

Rev 1
10/11/03

The Asymmetric Synthesis of 4,4-Disubstituted-2-Imidazolidinones: Potent NK₁ Antagonists

Gregory A. Reichard, Carmine Stengone, Sunil Paliwal, Ingrid Mergelsberg, Sapna Majmundar, Cheng Wang, Robert Tiberi, Andrew T. McPhail, John J. Piwinski, and Neng-Yang Shih*

Schering-Plough Research Institute, 2015 Galloping Hill Rd. Kenilworth, NJ 07033, and Werthenstein Chemie AG, Industriestrasse, CH-6105 Schachen, Switzerland
 Department of Chemistry, P.M. Gross Chemical Laboratory, Duke University, Durham, NC 27708

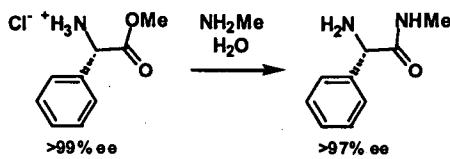
Supporting Information

General Procedures. Melting points were determined on a Mel-Temp apparatus and were uncorrected. Microanalysis and optical rotations were performed by Robertson Microlit Laboratories. ¹H NMR and ¹³C NMR were recorded at ambient temperature on an Avance-500 (500 MHz) Bruker nuclear magnetic resonance spectrometer at the frequency indicated. Chemical shifts for NMR spectra are reported as δ in units of parts per million (ppm) relative to residual CHCl_3 for proton (δ 7.26, singlet) and CDCl_3 for carbon (δ 77.0, triplet). The data are reported as follows: chemical shift, multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (reported as a J value in Hertz (Hz)), integration. The number of protons (n) for a given resonance is indicated by nH. Mass spectral analyses were recorded on JEOL model JMS-HX110A spectrometers and are reported in units of mass to charge (m/e). X-Ray data were collected on an Enraf-Nonius CAD4 diffractometer.

All moisture and / or air sensitive experiments were performed under a positive pressure of nitrogen or argon in flame dried glassware equipped with a rubber septum inlet. Solvents and liquid reagents were transferred by nitrogen flushed syringe or cannula. Reaction solutions were stirred with Teflon coated magnetic stir bars unless otherwise indicated. Commercial solvents and reagents were used without further purification.

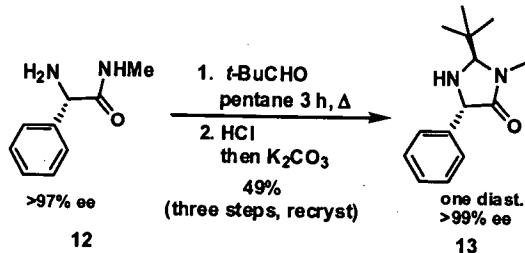
Analytical thin layer chromatography was performed using Merck 60 F₂₅₄ precoated silica gel plates (0.25 mm thickness). Subsequent to elution, ultraviolet illumination at 254 nm, while heating on a hot plate allowed for visualization of UV active material. Staining with a 5% ethanolic solution of phosphomolybdic acid (PMA) or an ethanolic solution of *p*-anisaldehyde (2.5%), sulfuric acid (3.5%) and acetic acid (1%) allowed for further visualization. Flash chromatography was performed using Selecto silica gel 60 (230-400 mesh) or Biotage and HPLC grade solvents. Columns were typically packed as a slurry (for Biotage commercial pre-packed columns were used) and equilibrated with the appropriate solvent prior to use.

Copies of ¹H and ¹³C spectra of all relevant compounds are provided.

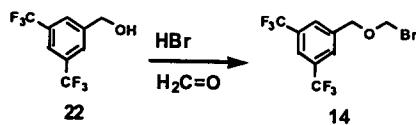


(S)-2-Amino-N-methyl-2-phenyl-acetamide (12). (S)-Phenylglycine methyl ester hydrochloride 11 (100g, 496 mmol, 1 equiv.) was added to methylamine (160 mL, 40% in H_2O , 4 equiv.) in a cool water bath at 10-16°C over a period of 15 minutes. After complete addition, the solution was warmed to room temperature and stirred for 1 h. The reaction was monitored by TLC in 98:2 EtOAc/MeOH. Upon completion, the reaction

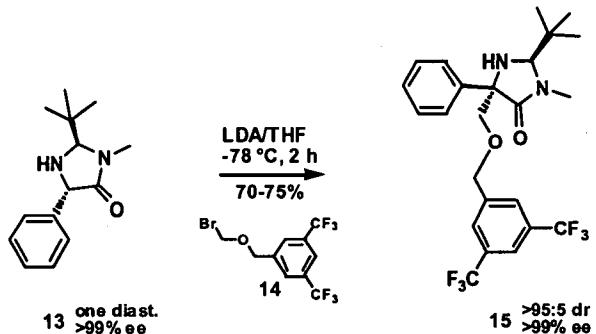
was quenched with brine (25% in H₂O, 500 mL). Extracted the solution with 1:1 THF/EtOAc (4 x 400 mL). Combined organic phases, dried (Na₂SO₄) and concentrated. Dried on high vacuum to give **12** (79.47 g, 98%) as a oil. TLC (EtOAc/MeOH 98:2): *R*_f sm 0.27, *R*_f prod 0.04; stain: pma. [α]²⁵_D = +93.56 (c 0.79, MeOH). ¹H NMR (500 MHz, CDCl₃): δ 2.83 (d, *J* = 4.73 Hz, 3H), 4.54 (s, 1H), 7.03 (br s, 1H), 7.27-7.4 (m, 5H); ¹³C NMR (500 MHz, CDCl₃): δ 25.9, 59.6, 126.8, 127.8, 128.6, 141, 173.6. HRMS: calcd. for C₁₀H₁₃N₂O (M+H) 165.1028; found (M+H) 165.1029. Anal. Calcd for C₁₀H₁₃N₂O: C, 65.83; H, 7.37; N, 17.06. Found: C, 63.63; H, 7.33; N, 16.39.



(R)-2-tert-Butyl-3-methyl-(S)-5-phenyl-imidazolidin-4-one (13). A mixture of **12** (79.44 g, 483.8 mmol, 1 equiv.), pentane (550 mL), and trimethylacetaldehyde (65.7 mL, 604.8 mmol, 1.25 equiv.) was heated to 65°C in a system equipped with a condenser, Dean-Stark trap and nitrogen inlet. The mixture was heated for 3 h and the suspension dissolved. The solution was cooled to room temperature and stirred overnight (16 h). Concentrated the solution and redissolved in MeOH (140-150 mL). Cooled in an ice bath for 30 min and then slowly added saturated HCl-MeOH (300 mL) via a dropping funnel over a 30 min period. The solution was stirred at 0°C and warmed to room temperature under nitrogen overnight. Concentrated on high vac to yield a crude, yellow oil (109.1 g). The oil was redissolved in methylene chloride (800 mL) and washed with 25% K₂CO₃ (w/w, 400 mL). The aqueous portion was washed again with methylene chloride (2 x 400 mL). Combined organics, dried (Na₂SO₄) and concentrated to give a yellow solid (98.7 g). The crude solid was recrystallized out of hot MTBE (300 mL). Cooled to 0°C to give **13** as a white solid (54.88 g, 49%), mp 110.4-111.5 °C. Mother liquor still contained product. This could be isolated by another recrystallization or by chromatography. TLC (CH₂Cl₂/MeOH(NH₃) 98:2): *R*_f sm 0.63, *R*_f prod 0.47; stain: pma. [α]²⁵_D = +60.61 (c 1.05, MeOH). ¹H NMR (500 MHz, CDCl₃): δ 1.04 (s, 9H), 2.26 (br s, 1H), 3.02 (s, 3H), 4.31 (s, 1H), 4.67 (s, 1H), 7.27-7.39 (m, 5H); ¹³C NMR (500 MHz, CDCl₃): δ 25.6, 31.4, 37.7, 62.5, 83.5, 127.2, 127.9, 128.7, 139.8, 174.2. HRMS: calcd. for C₁₄H₂₁N₂O (M+H) 233.1654; found (M+H) 233.1651. Anal. Calcd for C₁₄H₂₀N₂O: C, 72.38; H, 8.68; N, 12.06. Found: C, 72.12; H, 8.75; N, 12.02.

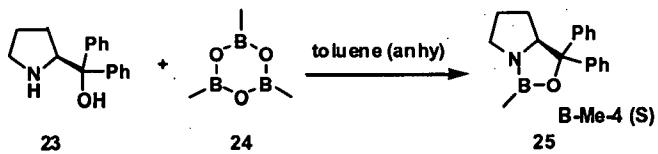


1-Bromomethoxymethyl-3,5-bis-trifluoromethyl-benzene (14). A flame-dried one-neck 200 mL RBF was charged with 3,5-bis(trifluoromethyl)benzyl alcohol **22** (50 g, 204.8 mmol, 1 equiv.) and paraformaldehyde (6.76 g, 225.3 mmol, 1.1 equiv.). The solid mixture was dissolved while under nitrogen with a heat gun until the solution was homogeneous. This process took approximately 20 min using a heat gun. Allowed solution to cool to room temperature. Next HBr gas was bubbled into the solution at a fast rate at ambient temperature. The reaction was continued for 2.5 h. Over this time period the solution changed from clear/white to orange. The layers were separated and the lower aqueous layer was drained. Diluted the upper layer with hexane (150 mL) and again removed any aqueous remnants. Dried light orange hexane layer over MgSO₄ overnight, during which time more of the color dissipated. Filtered and concentrated. Short path distillation (high vac, 75°C to give pure **14** (67.86 g, 98%) as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 4.83 (s, 2H), 5.76 (s, 2H), 7.81 (s, 2H), 7.85 (s, 1H).



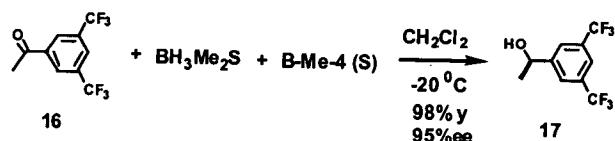
(S)-5-(3,5-Bis-trifluoromethyl-benzyloxymethyl)-(R)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidin-4-one (15). All reagents were deoxygenated under Ar prior to use. 13 (42.05 g, 181 mmol, 1 equiv.) was dissolved in dry THF from a still (550 mL) while agitating with a mechanical stirrer. The solution was cooled to approximately -78°C in dry ice/acetone and a solution of 1.5 M LDA•THF in cyclohexane (124.3 mL, 186.5 mmol, 1.03 equiv.) was added over a 20 min period. This led to the formation of a dark orange/brown solution. This solution was allowed to stir at -78°C for 30 min. Next, bromide 14 (64.0 g, 190 mmol, 1.05 equiv.) was slowly added via syringe over 20 min. Stirred at -78°C and monitored by TLC in 4:1 Hex/EtOAc. Reaction complete after 2 h. The reaction was quenched with sat. aq. NH₄Cl (300 mL) at -78°C and then warmed to room temperature while stirring vigorously. Separated phases and washed organic with H₂O (2 x 150 mL). Aqueous layer was washed with EtOAc (300 mL). Combined organics, dried (Na₂SO₄) and concentrated to give a crude, light yellow solid (90 g). Recrystallized out of hot pentane to give 15 (33.66 g). The mother liquor was again concentrated to an orange solid and recrystallized out of pentane (150 mL) to give an additional 10.50 g of product (Overall yield = 44.16 g, 50%), mp: 114.8-115.3 °C. The mother liquor (46.7 g, approximately 50% pure by NMR) still contained product which could be isolated. [α]²⁵_D = +14.84 (c 0.96, MeOH). ¹H NMR (500 MHz, CDCl₃): δ 0.91 (s, 9H), 2.5 (d, *J* = 6.0 Hz, 1H), 3.0 (s, 3H), 3.6 (d, *J* = 9.5 Hz, 1H), 4.04 (d, *J* = 9.5 Hz, 1H), 4.29 (d, *J* = 6.3 Hz, 1H), 4.61 (d, *J* = 12.9 Hz, 1H), 4.67 (d, *J* = 12.9 Hz, 1H), 7.26-7.29 (m, 2H), 7.35 (t, *J* = 7.25 Hz, 2H), 7.72 (s, 2H), 7.8 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 2 H); ¹³C NMR (500 MHz, CDCl₃): δ 25.6, 31.2, 36.2, 66.9, 71.6, 77.8, 82.8, 121.4, 122.2, 124.4, 126.3, 126.9, 127.6, 128.2, 1131.6 (q, *J* = 132.5 Hz), 139.9, 140.8, 174.0. HRMS: calcd. for C₂₄H₂₇N₂O₂ (M+H) 489.1977; found (M+H) 489.1983. Anal. Calcd for C₂₄H₂₆N₂O₂: C, 59.01; H, 5.37; N, 5.73. Found: C, 58.92; H, 5.32; N, 5.75.

STEP 1:

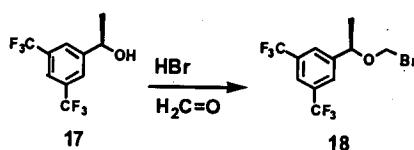


(R)-1-(3,5-Bis-trifluoromethyl-phenyl)-ethanol (17). (Step 1): A flame-dried 50mL one-necked flask was charged with S-Prolinol 22 (5.10 g, 20.1 mmol, 1.0 eq) and 56 mL of anhydrous toluene. This cloudy solution was heated up to 140~150 °C. 36 mL of dry toluene was azeotropically distilled through a Dean-Stark trap with an air condenser. Another 36 mL of toluene was added. This azeotropic distillation was repeated three times to ensure 23 was totally dry. After the third azotropical distillation was done, another 36 mL of anhydrous toluene was added. The solution was allowed to cool down to room temperature. Methylboroxin 24 (1.90 mL, 13.5 mmol, 0.67 eq) was syringed in within 5 minutes. White solid was formed at about 6 minutes after completion of the addition. The reaction mixture was stirred at room temperature for 30 minutes. Then 36 mL of toluene was distilled off ("Gel-like" material which came out first could be the excess boroxin 24). Another 36 mL of dry toluene was added and distilled off again. Repeated the distillation one more time, then 20 mL of 1.0 M of CBS catalyst B-Me-4(S) 25 solution in toluene was prepared. The almost colorless solution can be used in CBS reduction directly.

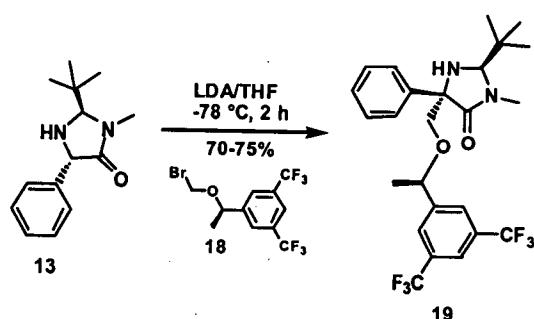
Note: The commercially available CBS was found to give lower %ee.

STEP 2:

(Step 2): A 1L oven-dried round-bottomed flask was charged with 3',5'-Bis(trifluoromethyl)acetophenone **16** (102.14 g, 0.4 mol, 1.0 eq) and 780 mL of anhydrous dichloromethane. The resulting colorless solution was transferred into a dry dropping funnel. Another oven-dried 3L round-bottomed flask was cooled to -20°C , and 20 mL of 1.0 M of CBS catalyst (S)B-Me-4 **25** toluene solution was syringed in, followed by 40 mL of 10.0~10.3 M Borane-Methylsulfide complex **26**. Then the 3',5'-Bis(trifluoromethyl)acetophenone **16** solution was added dropwise through the dropping funnel. (syringe pump is recommended to control the slow addition). The addition was carried out over 2 days. During the addition, the temperature was maintained at -20°C with Cryocool cooling apparatus. Once the addition was finished, the reaction was monitored by TLC in 4:1 Hexane/EtOAc. When **16** was completely consumed, 250 mL of methanol was added slowly. Hydrogen gas was emitted. The reaction solution was then concentrated to give white solid. The solid was dissolved in 500 mL of diethyl ether, then 45 ml of 2.0 M of hydrochloric acid in diethyl ether was added slowly at -20°C . White precipitate was formed. The reaction mixture was warmed up to room temperature and stirred for 30~40 minutes. The mixture was filtered through a funnel, the filtrate was concentrated to give 101.5 g (yield 98.7%) of **17** as a white solid. Chiral HPLC Chiral OD(Chiralcel) column (Hexane/IPA = 98/2) showed 94.6%ee. ^1H NMR (500 MHz, CDCl_3): δ 1.54 (d, J = 6.6 Hz, 3H), 5.04 (q, J = 6.6 Hz, 1H), 7.78 (s, 1H), 7.84 (s, 2H).

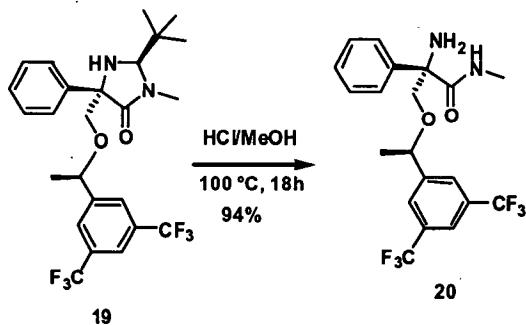


(R)-1-(1-Bromomethoxy-ethyl)-3,5-bis-trifluoromethyl-benzene (18). The compound **18** was prepared from **17** in a method analogous to that described for the preparation of **14** from 3,5-bis(trifluoromethyl)benzyl alcohol. ^1H NMR (500 MHz, CDCl_3): δ 1.56 (d, J = 6.6 Hz, 3H), 5.02 (q, J = 6.6 Hz, 1H), 5.41 (d, J = 4.4 Hz, 1H), 5.77 (d, J = 4.4 Hz, 1H), 7.8 (s, 2H), 7.85 (s, 1H).

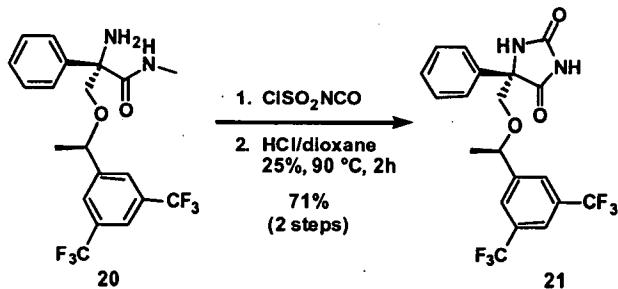


(S)-5-[(R)-1-(3,5-Bis-trifluoromethyl-phenyl)-ethoxymethyl]- (R)-2-tert-butyl-3-methyl-5-phenyl-4-imidazolidin-4-one (19). All reagents were deoxygenated under Ar prior to use. Compound **13** (16.0 g, 63.92 mmol, 1 equiv.) was dissolved in dry THF from a still (200 mL) while agitating with a mechanical stirrer. The solution was cooled to approximately -70°C and a solution of 1M LDA THF in cyclohexane (44 mL, 65.8 mmol, 1.03 equiv.) was added over a 20 min period. This led to the formation of a dark orange/brown solution. This solution was allowed to stir at -78°C for 30 min. Next, bromide **18** (22.6 g, 67.12 mmol, 1.05 equiv.) was slowly added via syringe over 20 min. The solution became a bit lighter with addition of the **18**. Stirred at -78°C and monitored by TLC in 4:1 Hex/EtOAc. Reaction complete after 2 h. The reaction was

quenched with sat. aq. NH₄Cl (100 mL) and then warmed to room temperature while stirring vigorously. Separated phases and washed organic with H₂O (2 x 50 mL). Dried (Na₂SO₄) and concentrated to give a crude, light yellow solid (32.63 g). Recrystallized out of hot pentane to give **19** (17.65 g, 55%). The mother liquor still contained starting product which could be isolated. mp 107.5–108 °C, TLC (hex/EtOAc 4:1): R_fsm 0.13, R_fprod 0.5; stain: pma. [α]_D²⁵ = +43.16 (c 1.04, MeOH). ¹H NMR (500 MHz, CDCl₃): δ 0.92 (s, 9H), 1.41 (d, J = 6.3 Hz, 3H), 2.43 (d, J = 7.25 Hz, 1H), 3.04 (s, 3H), 3.36 (d, J = 9.77 Hz, 1H), 3.88 (d, J = 9.77 Hz, 1H), 4.32 (d, J = 7.57 Hz, 1H), 4.6 (q, J = 6.6 Hz, 1H); 7.22–7.26 (m, 2H), 7.31 (t, J = 7.25 Hz, 2H), 7.69 (s, 2H), 7.72 (d, J = 8.5 Hz, 2H) 7.76 (s, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 23.8, 25.6, 31.2, 36.2, 67.0, 76.2, 77.7, 82.9, 121.4, 121.5, 122.2, 124.3, 126.0, 126.3, 127.5, 128.1, 131.8 (q, J = 132.5 Hz), 139.9, 146.5, 174.2. HRMS: calcd. for C₂₅H₂₉F₆N₂O₂ (M+H) 503.2133; found (M+H) 503.2126. Anal. Calcd for C₂₅H₂₈F₆N₂O₂: C, 59.76; H, 5.62; N, 5.57. Found: C, 59.71; H, 5.60; N, 5.53.

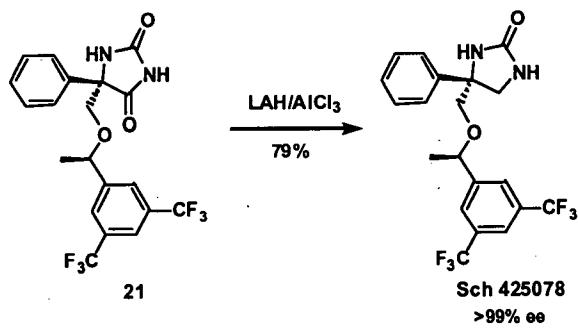


(S)-2-Amino-[*(R*)-1-(3,5-bis-trifluoromethyl-phenyl)-ethoxy]-N-methyl-2-phenyl-propionamide (20**).** Compound **19** (18.53 g, 36.87 mmol, 1 equiv.) was dissolved in 160 mL of MeOH. 160 mL concentrated HCl added and the mixture was heated at 87 °C overnight. Cooled to room temperature and concentrated. The resulting residue was taken in 300 mL CH₂Cl₂ and 200 mL saturated aq. K₂CO₃ was added and stirred for 30 minutes (pH of the solution should be higher than 10). Organic layer separated and aqueous layer washed with 2x 200 mL CH₂Cl₂. Combined organic layers were washed with 300 mL of saturated aq. NaCl. Organic layer dried over anhydrous Na₂SO₄, filtered and concentrated to give the product **20** (15 g, 94%) as colorless oil. TLC (hex/EtOAc) 1:1: R_fsm 0.81, R_fprod 0.29; stain: pma. [α]_D²⁵ = +48.83 (c 1.03, MeOH). ¹H NMR (500 MHz, CDCl₃): δ 1.44 (d, J = 6.6 Hz, 3H), 2.02 (br s, 2H), 2.81 (d, J = 5.0, 3H), 3.44 (d, J = 9.1 Hz, 1H), 4.3 (d, J = 9.1 Hz, 1H), 4.7 (q, J = 6.6 Hz, 1H); 7.24–7.3 (m, 1H), 7.31 (t, J = 6.9 Hz, 2H), 7.44 (d, J = 7.25 Hz, 2H), 7.6 (s, 1H), 7.7 (s, 2H), 7.78 (s, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 14.2, 21.0, 24.0, 26.2, 60.4, 63.6, 75.2, 78.1, 121.5, 122.2, 124.3, 125.1, 126.1, 126.2, 127.8, 128.6, 131.8 (q, J = 132.5 Hz), 140.2, 146.6, 173.7. HRMS: calcd. for C₂₀H₂₁F₆N₂O₂ (M+H) 435.1507; found (M+H) 435.1505. Anal. Calcd for C₂₀H₂₀F₆N₂O₂: C, 55.30; H, 4.64; N, 6.45. Found: C, 54.95; H, 4.71; N, 6.39.

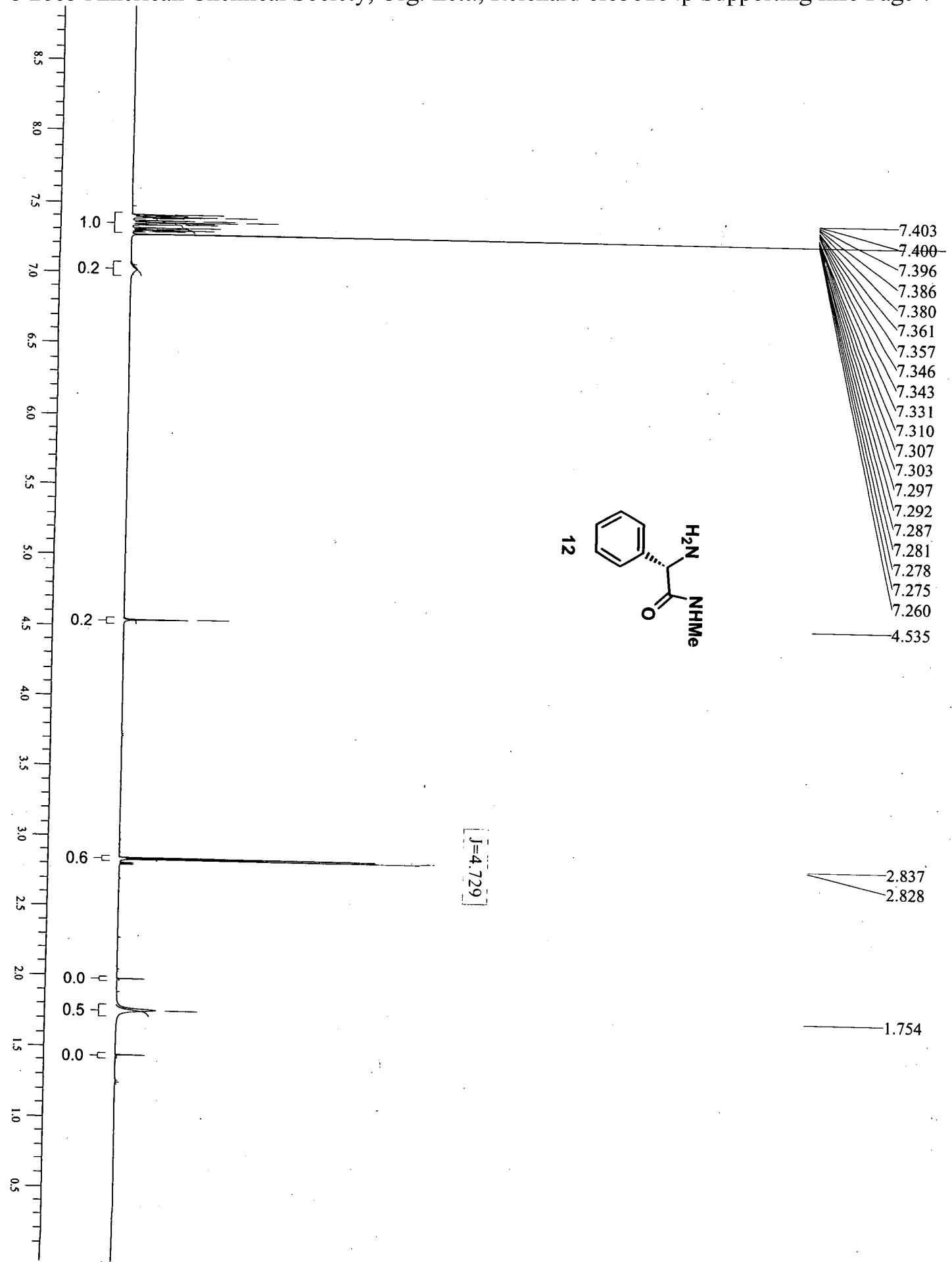


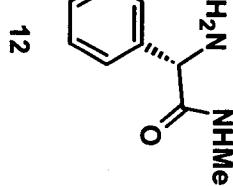
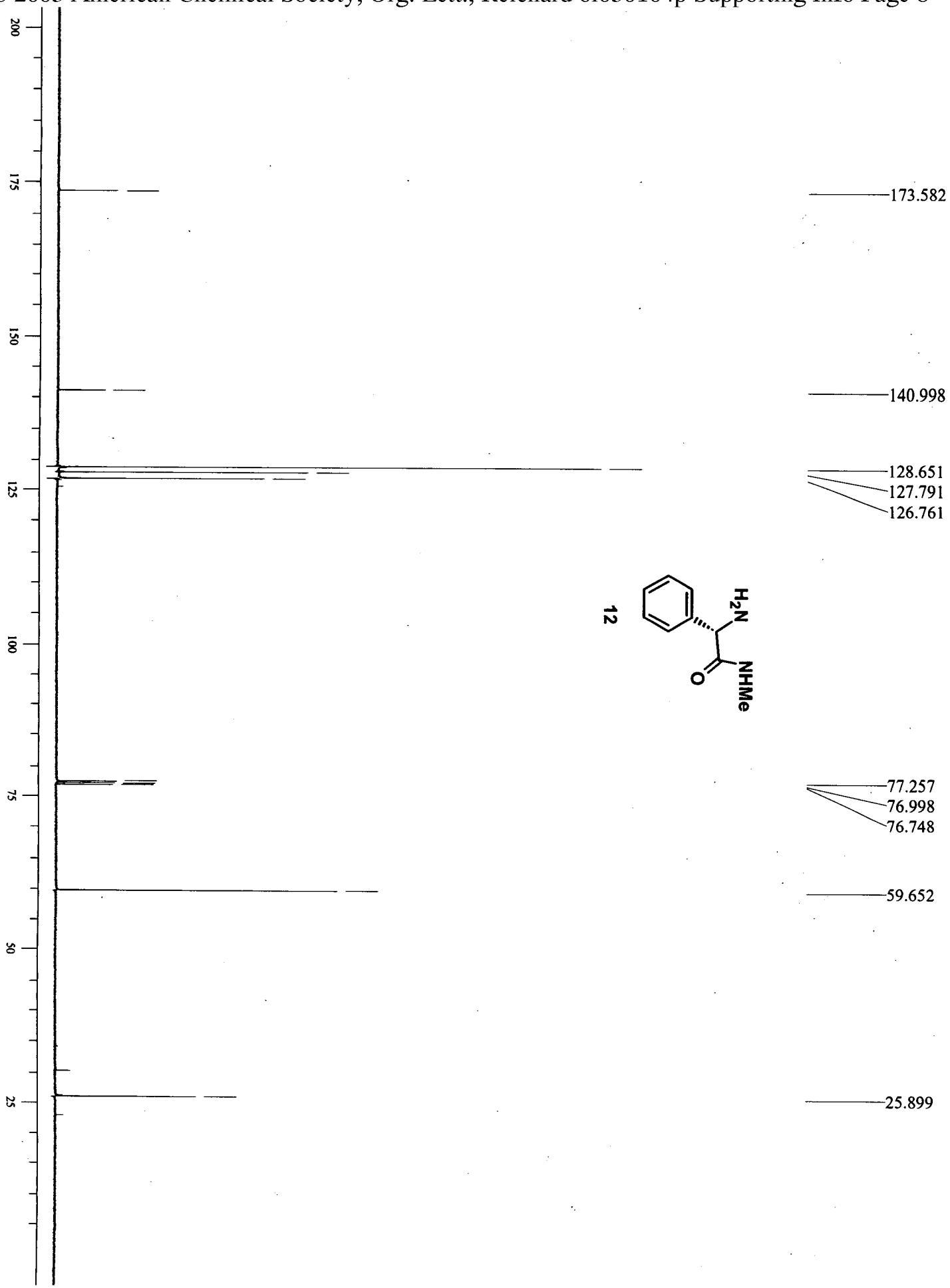
(S)-5-[*(R*)-1-(3,5-Bis-trifluoromethyl-phenyl)-ethoxymethyl]-5-phenyl-imidazolidine-2,4-dione (21**).** Amino amide **20** (14.14 g, 32.55 mmol, 1 equiv.) was taken up in dry methylene chloride (120 mL). The solution was cooled to -78°C and chlorosulfonyl isocyanate (2.84 mL, 32.55 mmol, 1 equiv.) was added. The reaction was stirred at 0°C for 3 h and then concentrated to a white solid. The solid was dissolved in 1,4-dioxane (120 mL) and 3 N aqueous HCl (120 mL). Stirred at 90°C for 5 h and stirred at room temperature overnight. Diluted solution with H₂O (250 mL) and extracted with EtOAc (3 x 400 mL). Combined organics,

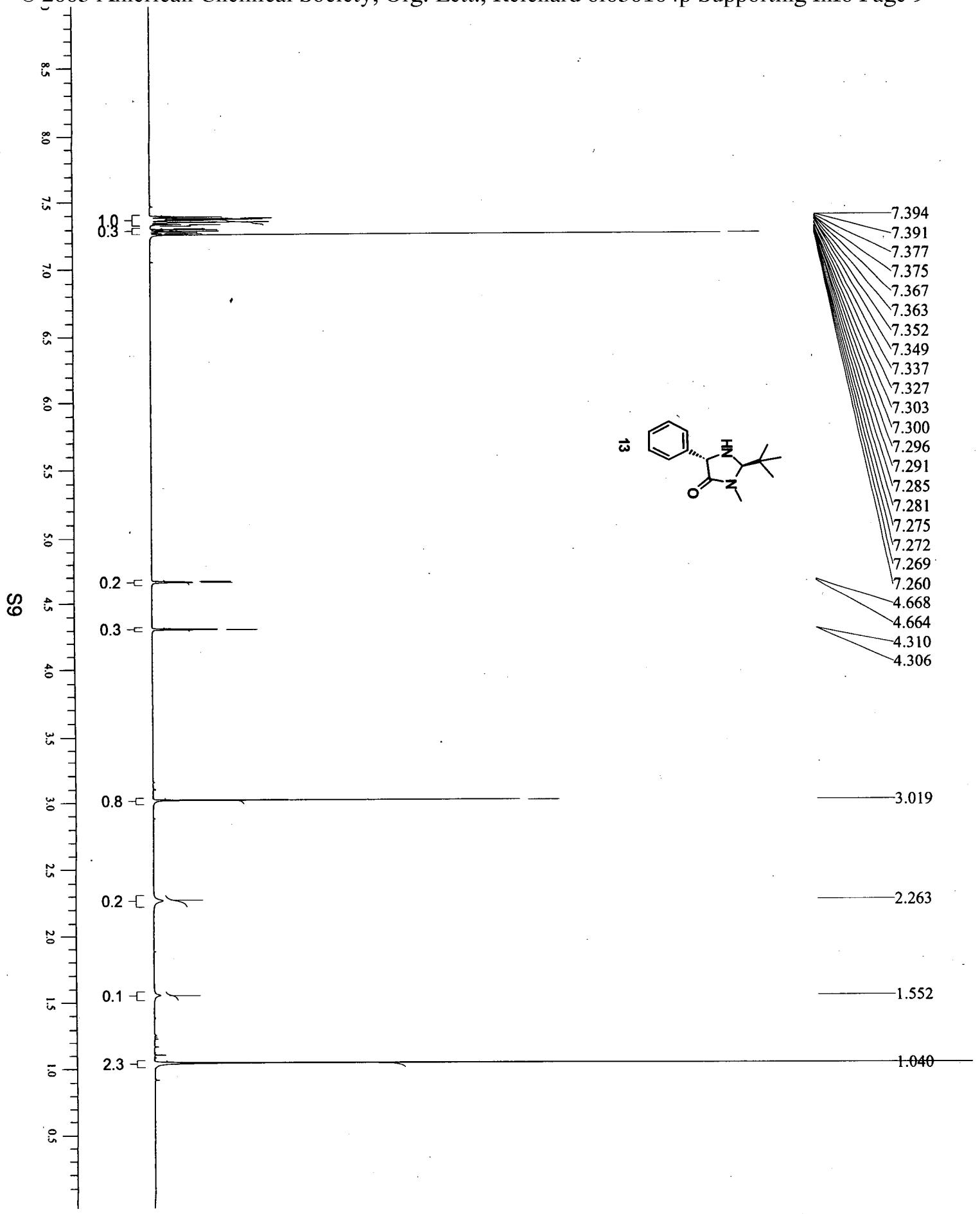
dried (Na_2SO_4), and concentrated to a crude, white foam (15.80 g). Performed plug chromatography on a 600 mL fritted funnel eluting with 2:1 Hex/EtOAc. Collected and concentrated fractions 2-8 to give pure **21** (10.26 g, 71%). TLC (hex/EtOAc 2:1): R_f sm 0.11, R_f prod 0.29; stain: pma. $[\alpha]^{25}_{D} = -32.82$ (c 1.02, MeOH). ^1H NMR (500 MHz, CDCl_3): δ 1.44 (d, $J = 6.6$ Hz, 3H), 3.7 (d, $J = 9.8$ Hz, 1H), 3.93 (d, $J = 9.5$ Hz, 1H), 4.58 (q, $J = 6.6$ Hz, 1H); 6.34 (br s, 1H), 7.37-7.39 (m, 3H), 7.47-7.49 (m, 2H), 7.6 (s, 2H), 7.78 (s, 1H), 7.9 (br s, 1H); ^{13}C NMR (500 MHz, CDCl_3): δ 23.8, 68.9, 72.9, 78.3, 121.8, 122.1, 124.2, 125.3, 126.1, 128.9, 132.0 (q, $J = 132$ Hz), 134.3, 145.4, 156.8, 173.2. HRMS: calcd. for $\text{C}_{20}\text{H}_{17}\text{F}_6\text{N}_2\text{O}_3$ ($M+\text{H}$) 447.1143; found ($M+\text{H}$) 447.1146. Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{F}_6\text{N}_2\text{O}_2$: C, 53.82; H, 3.61; N, 6.28. Found: C, 53.87; H, 3.54; N, 6.22.

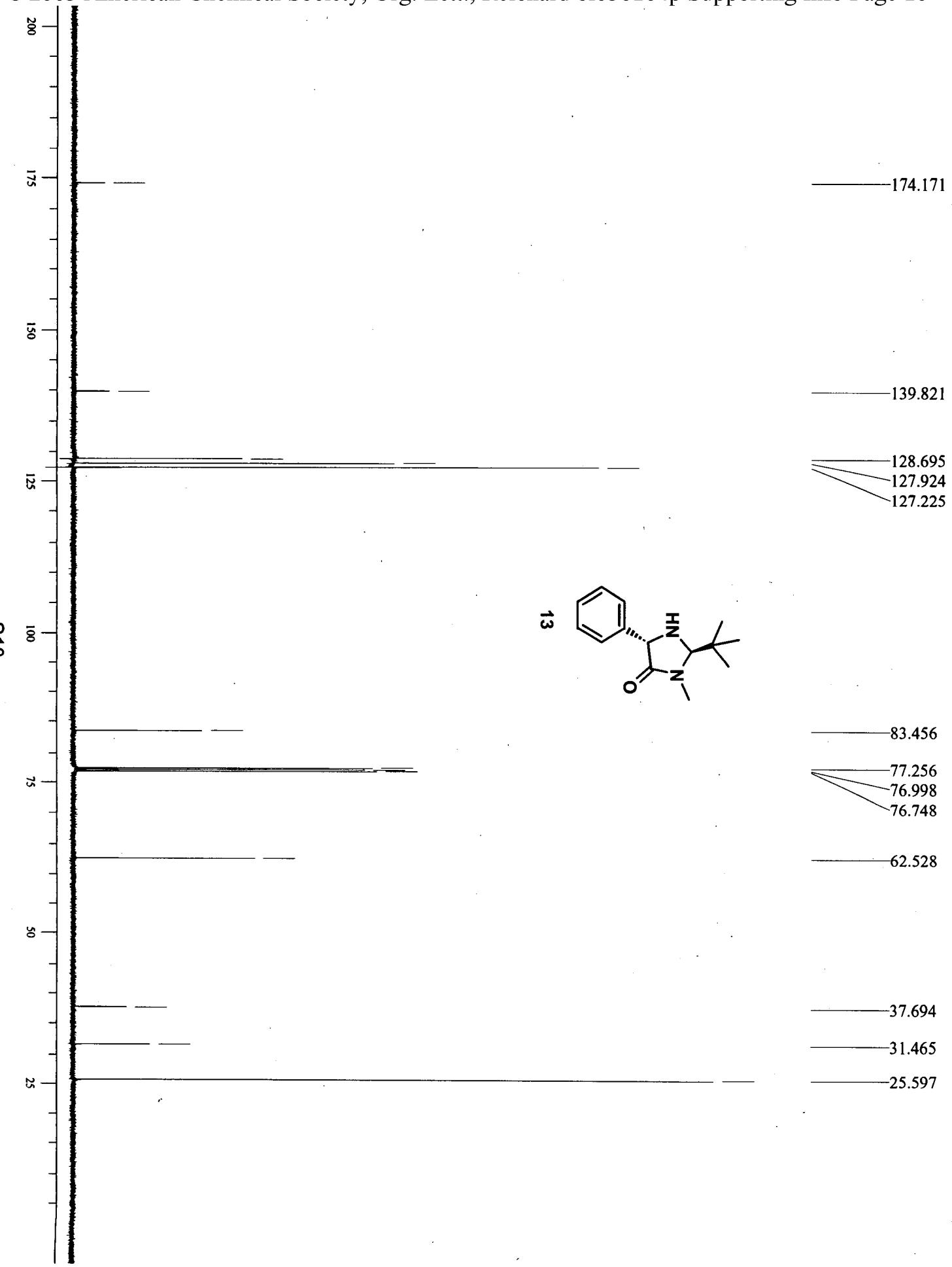


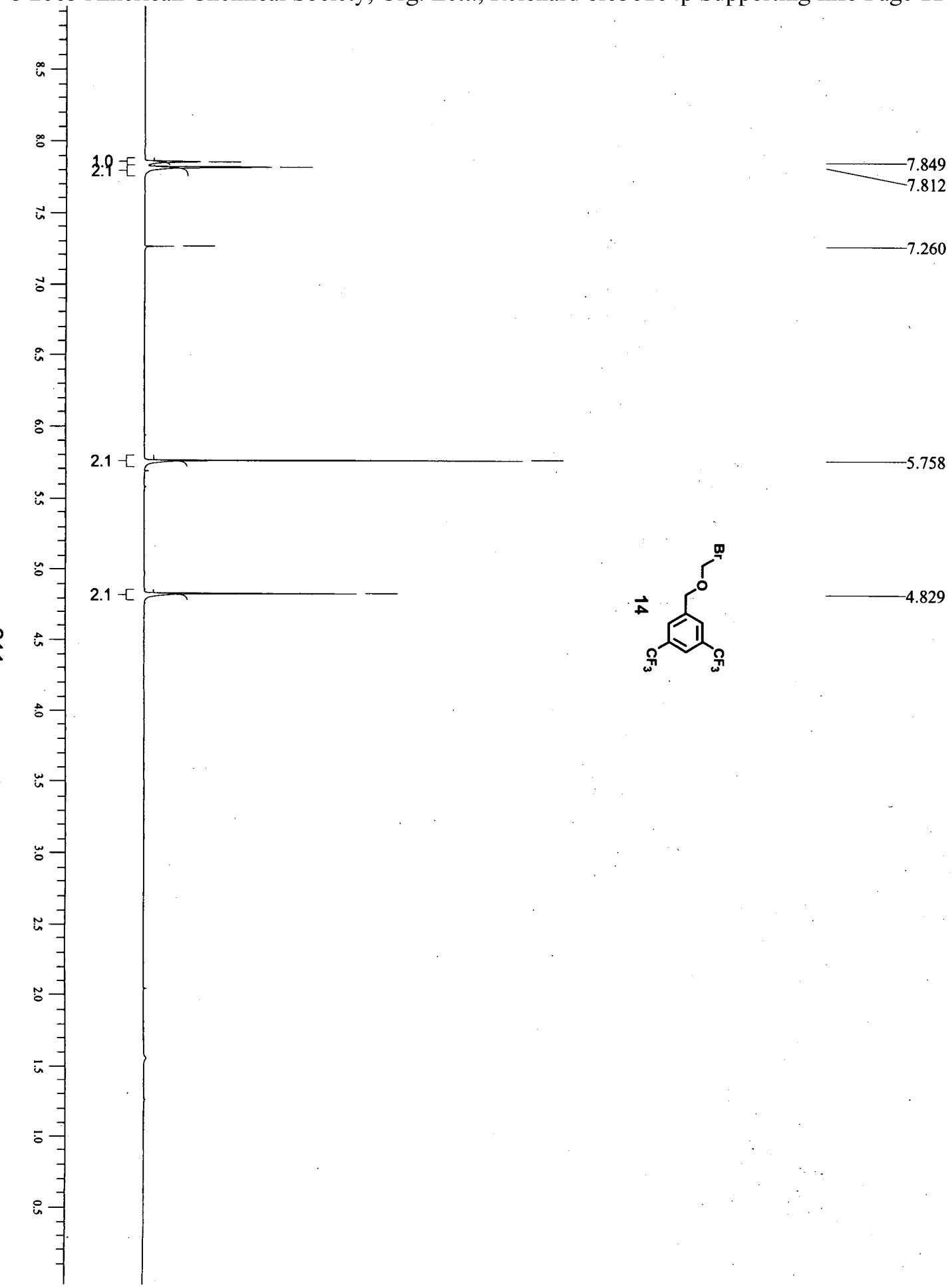
(R)-4-[(R)-1-(3,5-bistrifluoromethyl-phenyl)-ethoxymethyl]-4-phenyl-imidazolidin-2-one (Sch 425078). AlCl_3 (12.2 g, 91.4 mmol, 4 equiv.) was added to a flame-dried 1L 3-neck RBF equipped with stir bar and nitrogen inlet. The flask was cooled to 0°C and slowly added a solution of 1 M LAH in ether (68.6 mL, 68.6 mmol, 3 equiv.). This formed a white slurry which was stirred at 0°C for 15 min. Next, a solution of hydantoin **21** (10.2 g, 22.85 mmol, 1 equiv.) in 150 mL dry THF was added via canula. The solution was warmed to room temp. and stirred for 41 h. The solution was again cooled to 0°C and H_2O (20 mL) was added. Next, added 15% aq. NaOH (w/w, 20 mL) followed by more H_2O (60 mL). The biphasic solution was stirred for 30 min. All emulsion formed was dissolved with 1 N HCl (approximately 300-400 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 500 mL). Combined organics, washed with H_2O (200 mL), dried (Na_2SO_4), and concentrated to give the crude (9.86 g). The crude material was initially purified by plug chromatography on a 2L fritted funnel eluting with 1:1 Hex/EtOAc, followed by 98:2 EtOAc to give 8.0 g of material, which still contained 3% of a less polar impurity. The solid was recrystallized from hot MTBE (30 mL) to provide pure Sch 425078 (6.5 g, 79%). TLC (EtOAc/Et₃N 9:1): R_f sm 0.73, R_f prod 0.38; stain: pma. ^1H NMR (500 MHz, CDCl_3): δ 1.38 (d, $J = 6.6$ Hz, 3H), 3.46 (d, $J = 8.8$ Hz, 1H), 3.52 (d, $J = 8.8$ Hz, 1H), 3.63 (d, $J = 8.8$ Hz, 1H), 3.74 (d, $J = 8.8$ Hz, 1H), 4.48 (q, $J = 6.3$ Hz, 1H), 4.65 (br s, 1H), 5.42 (br s, 1H), 7.24-7.39 (m, 5H), 7.46 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (500 MHz, CDCl_3): δ 23.9, 50.7, 63.2, 74.7, 77.9, 121.6, 122.1, 124.2, 124.9, 126.1, 127.7, 128.7, 131.8 (q, $J = 132.5$ Hz), 142.1, 145.89, 162.7. HRMS: calcd. for $\text{C}_{20}\text{H}_{19}\text{F}_6\text{N}_2\text{O}_2$ ($M+\text{H}$) 433.1351; found ($M+\text{H}$) 433.1349.

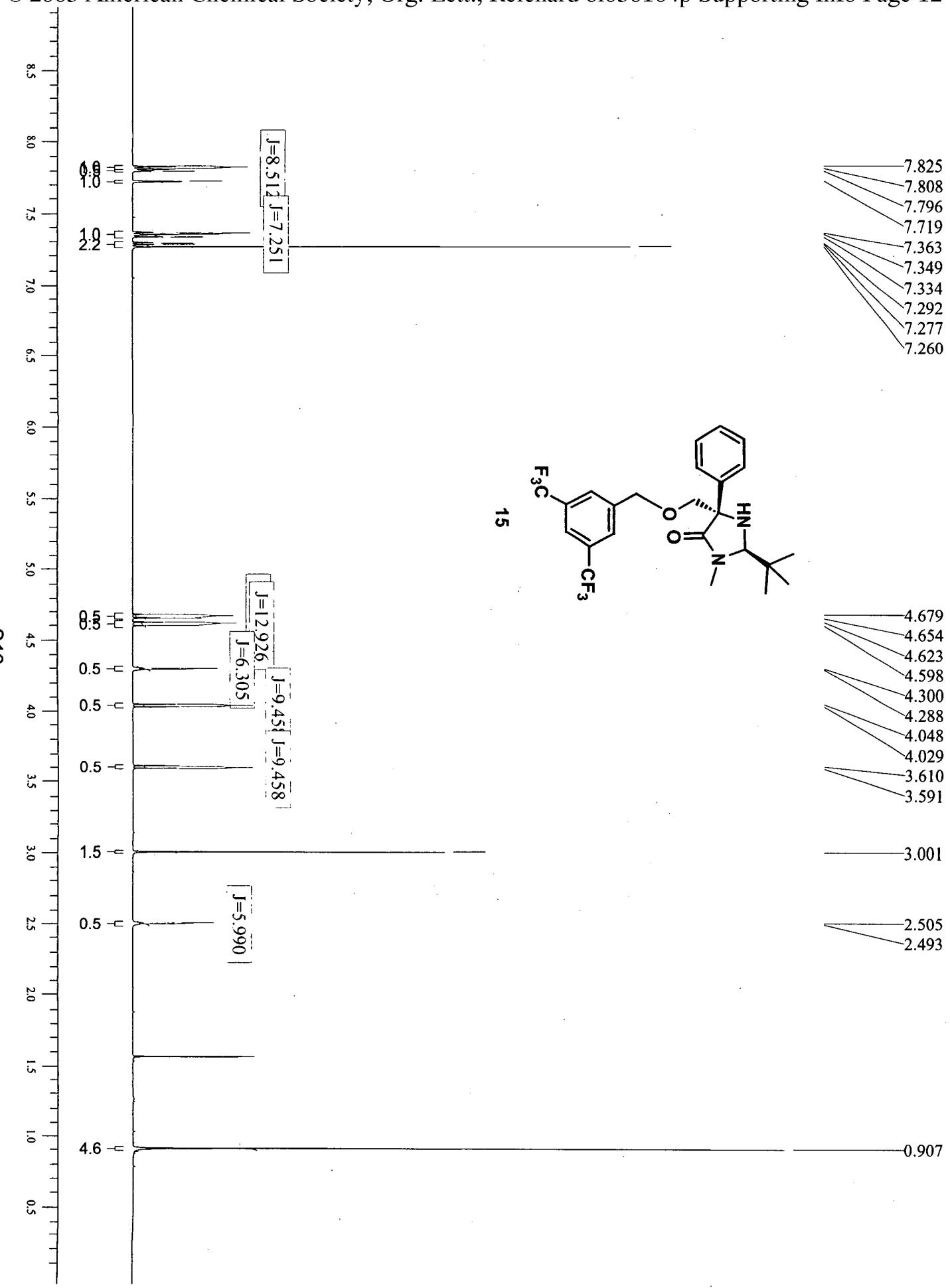


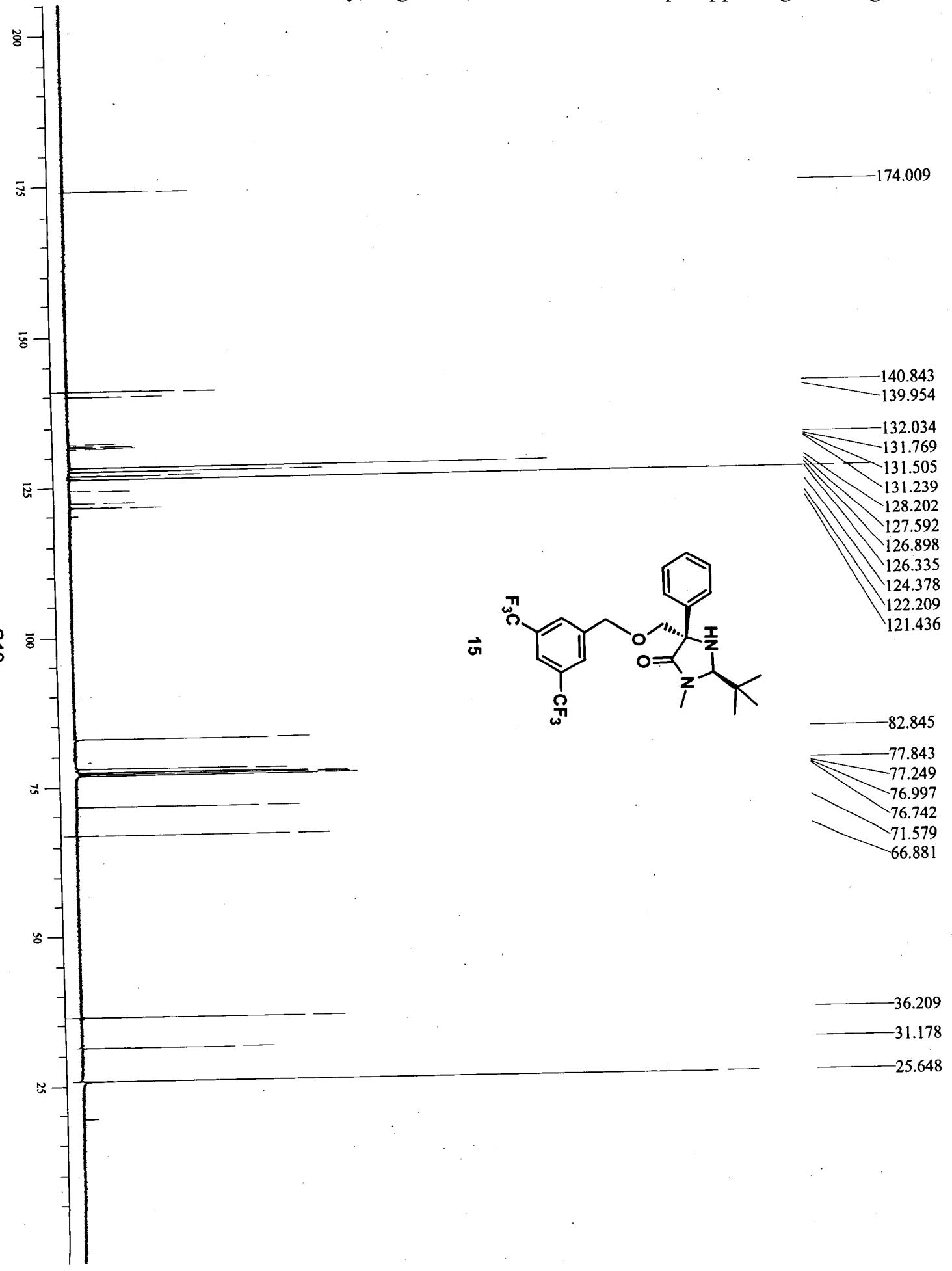




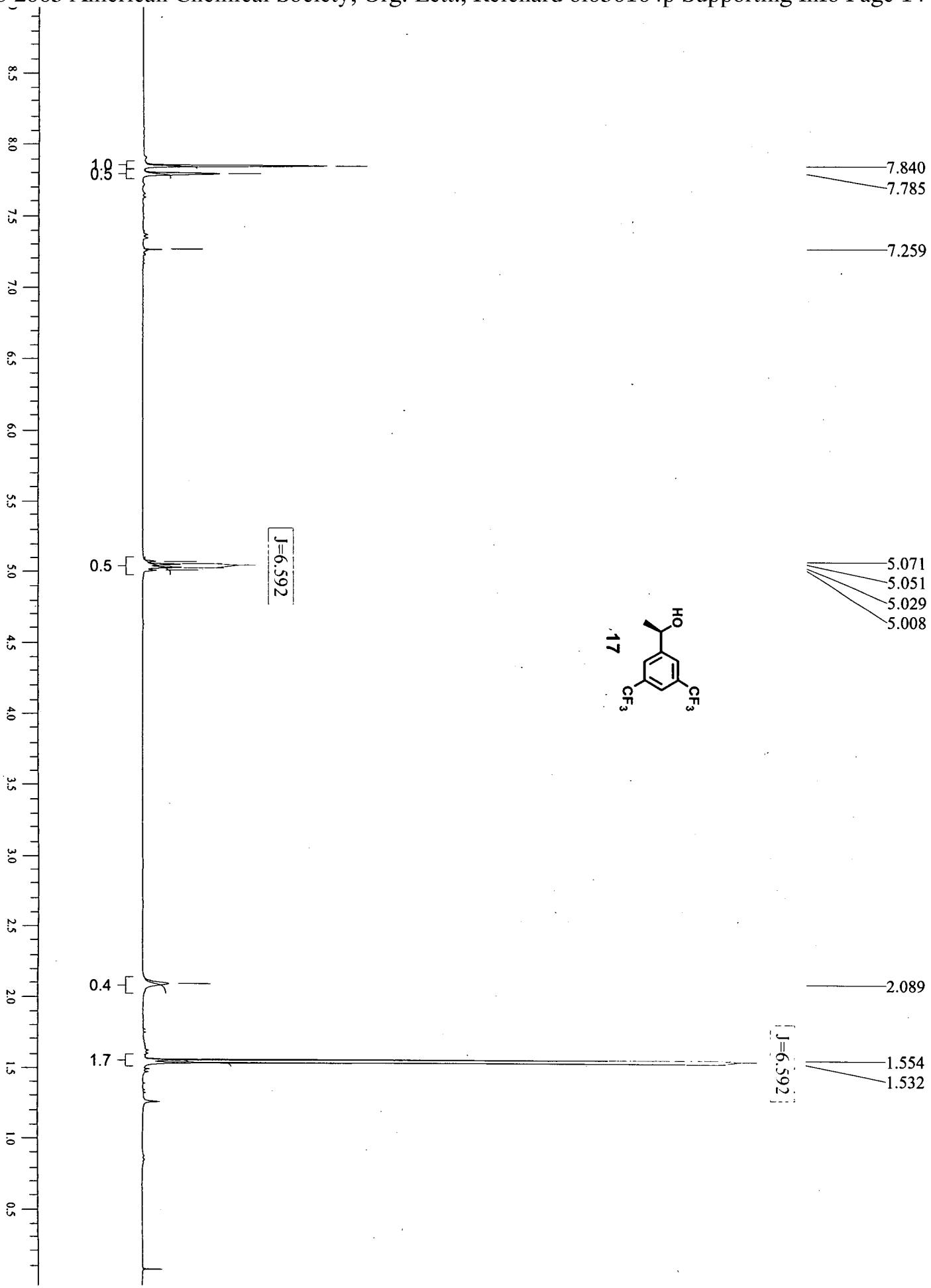


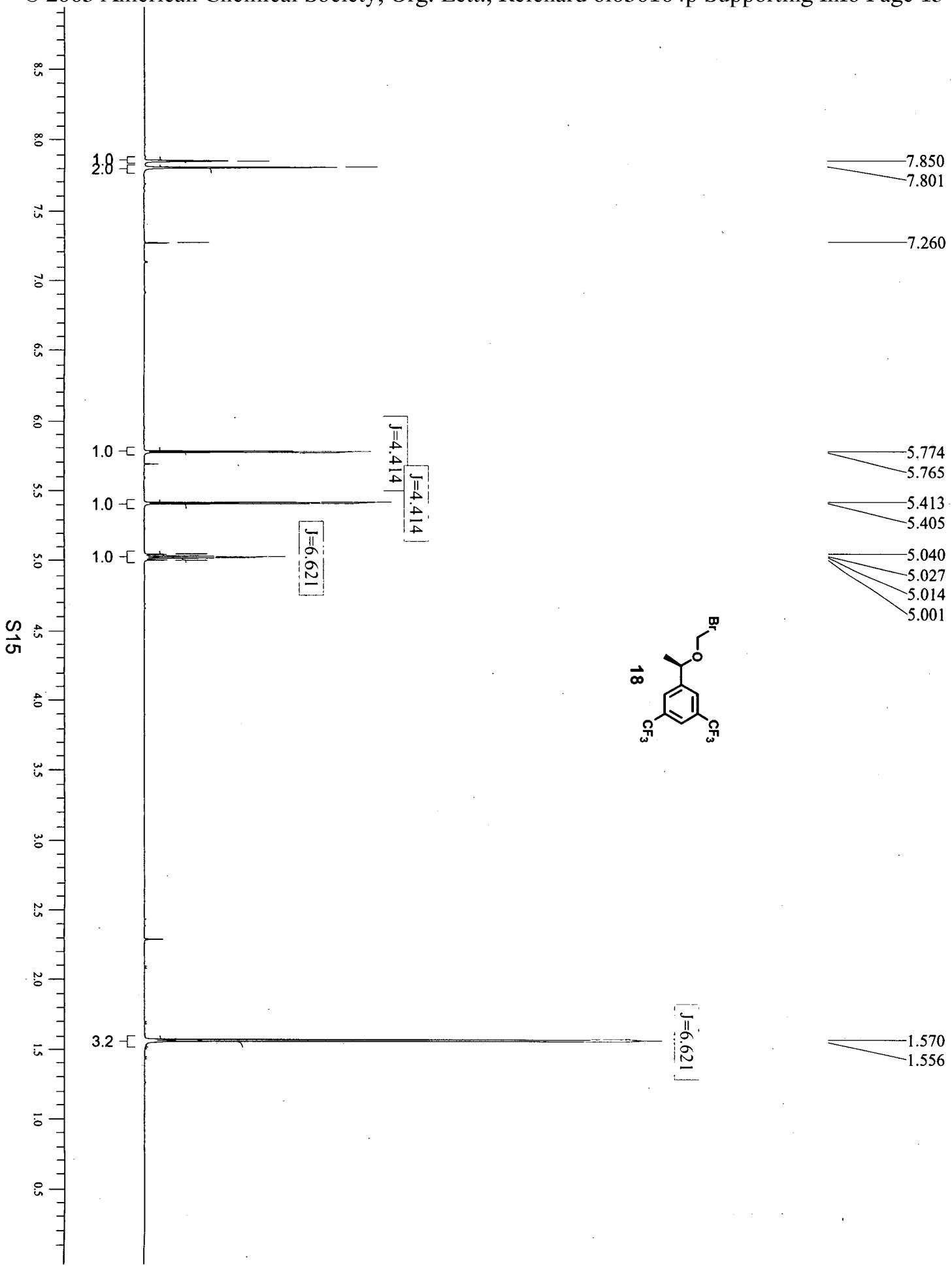


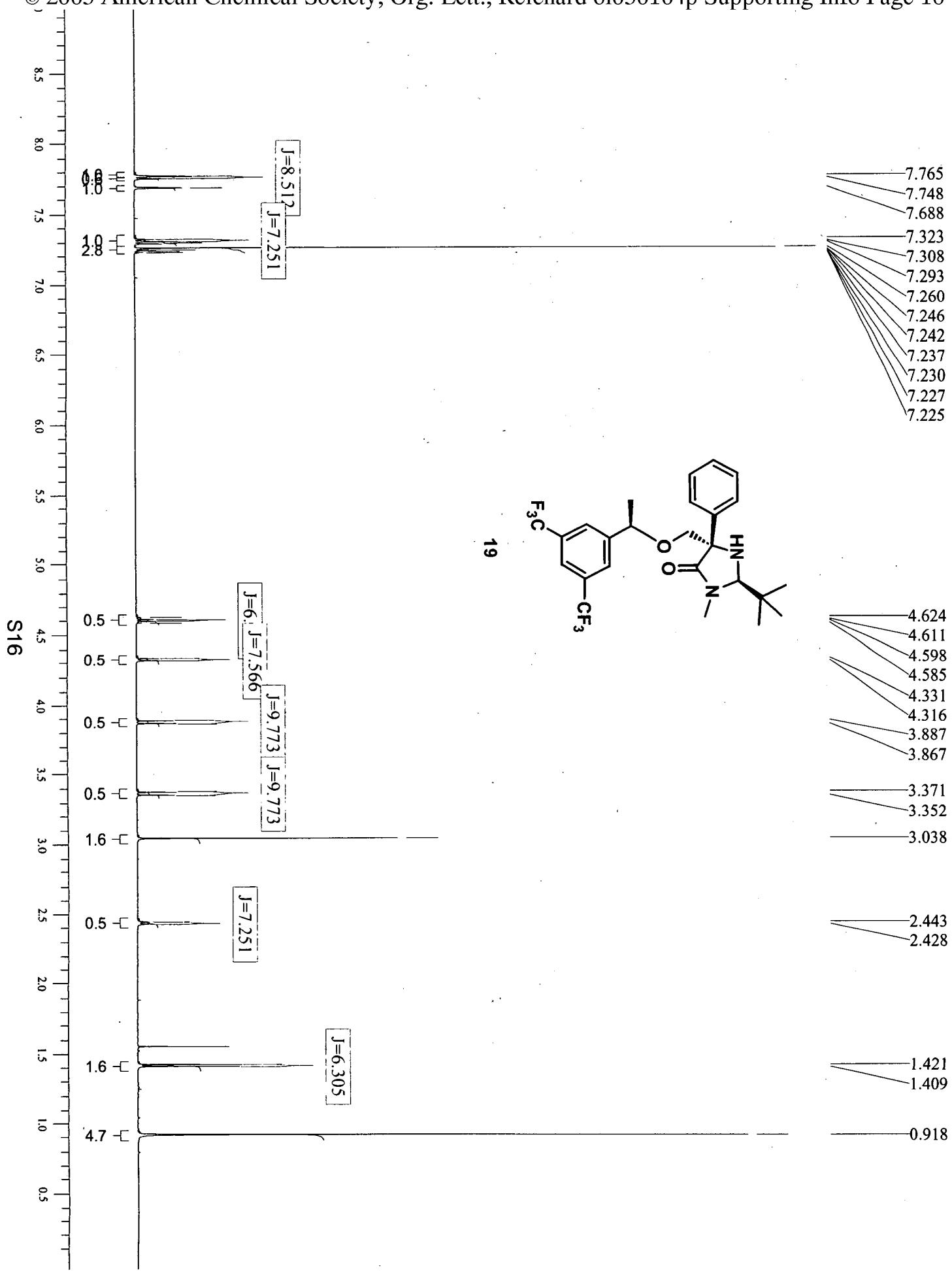


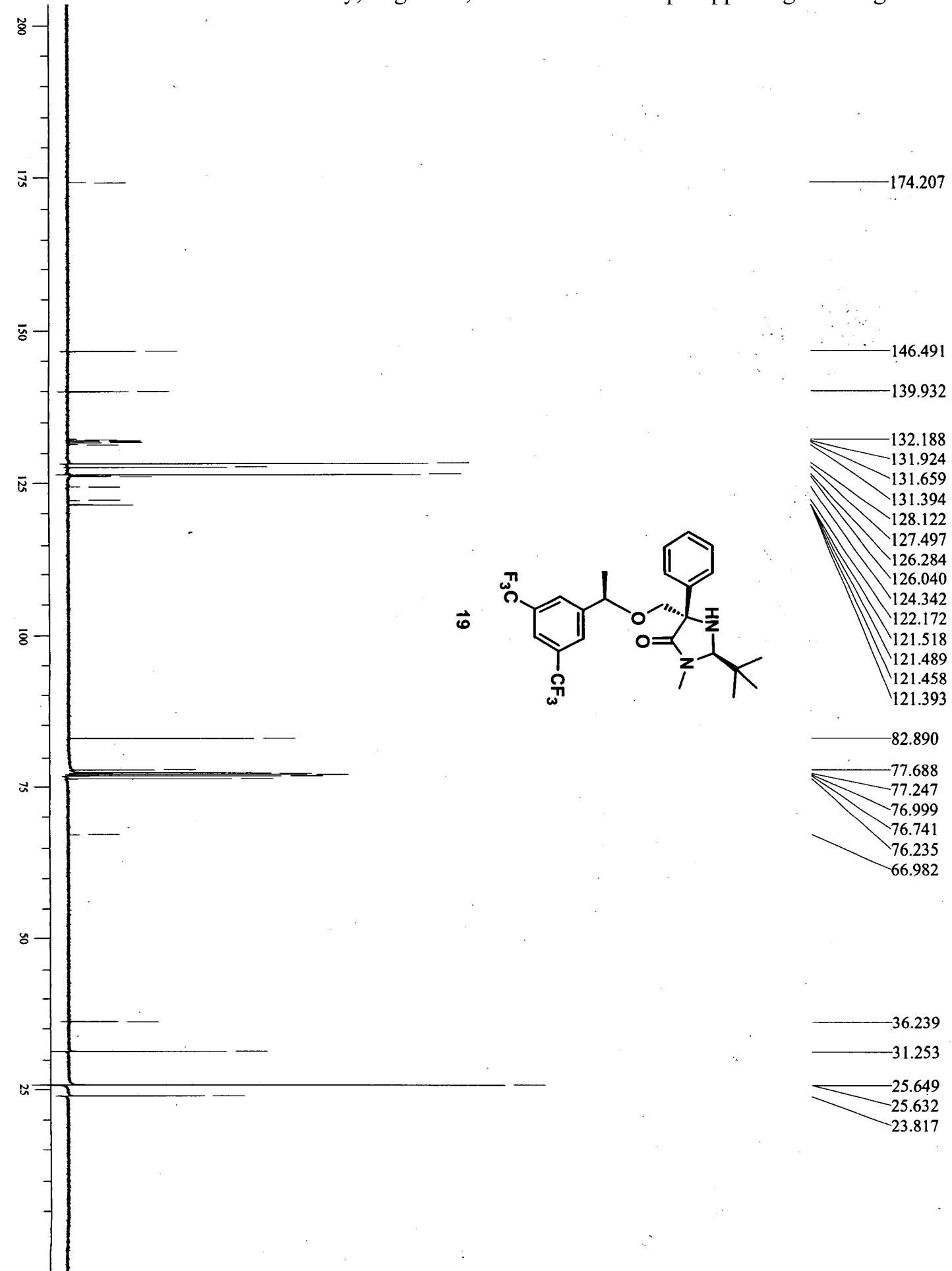


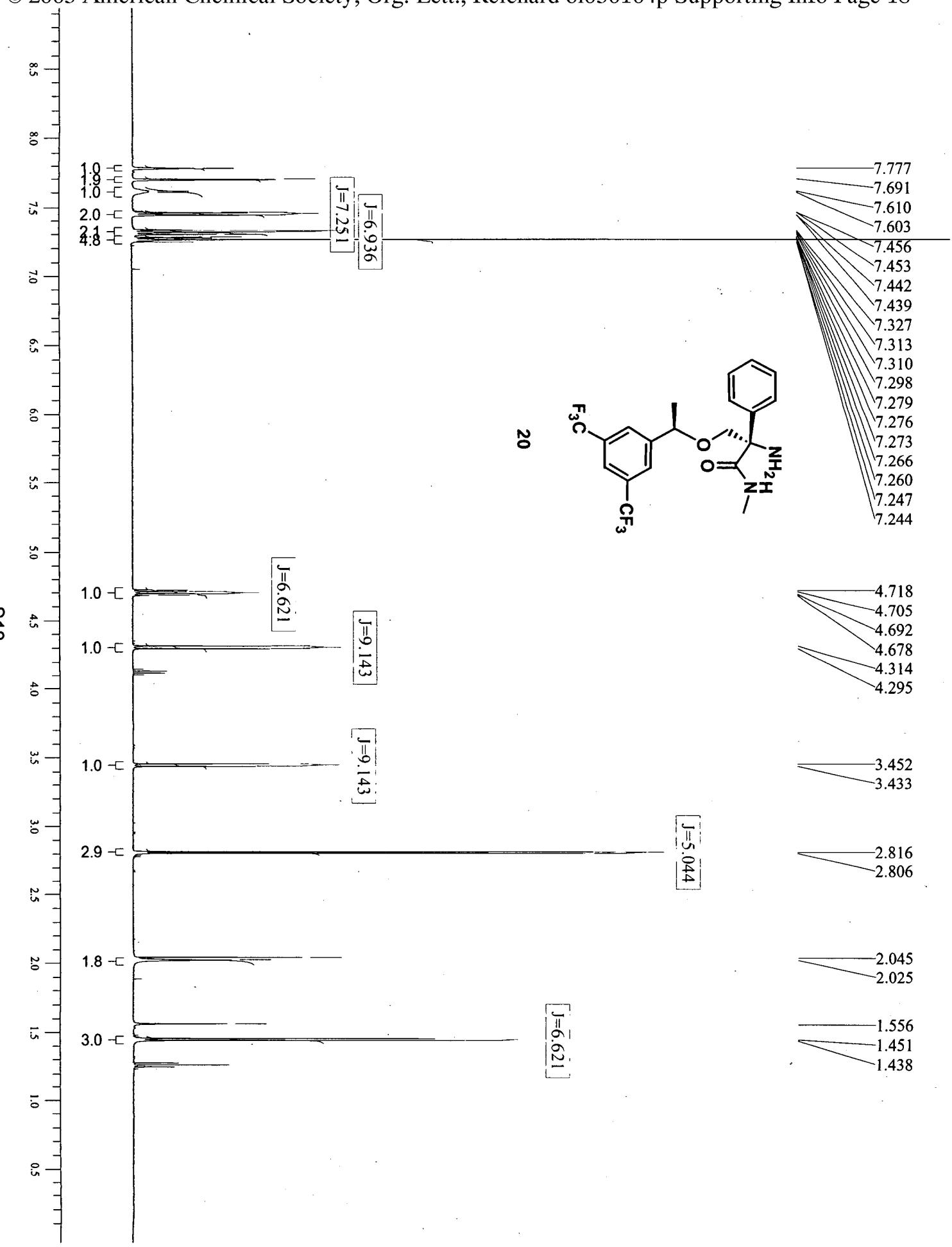
S14

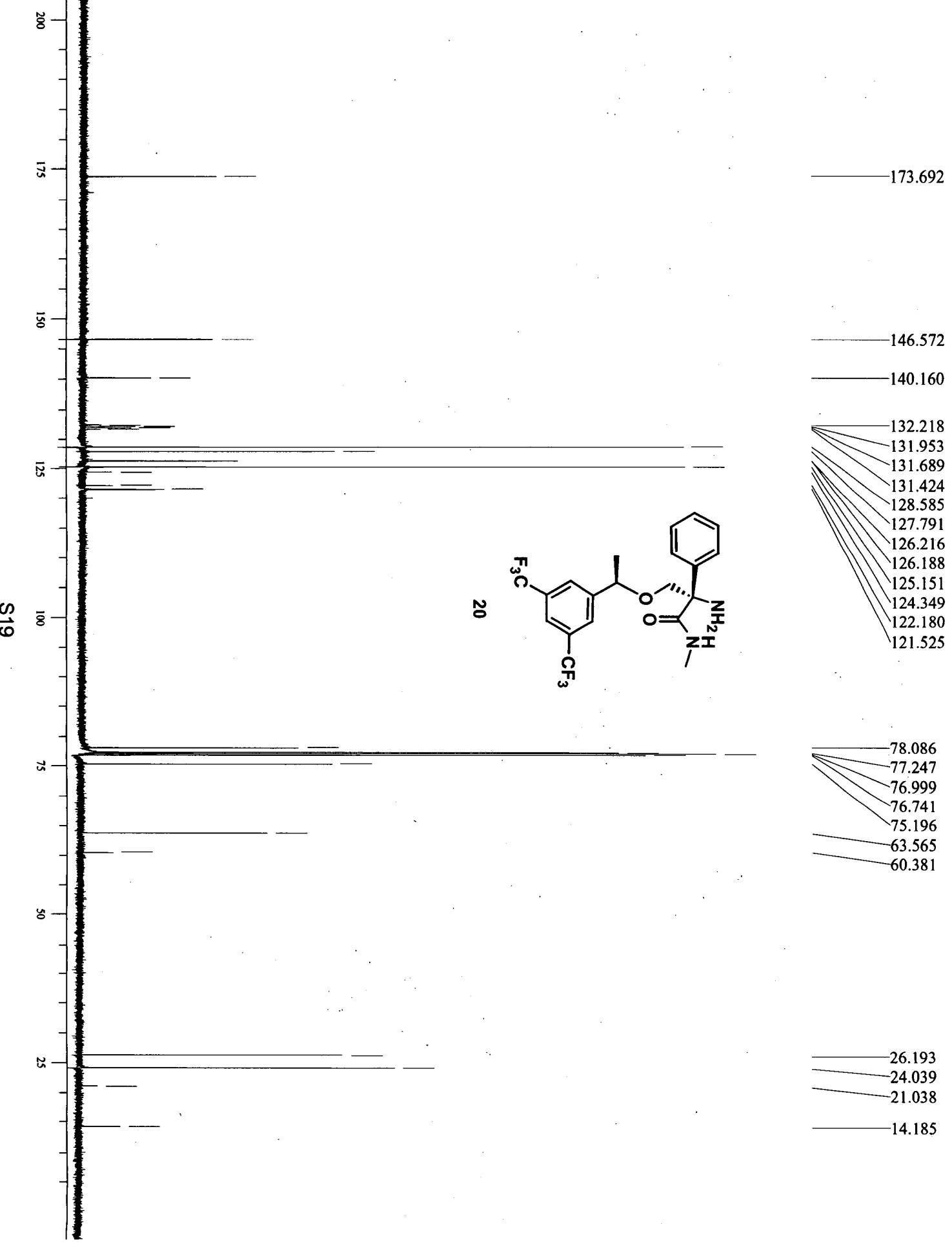


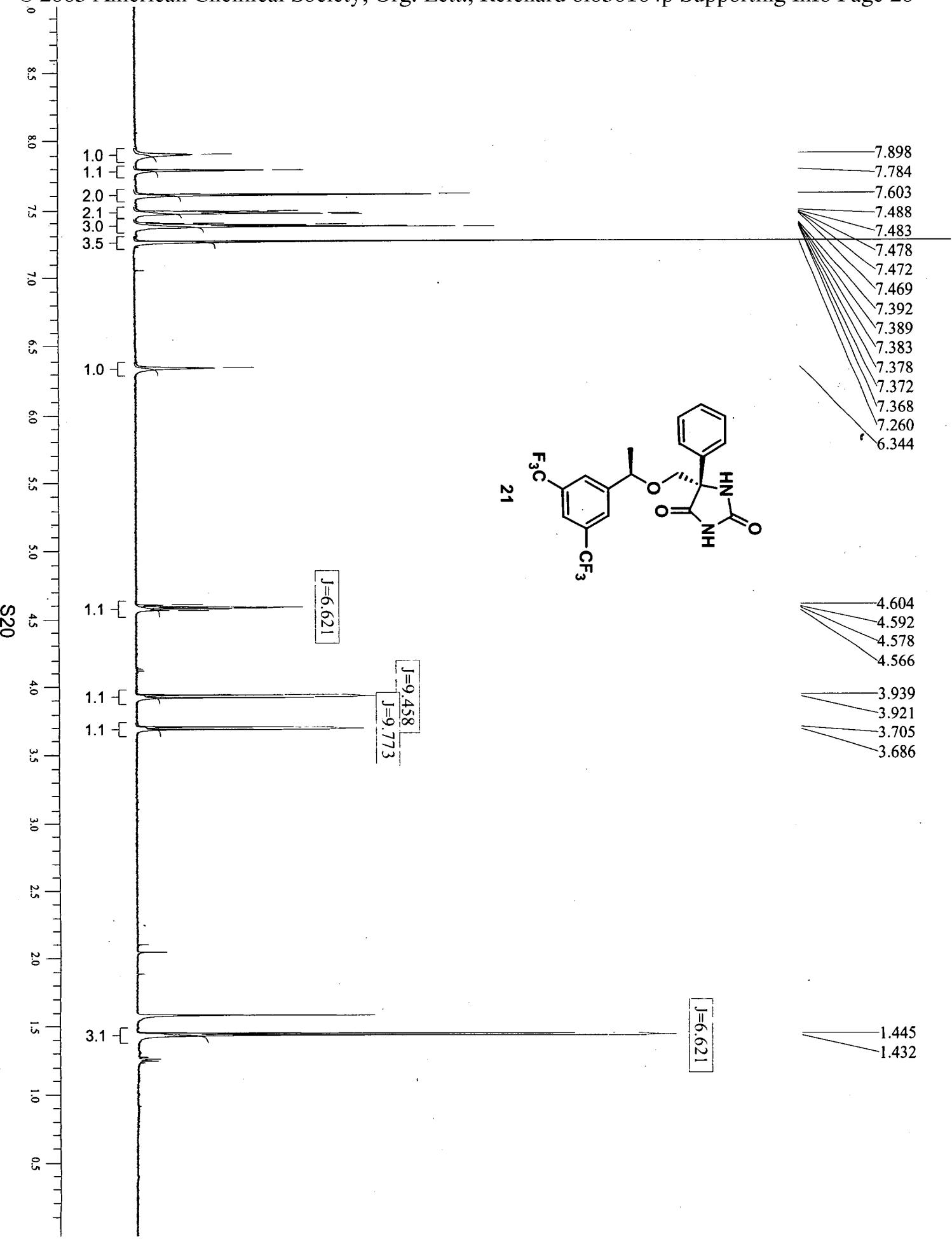


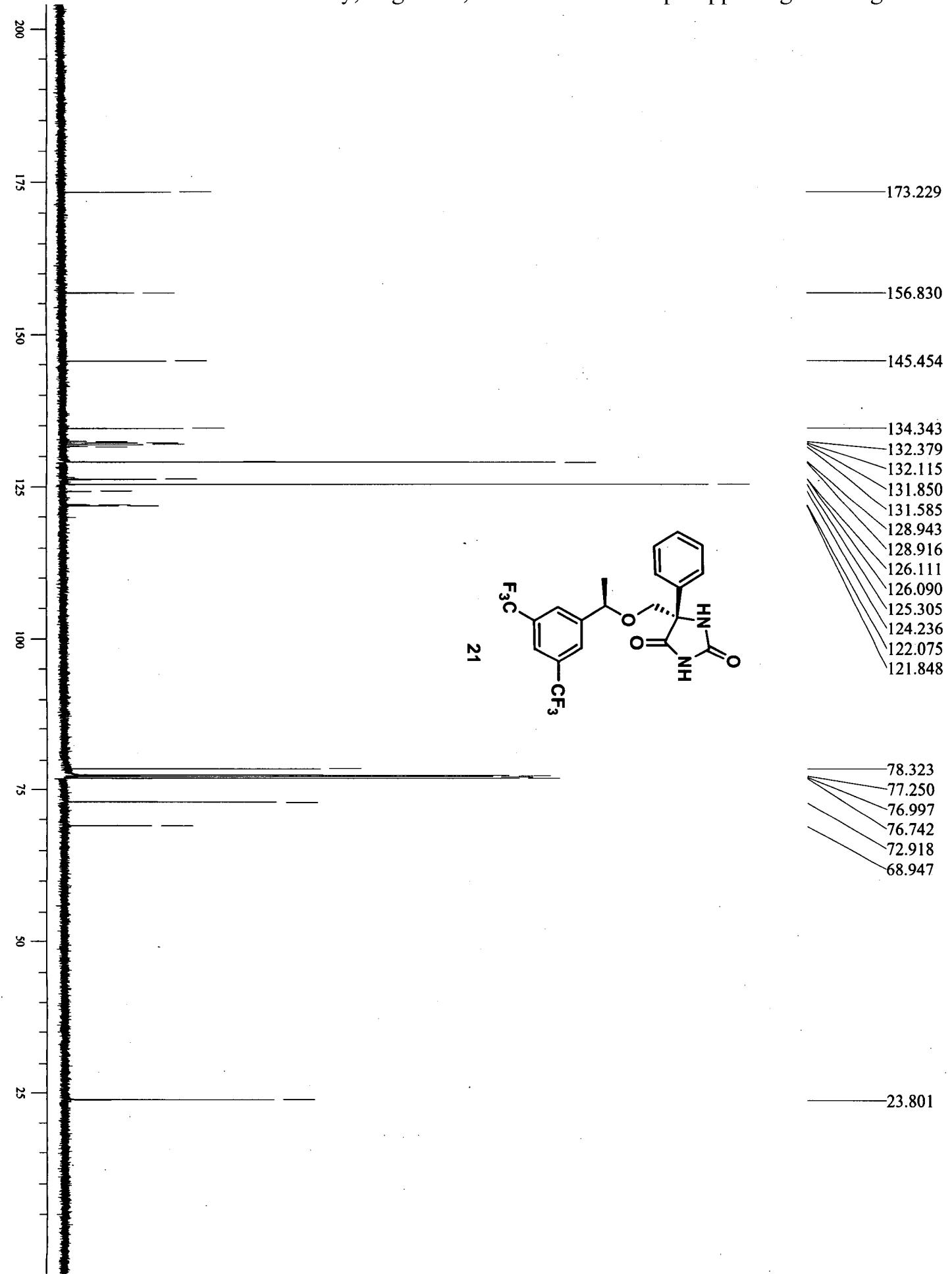




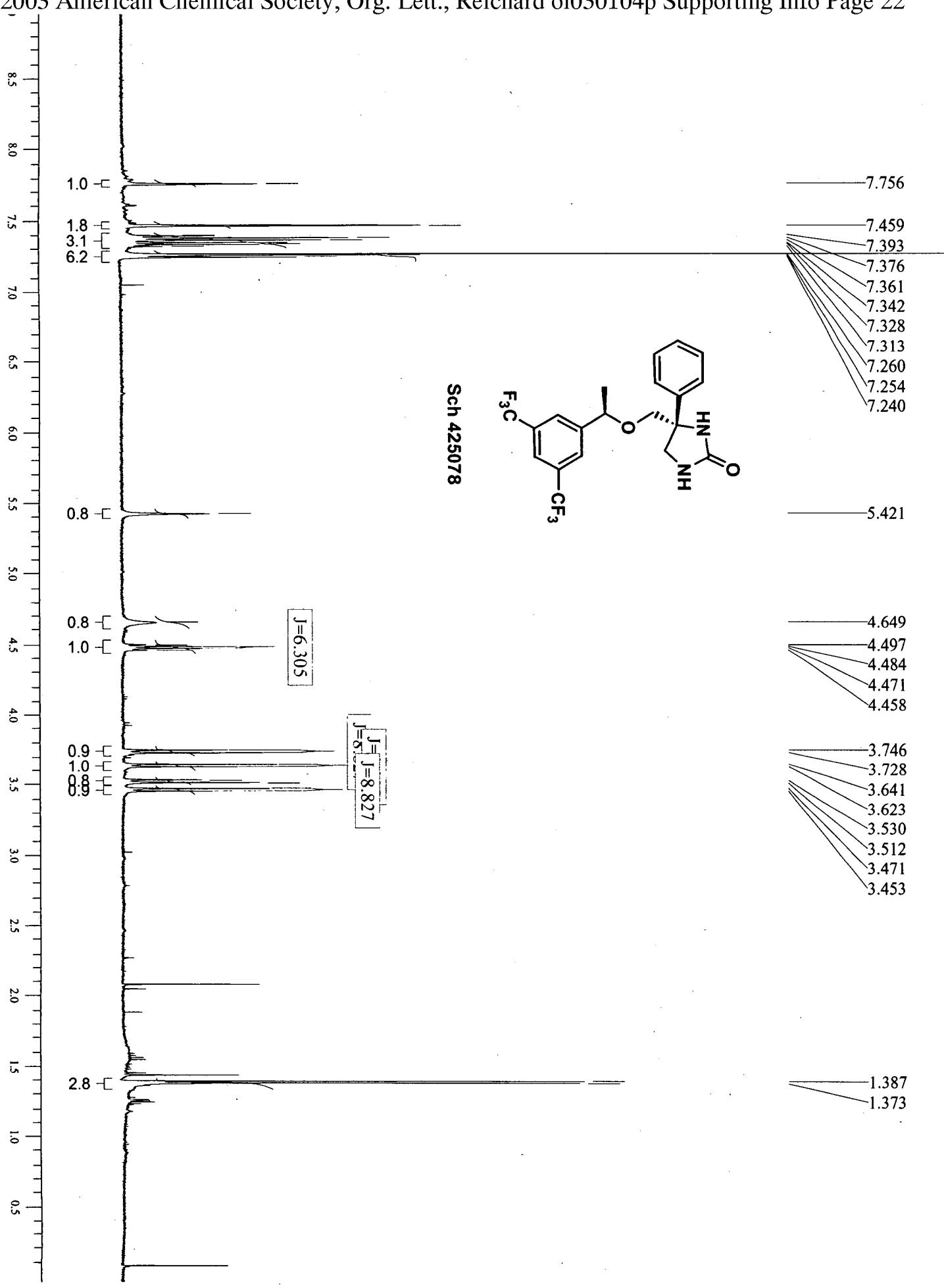


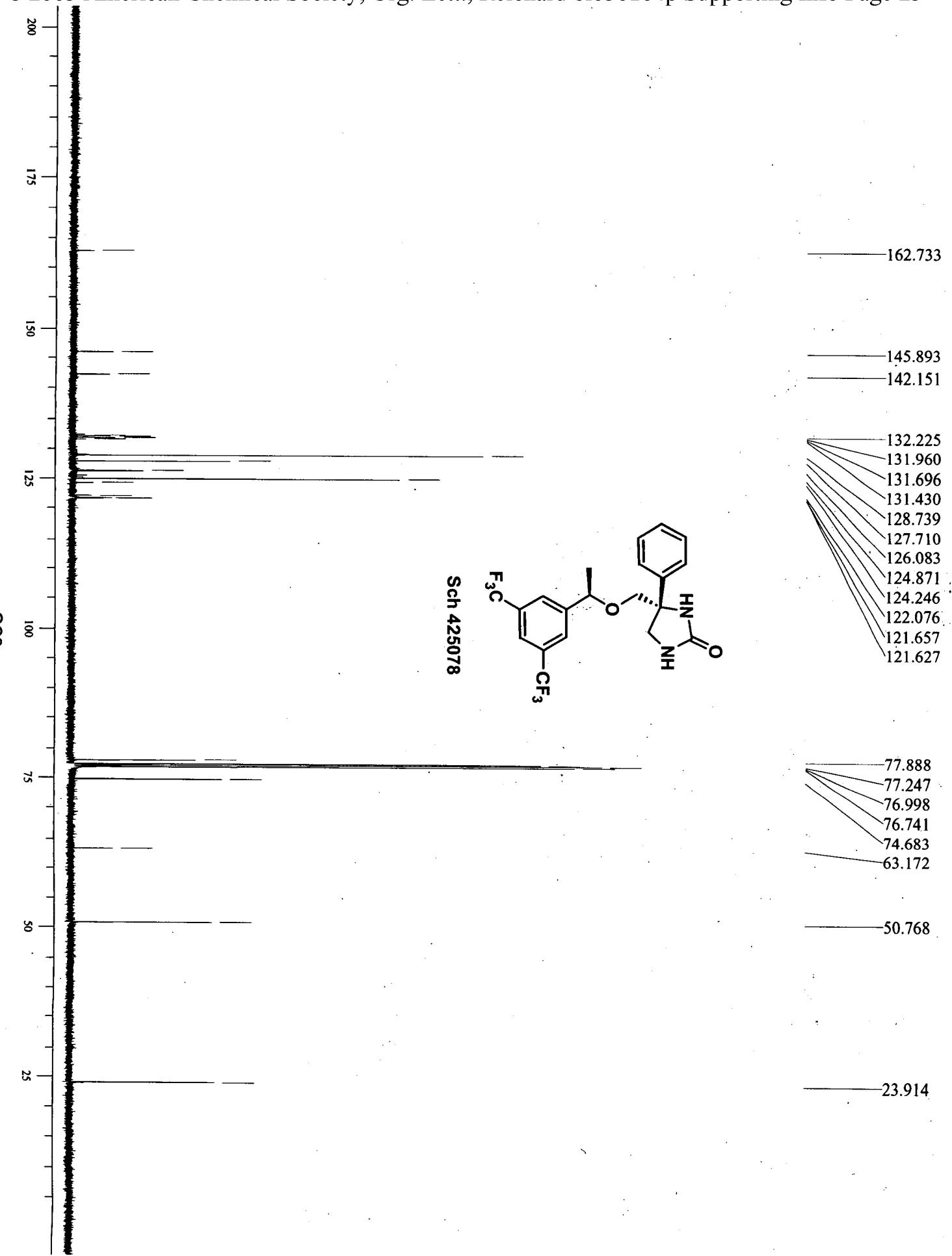






S22





```

# *.cif

data_global

_chemical_name_common 'compound 19'
_chemical_formula_moiety 'C25 H28 F6 N2 O2'
_chemical_formula_weight 502.50
_exptl_crystal_colour colourless
_chemical_melting_point 380.7-381.2
_exptl_crystal_description needle
_exptl_crystal_size_max 0.60
_exptl_crystal_size_mid 0.20
_exptl_crystal_size_min 0.20
_exptl_crystal_preparation 'prepared by the authors'
_exptl_crystal_solvent hexane
loop_
_atom_type_symbol
_atom_type_description
_atom_type_scat_dispersion_real
_atom_type_scat_dispersion_imag
_atom_type_scat_source
'C' 'C' 0.017 0.009
'International Tables Vol IV Tables 2.2B and 2.3.1'
'F' 'F' 0.069 0.053
'International Tables Vol IV Tables 2.2B and 2.3.1'
'O' 'O' 0.047 0.032
'International Tables Vol IV Tables 2.2B and 2.3.1'
'N' 'N' 0.029 0.018
'International Tables Vol IV Tables 2.2B and 2.3.1'
'H' 'H' 0.000 0.000
'International Tables Vol IV Tables 2.2B and 2.3.1'
_cell_length_a 17.566(2)
_cell_length_b 23.502(3)
_cell_length_c 6.082(1)
_cell_angle_alpha 90.00(-)
_cell_angle_beta 90.00(-)
_cell_angle_gamma 90.00(-)
_cell_volume 2511(1)
_symmetry_space_group_name_H-M 'P212121'

loop_
_symmetry_equiv_pos_as_xyz
'x,y,z'
'-x + 1/2, -y, +z + 1/2'
'+x + 1/2, -y + 1/2, -z'
-x, +y + 1/2, -z + 1/2
_cell_formula_units_Z 4
_cell_measurement_temperature 296
_cell_measurement_reflns_used 25
_cell_measurement_theta_min 36.00
_cell_measurement_theta_max 40.00
_exptl_crystal_density_diffrn 1.329
_exptl_crystal_density_method 'not measured'
_exptl_crystal_F_000 1048
_exptl_absorpt_coefficient_mu 0.97
_exptl_absorpt_correction_type 'psi-scan'

```

```

_exptl_absorpt_process_details) '(North, Phillips & Mathews, 1968)'
_exptl_absorpt_correction_T_min 0.92
_exptl_absorpt_correction_T_max 1.00
_diffrn_ambient_temperature 296
_refine_ls_number_reflections 2299
_refine_ls_number_of_parameters 344
_diffrn_radiation_wavelength 1.5418
_diffrn_radiation_type 'Cu K\alpha'
_diffrn_radiation_source 'X-ray tube'
_diffrn_radiation_monochromator graphite
_diffrn_measurement_device 'Enraf-Nonius CAD-4'
_diffrn_measurement_method '\q/2\q'
_diffrn_standards_number 4
_diffrn_standards_interval_time 120
_diffrn_standards_decay_% 'no decay, variation <1.0%'
loop_
    _diffrn_standard_refl_index_h
    _diffrn_standard_refl_index_k
    _diffrn_standard_refl_index_l
        7 6 0
        5 6 1
        6 3 2
        5 1 3
    _diffrn_reflns_number 2978
    _diffrn_reflns_limit_h_min 0
    _diffrn_reflns_limit_h_max 21
    _diffrn_reflns_limit_k_min 0
    _diffrn_reflns_limit_k_max 29
    _diffrn_reflns_limit_l_min 0
    _diffrn_reflns_limit_l_max 7
    _diffrn_reflns_theta_min 3.15
    _diffrn_reflns_theta_max 74.92
    _reflns_number_total 2978
    _reflns_number_gt 2299
    _reflns_threshold_expression I>2\s(I)
    _computing_data_collection 'CAD-4 Software (Enraf-Nonius, 1992)'
    _computing_cell_refinement
        ' CELDIM in CAD-4 Software (Enraf-Nonius, 1992)'
    _computing_data_reduction 'SDP 3.0 (Frenz & Enraf-Nonius, 1985)'
    _computing_structure_solution 'SDP 3.0 (Frenz & Enraf-Nonius, 1985)'
    _computing_structure_refinement 'SDP 3.0 (Frenz & Enraf-Nonius, 1985)'
    _refine_ls_structure_factor_coef F
    _refine_ls_matrix_type full
    _refine_ls_weighting_scheme calc
    _refine_ls_weighting_details
        'w=1/[\s^2^(Fo)+(0.0009)(Fo^2^)]'
    _atom_sites_solution_primary direct
    _atom_sites_solution_secondary difmap
    _atom_sites_solution_hydrogens geom
    _refine_ls_hydrogen_treatment constr
    _refine_ls_extinction_method 'SDP 3.0 (Frenz & Enraf-Nonius, 1985)'
    _refine_ls_extinction_coeff 0.0000059(2)
    _refine_ls_number_reflns 2299
    _refine_ls_number_parameters 344
    _refine_ls_number_restraints 0
    _refine_ls_R_factor_gt 0.052
    _refine_ls_wR_factor_gt 0.069

```

```

_refine_ls_goodness_of_fit_ref      1.68
_refine_ls_shift/su_max           0.03
_refine_diff_density_max          0.23
_refine_diff_density_min          -0.26

# Atomic Coordinates and Thermal Parameters

loop_
_atom_site_label
_atom_site_fract_x
_atom_site_fract_y
_atom_site_fract_z
_atom_site_U_iso_or_equiv
_atom_site_occupancy
C1 0.3308(2) 0.3280(1) -0.5234(5) 0.0481(8) 1.0
N2 0.2563(1) 0.3245(1) -0.4743(4) 0.0484(6) 1.0
C3 0.2375(2) 0.3465(1) -0.2564(5) 0.0417(6) 1.0
N4 0.3114(1) 0.3626(1) -0.1641(4) 0.0434(5) 1.0
C5 0.3726(2) 0.3514(1) -0.3217(5) 0.0424(6) 1.0
O6 0.3600(1) 0.3122(1) -0.6960(4) 0.0631(6) 1.0
C7 0.2069(2) 0.2890(2) -0.6054(6) 0.0655(9) 1.0
C8 0.1818(2) 0.3978(1) -0.2578(5) 0.0474(6) 1.0
C9 0.2144(2) 0.4470(2) -0.3909(7) 0.0686(10) 1.0
C10 0.1716(2) 0.4162(2) -0.0190(6) 0.0655(9) 1.0
C11 0.1035(2) 0.3809(2) -0.3490(8) 0.0733(11) 1.0
C12 0.4222(2) 0.4033(1) -0.3630(5) 0.0485(6) 1.0
C13 0.4307(2) 0.4442(1) -0.2006(6) 0.0599(9) 1.0
C14 0.4804(2) 0.4892(2) -0.2277(8) 0.0711(10) 1.0
C15 0.5212(2) 0.4952(2) -0.4174(9) 0.0771(11) 1.0
C16 0.5126(3) 0.4558(2) -0.5811(9) 0.0950(13) 1.0
C17 0.4636(3) 0.4095(2) -0.5558(7) 0.0826(10) 1.0
C18 0.4250(2) 0.3039(1) -0.2373(6) 0.0485(8) 1.0
O19 0.3800(1) 0.2547(1) -0.2056(4) 0.0514(5) 1.0
C20 0.4105(2) 0.2137(1) -0.0604(6) 0.0479(6) 1.0
C21 0.4708(2) 0.1781(2) -0.1745(9) 0.0745(11) 1.0
C22 0.3444(2) 0.1779(1) 0.0227(6) 0.0464(6) 1.0
C23 0.2720(2) 0.1860(1) -0.0624(7) 0.0524(8) 1.0
C24 0.2116(2) 0.1535(1) 0.0180(7) 0.0588(9) 1.0
C25 0.2219(2) 0.1134(1) 0.1784(7) 0.0647(9) 1.0
C26 0.2952(2) 0.1054(1) 0.2625(7) 0.0605(9) 1.0
C27 0.3554(2) 0.1373(1) 0.1857(6) 0.0552(8) 1.0
C28 0.1334(2) 0.1655(2) -0.0747(10) 0.0849(13) 1.0
F29 0.0819(1) 0.1293(1) -0.0106(7) 0.1155(10) 1.0
F30 0.1326(2) 0.1637(2) -0.2919(7) 0.1570(13) 1.0
F31 0.1101(1) 0.2162(1) -0.0287(11) 0.1684(13) 1.0
C32 0.3085(3) 0.0617(2) 0.4359(8) 0.0811(13) 1.0
F33 0.2431(3) 0.0324(2) 0.4842(10) 0.166(1) 0.67
F34 0.3532(3) 0.0220(2) 0.3735(9) 0.141(1) 0.67
F35 0.3293(4) 0.0829(2) 0.6188(7) 0.152(3) 0.67
F33' 0.3874(6) 0.0617(4) 0.5069(19) 0.158(4) 0.33
F34' 0.2944(8) 0.0154(3) 0.3977(16) 0.165(5) 0.33
F35' 0.2700(8) 0.0721(5) 0.6101(16) 0.151(4) 0.33
H3 0.2083 0.3157 -0.1639 0.0417 1.0
H4 0.3206 0.3405 -0.0301 0.0434 1.0
H7A 0.1688 0.2672 -0.5023 0.0655 1.0
H7B 0.2400 0.2595 -0.6931 0.0655 1.0
H7C 0.1762 0.3144 -0.7161 0.0655 1.0

```

H9A 0.1758 0.4811 -0.3895 0.0686 1.0
H9B 0.2662 0.4600 -0.3213 0.0686 1:0
H9C 0.2236 0.4337 -0.5536 0.0686 1.0
H10A 0.1342 0.4510 -0.0119 0.0655 1.0
H10B 0.1491 0.3823 0.0725 0.0655 1.0
H10C 0.2246 0.4280 0.0467 0.0655 1.0
H11A 0.0673 0.4165 -0.3477 0.0733 1.0
H11B 0.1096 0.3661 -0.5109 0.0733 1.0
H11C 0.0800 0.3486 -0.2508 0.0733 1.0
H13 0.4004 0.4411 -0.0619 0.0599 1.0
H14 0.4866 0.5177 -0.1070 0.0711 1.0
H15 0.5569 0.5280 -0.4364 0.0771 1.0
H16 0.5419 0.4602 -0.7211 0.0950 1.0
H17 0.4583 0.3809 -0.6764 0.0826 1.0
H18A 0.4500 0.3162 -0.0878 0.0485 1.0
H18B 0.4678 0.2956 -0.3533 0.0485 1.0
H20 0.4380 0.2332 0.0732 0.0479 1.0
H21A 0.4926 0.1480 -0.0637 0.0745 1.0
H21B 0.4465 0.1571 -0.3096 0.0745 1.0
H21C 0.5150 0.2046 -0.2291 0.0745 1.0
H23 0.2631 0.2149 -0.1804 0.0524 1.0
H25 0.1781 0.0904 0.2341 0.0647 1.0
H27 0.4075 0.1312 0.2478 0.0605 1.0
=====

loop_

- _atom_site_aniso_label
- _atom_site_aniso_U_11
- _atom_site_aniso_U_22
- _atom_site_aniso_U_33
- _atom_site_aniso_U_12
- _atom_site_aniso_U_13
- _atom_site_aniso_U_23

C1 0.053(1) 0.055(1) 0.036(1) 0.002(1) 0.002(1) -0.004(1)
N2 0.045(1) 0.062(1) 0.038(1) 0.000(1) -0.001(1) -0.008(1)
C3 0.038(1) 0.054(1) 0.033(1) -0.001(1) 0.001(1) -0.002(1)
N4 0.036(1) 0.061(1) 0.033(1) 0.002(1) 0.001(1) -0.005(1)
C5 0.041(1) 0.052(1) 0.035(1) 0.001(1) 0.005(1) -0.002(1)
O6 0.071(1) 0.078(1) 0.040(1) 0.002(1) 0.013(1) -0.013(1)
C7 0.067(2) 0.072(2) 0.057(2) -0.006(2) -0.019(2) -0.014(2)
C8 0.042(1) 0.056(1) 0.044(1) 0.008(1) -0.002(1) 0.001(1)
C9 0.073(2) 0.063(2) 0.070(2) 0.009(2) -0.004(2) 0.016(2)
C10 0.063(2) 0.080(2) 0.054(2) 0.020(2) 0.009(2) -0.009(2)
C11 0.044(1) 0.095(2) 0.081(3) 0.008(2) -0.011(2) 0.001(2)
C12 0.046(1) 0.055(1) 0.045(2) 0.005(1) 0.001(1) -0.001(1)
C13 0.050(1) 0.069(2) 0.061(2) -0.005(1) 0.003(2) -0.015(2)
C14 0.069(2) 0.067(2) 0.078(2) -0.008(2) -0.003(2) -0.017(2)
C15 0.070(2) 0.060(2) 0.101(3) -0.012(2) 0.007(2) 0.002(2)
C16 0.108(3) 0.094(2) 0.084(3) -0.044(2) 0.039(2) -0.008(2)
C17 0.108(2) 0.074(2) 0.065(2) -0.034(2) 0.037(2) -0.015(2)
C18 0.035(1) 0.053(1) 0.057(2) -0.003(1) 0.003(1) 0.003(1)
O19 0.038(1) 0.054(1) 0.063(1) -0.004(1) -0.007(1) 0.008(1)
C20 0.036(1) 0.053(1) 0.055(2) 0.003(1) -0.004(1) 0.002(1)
C21 0.051(2) 0.070(2) 0.102(3) 0.012(2) 0.022(2) -0.001(2)
C22 0.042(1) 0.044(1) 0.052(2) 0.006(1) 0.000(1) -0.004(1)
C23 0.041(1) 0.050(1) 0.066(2) 0.002(1) 0.000(2) -0.002(2)
C24 0.042(1) 0.053(1) 0.081(2) -0.003(1) 0.007(2) -0.002(2)
C25 0.064(2) 0.054(2) 0.076(2) -0.006(1) 0.015(2) -0.002(2)

C26 0.072(2) 0.050(1) 0.060(2) 0.003(1) 0.007(2) 0.002(2)
 C27 0.057(2) 0.054(1) 0.055(2) 0.005(1) -0.002(2) 0.001(2)
 C28 0.046(2) 0.079(2) 0.131(4) -0.009(2) 0.001(2) 0.017(3)
 F29 0.053(1) 0.130(2) 0.163(3) -0.033(1) -0.001(2) 0.022(2)
 F30 0.068(1) 0.273(4) 0.130(2) -0.022(2) -0.034(2) 0.055(3)
 F31 0.064(1) 0.104(2) 0.338(6) 0.023(1) -0.043(3) -0.012(3)
 C32 0.110(3) 0.067(2) 0.068(2) 0.001(2) 0.009(3) 0.008(2)
 F33 0.139(4) 0.178(3) 0.181(4) -0.038(3) 0.008(4) 0.113(3)
 F34 0.195(3) 0.104(2) 0.124(3) 0.085(2) 0.052(3) 0.045(2)
 F35 0.304(7) 0.083(2) 0.067(2) -0.013(4) -0.059(3) 0.007(2)
 F33' 0.159(8) 0.153(7) 0.163(8) -0.026(7) -0.063(7) 0.092(5)
 F34' 0.366(15) 0.043(3) 0.087(6) -0.051(5) -0.034(9) -0.001(4)
 F35' 0.234(11) 0.154(8) 0.064(5) -0.016(9) 0.045(7) -0.001(6)

#Molecular geometry

loop_
 _geom_bond_atom_site_label_1
 _geom_bond_atom_site_label_2
 _geom_bond_distance

C1-N2 1.345(4)
 C1-C5 1.532(4)
 C1-O6 1.226(4)
 N2-C3 1.460(4)
 N2-C7 1.444(5)
 C3-N4 1.464(4)
 C3-C8 1.553(4)
 N4-C5 1.464(4)
 C5-C12 1.520(4)
 C5-C18 1.535(4)
 C8-C9 1.523(5)
 C8-C10 1.526(5)
 C8-C11 1.535(5)
 C12-C13 1.386(4)
 C12-C17 1.387(6)
 C13-C14 1.381(5)
 C14-C15 1.366(7)
 C15-C16 1.368(7)
 C16-C17 1.396(7)
 C18-O19 1.414(4)
 O19-C20 1.413(4)
 C20-C21 1.518(5)
 C21-C22 1.520(5)
 C22-C23 1.386(5)
 C22-C27 1.389(4)
 C23-C24 1.396(5)
 C24-C25 1.368(5)
 C24-C28 1.511(5)
 C25-C26 1.398(5)
 C26-C27 1.378(5)
 C26-C32 1.491(6)
 C28-F29 1.302(5)
 C28-F30 1.322(7)
 C28-F31 1.291(5)
 C32-F33 1.371(7)
 C32-F34 1.277(7)

C32-F35 1.272(7)
C32-F33' 1.407(12)
C32-F34' 1.140(9)
C32-F35' 1.281(12)
C3-H3 1.05
N4-H4 0.98
C7-H7A 1.05
C7-H7B 1.05
C7-H7C 1.05
C9-H9A 1.05
C9-H9B 1.05
C9-H9C 1.05
C10-H10A 1.05
C10-H10B 1.05
C10-H10C 1.05
C11-H11A 1.05
C11-H11B 1.05
C11-H11C 1.05
C13-H13 1.00
C14-H14 1.00
C15-H15 1.00
C16-H16 1.00
C17-H17 1.00
C18-H18A 1.05
C18-H18B 1.05
C20-H20 1.05
C21-H21A 1.05
C21-H21B 1.05
C21-H21C 1.05
C23-H23 1.00
C25-H25 1.00
C27-H27 1.00

loop_
 _geom_angle_atom_site_label_1
 _geom_angle_atom_site_label_2
 _geom_angle_atom_site_label_3
 _geom_angle

N2-C1-C5 108.1(3)
N2-C1-O6 125.4(3)
C5-C1-O6 126.4(3)
C1-N2-C3 113.6(2)
C1-N2-C7 119.8(3)
C3-N2-C7 124.7(2)
N2-C3-N4 103.8(2)
N2-C3-C8 114.4(2)
N4-C3-C8 111.1(2)
C3-N4-C5 110.7(2)
C1-C5-N4 103.7(3)
C1-C5-C12 115.5(2)
C1-C5-C18 107.1(2)
N4-C5-C12 112.6(2)
N4-C5-C18 110.6(2)
C12-C5-C18 107.2(3)
C3-C8-C9 110.8(3)

C3-C8-C10 106.8(3)
C3-C8-C11 111.4(3)
C9-C8-C10 109.6(3)
C9-C8-C11 109.9(3)
C10-C8-C11 108.2(3)
C5-C12-C13 120.0(3)
C5-C12-C17 121.6(3)
C13-C12-C17 118.2(3)
C12-C13-C14 120.9(4)
C13-C14-C15 120.8(4)
C14-C15-C16 119.1(4)
C15-C16-C17 121.0(5)
C12-C17-C16 119.9(4)
C5-C18-O19 107.8(3)
C18-O19-C20 115.5(2)
O19-C20-C21 110.8(3)
O19-C20-C22 107.2(3)
C21-C20-C22 112.3(2)
C20-C22-C23 120.0(3)
C20-C22-C27 120.7(3)
C23-C22-C27 119.2(3)
C22-C23-C24 119.4(3)
C23-C24-C25 121.7(3)
C23-C24-C28 117.3(3)
C25-C24-C28 121.0(3)
C24-C25-C26 118.4(3)
C25-C26-C27 120.6(3)
C25-C26-C32 119.7(3)
C27-C26-C32 119.6(3)
C22-C27-C26 120.6(3)
C24-C28-F29 113.5(4)
C24-C28-F30 112.1(4)
C24-C28-F31 112.3(4)
F29-C28-F30 105.7(4)
F29-C28-F31 108.6(3)
F30-C28-F31 104.1(5)
C26-C32-F33 111.5(4)
C26-C32-F34 112.9(4)
C26-C32-F35 113.2(4)
C26-C32-F33' 111.5(6)
C26-C32-F34' 118.7(6)
C26-C32-F35' 111.8(6)
F33-C32-F34 102.2(4)
F33-C32-F35 104.5(5)
F34-C32-F35 111.7(5)
F33'-C32-F34' 105.6(9)
F33'-C32-F35' 104.4(8)
F34'-C32-F35' 103.7(9)
N2-C3-H3 110.7
N4-C3-H3 113.9
C8-C3-H3 103.3
C3-N4-H4 109.2
C5-N4-H4 109.2
N2-C7-H7A 109.5
N2-C7-H7B 109.2
N2-C7-H7C 109.5
H7A-C7-H7B 109.5

H7A-C7-H7C 109.5
H7B-C7-H7C 109.5
C8-C9-H9A 109.5
C8-C9-H9B 109.5
C8-C9-H9C 109.5
H9A-C9-H9B 109.5
H9A-C9-H9C 109.5
H9B-C9-H9C 109.5
C8-C10-H10A 109.5
C8-C10-H10B 109.5
C8-C10-H10C 109.5
H10A-C10-H10B 109.5
H10A-C10-H10C 109.5
H10B-C10-H10C 109.5
C8-C11-H11A 109.5
C8-C11-H11B 109.5
C8-C11-C11C 109.5
H11A-C11-H11B 109.5
H11A-C11-H11C 109.5
H11B-C11-H11C 109.5
C12-C13-H13 119.5
C14-C13-H13 119.5
C13-C14-H14 119.6
C15-C14-H14 119.6
C14-C15-H15 120.4
C16-C15-H15 120.4
C15-C16-H16 119.5
C17-C16-H16 119.5
C12-C17-H17 120.1
C16-C17-H17 120.1
C5-C18-H18A 109.9
C5-C18-H18B 109.9
O19-C18-H18A 109.9
O19-C18-H18B 109.9
H18A-C18-H18B 109.5
O19-C20-H20 111.1
C21-C20-H20 105.9
C22-C20-H20 109.6
C20-C21-H21A 109.5
C20-C21-H21B 109.5
C20-C21-H21C 109.5
H21A-C21-H21B 109.5
H21A-C21-H21C 109.5
H21B-C21-H21C 109.5
C22-C23-H23 120.3
C24-C23-H23 120.3
C24-C25-H25 120.8
C26-C25-H25 120.8
C22-C27-H27 119.7
C26-C27-H27 119.7

loop_
 _geom_torsion_atom_site_label_1
 _geom_torsion_atom_site_label_2
 _geom_torsion_atom_site_label_3
 _geom_torsion_atom_site_label_4
 _geom_torsion

C5-C1-N2-C3 3.4(3)
C5-C1-N2-C7 -161.8(3)
O6-C1-N2-C3 179.9(2)
O6-C1-N2-C7 14.7(4)
N2-C1-C5-N4 -2.7(3)
N2-C1-C5-C12 -126.5(3)
N2-C1-C5-C18 114.3(3)
O6-C1-C5-N4 -179.1(3)
O6-C1-C5-C12 57.1(4)
O6-C1-C5-C18 -62.1(4)
C1-N2-C3-N4 -2.7(3)
C1-N2-C3-C8 118.6(3)
C7-N2-C3-N4 161.7(3)
C7-N2-C3-C8 -77.0(4)
N2-C3-N4-C5 0.7(3)
C8-C3-N4-C5 -122.7(3)
N2-C3-C8-C9 -58.5(4)
N2-C3-C8-C10 -177.8(3)
N2-C3-C8-C11 64.3(4)
N4-C3-C8-C9 58.6(3)
N4-C3-C8-C10 -60.6(3)
N4-C3-C8-C11 -178.6(3)
C3-N4-C5-C1 1.2(3)
C3-N4-C5-C12 126.7(3)
C3-N4-C5-C18 -113.4(3)
C1-C5-C12-C13 147.0(3)
C1-C5-C12-C17 -37.0(5)
N4-C5-C12-C13 28.2(4)
N4-C5-C12-C17 -155.9(3)
C18-C5-C12-C13 -93.7(4)
C18-C5-C12-C17 82.2(4)
C1-C5-C18-O19 -53.5(3)
N4-C5-C18-O19 58.9(3)
C12-C5-C18-O19 -178.0(3)
C5-C12-C13-C14 174.6(3)
C17-C12-C13-C14 -1.5(5)
C5-C12-C17-C16 -175.5(4)
C13-C12-C17-C16 0.5(6)
C12-C13-C14-C15 1.5(6)
C13-C14-C15-C16 -0.3(7)
C14-C15-C16-C17 -0.7(7)
C15-C16-C17-C12 0.6(7)
C5-C18-O19-C20 -158.8(3)
C18-O19-C20-C21 -79.4(3)
C18-O19-C20-C22 157.7(3)
O19-C20-C22-C23 5.6(4)
O19-C20-C22-C27 -173.7(3)
C21-C20-C22-C23 -116.3(4)
C21-C20-C22-C27 64.4(4)
C20-C22-C23-C24 -178.9(3)
C27-C22-C23-C24 0.4(5)
C20-C22-C27-C26 179.2(3)
C23-C22-C27-C26 -0.1(5)
C22-C23-C24-C25 -0.4(5)
C22-C23-C24-C28 177.9(4)
C23-C24-C25-C26 0.1(5)
C28-C24-C25-C26 -178.1(4)

C23-C24-C28-F29 172.6(4)
C23-C24-C28-F30 52.9(5)
C23-C24-C28-F31 -63.9(6)
C25-C24-C28-F29 -9.2(6)
C25-C24-C28-F30 -128.8(4)
C25-C24-C28-F31 114.4(5)
C24-C25-C26-C27 0.2(5)
C24-C25-C26-C32 -179.5(4)
C25-C26-C27-C22 -0.2(5)
C32-C26-C27-C22 179.4(3)
C25-C26-C32-F33 2.5(6)
C25-C26-C32-F34 117.0(5)
C25-C26-C32-F35 -114.9(5)
C25-C26-C32-F33' -177.2(6)
C25-C26-C32-F34' 59.7(10)
C25-C26-C32-F35' -60.8(8)
C27-C26-C32-F33 -177.1(4)
C27-C26-C32-F34 -62.7(6)
C27-C26-C32-F35 65.5(6)
C27-C26-C32-F33' 3.2(7)
C27-C26-C32-F34' -119.9(9)
C27-C26-C32-F35' 119.6(7)

#=====

Hydrogen_bonded_distance_(Donor_Acceptor) 'N4...O6 (at x, y, 1 + z) 3.200(3)'

#==END