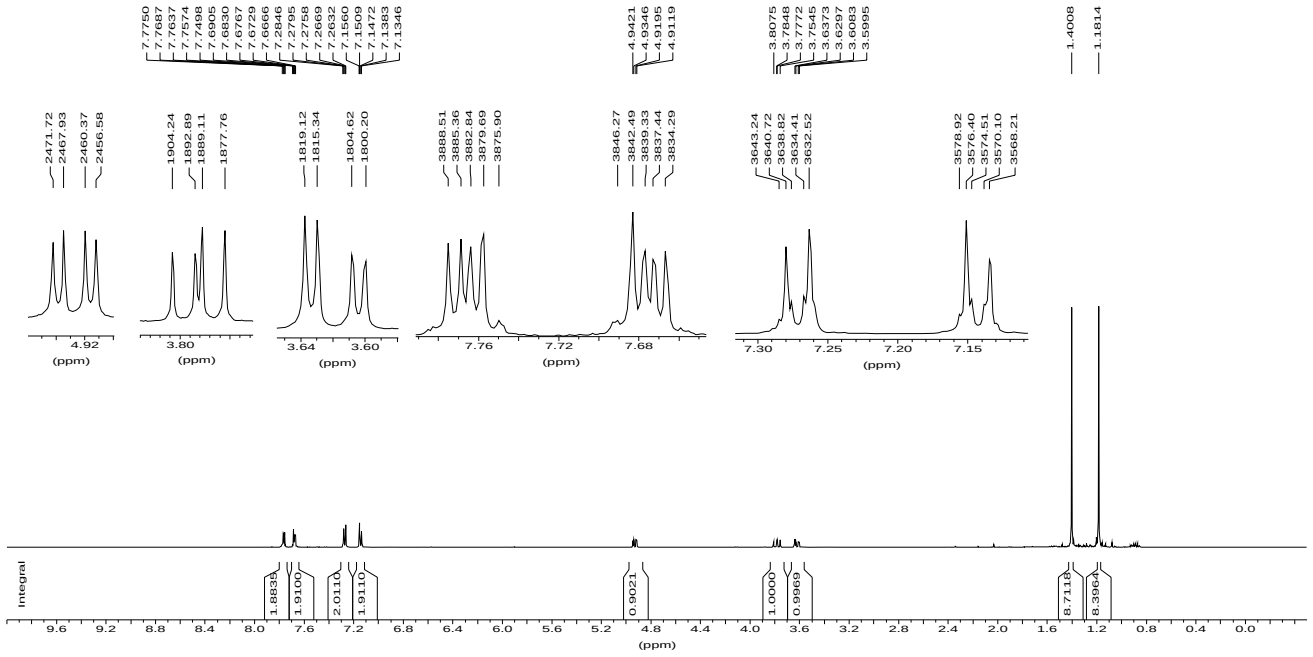

O
O
N
O
O
S
Br


1H AMX500 ds11101 lds8233
7.7876
7.7801
7.7738
7.7687
7.7624
7.7548
7.7271
7.7195
7.7132
7.7082
7.7019
7.6943
7.6918
7.2606
7.2203
7.2165
7.2077
7.2026
7.1926
7.1888
7.1837
7.1749
7.1711
4.9069
4.8980
4.8842
4.8766
3.8088
3.7861
3.7798
3.7571
3.6348
3.6272
3.6058
3.5982
1.4083
2454.07
2449.65
2442.72
2438.93
1904.88
1893.53
1890.37
1879.03
1817.86
1814.08
1803.36
1799.58
3894.83
3891.04
3887.89
3885.37
3882.21
3878.43
3864.56
3860.78
3857.62
3855.10
3851.95
3848.17
3846.90
3611.09
3609.20
3604.78
3602.26
3597.22
3595.32
3592.80
3588.39
3586.50
(ppm)
Integral
2.0611
2.1261
4.0849
1.0000
1.0847
1.0851
9.2401

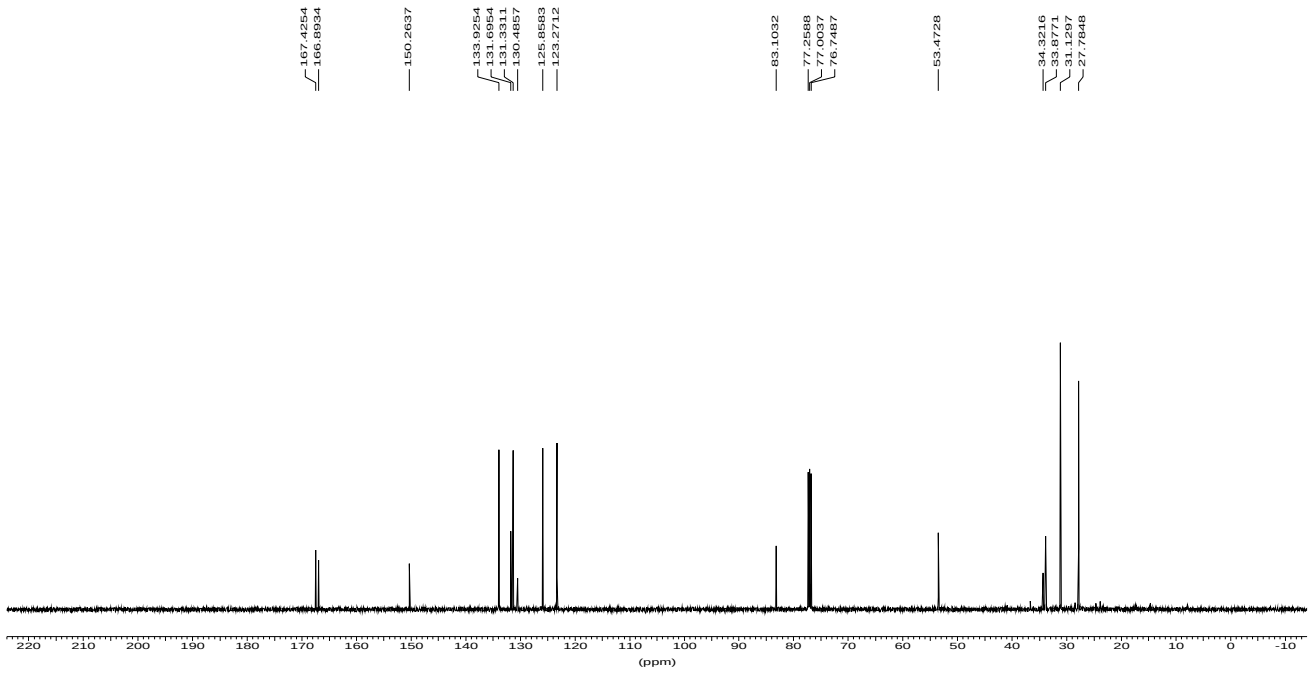

13C AMX500 ds11102 lds8233
167.3743
166.6456
134.1439
134.2476
132.7520
131.9358
131.5496
123.3367
121.1214
83.3291
77.2587
77.0036
76.7486
53.1375
33.5563
27.7993
16869.64
16756.92
16694.60
16591.96
16543.39
(ppm)

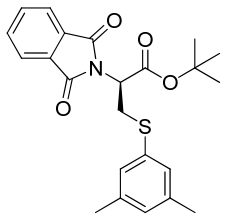


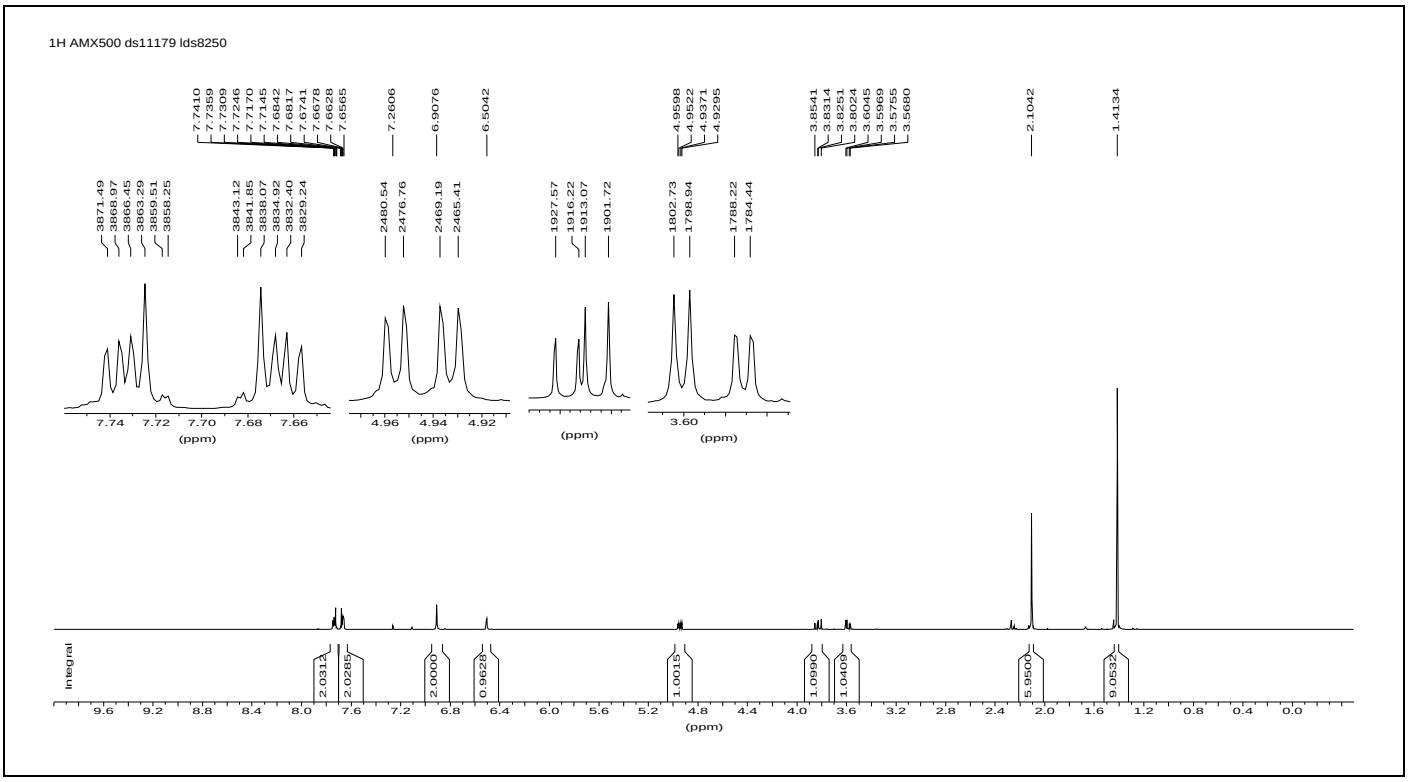
1H AMX500 ds11173 lds8246



13C AMX500 ds11174 lds8246






1H AMX500 ds11179 lds8250
7.7410
7.7359
7.7309
7.7246
7.7170
7.7145
7.6842
7.6817
7.6741
7.6678
7.6628
7.6565
7.2606
6.9076
6.5042
4.9598
4.9522
4.9371
4.9295
3.8541
3.8514
3.8351
3.8024
3.6045
3.5969
3.5755
3.5680
2.1042
1.4134
3871.49
3868.97
3866.45
3863.29
3861.51
3858.25
3843.12
3841.85
3838.07
3834.92
3832.40
3829.24
2480.54
2476.76
2469.19
2465.41
1927.57
1916.22
1913.07
1901.72
1802.73
1798.94
1788.22
1784.44
(ppm)
Integral
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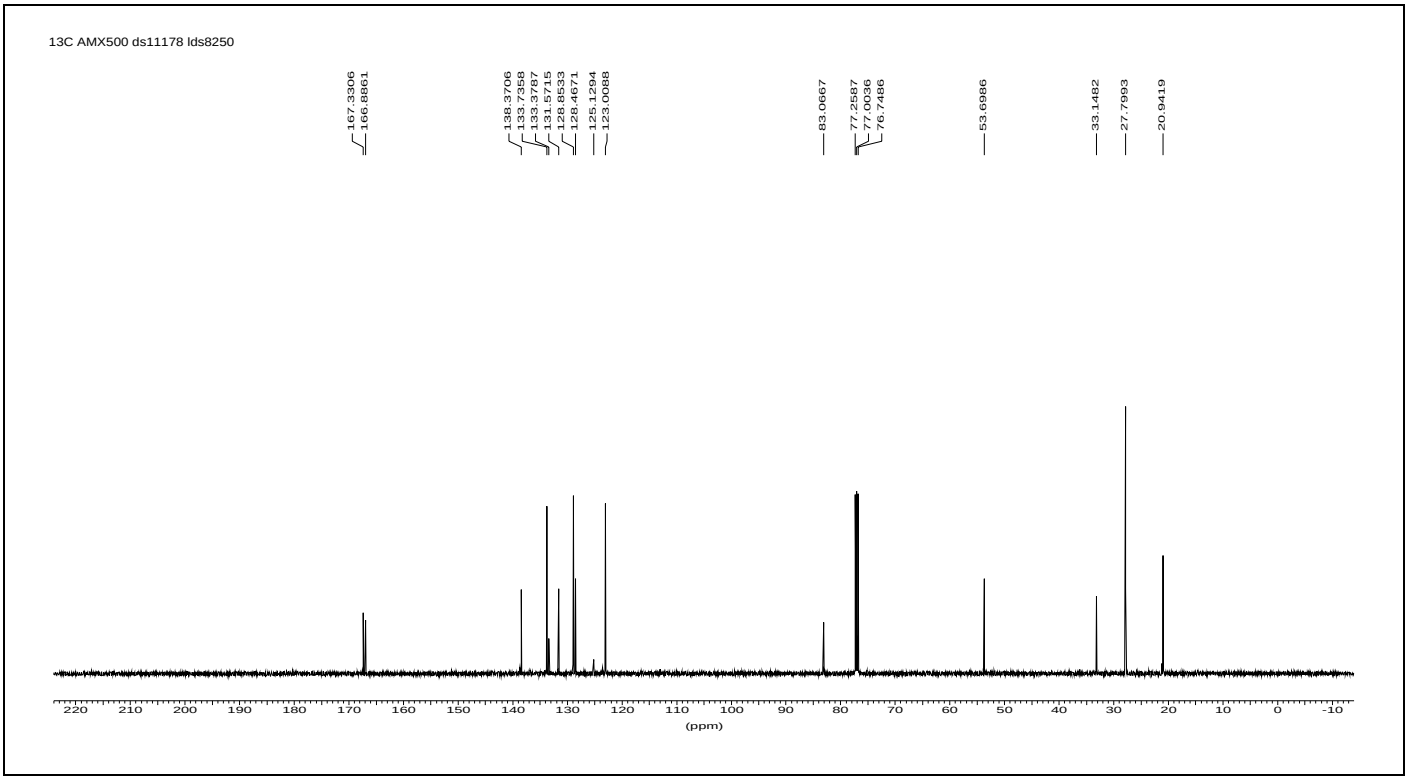
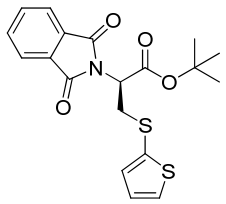
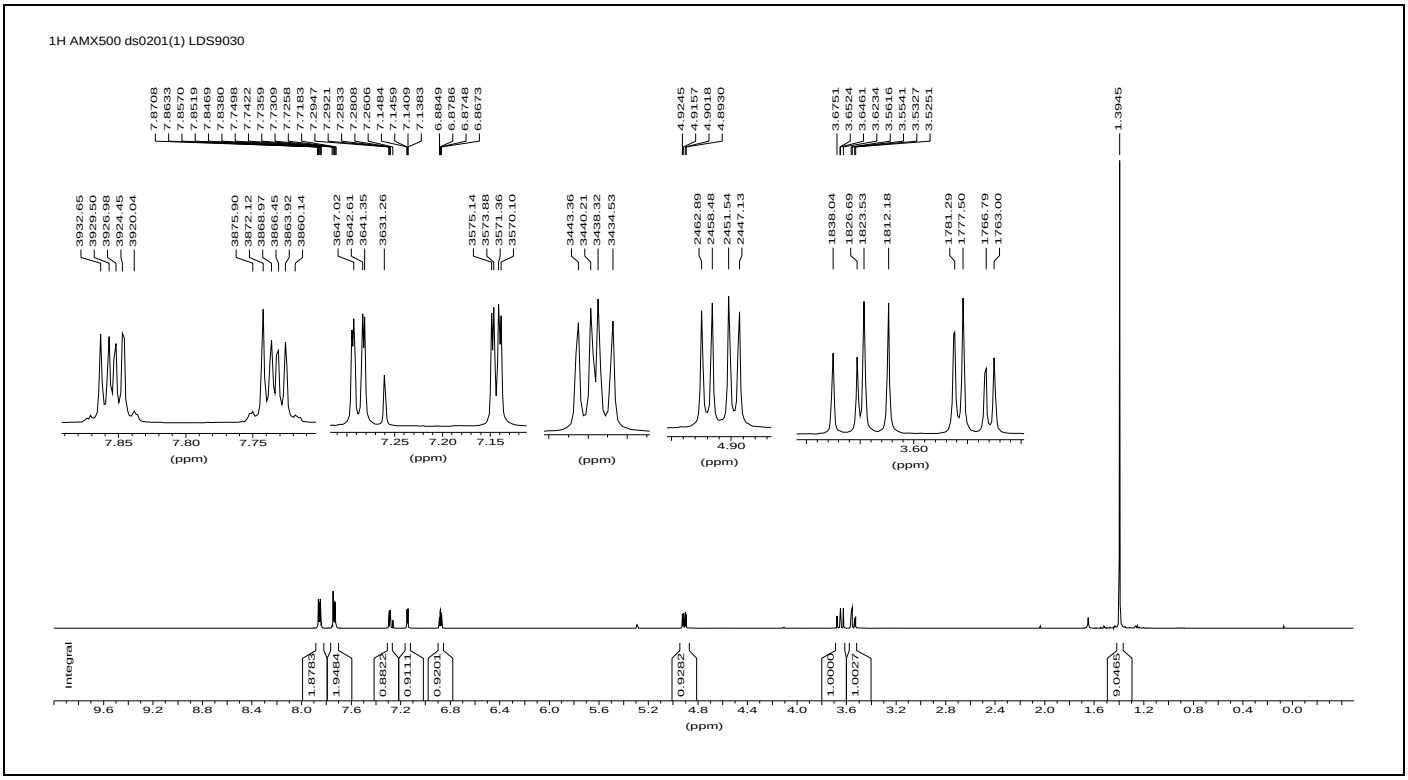
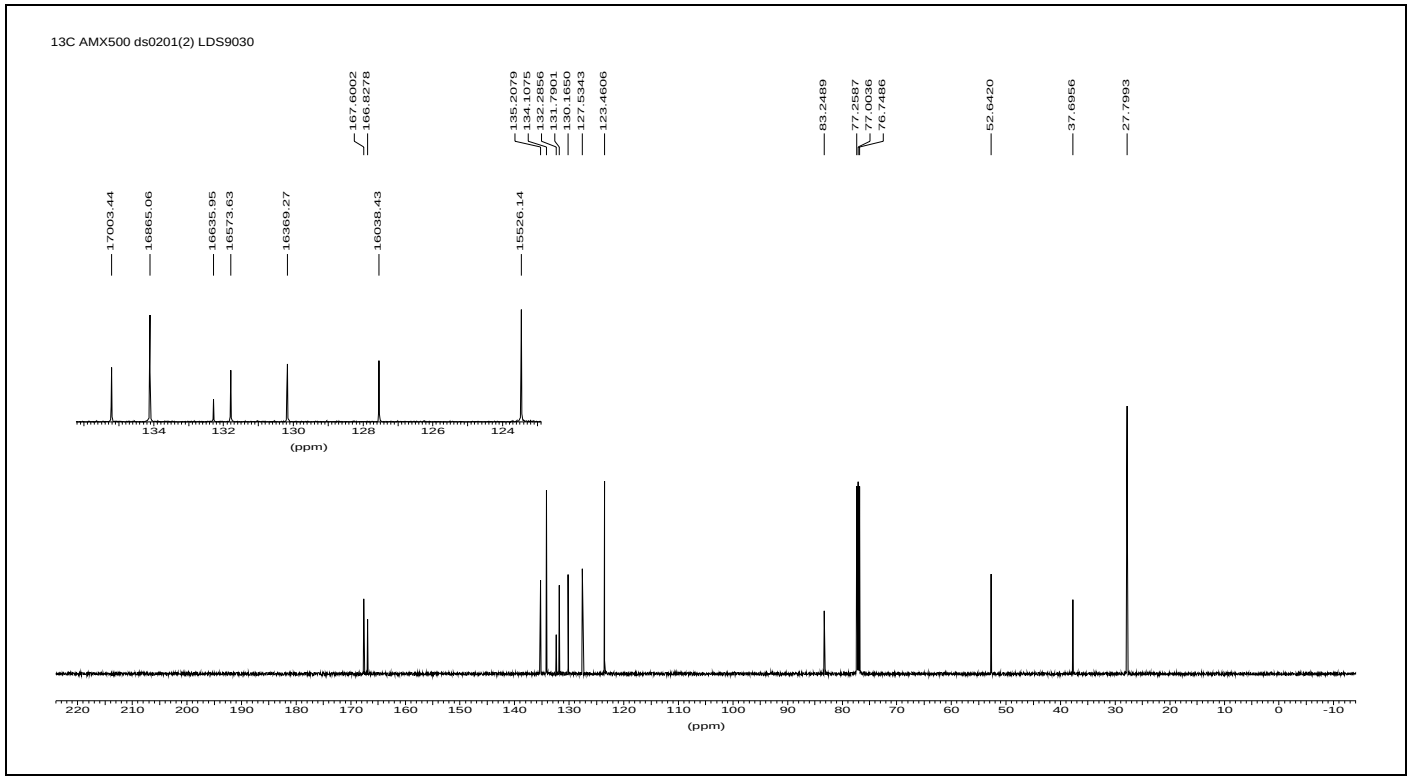
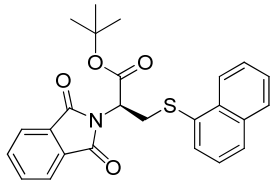
2.0285
2.0000
0.9628
1.0015
1.0990
1.0409
5.9500
9.0532

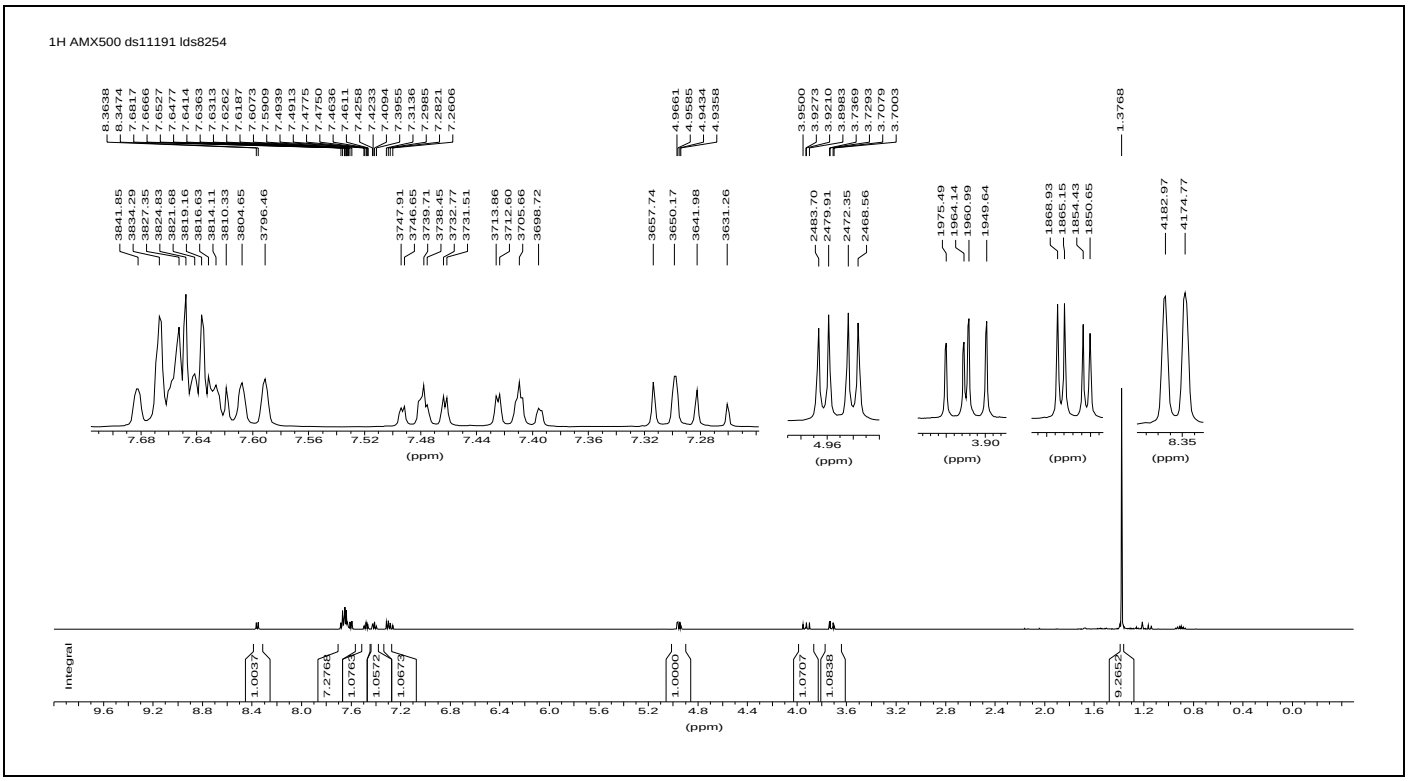

13C AMX500 ds11178 lds8250
167.3306
165.8861
138.3706
133.7358
133.3787
131.5715
128.8533
128.4671
125.1294
123.0088
83.0667
77.2587
77.0036
76.7486
53.6986
33.1482
27.7993
20.9419
(ppm)

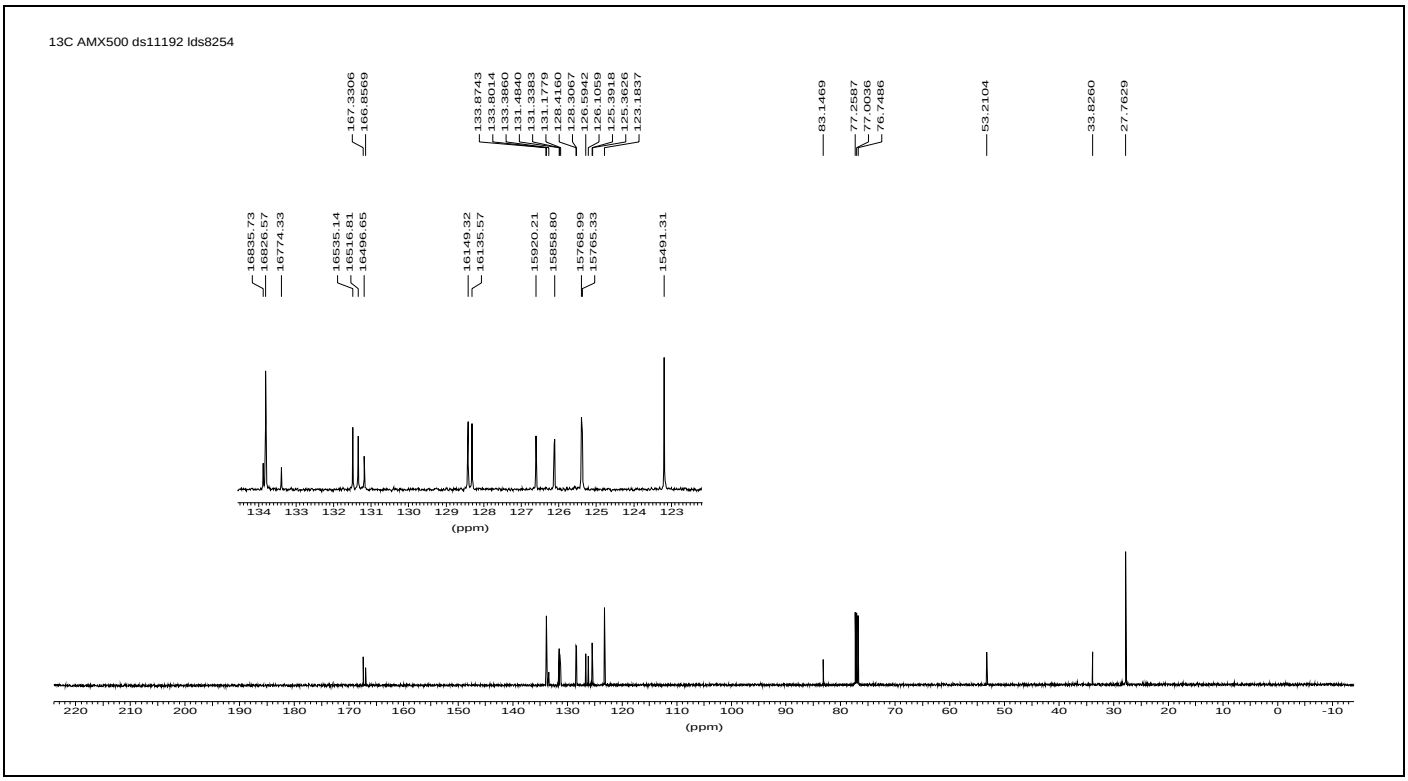


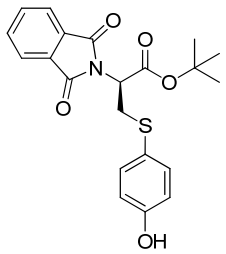

1H AMX500 ds0201(1) LDS9030
7.8708
7.8633
7.8570
7.8519
7.8469
7.8380
7.7498
7.7422
7.7359
7.7309
7.7258
7.7183
7.2947
7.2921
7.2833
7.2808
7.2606
7.1484
7.1459
7.1409
7.1383
6.8849
6.8786
6.8748
6.8673
4.9245
4.9157
4.9018
4.8930
3.6751
3.6524
3.6461
3.6234
3.5616
3.5541
3.5327
3.5251
1.3945
3932.65
3929.50
3926.98
3924.45
3920.04
3875.90
3872.12
3868.97
3866.45
3863.92
3860.14
3647.02
3642.61
3641.35
3631.26
3575.14
3573.88
3571.36
3570.10
3443.36
3440.21
3438.32
3434.53
2462.89
2458.48
2451.54
2447.13
1838.04
1826.69
1823.53
1812.18
1781.29
1777.50
1766.79
1763.00
7.85
7.80
7.75
7.25
7.20
7.15
4.90
3.60
(ppm)
Integral
1.8783
1.9484
0.8822
0.9111
0.9201
0.9282
1.0000
1.0027
9.0465
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0


13C AMX500 ds0201(2) LDS9030
167.6002
166.8278
135.2079
134.1075
132.2856
131.7901
130.1650
127.5343
123.4606
83.2489
77.2587
77.0036
76.7486
52.6420
37.6956
27.7993
17003.44
16865.06
16635.95
16573.63
16369.27
16038.43
15526.14
134
132
130
128
126
124
(ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

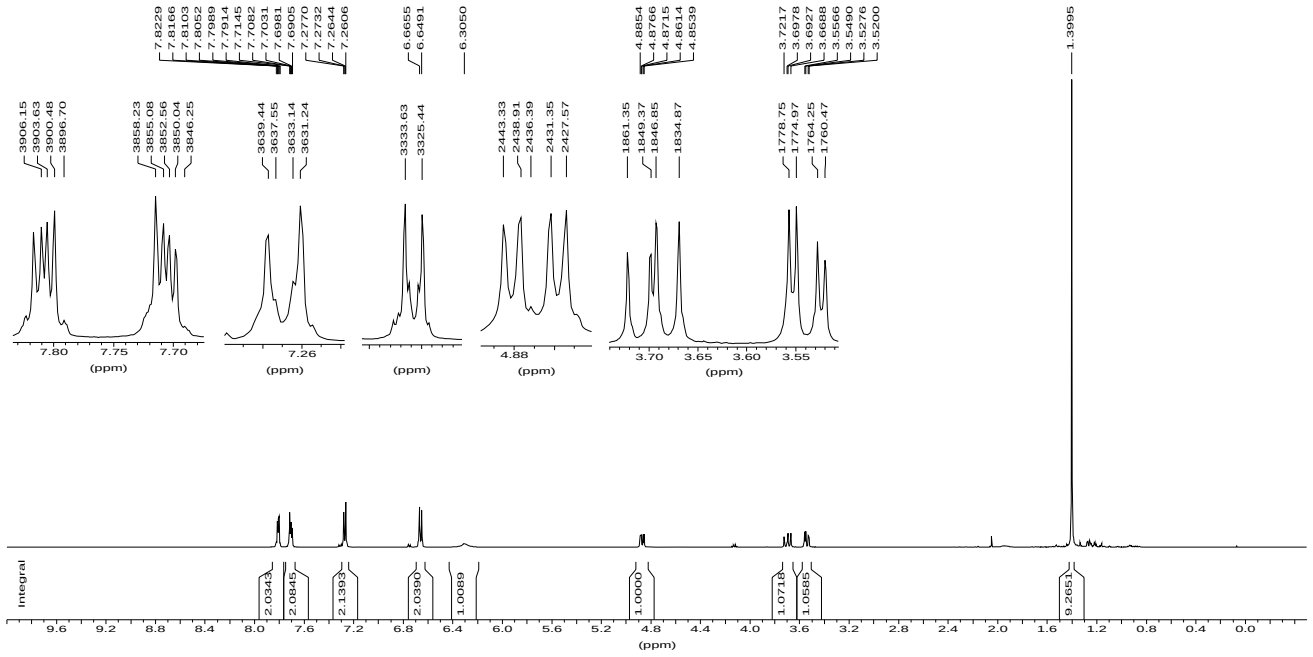



1H AMX500 ds11191 lds8254
(ppm)

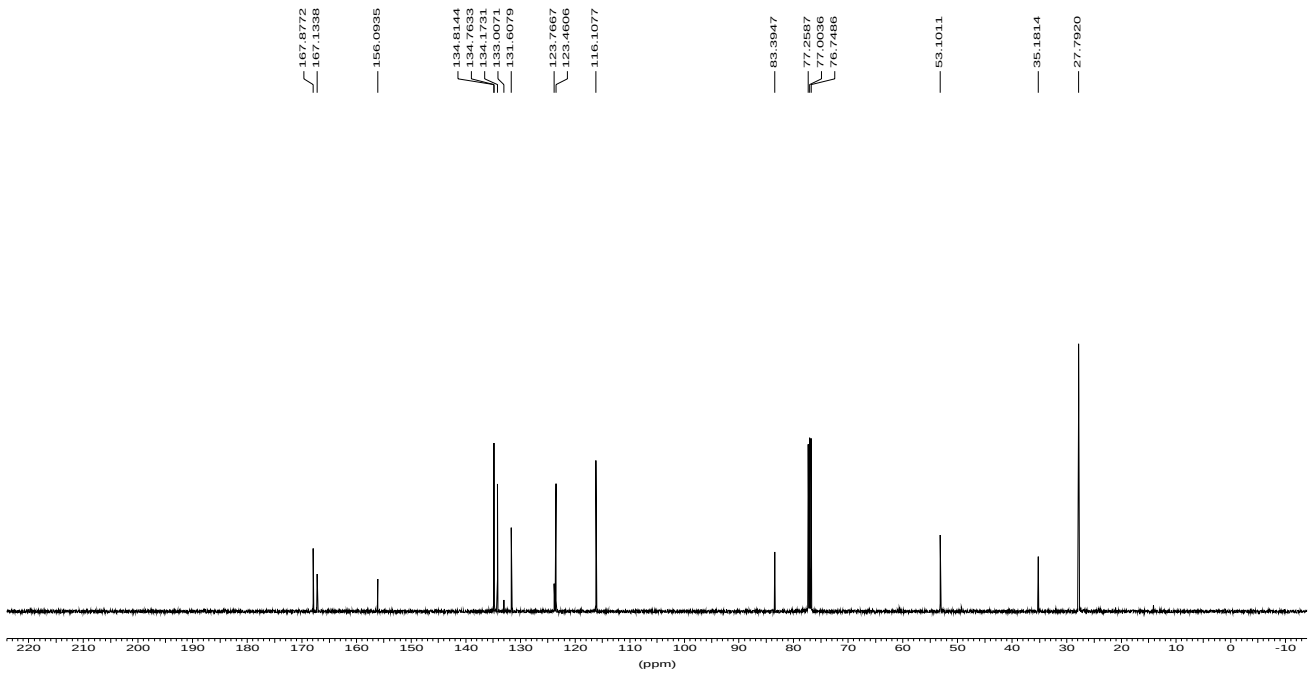

13C AMX500 ds11192 lds8254
(ppm)

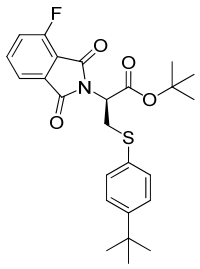


1H AMX500 ds0223(2) lds9062

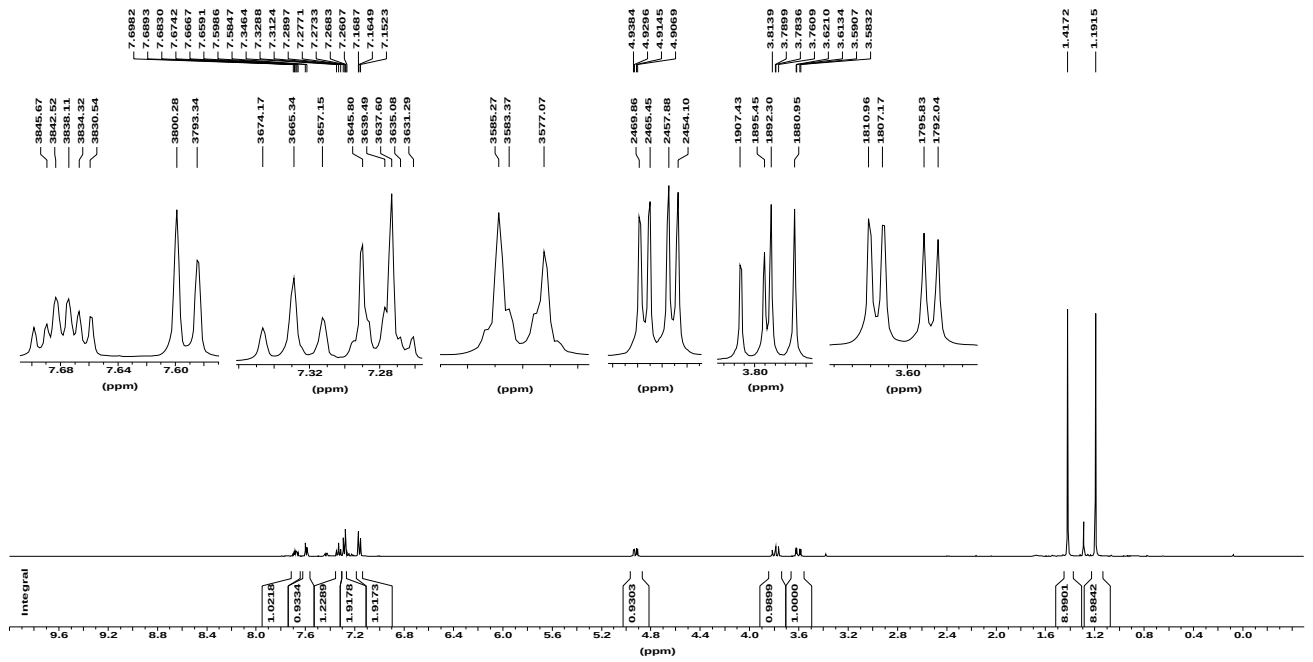


13C AMX500 ds0223(1) LDS9062

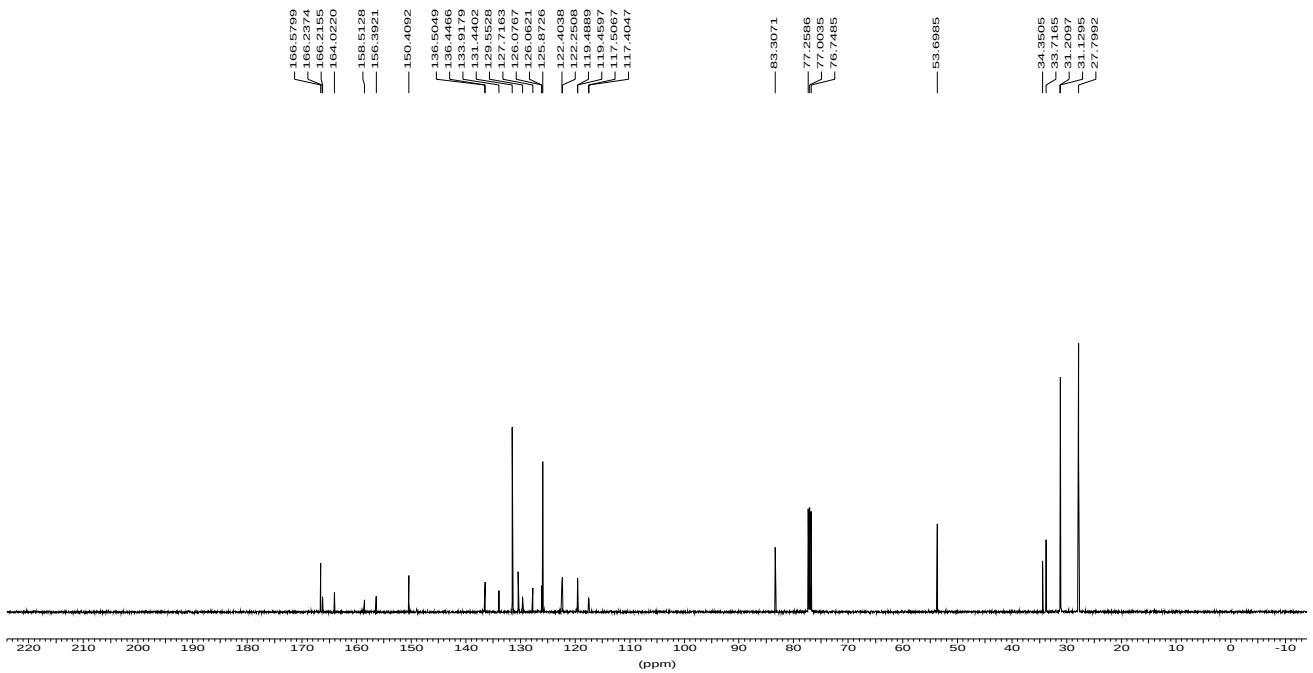


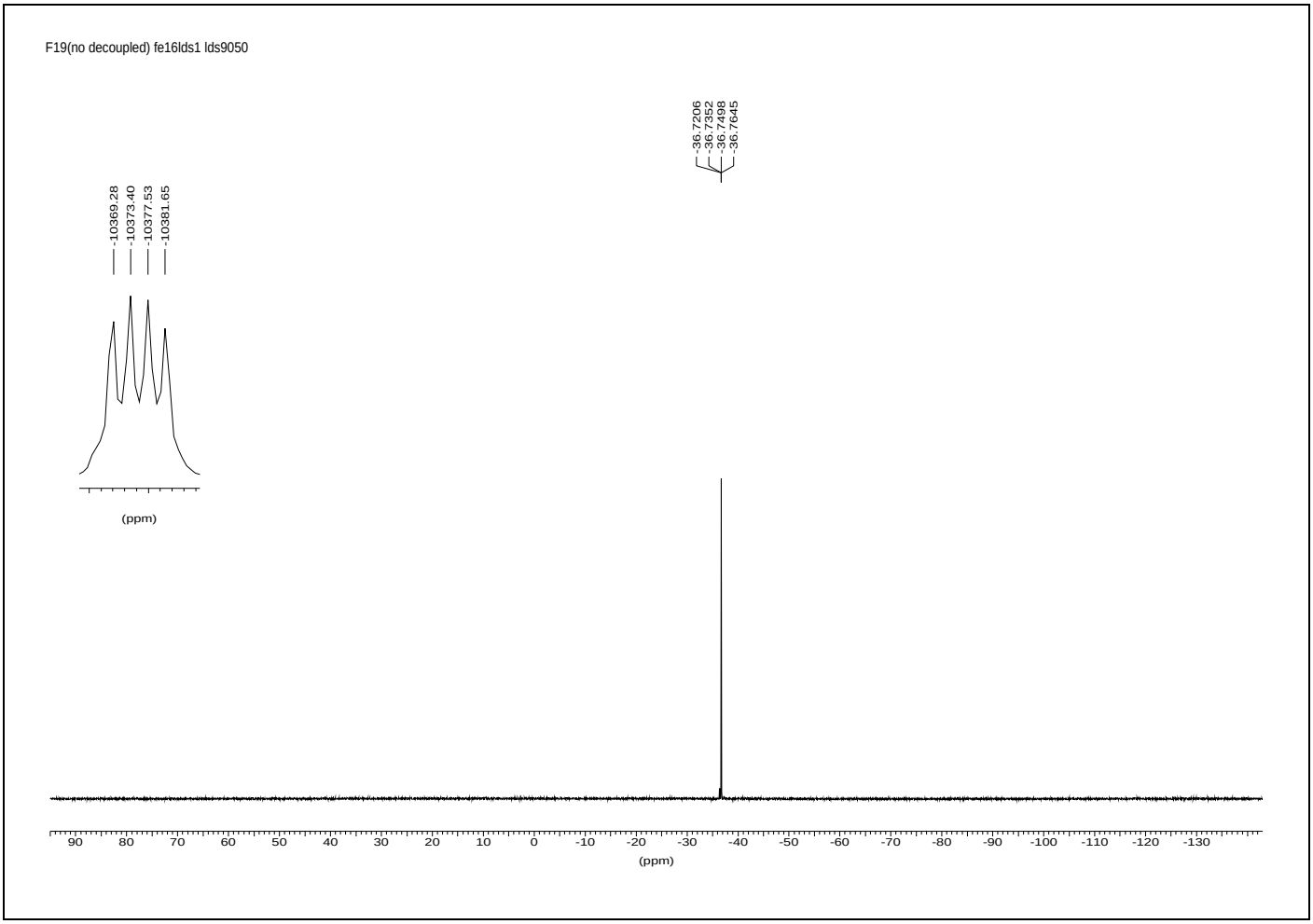


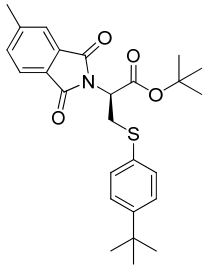
1H AMX500 ds02162 LDS9050

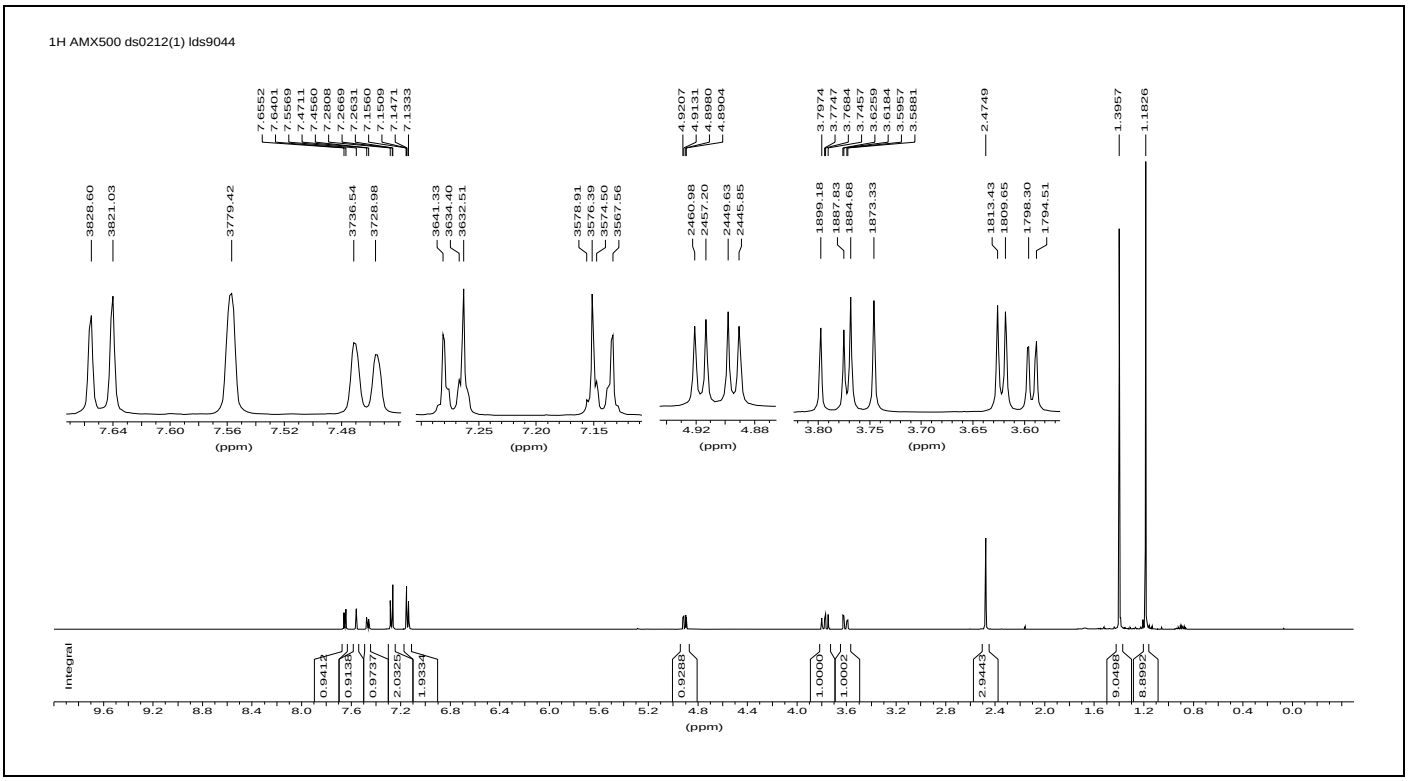


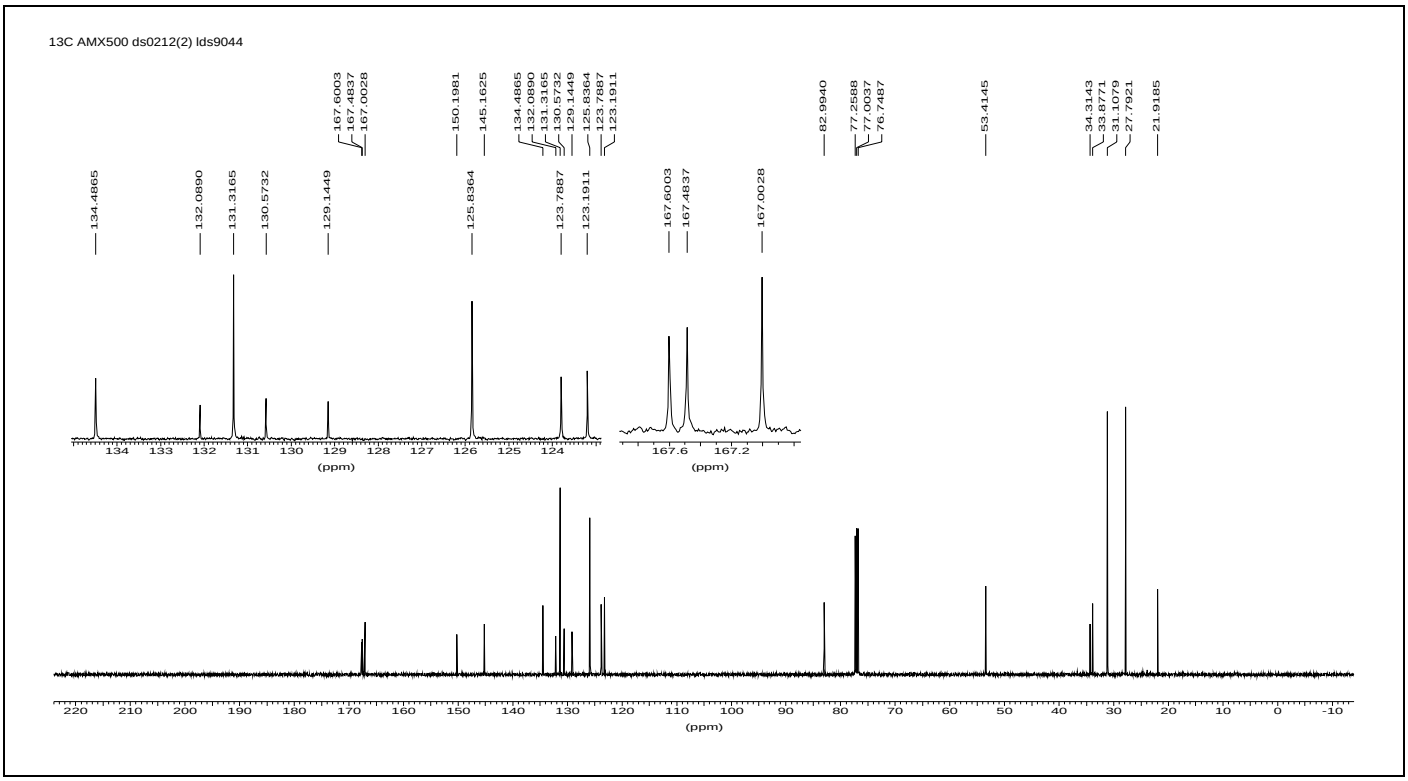
13C AMX500 ds02161 LDS9050

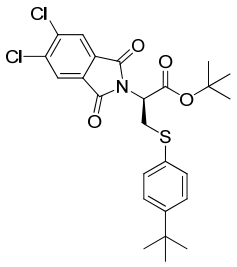



F19(no decoupled) fe16lds1 lds9050
-36.7206
-36.7352
-36.7498
-36.7645
-10369.28
-10373.40
-10377.53
-10381.65
(ppm)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130
(ppm)

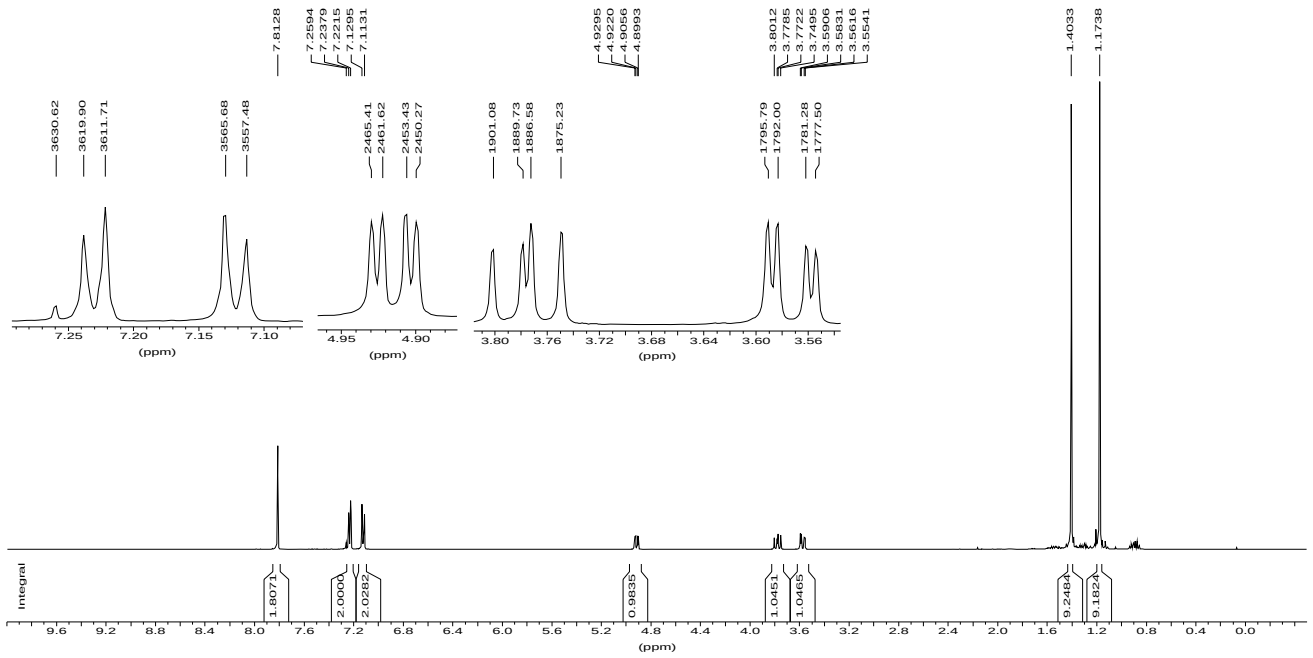



1H AMX500 ds0212(1) lds9044
7.6552
7.6401
7.5569
7.4711
7.4560
7.2808
7.2669
7.2631
7.1560
7.1509
7.1471
7.1333
4.9207
4.9131
4.8980
4.8904
3.7974
3.7747
3.7684
3.7457
3.6259
3.6184
3.5957
3.5881
2.4749
1.3957
1.1826
3828.60
3821.03
3779.42
3736.54
3728.98
3641.33
3634.40
3632.51
3578.91
3576.39
3574.50
3567.56
2460.98
2457.20
2449.63
2445.85
1899.18
1887.83
1884.68
1873.33
1813.43
1809.65
1798.30
1794.51
(ppm)
Integral
0.9411
0.9138
0.9737
2.0325
1.9334
0.9288
1.0000
1.0002
2.9443
9.0498
8.8992
(ppm)

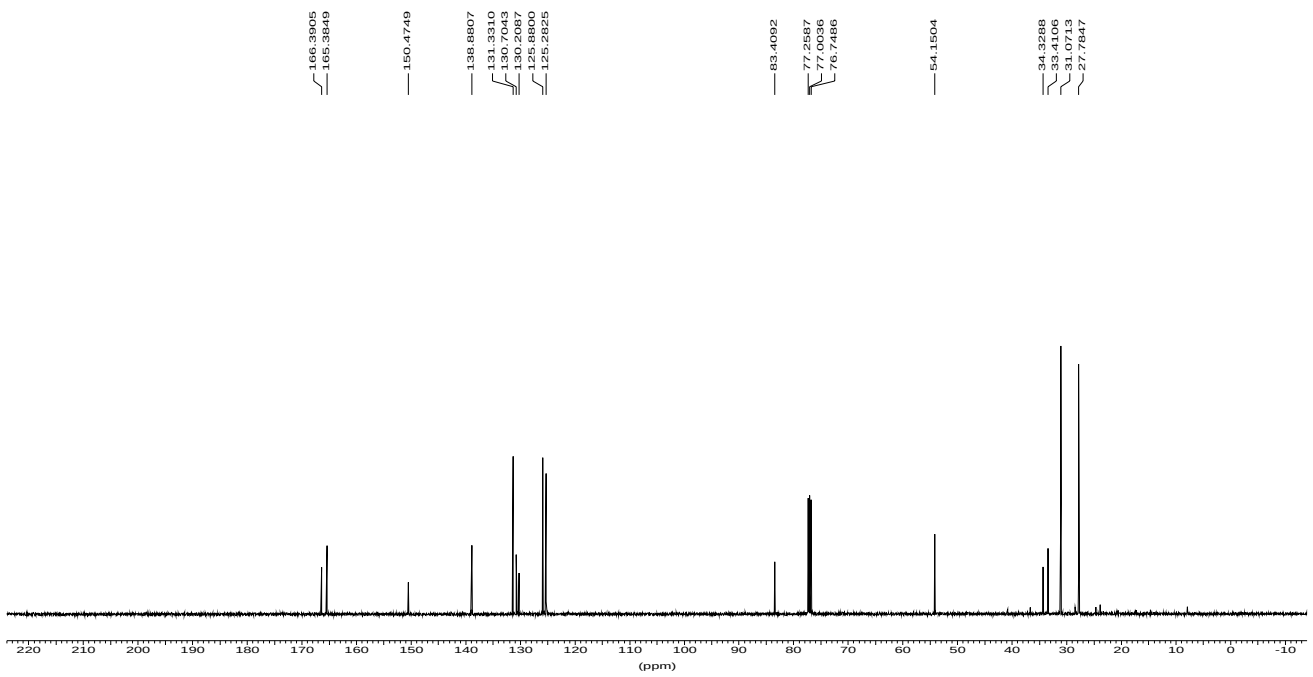

13C AMX500 ds0212(2) lds9044
167.6003
167.4837
167.0028
150.1981
145.1625
134.4865
132.0890
131.3165
130.5732
129.1449
125.8364
123.7887
123.1911
82.9940
77.2588
77.0037
76.7487
53.4145
34.3143
33.8771
31.1079
27.7921
21.9185
(ppm)

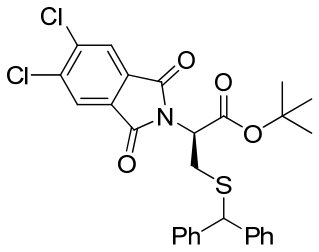


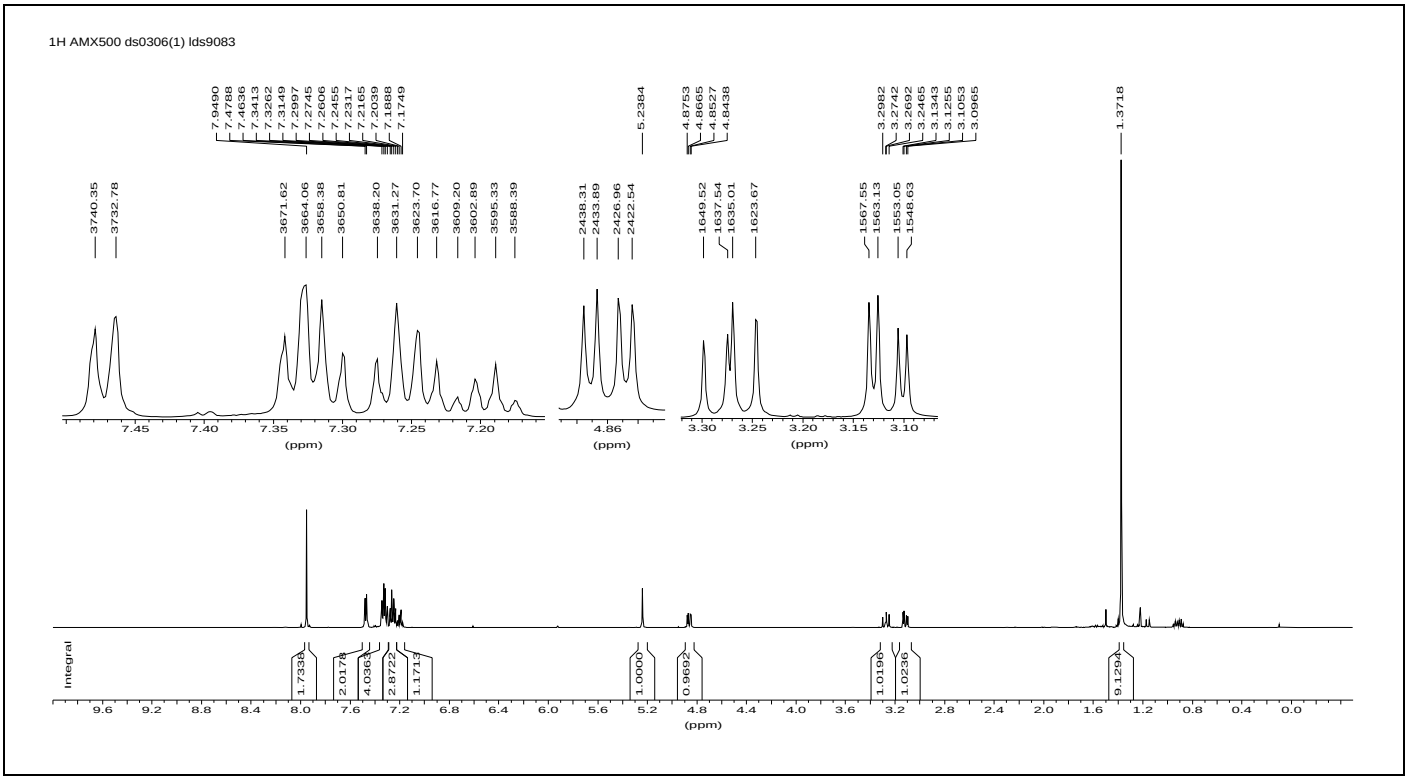
1H AMX500 ds0213(1) LSS2022



13C AMX500 ds0213(2) LSS2022




Cl
Cl
O
O
N
O
O
S
Ph
Ph


1H AMX500 ds0306(1) lds9083
7.9490
7.4788
7.4636
7.3413
7.3262
7.3149
7.2997
7.2745
7.2606
7.2455
7.2317
7.2165
7.2039
7.1888
7.1749
5.2384
4.8753
4.8665
4.8527
4.8438
3.2982
3.2742
3.2692
3.2465
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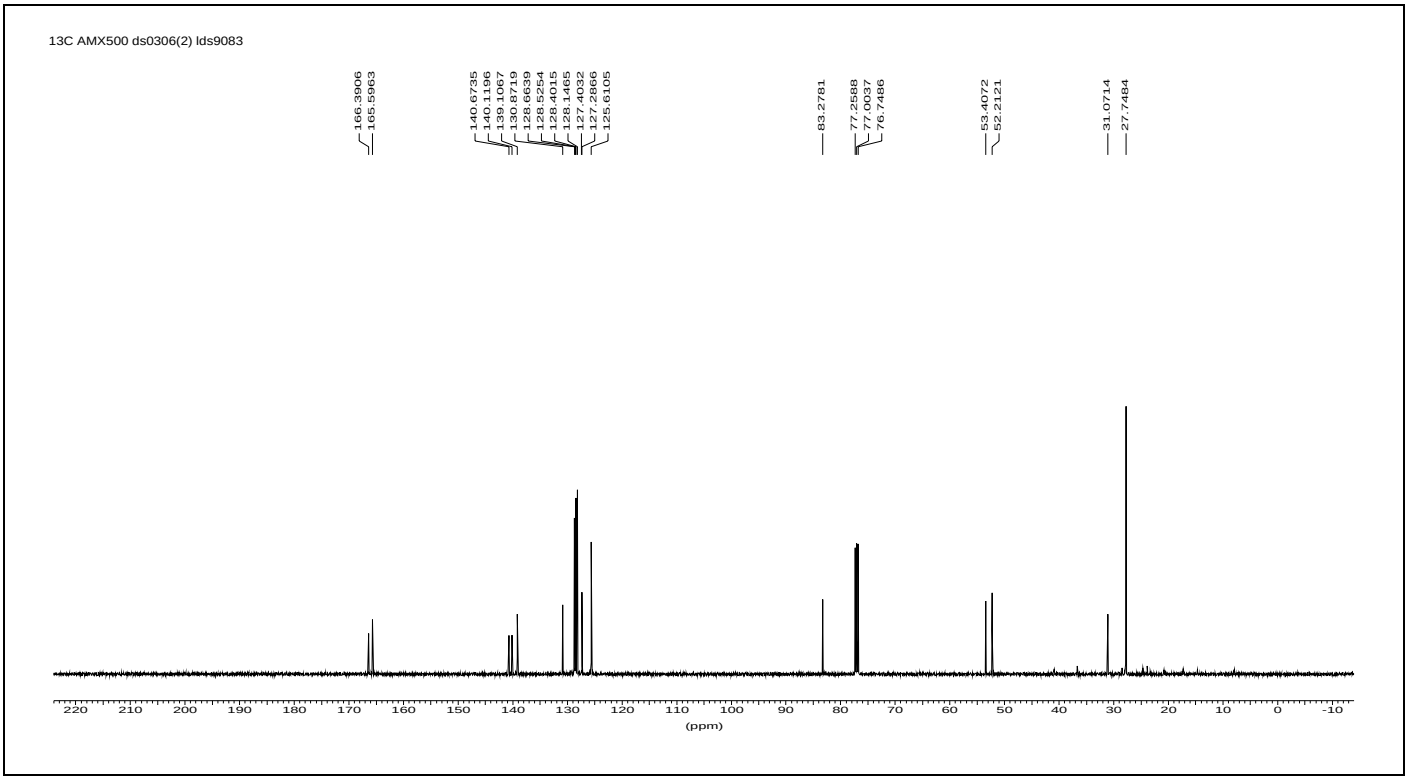
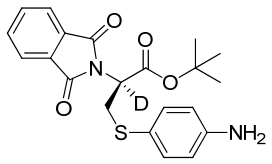
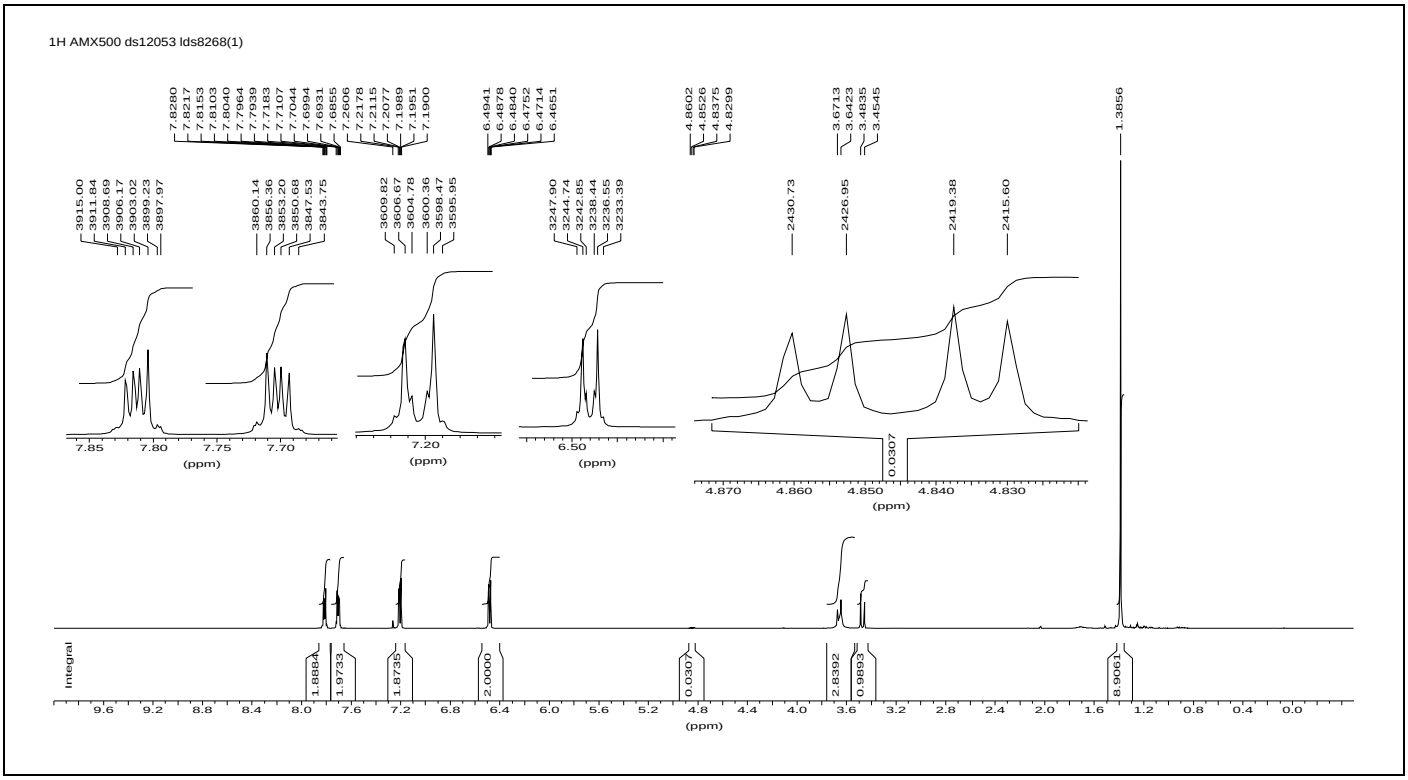
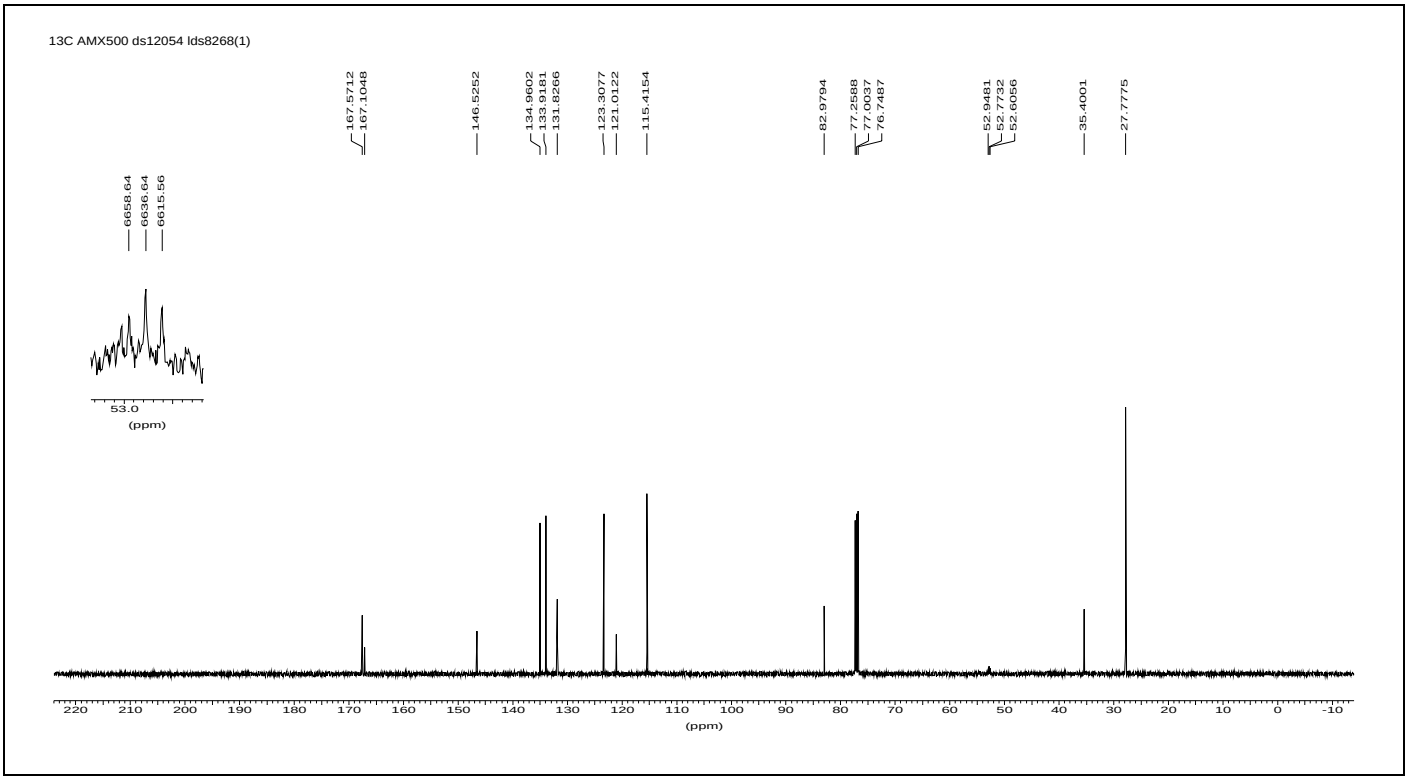
3.1255
3.1053
3.0965
1.3718
3740.35
3732.78
3671.62
3664.06
3658.38
3650.81
3638.20
3631.27
3623.70
3616.77
3609.20
3602.89
3595.33
3588.39
2438.31
2433.89
2426.96
2422.54
1649.52
1637.54
1635.01
1623.67
1567.55
1563.13
1553.05
1548.63
7.45
7.40
7.35
7.30
7.25
7.20
(ppm)
4.86
(ppm)
3.30
3.25
3.20
3.15
3.10
(ppm)
integral
1.7338
2.0178
4.0363
2.8722
1.1713
1.0000
0.9692
1.0198
1.0236
9.1294
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
(ppm)

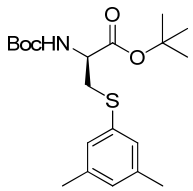

13C AMX500 ds0306(2) lds9083
166.3906
165.5963
140.6735
140.1196
139.1067
130.8719
128.6639
128.5254
128.4015
128.1465
127.4032
127.2866
125.6105
83.2781
77.2588
77.0037
76.7486
53.4072
52.2121
31.0714
27.7484
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
(ppm)

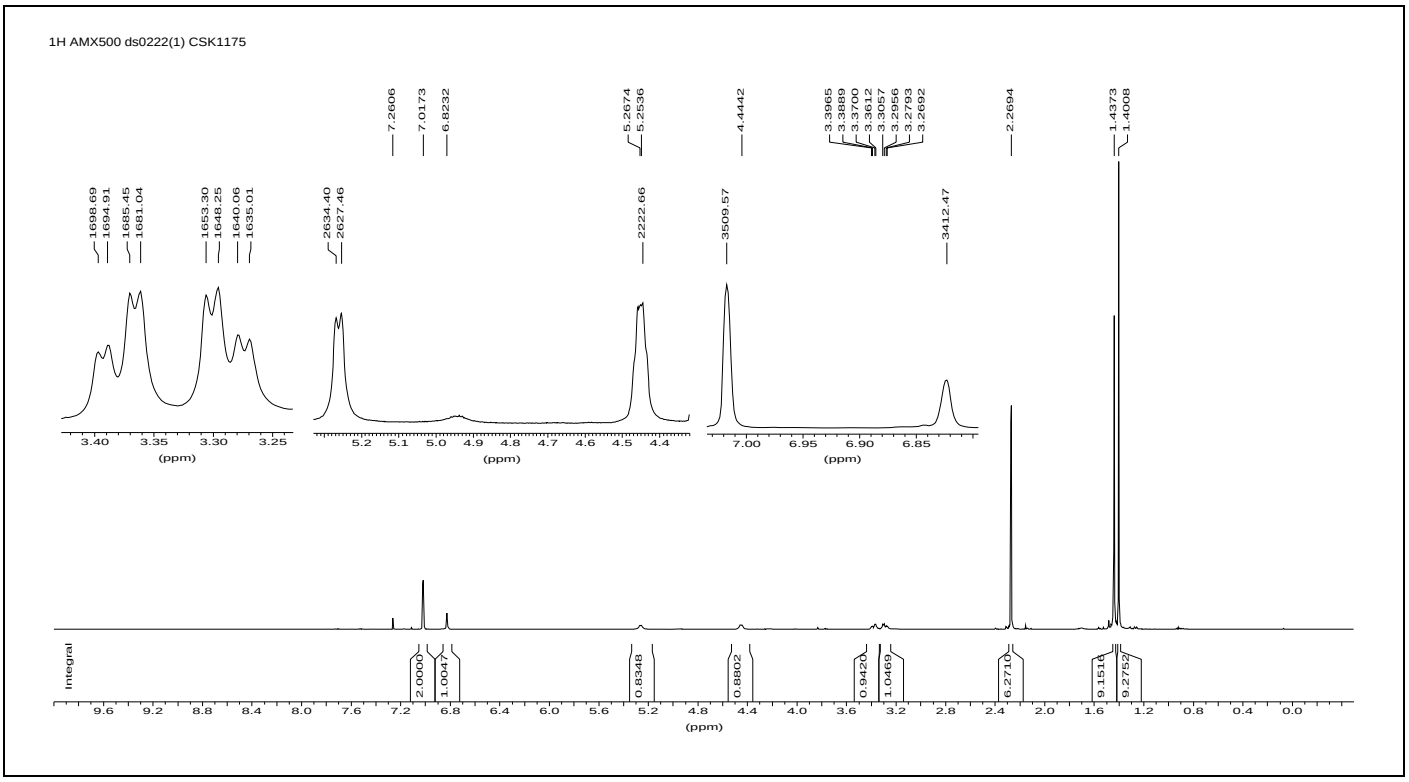


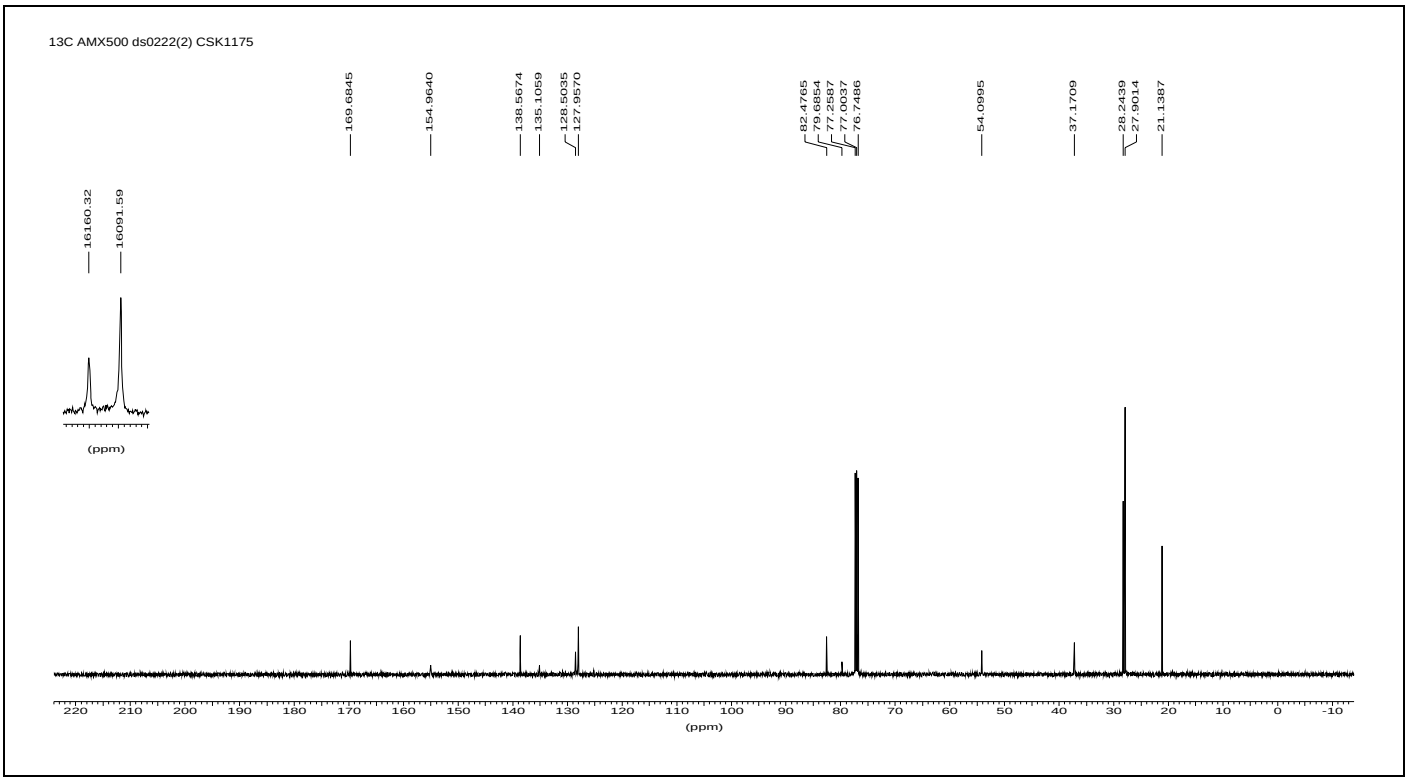
11f-d_1

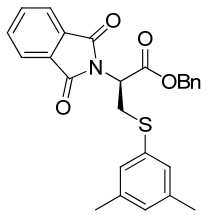

1H AMX500 ds12053 lds8268(1)
(ppm)
Integral

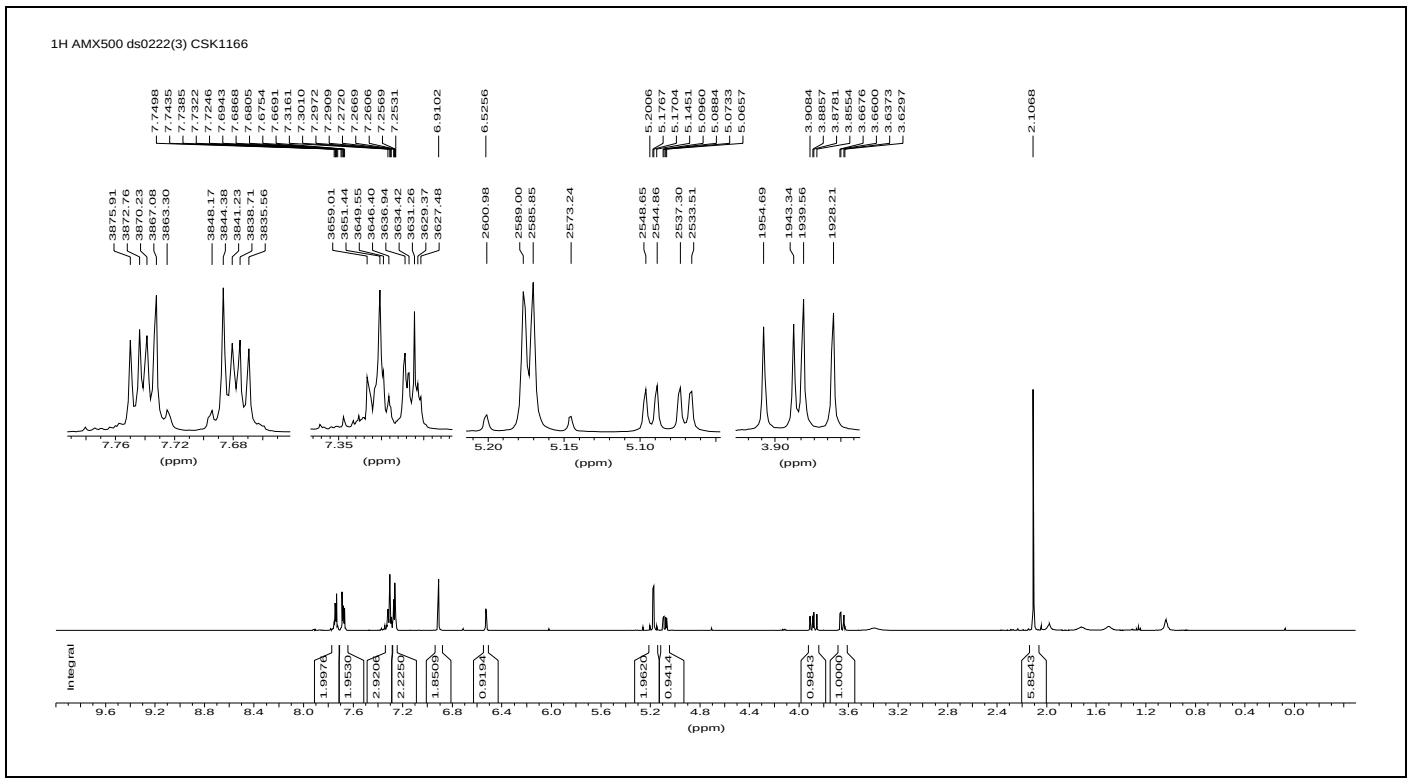

13C AMX500 ds12054 lds8268(1)
(ppm)

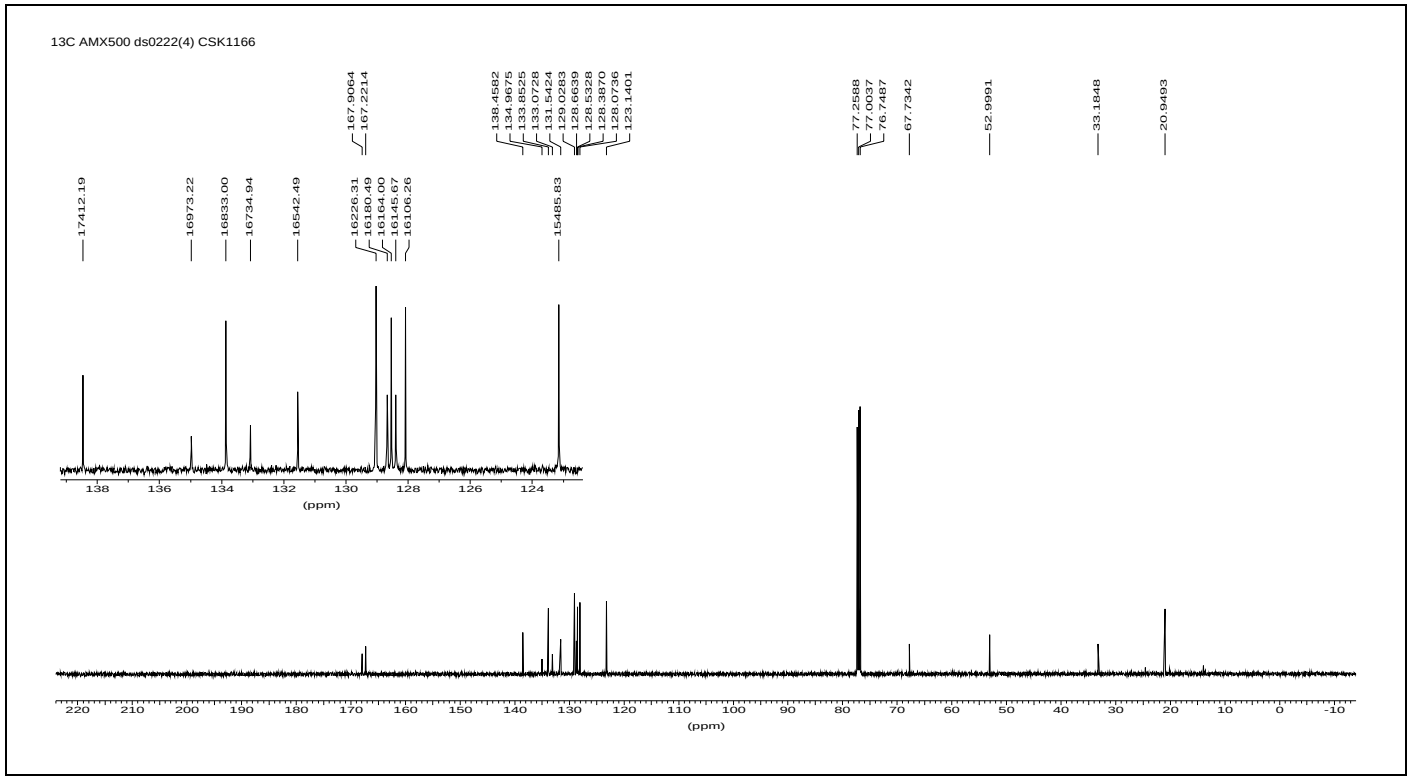

BocHN
O
O
S

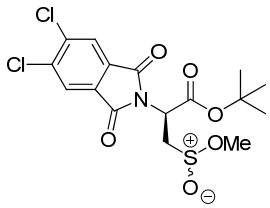

1H AMX500 ds0222(1) CSK1175
7.2606
7.0173
6.8232
5.2674
5.2536
4.4442
3.3965
3.3889
3.3700
3.3612
3.3057
3.2956
3.2793
3.2692
2.2694
1.4373
1.4008
1698.69
1694.91
1685.45
1681.04
1653.30
1648.25
1640.06
1635.01
2634.40
2627.46
2222.66
3509.57
3412.47
integral
2.0000
1.0047
0.8348
0.8802
0.9420
1.0469
6.2710
9.1518
9.2752
(ppm)

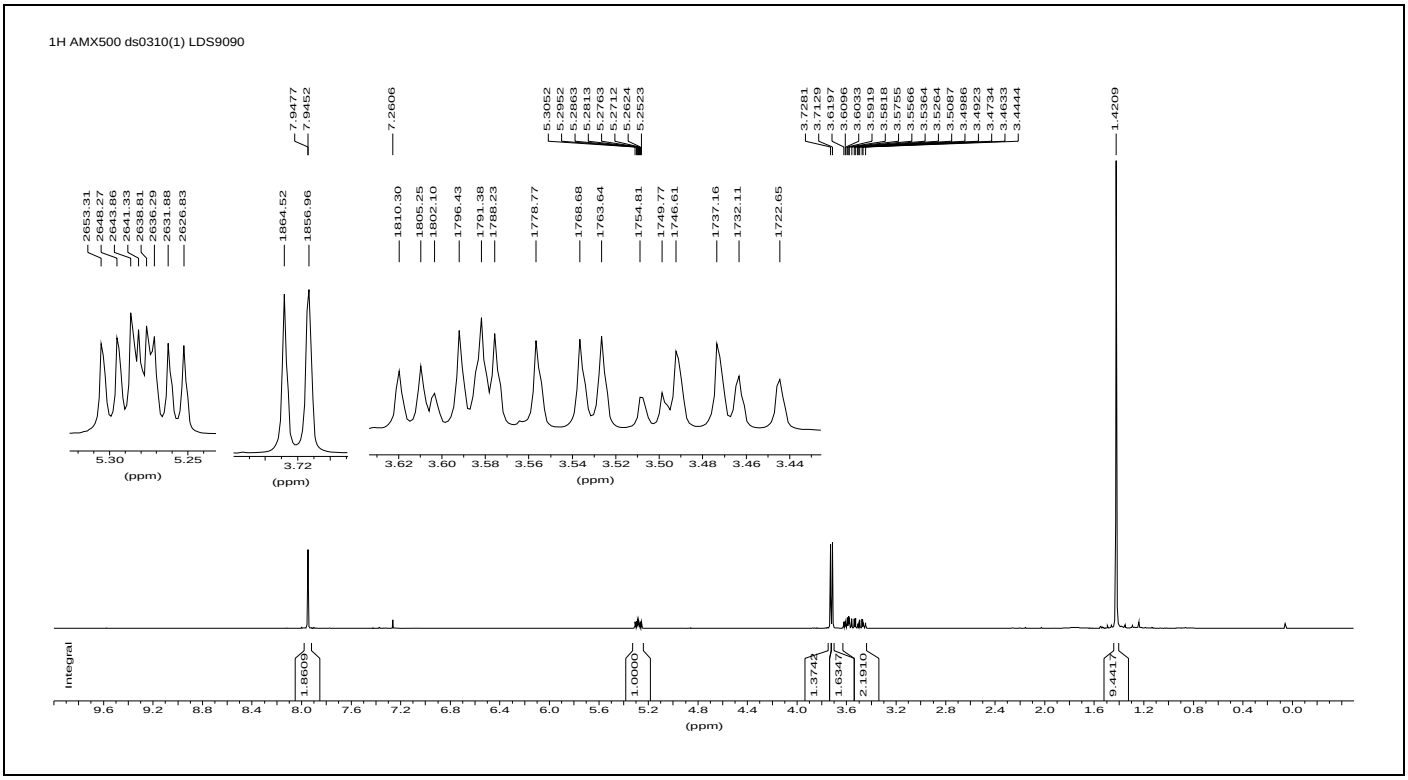

13C AMX500 ds0222(2) CSK1175
169.6845
154.9640
138.5674
135.1059
128.5035
127.9570
82.4765
79.6854
77.2587
77.0037
76.7486
54.0995
37.1709
28.2439
27.9014
21.1387
16160.32
16091.59
(ppm)

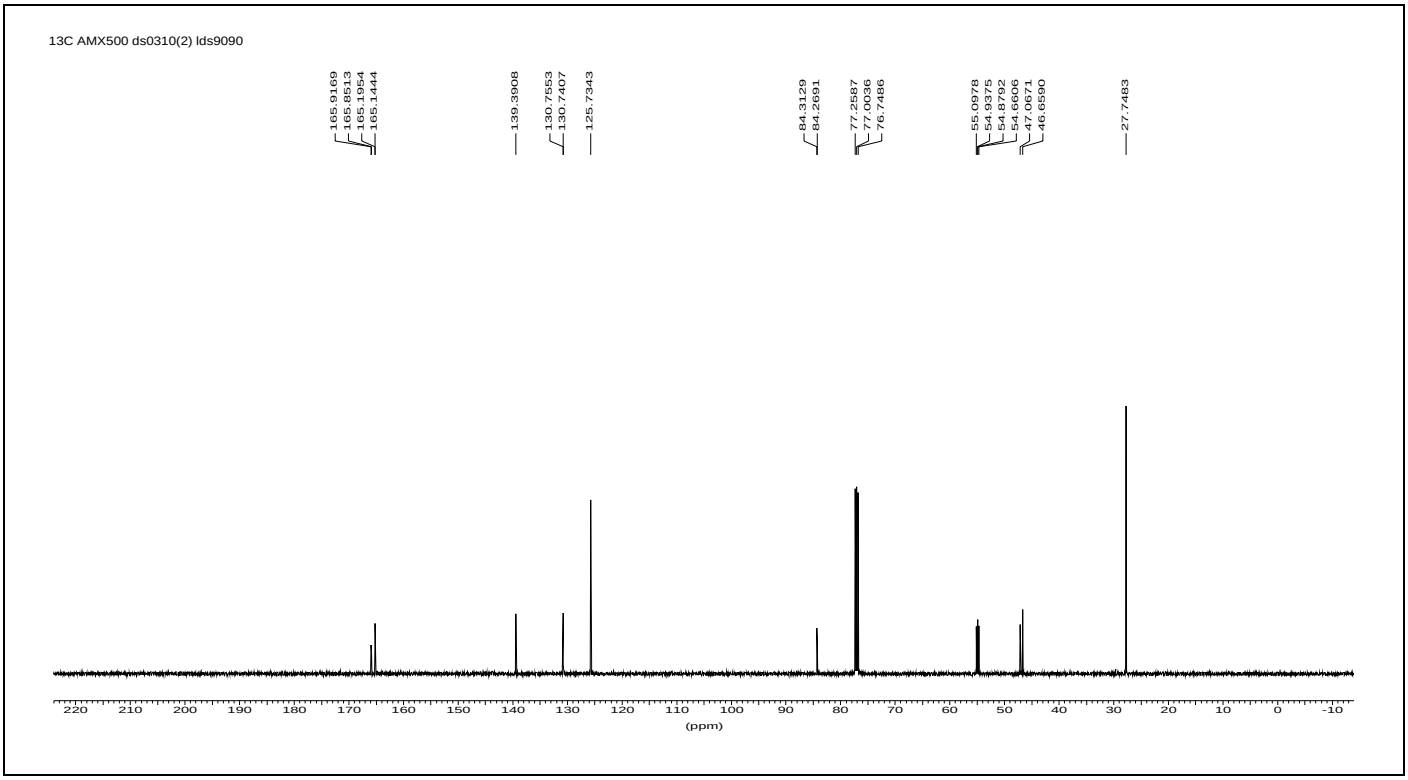

O
O
N
O
OBn
O
S

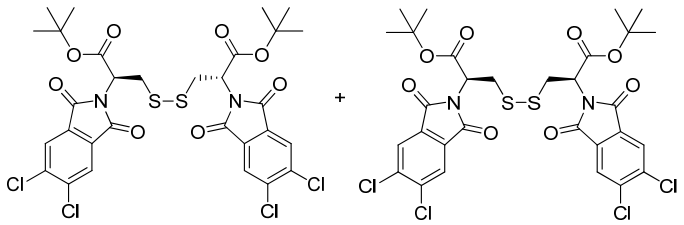

1H AMX500 ds0222(3) CSK1166
7.7498
7.7435
7.7385
7.7322
7.7246
7.6943
7.6868
7.6805
7.6754
7.6691
7.3161
7.3010
7.2972
7.2909
7.2720
7.2669
7.2606
7.2569
7.2531
6.9102
6.5256
5.2006
5.1767
5.1704
5.1451
5.0960
5.0884
5.0733
5.0657
3.9084
3.8857
3.8781
3.8554
3.6676
3.6600
3.6373
3.6297
2.1068
3875.91
3872.76
3870.23
3867.08
3863.30
3848.17
3844.38
3841.23
3838.71
3835.56
3659.01
3651.44
3649.55
3646.40
3636.94
3634.42
3631.26
3629.37
3627.48
2600.98
2589.00
2585.85
2573.24
2548.65
2544.86
2537.30
2533.51
1954.69
1943.34
1939.56
1928.21
7.76
7.72
7.68
(ppm)
7.35
(ppm)
5.20
5.15
5.10
(ppm)
3.90
(ppm)
integral
1.9970
1.9530
2.9204
2.2259
1.8509
0.9194
1.9620
0.9414
0.9843
1.0000
5.8543
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
(ppm)


13C AMX500 ds0222(4) CSK1166
167.9064
167.2214
138.4582
134.9675
133.8525
133.0728
131.5424
129.2083
128.6639
128.5328
128.3870
128.0736
123.1401
77.2588
77.0037
76.7487
67.7342
52.9991
33.1848
20.9493
17412.19
16973.22
16833.00
16734.94
16542.49
16226.31
16180.49
16164.00
16145.67
16100.26
15485.83
138
136
134
132
130
128
126
124
(ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
(ppm)

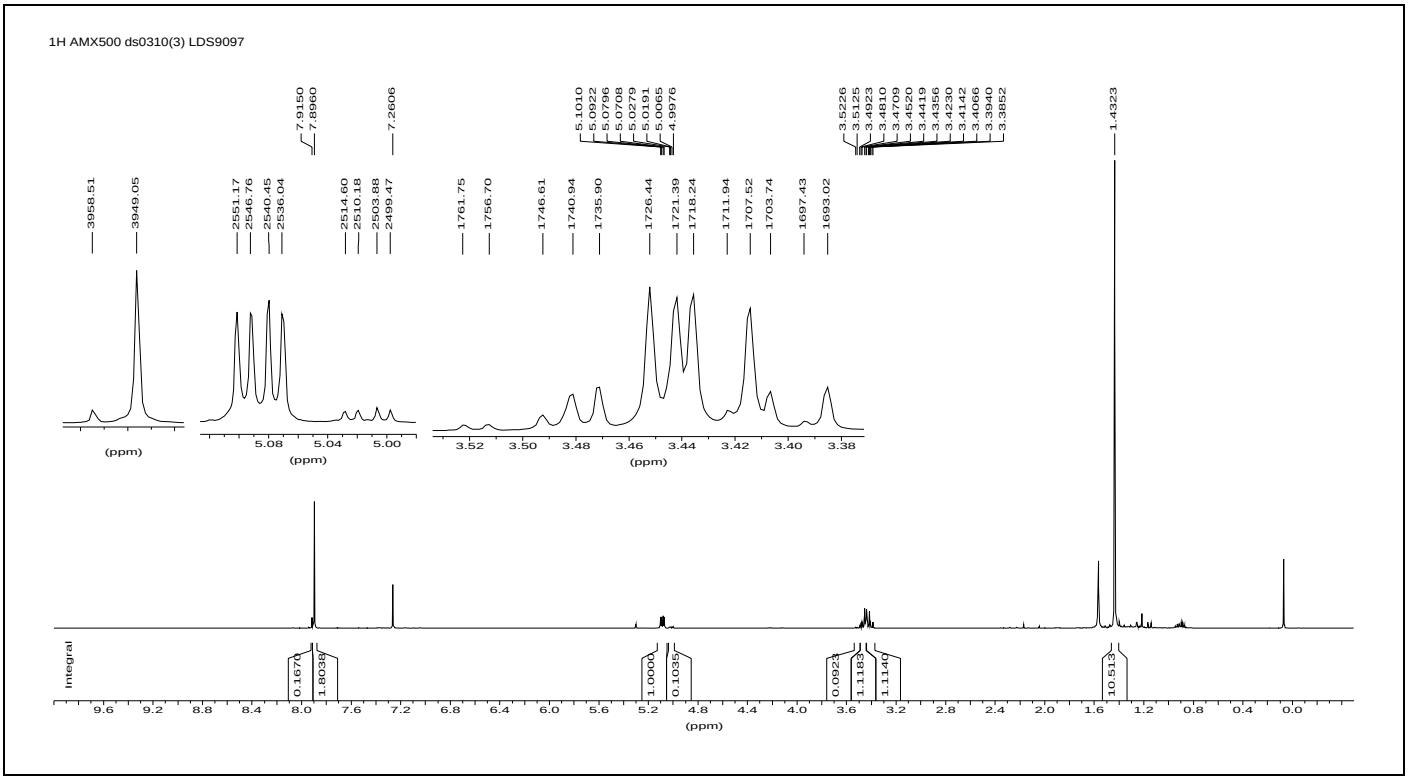

Cl
Cl
O
O
N
O
O
O
S
OMe
O

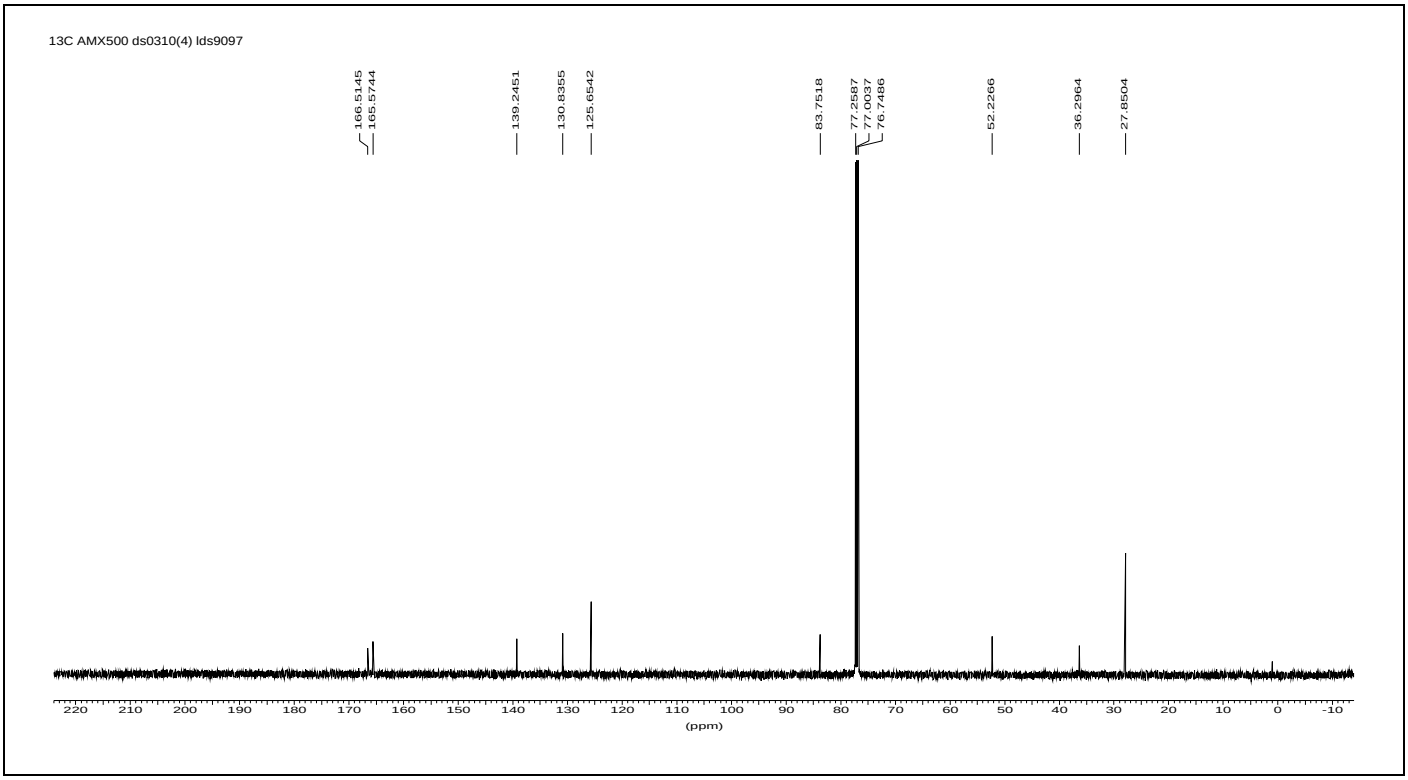

1H AMX500 ds0310(1) LDS9090
7.9477
7.9452
7.2606
5.3052
5.2952
5.2883
5.2813
5.2763
5.2712
5.2624
5.2523
3.7281
3.7129
3.6197
3.6096
3.6033
3.5919
3.5818
3.5755
3.5566
3.5364
3.5264
3.5087
3.4986
3.4923
3.4734
3.4633
3.4444
1.4209
2653.31
2648.27
2643.86
2641.33
2638.81
2636.29
2631.88
2626.83
1864.52
1856.96
1810.30
1805.25
1802.10
1796.43
1791.38
1788.23
1778.77
1768.68
1763.64
1754.81
1749.77
1746.61
1737.16
1732.11
1722.65
5.30
5.25
(ppm)
3.72
(ppm)
3.62
3.60
3.58
3.56
3.54
3.52
3.50
3.48
3.46
3.44
(ppm)
Integral
1.8609
1.0000
1.3742
1.6347
2.1910
9.4417
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
(ppm)

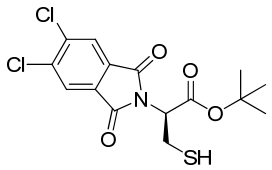

13C AMX500 ds0310(2) lds9090
165.9169
165.8513
165.1954
165.1444
139.3908
130.7553
130.7407
125.7343
84.3129
84.2691
77.2587
77.0036
76.7486
55.0978
54.9375
54.8792
54.6606
47.0671
46.6590
27.7483
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
(ppm)

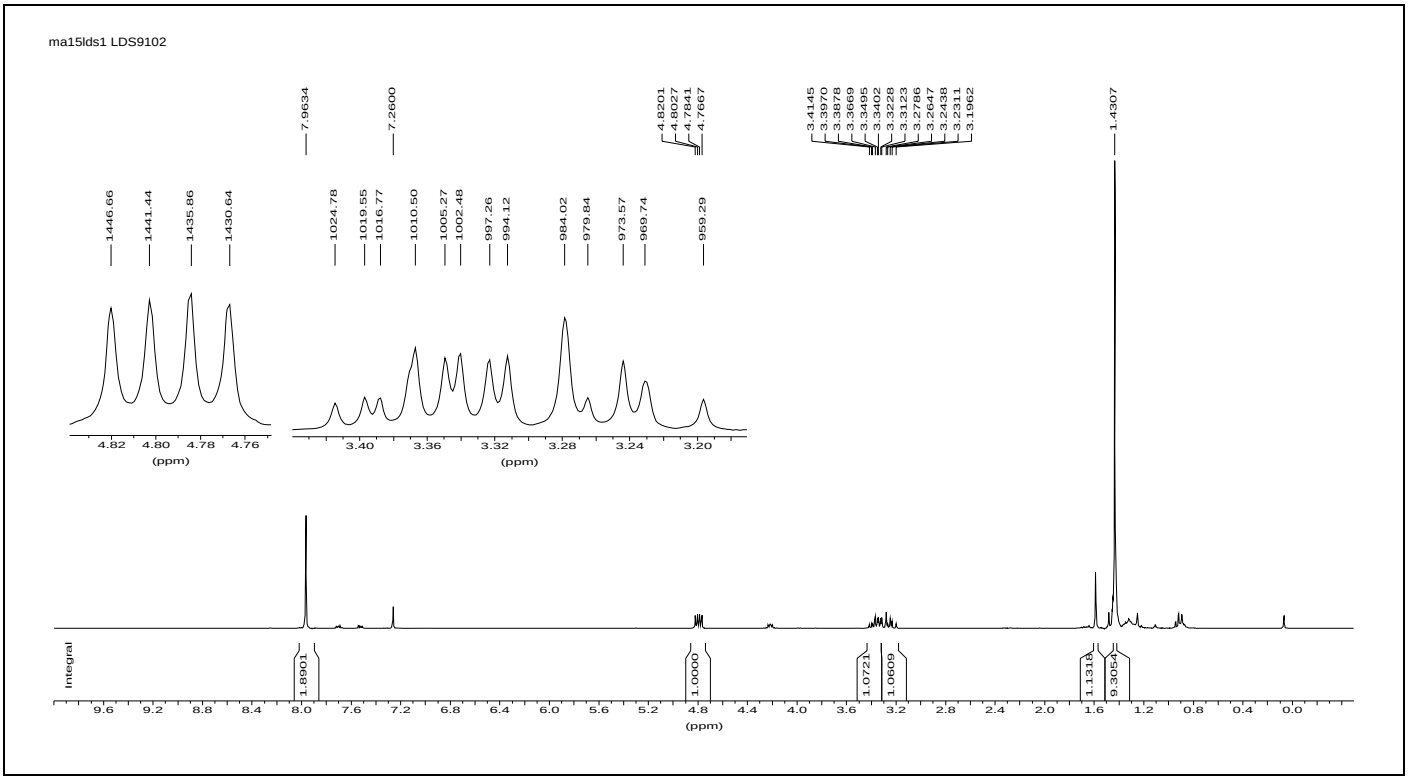


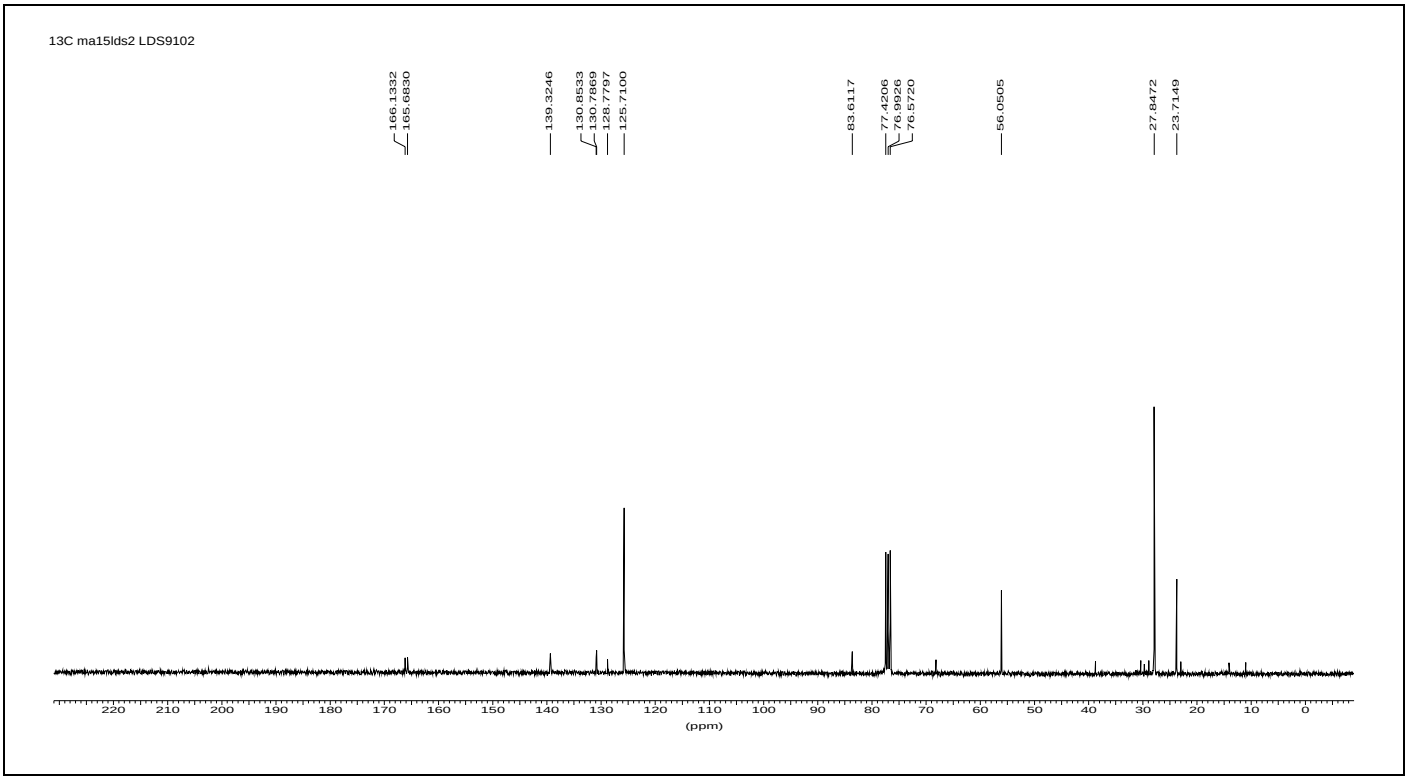
(*S*,*S*)-**8** *meso*-**8**

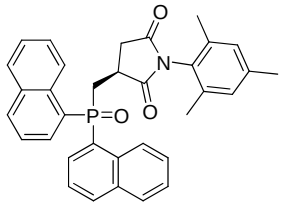

1H AMX500 ds0310(3) LDS9097
7.9150
7.8960
7.2606
5.1010
5.0922
5.0796
5.0708
5.0279
5.0191
5.0065
4.9976
3.5226
3.5125
3.4923
3.4810
3.4709
3.4520
3.4419
3.4356
3.4230
3.4142
3.4066
3.3940
3.3852
1.4323
3958.51
3949.05
2551.17
2546.76
2540.45
2536.04
2514.60
2510.18
2503.88
2499.47
1761.75
1756.70
1746.61
1740.94
1735.90
1726.44
1721.39
1718.24
1711.94
1707.52
1703.74
1697.43
1693.02
(ppm)
Integral
0.1670
1.8038
1.0000
0.1039
0.0923
1.1183
1.1140
10.513
(ppm)

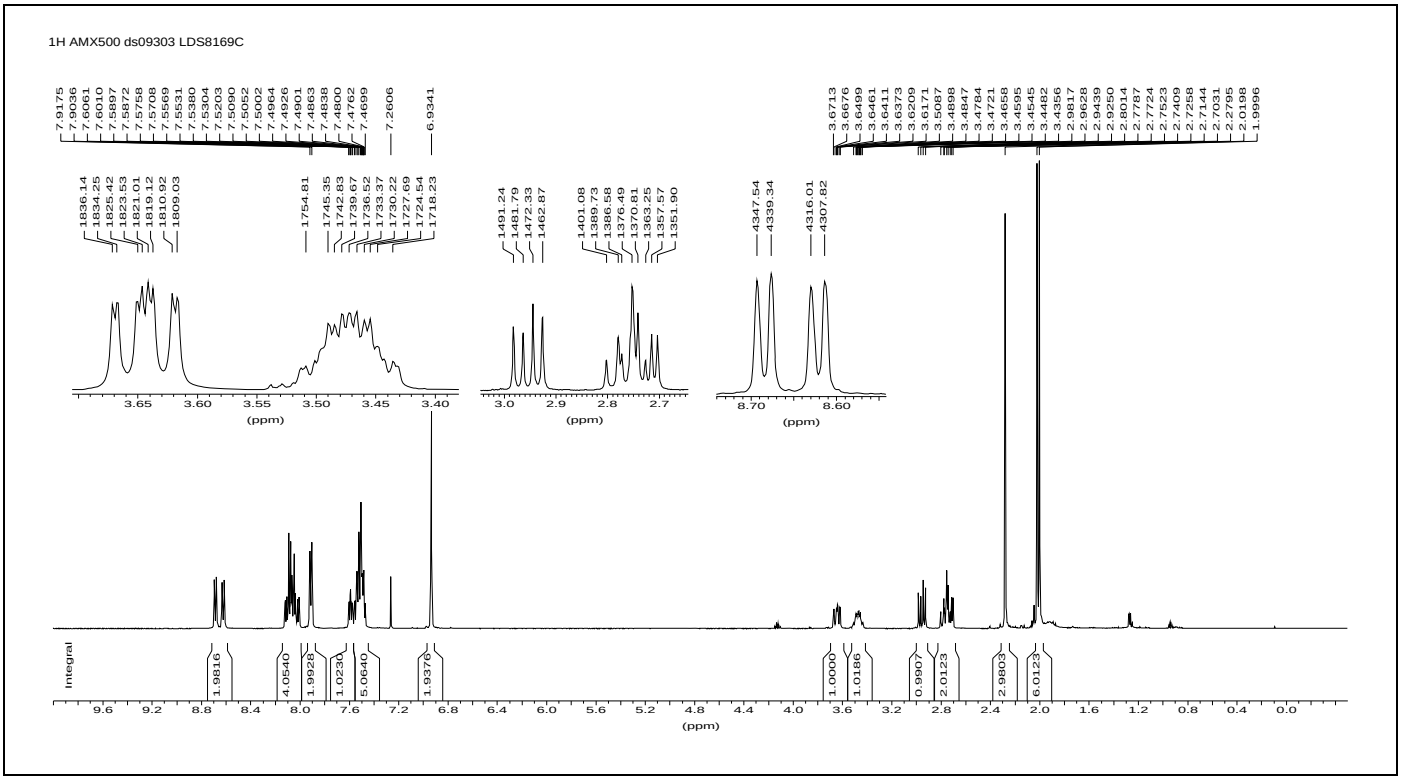

13C AMX500 ds0310(4) lds9097
166.5145
165.5744
139.2451
130.8355
125.6542
83.7518
77.2587
77.0037
76.7486
52.2266
36.2964
27.8504
(ppm)

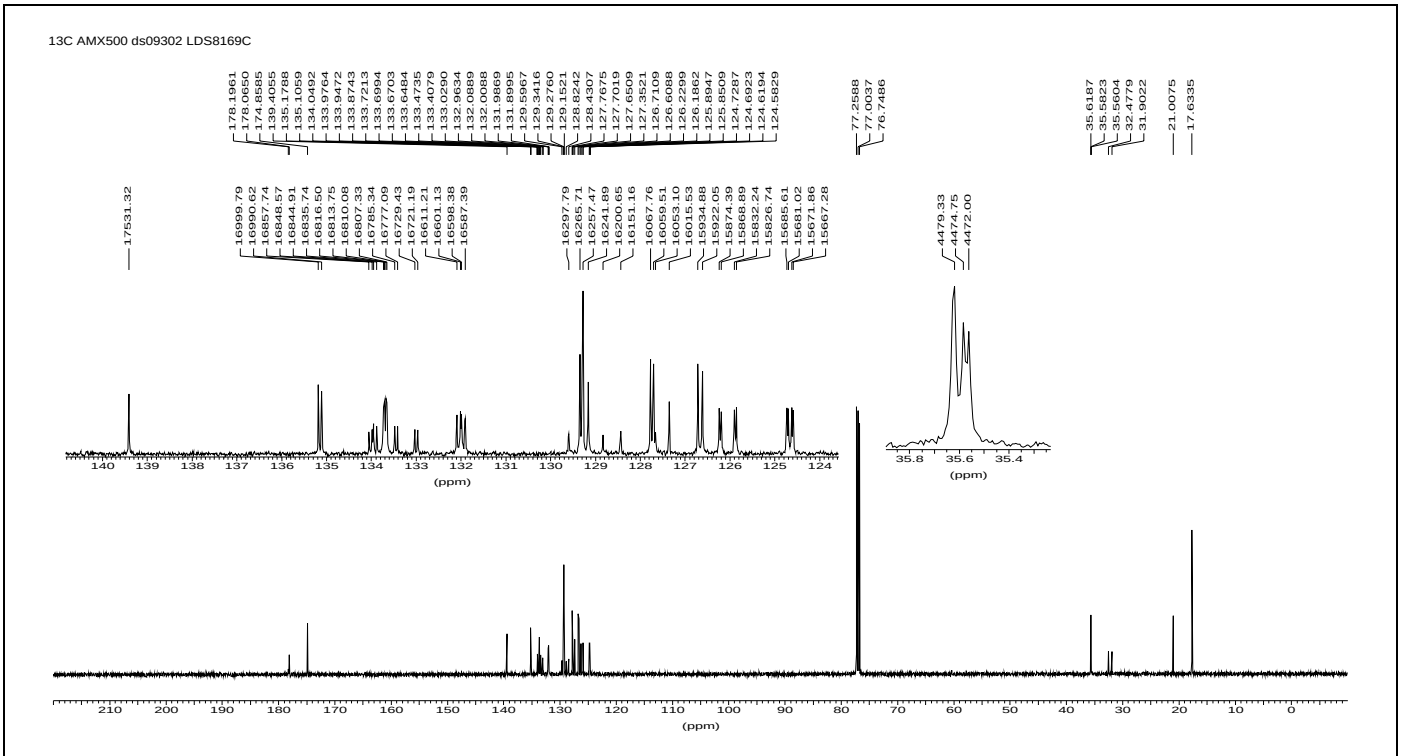

Cl
Cl
O
O
N
O
O
SH

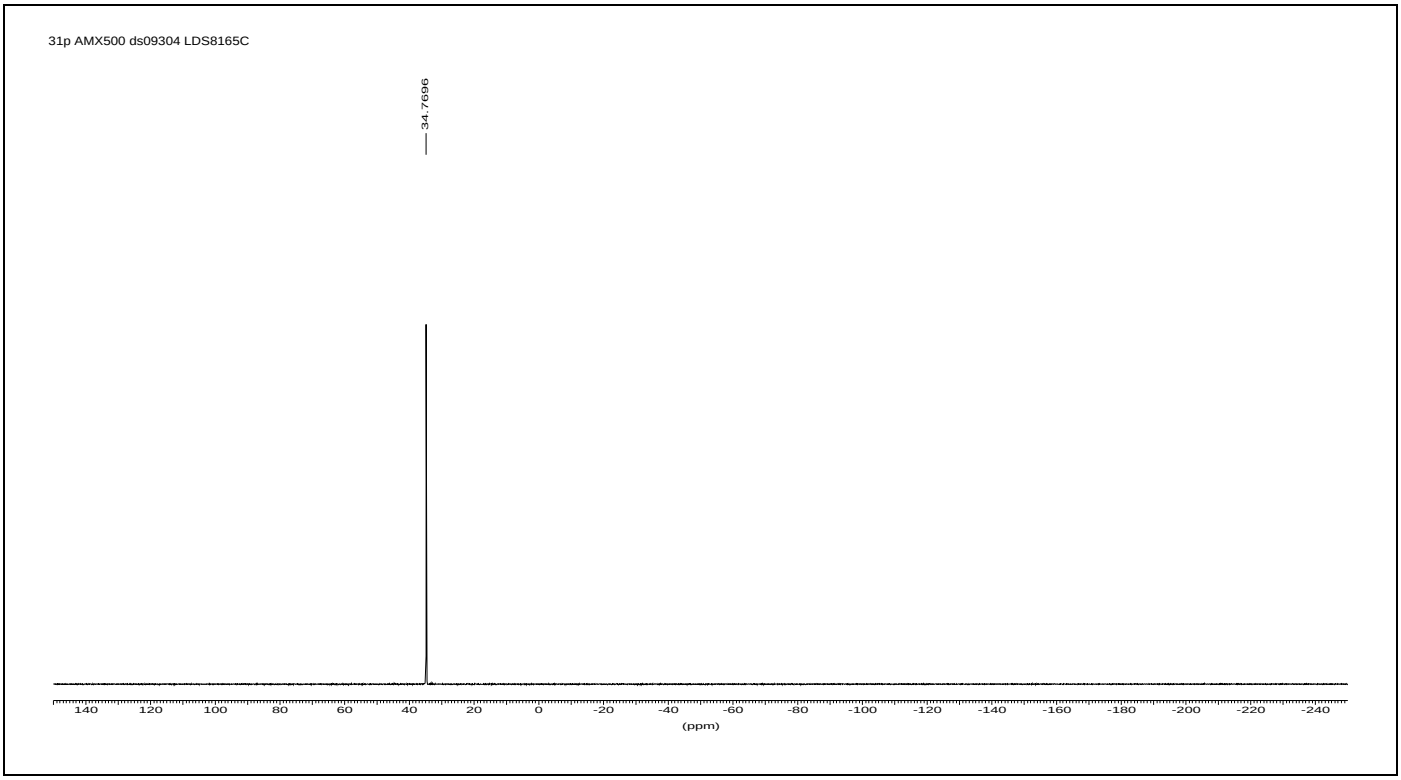

ma15lds1 LDS9102
7.9634
7.2600
4.8201
4.8027
4.7841
4.7667
3.4145
3.3970
3.3878
3.3669
3.3495
3.3402
3.3228
3.3123
3.2786
3.2647
3.2438
3.2311
3.1962
1.4307
1446.66
1441.44
1435.86
1430.64
1024.78
1019.55
1016.77
1010.50
1005.27
1002.48
997.26
994.12
984.02
979.84
973.57
969.74
959.29
4.82 4.80 4.78 4.76
(ppm)
3.40 3.36 3.32 3.28 3.24 3.20
(ppm)
Integral
1.8901
1.0000
1.0721
1.0609
1.1318
9.3054
9.6 9.2 8.8 8.4 8.0 7.6 7.2 6.8 6.4 6.0 5.6 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8 0.4 0.0
(ppm)

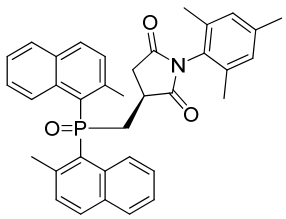

13C ma15lds2 LDS9102
166.1332
165.6830
139.3246
130.8533
130.7869
128.7797
125.7100
83.6117
77.4206
76.9926
76.5720
56.0505
27.8472
23.7149
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

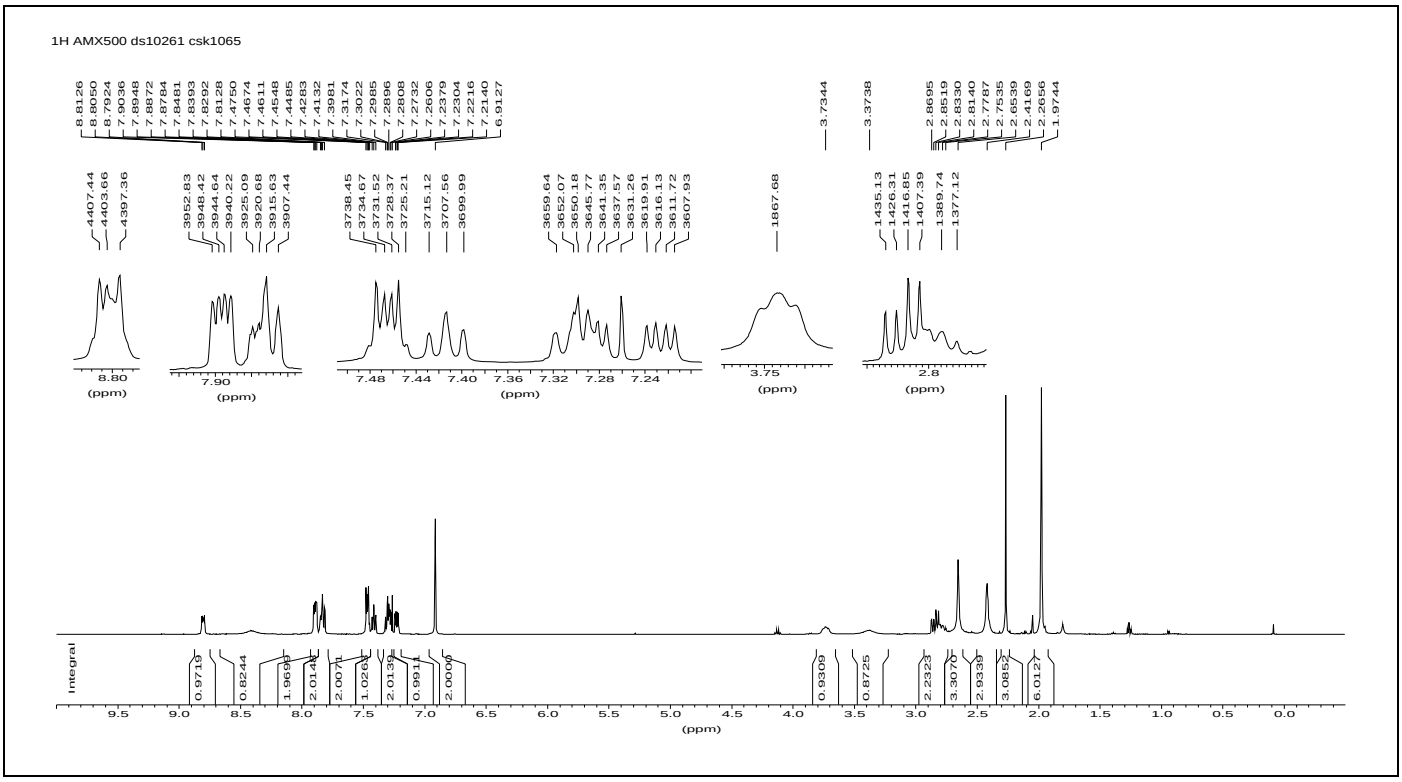


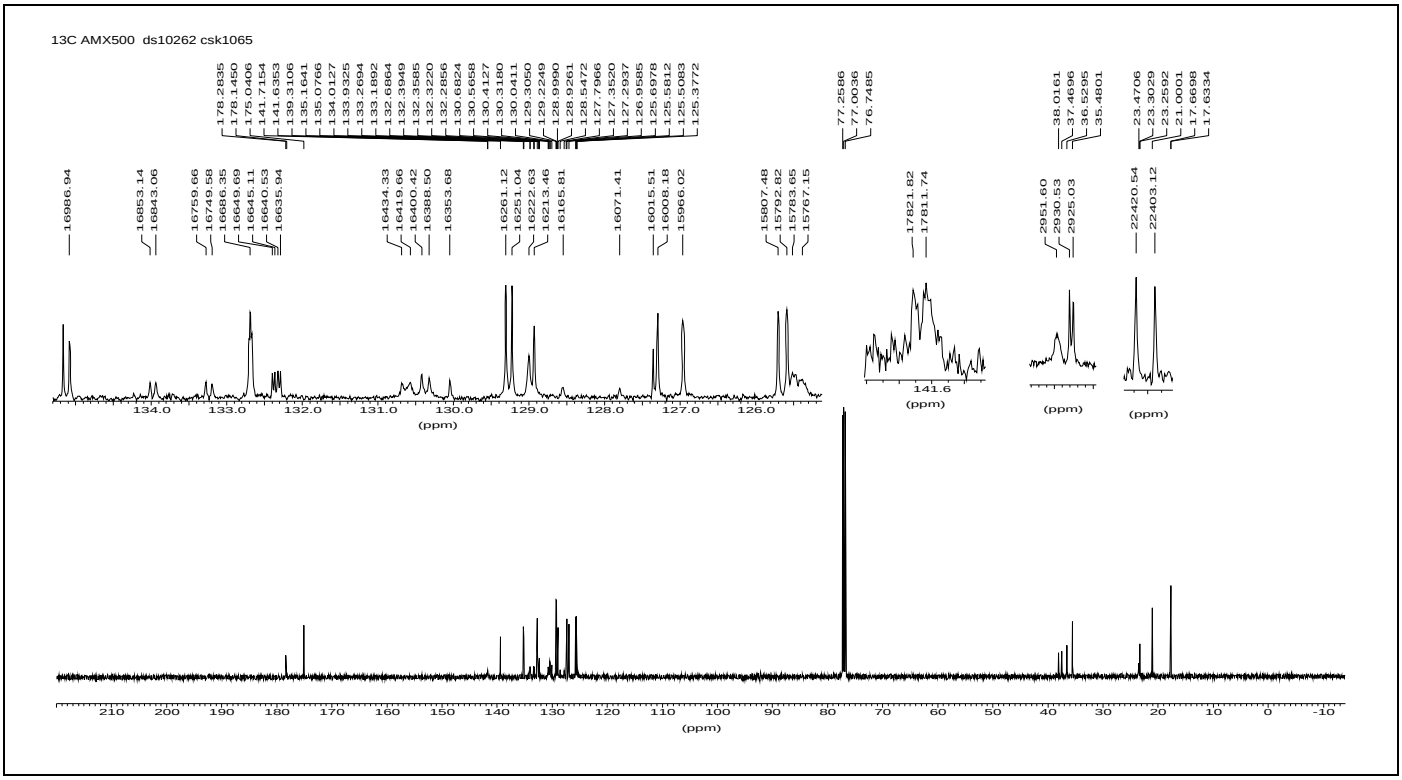

1H AMX500 ds09303 LDS8169C
Integral
(ppm)

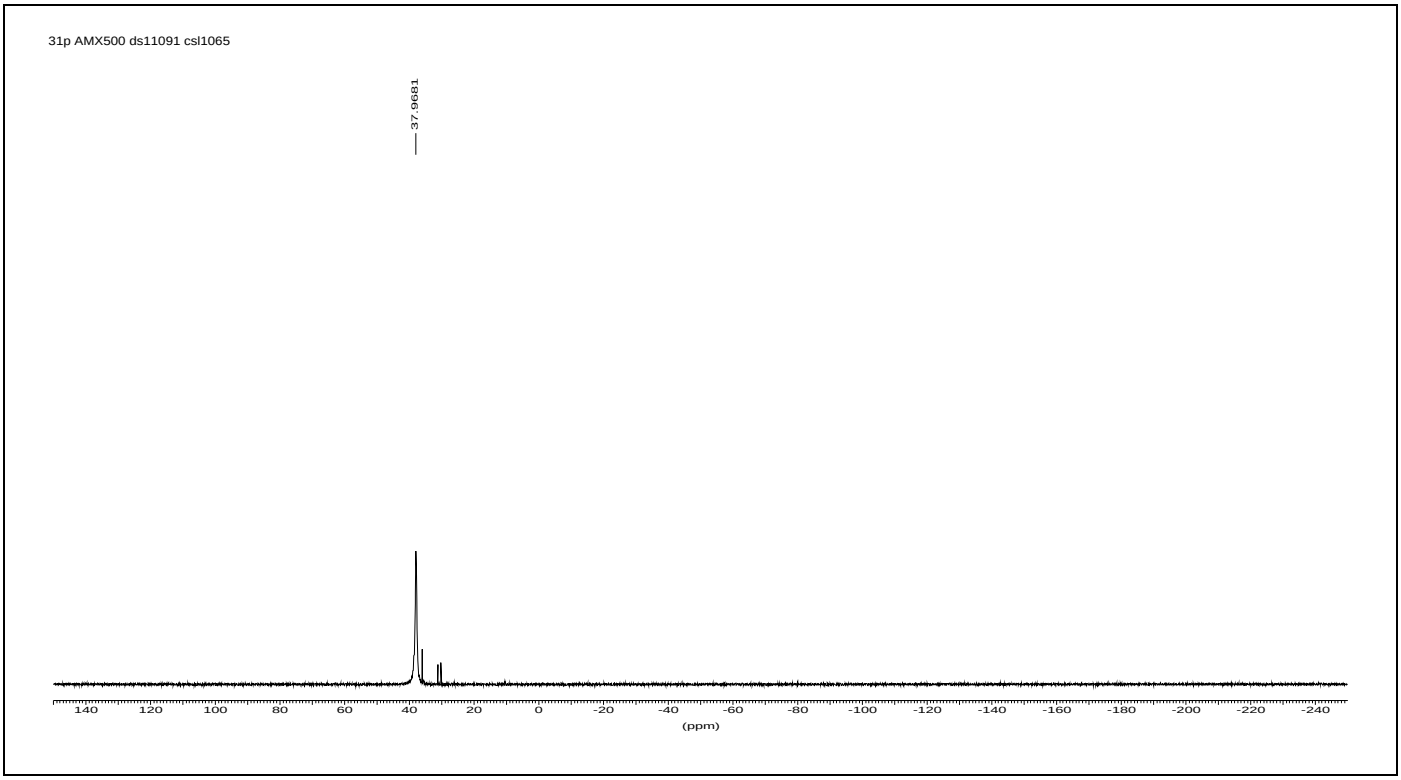

13C AMX500 ds09302 LDS8169C
(ppm)

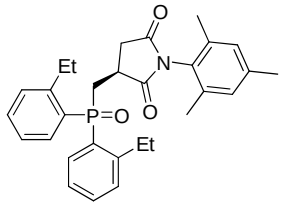

31p AMX500 ds09304 LDS8165C
34.7696
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
(ppm)

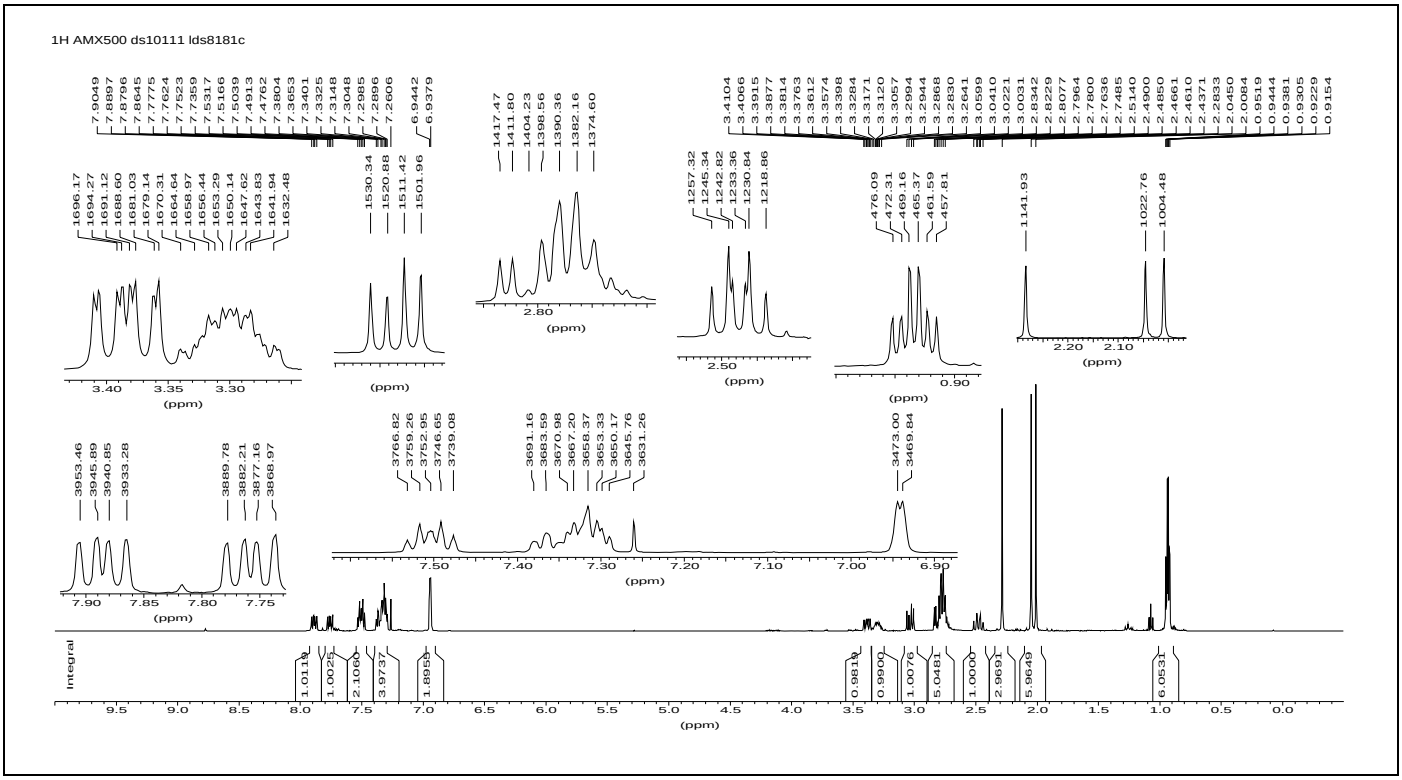

O
N
O
O=P
O

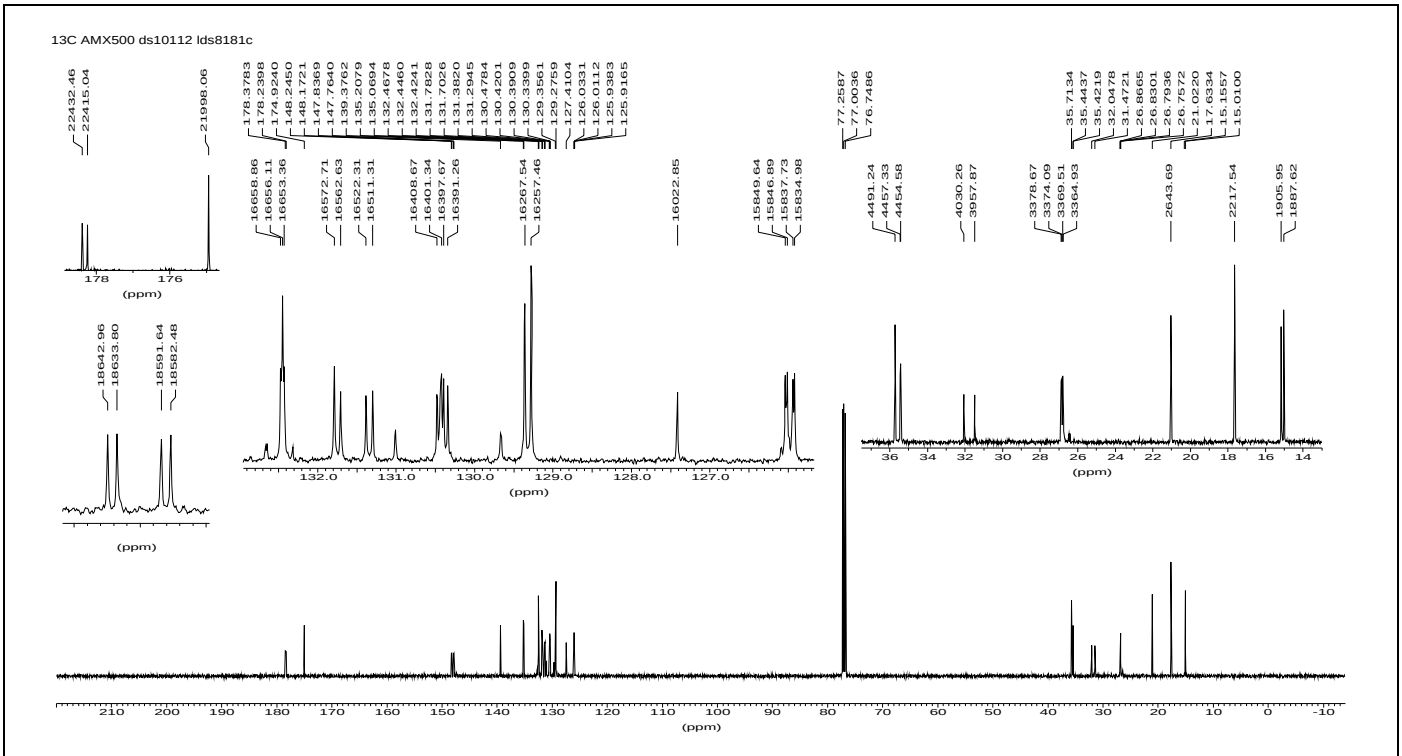

1H AMX500 ds10261 csk1065
8.81 8.80 7.92 7.90 7.89 7.88 7.88 7.85 7.84 7.83 7.83 7.81 7.48 7.47 7.46 7.45 7.43 7.41 7.40 7.32 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.24 7.23 7.22 7.21 6.93
3.74 3.37
2.87 2.85 2.84 2.81 2.79 2.75 2.66 2.42 2.27 1.98
4407.44 4403.66 4397.36 3952.83 3948.42 3944.64 3940.22 3925.09 3920.68 3915.63 3907.44 3738.45 3734.67 3731.52 3728.37 3725.21 3715.12 3707.56 3699.99 3659.64 3652.07 3650.18 3645.77 3641.35 3637.57 3631.26 3619.91 3616.13 3611.72 3607.93 1867.68 1435.13 1426.31 1416.85 1407.39 1389.74 1377.12
8.80 (ppm)
7.90 (ppm)
7.48 7.44 7.40 7.36 7.32 7.28 7.24 (ppm)
3.75 (ppm)
2.8 (ppm)
Integral
0.97 0.82 1.96 2.01 2.00 1.02 2.01 0.99 2.00 0.93 0.87 2.23 3.30 2.93 3.08 6.01
(ppm)

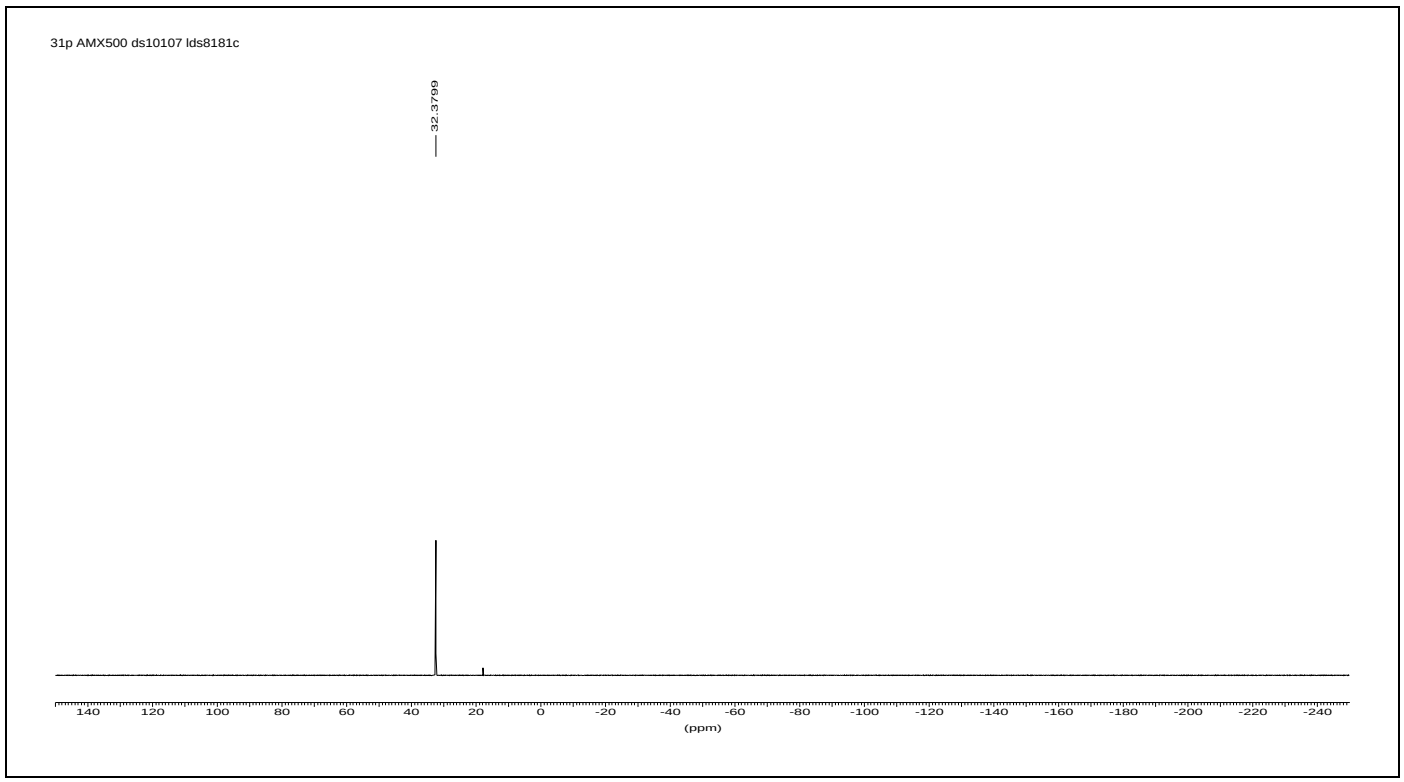

13C AMX500 ds10262 csk1065
178.28 178.14 175.04 141.71 141.63 139.31 135.16 135.07 134.01 133.93 133.26 133.18 132.68 132.39 132.35 132.32 132.28 130.68 130.56 130.41 130.31 130.04 129.30 129.22 128.99 128.92 128.54 127.79 127.35 127.29 126.95 125.69 125.58 125.50 125.37
77.25 77.00 76.74
38.01 37.46 36.52 35.48
23.47 23.30 23.25 21.00 17.66 17.63
16986.94 16853.14 16843.06 16759.66 16749.58 16686.35 16649.69 16645.11 16640.53 16635.94 16434.33 16419.66 16400.42 16388.50 16353.68 16261.12 16251.04 16222.63 16213.46 16165.81 16071.41 16015.51 16008.18 15966.02 15807.48 15792.82 15783.65 15767.15 17821.82 17811.74 2951.60 2930.53 2925.03 22420.54 22403.12
134.0 133.0 132.0 131.0 130.0 129.0 128.0 127.0 126.0 (ppm)
141.6 (ppm)
(ppm)
(ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 (ppm)

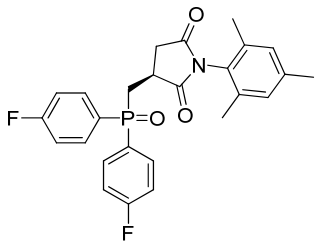

31p AMX500 ds11091 csl1065
37.9681
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
(ppm)

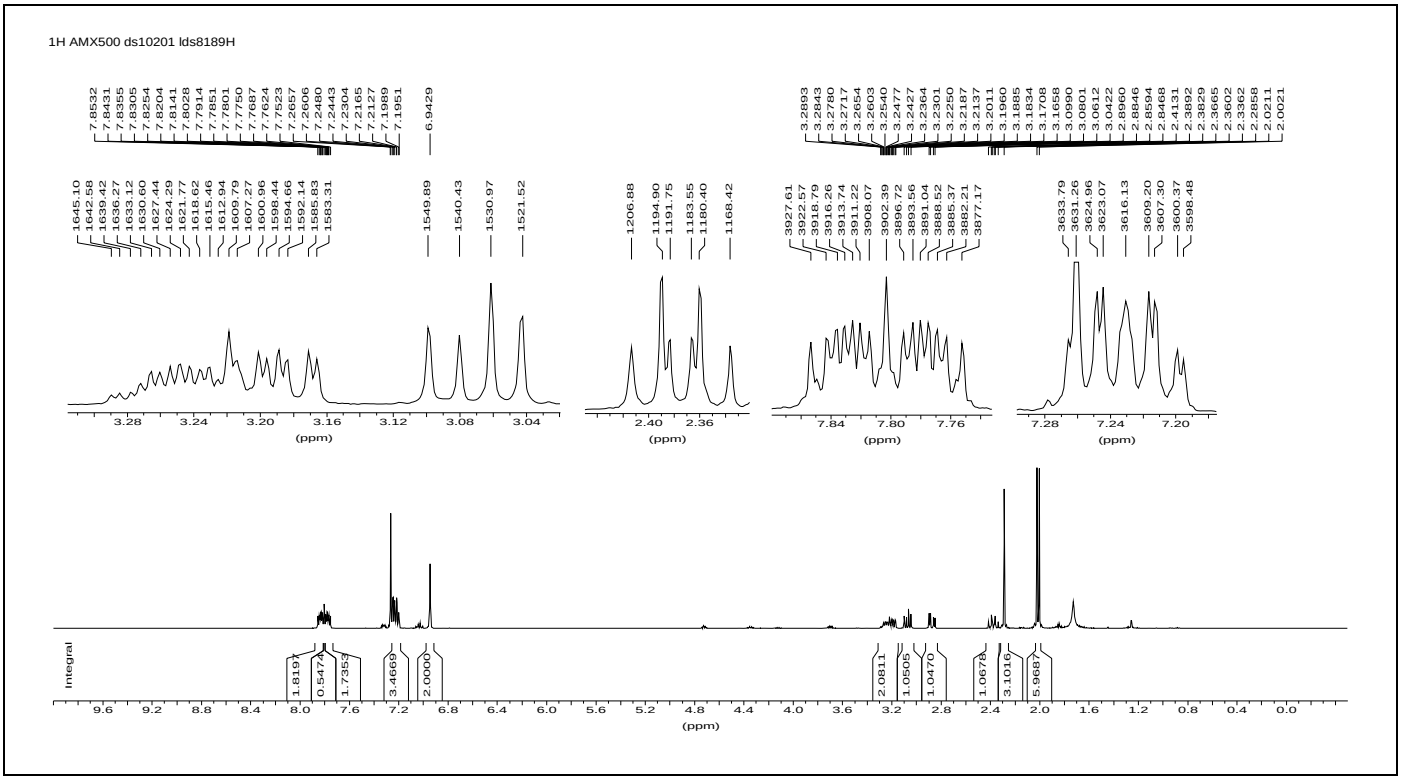

O
N
O
Et
P=O
Et

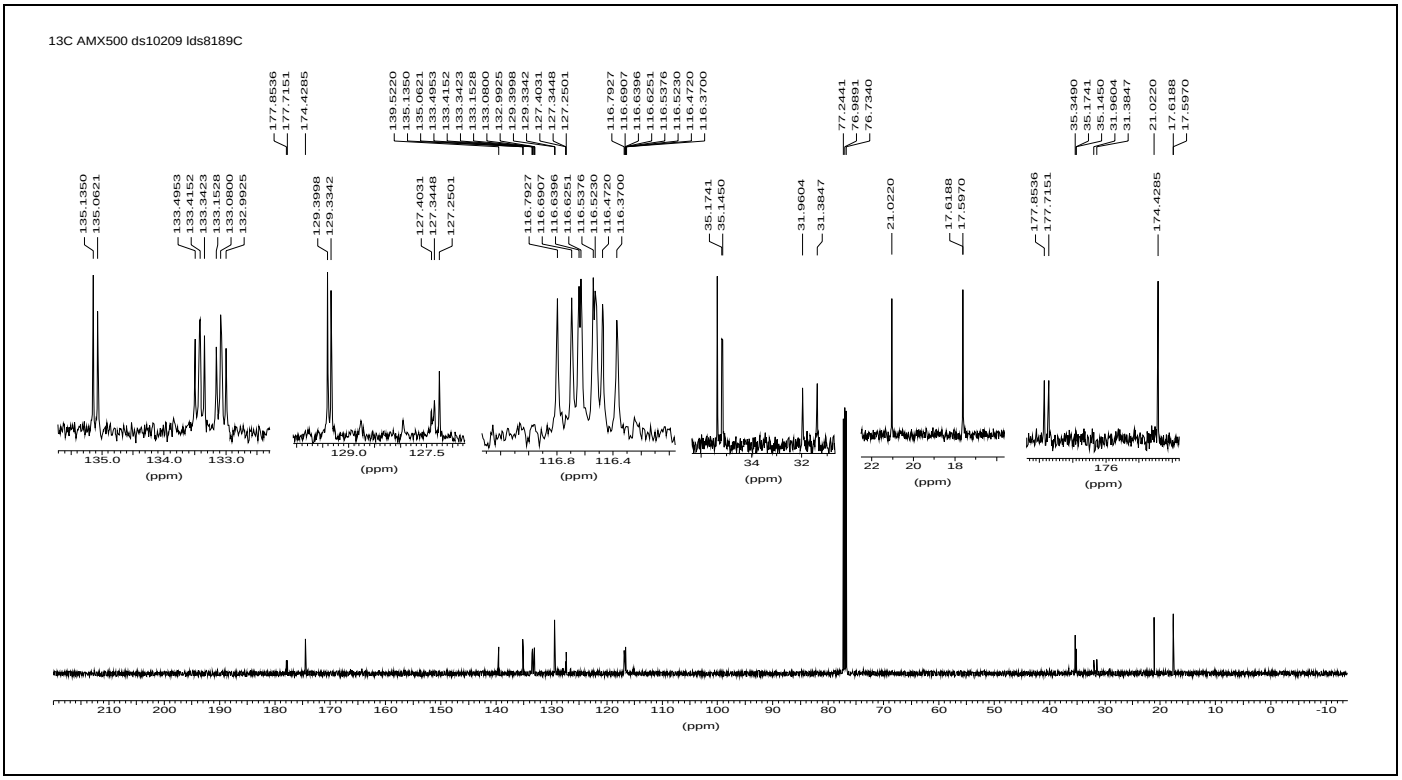

1H AMX500 ds10111 lds8181c
(ppm)
Integral

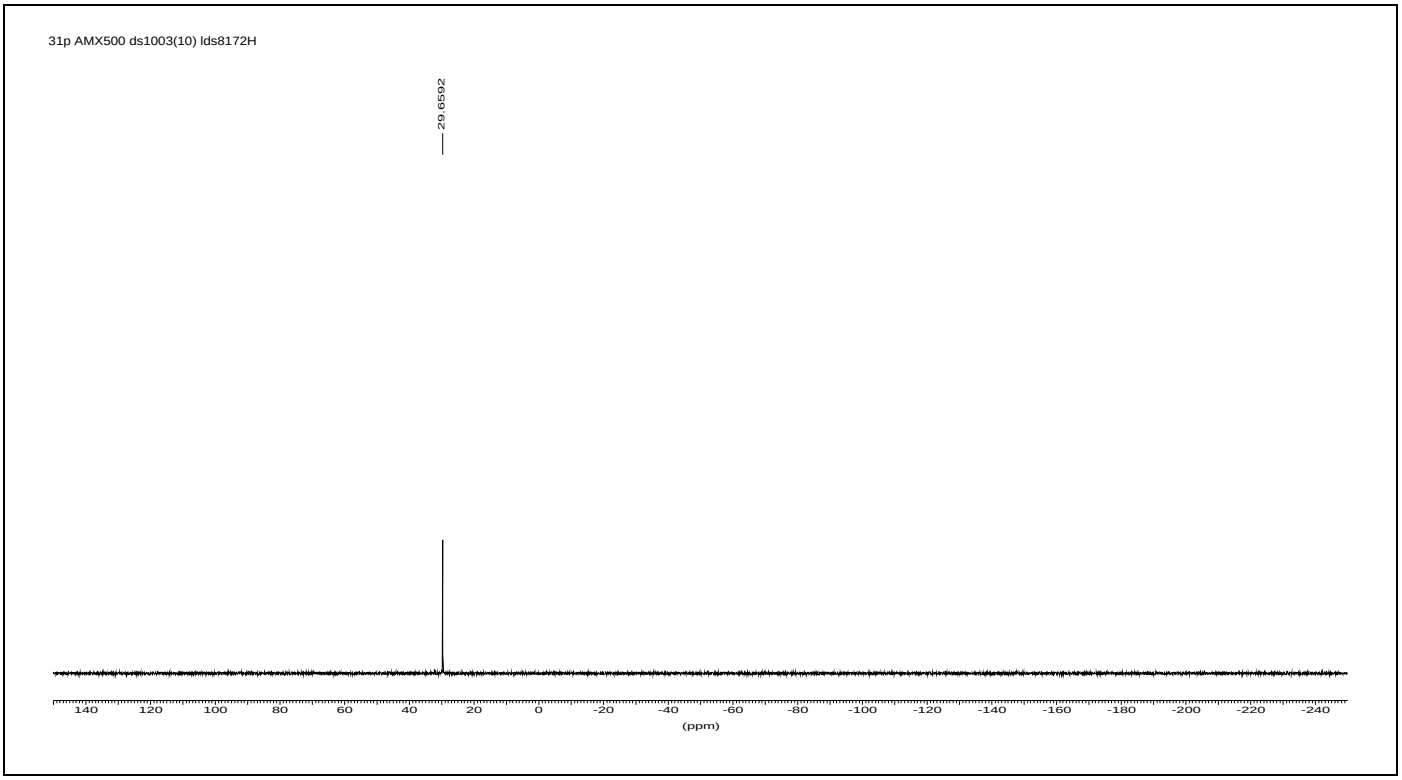

13C AMX500 ds10112 lds8181c
(ppm)

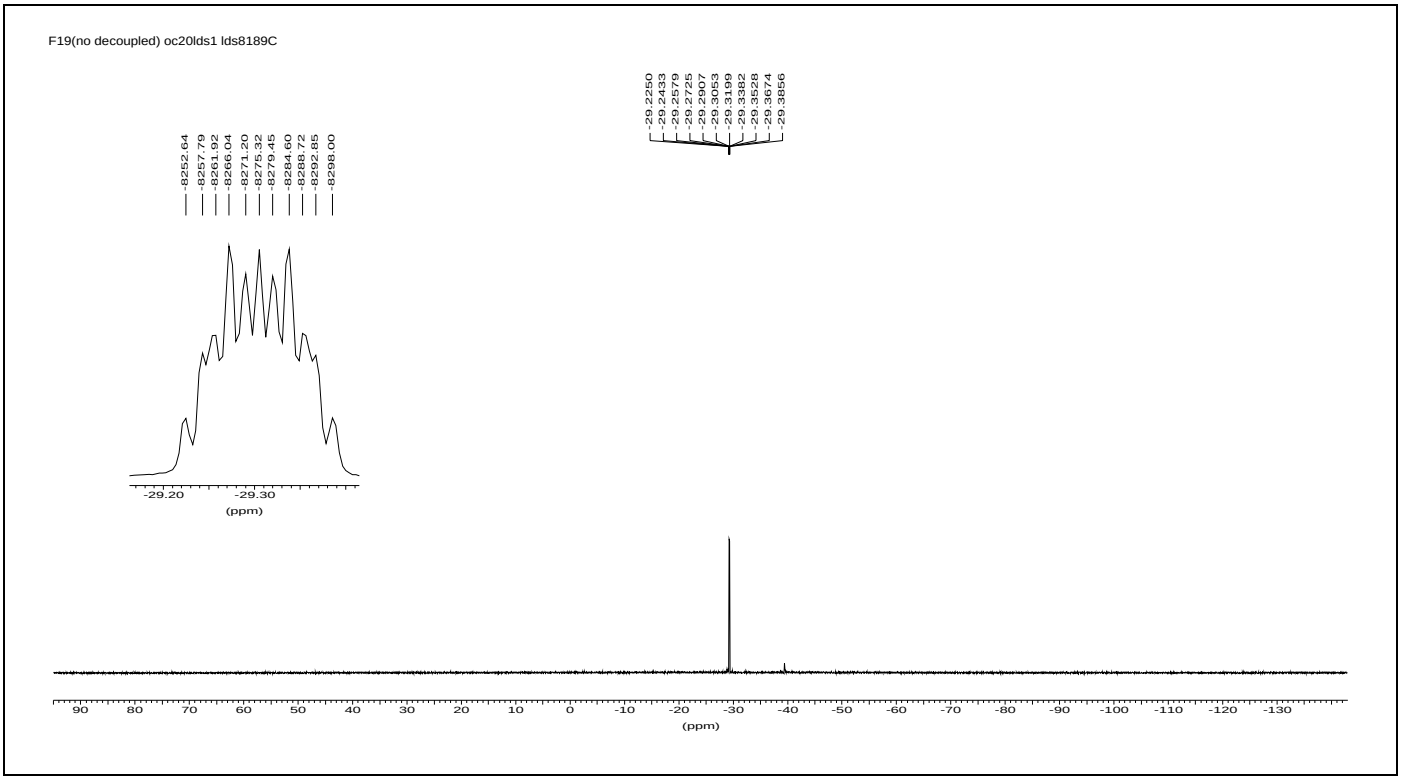

31p AMX500 ds10107 lds8181c
32.3799
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
(ppm)

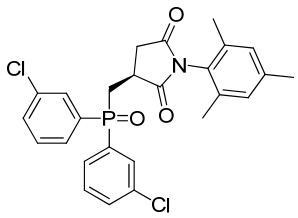

O
N
O
O
F
P=O
F

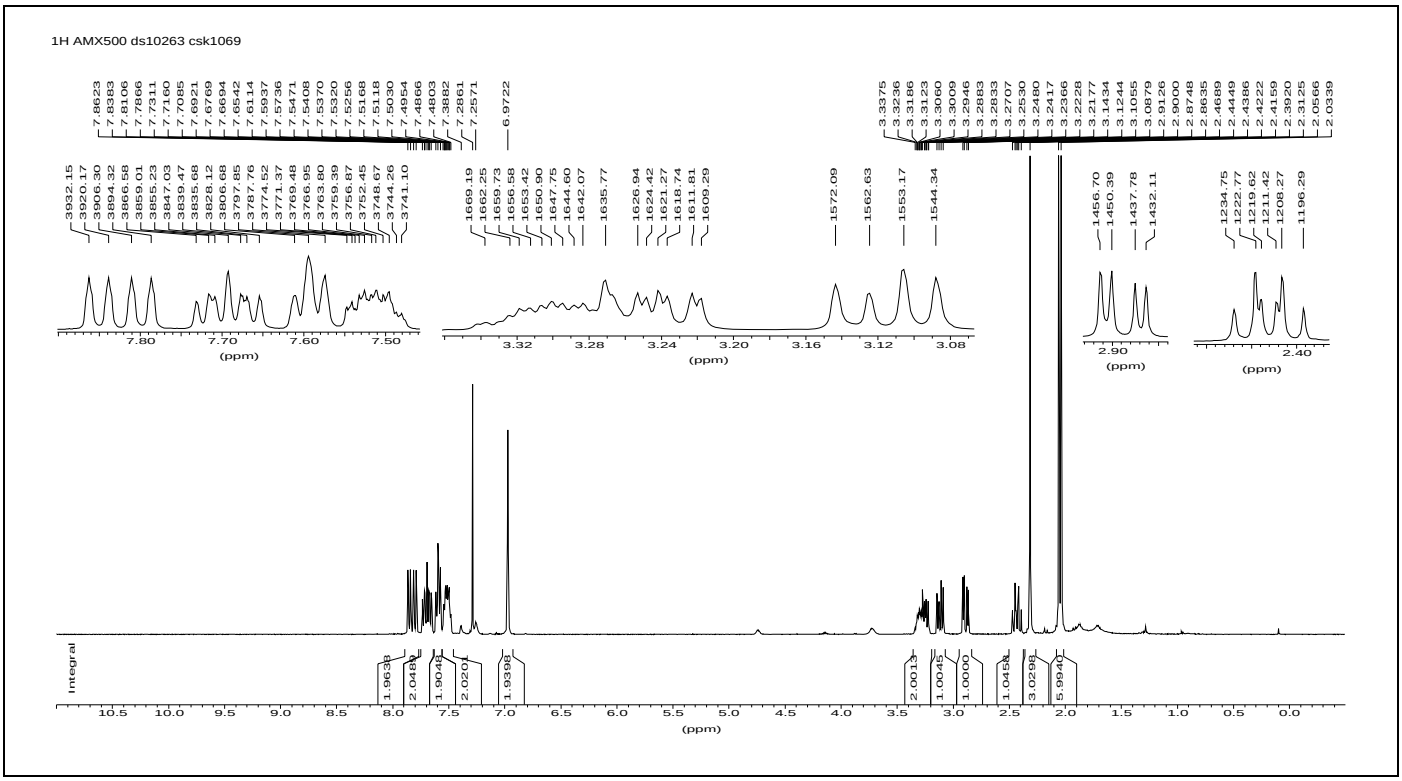

1H AMX500 ds10201 lds8189H
(ppm)
Integral

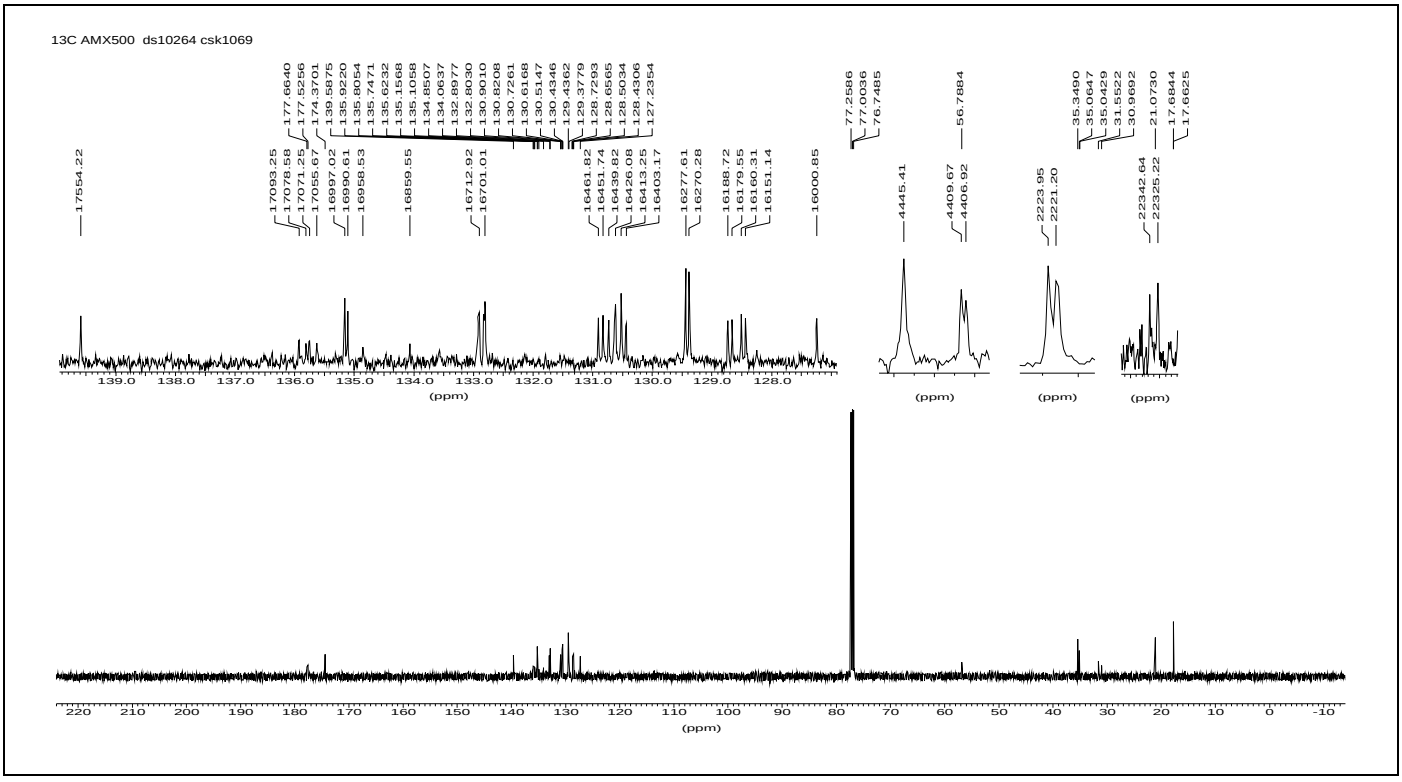

13C AMX500 ds10209 lds8189C
(ppm)

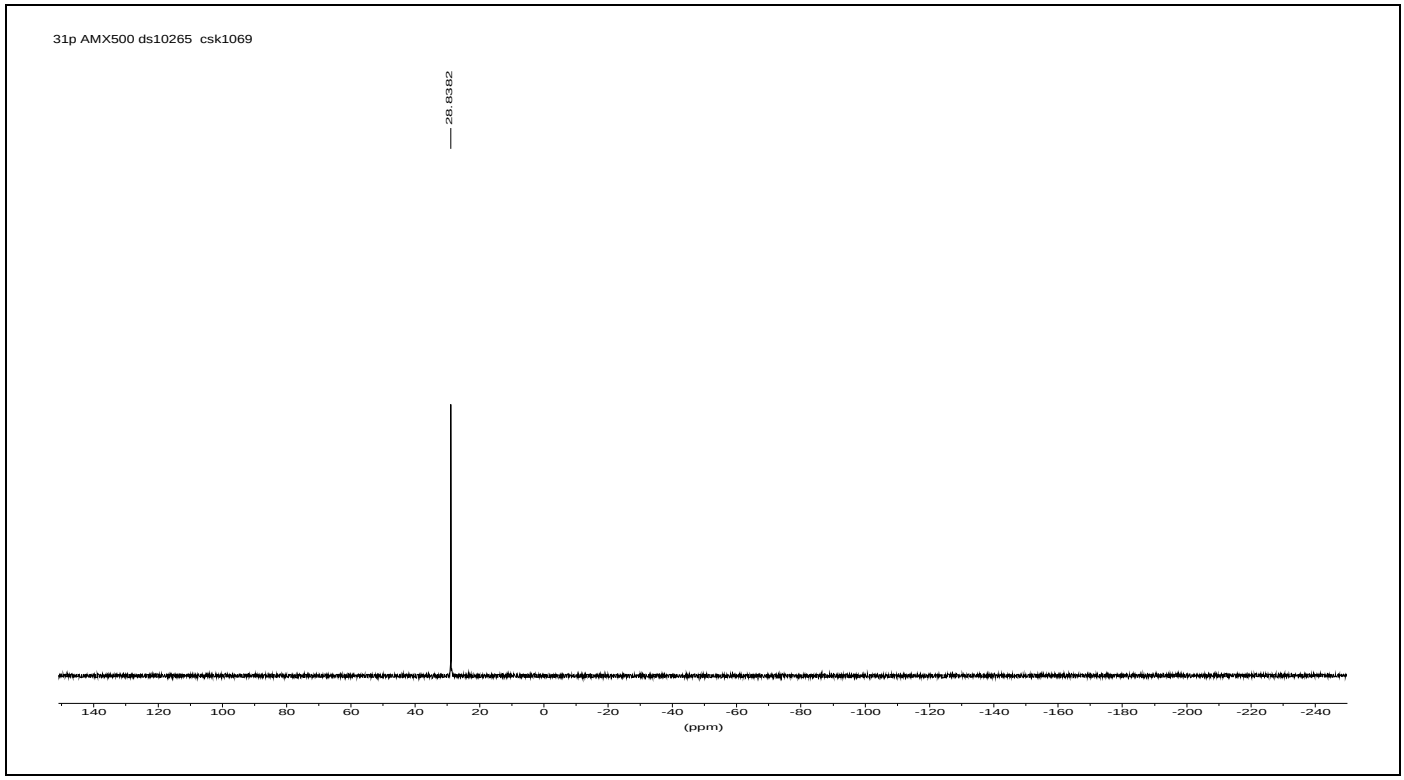

31p AMX500 ds1003(10) lds8172H
29.6592
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
(ppm)

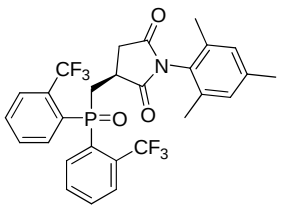

F19(no decoupled) oc20lds1 lds8189C
-252.64
-257.79
-261.92
-266.04
-271.20
-275.32
-279.45
-284.60
-288.72
-292.85
-298.00
-29.20
-29.30
(ppm)
-29.2250
-29.2433
-29.2579
-29.2725
-29.2907
-29.3053
-29.3199
-29.3382
-29.3528
-29.3674
-29.3856
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130
(ppm)


O
N
O
Cl
P=O
O
Cl

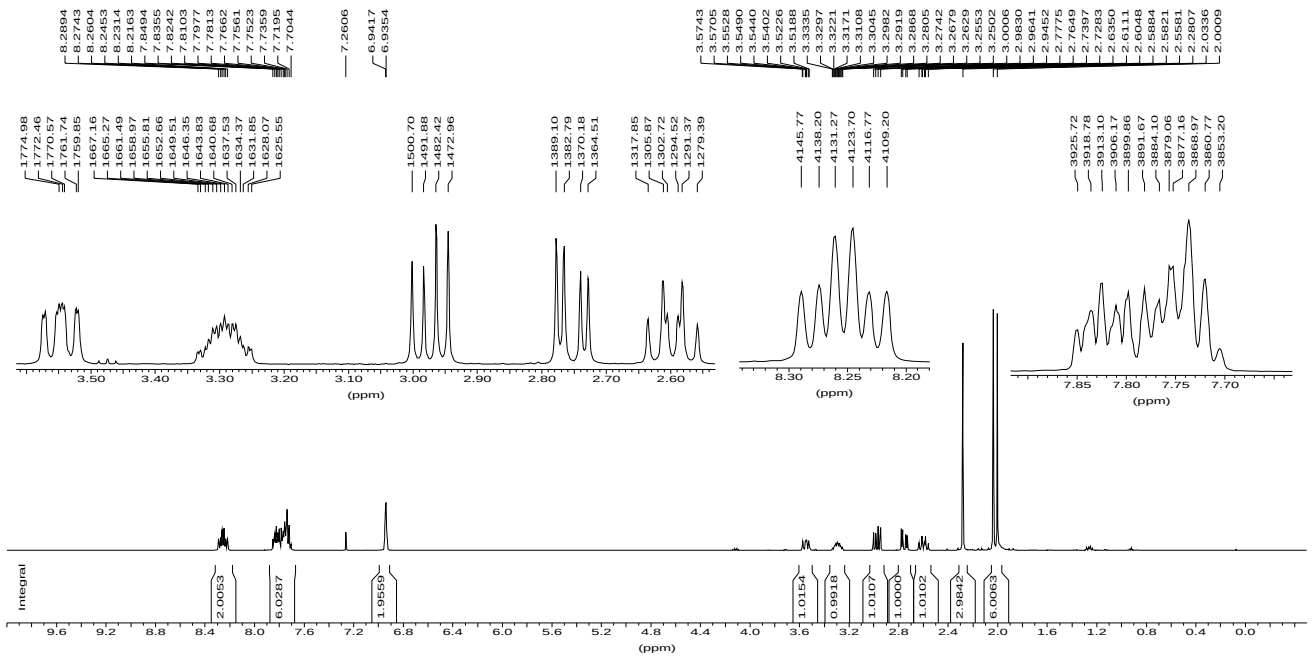

1H AMX500 ds10263 csk1069
(ppm)
Integral


13C AMX500 ds10264 csk1069
(ppm)

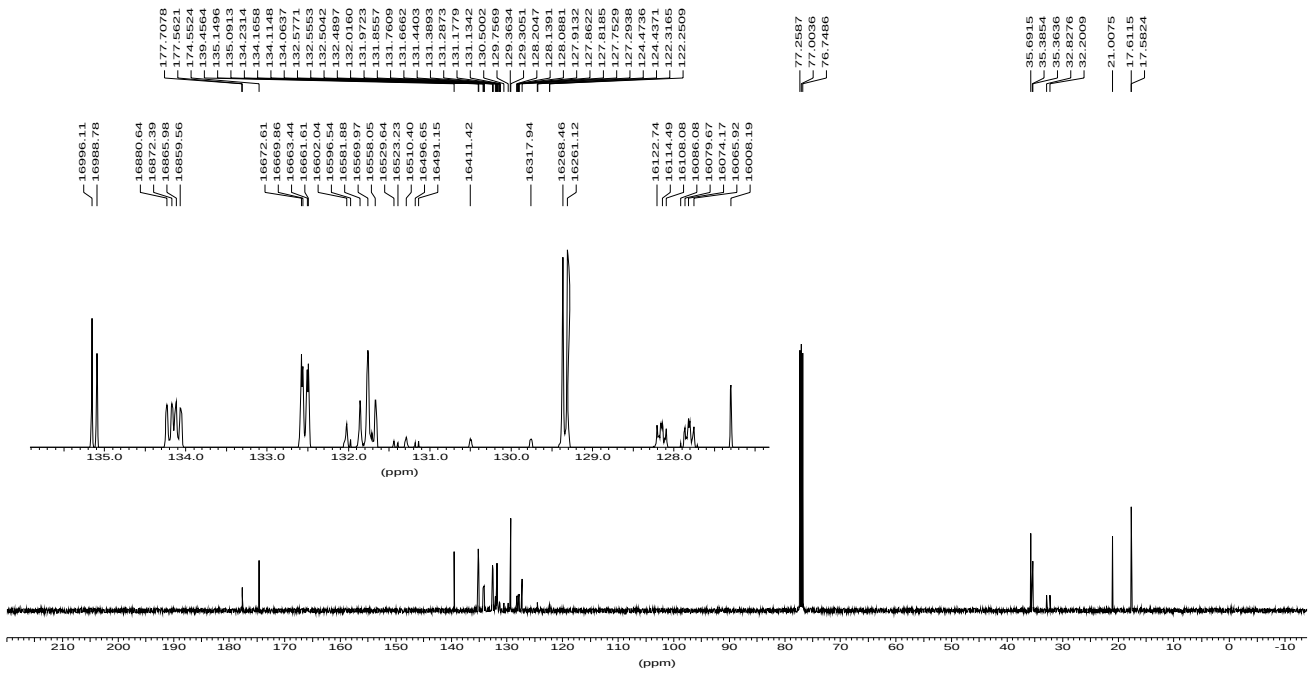

31p AMX500 ds10265 csk1069
28.8382
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
(ppm)



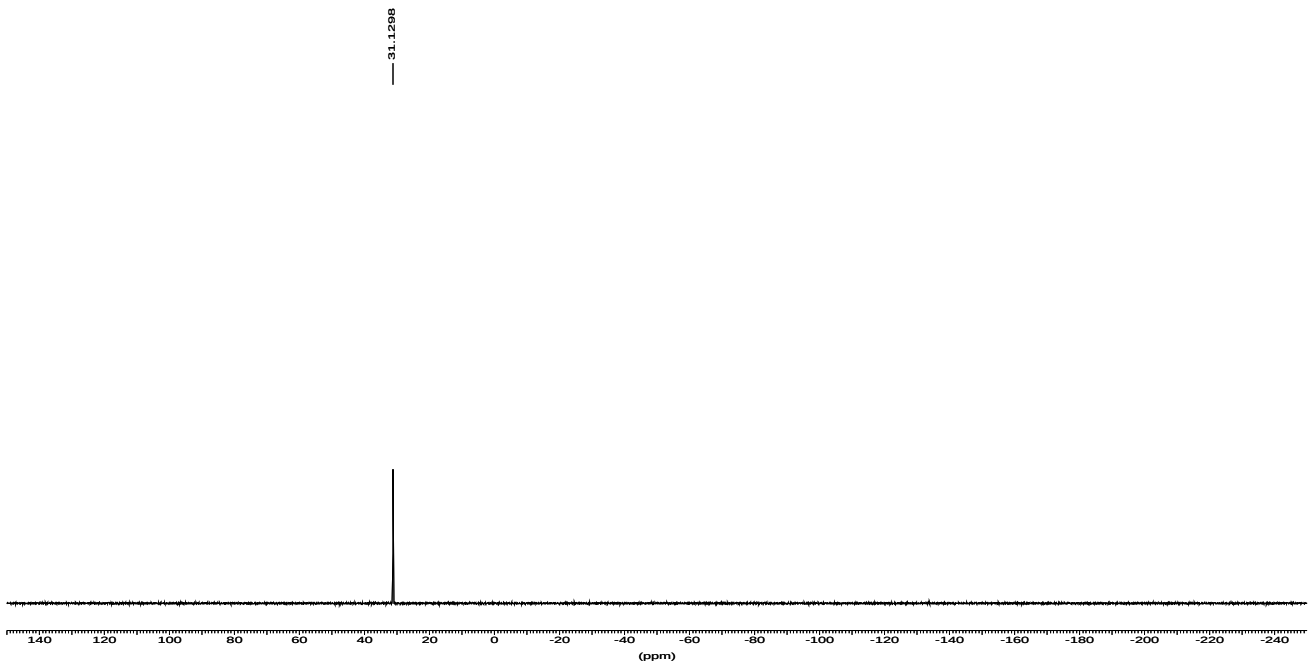
1H AMX500 ds10034 LDS8171C



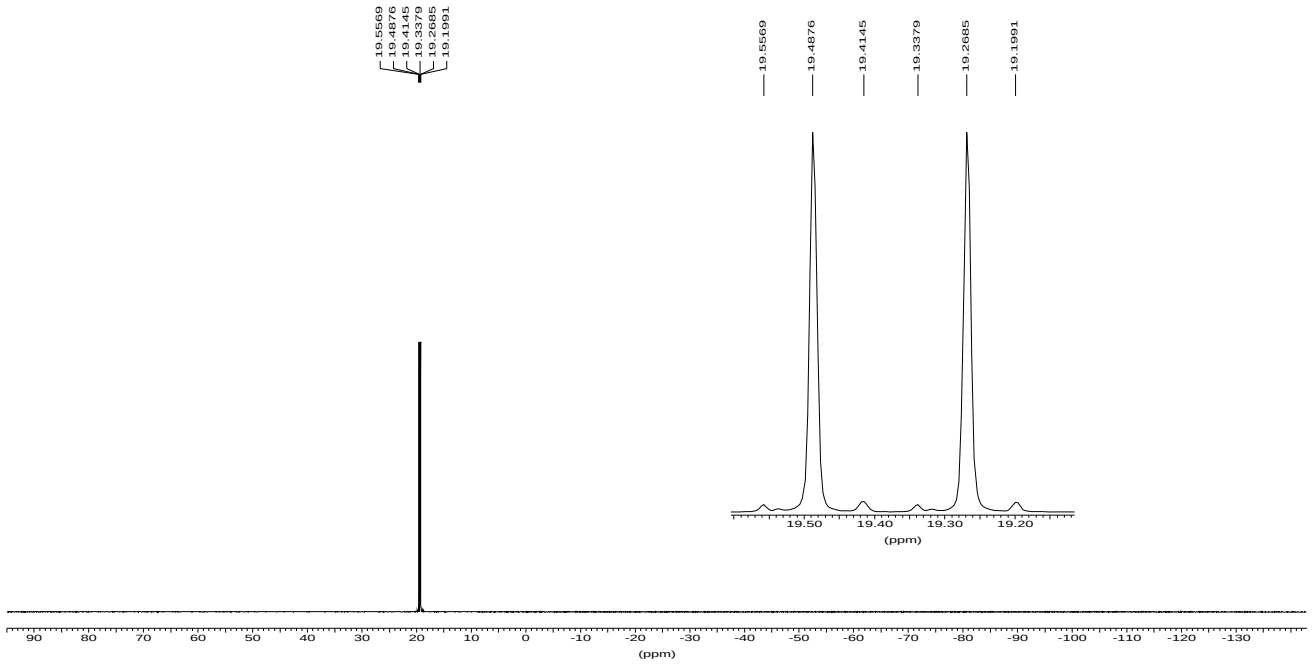
13C AMX500 ds10033 LDS8171C

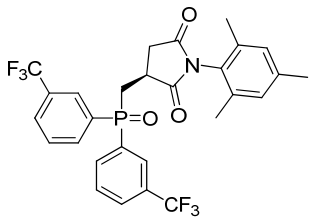


31p AMX500 ds10038 lds8171H

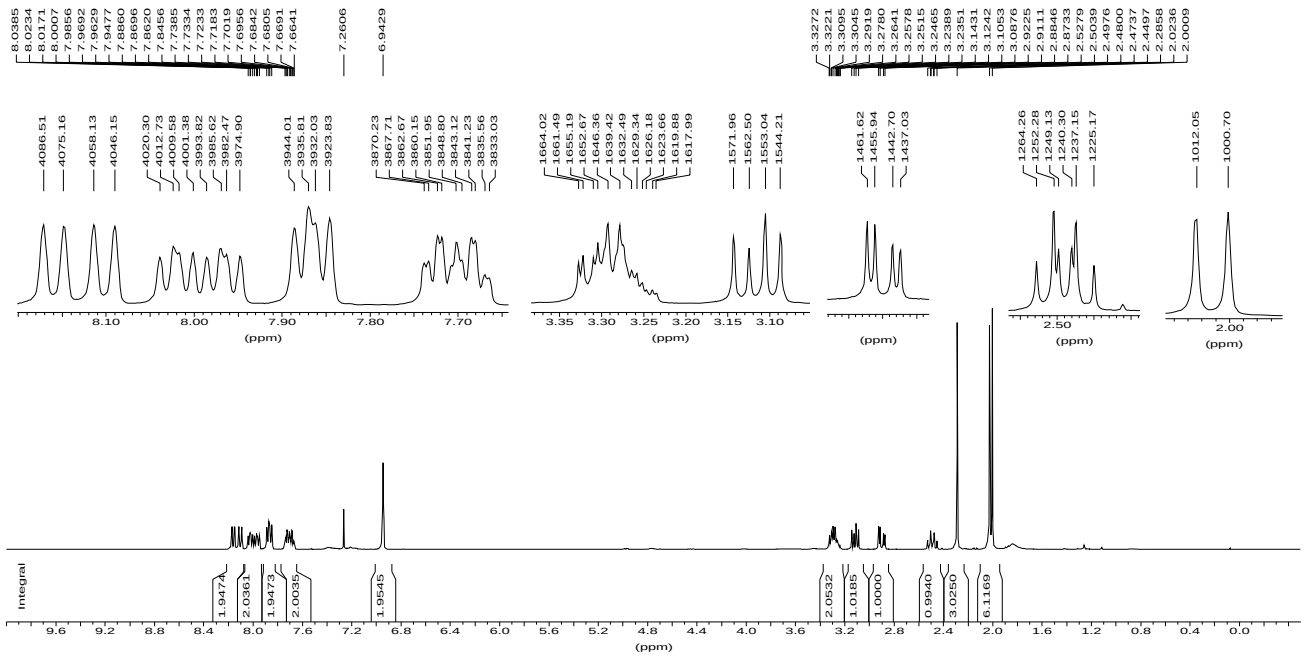


F19(no decoupled) oc03lds2 LDS8171C

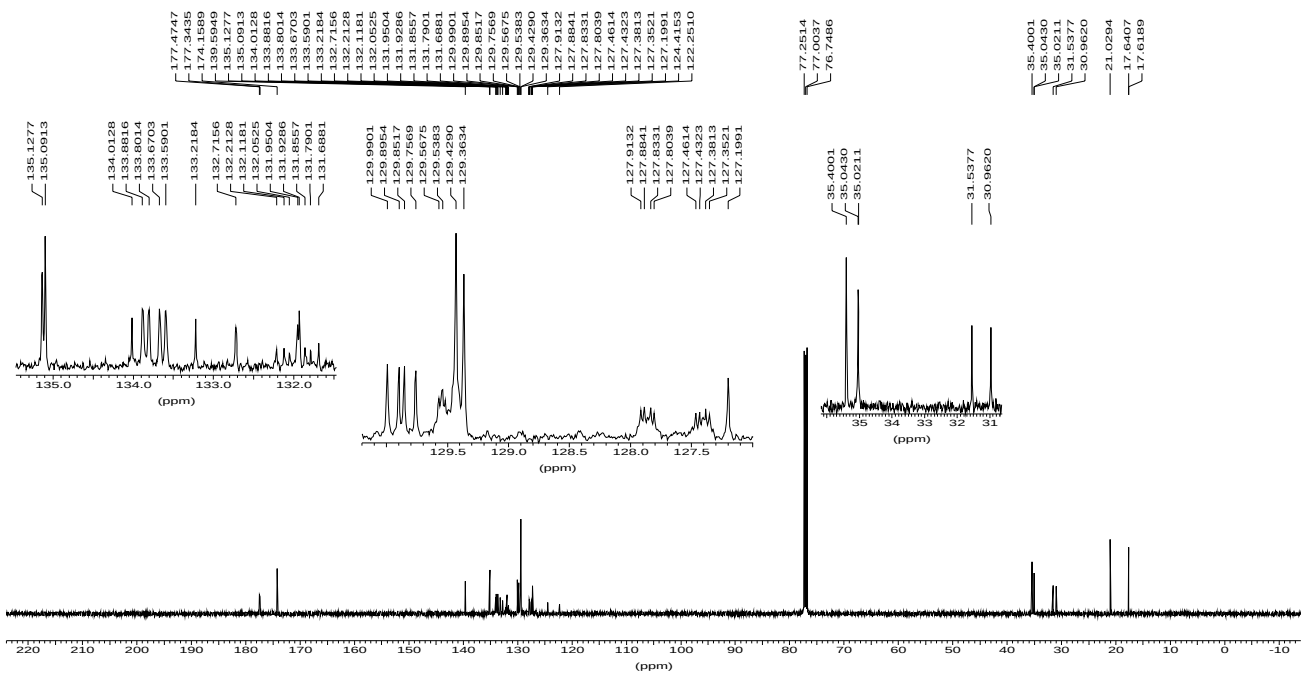




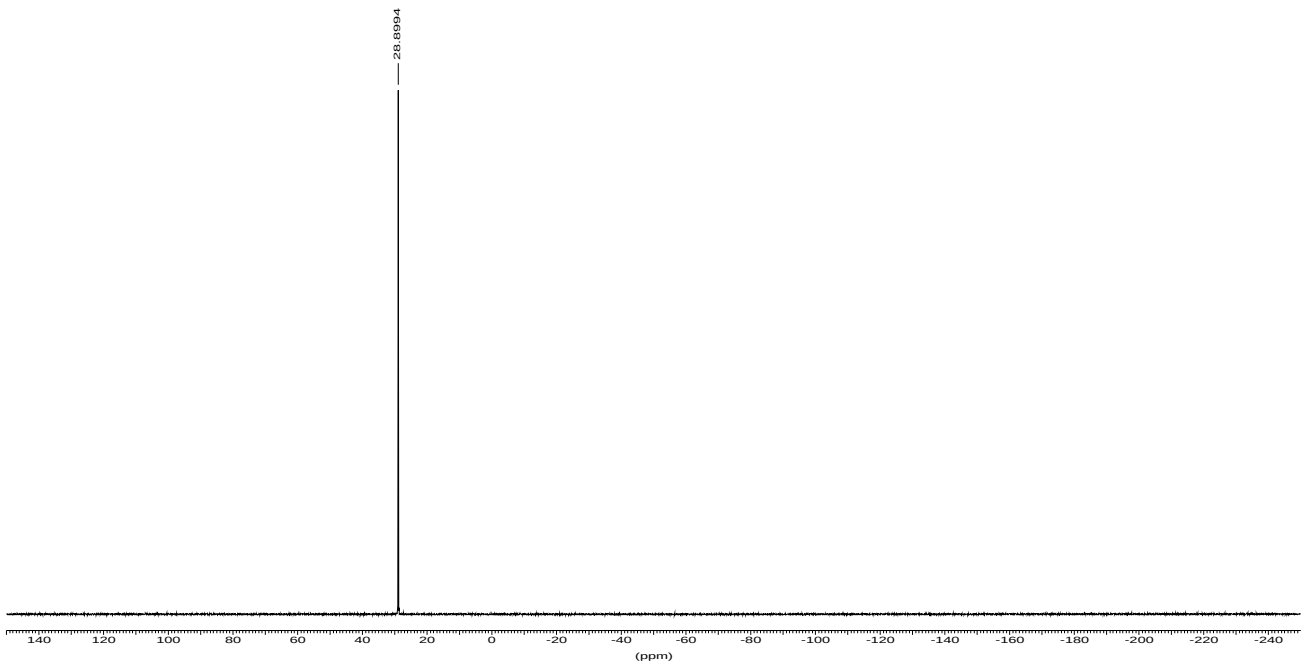
1H AMX500 ds11203 csk1091



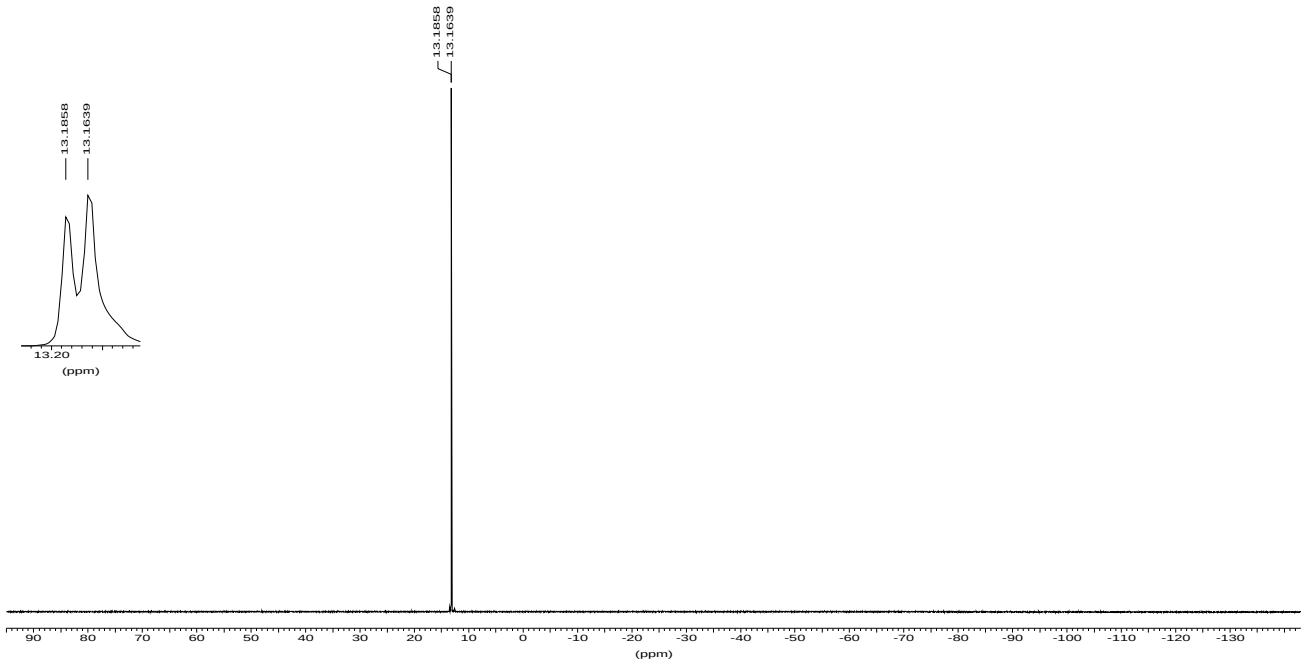
13C AMX500 ds11204 csk1091

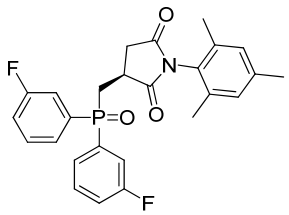


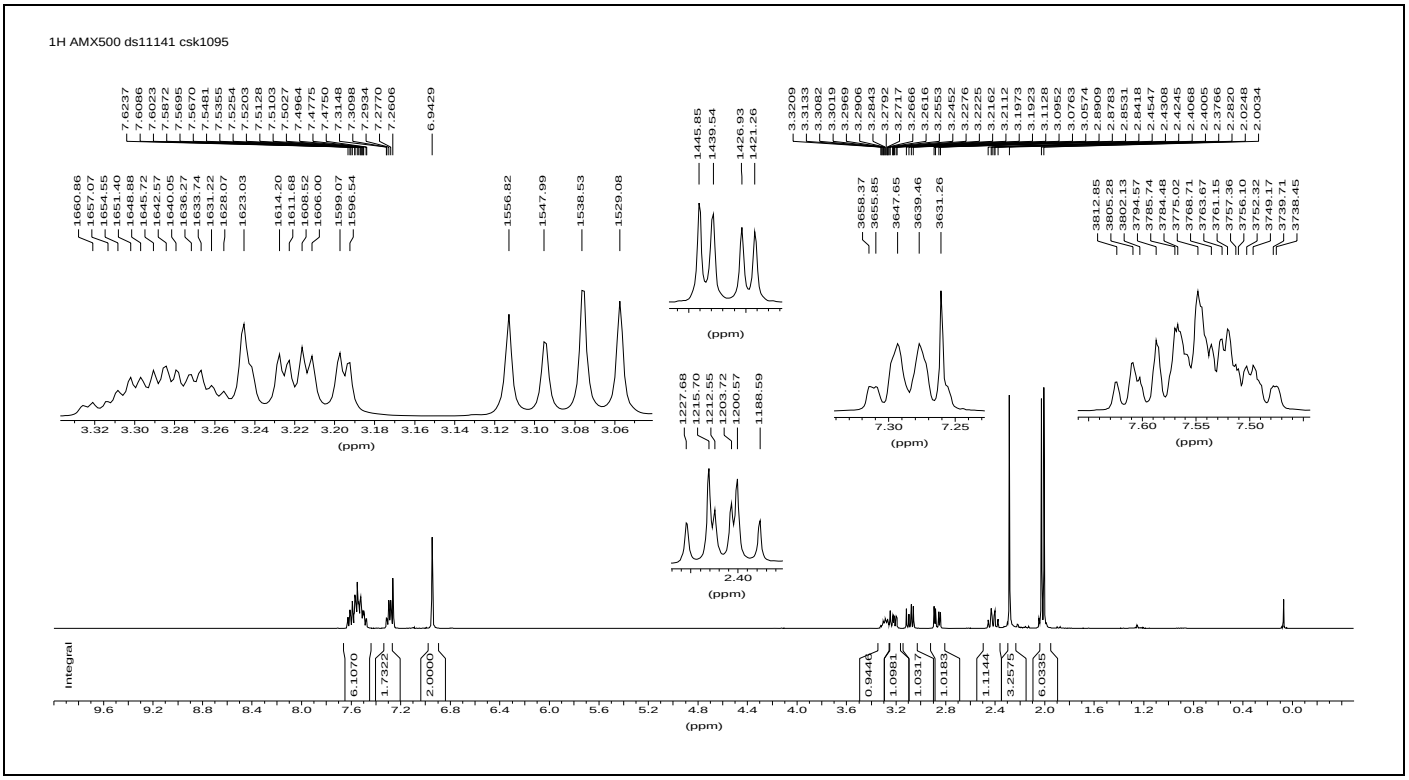
31p AMX500 ds11145 csk1091

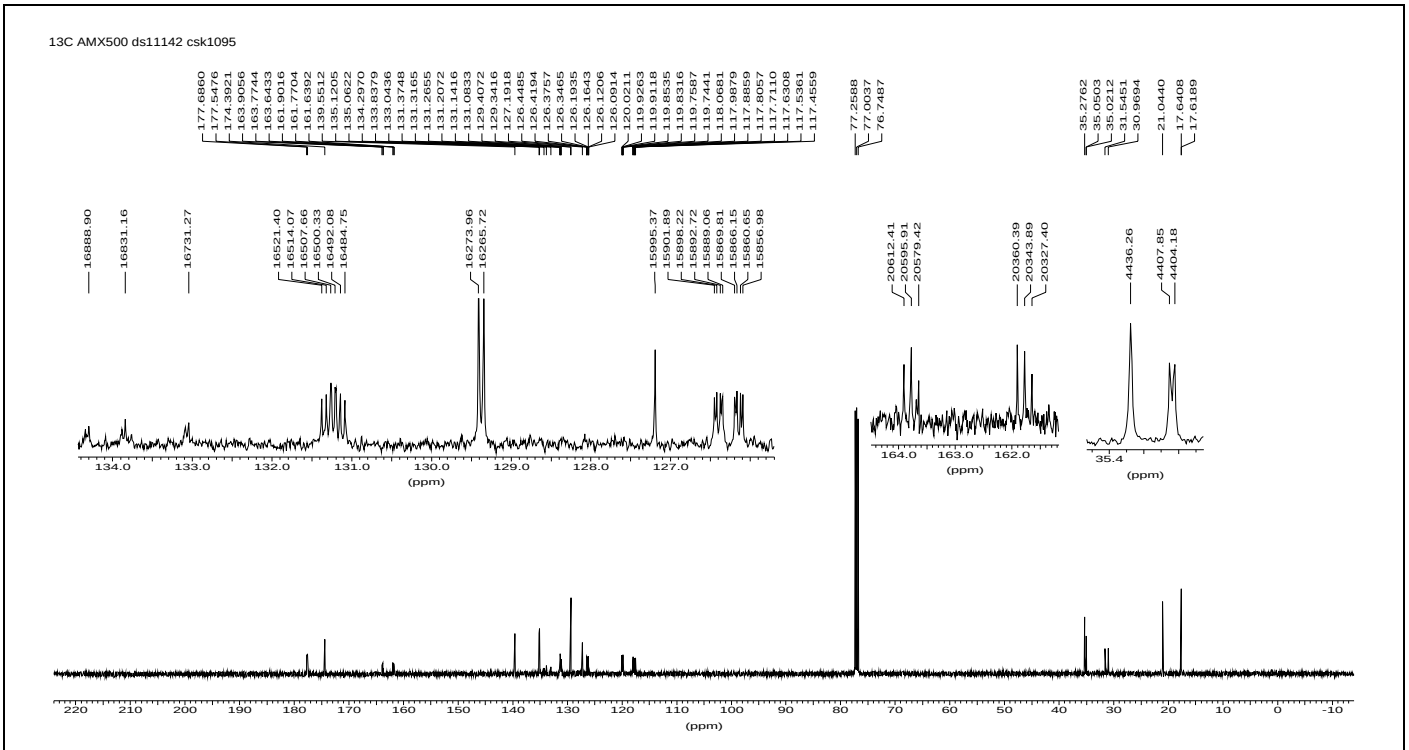


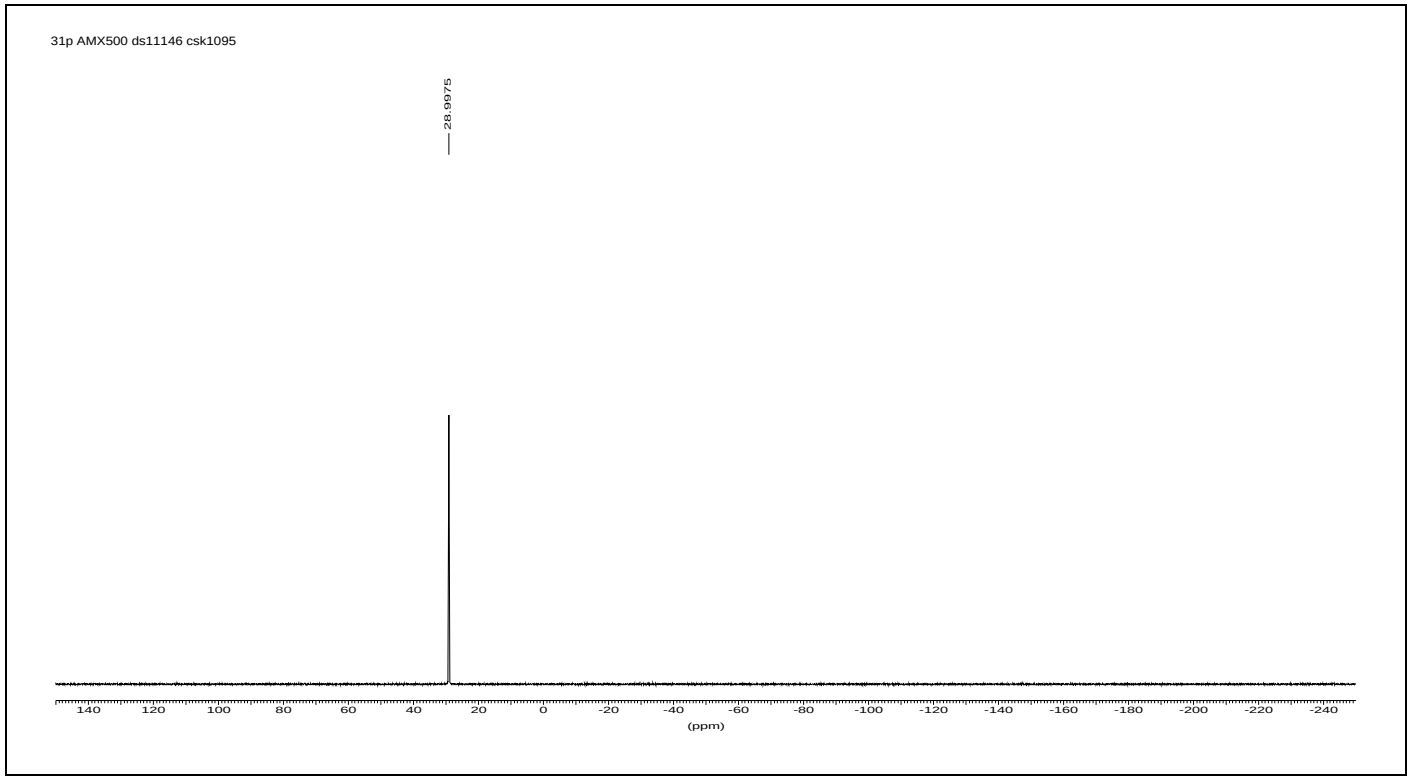
F19(no decoupled) nv14lds1 csk1091

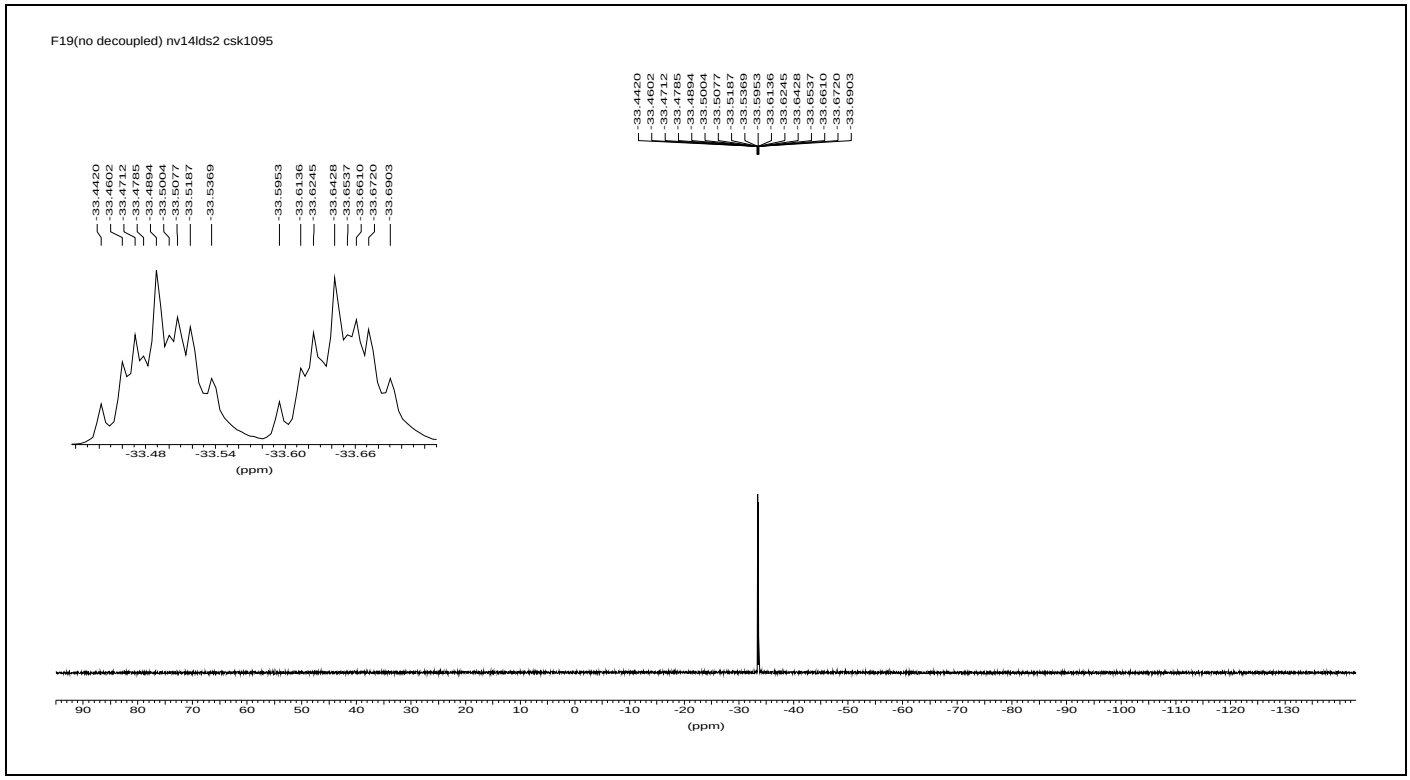


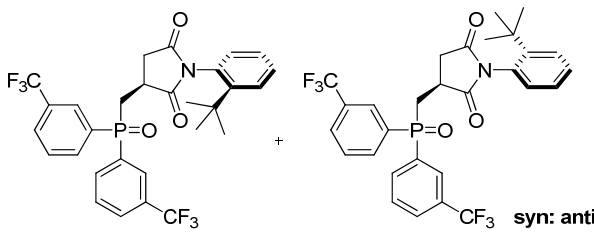

O
N
O
O
F
P=O
F


1H AMX500 ds11141 csk1095
(ppm)
Integral

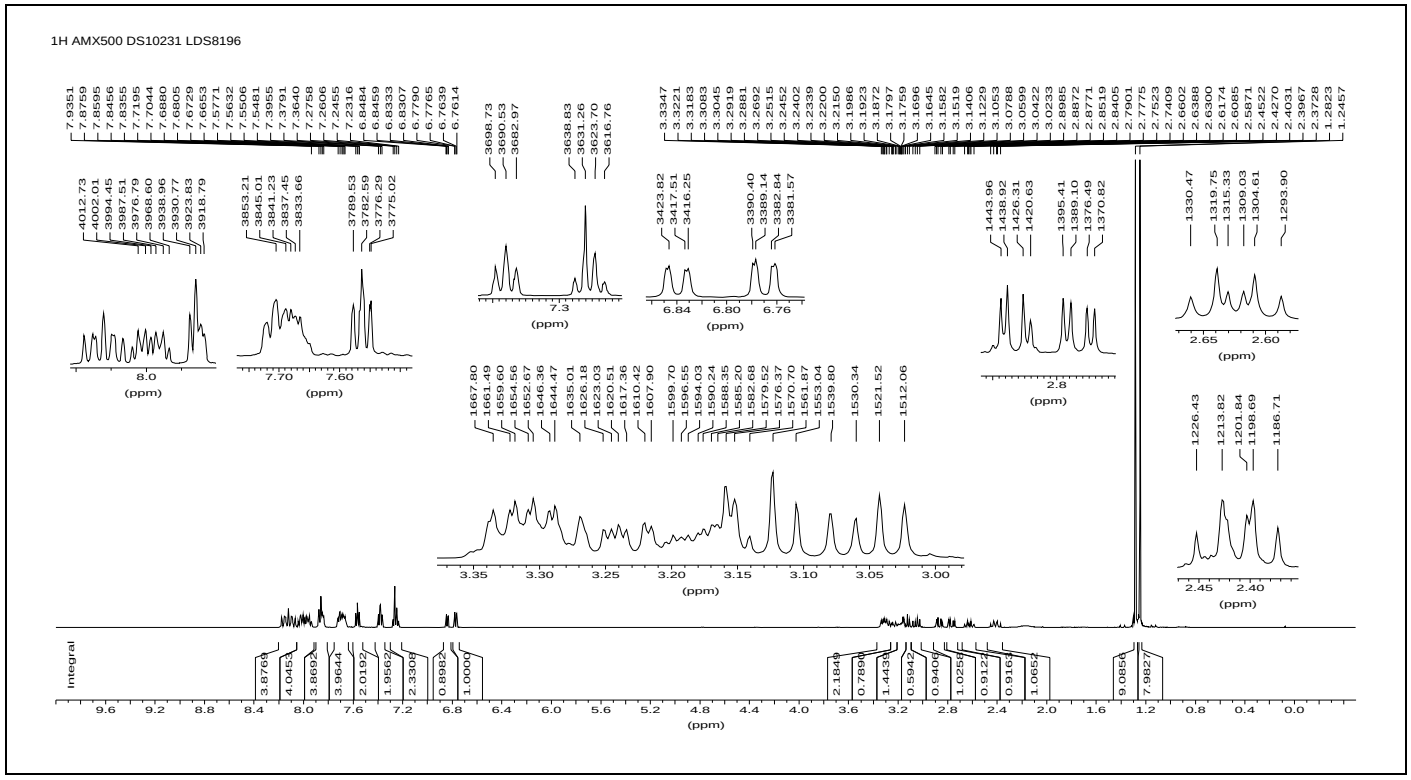

13C AMX500 ds11142 csk1095
(ppm)

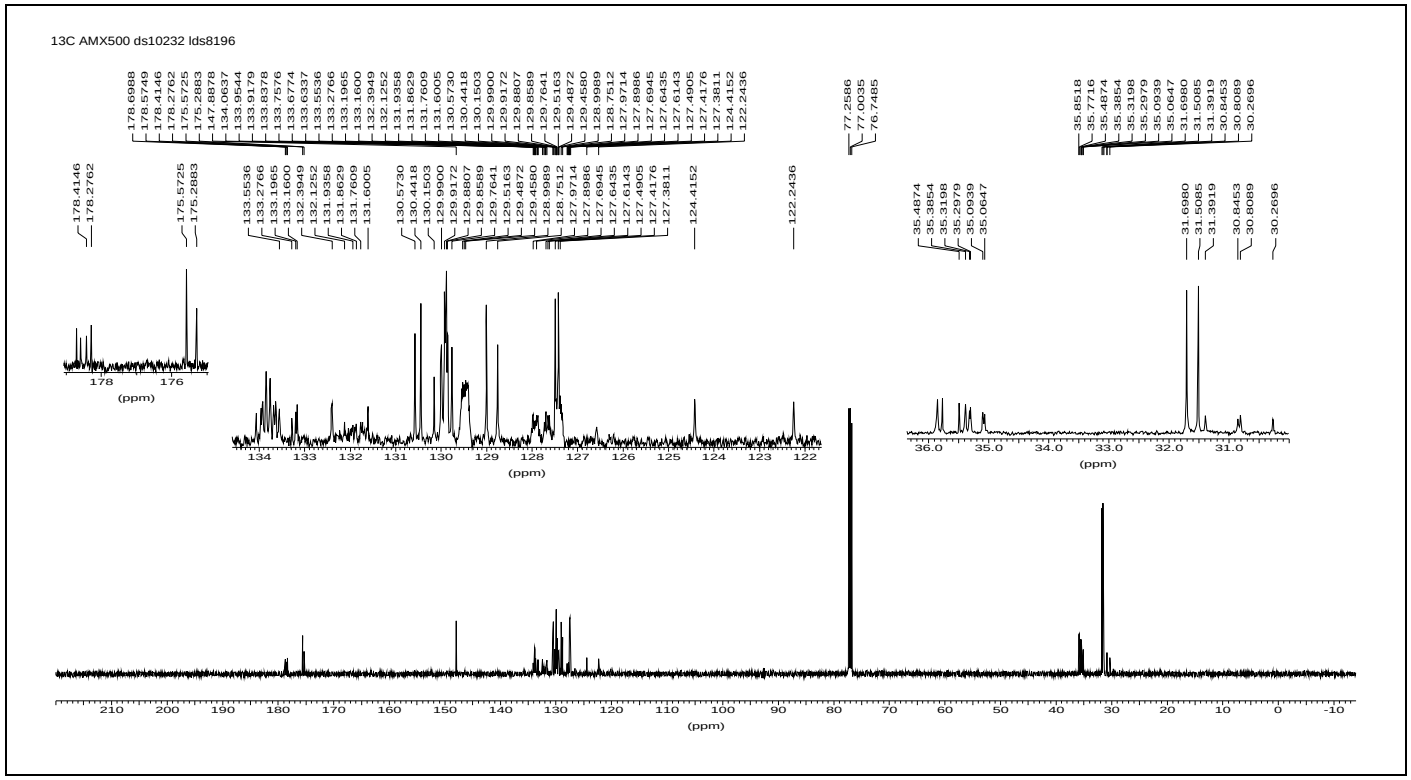

31p AMX500 ds11146 csk1095
28.9975
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
(ppm)

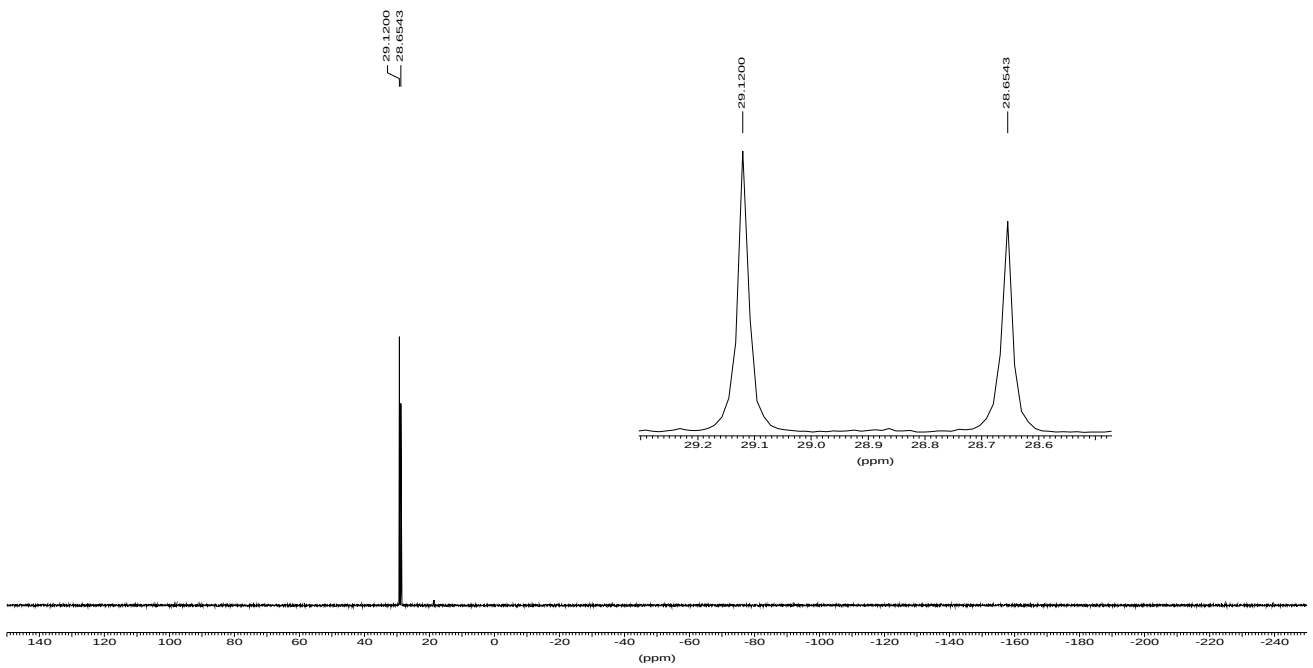

F19(no decoupled) nv14lds2 csk1095
-33.4420
-33.4602
-33.4712
-33.4785
-33.4894
-33.5004
-33.5077
-33.5187
-33.5369
-33.5953
-33.6136
-33.6245
-33.6428
-33.6537
-33.6610
-33.6720
-33.6903
-33.48 -33.54 -33.60 -33.66
(ppm)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130
(ppm)

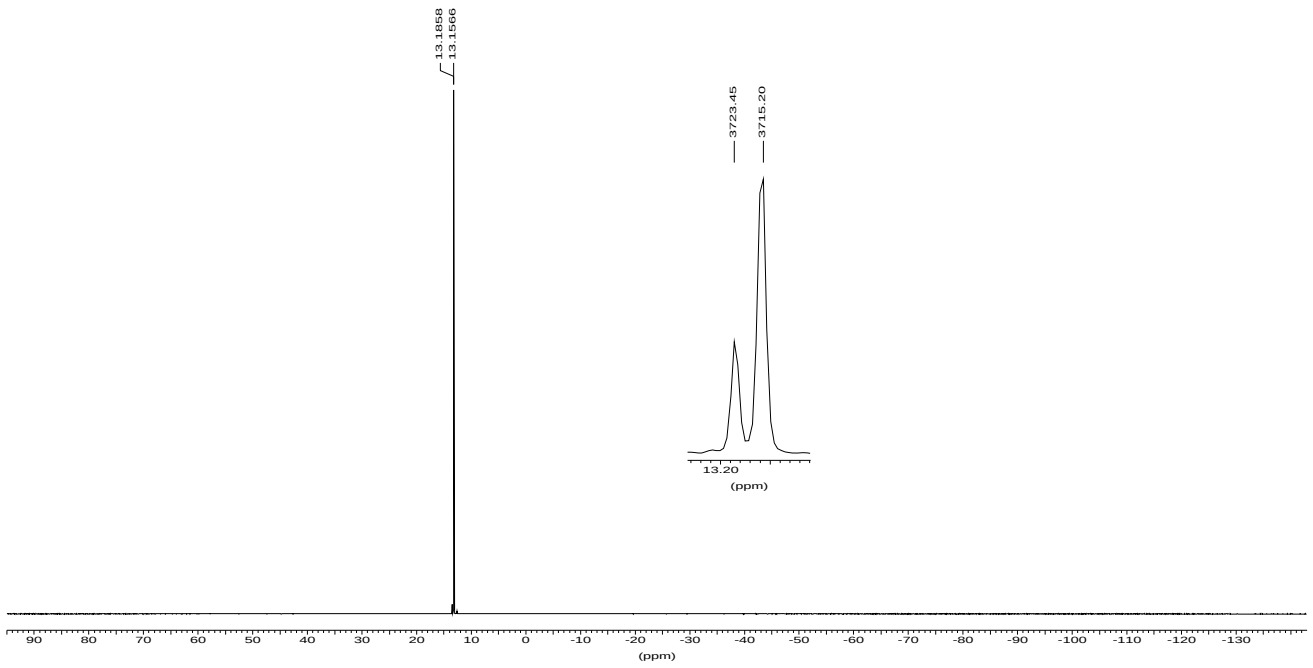


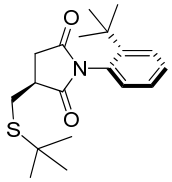
syn: anti = 1:2.4 (racemic), 1.1:1 (chiral)

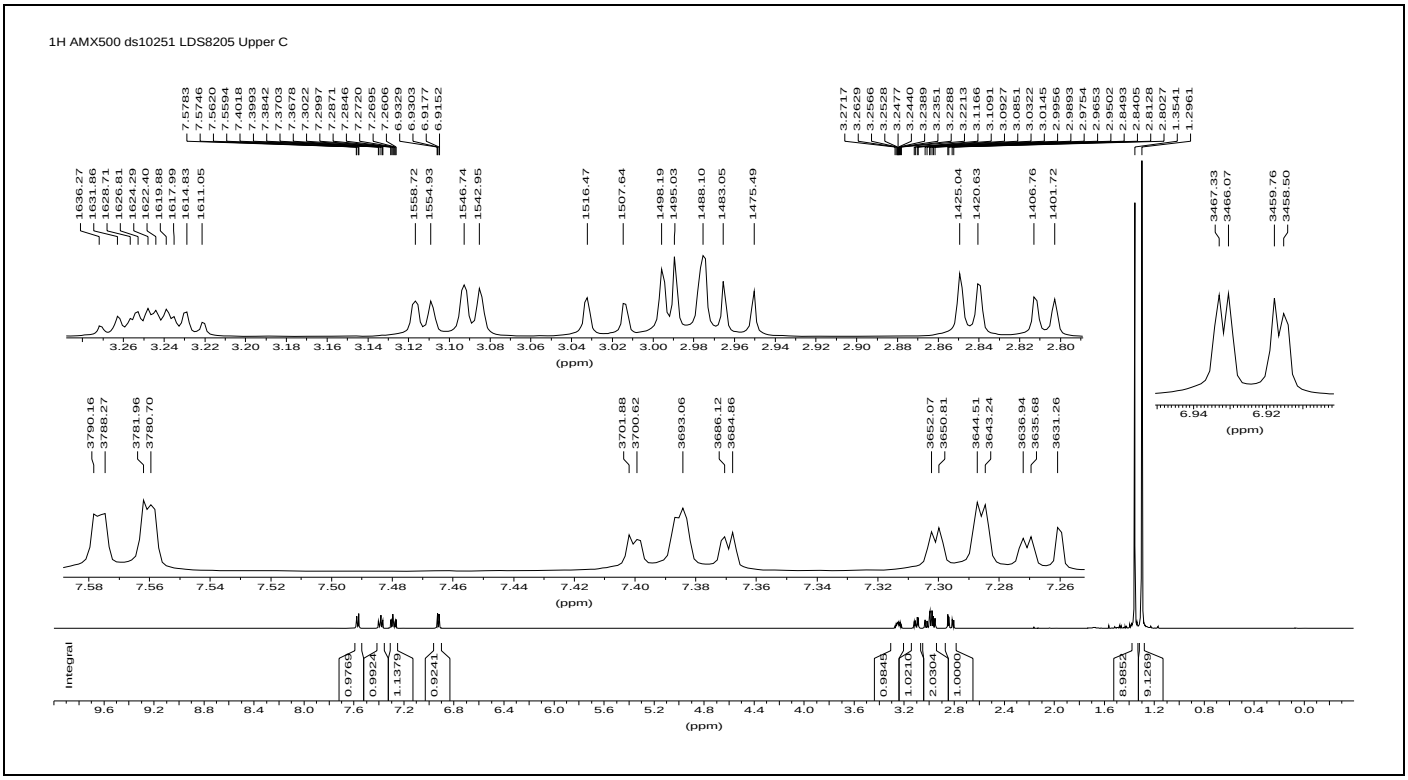


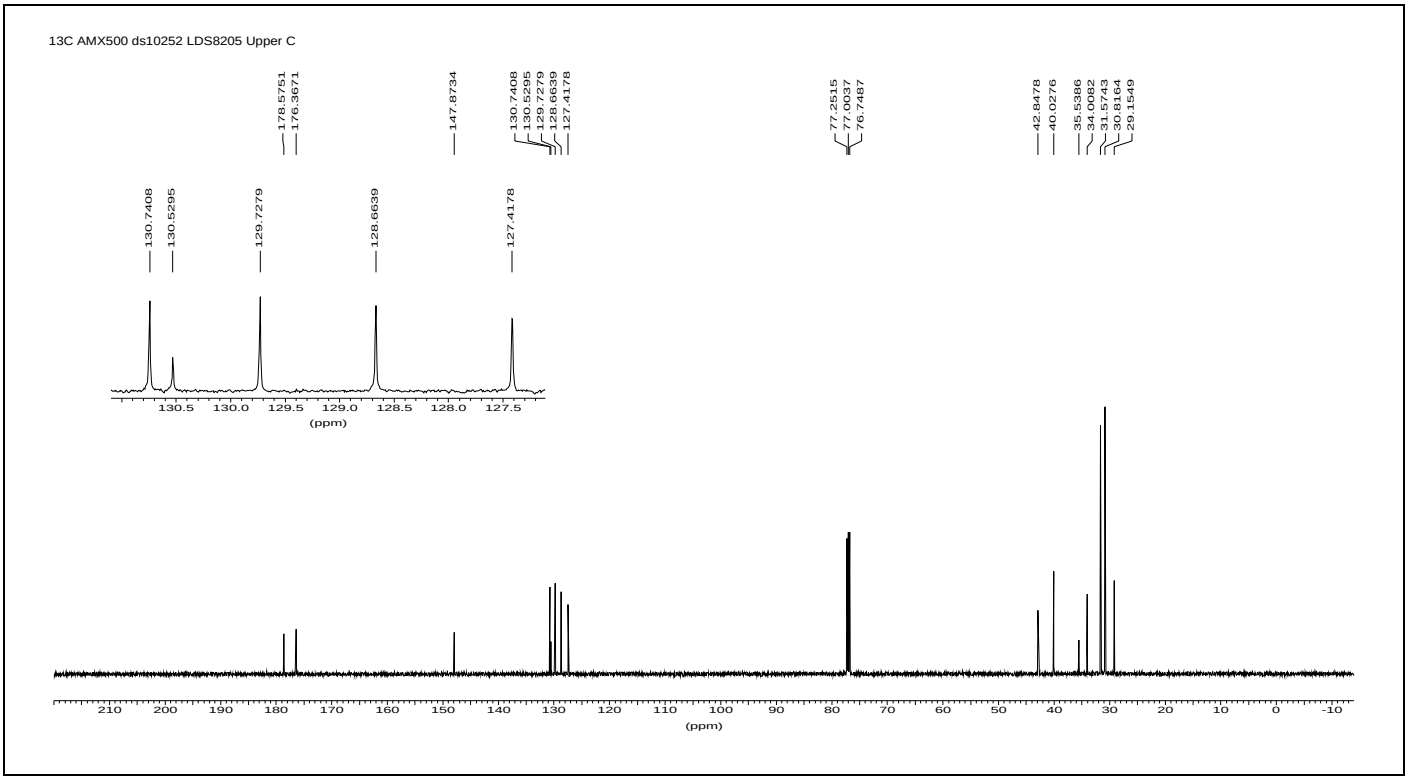


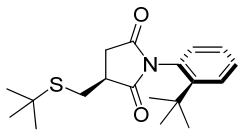

31p AMX500 ds09283 lss1257
29.1200
28.6543
29.1200
28.6543
29.2 29.1 29.0 28.9 28.8 28.7 28.6
(ppm)
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
(ppm)

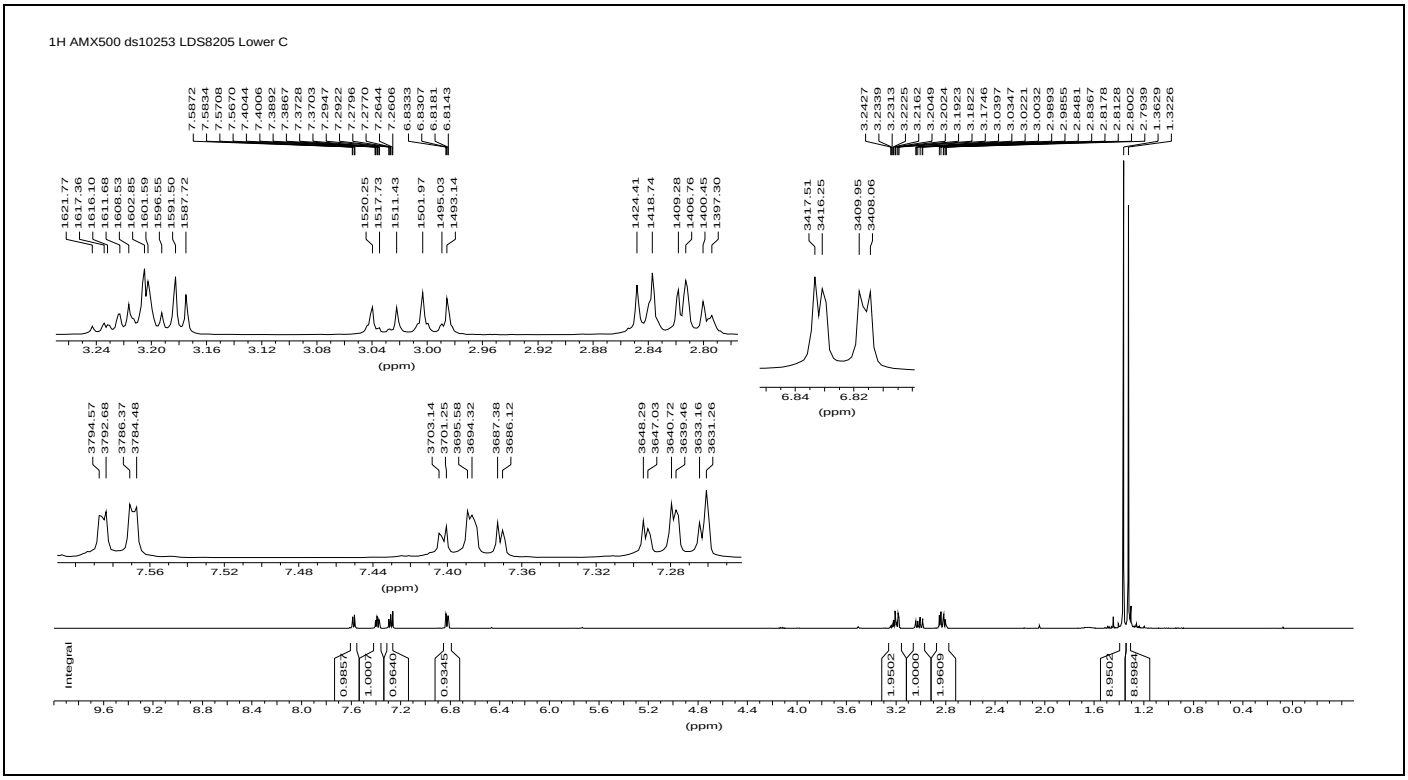

F19(no decoupled) oc20lds3 lds8196
13.1858
13.1566
3723.45
3715.20
13.20
(ppm)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130
(ppm)

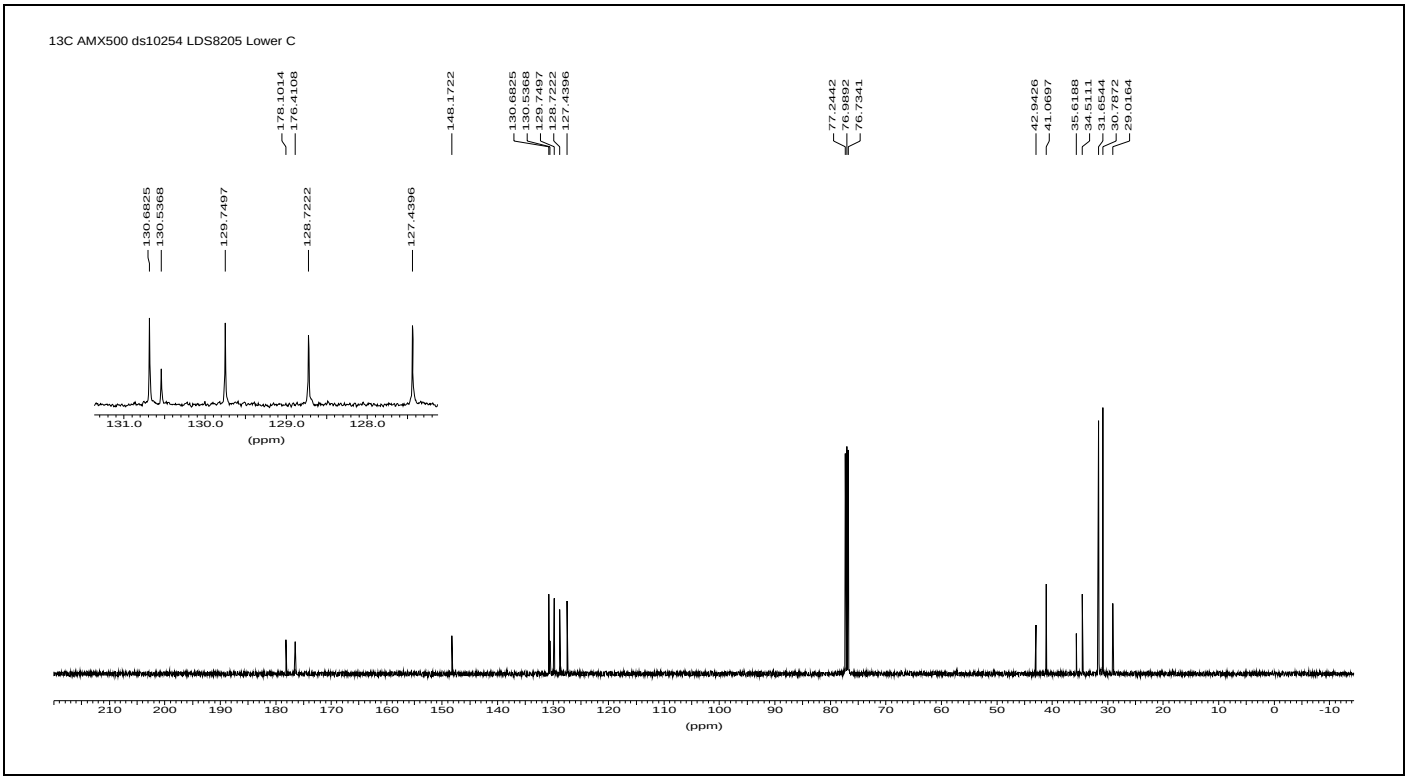



1H AMX500 ds10251 LDS8205 Upper C
(ppm)

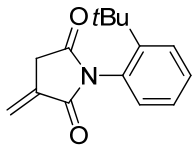

13C AMX500 ds10252 LDS8205 Upper C
(ppm)

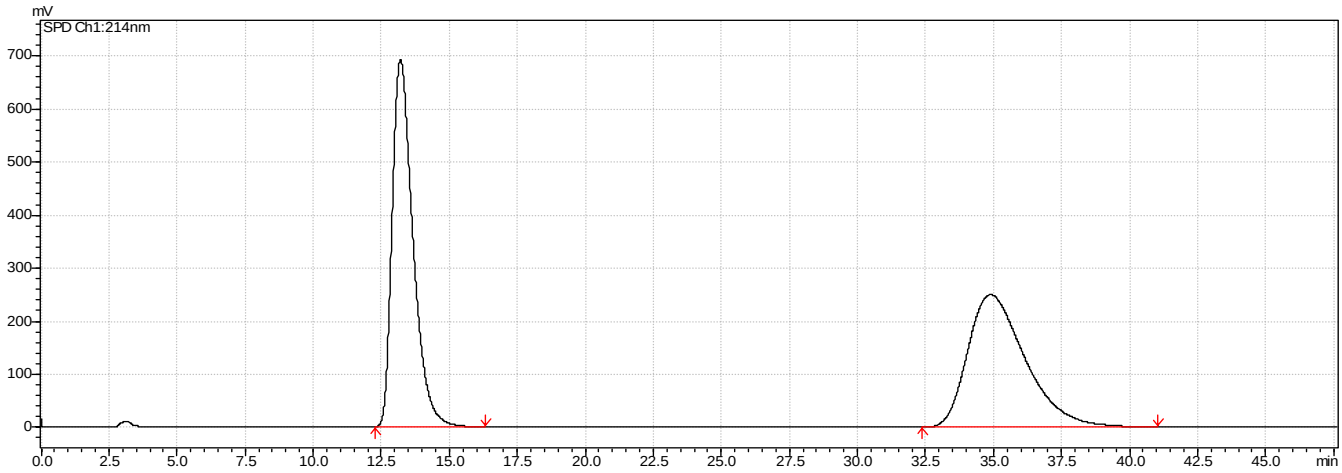


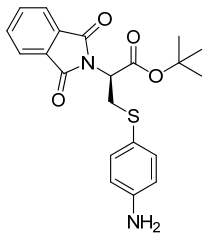

1H AMX500 ds10253 LDS8205 Lower C
7.5872
7.5834
7.5708
7.5670
7.4044
7.4006
7.3892
7.3867
7.3728
7.3703
7.2947
7.2922
7.2796
7.2770
7.2644
7.2606
6.8333
6.8307
6.8171
6.8143
3.2427
3.2339
3.2313
3.2225
3.2162
3.2049
3.2024
3.1923
3.1822
3.1746
3.0397
3.0347
3.0221
3.0032
2.9883
2.9555
2.8481
2.8367
2.8178
2.8128
2.8002
2.7939
1.3629
1.3226
1621.77
1617.36
1616.10
1611.68
1608.53
1602.85
1601.59
1596.55
1591.50
1587.72
1520.25
1517.73
1511.43
1501.97
1495.03
1493.14
1424.41
1418.74
1409.28
1406.76
1400.45
1397.30
3417.51
3416.25
3409.95
3408.06
3794.57
3792.68
3786.37
3784.48
3703.14
3701.25
3695.58
3694.32
3687.38
3686.12
3648.29
3647.03
3640.72
3639.46
3633.16
3631.26
Integral
0.985
1.000
0.964
0.934
1.950
1.000
1.960
8.950
8.898
(ppm)

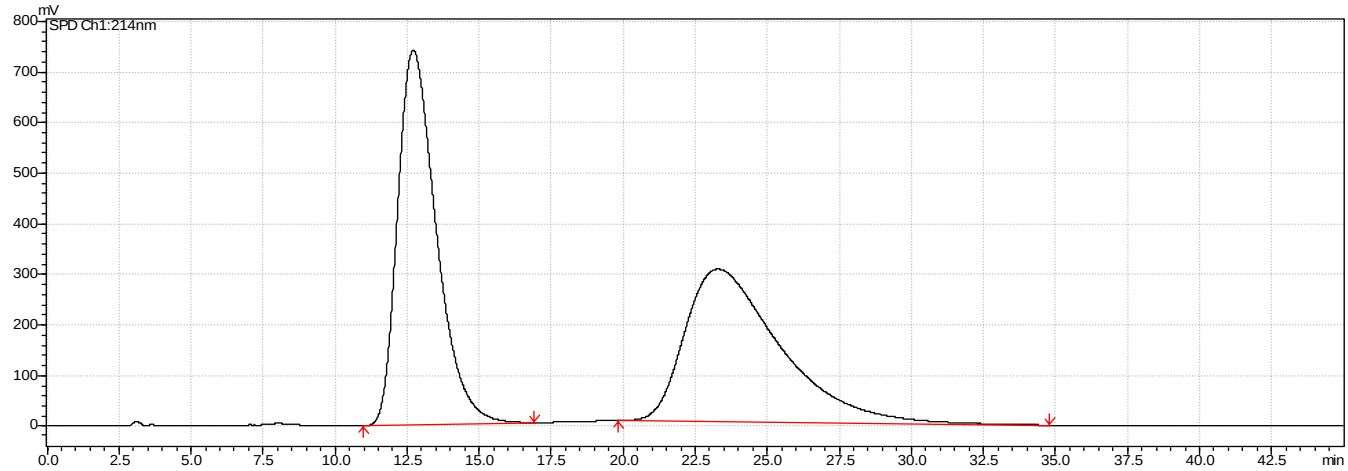

13C AMX500 ds10254 LDS8205 Lower C
178.1014
176.4108
148.1722
130.6825
130.5368
129.7497
128.7222
127.4396
77.2442
76.9892
76.7341
42.9426
41.0697
35.6188
34.5111
31.6544
30.7872
29.0164
(ppm)

Chiral HPLC Chromatograms

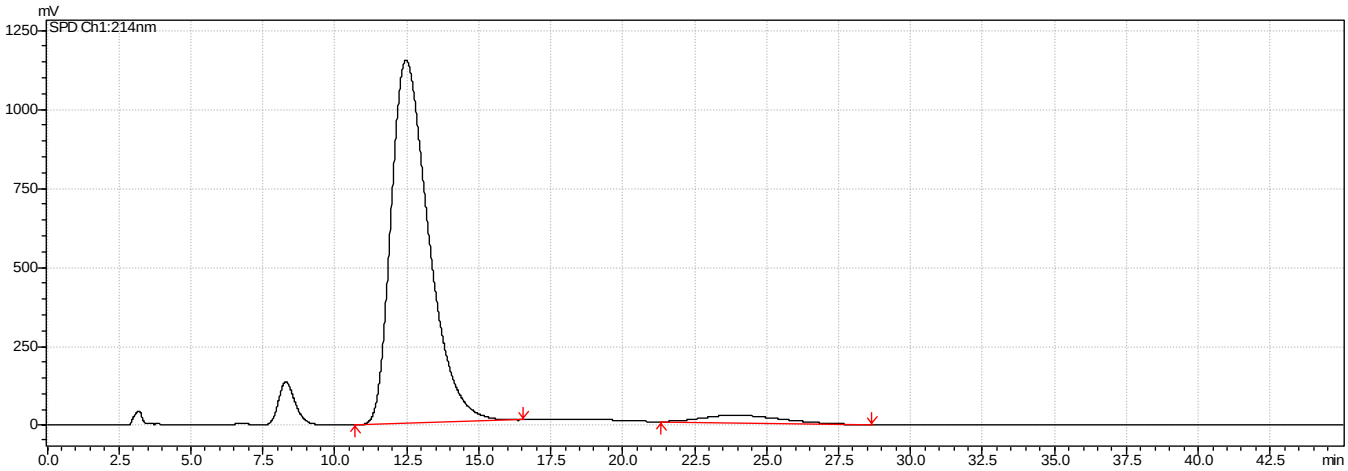




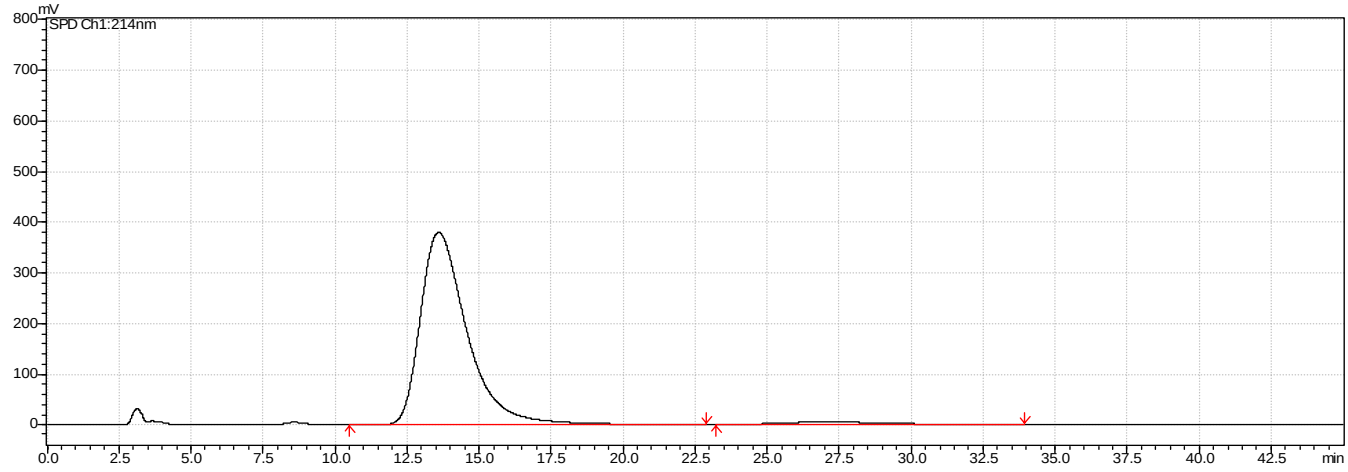




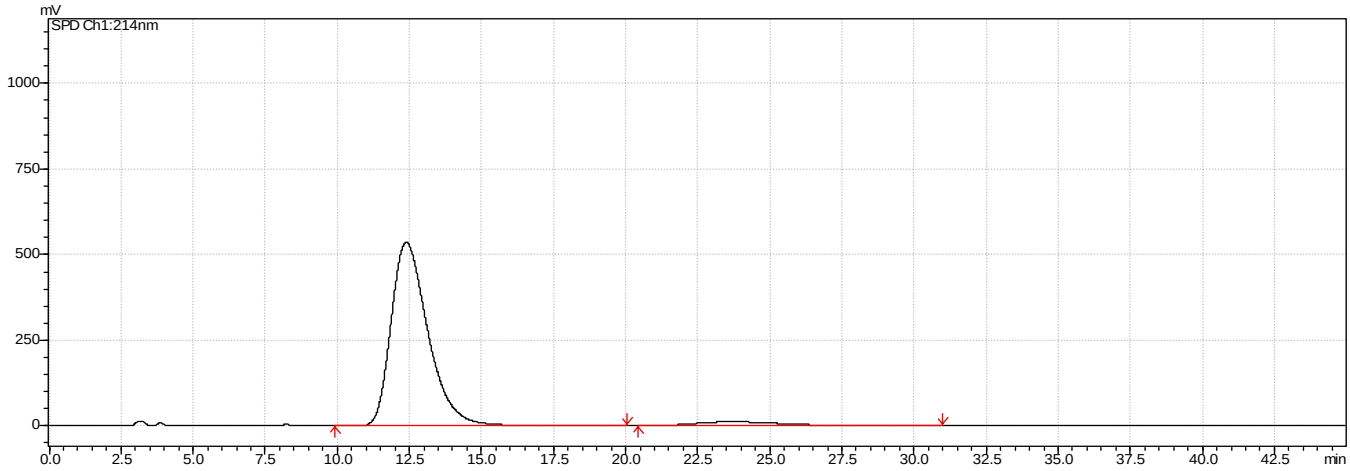
With 10 mol% catalyst at −50°C

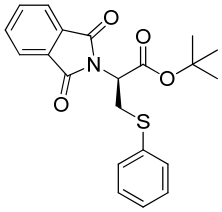


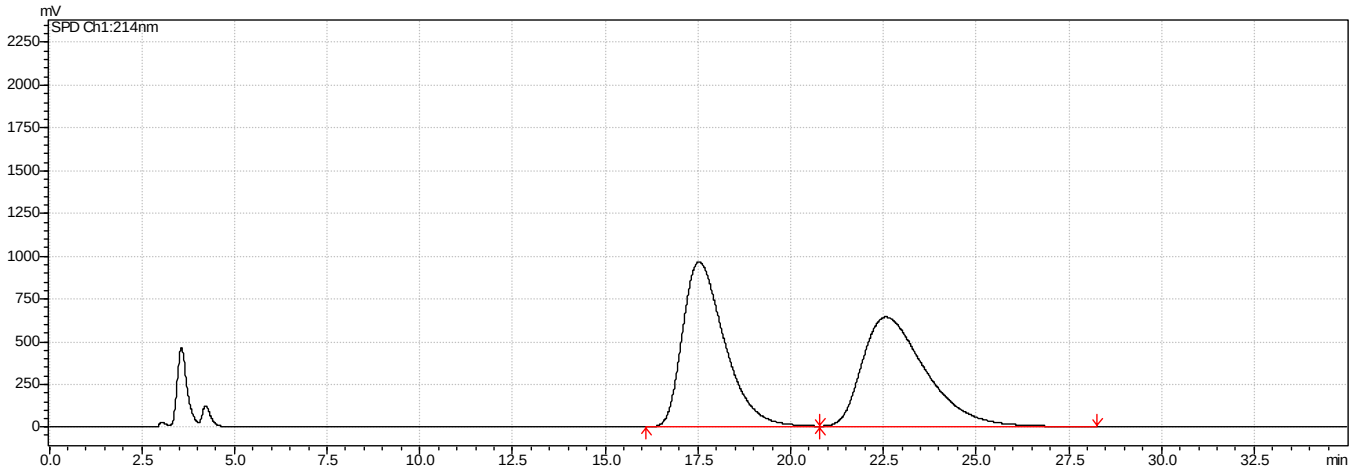
With 5 mol% catalyst at −116°C

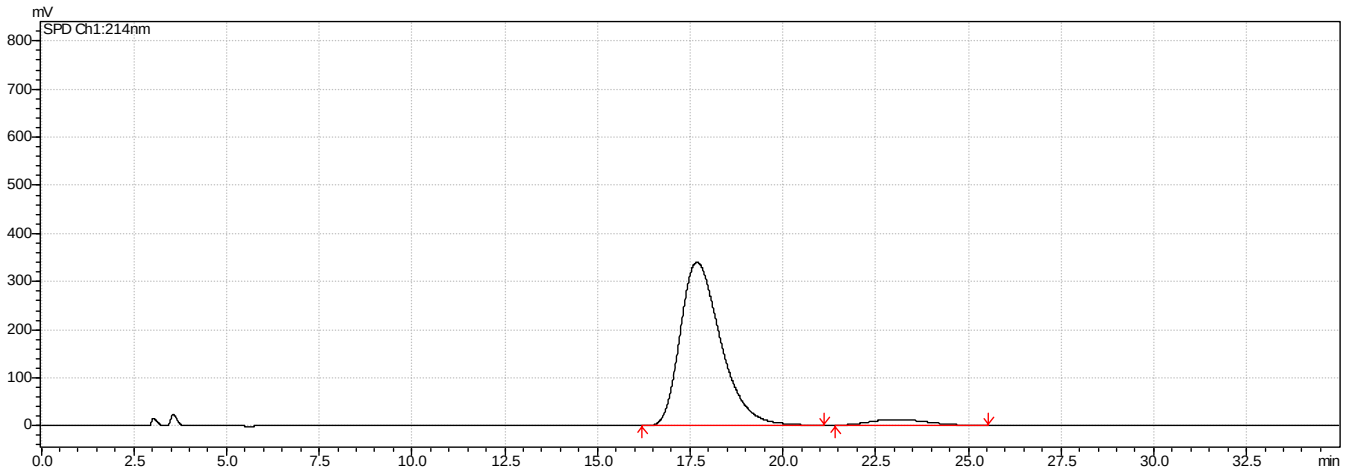


With 1 mol% catalyst at −116°C




O
O
N
O
O
S


mV
SPD Ch1:214nm
2250
2000
1750
1500
1250
1000
750
500
250
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
22.5
25.0
27.5
30.0
32.5
min


mV
SPD Ch1:214nm
800
700
600
500
400
300
200
100
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
22.5
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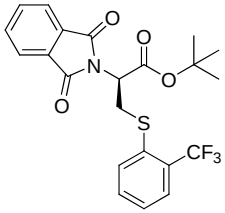
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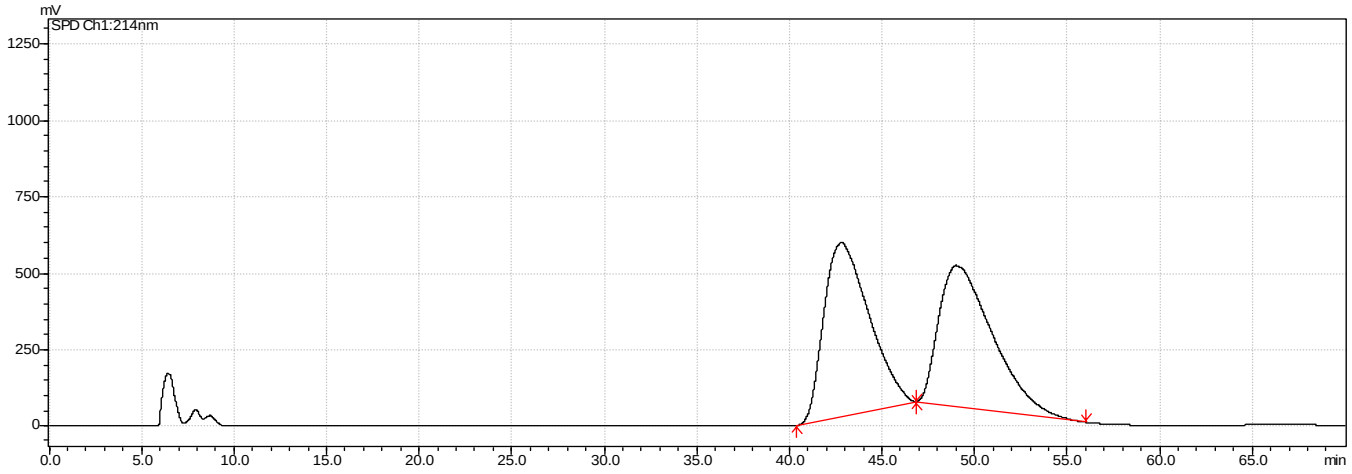
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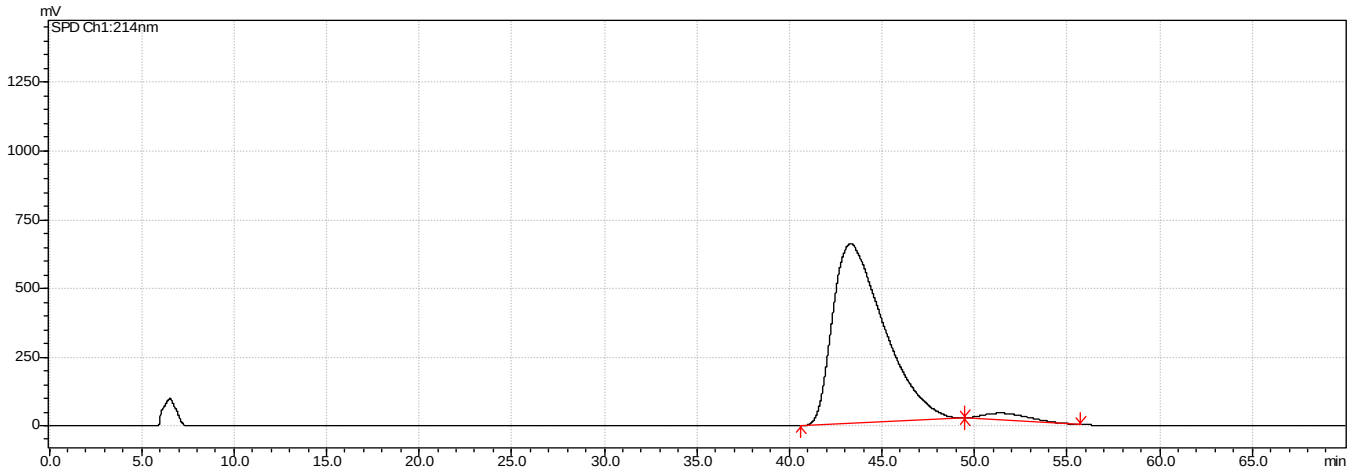
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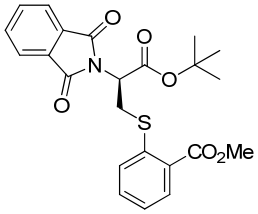
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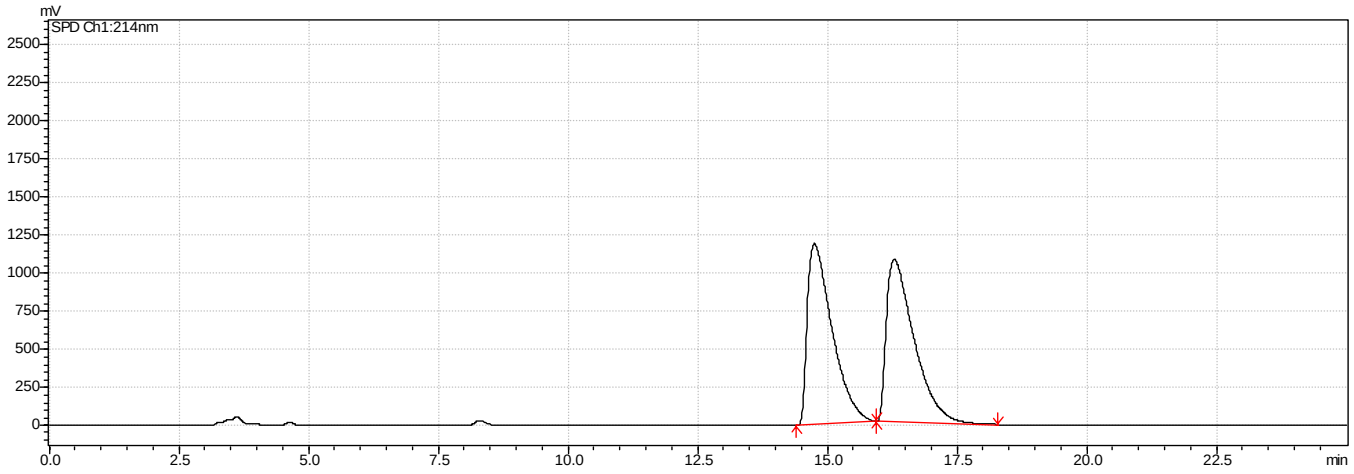
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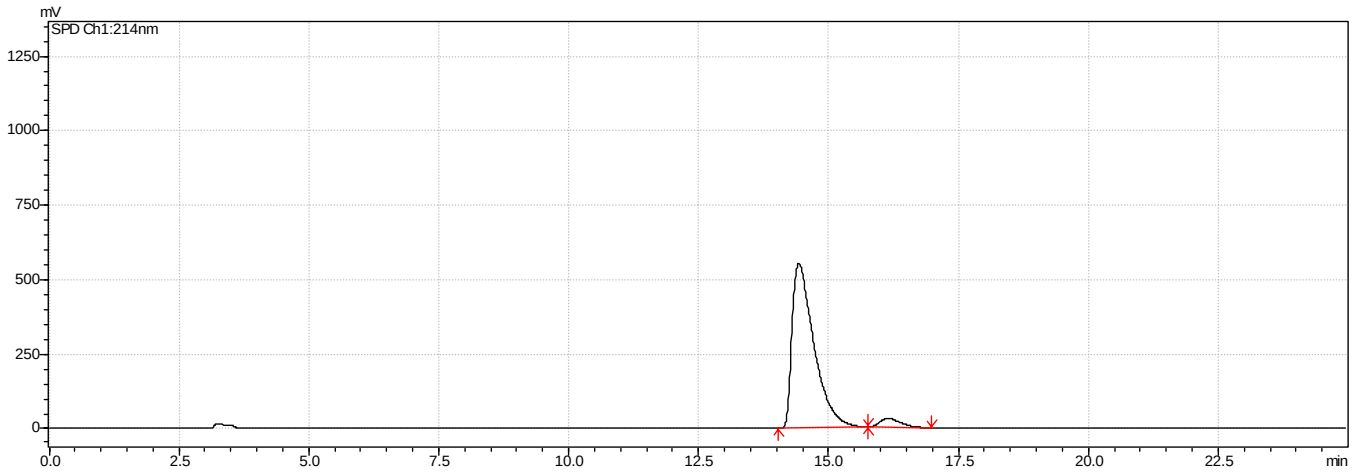
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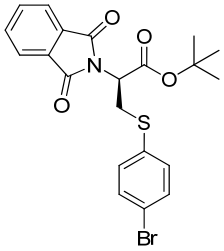
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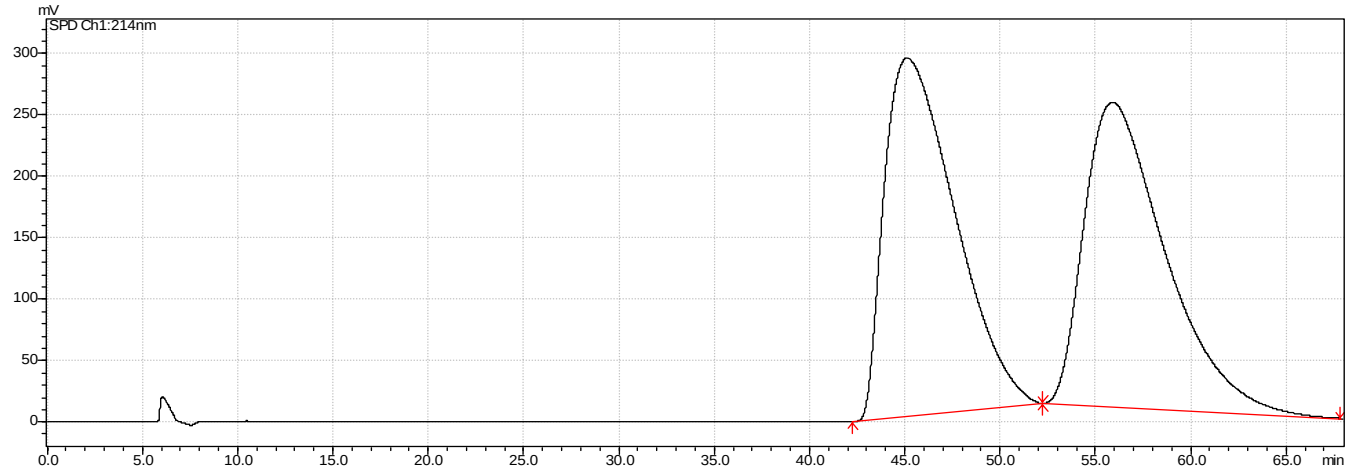
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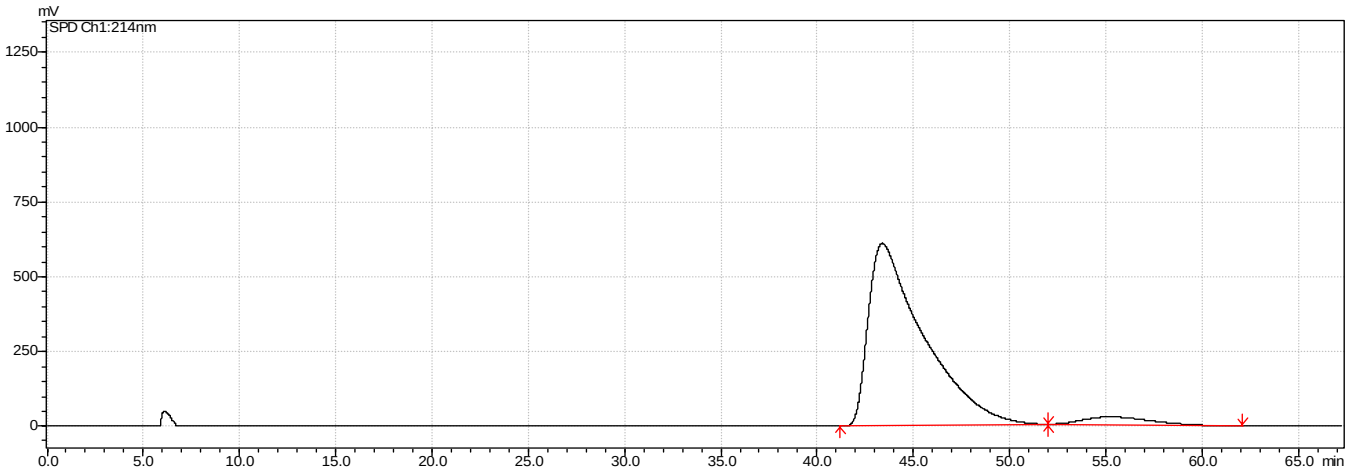
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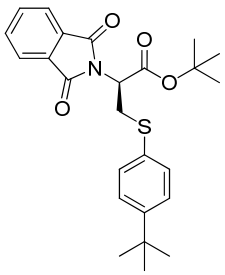
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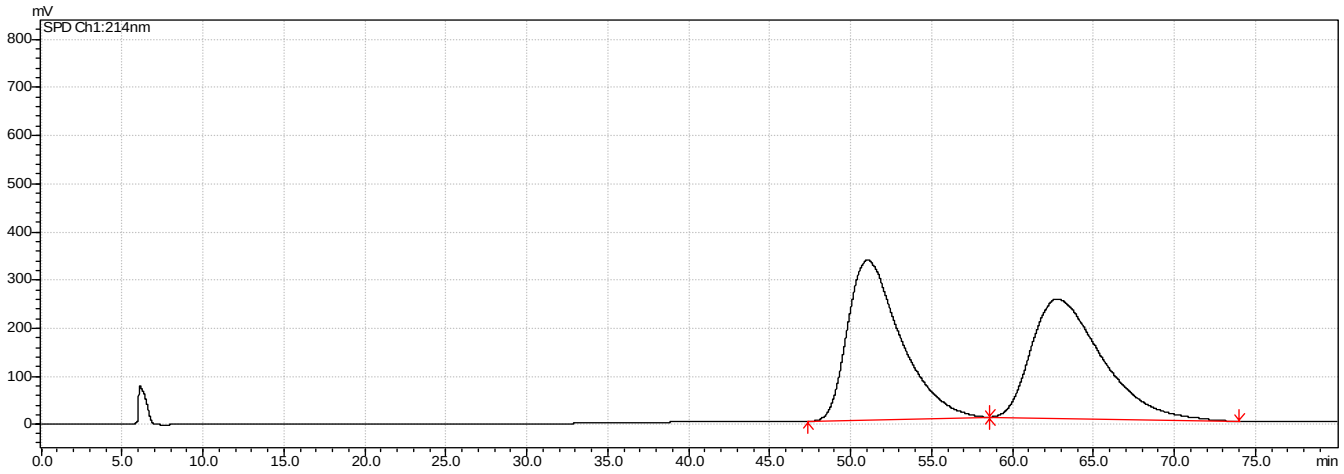
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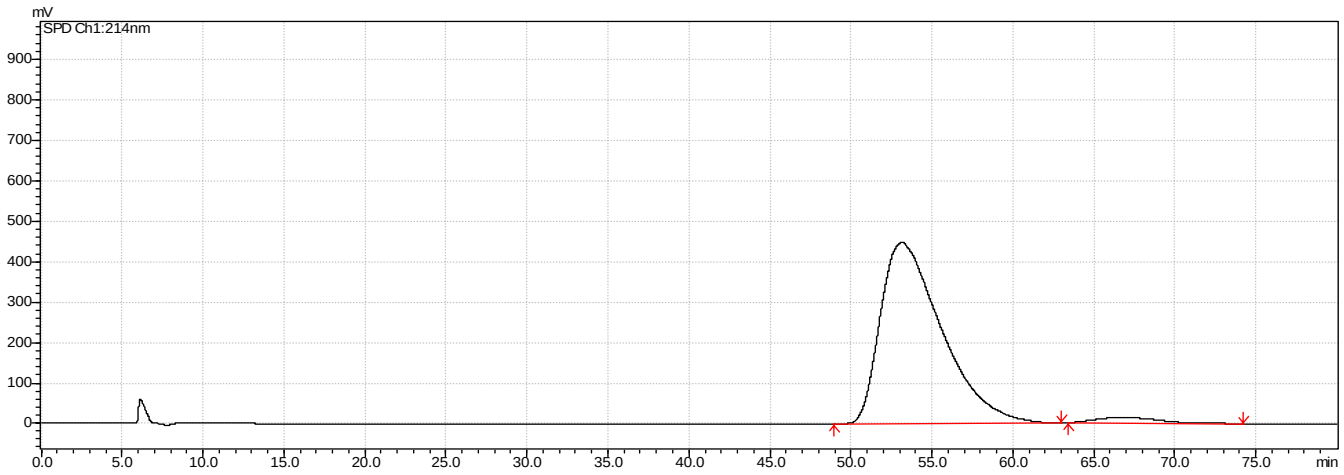
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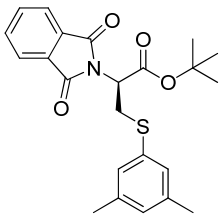
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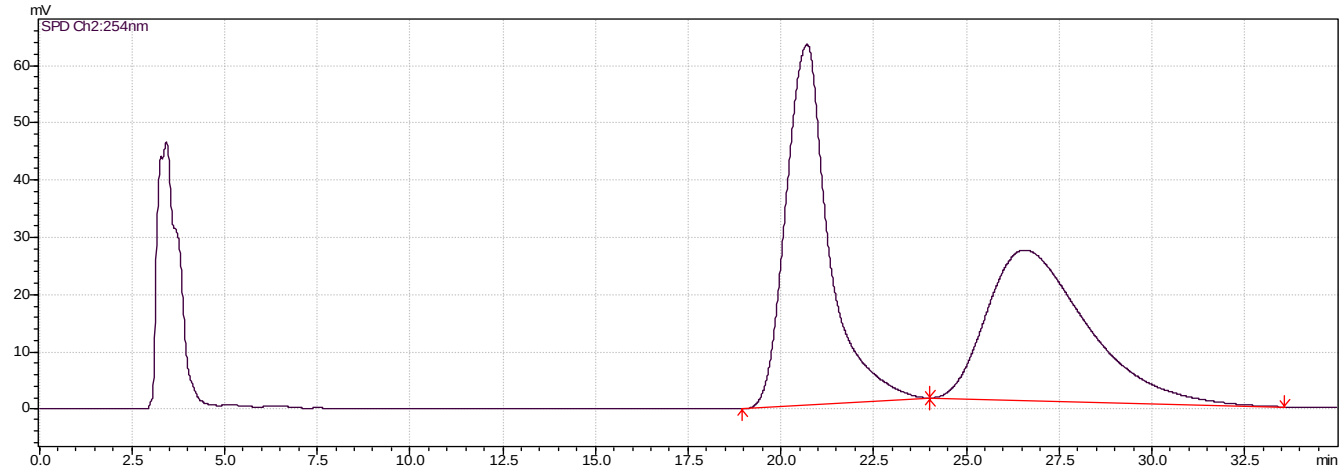
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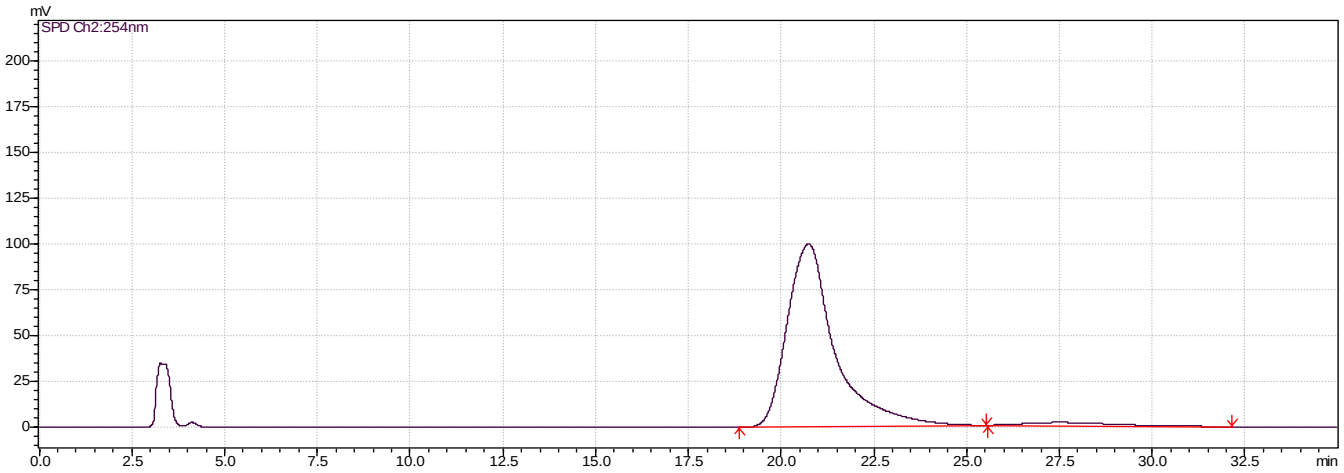
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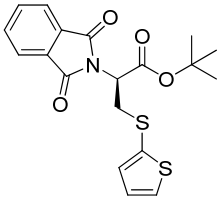
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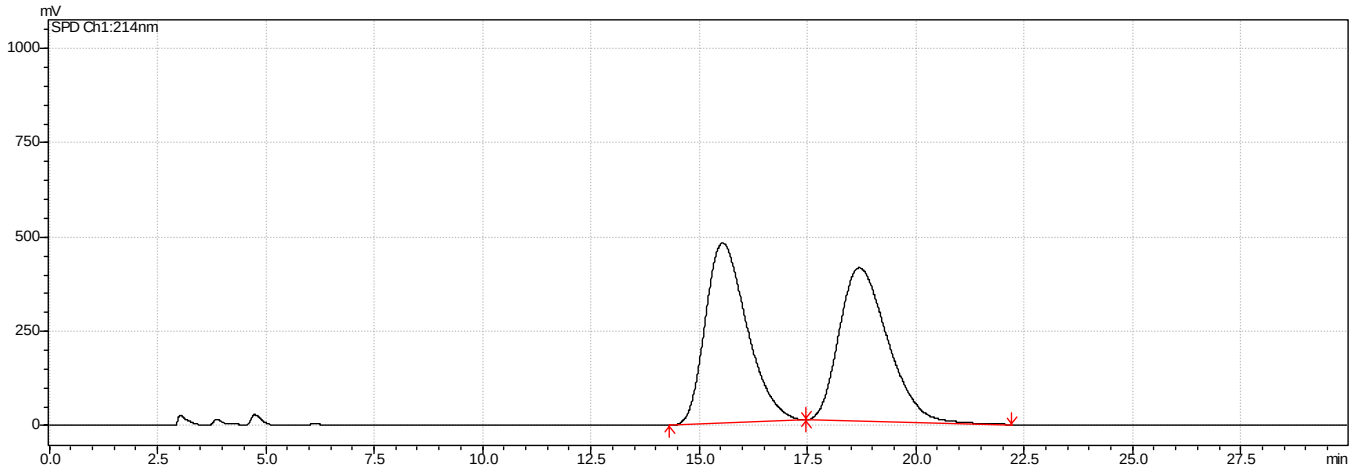
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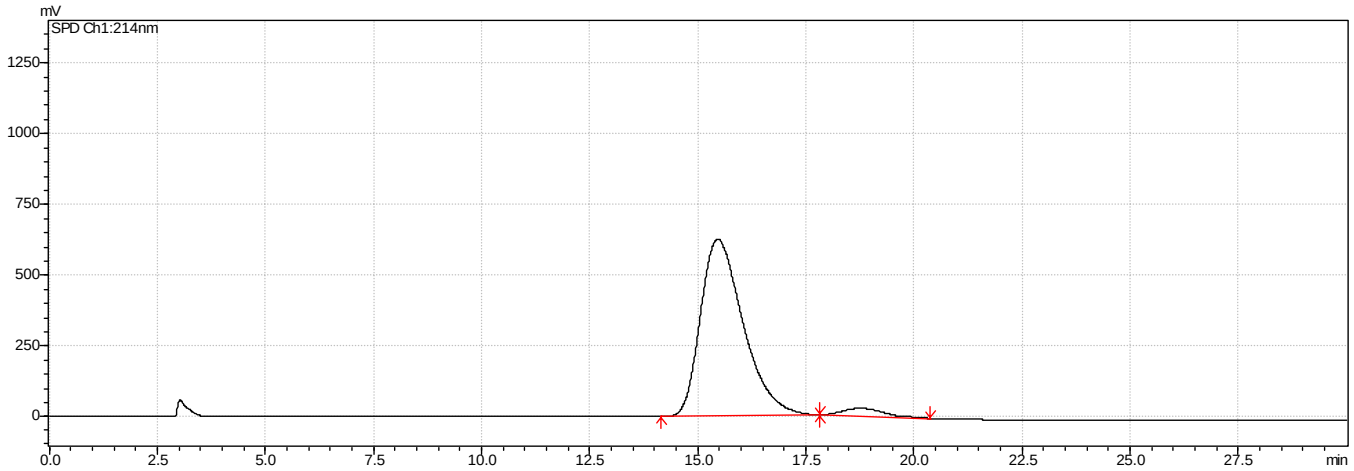
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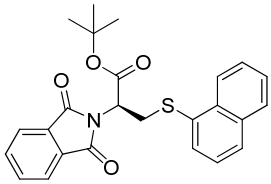
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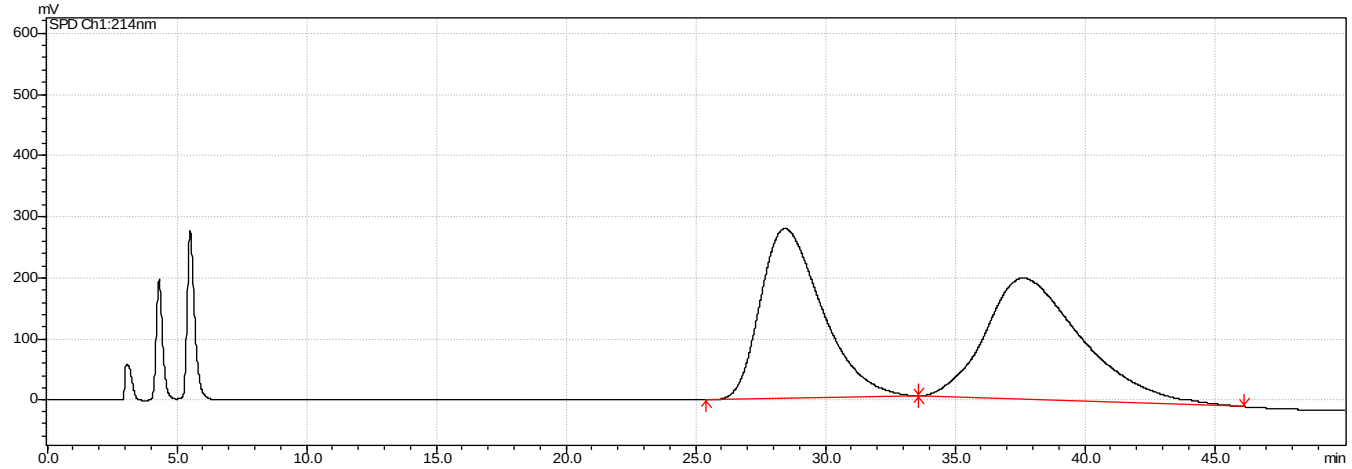
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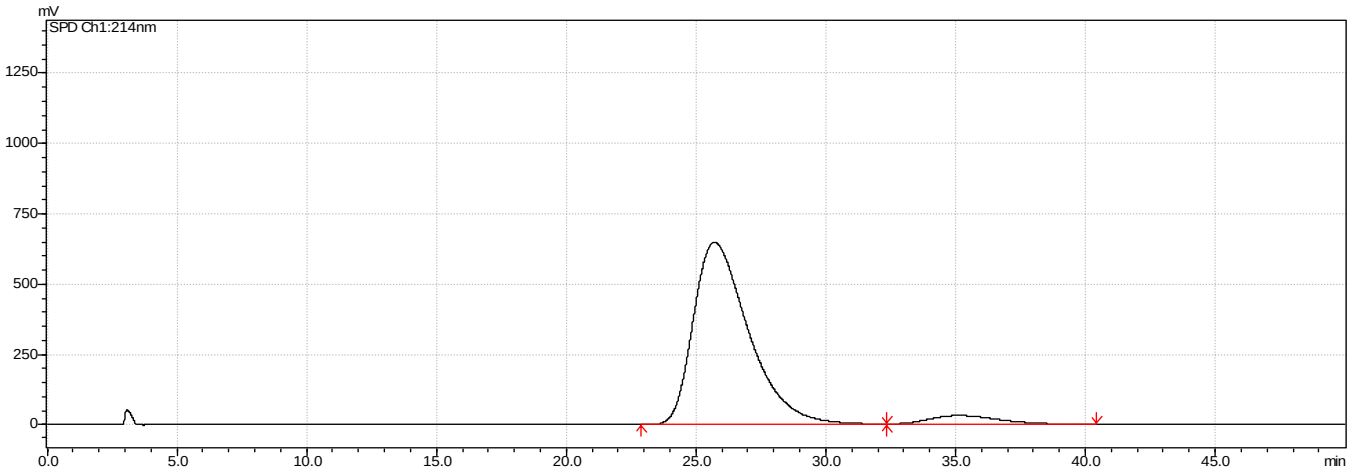
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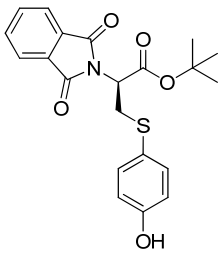
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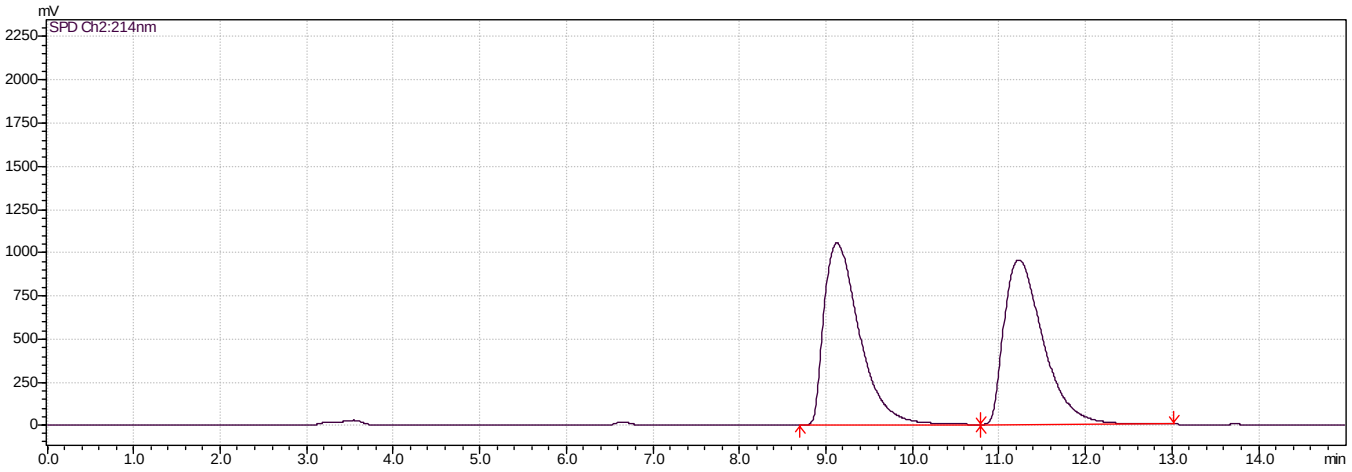
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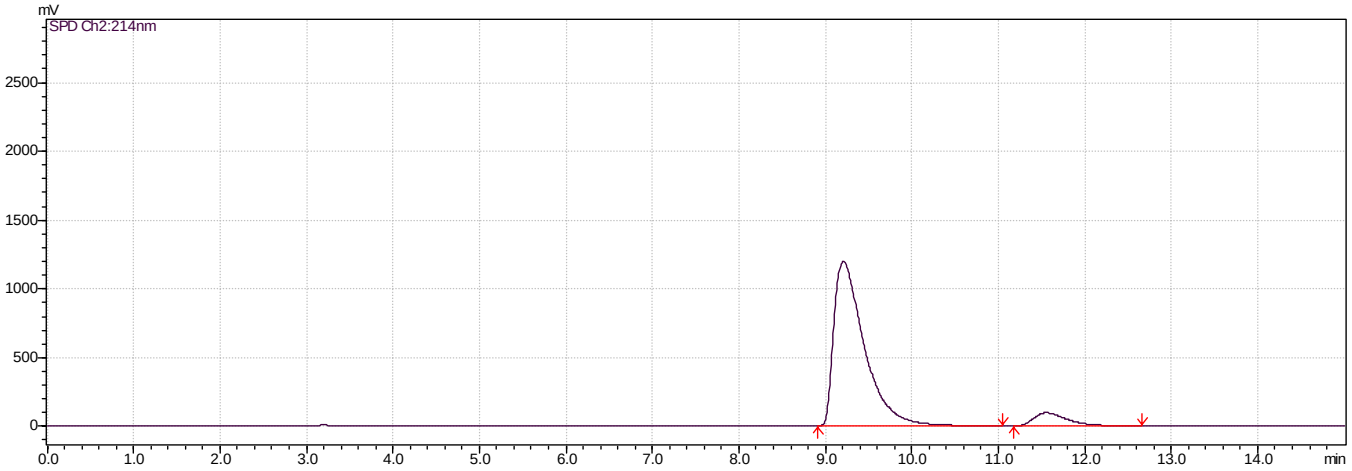
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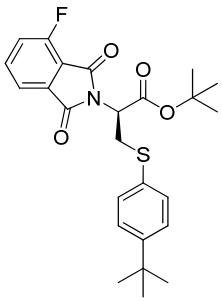
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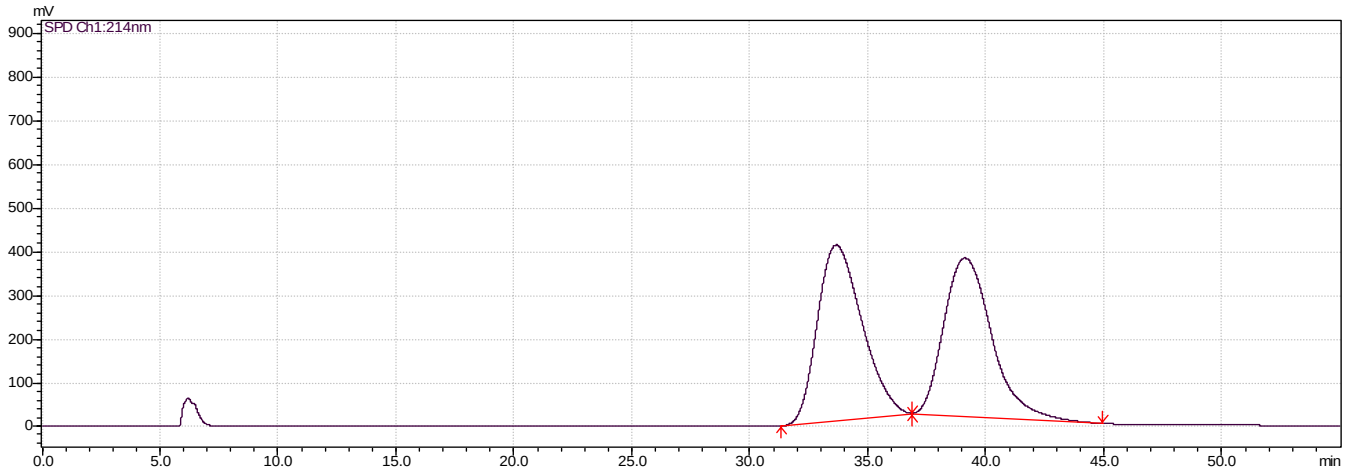
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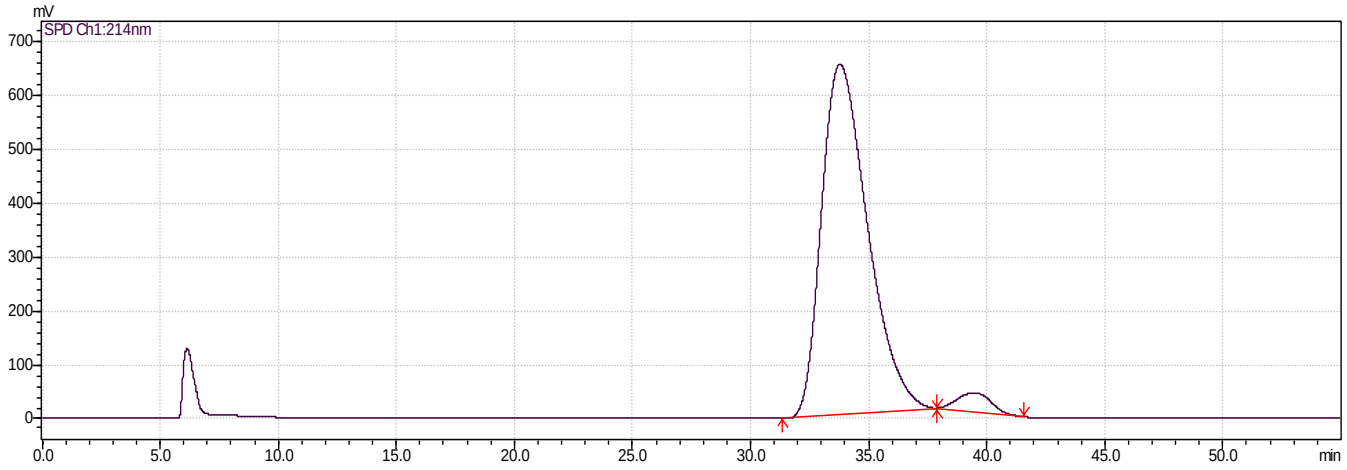
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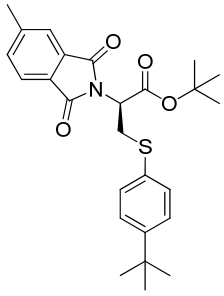
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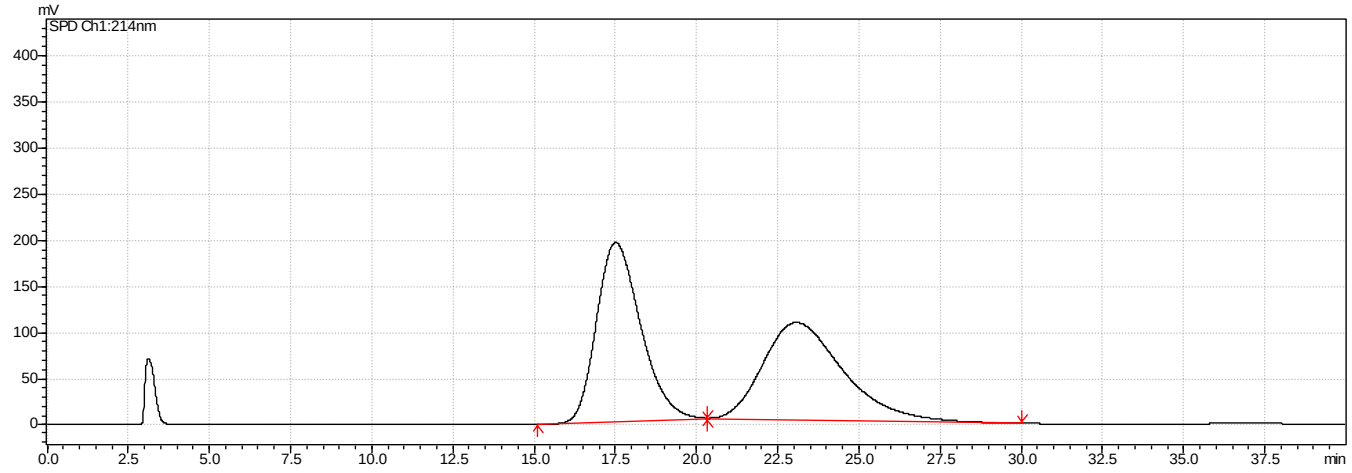
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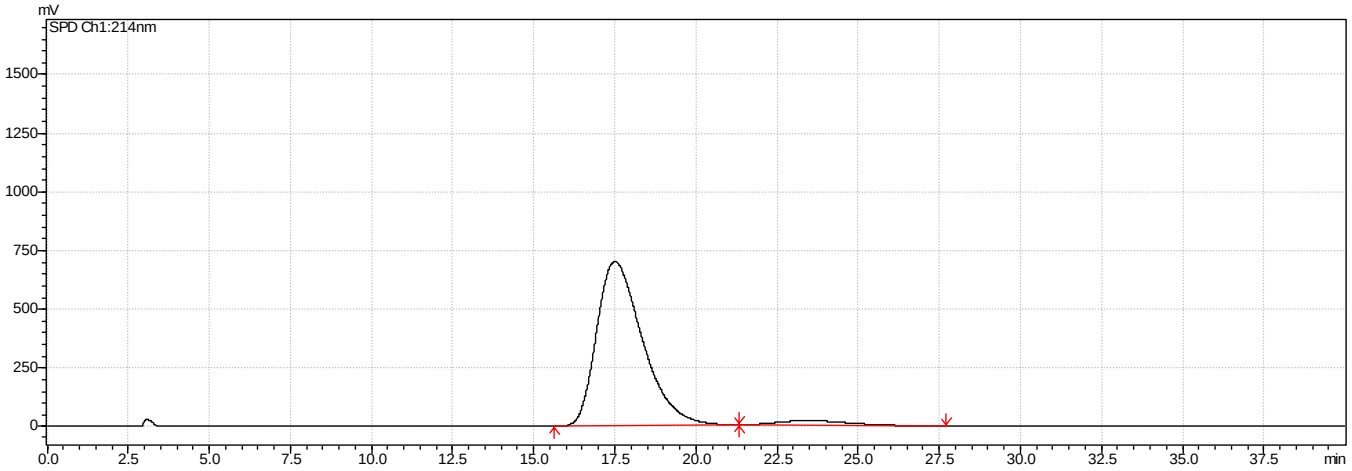
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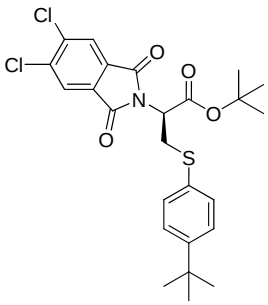
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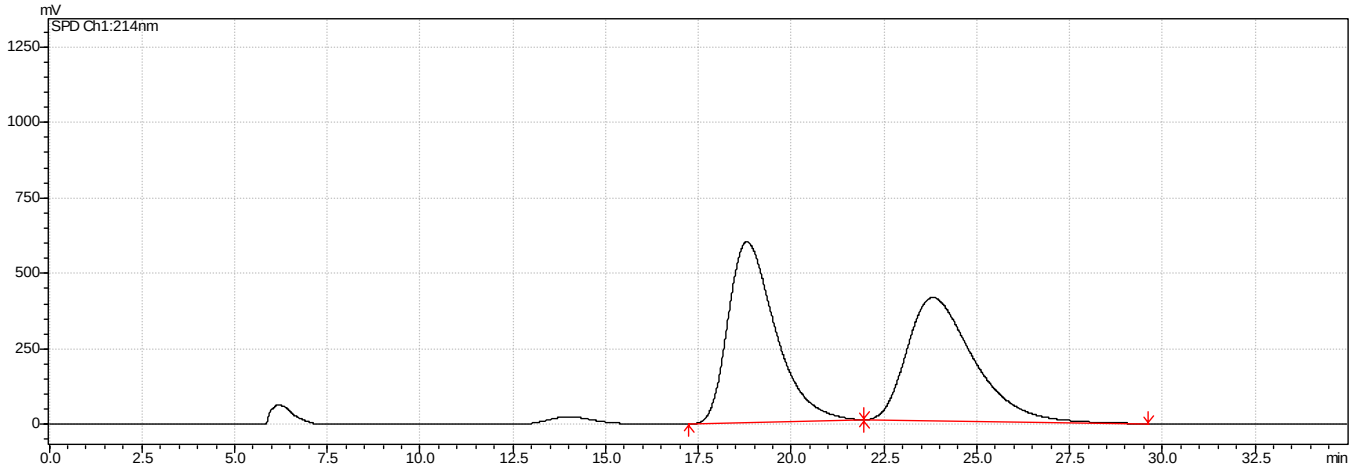
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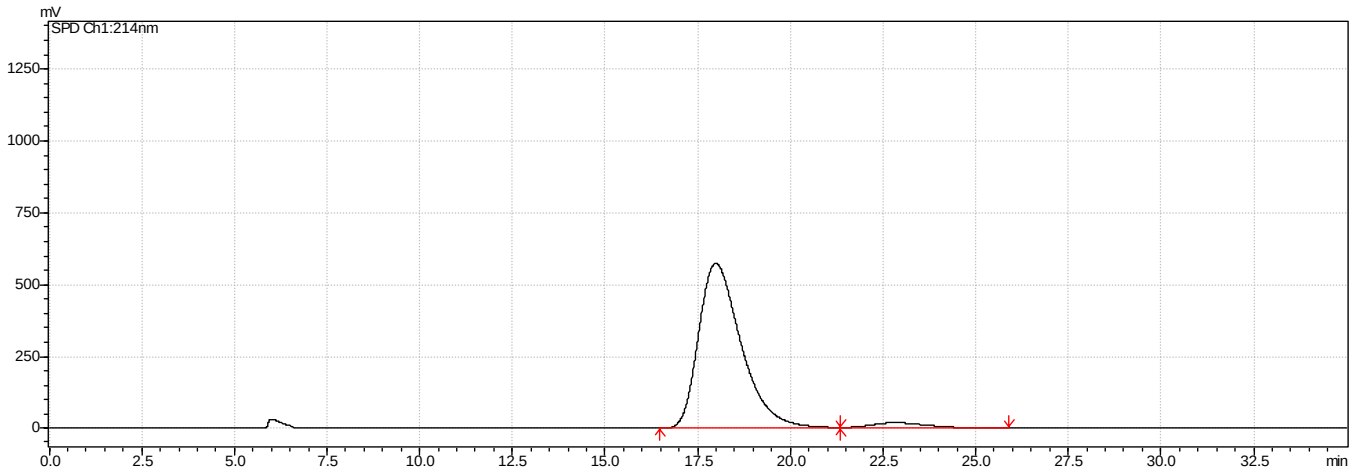
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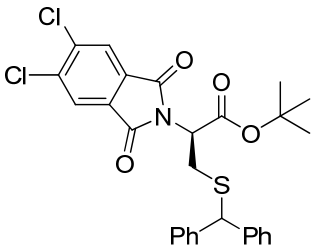
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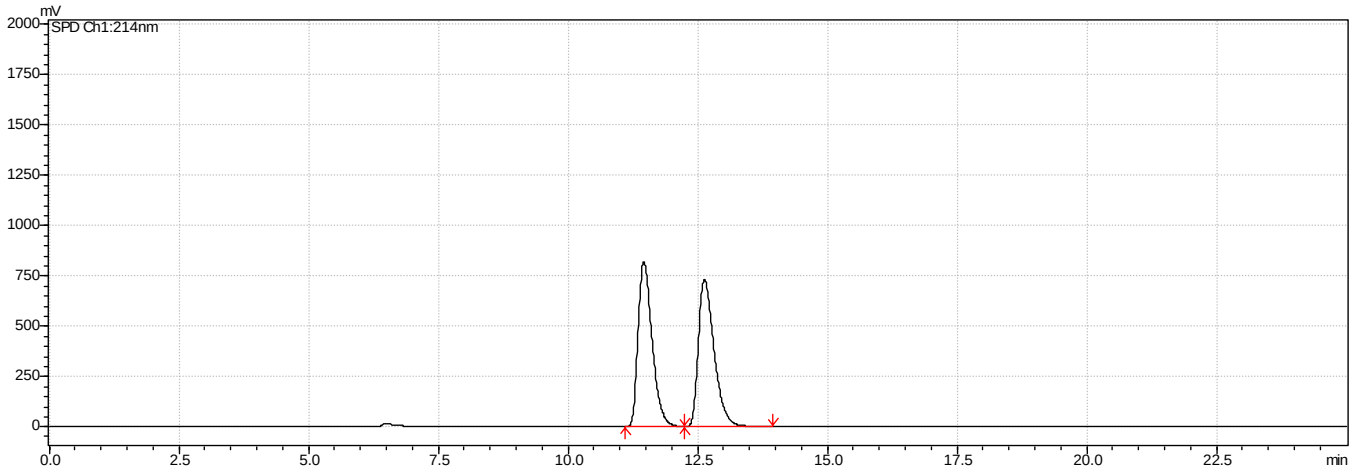
Ph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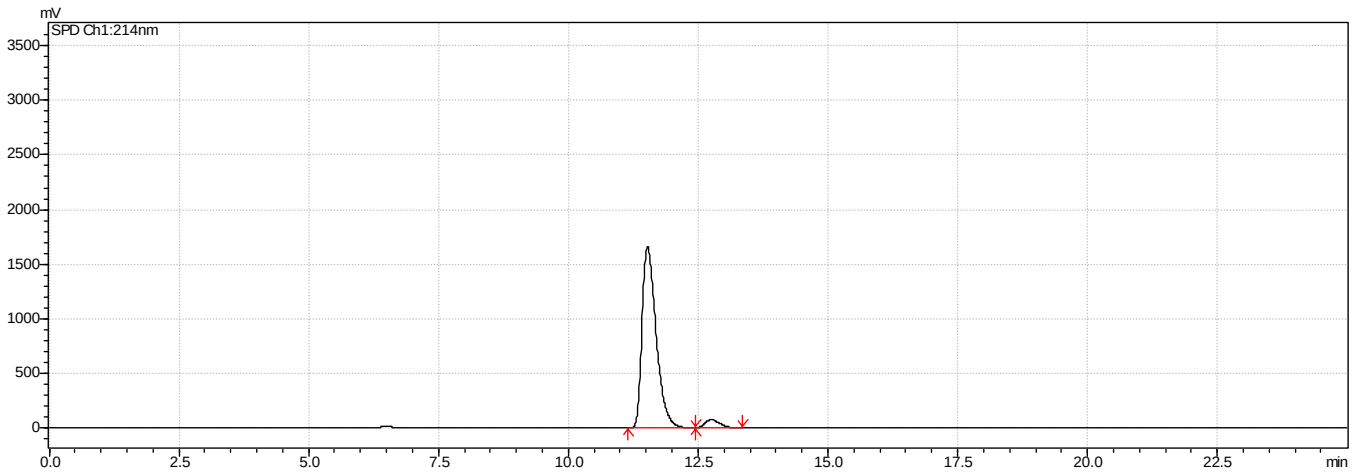
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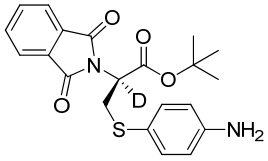
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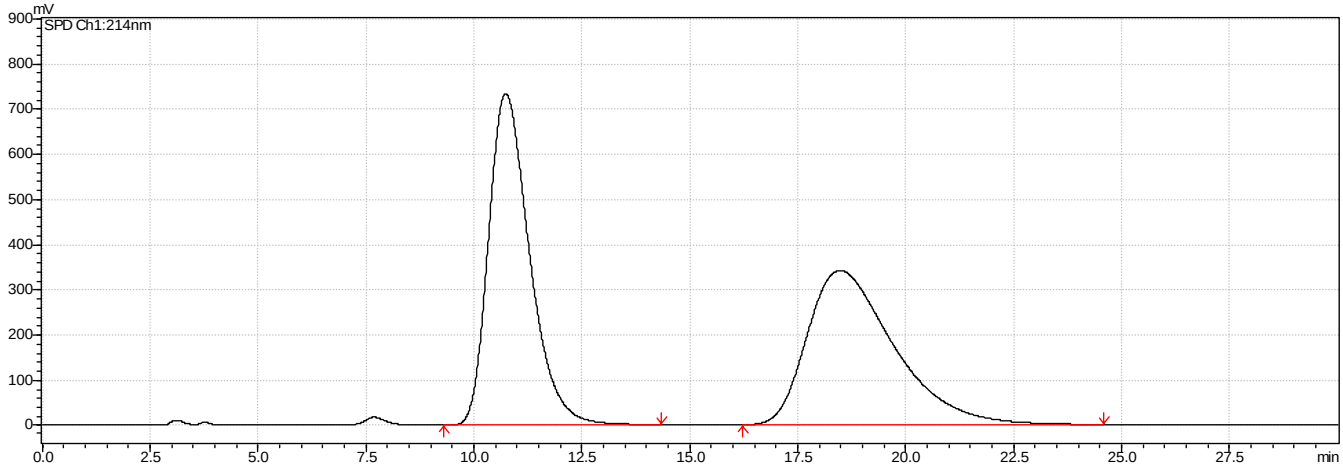
11f-d_1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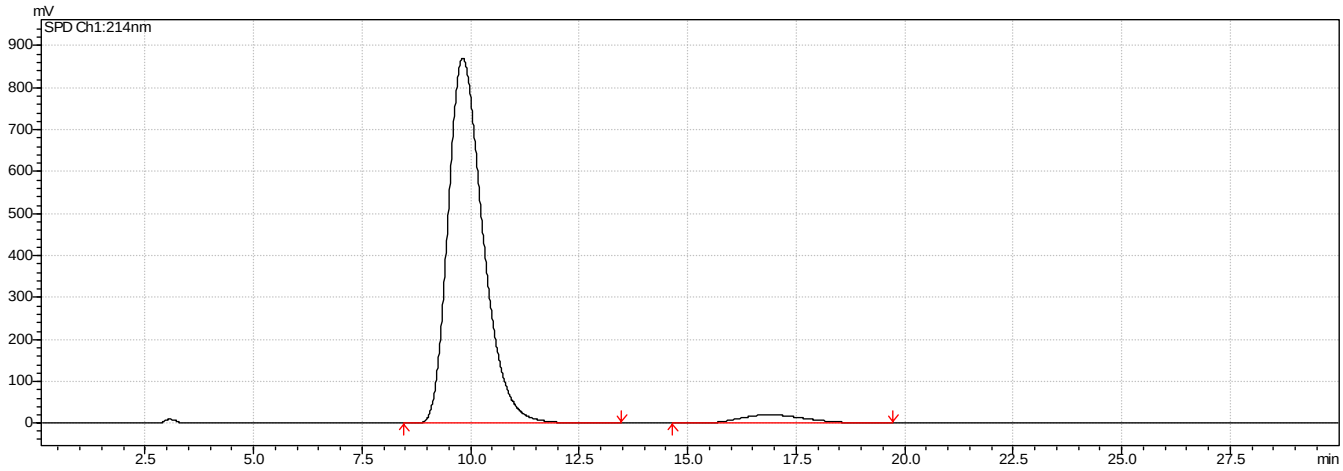
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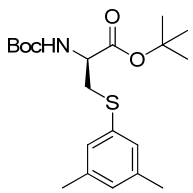
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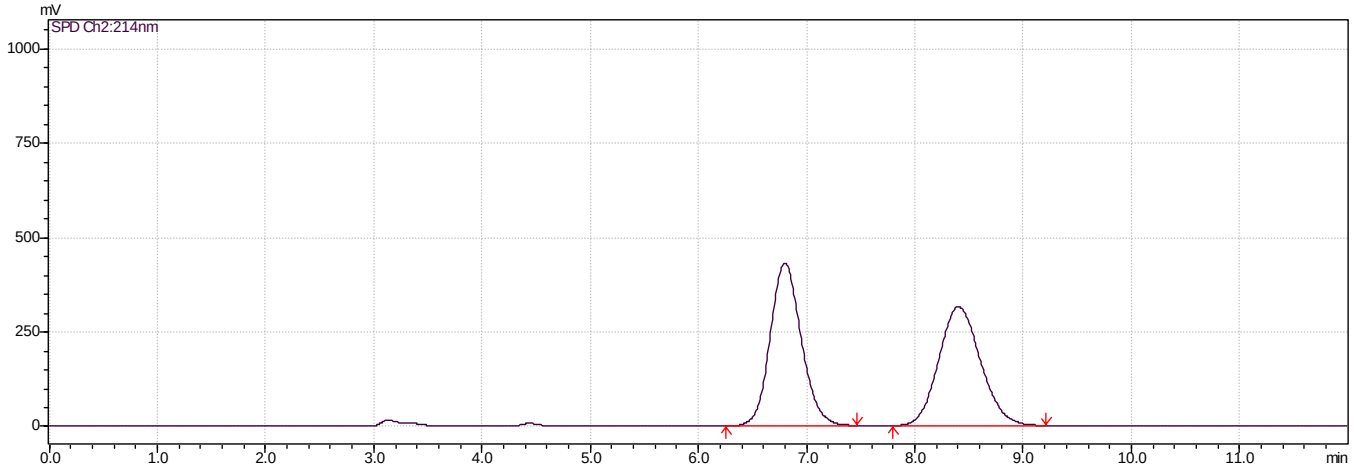
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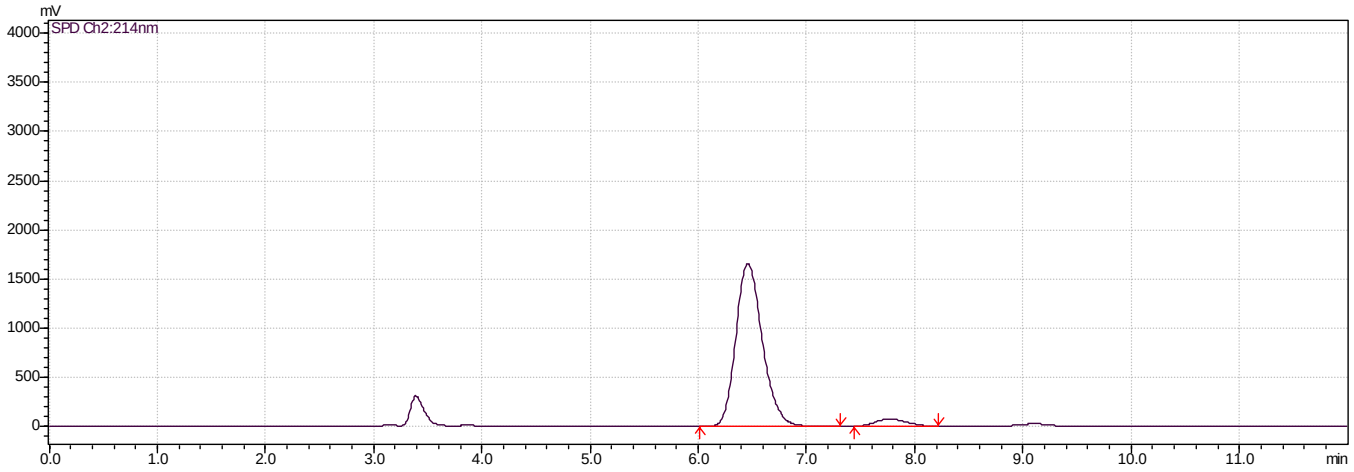
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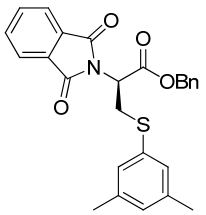
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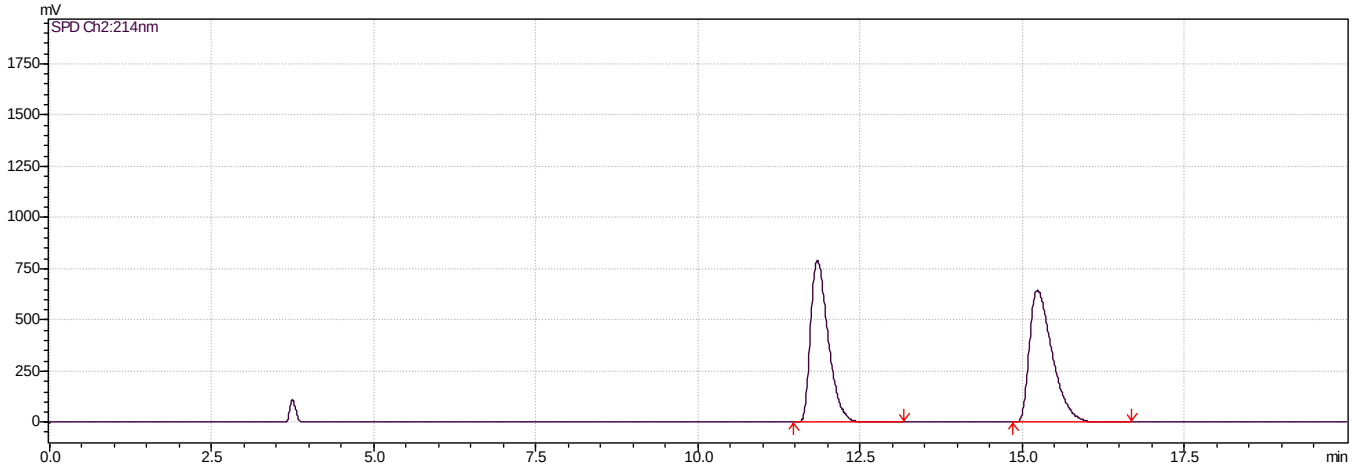
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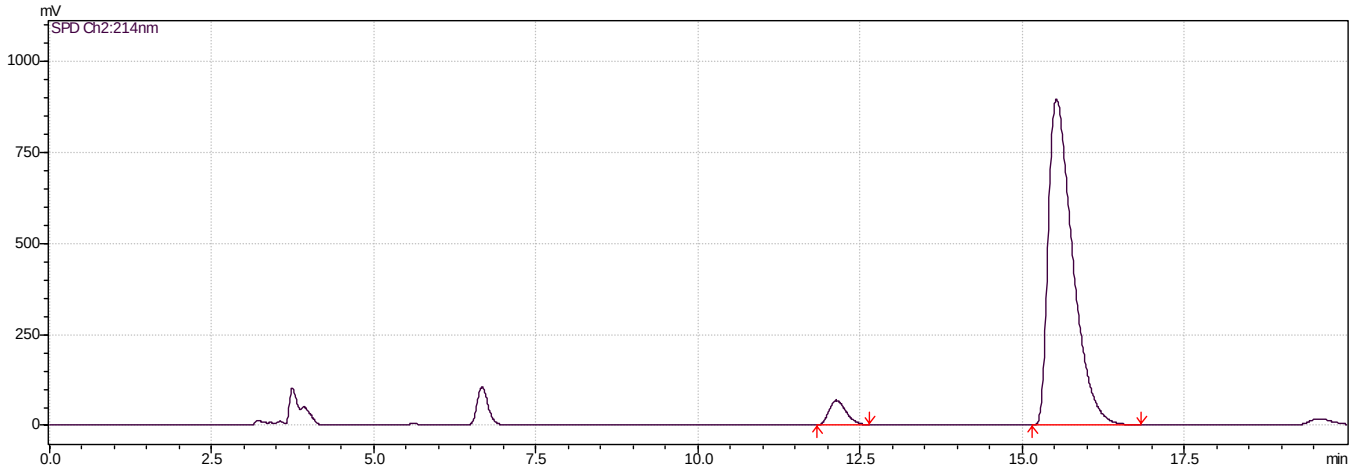
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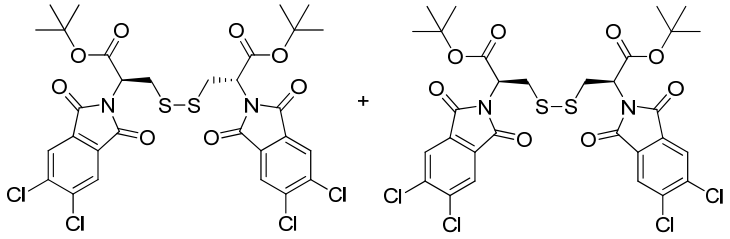
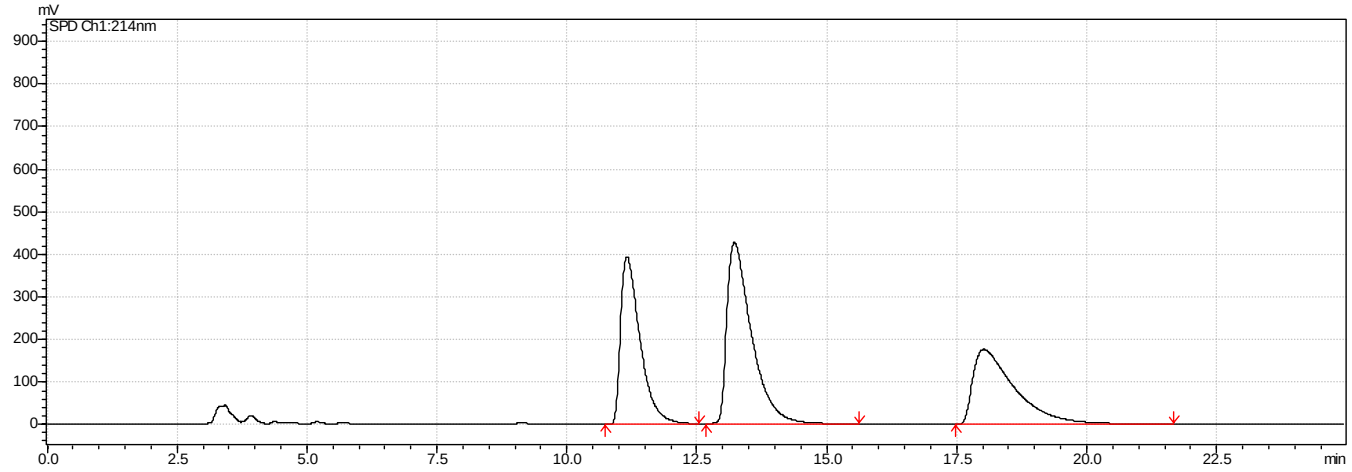


(*S*,*S*)-**8**

meso-**8**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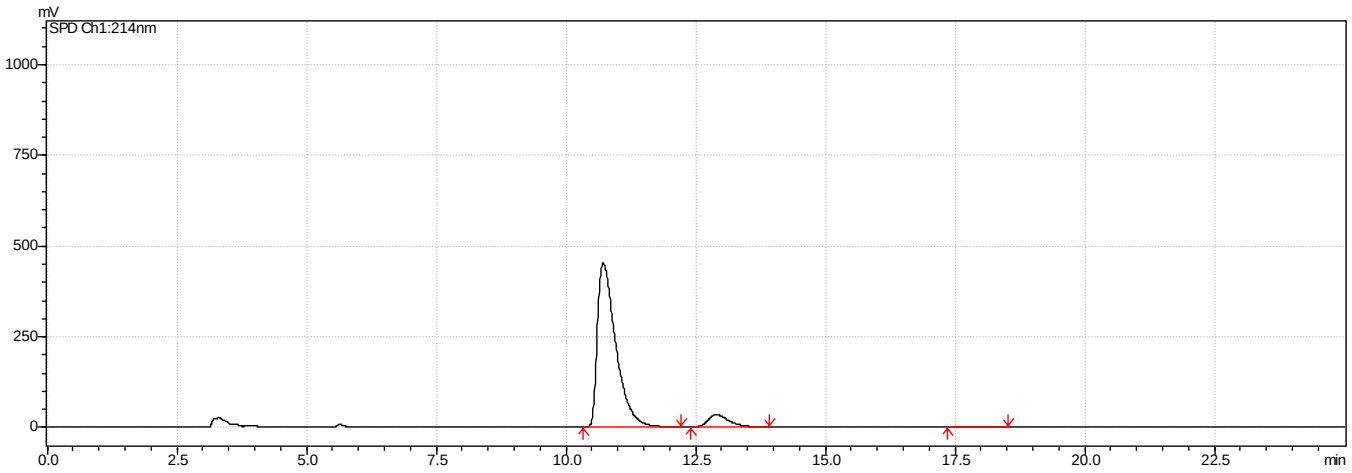
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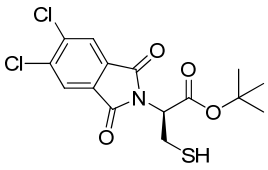
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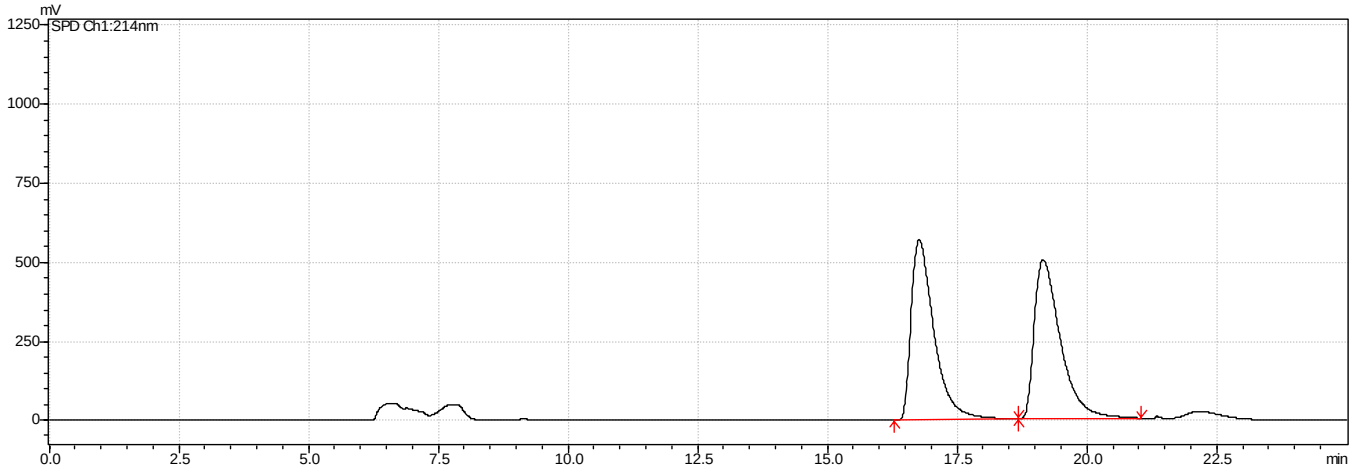
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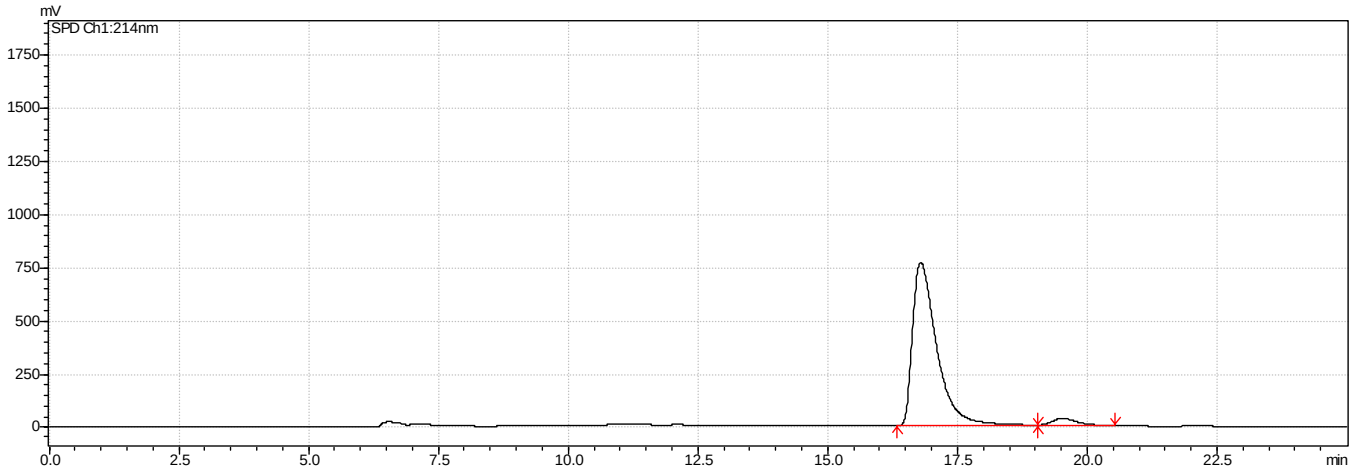
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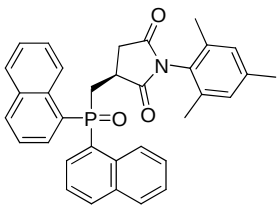
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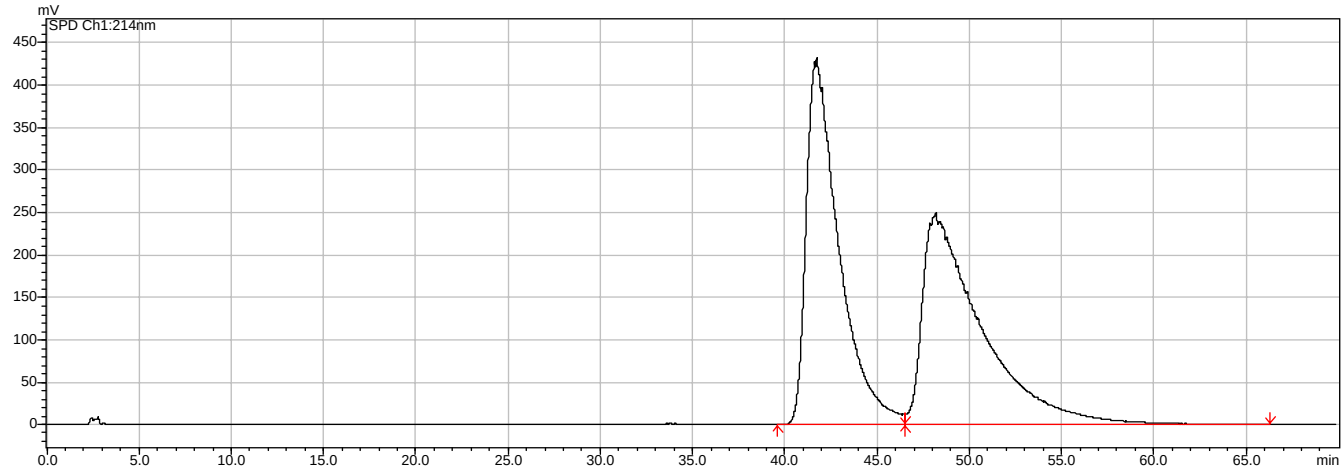
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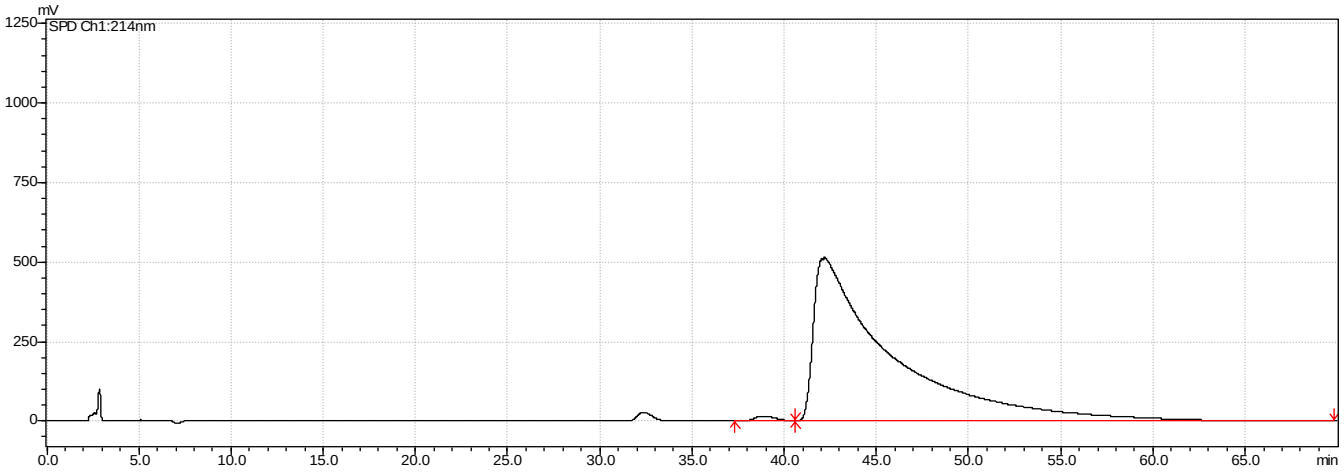
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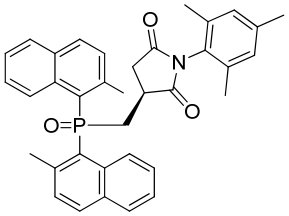
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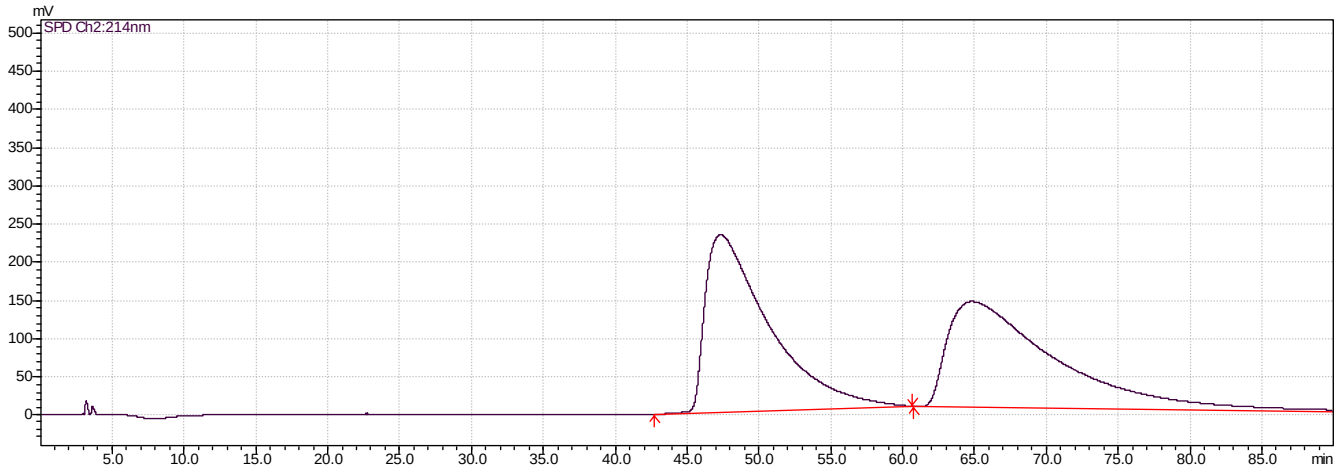
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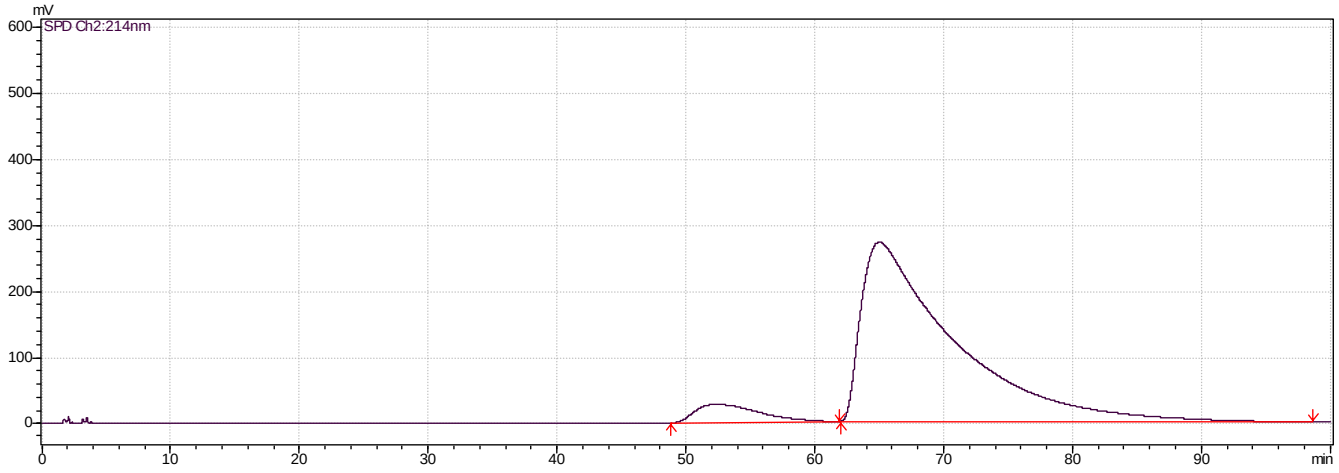
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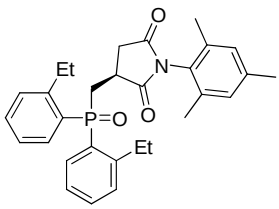
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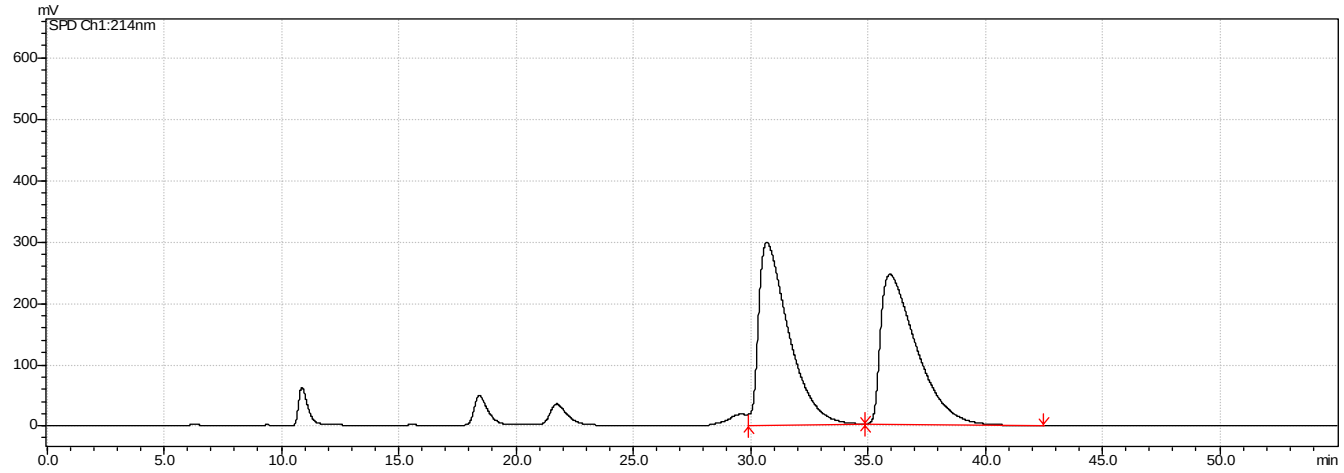
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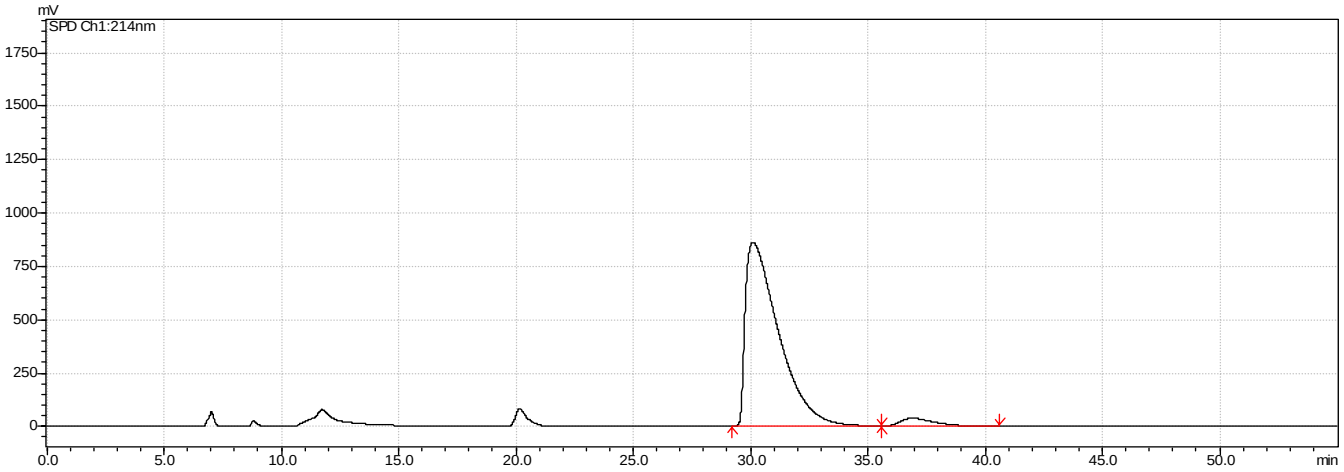
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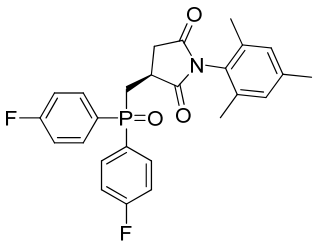
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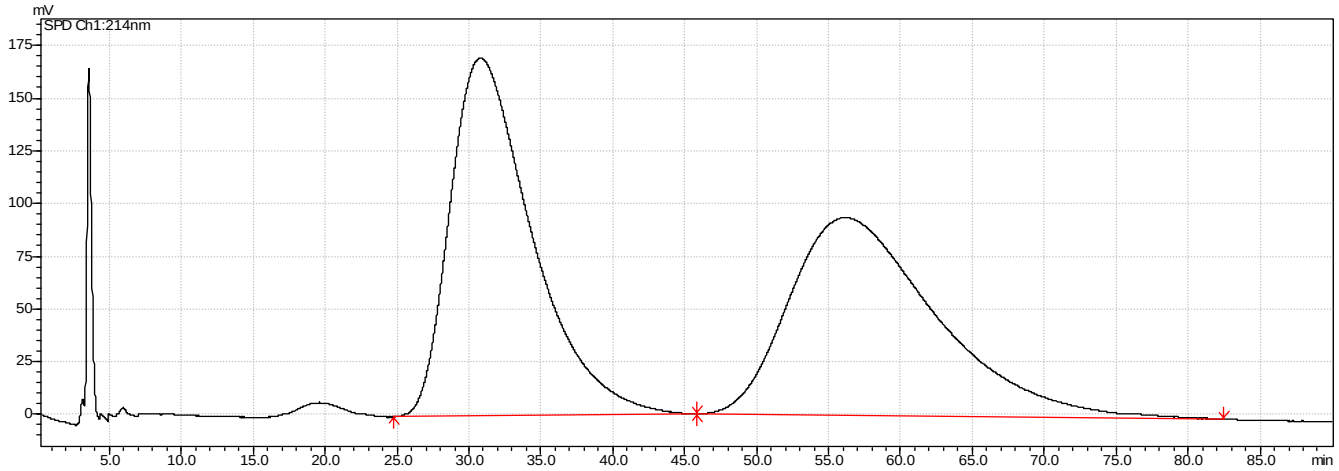
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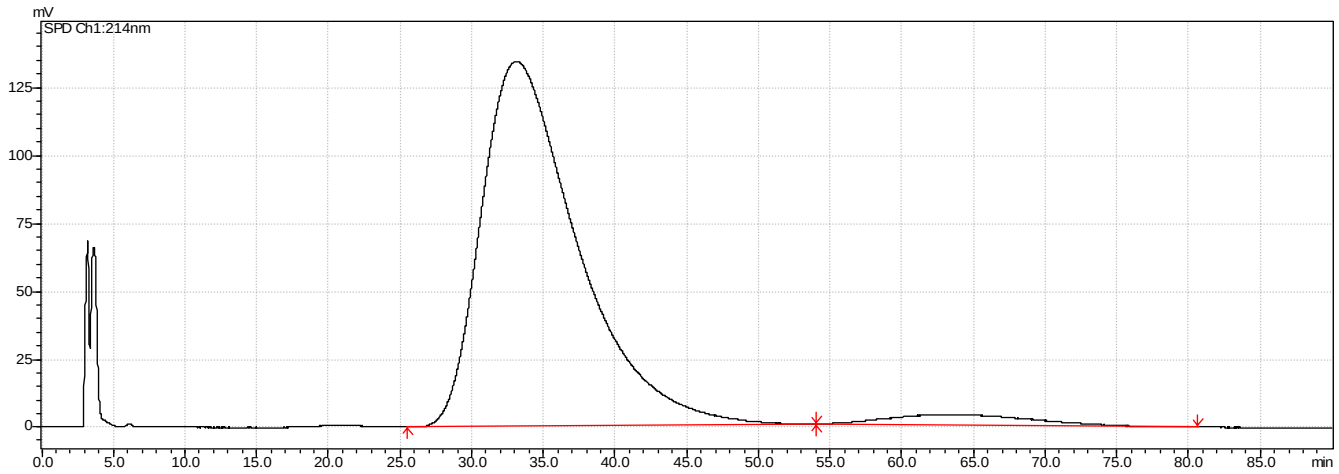
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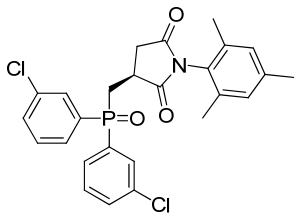
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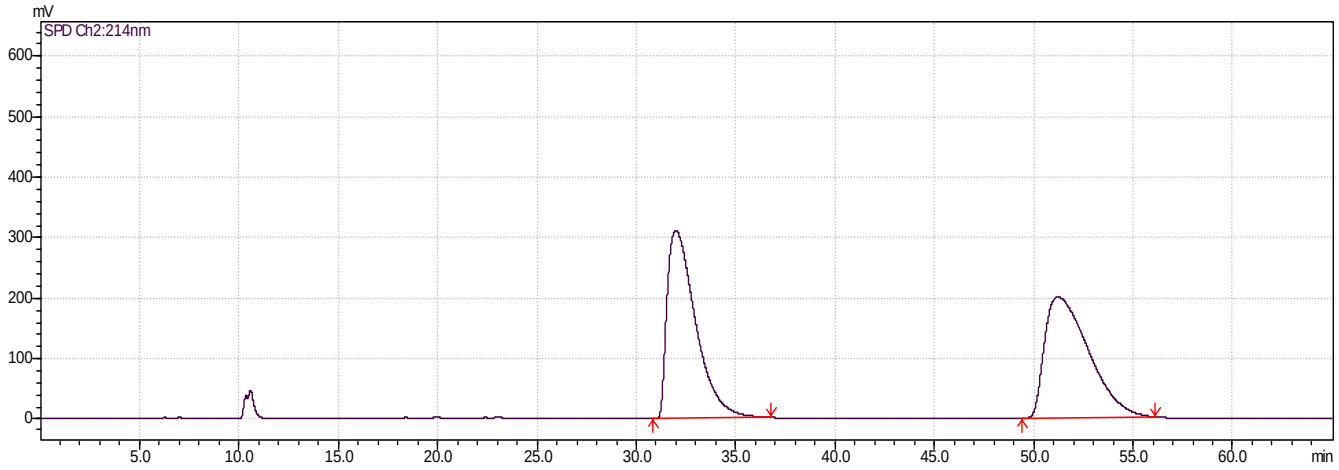
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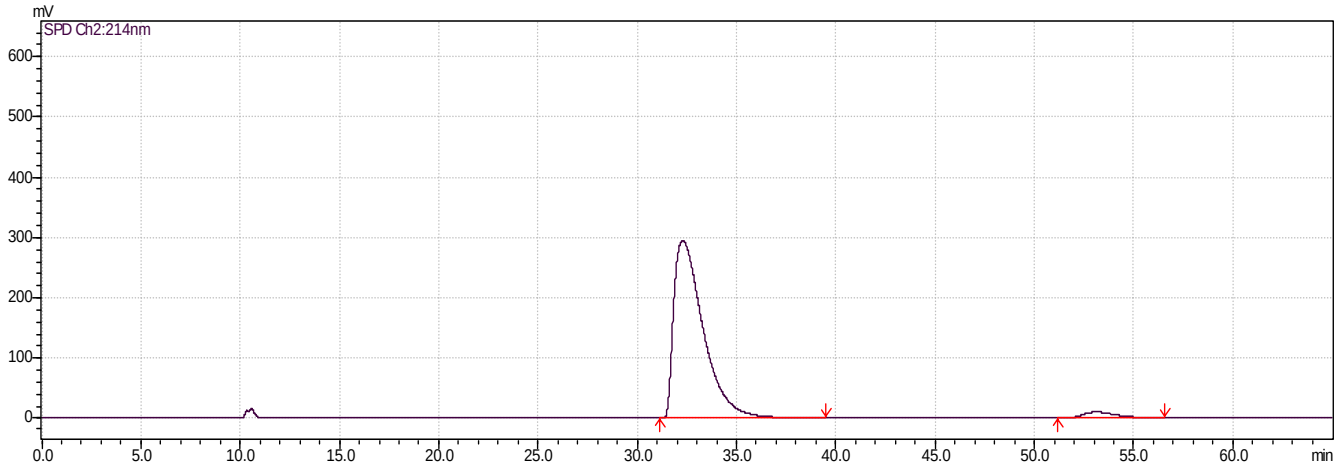
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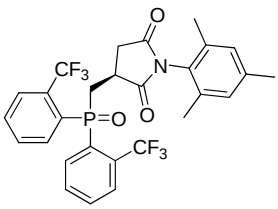
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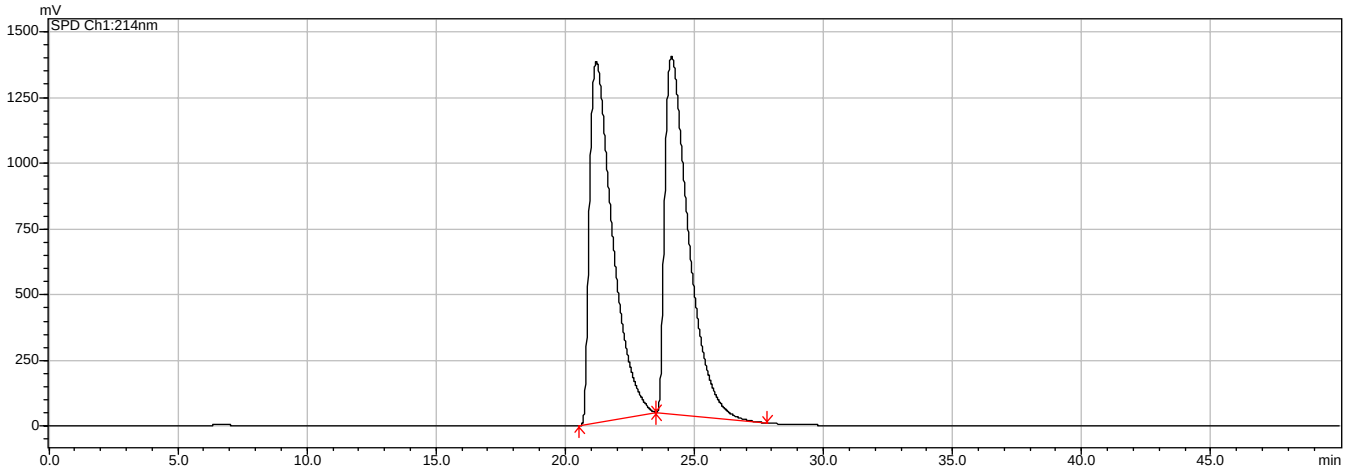
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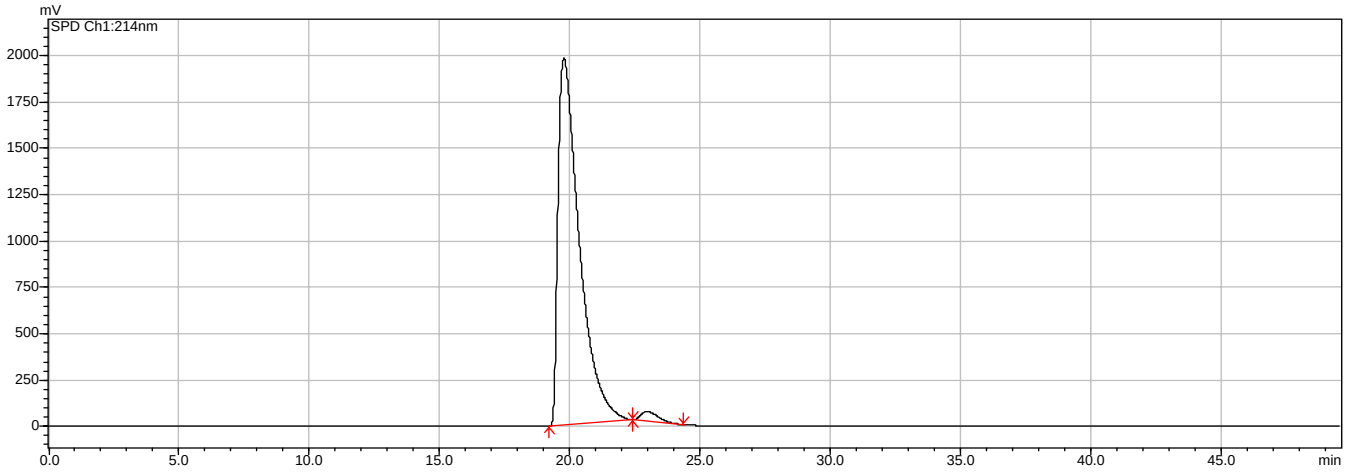
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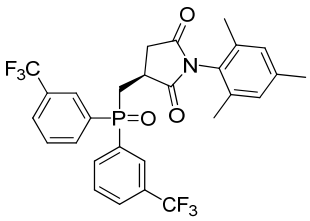
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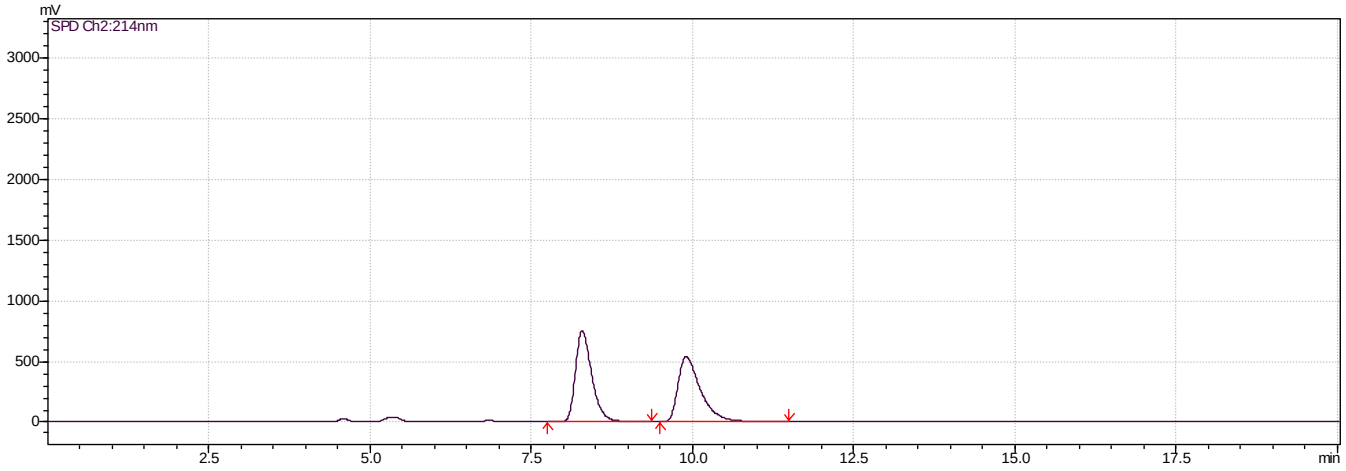
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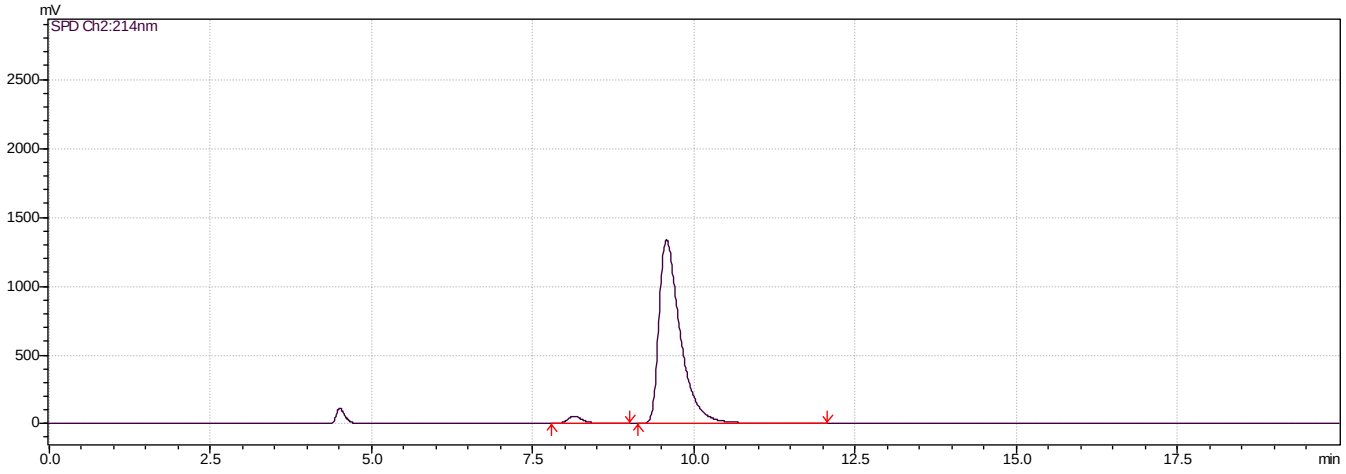
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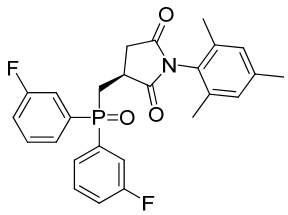
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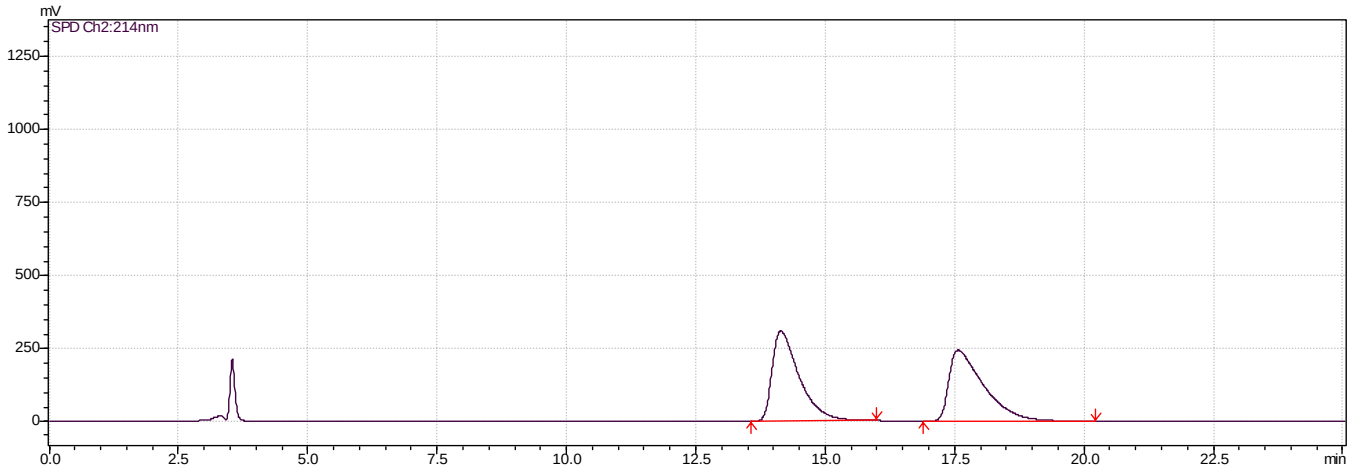
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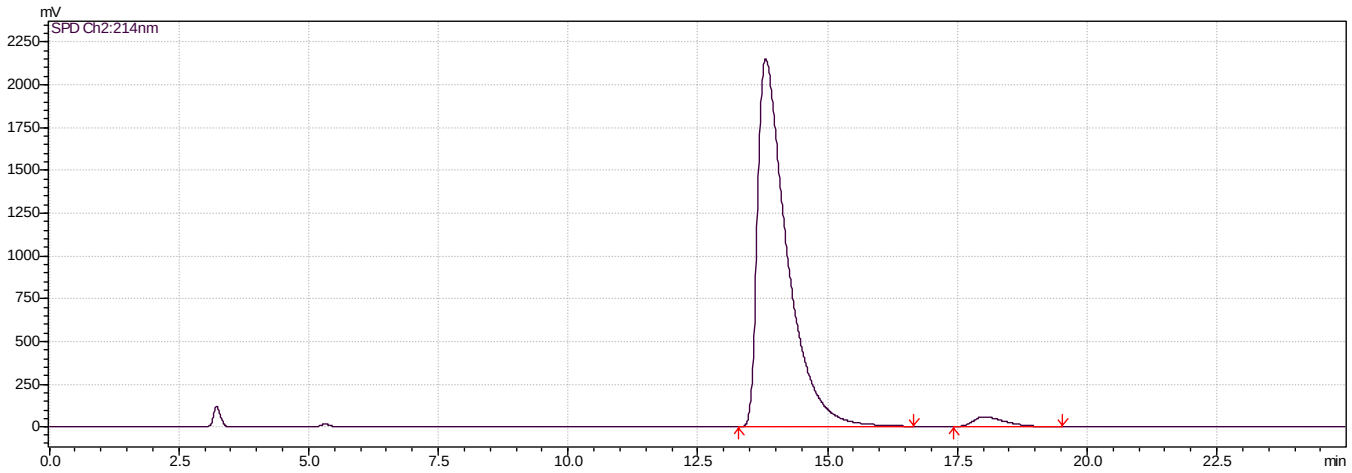
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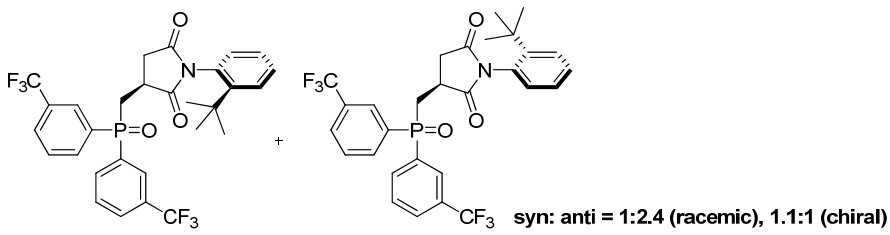
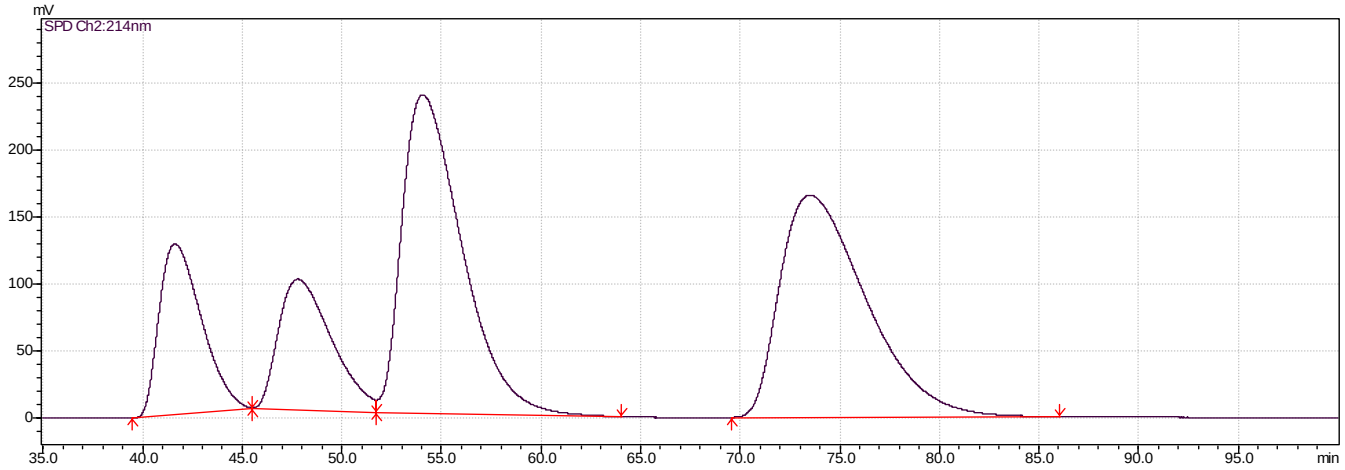
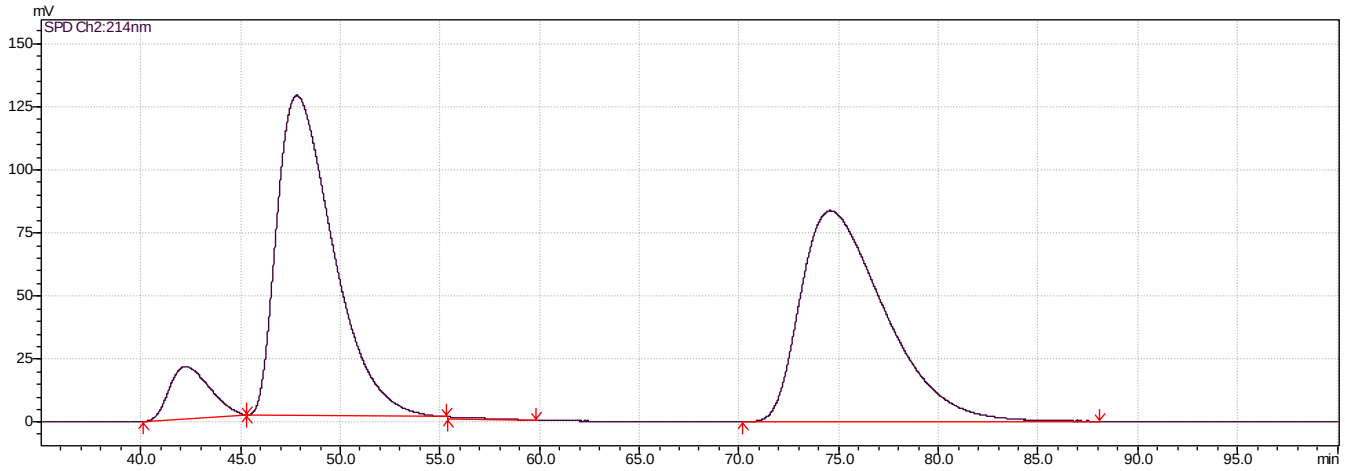
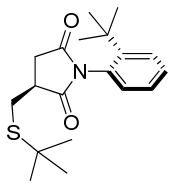


syn: anti = 1:2.4 (racemic), 1.1:1 (chiral)



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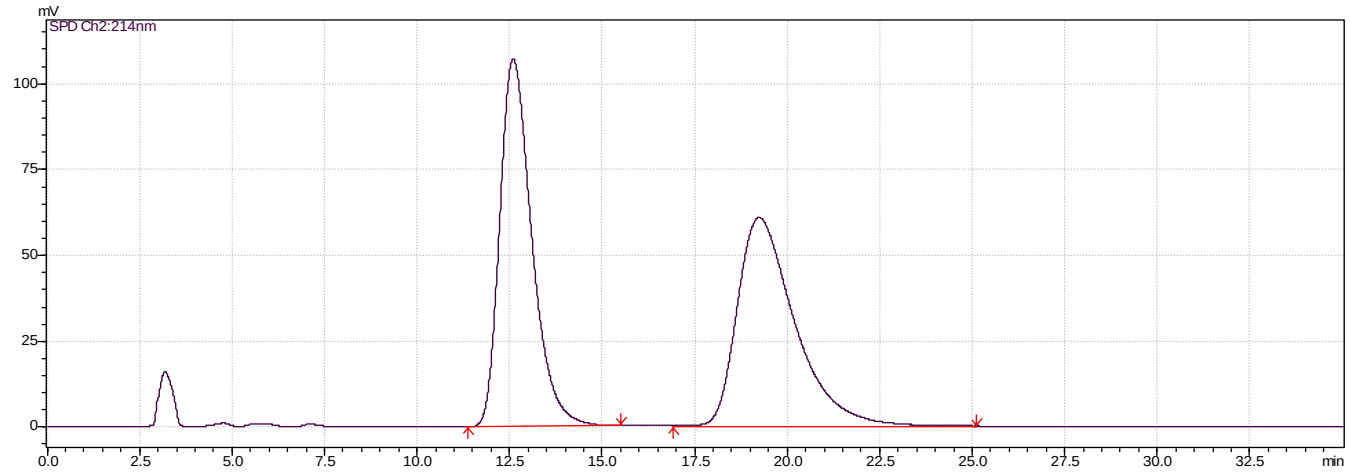
O
S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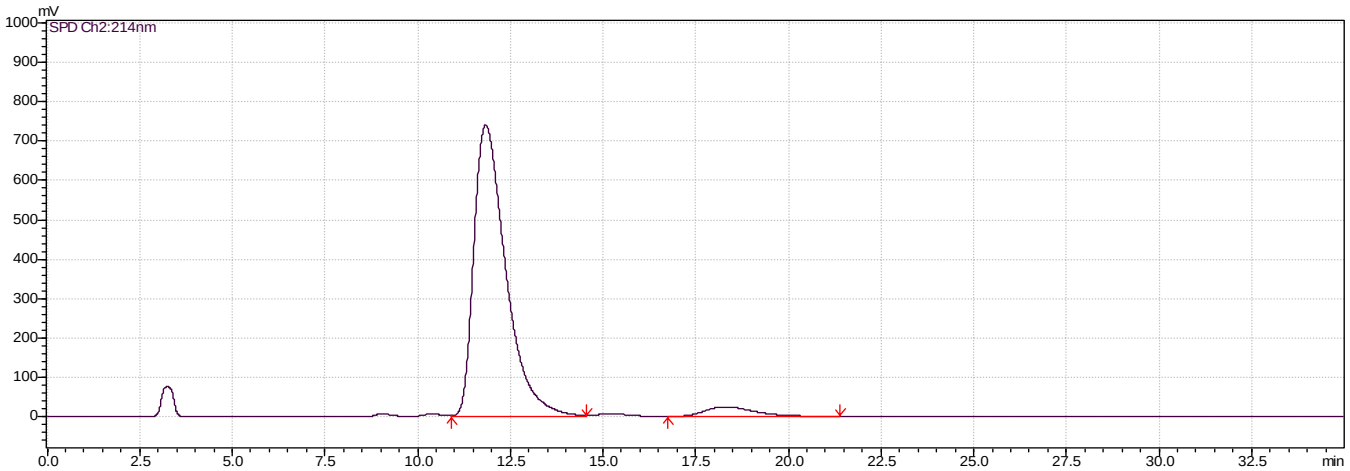
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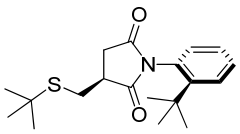
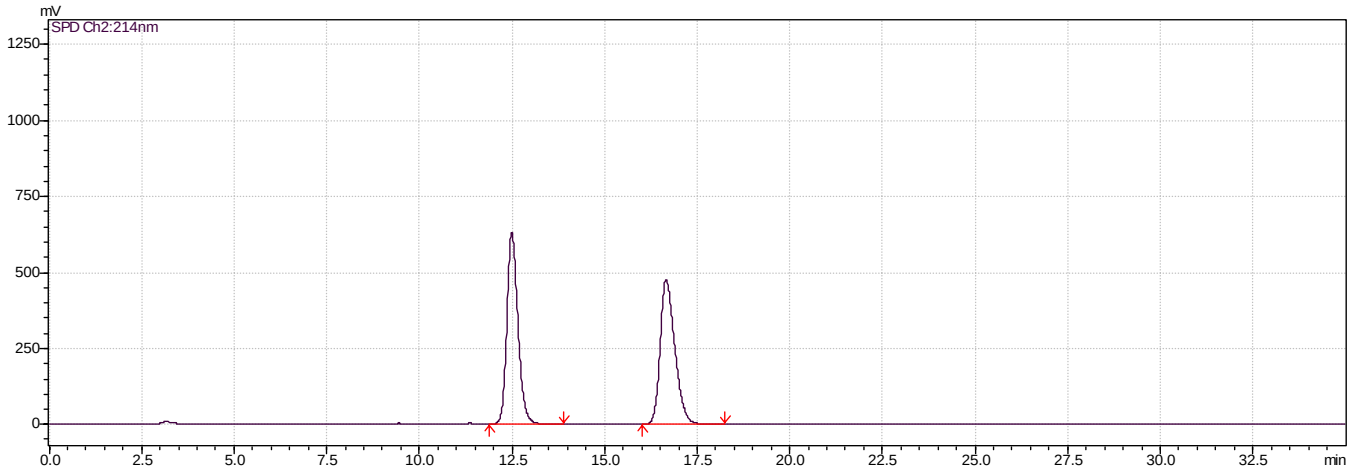
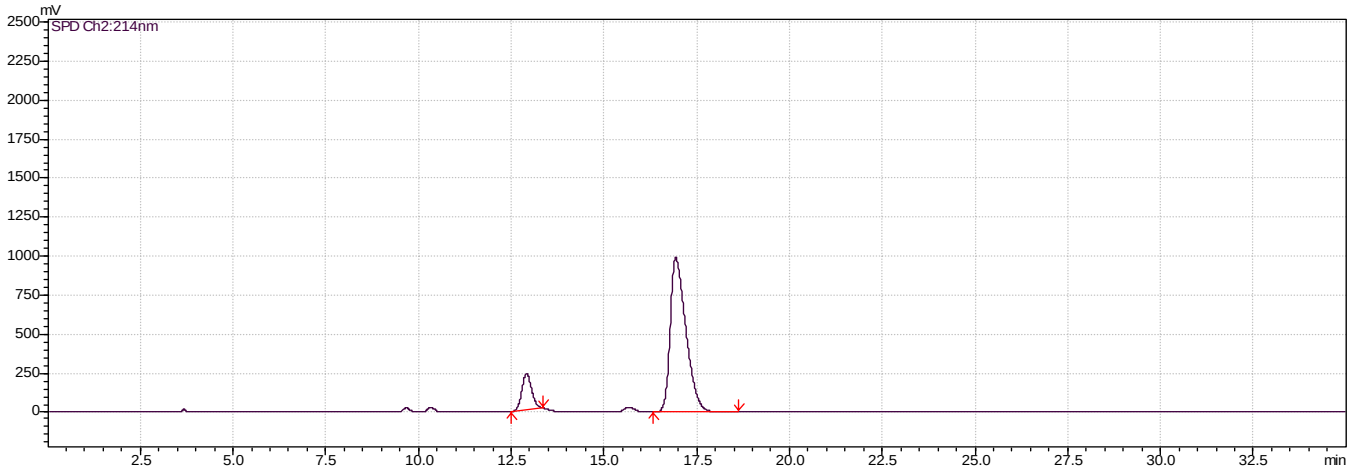
SPD Ch2:214nm
1000
900
800
700
600
500
400
300
200
100
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
22.5
25.0
27.5
30.0
32.5
min


O
N
S
O


mV
SPD Ch2:214nm
1250
1000
750
500
250
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
22.5
25.0
27.5
30.0
32.5
min


mV
SPD Ch2:214nm
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
22.5
25.0
27.5
30.0
32.5
min