

Lithiation-Electrophilic Trapping of *N*-Sulfonyl-activated Ethylene Aziridines

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Supporting Information Available: Full experimental procedures and characterisation data.

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General

Water is distilled water. Et₂O and THF were freshly distilled from sodium and benzophenone whereas CH₂Cl₂ was freshly distilled from CaH₂. *s*-BuLi was titrated against *N*-benzylbenzamide before use. Petrol refers to the fraction of petroleum ether with a boiling point range of 40-60 °C. PMDETA and diamines used in lithiation reactions were distilled before use. All reactions were carried out under O₂-free N₂ or Ar using oven-dried and/or flame dried glassware. Flash column chromatography was carried out using Fluka Silica gel 60 (0.035-0.070 mm particle size). Thin layer chromatography was carried using Merck F₂₅₄ aluminium-backed silica plates.

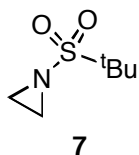
Proton (400 MHz) and carbon (100.6 MHz) NMR spectra were recorded on a Jeol ECX-400 instrument using an internal deuterium lock. All samples were recorded in CDCl₃. Chemical shifts are quoted in parts per million and referenced to CHCl₃ (7.27 for ¹H NMR and 77.0 for ¹³C NMR spectroscopy). Carbon NMR spectra were recorded with broadband proton decoupling and were assigned using DEPT and HSQC experiments. Infra-red spectra were recorded on an ATI Matteson Genesis FT-IR spectrometer. Chemical ionisation and high resolution mass spectra were recorded on a Fisons Analytical (VG) Autospec spectrometer. Electrospray ionisation low and high resolution mass spectra were recorded on a Bruker Daltronics micrOTOF spectrometer. Melting points were measured on a Gallenkamp melting point apparatus.

Experimental procedures and characterisation data

General procedure A: Lithiation-trapping of *N*-sulfonyl aziridines (external)

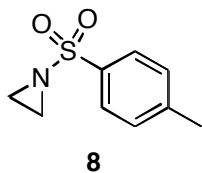
sec-BuLi (1.2-3.0 eq) was added dropwise to a stirred solution of PMDETA (pentamethyldiethylenetriamine), TMEDA or (–)-sparteine (1.2-3.0 eq) in THF or Et₂O (2 mL) at –78 °C under N₂. After stirring for 15 min at –78 °C, the solution was added dropwise *via* canula to a stirred solution of aziridine (0.30 mmol) in THF or Et₂O (3 mL) at –78 °C under N₂. After stirring for 1 min at –78 °C, freshly distilled electrophile (0.90 mmol, 3.0 eq) was added and stirred at –78 °C for a further 1 h. Then, saturated NH₄Cl_(aq) (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined Et₂O extracts were dried (MgSO₄) and evaporated under reduced pressure to give the crude product.

1-(*tert*-Butylsulfonyl)aziridine **7**



tert-Butylsulfinyl chloride (2.54 g, 18.0 mmol) was added to a stirred solution of ethanolamine (500 mg, 8.2 mmol) and Et₃N (2.85 mL, 16.4 mmol) in 5:1 MeCN-DMF (25 mL) at 0 °C under N₂. The resulting solution was allowed to warm to rt and stirred at rt for 16 h. Then, the reaction mixture was washed with 5% NaHCO_{3(aq)} (2 x 20 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude sulfinamido sulfinate. Then, *m*-CPBA (4.45 g, 18.0 mmol) was added to a stirred solution of the crude sulfinamido sulfinate in CH₂Cl₂ (60 mL) at 0 °C under N₂. After stirring at rt for 16 h, 20% Na₂SO_{3(aq)} (20 mL) was added and the mixture was stirred for 20 min. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 x 20 mL). The combined organic extracts were washed with 20% Na₂SO_{3(aq)} (20 mL) and saturated NaHCO_{3(aq)} (20 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude sulfonamide. A stirred mixture of crude sulfonamide and K₂CO₃ (2.26 g, 16.4 mmol) in MeCN (60 mL) was heated at 45 °C under N₂ for 16 h. After cooling, the reaction mixture was diluted with CH₂Cl₂ (20 mL). The mixture was washed with water (20 mL) and brine (20 mL), dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-Et₂O (1:1) as eluent gave aziridine **7** (584 mg, 48%) as a colourless oil, *R*_F (1:1 petrol-Et₂O) 0.3; ν_{max} (CH₂Cl₂)/cm⁻¹ 1305 (SO₂) and 1128 (SO₂); δ_{H} (400 MHz, CDCl₃) 2.30 (4 H, s, CH₂N) and 1.45 (9 H, s, CMe₃); δ_{C} (100.6 MHz; CDCl₃) 59.3 (CMe₃), 26.7 (CH₂N) and 24.0 (CMe₃); *m/z* (CI; NH₃) 181 [100%, (M + NH₄)⁺] and 164 (10) [Found (M + NH₄)⁺ 181.1006 C₆H₁₃NO₂S requires M + NH₄, 181.1011]. Spectroscopic data are identical with those reported in the literature.¹

1-(4-Methylphenylsulfonyl) aziridine **8**

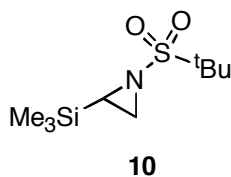


p-Toluenesulfonyl chloride (1.15 g, 6.0 mmol) was added to a stirred solution of ethanolamine (366 mg, 6.0 mmol) and Et₃N (1.68 mL, 2.0 mmol) in CH₂Cl₂ (10 mL) at 0 °C under N₂. The resulting solution was

allowed to warm to rt and stirred at rt for 16 h. Then, the reaction mixture was washed with 5% $\text{NaHCO}_{3(\text{aq})}$ (2 x 10 mL), dried (MgSO_4) and evaporated under reduced pressure to give the crude sulfonamido alcohol. Then, pyridine (2.74 mL, 30.0 mmol) was added dropwise to a stirred solution of methanesulfonyl chloride (2.54 mL, 30.0 mmol) in CH_2Cl_2 (70 mL) at 0 °C under N_2 . After stirring for 20 min, a solution of the crude sulfonamido alcohol in CH_2Cl_2 (5 mL) was added and the resulting solution was stirred for 20 min. Then, the solution was heated at reflux for 16 h. The solution was allowed to cool to rt and washed with brine (20 mL), dried (MgSO_4) and evaporated under reduced pressure to give the crude sulfonamido mesylate. A stirred mixture of the crude sulfonamido mesylate and K_2CO_3 (3.32 g, 24.0 mmol) in MeCN (70 mL) was heated at 45 °C under N_2 for 16 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (20 mL). The mixture was washed with water (20 mL) and brine (20 mL), dried (MgSO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-EtOAc (1:1) as eluent gave aziridine **8** (587 mg, 53%) as a colourless oil, δ_{H} (400 MHz, CDCl_3) 7.78 (2 H, d, J 8.0, $o\text{-C}_6\text{H}_4\text{SO}_2$), 7.31 (2 H, d, J 8.0, $m\text{-C}_6\text{H}_4\text{SO}_2$), 2.40 (3 H, s, Me) and 2.32 (4 H, br s, CH_2N). Spectroscopic data are identical with those reported in the literature.²

1-(*tert*-Butylsulfonyl)-2-(trimethylsilyl)aziridine **10**

(Table 1, entry 1)

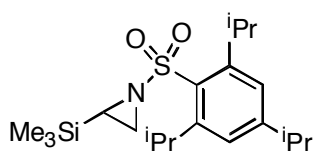


sec-BuLi (0.92 mL of a 1.0 M solution in cyclohexane, 0.92 mmol) was added dropwise to a stirred solution of PMDETA (0.19 mL, 0.92 mmol) in THF (3 mL) at –78 °C under N_2 . After stirring for 15 min at –78 °C, the solution was added dropwise *via* a canula to a stirred solution of aziridine **7** (50 mg, 0.31 mmol) and trimethylsilyl chloride (0.11 mL, 0.93 mmol) in THF (2 mL) at –78 °C under N_2 . After stirring for 1 h at –78 °C, saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined Et_2O extracts were dried (MgSO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **10** (26 mg, 36%) as a colourless oil, R_{F} (1:1 petrol-Et₂O) 0.3; $\nu_{\text{max}}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$ 1310 (SO_2), 1212 (SiMe_3) and 1130 (SO_2); δ_{H} (400 MHz, CDCl_3) 2.58 (1 H, d, J

8.0, CHNSi), 2.03 (1 H, d, J 5.5, CH₂N), 1.96 (1 H, dd, J 8.0 and 5.5, CH₂N), 1.48 (9 H, s, CMe₃) and 0.09 (9 H, s, SiMe₃); δ_c (100.6 MHz; CDCl₃) 59.2 (CMe₃), 31.1 (CH₂N), 27.5 (CHN), 24.3 (CMe₃) and -3.4 (SiMe₃); m/z (CI; NH₃) 236 [100%, (M + H)⁺] and 116 (30) [Found (M + H)⁺ 236.1150. C₉H₂₁NO₂SiS requires $M + H$, 236.1141] and starting aziridine **7** (25 mg, 50%). Spectroscopic data are identical with those reported in the literature.¹

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 1, entry 4)

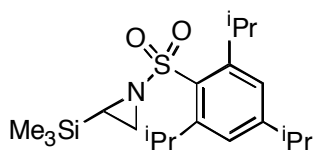


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sec-BuLi (0.8 mL of a 1.2 M solution in cyclohexane, 0.96 mmol) was added dropwise to a stirred solution of (–)-sparteine (0.22 mL, 0.96 mmol) in THF (3 mL) at –78 °C under N₂. After stirring for 15 min at –78 °C, the solution was added dropwise *via* a canula to a stirred solution of aziridine **9** (100 mg, 0.32 mmol) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) in THF (2 mL) at –78 °C under N₂. After stirring for 1 h at –78 °C, saturated NH₄Cl_(aq) (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined Et₂O extracts were dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **12** (81 mg, 12%) and starting aziridine **9** (15 mg, 52%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 1, entry 5)



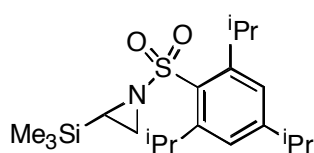
12

sec-BuLi (0.8 mL of a 1.2 M solution in cyclohexane, 0.96 mmol) was added dropwise to a stirred solution of PMDETA (0.2 mL, 0.96 mmol) in THF (3 mL) at –78 °C under N₂. After stirring for 15 min at

–78 °C, the solution was added dropwise *via* a canula to a stirred solution of aziridine **9** (100 mg, 0.32 mmol) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) in THF (2 mL) at –78 °C under N₂. After stirring for 4 h at –78 °C, saturated NH₄Cl_(aq) (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined Et₂O extracts were dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **12** (77 mg, 63%) and starting aziridine **9** (30 mg, 30%).

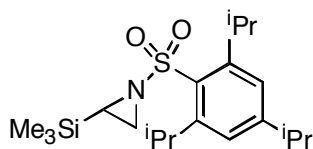
1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 1, entry 6)

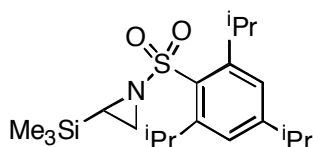


12

sec-BuLi (0.8 mL of a 1.2 M solution in cyclohexane, 0.96 mmol) was added dropwise to a stirred solution of PMDETA (0.2 mL, 0.96 mmol) in THF (3 mL) at –78 °C under N₂. After stirring for 15 min at –78 °C, the solution was added dropwise *via* a canula to a stirred solution of aziridine **9** (100 mg, 0.32 mmol) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) in THF (2 mL) at –78 °C under N₂. After stirring for 1 h at –78 °C and allowing the mixture to warm to rt over 3 h, saturated NH₄Cl_(aq) (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined Et₂O extracts were dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **12** (71 mg, 58%) and starting aziridine **9** (18 mg, 18%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine 12**(Table 1, entry 7)****12**

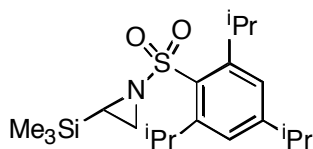
sec-BuLi (0.32 mL of a 1.2 M solution in cyclohexane, 0.38 mmol) was added dropwise to a stirred solution of PMDETA (0.08 mL, 0.38 mmol) in THF (3 mL) at -78°C under N_2 . After stirring for 15 min at -78°C , the solution was added dropwise *via* a canula to a stirred solution of aziridine **219** (100 mg, 0.32 mmol) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) in THF (2 mL) at -78°C under N_2 . After stirring for 1 h at -78°C , the solution was left in the dry-ice bath and allowed to warm slowly over 16 h and then saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined Et_2O extracts were dried (MgSO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol- Et_2O (10:1) as eluent gave silyl aziridine **12** (34 mg, 28%) and starting aziridine **9** (59 mg, 59%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine 12**(Table 2, entry 2)****12**

Using general procedure A, *sec*-BuLi (0.67 mL of a 1.2 M solution in cyclohexane, 0.80 mmol, 2.5 eq), PMDETA (0.17 mL, 0.80 mmol, 2.5 eq) in THF (2 mL), aziridine **9** (100 mg, 0.32 mmol) in THF (3 mL) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) gave the crude product. Purification by flash chromatography on silica with petrol- Et_2O (10:1) as eluent gave silyl aziridine **12** (56 mg, 46%) and starting aziridine **9** (40 mg, 40%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 2, entry 3)

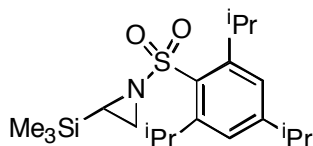


12

Using general procedure A, *sec*-BuLi (0.32 mL of a 1.2 M solution in cyclohexane, 0.38 mmol, 1.2 eq), PMDETA (0.08 mL, 0.38 mmol, 1.2 eq) in THF (2 mL), aziridine **9** (100 mg, 0.32 mmol) in THF (3 mL) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) gave the crude product. Only starting material was observed in the ¹H NMR spectrum of the crude product.

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 2, entry 4)

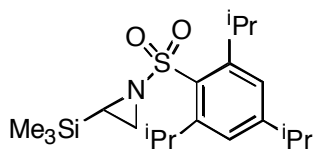


12

sec-BuLi (0.8 mL of a 1.2 M solution in cyclohexane, 0.96 mmol) was added dropwise to a stirred solution of PMDETA (0.2 mL, 0.96 mmol) in THF (3 mL) at -78°C under N_2 . After stirring for 15 min at -78°C , the solution was added dropwise *via* a canula to a stirred solution of aziridine **219** (100 mg, 0.32 mmol) in THF (2 mL) at -78°C under N_2 . After stirring for 15 min at -78°C , trimethylsilyl chloride (0.12 mL, 0.96 mmol) was added dropwise. After stirring for 1 h at -78°C , saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined Et_2O extracts were dried (MgSO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol- Et_2O (10:1) as eluent gave 2,4,6-tri-*iso*-propylsulfonamide **13** (70 mg, 78%) as a white solid.

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 2, entry 5)

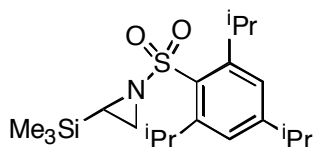


12

Using general procedure A, *sec*-BuLi (0.87 mL of a 1.1 M solution in cyclohexane, 0.96 mmol), TMEDA (0.15 mL, 0.96 mmol) in THF (2 mL), aziridine **9** (100 mg, 0.32 mmol) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) gave the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **12** (42 mg, 34%) and 2,4,6-tri-*iso*-propylsulfonamide **13** (57 mg, 62%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 2, entry 6)

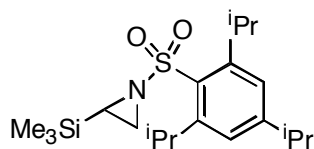


12

Using general procedure A, *sec*-BuLi (0.8 mL of a 1.0 M solution in cyclohexane, 0.8 mmol, 2.5 eq), TMEDA (0.12 mL, 0.8 mmol, 2.5 eq) in THF (2 mL), aziridine **9** (100 mg, 0.32 mmol) in THF (3 mL) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) gave the crude product. Purification by flash chromatography on silica with petrol-Et₂O (10:1) as eluent gave silyl aziridine **12** (27 mg, 22%) and 2,4,6-tri-*iso*-propylsulfonamide **13** (49 mg, 54%).

1-(2,4,6-Triisopropylphenylsulfonyl)-2-(trimethylsilyl)aziridine **12**

(Table 2, entry 7)



12

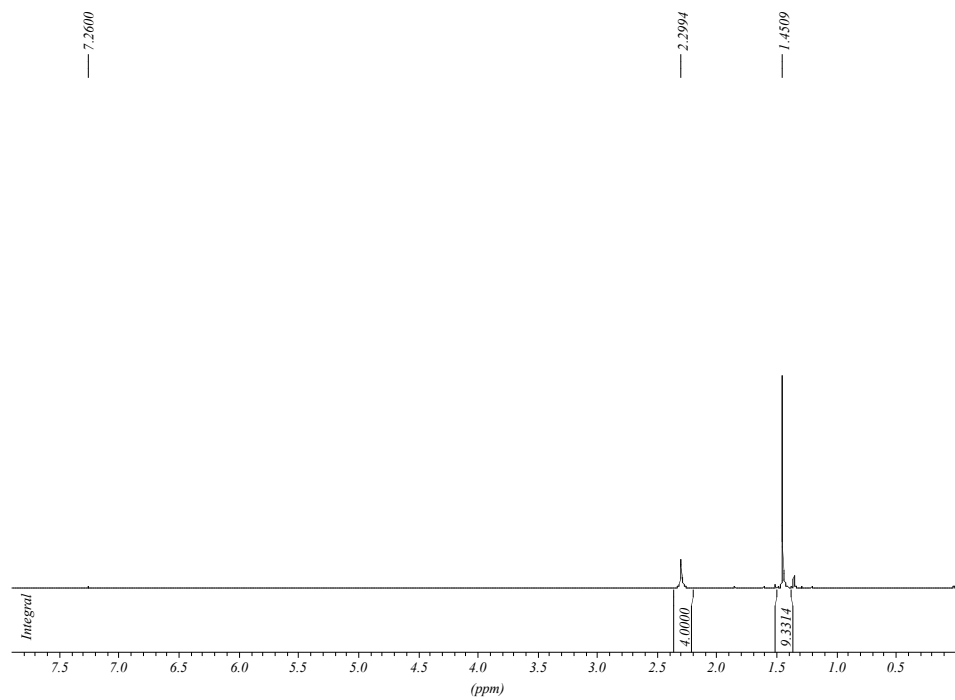
Using general procedure A, *sec*-BuLi (0.46 mL of a 1.05 M solution in cyclohexane, 0.48 mmol, 1.5 eq), TMEDA (0.08 mL, 0.48 mmol, 1.5 eq) in THF (2 mL), aziridine **9** (100 mg, 0.32 mmol) in THF (3 mL) and trimethylsilyl chloride (0.12 mL, 0.96 mmol) gave the crude product. Only starting material was observed in the ¹H NMR spectrum of the crude product.

References for supporting information:

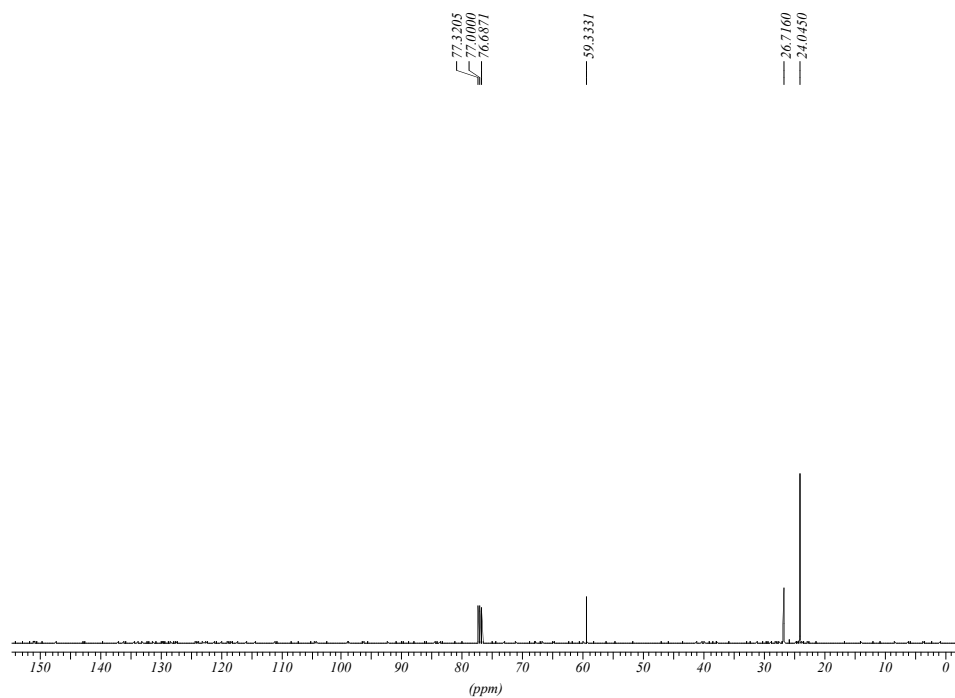
- (1) D. M. Hodgson, S. P. Hughes, A. L. Thompson and T. D. Heightman, *Org. Lett.* 2008, **10**, 3453.
- (2) R. Herges, A. Dikmans, U. Jana, F. Köhler, P. G. Jones, I. Dix, T. Fricke and D. König, *Eur. J. Org. Chem.* 2002, 3004.

$^1\text{H}/^{13}\text{C}$ NMR spectra:

Compound 7

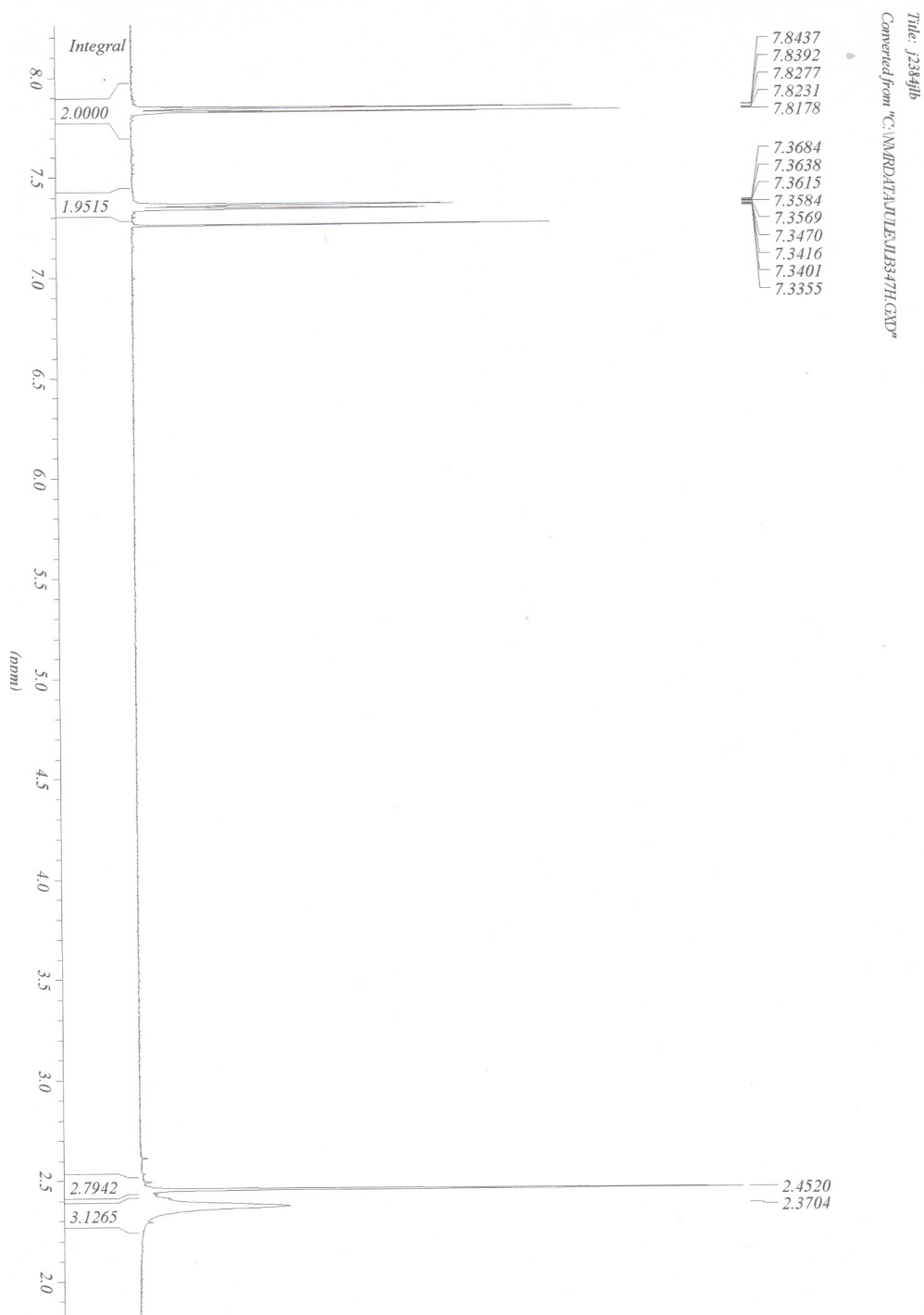
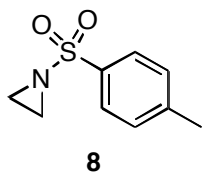


▷ NBus

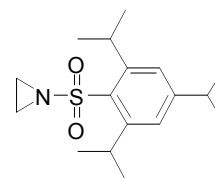
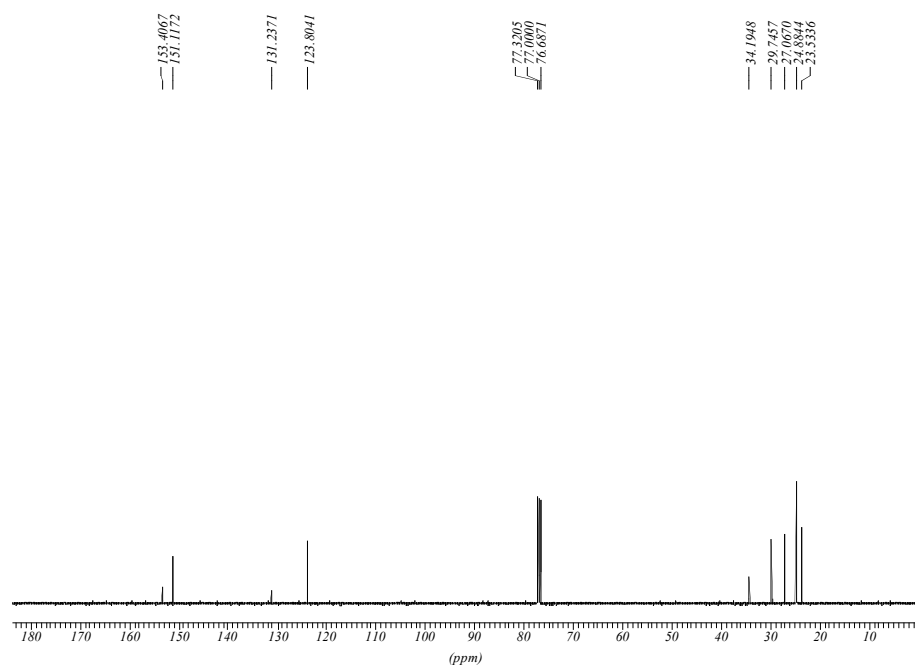
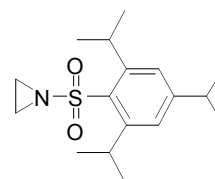
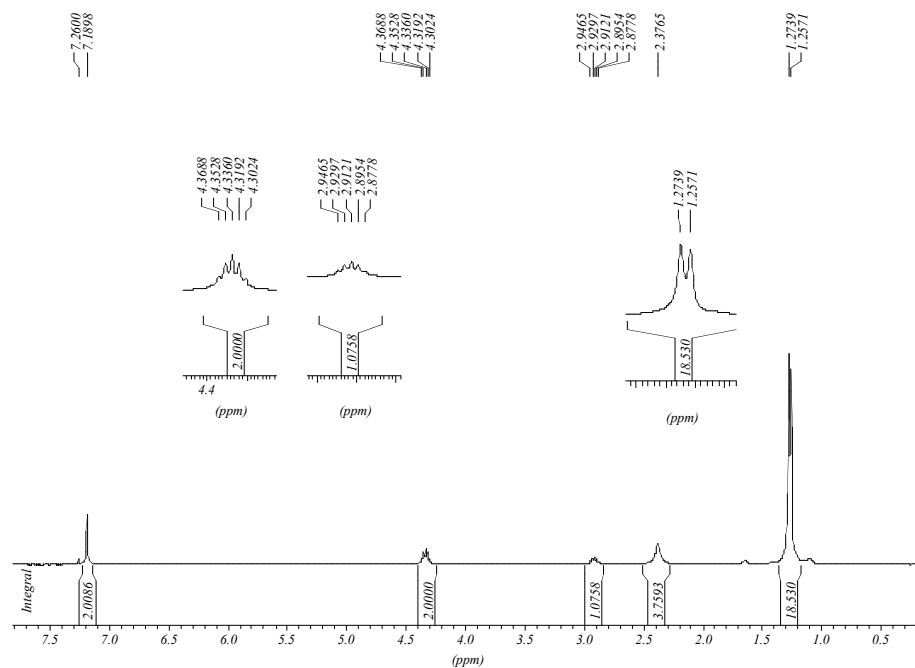


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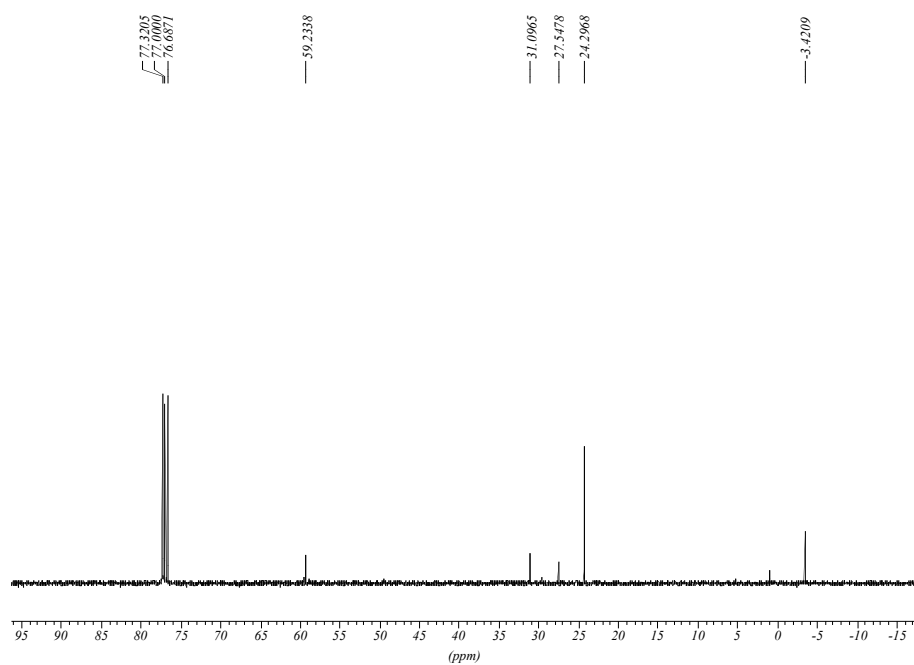
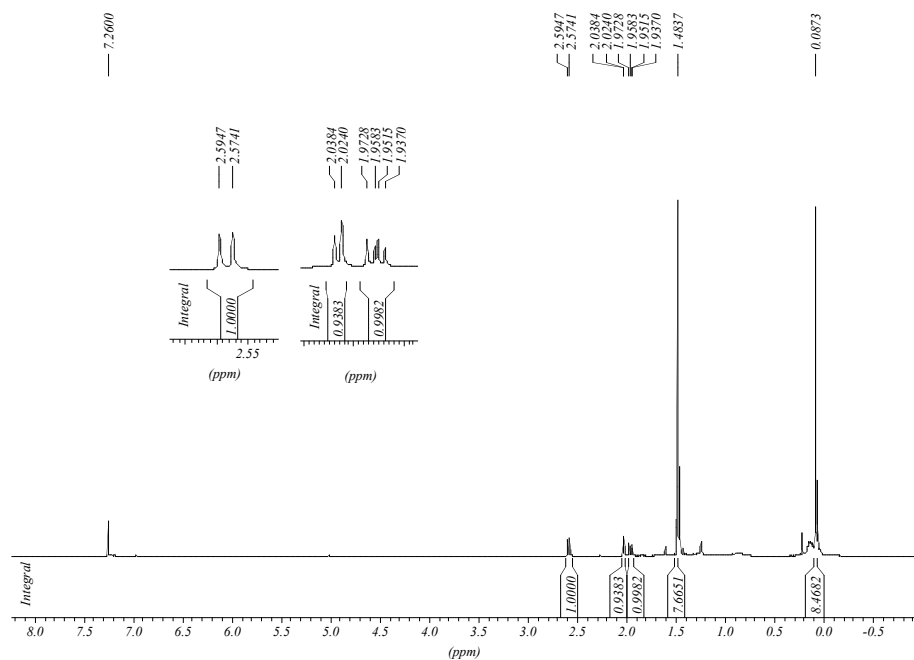
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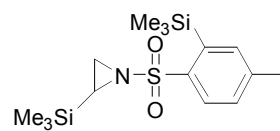
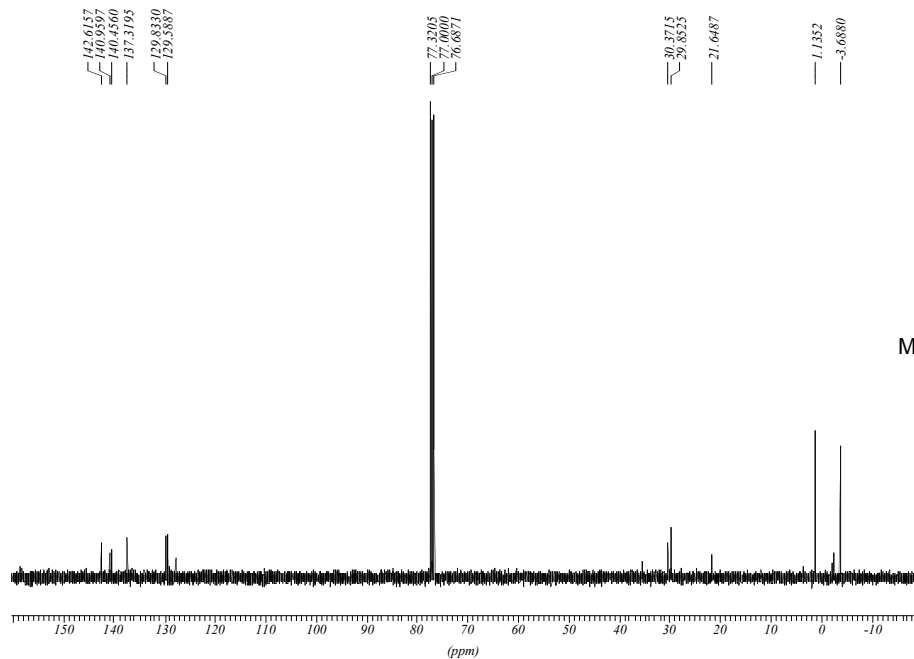
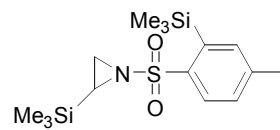
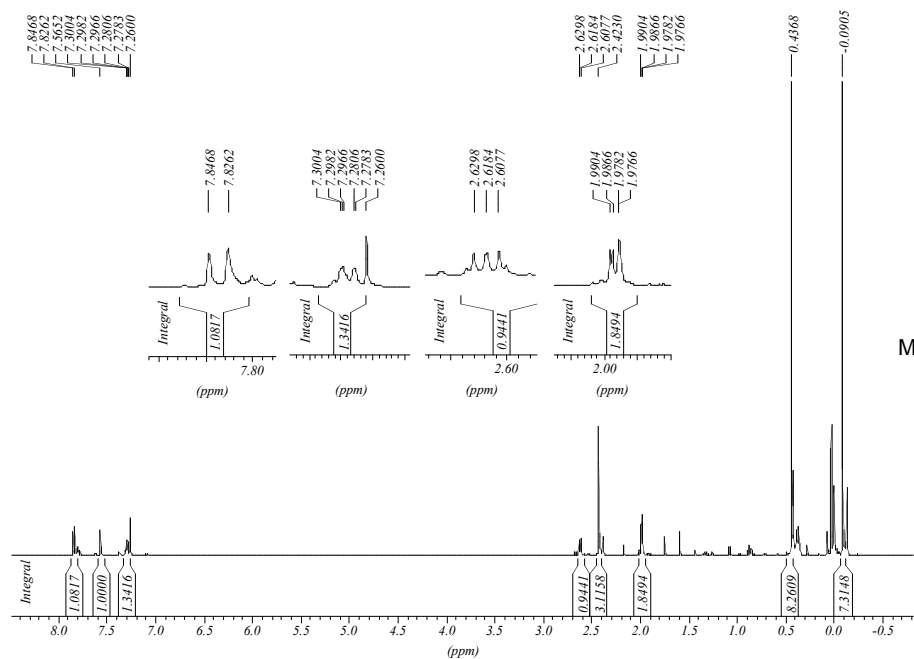
Compound 9



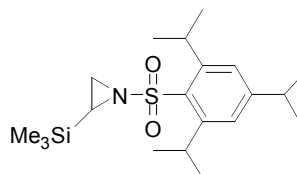
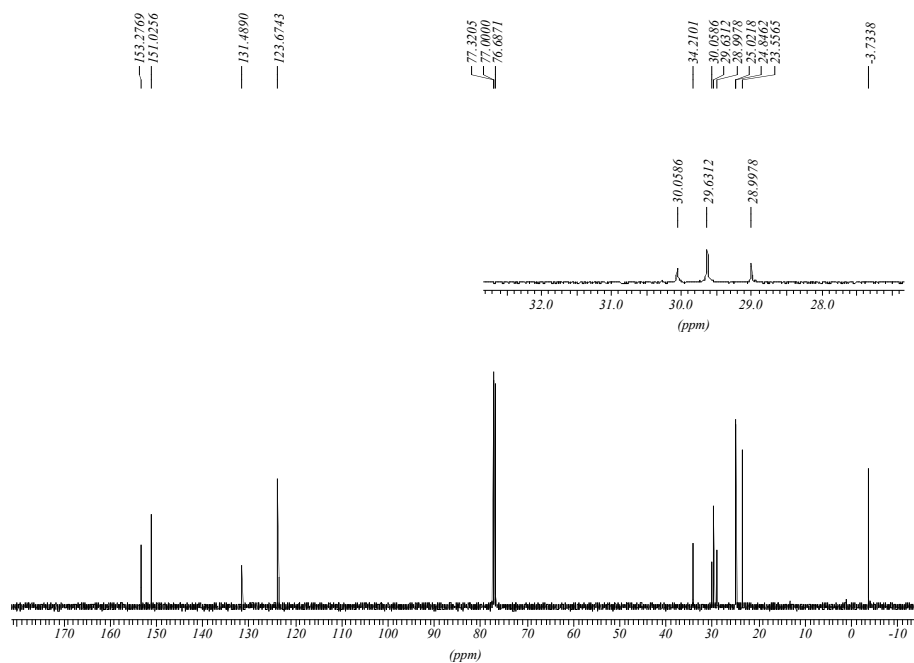
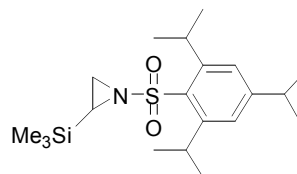
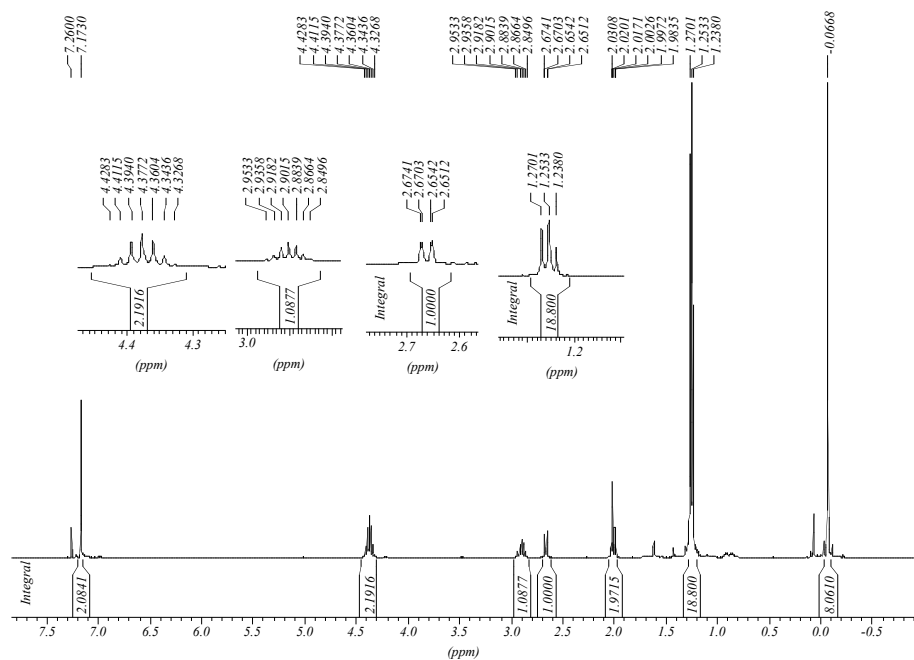
Compound 10



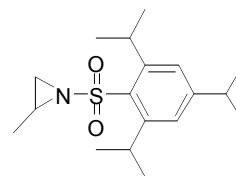
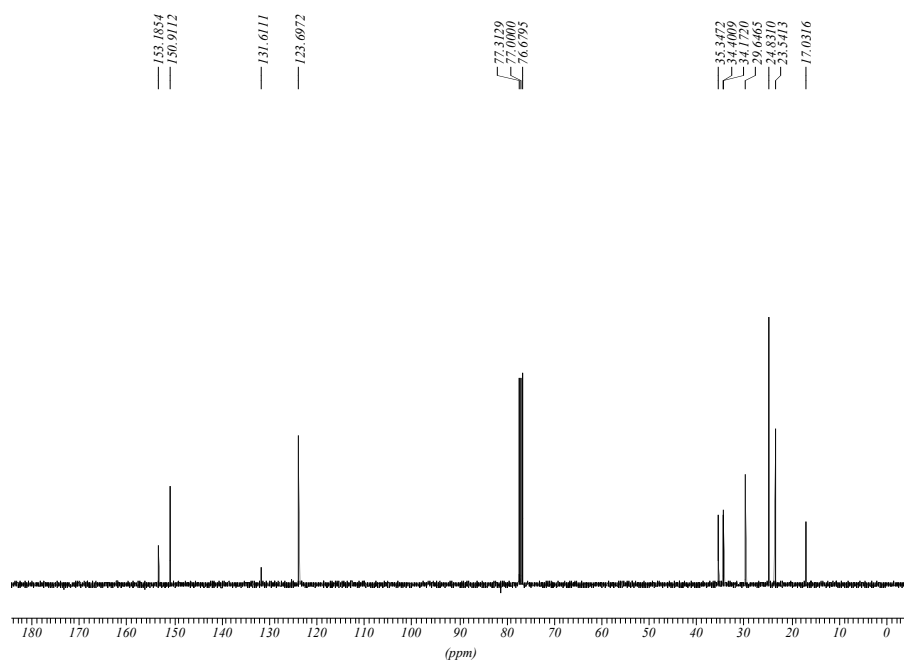
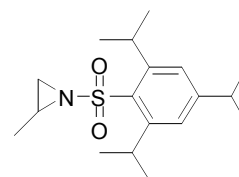
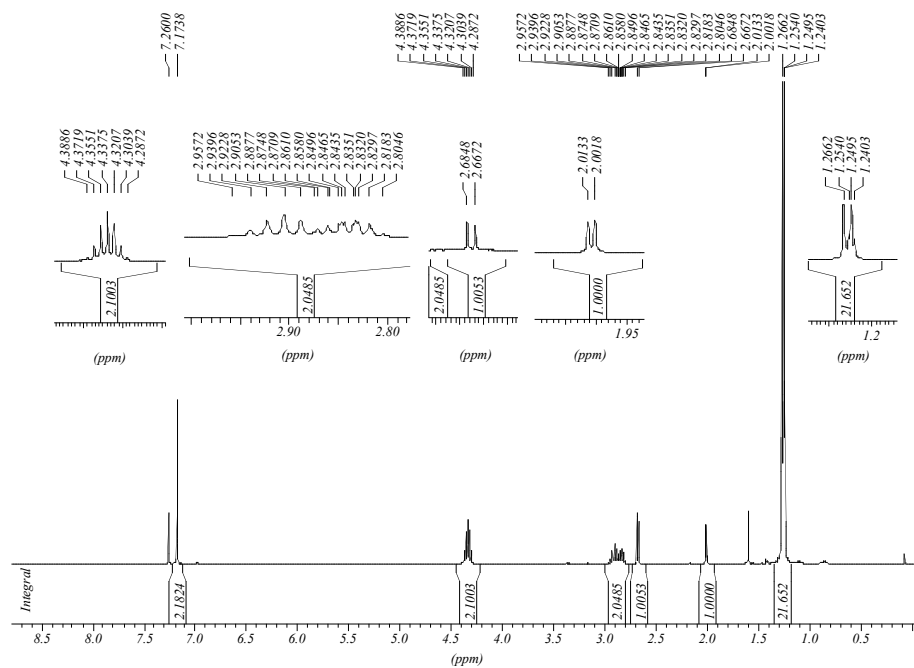
Compound 11



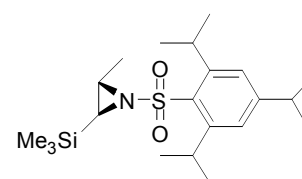
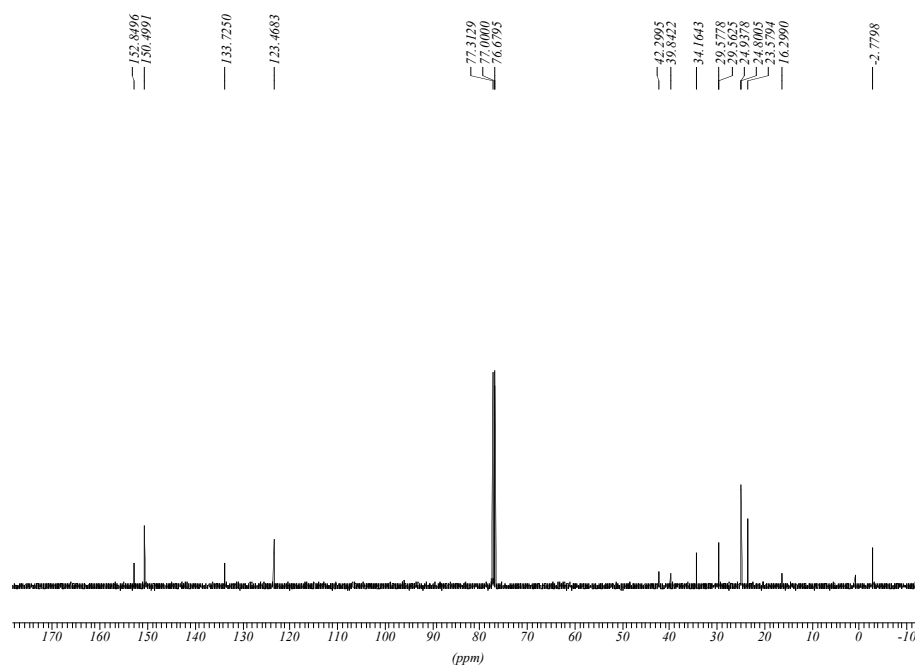
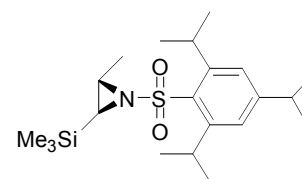
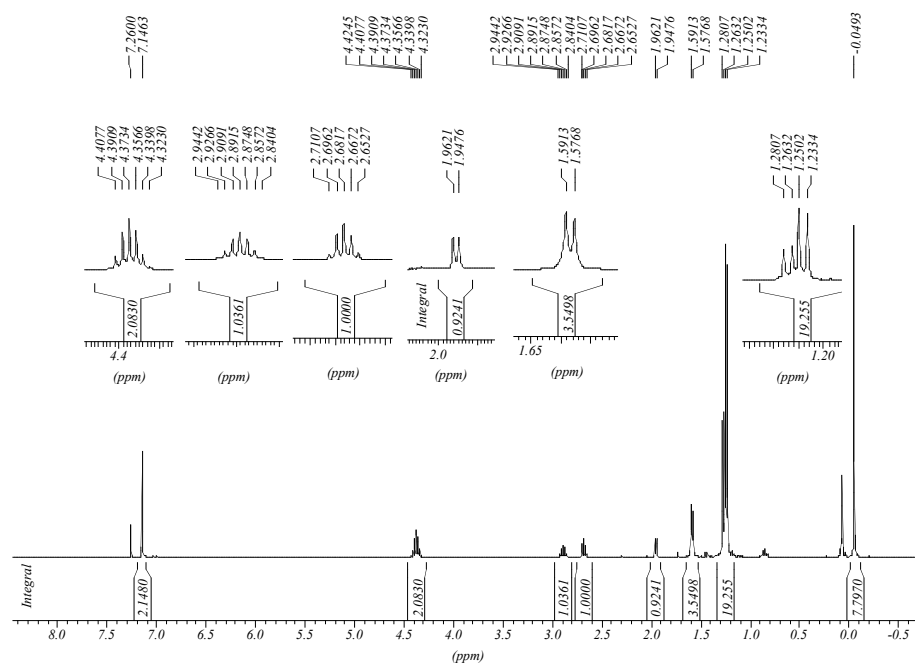
Compound 12



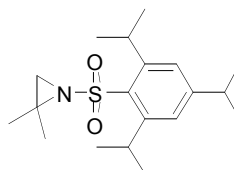
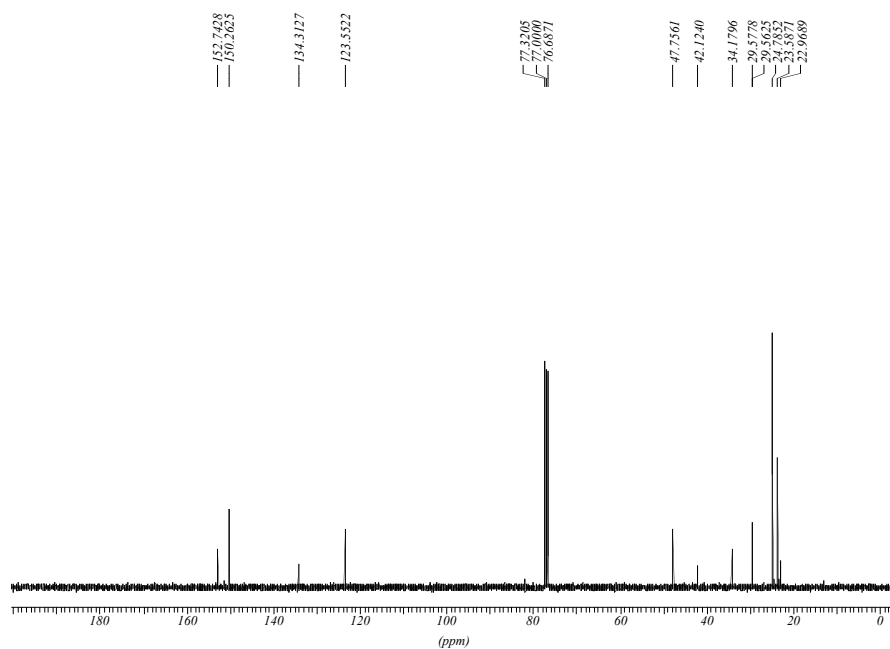
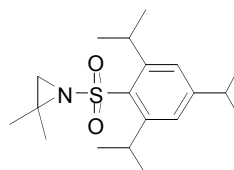
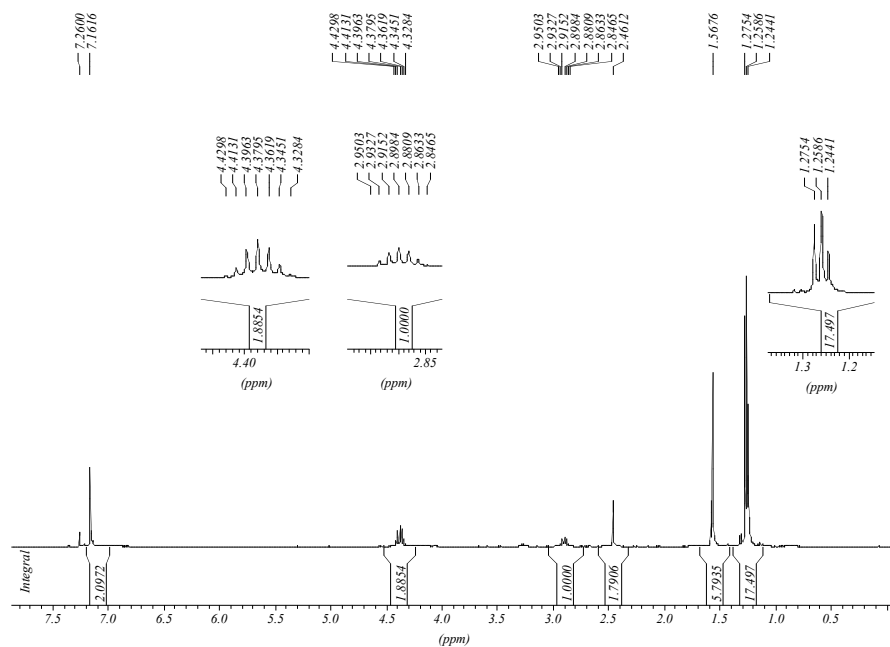
Compound 14



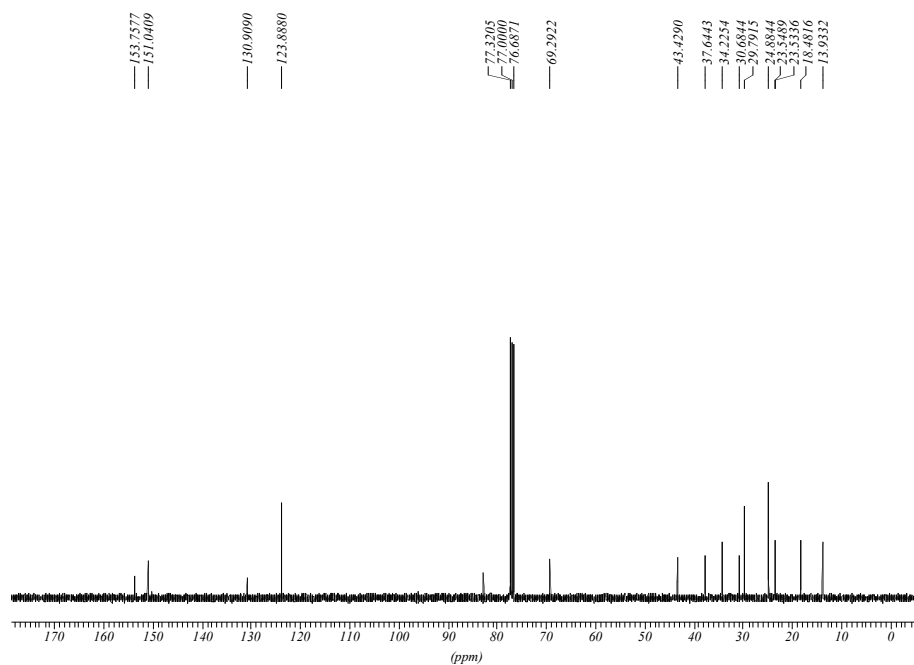
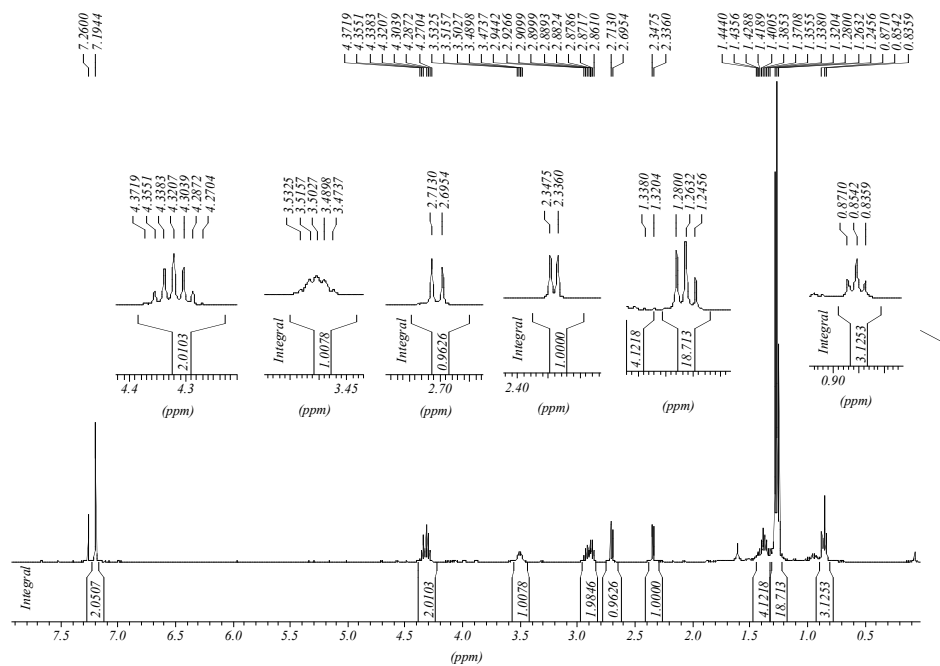
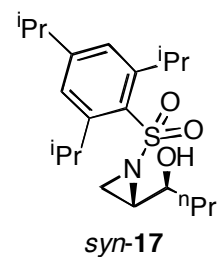
Compound 15



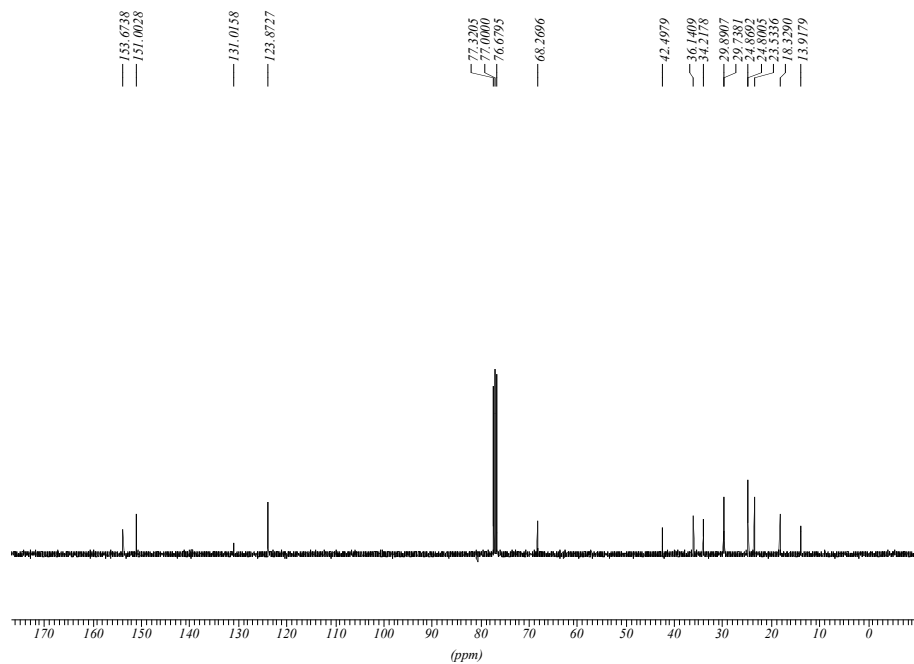
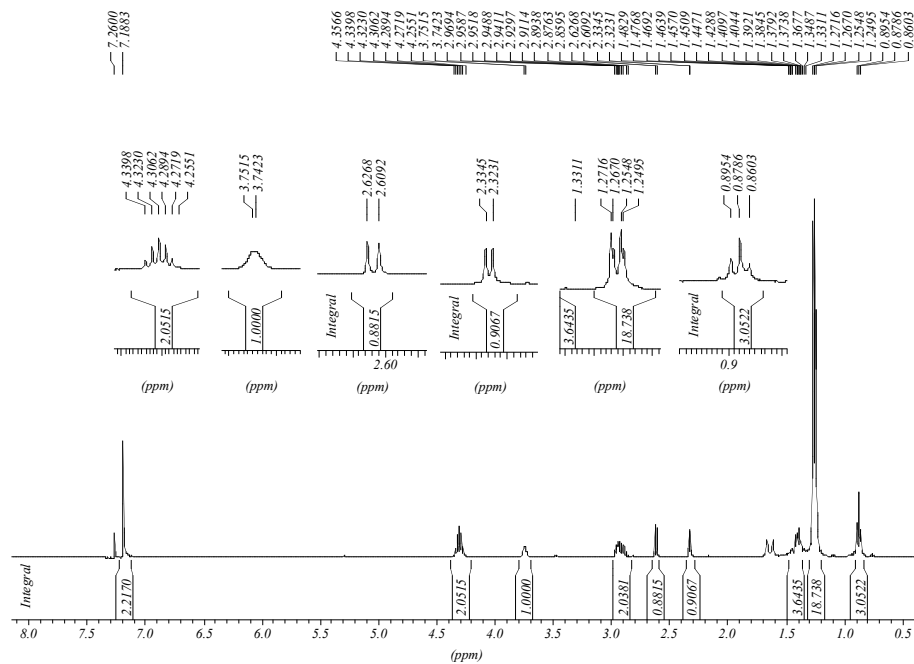
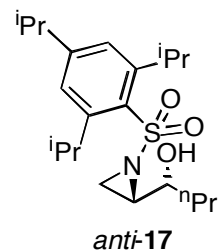
Compound 16



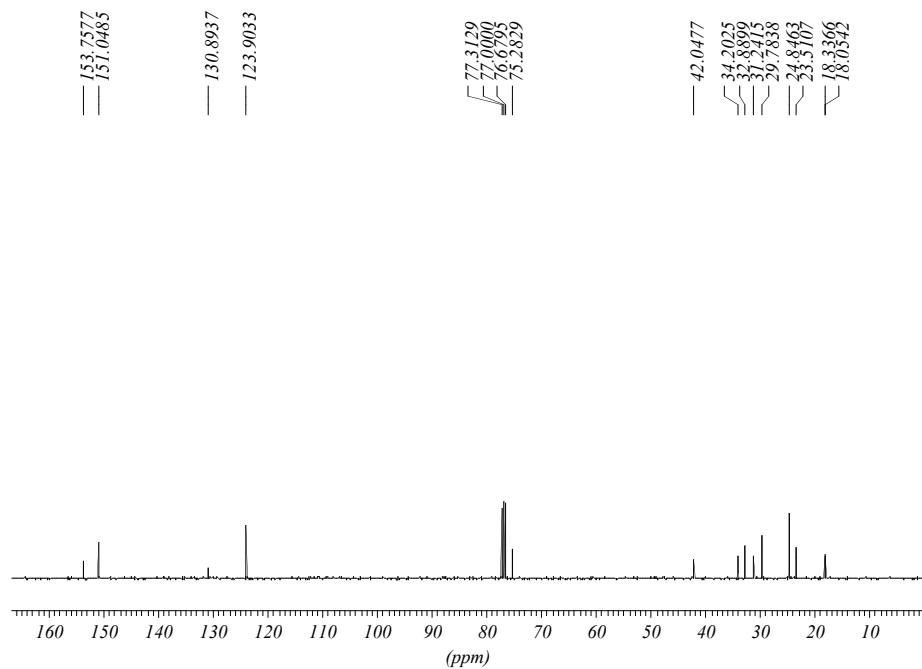
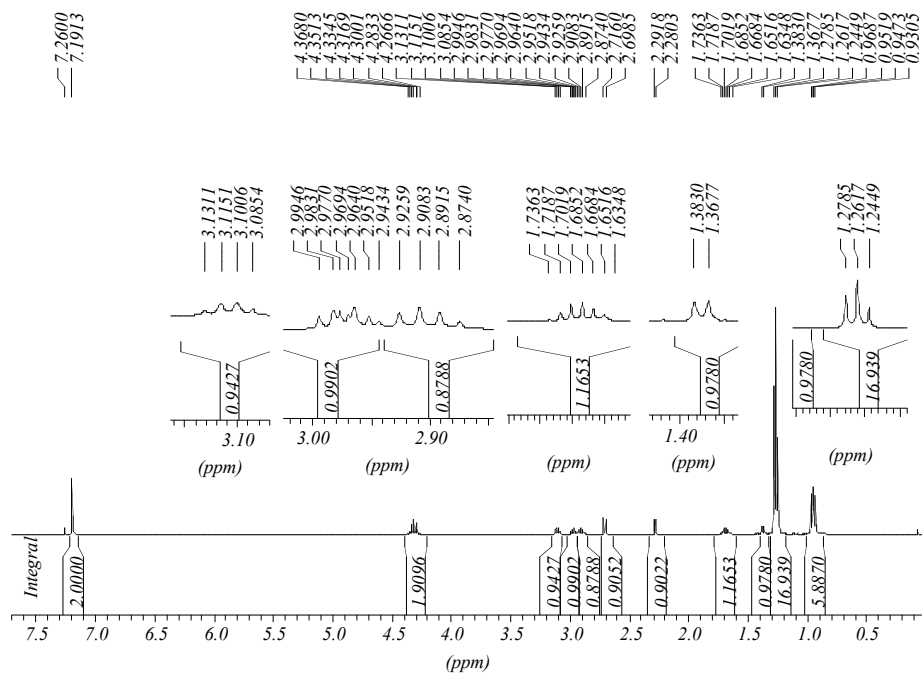
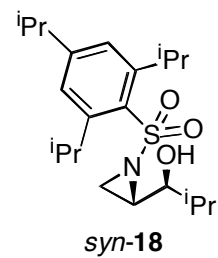
Compound *syn-17*



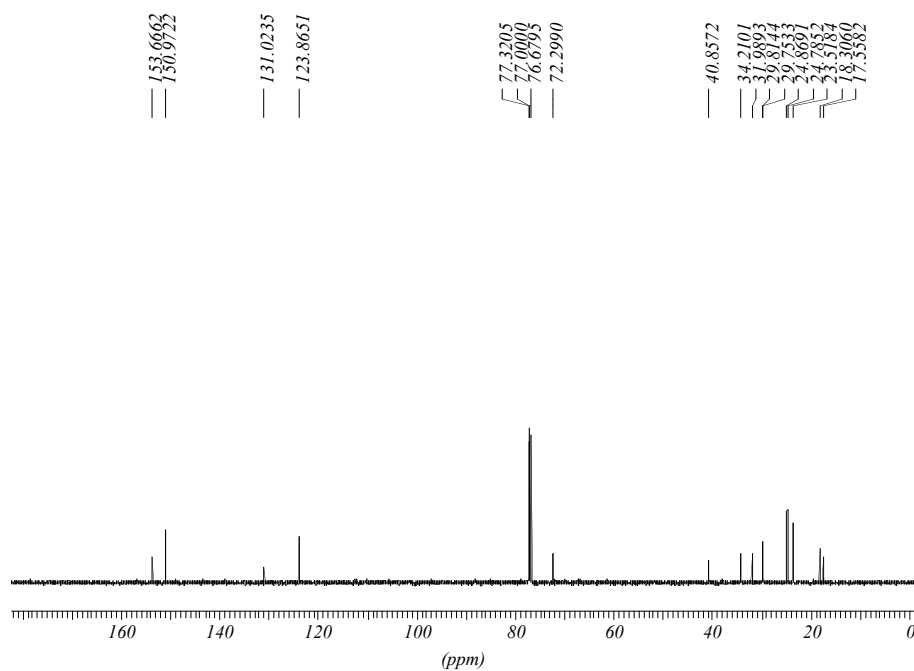
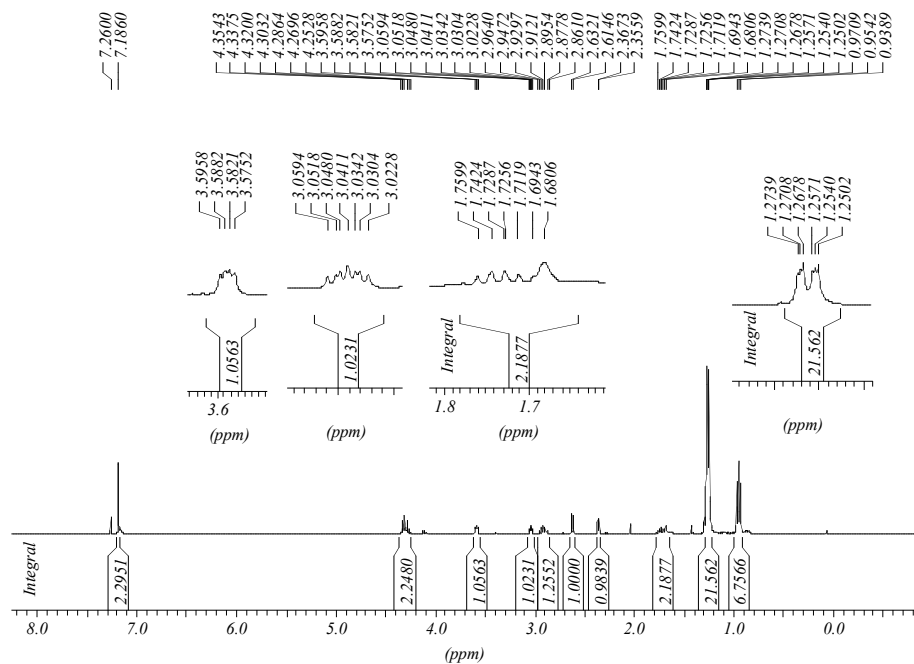
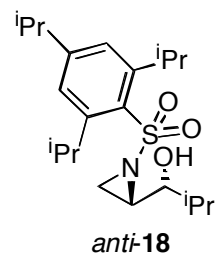
Compound *anti*-17



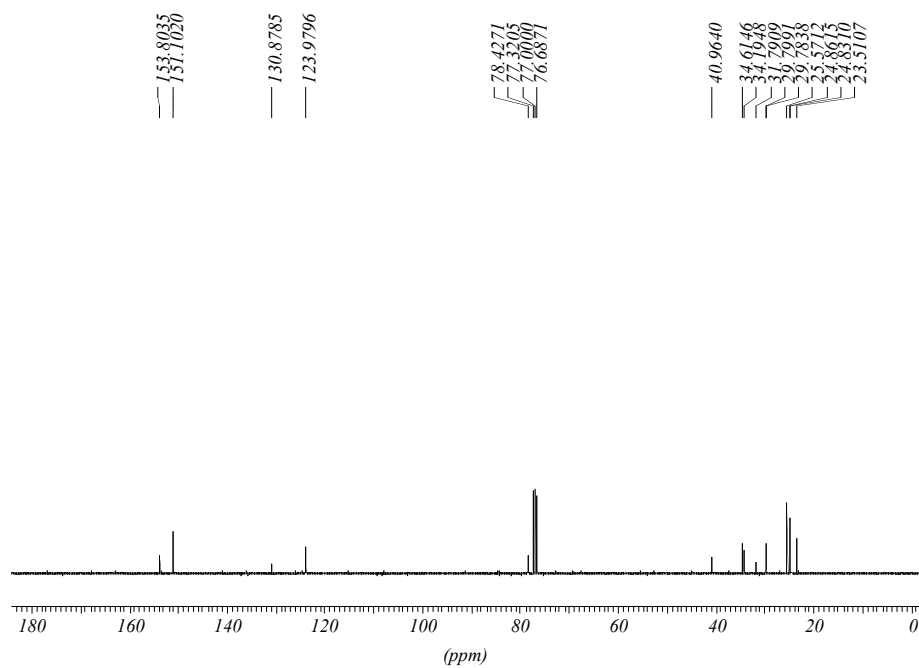
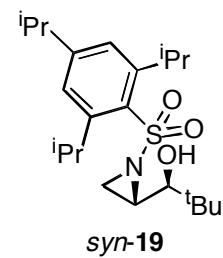
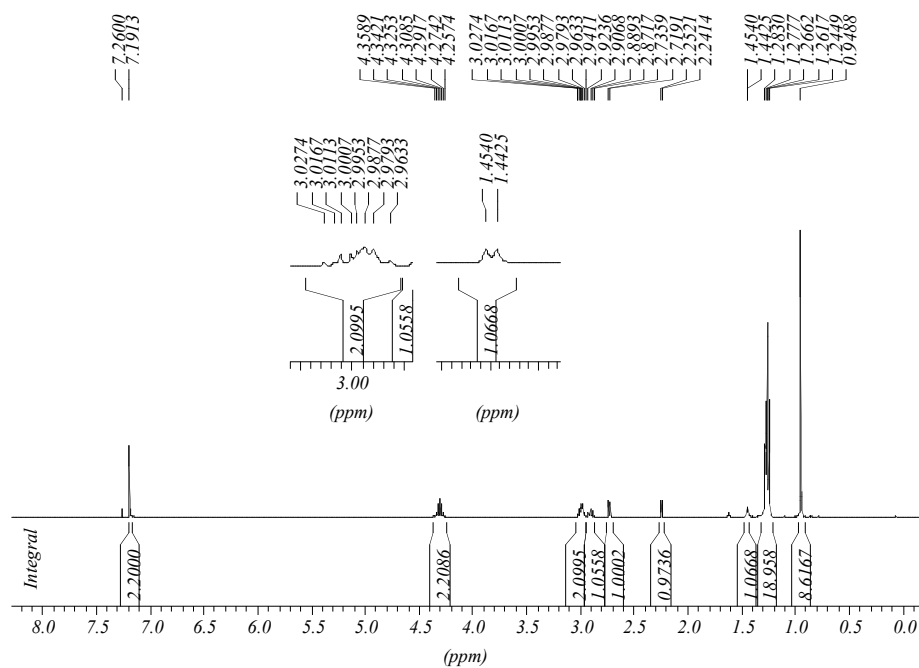
Compound *syn*-18



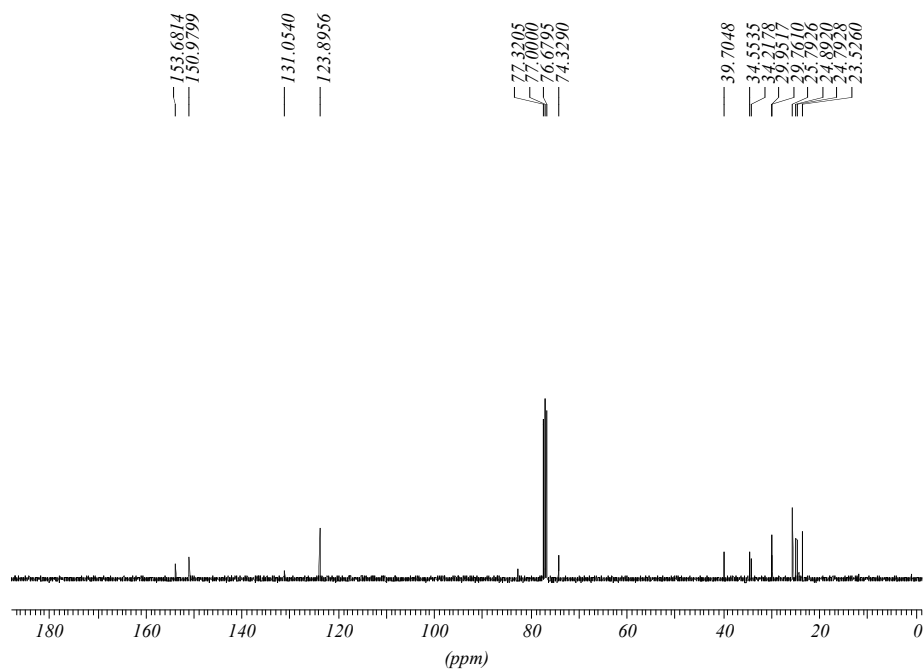
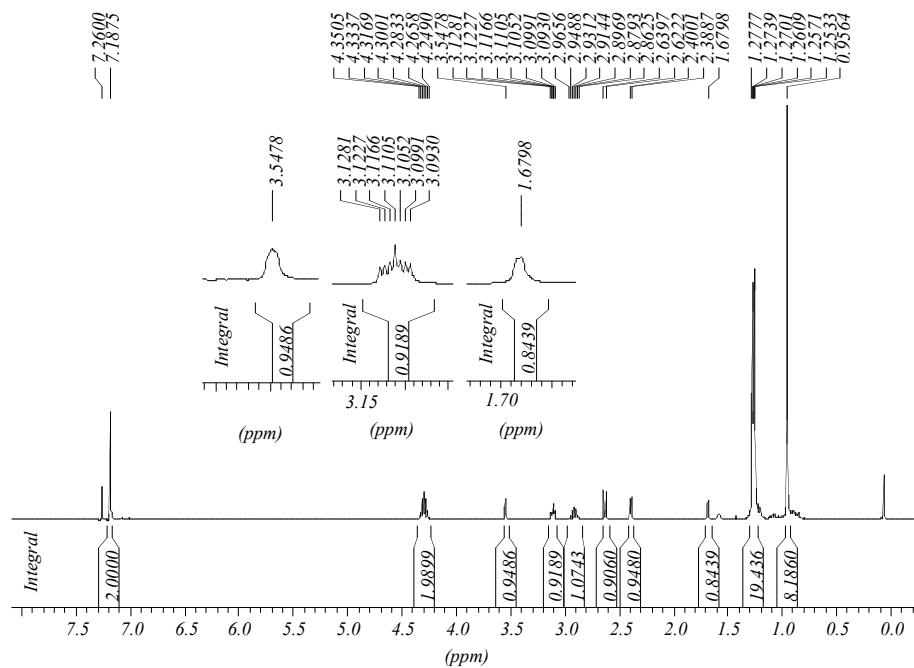
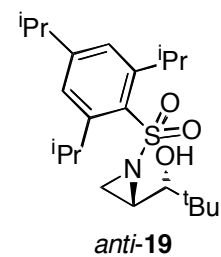
Compound *anti*-18



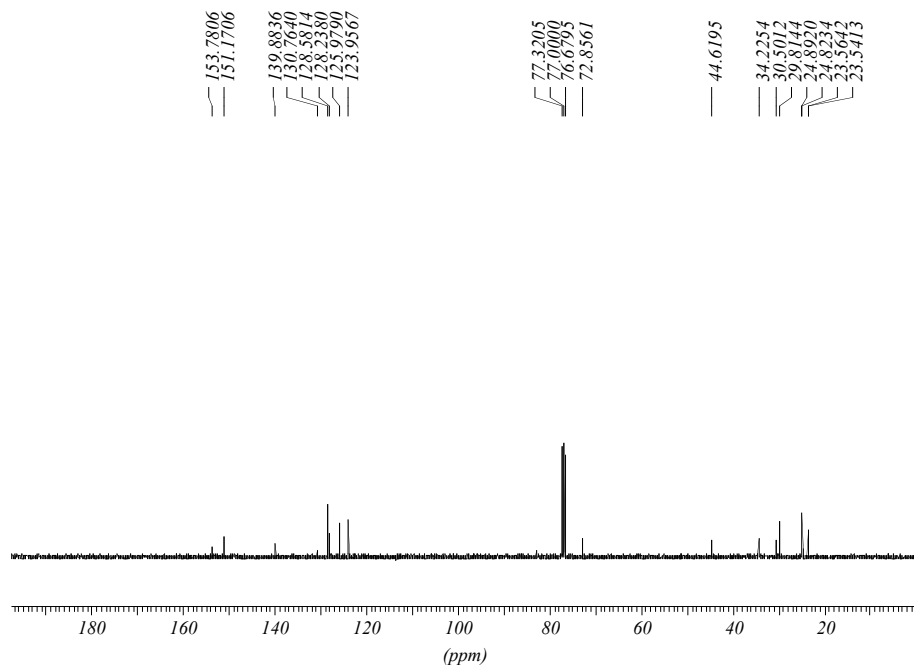
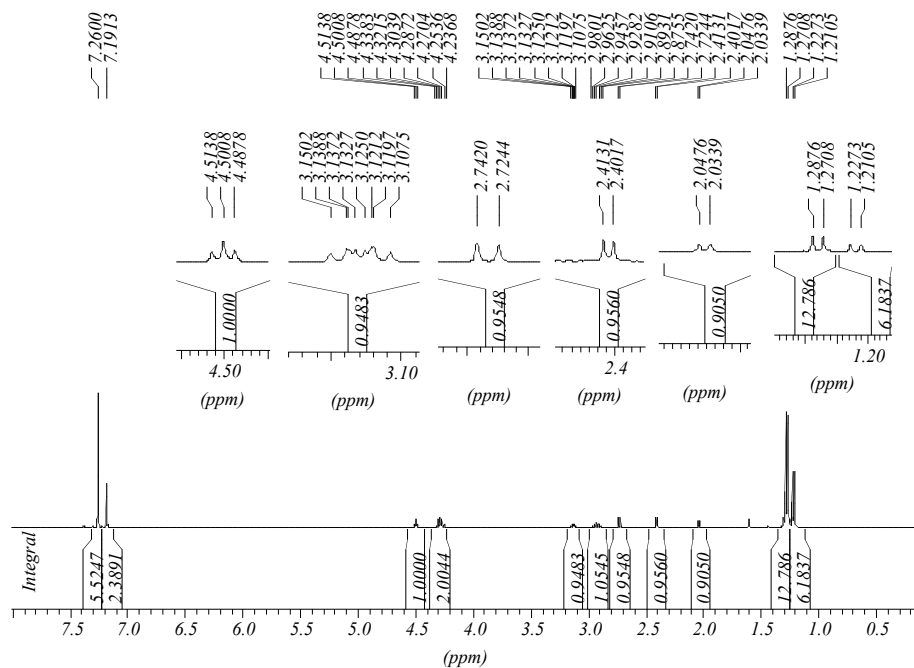
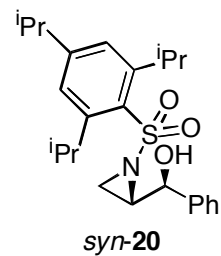
Compound *syn*-19



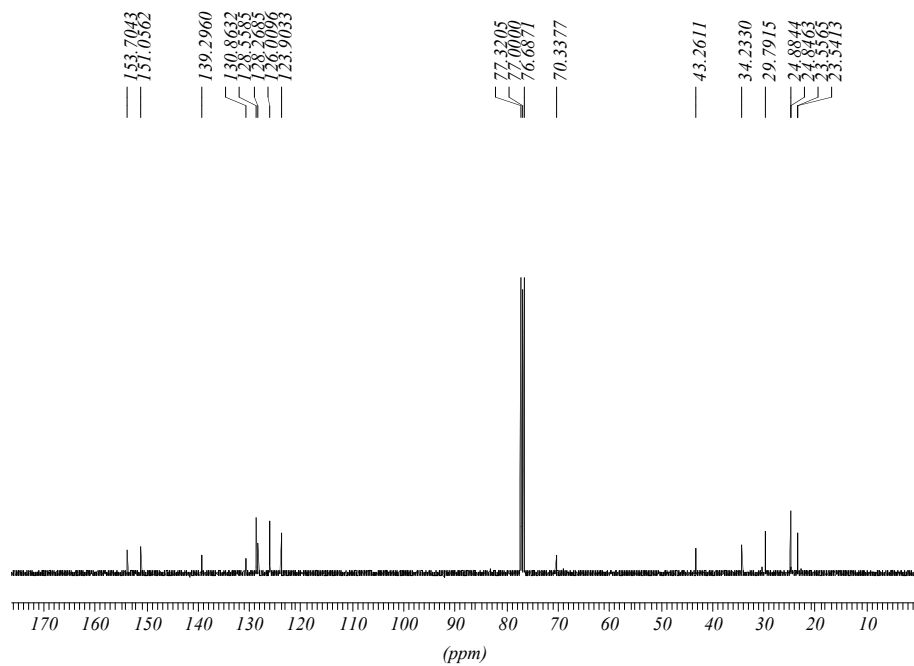
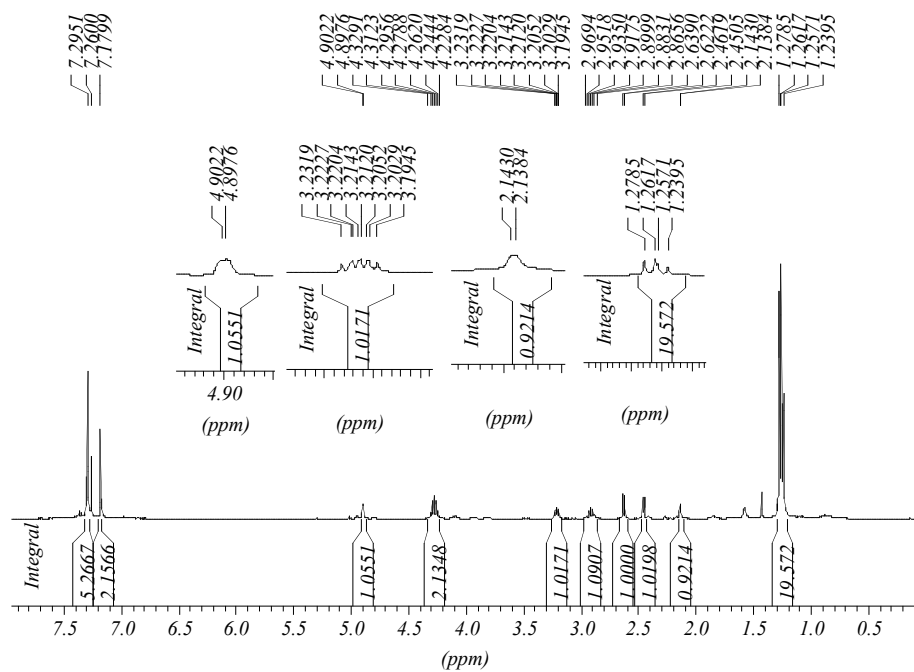
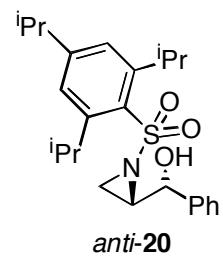
Compound *anti*-19



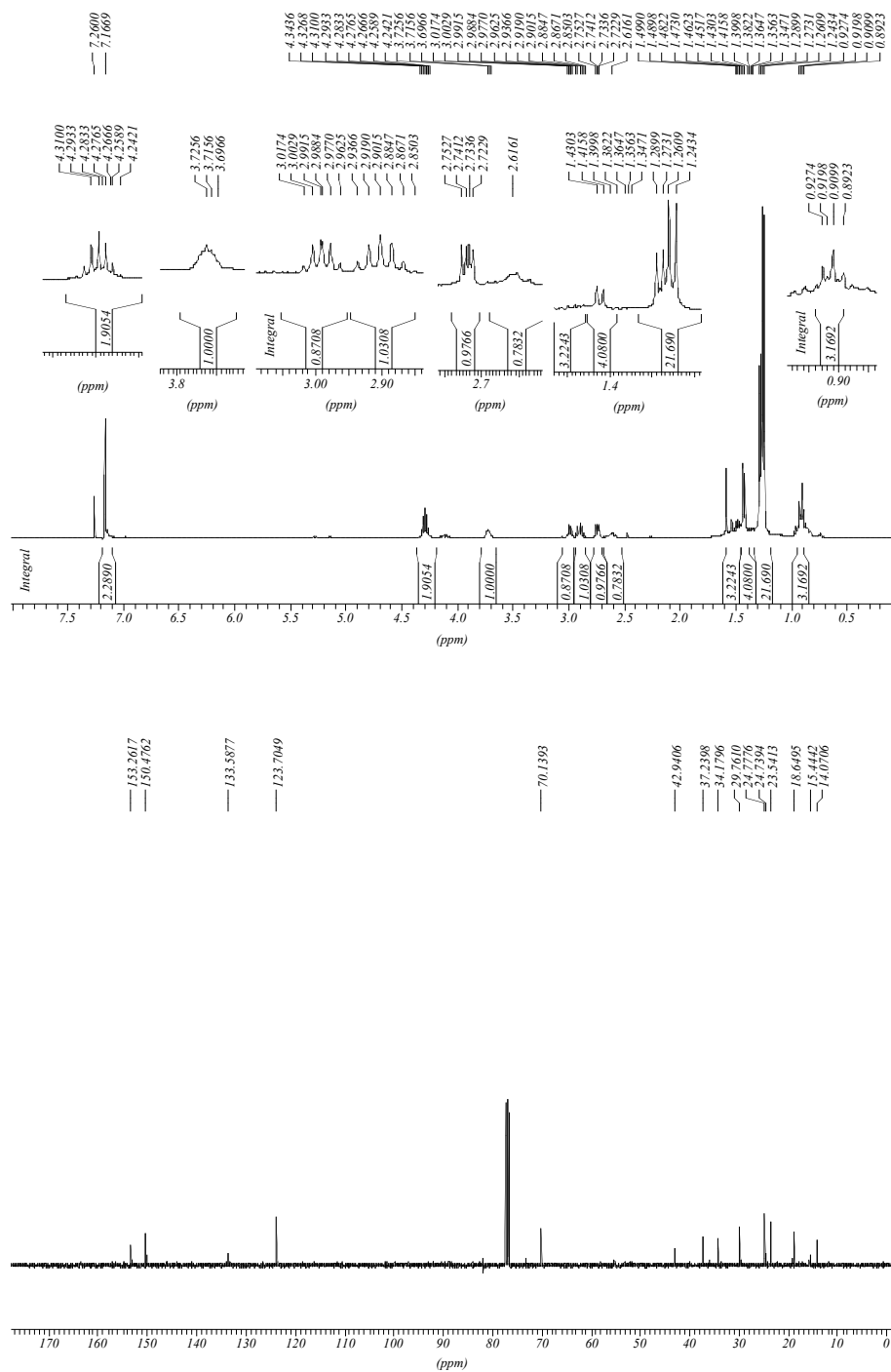
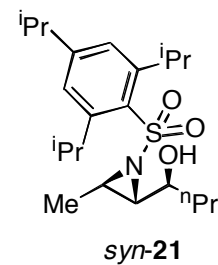
Compound *syn-20*



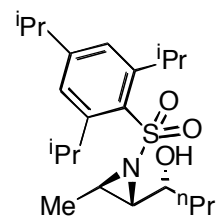
Compound *anti*-20



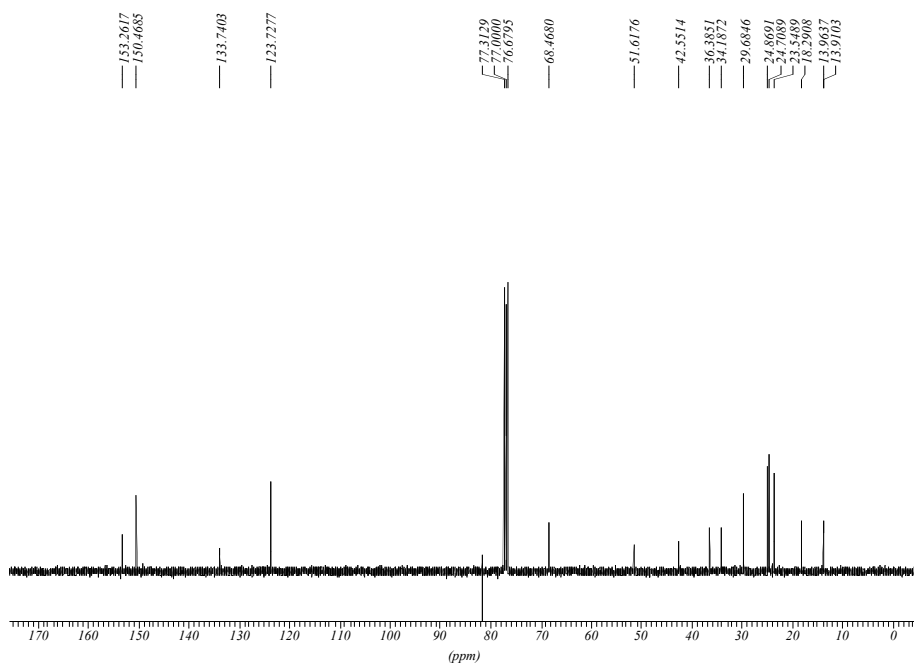
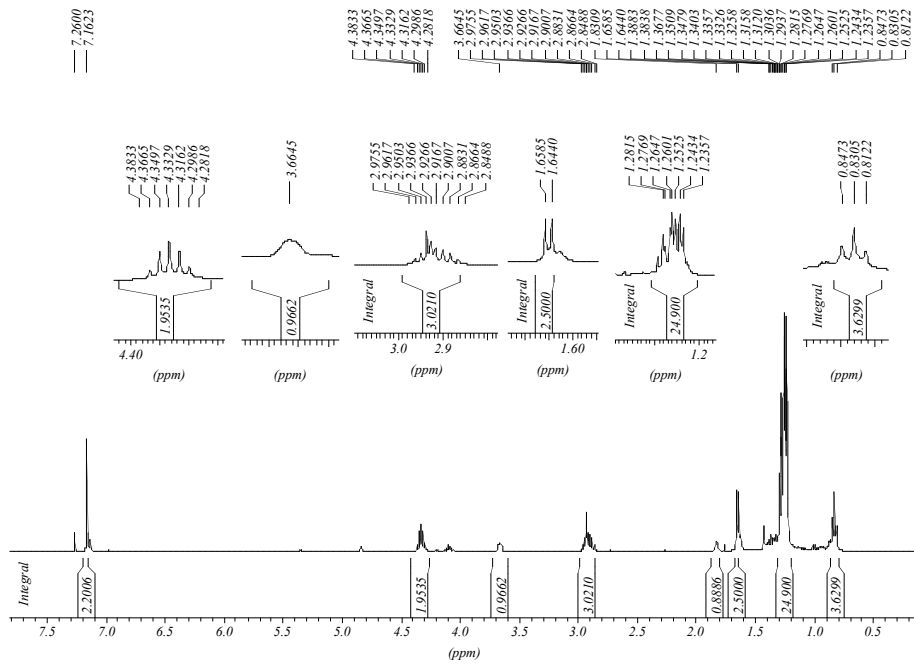
Compound *syn*-21



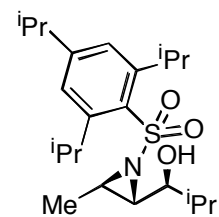
Compound *anti*-21



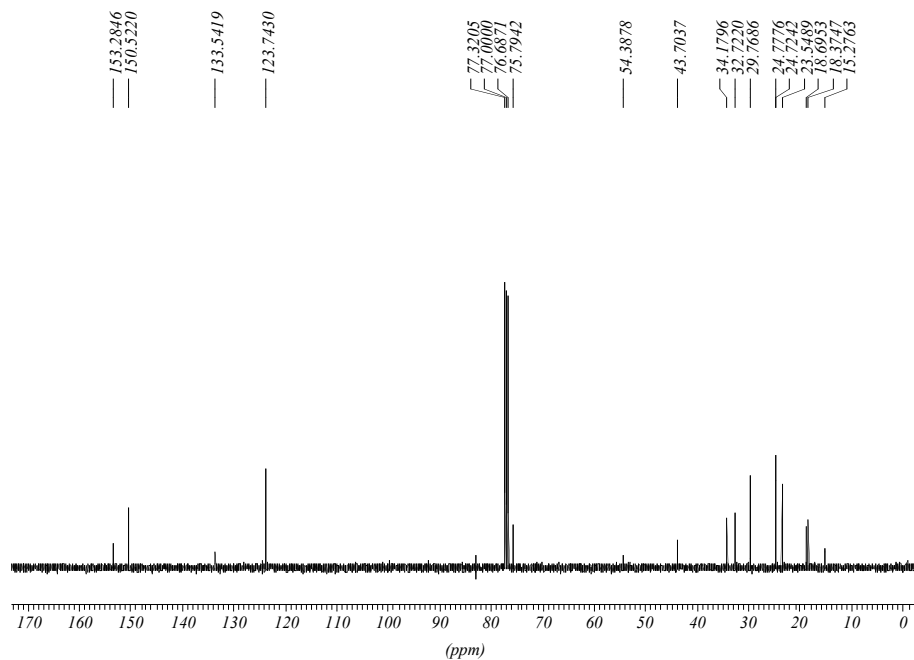
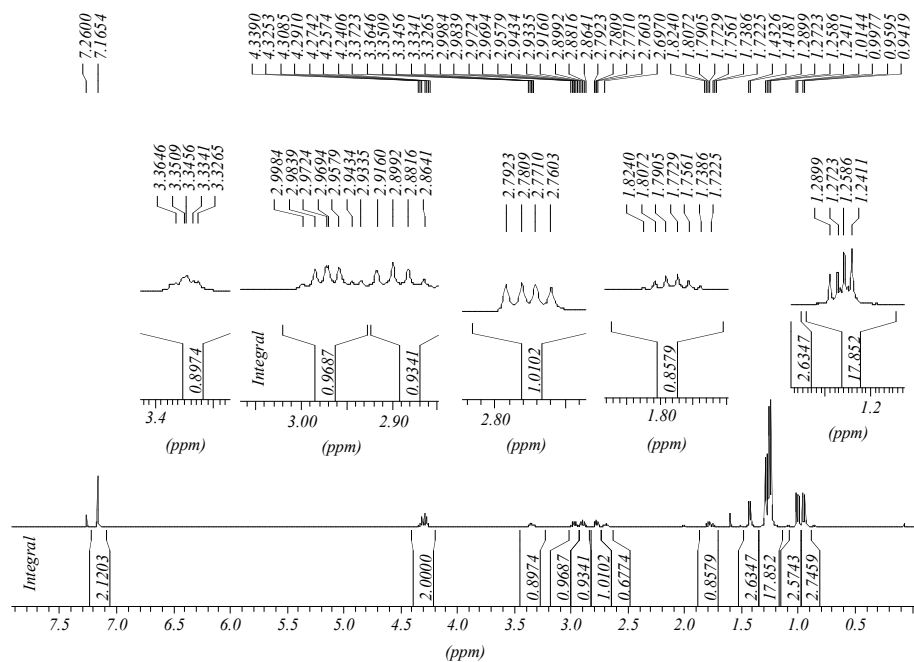
anti-21



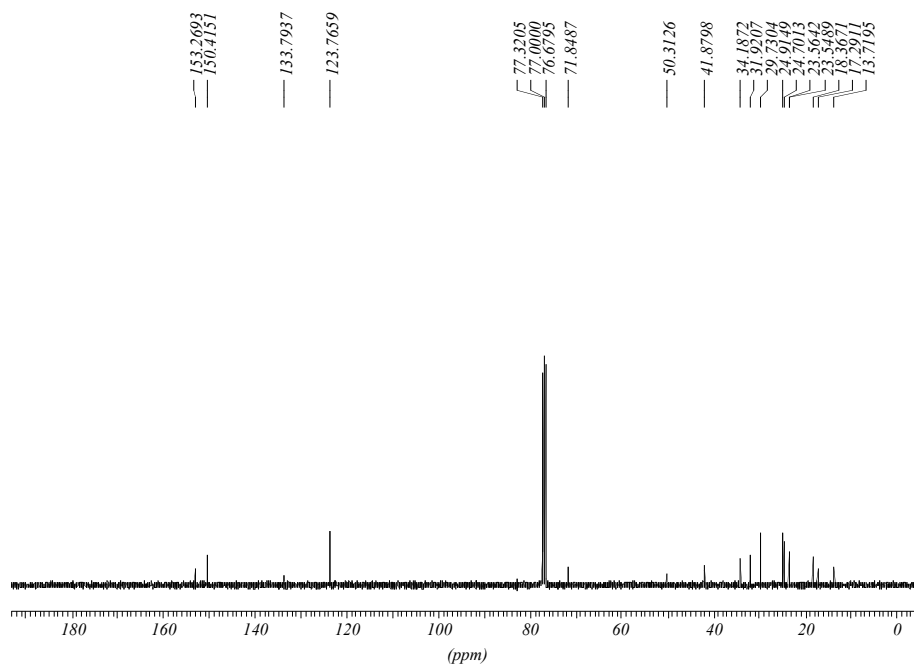
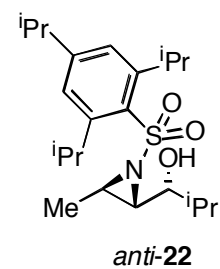
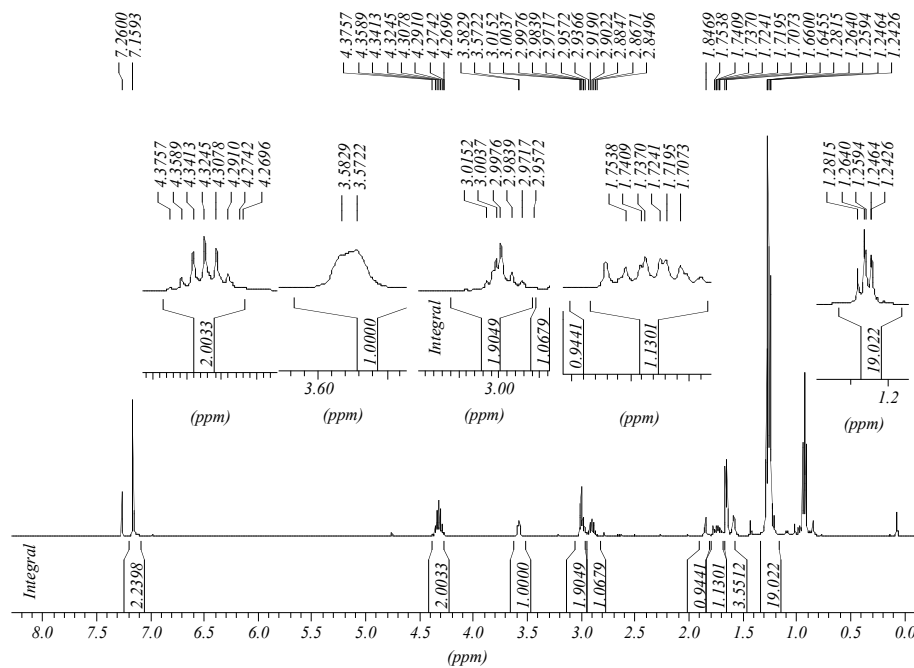
Compound *syn*-22



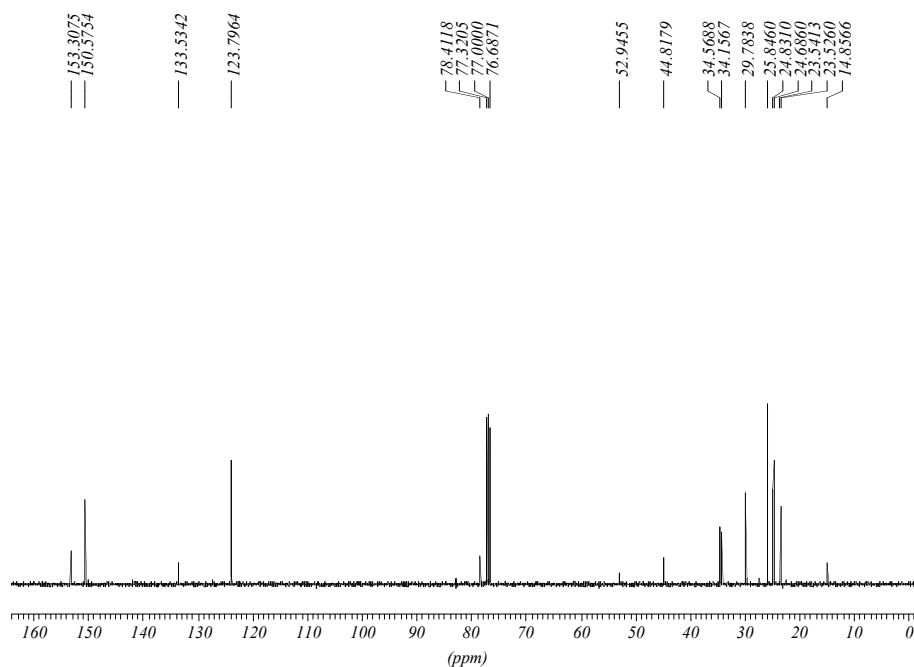
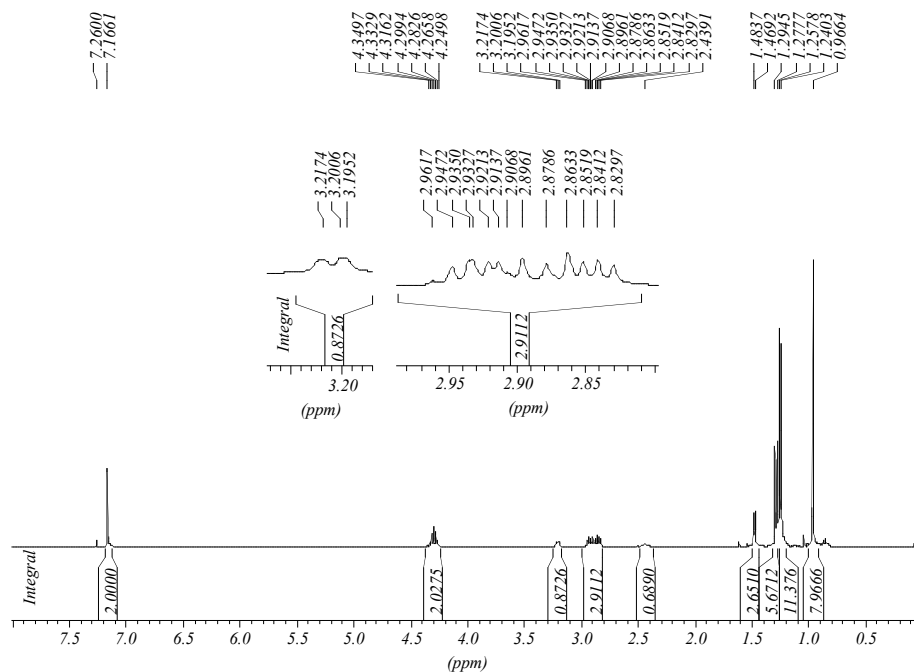
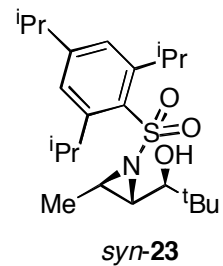
syn-22



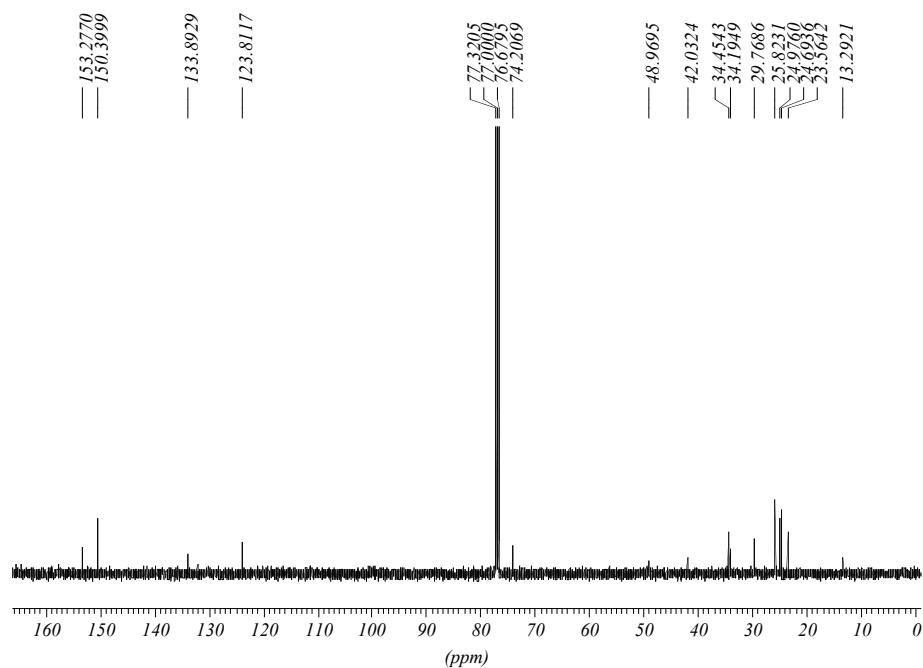
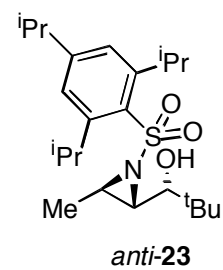
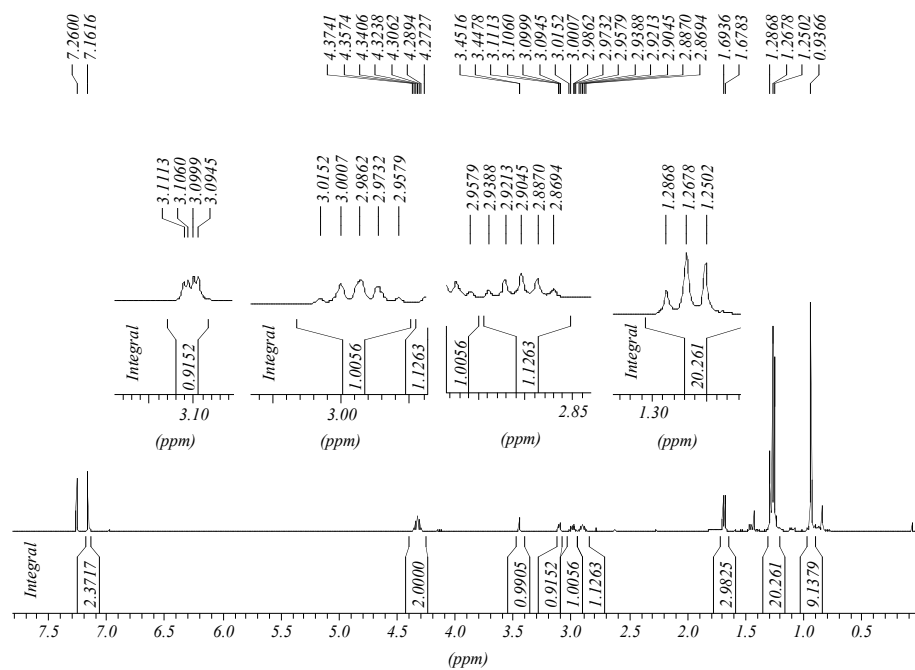
Compound *anti*-22



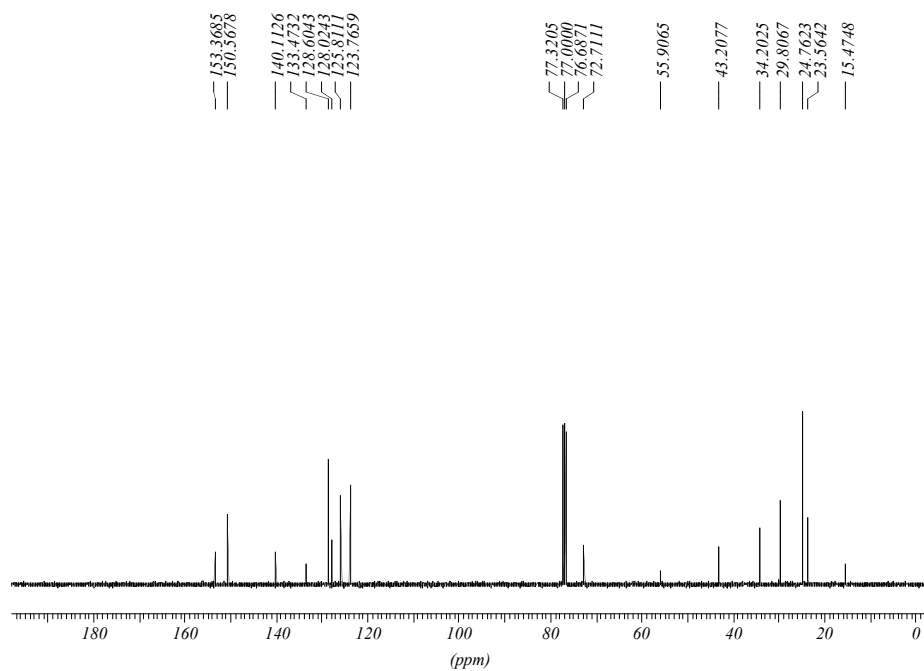
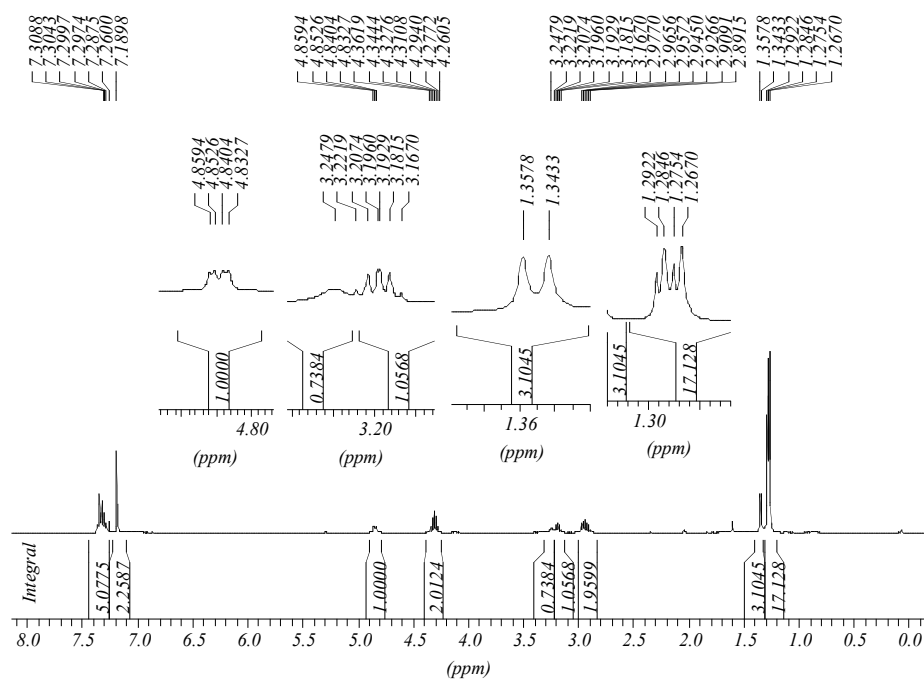
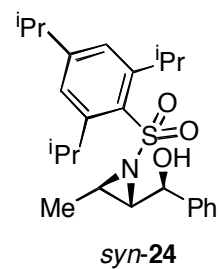
Compound *syn*-23



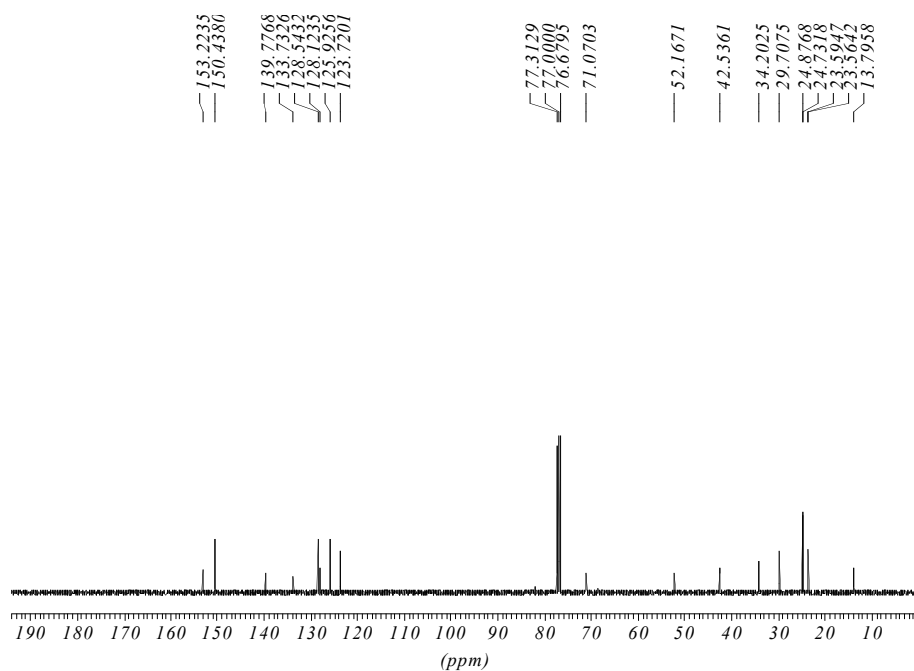
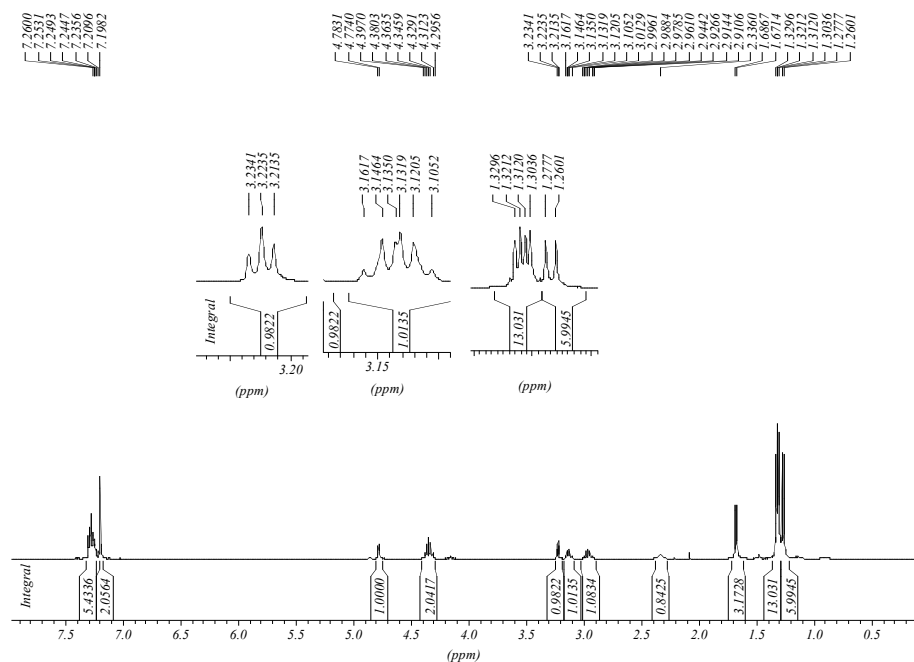
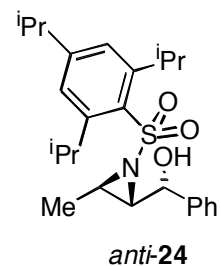
Compound *anti*-23



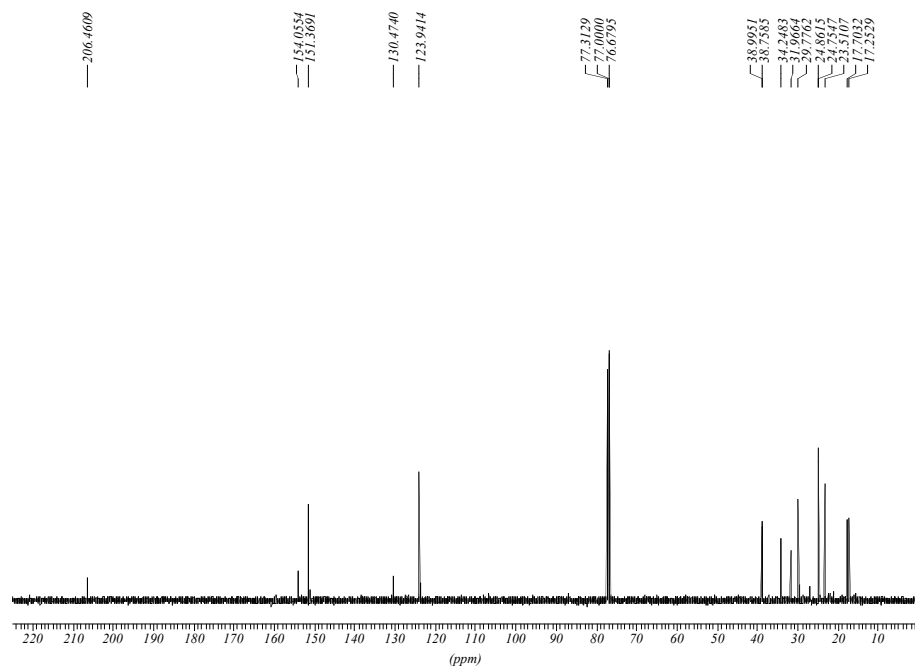
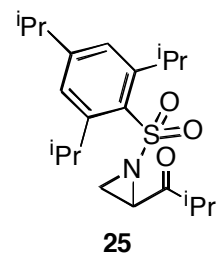
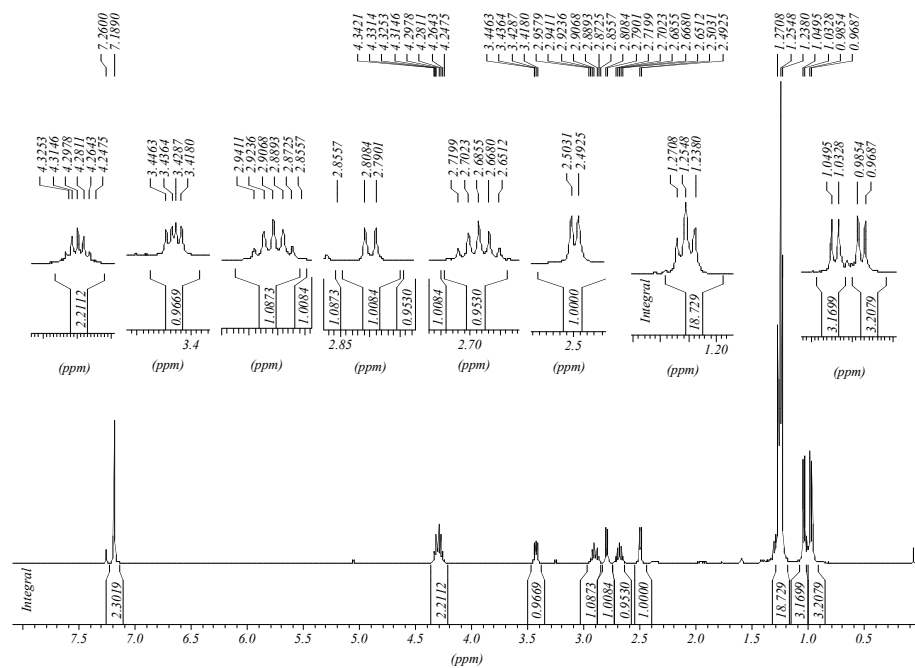
Compound *syn-24*



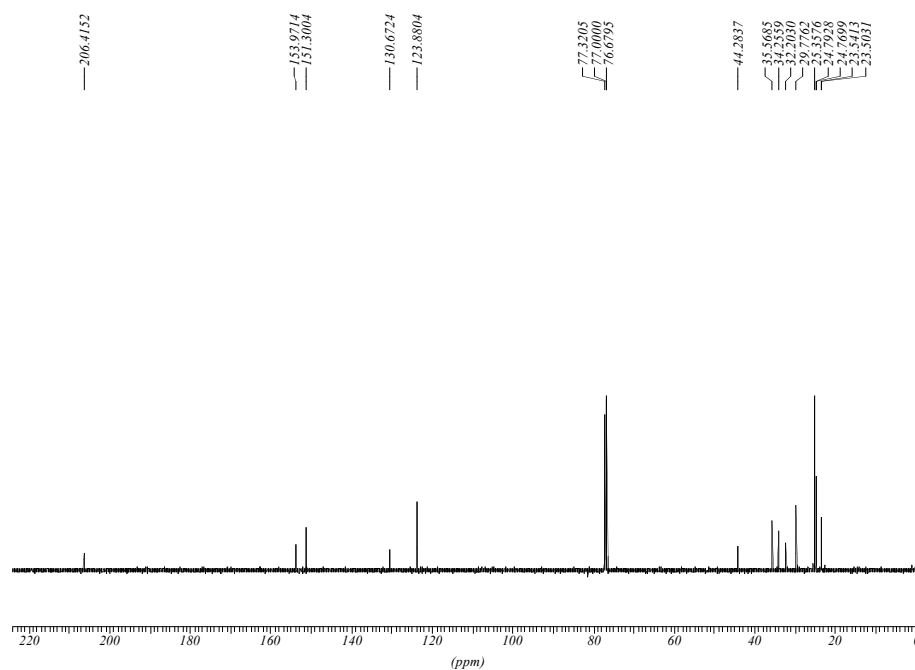
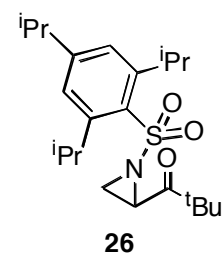
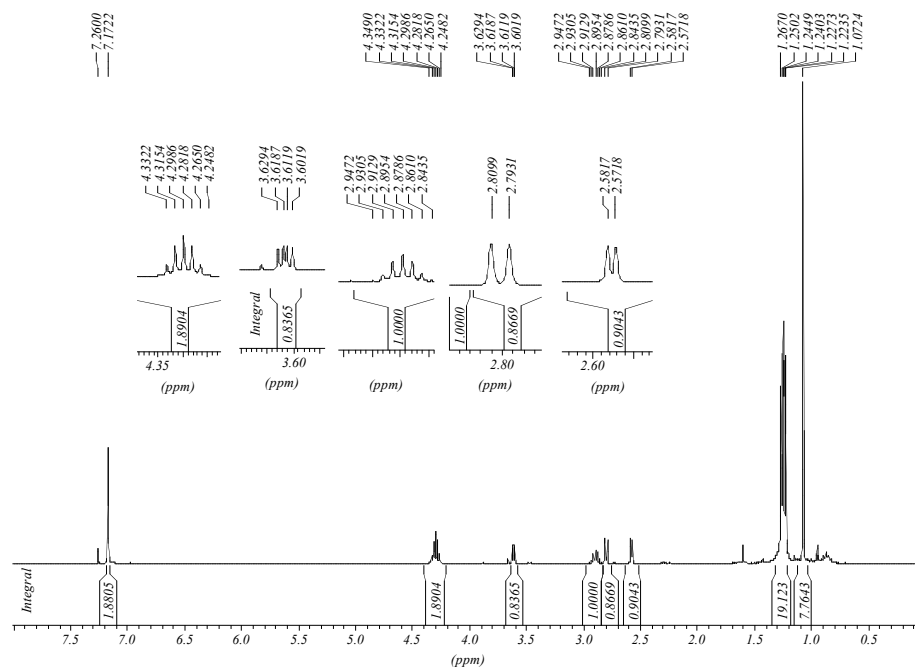
Compound *anti*-24



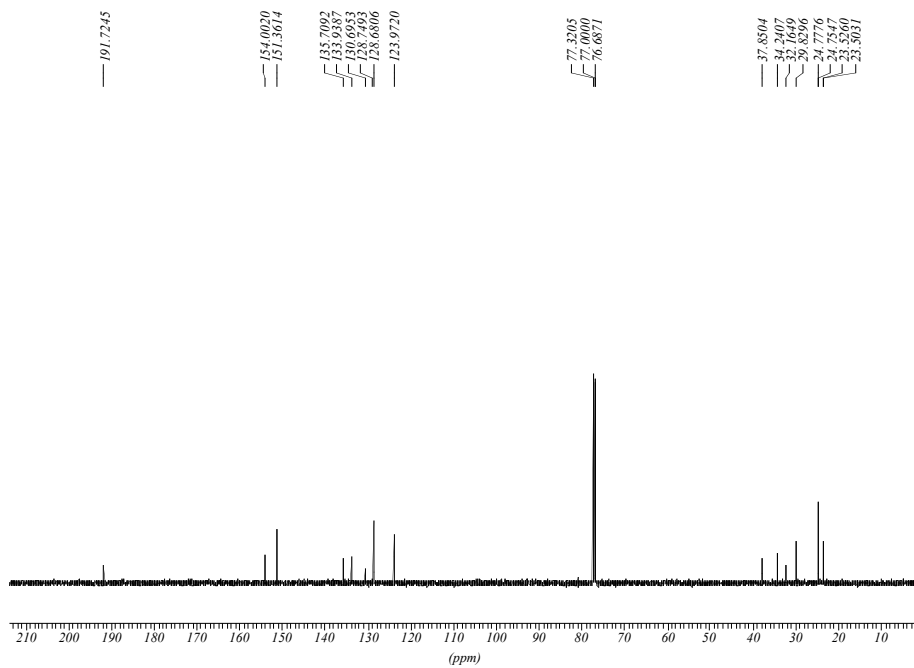
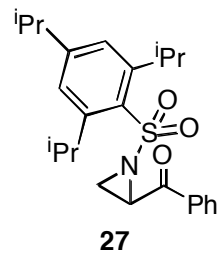
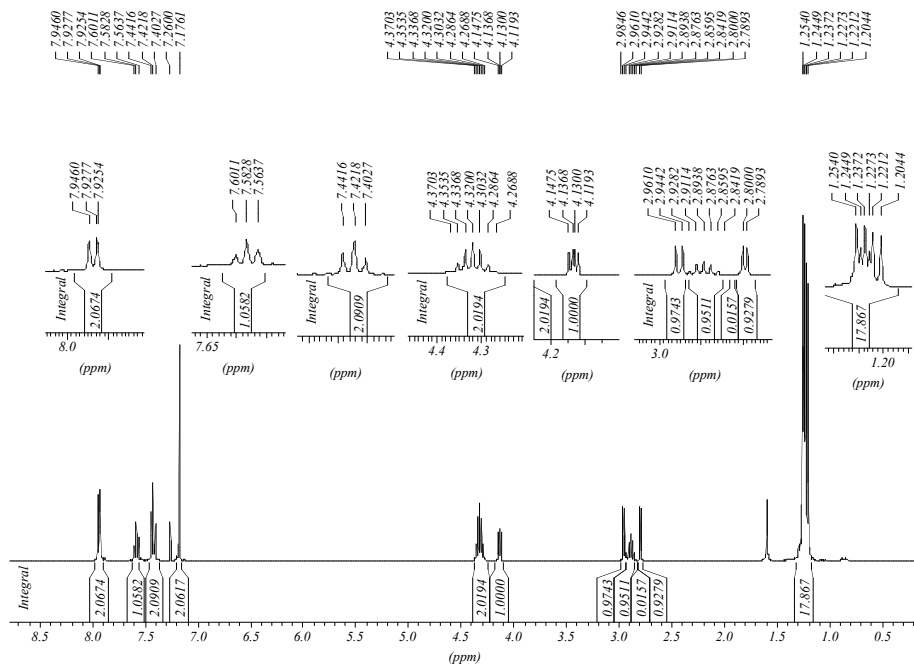
Compound 25



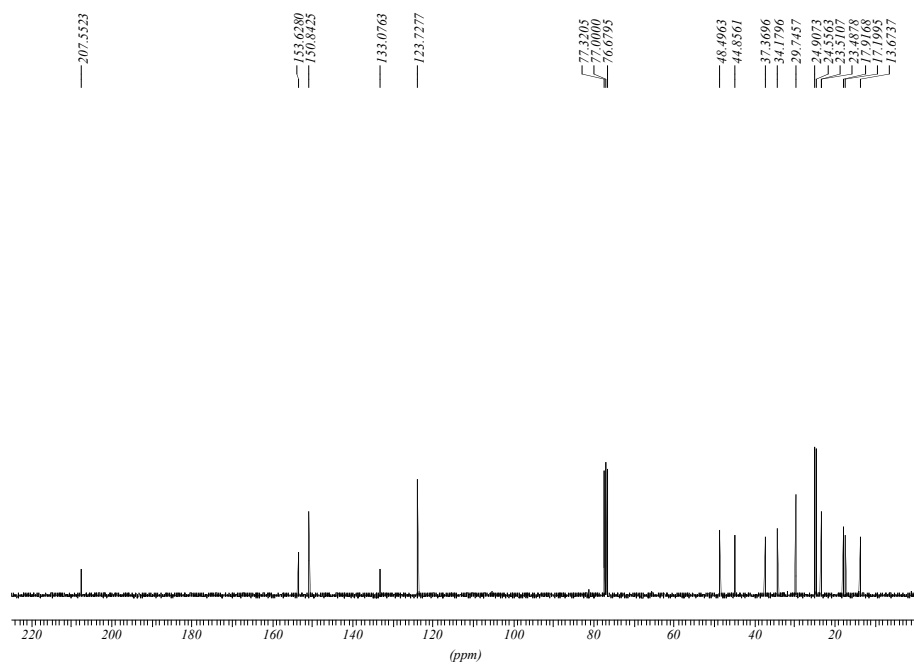
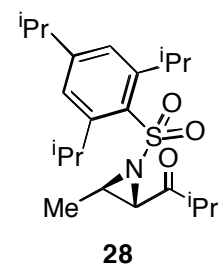
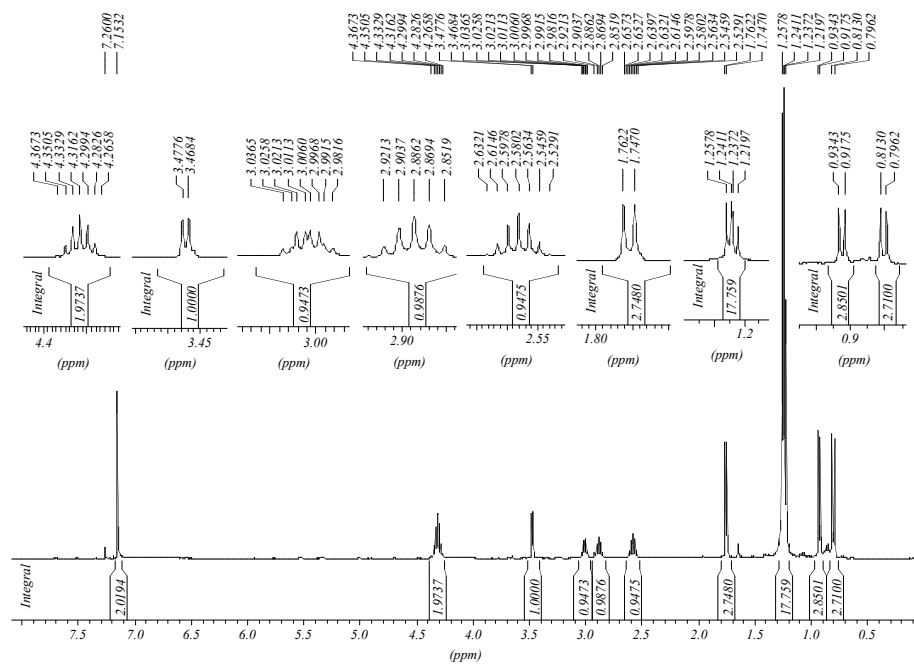
Compound 26



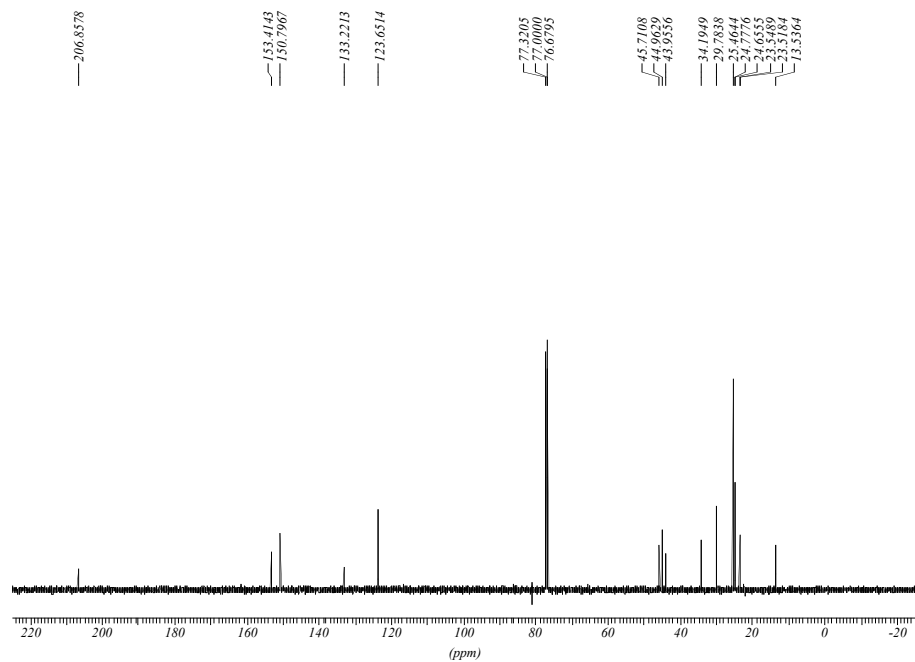
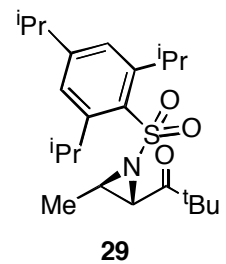
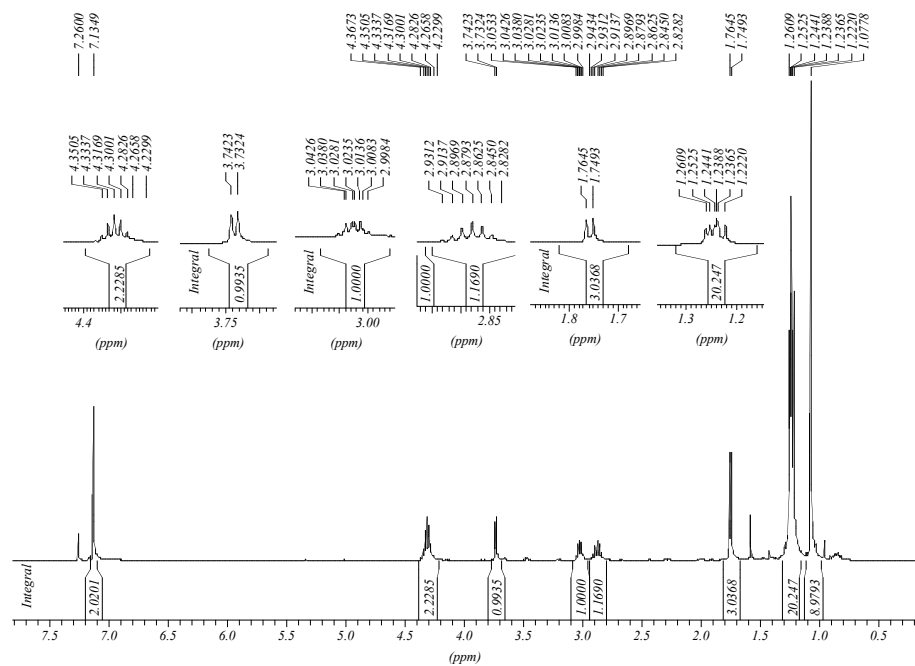
Compound 27



Compound 28



Compound 29



Compound 30

