

Design, synthesis and evaluation *in vitro* of quinoline-8-carboxamides, a new class of PARP-1 inhibitor

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Supplementary Information

Experimental Section	2
Crystal data	9
Analytical data for 17a,e-l,o, 18c, 21, 29b, 30, 31	10
Biochemical evaluation	13
Elemental microanalysis data	14
Selected NMR spectra	15
References cited in Supplementary Information	45

Experimental Section

NMR spectra were recorded on JEOL/Varian GX270 and EX400 spectrometers of samples in CDCl₃, unless otherwise stated. IR spectra were measured as thin films or as KBr discs on a Perkin-Elmer RXI FT-IR spectrometer. The stationary phase for chromatography was silica gel. Solvents were evaporated under reduced pressure. Solutions in organic solvents were dried with MgSO₄. Melting points were determined using a Reichert-Jung Thermo Galen instrument and are uncorrected.

General Coupling Procedure 1. The haloquinoline (1.0 mmol), Pd(PPh₃)₄ (0.1 mmol), Na₂CO₃ (1.2 mmol) and the arylboronic acid (1.1 mmol) were heated at reflux for 24 h under N₂ in toluene / EtOH / H₂O (10 mL : 1 mL : 1 mL). The evaporation residue, in EtOAc, was washed with water and brine. Drying, evaporation and chromatography (hexane / EtOAc 10:1) gave the coupled product.

General Coupling Procedure 2. The haloquinoline (1.0 mmol), arylboronic acid (1.6 mmol) and Pd(PPh₃)₄ (0.05 mmol) were sequentially added to degassed DMF (1.0 mL) and the mixture was stirred for 30 min. Degassed aq. Na₂CO₃ (1.0 M, 0.25 mL) was added and the mixture was heated under N₂ at 80°C until TLC monitoring showed that the reaction was complete (8-48 h). The evaporation residue, in EtOAc, was washed with water and brine. Drying, evaporation and chromatography (hexane / EtOAc 3:2) gave the coupled product.

General Coupling Procedure 3. The haloquinoline (1.0 mmol), Pd(PPh₃)₄ (0.1 mmol) and the substituted stannane (2.0 mmol) in NMP (5.0 mL) were heated at 80°C for 24 h under N₂. The mixture was extracted with EtOAc. Drying, evaporation and chromatography (hexane / EtOAc 3:2) gave the coupled product.

3-Iodo-8-nitroquinoline (12). N-Iodosuccinimide (452 mg, 2.0 mmol) was added in portions to 8-nitroquinoline **11** (348 mg, 2.0 mmol) in AcOH (15 mL) during 1 h at 110°C. The mixture was stirred for 8 h at 20°C, before being poured into water. The pH was adjusted to 6 with aq. NH₃. The product was collected by filtration, washed with water and dried to give **12** (429 mg, 71%) as a pale yellow solid: mp 121-122°C (lit.⁵¹ mp 119-120°C); ¹H NMR δ 7.64 (1 H, t, *J* = 8.0 Hz, 6-H), 7.91 (1 H, dd, *J* = 8.2, 1.2 Hz, 5-H), 8.06 (1 H, dd, *J* = 8.2, 1.2 Hz, 7-H), 8.64 (1 H, d, *J* = 2.0 Hz, 4-H), 9.17 (1 H, d, *J* = 2.0 Hz, 2-H); MS (FAB) *m/z* 301.9522 (M + H) (C₉H₆IN₂O₂ requires 301.9527), 255 (M - NO₂), 175 (M - I).

8-Nitro-3-phenylquinoline (13a). Compound **12** was treated with PhB(OH)₂ by General Coupling Procedure 1 to give **13a** (97%) as an off-white solid: mp 115-116°C (lit.⁵² mp 116-117°C); ¹H NMR δ 7.50 (1 H, tt, *J* = 8.2, 1.2 Hz, Ph 4-H), 7.56 (2 H, t, *J* = 8.2 Hz, Ph 3,5-H₂), 7.66 (1 H, t, *J* = 8.2 Hz, 6-H), 7.72 (2 H, dd, *J* = 8.2, 1.2 Hz, Ph 2,6-H₂), 8.06 (1 H, dd, *J* = 8.2, 1.2 Hz, 5-H), 8.11 (1 H, dd, *J* = 8.2, 1.2 Hz, 7-H), 8.39 (1 H, d, *J* = 2.3 Hz, 4-H), 9.34 (1 H, d, *J* = 2.3 Hz, 2-H); ¹³C NMR δ 123.7 (7-C), 125.8 (6-C), 127.5 (Ph 2,6-C₂), 128.0 (Ph 4-C), 129.0 (4a,8-C₂), 129.5 (Ph 3,5-C₂), 132.3 (5-C), 133.0 (4-C), 135.7 (3-C), 136.7 (Ph 1-C), 138.5 (8a-C), 152.3 (2-C).

8-Nitro-3-(2-trifluoromethylphenyl)quinoline (13b). Compound **12** was treated with 2-trifluoromethylphenylboronic acid by General Coupling Procedure 1 to give **13b** (66%) as an off-white solid: mp 85-87°C; ¹H NMR δ 7.38 (1 H, d, *J* = 7.8 Hz, Ph 6-H), 7.60 (1 H, t, *J* = 7.8 Hz, Ph 4-H), 7.67 (2 H, t, *J* = 8.0 Hz, 6-H + Ph 5-H), 7.82 (1 H, d, *J* = 7.8 Hz, Ph 3-H), 8.08 (1 H, d, *J* = 7.4 Hz, 5-H), 8.10 (1 H, d, *J* = 7.4 Hz, 7-H), 8.22 (1 H, d, *J* = 1.8 Hz, 4-H), 9.03 (1 H, d, *J* = 1.8 Hz, 2-H); ¹³C NMR (HMQC / HMBC) δ 123.8 (q, *J* = 273.7 Hz, CF₃), 124.2 (7-C), 125.9 (6-C), 126.5 (q, *J* = 5.3 Hz, Ph 3-C), 128.0 (3-C), 128.8 (Ph 4-C), 129.0 (q, *J* = 29.9 Hz, Ph 2-C), 131.9 (Ph 5-C), 132.1 (Ph 6-C), 132.3 (5-C), 134.6 (3-C), 135.5 (4-C), 136.2 (8a-C), 138.6 (Ph 1-C), 148.2 (4a,8-C₂), 152.8 (2-C); ¹⁹F NMR δ -56.63 (3 F, s, CF₃); MS (ES) *m/z* 319.0673 (M + H) (C₁₆H₁₀F₃N₂O₂ requires 319.0689), 249 (M - CF₃).

8-Nitro-3-(3-trifluoromethylphenyl)quinoline (13c). Compound **12** was treated with 3-trifluoromethylphenylboronic acid by General Coupling Procedure 1 to give **13c** (97%) as a pale yellow solid: mp 119-120°C; ¹H NMR δ 7.62-7.76 (3 H, m, 6-H + Ph 5,6-H₂), 7.88 (1 H, d, *J* = 7.4 Hz, Ph 4-H), 7.94 (1 H, s, Ph 2-H), 8.08 (1 H, dd, *J* = 7.4, 1.2 Hz, 5-H), 8.13 (1 H, dd, *J* = 7.4, 1.2 Hz, 7-H), 8.42 (1 H, d, *J* = 2.3 Hz, 4-H), 9.30 (1 H, d, *J* = 1.9 Hz, 2-H); ¹³C NMR δ 123.8 (q, *J* = 272.2 Hz, CF₃), 124.2, 124.3 (q, *J* = 3.8 Hz), 125.5 (q, *J* = 3.8 Hz), 126.1, 128.2 (q, *J* = 64.4 Hz, Ph 3-C), 128.7, 130.0, 130.7, 132.3, 133.5, 134.2, 137.5, 138.8, 148.1, 151.7; MS (ES) *m/z* 319.0689 (M + H) (C₁₆H₁₀F₃N₂O₂ requires 319.0689).

8-Nitro-3-(4-trifluoromethylphenyl)quinoline (13d). Compound **12** was treated with 4-trifluoromethylphenylboronic acid by General Coupling Procedure 1 to give **13d** (74%) as an off-white solid: mp 120-123°C; ¹H NMR δ 7.67 (1 H, t, *J* = 7.8 Hz, 6-H), 7.80 (4 H, s, Ph 2,3,5,6-H₄), 8.08 (1 H, d, *J* = 8.2 Hz, 5-H), 8.12 (1 H, d, *J* = 8.2 Hz, 7-H), 8.42 (1 H, d, *J* = 2.3 Hz, 4-H), 9.30 (1 H, d, *J* = 1.9 Hz, 2-H); ¹³C NMR (HMQC / HMBC) δ 123.9 (q, *J* = 271.4 Hz, CF₃), 124.2 (6-C), 126.1 (C-3), 126.4 (q, *J* = 3.8 Hz, Ph 3,5-C₂), 127.9 (Ph 2,6-C₂), 128.7 (7-C), 130.9 (q, *J* = 32.9 Hz, Ph 4-C), 133.6 (5-C), 134.2 (4-C), 138.9 (8a-C), 140.2 (Ph 1-C), 148.2 (8-C), 151.8 (2-C); ¹⁹F NMR δ -62.62 (3 F, s, CF₃); MS (ES) *m/z* 319.0686 (M + H) (C₁₆H₁₀F₃N₂O₂ requires 319.0689), 249 (M - CF₃).

3-Phenylquinolin-8-amine (14). SnCl₂·6H₂O (3.04 g, 10 mmol) was stirred with **13a** (800 mg, 3.2 mmol) in EtOH (50 mL) for 6 h before the mixture was poured into water. The solution was made strongly alkaline with aq. NaOH. The precipitate, in EtOAc, was dried. Evaporation and chromatography (EtOAc / hexane 1:10) gave **14** (610 mg, 82%) as a pale buff solid: mp 74-76°C (lit.⁵² mp 74-75°C); ¹H NMR δ 4.96 (2 H, br, NH₂), 6.92 (1 H, dd, *J* = 7.7, 1.5 Hz, 7-H), 7.20 (dd, *J* = 7.7, 2.0 Hz, 5-H), 7.35 (1 H, t, *J* = 7.7 Hz, 6-H), 7.42 (1 H, tt, *J* = 8.0, 2.3 Hz, Ph 4-H), 7.51 (2 H, t, *J* = 8.0 Hz, Ph 3,5-H₂), 7.70 (dd, *J* = 8.3, 1.5 Hz, Ph 2,6-H₂), 8.20 (1 H, d, *J* = 2.4 Hz, 4-H), 9.02 (1 H, d, *J* = 2.4 Hz, 2-H).

3-Phenylquinolin-8-diazonium tetrafluoroborate (15) and 3-phenylquinoline-8-carbonitrile (16). NaNO₂ (250 mg, 3.6 mmol) in ice-water (2.0 mL) was added dropwise to **14** (500 mg, 2.3 mmol) in aq. HBF₄ (40%, 10 mL) at 0°C. The precipitate was collected and washed (cold aq. HBF₄ (40%), cold EtOH, Et₂O (4 ×)) to give **15** (300 mg, 41%) as a pale yellow solid: IR (KBr) ν_{\max} 2261 cm⁻¹. This material (200 mg, 0.6 mmol)

was stirred with CuCN (203 mg, 2.0 mmol) and KCN (290 mg, 4.5 mmol) in water (8.0 mL) at 50°C for 1 h and at 20°C for 8 h. The mixture was extracted (EtOAc). Washing (water), drying, evaporation and chromatography (EtOAc / hexane 1:10) gave **16** (110 mg, 78%) as a pale buff solid: mp 122-124°C; IR (KBr) ν_{\max} 2230 cm^{-1} ; ^1H NMR δ 7.47 (1 H, t, $J = 7.4$ Hz, Ph 4-H), 7.53 (2 H, t, $J = 7.4$ Hz, Ph 3,5-H₂), 7.64 (1 H, t, $J = 7.8$ Hz, 6-H), 7.71 (2 H, d, $J = 7.4$ Hz, Ph 2,6-H₂), 8.10 (1 H, dd, $J = 7.4, 2.0$ Hz, 5-H), 8.13 (1 H, dd, $J = 7.4, 2.0$ Hz, 7-H), 8.36 (1 H, d, $J = 2.4$ Hz, 4-H), 9.34 (1 H, d, $J = 2.4$ Hz, 2-H); ^{13}C NMR (HMQC / HMBC) δ 113.0 (8-C), 117.2 (CN), 126.3 (6-C), 127.5 (Ph 2,6-C₂), 128.0 (4a-C), 128.7 (Ph 4-C), 129.4 (Ph 3,5-C₂), 133.0 (5-C), 133.3 (4-C), 135.2 (7-C), 135.6 (3-C), 136.8 (Ph 1-C), 146.5 (8a-C), 152.1 (2-C); MS (ES) m/z 483 (2 M + Na), 231.0909 (M + H) (C₁₆H₁₁N₂ requires 231.0917); Anal. (C₁₆H₁₀N₂) C, H, N.

3-(2-Trifluoromethylphenyl)quinoline-8-carboxamide (17b). Compound **17f** was treated with 2-trifluoromethylphenylboronic acid by General Coupling Procedure 1 to give **17b** (27%) as a white solid: mp 165-167°C; IR ν_{\max} (KBr) 3468, 3100, 1669, 1571 cm^{-1} ; ^1H NMR δ 6.21 (1 H, br, NH), 7.42 (1 H, d, $J = 7.3$ Hz, Ph 6-H), 7.60 (1 H, t, $J = 7.6$ Hz, Ph 4-H), 7.66 (1 H, t, $J = 7.3$ Hz, Ph 5-H), 7.73 (1 H, t, $J = 7.6$ Hz, 6-H), 7.85 (1 H, d, $J = 7.7$ Hz, Ph 3-H), 8.03 (1 H, d, $J = 1.4$ Hz, 5-H), 8.24 (1 H, d, $J = 2.0$ Hz, 7-H), 8.88 (1 H, d, $J = 1.0$ Hz, 4-H), 8.90 (1 H, d, $J = 1.4$ Hz, 2-H), 10.91 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 126.5 (q, $J = 5.4$ Hz, Ph 3-C), 127.0 (6-C), 127.5 (4a-C or 8-C), 128.6 (Ph 4-C), 129.1 (q, $J = 30.6$ Hz, Ph 2-C), 131.8 (Ph 6-C), 132.7 (5-C), 134.6 (7-C), 136.6 (q, $J = <2$ Hz, Ph 1-C), 137.0 (4-C), 144.7 (8-C), 149.6 (2-C), 167.5 (2-C); ^{19}F NMR δ -56.70 (s, CF₃); 655 (2 M + Na); MS (ES) m/z 317.0896 (M + H) (C₁₇H₁₂F₃N₂O requires 317.0896).

3-(3-Trifluoromethylphenyl)quinoline-8-carboxamide (17c). Compound **17f** was treated with 3-trifluoromethylphenylboronic acid by General Coupling Procedure 1 to give **17c** (43%) as a white solid: mp 228-229°C; IR ν_{\max} (KBr) 3466, 3058, 1669, 1571 cm^{-1} ; ^1H NMR ((CD₃)₂SO) δ 7.80-7.87 (3 H, m, Ph 4,5,6-H₃), 8.00 (1 H, br, NH), 8.26 (1 H, d, $J = 7.4$ Hz, Ph 2-H), 8.27-8.34 (2 H, m, 5,6-H₂), 8.58 (1 H, dd, $J = 7.4, 1.9$ Hz, 7-H), 9.00 (1 H, d, $J = 2.3$ Hz, 4-H), 9.47 (1 H, d, $J = 2.3$ Hz, 2-H), 10.14 (1 H, br, NH); ^{13}C NMR ((CD₃)₂SO) δ 123.9 (m), 125.1 (m), 127.0, 128.0, 129.5, 130.4, 131.3, 131.4, 132.8, 133.1, 135.4, 137.6, 144.2, 149.2, 166.3; ^{19}F NMR ((CD₃)₂SO) δ -62.56 (3 F, s, CF₃); MS (ES) m/z 655 (2 M + Na), 317.0896 (M + H) (C₁₇H₁₂F₃N₂O requires 317.0896); Anal. (C₁₇H₁₁F₃N₂O) C, H, N.

3-(4-Trifluoromethylphenyl)quinoline-8-carboxamide (17d). Compound **17f** was treated with 4-trifluoromethylphenylboronic acid by General Coupling Procedure 1 (chromatography eluant EtOAc / hexane, 5:2) to give **17d** (38%) as a white solid: mp 184-185°C; IR ν_{\max} (KBr) 3469, 3120, 1671, 1572 cm^{-1} ; ^1H NMR δ 6.18 (1 H, br, NH), 7.73 (1 H, t, $J = 8.0$ Hz, 6-H), 7.80 (2 H, d, $J = 8.7$ Hz, Ph 3,5-H₂), 7.84 (2 H, d, $J = 8.7$ Hz, Ph 3,5-H₂), 8.45 (1 H, d, $J = 2.4$ Hz, 4-H), 8.89 (1 H, dd, $J = 7.2, 1.4$ Hz, 7-H), 9.20 (1 H, d, $J = 2.4$ Hz, 2-H), 10.86 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 124.0 (q, $J = 272.2$ Hz, CF₃), 126.3 (q, $J = 3.8$ Hz, Ph 3,5-C₂), 127.3 (6-C), 127.7 (Ph 2,6-C₂), 128.2 (4a-C or 8-C), 128.5 (8-C or 4a-C), 130.6 (q, $J = 32.2$ Hz, Ph 4-C), 132.4 (Ph 1-C), 132.8 (5-C), 134.7 (7-C), 135.2 (4-C), 140.6 (3-C), 148.6 (2-C), 167.4 (CONH₂); ^{19}F NMR δ

-62.56 (s, CF₃); MS (FAB) *m/z* 317.0897 (M + H) (C₁₇H₁₂F₃N₂O requires 317.0896), 299 (M – NH₂), 273 (M – CONH₂).

3-(4-Methoxyphenyl)quinoline-8-carboxamide (17m). Compound **17f** was treated with 4-methoxyphenylboronic acid by General Coupling Procedure 1 to give **17m** (95%) as a pale yellow solid: mp 190-192°C; IR ν_{\max} (KBr) 3468, 3200, 1657, 1607 cm⁻¹; ¹H NMR δ 3.88 (3 H, s, Me), 6.21 (1 H, br, NH), 7.06 (2 H, d, *J* = 8.6 Hz, Ph 3,5-H₂) 7.64 (2 H, d, *J* = 8.6 Hz, Ph 2,6-H₂), 7.66 (1 H, t, *J* = 8.0 Hz, 6-H), 8.00 (1 H, dd, *J* = 8.2, 1.2 Hz, 5-H), 8.33 (1 H, d, *J* = 2.3 Hz, 4-H), 8.80 (1 H, dd, *J* = 8.0, 2.0 Hz, 7-H), 9.16 (1 H, d, *J* = 2.3 Hz, 2-H), 10.96 (1 H, br, NH); ¹³C NMR (HMQC / HMBC) δ 55.4 (Me), 114.8 (Ph 3,5-C₂), 126.8 (6-C), 128.4 (Ph 2,6-C₂), 128.3 (Ph 1-C), 128.4 (4a-C or 8-C), 129.3 (8-C or 4a-C), 132.5 (5-C), 133.5 (3-C), 133.6 (7-C), 133.7 (4-C), 144.3 (8a-C), 148.8 (2-C), 160.4 (Ph 4-C), 167.6 (C=O); MS (FAB) *m/z* 279.1129 (M + H) (C₁₇H₁₅N₂O₂ requires 279.1128), 261 (M – NH₂), 235 (M – CONH₂); Anal. (C₁₇H₁₄N₂O₂) C, H, N.

3-(3,5-Dimethylphenyl)quinoline-8-carboxamide (17n). Compound **17f** was treated with 3,5-methylphenylboronic acid by General Coupling Procedure 1. Recrystallisation (hexane / EtOAc) gave **17n** (65%) as a white solid: mp 209-211°C; IR ν_{\max} (KBr) 3468, 3281, 1665, 1597 cm⁻¹; ¹H NMR δ 2.43 (6 H, s, 2 × Me), 6.13 (1 H, br, NH), 7.11 (1 H, s, Ph 4-H), 7.32 (2 H, s, Ph 2,6-H₂), 7.70 (1 H, t, *J* = 8.1 Hz, 6-H), 8.04 (1 H, dd, *J* = 8.1, 1.3 Hz, 5-H), 8.39 (1 H, d, *J* = 2.5 Hz, 4-H), 8.84 (1 H, dd, *J* = 8.0, 1.4 Hz, 7-H) 9.17 (1 H, d, *J* = 2.5 Hz, 2-H), 10.98 (1 H, br, NH); ¹³C NMR (HMQC / HMBC) δ 21.4 (2 × Me), 125.2 (Ph 2,6-C₂), 128.1 (4a-C or 8-C), 128.4 (8-C or 4a-C), 128.4 (6-C), 130.2 (Ph 4-C), 132.6 (4-C), 133.9 (7-C), 134.0 (3-C), 134.5 (5-C), 136.1 (Ph 1-C), 139.0 (Ph 3,5-C₂), 144.6 (8a-C), 149.1 (2-C), 167.6 (C=O); MS (FAB) *m/z* 277.1334 (M + H) (C₁₈H₁₇N₂O requires 277.1335), 233 (M – CONH₂).

3-(3-Bromophenyl)quinoline-8-carboxamide (17p). Compound **17f** was treated with 3-bromophenylboronic acid by General Coupling Procedure 1 to give **17p** (31%) as a white solid: mp 178-180°C; IR ν_{\max} (KBr) 3454, 3282, 1665, 1597 cm⁻¹; ¹H NMR δ 6.26 (1 H, br, NH), 7.42 (1 H, t, *J* = 7.8 Hz, Ph 5-H), 7.60 (1 H, dd, *J* = 8.2, 2.0 Hz, Ph 4-H), 7.64 (1 H, dd, *J* = 7.8, 2.1 Hz, Ph 6-H), 7.73 (1 H, t, *J* = 7.8 Hz, 6-H), 7.86 (1 H, t, *J* = 1.6 Hz, Ph 2-H), 8.06 (1 H, dd, *J* = 7.8, 1.6 Hz, 5-H), 8.40 (1 H, d, *J* = 2.3 Hz, 4-H), 8.85 (1 H, dd, *J* = 7.4, 1.6 Hz, 7-H), 9.14 (1 H, d, *J* = 2.3 Hz, 2-H), 10.92 (1 H, br, NH); ¹³C NMR (HMQC / HMBC) δ 123.4 (Ph 3-C), 125.9 (Ph 6-C), 127.1 (6-C), 128.2 (4a-C or 8-C), 128.3 (8-C or 4a-C), 130.4 (Ph 5-C), 131.5 (Ph 4-C), 132.4 (3-C), 132.8 (Ph 2-C), 134.5 (5-C), 134.9 (7-C), 135.2 (4-C), 139.1 (Ph 1-C), 144.8 (8a-C), 148.6 (2-C), 167.5 (C=O); MS (FAB) *m/z* 329.0112 (M + H) (C₁₆H₁₁⁸¹BrN₂O requires 329.0102), 327.0133 (M + H) (C₁₆H₁₁⁷⁹BrN₂O requires 327.0119). Anal. (C₁₆H₁₁BrN₂O.0.75 CHCl₃) C, H, N.

3-(4-Cyanophenyl)quinoline-8-carboxamide (17q). Compound **17f** was treated with 4-cyanophenylboronic acid by General Coupling Procedure 1 (chromatographic eluant hexane / EtOAc 3:2) to give **17q** (40%) as a white solid: mp 209-211°C; IR ν_{\max} (KBr) 3467, 3268, 1674, 1600 cm⁻¹; ¹H NMR δ 6.20 (1 H, br, NH), 7.74 (1 H, t, *J* = 7.8 Hz, 6-H), 7.82 (4 H, s, Ph 2,3,5,6-H₄), 8.08 (1 H, dd, *J* = 7.8, 1.2 Hz, 5-H), 8.45 (1 H, d, *J* = 2.3 Hz, 4-H), 8.85 (1 H, dd, *J* = 7.4, 1.6 Hz, 7-H), 9.18 (1 H, d, *J* = 2.3 Hz, 2-H), 10.91 (1 H,

br, NH); ^{13}C NMR (HMQC / HMBC) δ 112.2 (Ph 4-C), 118.4 (C \equiv N), 127.4 (Ph 2,6-C $_2$), 127.9 (6-C), 128.0 (4a-C or 8-C), 128.3 (8-C or 4a-C), 131.8 (Ph 3,5-C $_2$), 132.9 (7-C), 133.1 (4-C), 134.9 (5-C), 135.4 (3-C), 141.5 (Ph 1-C), 145.1 (8a-C), 148.3 (2-C), 167.3 (C=O); MS (ES) m/z 274.0974 (M + H) (C $_{17}$ H $_{12}$ N $_3$ O requires 274.0975), 230 (M - CONH $_2$).

3-(Pyridin-3-yl)quinoline-8-carboxamide (17r). Compound **17f** was treated with pyridine-3-boronic acid by General Coupling Procedure 2 to give **17r** (26%) as a pale yellow solid: mp 136-137°C; IR ν_{max} (KBr) 3436, 3055, 1647, 1591 cm^{-1} ; ^1H NMR δ 6.23 (1 H, br, NH), 7.48 (1 H, dd, J = 8.0, 4.8 Hz, pyridine 5-H), 7.74 (1 H, t, J = 8.0 Hz, 6-H), 8.02 (1 H, dt, J = 7.6, 1.7 Hz, pyridine 4-H), 8.07 (1 H, dd, J = 8.3, 1.7 Hz, 5-H), 8.44 (1 H, d, J = 2.4 Hz, 4-H), 8.71 (1 H, dd, J = 4.9, 1.4 Hz, pyridine 6-H) 8.88 (1 H, dd, J = 7.6, 1.0 Hz, 7-H), 8.99 (1 H, d, J = 1.5 Hz, pyridine 2-H), 9.17 (1 H, d, J = 2.4 Hz, 2-H), 10.83 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 124.0 (pyridine 5-C), 127.3 (6-C), 128.2 (4a-C or 8-C), 128.6 (8-C or 4a-C), 130.6 (pyridine 1-C), 132.7 (5-C), 132.8 (3-C), 134.6 (7-C, pyridine 6-C), 135.0 (4-C), 144.9 (8a-C), 148.4 (pyridine 2,4-C $_2$), 149.2 (2-C), 167.3 (C=O); MS (ES) m/z 521 (2 M + Na), 250.0975 (M + H) (C $_{15}$ H $_{12}$ N $_3$ O requires 250.0902); Anal. (C $_{15}$ H $_{11}$ N $_3$ O) C, H, N.

3-(Pyridin-4-yl)quinoline-8-carboxamide (17s). Compound **17f** was treated with pyridine-4-boronic acid by General Coupling Procedure 2 to give **17s** (40%) as a pale yellow solid: mp 190-193°C; IR ν_{max} (KBr) 3462, 3055, 1654, 1591 cm^{-1} ; ^1H NMR (CD $_3$ OD) δ 7.80 (1 H, t, J = 8.2 Hz, 6-H), 7.97 (2 H, d, J = 5.9 Hz, pyridine 3,5-H $_2$), 8.28 (1 H, dd, J = 8.2, 1.6 Hz, 5-H), 8.71 (2 H, d, J = 5.9 Hz, pyridine 2,6-H $_2$), 8.74 (1 H, d, J = 7.4, 1.6 Hz, 7-H), 8.88 (1 H, d, J = 2.3 Hz, 4-H), 9.40 (1 H, d, J = 2.7 Hz, 2-H); ^{13}C NMR (CD $_3$ OD) (HMQC / HMBC) δ 123.4 (pyridine 3,5-C $_2$), 128.2 (6-C), 129.7 (4a,8-C $_2$), 131.9 (3-C), 134.8 (5-C), 135.4 (7-C), 137.1 (4-C), 146.7 (8a-C), 146.8 (pyridine 4-C), 149.8 (pyridine 2,6-C $_2$), 151.0 (2-C); MS (ES) 521 (2 M + Na), m/z 250.0975 (M + H) (C $_{15}$ H $_{12}$ N $_3$ O requires 250.0975).

E-3-(2-Phenylethenyl)quinoline-8-carboxamide (17t). and **Z-3-(2-phenylethenyl)quinoline-8-carboxamide (17u).** Compound **17f** was treated with *E*-2-phenylethenylboronic acid by General Coupling Procedure 1 (chromatographic eluant hexane / EtOAc 3:2) to give **17t** (52%) as a white solid: mp 158-160°C; ^1H NMR δ 6.12 (1 H, br, NH), 7.28 (1 H, d, J = 20.0 Hz, alkene-H), 7.35 (1 H, d, J = 19.7 Hz, alkene-H), 7.38-7.59 (5 H, m, Ph 2,3,4,5,6-H $_5$), 7.67 (1 H, t, J = 7.9 Hz, 6-H), 7.98 (1 H, dd, J = 8.2, 1.5 Hz, 5-H), 8.28 (1 H, d, J = 2.2 Hz, 4-H), 8.80 (1 H, dd, J = 8.0, 1.5 Hz, 7-H) 9.13 (1 H, d, J = 2.5 Hz, 2-H), 10.92 (1 H, br, NH); MS (ES) m/z 275.1179 (M + H) (C $_{18}$ H $_{15}$ N $_2$ O requires 275.1179). Compound **17t** (10 mg) in CD $_3$ OD (0.6 mL) was allowed to stand under laboratory lighting conditions for 3 d; the ^1H NMR spectrum showed a mixture of **17t** and **17u** (4:1): ^1H NMR (**17u**) δ 6.05 (1 H, br, NH), 6.79 (1 H, d, J = 10.8 Hz, alkene-H), 6.81 (1 H, d, J = 10.8 Hz, alkene-H), 7.32-7.60 (5 H, m, Ph 2,3,4,5,6-H $_5$), 7.65 (1 H, t, J = 8.0 Hz, 6-H), 7.83 (1 H, dd, J = 8.2, 1.6 Hz, 5-H), 8.08 (1 H, d, J = 2.0 Hz, 4-H), 8.74 (1 H, dd, J = 8.2, 1.6 Hz, 7-H), 8.76 (1 H, d, J = 2.0 Hz, 2-H), 10.91 (1 H, br, NH).

8-Trifluoromethanesulfonyloxyquinoline (20). Tf₂O (9.32 g, 33 mmol) was added dropwise to quinolin-8-ol **19** (4.00 g, 27.6 mmol) in pyridine (10 mL) at 0°C. The mixture was stirred for 5 min at 0°C and for 5 h at 23°C, before being poured into water and extracted (EtOAc). Washing (water, aq. HCl (10%), water), drying, evaporation and chromatography (EtOAc / hexane 1:10) gave **20** (5.61 g, 73%) as a pale yellow solid: mp 61-62°C (lit.⁴¹ mp 61-62°C); IR ν_{\max} 1318, 1212 cm⁻¹; ¹H NMR δ 7.50 (1 H, dd, *J* = 8.6, 4.3 Hz, 3-H), 7.54 (1 H, t, *J* = 8.2 Hz, 6-H), 7.61 (1 H, dd, *J* = 7.8, 1.2 Hz, 7-H), 7.84 (1 H, dd, *J* = 7.8, 1.8 Hz, 5-H), 8.20 (1 H, dd, *J* = 8.0, 2.0 Hz, 4-H), 9.04 (1 H, dd, *J* = 4.3, 2.0 Hz, 2-H); ¹³C NMR (HMQC) δ 118.86 (q, *J* = 351 Hz, CF₃), 120.95 (7-C), 122.62 (3-C), 125.90 (6-C), 128.26 (5-C), 129.70 (C_q), 135.80 (4-C), 140.93 (C_q), 145.97 (C_q), 151.62 (2-C); ¹⁹F NMR δ -73.81 (s, CF₃).

***E-N*-(2-Bromophenyl)-3-phenylpropenamide (23).** *E*-3-phenylpropenoyl chloride (5.51 g, 33.2 mmol) was stirred vigorously with 2-bromoaniline **22** (5.67 g, 33.2 mmol) and K₂CO₃ (7.10 g, 51.5 mmol) in water (16.5 mL) and acetone (16 mL) at 0°C for 2 h. The mixture was then poured into ice-water (20 mL). Recrystallisation (hexane) of the precipitate gave **23** (9.8 g, 97%) as white crystals: mp 145-146°C (lit.⁵⁴ mp 148-149°C); ¹H NMR δ 6.58 (1 H, d, *J* = 15.5 Hz, 2-H), 6.98 (1 H, dd, *J* = 7.9, 1.5 Hz, BrPh 6-H), 7.35 (1 H, dd, *J* = 7.9, 1.5 Hz, BrPh 4-H), 7.38-7.60 (6 H, m, Ph 2,3,4,5,6-H₅ + BrPh 5-H), 7.76 (1 H, d, *J* = 15.5 Hz, 3-H), 7.79 (1 H, br, NH), 8.50 (1 H, d, *J* = 8.2 Hz, BrPh 3-H).

8-Bromoquinolin-2-one (24). Compound **23** (9.78 g, 32.5 mmol) and AlCl₃ (26 g, 0.20 mol) were heated to 125°C in chlorobenzene (32 mL) for 24 h. The mixture was cooled to 50°C and poured onto ice. Recrystallisation (ethanol) of the precipitate gave **24** (3.0 g, 41%) as white crystals: mp 194-196°C (lit.⁴⁴ mp 196-198°C); ¹H NMR δ 6.63 (1 H, d, *J* = 9.4 Hz, 3-H), 7.07 (1 H, t, *J* = 7.8 Hz, 6-H), 7.48 (1 H, dd, *J* = 7.8, 1.2 Hz, 5-H), 7.71 (1 H, d, *J* = 9.8 Hz, 4-H), 7.71 (1 H, dd, *J* = 7.8, 1.2 Hz, 7-H), 9.08 (1 H, br, NH); ¹³C NMR δ 109.1, 121.0, 123.0, 123.3, 127.5, 133.6, 140.4, 162.1.

2,8-Dibromoquinoline (26). POBr₃ (1.07 g, 3.7 mmol) was heated with **24** (410 mg, 1.8 mmol) at 140°C for 3 h. The cooled mixture was poured into ice-water. The precipitate was collected and dried. Chromatography (CH₂Cl₂ / EtOAc 1:1) gave **26** (430 mg, 82%) as a pale buff solid: mp 118-119°C (lit.⁵⁵ mp 118-119°C); ¹H NMR δ 7.71 (1 H, t, *J* = 7.8 Hz, 6-H), 7.57 (1 H, d, *J* = 8.6 Hz, 3-H), 7.76 (1 H, dd, *J* = 7.8, 1.1 Hz, 5-H), 7.98 (1 H, d, *J* = 8.6 Hz, 4-H), 8.05 (1 H, d, *J* = 7.4 Hz, 7-H); ¹³C NMR (HMQC / HMBC) δ 123.6 (8-C), 126.9 (3-C), 127.5 (6-C), 127.6 (4a-C), 128.2 (5-C), 134.1 (7-C), 138.7 (4-C), 143.1 (8a-C), 145.2 (2-C).

8-Bromo-2-methylquinoline (18b) and 2,8-dimethylquinoline (27). Compound **26** (108 mg, 0.38 mmol) was heated with Me₄Sn (67 mg, 0.37 mmol) and Pd(PPh₃)₄ (43 mg, 40 μ mol) in NMP (2.0 mL) at 80°C for 8 h under Ar. The mixture was extracted with EtOAc. Washing (water, brine), evaporation and chromatography (hexane / EtOAc 10:1) gave an inseparable mixture of **18b** (39 mg, 46%) and **27** (14 mg, 23%) as a pale brown oil: ¹H NMR (**18b**) δ 2.73 (3 H, s, Me), 7.34 (1 H, d, *J* = 8.2 Hz, 3-H), 7.44 (1 H, t, *J* = 8.2 Hz, 6-H), 7.67 (1 H, dd, *J* = 8.0, 1.2 Hz, 5-H), 7.98 (1 H, d, *J* = 8.0, 1.2 Hz, 7-H), 7.99

(1 H, d, $J = 8.2$ Hz, 4-H); $^1\text{H NMR}$ (**27**) δ 2.75 (3 H, s, Me), 2.81 (3 H, s, Me), 7.27 (1 H, d, $J = 8.2$ Hz, 3-H), 7.32 (1 H, t, $J = 7.8$ Hz, 6-H), 7.72 (1 H, $J = 8.2$, 1.2 Hz, 5-H), 8.00 (1 H, dd, $J = 7.8$, 1.2 Hz, 7-H), 8.09 (1 H, d, 8.2 Hz, 4-H).

8-Bromo-2-methylquinoline (18b). *E*-But-2-enal (0.61 g, 8.7 mmol) was added dropwise to 2-bromoaniline **22** (1.48 g, 8.7 mmol) in boiling aq. HCl (6 M, 4.0 mL) during 30 min. Heating continued for a further 30 min. The mixture was cooled to 20°C and washed (Et₂O). ZnCl₂ (1.20 g, 8.8 mmol) was added with vigorous stirring. The precipitate was filtered, washed with cold 3 M aq. HCl and dried in air. The solid was washed with Et₂O and dried to provide **18b.ZnCl₂ complex** (0.62 g, 73%) as yellow crystals. This material was treated with water (15 mL) and 35% aq. NH₃ (5 mL). The oil was extracted with Et₂O. Drying and evaporation gave **18b** (280 mg, 59%) as a pale yellow solid: mp 63-65°C (lit.⁴⁵ mp 67-68°C); $^1\text{H NMR}$ δ 2.73 (3 H, s, Me), 7.34 (1 H, d, $J = 8.2$ Hz, 3-H), 7.44 (1 H, t, $J = 8.2$ Hz, 6-H), 7.67 (1 H, dd, $J = 8.0$, 1.2 Hz, 5-H), 7.98 (1 H, d, $J = 8.0$, 1.2 Hz, 7-H), 7.99 (1 H, d, $J = 8.2$ Hz, 4-H).

8-Bromo-2-phenylquinoline (18d). Compound **26** was treated with PhB(OH)₂ by General Coupling Procedure 1 (chromatographic eluant CH₂Cl₂ / hexane 1:10) to give **18d** (43%) as a pale brown oil (lit.⁵⁵ oil): $^1\text{H NMR}$ δ 7.35 (1 H, t, $J = 7.8$ Hz, 6-H), 7.48 (2 H, t, $J = 7.0$ Hz, Ph 3,5-H₂), 7.54 (1 H, t, $J = 7.8$ Hz, Ph 4-H), 7.76 (1 H, dd, $J = 8.2$, 1.1 Hz, 5-H), 7.95 (1 H, d, $J = 8.6$ Hz, 3-H), 8.05 (1 H, dd, $J = 7.8$, 1.2 Hz, 7-H), 8.18 (1 H, d, $J = 8.6$ Hz, 4-H), 8.31 (2 H, d, $J = 8.0$ Hz, Ph 2,6-H₂); $^{13}\text{C NMR}$ (HMOC / HMBC) δ 119.3 (3-C), 126.7 (6-C), 127.0 (4a-C or 8-C), 127.4 (5-C), 127.5 (8-C or 4a-C), 127.6 (1'-C), 127.7 (4'-C), 129.0 (2',6'-C₂), 129.9 (3',5'-C₂), 133.3 (4-C), 134.2 (8a-C), 137.3 (7-C), 138.8 (2-C).

8-Bromo-2-(4-methoxyphenyl)quinoline (18e) and 2-(4-methoxyphenyl)quinoline (28). Compound **26** was treated with 4-methoxyphenylboronic acid by General Coupling Procedure 1 (chromatographic eluant PhMe) to give **18e** (322 mg, 84%) as a pale orange oil: $^1\text{H NMR}$ δ 3.88 (3 H, s, Me), 7.04 (2 H, d, $J = 8.1$ Hz, Ph 3,5-H₂), 7.31 (1 H, t, $J = 7.8$ Hz, 6-H), 7.71 (1 H, dd, $J = 8.2$, 1.2 Hz, 5-H), 7.86 (1 H, d, $J = 9.0$ Hz, 3-H), 8.01 (1 H, dd, $J = 7.8$, 1.2 Hz, 7-H), 8.10 (1 H, d, $J = 8.6$ Hz, 4-H), 8.28 (2 H, d, $J = 8.2$ Hz, Ph 2,6-H₂); $^{13}\text{C NMR}$ (HMBC) δ 55.3 (Me), 114.2 (Ph 3,5-C₂), 118.7 (3-C), 125.2 (8-C), 126.1 (6-C), 127.2 (5-C), 128.0 (4a-C), 129.0 (Ph 2,6-C₂), 131.1 (4-C), 131.4 (Ph 1-C), 137.0 (7-C), 145.0 (8a-C), 157.1 (2-C), 161.1 (Ph 4-C); MS (ES) m/z 314.0163 (M + H) (C₁₆H₁₃⁷⁹BrNO requires 314.0175). Further elution gave **28** (21 mg, 7%) as a pale buff solid: mp 118-119°C (lit.⁵⁶ mp 122-123°C); $^1\text{H NMR}$ δ 3.88 (3 H, s, Me), 7.05 (2 H, d, $J = 8.0$ Hz, Ph 3,5-H₂), 7.49 (1 H, t, $J = 8.2$ Hz, 6-H), 7.71 (1 H, t, $J = 8.0$ Hz, 7-H), 7.81 (1 H, dd, $J = 8.2$, 1.2 Hz, 5-H), 7.83 (1 H, d, $J = 8.6$ Hz, 3-H), 8.12 (3 H, m, 8-H + Ph 2,6-H₂), 8.17 (1 H, $J = 8.6$ Hz, 4-H).

2-Ethylquinoline-8-carboxamide (29c). Compound **18c** was treated with BuLi and trimethylsilylisocyanate, as for the synthesis of **29b**, to give **29c** (43%) as a pale yellow solid: mp 172-175°C; IR ν_{max} (KBr) 3469, 3300, 1681, 1593 cm⁻¹; $^1\text{H NMR}$ δ 1.41 (3 H, t, $J = 7.4$ Hz, Me), 3.03 (2 H, q, $J = 7.8$ Hz, CH₂), 6.47 (1 H, br, NH), 7.34 (1 H, d, $J = 8.6$ Hz, 3-H), 7.58 (1 H, t, $J = 7.8$ Hz, 6-H), 7.91 (1 H, dd, $J = 7.8$, 1.6 Hz, 5-H), 8.13 (1

H, d, $J = 8.6$ Hz, 4-H). 8.79 (1 H, dd, $J = 8.0, 1.2$ Hz, 7-H), 11.30 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 13.0 (Me), 31.8 (CH₂), 121.0 (3-C), 125.4 (6-C), 126.9 (4a-C or 8-C), 127.7 (8-C or 4a-C), 132.2 (7-C), 133.9 (5-C), 137.6 (4-C), 145.1 (8a-C), 163.4 (2-C), 168.1 (CONH₂); MS (ES) m/z 201.1016 (M + H) (C₁₂H₁₃N₂O requires 201.1022).

2-Phenylquinoline-8-carboxamide (29d). Compound **18d** was treated with BuLi and trimethylsilylisocyanate, as for the synthesis of **29b** (chromatographic eluant CH₂Cl₂ / EtOAc 2:1) to give **29d** (34%) as a pale yellow solid: mp 209-210°C (lit.⁵⁸ mp 210-212°C); IR ν_{max} (KBr) 3470, 3270, 1674, 1600 cm⁻¹; ^1H NMR δ 6.16 (1 H, br, NH), 7.52-7.58 (3 H, m, Ph 3,4,5-H₃), 7.66 (1 H, t, $J = 7.8$ Hz, 6-H), 7.92 (1 H, d, $J = 8.6$ Hz, 3-H), 7.99-8.04 (3 H, m, 5-H + Ph 2,6-H₂), 8.34 (1 H, d, $J = 8.6$ Hz, 4-H), 8.87 (1 H, dd, $J = 7.4, 1.6$ Hz, 7-H), 11.20 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 119.2 (3-C), 126.2 (6-C), 127.4 (4a-C or 8-C), 127.7 (Ph 2,6-C₂), 128.4 (8-C or 4a-C), 129.2 (Ph 4-C), 130.0 (Ph 3,5-C₂), 132.2 (4-C), 134.6 (7-C), 138.5 (5-C), 139.2 (Ph 1-C), 145.5 (8a-C), 157.3 (2-C), 167.8 (CONH₂).

2-(4-Methoxyphenyl)quinoline-8-carboxamide (29e). Compound **18e** was treated with BuLi and trimethylsilylisocyanate, as for the synthesis of **29b** (chromatographic eluant CH₂Cl₂ / EtOAc 2:1) to give **29e** (43%) as a pale yellow solid: mp 221-224°C; IR ν_{max} (KBr) 3448, 3257, 1662, 1602 cm⁻¹; ^1H NMR δ 3.90 (3 H, s, Me), 6.27 (1 H, br, NH), 7.07 (2 H, d, $J = 8.0$ Hz, Ph 3,5-H₂), 7.63 (1 H, t, $J = 7.8$ Hz, 6-H), 7.87 (1 H, d, $J = 8.6$ Hz, 3-H), 7.96 (1 H, dd, $J = 8.0, 1.6$ Hz, 5-H), 7.98 (2 H, d, $J = 8.0$ Hz, Ph 2,6-H₂), 8.27 (1 H, d, $J = 8.6$ Hz, 4-H), 8.83 (1 H, dd, $J = 8.0, 1.6$ Hz, 7-H); 11.20 (1 H, br, NH), ^{13}C NMR (HMQC / HMBC) δ 55.5 (Me), 114.6 (Ph 3,5-C₂), 118.8 (3-C), 125.8 (6-C), 127.8 (4a-C or 8-C), 128.2 (8-C or 4a-C), 129.1 (Ph 2,6-C₂), 131.6 (Ph 1-C), 132.2 (7-C), 134.4 (5-C), 138.3 (4-C), 145.6 (8a-C), 156.9 (Ph 4-C), 161.3 (2-C), 168.0 (CONH₂); MS (ES) m/z 279.1128 (M + H) (C₁₇H₁₅N₂O₂ requires 279.1128).

Crystal Data for 17a: C₁₆H₁₂N₂O, $M = 248.28$, $\lambda = 0.71073$ Å, monoclinic, space group $C2/c$, $a = 16.2950(4)$, $b = 11.1110(3)$, $c = 14.3230(4)$ Å, $\beta = 108.069(1)^\circ$, $V = 2465.34(11)$ Å³, $Z = 8$, $D_c = 1.338$ g cm⁻³, $\mu = 0.085$ mm⁻¹, $F(000) = 1040$, crystal size $0.50 \times 0.50 \times 0.13$ mm, unique reflections = 2827 [$R_{\text{int}} = 0.0610$], observed $I > 2\sigma(I) = 2037$, data/restraints/parameters = 2827 / 2 / 181, obs. data; $R1 = 0.0471$, $wR2 = 0.1141$, all data; $R1 = 0.0712$, $wR2 = 0.1300$, max peak/hole 0.221 and -0.247 eÅ⁻³, software used, SHELXS, SHELXL and ORTEX.⁵⁹⁻⁶¹

Crystal data for 17b: C₁₇H₁₁F₃N₂O, $M = 316.28$, $\lambda = 0.71073$ Å, triclinic, space group $P-1$, $a = 8.0440(3)$, $b = 9.1370(3)$, $c = 9.8910(4)$ Å, $\alpha = 83.548(1)^\circ$, $\beta = 81.155(2)^\circ$, $\gamma = 76.326(2)^\circ$, $V = 695.77(4)$ Å³, $Z = 2$, $D_c = 1.510$ g cm⁻³, $\mu = 0.123$ mm⁻¹, $F(000) = 324$, crystal size $0.35 \times 0.20 \times 0.15$ mm, unique reflections = 3395 [$R_{\text{int}} = 0.0360$], observed $I > 2\sigma(I) = 2602$, data/restraints/parameters = 3395 / 2 / 217, obs. data; $R1 = 0.0432$, $wR2 = 0.1093$, all data; $R1 = 0.0629$, $wR2 = 0.1202$, max peak/hole 0.365 and -0.386 eÅ⁻³, software used, SHELXS, SHELXL and ORTEX.⁵⁹⁻⁶¹

Analytical data

17a. IR (KBr) ν_{\max} 3468, 3270, 1674, 1600 cm^{-1} ; ^1H NMR δ 6.17 (1 H, br, NH), 7.48 (1 H, t, $J = 8.0$ Hz, Ph 4-H), 7.56 (2 H, t, $J = 8.0$ Hz, Ph 3,5- H_2), 7.60 (1 H, t, $J = 8.0$ Hz, 6-H), 7.65 (2 H, m, Ph 2,6- H_2), 8.06 (1 H, dd, $J = 7.8, 1.6$ Hz, 5-H), 8.42 (1 H, d, $J = 2.3$ Hz, 4-H), 8.86 (1 H, dd, $J = 8.0, 1.2$ Hz, 7-H), 9.20 (1 H, d, $J = 2.3$ Hz, 2-H), 10.95 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 126.8 (8-C), 127.4 (6-C), 128.4 (Ph 2,6- C_2), 128.4 (4a-C), 128.6 (Ph 3,5- C_2), 129.3 (Ph 4-C), 132.7 (4-C), 133.8 (5-C), 134.1 (7-C), 134.6 (3-C), 137.1 (Ph 1-C), 144.7 (8a-C), 149.0 (2-C), 167.6 (C=O); MS (FAB) m/z 249.1030 (M + H) ($\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}$ requires 249.0983), 232 (M - NH_2).

17e. IR ν_{\max} 3468, 3330, 1654, 1593 cm^{-1} ; ^1H NMR δ 6.49 (1 H, br, NH), 7.44 (1 H, dd, $J = 8.2, 4.4$ Hz, 3-H), 7.63 (1 H, t, $J = 7.8$ Hz, 6-H), 7.94 (1 H, dd, $J = 7.8, 2.2$ Hz, 5-H), 8.23 (1 H, dd, $J = 8.2, 2.0$ Hz, 7-H), 8.82 (1 H, dd, $J = 7.4, 2.2$ Hz, 4-H), 8.88 (1 H, dd, $J = 4.3, 2.3$ Hz, 2-H), 10.95 (1 H, br, NH); ^{13}C NMR δ 120.92, 126.30, 128.40, 128.43, 132.40, 134.05, 137.56, 145.55, 149.42, 156.84, 167.68; MS (FAB) m/z 173.0717 (M + H) ($\text{C}_{10}\text{H}_9\text{N}_2\text{O}$ requires 173.0715); Anal. ($\text{C}_{10}\text{H}_8\text{N}_2\text{O}$) C, H, N.

17f. IR ν_{\max} 3420, 3302, 1668, 1562 cm^{-1} ; ^1H NMR δ 6.11 (1 H, br, NH), 7.72 (1 H, t, $J = 7.7$ Hz, 6-H), 7.89 (1 H, dd, $J = 8.2, 1.5$ Hz, 5-H), 8.64 (1 H, d, $J = 2.2$ Hz, 4-H), 8.86 (1 H, dd, $J = 8.0, 1.5$ Hz, 7-H), 9.05 (1 H, d, $J = 2.2$ Hz, 2-H), 10.53 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 89.4 (3-C), 127.5 (6-C), 128.8 (4a-C or 8-C), 130.2 (8-C or 4a-C), 131.4 (5-C), 134.9 (7-C), 143.8 (8a-C), 145.2 (5-C), 154.9 (2-C), 167.0 (C=O); MS (FAB) m/z 299.9715 (M + H) ($\text{C}_{10}\text{H}_7\text{IN}_2\text{O}$ requires 299.9760).

17g. IR ν_{\max} 3468, 3019, 1665, 1570 cm^{-1} ; ^1H NMR δ 2.53 (3 H, s, Me), 6.20 (1 H, br, NH), 7.62 (1 H, t, $J = 8.2$ Hz, 6-H), 7.88 (1 H, dd, $J = 8.2, 1.6$ Hz, 5-H), 8.01 (1 H, d, $J = 2.0$ Hz, 4-H), 8.73 (1 H, dd, $J = 8.2, 1.6$ Hz, 7-H), 8.75 (1 H, d, $J = 2.0$ Hz, 2-H), 10.99 (1 H, br, NH); ^{13}C NMR δ 18.5, 126.4, 128.2, 128.4, 130.5, 131.9, 133.1, 136.3, 143.9, 151.4, 167.9; MS (ES) m/z 187.0866 (M + H) ($\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}$ requires 187.0866), 143 (M - CONH_2); Anal. ($\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}$) C, H, N.

17h. IR (KBr) ν_{\max} 3276, 3131, 2164, 1680, 1610 cm^{-1} ; ^1H NMR δ 0.29 (9 H, s, SiMe_3), 6.21 (1 H, br, NH), 7.68 (1 H, t, $J = 7.5$ Hz, 6-H), 7.92 (1 H, dd, $J = 7.9, 1.8$ Hz, 5-H), 8.34 (1 H, d, $J = 2.1$ Hz, 4-H), 8.83 (1 H, dd, $J = 7.5, 1.4$ Hz, 7-H), 8.91 (1 H, d, $J = 2.1$ Hz, 2-H), 10.70 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 0.20 (Me), 99.4 (Si-C), 101.0 (C \equiv CSi), 117.4 (3-C), 127.2 (6-C), 127.4 (4-C or 8-C), 128.6 (8-C or 4-C), 132.2 (5-C), 134.8 (7-C), 140.2 (4-C), 144.1 (8a-C), 151.5 (2-C), 167.2 (C=O); MS (ES) m/z 559 (2 M + Na), 269.1105 (M + H) ($\text{C}_{15}\text{H}_{17}\text{N}_2\text{OSi}$ requires 269.1032); Anal. ($\text{C}_{15}\text{H}_{16}\text{N}_2\text{OSi}$) C, H, N.

17i. IR ν_{\max} 3468, 3190, 2099, 1687, 1639 cm^{-1} ; ^1H NMR δ 3.32 (1 H, s, ethynyl 2-H), 6.07 (1 H, br, NH), 7.71 (1 H, t, $J = 7.8$ Hz, 6-H), 7.96 (1 H, dd, $J = 8.4, 1.5$ Hz, 5-H), 8.40 (1 H, d, $J = 2.0$ Hz, 4-H), 8.86 (1 H, dd, $J = 8.4, 1.6$ Hz, 7-H), 8.96 (1 H, d, $J = 2.0$ Hz, 2-H), 10.67 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 80.0 (ethynyl 1-C), 81.4 (ethynyl 2-C), 116.4 (3-C), 127.3 (6-C), 127.4 (4a-C or 8-C), 128.7 (8-C or 4a-C), 132.2

(5-C), 135.1 (7-C), 140.7 (4-C), 144.3 (8a-C), 151.5 (2-C), 167.1 (C=O); MS (ES) m/z 197.0702 (M + H) ($C_{12}H_9N_2O$ requires 197.0709).

17j. IR (KBr) ν_{\max} 3350, 2928, 1666, 1600 cm^{-1} ; 1H NMR δ 1.37 (3 H, t, $J = 7.8$ Hz, Me), 2.88 (2 H, q, $J = 7.6$ Hz, CH_2), 6.08 (1 H, br, NH), 7.64 (1 H, t, $J = 7.8$ Hz, 6-H), 7.94 (1 H, dd, $J = 7.8, 1.6$ Hz, 5-H), 8.03 (1 H, d, $J = 2.3$ Hz, 4-H), 8.78 (1 H, dd, $J = 8.2, 1.6$ Hz, 7-H), 8.81 (1 H, d, $J = 2.3$ Hz, 2-H), 11.01 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 15.1 (Me), 26.0 (CH_2), 126.4 (6-C), 128.3 (4a-C or 8-C), 128.5 (8-C or 4a-C), 132.1 (7-C), 133.2 (4-C), 135.0 (5-C), 136.6 (3-C), 144.1 (8a-C), 150.9 (2-C), 167.8 (CONH₂); MS (ES) m/z 201.1022 (M + H) ($C_{12}H_{13}N_2O$ requires 201.0950).

17k. 1H NMR δ 5.50 (1 H, d, $J = 11.0$ Hz, ethenyl 2- H_{trans}), 6.60 (1 H, d, $J = 17.6$ Hz, ethenyl 2- H_{cis}), 6.13 (1 H, br, NH), 6.89 (1 H, q, $J = 17.7, 11.0$ Hz, ethenyl 1-H), 7.68 (1 H, t, $J = 7.8$ Hz, 6-H), 7.96 (1 H, dd, $J = 8.2, 1.6$ Hz, 5-H), 8.17 (1 H, d, $J = 2.3$ Hz, 4-H), 8.78 (1 H, dd, $J = 7.4, 1.6$ Hz, 7-H), 9.03 (1 H, d, $J = 2.3$ Hz, 2-H), 10.90 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 117.3 (ethenyl 2-C), 126.8 (6-C), 128.3 (4a-C or 8-C), 128.4 (8-C or 4a-C), 130.3 (3-C), 132.5 (5-C), 133.0 (ethenyl 1-C), 133.8 (7-C), 133.9 (4-C), 144.9 (8a-C), 148.2 (2-C), 167.5 (C=O). MS (ES) m/z 220.0481 (M + Na) ($C_{11}H_7N_3NaO$ requires 220.0487).

17l. IR ν_{\max} (KBr) 3470, 3210, 2363, 1674, 1590; 1H NMR δ 2.13 (3 H, s, Me), 6.13 (1 H, br, NH), 7.68 (1 H, t, $J = 7.8$ Hz, 6-H), 7.90 (1 H, dd, $J = 7.8, 1.6$ Hz, 5-H), 8.24 (1 H, d, $J = 2.3$ Hz, 4-H), 8.84 (1 H, dd, $J = 7.8, 1.6$ Hz, 7-H), 9.05 (1 H, d, $J = 2.3$ Hz, 2-H), 10.75 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 4.5 (Me), 90.6 (propynyl 1-C), 118.3 (propynyl 2-C), 127.0 (3-C), 127.7 (6-C), 128.2 (4a-C or 8-C), 128.5 (8-C or 4a-C), 132.1 (5-C), 134.4 (7-C), 139.3 (4-C), 143.8 (8a-C), 151.6 (2-C), 167.4 (C=O); MS (ES) m/z 211.0866 (M + H) ($C_{13}H_{11}N_2O$ requires 211.0793); Anal. ($C_{13}H_{10}N_2O$) C, H, N.

17o. IR ν_{\max} 3468, 3283, 1675, 1599 cm^{-1} ; 1H NMR δ 2.44 (3 H, s, Me), 6.17 (1 H, br, NH), 7.36 (2 H, d, $J = 7.8$ Hz, Ph 3,5- H_2), 7.63 (2 H, d, $J = 8.2$ Hz, Ph 2,6- H_2), 7.69 (1 H, t, $J = 7.8$ Hz, 6-H), 8.04 (1 H, dd, $J = 8.2, 1.5$ Hz, 5-H), 8.39 (1 H, d, $J = 2.0$ Hz, 4-H), 8.83 (1 H, dd, $J = 8.0, 1.5$ Hz, 7-H) 9.19 (1 H, d, $J = 2.0$ Hz, 2-H), 10.96 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 21.2 (Me), 126.8 (6-C), 127.2 (Ph 3,5- C_2), 128.4 (4a,8- C_2), 130.1 (Ph 2,6- C_2), 132.6 (5-C), 133.7 (3-H or Ph 1-C), 133.8 (3-H or Ph 1-C), 134.1 (4-C), 134.2 (7-C), 138.6 (Ph 4-C), 144.5 (8a-C), 149.0 (2-C), 167.6 (C=O); MS (ES) m/z 263.1176 (M + H) ($C_{17}H_{15}N_2O$ requires 263.1176), 219 (M - CONH₂); Anal. ($C_{17}H_{14}N_2O$) C, H, N.

18c. 1H NMR δ 1.43 (3 H, t, $J = 7.4$ Hz, Me), 3.08 (2 H, q, $J = 7.8$ Hz, CH_2), 7.30 (1 H, t, $J = 7.8$ Hz, 6-H), 7.34 (1 H, d, $J = 8.2$ Hz, 3-H), 7.73 (1 H, dd, $J = 8.2, 1.2$ Hz, 5-H), 8.01 (1 H, dd, $J = 7.8, 1.6$ Hz, 7-H), 8.03 (1 H, d, $J = 8.6$ Hz, 4-H); ^{13}C NMR (HMQC / HMBC) δ 13.5 (Me), 32.3 (CH_2), 121.7 (3-C), 124.5 (8-C), 126.0 (6-C), 127.41 (5-C), 128.0 (4a-C), 132.9 (7-C), 136.6 (4-C), 144.8 (8a-C), 165.1 (2-C); MS (EI) m/z 236 (M - H) ($C_{11}H_9^{81}BrN$), 233.9911 (M - H) ($C_{11}H_9^{79}BrN$ requires 233.9913).

21. IR ν_{\max} 2232 cm^{-1} ; ^1H NMR δ 7.48-7.58 (2 H, m, 3,6- H_2), 8.02-8.08 (2 H, m, 5,7- H_2), 8.21 (1 H, dd, $J = 8.6, 1.6$ Hz, 4-H), 9.03 (1 H, dd, $J = 4.3, 1.6$ Hz, 2-H); ^{13}C NMR δ 112.84, 117.18, 122.68, 125.76, 127.98, 132.86, 135.42, 136.43, 147.29, 152.38; MS (EI) m/z 154.0531 (M) ($\text{C}_{10}\text{H}_6\text{N}_2$) requires 154.0525), 128 (M – CN).

29b. IR ν_{\max} (KBr) 3480, 3236, 1661, 1616 cm^{-1} ; ^1H NMR δ 2.77 (3 H, s, Me), 6.40 (1 H, br, NH), 7.35 (1 H, d, $J = 8.2$ Hz, 3-H), 7.60 (1 H, t, $J = 7.8$ Hz, 6-H), 7.93 (1 H, dd, $J = 8.2, 1.6$ Hz, 5-H), 8.15 (1 H, d, $J = 8.2$ Hz, 4-H), 8.82 (1 H, dd, $J = 7.8, 1.6$ Hz, 7-H), 11.25 (1 H, br, NH); ^{13}C NMR (HMQC / HMBC) δ 25.5 (Me), 121.8 (2-C), 125.4 (6-C), 126.7 (4a-C or 8-C), 127.7 (8-C or 4a-C), 132.2 (7-C), 133.2 (5-C), 137.6 (4-C), 145.2 (8a-C), 158.7 (3-C), 168.0 (CONH₂); MS (ES) m/z 187.0857 (M + H) ($\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}$ requires 187.0866).

30. IR ν_{\max} (KBr) 2364, 1227 cm^{-1} ; ^1H NMR δ 7.48-7.56 (3 H, m, Ph 3,4,5- H_3), 7.64 (2 H, d, $J = 8.2$ Hz, Ph 2,6- H_2), 7.72 (1 H, t, $J = 7.4$ Hz, 6-H), 7.91 (1 H, d, $J = 1.6$ Hz, 4-H), 8.13 (1 H, d, $J = 7.4, 1.6$ Hz, 7-H), 8.14 (1 H, dd, $J = 7.4, 1.6$ Hz, 5-H), 8.83 (1 H, d, $J = 1.6$ Hz, 2-H); ^{13}C NMR δ 106.0 (8-C), 117.7 (CN), 122.9 (4-C), 127.1 (Ph 2,6- C_2), 128.4 (6-C), 129.6 (Ph 3,4,5- C_3), 131.1 (4a-C), 133.2 (7-C), 134.8 (Ph 1-C), 136.2 (5-C), 136.9 (8a-C), 138.9 (3-C), 139.0 (2-C); MS (ES) m/z 247.0865 (M + H) ($\text{C}_{16}\text{H}_{11}\text{N}_2\text{O}$ requires 247.0866), 231 (M + H – O); Anal. ($\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}$) C, H, N. Further elution gave **16** (22 mg, 31%).

31. IR ν_{\max} (KBr) 3420, 1219 cm^{-1} ; ^1H NMR ($(\text{CD}_3)_2\text{SO}$) δ 7.28 (1 H, br, NH), 7.48 (1 H, br, NH), 7.48 (1 H, t, $J = 8.0$ Hz, Ph 4-H), 7.53 (1 H, dd, $J = 8.2, 1.2$ Hz, 5-H), 7.56 (2 H, t, $J = 8.0$ Hz, Ph 3,5- H_2), 7.72 (1 H, t, $J = 7.8$ Hz, 6-H), 7.89 (2 H, d, $J = 8.0$ Hz, Ph 2,6- H_2), 8.13 (1 H, dd, $J = 8.2, 1.2$ Hz, 7-H), 8.31 (1 H, d, $J = 1.6$ Hz, 4-H), 8.92 (1 H, d, $J = 2.0$ Hz, 2-H); ^{13}C NMR (HMQC / HMBC) ($(\text{CD}_3)_2\text{SO}$) δ 122.2 (4-C), 127.2 (Ph 2,6- C_2), 128.7 (6-C), 129.2 (4a-C or 8-C), 129.4 (8-C or 4a-C), 129.5 (Ph 3,5- C_2), 129.7 (5-C), 130.9 (7-C), 131.8 (Ph 4-C), 134.2 (3-C), 134.3 (2-C), 135.2 (Ph 1-C), 136.2 (C-8a), 170.4 (CONH₂); MS (ES) m/z 551 (2 M + Na), 265.0960 (M + H) ($\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}_2$ requires 265.0972); Anal. ($\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$) C, H, N.

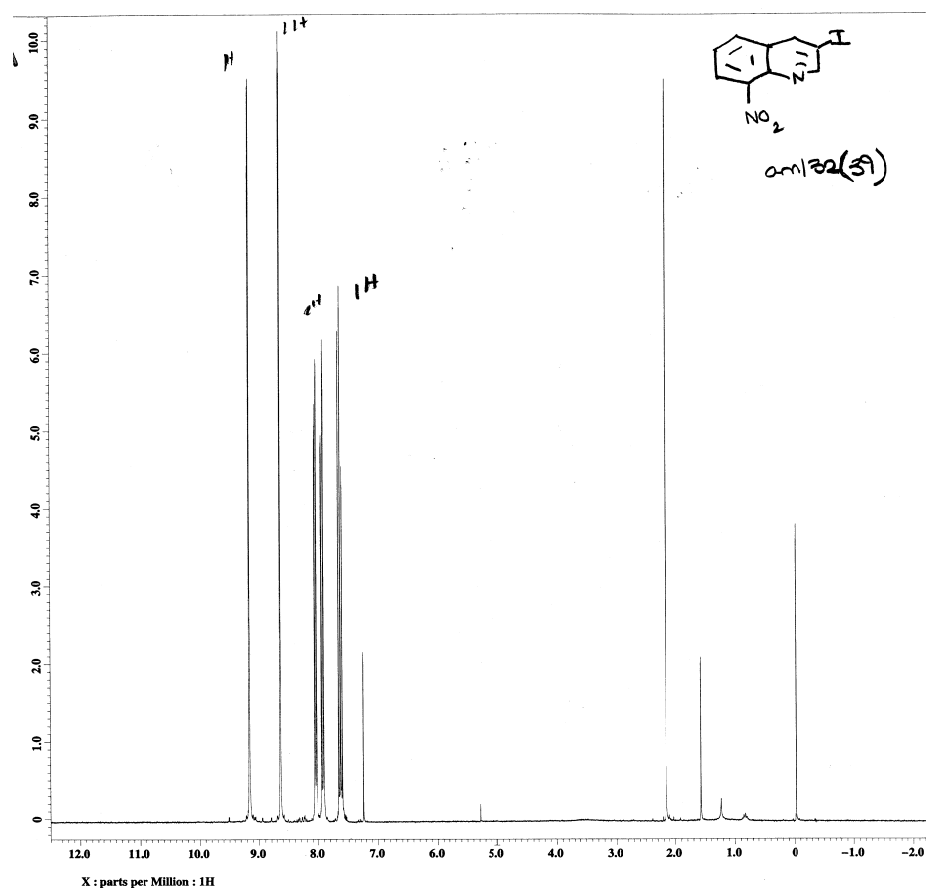
Biochemical assay

Inhibition of human recombinant PARP-1 activity was measured using the Universal PARP assay kit (Trevigen Inc, Gaithersburg, USA), with some modification of the protocol supplied with the kit. The assays were performed in 96-well plates pre-coated with histones. Briefly, stock solutions (50 mM in DMSO) of inhibitors **17**, **29** and **31** were prepared. To generate inhibition curves, the stock solutions were diluted with 1 × PARP Buffer (supplied) to give seven different concentrations at 5 × stock solution, such that the final concentrations in the assay were 100, 30, 10, 3, 1, 0.3, and 0.1 μM. The final concentration of DMSO in the assay was less than 0.2 % (v/v). A positive control (no inhibitor) and negative control (no enzyme) were included in each assay. The PARP-1 was diluted to 0.8 units / 15 μL with 1 × PARP Buffer. Diluted PARP inhibitor (40 μL) was mixed with diluted PARP enzyme (60 μL), centrifuged and incubated for 10 min at ambient temperature. Aliquots (25 μL) of each solution was distributed into wells in triplicate. To initiate the reaction, of PARP cocktail ((10 × PARP Cocktail (supplied), 10 × Activated DNA (supplied), 1 10 × PARP buffer (1:1:8) (v/v/v)) (25 μL) was added to each well. The reaction was allowed to proceed for 1 h at ambient temperature. Plates were washed four times with PBS + 0.1 % (v/v) Triton X-100 (200 μL). Then 50 μL Strep-HRP (50 μL) (1000 fold with 1 × Strep diluent) was added to each well with a multi-channel pipettor, and the plate incubated for 30 min at ambient temperature before washing with PBS + 0.1 % (v/v) Triton X-100 (200 μL). Substrate TACS Sapphire (supplied) (50 μL well⁻¹) was added and the plates incubated in the dark for 30 min. Absorbance at 630 nm was measured using a Versamax microplate reader with SoftMax Pro 4.7.1 software. The colourimetric reaction was stopped by adding HCl (0.2 M, 50 μL) and the absorbance read at 450 nm. Data were analysed using GraphPad Prism 2.01 software. The IC₅₀ values were calculated by plotting log₁₀ [inhibitor] versus absorbance for the replicant data. Quoted IC₅₀ values are an average for the three replicant curves.

Elemental microanalysis data.

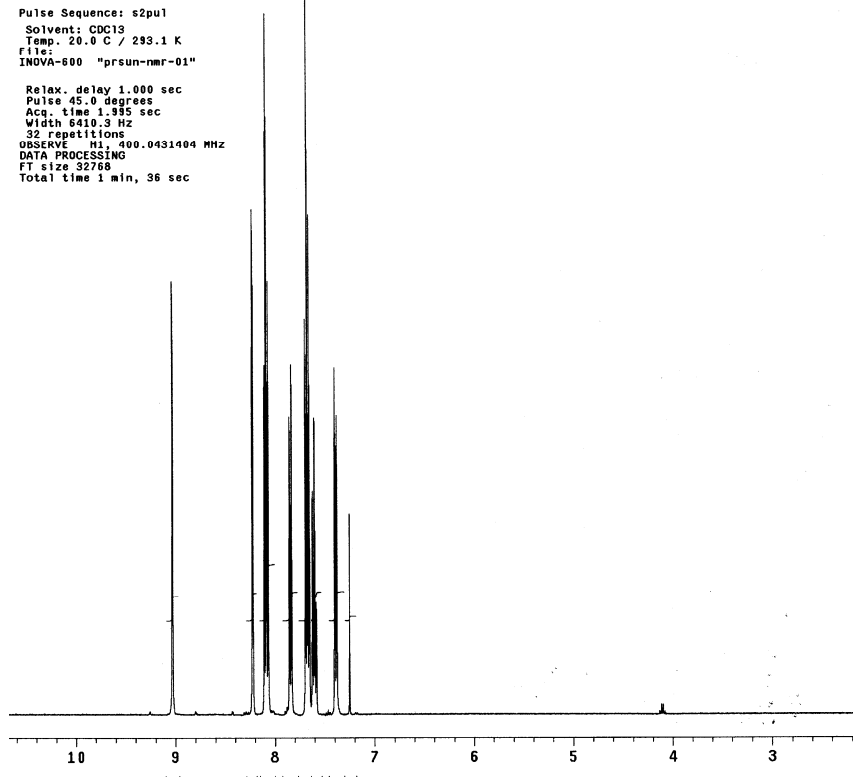
Cpd.	Formula	Found			Calculated		
		C	H	N	C	H	N
16	C ₁₆ H ₁₀ N ₂	83.39	4.39	12.09	83.46	4.38	12.17
17c	C ₁₇ H ₁₁ F ₃ N ₂ O	64.78	3.49	8.84	64.56	3.51	8.86
17e	C ₁₀ H ₈ N ₂ O	69.62	4.77	16.12	69.76	4.68	16.27
17g	C ₁₁ H ₁₀ N ₂ O	71.00	5.69	14.97	70.95	5.41	15.04
17h	C ₁₅ H ₁₆ N ₂ OSi	67.35	5.81	10.30	67.13	6.01	10.44
17l	C ₁₃ H ₁₀ N ₂ O	74.25	4.85	13.31	74.27	4.79	13.33
17m	C ₁₇ H ₁₄ N ₂ O ₂	72.92	4.69	9.63	73.37	5.07	10.07
17o	C ₁₇ H ₁₄ N ₂ O	77.54	5.21	10.47	77.84	5.38	10.68
17p	C ₁₆ H ₁₁ BrN ₂ O. 0.75 CHCl ₃	48.55	2.70	6.03	48.37	2.84	6.02
17r	C ₁₅ H ₁₁ N ₃ O	72.38	4.48	16.41	72.28	4.45	16.86
30	C ₁₆ H ₁₀ N ₂ O	78.05	3.99	11.12	78.03	4.09	11.38
31	C ₁₆ H ₁₂ N ₂ O ₂	72.74	4.46	10.47	72.72	4.58	10.60

Selected NMR spectra



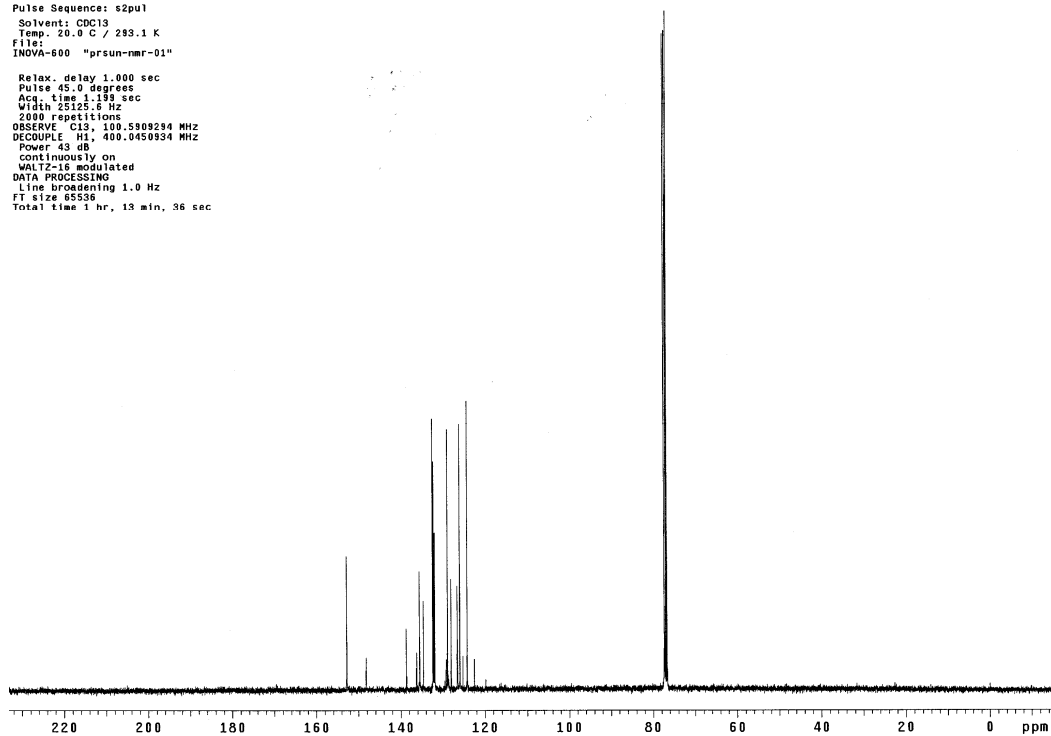
^1H NMR spectrum of **12**.

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Sample directory: amlorho_2007-01-18
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Pulse 45.0 degrees
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FT size 32768
Total time 1 min, 36 sec



¹H NMR spectrum of **13b**.

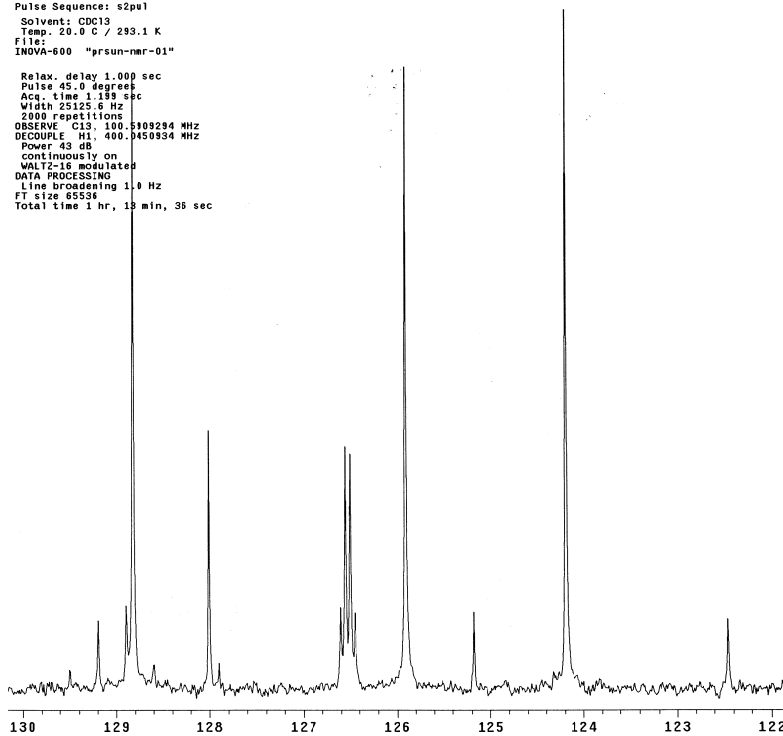
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DECOUPLE H1, 400.0450934 MHz
Power 43 dB
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 13 min, 36 sec



¹³C NMR spectrum of **13b**.

Pulse Sequence: s2pul
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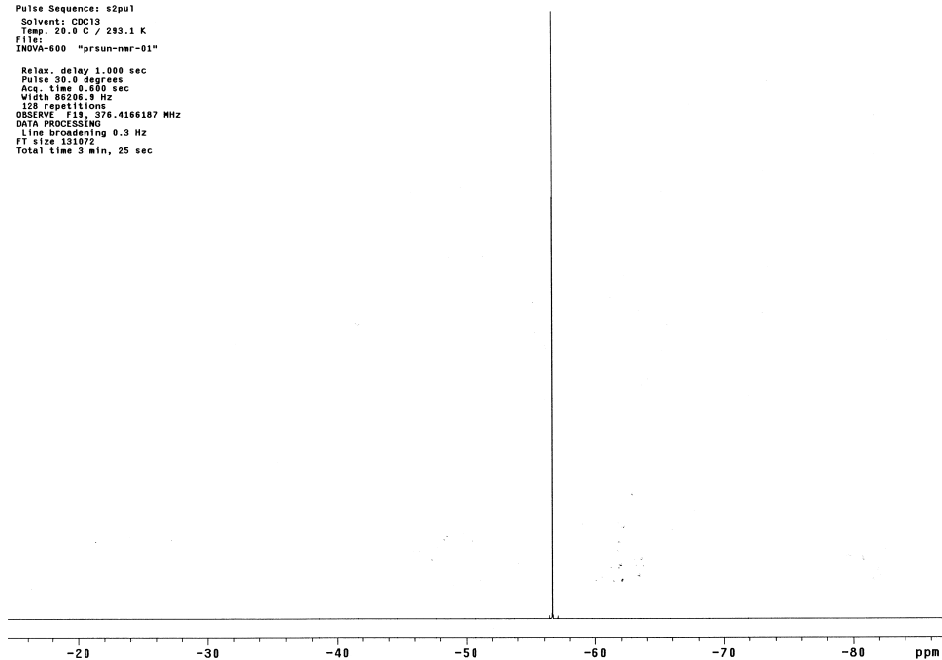
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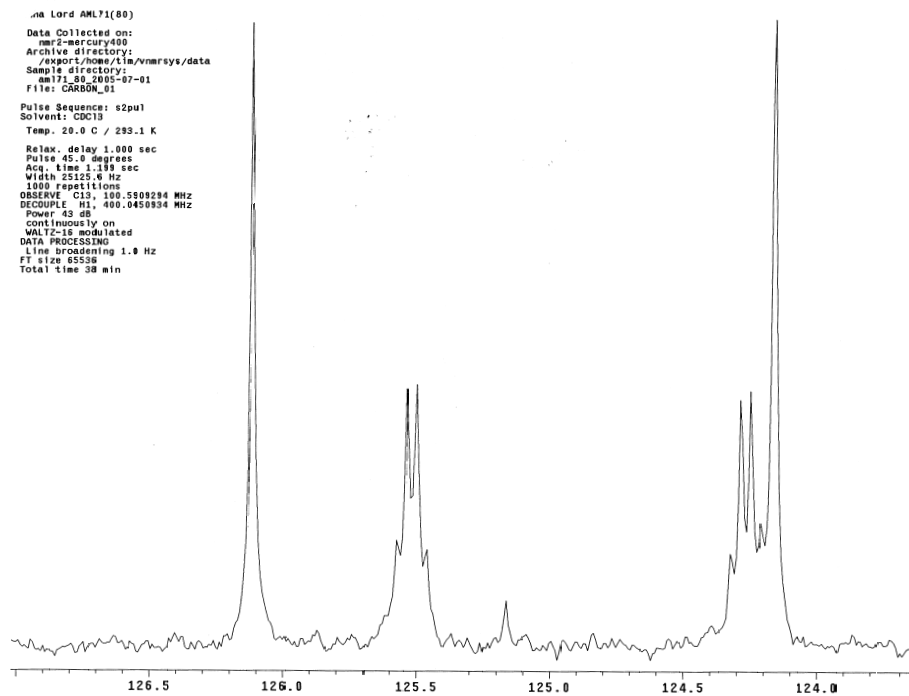
Expansion of part of ¹³C NMR spectrum of **13b**.

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Temp. 20.0 C / 293.1 K
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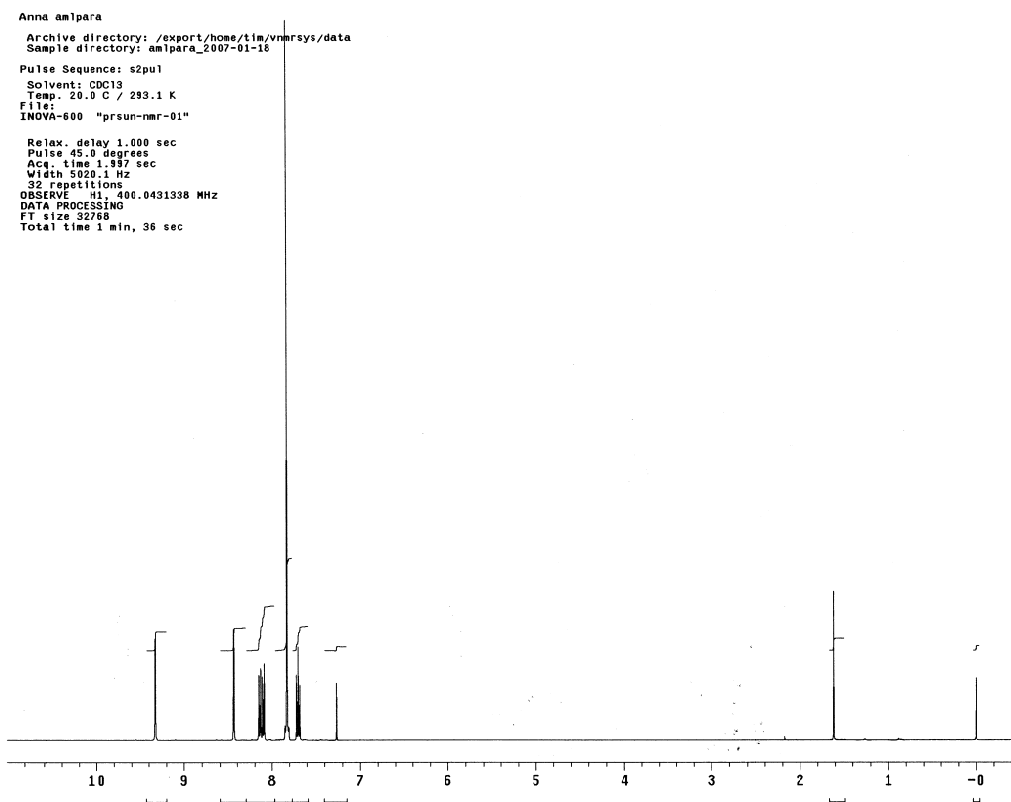
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Line broadening 0.3 Hz
FT size 131072
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¹⁹F NMR spectrum of **13b**.

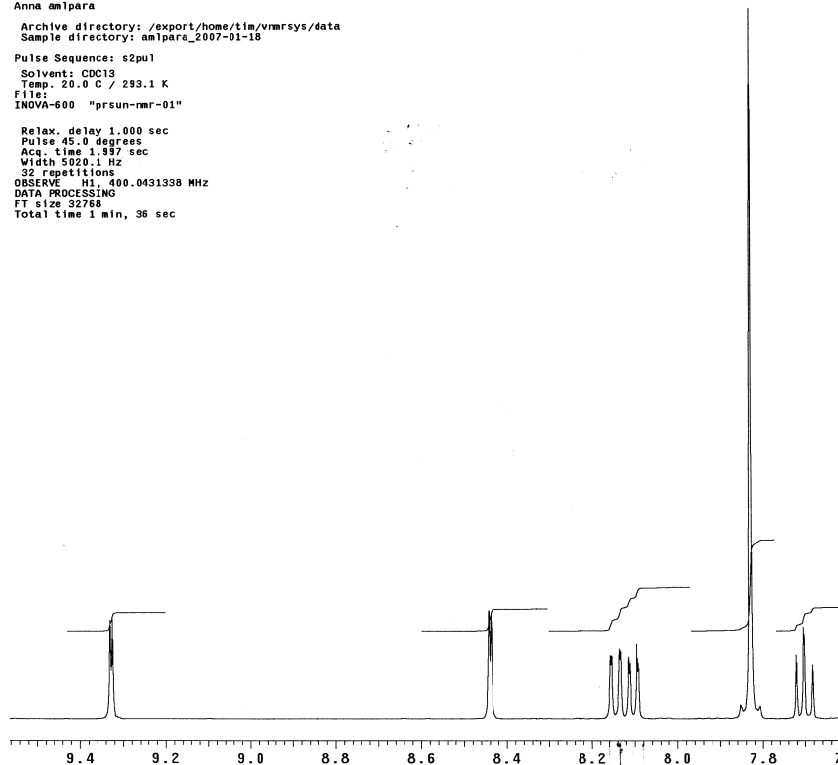


Expansion of part of ^{13}C NMR spectrum of **13c**.

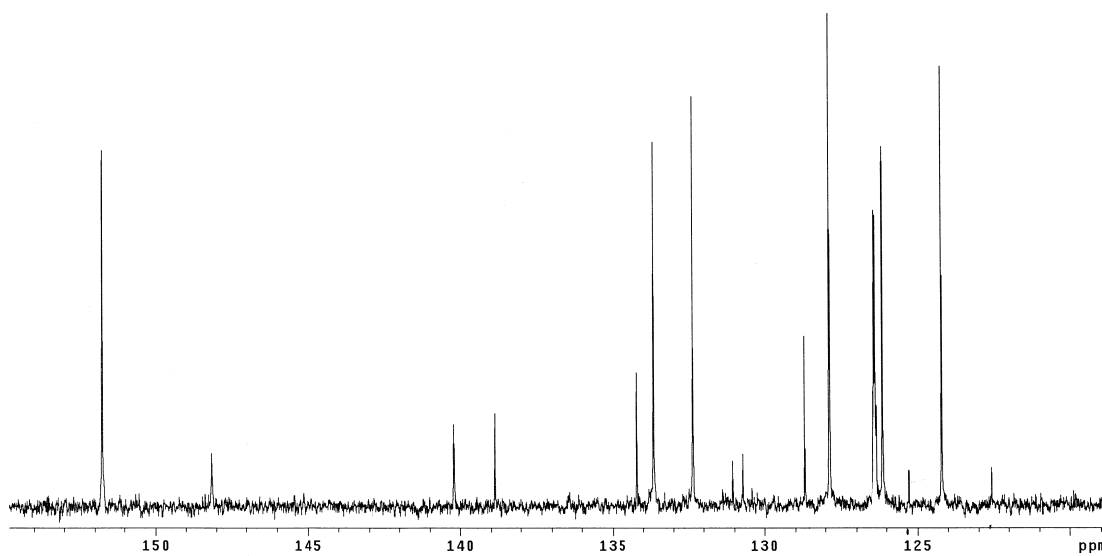


^1H NMR spectrum of **13d**.

Anna ampara
Archive directory: /export/home/tim/vmrsys/data
Sample directory: ampapa_2007-01-18
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
File:
INOVA-600 "prsun-nmf-01"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.997 sec
Width 5020.1 Hz
32 repetitions
OBSERVE H1, 400.0431338 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 36 sec

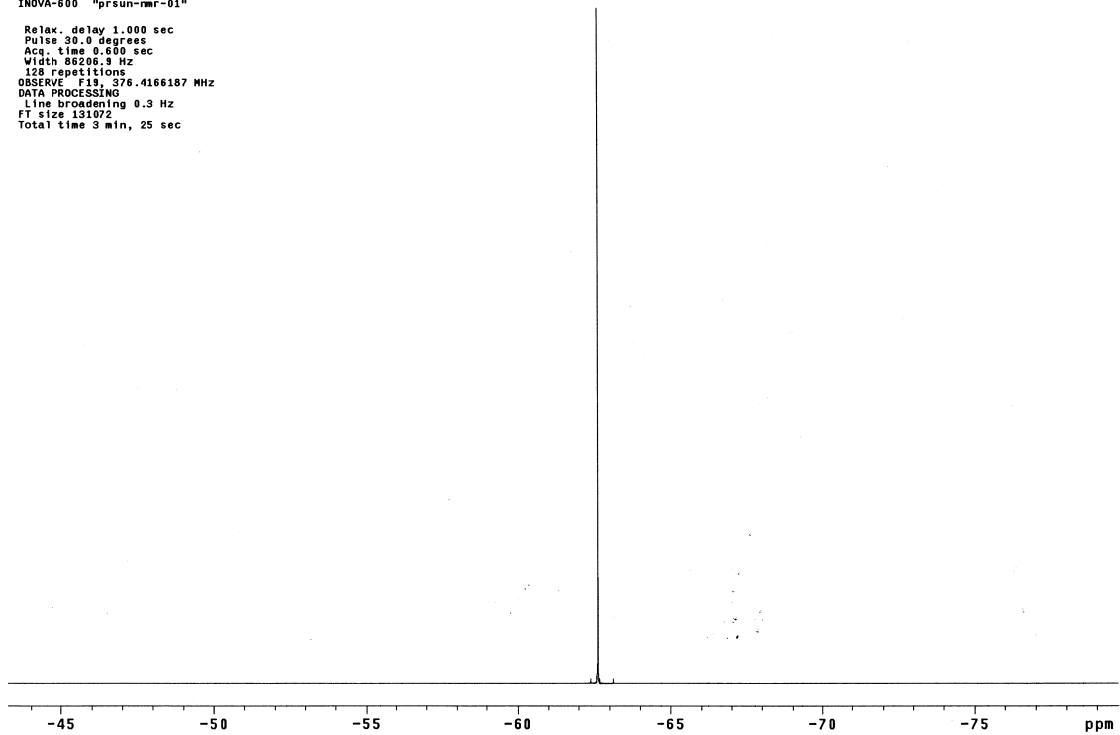


Expansion of part of ^1H NMR spectrum of **13d**.

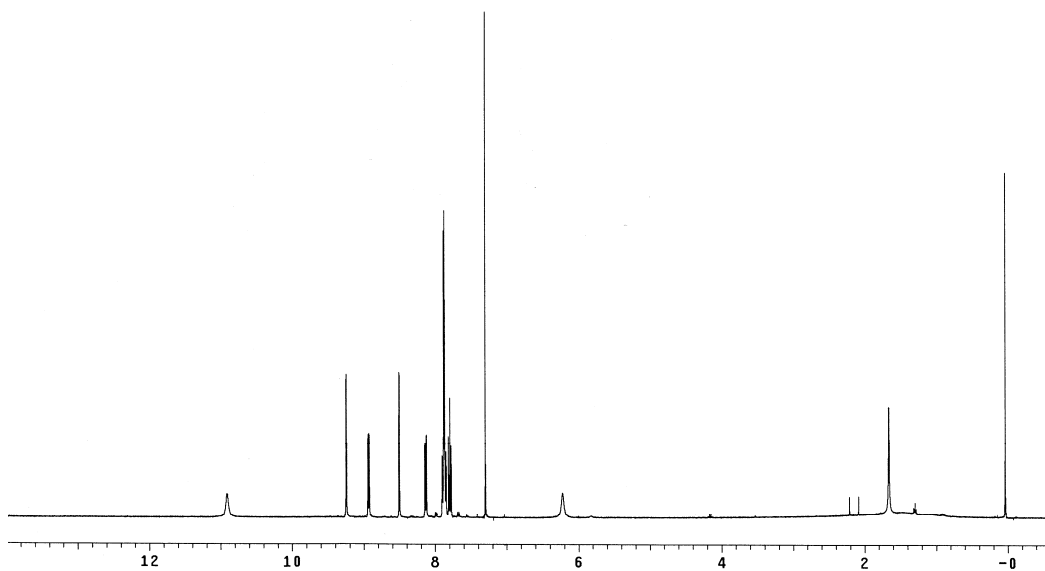


^{13}C NMR spectrum of **13d**.

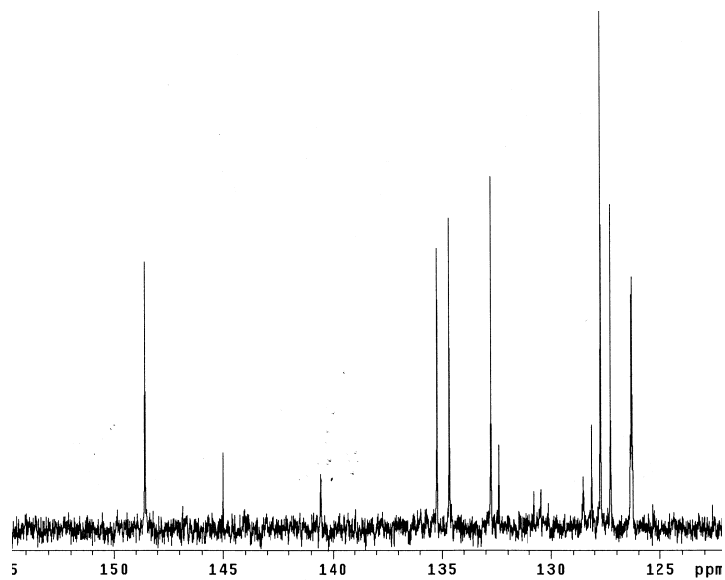
temp. 20.0 C / 293.2 K
File: INOVA-600 "prsun-nmr-01"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 0.600 sec
Width 86206.9 Hz
128 repetitions
OBSERVE F19, 376.4166187 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 3 min, 25 sec



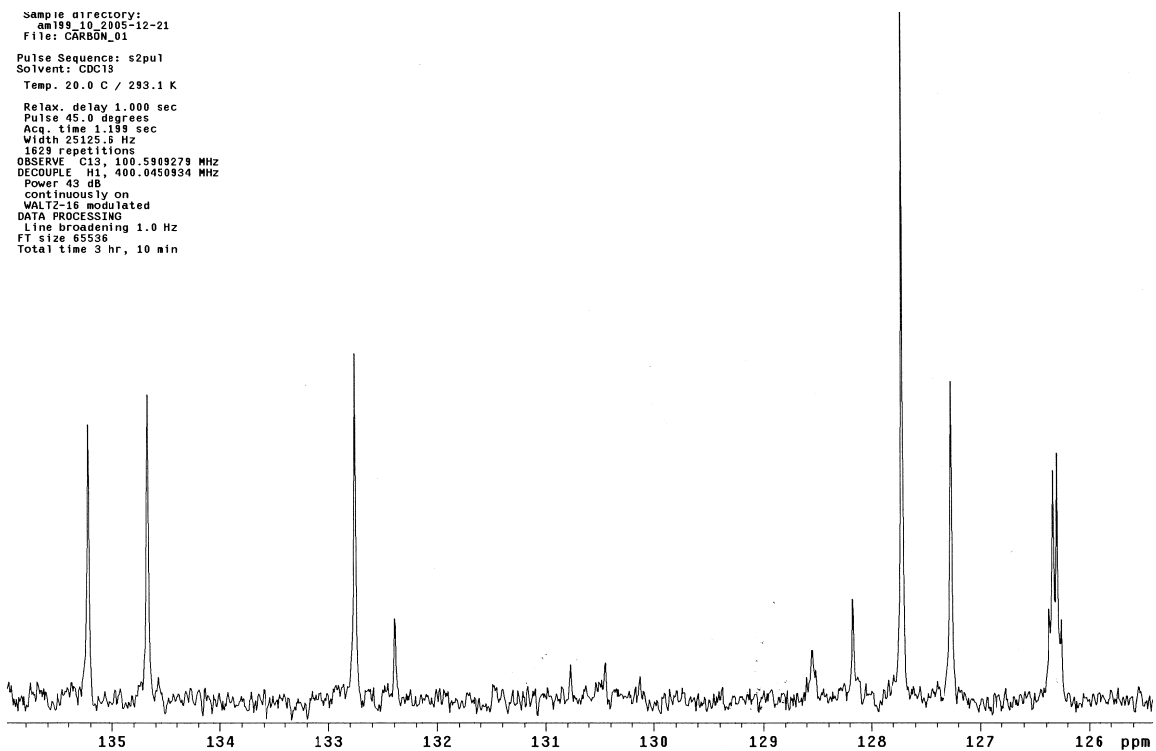
^{19}F NMR spectrum of **13d**.



^1H NMR spectrum of **17d**.

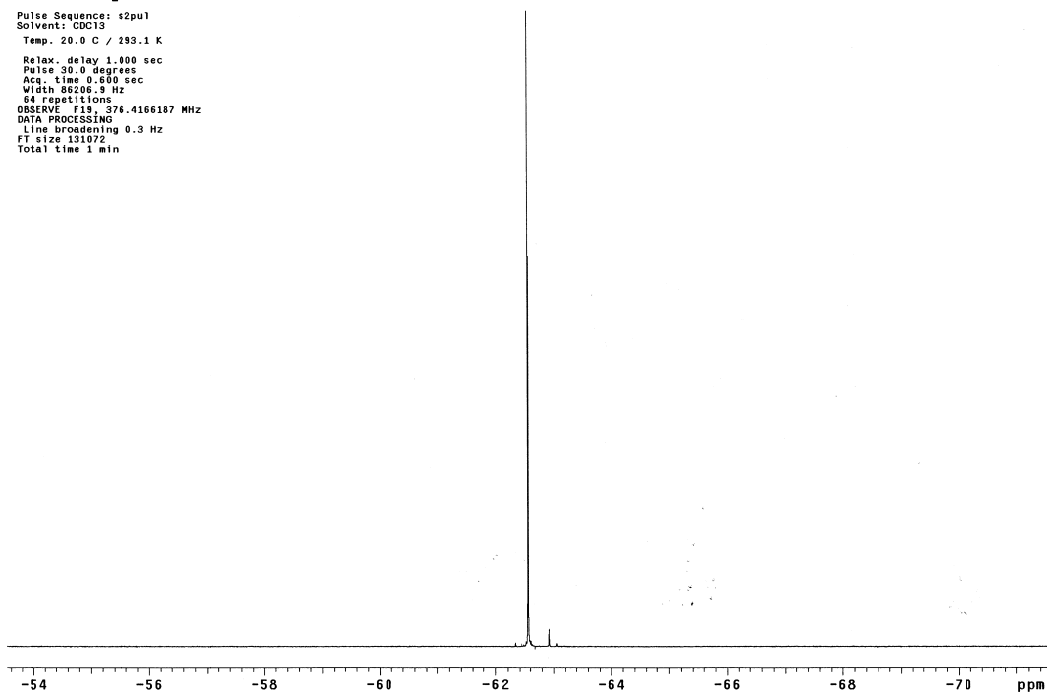


^{13}C NMR spectrum of **17d**.



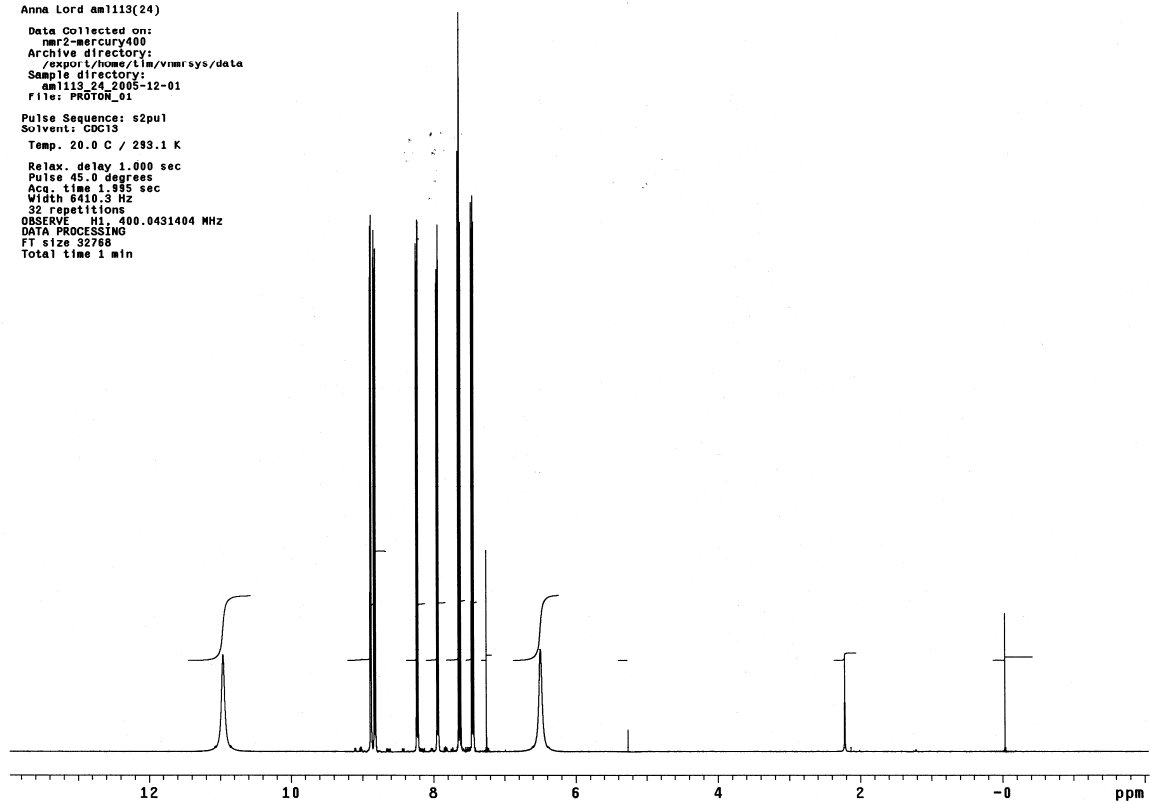
Expansion of part of ^{13}C NMR spectrum of **17d**.

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 0.600 sec
Width 86206.8 Hz
64 repetitions
OBSERVE F1 376.4166187 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 1 min



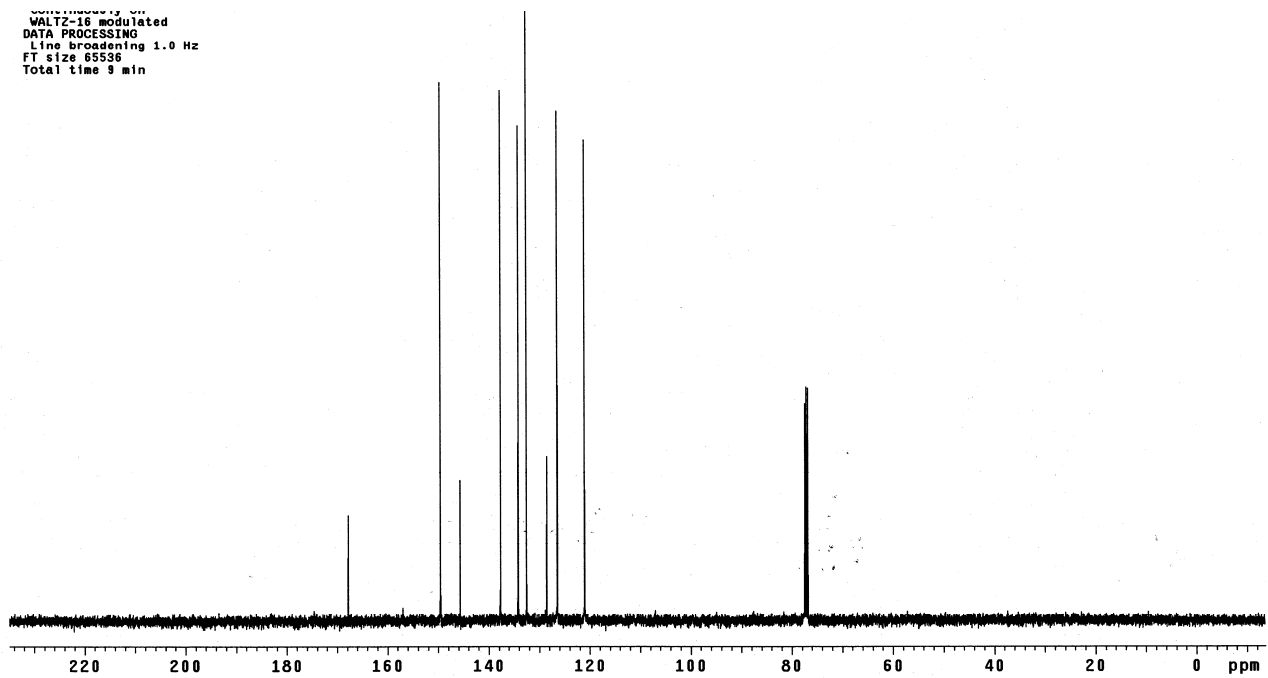
¹⁹F NMR spectrum of **17d**.

Anna Lord am1113(24)
Data Collected on:
nmr2-mercury400
Archive directory:
/export/home/tim/vnmr/sys/data
Sample directory:
am1113_24_2005-12-01
file: PROTON_01
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.935 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1 400.0431404 MHz
DATA PROCESSING
FT size 32768
Total time 1 min

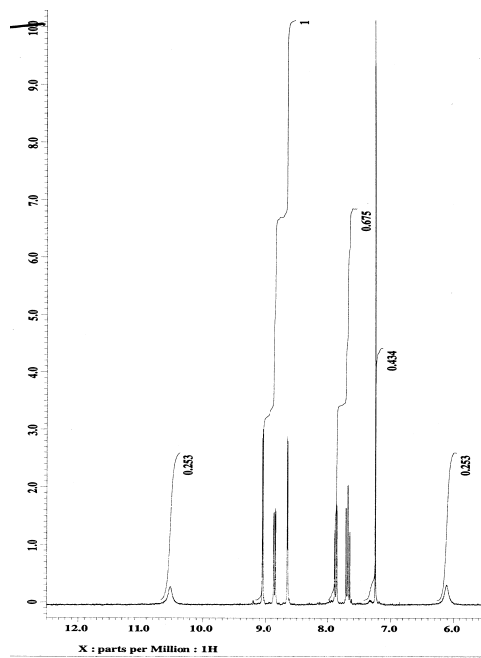


¹H NMR spectrum of **17e**.

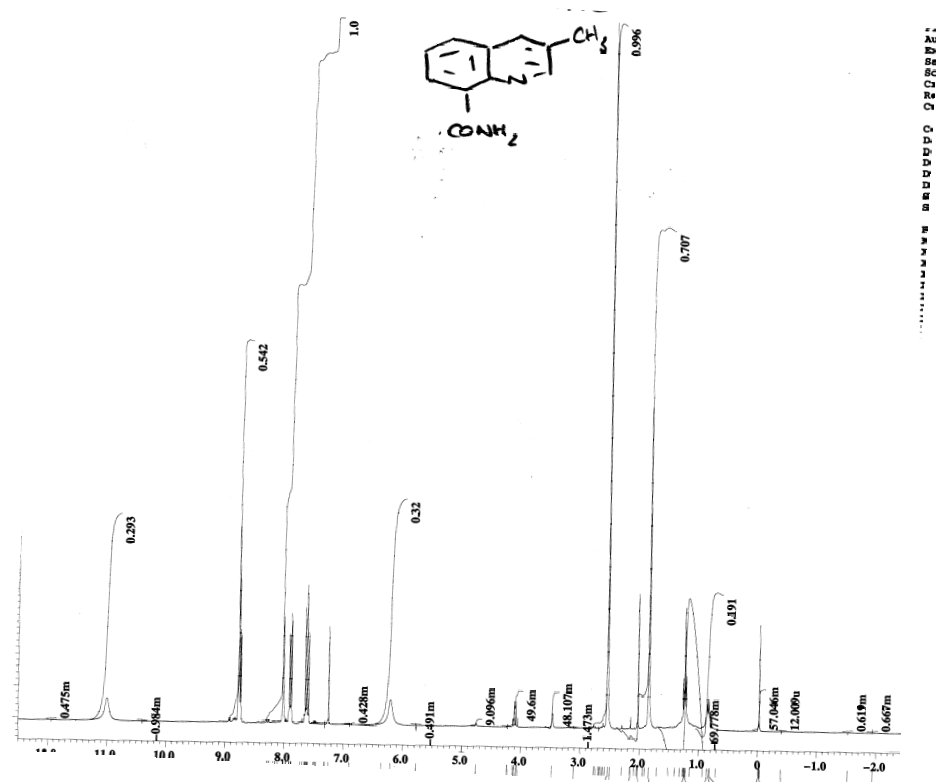
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 8536
Total time 9 min



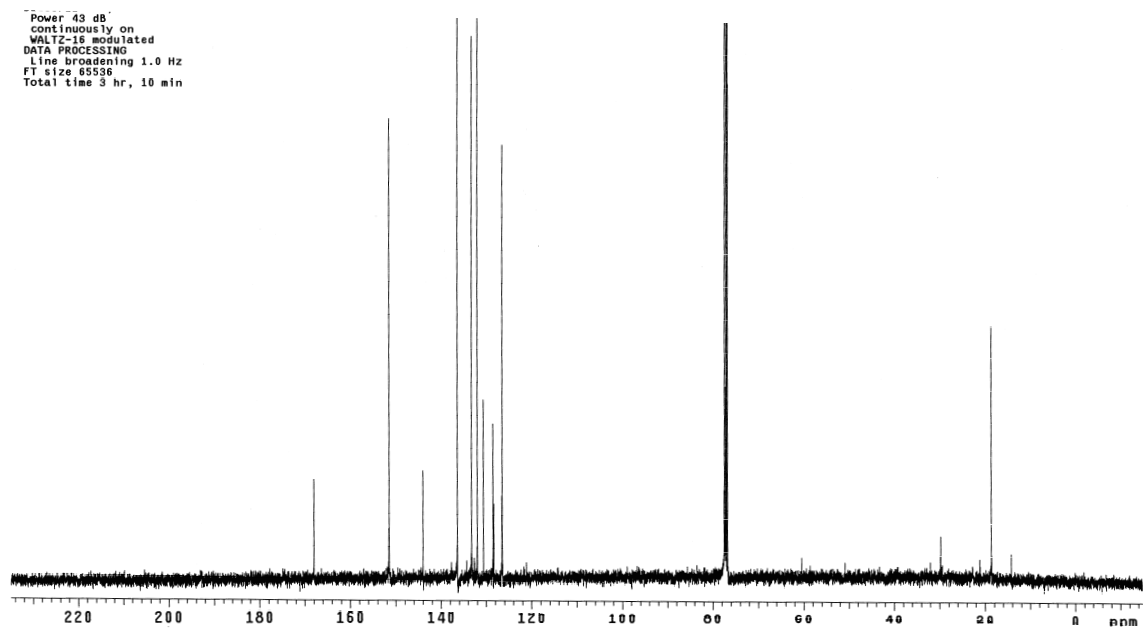
^{13}C NMR spectrum of **17e**.



^1H NMR spectrum of **17f**.

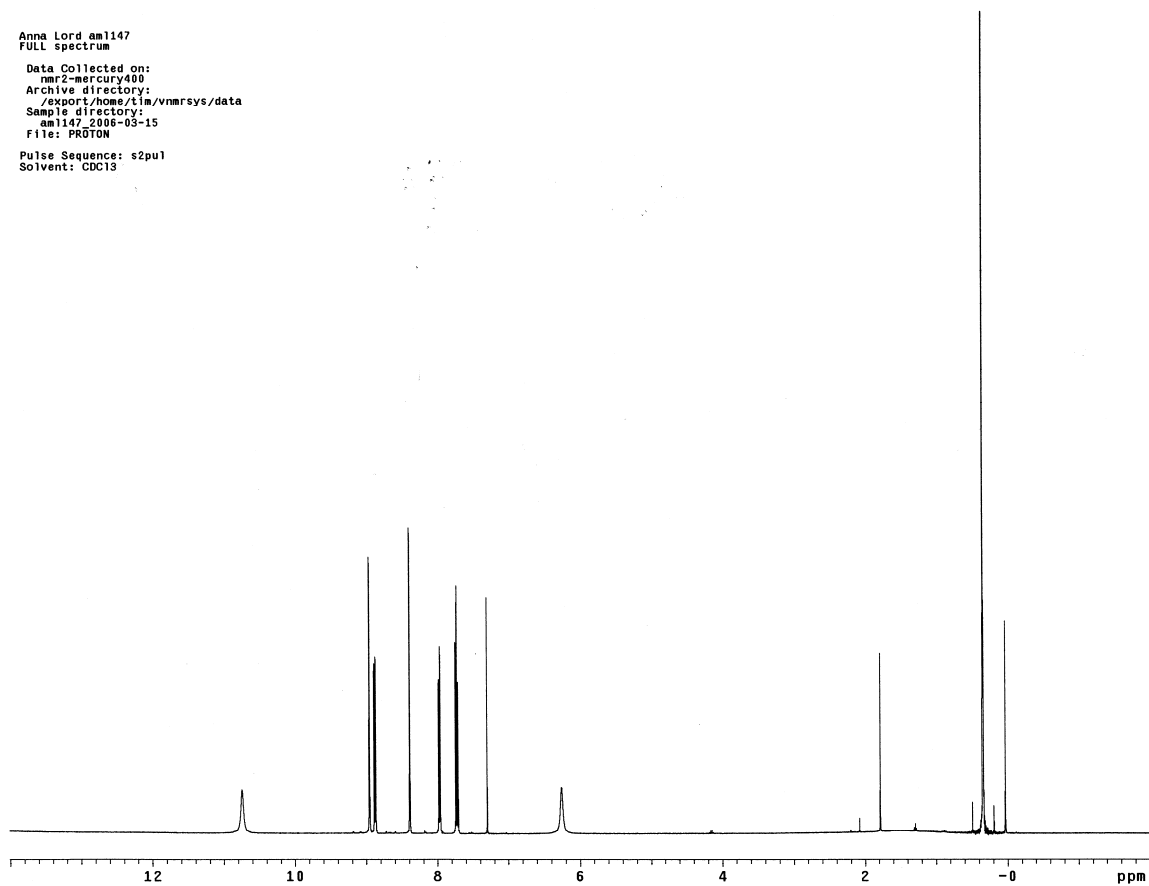


¹H NMR spectrum of 17g.



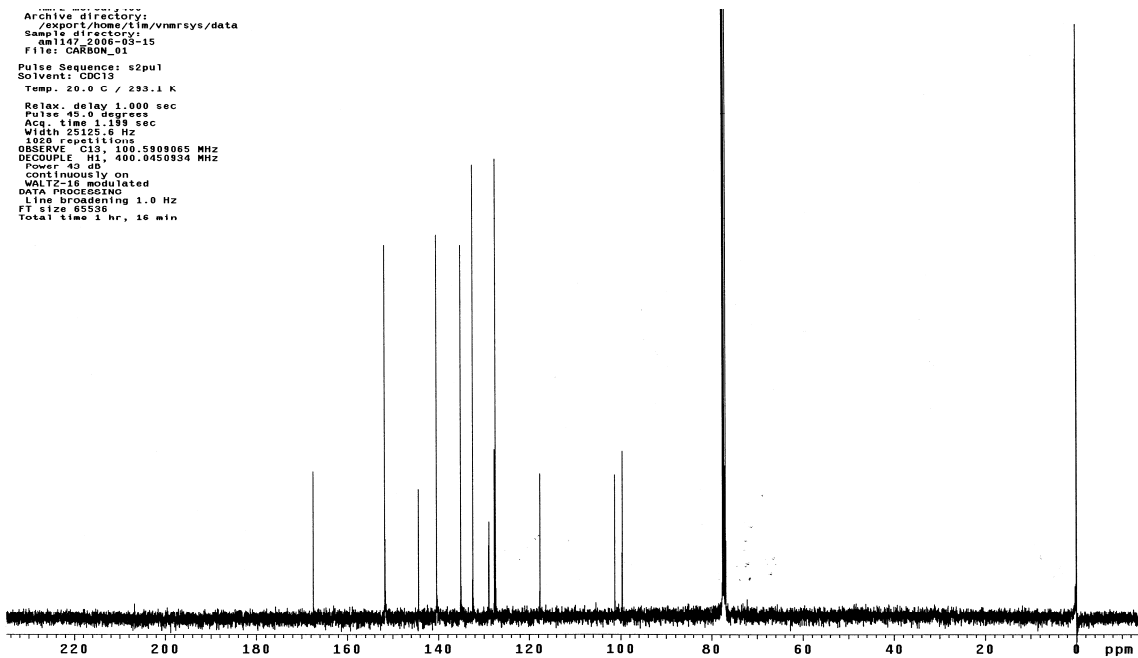
¹³C NMR spectrum of 17g.

Anna Lord am1147
FULL spectrum
Data Collected on:
nmr2-mercury400
Archive directory:
/export/home/l1a/vnmrSYS/data
Sample directory:
am1147_2006-03-15
File: PROTON
Pulse Sequence: s2pu1
Solvent: CDCl3



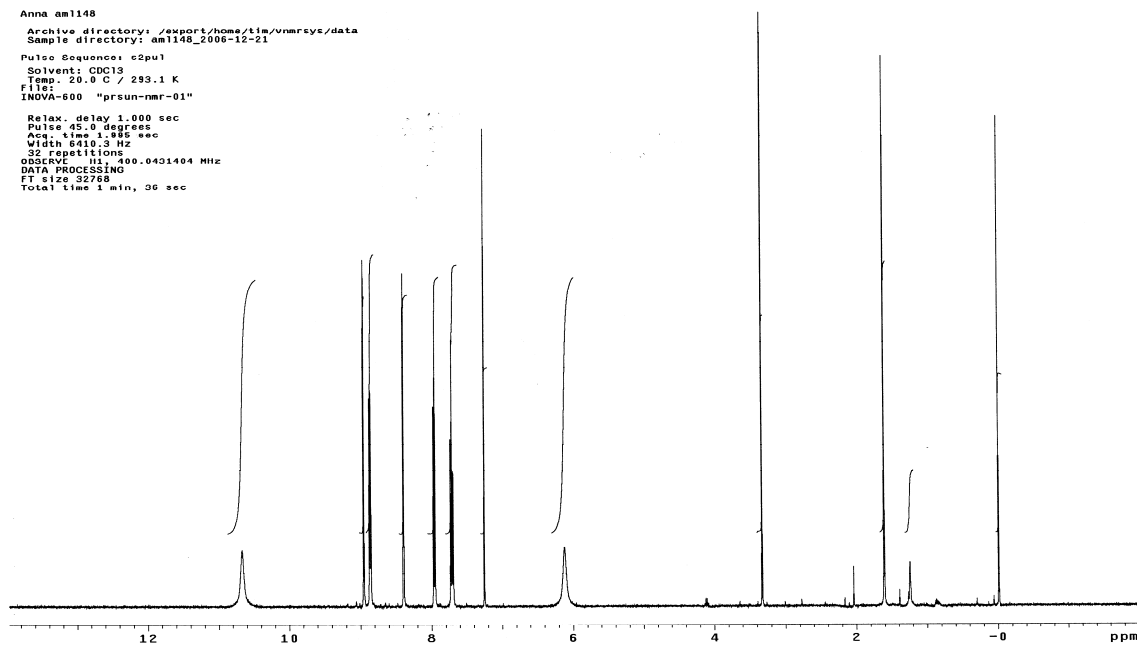
¹H NMR spectrum of **17h**.

Archive directory:
/export/home/l1a/vnmrSYS/data
sample directory:
am1147_2006-03-15
File: CARBON_01
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degree
Acq. time 1.199 sec
Width 25125.6 Hz
1024 repetitions
OBSERVE C13, 100.590865 MHz
DECOUPLE H1, 400.9450934 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCS230
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 16 min



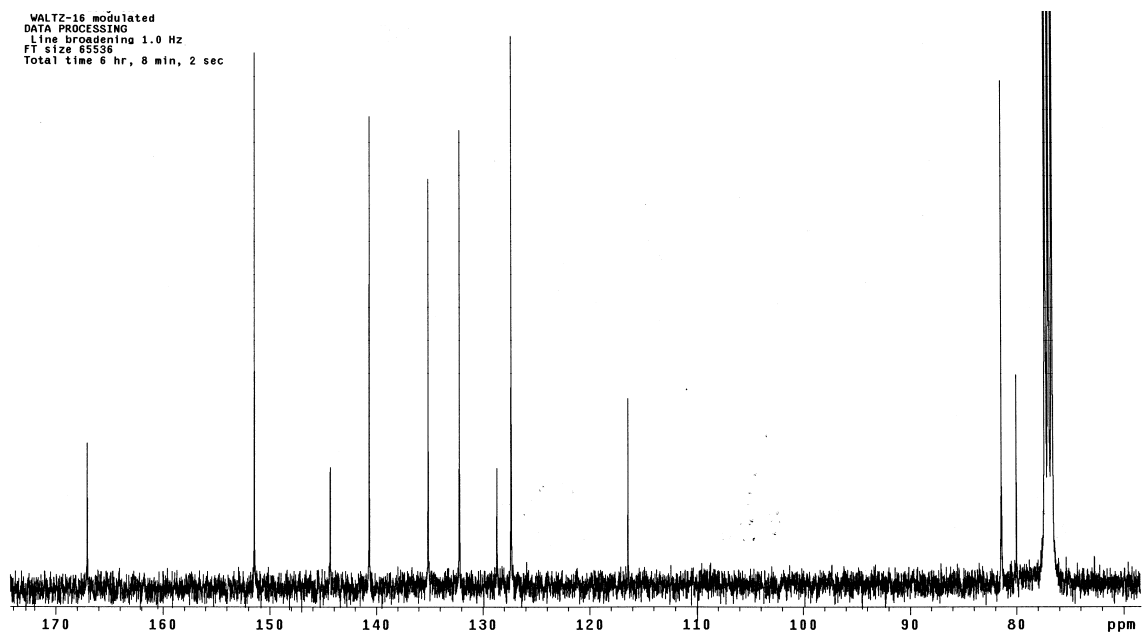
¹³C NMR spectrum of **17h**.

Anna am1148
Archive directory: /export/home/tim/vnmrcys/data
Sample directory: am1148_2006-12-21
Pulse Sequence: c2pu1
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
File:
INOVA-600 "prsun-nmr-01"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSWID Hz 400.0431404 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 36 sec

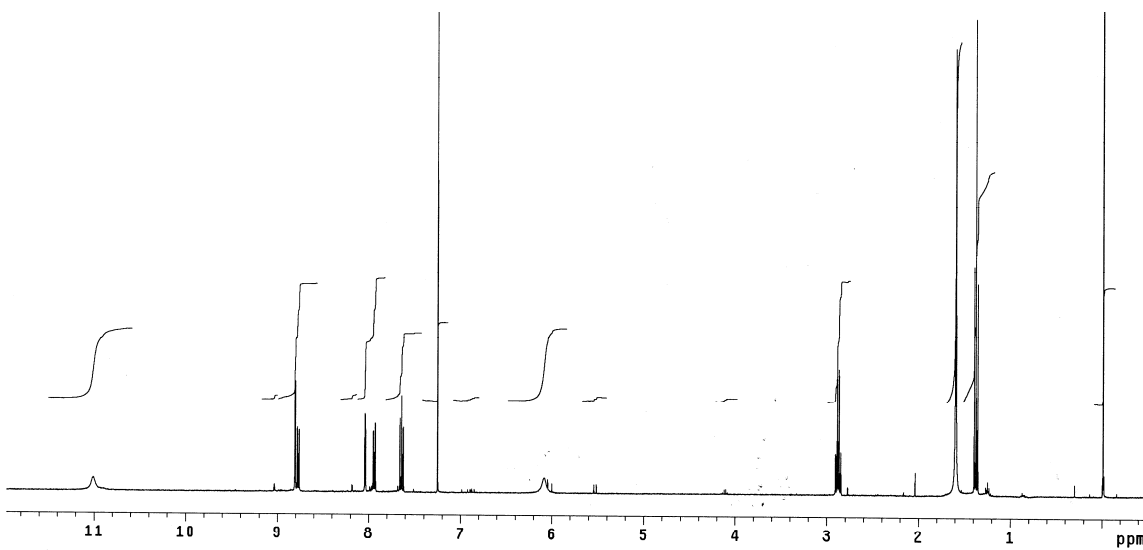


^1H NMR spectrum of **17i**.

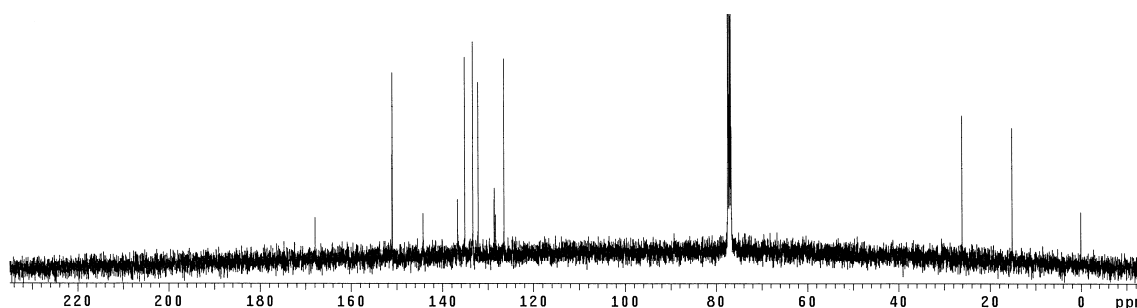
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 6 hr, 8 min, 2 sec



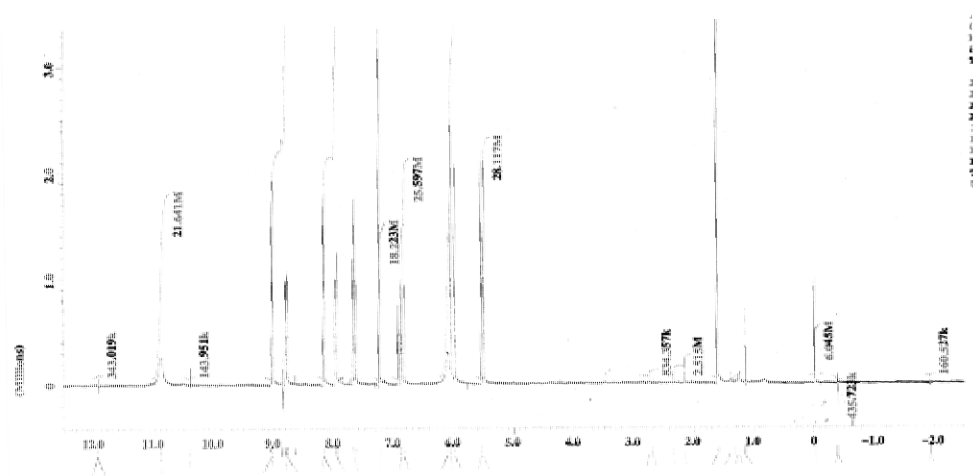
^{13}C NMR spectrum of **17i**.



^1H NMR spectrum of **17j**.

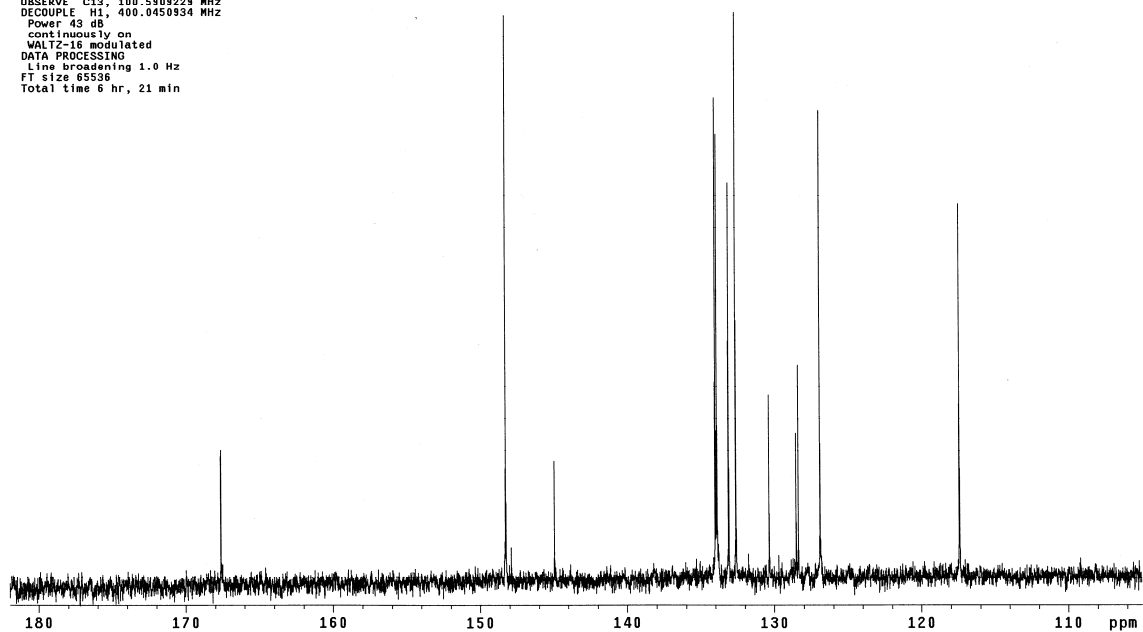


^{13}C NMR spectrum of **17j**.



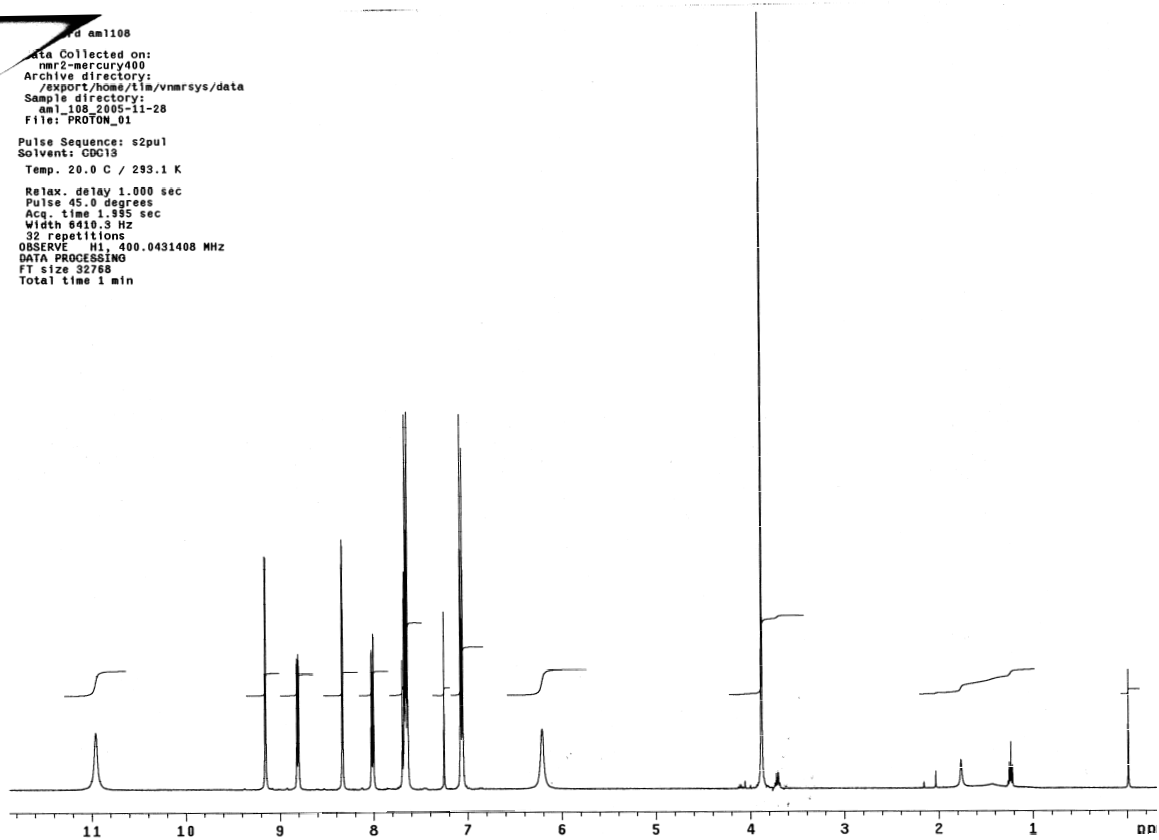
^1H NMR spectrum of **17k**.

Width 25125.6 Hz
10000 repetitions
OBSERVE C13, 100.5309229 MHz
DECOUPLE H1, 400.0450934 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 6 hr, 21 min

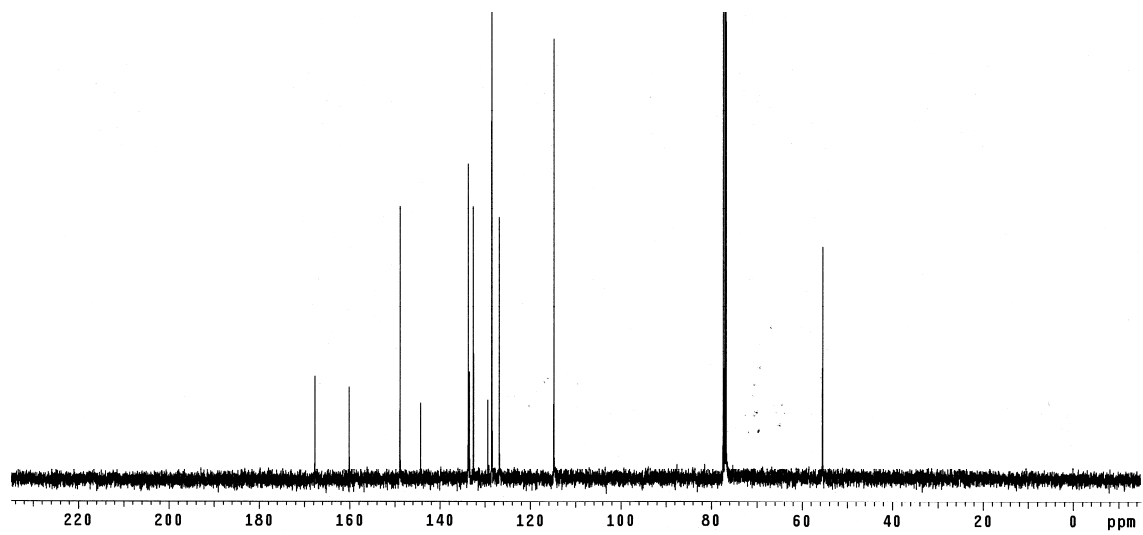


Expansion of part of ^{13}C NMR spectrum of **17k**.

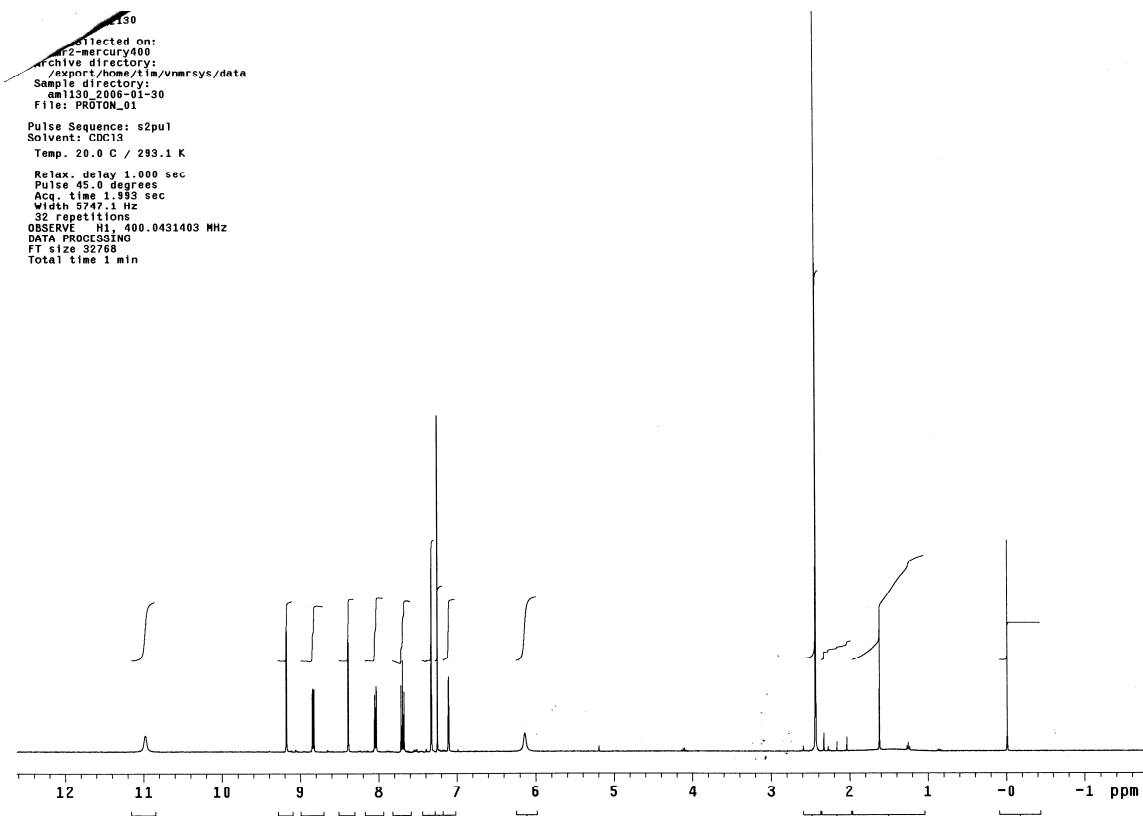
rd am108
Data Collected on:
mer2-mercury400
Archive directory:
/export/home/tia/vnmrsws/data
Sample directory:
am1_08_2005-11-28
File: PROTON_01
Pulse Sequence: s2pul
Solvent: GDC13
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. Time 1.935 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0431408 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



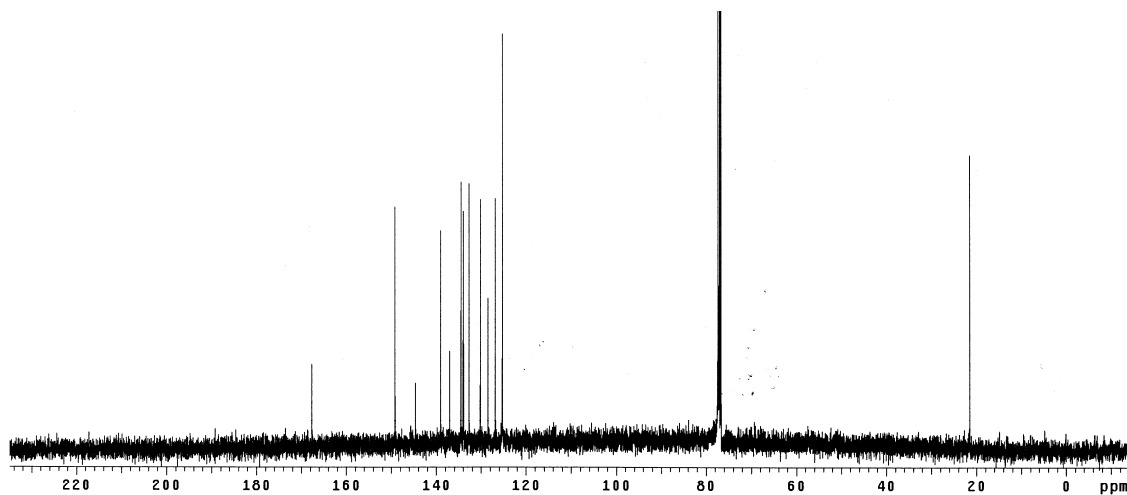
^1H NMR spectrum of **17m**.



^{13}C NMR spectrum of **17m**.

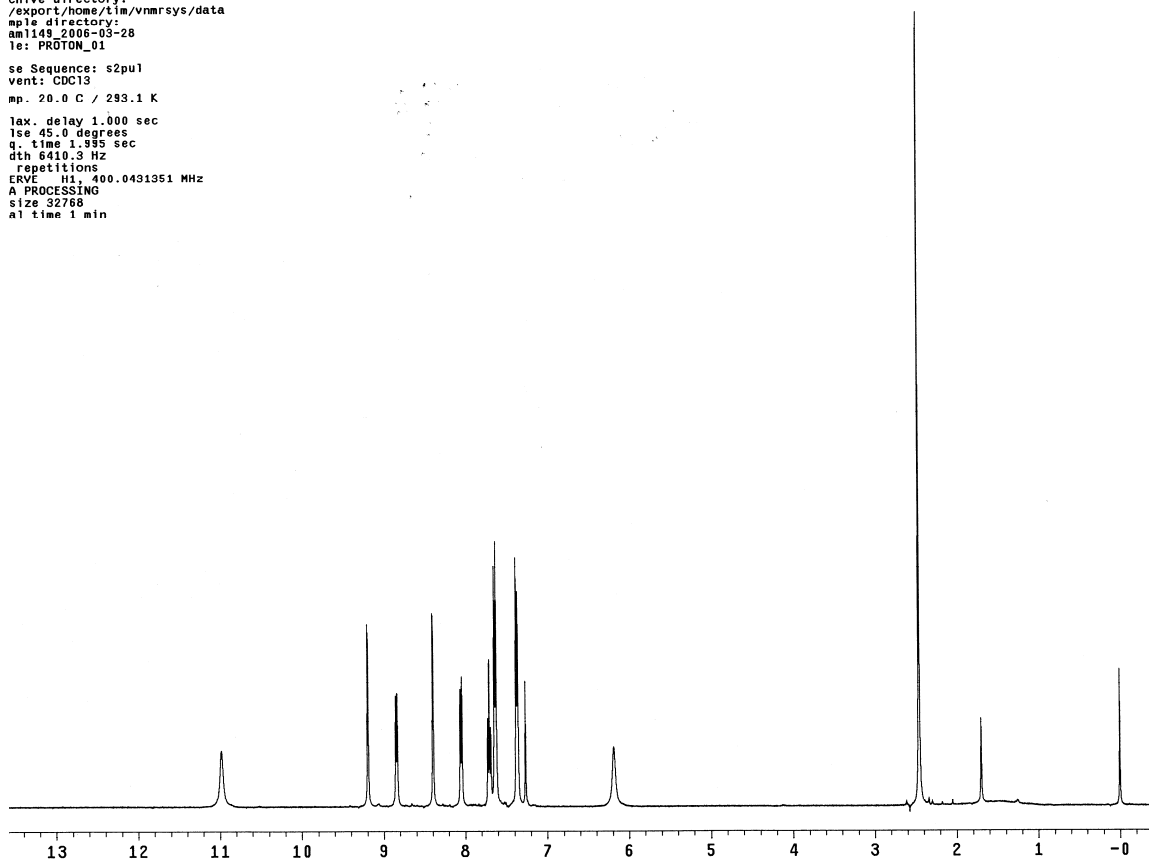


^1H NMR spectrum of **17n**.



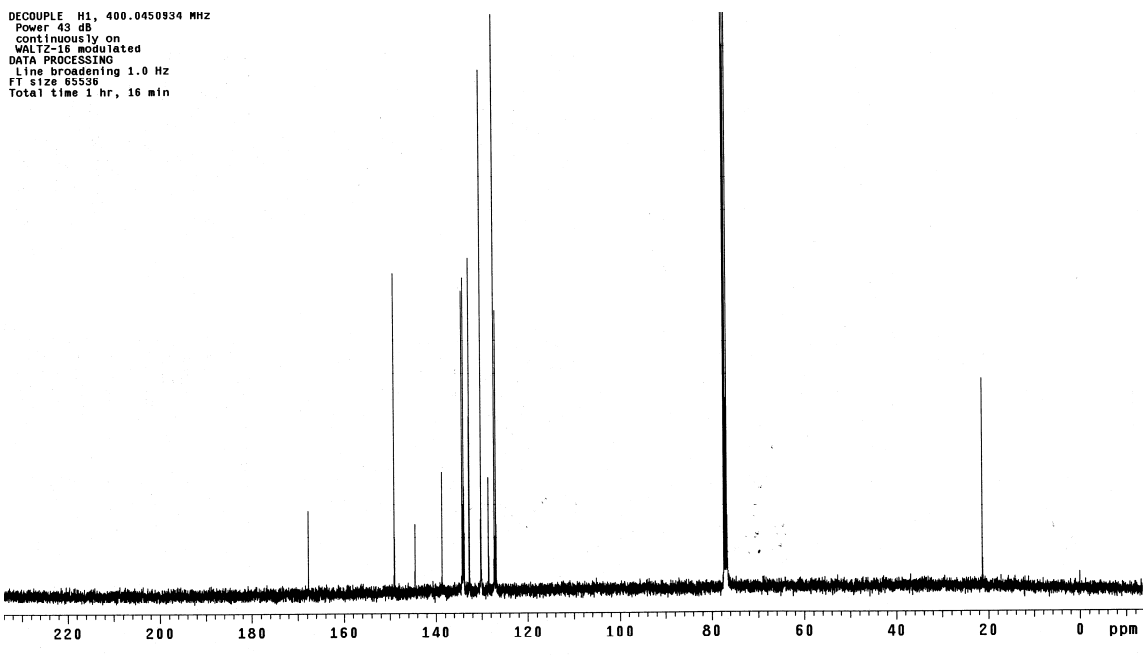
^{13}C NMR spectrum of **17n**.

```
nmr2-mercury400
chive directory:
/export/home/tim/vnmrSYS/data
nple directory:
am1149_2006-03-28
le: PROTON_01
se Sequence: s2pu1
vent: CDC13
mp. 20.0 C / 293.1 K
lax. delay 1.000 sec
lse 45.0 degrees
q. time 1.995 sec
dth 6410.3 Hz
repetitions
ERVE H1, 400.0491951 MHz
A PROCESSING
size 32768
at time 1 min
```



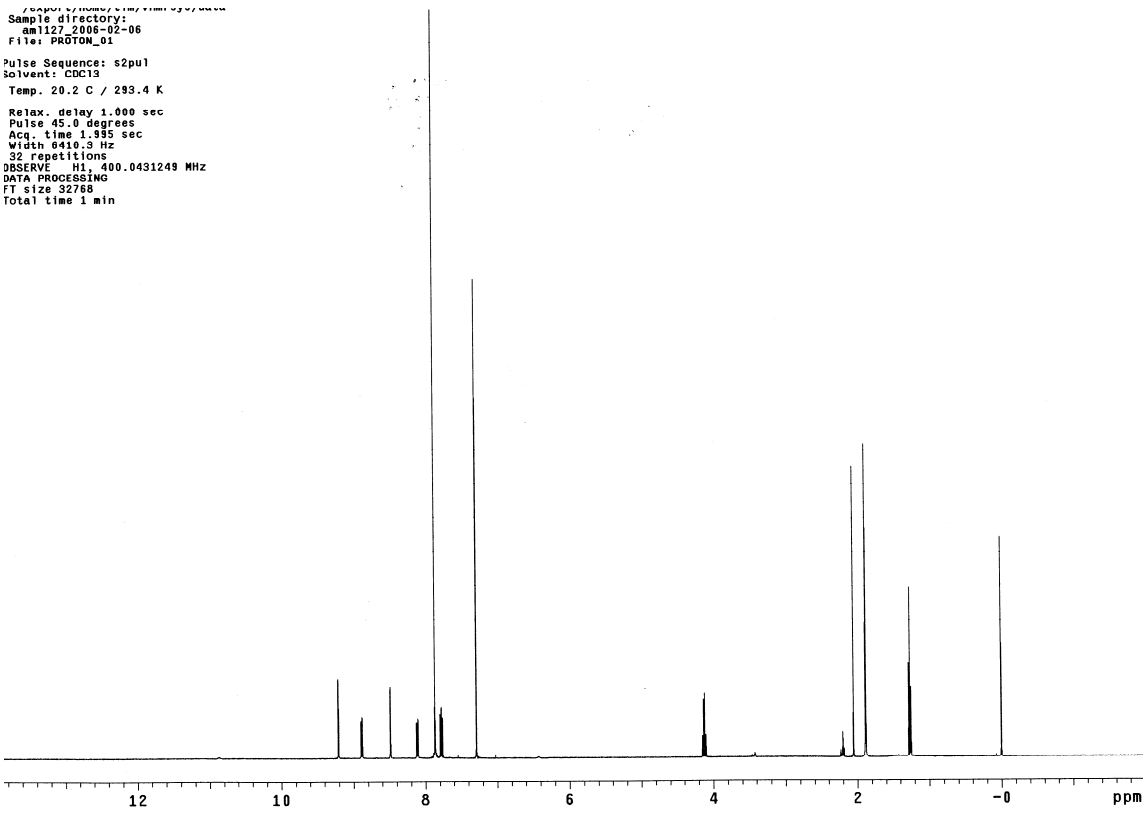
^1H NMR spectrum of **17o**.

DECOUPLE H1, 400.0450934 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 16 min

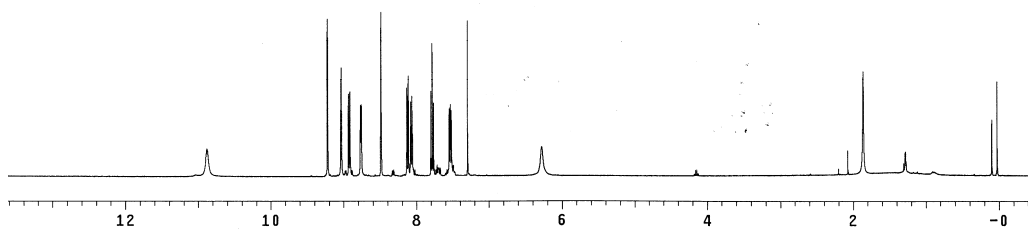


¹³C NMR spectrum of **17o**.

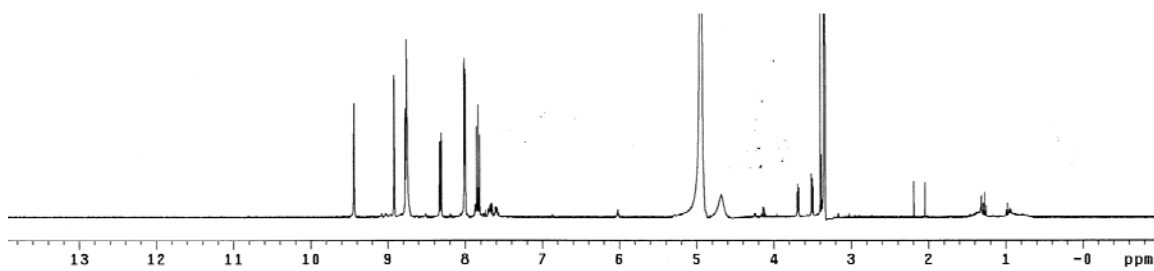
Sample directory:
am127_2006-02-06
File: PROTON_01
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.2 C / 293.4 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0431249 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



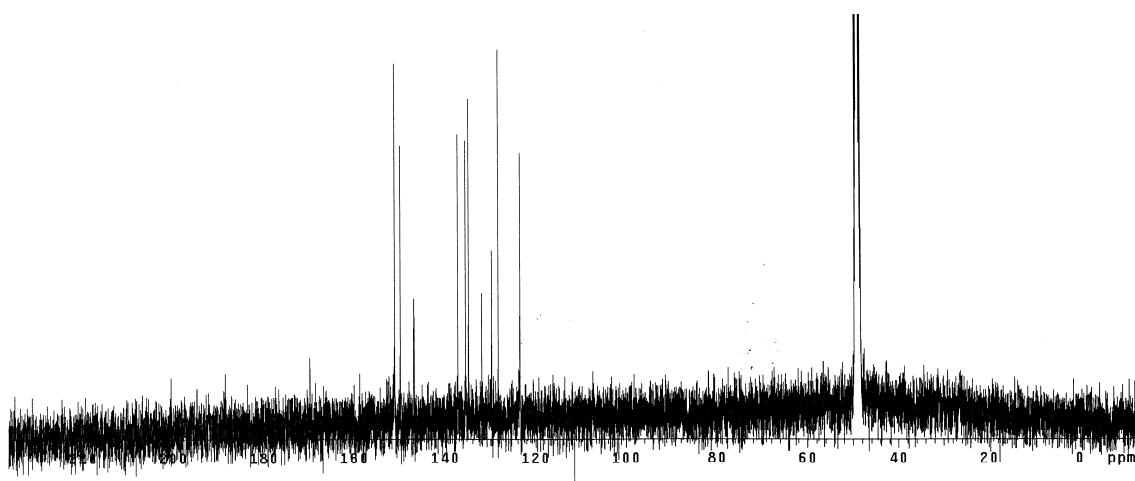
¹H NMR spectrum of **17q**.



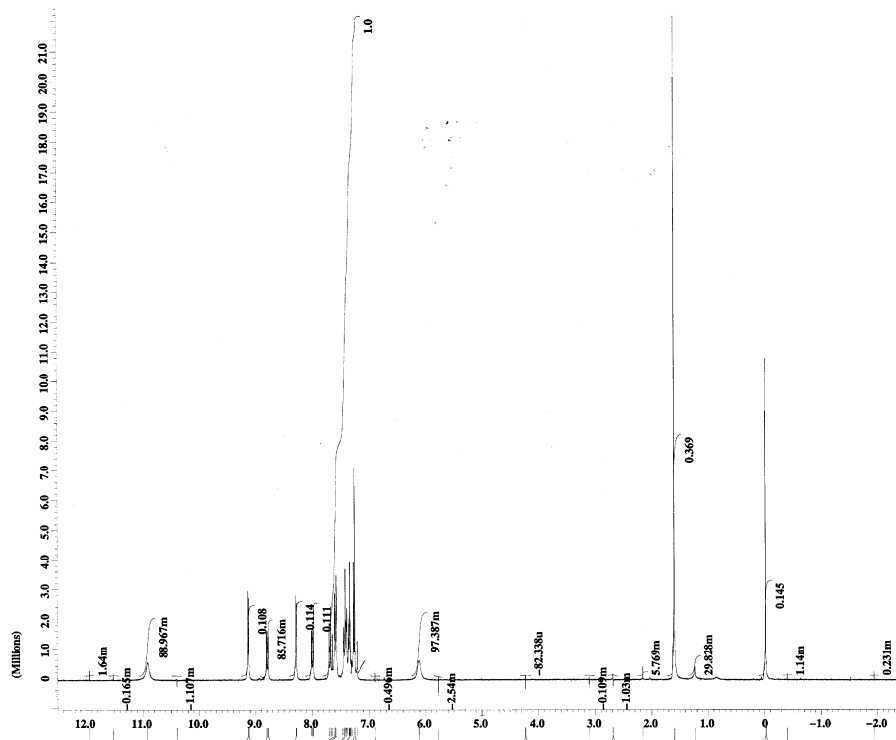
^1H NMR spectrum of **17r**.



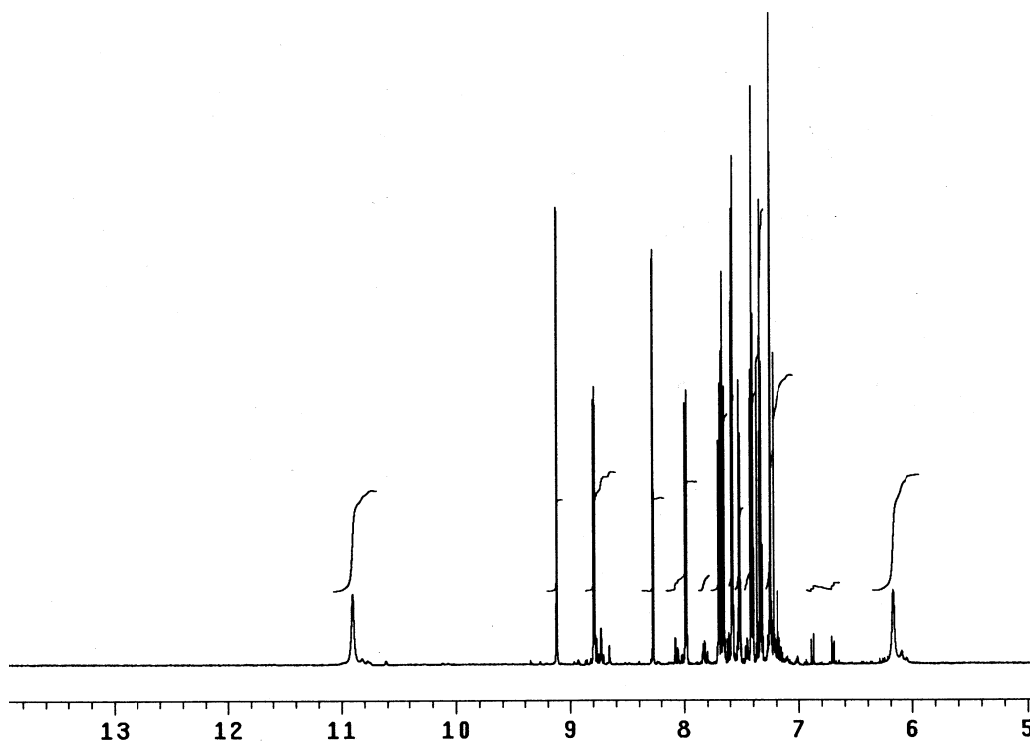
^1H NMR spectrum of **17s**.



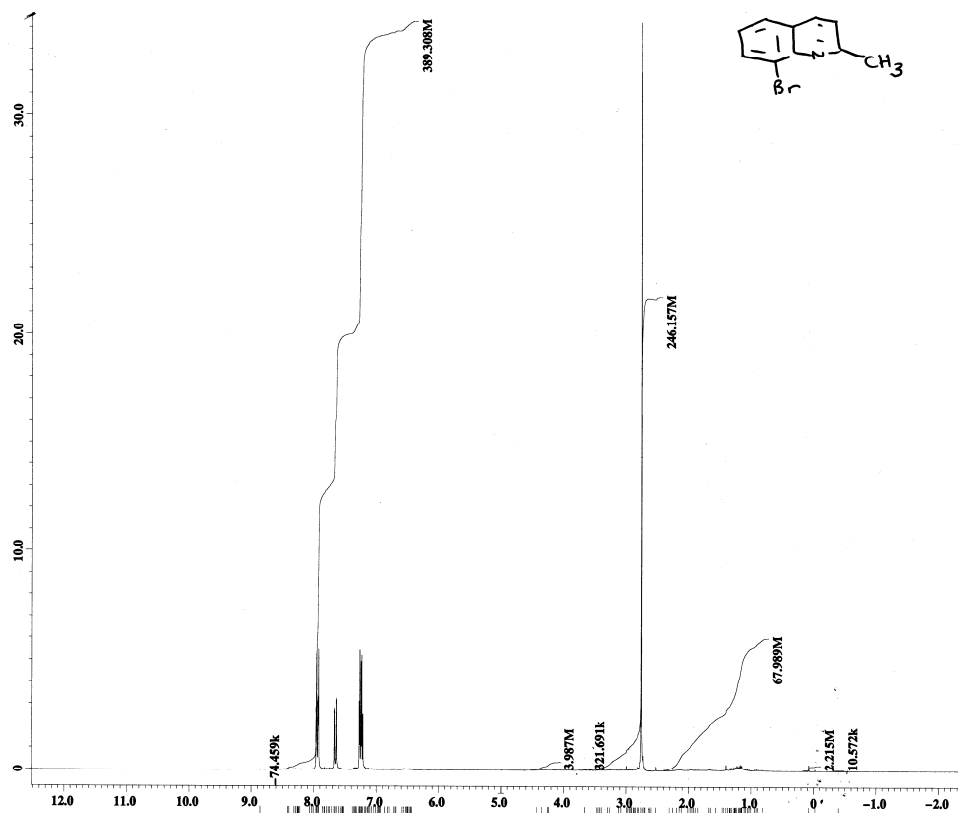
^{13}C NMR spectrum of **17s**.



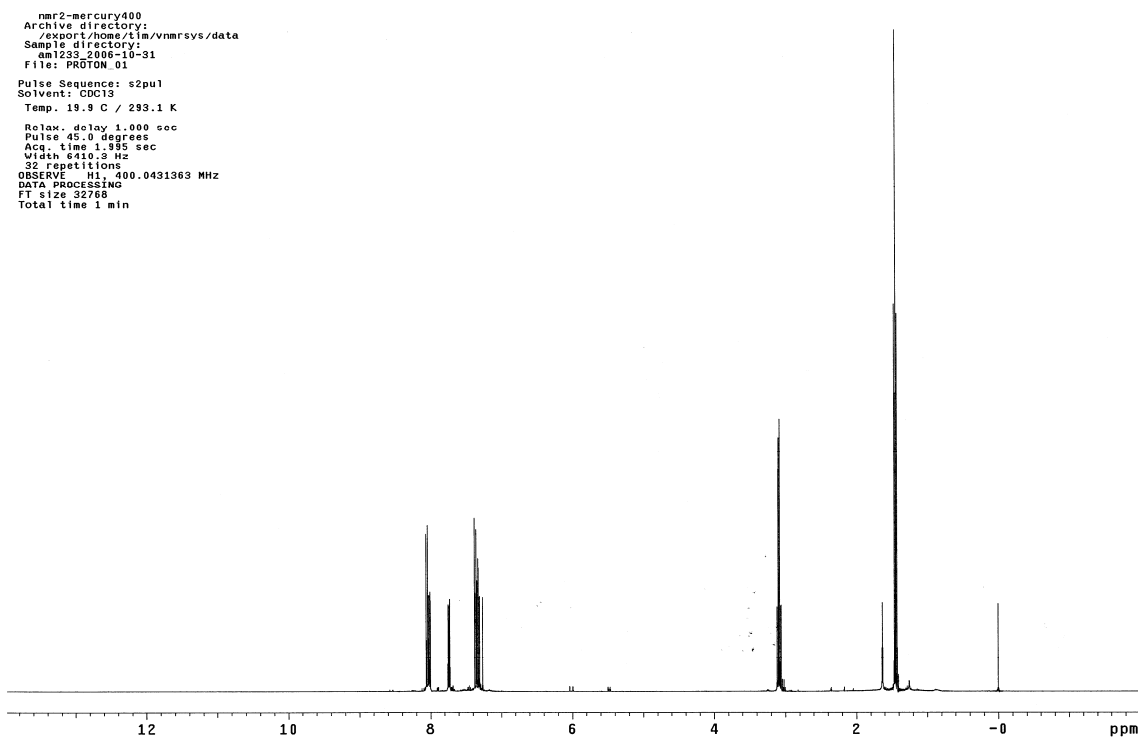
^1H NMR spectrum of **17t**.



Expansion of part of ^1H NMR spectrum of mixture of **17t** and **17u**.

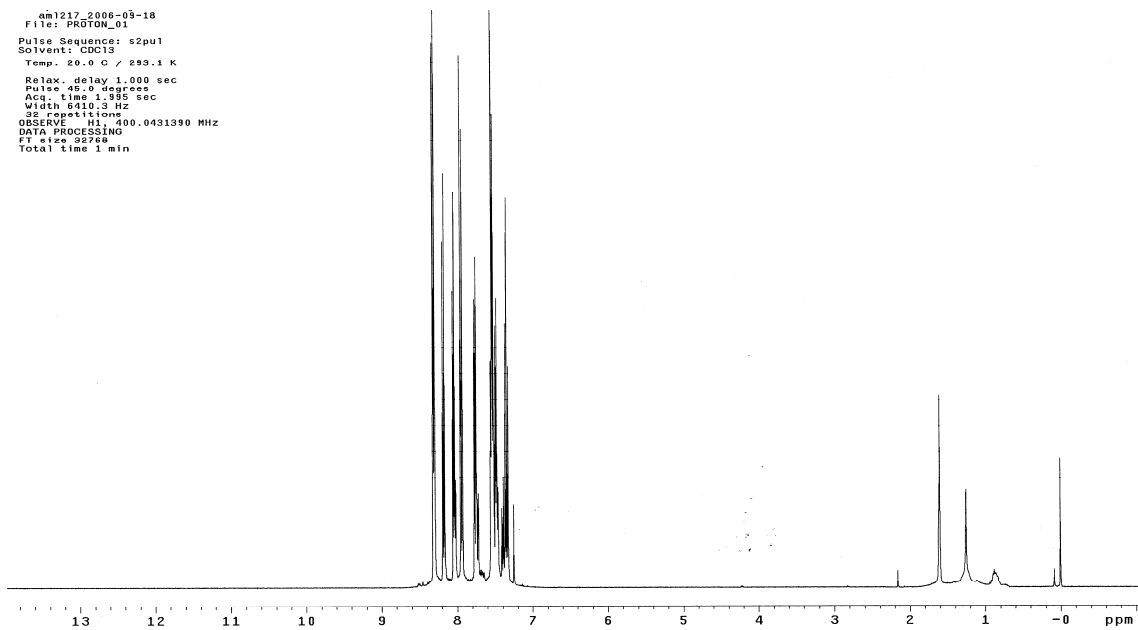


¹H NMR spectrum of **18b**.



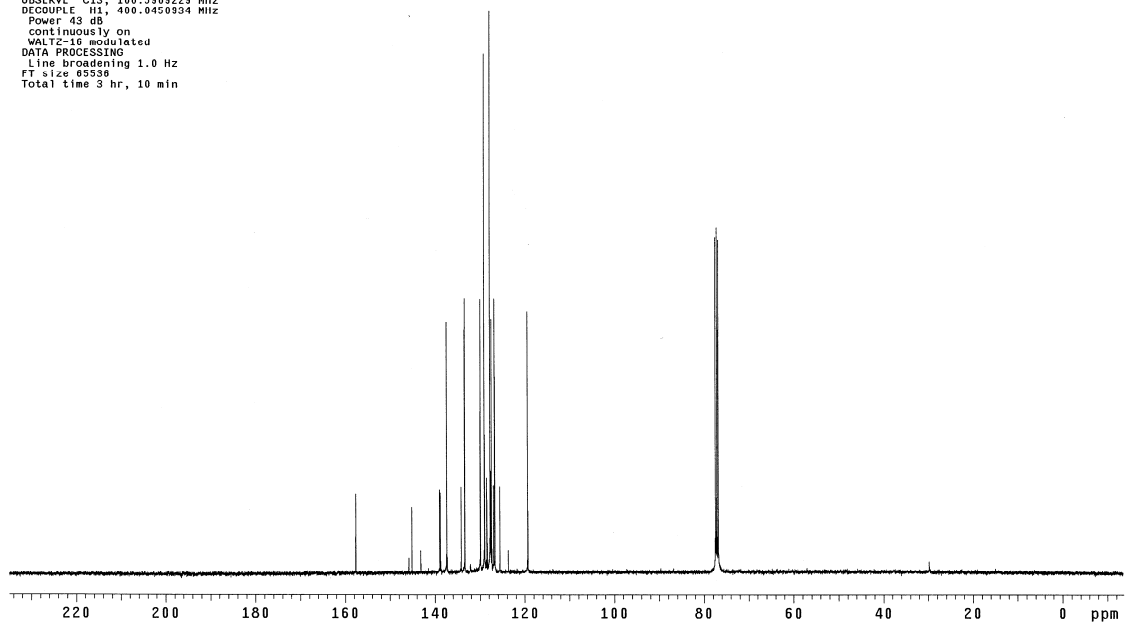
¹H NMR spectrum of **18c**.

dm1217_2006-09-18
File: PROTON_01
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 95.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0491390 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



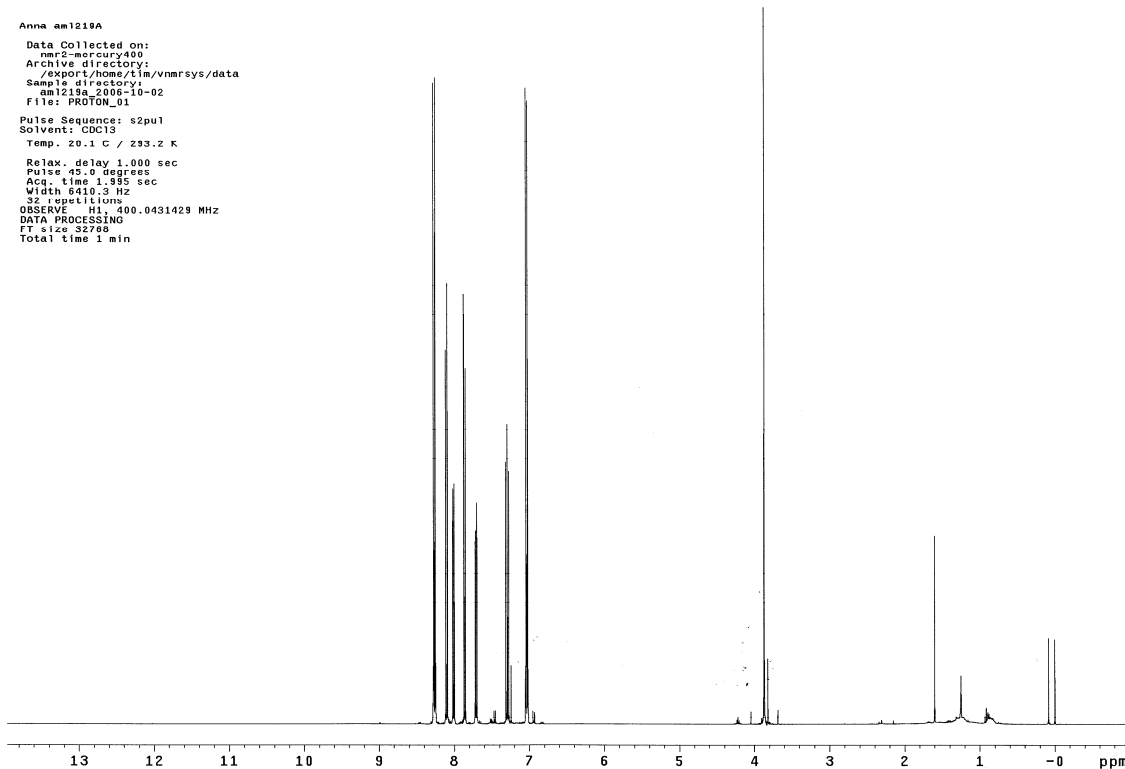
¹H NMR spectrum of **18d**.

5000 repetitions
OBSERVE C13, 100.5909229 MHz
DECOUPLE H1, 400.0450934 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 85336
Total time 3 hr, 10 min



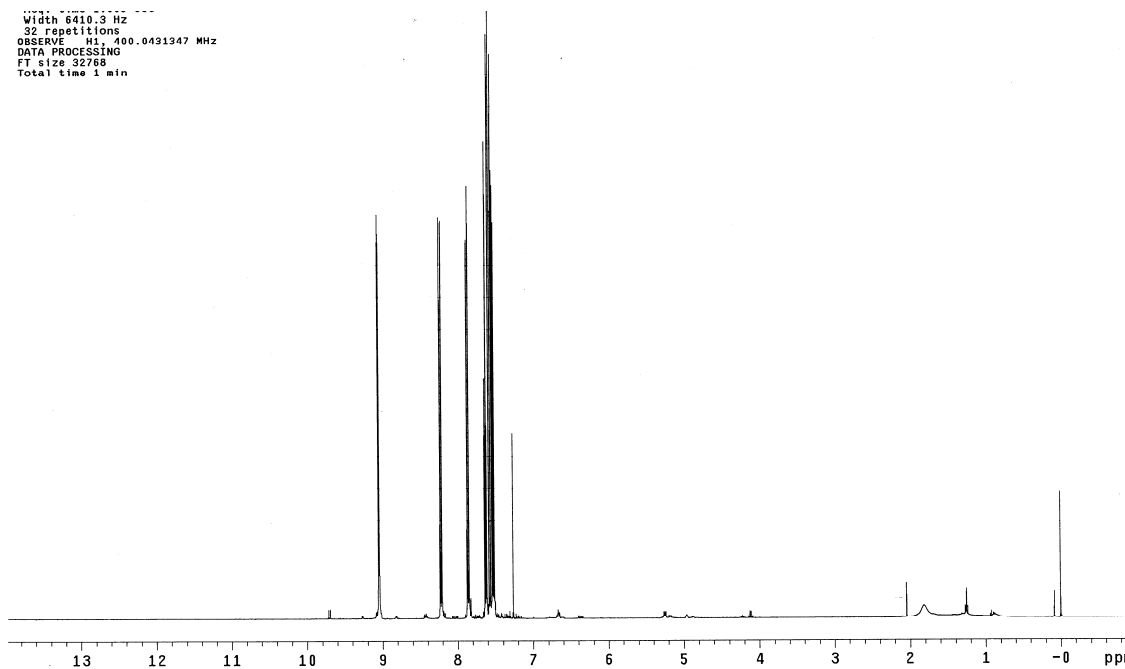
¹³C NMR spectrum of **18d**.

Anna am1219A
Data Collected on:
nmr2-mercury400
Archive directory:
/export/home/fin/vnmr/sys/data
Sample directory:
am1219a_2006-10-02
File: PROTON_01
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.1 C / 293.2 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0431429 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



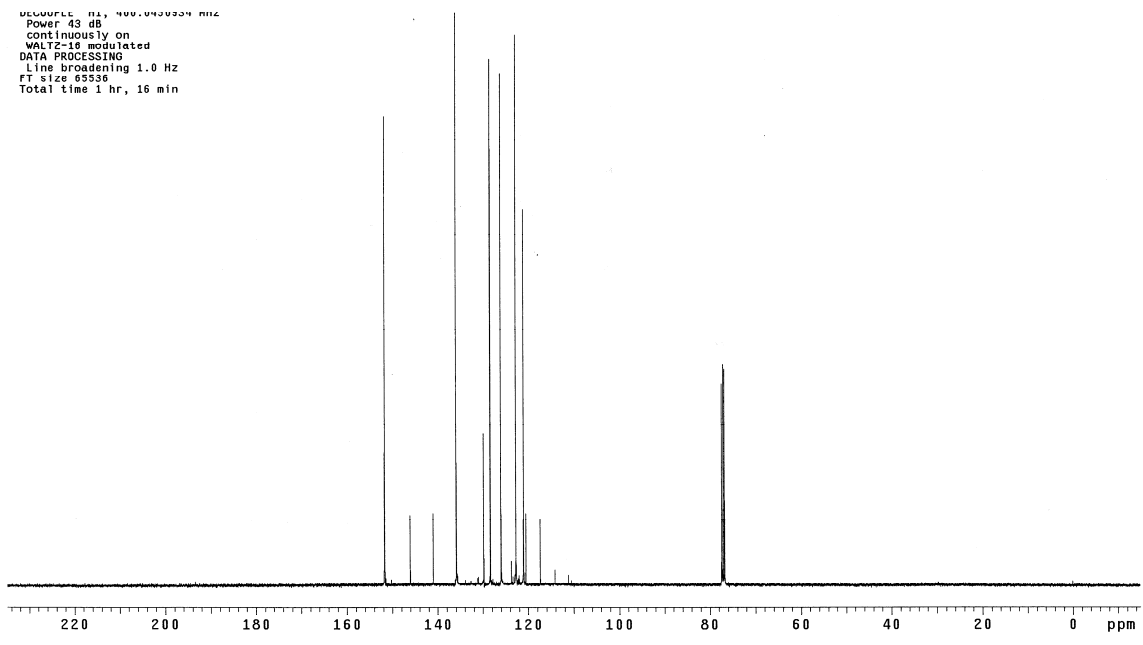
^1H NMR spectrum of **18e**.

Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0431347 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



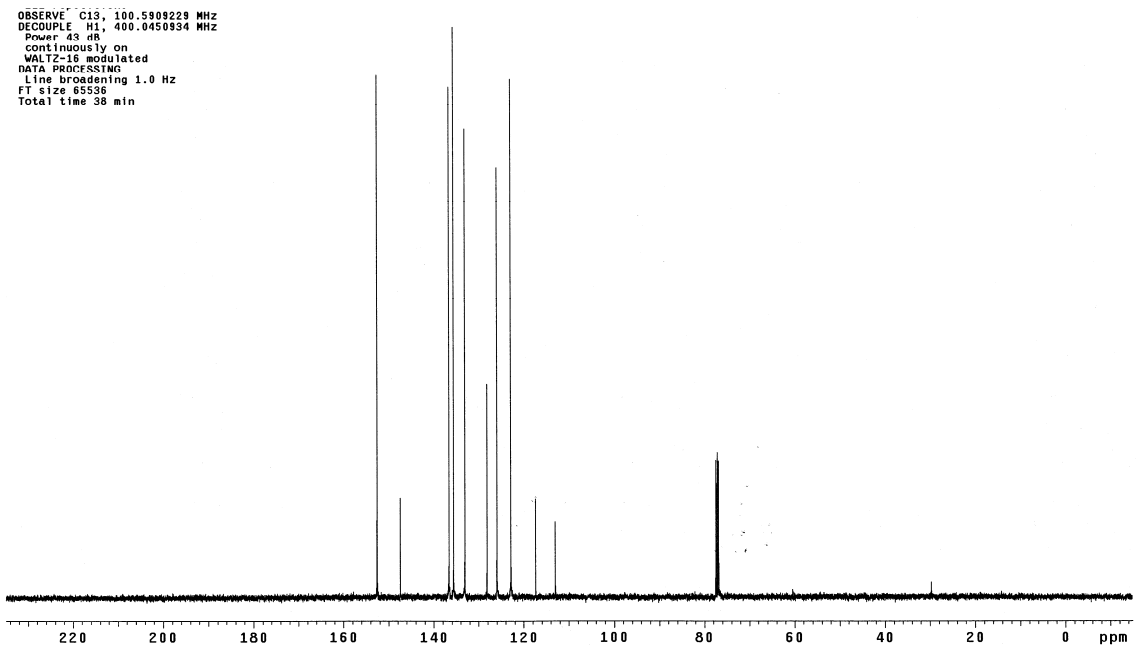
^1H NMR spectrum of **20**.

DECOUPLE H1, 400.0450534 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 16 min

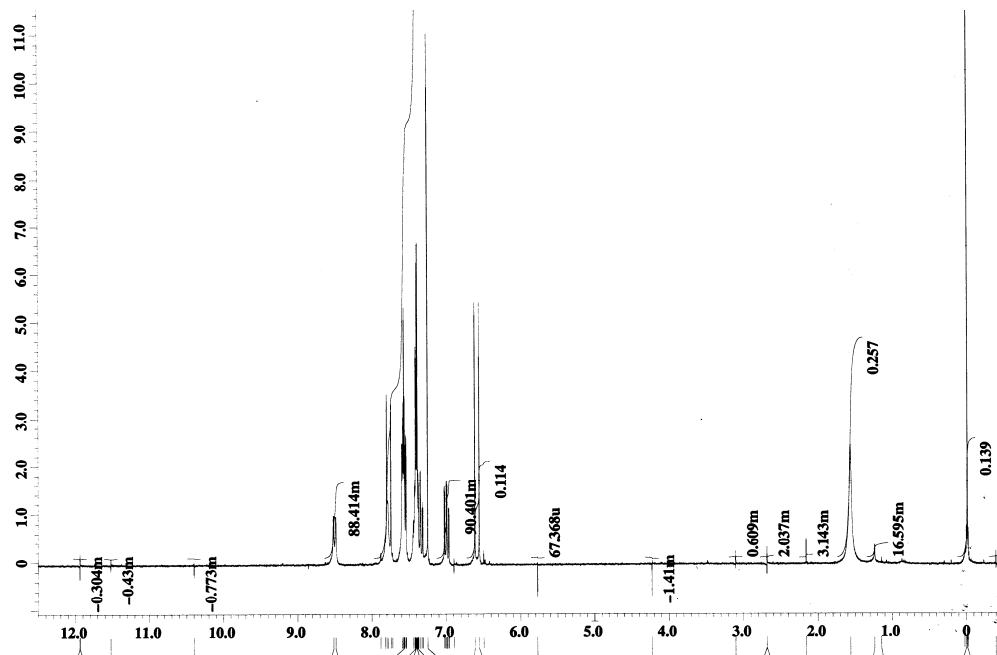


¹³C NMR spectrum of **20**.

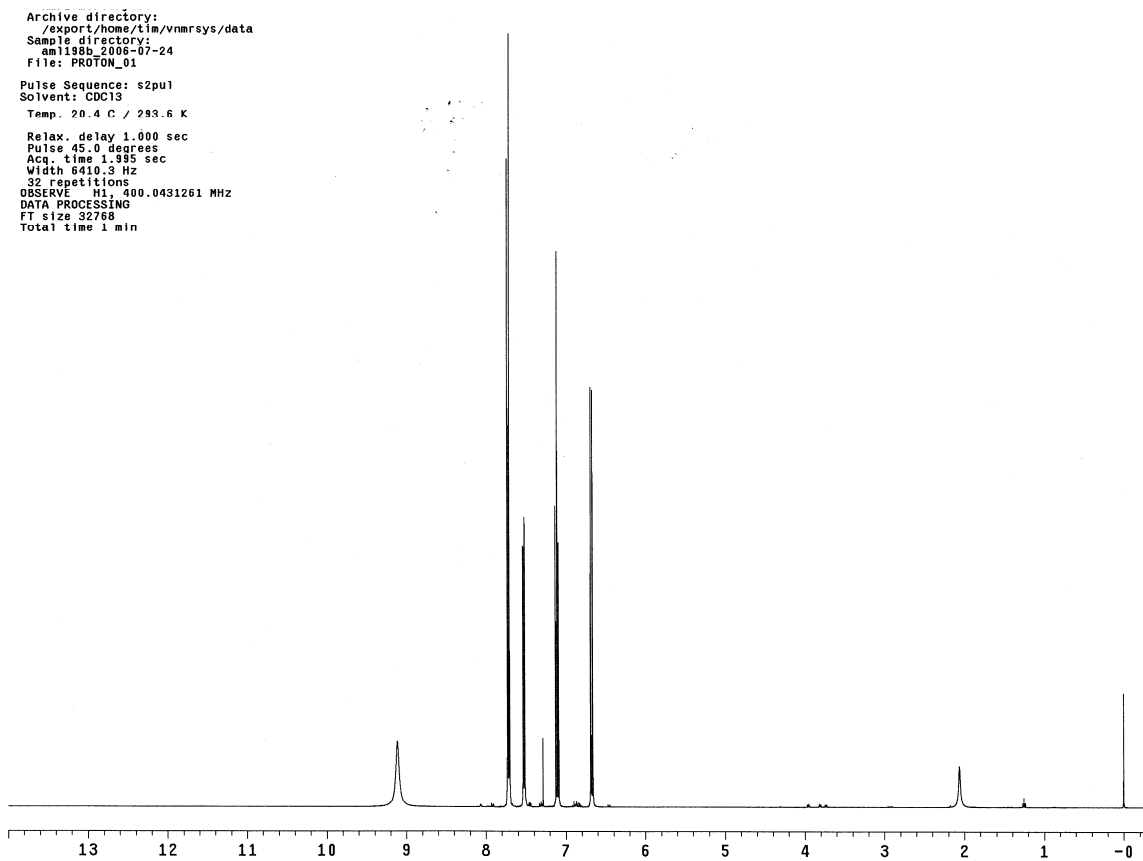
OBSERVE C13, 100.5908229 MHz
DECOUPLE H1, 400.0450534 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 38 min



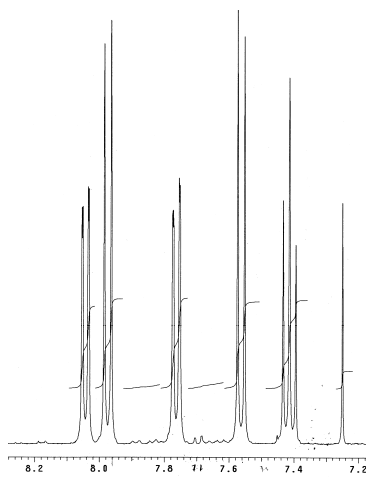
¹³C NMR spectrum of **21**.



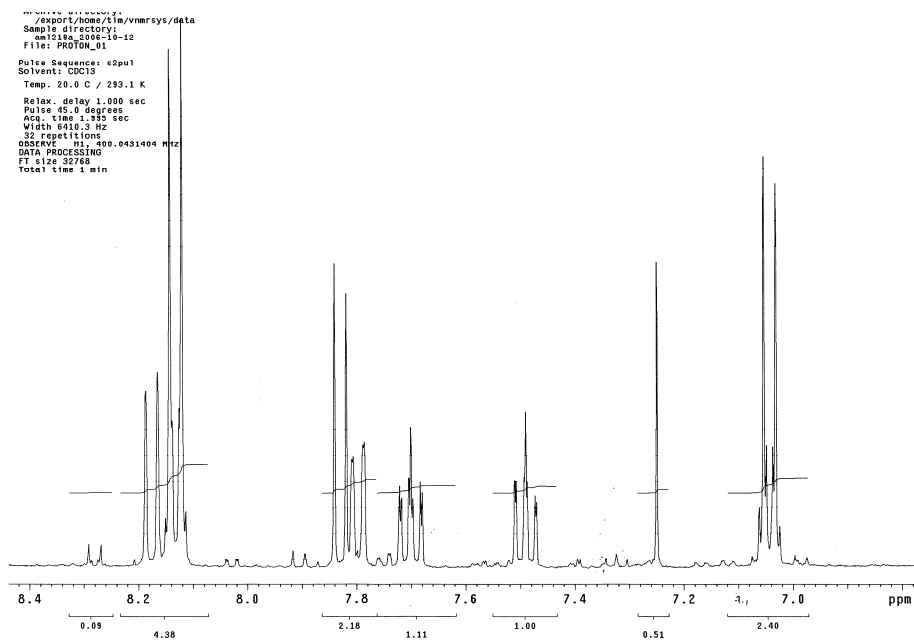
^1H NMR spectrum of **23**.



^1H NMR spectrum of **24**.

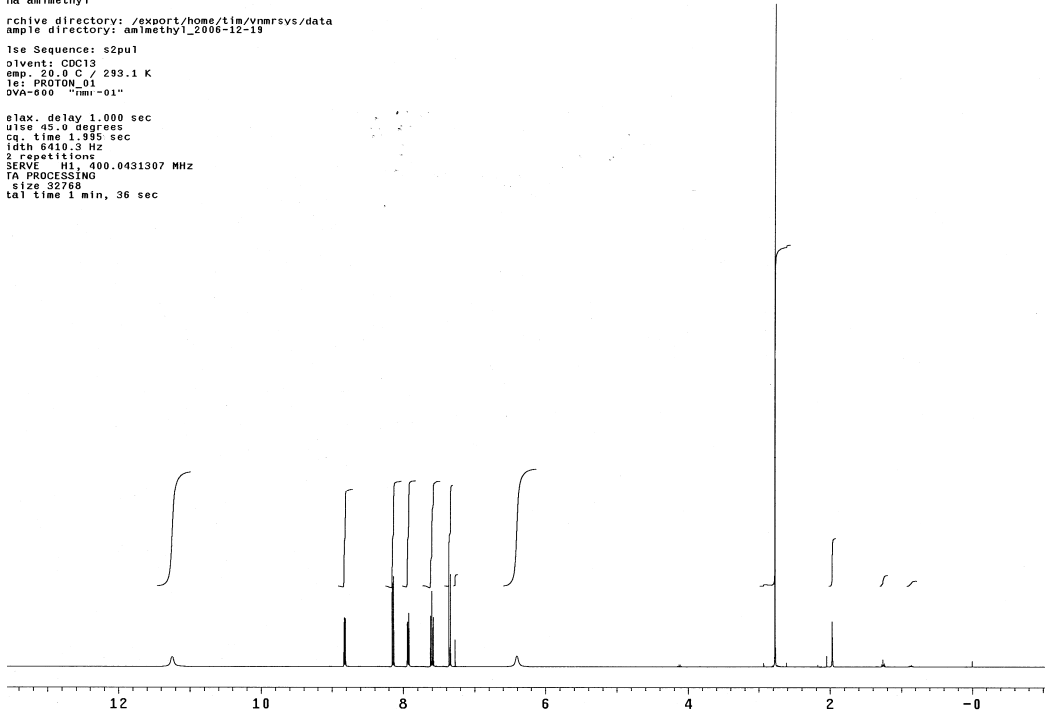


Expansion of part of ^1H NMR spectrum of **26**.



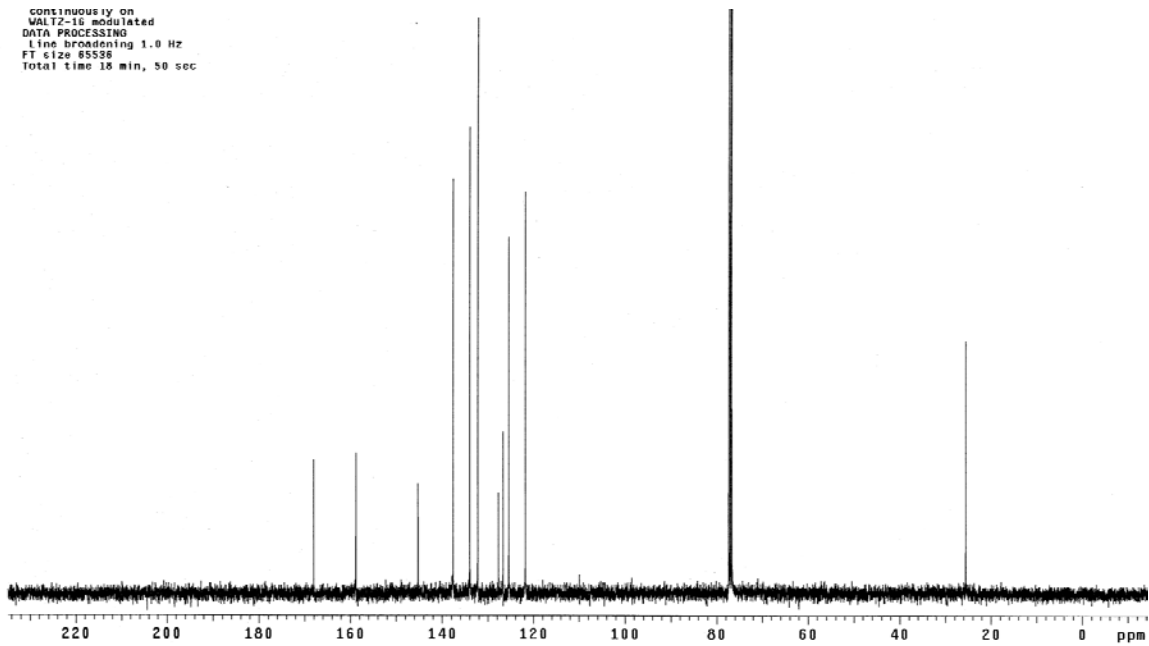
Expansion of part of ^1H NMR spectrum of **28**.

na am1methy1
rchive directory: /export/home/tjm/vnmrsvs/data
mple directory: am1methy1_2006-12-19
lse Sequence: s2pu1
olvent: CDCl3
mp: 29.0 C / 293.1 K
lc: PROTON_01
VA-600 "rmi-01"
elax. delay 1.000 sec
ulse 45.0 degrees
cp. time 1.995 sec
idth 6410.3 Hz
2 repetitions
SERVE HI, 400.0431307 MHz
TA PROCESSING
Size 32768
tal time 1 min, 36 sec

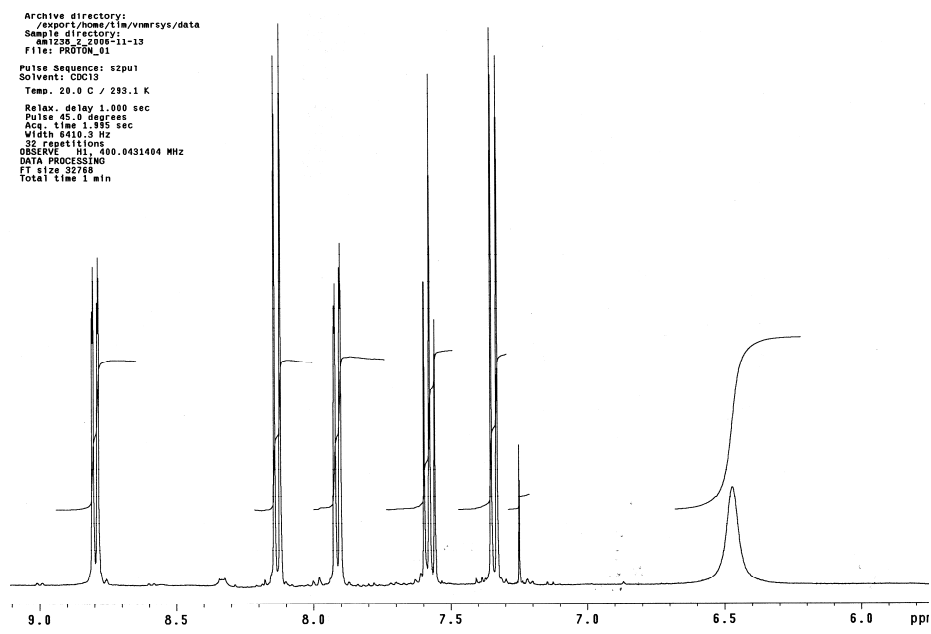


¹H NMR spectrum of **29b**.

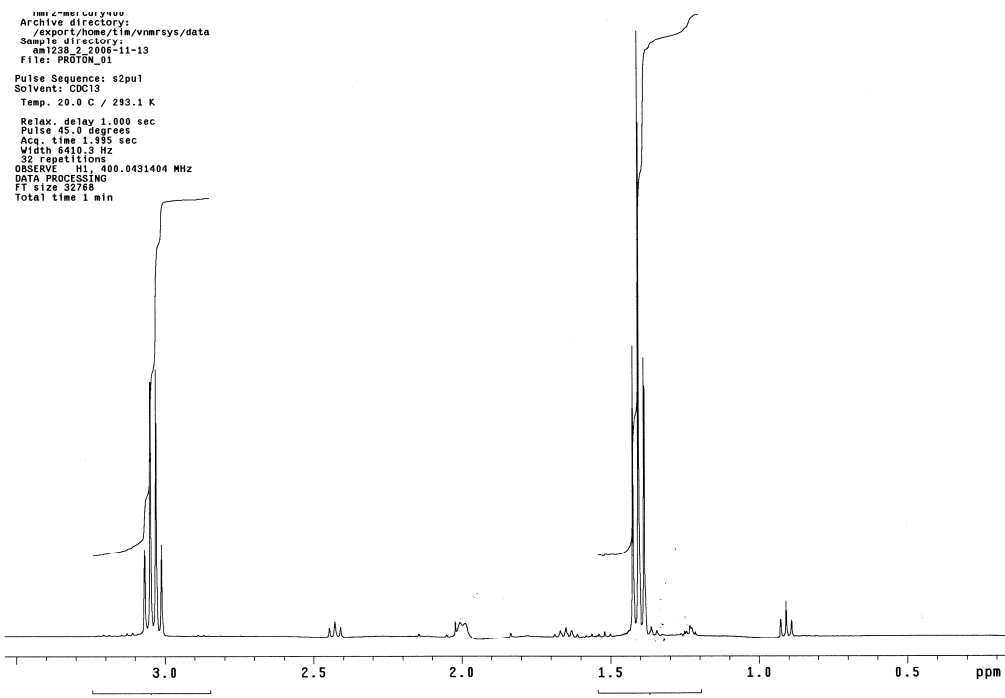
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 18 min, 50 sec



¹³C NMR spectrum of **29b**.

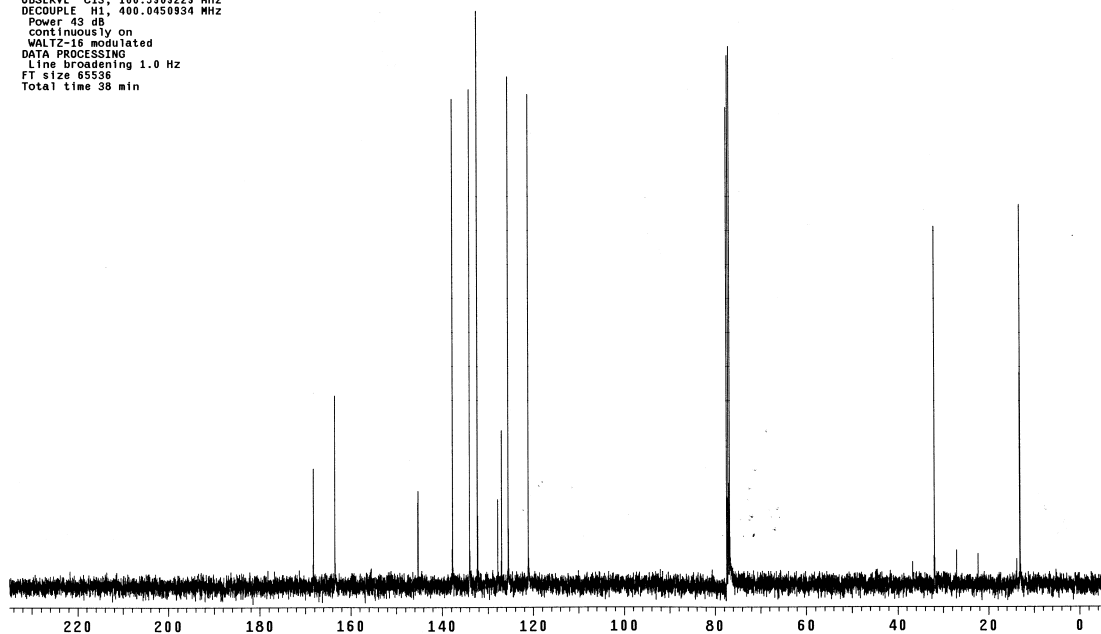


Expansion of part of ¹H NMR spectrum of **29c**.



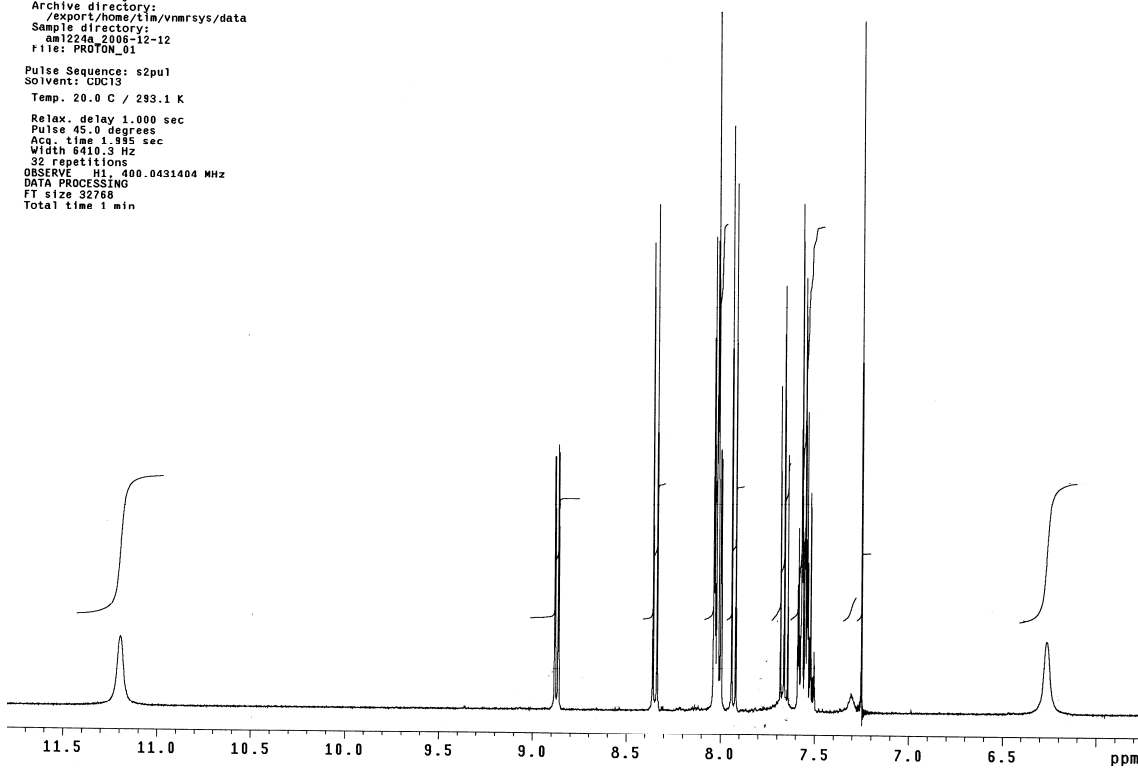
Expansion of part of ¹H NMR spectrum of **29c**.

OBSERVE C13, 100.5909229 MHz
DECOUPLE H1, 400.0450934 MHz
Power 43 db
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 38 min



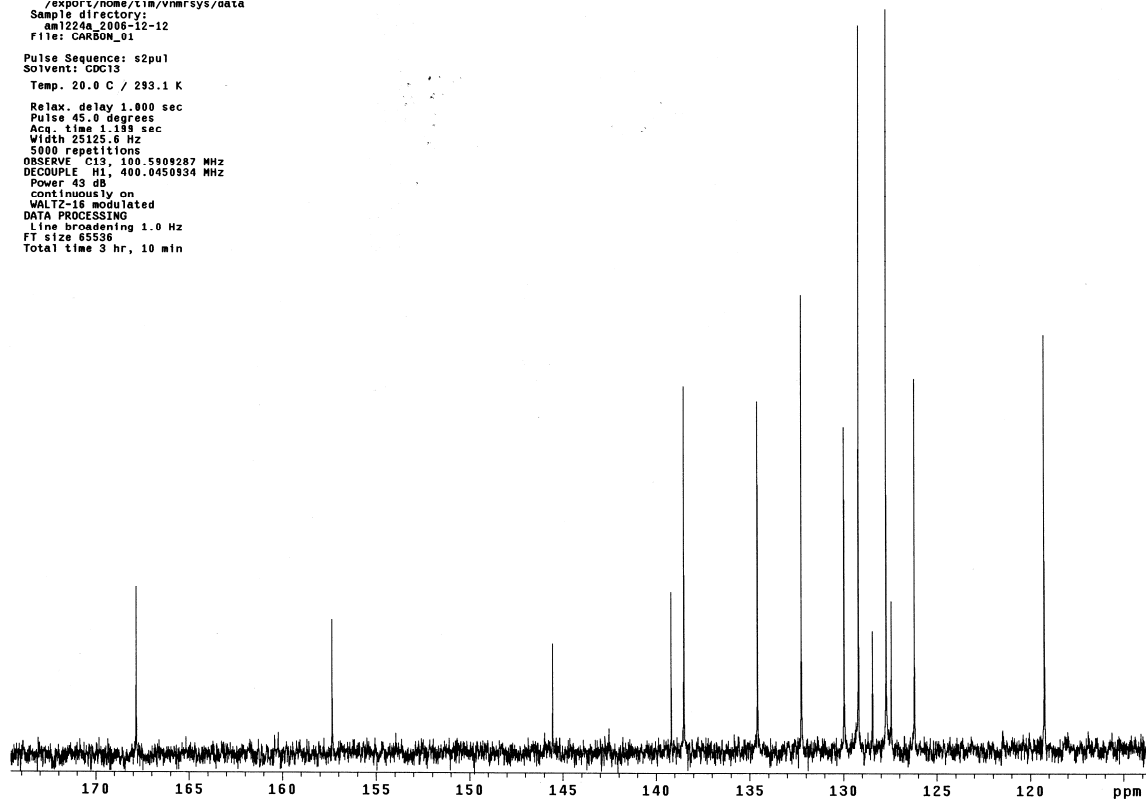
¹³C NMR spectrum of **29c**.

Anna am1224
Data Collected on:
nmr2-mercury400
Archive directory:
/export/home/tim/vnmrsys/data
Sample directory:
am1224a_2006-12-12
File: PROTON_01
Pulse Sequence: s2pu1
Solvent: CDC13
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.0431404 MHz
DATA PROCESSING
FT size 32768
Total time 1 min



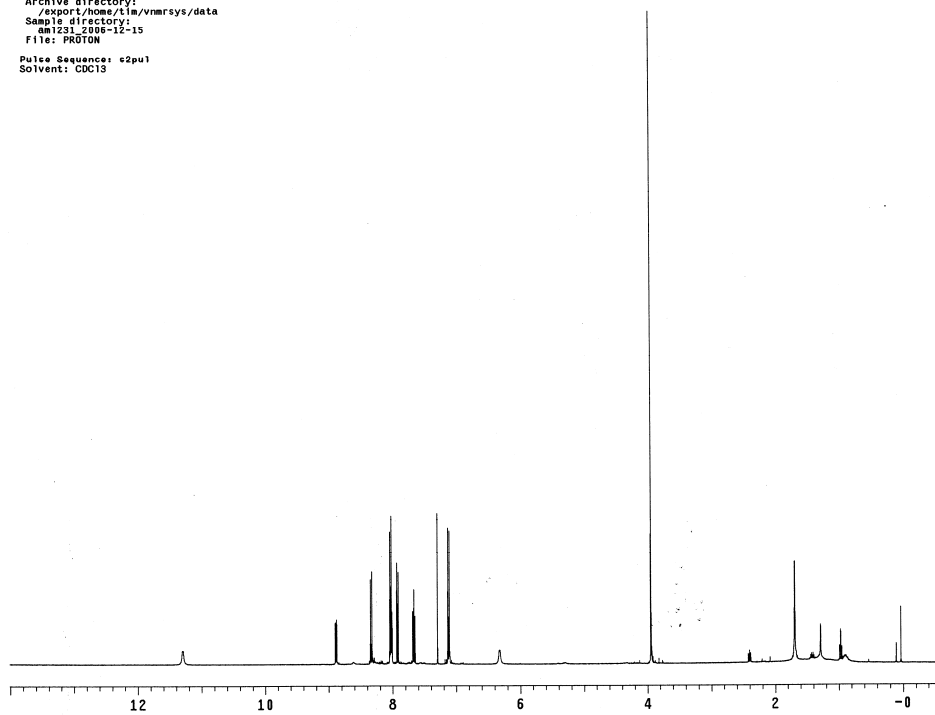
Expansion of part of ¹H NMR spectrum of **29d**.

/export/home/tim/vnmrsys/data
Sample directory:
am1224a_2006-12-12
File: CAR60N_01
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.189 sec
Width 25125.6 Hz
5000 repetitions
OBSERVE C13, 100.5909287 MHz
DECOUPLE H1, 400.0450834 MHz
Power 43 dB
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
F1 size 65536
Total time 3 hr, 10 min



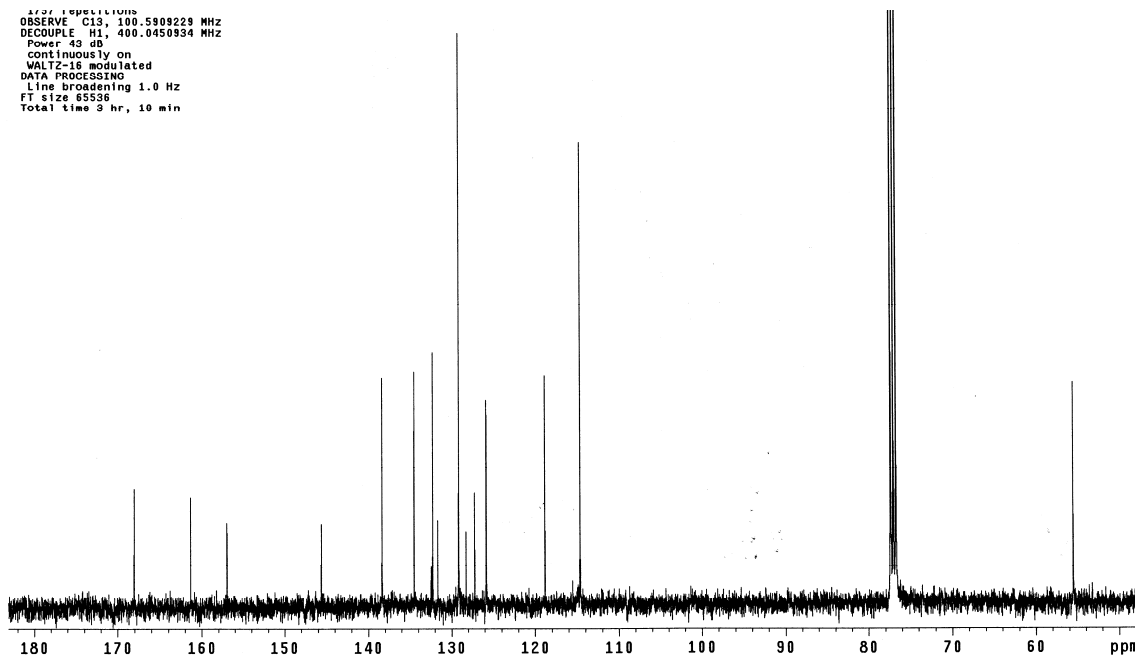
Expansion of part of ^{13}C NMR spectrum of **29d**.

Archive directory:
/export/home/tim/vnmrsys/data
Sample directory:
am1231_2006-12-15
File: PROTON
Pulse Sequence: s2pu1
Solvent: CDCl3



^1H NMR spectrum of **29e**.

2701 1000000000
OBSERVE C13, 100.5909229 MHz
DECOUPLE H1, 400.0450934 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 10 min



¹³C NMR spectrum of **29e**.

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