Supporting Information

Synthesis of Diverse 3-Azido-5-(azidomethyl)benzene Derivatives via Formal C–H Azidation and Functional Group-selective Transformations

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Contents

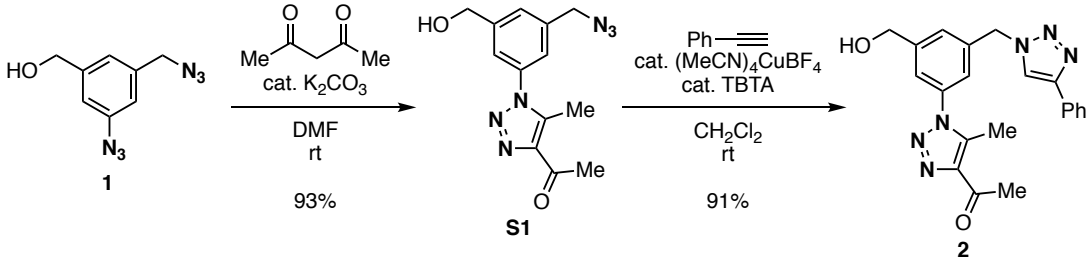
General Remarks

All reactions were performed with dry glassware under atmosphere of argon otherwise noted. ^{1}H and ^{13}C NMR spectra were obtained with a Bruker AVANCE 500 spectrometer at 500 and 126 MHz, respectively. $CDCl_3$ and DMSO-d_6 were used as solvents for obtaining NMR spectra. Chemical shifts (δ) are given in parts per million (ppm) downfield from $(CH_3)_4Si$ (δ 0.00 for ^{1}H in $CDCl_3$) or the solvent peak (δ 77.00 for ^{13}C NMR in $CDCl_3$, and δ 2.50 for ^{1}H NMR and δ 39.5 for ^{13}C NMR in DMSO-d_6) as an internal reference, or α,α,α-trifluorotoluene in $CDCl_3$ (δ –63.0 ppm for ^{19}F NMR) as external standards with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, m, and br signify singlet, doublet, triplet, multiplet, and broad, respectively. IR spectra were measured by diffuse reflectance method on a Shimadzu IRPrestige-21 spectrometer attached with DRS-8000A with the absorption band given in cm^{-1}. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals, Silica Gel 60 F_{254}). Column chromatography was conducted using Biotage® ZIP sphere cartridge [silica], and Biotage SNAP Ultra with medium pressure liquid chromatography (Yamazen, W-Prep 2XY A-type), or using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60, spherical, particle size 40–50 μm). Melting points (Mp) were measured on a YANACO MP-J3 instrument or with an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. High-resolution mass spectra (HRMS) were measured on a Bruker micrOTOF mass spectrometer under positive electrospray ionization (ESI^+) conditions. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

CAUTION! **Azido-containing compounds are presumed to be potentially explosive. Although we have never experienced such an explosion with azido compounds used in this study, all manipulations should be carefully carried out behind a safety shield in a hood.**

Experimental Section

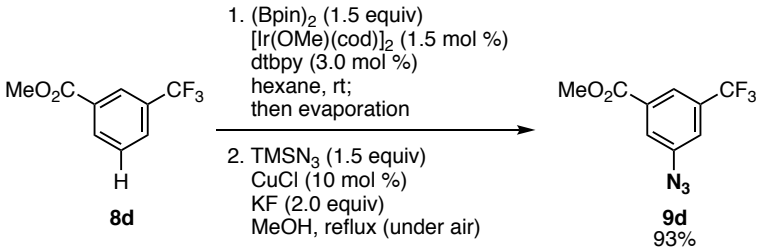
Bistriazole synthesis via sequential azido-type-selective triazole formations



To a solution of 3-azido-5-(azidomethyl)benzyl alcohol (**1**) (33.5 mg, 0.164 mmol) and acetylacetone (20 μL, 0.20 mmol) dissolved in DMF (1.6 mL) was added potassium carbonate (4.5 mg, 33 μmol) at room temperature. After stirring for 2 h at the same temperature, to the mixture was added a saturated aqueous NH_4Cl solution (5 mL). The mixture was extracted with EtOAc (5 mL × 3), and the combined organic extract was dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 51/49 to 30/70) to afford 4-acetyl-1-(3-(azidomethyl)-5-(hydroxymethyl)phenyl)-5-methyl-1*H*-1,2,3-triazole (**S1**) (43.8 mg, 0.153 mmol, 93.2%) as a colorless oil.

To a solution of 4-acetyl-1-(3-(azidomethyl)-5-(hydroxymethyl)phenyl)-5-methyl-1*H*-1,2,3-triazole (**S1**) (21.2 mg, 74.0 μmol), phenylacetylene (9.8 μL, 89 μmol) and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) (1.7 mg, 3.2 μmol) dissolved in CH_2Cl_2 (0.74 mL) was added tetrakis(acetonitrile)copper(I) tetrafluoroborate (1.4 mg, 4.5 μmol) at room temperature. After stirring for 2 h at the same temperature, the mixture was purified by flash column chromatography (*n*-hexane/EtOAc = 22/78 to 1/99) to afford 4-acetyl-1-(5-(hydroxymethyl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-ylmethyl)phenyl)-5-methyl-1*H*-1,2,3-triazole (**2**) (26.3 mg, 67.7 μmol, 91.4%) as a colorless oil.

A typical procedure for formal C–H azidation of 1,3-disubstituted benzenes

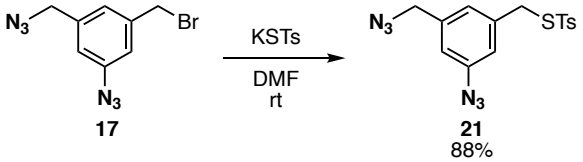


To a solution of bis(pinacolato)diboron (3.83 g, 15.1 mmol), $[Ir(OMe)(cod)]_2$ (105 mg, 0.158 mmol), and 4,4'-di-*tert*-butyl-2,2'-bipyridyl (82.7 mg, 0.308 mmol) dissolved in *n*-hexane (90 mL) was added methyl 3-(trifluoromethyl)benzoate (**8d**) (2.04 g, 9.99 mmol) at room temperature. After stirring for 43 h at the same temperature, the mixture was concentrated under reduced pressure to afford a crude mixture containing (3-methoxycarbonyl-5-(trifluoromethyl))phenylboronic acid pinacol ester.

Under air, the crude mixture was dissolved in methanol (200 mL), and to this solution was added trimethylsilyl azide (1.96 mL, 15.0 mmol), copper(I) chloride (99.0 mg, 1.00 mmol), and potassium fluoride (1.16 g, 20.0 mmol) at room temperature. After stirring for 8 h under reflux (70 °C, bath temperature), the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 30/1) to afford methyl 3-azido-5-(trifluoromethyl)-benzoate (**9d**) (2.28 g, 9.27 mmol, 92.7% from **8d**) as a pale yellow oil.

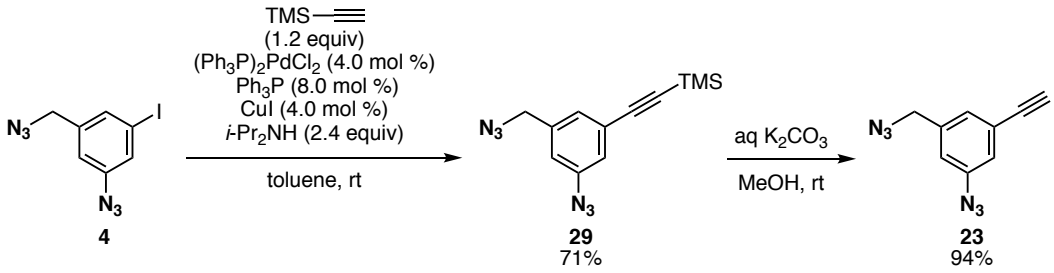
Azides **9c** and **9g** were also prepared from **8c** and **8g** by the same procedure.

*Synthesis of thiosulfonate **21***



To a solution of potassium 4-toluenethiosulfonate (45.4 mg, 0.201 mmol) in DMF (0.12 mL) was added 3-azido-5-(azidomethyl)benzyl bromide (**17**) (53.5 mg, 0.200 mmol) at room temperature. After stirring for 12 h at the same temperature, to the mixture was added water (1 mL). The mixture was extracted with EtOAc (2 mL × 3), and the combined organic extract was washed with water (5 mL × 2) and brine (5 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 7/1) to afford *S*-(3-azido-5-(azidomethyl)benzyl) 4-toluenethiosulfonate (**21**) (65.9 mg, 0.176 mmol, 87.9%) as a yellow oil.

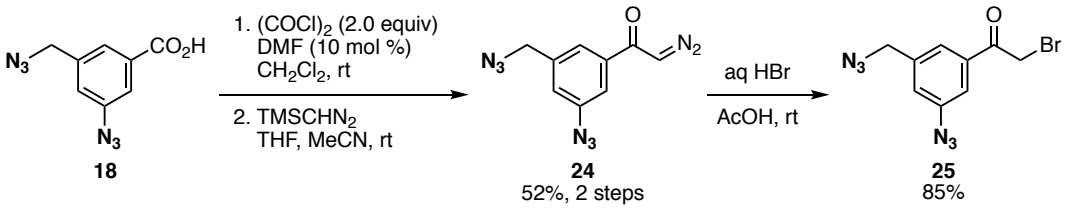
*Synthesis of terminal alkyne **23***



To a solution of $(Ph_3P)_2PdCl_2$ (281 mg, 0.400 mmol), triphenylphosphine (210 mg, 0.801 mmol), copper(I) iodide (76.0 mg, 0.399 mmol), and diisopropylamine (2.48 g, 24.5 mmol) in toluene (4.0 mL) was added a solution of 3-azido-5-(azidomethyl)phenyl iodide (**4**) (3.00 g, 10.0 mmol) and trimethylsilylacetylene (1.20 g, 12.2 mmol) in toluene (6.0 mL) at 0 °C. After stirring for 18 h at room temperature, the mixture was filtered through Kiriyama filter paper, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/CH_2Cl_2 = 88/12) to give 3-azido-5-(trimethylsilylethynyl)benzyl azide (**29**) (1.93 g, 7.14 mmol, 71.4%) as a yellow oil.

To a solution of 3-azido-5-(trimethylsilylethynyl)benzyl azide (**29**) (1.01 g, 3.74 mmol) in methanol (37 mL) was added saturated aqueous potassium carbonate (3.7 mL) at room temperature. After stirring for 15 h at the same temperature, to the mixture was added water (100 mL). The mixture was extracted with EtOAc (20 mL × 3), and the combined organic extract was washed with brine (20 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/CH_2Cl_2 = 80/20) to give 3-azido-5-(azidomethyl)phenylacetylene (**23**) (697 mg, 3.52 mmol, 94.1%) as a yellow oil.

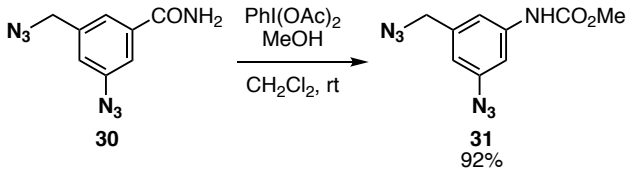
Synthesis of phenacyl bromide ***25***



To a solution of 3-azido-5-(azidomethyl)benzoic acid (**18**) (1.75 g, 8.02 mmol) and DMF (59.7 mg, 0.817 mmol) in CH_2Cl_2 (6.0 mL) was added a solution of oxalyl chloride (2.05 g, 16.2 mmol) in CH_2Cl_2 (6.0 mL) at 0 °C. After stirring for 3 h at room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in a mixed solvent of MeCN (5.0 mL) and THF (5.0 mL), and to the solution was added a solution of trimethylsilyldiazomethane in Et_2O (2.0 M, 16.0 mL, 32.0 mmol) at 0 °C. After stirring for 17 h at room temperature, the mixture was filtered through a plug of cotton, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/CH_2Cl_2 = 76/24 to 55/45) to give 3'-azido-5'-(azidomethyl)-α-diazoacetophenone (**24**) (1.01 g, 4.17 mmol, 52.0% from **18**) as a yellow solid.

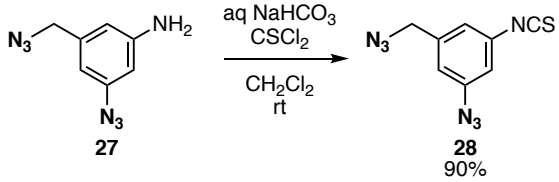
To a solution of 3'-azido-5'-(azidomethyl)-α-diazoacetophenone (**24**) (401 mg, 1.66 mmol) in acetic acid (2.5 mL) was added aqueous hydrobromic acid (48%, 0.57 mL, 5.0 mmol) at 0 °C. After stirring for 70 min at room temperature, to the mixture was added saturated aqueous sodium bicarbonate to adjust the pH to 8. The mixture was extracted with EtOAc (20 mL × 3), and the combined organic extract was washed with brine (20 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 92/8) to give 3-azido-5-(azidomethyl)phenacyl bromide (**25**) (413 mg, 1.40 mmol, 84.5%) as a brown oil.

Synthesis of methyl carbamate **31**



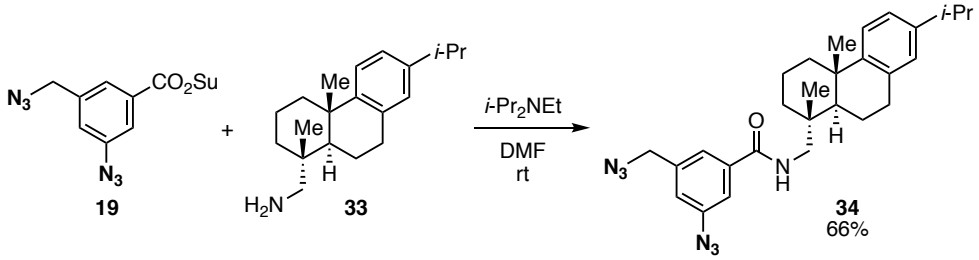
To a solution of 3-azido-5-(azidomethyl)benzamide (**30**) (109 mg, 0.502 mmol) in CH_2Cl_2 was added $PhI(OAc)_2$ (322 mg, 1.00 mmol) at room temperature. After stirring for 40 min at the same temperature, to the mixture was added methanol (15 mL). After stirring for 20 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 86/14 to 65/35) to give methyl (3-azido-5-(azidomethyl)-phenyl)carbamate (**31**) (114 mg, 0.461 mmol, 91.9%) as a pale brown solid.

*Synthesis of isothiocyanate **28***



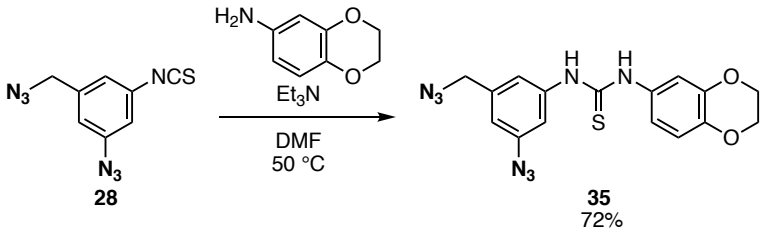
To a solution of sodium bicarbonate (175 mg, 2.08 mmol) in water (0.90 mL) was added a solution of 3-azido-5-(azidomethyl)aniline (**27**) (100 mg, 0.529 mmol) in CH_2Cl_2 (0.90 mL). To the resulting biphasic mixture was added thiophosgene (60 μL, 0.78 mmol) at 0 °C. After stirring for 2 h at room temperature, the mixture was extracted with CH_2Cl_2 (5 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 95/5) to give 3-azido-5-(azidomethyl)phenyl isothiocyanate (**28**) (110 mg, 0.476 mmol, 90.0%) as a yellow oil.

Synthesis of amide **34**



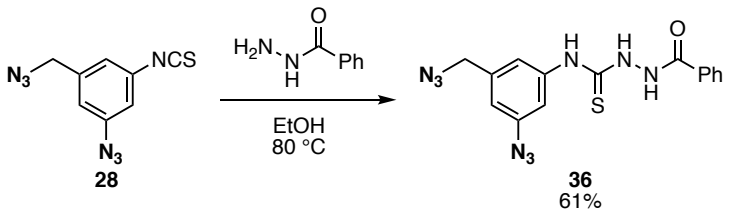
To a solution of (+)-dehydroabietylamine (**33**) (28.5 mg, 99.8 μmol) and *N*-ethyldiisopropylamine (19.3 mg, 0.149 mmol) in DMF (1.0 mL) was added succinimido 3-azido-5-(azidomethyl)benzoate (**19**) (47.5 mg, 0.151 mmol). After stirring for 17 h at room temperature, the mixture was dried under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 84/16 to 63/37) to give *N*-(+)-dehydroabietyl 3-azido-5-(azidomethyl)benzamide (**34**) (32.1 mg, 66.1 μmol, 66.2%) as a pale yellow oil.

*Synthesis of thiourea **35***



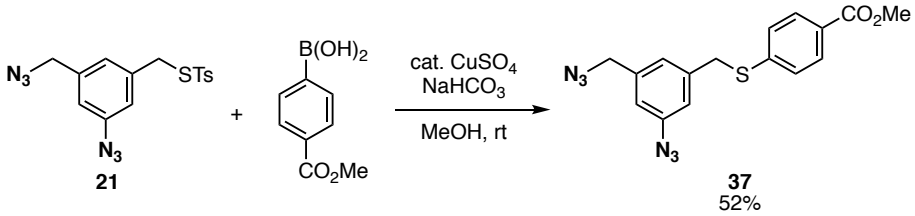
To a solution of 3-azido-5-(azidomethyl)phenyl isothiocyanate (**28**) (10.5 mg, 45.4 μmol) and 3,4-ethylenedioxyaniline (9.8 mg, 65 μmol) in DMF (0.80 mL) was added triethylamine (10 μL, 69 μmol) at room temperature. After stirring for 18 h at 50 °C, to the mixture was added water (5 mL). The mixture was extracted with a mixed solvent of *n*-hexane and EtOAc (1:4) (5 mL × 3), and the combined organic extract was washed with water (5 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 5/2) to give 1-(3-azido-5-(azidomethyl)phenyl)-3-(3,4-ethylenedioxyphenyl)-thiourea (**35**) (12.5 mg, 32.7 μmol, 72.0%) as a yellow oil.

*Synthesis of thiourea **36***



To a solution of 3-azido-5-(azidomethyl)phenyl isothiocyanate (**28**) (23.6 mg, 0.102 mmol) in EtOH (0.4 mL) was added benzohydrazide (14.0 mg, 0.103 mmol). After stirring the mixture for 80 min at 80 °C, the resulting precipitate was collected by filtration and then dried under reduced pressure to give *N*-(3-azido-5-(azidomethyl)phenyl)-2-benzoylhydrazine-1-carbothioamide (**36**) (22.9 mg, 62.3 μmol, 61.1%) as a colorless solid.

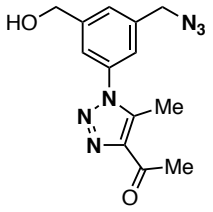
*Synthesis of sulfide **37***



To a mixture of copper(II) sulfate (0.82 mg, 5.1 μmol) and sodium bicarbonate (16.8 mg, 0.200 mmol) was added a solution of *S*-(3-azido-5-(azidomethyl)benzyl) 4-toluenethiosulfonate (**21**) (34.0 mg, 90.8 μmol) and 4-methoxycarbonylphenylboronic acid (26.9 mg, 0.149 mmol) in MeOH (1.0 mL) at room temperature. After stirring for 25 h at the same temperature, to the mixture was added water (5 mL). The mixture was extracted with EtOAc (5 mL × 3), and the combined organic extract was washed with brine (5 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified twice by preparative TLC (*n*-hexane/EtOAc = 3/1 and *n*-hexane/CH_2Cl_2 = 1/6) to give 3-azido-5-(azidomethyl)benzyl 4-methoxycarbonylphenyl sulfide (**37**) (16.6 mg, 46.8 μmol, 51.6%) as a colorless solid.

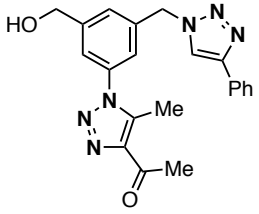
Characterization Data of New Compounds

4-Acetyl-1-(3-(azidomethyl)-5-(hydroxymethyl)phenyl)-5-methyl-1*H*-1,2,3-triazole (**S1**)



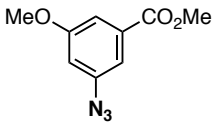
Colorless oil; TLC R_f 0.36 (*n*-hexane/EtOAc = 4/6); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.41 (t, 1H, J = 5.0 Hz), 2.60 (s, 3H), 2.75 (s, 3H), 4.49 (s, 2H), 4.84 (d, 2H, J = 5.0 Hz), 7.33 (s, 1H), 7.46 (s, 1H), 7.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 10.2 (1C), 27.9 (1C), 53.9 (1C), 63.9 (1C), 123.0 (1C), 123.5 (1C), 127.4 (1C), 135.8 (1C), 137.5 (1C), 137.9 (1C), 143.7 (1C), 144.0 (1C), 194.4 (1C); IR (KBr, cm^{-1}) 546, 1285, 1418, 1485, 1557, 1682, 2100, 3418; HRMS (ESI^+) m/z 309.1063 ($[M+Na]^+$, $C_{13}H_{14}N_6NaO_2^+$ requires 309.1070)

4-Acetyl-1-(5-(hydroxymethyl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-ylmethyl)phenyl)-5-methyl-1*H*-1,2,3-triazole (**2**)



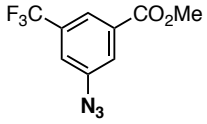
Colorless oil; TLC R_f 0.51 (EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.52 (s, 3H), 2.71 (s, 3H), 3.33 (br s, 1H), 4.77 (s, 2H), 5.62 (s, 2H), 7.26–7.28 (m, 1H), 7.29–7.34 (m, 1H), 7.36–7.40 (m, 2H), 7.44 (s, 1H), 7.46 (s, 1H), 7.73–7.76 (m, 2H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 10.1 (1C), 27.9 (1C), 53.3 (1C), 63.6 (1C), 120.0 (1C), 123.2 (1C), 123.3 (1C), 125.7 (2C), 127.3 (1C), 128.5 (1C), 128.9 (2C), 130.0 (1C), 135.9 (1C), 136.9 (1C), 137.5 (1C), 143.6 (1C), 144.7 (1C), 148.4 (1C), 194.2 (1C); IR (KBr, cm^{-1}) 768, 912, 1076, 1485, 1557, 1672, 3379; HRMS (ESI^+) m/z 411.1530 ($[M+Na]^+$, $C_{21}H_{20}N_6NaO_2^+$ requires 411.1540).

Methyl 3-azido-5-methoxybenzoate (**9c**)



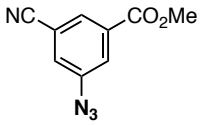
Orange solid; Mp 44–45 ºC; TLC R_f 0.38 (*n*-hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.85 (s, 3H), 3.93 (s, 3H), 6.72 (dd, 1H, J = 2.3, 2.3 Hz), 7.33 (dd, 1H, J = 2.3, 1.3 Hz), 7.35 (dd, 1H, J = 2.3, 1.3 Hz); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 52.4 (1C), 55.7 (1C), 109.8 (1C), 111.0 (1C), 112.4 (1C), 132.7 (1C), 141.7 (1C), 160.7 (1C), 166.1 (1C); IR (KBr, cm^{-1}) 766, 1057, 1225, 1262, 1314, 1340, 1434, 1603, 1726, 2110; HRMS (ESI^+) m/z 230.0539 ($[M+Na]^+$, $C_9H_9N_3NaO_3^+$ requires 230.0536).

Methyl 3-azido-5-(trifluoromethyl)benzoate (**9d**)



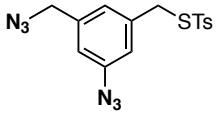
Pale yellow oil; TLC R_f 0.45 (*n*-hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.97 (s, 3H), 7.39 (s, 1H), 7.84 (s, 1H), 8.03 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 52.6 (1C), 119.9 (d, 1C, $^3J_{C–F}$ = 3.4 Hz), 122.4 (d, 1C, $^3J_{C–F}$ = 3.6 Hz), 122.8 (1C), 123.0 (q, 1C, $^1J_{C–F}$ = 273.4 Hz), 132.6 (q, 1C, $^2J_{C–F}$ = 33.6 Hz), 132.7 (1C), 141.7 (1C), 164.7 (1C); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –63.4 (s); IR (KBr, cm^{-1}) 691, 769, 1136, 1177, 1259, 1356, 1438, 1462, 2056; HRMS (ESI^+) *m*/*z* 246.0496 ($[M+H]^+$, $C_9H_7F_3N_3O_2^+$ requires 246.0485).

Methyl 3-azido-5-cyanobenzoate (**9e**)



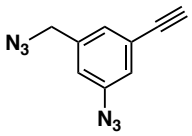
Colorless solid; Mp 129–133 ºC; TLC R_f 0.64 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.98 (s, 3H), 7.43 (dd, 1H, *J* = 2.2, 1.5 Hz), 7.92 (dd, 1H, *J* = 2.2, 1.5 Hz), 8.07 (dd, 1H, *J* = 1.5, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 53.0 (1C), 114.4 (1C), 117.0 (1C), 124.0 (1C), 126.1 (1C), 129.2 (1C), 133.2 (1C), 142.2 (1C), 164.3 (1C); IR (KBr, cm^{-1}) 767, 888, 1183, 1201, 1252, 1275, 1335, 1735, 2131; HRMS (ESI^+) *m*/*z* 225.0383 ($[M+Na]^+$, $C_9H_6N_4NaO_2^+$ requires 225.0383).

S-(3-Azido-5-(azidomethyl)benzyl) 4-toluenethiosulfonate (**21**)



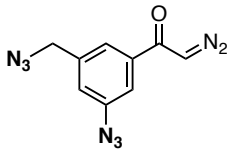
Yellow oil; TLC R_f 0.35 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.44 (s, 3H), 4.23 (s, 2H), 4.26 (s, 2H), 6.74 (s, 1H), 6.81 (s, 1H), 6.89 (s, 1H), 7.25–7.29 (AA'BB', 2H), 7.68–7.72 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 21.6 (1C), 39.6 (1C), 53.9 (1C), 117.9 (1C), 119.1 (1C), 124.9 (1C), 127.0 (2C), 129.8 (2C), 136.8 (1C), 138.0 (1C), 141.1 (1C), 142.0 (1C), 144.9 (1C); IR (KBr, cm^{-1}) 419, 519, 546, 586, 654, 1142, 1321, 2108; HRMS (ESI^+) *m*/*z* 397.0504 ($[M+Na]^+$, $C_{15}H_{14}N_6NaO_2S_2^+$ requires 397.0512).

3-Azido-5-(azidomethyl)phenylacetylene (**23**)



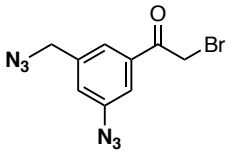
Yellow oil; TLC R_f 0.20 (*n*-hexane/CH_2Cl_2 = 9/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.14 (s, 1H), 4.33 (s, 2H), 6.96 (s, 1H), 7.12 (s, 1H), 7.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 53.9 (1C), 78.8 (1C), 82.1 (1C), 119.0 (1C), 122.1 (1C), 124.3 (1C), 128.0 (1C), 137.8 (1C), 141.0 (1C); IR (KBr, cm^{-1}) 856, 1229, 1306, 1342, 1435, 1599, 2108, 3292; HRMS (ESI^+) *m*/*z* 199.0733 ($[M+H]^+$, $C_9H_7N_6^+$ requires 199.0727).

3'-Azido-5'-(azidomethyl)-α-diazoacetophenone (**24**)



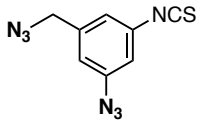
Yellow solid; Mp 57–58 ºC; TLC R_f 0.21 (*n*-hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.42 (s, 2H), 5.91 (s, 1H), 7.13–7.15 (m, 1H), 7.38–7.40 (m, 1H), 7.43–7.45 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 53.9 (1C), 54.9 (1C), 117.0 (1C), 122.1 (1C), 122.3 (1C), 138.2 (1C), 138.7 (1C), 141.6 (1C), 184.7 (1C); IR (KBr, cm^{-1}) 740, 1177, 1236, 1307, 1366, 1442, 1589, 2107; Anal. calcd. for $C_9H_6N_8O$: C, 44.63; H, 2.50; N, 46.27%; Found: C, 44,71; H, 2,49; N, 46.33%.

3-Azido-5-(azidomethyl)phenacyl bromide (**25**)



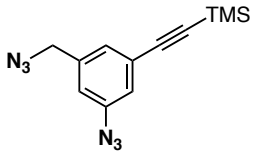
Brown oil; TLC R_f 0.51 (*n*-hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.44 (s, 2H), 4.46 (s, 2H), 7.20–7.23 (m, 1H), 7.57–7.59 (m, 1H), 7.66–7.68 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 30.5 (1C), 53.7 (1C), 118.8 (1C), 123.3 (1C), 124.4 (1C), 135.8 (1C), 138.5 (1C), 141.8 (1C), 190.1 (1C); IR (KBr, cm^{-1}) 851, 1261, 1312, 1347, 1443, 1592, 1688, 2108; HRMS (ESI^+) *m*/*z* 316.9760 ($[M+Na]^+$, $C_9H_7{}^{79}BrN_6NaO^+$ requires 316.9757).

3-Azido-5-(azidomethyl)phenyl isothiocyanate (**28**)



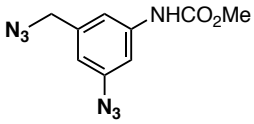
Yellow oil; TLC R_f 0.35 (*n*-hexane/EtOAc = 20/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.35 (s, 2H), 6.81–6.83 (m, 1H), 6.87–6.89 (m, 1H), 6.95–6.97 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 53.6 (1C), 115.7 (1C), 117.1 (1C), 121.4 (1C), 133.4 (1C), 137.8 (1C), 139.1 (1C), 142.2 (1C); IR (KBr, cm^{-1}) 706, 800, 849, 1238, 1323, 1344, 1458, 1599, 2104; HRMS (ESI^+) *m*/*z* 232.0411 ($[M+H]^+$, $C_8H_6N_7S^+$ requires 232.0400).

3-Azido-5-(trimethylsilylethynyl)benzyl azide (**29**)



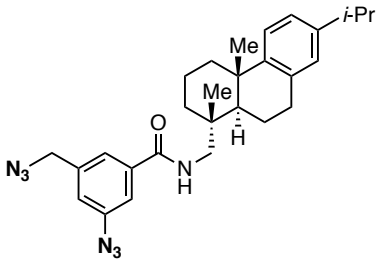
Yellow oil; TLC R_f 0.24 (*n*-hexane/CH_2Cl_2 = 9/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.26 (s, 9H), 4.31 (s, 2H), 6.90–6.92 (m, 1H), 7.09–7.10 (m, 1H), 7.19–7.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ –0.19 (3C), 53.9 (1C), 96.2 (1C), 103.2 (1C), 118.7 (1C), 121.8 (1C), 125.3 (1C), 127.9 (1C), 137.6 (1C), 140.8 (1C); IR (KBr, cm^{-1}) 760, 845, 1250, 1317, 1342, 1589, 2110, 2959; HRMS (ESI^+) *m*/*z* 271.1115 ($[M+H]^+$, $C_{12}H_{15}N_6Si^+$ requires 271.1122).

Methyl (3-azido-5-(azidomethyl)phenyl)carbamate (**31**)



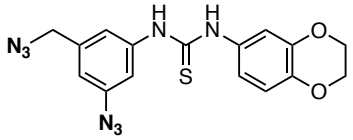
Pale brown solid; Mp 66–67 ºC; TLC R_f 0.45 (*n*-hexane/EtOAc = 7/3); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.79 (s, 3H), 4.31 (s, 2H), 6.68 (s, 1H), 6.78 (s, 1H), 7.09 (s, 1H), 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 52.6 (1C), 54.2 (1C), 108.7 (1C), 113.3 (1C), 114.2 (1C), 138.2 (1C), 139.8 (1C), 141.6 (1C), 153.7 (1C); IR (KBr, cm^{-1}) 847, 1088, 1227, 1348, 1445, 1557, 1609, 1715, 2110, 3321; HRMS (ESI^+) *m*/*z* 270.0704 ($[M+Na]^+$, $C_9H_9N_7NaO_2^+$ requires 270.0710).

N-(+)-Dehydroabietyl 3-azido-5-(azidomethyl)benzamide (**34**)



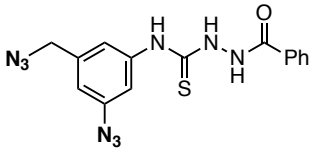
Pale yellow oil; TLC R_f 0.45 (*n*-hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.01 (s, 3H), 1.21 (d, 6H, *J* = 6.9 Hz), 1.23 (s, 3H), 1.26–1.42 (m, 2H), 1.46 (dd, 1H, *J* = 12.3, 1.8 Hz), 1.48–1.54 (m, 1H), 1.64–1.83 (m, 3H), 1.93–1.99 (m, 1H), 2.27–2.33 (m, 1H), 2.78–2.87 (m, 2H), 2.90–2.96 (m, 1H), 3.32 (dd, 1H, *J* = 13.7, 6.5 Hz), 3.43 (dd, 1H, *J* = 13.7, 6.5 Hz), 4.38 (s, 2H), 6.13–6.21 (m, 1H), 6.89 (s, 1H), 6.99 (d, 1H, *J* = 8.2 Hz), 7.07 (s, 1H), 7.16 (d, 1H, *J* = 8.2 Hz), 7.36 (s, 1H), 7.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 18.6 (1C), 18.8 (1C), 19.1 (1C), 23.9 (2C), 25.4 (1C), 30.3 (1C), 33.4 (1C), 36.5 (1C), 37.5 (1C), 37.8 (1C), 38.3 (1C), 45.8 (1C), 50.6 (1C), 53.9 (1C), 117.5 (1C), 121.0 (1C), 122.4 (1C), 123.9 (1C), 124.2 (1C), 127.0 (1C), 134.7 (1C), 137.3 (1C), 138.1 (1C), 141.4 (1C), 145.7 (1C), 147.0 (1C), 166.3 (1C); IR (KBr, cm^{-1}) 729, 908, 1344,1435, 1520, 1593, 1643, 2112, 2959, 3316; HRMS (ESI^+) *m*/*z* 508.2784 ($[M+Na]^+$, $C_{28}H_{35}N_7NaO^+$ requires 508.2795).

1-(3-Azido-5-(azidomethyl)phenyl)-3-(3,4-ethylenedioxyphenyl)thiourea (**35**)



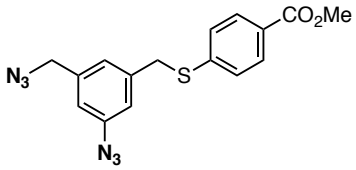
Yellow oil; TLC R_f 0.52 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.27–4.31 (m, 4H), 4.34 (s, 2H), 6.80 (dd, 1H, *J* = 8.5, 2.5 Hz), 6.83 (s, 1H), 6.86 (d, 1H, *J* = 2.5 Hz), 6.93 (d, 1H, *J* = 8.5 Hz), 7.14 (s, 1H), 7.22 (s, 1H), 7.60 (s, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 54.0 (1C), 64.28 (1C), 64.32 (1C), 115.1 (1C), 115.3 (1C), 116.1 (1C), 118.5 (1C), 119.3 (1C), 120.4 (1C), 128.9 (1C), 138.2 (1C), 139.8 (1C), 141.4 (1C), 143.6 (1C), 144.4 (1C), 180.0 (1C); IR (KBr, cm^{-1}) 731, 887, 1065, 1242, 1305, 1506, 1595, 2112, 3221; HRMS (ESI^+) *m*/*z* 405.0844 ($[M+Na]^+$, $C_{16}H_{14}N_8NaO_2S^+$ requires 405.0853).

N-(3-azido-5-(azidomethyl)phenyl)-2-benzoylhydrazine-1-carbothioamide (**36**)



Colorless solid; Mp 165–167 ºC; TLC R_f 0.57 (*n*-hexane/EtOAc = 3/7); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 4.48 (s, 2H), 6.93 (s, 1H), 7.33 (s, 1H), 7.40 (s, 1H), 7.49–7.55 (AA'BB'C, 2H), 7.58–7.62 (AA'BB'C, 1H), 7.94–7.99 (AA'BB'C, 2H), 9.91 (br, 2H), 10.6 (br, 1H); ^{13}C NMR (DMSO-d_6, 126 MHz) δ 53.4 (1C), 115.7 (1C), 115.9 (1C), 122.2 (1C), 128.4 (2C), 128.7 (2C), 132.4 (1C), 132.8 (1C), 138.0 (1C), 139.6 (1C), 141.2 (1C), 166.4 (1C), 181.3 (1C); IR (KBr, cm^{-1}) 685, 704, 1364, 1541, 1578, 1630, 2112, 3312; HRMS (ESI$^+$) *m*/*z* 390.0844 ([M+Na]$^+$, $C_{15}H_{13}N_9NaOS^+$ requires 390.0856).

3-Azido-5-(azidomethyl)benzyl 4-methoxycarbonylphenyl sulfide (**37**)

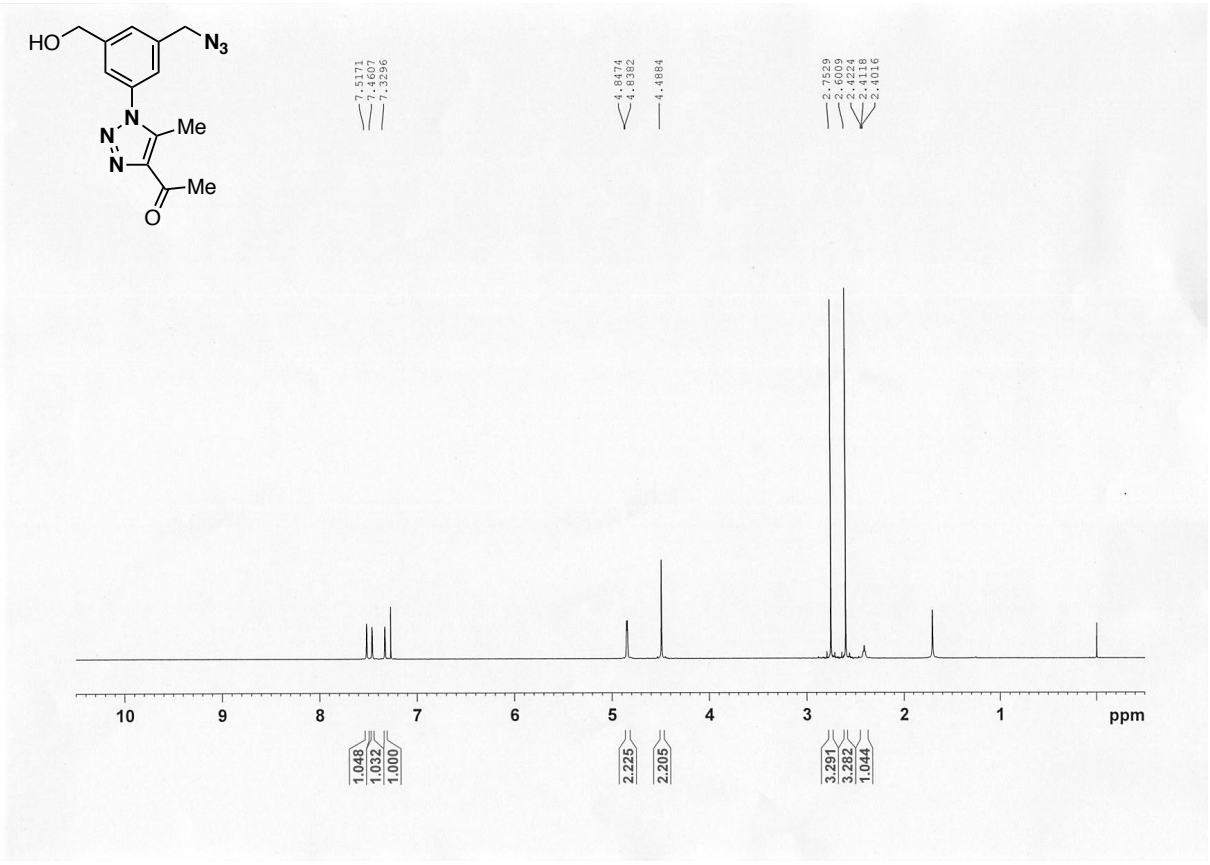


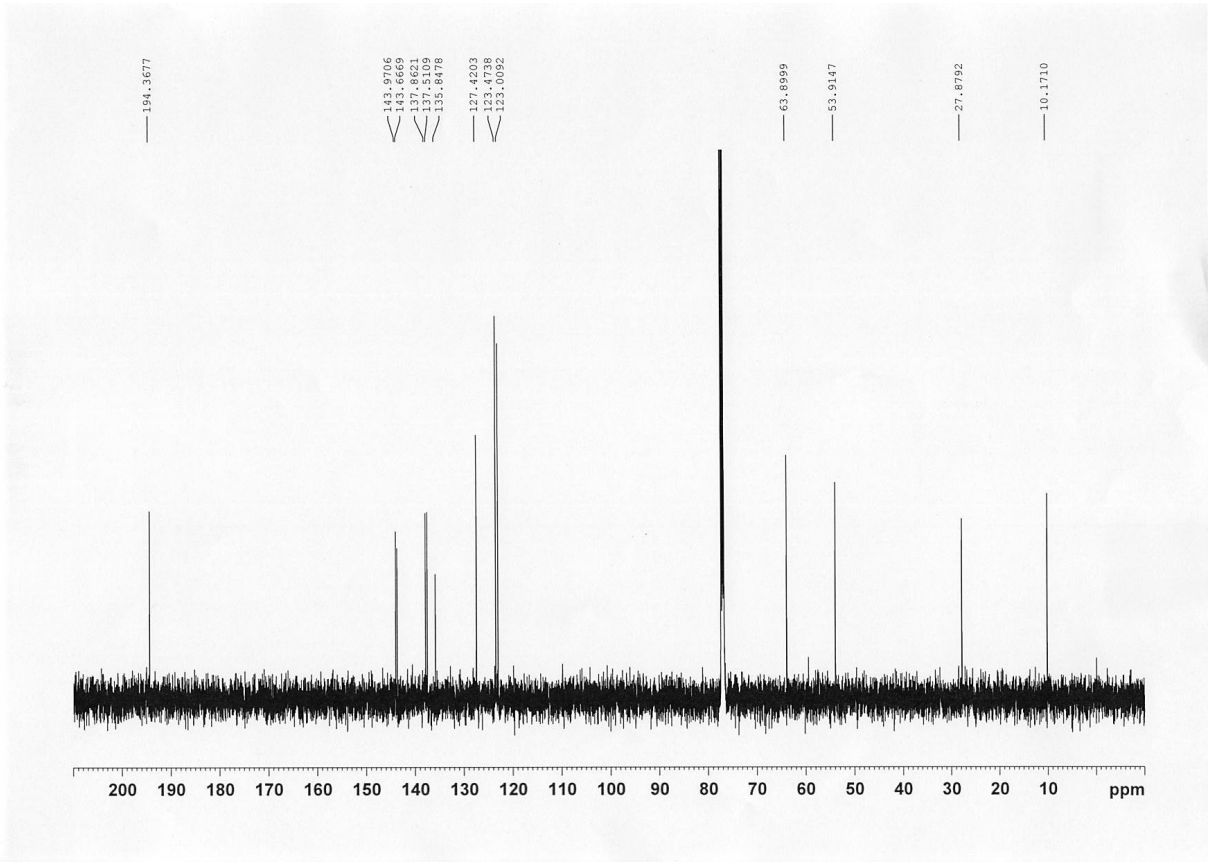
Colorless solid; Mp 90–93 ºC; TLC R_f 0.57 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.89 (s, 3H), 4.17 (s, 2H), 4.31 (s, 2H), 6.87 (s, 1H), 6.98 (s, 1H), 7.07 (s, 1H), 7.27–7.31 (AA'BB', 2H), 7.90–7.93 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 37.1 (1C), 52.1 (1C), 54.1 (1C), 117.7 (1C), 119.0 (1C), 124.8 (1C), 127.5 (2C), 127.6 (1C), 130.0 (2C), 137.8 (1C), 139.3 (1C), 141.1 (1C), 142.6 (1C), 166.6 (1C); IR (KBr, cm^{-1}) 758, 1113, 1294, 1433, 1454, 1593, 1713, 2106; HRMS (ESI$^+$) *m*/*z* 377.0791 ([M+Na]$^+$, $C_{16}H_{14}N_6NaO_2S^+$ requires 377.0791).

For other materials reported previously, see *Eur. J. Org. Chem.* **2014**, 3991.

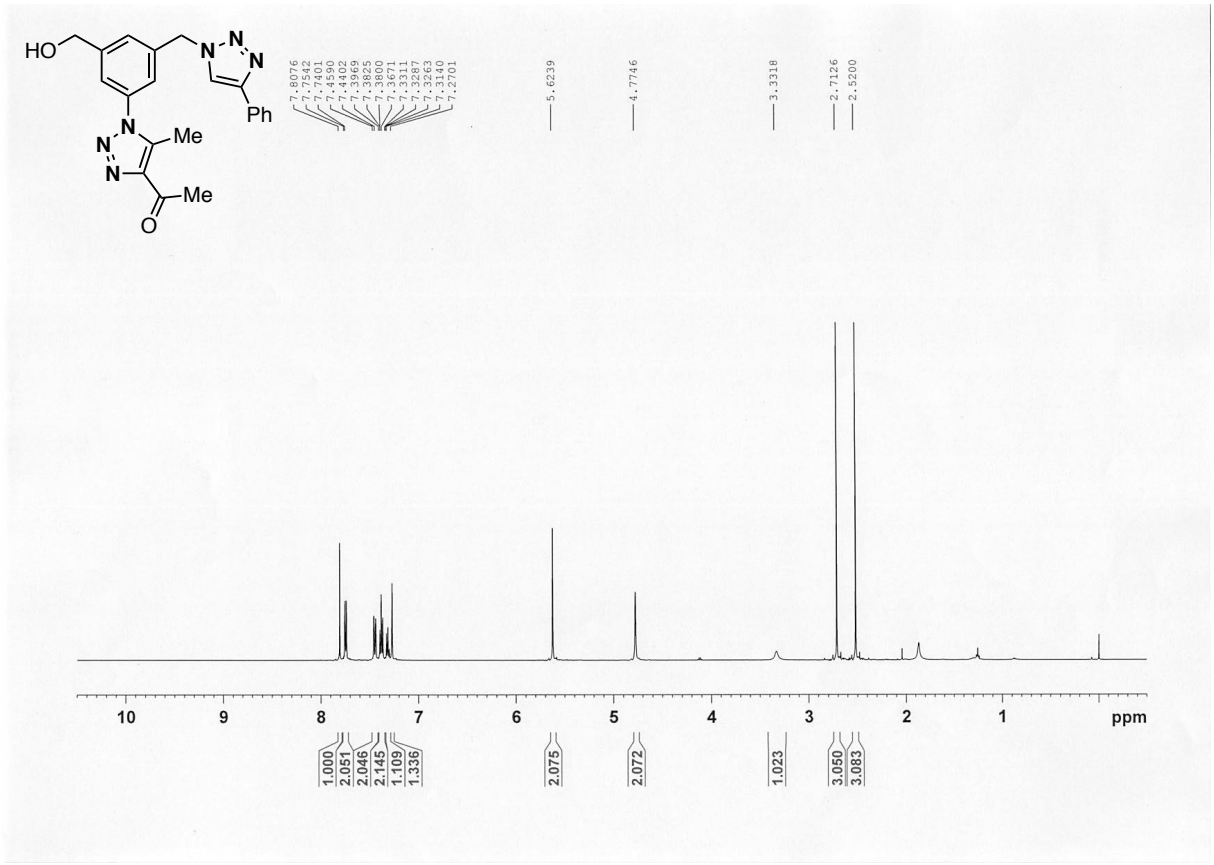
^{1}H and ^{13}C NMR Spectra of New Compounds

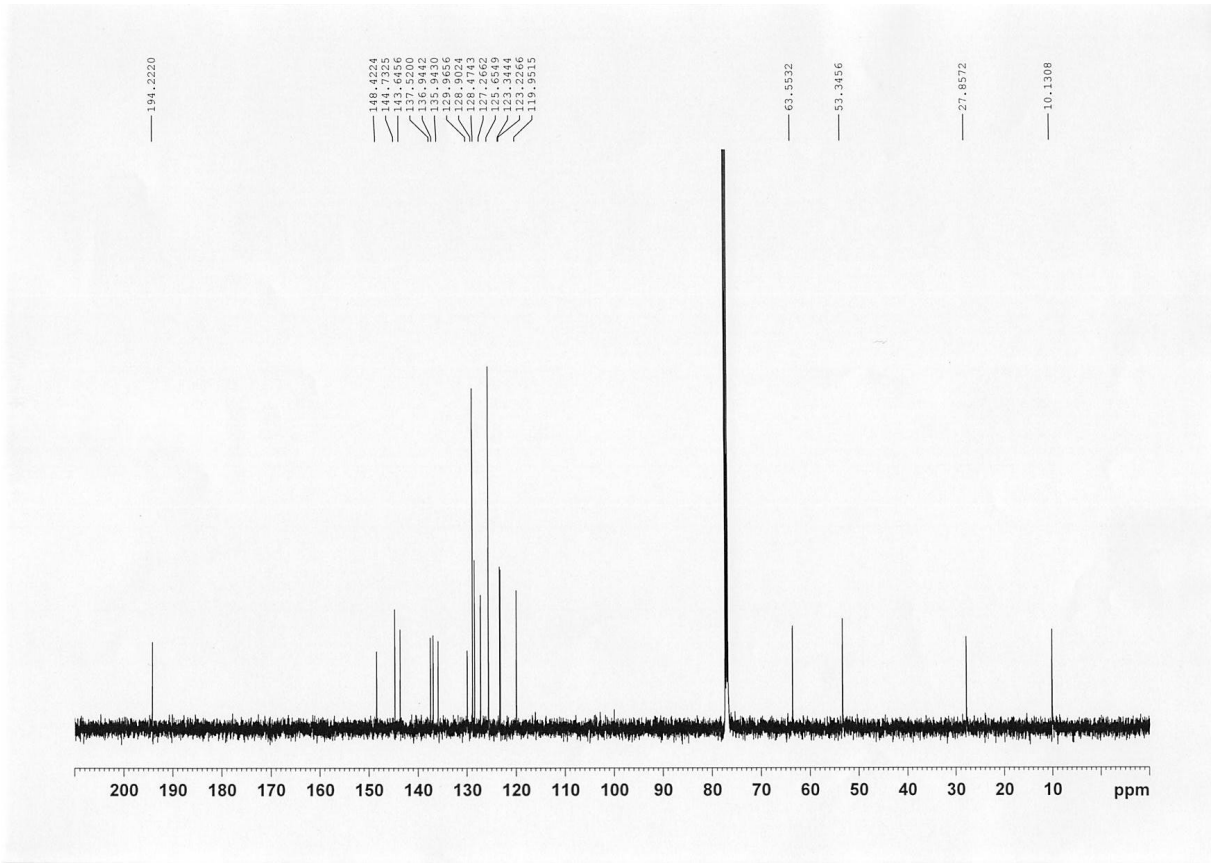
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **S1** ($CDCl_3$)



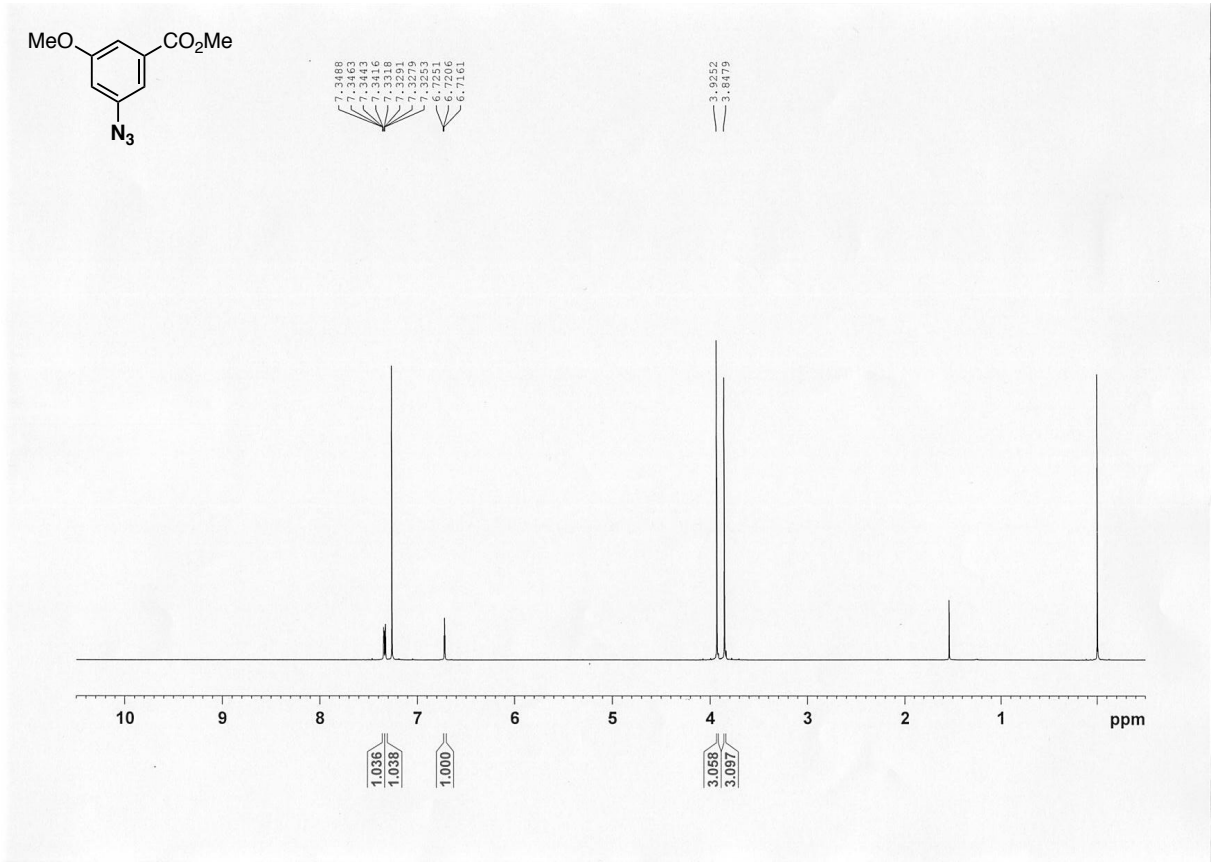


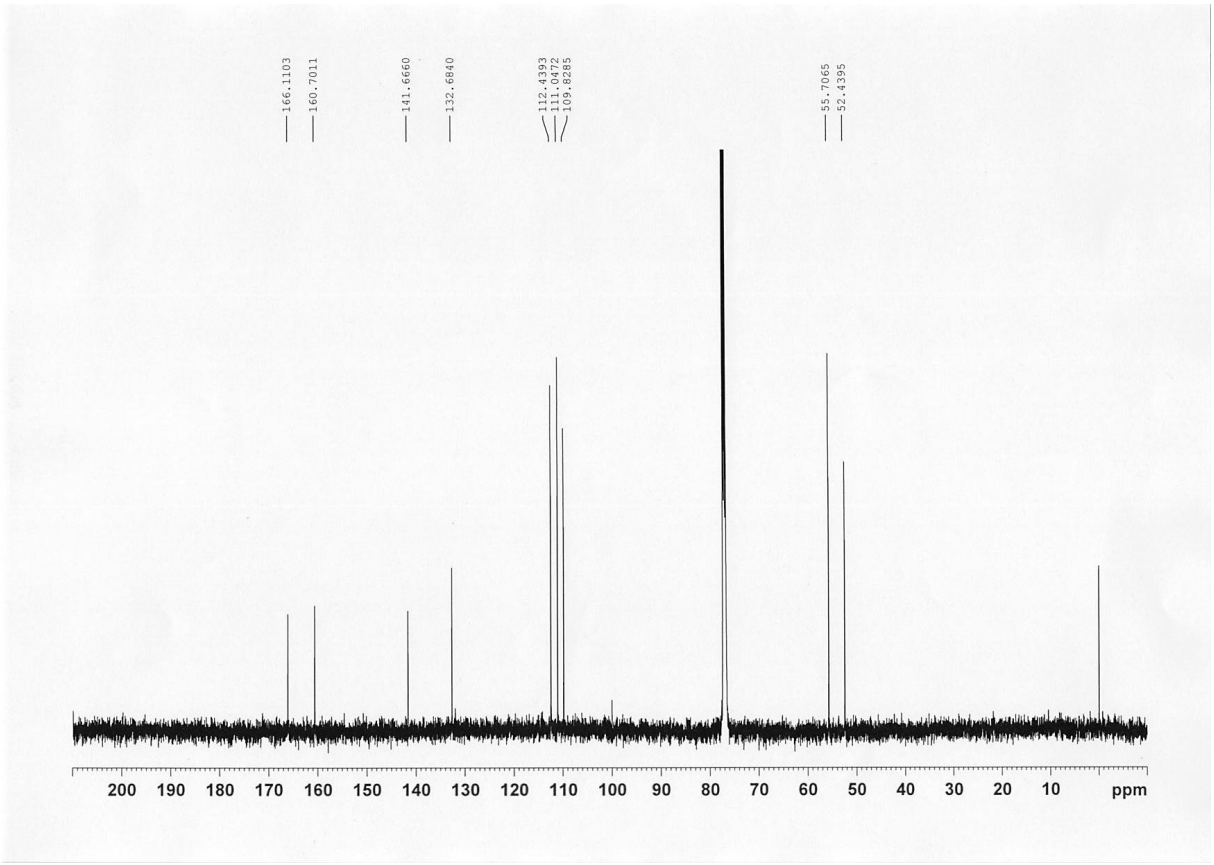
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **2** ($CDCl_3$)



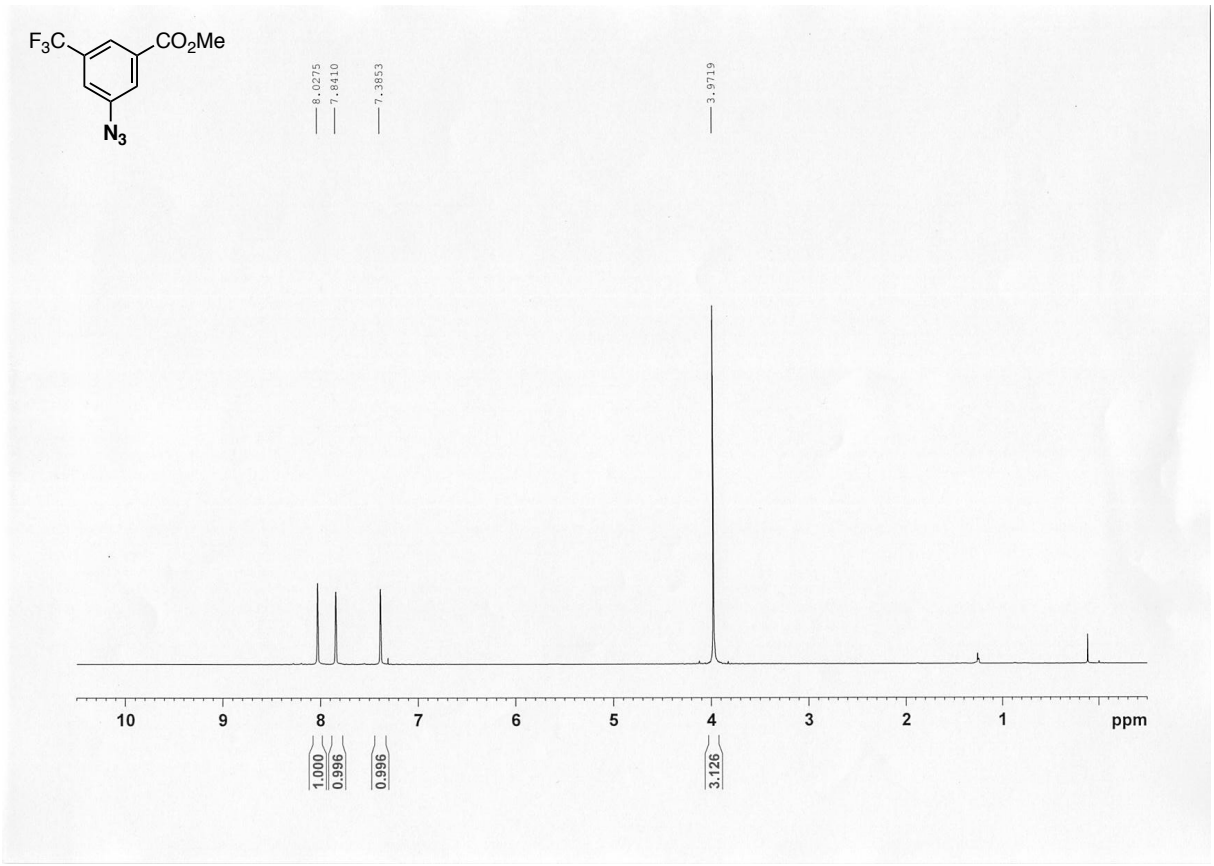


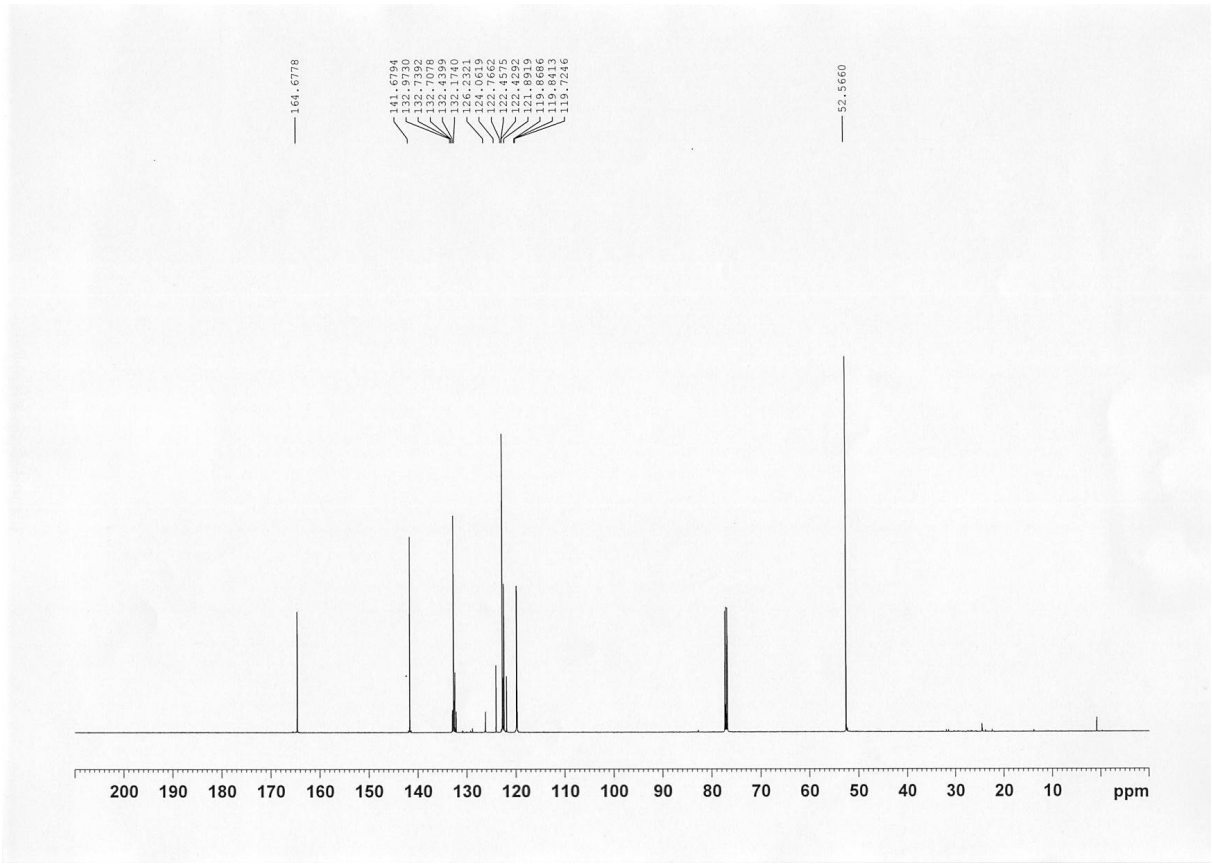
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **9c** ($CDCl_3$)



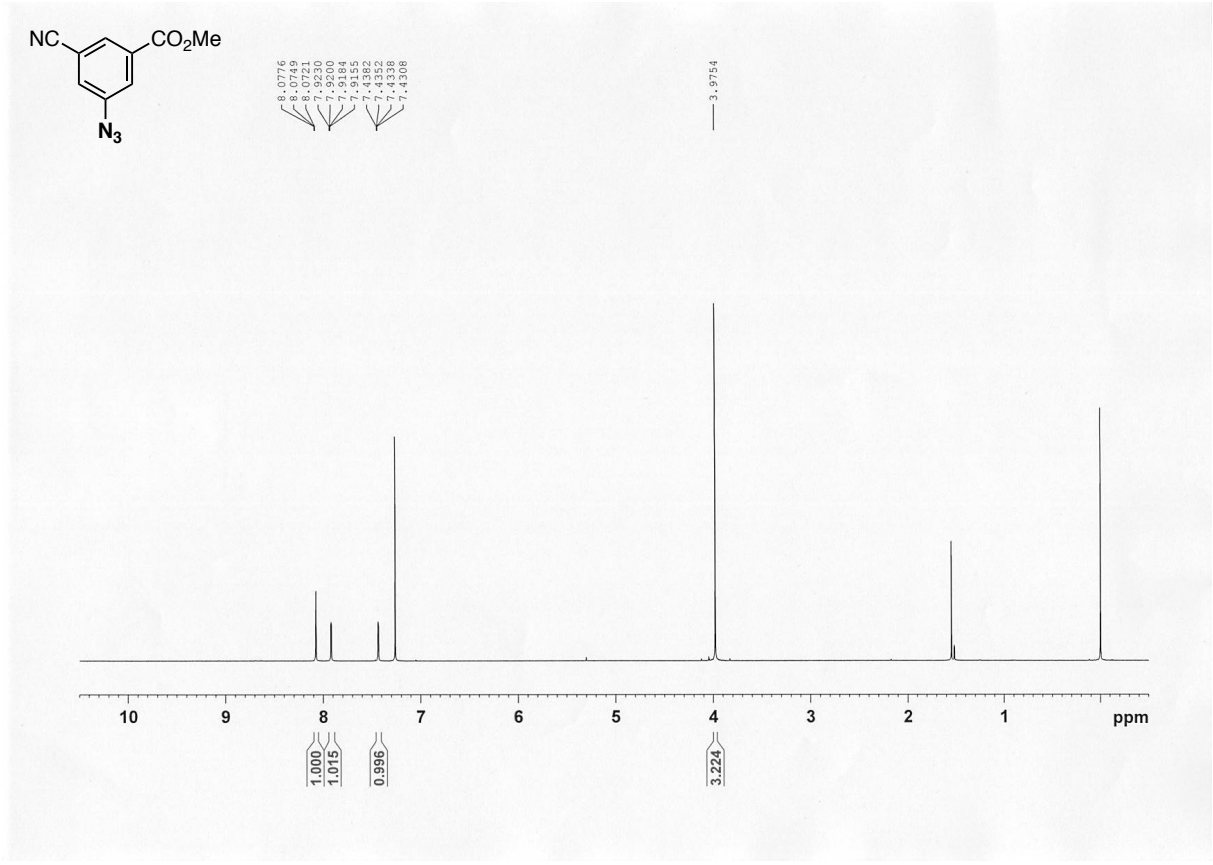


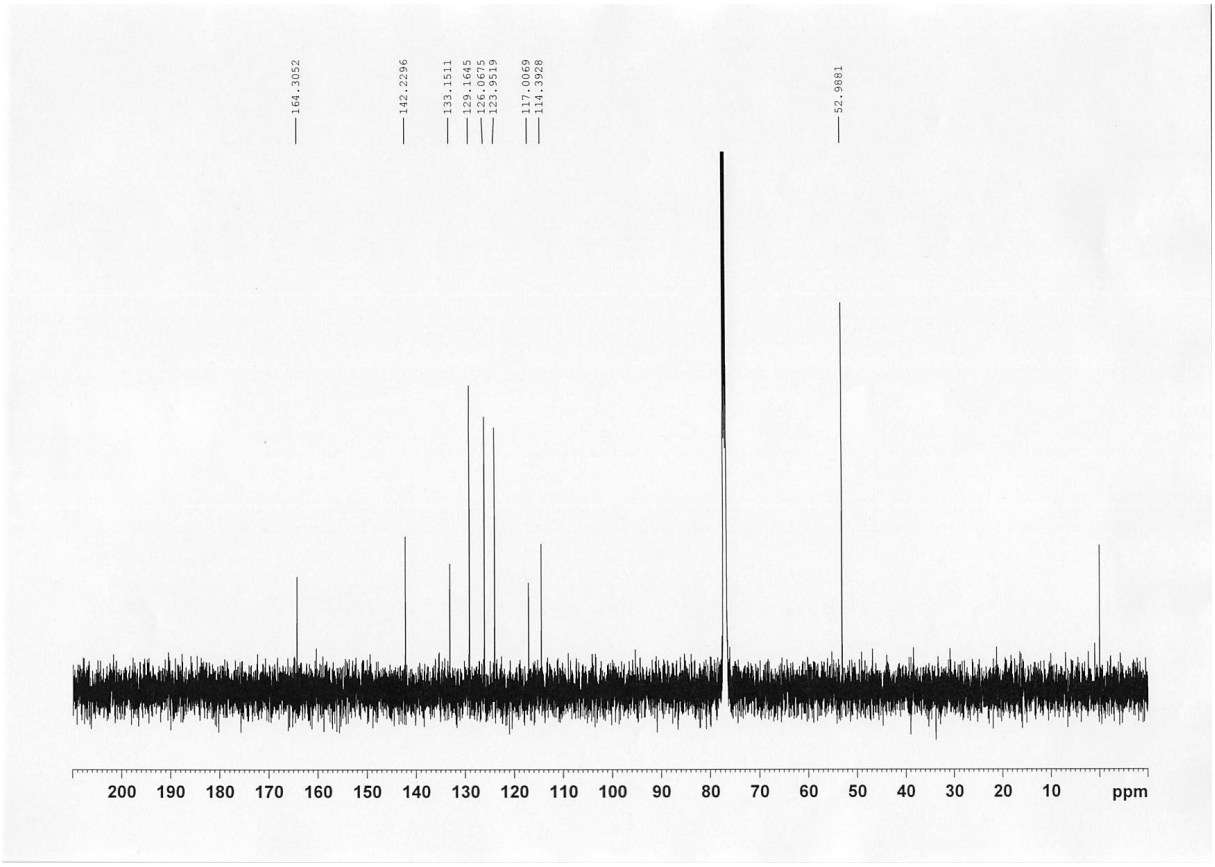
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **9d** ($CDCl_3$)



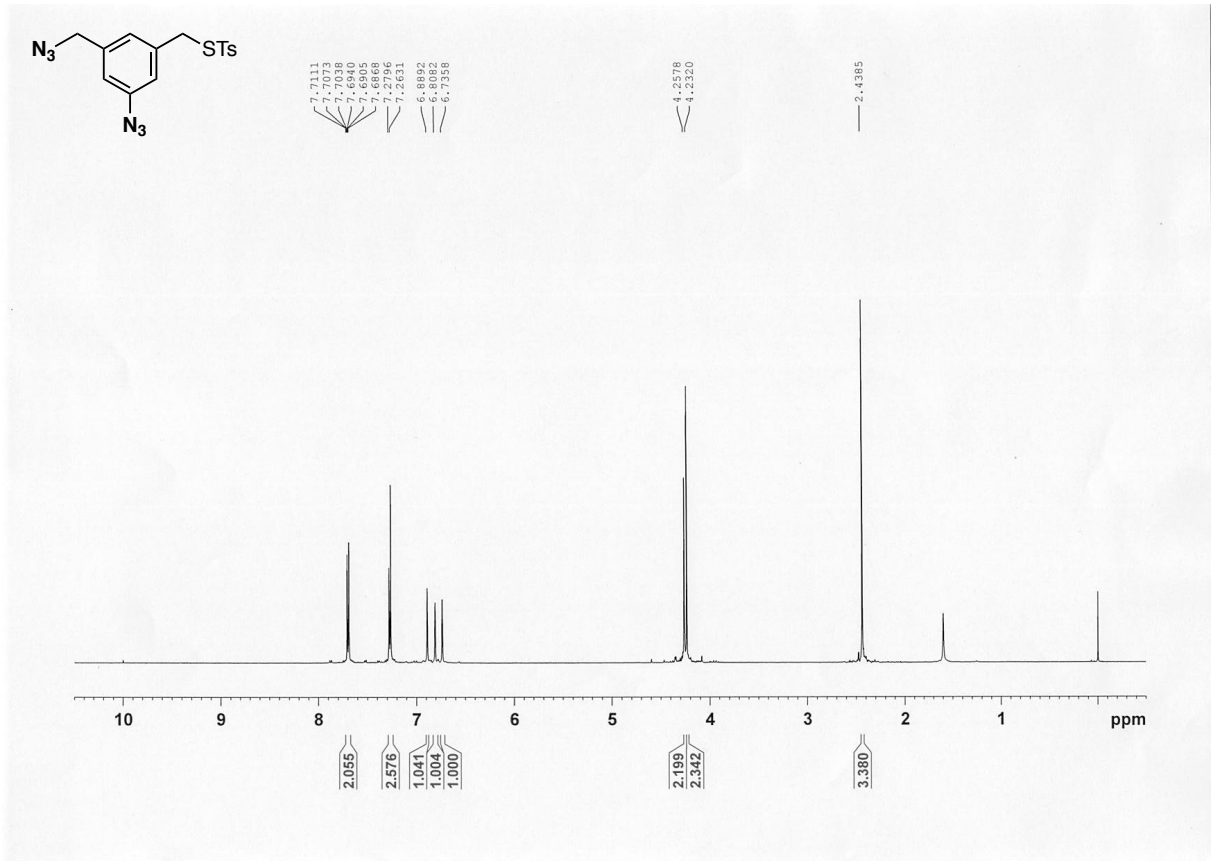


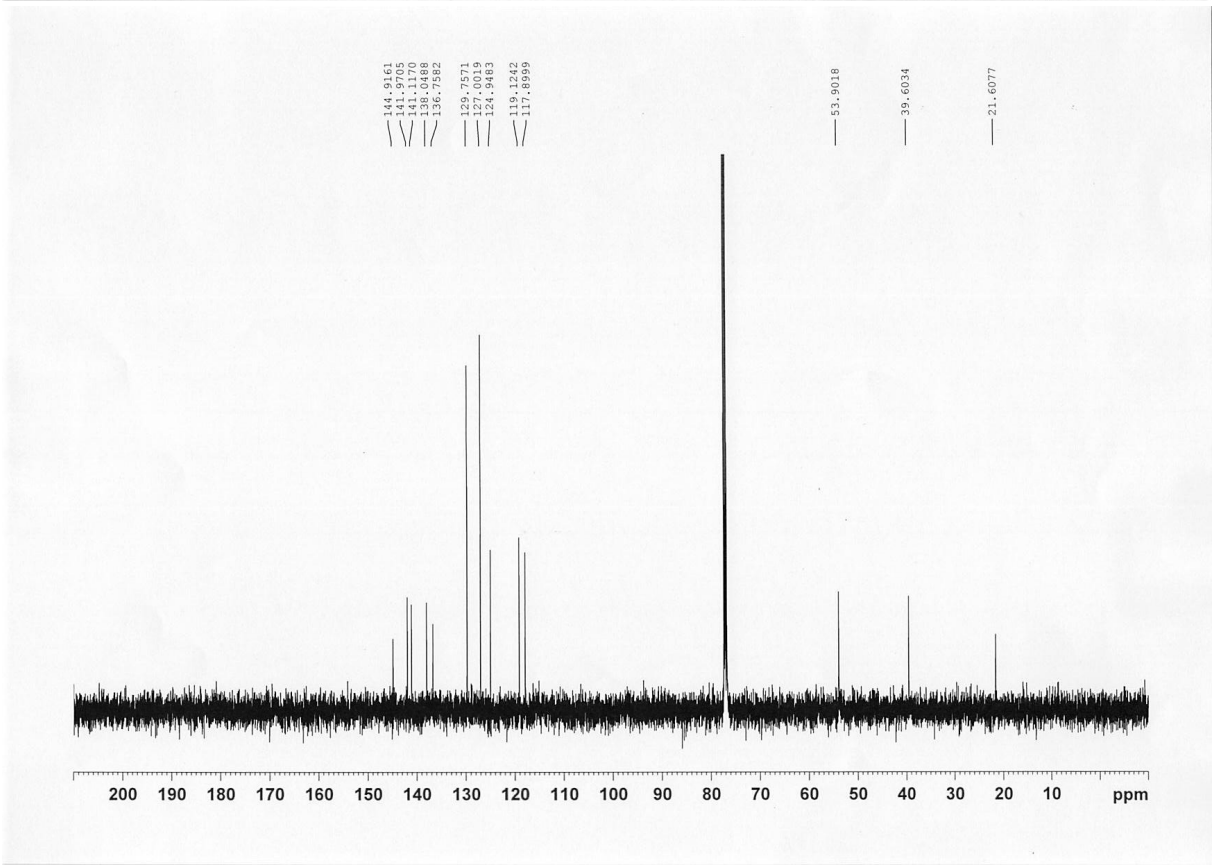
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **9e** ($CDCl_3$)



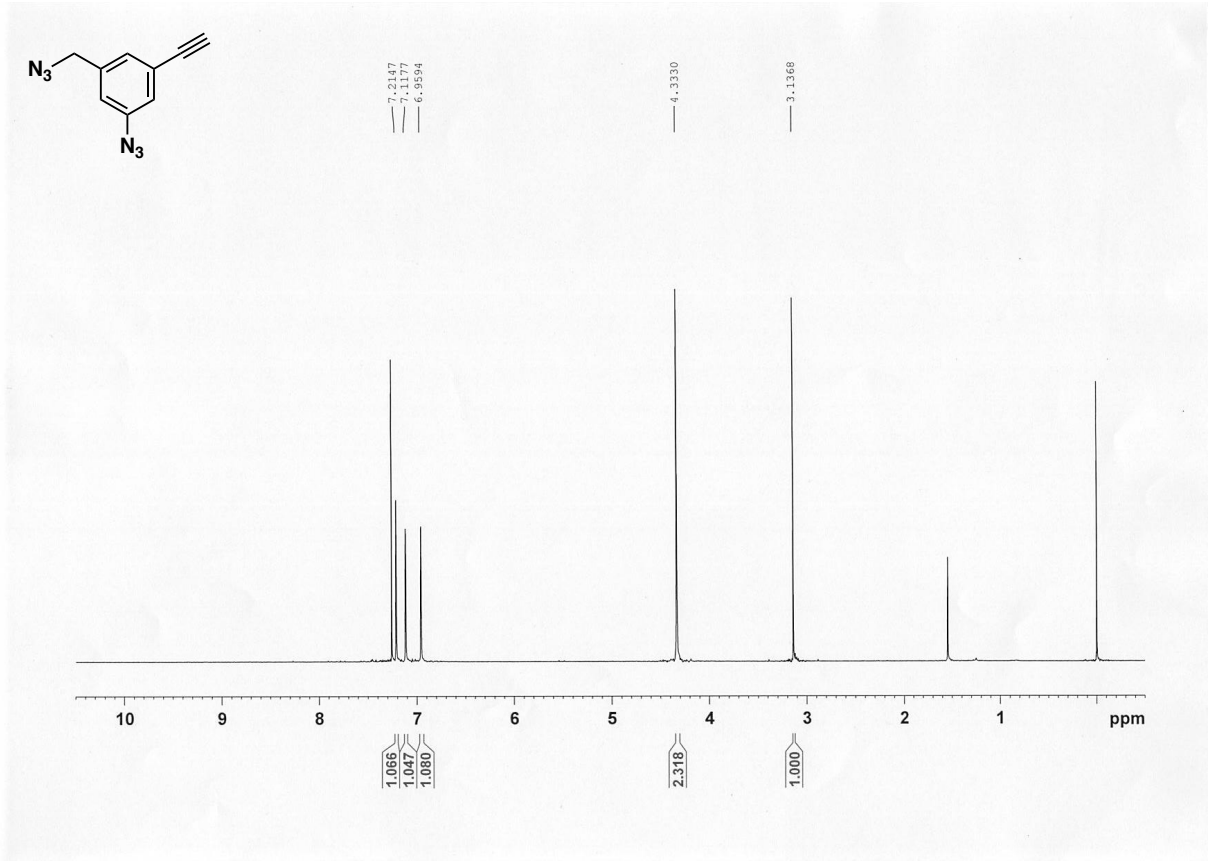


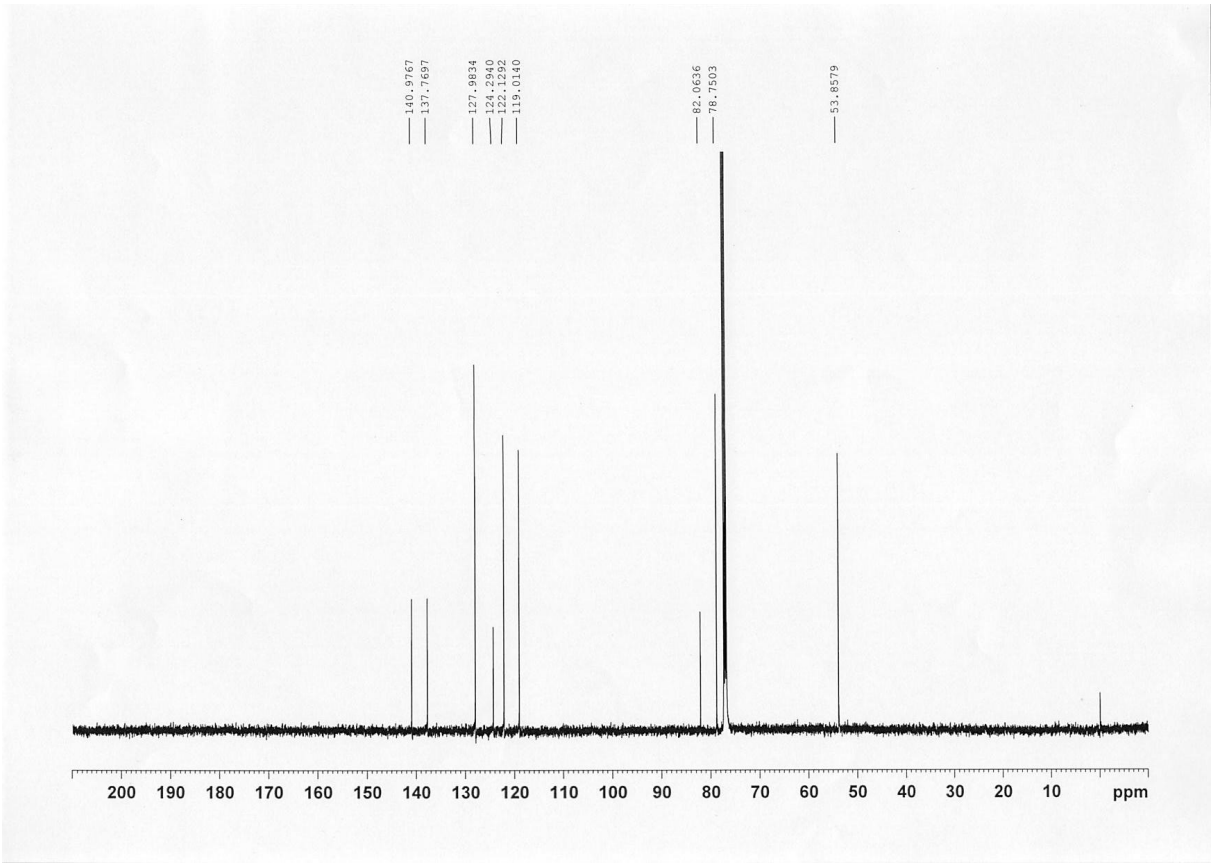
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **21** ($CDCl_3$)



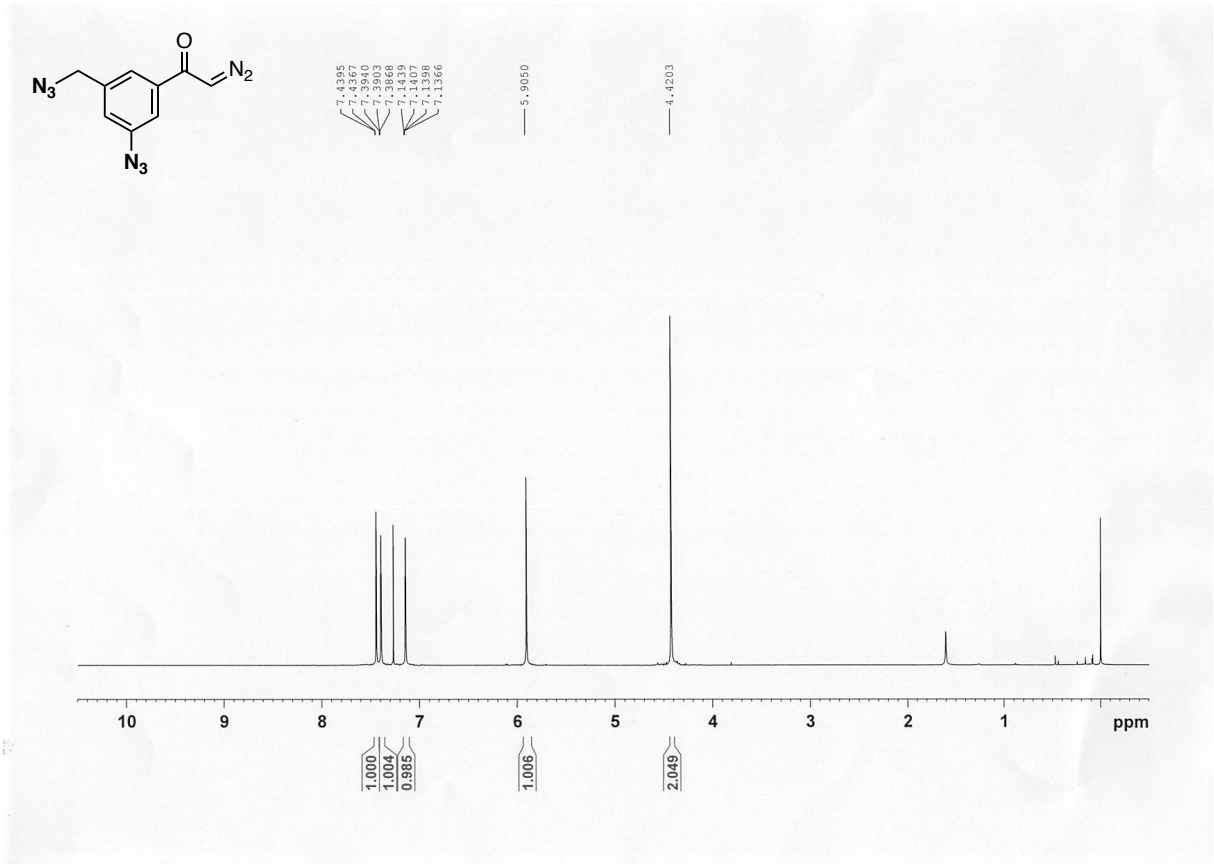


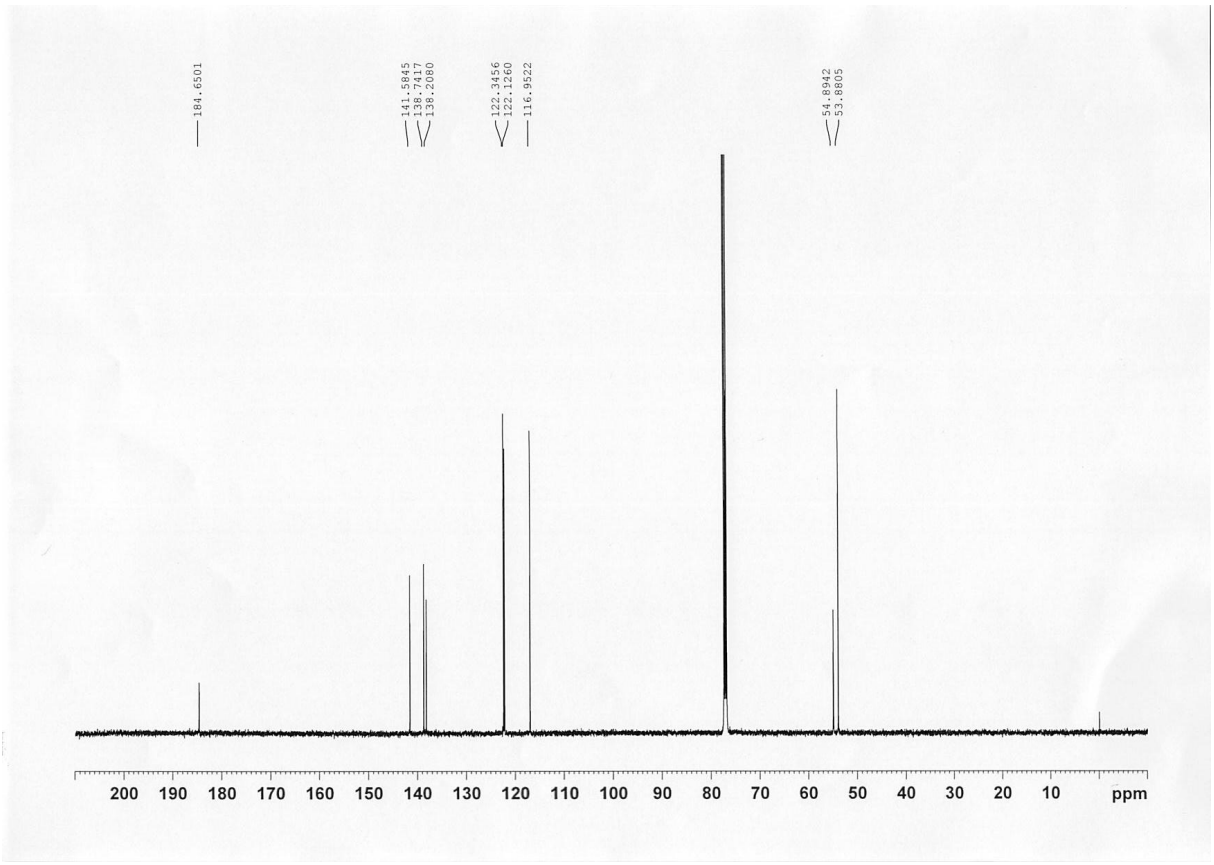
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **23** ($CDCl_3$)



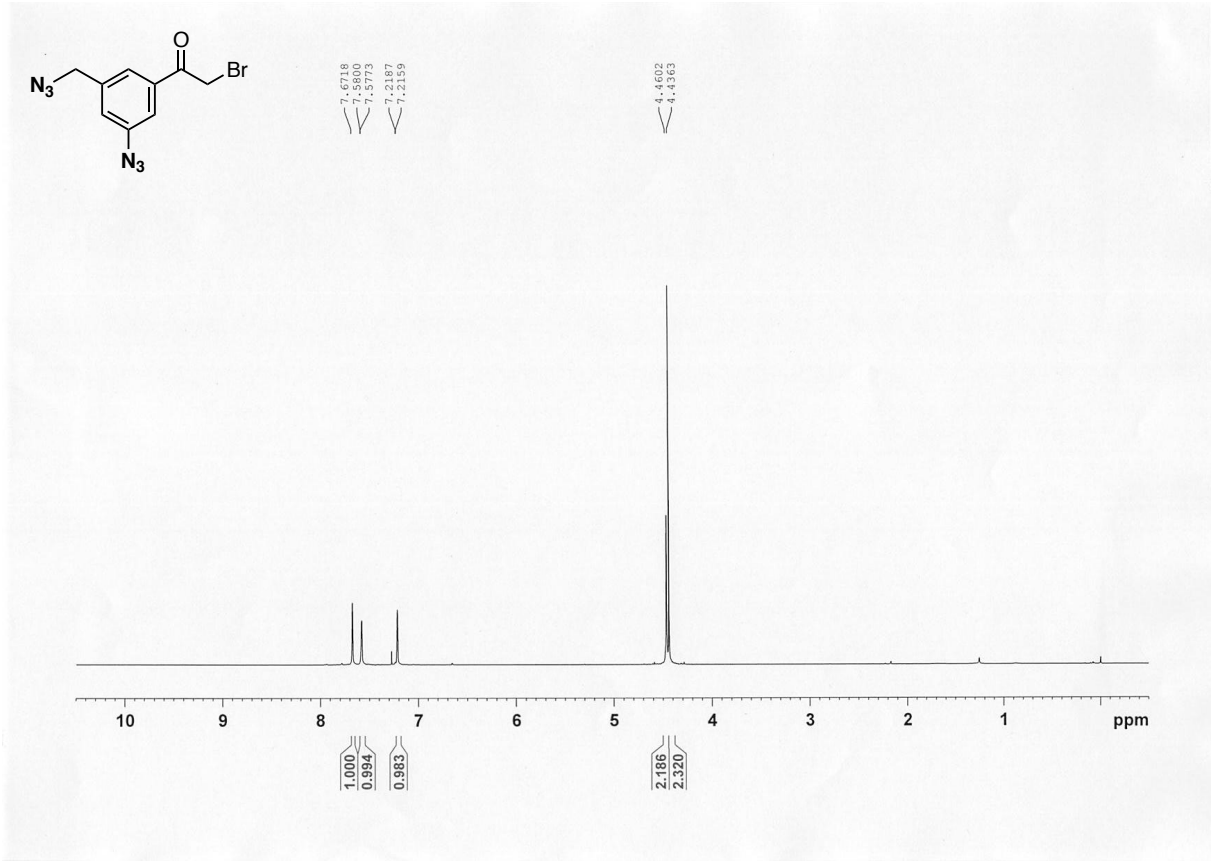


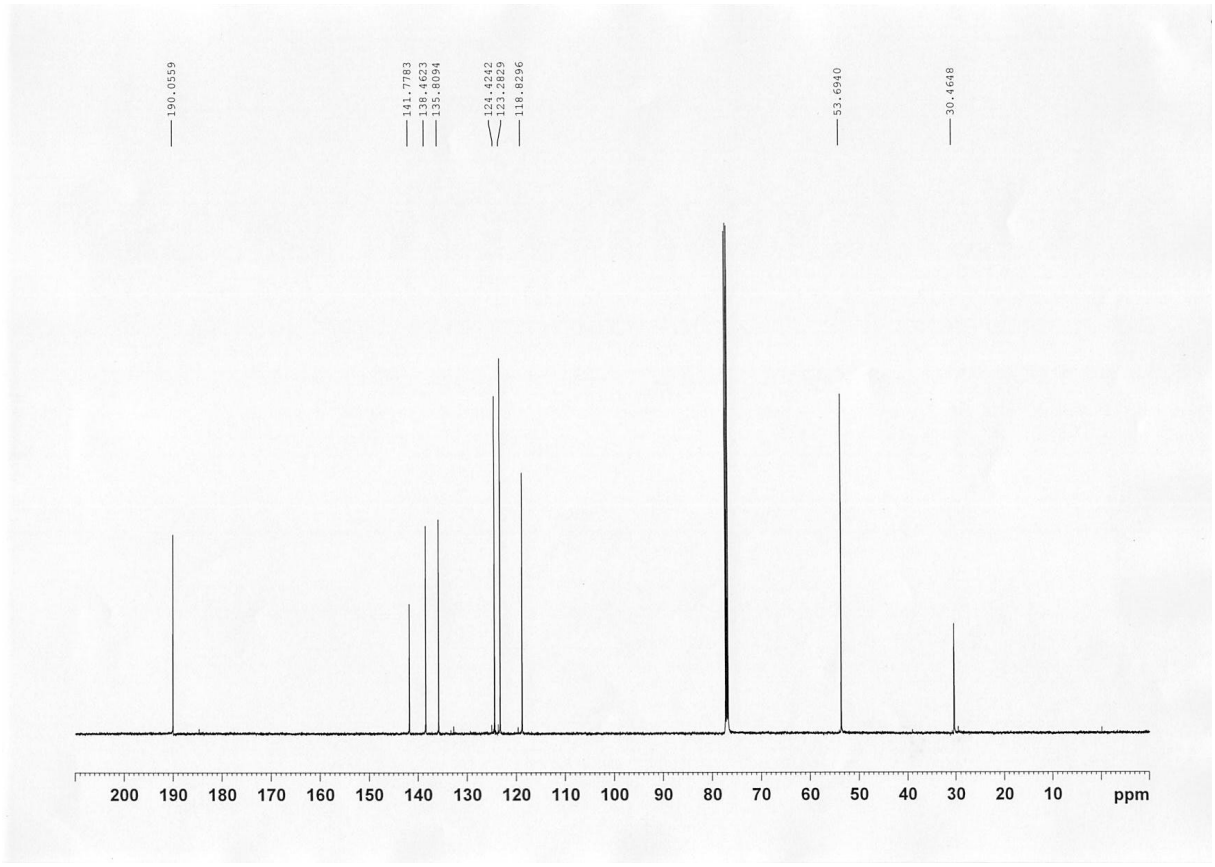
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **24** ($CDCl_3$)



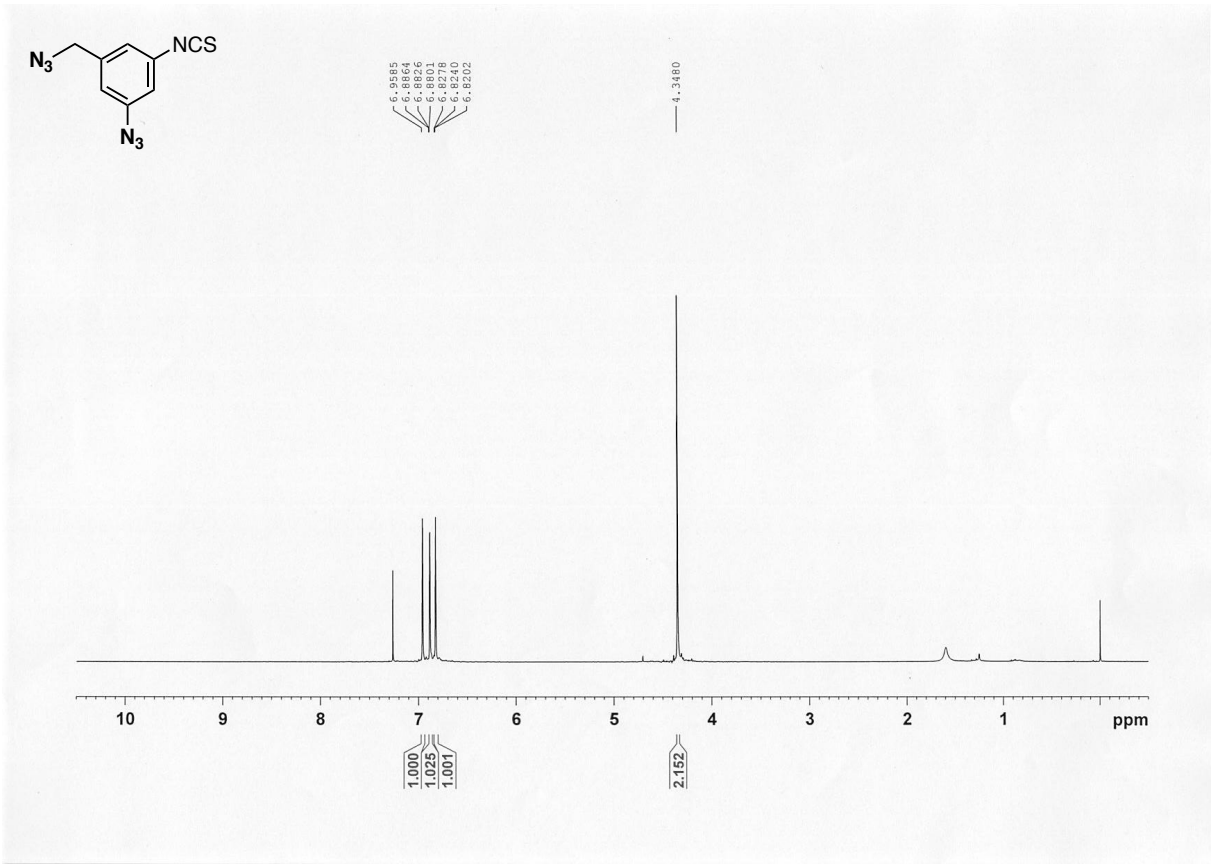


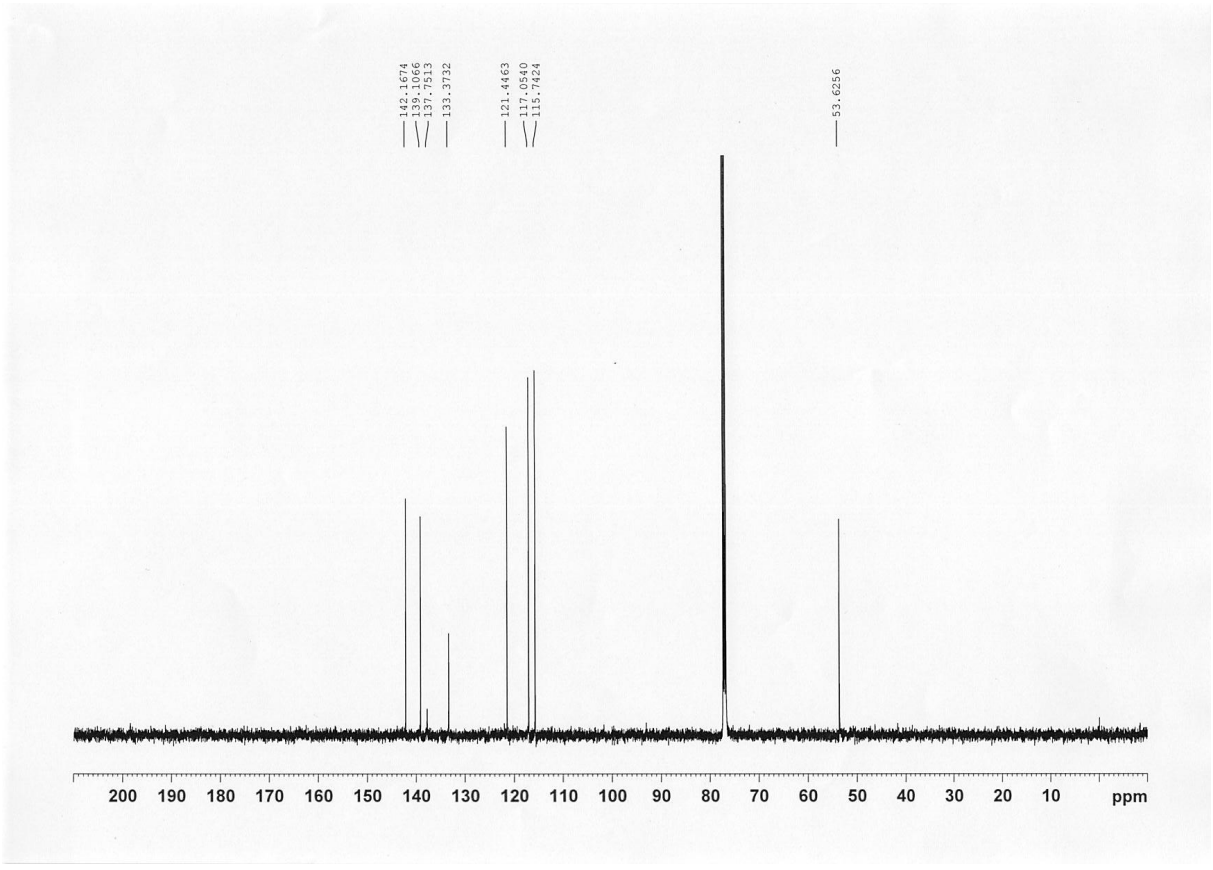
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **25** ($CDCl_3$)



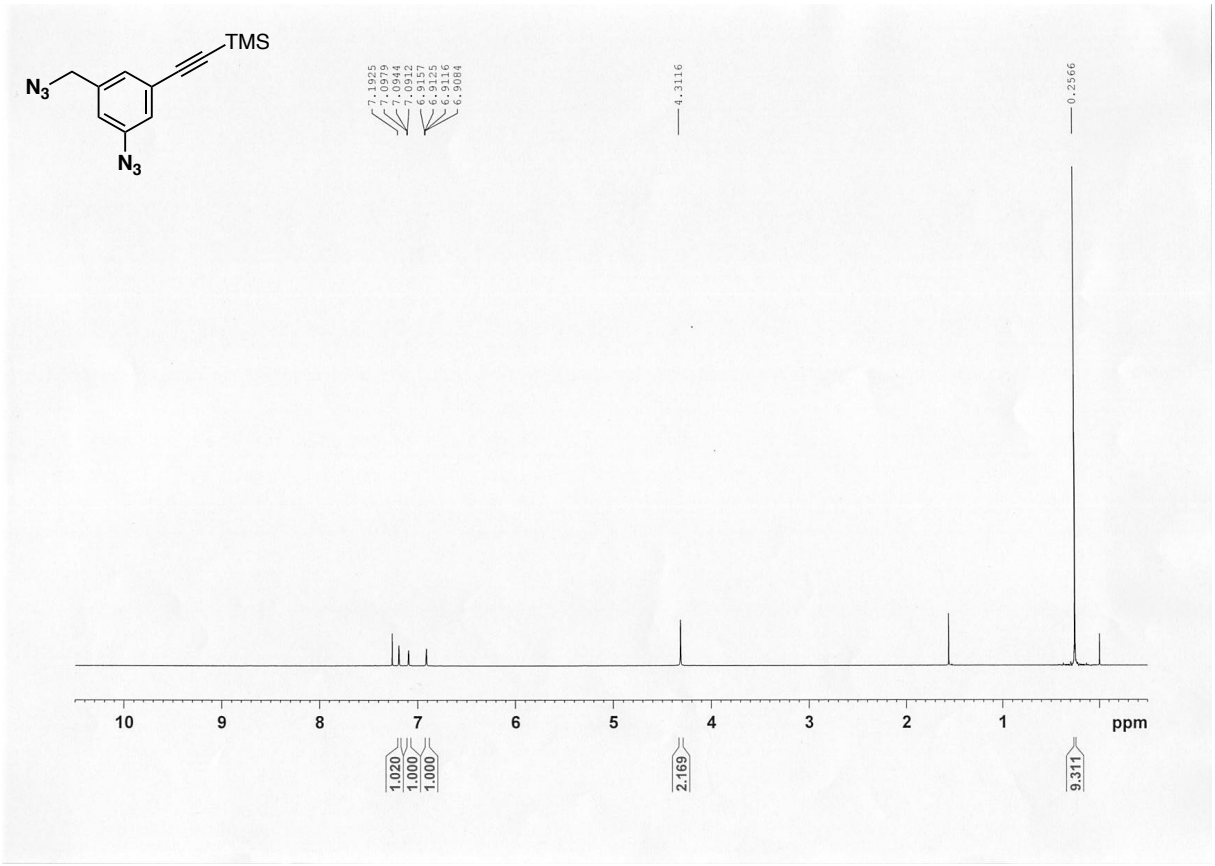


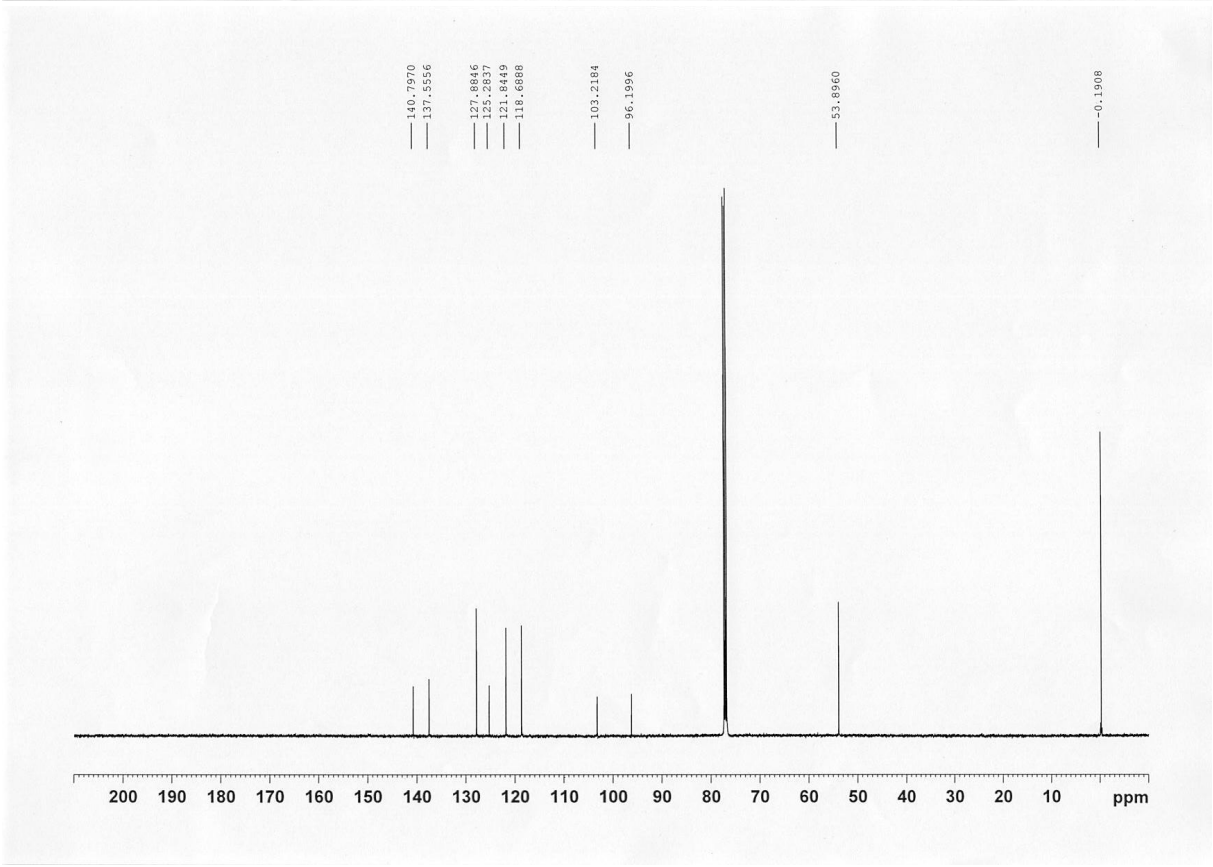
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **28** ($CDCl_3$)



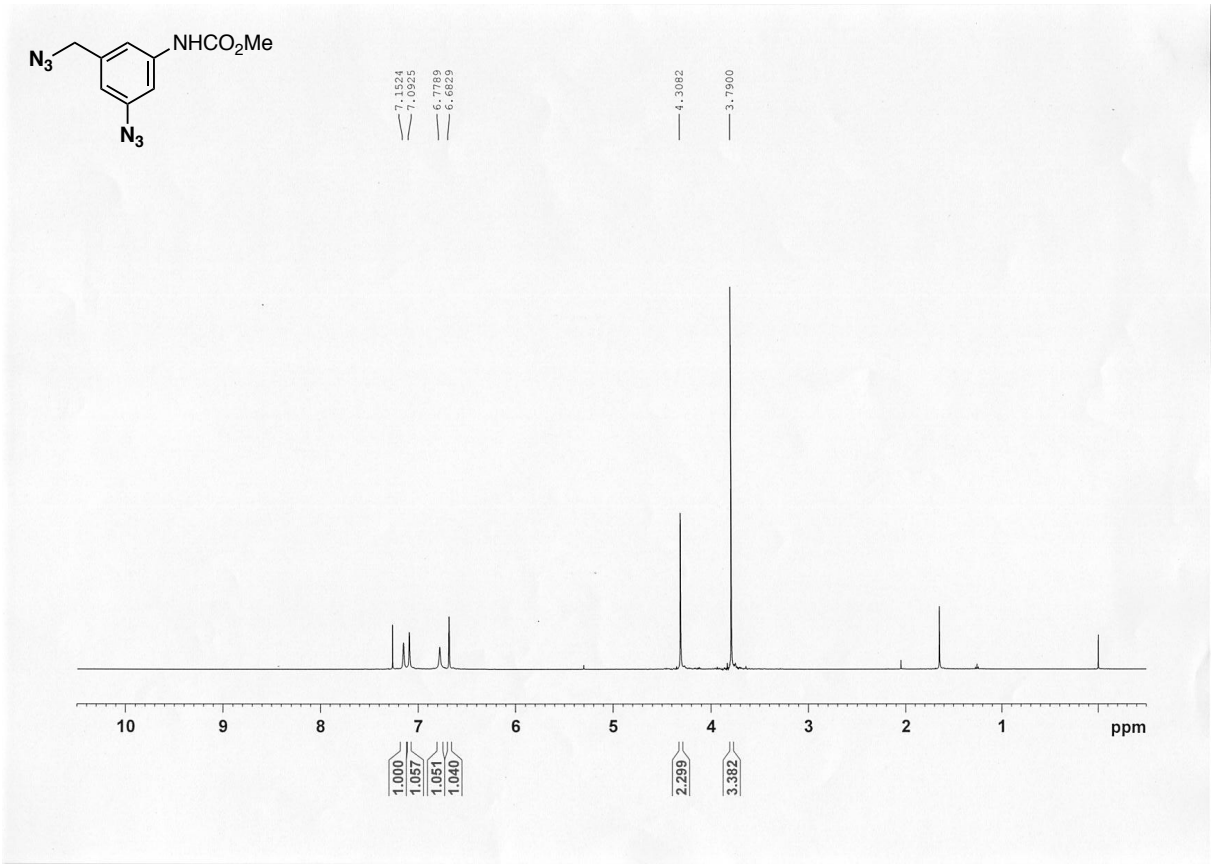


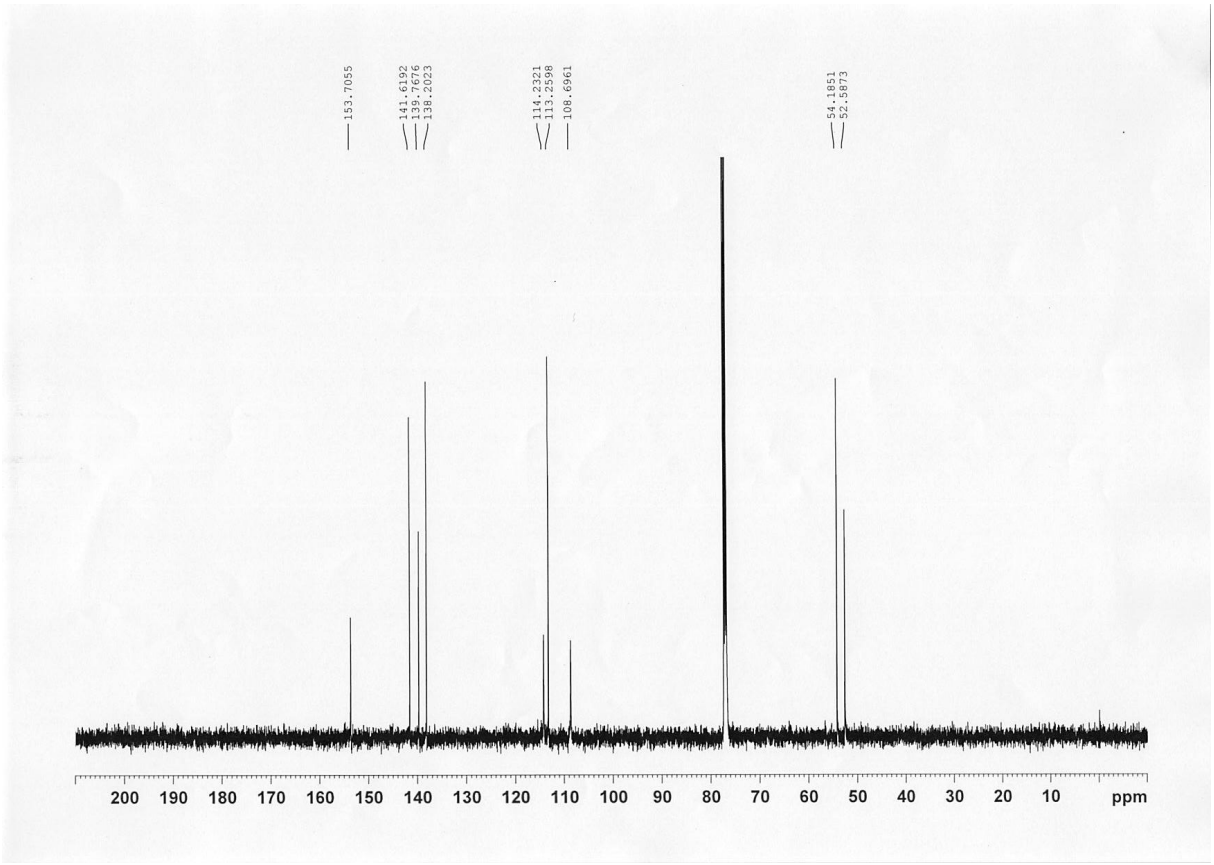
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **29** ($CDCl_3$)



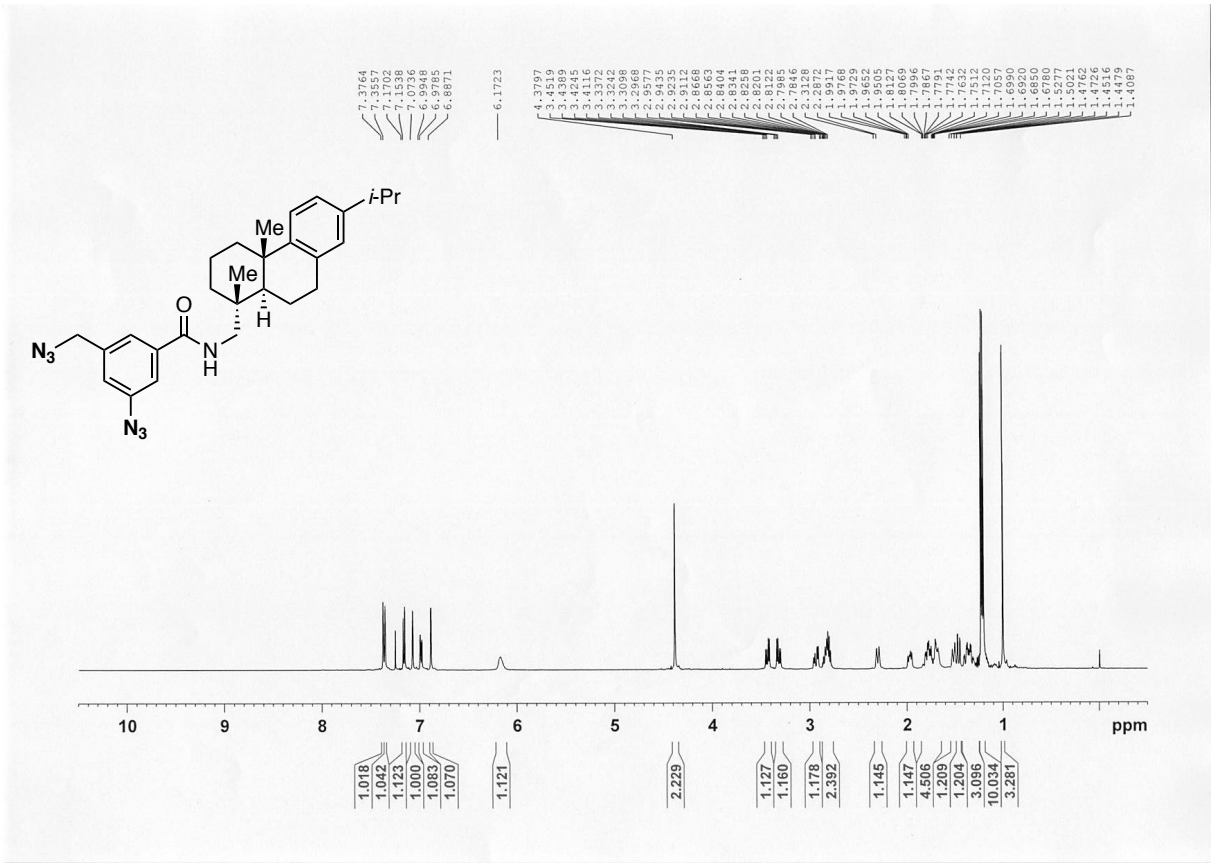


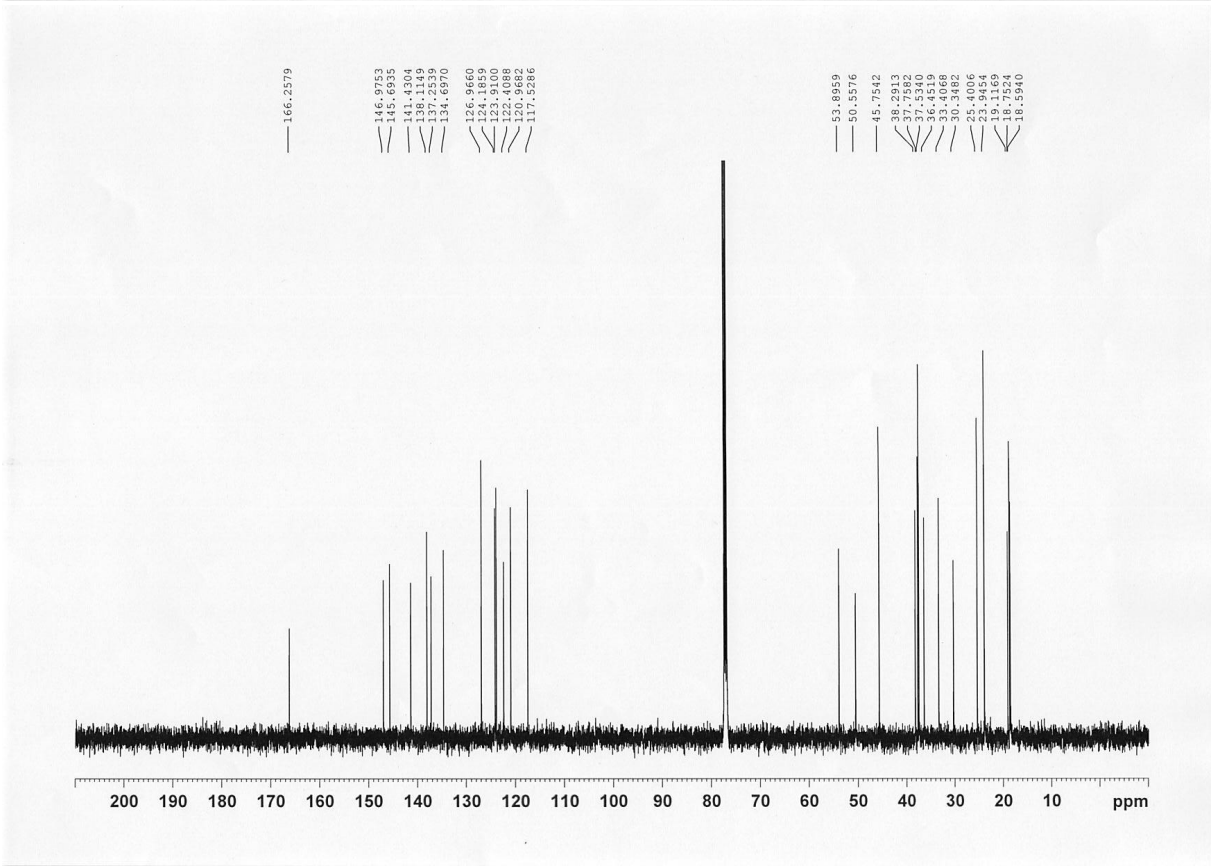
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **31** ($CDCl_3$)



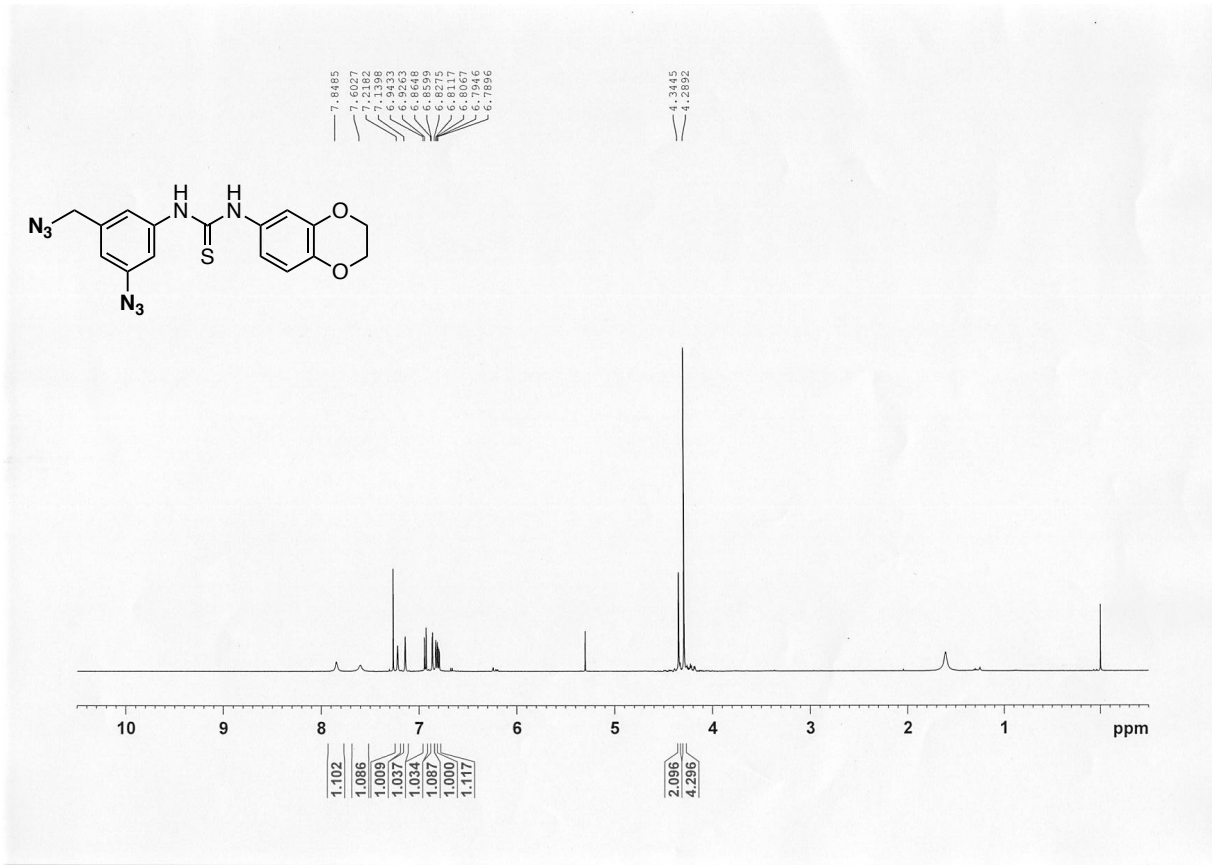


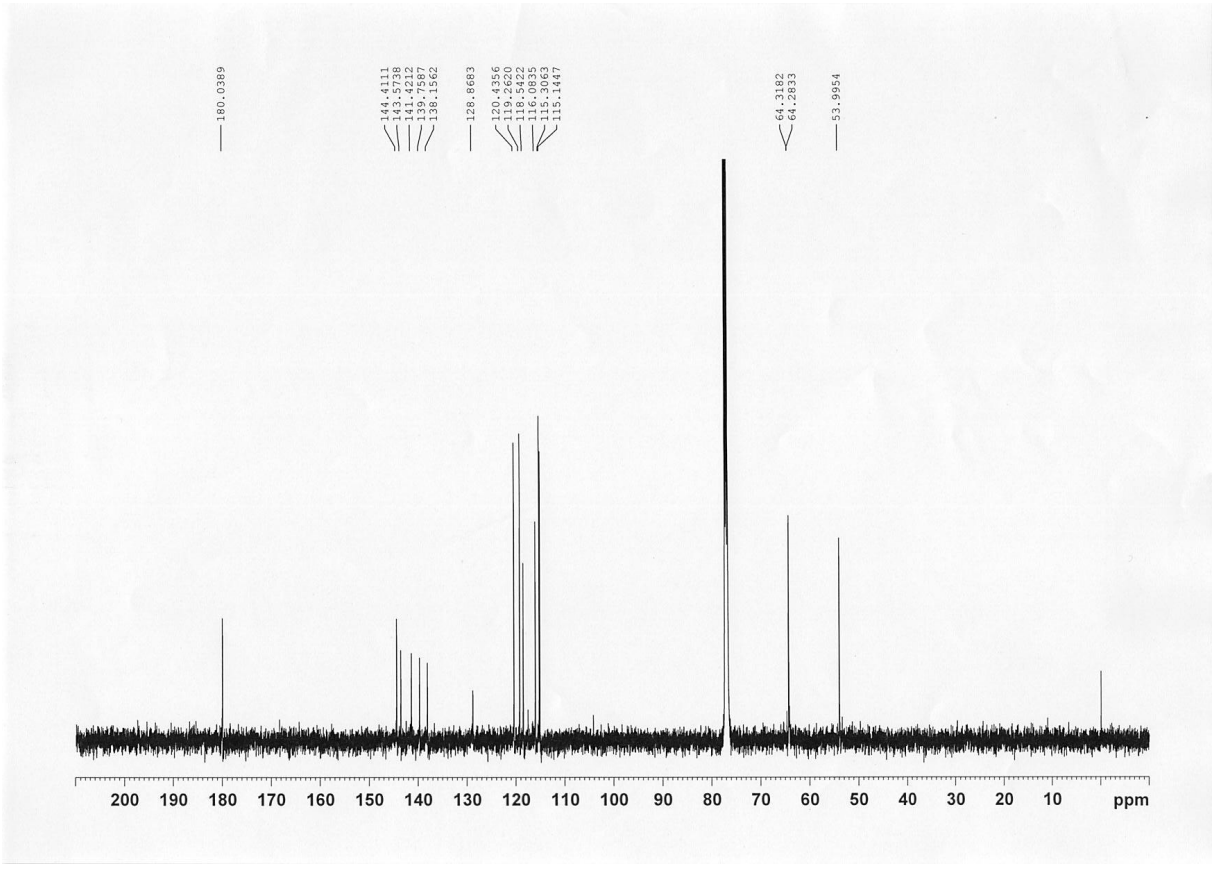
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **34** ($CDCl_3$)



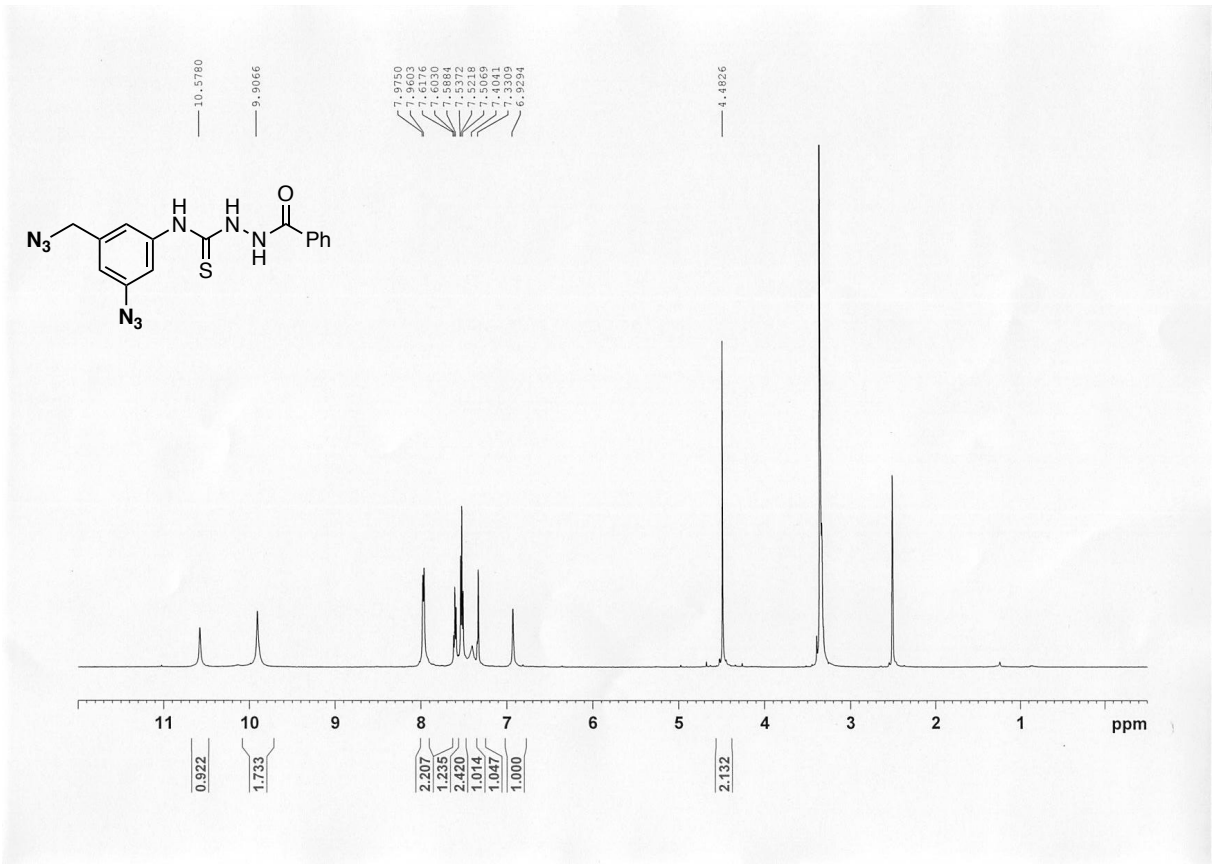


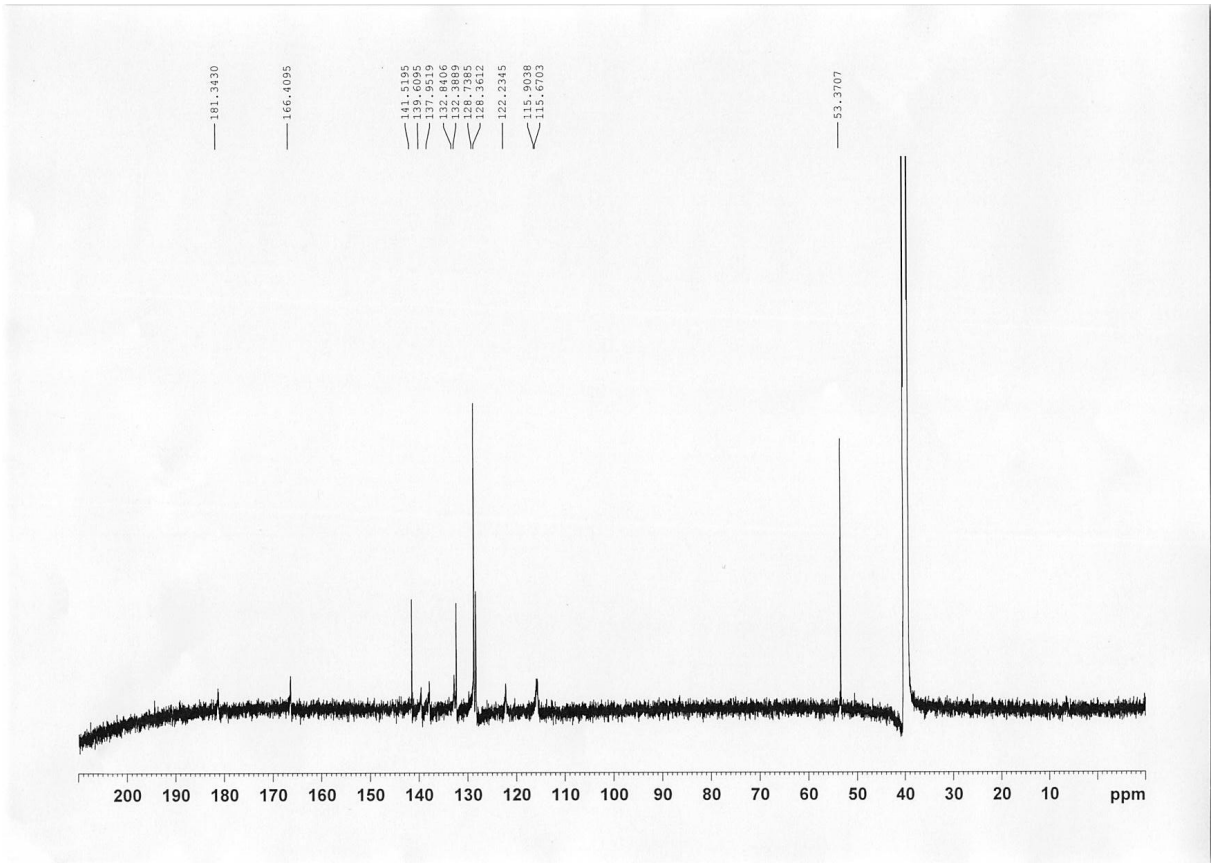
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **35** ($CDCl_3$)





^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **36** (DMSO-d_6)





^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **37** ($CDCl_3$)