

Single-step Synthesis of Pyrimidine Derivatives

Mohammad Movassaghi* and Matthew D. Hill

Massachusetts Institute of Technology, Department of Chemistry, Massachusetts 02139

Contents:

<u>General Procedures</u>	<u>S1</u>
<u>Materials</u>	<u>S1</u>
<u>Instrumentation</u>	<u>S2</u>
<u>Synthesis of pyrimidine derivatives: Table 2, entries 1-21</u>	<u>S3-S24</u>
<u>Direct conversion of secondary amide 1a and primary amide 4 to quinazoline 3a</u>	<u>S25</u>
<u>Reat-IR monitoring of the conversion of amide 1a and nitrile 2a to quinazoline 3a</u>	<u>S26-S27</u>
<u>¹H and ¹⁹F NMR monitoring of the conversion of amide 1a and nitrile 2a to quinazoline 3a</u>	<u>S28-S29</u>
<u>¹³C NMR monitoring of the conversion of amide 1a-¹³C and nitrile 2a to quinazoline 3a-¹³C</u>	<u>S30</u>
<u>Additional notes on the mechanism (Scheme S1)</u>	<u>S30</u>

Supporting Information

General Procedures. All reactions were performed in oven-dried or flame-dried round bottomed flasks, modified Schlenk (Kjeldahl shape) flasks, or glass pressure vessels. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 32–63 µm, standard grade, Sorbent Technologies) or non-activated alumina gel (80–325 mesh, chromatographic grade, EM Science).¹ Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel or neutral alumina gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to an ethanolic phosphomolybdic acid (PMA), an acidic solution of *p*-anisaldehyde (anis), an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate (KMnO₄) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~10 Torr (house vacuum) at 25–35 °C, then at ~0.5 Torr (vacuum pump) unless otherwise indicated.

Materials. Commercial reagents and solvents were used as received with the following exceptions: Dichloromethane, diethyl ether, tetrahydrofuran, acetonitrile, and toluene were purchased from J.T. Baker (CycletainerTM) and were purified by the method of Grubbs et al. under positive argon pressure.² 2-chloropyridine was distilled from calcium hydride and stored sealed under an argon atmosphere. The starting amides were prepared by acylation of the corresponding anilines³ or via previously reported copper-catalyzed C–N bond-forming reactions.^{4,5}

¹ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

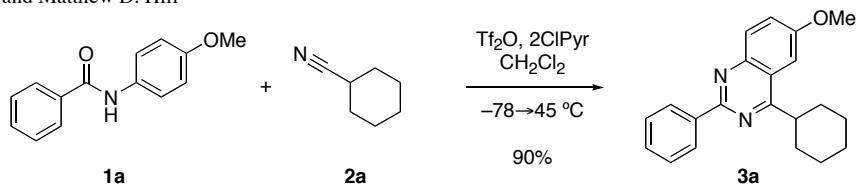
² Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

³ For a general procedure, see: DeRuiter, J.; Swearingen, B. E.; Wandrekar, V.; Mayfield, C. A. *J. Med. Chem.* **1989**, *32*, 1033–1038.

⁴ For the general procedure used for the synthesis of all *N*-vinyl amides, see: Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 3667–3669.

⁵ For related reports, see: (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805–818. (b) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852–860. (c) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131–209. (d) Beletskaya, I. P.; Cheprakov, A. V. *Coordin. Chem. Rev.* **2004**, *248*, 2337–2364. (e) Dehli, J. R.; Legros, J.; Bolm, C. *Chem. Commun.* **2005**, 973–986.

Instrumentation. All reaction conducted at 140 °C were performed in a CEM Discover Lab Mate microwave reactor. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded with a Varian inverse probe 500 INOVA spectrometer. Chemical shifts are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the residual protium in the NMR solvent (CHCl_3 : δ 7.27, C_6HD_5 : δ 7.16, CHDCl_2 : δ 5.32). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance spectra were recorded with a Varian 500 INOVA spectrometer and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the carbon resonances of the solvent (CDCl_3 : δ 77.2, benzene- d_6 : δ 128.0, $\text{DMF-}d_7$: δ 163.2, CD_2Cl_2 : δ 54.0). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constant(s) in Hertz, assignment]. Fluorine-19 nuclear magnetic resonance spectra were recorded with a Varian 300 INOVA spectrometer and are recorded in parts per million on the δ scale and are referenced from the fluorine resonances of trifluoroacetic acid (CD_2Cl_2 : δ -76.6). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q = quartet, quint = quintet, m = multiplet), coupling constant(s) in Hertz, assignment]. Infrared data were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad), assignment]. In situ IR reaction monitoring was performed on an ASI ReactIR 1000 spectrometer. Chiral HPLC analysis was performed on an Agilent 1100 Series HPLC with a Chiralpak AD-H column. We thank Dr. Li Li at the Massachusetts Institute of Technology Department of Chemistry instrumentation facility for obtaining mass spectroscopic data.



4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline (3a, Table 2, entry 1):

Trifluoromethanesulfonic anhydride (92 μL , 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv) and 2-chloropyridine (58 μL , 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at $-78\text{ }^\circ\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to $0\text{ }^\circ\text{C}$, the nitrile **2a** (61 mg, 0.56 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a preheated oil bath at $45\text{ }^\circ\text{C}$ and maintained at that temperature. After 16 h, the reaction mixture was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 7.5% EtOAc in hexanes; SiO_2 : $15 \times 1.5\text{ cm}$) on neutralized silica gel to give the quinazoline product **3a** as a white solid (145 mg, 90%).

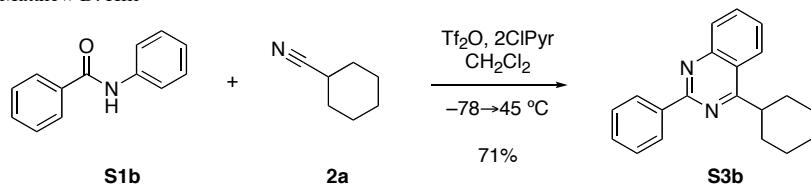
¹H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.67–8.63 (m, 2H, ArH), 8.02 (d, 1H, $J = 9.1\text{ Hz}$, ArH), 7.56–7.46 (m, 4H, ArH), 7.37 (d, 1H, $J = 2.6\text{ Hz}$, ArH), 4.00 (s, 3H, OCH_3), 3.49 (tt, 1H, $J = 11.1, 3.3\text{ Hz}$, $^3\text{C}_6\text{H}_{11}$), 2.09–1.84 (m, 7H, $^3\text{C}_6\text{H}_{11}$), 1.64–1.52 (m, 2H, $^3\text{C}_6\text{H}_{11}$), 1.45 (qt, 1H, $J = 12.7, 2.8\text{ Hz}$, $^3\text{C}_6\text{H}_{11}$).

¹³C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 173.0, 158.6, 157.9, 147.2, 139.0, 131.3, 130.1, 128.6, 128.4, 125.4, 122.6, 102.3, 55.9, 41.7, 32.1, 26.8, 26.4.

FTIR (neat) cm^{-1} : 3064 (w), 2931 (m), 2852 (w), 1622 (w), 1567 (w), 1546 (s), 1222 (s).

HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 319.1810, found: 319.1807.

TLC (15% EtOAc/hexanes), R_f : 0.50 (UV, CAM).



4-Cyclohexyl-2-phenyl-quinazoline (S3b, Table 2, entry 2):

Trifluoromethanesulfonic anhydride (92 μ L, 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1b** (100 mg, 0.507 mmol, 1 equiv) and 2-chloropyridine (57 μ L, 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78 $^{\circ}\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 $^{\circ}\text{C}$, the nitrile **2a** (61 mg, 0.56 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a preheated oil bath at 45 $^{\circ}\text{C}$ and maintained at that temperature. After 16 h, the reaction mixture was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3b** as a white solid (104 mg, 71%).

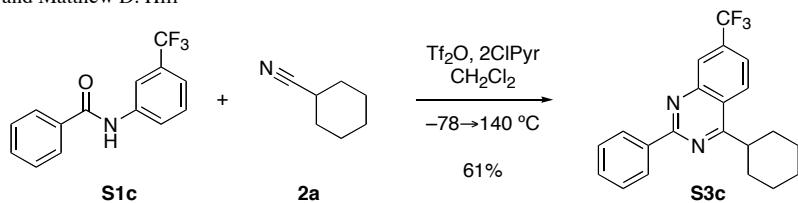
^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}\text{C}$) δ : 8.72–8.67 (m, 2H, ArH), 8.18 (dd, 1H, J = 8.3, 1.3 Hz, ArH), 8.10 (dd, 1H, J = 8.5, 1.3 Hz, ArH), 7.86 (ddd, 1H, J = 8.3, 6.9, 1.3 Hz, ArH), 7.61–7.48 (m, 4H, ArH), 3.60 (tt, 1H, J = 11.2, 3.4 Hz, $^6\text{C}_6\text{H}_{11}$), 2.09–1.84 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.62–1.52 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.45 (qt, 1H, J = 12.8, 3.0 Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}\text{C}$) δ : 174.9, 160.2, 151.2, 138.9, 133.3, 130.5, 129.8, 128.8, 128.7, 126.8, 124.3, 121.9, 41.7, 32.3, 26.8, 26.4.

FTIR (neat) cm^{-1} : 3066 (w), 2933 (s), 2852 (s), 1615 (m), 1570 (s), 1546 (s), 1497 (s), 1344 (s), 1027 (m).

HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2$ $[\text{M}+\text{H}]^+$: 289.1705, found: 289.1704.

TLC (15% EtOAc/hexanes), R_f : 0.56 (UV, CAM).



4-Cyclohexyl-2-phenyl-7-trifluoromethyl-quinazoline (S3c, Table 2, entry 3):

Trifluoromethanesulfonic anhydride (82 μL , 0.50 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1c** (120 mg, 0.450 mmol, 1 equiv) and 2-chloropyridine (51 μL , 0.54 mmol, 1.2 equiv) in dichloromethane (1.5 mL) at -78 °C . After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 °C , the nitrile **2a** (54 mg, 0.50 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140 °C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : $15 \times 1.5 \text{ cm}$) on neutralized silica gel to give the quinazoline product **S3c** as a white solid (97 mg, 61%).

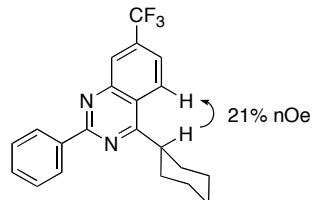
^1H NMR (500 MHz, CDCl_3 , 20 °C) δ : 8.72–8.69 (m, 2H, ArH), 8.40 (s, 1H, ArH), 8.29 (d, 1H, $J = 8.7 \text{ Hz}$, ArH), 7.74 (d, 1H, $J = 8.7 \text{ Hz}$, ArH), 7.59–7.54 (m, 3H, ArH), 3.60 (tt, 1H, $J = 11.4, 3.4 \text{ Hz}$, $^6\text{C}_6\text{H}_{11}$), 2.10–1.86 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.64–1.53 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.45 (qt, 1H, $J = 12.7, 3.0 \text{ Hz}$, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 °C) δ : 175.4, 161.3, 150.6, 138.1, 134.8 (q, $J = 33 \text{ Hz}$), 131.1, 131.0, 128.9, 128.8, 127.7 (q, $J = 4.3 \text{ Hz}$), 125.7, 123.8 (q, $J = 271 \text{ Hz}$), 123.1, 122.3 (q, $J = 4.1 \text{ Hz}$), 42.0, 32.3, 26.7, 26.3.

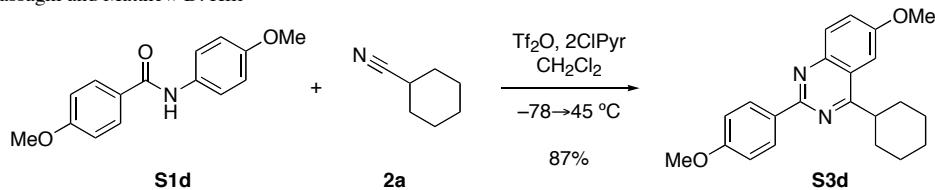
FTIR (neat) cm^{-1} : 2929 (s), 2857 (m), 1575 (s), 1549 (s), 1499 (m), 1344 (s), 1126 (s).

HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{20}\text{F}_3\text{N}_2$ $[\text{M}+\text{H}]^+$: 357.1579, found: 357.1587.

TLC (20% EtOAc/hexanes), R_f : 0.74 (UV, CAM).



nOe data:



4-Cyclohexyl-6-methoxy-2-(4-methoxy-phenyl)-quinazoline (S3d, Table 2, entry 4):

Trifluoromethanesulfonic anhydride (71 μ L, 0.43 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1d** (100 mg, 0.389 mmol, 1 equiv) and 2-chloropyridine (44 μ L, 0.47 mmol, 1.2 equiv) in dichloromethane (1.3 mL) at -78 $^{\circ}$ C. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 $^{\circ}$ C, the nitrile **2a** (47 mg, 0.43 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a preheated oil bath at 45 $^{\circ}$ C and maintained at that temperature. After 18 h, the reaction mixture was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3d** as a white solid (118 mg, 87%).

^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}$ C) δ :

8.62–8.58 (m, 2H, ArH), 7.97 (d, 1H, J = 9.1 Hz, ArH), 7.50 (dd, 1H, J = 9.1, 2.7 Hz, ArH), 7.35 (d, 1H, J = 2.7 Hz, ArH), 7.06–7.03 (m, 2H, ArH), 3.99 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.46 (tt, 1H, J = 11.2, 3.2 Hz, $^6\text{C}_6\text{H}_{11}$), 2.08–1.84 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.62–1.51 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.45 (qt, 1H, J = 12.7, 3.2 Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}$ C) δ :

172.9, 161.4, 158.4, 157.6, 147.2, 131.7, 131.0, 129.9, 125.3, 122.2, 113.9, 102.4, 55.8, 55.5, 41.7, 32.0, 26.8, 26.4.

FTIR (neat) cm^{-1} :

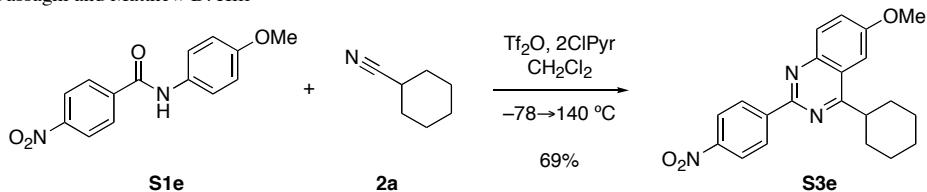
3001 (w), 2932 (s), 2852 (w), 1623 (m), 1545 (s), 1515 (s), 1250 (s), 1223 (s), 1167 (s).

HRMS (ESI):

calcd for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 349.1916,
found: 349.1913.

TLC (20% EtOAc/hexanes), R_f :

0.45 (UV, CAM).



4-Cyclohexyl-6-methoxy-2-(4-nitro-phenyl)-quinazoline (S3e, Table 2, entry 5):

Trifluoromethanesulfonic anhydride (80 μ L, 0.49 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1e** (120 mg, 0.440 mmol, 1 equiv) and 2-chloropyridine (50 μ L, 0.53 mmol, 1.2 equiv) in dichloromethane (1.5 mL) at -78 °C. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 °C, the nitrile **2a** (53 mg, 0.49 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140 °C. After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the quinazoline product **S3e** as a yellow solid (111 mg, 69%).

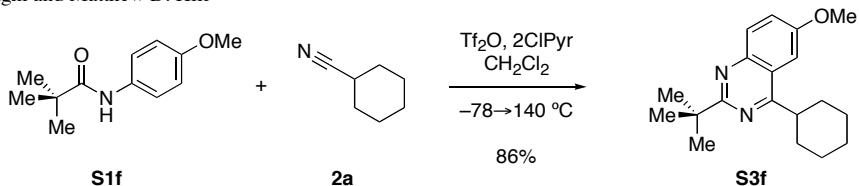
^1H NMR (500 MHz, CDCl_3 , 20 °C) δ : 8.84–8.81 (m, 2H, ArH), 8.38–8.35 (m, 2H, ArH), 8.05 (d, 1H, J = 9.1 Hz, ArH), 7.57 (dd, 1H, J = 9.1, 2.6 Hz, ArH), 7.39 (d, 1H, J = 2.7 Hz, ArH), 4.02 (s, 3H, OCH_3), 3.51 (tt, 1H, J = 11.4, 3.4 Hz, $^6\text{C}_6\text{H}_{11}$), 2.09–1.86 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.64–1.53 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.46 (qt, 1H, J = 12.5, 3.1 Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 °C) δ : 173.5, 158.8, 156.2, 148.9, 147.0, 144.9, 131.5, 129.1, 126.1, 123.8, 123.1, 102.3, 56.0, 41.8, 32.1, 26.7, 26.3.

FTIR (neat) cm^{-1} : 2929 (s), 2851 (m), 1621 (w), 1595 (w), 1544 (m), 1512 (s), 1339 (s), 1256 (m), 1223 (m).

HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{21}\text{N}_3\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 386.1481, found: 386.1459.

TLC (30% EtOAc/hexanes), R_f : 0.58 (UV, CAM).



2-tert-Butyl-4-cyclohexyl-6-methoxy-quinazoline (S3f, Table 2, entry 6):

Trifluoromethanesulfonic anhydride (88 μL , 0.53 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1f** (100 mg, 0.480 mmol, 1 equiv) and 2-chloropyridine (55 μL , 0.58 mmol, 1.2 equiv) in dichloromethane (1.6 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0°C , the nitrile **2a** (58 mg, 0.53 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3f** as a pale yellow solid (124 mg, 86%).

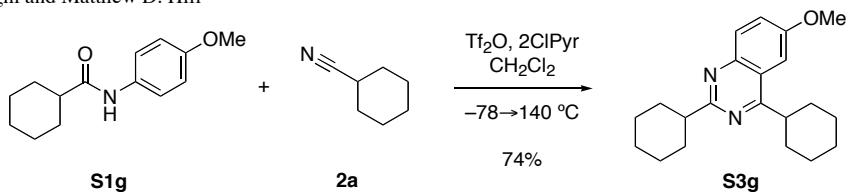
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 7.91 (d, 1H, $J = 9.1$ Hz, ArH), 7.46 (dd, 1H, $J = 9.1, 2.7$ Hz, ArH), 7.32 (d, 1H, $J = 2.7$ Hz, ArH), 3.97 (s, 3H, OCH_3), 3.40 (tt, 1H, $J = 11.4, 3.2$ Hz, $^6\text{C}_6\text{H}_{11}$), 1.98–1.80 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.58–1.50 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.49 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.40 (qt, 1H, $J = 12.7, 3.1$ Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 172.2, 170.9, 157.5, 146.5, 130.9, 124.6, 121.6, 102.1, 55.8, 41.5, 39.6, 32.0, 29.9, 26.7, 26.4.

FTIR (neat) cm^{-1} : 2948 (w), 2912 (m), 2848 (m), 1619 (w), 1556 (m), 1497 (m), 1221 (s).

HRMS (ESI): calcd for $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 299.2123, found: 299.2121.

TLC (20% EtOAc/hexanes), R_f : 0.60 (UV, CAM).



2,4-Dicyclohexyl-6-methoxy-quinazoline (S3g, Table 2, entry 7):

Trifluoromethanesulfonic anhydride (90 μL , 0.54 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1g** (115 mg, 0.493 mmol, 1 equiv) and 2-chloropyridine (56 μL , 0.59 mmol, 1.2 equiv) in dichloromethane (1.6 mL) at $-78 \text{ }^{\circ}\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to $0 \text{ }^{\circ}\text{C}$, the nitrile **2a** (59 mg, 0.54 mmol, 1.1 equiv) was added via syringe, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to $140 \text{ }^{\circ}\text{C}$. After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : $15 \times 1.5 \text{ cm}$) on neutralized silica gel to give the quinazoline product **S3g** as a white solid (119 mg, 74%).

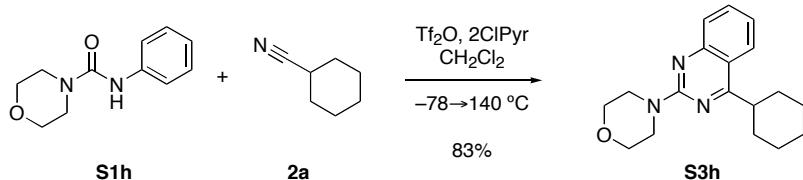
^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}\text{C}$) δ : 7.89 (d, 1H, $J = 9.1 \text{ Hz}$, ArH), 7.47 (dd, 1H, $J = 9.1, 2.9 \text{ Hz}$, ArH), 7.32 (d, 1H, $J = 2.9 \text{ Hz}$, ArH), 3.97 (s, 3H, OCH_3), 3.44 (tt, 1H, $J = 11.5, 3.2 \text{ Hz}$, $^6\text{C}_6\text{H}_{11}$), 2.95 (tt, 1H, $J = 11.7, 3.5 \text{ Hz}$, $^6\text{C}_6\text{H}_{11}$), 2.08–1.72 (m, 14 H, $^6\text{C}_6\text{H}_{11}$, $^6\text{C}_6\text{H}_{11}$), 1.58–1.34 (m, 6H, $^6\text{C}_6\text{H}_{11}$, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}\text{C}$) δ : 172.9, 168.4, 157.4, 146.7, 130.5, 125.0, 122.1, 102.2, 55.8, 47.9, 41.5, 32.2, 32.0, 26.7, 26.6, 26.4, 26.3.

FTIR (neat) cm^{-1} : 2927 (s), 2852 (m), 1623 (w), 1556 (m), 1449 (m), 1222 (s).

HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 325.2280, found: 325.2274.

TLC (20% EtOAc/hexanes), R_f : 0.56 (UV, CAM).



4-Cyclohexyl-2-morpholin-4-yl-quinazoline (S3h, Table 2, entry 8):

Trifluoromethanesulfonic anhydride (97 μL , 0.59 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1h** (110 mg, 0.530 mmol, 1 equiv), nitrile **2a** (64 mg, 0.59 mmol, 1.1 equiv) and 2-chloropyridine (61 μL , 0.64 mmol, 1.2 equiv) in dichloromethane (1.8 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0°C . The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3h** as a white solid (131 mg, 83%).

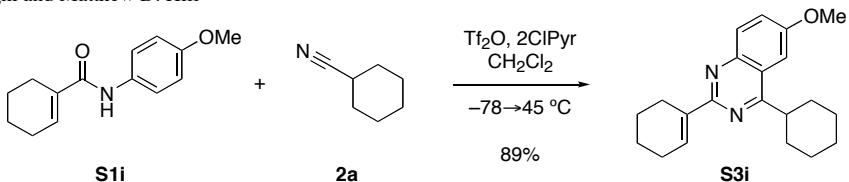
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 7.92 (d, 1H, $J = 8.3$ Hz, ArH), 7.65–7.58 (m, 2H, ArH), 7.21 (ddd, 1H, $J = 8.2, 6.4, 1.6$ Hz, ArH), 3.97 (t, 4H, $J = 4.7$ Hz, $\text{OCH}_2\text{CH}_2\text{N}$), 3.83 (t, 4H, $J = 4.7$ Hz, $\text{OCH}_2\text{CH}_2\text{N}$), 3.41 (tt, 1H, $J = 11.4, 2.9$ Hz, $^6\text{C}_6\text{H}_{11}$), 1.98–1.69 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.51 (tt, 2H, $J = 9.6, 4.2$ Hz, $^6\text{C}_6\text{H}_{11}$) 1.35 (tt, 1H, $J = 12.8, 3.4$ Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 175.8, 158.9, 152.6, 133.3, 126.8, 124.6, 122.3, 118.1, 67.2, 44.7, 41.5, 32.1, 26.7, 26.4.

FTIR (neat) cm^{-1} : 3064 (w), 2930 (s), 2852 (s), 1615 (s), 1579 (s), 1554 (s), 1486 (s), 1227 (s).

HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{24}\text{N}_3\text{O} [\text{M}+\text{H}]^+$: 298.1919, found: 298.1911.

TLC (20% EtOAc/hexanes), R_f : 0.48 (UV, CAM).



2-Cyclohex-1-enyl-4-cyclohexyl-6-methoxy-quinazoline (S3i, Table 2, entry 9):

Trifluoromethanesulfonic anhydride (79 μ L, 0.48 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1i** (100 mg, 0.432 mmol, 1 equiv), 2-chloropyridine (49 μ L, 0.53 mmol, 1.2 equiv), and nitrile **2a** (236 mg, 2.16 mmol, 5.00 equiv) in dichloromethane (1.4 mL) at -78 $^{\circ}$ C. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 $^{\circ}$ C. The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a preheated oil bath at 45 $^{\circ}$ C and maintained at that temperature. After 16 h, the reaction mixture was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3i** as a white solid (124 mg, 89%).

^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}$ C) δ :

7.90 (d, 1H, J = 9.1 Hz, ArH), 7.47–7.44 (m, 2H, ArH, $\text{C}=\text{CHCH}_2$), 7.32 (d, 1H, J = 2.7 Hz, ArH), 3.97 (s, 3H, OCH_3), 3.41 (tt, 1H, J = 10.9, 2.7 Hz, $^6\text{C}_6\text{H}_{11}$), 2.77–2.72 (m, 2H, $^6\text{C}_6\text{H}_9$), 2.39–2.34 (m, 2H, $^6\text{C}_6\text{H}_9$), 2.02–1.70 (m, 11H, $^6\text{C}_6\text{H}_{11}$, $^6\text{C}_6\text{H}_9$), 1.60–1.49 (m, 2H, $^6\text{C}_6\text{H}_{11}$), 1.41 (qt, 1H, J = 12.7, 3.4 Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}$ C) δ :

172.0, 160.1, 157.5, 146.7, 137.4, 132.9, 131.0, 124.8, 122.1, 102.5, 55.8, 41.6, 32.0, 26.8, 26.4, 26.4, 25.6, 23.1, 22.5.

FTIR (neat) cm^{-1} :

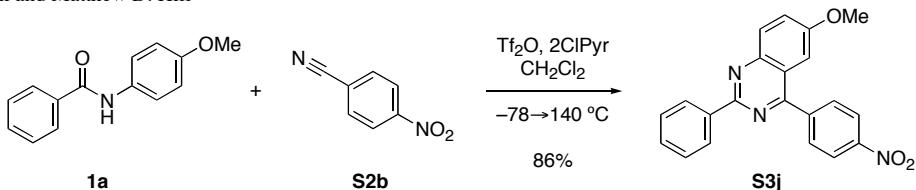
2929 (s), 2853 (m), 1621 (w), 1547 (s), 1496 (m), 1226 (s).

HRMS (ESI):

calcd for $\text{C}_{21}\text{H}_{27}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 323.2123,
found: 323.2126.

TLC (20% EtOAc/hexanes), R_f :

0.67 (UV, CAM).



6-Methoxy-4-(4-nitro-phenyl)-2-phenyl-quinazoline (S3j, Table 2, entry 10):

Trifluoromethanesulfonic anhydride (92 μ L, 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv), nitrile **S2b** (83 mg, 0.56 mmol, 1.1 equiv) and 2-chloropyridine (58 μ L, 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78 $^{\circ}$ C. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 $^{\circ}$ C. The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140 $^{\circ}$ C. After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 20% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3j** as a pale yellow solid (156 mg, 86%).

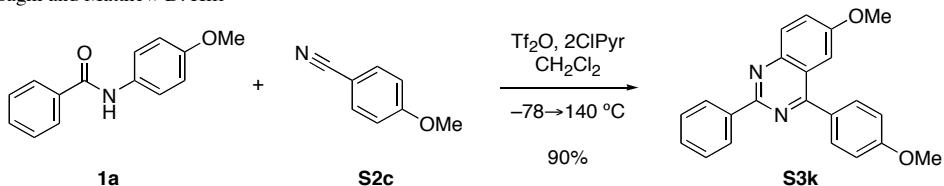
^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}$ C) δ : 8.66–8.62 (m, 2H, ArH), 8.51–8.47 (m, 2H, ArH), 8.13 (d, 1H, J = 9.3 Hz, ArH), 8.11–8.07 (m, 2H, ArH), 7.64 (dd, 1H, J = 9.3, 2.7 Hz, ArH), 7.57–7.50 (m, 3H, ArH), 7.24 (d, 1H, J = 2.7 Hz, ArH), 3.89 (s, 3H, OCH_3).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}$ C) δ : 164.2, 158.8, 158.7, 148.8, 148.6, 144.4, 138.0, 131.3, 131.0, 130.6, 128.8, 128.4, 127.1, 124.1, 122.3, 103.3, 55.9.

FTIR (neat) cm^{-1} : 3056 (w), 2971 (w), 1996 (w), 1621 (m), 1543 (s), 1513 (s), 1350 (s), 1222 (m).

HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$: 358.1192, found: 358.1183.

TLC (20% EtOAc/hexanes), R_f : 0.36 (UV, CAM).



6-Methoxy-4-(4-methoxy-phenyl)-2-phenyl-quinazoline (S3k, Table 2, entry 11):

Trifluoromethanesulfonic anhydride (92 μL , 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv), nitrile **S2c** (74 mg, 0.56 mmol, 1.1 equiv) and 2-chloropyridine (58 μL , 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0°C . The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 20% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3k** as a pale yellow solid (156 mg, 90%).

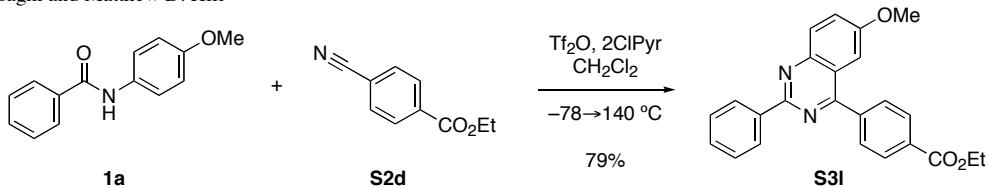
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.67–8.64 (m, 2H, ArH), 8.07 (d, 1H, $J = 9.1$ Hz, ArH), 7.94–7.90 (m, 2H, ArH), 7.57–7.45 (m, 5H, ArH), 7.16–7.12 (m, 2H, ArH), 3.95 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 166.1, 161.1, 158.7, 158.1, 148.3, 138.6, 131.6, 130.7, 130.6, 130.2, 128.6, 128.4, 126.1, 122.5, 114.2, 104.6, 55.7, 55.6.

FTIR (neat) cm^{-1} : 3006 (w), 2957 (m), 2839 (w), 1608 (s), 1564 (m), 1534 (s), 1499 (s), 1404 (s), 1259 (s), 1221 (m).

HRMS (ESI): calcd for $\text{C}_{22}\text{H}_{19}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 343.1447, found: 343.1437.

TLC (20% EtOAc/hexanes), R_f : 0.33 (UV, CAM).



4-(6-Methoxy-2-phenyl-quinazolin-4-yl)-benzoic acid ethyl ester (S3I, Table 2, entry 12):

Trifluoromethanesulfonic anhydride (92 μ L, 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv), nitrile **S2d** (98 mg, 0.56 mmol, 1.1 equiv) and 2-chloropyridine (58 μ L, 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78 °C. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 °C. The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140 °C. After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the quinazoline product **S3I** as a white solid (154 mg, 79%).

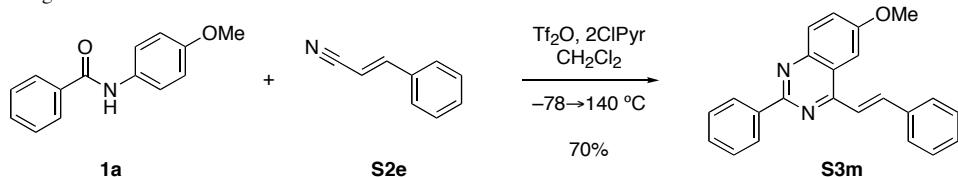
^1H NMR (500 MHz, CDCl_3 , 20 °C) δ : 8.67–8.63 (m, 2H, ArH), 8.30 (d, 2H, J = 8.0 Hz, ArH), 8.10 (d, 1H, J = 9.1 Hz, ArH), 7.98 (d, 2H, J = 7.9 Hz, ArH), 7.58 (dd, 1H, J = 9.1, 2.7 Hz, ArH), 7.56–7.48 (m, 3H, ArH), 7.31 (d, 1H, J = 2.7 Hz, ArH), 4.48 (q, 2H, J = 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 3.87 (s, 3H, OCH_3), 1.48 (t, 3H, J = 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$).

^{13}C NMR (125 MHz, CDCl_3 , 20 °C) δ : 166.4, 165.7, 158.9, 158.4, 148.5, 142.4, 138.3, 131.7, 131.0, 130.4, 130.0, 130.0, 128.8, 128.5, 126.8, 122.5, 103.9, 61.5, 55.8, 14.6.

FTIR (neat) cm^{-1} : 2961 (w), 1717 (s), 1621 (w), 1536 (m), 1407 (m), 1271 (s), 1222 (s).

HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 385.1552, found: 385.1544.

TLC (20% EtOAc/hexanes), R_f : 0.39 (UV, CAM).



6-Methoxy-2-phenyl-4-styryl-quinazoline (S3m, Table 2, entry 13):

Trifluoromethanesulfonic anhydride (92 μL , 0.56 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv), nitrile **S2e** (72 mg, 0.56 mmol, 1.1 equiv) and 2-chloropyridine (58 μL , 0.61 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0°C . The resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 20% EtOAc in hexanes; SiO_2 : 15×1.5 cm) on neutralized silica gel to give the quinazoline product **S3m** as a white solid (120 mg, 70%).

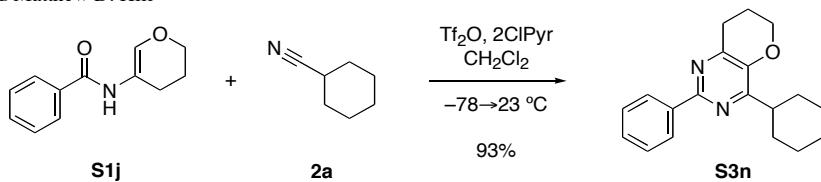
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.71–8.68 (m, 2H, ArH), 8.45 (d, 1H, $J = 15.4$ Hz, $\text{CH}=\text{CH}$), 8.03 (d, 1H, $J = 9.1$ Hz, ArH), 7.89 (d, 1H, $J = 15.4$ Hz, ArH), 7.80 (d, 2H, $J = 7.4$ Hz, ArH), 7.59–7.55 (m, 3H, ArH), 7.54–7.47 (m, 4H, ArH), 7.45–7.41 (m, 1H, ArH), 4.04 (s, 3H, OCH_3).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 160.3, 158.5, 158.1, 148.4, 139.1, 138.8, 136.4, 131.0, 130.2, 129.7, 129.1, 128.7, 128.4, 128.2, 126.3, 122.5, 121.3, 101.6, 55.9.

FTIR (neat) cm^{-1} : 3059 (w), 2936 (w), 1621 (m), 1560 (m), 1533 (s), 1499 (m), 1408 (s), 1224 (s).

HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 339.1497, found: 339.1492.

TLC (20% EtOAc/hexanes), R_f : 0.38 (UV, CAM).



4-Cyclohexyl-2-phenyl-7,8-dihydro-6H-pyran-2,3-dione (S3n, Table 2, entry 14):

Trifluoromethanesulfonic anhydride (63 μ L, 0.38 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1j** (70 mg, 0.34 mmol, 1 equiv), nitrile **2a** (41 mg, 0.38 mmol, 1.1 equiv) and 2-chloropyridine (39 μ L, 0.41 mmol, 1.2 equiv) in dichloromethane (1.0 mL) at -78 °C. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 °C. The resulting solution was allowed to warm to ambient temperature. After 1 h, aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3n** as a white solid (94 mg, 93%).

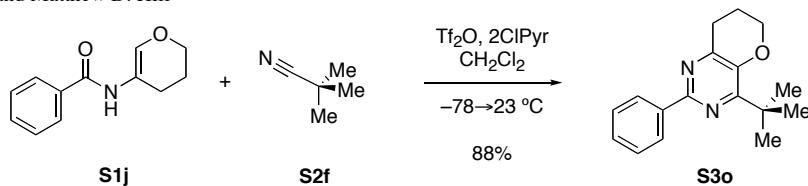
^1H NMR (500 MHz, CDCl_3 , 20 °C) δ : 8.40–8.36 (m, 2H, ArH), 7.47–7.38 (m, 3H, ArH), 4.27 (t, 2H, J = 5.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 3.06 (tt, 1H, J = 11.9, 3.5 Hz, $^6\text{C}_6\text{H}_{11}$), 2.98 (t, 2H, J = 6.6 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.18–2.13 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 1.91–1.69 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.44 (qt, 2H, J = 12.7, 3.2 Hz, $^6\text{C}_6\text{H}_{11}$), 1.35 (qt, 1H, J = 12.7, 3.2 Hz, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 °C) δ : 161.7, 155.8, 149.6, 146.0, 138.7, 129.3, 128.5, 127.7, 66.7, 38.8, 30.8, 28.1, 26.6, 26.3, 22.2.

FTIR (neat) cm^{-1} : 3065 (w), 2930 (s), 2852 (m), 1587 (w), 1565 (s), 1430 (s), 1410 (s), 1208 (m).

HRMS (ESI): calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 295.1810, found: 295.1796.

TLC (20% EtOAc/hexanes), R_f : 0.52 (UV, CAM).



4-*tert*-Butyl-2-phenyl-7,8-dihydro-6*H*-pyranopyrimidine (S3o, Table 2, entry 15):

Trifluoromethanesulfonic anhydride (890 μ L, 5.41 mmol, 1.1 equiv) was added via syringe over 3 min to a stirred mixture of amide **S1j** (1.0 g, 4.9 mmol, 1 equiv), nitrile **S2f** (450 mg, 5.41 mmol, 1.1 equiv) and 2-chloropyridine (560 μ L, 5.90 mmol, 1.2 equiv) in dichloromethane (16 mL) at -78 $^\circ\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 $^\circ\text{C}$. The resulting solution was allowed to warm to ambient temperature. After 3 h, aqueous sodium hydroxide solution (5 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (50 mL) was added to dilute the mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (2×50 mL) and the organic fractions were combined, dried over anhydrous sodium sulfate, and were filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 12×3 cm) on neutralized silica gel to give the pyrimidine product **S3o** as a white solid (1.17 g, 88%).

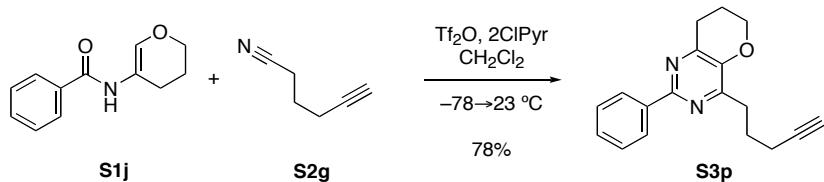
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.42–8.37 (m, 2H, ArH), 7.48–7.38 (m, 3H, ArH), 4.27 (t, 2H, $J = 5.1$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.98 (t, 2H, $J = 6.7$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.20–2.14 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 1.46 (s, 9H, $\text{C}(\text{CH}_3)_3$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 163.3, 154.8, 150.4, 147.6, 138.6, 129.4, 128.5, 127.7, 66.3, 38.2, 28.3, 28.1, 22.1.

FTIR (neat) cm^{-1} : 3065 (w), 2955 (m), 2868 (w), 1558 (m), 1429 (m), 1406 (s), 1366 (m), 1353 (m).

HRMS (ESI): calcd for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 269.1654, found: 269.1653.

TLC (20% EtOAc/hexanes), R_f : 0.67 (UV, CAM).



4-Pent-4-ynyl-2-phenyl-7,8-dihydro-6H-pyranopyrimidine (S3p, Table 2, entry 16):

Trifluoromethanesulfonic anhydride (89 μL , 0.54 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1j** (100 mg, 0.490 mmol, 1 equiv), nitrile **S2g** (50 mg, 0.54 mmol, 1.1 equiv) and 2-chloropyridine (56 μL , 0.59 mmol, 1.2 equiv) in dichloromethane (1.6 mL) at -78 $^\circ\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 $^\circ\text{C}$. The resulting solution was allowed to warm to ambient temperature. After 1 h, aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3p** as a colorless oil (107 mg, 78%).

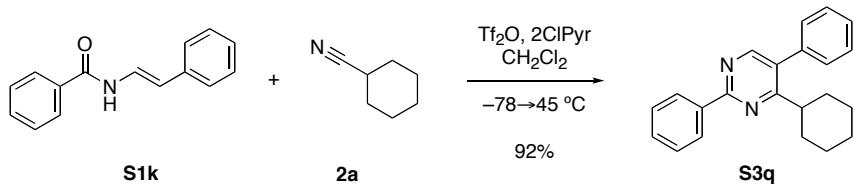
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.36–8.33 (m, 2H, ArH), 7.48–7.38 (m, 3H, ArH), 4.28 (t, 2H, J = 5.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.98 (t, 2H, J = 6.6 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.92 (t, 2H, J = 7.2 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CCH}$), 2.37 td, 2H, J = 7.1, 2.6 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CCH}$), 2.20–2.14 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.08 (quint, 2H, J = 7.4 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CCH}$), 2.01 (1H, t, J = 2.7 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CCH}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 157.2, 155.9, 149.7, 146.9, 138.4, 129.5, 128.6, 127.7, 84.5, 68.8, 66.9, 30.4, 28.1, 26.0, 22.2, 18.5.

FTIR (neat) cm^{-1} : 3297 (s), 3066 (m), 2939 (s), 2117 (w), 1587 (s), 1569 (s), 1411 (s), 1202 (m).

HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O} [\text{M}+\text{H}]^+$: 279.1497, found: 279.1496.

TLC (20% EtOAc/hexanes), R_f : 0.41 (UV, CAM).



4-Cyclohexyl-2,5-diphenyl-pyrimidine (S3q, Table 2, entry 17):

Trifluoromethanesulfonic anhydride (90 μL , 0.54 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1k** (110 mg, 0.493 mmol, 1 equiv), nitrile **2a** (269 mg, 2.47 mmol, 5.00 equiv) and 2-chloropyridine (56 μL , 0.59 mmol, 1.2 equiv) in dichloromethane (1.7 mL) at -78 °C. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 °C, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a preheated oil bath at 45 °C and maintained at that temperature. After 1 h, the reaction vessel was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure, and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3q** as a white solid (142 mg, 92%).

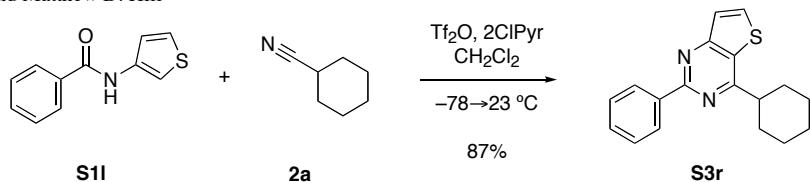
^1H NMR (500 MHz, CDCl_3 , 20 °C) δ : 8.59 (s, 1H, ArH), 8.57–8.54 (m, 2H, ArH), 7.55–7.44 (m, 6H, ArH), 7.38–7.35 (m, 2H, ArH), 2.90 (tt, 1H, J = 11.5, 3.5 Hz, $^6\text{C}_6\text{H}_{11}$), 1.94–1.69 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.37 (qt, 1H, J = 12.8, 3.2 Hz, $^6\text{C}_6\text{H}_{11}$), 1.30–1.20 (m, 2H, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 °C) δ : 171.6, 163.1, 157.4, 138.2, 136.6, 131.7, 130.6, 129.4, 128.9, 128.7, 128.3, 128.1, 42.0, 32.2, 26.3, 26.1.

FTIR (neat) cm^{-1} : 3060 (w), 2929 (s), 2853 (m), 1586 (w), 1568 (s), 1525 (s), 1425 (s), 1378 (m).

HRMS (ESI): calcd for $\text{C}_{22}\text{H}_{23}\text{N}_2$ $[\text{M}+\text{H}]^+$: 315.1861, found: 315.1861.

TLC (20% EtOAc/hexanes), R_f : 0.69 (UV, CAM).



4-Cyclohexyl-2-phenyl-thieno[3,2-d]pyrimidine (S3r, Table 2, entry 18):

Trifluoromethanesulfonic anhydride (72 μ L, 0.43 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S11** (80 mg, 0.39 mmol, 1 equiv), nitrile **2a** (47 mg, 0.54 mmol, 1.1 equiv) and 2-chloropyridine (45 μ L, 0.47 mmol, 1.2 equiv) in dichloromethane (1.3 mL) at -78 $^{\circ}$ C. After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0 $^{\circ}$ C. The resulting solution was allowed to warm to ambient temperature. After 1 h, aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3r** as a pale yellow solid (101 mg, 87%).

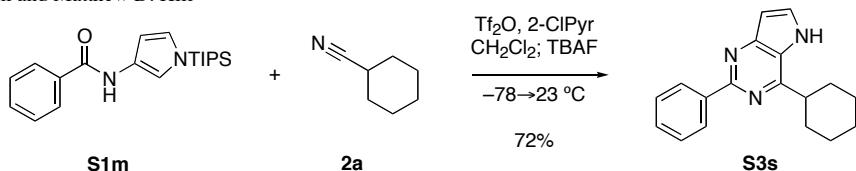
^1H NMR (500 MHz, CDCl_3 , 20 $^{\circ}$ C) δ : 8.60–8.58 (m, 2H, ArH), 7.92 (d, 1H, J = 5.5 Hz, ArH), 7.60 (d, 1H, J = 5.5 Hz, ArH), 7.54–7.48 (m, 3H, ArH), 3.05 (tt, 1H, J = 11.5, 3.8 Hz, $^c\text{C}_6\text{H}_{11}$), 2.10–1.81 (m, 7H, $^c\text{C}_6\text{H}_{11}$), 1.56–1.38 (m, 3H, $^c\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^{\circ}$ C) δ : 168.8, 162.0, 161.4, 138.7, 134.5, 130.3, 128.7, 128.5, 127.4, 125.4, 46.3, 31.3, 26.5, 26.2.

FTIR (neat) cm^{-1} : 2928 (m), 2852 (w), 1535 (s), 1365 (w), 1341 (w).

HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{S}$ $[\text{M}+\text{H}]^+$: 295.1269, found: 295.1259.

TLC (20% EtOAc/hexanes), R_f : 0.52 (UV, CAM).



4-Cyclohexyl-2-phenyl-5H-pyrrolo[3,2-d]pyrimidine (S3s, Table 2, entry 19):

Trifluoromethanesulfonic anhydride (37 μL , 0.23 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1m** (70 mg, 0.20 mmol, 1 equiv), nitrile **2a** (46 mg, 0.41 mmol, 2.00 equiv) and 2-chloropyridine (39 μL , 0.41 mmol, 2.00 equiv) in dichloromethane (0.7 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0°C . The resulting solution was allowed to warm to ambient temperature. After 1 h, triethylamine (1 mL) was introduced to neutralize the trifluoromethanesulfonate salts, followed by TBAF (204 μL , 1.00 equiv, 1.0 M) to protodesilylate the pyrimidine product. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10 \rightarrow 40% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3s** as a pale tan solid (41 mg, 72%).

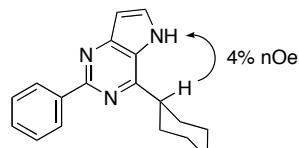
^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.57–8.52 (m, 2H, ArH), 8.45 (s, 1H, NH), 7.54–7.47 (m, 3H, ArH), 7.45–7.40 (m, 1H, ArH), 6.79 (dd, 1H, J = 3.1, 2.0 Hz, ArH), 3.05 (tt, 1H, J = 11.4, 3.5 Hz, $^6\text{C}_6\text{H}_{11}$), 2.09–1.80 (m, 7H, $^6\text{C}_6\text{H}_{11}$), 1.54–1.38 (m, 3H, $^6\text{C}_6\text{H}_{11}$).

^{13}C NMR (125 MHz, $\text{DMF}-d_7$, 20 $^\circ\text{C}$) δ : 157.9, 156.9, 151.9, 141.1, 133.6, 130.0, 129.3, 128.6, 125.2, 102.9, 42.4, 32.2, 27.3, 27.0.

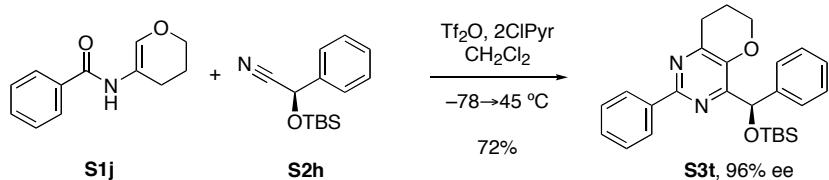
FTIR (neat) cm^{-1} : 3073 (m), 3019 (m), 2924 (s), 2849 (s), 1996 (w), 1738 (w), 1609 (m), 1543 (s), 1445 (m), 1386 (s).

HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3$ $[\text{M}+\text{H}]^+$: 278.1657, found: 278.1656.

TLC (40% EtOAc/hexanes), R_f : 0.38 (UV, CAM).



nOe data:



(R)-4-[(tert-Butyl-dimethyl-silyloxy)-phenyl-methyl]-2-phenyl-7,8-dihydro-6H-pyran-3,2-dipyrimidine (S3t, Table 2, entry 20):

Trifluoromethanesulfonic anhydride (54 μ L, 0.33 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1j** (60 mg, 0.30 mmol, 1 equiv), nitrile **S2h**⁶ (219 mg, 0.885 mmol, 3.00 equiv) and 2-chloropyridine (34 μ L, 0.35 mmol, 1.2 equiv) in dichloromethane (1.0 mL) at -78 °C. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 °C, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before being placed into a preheated oil bath at 45 °C and maintained at that temperature. After 1 h, the reaction vessel was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO₂: 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3t** as a colorless oil (91 mg, 72%, 96% ee). The ee of the product was determined by chiral HPLC analysis of the corresponding desilylated alcohol. The enantiomeric excess of the pyrimidine product was determined to be 95% ee by chiral HPLC analysis [Chiralpak AD-H; 2.5 mL/min; 7% ¹PrOH in hexanes; *t*_R (minor) = 6.74 min, *t*_R (major) = 9.95 min].

¹H NMR (500 MHz, CDCl₃, 20 °C) δ : 8.44–8.38 (m, 2H, ArH), 7.62–7.57 (m, 2H, ArH), 7.48–7.38 (m, 3H, ArH), 7.35–7.30 (m, 2H, ArH), 7.27–7.24 (m, 1H, ArH), 6.20 (s, 1H, CHOTBS), 4.32–4.21 (m, 2H, CH₂CH₂CH₂O), 3.03–2.92 (m, 2H, CH₂CH₂CH₂O), 2.20–2.11 (m, 2H, CH₂CH₂CH₂O), 0.95 (s, 9H, Si(CH₃)₂C(CH₃)₃), 0.05 (s, 3H, Si(CH₃)₂C(CH₃)₃), 0.00 (s, 3H, Si(CH₃)₂C(CH₃)₃).

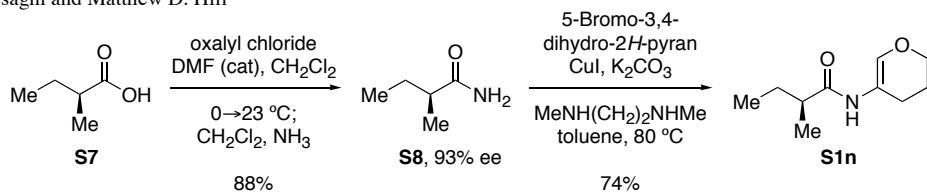
¹³C NMR (125 MHz, CDCl₃, 20 °C) δ : 157.4, 156.0, 151.3, 145.7, 142.6, 138.3, 129.5, 128.5, 128.1, 127.8, 127.3, 127.0, 71.8, 66.8, 28.2, 26.0, 22.0, 18.5, -4.5, -4.7.

FTIR (neat) cm⁻¹: 3065 (m), 3032 (m), 2954 (s), 2886 (s), 2856 (s), 1957 (w), 1819 (w), 1586 (m), 1564 (s), 1409 (s), 1252 (s).

HRMS (ESI): calcd for C₂₆H₃₃N₂O₂Si [M+H]⁺: 433.2311, found: 433.2303.

TLC (20% EtOAc/hexanes), *R*_F: 0.67 (UV, CAM).

⁶ The nitrile **S2h** was prepared by silylation of the corresponding commercially available cyanohydrin. The optical activity of the starting cyanohydrin was determined to be 96% ee by chiral HPLC analysis.



(S)-N-(5,6-Dihydro-4H-pyran-3-yl)-2-methylbutyramide (S1n, Table 2, entry 21):

Oxalyl chloride (1.30 g, 10.3 mmol, 1.05 equiv) was added over 1 minute via syringe to a stirred solution of (S)-(+)-2-methylbutyric acid (**S7**, 1.0 g, 9.8 mmol, 1 equiv) and *N,N*-dimethylformamide (10 μL) in dichloromethane (33 mL) in an ice-bath at 0 °C. The reaction mixture was removed from the ice-bath after 15 minutes and allowed to warm to ambient temperature. After 1.5 h, gas evolution had ceased and dichloromethane saturated with ammonia (33 mL) was added via cannula at ambient temperature. Water (10 mL) was added after 5 minutes to remove ammonium salts and the layers were separated. The aqueous layer was extracted with dichloromethane (2 \times 50 mL), the organic layers were combined and dried over anhydrous sodium sulfate and filtered, and the volatiles were removed under reduced pressure to afford pure primary amide **S8** as a white solid (870 mg, 88%). The enantiomeric excess of the amide was determined to be 93% ee by chiral HPLC analysis [Chiralpak AD-H; 1.0 mL/min; 7% *i*PrOH in hexanes; t_{R} (minor) = 14.2 min, t_{R} (major) = 15.7 min]. The primary amide (850 mg, 8.40 mmol, 1 equiv) was then combined with 5-Bromo-3,4-dihydro-2H-pyran⁷ (1.1 g, 7.0 mmol, 0.83 equiv), copper iodide (160 mg, 0.840 mmol, 0.100 equiv), *N,N'*-dimethylethylenediamine (148 mg, 1.68 mmol, 0.200 equiv), and potassium carbonate (1.97 g, 14.3 mmol, 1.70 equiv) in toluene (8.4 mL) in a pressure vessel. The resulting reaction mixture was placed in a preheated oil bath at 80 °C and maintained at that temperature. After 16 h, the solution was removed from the bath and allowed to cool to ambient temperature. The crude mixture was diluted with ethyl acetate (30 mL) and filtered through celite; the volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 40% EtOAc in hexanes; SiO_2 : 25 \times 3 cm) on silica gel to give the amide product **S1n** as a white solid (950 mg, 74%). The copper catalyzed C–N bond formation occurred without loss of optical activity as confirmed by measuring the enantiomeric excess of the corresponding pyrimidine **S3u** (see page S24).

¹H NMR (500 MHz, CDCl_3 , 20 °C) δ : 6.93 (s, 1H, C=CH), 6.15 (br s, 1H, NH), 3.95 (t, 2H, J = 5.3 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.26–2.22 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.16–2.07 (m, 1H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 1.98–1.92 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 1.74–1.64 (m, 1H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 1.51–1.42 (m, 1H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 1.16 (d, 3H, J = 6.7 Hz, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 0.94 (t, 3H, J = 7.4 Hz, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$).

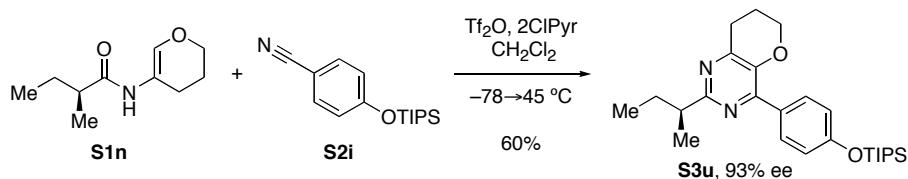
¹³C NMR (125 MHz, CDCl_3 , 20 °C) δ : 175.8, 139.5, 113.7, 65.4, 43.3, 27.6, 23.9, 22.1, 17.7, 12.1.

FTIR (neat) cm^{-1} : 3292 (w), 2968 (m), 2936 (m), 2878 (w), 1727 (s), 1699 (m), 1651 (s), 1510 (m), 1463 (m), 1382 (w), 1165 (m).

HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_2$ [$\text{M}+\text{H}$]⁺: 184.1332, found: 184.1337.

TLC (40% EtOAc in hexanes), R_f : 0.34 (UV, CAM).

⁷ Bonner, W. A.; Werth, P. J.; Roth, J. M. *J. Org. Chem.* **1962**, 27, 1575.



(S)-2-sec-Butyl-4-[4-(triisopropyl-silanyloxy)-phenyl]-7,8-dihydro-6H-pyranolo[3,2-d]pyrimidine (S3u, Table 2, entry 21):

Trifluoromethanesulfonic anhydride (79 μL , 0.48 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **S1n** (80 mg, 0.44 mmol, 1 equiv), nitrile **S2i** (361 mg, 1.31 mmol, 3.00 equiv) and 2-chloropyridine (50 μL , 0.52 mmol, 1.2 equiv) in dichloromethane (1.5 mL) at $-78\text{ }^\circ\text{C}$. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to $0\text{ }^\circ\text{C}$, and the resulting solution was allowed to warm to ambient temperature for 5 minutes before being placed into a preheated oil bath at $45\text{ }^\circ\text{C}$ and maintained at that temperature. After 1 h, the reaction vessel was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10 \rightarrow 20% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the pyrimidine product **S3u** as a colorless oil (115 mg, 60%). The enantiomeric excess of the pyrimidine product was determined to be 93% ee by protodesilylation and chiral HPLC analysis [Chiralpak AD-H; 2.0 mL/min; 3% $^i\text{PrOH}$ in hexanes; t_{R} (major) = 9.36 min, t_{R} (minor) = 11.1 min] of the corresponding alcohol.⁸

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 8.16–8.12 (m, 2H, ArH), 6.97–6.93 (m, 2H, ArH), 4.28 (t, 2H, J = 5.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2.98–2.87 (m, 3H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 2.20–2.15 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 1.96–1.86 (m, 1H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 1.70–1.61 (m, 1H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$), 1.34–1.26 (m, 6H, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$, $\text{Si}(\text{CH}(\text{CH}_3)_2)_3$), 1.14 (d, 18H, J = 7.5 Hz, $\text{Si}(\text{CH}(\text{CH}_3)_2)_3$), 0.90 (t, 3H, J = 7.4 Hz, $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$).

^{13}C NMR (125 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ : 165.5, 157.7, 151.4, 150.9, 145.6, 131.3, 128.9, 119.5, 66.7, 44.2, 29.6, 28.4, 22.1, 20.0, 18.1, 12.9, 12.4.

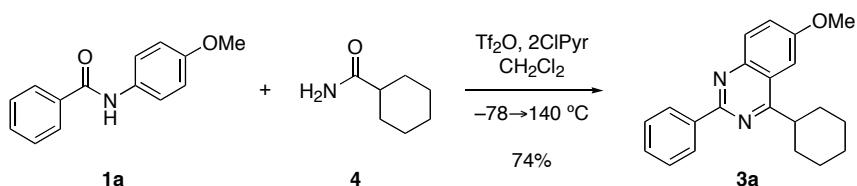
FTIR (neat) cm^{-1} : 2961 (s), 2868 (s), 1605 (s), 1558 (m), 1541 (w), 1508 (s), 1463 (m), 1270 (s).

HRMS (EI): calcd for $\text{C}_{26}\text{H}_{40}\text{N}_2\text{O}_2\text{Si} [\text{M}]^+$: 440.2859, found: 440.2865.

TLC (20% EtOAc in hexanes), R_f : 0.37 (UV, CAM)

⁸ The use of the (S)-*N*-(4-methoxyphenyl)-2-methylbutyramide variant of amide **S1n** as the substrate with the same nitrile (**S2i**, 1.1 equiv) under standard conditions (B or C, see text) provided the corresponding quinazoline in 58% yield (condition C) but with complete racemization (0% ee). This is likely due to the compounded effect of the low reactivity of the amide and the nitrile in addition to the likely slower rate of cyclization of intermediate **6** (Scheme 1) leading to quinazolines.

Direct conversion of secondary amide **1a and primary amide **4** to quinazoline **3a**.**



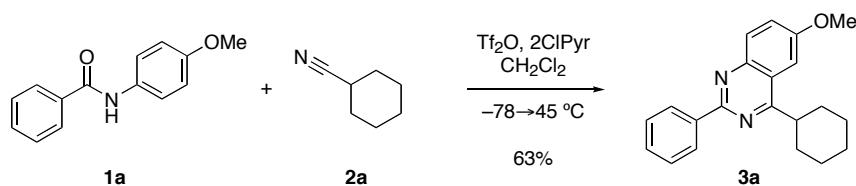
4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline (eq 2):

Trifluoromethanesulfonic anhydride (193 μL , 1.17 mmol, 2.30 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (115 mg, 0.506 mmol, 1 equiv), cyclohexanecarboxamide **4** (71 mg, 0.56 mmol, 1.1 equiv) and 2-chloropyridine (125 μL , 1.32 mmol, 2.60 equiv) in dichloromethane (1.7 mL) at -78°C . After 5 min, the reaction mixture was placed in an ice-water bath for 5 minutes and warmed to 0°C . The resulting solution was warmed to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and allowed to cool to ambient temperature before aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 5% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the quinazoline product **3a** as a white solid (119 mg, 74%).

See page S3 for spectroscopic data.

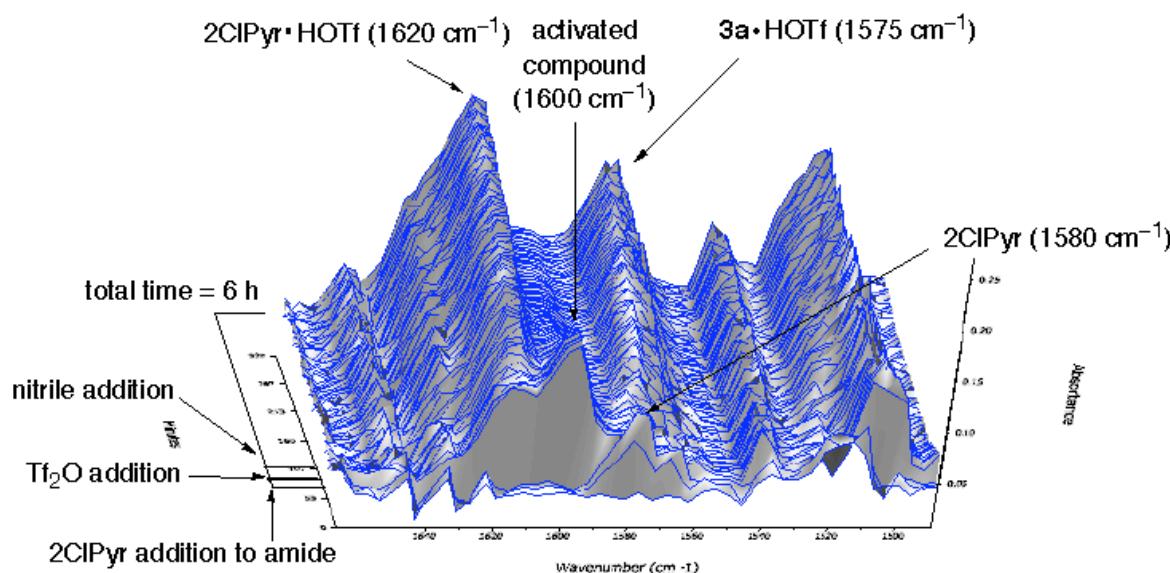
In situ IR analysis of the conversion of amide 1a and nitrile 2a to quinazoline 3a:

All reactions were performed in a reaction vessel under an atmosphere of argon with the React-IR probe submerged completely in the reaction mixture.



4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline (3a):

In situ IR monitoring of the addition of trifluoromethanesulfonic anhydride (96 μ L, 0.58 mmol, 1.1 equiv) via syringe over 1 min to a mixture of amide **1a** (120 mg, 0.528 mmol, 1 equiv) and 2-chloropyridine (60 μ L, 0.63 mmol, 1.2 equiv) in dichloromethane (2.7 mL) at 0 $^{\circ}$ C revealed consumption of both amide **1a** and 2-chloropyridine with concomitant appearance of a persistent band at 1600 cm^{-1} corresponding to the activated compound. After 5 min, nitrile **2a** (63 mg, 0.58 mmol, 1.1 equiv) was added via syringe, and the resulting solution was placed into a preheated oil bath at 45 $^{\circ}$ C and maintained at that temperature. After 6 h, the reaction vessel was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 20% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the quinazoline product **3a** as a white solid (106 mg, 63%). See page S3 for full characterization of product **3a**. See control experiments for assignment of observed band (page S27).⁸



⁸ Dines, T. J.; MacGregor, L. D.; Rochester, C. H. *Spectrochimica Acta Part A* **2003**, 59, 3205–3217.

Control IR Experiments:

Assignment of the 2-chloropyridine and the 2-chloropyridinium triflate characteristic stretches:

1) In situ IR monitoring of the addition of trifluoromethanesulfonic acid (47 μ L, 0.53 mmol, 1 equiv) via syringe to a solution of 2-chloropyridine (50 μ L, 0.53 mmol, 1 equiv, 1580 cm^{-1}) in CH_2Cl_2 (2.2 mL) at 0 $^{\circ}\text{C}$ resulted in the expected 2-chloropyridinium triflate salt (1620 cm^{-1}).

Assignment of the 4-Cyclohexyl-6-methoxy-2-phenyl-quinazolin-1-i um triflate (**3a**•HOTf) characteristic stretch:

2) In situ IR monitoring of the addition of trifluoromethanesulfonic acid (78 μ L, 0.88 mmol, 2.0 equiv) via syringe to a solution of quinazoline **3a** (140 mg, 0.29 mmol, 1 equiv, 1550 cm^{-1}) and 2-chloropyridine (50 μ L, 0.53 mmol, 1 equiv, 1580 cm^{-1}) in CH_2Cl_2 (2.2 mL) at 0 $^{\circ}\text{C}$ resulted in the expected mixture containing 2-chloropyridinium triflate salt (1620 cm^{-1}) and the 4-cyclohexyl-6-methoxy-2-phenyl-quinazolin-1-i um triflate salt (**3a**•HOTf, 1575 cm^{-1}).

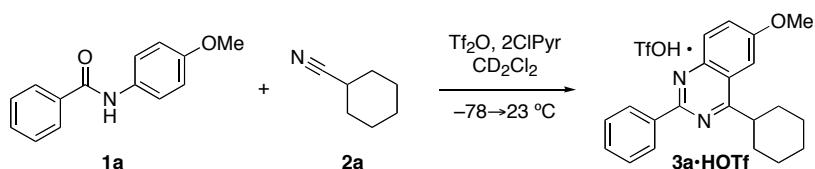
3) The same characteristic resonance for **3a**•HOTf was observed in the absence of 2-chloropyridine. In situ IR monitoring of the addition of trifluoromethanesulfonic acid (43 μ L, 0.49 mmol, 1 equiv) to a solution of quinazoline **3a** (140 mg, 0.29 mmol, 1 equiv, 1550 cm^{-1}) in CH_2Cl_2 (2.2 mL) at 0 $^{\circ}\text{C}$ resulted in the expected 4-cyclohexyl-6-methoxy-2-phenyl-quinazolin-1-i um triflate salt (**3a**•HOTf, 1575 cm^{-1}).

Assignment of the characteristic stretch at 1600 cm^{-1} to the activated intermediate in the presence of 2-chloropyridine:

4) Trifluoromethanesulfonic anhydride (96 μ L, 0.58 mmol, 1.1 equiv) was added via syringe over 1 min to a solution of amide **1a** (120 mg, 0.528 mmol, 1 equiv) in dichloromethane (2.7 mL) at 0 $^{\circ}\text{C}$. After 5 min, 2-chloropyridine (60 μ L, 0.63 mmol, 1.2 equiv) was added via syringe resulting in the appearance of the characteristic stretch at 1600 cm^{-1} . The nitrile **2a** (63 mg, 0.58 mmol, 1.1 equiv) was immediately added via syringe, and the resulting solution was placed into a preheated oil bath at 45 $^{\circ}\text{C}$ and maintained at that temperature. After 3 h, the reaction mixture was allowed to cool to ambient temperature and aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 20% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on neutralized silica gel to give the quinazoline product **3a** as a white solid (58 mg, 35%). This non-ideal procedure (order of reagent addition and time) was used to verify the involvement of 2-chloropyridine in the formation of the activated intermediate resulting in the observed stretch at 1600 cm^{-1} .

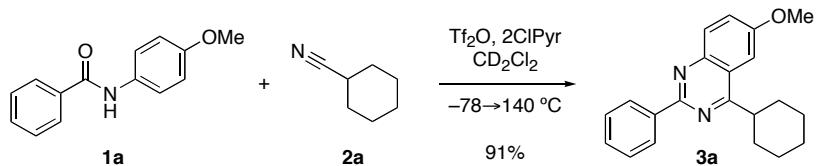
5) Additionally, in situ IR monitoring of the addition of trifluoromethanesulfonic anhydride (73 μ L, 0.44 mmol, 1 equiv) via syringe to 2-chloropyridine (42 μ L, 0.44 mmol, 1 equiv, 1580 cm^{-1}) in CH_2Cl_2 (2.2 mL) at ambient temperature resulted in no observable change. The band at 1580 cm^{-1} related to 2-chloropyridine persisted with out loss in intensity. After 4.5 h, water (70 μ L, 4.4 mmol, 10 equiv) was added via syringe and as expected the 2-chloropyridine stretch (1580 cm^{-1}) disappeared completely with a concomitant appearance of a band consistent with 2-chloropyridinium triflate salt (1620 cm^{-1}).

¹H and ¹⁹F NMR monitoring of the conversion of amide **1a and nitrile **2a** to quinazoline **3a**:**



4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline (3a**·HOTf):**

Trifluoromethanesulfonic anhydride (80 μL , 0.48 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (100 mg, 0.440 mmol, 1 equiv) and 2-chloropyridine (50 μL , 0.53 mmol, 1.2 equiv) in CD_2Cl_2 (1.5 mL) at -78°C . After 5 min the reaction vessel was placed in an ice-water bath and warmed to 0°C . ¹H (500 MHz) and ¹⁹F (282 MHz) NMR analysis revealed broad resonances. Additionally, complete consumption of 2-chloropyridine and the starting amide **1a** was confirmed. ¹⁹F NMR was informative and revealed a broad peak corresponding to a triflate ion at δ -79.6 along with remaining trifluoromethanesulfonic anhydride (δ -72.4, ~16%). The nitrile **2a** (53 mg, 0.48 mmol, 1.1 equiv) was added via syringe. After 5 min, ¹H and ¹⁹F NMR analysis revealed a small set of resonances consistent with the protonated quinazoline product **3a**·HOTf along with dominant resonances corresponding to those observed during activation of the amide as described above. Again, the ¹⁹F NMR was informative and revealed predominantly a broad resonance corresponding to a triflate ion at δ -79.6 along with un-reacted trifluoromethanesulfonic anhydride (13%) at δ -72.4. While a trace amount of the product was observed, the best conditions for the synthesis of **3a** involve heating to 140°C .



4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline (3a**):**

Trifluoromethanesulfonic anhydride (80 μL , 0.48 mmol, 1.1 equiv) was added via syringe over 1 min to a stirred mixture of amide **1a** (100 mg, 0.440 mmol, 1 equiv), nitrile **2a** (53 mg, 0.48 mmol, 1.1 equiv) and 2-chloropyridine (50 μL , 0.53 mmol, 1.2 equiv) in CD_2Cl_2 (1.5 mL) at -78°C . After 5 min, the reaction vessel was placed in an ice-water bath for 5 minutes and warmed to 0°C ; the resulting solution was allowed to warm to ambient temperature for 5 minutes before the reaction vessel was placed into a microwave reactor and heated to 140°C . After 20 min, the reaction vessel was removed from the microwave reactor and a sample was subject to ¹H (500 MHz) and ¹⁹F NMR (282 MHz) analysis. Complete conversion to the desired product was observed by this crude ¹H NMR analysis. The observed resonances corresponded to 2-chloropyridinium trifluoromethanesulfonate, protonated quinazoline **3a**·HOTf, and the remaining nitrile **2a**. ¹⁹F NMR analysis of the crude reaction mixture revealed only a broad resonance corresponding to triflate anion at δ -79.6 and weak resonance at δ -72.4 for the trace amount of remaining trifluoromethanesulfonic anhydride. Aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO_2 : 15 \times 1.5 cm) on

neutralized silica gel to give the quinazoline product **3a** as a white solid (127 mg, 91%). See page S3 for full characterization of the quinazoline product **3a**.

Control ¹H and ¹⁹F NMR Experiments:

Assignment of the 2-chloropyridinium triflate resonances:

1) Addition of trifluoromethanesulfonic acid (1 equiv) via syringe to 2-chloropyridine (1 equiv) in CD₂Cl₂ (700 μ L) at 23 °C followed by ¹H and ¹⁹F NMR analysis revealed the formation of the expected 2-chloropyridinium triflate. ¹H NMR (500 MHz) δ : 15.8 (br-s, 1H), 8.76 (br-m, 1H), 8.54 (m, 1H), 8.02–7.98 (m, 2H). ¹⁹F NMR (282 MHz) δ : -79.3.

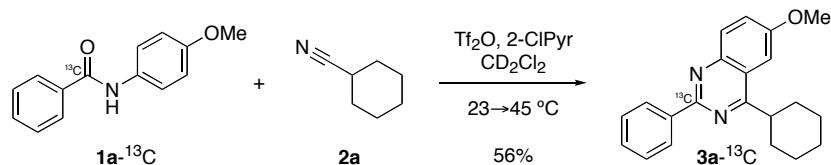
2) Consistent with the IR experiments described above, the addition of trifluoromethanesulfonic anhydride (32 μ L, 0.19 mmol, 1.1 equiv) via syringe to a solution of 2-chloropyridine (17 μ L, 0.18 mmol, 1 equiv) in CD₂Cl₂ (600 μ L) at 23 °C under an atmosphere of argon followed by ¹H and ¹⁹F NMR analysis revealed no change after 24 h. Importantly, ¹⁹F NMR (282 MHz) analysis only reveals a persistent resonance at δ -72.4 (Tf₂O). After 24 hours, water (50 μ L) was added to this sample to give the expected 2-chloropyridinium triflate (δ -79.5).

Assignment of the 4-Cyclohexyl-6-methoxy-2-phenyl-quinazolin-1-ium triflate (**3a**•HOTf) resonances:

3) Addition of trifluoromethanesulfonic acid (56 μ L, 0.63 mmol, 2.0 equiv) via syringe to a solution of 2-chloropyridine (36 μ L, 0.38 mmol, 1.2 equiv) and quinazoline **3a** (100 mg, 0.310 mmol, 1 equiv) in CD₂Cl₂ (1 mL) at 23 °C followed by ¹H and ¹⁹F NMR analysis revealed the formation of the expected 2-chloropyridinium triflate and the 4-cyclohexyl-6-methoxy-2-phenyl-quinazolin-1-ium triflate (**3a**•HOTf). ¹H NMR (500 MHz) δ : 14.9 (br-s, 2.6H), 9.05 (br-s, 2.2H), 8.72 (dd, 1.1H, J = 5.5, 1.8 Hz), 8.70–8.63 (m, 3.0H), 8.28 (ddd, 1.0H, J = 8.2, 7.7, 1.9 Hz), 7.92 (dd, 0.9H, J = 9.3, 2.6 Hz), 7.82–7.75 (m, 2.8H), 7.75–7.70 (m, 2.0H), 7.61 (d, 1.1H, J = 2.7 Hz), 4.10 (s, 3.0H), 3.74 (tt, 1.1H, J = 11.4, 3.4 Hz), 2.14–1.90 (m, 7.2H), 1.70–1.59 (m, 2.1H), 1.48 (qt, 1.1H, J = 13.0, 3.5 Hz). ¹⁹F NMR (282 MHz) δ : -79.6.

4) Addition of trifluoromethanesulfonic acid (56 μ L, 0.63 mmol, 2.0 equiv) via syringe to a solution of quinazoline **3a** (100 mg, 0.310 mmol, 1 equiv) in CD₂Cl₂ (1 mL) at 23 °C followed by ¹⁹F NMR analysis of the mixture suggests *mono*-protonation to give the quinazolinium triflate **3a**•HOTf. ¹⁹F NMR (282 MHz) δ : -78.0, -79.1.

¹³C NMR monitoring of the conversion of amide **1a**-¹³C and nitrile **2a** to quinazoline **3a**-¹³C:



4-Cyclohexyl-6-methoxy-2-phenyl-quinazoline-¹³C (**3a**-¹³C):

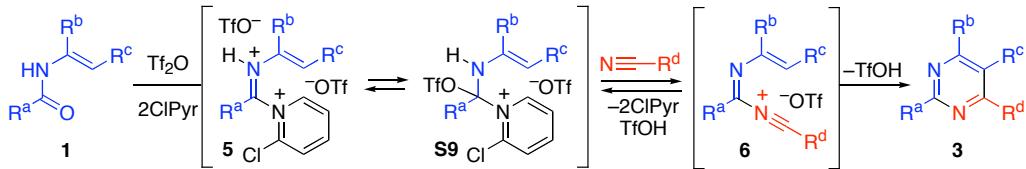
2-Chloropyridine (50 μ L, 0.53 mmol, 1.2 equiv) was added via syringe to a solution of amide⁹ **1a**-¹³C (¹³C=O, 100 mg, 0.439 mmol, 1 equiv) in CD₂Cl₂ (1.1 mL) at ambient temperature in an NMR tube under an atmosphere of argon. A sharp resonance corresponding to the carbonyl of amide

⁹ Amide **1a**-¹³C was readily prepared from the commercially available benzoic acid-*carboxy*-¹³C (99% atom % ¹³C, C₆H₅¹³CO₂H).

1a-¹³C (δ 166.0) was observed. Trifluoromethanesulfonic anhydride (80 μ L, 0.48 mmol, 1.1 equiv) was added via syringe at 23 °C and the ¹³C NMR spectrum of the resulting mixture was immediately recorded. The starting amide was completely consumed and a new and persistent broad resonance was detected (δ 149.8). Addition of nitrile **2a** (53 mg, 0.48 mmol, 1.1 equiv) at 23 °C and immediate ¹³C NMR monitoring led to observation of two new sharp resonance at δ 166.9 and δ 96.9 along with the remaining broad resonance at δ 149.8 (~0.9:0.4,1.0, respectively). After 2 h heating of the mixture at 45 °C, the sample was cooled to 23 °C and the ¹³C NMR analysis of the reaction mixture revealed a dominant new resonance at δ 155.1 attributed to the desired product quinazoline **3a-¹³C**•HOTf and disappearance of the broad resonance at δ 149.8. The resonances at δ 166.9 and δ 96.9 were weak (~5%) but remained detectable. The assignment of the resonance at δ 155.1 to **3a-¹³C**•HOTf was confirmed independently by protonation of a sample of product **3a-¹³C** with TfOH (1 equiv) in CD₂Cl₂. The NMR tube was placed in a 45 °C oil bath and maintained at that temperature for an additional 14 h. At this time, the only dominant ¹³C resonance was that attributed to the desired product quinazoline **3a-¹³C**•HOTf (δ 155.1). An aqueous sodium hydroxide solution (1 mL, 1N) was introduced to neutralize the trifluoromethanesulfonate salts. Dichloromethane (5 mL) was added to dilute the mixture and the layers were separated. The organic layer was washed with brine (2 mL), was dried over anhydrous sodium sulfate, and was filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (eluent: 10% EtOAc in hexanes; SiO₂: 15 \times 1.5 cm) on neutralized silica gel to give the isotopically enriched quinazoline product **3a-¹³C** as a white solid (79 mg, 56%).

The ¹H, ¹³C, and ¹⁹F NMR and the in situ React-IR experiments described above are consistent with the activation of the starting amide to a reactive amidinium intermediate such as **5** that is likely to be in equilibrium with the corresponding triflate adduct **S9**.¹⁰ Nucleophilic displacement of the 2-chloropyridine could result in formation of the adduct **6** followed by cycloisomerization to **3**.¹¹ The conversion of **6** to **3** may be facilitated by net addition of 2-chloropyridinium triflate across the nitrilium ion. The product **3** serves as the second equivalent of base under the reaction conditions as described above. Rapid exchange of the trifluoromethane sulfonates is likely responsible for observation of a single broad ¹⁹F NMR resonance for the activated intermediate.

Scheme S1.



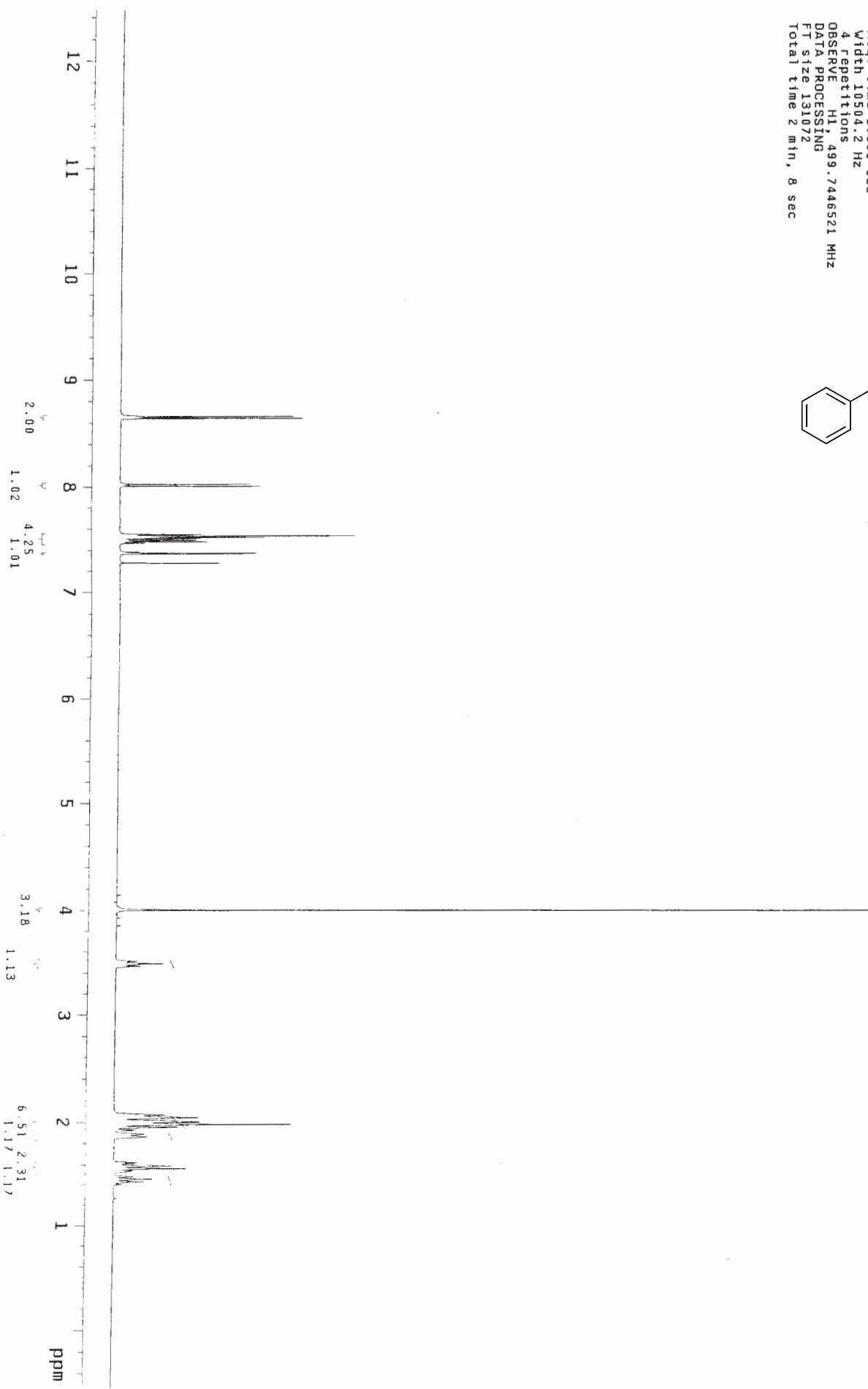
While the broad ¹³C-resonance at δ 149.8 described above is likely a time averaged value for the activated forms of the amide, the observed transient resonances at δ 166.9 and δ 96.9 may be related to derivatives of **5** and **S9**, respectively.^{12,13}

¹⁰ a) The presence of a persistent nitrilium intermediate was not observed, but its transient formation cannot be ruled out. Please see Booth, B. L.; Jibodu, K. O.; Proen  a, M. F. *Chem. Commun.* **1980**, 1151. b) For ¹⁹F NMR detection of a related anomeric trifluoromethanesulfonate adduct, see Rencurosi, A.; Lay, L.; Russo, G.; Caneva, E.; Poletti, L. *Carbohydrate Research* **2006**, 341, 903.

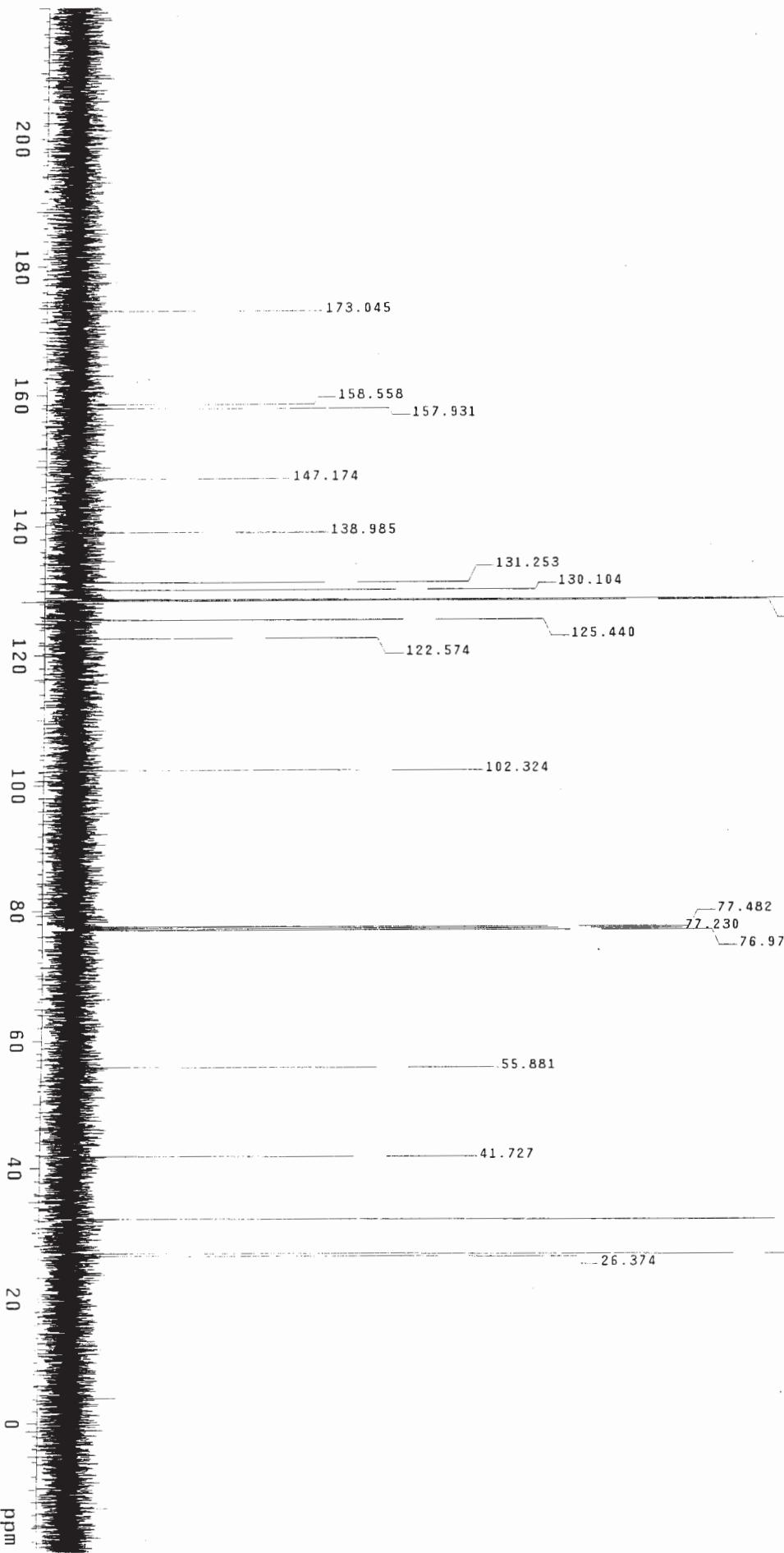
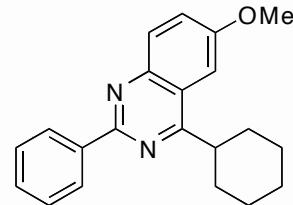
¹¹ The conversion of **6** to **3** may be facilitated by net addition of 2-chloropyridinium triflate across the nitrilium ion.

¹² For spectroscopic study of related structures, see: a) Coustard, J.-M. *Tetrahedron* **1999**, 55, 5809. b) Charette, A. B.; Mathieu, S.; Martel, J. *Org. Lett.* **2005**, 7, 5401. c) Charette, A. B.; Grenon, M. *Can. J. Chem.* **2001**, 79, 1694.

¹³ Unlike the amidinium derivatives of pyridine (see references 12b and 12c), we expect those derived from 2-chloropyridine to be far more electrophilic, allowing the formation of adducts and disfavoring a persistent doubly cationic amidinium ion. An alternative to **5** may be the hydrogen bonded complex of trifluoromethanesulfonic acid as opposed to the fully protonated form.



Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "rocky"
 PULSE SEQUENCE
 Relax. delay 0.500 sec
 Pulse 65.4 degrees
 Acq. time 1.736 sec
 Width 37735.8 Hz
 40 repetitions
 OBSERVE C13, 125.783274 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 Continuous on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 1 minutes



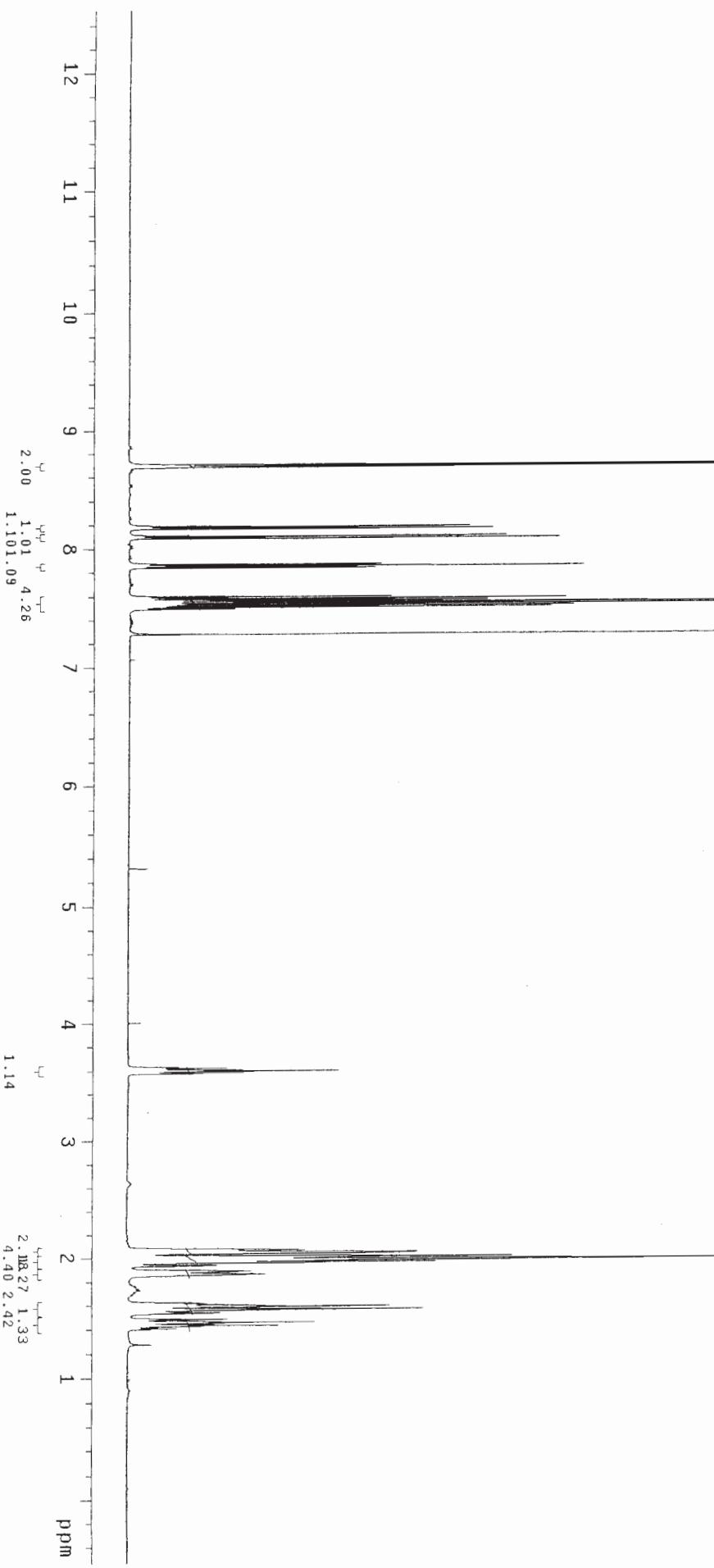
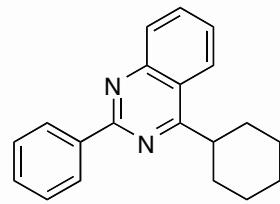
Pulse Sequence: $\text{52}\mu\text{t}$
 Solvent: CDCl_3
 Ambient temperature

```

File: mh-IV-25c1e
INOVA-500 "bullwinkle"

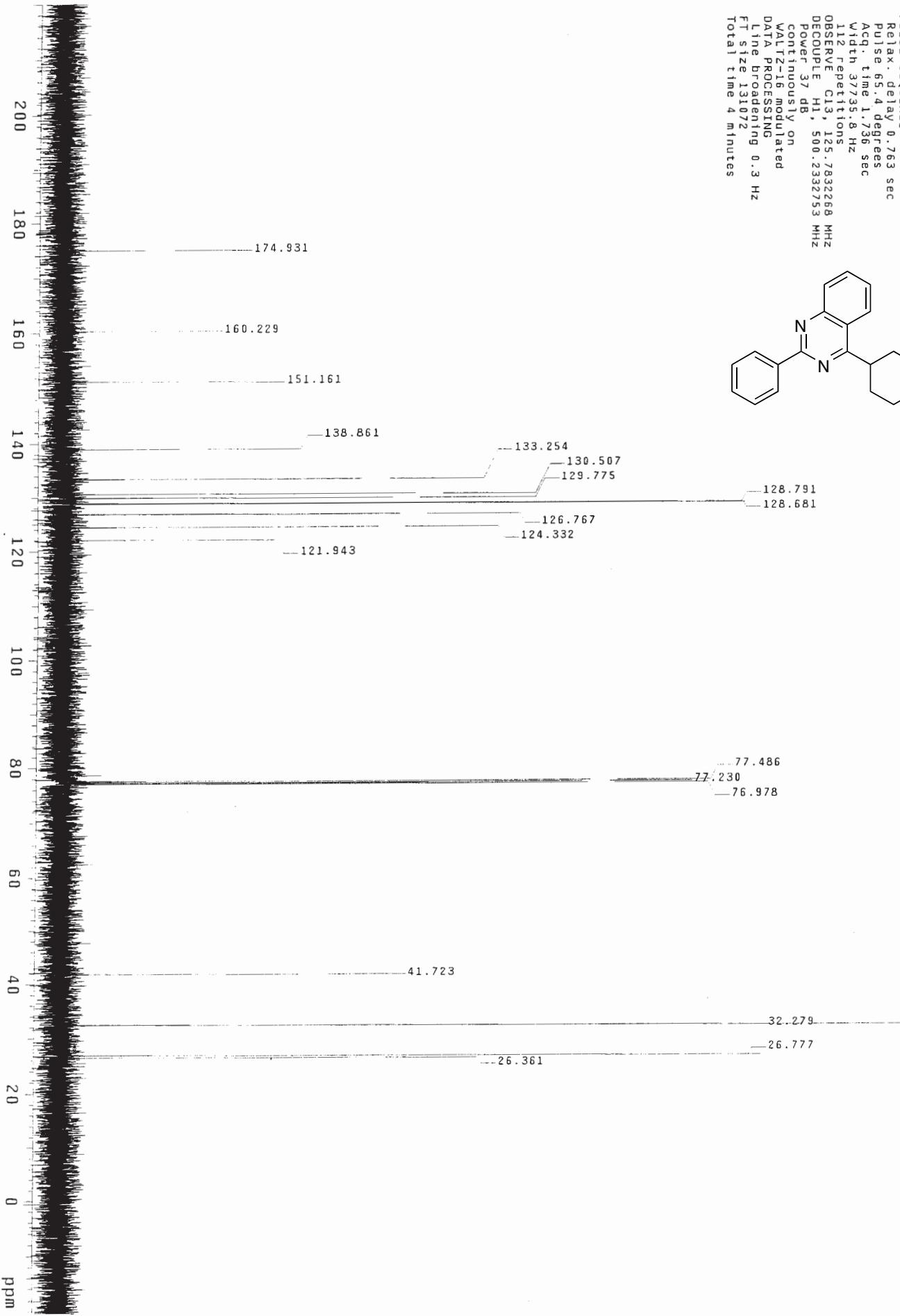
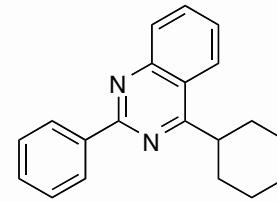
Relax. delay 5.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
g repeat time
OBSERVE H1,499.7446521 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 8 sec

```



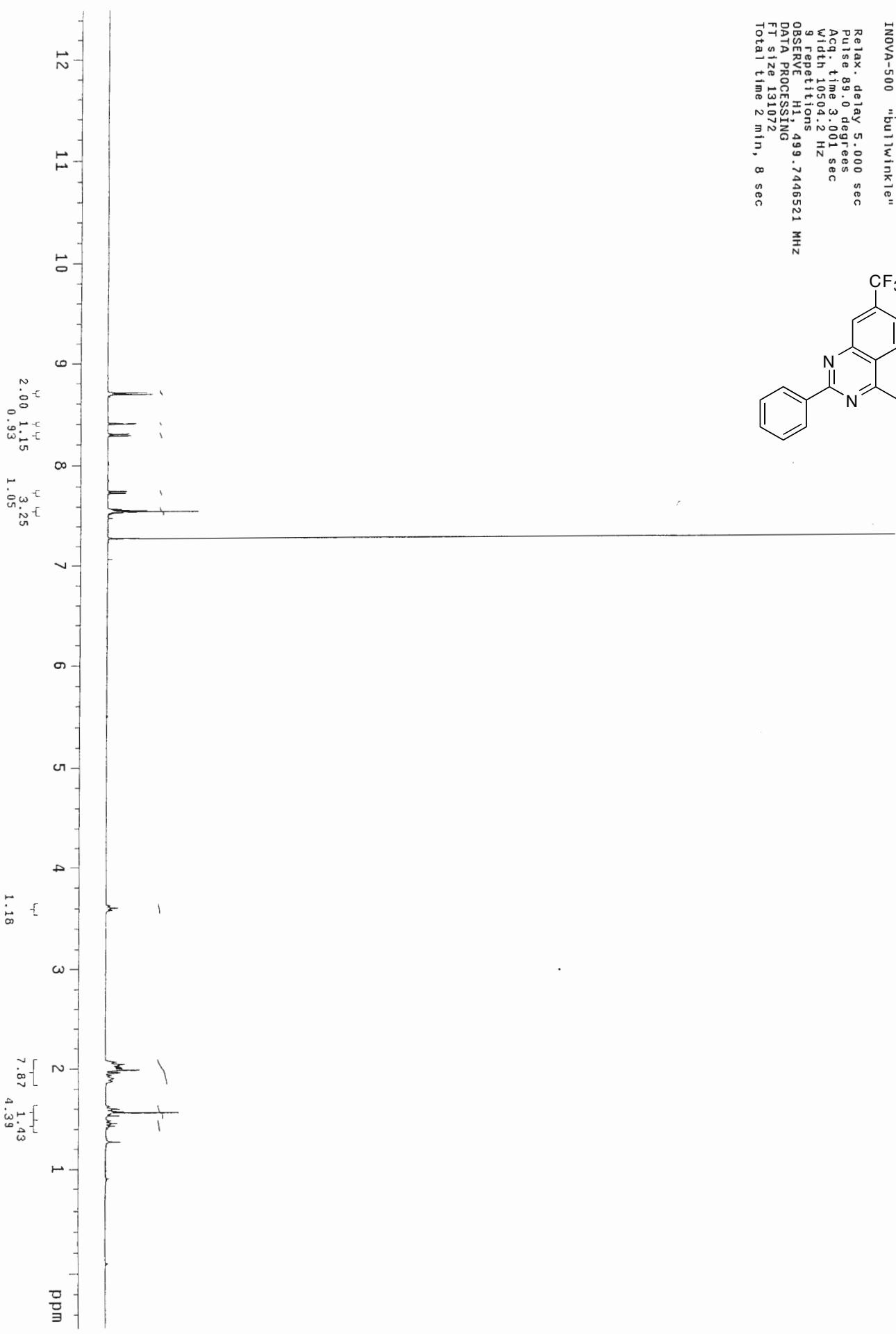
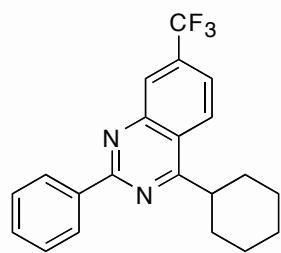
S34/S80

Solvent: CDCl₃
Ambient temperature
User: 1-14-87
INDA-500 "Rocky"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acc. time 1.736 sec
Width 37/35.8 Hz
112 repetitions
OBSERVE C13, 125.7832268 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WATER-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 4 minutes



Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 width 10504.2 Hz
 9 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



Pulse Sequence: s2pul1

Solvent: CDCl₃

Ambient temperature

User: 1-14-87

File: mh-1V-265carbon

INOVA-500 "zippy"

PULSE SEQUENCE

Relax. delay 0.763 sec

Pulse 65.4 degrees

Acq. time 1.736 sec

Width 3775.8 Hz

368 repetitions

OBSERVE C13, 125.783268 MHz

DECOUPLE H1, 500.2332753 MHz

Power 37 dB

continuously on

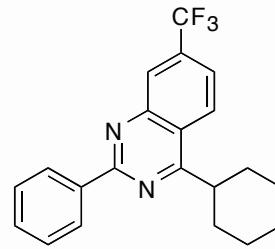
WALTZ16 modulated

DATA PROCESSING

Line broadening 0.3 Hz

FT size 131072

Total time 6966 hr, 51 min, 36 sec



131.090

128.948

128.797

125.712

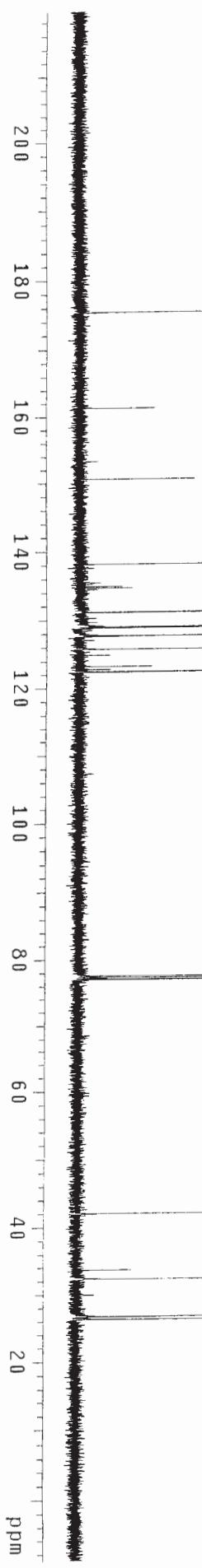
77.489
77.233
76.981

41.950

32.278

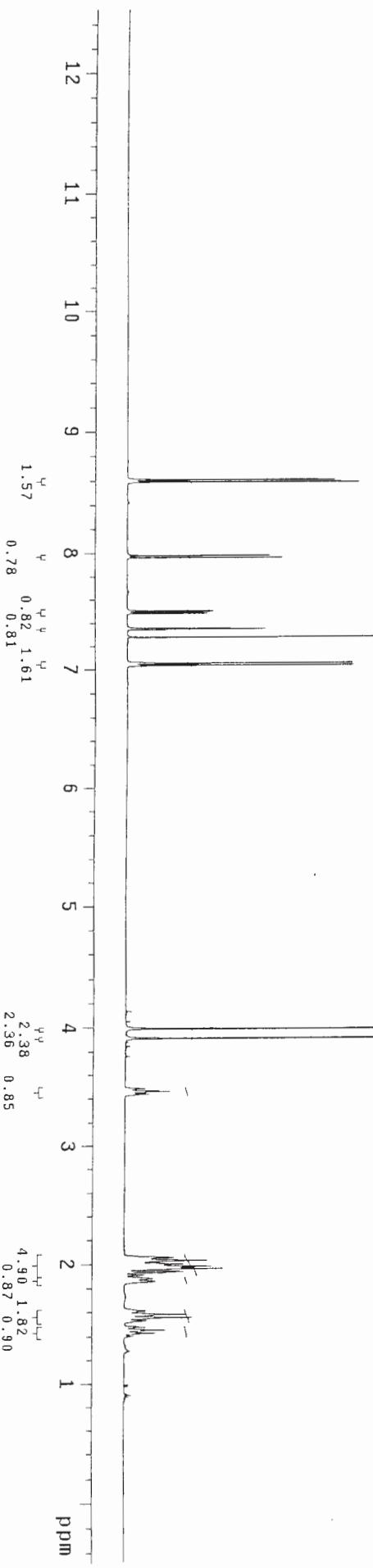
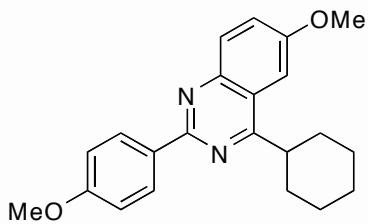
26.671

26.259



Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Time 3.001 sec
 Acq. width 10504.2 Hz
 7 repetitions
 OBSERVE H1 499.7446521 MHZ
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



S38/S80

Solvent: CDCl₃
Ambient temperature
User: 1-14-87
INNOVA-500 "Rocky"

PULSE SEQUENCE

Relax. delay 0.763 sec

Pulse 65.4 degrees

Acc. time 1.736 sec

Width 3735.8 Hz

40 repetitions

DESYERVE C13, 125.7832297 MHz

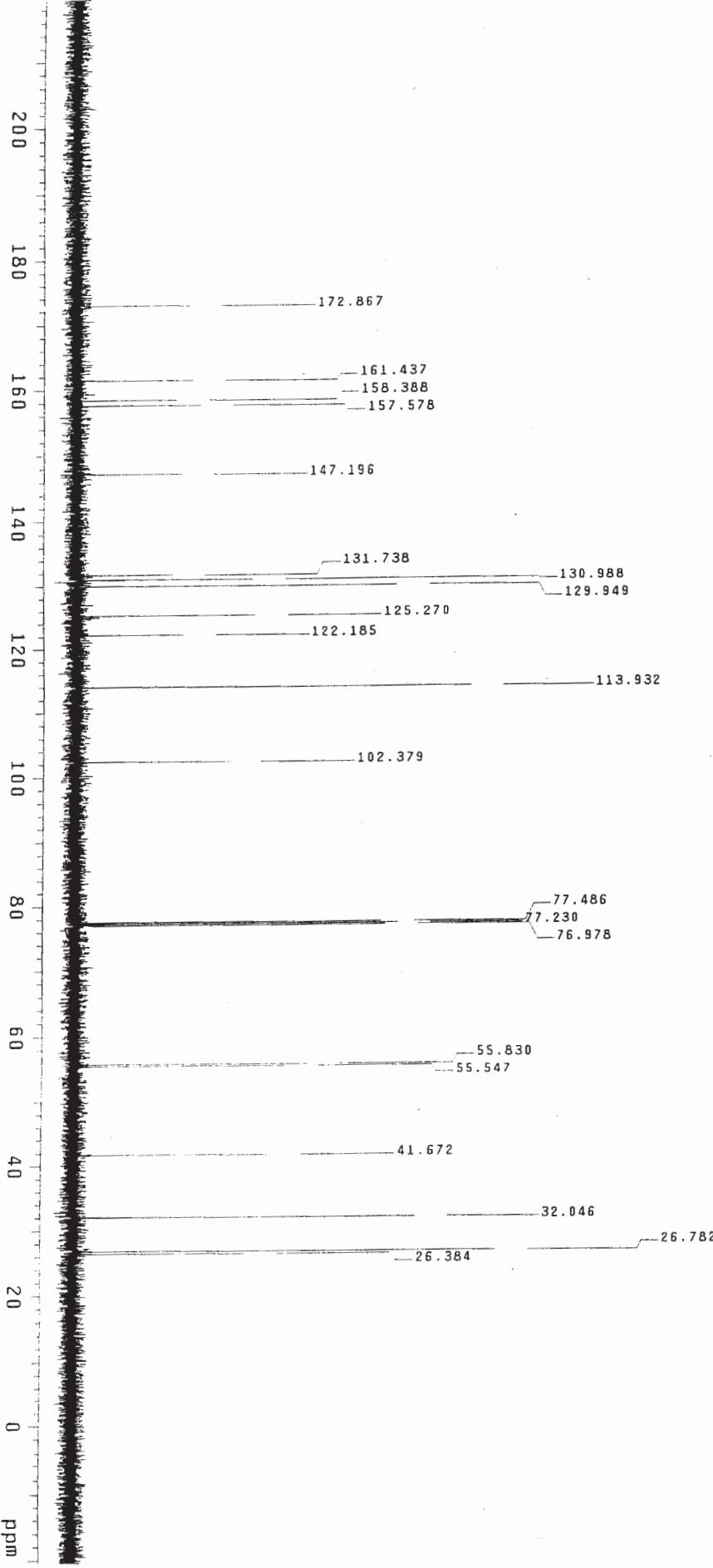
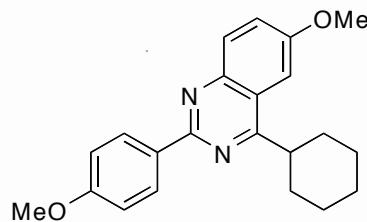
DECOUPLE H1, 500.28332753 MHz

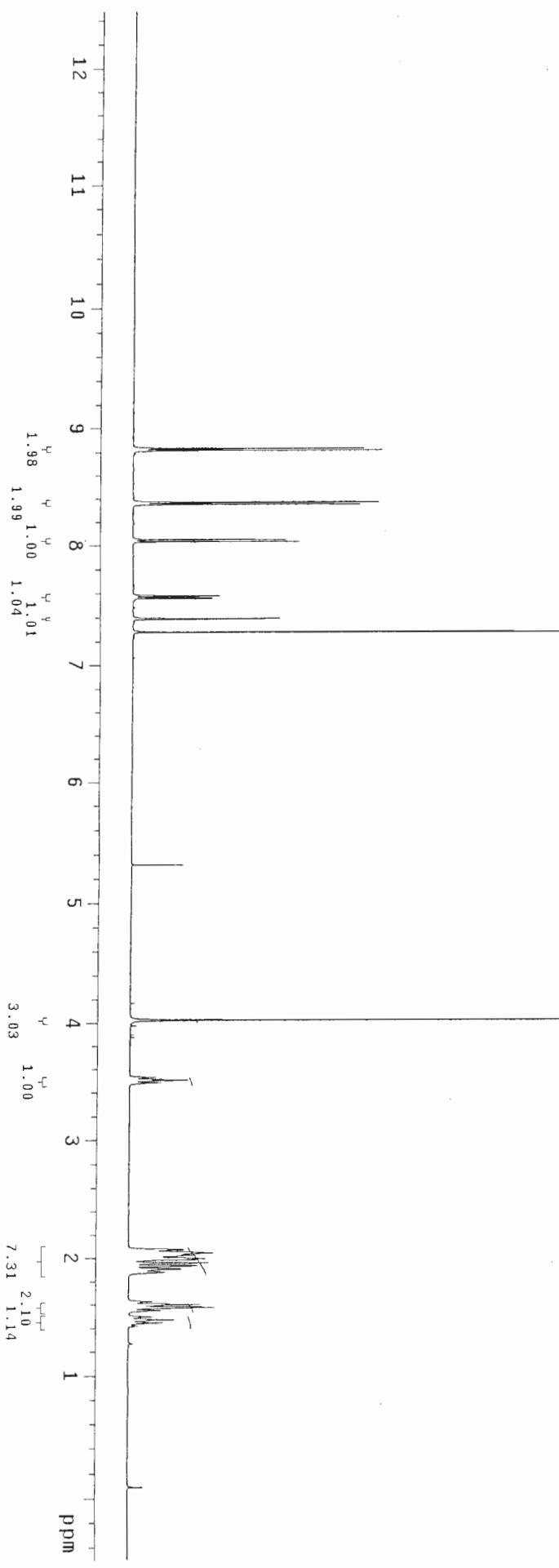
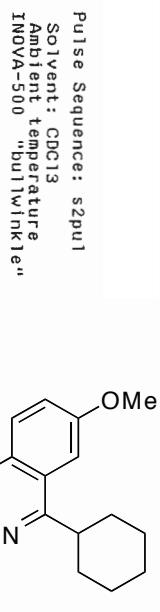
Power 37 dB

Line broadening 0.3 Hz

FT size 131072

Continuous on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 1 minutes

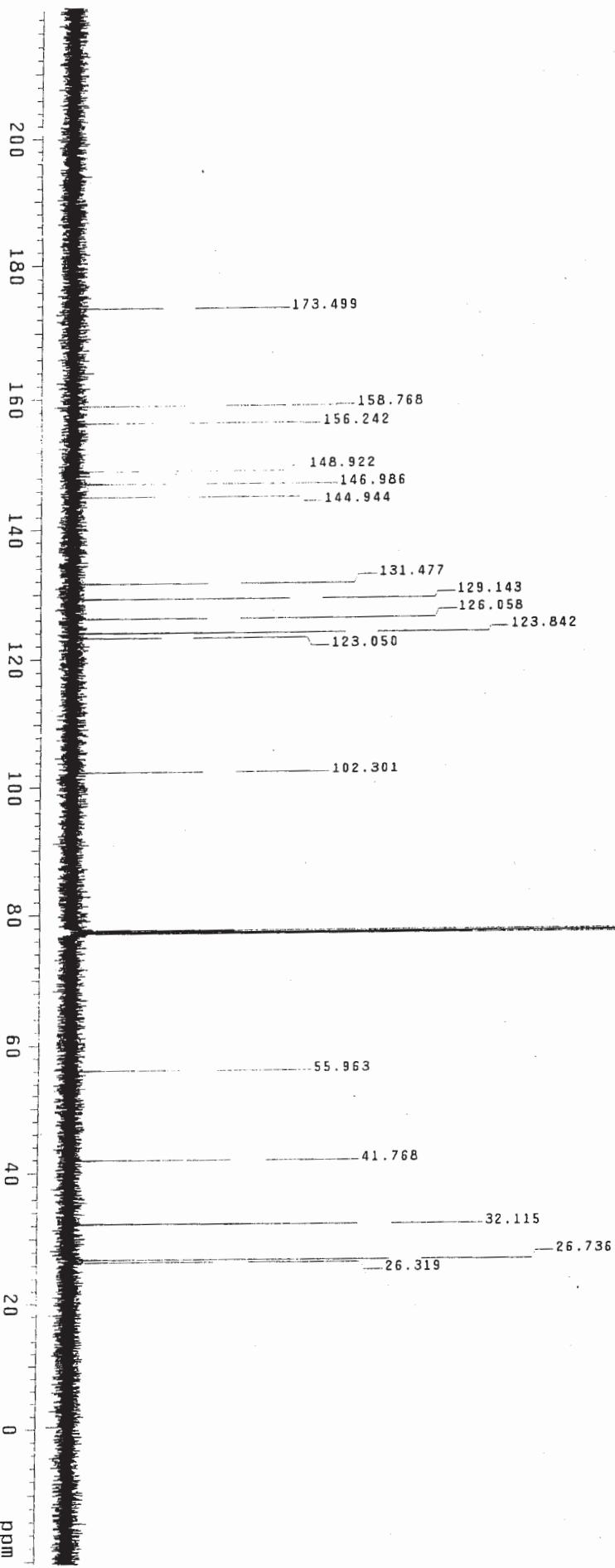
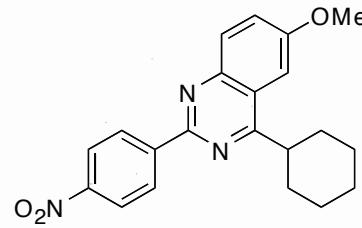




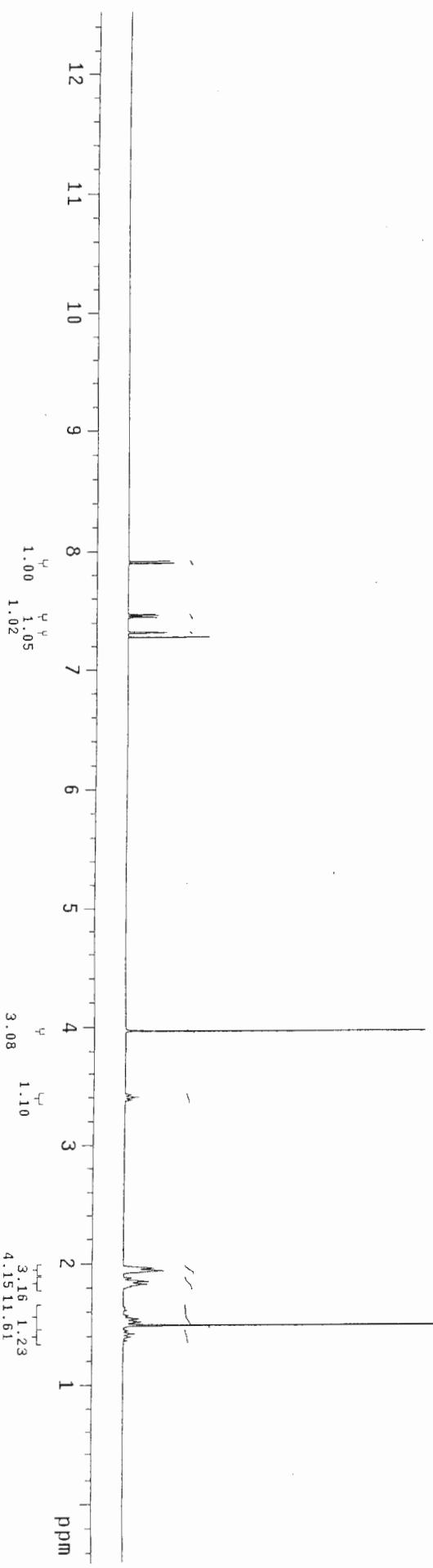
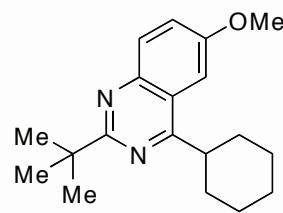
mh-IV-274

Solvent: CDCl₃
 Ambient temperature
 User: 1-4-87
 File: mh-IV-274carbon
 INNOVA-500 "rocky"

PULSE SEQUENCE
 Relax. delay 0.763 sec
 Pulse 65.4 degrees
 Acq. time 1.736 sec
 Width 37735.8 Hz
 648 repetitions
 OBSERVE C13, 125.7832268 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WAL12-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 27 minutes



Pulse Sequence: s2pul

Solvent: CDCl₃
Ambient temperature
INOVIA-500 "Bruylants"Relax. delay 5.000 sec
Pulse 89.0 degrees
Aq. time 3.001 sec
Width 10504.2 Hz
5 repetitions
OBSERVE H1, 499.7446521 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 8 sec

Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "Rocky"

PULSE SEQUENCE

Relax. delay 0.500 sec

Pulse 65.4 degrees

Acq. time 1.736 sec

Width 3735.8 Hz

72 repetitions

OBSERVE C13, 125.7832274 MHz

DECOUPLE H1, 500.2332753 MHz

Power 37 dB

CONTINUOUSLY ON

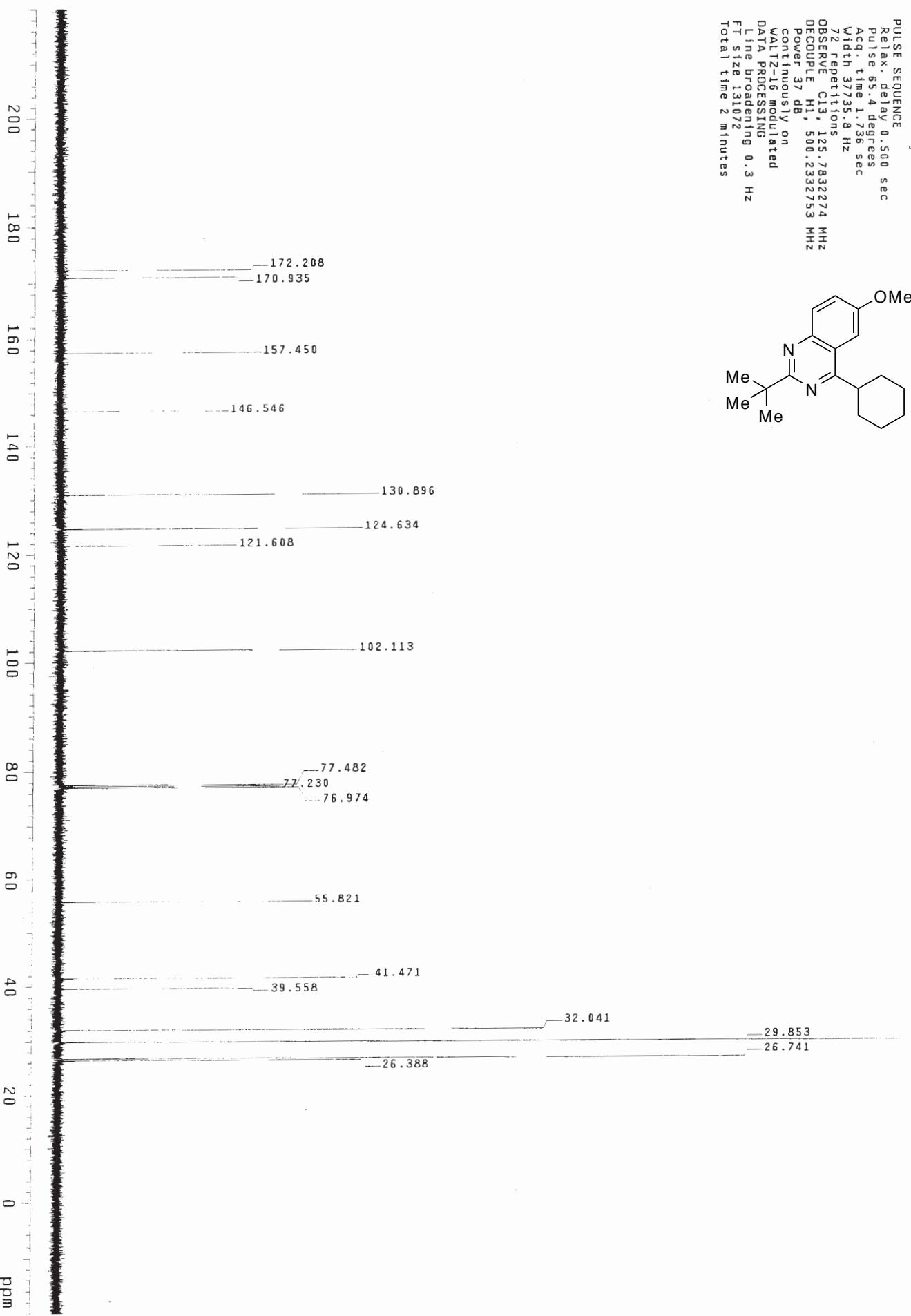
WALTZ-16 MODULATED

DATA PROCESSING

LINE BROADENING 0.3 Hz

FT SIZE 131072

TOTAL TIME 2 MINUTES



Pulse Sequence: s2pu1

Solvent: CDCl₃

Ambient temperature

File: mh-IV-223fr12-22

INOVA-500 "Zippy"

PULSE SEQUENCE

Relax. delay 5.000 sec

Pulse 89.0 degrees

Acq. time 3.001 sec

Width 1.0504.2 Hz

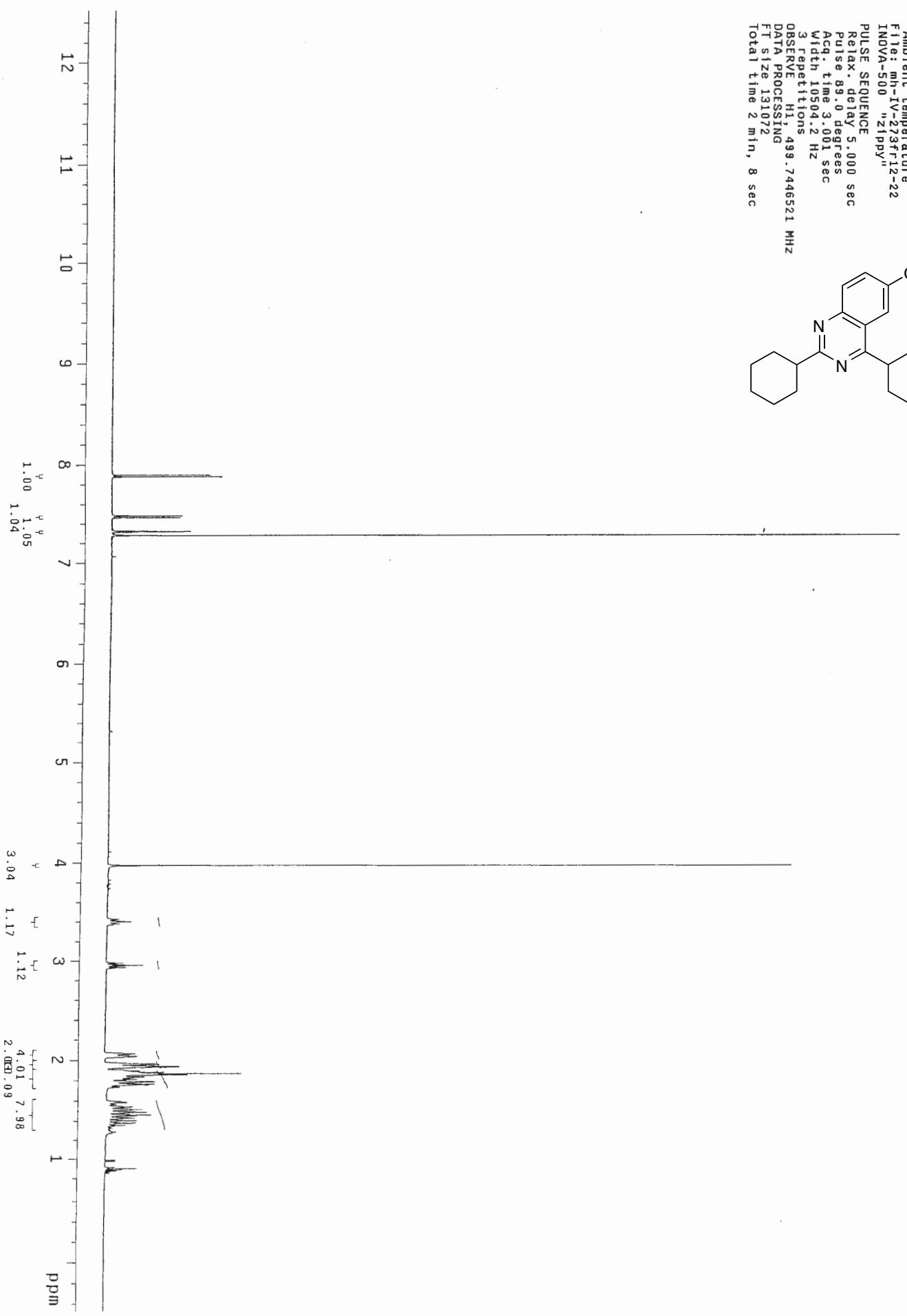
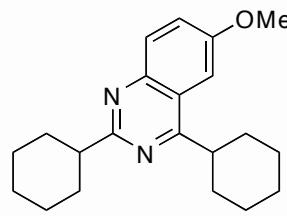
3 repetitions

OBSERVE H1, 499.7446521 MHz

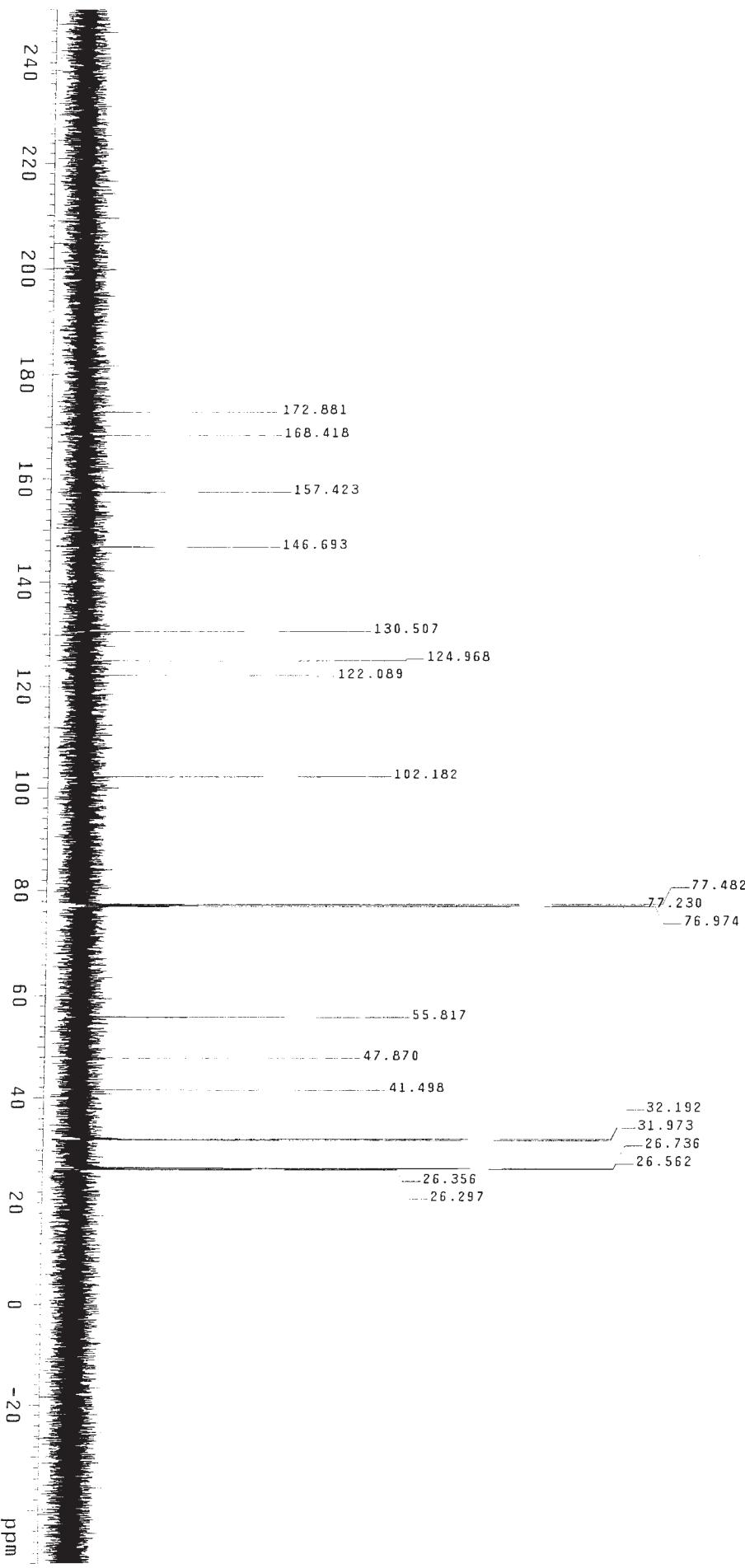
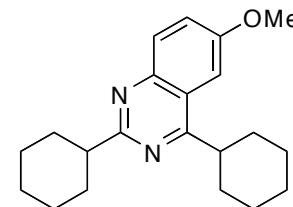
DATA PROCESSING

FT size 131072

Total time 2 min, 8 sec



Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "Rocky"
 PULSE SEQUENCE
 Relax. Delay 0.763 sec
 Pulse 65.4 degrees
 Acc. time 1.736 sec
 Width 37.35.8 Hz
 88 repetitions
 OBSERVE C13, 125.7832286 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT Size 131072
 Total time 3 minutes

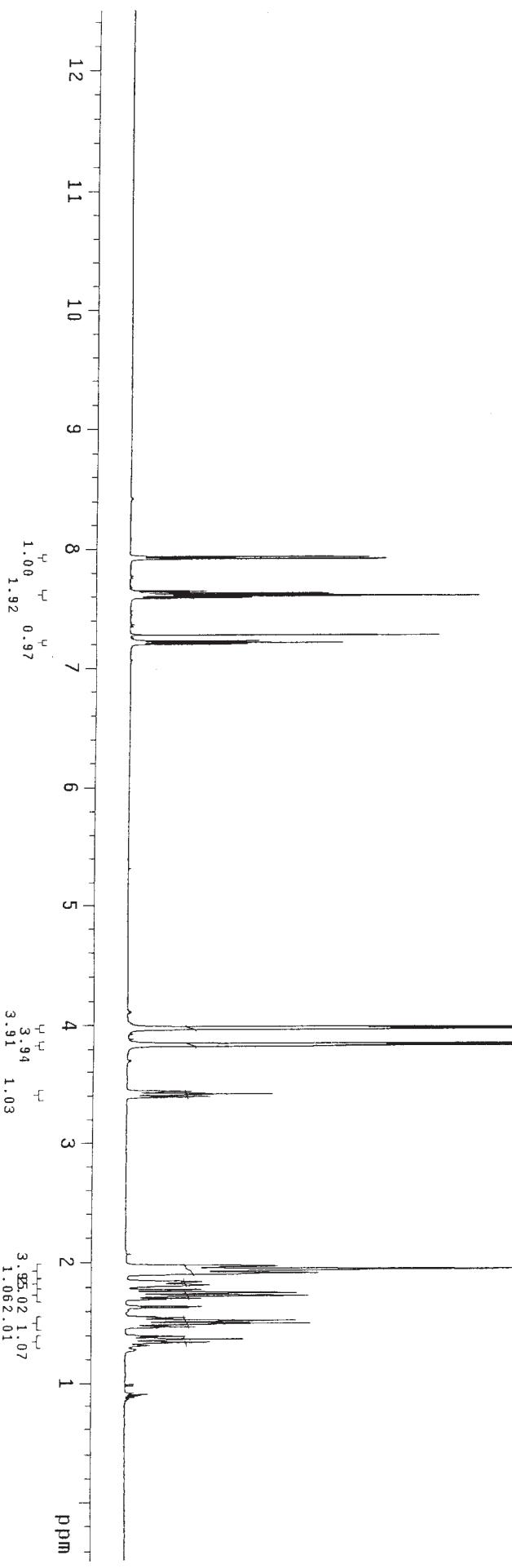
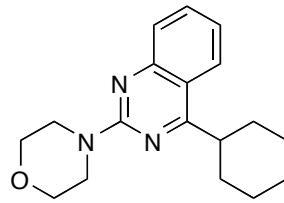


Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 File: mh-v-65clean
 INova-500 "bulwinkle"

```

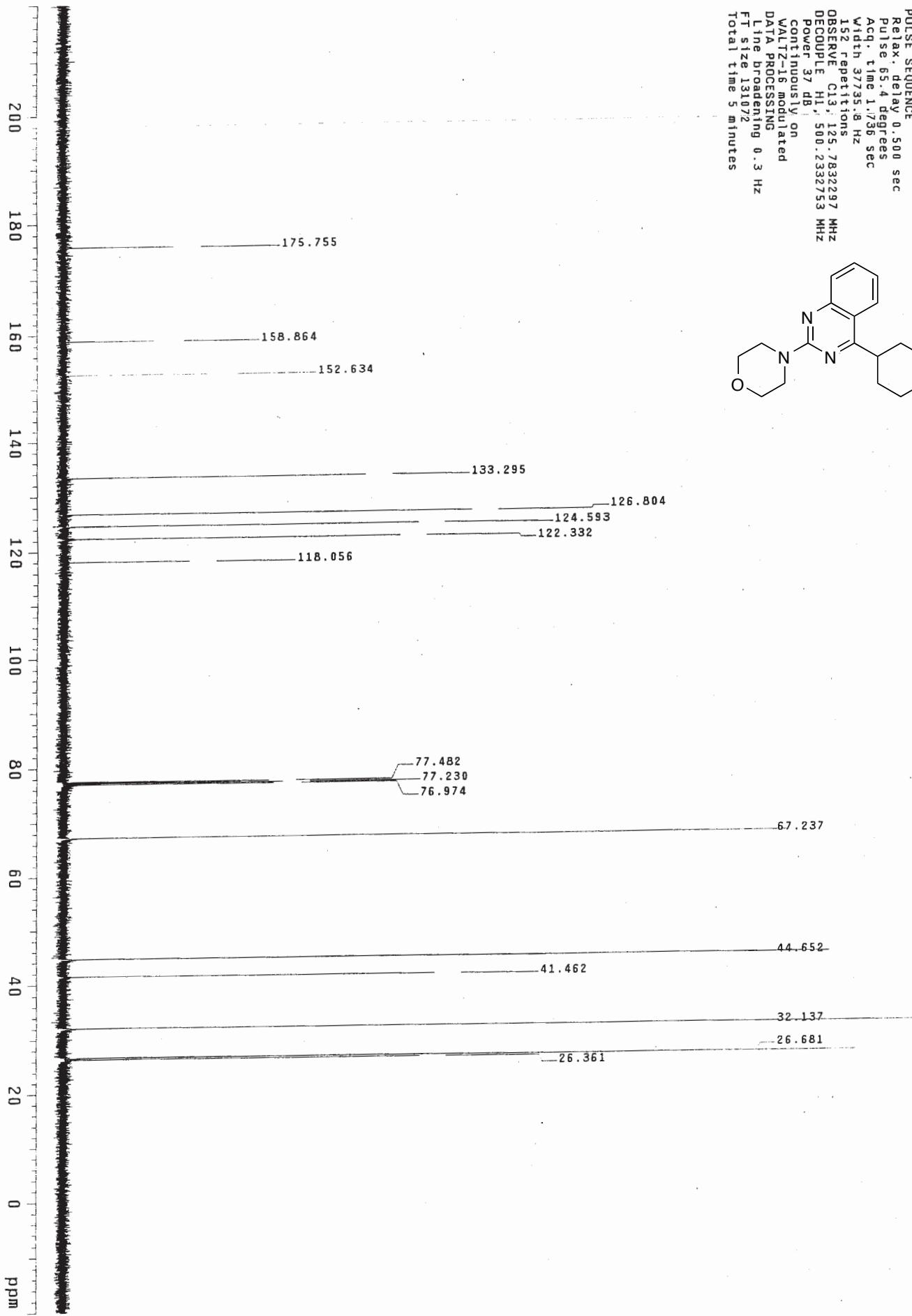
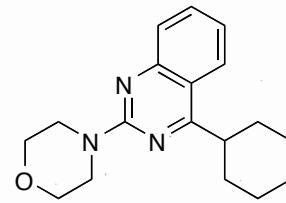
Relax. delay 5.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 105.04.2 Hz
7 repetitions
OBSERVE H1 499.7446521 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 8 sec

```



Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "rocky"

PULSE SEQUENCE
 Relax. delay 0.500 sec
 Pulse 65.4 degrees
 Acc. time 1.736 sec
 Width 37.351.8 Hz
 152 repetitions
 OBSERVE C13; 125.7832297 MHz
 DECOUPLE H1; 500.2332753 MHz
 Power 37 dB
 CONTINUOUSLY ON
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 5 minutes



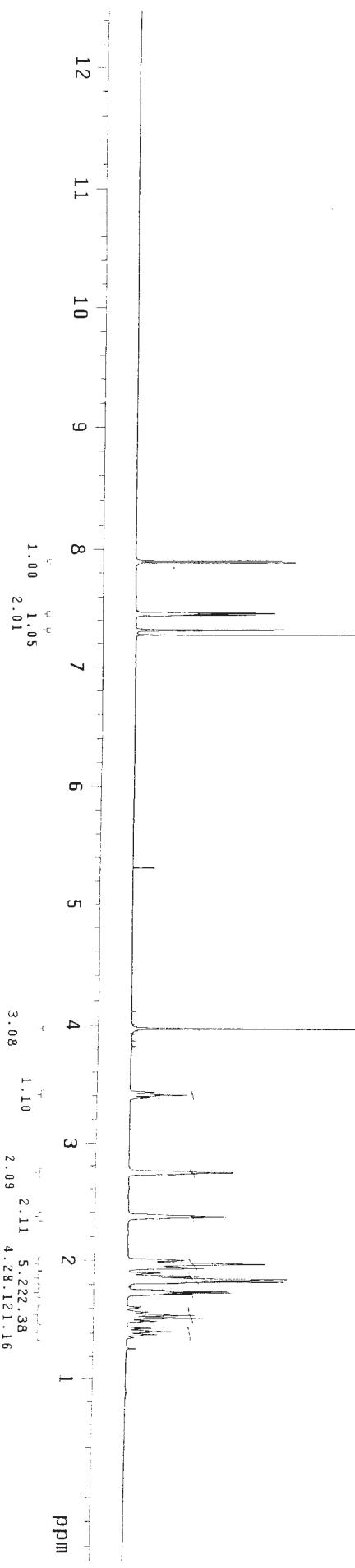
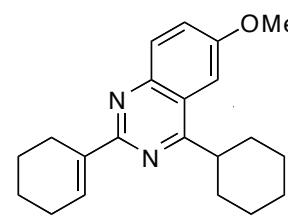
Pulse Sequence: s2pu1

Solvent: CDCl₃
Ambient temperature

File: mh-10-287
INOVA-500 "zippy"

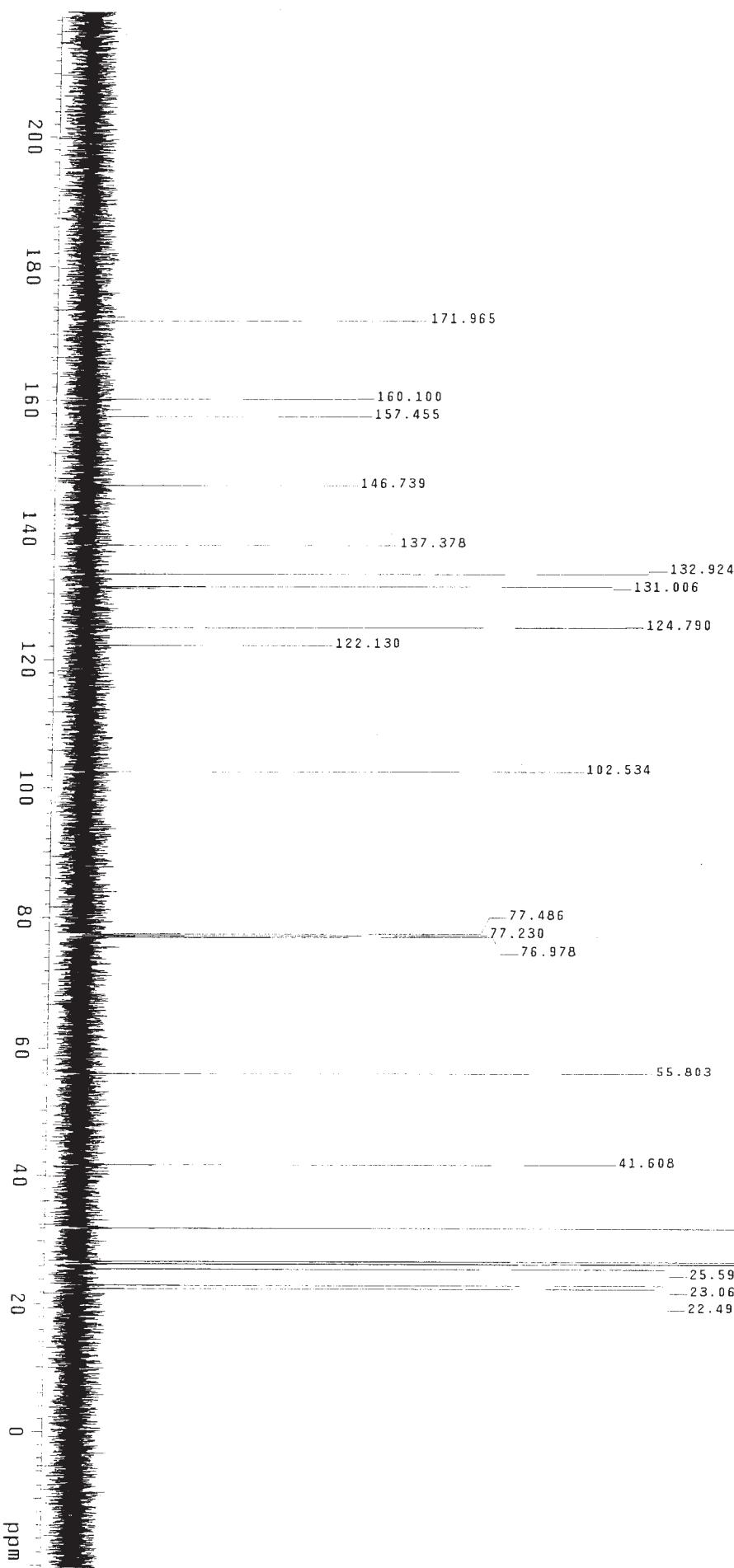
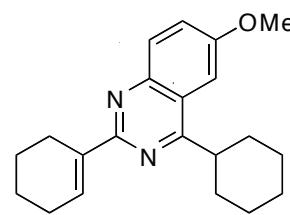
PULSE SEQUENCE

Relax. delay 5.000 sec
pulse 89.0 degrees
Acq. time 3.001 sec
Width 10544.2 Hz
2 repetitions
OBSERVE H1, 499.7446521 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 8 sec

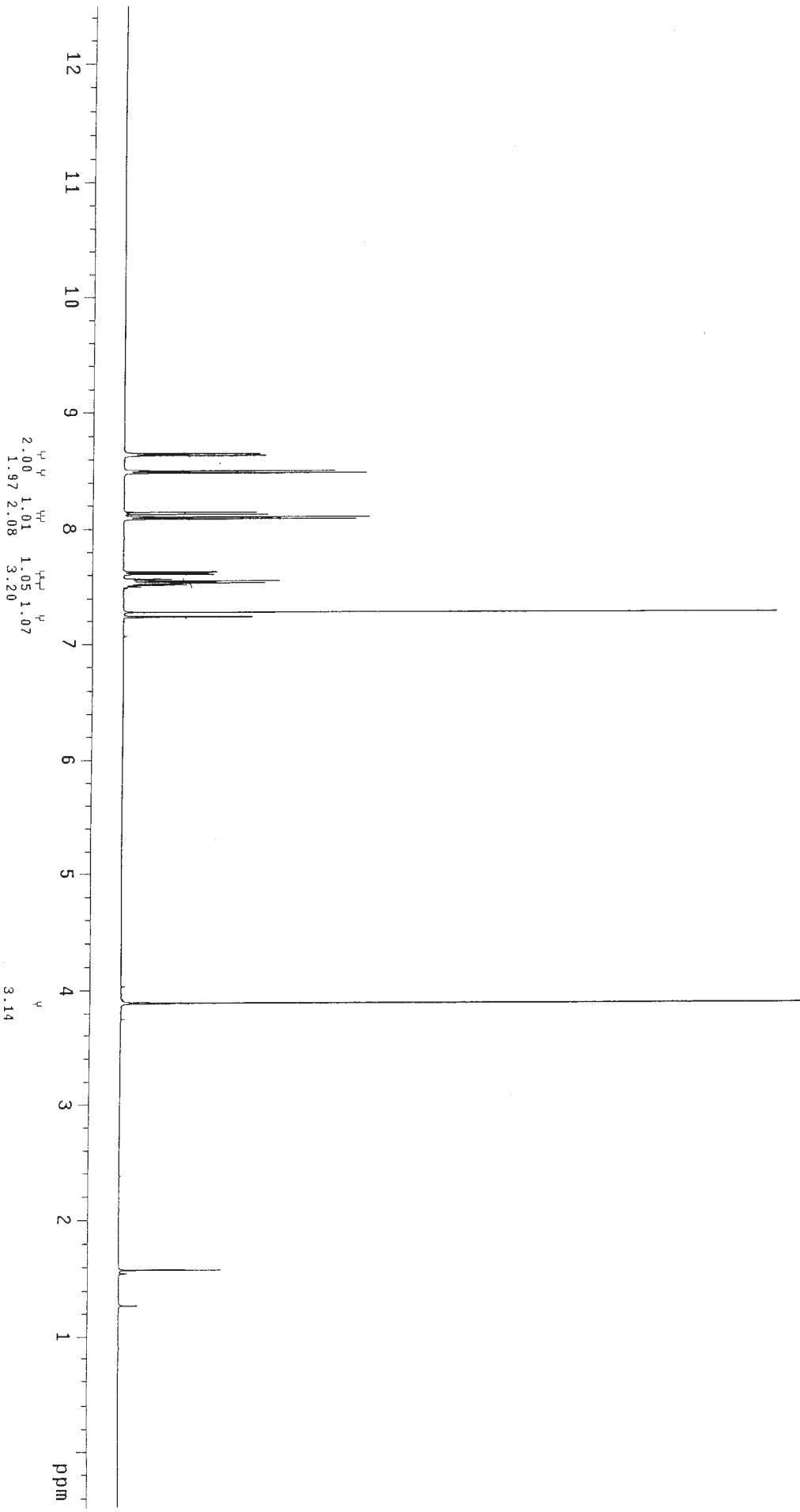
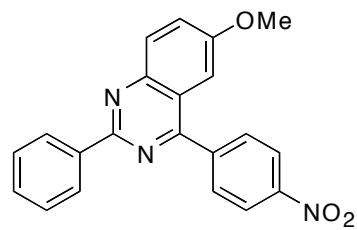


Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INOVA-500 "Rocky"

PULSE SEQUENCE
 Relax. delay 0.763 sec
 Pulse 65.4 degrees
 Acc. time 1.736 sec
 Width 37.35.8 Hz
 48 repetitions
 OBSERVE C13, 125.783286 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 VALT2-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 2 minutes



Pulse Sequence: s2pu1

Solvent: CDCl₃
Ambient temperature
INOVA-500 "bulletwinkle"Relax. delay 5.000 sec
Pulse 89.0 degrees
Acc. time 3.001 sec
width 1504.2 Hz
9 repetitions
OBSERVE H1, 499.7446521 MHz
DATA PROCESSING 499.7446521 MHz
FT size 131072
Total time 2 min, 8 sec

Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "Rocky"

PULSE SEQUENCE

Relax. delay 0.500 sec

pulse 65.4 degrees

Acq. time 1.736 sec

Width 37.35.8 Hz

160 repetitions

OBSERVE C13, 125.7832274 MHz

DECUPLE H1, 500.2332753 MHz

Power 37 dB

continuously on

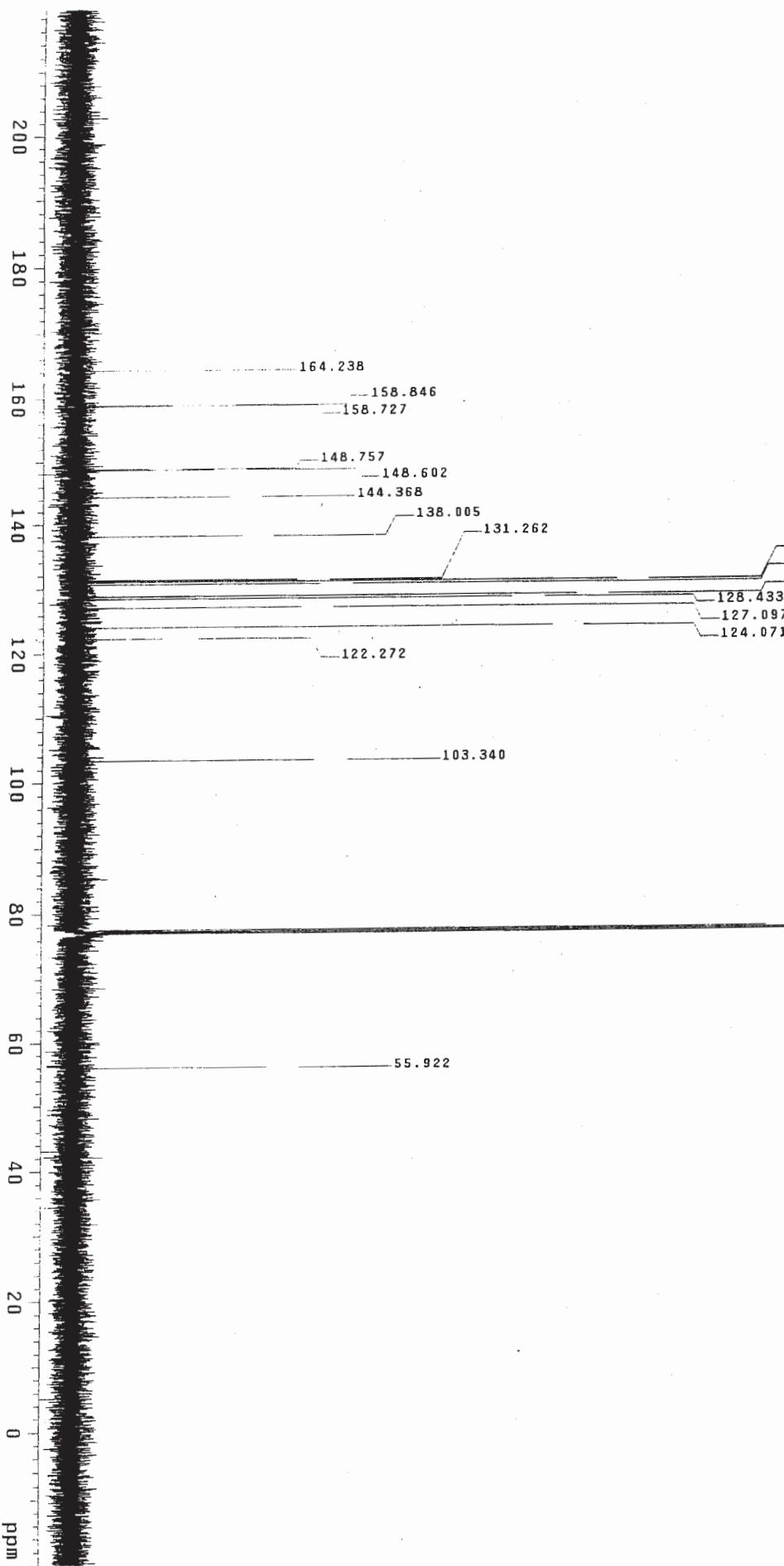
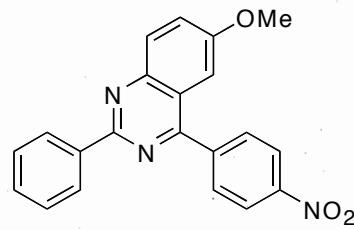
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.3 Hz

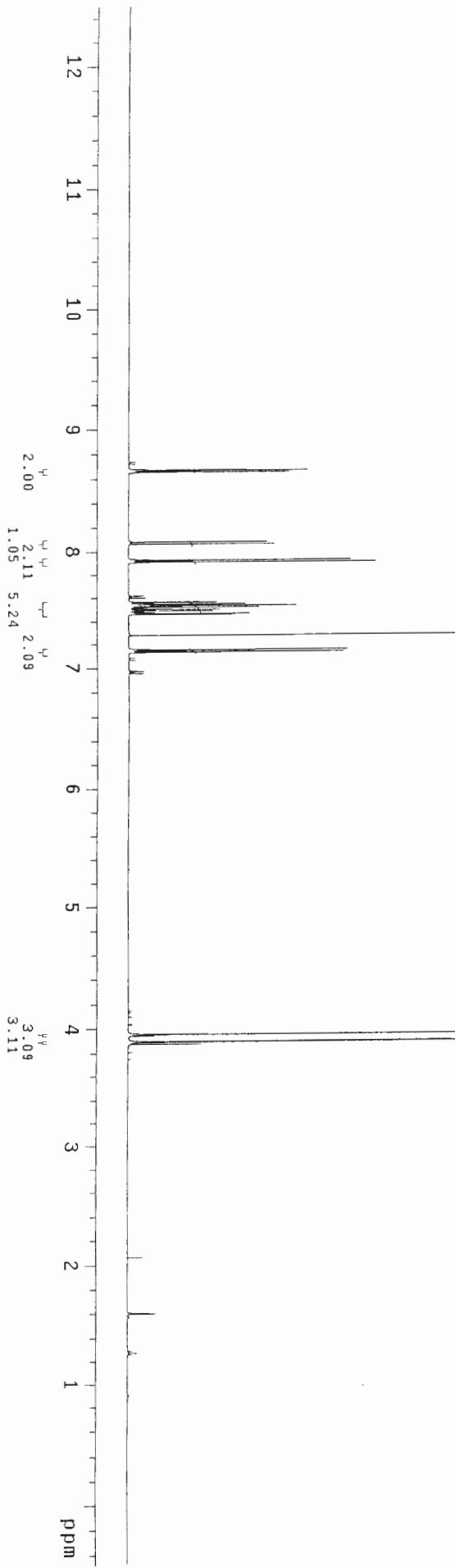
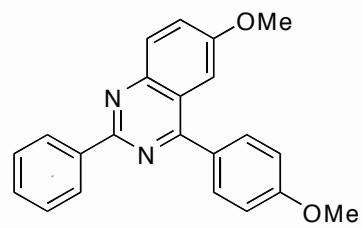
FT size 131024

Total time 6 minutes



Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 Width 10504.2 Hz
 9 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "rocky"

PULSE SEQUENCE

Relax. delay 0.500 sec

Pulse 65.4 degrees

Acc. time 1.736 sec

Width 37735.8 Hz

32 repetitions

OBSERVE C13, 125.7832360 MHz

DECOPPLE H1, 500.2332753 MHz

Power 37 dB

continuously on

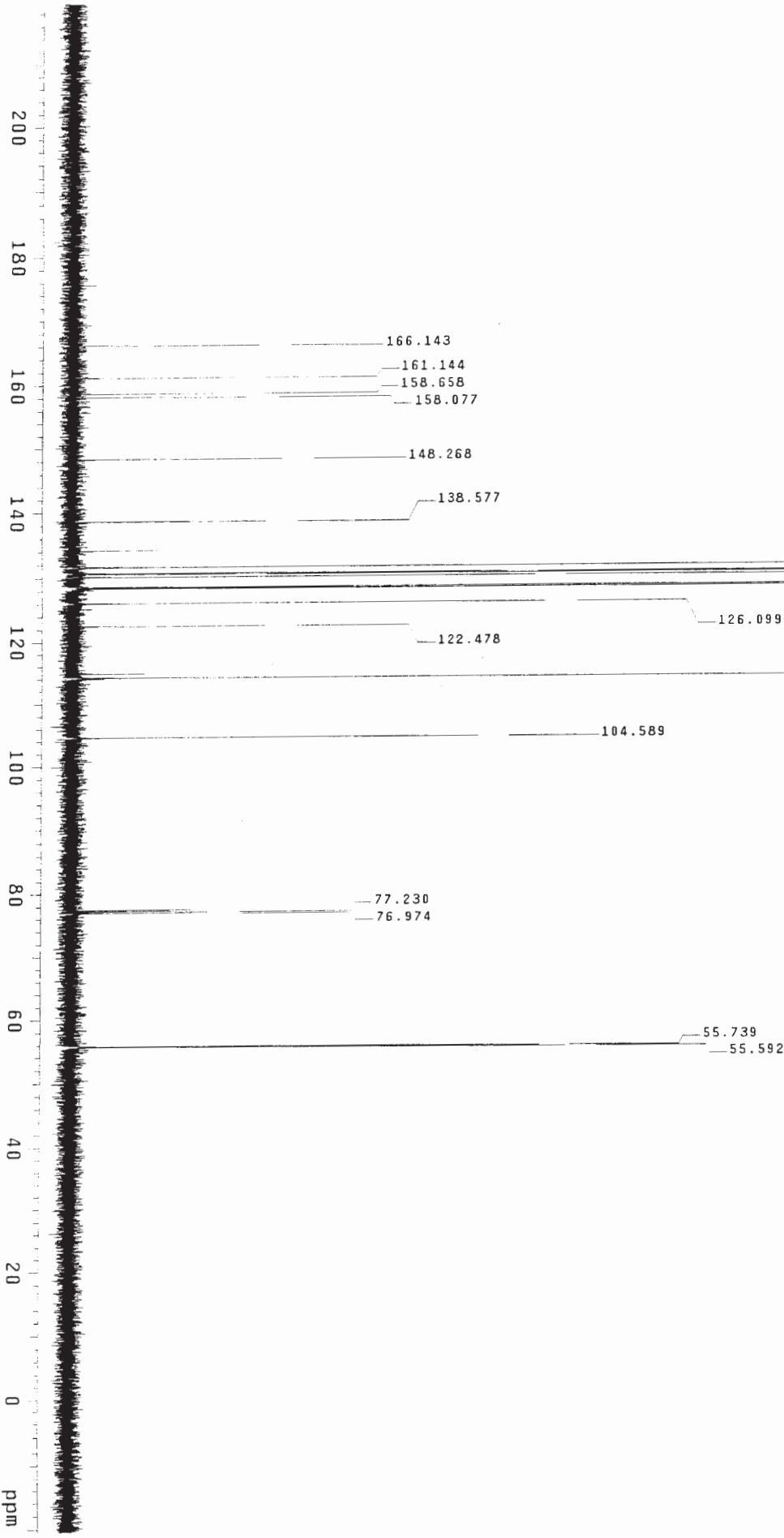
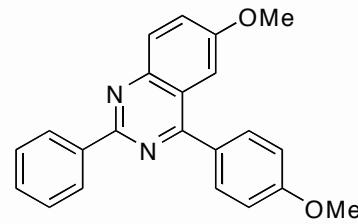
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.3 Hz

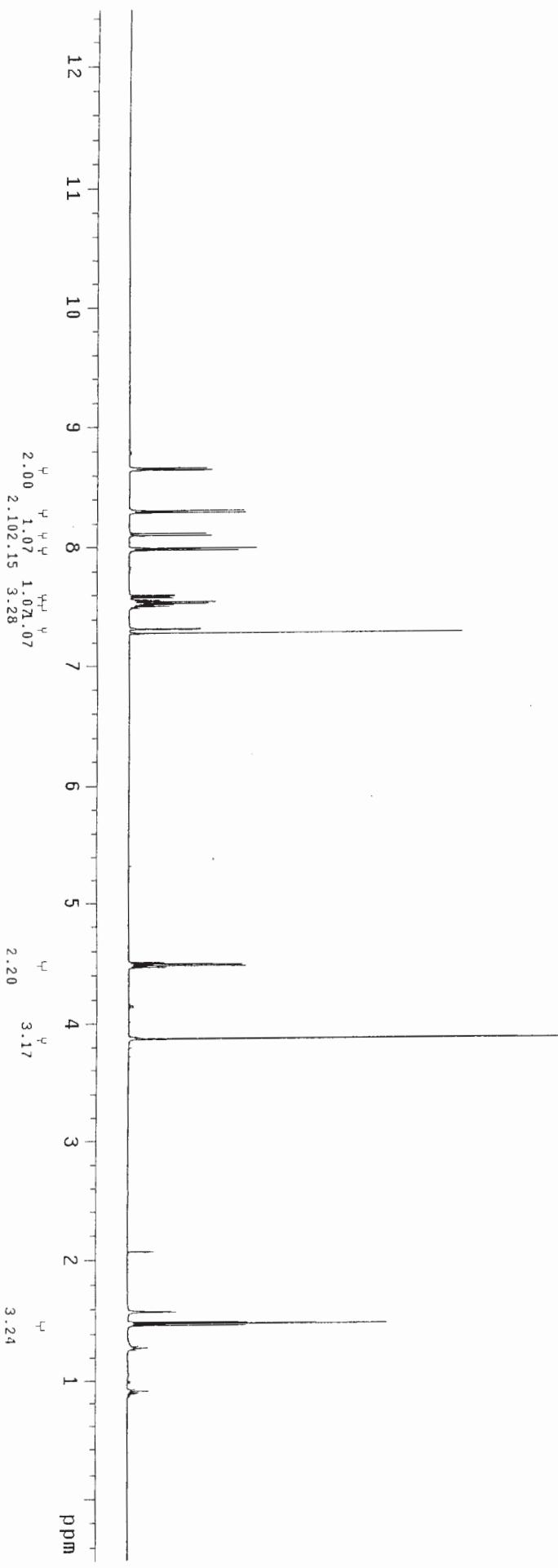
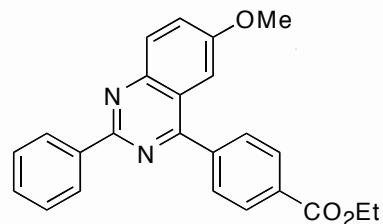
FT size 131072

Total time 1 minute



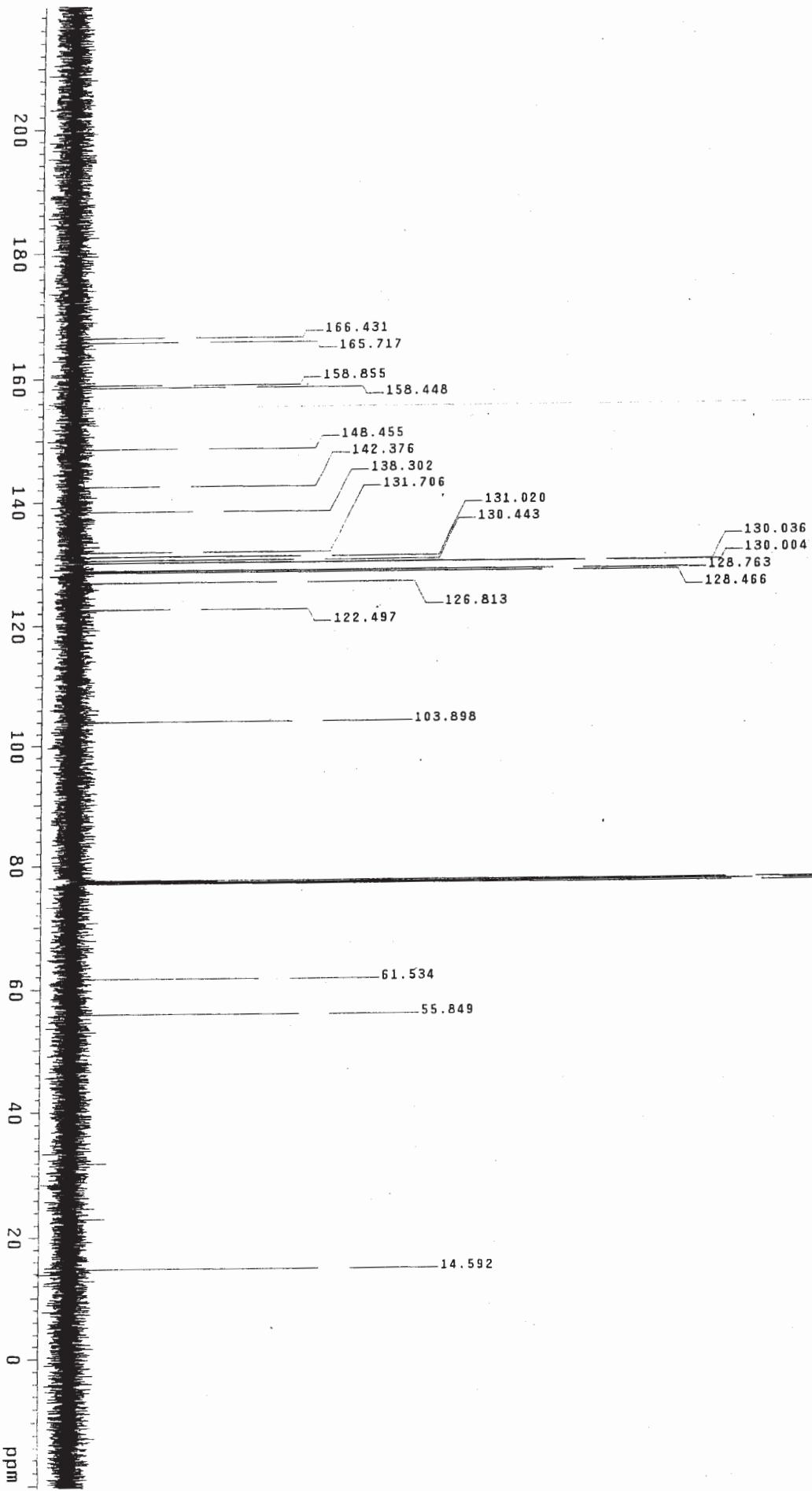
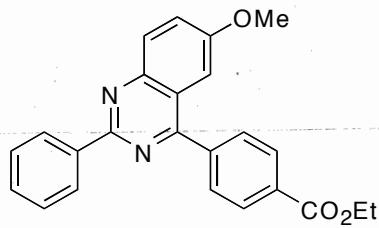
Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INNOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 pulse 89.0 degrees
 Acq. time 3.001 sec
 width 10504.2 Hz
 10 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



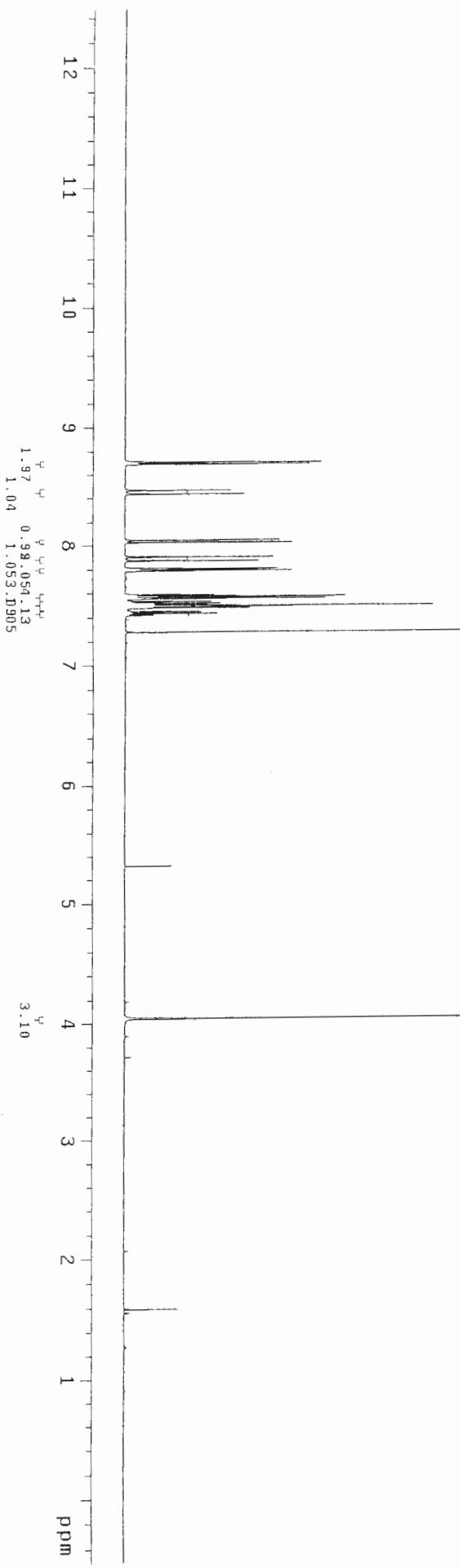
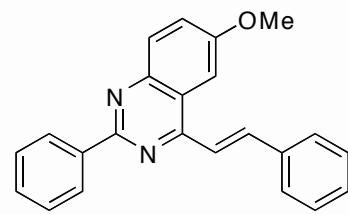
Solvent: CDCl₃
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"
PULSE SEQUENCE

Pulse delay 0.500 sec
 ACQ. TIME 1.736 SEC
 WIDTH 37735.8 Hz
 120 repetitions
 OBSERVE GL3, 125.7832274 MHz
 DECOUPLE HI, 500.2332753 MHz
 POWER 37 dB
 continuously on
 WAIT-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 4 minutes



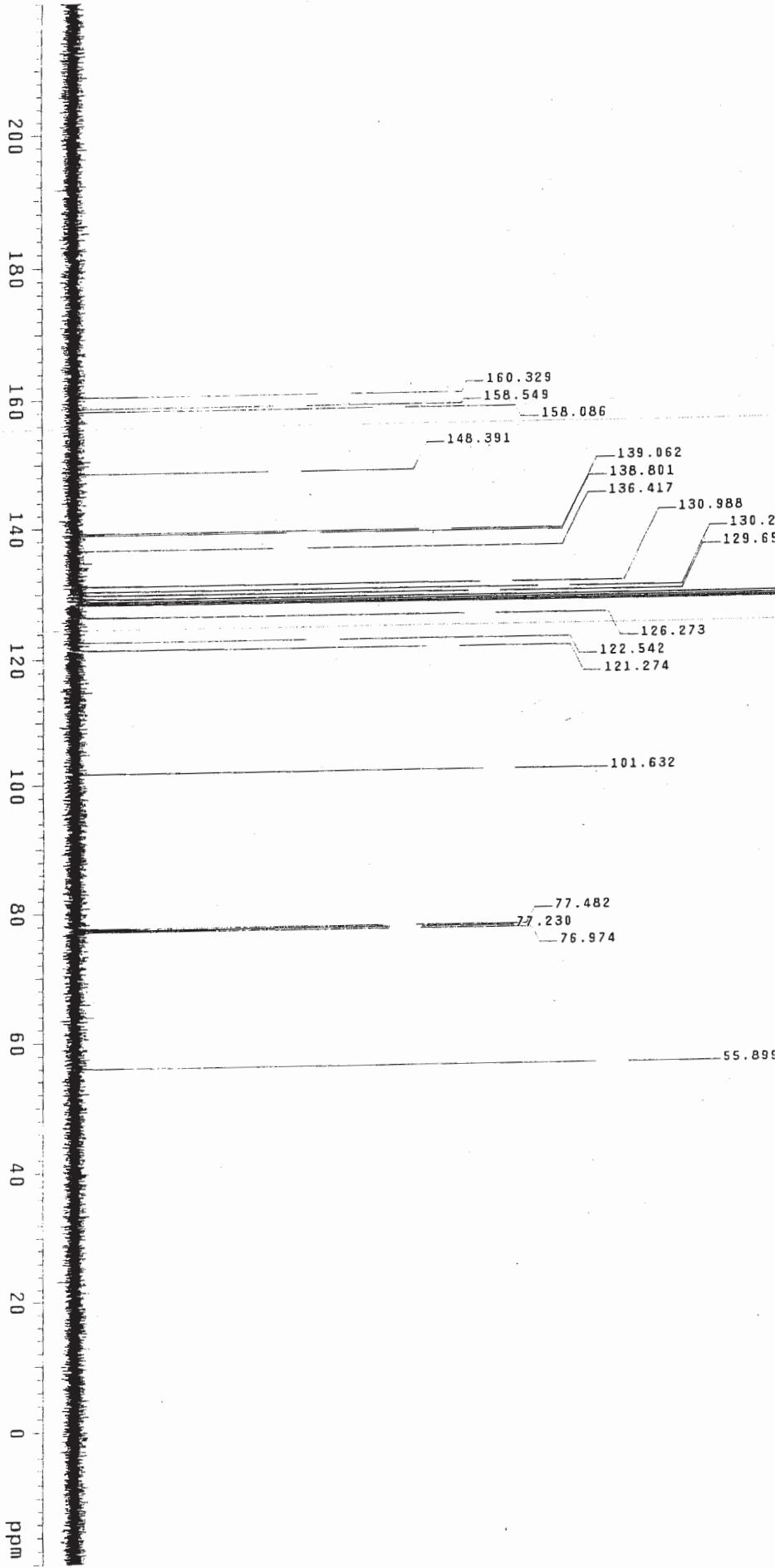
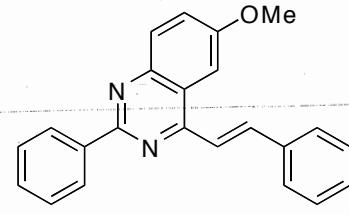
Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INNOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 pulse 89.0 degrees
 pulse width 1054.2 Hz
 Acc. time 3.001 sec
 7 repetitions
 OBSERVE H1 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



Solvent: CDCl_3
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "Rocky"

PULSE SEQUENCE
 Relax. delay 0.500 sec
 Pulse 65.4 degrees
 Acc. time 1.736 sec
 Width 37.358 Hz
 120 repetitions
 DESERVE C13, 125.7832309 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 Continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT Size 131072
 Total time 4 minutes



Pulse Sequence: $s2pu1$

Solvent: tBCl3
Ambient temperature

File: mh-V-14
TNOVA=500 "zippy"

REVUE GÉOLOGIQUE

PULSE SEQUENCE
RELAX · DELAY 5 · 000 SEC

Pulse 89.0 degrees
ACQ: time 3.001 sec

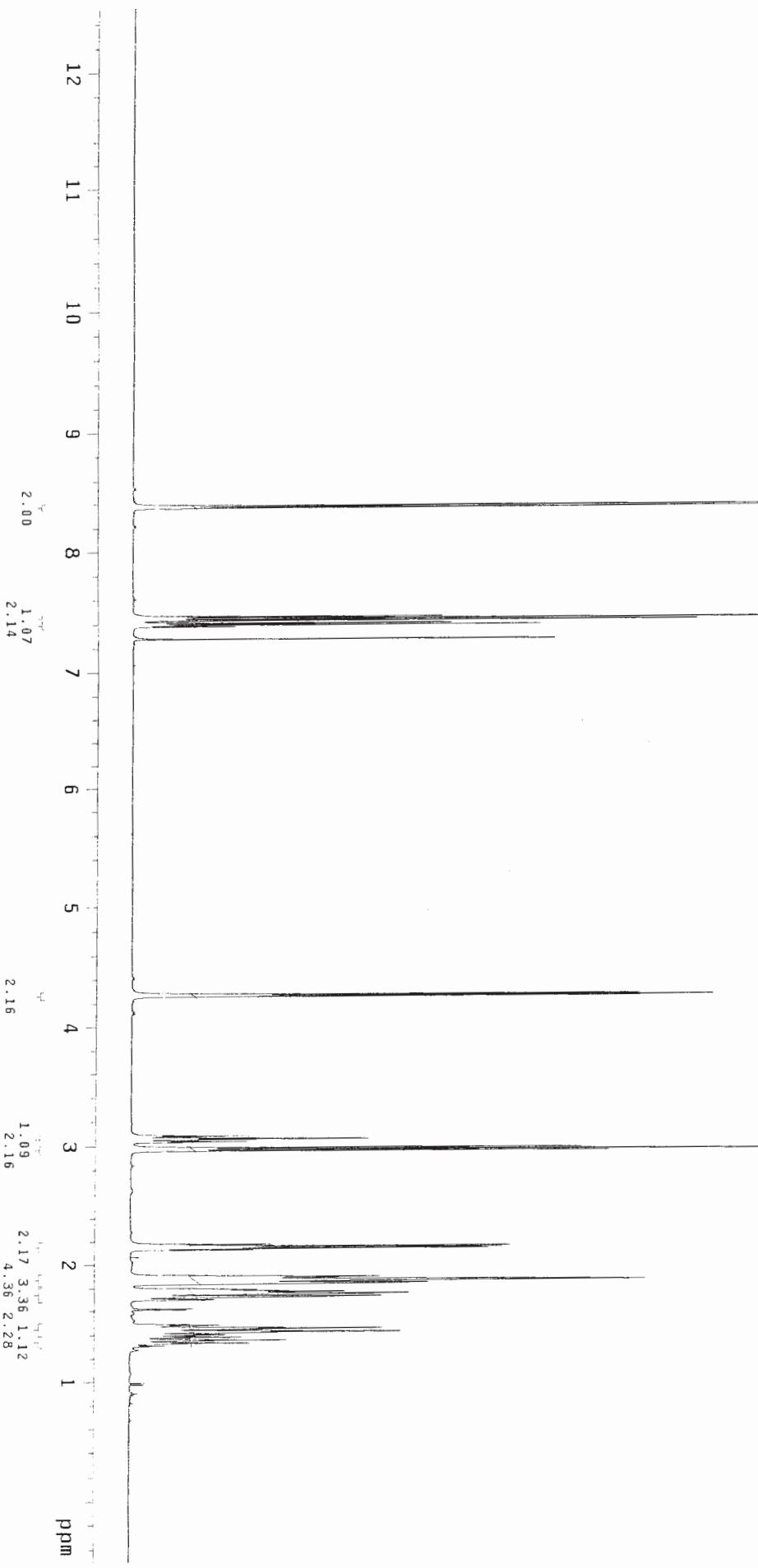
width 10504.2 Hz

5 repetitions
GBSERVE H1 100 71165

UBSLRV HI 433 : / 4483
DATA PROCESSING

FT size 131072

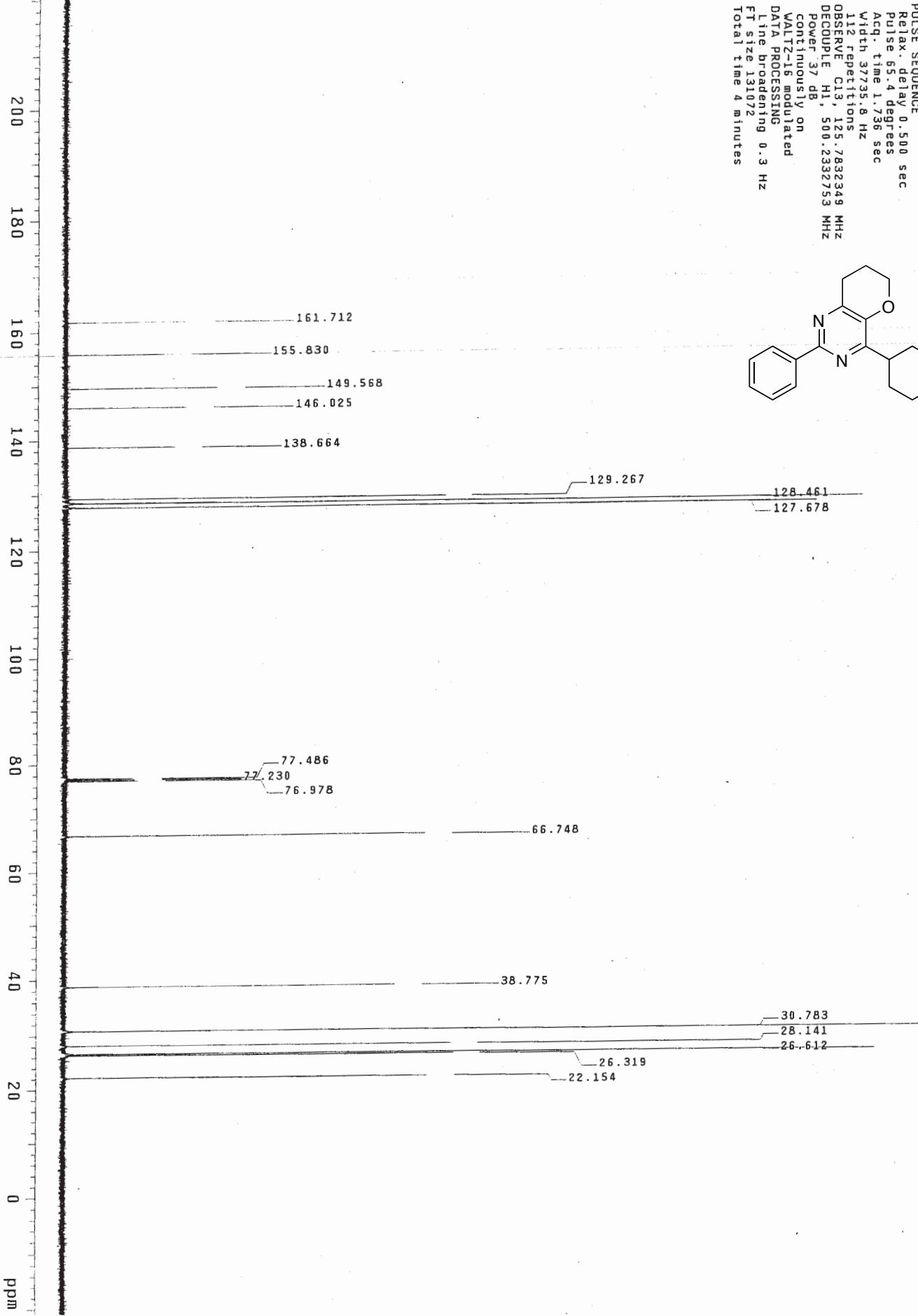
total time 2 min, 8 sec



S58/S80

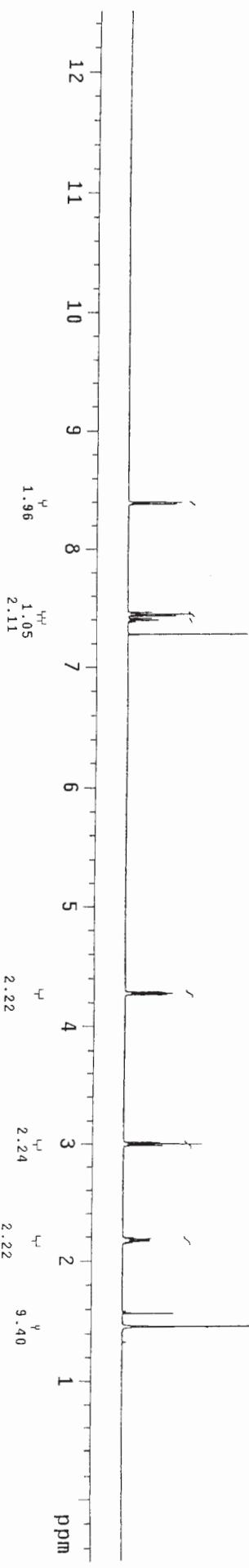
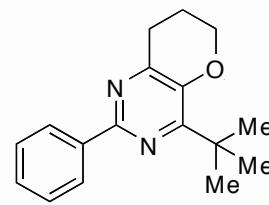
Solvent: C6E13
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

Relax. delay 0.500 sec
pulse 65.4 degrees
Acq. time 1.736 sec
width 37.35.8 Hz
112 repetitions
OBSERVE C13, 125.783233
DECOPLE H1, 500.2332795
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 4 minutes



Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 INNOVA-500 "bulwinkle"

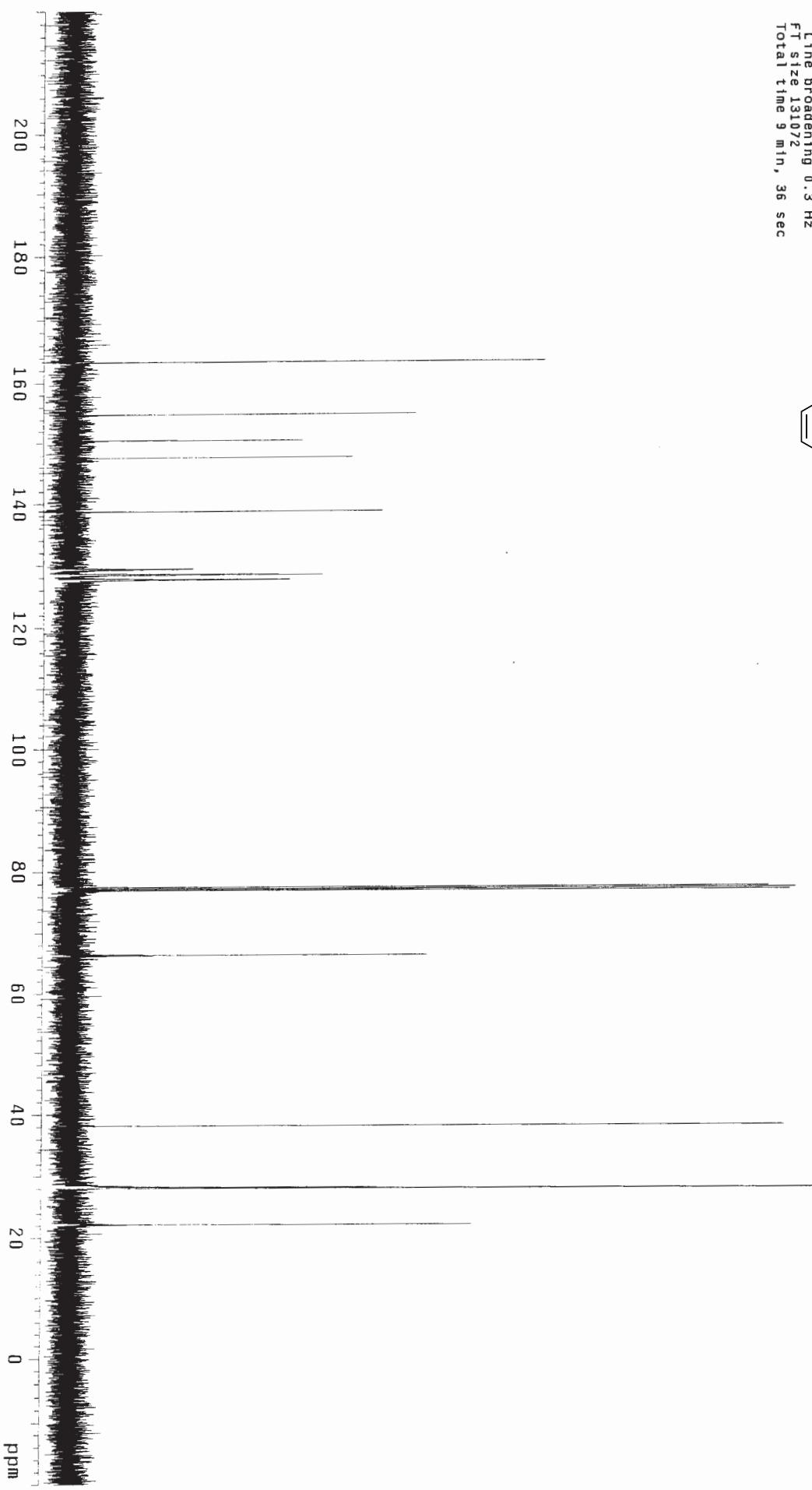
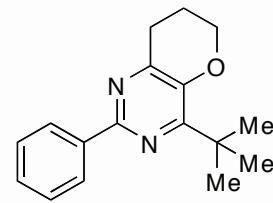
Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 Width 10504.2 Hz
 7 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING FT size 131072
 Total time 2 min, 8 sec



Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 File: mh-v-52carbon
 INNOVA-500 "zipy"

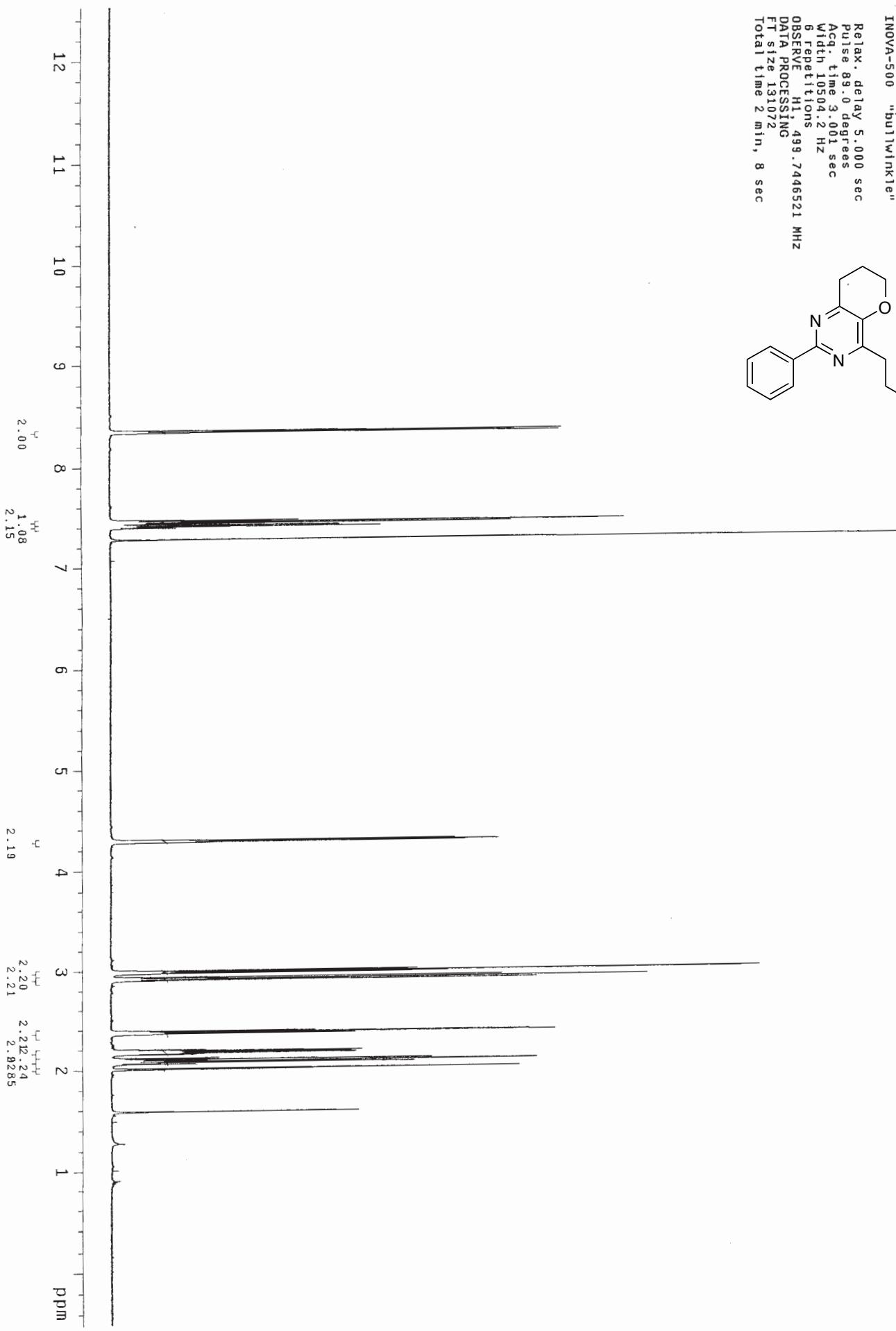
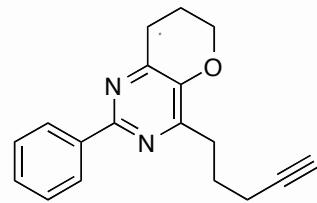
PULSE SEQUENCE
 R1ax. delay 0.500 sec
 pulse 65.4 degrees
 Acq. time 1.736 sec
 width 3775.8 Hz
 256 repetitions
 OBSERVE C13, 125.783309 MHz
 DECOUPLE H1, 500.2332753 MHz
 power 37 dB
 continuously on
 WALTZ-16 modulated

DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 9 min, 36 sec



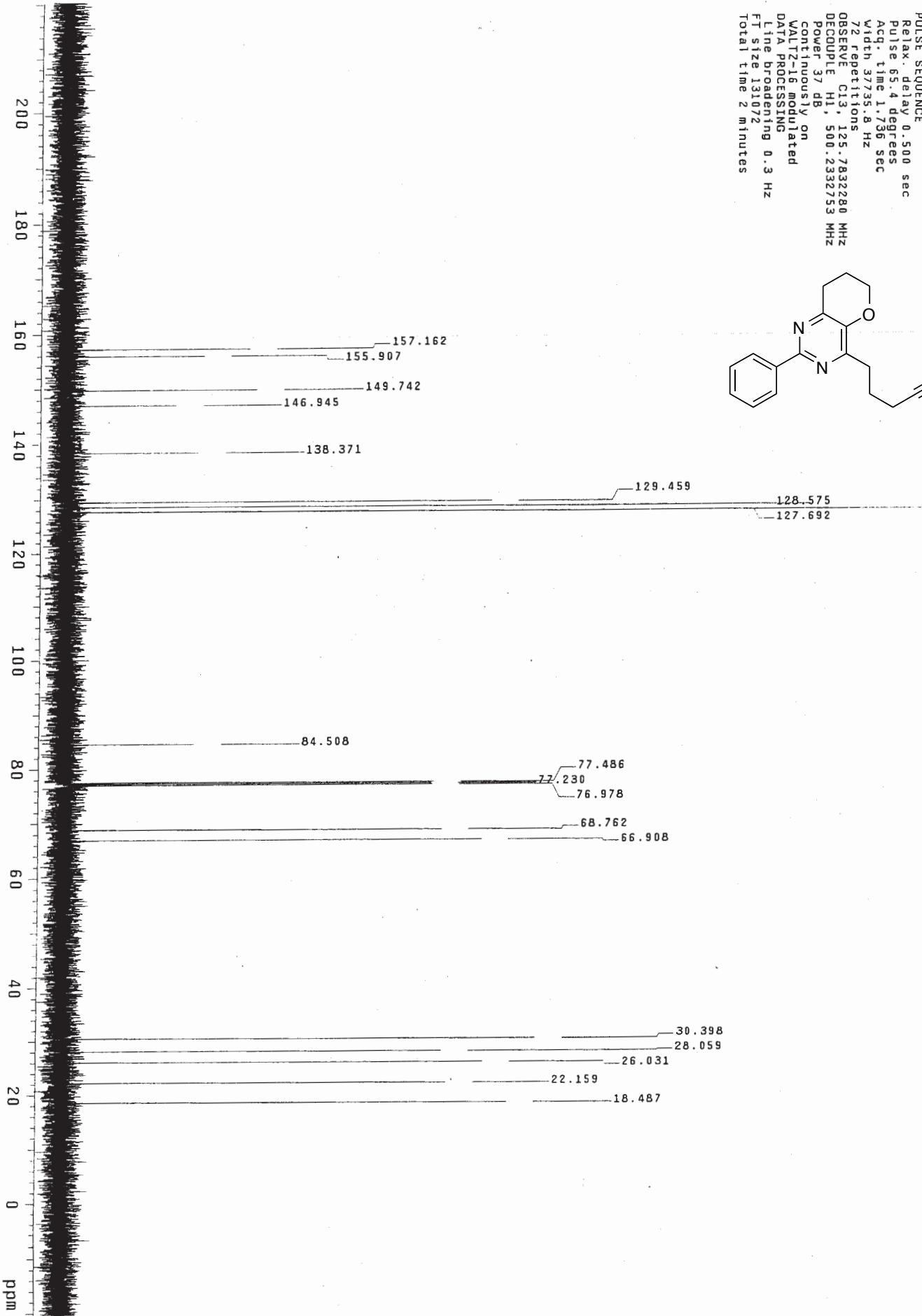
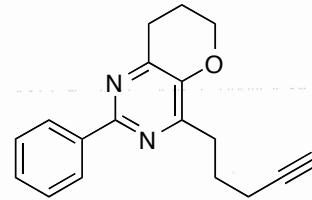
Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INNOVA-500 "bulwinkle"

Relax. delay 5.000 sec
 pulse 89.0 degrees
 Acq. time 3.001 sec
 width 1054.2 Hz
 6 repetitions
 OBSERVE H1; 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



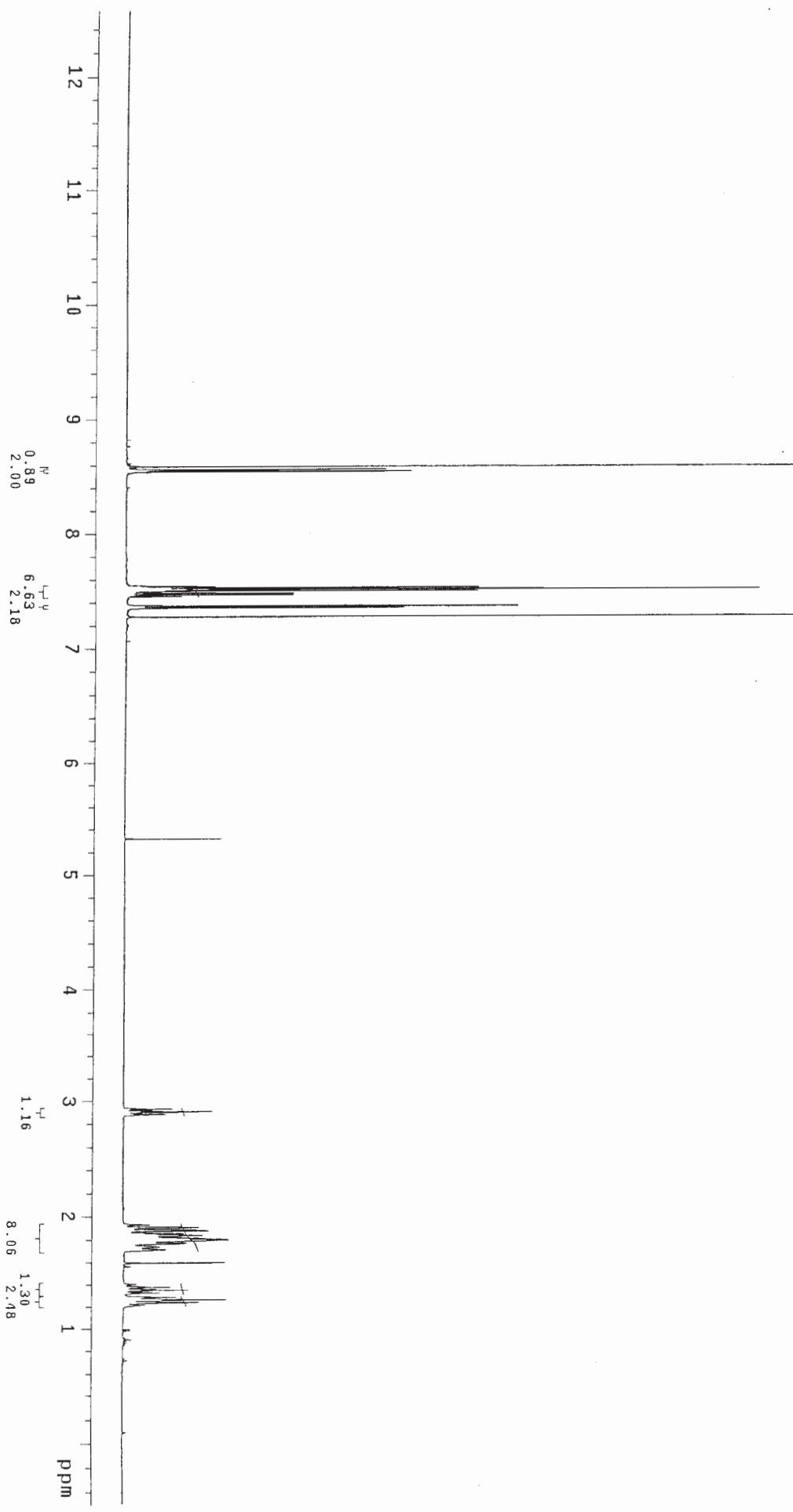
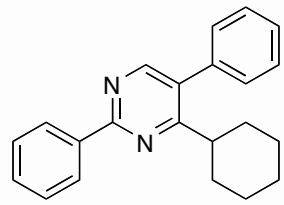
S62/S80

Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "rocky"
 PULSE SEQUENCE
 Relax. delay 0.500 sec
 Pulse 65.4 degrees
 Acc. time 1.736 sec
 width 37.35.8 Hz
 72 repetitions
 OBSERVE C13, 125.7832280 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 2 minutes



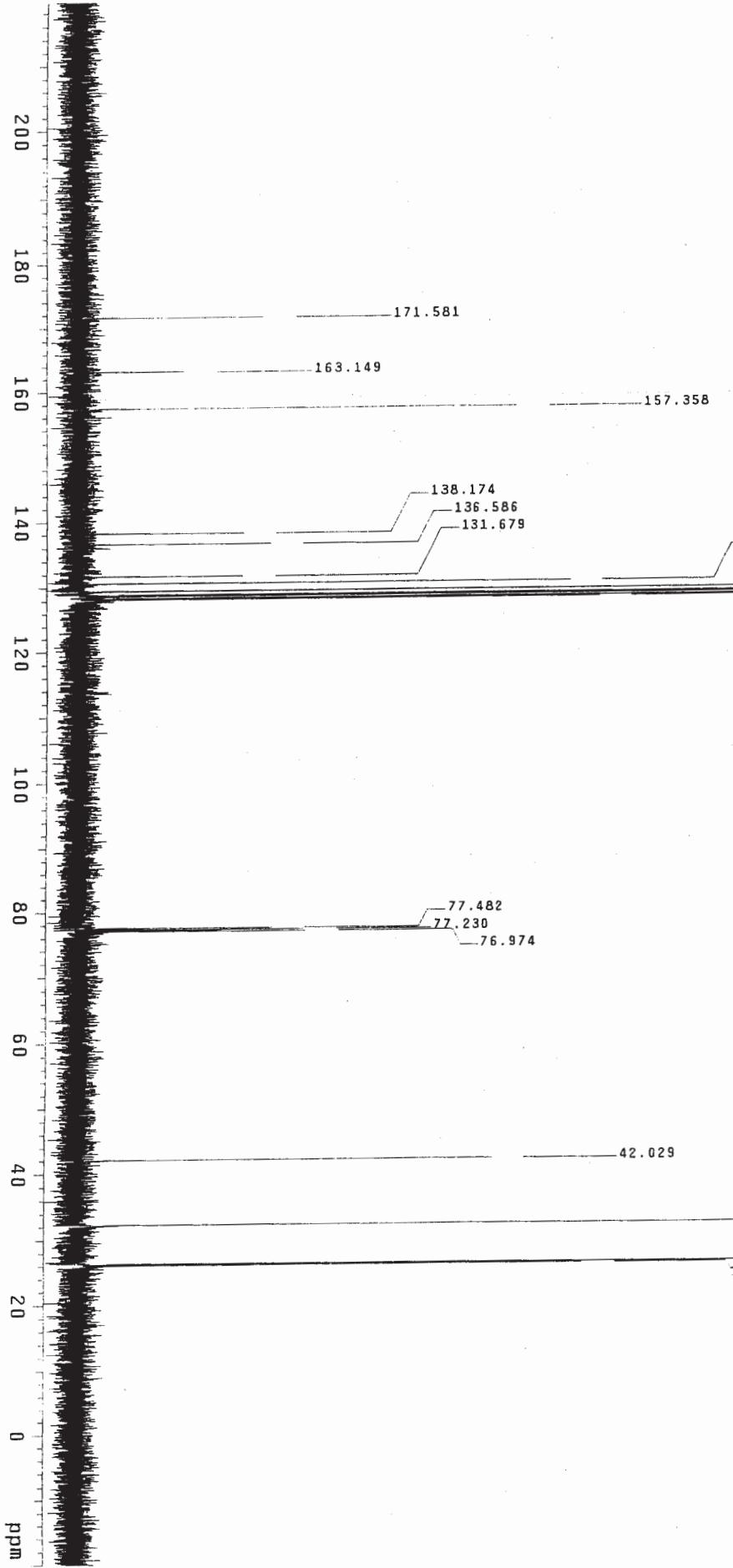
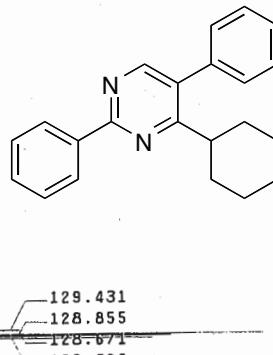
Pulse Sequence: s2pu
 Solvent: CDCl_3
 Ambient temperature
 INOVA-500 "bullewinkle"

Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 Width 10.04.2 Hz
 7 repetitions
 OBSERVE HI, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



Solvent: CDCl₃
 Ambient temperature
 User: 1-14-87
 INDO-500 "rocky"

PULSE SEQUENCE
 Relax. delay 0.500 sec
 pulse 65.4 degrees
 Acq. time 1.736 sec
 Width 37.35.8 Hz
 40 repetitions
 OBSERVE Cl3, 125.7832314 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 1 minutes



Pulse Sequence: s2pul

Solvent: CDCl₃

Ambient temperature

File: mh-IV-285

INOVA-500 "zippy"

PULSE SEQUENCE

Relax. delay 5.000 sec

Pulse 89.0 degrees

Acq. time 3.001 sec

Width 10504.2 Hz

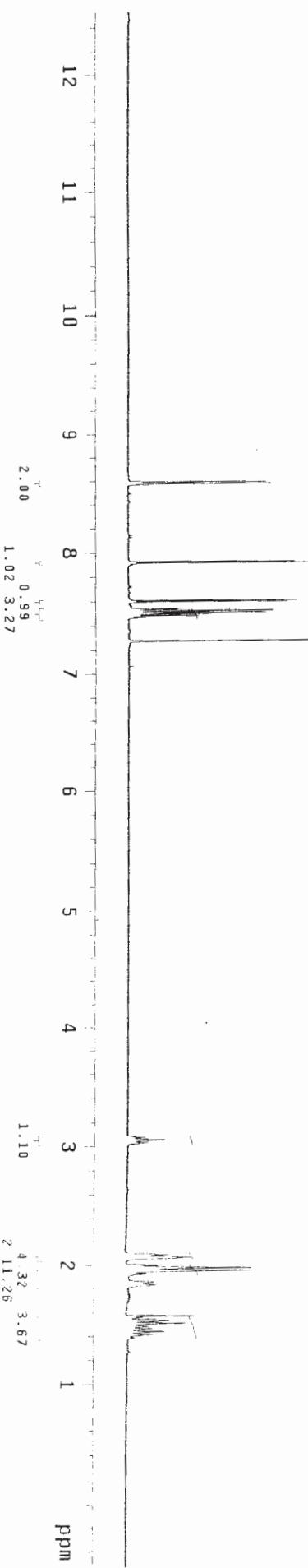
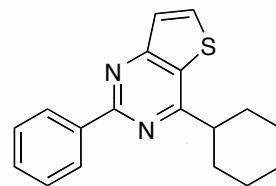
3 repetitions

OBSERVE H1 499.7446521 MHz

DATA PROCESSING

FT size 131072

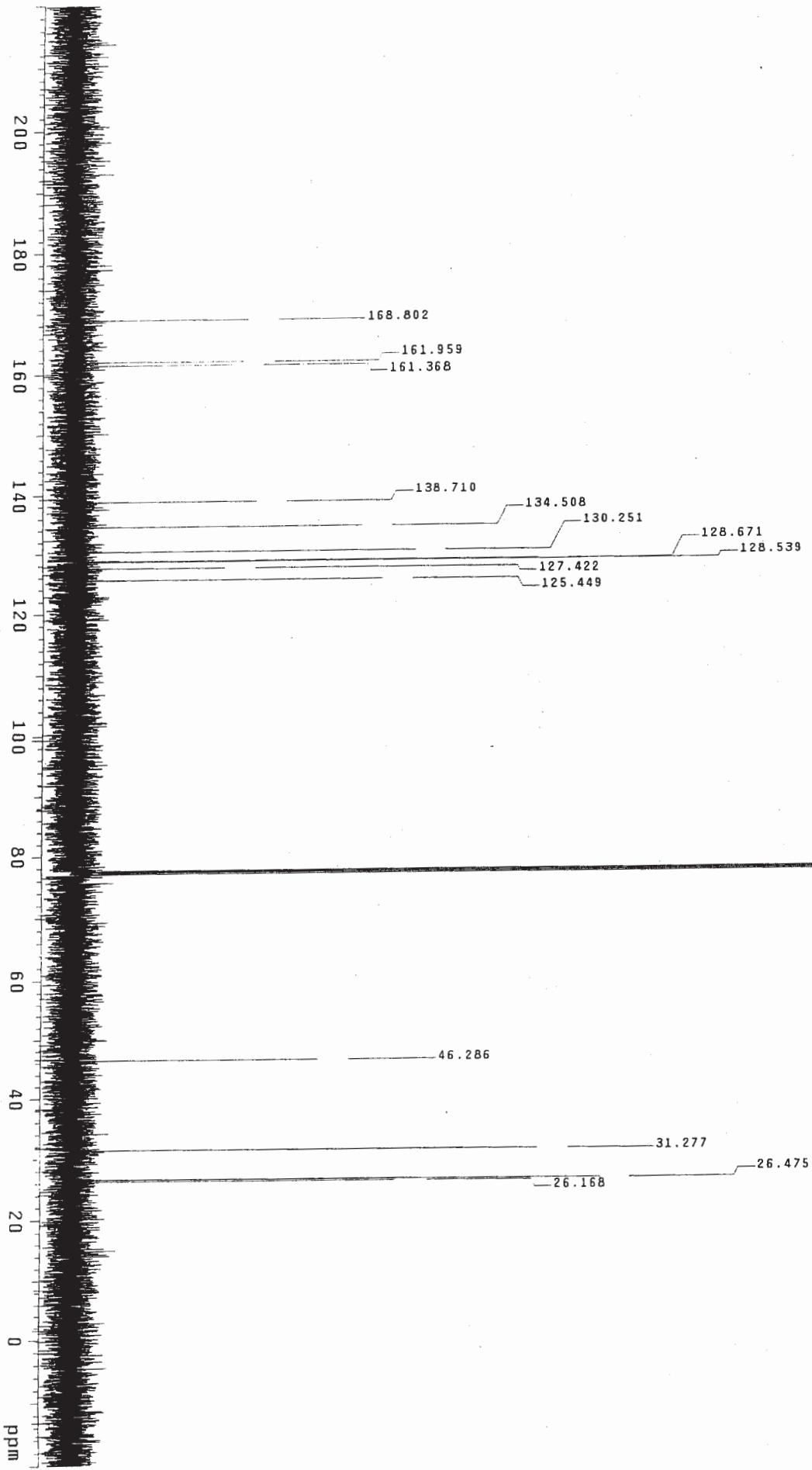
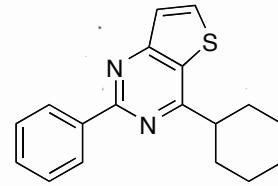
Total time 2 min, 8 sec



S66/S80

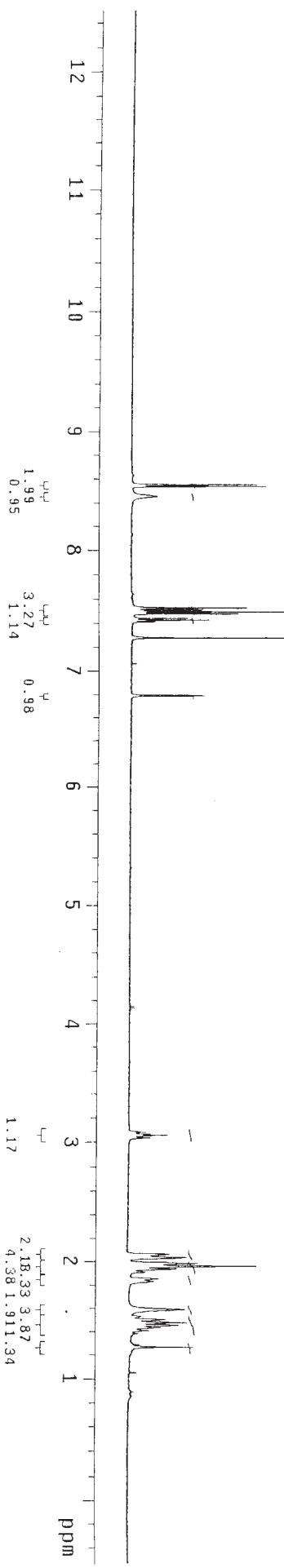
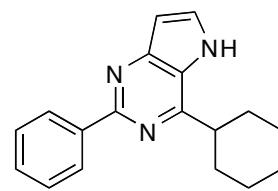
Solvent: CDCl₃
Ambient temperature
User: 1-14-87
INOVA-500 "Rocky"

PULSE SEQUENCE
Relax. delay 0.763 sec
pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
112 repetitions
OBSERVE C13, 125.7832286 MHz
DECUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 4 minutes



Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "bulletwinkle"

Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 Width 10504.2 Hz
 7 repetitions
 OBSERVE H1 499.7446521 MHz
 DATA PROCESSING
 FT size 131024
 Total time 2 min, 8 sec



Solvent: DMF
 Ambient temperature
 User: 1-14-87
 INNOVA-500 "rocky"

PULSE SEQUENCE

Pulse 65.4 degrees

Acq. t. time 1.736 sec

Width 37735.8 Hz

168 repetitions

OBSERVE C13, 125.7836630 MHz

DECOPLE H1, 500.2354363 MHz

Power 37 dB

continuously on

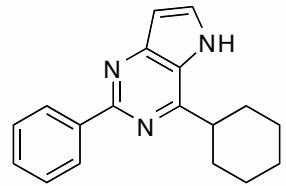
VALTZ-16 modulated

DATA PROCESSING

Line broadening 0.3 Hz

FT size 131072

Total time 6 minutes



— 163.383
 — 163.150
 — 162.917

— 157.886
 — 156.907
 — 151.936

— 141.052

— 133.550
 — 130.008

— 125.179

— 128.321
 — 128.639

— 102.879

— 42.412
 — 36.009
 — 35.844
 — 35.679
 — 35.510
 — 35.340

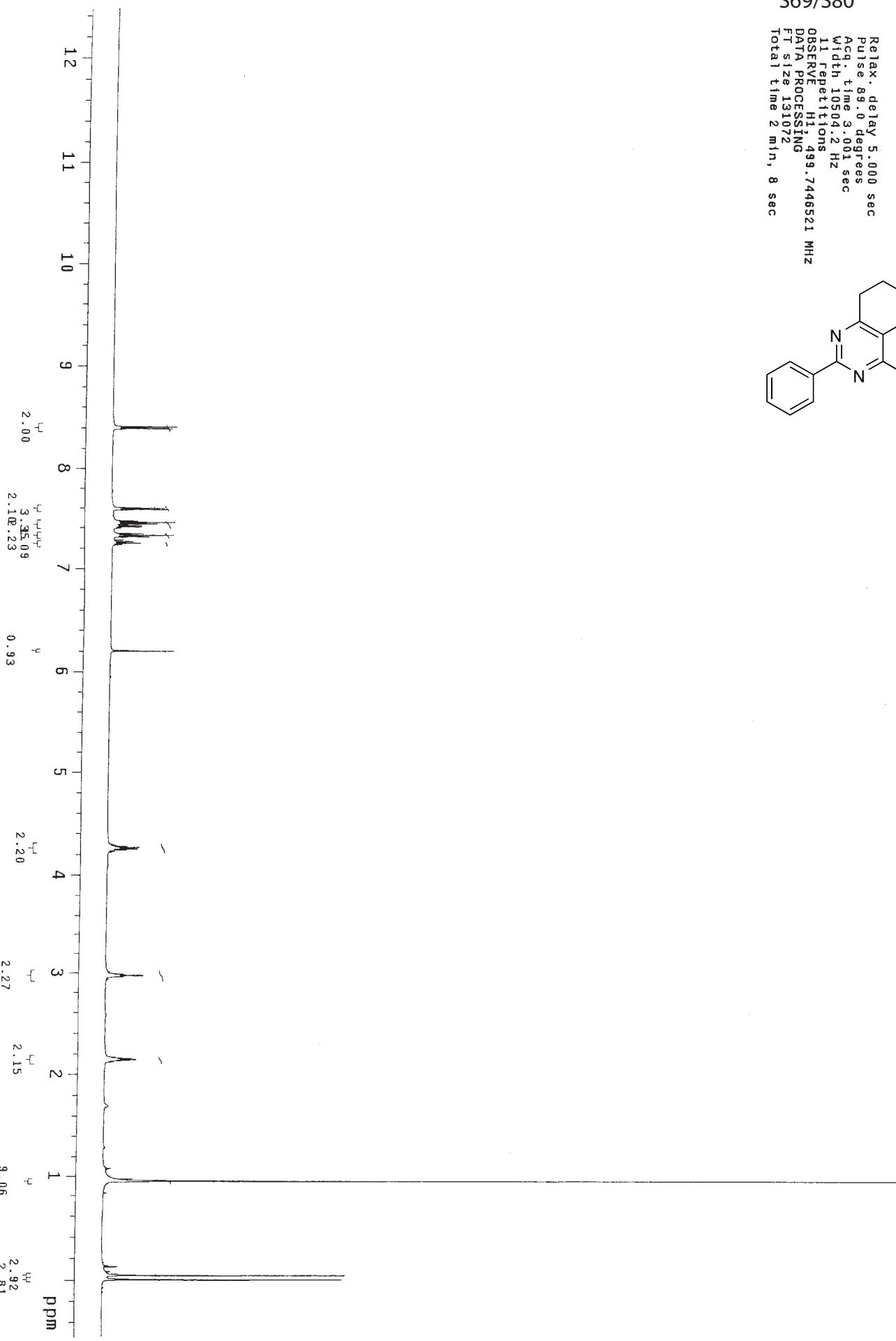
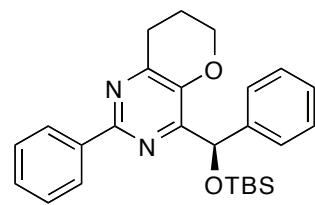
— 32.182
 — 30.887
 — 30.718
 — 30.548
 — 30.388
 — 30.214
 — 27.285

— 27.047



Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "bullwinkl"

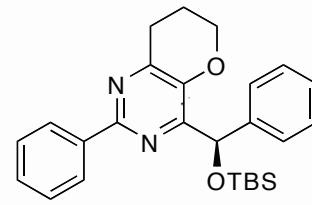
Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 width 10504.2 Hz
 11 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec



S70/S80

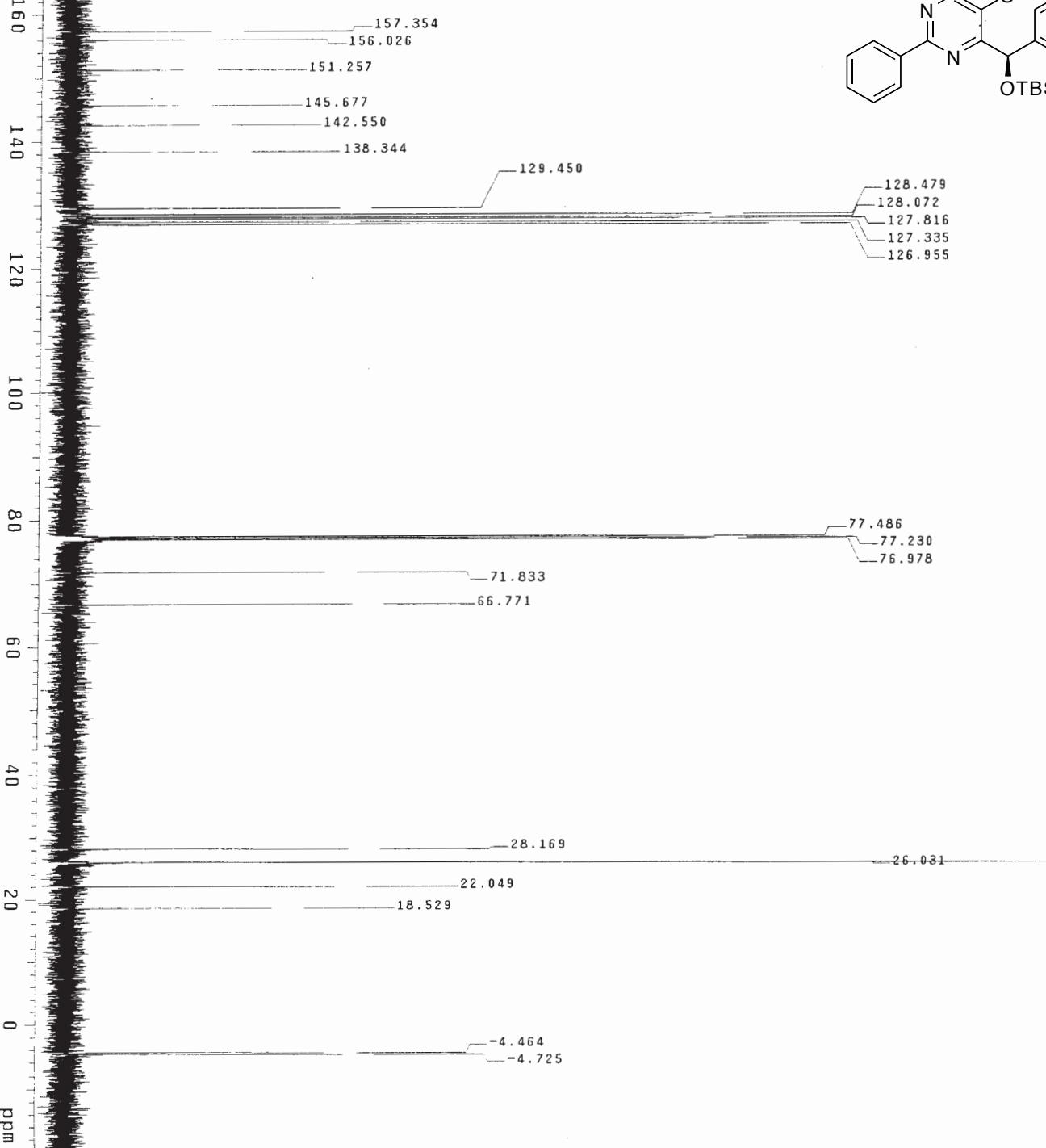
Solvent: CDCl₃
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

PULSE SEQUENCE
Relax delay 0.500 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37.33, 8 Hz
488 repetitions
OBSERVE C13, 125.7832280 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT Size 131072
Total time 18 minutes

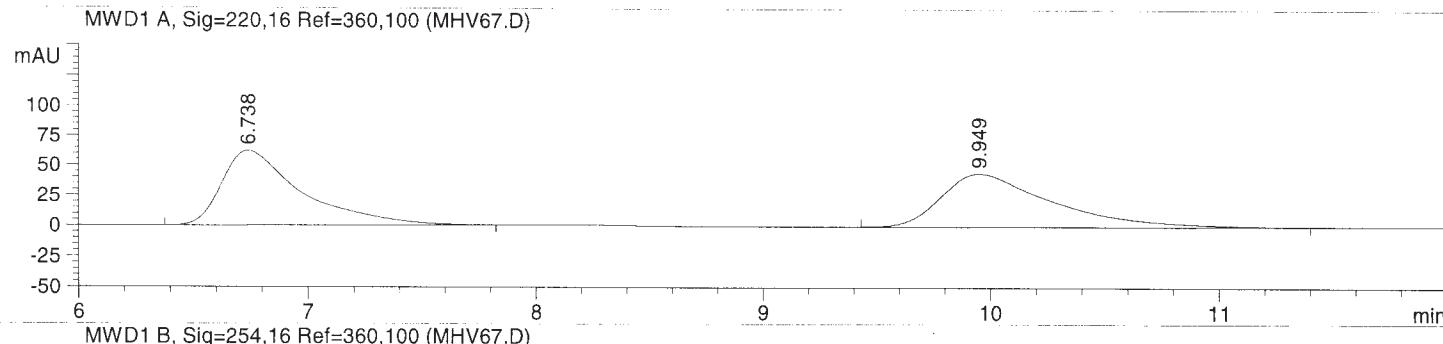


128.479
128.072
127.816
127.335
126.955

77.486
77.230
76.978



```
=====
Injection Date : 5/17/2006 6:45:12 PM           Seq. Line : 1           S71/S80
Sample Name    : mh-V-67                      Location : Vial 44
Acq. Operator  : Pete                         Inj : 1
                                         Inj Volume : 1  $\mu$ l
Acq. Method    : C:\HPCHEM\2\METHODS\MATT.M
Last changed   : 5/16/2006 6:11:26 PM by Pete
Analysis Method: C:\HPCHEM\2\METHODS\3087.M
Last changed   : 9/2/2006 12:47:50 PM by Mike
                                         (modified after loading)
=====
```



```
=====
Area Percent Report
=====
```

```
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.738	PB	0.3448	1484.55396	62.12878	49.9781
2	9.949	BB	0.4865	1485.85620	43.93668	50.0219

Totals : 2970.41016 106.06546

Results obtained with enhanced integrator!

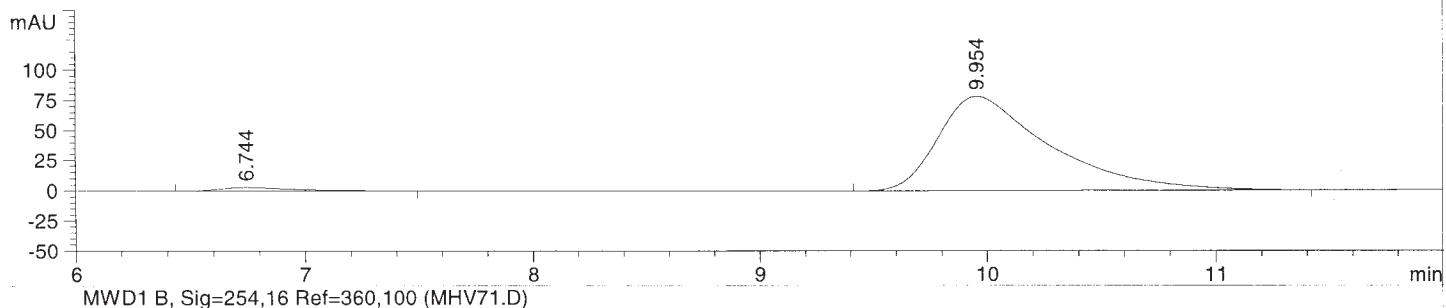
Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.738	PB	0.3444	1275.83508	53.46923	49.9666
2	9.949	BB	0.4879	1277.54297	37.83992	50.0334

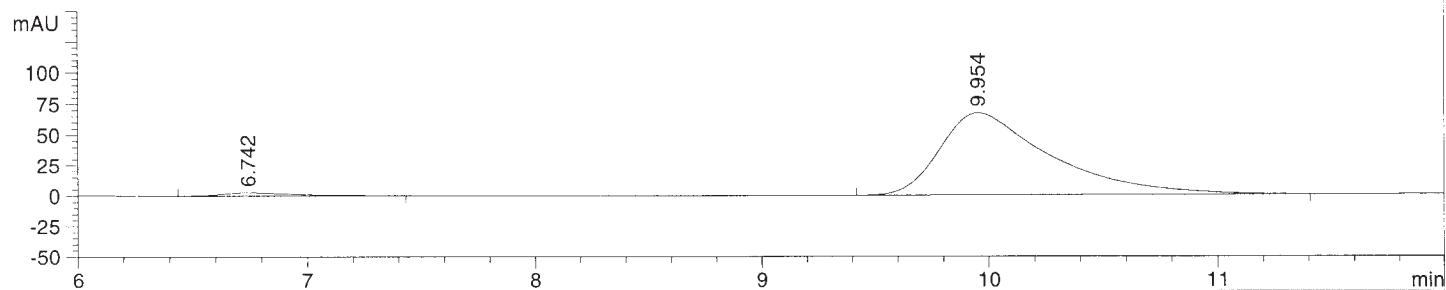
Totals : 2553.37805 91.30915

=====
 Injection Date : 5/17/2006 6:27:00 PM Seq. Line : 1
 Sample Name : mh-V-71 Location : Vial 45
 Acq. Operator : Pete Inj : 1
 Inj Volume : 1 μ l
 Acq. Method : C:\HPCHEM\2\METHODS\MATT.M
 Last changed : 5/16/2006 6:11:26 PM by Pete
 Analysis Method : C:\HPCHEM\2\METHODS\3087.M
 Last changed : 9/2/2006 12:47:50 PM by Mike
 (modified after loading)
 =====

MWD1 A, Sig=220,16 Ref=360,100 (MHV71.D)



MWD1 B, Sig=254,16 Ref=360,100 (MHV71.D)



===== Area Percent Report =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.744	BB	0.3266	67.53790	2.97821	2.4983
2	9.954	PB	0.4889	2635.80933	77.87540	97.5017

Totals : 2703.34723 80.85362

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.742	PB	0.3238	58.46334	2.56659	2.5113
2	9.954	BB	0.4869	2269.58228	67.04366	97.4887

Totals : 2328.04562 69.61026

Pulse Sequence: s2pul

Solvent: CDCl₃

Ambient temperature

File: mh-v-151

INOVA-500 "zippy"

PULSE SEQUENCE

Relax. delay 5.000 sec

Pulse 89.0 degrees

Acq. time 3.001 sec

Width 1504.2 Hz

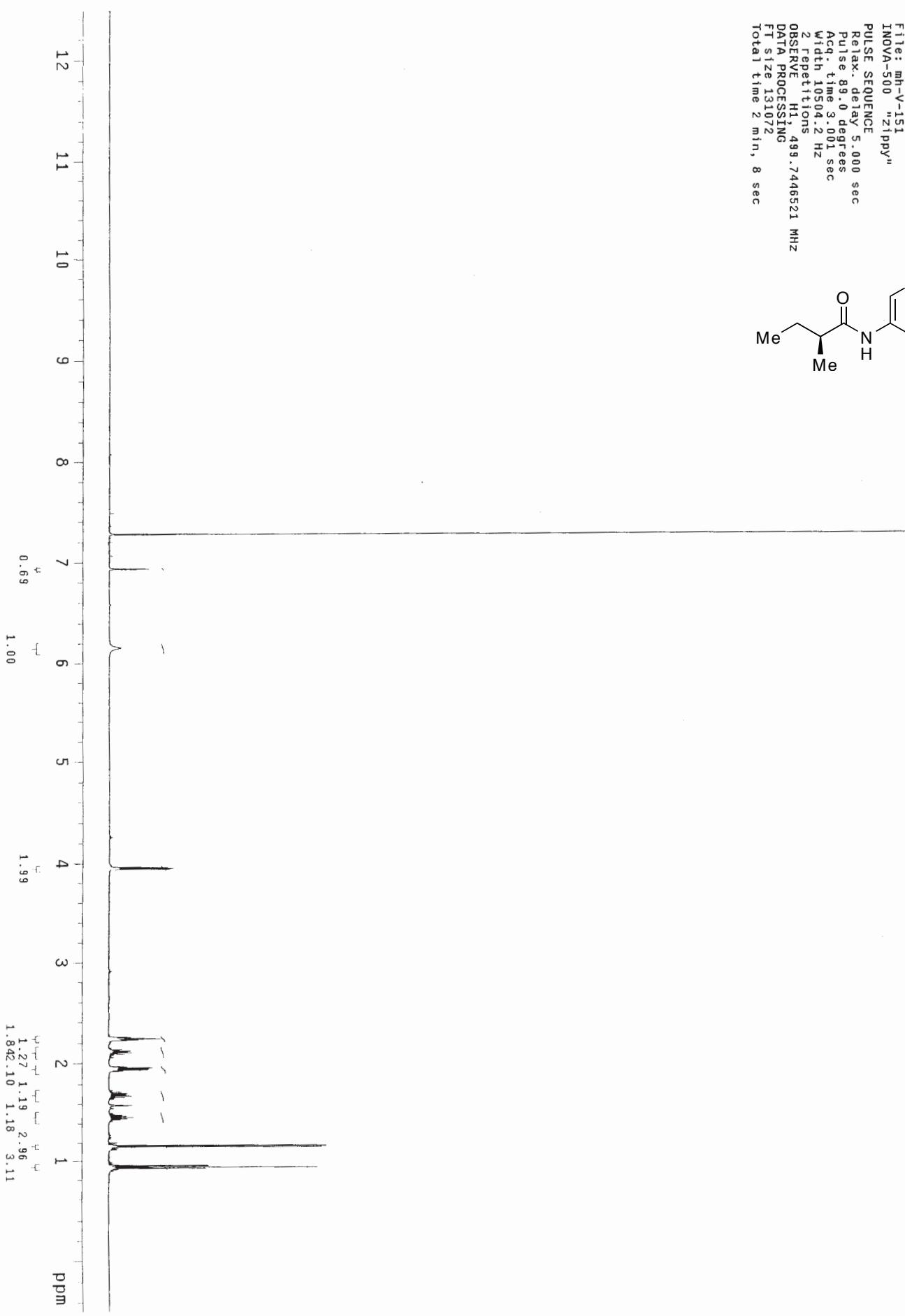
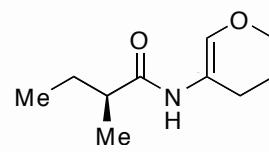
2 repetitions

OBSERVE H1, 499.7446521 MHz

DATA PROCESSING

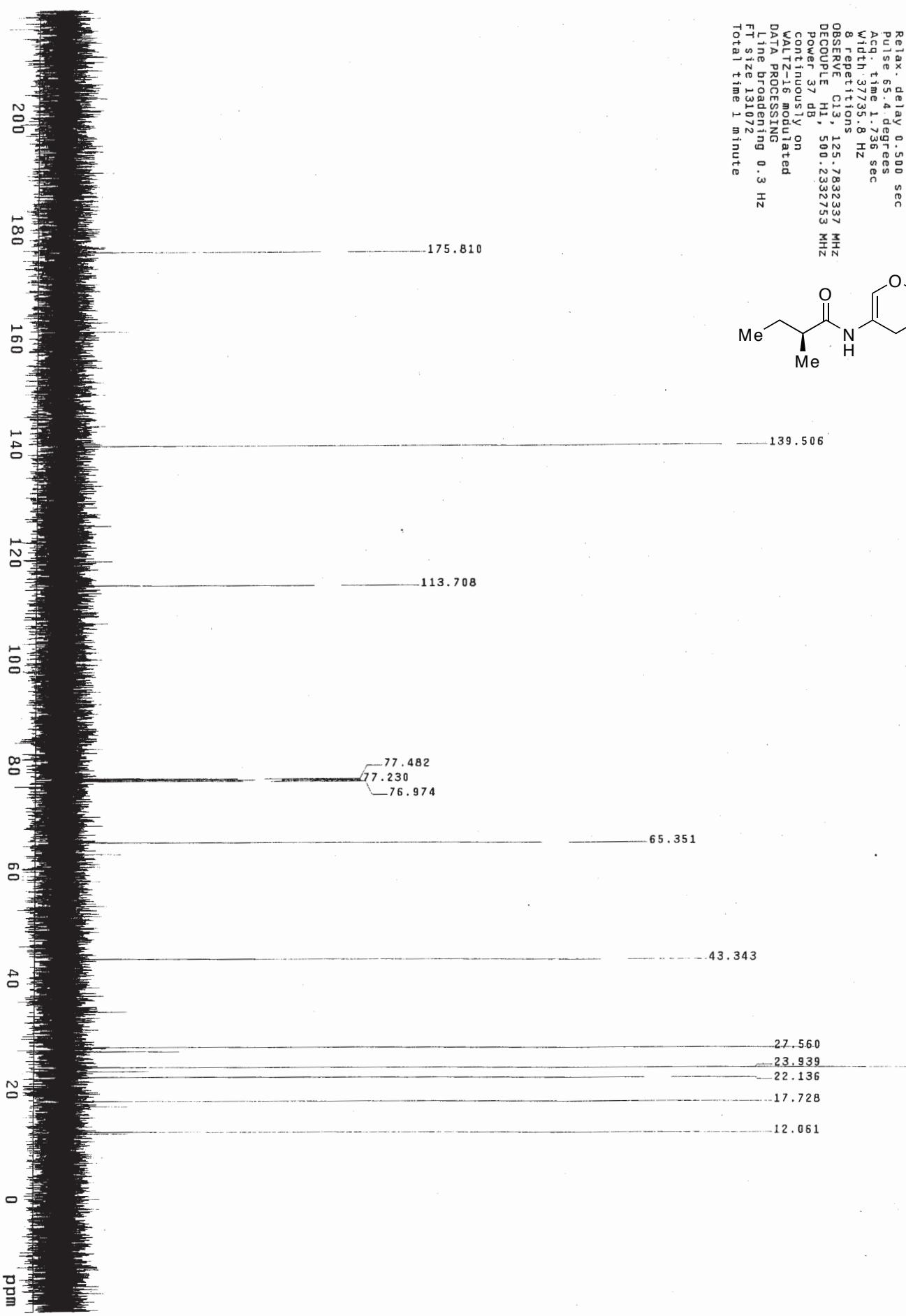
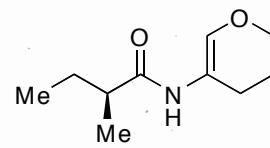
FT size 131072

Total time 2 min, 8 sec



Solvent: C6C13
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

RELAX- DELAY 0.500 sec
 PULSE 65.4 degrees
 Acc. time 1.736 sec
 Width 37.535 8 Hz
 8 repetitions
 OBSERVE C13, 125.7832337 MHz
 DECODE H1, 500.2332753 MHz
 Power 37 dB
 Continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131022
 Total time 1 minute

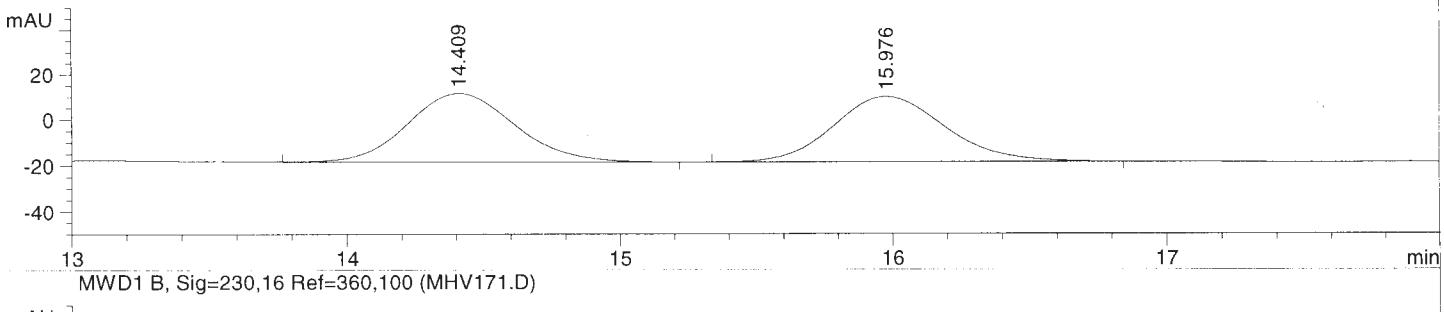


Data File C:\HPCHEM\2\DATA\MHV171.D
Racemis; Chiralcel OD 99% hex 1% IPA 0.5ml/min

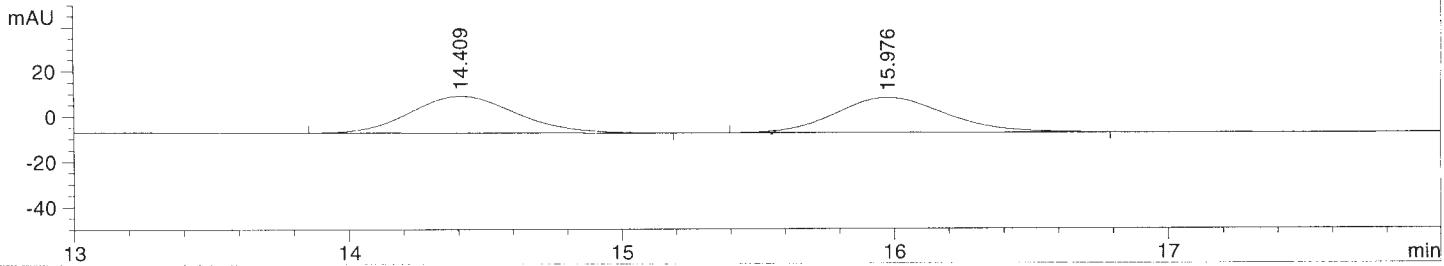
S75/S80

=====
Injection Date : 8/22/2006 10:50:07 AM Seq. Line : 1
Sample Name : mh-v-171 Location : Vial 52
Acq. Operator : Mike Inj : 1
Inj Volume : 1 μ l
Acq. Method : C:\HPCHEM\2\METHODS\3087.M
Last changed : 8/22/2006 10:50:23 AM by Mike
(modified after loading)
Analysis Method : C:\HPCHEM\2\METHODS\3087.M
Last changed : 9/2/2006 12:14:09 PM by Mike
(modified after loading)
=====

MWD1 A, Sig=220,16 Ref=360,100 (MHV171.D)



MWD1 B, Sig=230,16 Ref=360,100 (MHV171.D)



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.409	VP	0.4294	817.90497	29.87720	50.6648
2	15.976	BB	0.4386	796.44165	28.27765	49.3352

Totals : 1614.34662 58.15485

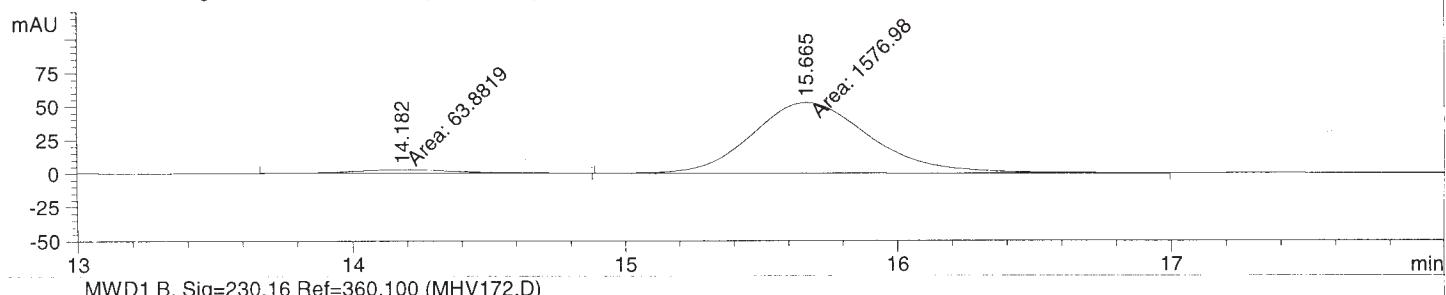
Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=230,16 Ref=360,100

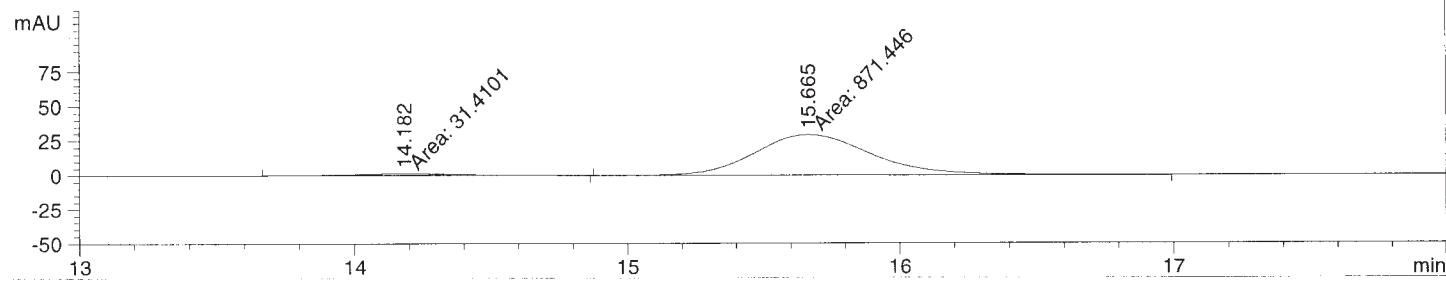
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.409	BB	0.4259	445.15985	16.43794	50.3785
2	15.976	BB	0.4316	438.47003	15.61679	49.6215

=====
Injection Date : 8/22/2006 11:58:22 AM Seq. Line : 1
Sample Name : mh-v-172 Location : Vial 51
Acq. Operator : Mike Inj : 1
Inj Volume : 1 μ l
Acq. Method : C:\HPCHEM\2\METHODS\3087.M
Last changed : 8/22/2006 11:57:39 AM by Mike
Analysis Method : C:\HPCHEM\2\METHODS\3087.M
Last changed : 9/2/2006 12:26:23 PM by Mike
(modified after loading)
=====

MWD1 A, Sig=220,16 Ref=360,100 (MHV172.D)



MWD1 B, Sig=230,16 Ref=360,100 (MHV172.D)



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.182	MM	0.4311	63.88190	2.46999	3.8932
2	15.665	MM	0.5027	1576.97693	52.28671	96.1068

Totals : 1640.85883 54.75670

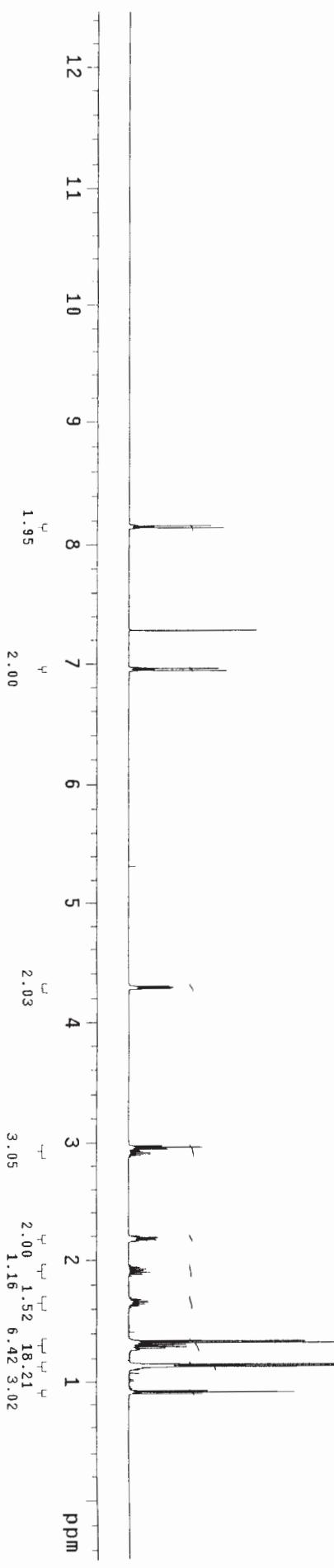
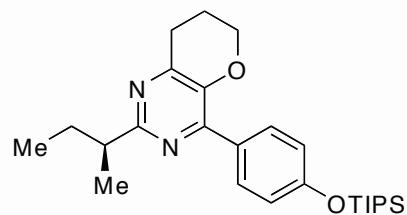
Results obtained with enhanced integrator!

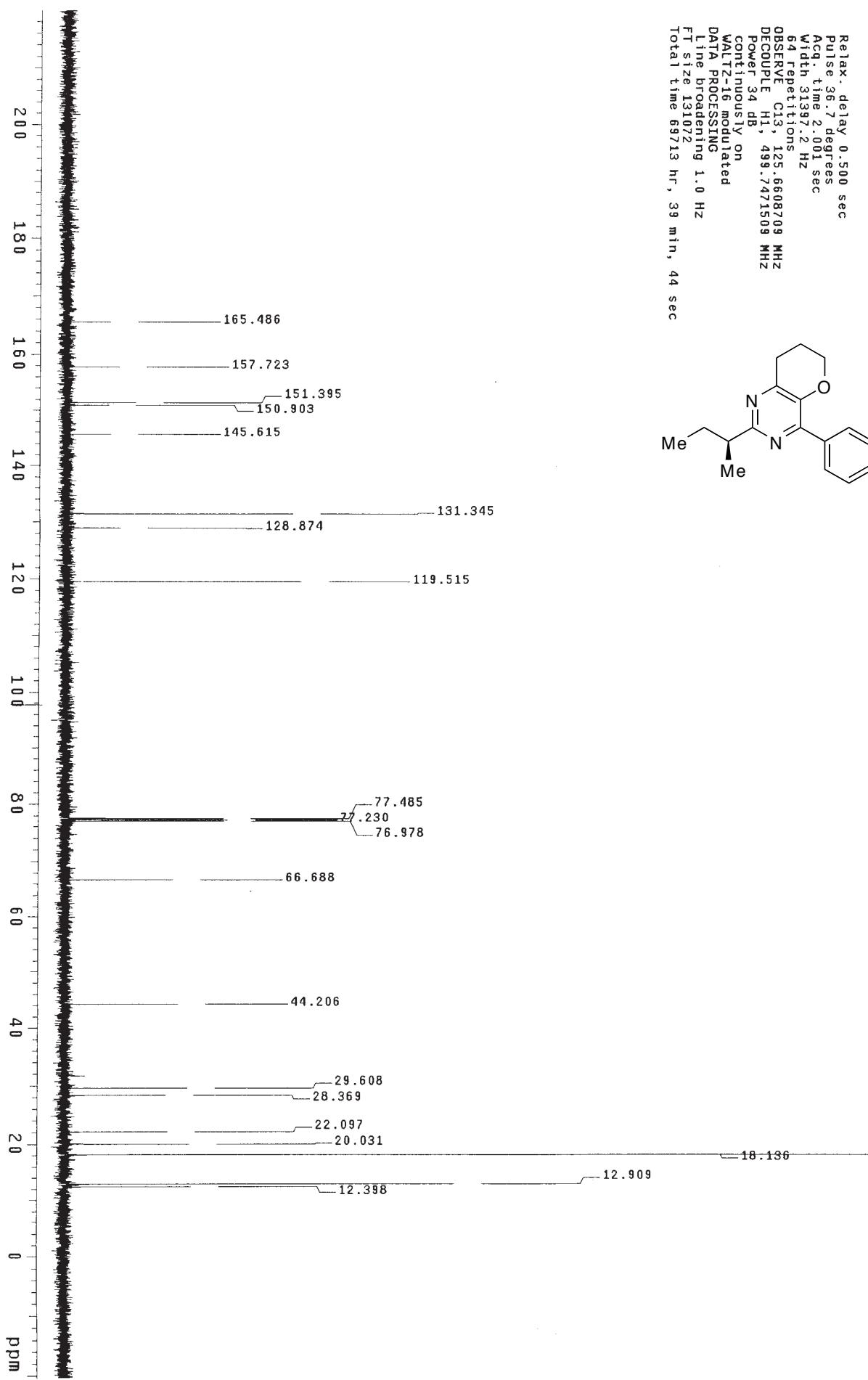
Signal 2: MWD1 B, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.182	MM	0.4046	31.41007	1.29372	3.4790
2	15.665	MM	0.5021	871.44592	28.92579	96.5210

Totals : 902.85600 30.21951

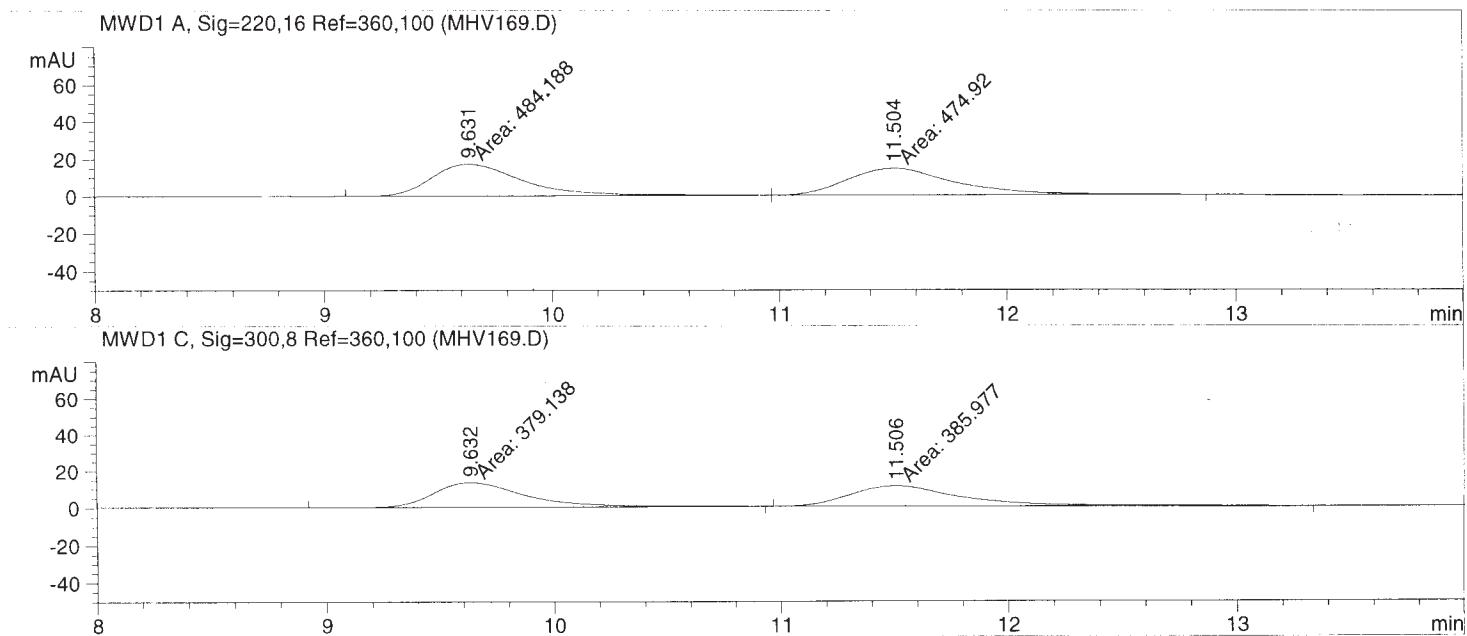
Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-500 "Bruylants"
 Relax. delay 5.000 sec
 Pulse 89.0 degrees
 Acq. time 3.001 sec
 Width 10504.2 Hz
 8 repetitions
 OBSERVE H1, 499.7446521 MHz
 DATA PROCESSING
 FT size 131072
 Total time 2 min, 8 sec





=====
 Injection Date : 9/2/2006 12:22:20 PM Seq. Line : 1
 Sample Name : mh-V-169 Location : Vial 31
 Acq. Operator : Mike Inj : 1
 Inj Volume : 1 μ l
 Acq. Method : C:\HPCHEM\2\METHODS\MATT.M
 Last changed : 9/2/2006 12:21:32 PM by Mike
 Analysis Method : C:\HPCHEM\2\METHODS\3087.M
 Last changed : 9/2/2006 12:43:49 PM by Mike
 (modified after loading)
 =====

S79/S80



===== Area Percent Report =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.631	MM	0.4723	484.18787	17.08654	50.4831
2	11.504	MM	0.5551	474.92029	14.26056	49.5169

Totals : 959.10815 31.34710

Results obtained with enhanced integrator!

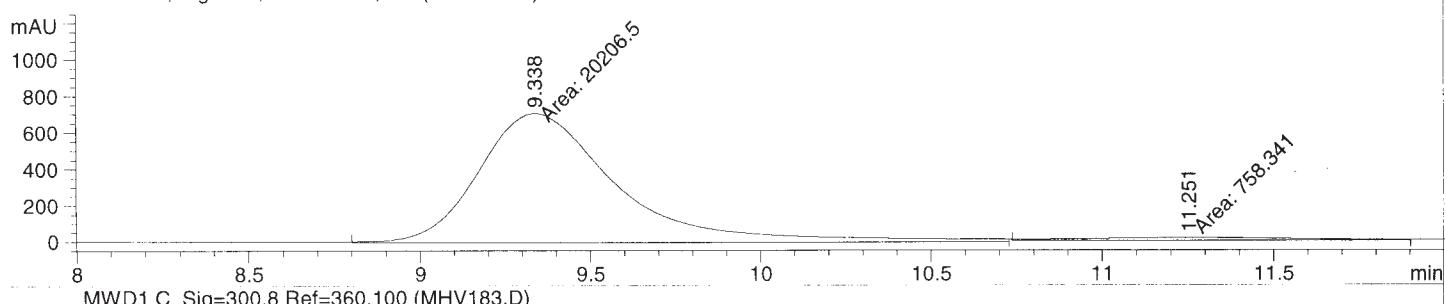
Signal 2: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.632	MM	0.4717	379.13776	13.39615	49.5530
2	11.506	MM	0.5841	385.97714	11.01431	50.4470

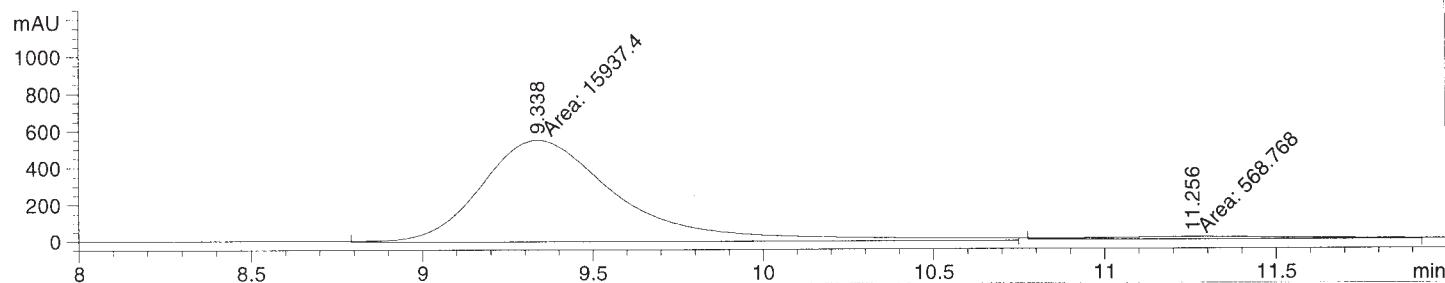
Totals : 765.11490 24.41047

=====
 Injection Date : 8/26/2006 10:53:00 AM Seq. Line : 1 S80/S80
 Sample Name : mh-V-183 Location : Vial 81
 Acq. Operator : Mike Inj : 1
 Inj Volume : 1 μ l
 Acq. Method : C:\HPCHEM\2\METHODS\MATT.M
 Last changed : 8/26/2006 10:53:06 AM by Mike
 (modified after loading)
 Analysis Method : C:\HPCHEM\2\METHODS\3087.M
 Last changed : 9/2/2006 12:02:15 PM by Mike
 (modified after loading)
 =====

MWD1 A, Sig=220,16 Ref=360,100 (MHV183.D)



MWD1 C, Sig=300,8 Ref=360,100 (MHV183.D)



===== Area Percent Report =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.338	MM	0.4737	2.02065e4	711.01727	96.3828
2	11.251	MM	0.7658	758.34058	16.50354	3.6172

Totals : 2.09649e4 727.52081

Results obtained with enhanced integrator!

Signal 2: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.338	MM	0.4781	1.59374e4	555.53772	96.5542
2	11.256	MM	0.7484	568.76819	12.66714	3.4458

Totals : 1.65062e4 568.20486