

Total Synthesis of (*S*)-(+)-Tylophorine via Enantioselective Intramolecular Alkene Carboamination

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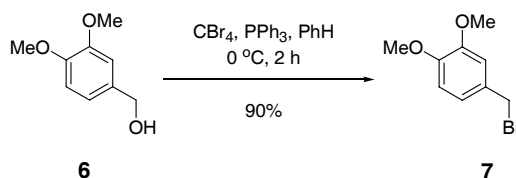
Supplementary Material

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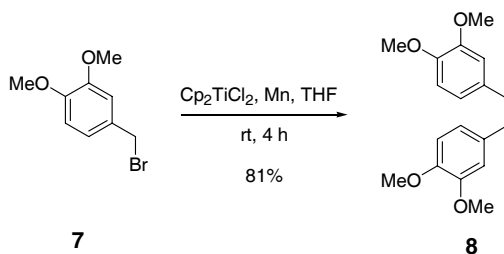
General Information:

All reactions were performed under an Ar atmosphere with stirring. All reagents (including chiral ligand) were commercially available unless otherwise noted. Solvents were purified using a solvent filtration system. All ^1H NMR (400 MHz) and ^{13}C NMR (75 MHz) spectra were recorded at 25.0 °C. Coupling constants (J) are in hertz. Abbreviations used are s = singlet, d = doublet, t = triplet, m = multiplet and br = broad. IR spectra were taken neat using an FTIR. Wave numbers in cm^{-1} are reported for characteristic peaks. High resolution mass spectra were obtained at SUNY, Buffalo's mass spec. facility. Optical rotations were obtained using a Polarimeter fitted with a micro cell with a 1 dm path length. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) using Chiralcel AD-H chiral analytical column (UV detection at 254 nm). Melting points were obtained on an electrothermal melting point apparatus and uncorrected.



3, 4-Dimethoxybenzyl bromide (**7**)¹

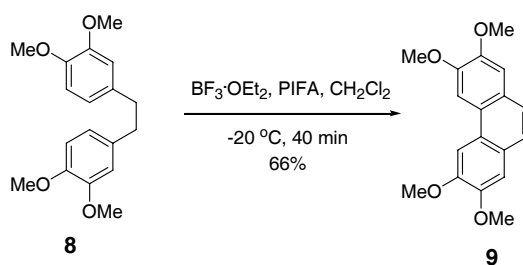
3, 4-Dimethoxybenzyl bromide (**7**) was prepared as described by Barrero.^{1a} CBr_4 (0.66 g, 2.0 mmol) and Ph_3P (0.53 g, 2.0 mmol) at 0 °C under Ar atmosphere were added to a stirred solution of 3, 4-dimethoxybenzyl alcohol (0.17 g, 1.0 mmol) in benzene (7 mL). The solution was stirred at the same temperature for 2 h (TLC monitoring), then diluted with hexane (10 mL). The resulting mixture was filtered to remove triphenylphosphine oxide. The filtrate was concentrated under reduced pressure and the resulting crude purified by flash chromatography on silica gel (EtOAc/hexane, 1 : 5) to afford the corresponding 3, 4-dimethoxybenzyl bromide (0.21 g, 90% yield) as yellow solid. Mp 47-49 °C, lit² 47- 50 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.96-6.93 (m, 1 H), 6.90 (d, 1 H, J = 2.0 Hz), 6.79 (d, 1 H, J = 8.4 Hz), 4.50 (s, 2 H), 3.89 (s, 3 H), 3.88 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 149.3, 149.1, 130.3, 121.6, 112.1, 111.1, 55.9, 34.4.



1, 2-Bis (3, 4-dimethoxyphenyl) ethane (**8**)

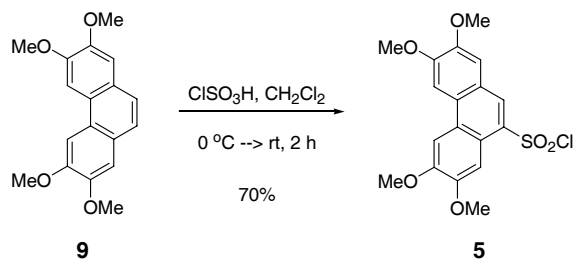
1, 2-Bis (3, 4-dimethoxyphenyl) ethane (**8**) was prepared as described by Barrero.^{1a} A mixture of Cp_2TiCl_2 (69.7 mg, 0.280 mmol) and Mn dust (0.610 g, 11.1 mmol) in thoroughly deoxygenate THF (20 mL) was stirred under an Ar atmosphere at room

temperature until the red solution turned green. The corresponding 3, 4-dimethoxybenzyl bromide (0.320 g, 1.39 mmol) in strictly deoxygenated THF (0.8 mL, $C_f = 0.07$ M) was then added to the Cp_2TiCl solution, and the mixture was stirred at room temperature for 4 h. The THF was removed in vacuo and the remaining mixture was treated with 1 N HCl and extracted with Et_2O . The organic extract was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by flash chromatography on silica gel (EtOAc / hexane, 1 : 3) to afford the corresponding 1, 2-bis (3, 4-dimethoxyphenyl) ethane (**8**)^{1a, 3} (0.34 g, 81%) as a white solid. Mp 108-110 °C, lit⁴. 110.5-111 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.80- 6.78 (d, 2 H, $J = 8.0$ Hz), 6.72- 6.70 (d, 2 H, $J = 8.0$ Hz), 6.66 (s, 2 H), 3.87 (s, 6 H), 3.86 (s, 6 H), 2.85 (s, 4 H); ^{13}C NMR (75 MHz, CDCl_3): δ 149.3, 147.8, 134.9, 120.9, 112.5, 111.7, 56.5, 56.3, 38.2.



2, 3, 6, 7-Tetramethoxyphenanthrene (**9**)

2, 3, 6, 7-Tetramethoxyphenanthrene (**9**) was prepared as described by Domínguez.⁵ A solution of PIFA (165 mg, 0.380 mmol) and $\text{BF}_3\cdot\text{OEt}_2$ (0.10 mL, 0.76 mmol) in CH_2Cl_2 (8 mL) was added dropwise at -20 °C to a solution of 1, 2-bis (3, 4-dimethoxyphenyl) ethane (**8**) (100 mg, 0.33 mmol) in CH_2Cl_2 (5 mL) over 15 min. The mixture was stirred at same temperature for 40 min, and the solvent was removed in vacuo. The resulting crude was purified by flash chromatography on silica gel (EtOAc / hexane, 1: 2) to afford 2, 3, 6, 7-tetramethoxyphenanthrene (**9**)⁵ (65 mg, 66%) as light yellow solid. Mp 179-181 °C, lit⁶. 178-180 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.80 (s, 2 H), 7.56 (s, 2 H), 7.22 (s, 2 H), 4.13 (s, 6 H), 4.04 (s, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ 149.8, 149.3, 127.0, 124.9, 124.8, 108.9, 103.4, 56.6, 56.4.

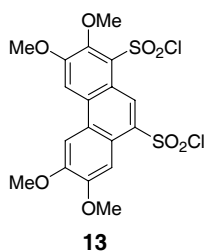


2, 3, 6, 7-Tetramethoxy-phenanthrene-9-sulfonyl chloride (**5**)

The chlorosulfonation was performed by modification of the procedure reported by Teranishi.⁷ To a solution of 2, 3, 6, 7- tetramethoxyphenanthrene (**9**) (100 mg, 0.34 mmol) in dry CH_2Cl_2 (0.64 mL) was added dropwise chlorosulfonic acid (0.10 mL, 175 mg, 1.50 mmol) under cooling with an ice-water bath and Ar. The mixture was stirred at room temperature for 2 h, then poured onto crushed ice (approx 2.0 g). The aqueous phase was thoroughly extracted with CH_2Cl_2 (3 \times 2 mL), and the combined organic layer was

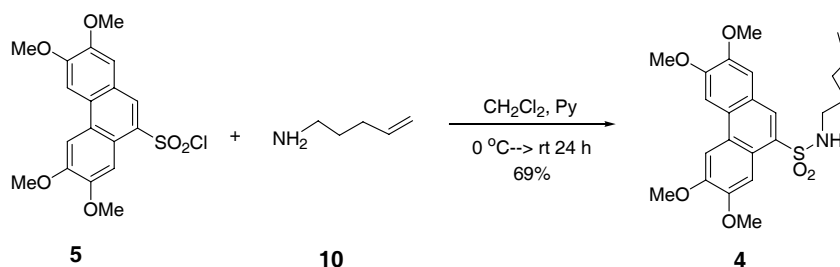
washed with H₂O (2 mL), then dried over MgSO₄, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel (EtOAc / hexane, 1 : 1.5) to afford 2, 3, 6, 7-tetramethoxyphenanthrene-9-sulfonyl chloride (**5**) (93.3 mg, 70%) as yellow solid. Mp 207- 209 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.47 (s, 1 H), 8.14 (s, 1 H), 7.78 (s, 1 H), 7.72 (s, 1 H), 7.29 (s, 1 H), 4.18 (s, 3 H), 4.16 (s, 3 H), 4.10 (s, 3 H), 4.06 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 153.5, 150.6, 150.4, 150.3, 135.6, 129.9, 129.0, 126.4, 123.5, 119.9, 110.5, 105.7, 103.7, 103.0, 56.7, 56.6. IR (neat): 3008, 2932, 2839, 1618, 1512, 1477, 1429, 1364, 1263, 1214, 1166, 1132, 1004, 910, 535 cm⁻¹; HRMS (EI) calcd for [M]⁺ C₁₈H₁₇ClO₆S: 396.0451, found: 396.0441.

Over sulfonylation was observed if a higher concentration of chlorosulfonic acid was used, 2, 3, 6, 7-tetramethoxyphenanthrene-1, 9-disulfonyl chloride (**13**) was the major byproduct.



2, 3, 6, 7-Tetramethoxy-phenanthrene-1, 9-disulfonyl chloride (**13**)

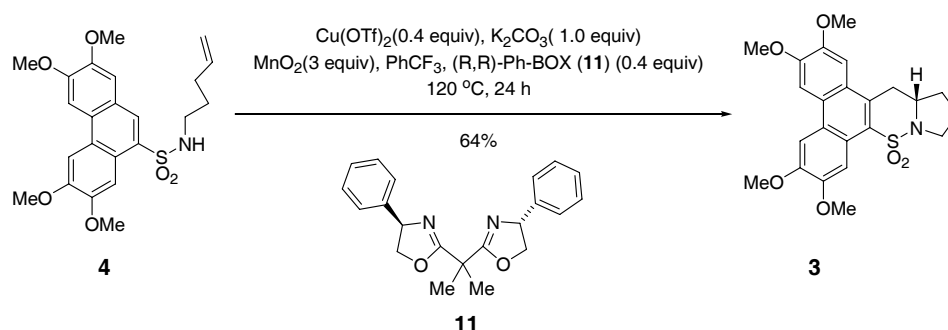
Data for **13**: Yellow solid, Mp 205- 208 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.84 (s, 1 H), 8.08 (s, 1 H), 7.74 (s, 1 H), 7.66(s, 1 H), 4.16 (s, 3 H), 4.15 (s, 3 H), 4.09 (s, 3H), 4.01 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 156.6, 151.0, 150.8, 146.8, 136.5, 131.3, 128.4, 126.6, 126.0, 121.2, 120.4, 105.6, 104.2, 102.4, 61.6, 56.7, 56.6. IR (neat): 3004, 2937, 2835, 1618, 1605, 1526, 1490, 1467, 1421, 1398, 1372, 1280, 1259, 1205, 1162, 1131, 1041, 998, 913, 729, 591 cm⁻¹; HRMS (EI) calcd for [M]⁺ C₁₈H₁₆Cl₂O₈S₂: 430.0039, found: 430.0028.



2, 3, 6, 7-Tetramethoxyphenanthrene-9-sulfonic acid pent- 4- enylamide (**4**)

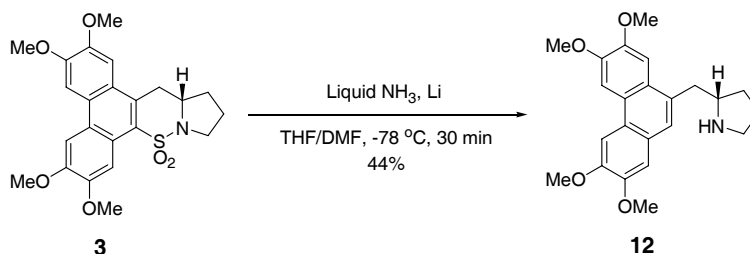
Dry pyridine (158 mg, 2.00 mmol) and 2,3,6,7-tetramethoxy-phenanthrene-9-sulfonyl chloride (**5**) (475.8 mg, 1.20 mmol) were added to a solution of pent-4-enylamine⁸ (**10**) (85 mg, 1.0 mmol) in dry CH₂Cl₂ (8 mL) at 0 °C. The mixture was then warmed to room temperature and allowed to stir for 24 h (monitoring by TLC). 1N HCl (10 mL) was added and the mixture was extracted with Et₂O (3 × 20 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude residue was purified by flash chromatography on silica gel (EtOAc/ hexane, 1: 1) to afford 2,3,6,7-tetramethoxyphenanthrene-9-sulfonic acid pent-4-enylamide (**4**) (307.1 mg, 69%) as a yellow solid. Mp 182-184 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.39 (s, 1 H), 8.11 (s, 1 H),

7.81 (s, 1 H), 7.75 (s, 1 H), 7.28 (s, 1 H), 5.70-5.51 (m, 1 H), 4.87- 4.82 (m, 2 H), 4.61 (t, 1 H, J = 6.0 Hz), 4.16 (s, 3 H), 4.15 (s, 3 H), 4.07 (s, 3 H), 4.04 (s, 3 H), 2.96-2.91 (dd, 2 H, J = 6.4, 20 Hz), 1.98-1.93 (dd, 2 H, J = 7.2, 20.8 Hz), 1.54-1.47 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 152.1, 150.0, 149.9, 137.7, 130.1, 130.0, 127.6, 126.3, 124.3, 121.1, 116.1, 110.0, 109.9, 106.0, 103.8, 103.7, 103.0, 102.9, 56.6, 43.3, 31.2, 29.2. IR (neat): 3292, 3002, 2938, 2838, 2255, 1620, 1510, 1472, 1428, 1319, 1256, 1128, 1042, 1004, 916, 842, 731, 593 cm^{-1} ; HRMS (EI) calcd for $[\text{M} + 1]^+$ $\text{C}_{23}\text{H}_{27}\text{NO}_6\text{S}$: 446.1632, found: 446.1629.



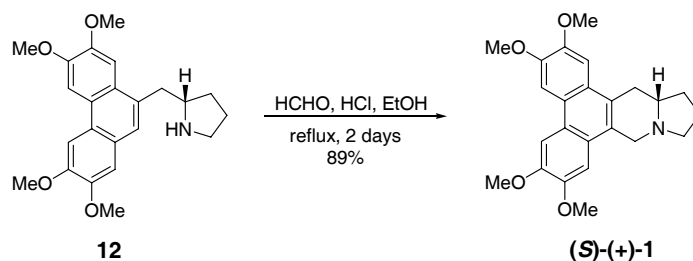
(S)-2, 3, 6, 7-Tetramethoxy-11, 12, 12a, 13-tetrahydro-10H-9- thia- 9- a-aza-cyclopenta[b] triphenylene-9, 9-dioxide (3)

$\text{Cu}(\text{OTf})_2$ (10.0 mg, 0.028 mmol, 0.4 equiv), 2, 2- bis[(4*R*)- 4-phenyl- 2- oxazolin-2- yl]-propane (**11**) (9.2 mg, 0.028 mmol, 0.4 equiv) and 2.5 mL of PhCF_3 were combined in a pressure tube equipped with a stir bar under Ar, and the mixture was stirred at 45-50 °C for 1 h in order to make the Cu(II) salt coordinate with the ligand completely. This mixture was then treated with K_2CO_3 (9.5 mg, 0.069 mmol, 1 equiv), MnO_2 (18.0 mg, 0.206 mmol, 3 equiv) and 2,3,6,7-tetramethoxyphenanthrene-9-sulfonic acid pent-4-enylamide (**4**) (30.6 mg, 0.069 mmol, 1 equiv), then the tube was refreshed by Ar for 5 min, sealed and heated at 120 °C in an oil bath for 24 h. Upon cooling to rt, the mixture was diluted with CHCl_3 (2.0 mL) and stirred for about 5 min. Filtration of the cooled solution and removal of the solvent *in vacuo* afforded a crude residue. Successive chromatography on SiO_2 (EtOAc / hexane, 3: 1; CHCl_3 / EtOAc , 20 : 1) afforded purified sultam **3** (20.0 mg, 64%) as light yellow solid. This reaction was performed on 0.344 mmol (0.153 g) **4** as well, and a 61% yield was obtained. Mp 289- 291 °C (decomposed); $[\alpha]_{\text{D}}^{23} = +47.1^\circ$ ($c = 2$ in CH_2Cl_2), ^1H NMR (400 MHz, CDCl_3): δ 8.32 (s, 1 H), 7.79 (s, 1 H), 7.77 (s, 1 H), 7.30(s, 1H), 4.31(m, 1H), 4.14 (s, 3 H), 4.12 (s, 3 H), 4.10 (s, 3 H), 4.06 (s, 3 H), 3.80-3.70 (m, 1 H), 3.51- 3.39 (m, 2 H), 3.20 (dd, J = 16.0, 8.0 Hz, 1 H), 2.52-2.40 (m, 1 H), 2.13-2.08 (m, 2H), 2.00-1.90 (m, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ 151.3, 150.0, 149.8, 149.7, 130.1, 129.6, 127.0, 125.0, 123.9, 120.9, 107.0, 105.3, 103.7, 103.4, 56.9, 56.5, 46.6, 33.2, 31.3, 23.0. IR (neat): 2959, 2938, 2253, 1619, 1533, 1515, 1476, 1466, 1421, 1278, 1264, 1247, 1213, 1199, 1147, 1044, 1005, 728, 607 cm^{-1} ; HRMS (EI) calcd for $[\text{M}]^+$ $\text{C}_{23}\text{H}_{25}\text{NO}_6\text{S}$: 443.1397, found: 443.1407.



(S)-2-(2, 3, 6, 7-tetramethoxyphenanthren- 9-ylmethyl)-pyrrolidine (12)

The desulfonation was performed by modification of the procedure reported by Evans.⁹ Ammonia (10.0 mL) was condensed in a volume-marked two-neck flask containing sultam **3** (22.5 mg, 0.0508 mmol) and dry THF/DMSO (1.0 mL, 1: 2) at -78 °C under Ar. Lithium metal (3.0 mg, 0.43 mmol, 8.4 equiv) was added over 15 min (1.0 mg of lithium per 5 min was added). After the mixture was stirred at -78 °C under Ar for 30 min, solid NH₄Cl (1.0 g) was added, and the solution was warmed to room temperature, and allowed to evaporate overnight. EtOAc (10 mL) and aqueous KOH (20%, 10 mL) were added to the resulting residue. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over Na₂SO₄. The solvents were removed *in vacuo* and flash chromatography of the resulting crude oil on SiO₂ using CH₃OH/aqueous 37% NH₄OH (3 : 0.1) as eluent afforded 8.5 mg (44%) of (S)- 2- (2, 3, 6, 7-tetramethoxyphenanthren-9-ylmethyl)-pyrrolidine (**12**) as a light yellow oil, whose NMR spectra was identical to that previously reported for **12**.¹⁰ [α]_D²³ = + 3.5° (c = 0.94, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): δ 7.84 (s, 1 H), 7.77 (s, 1 H), 7.48 (s, 1 H), 7.44 (s, 1 H), 7.19 (s, 1 H), 4.12 (s, 3 H), 4.11 (s, 3 H), 4.05 (s, 3 H), 4.03 (s, 3 H), 3.53 (m, 1 H), 3.19 (d, 2 H, *J* = 6.8 Hz), 3.18-3.08 (m, 1 H), 2.90-2.80 (m, 1 H), 1.91-1.88 (m, 2 H), 1.78-1.73 (m, 2 H), 1.60-1.50 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 149.4, 149.1, 132.4, 126.9, 126.1, 125.5, 125.2, 124.2, 108.6, 105.5, 104.0, 103.4, 59.2, 56.7, 56.6, 56.5, 56.4, 46.8, 40.8, 32.3, 25.5.



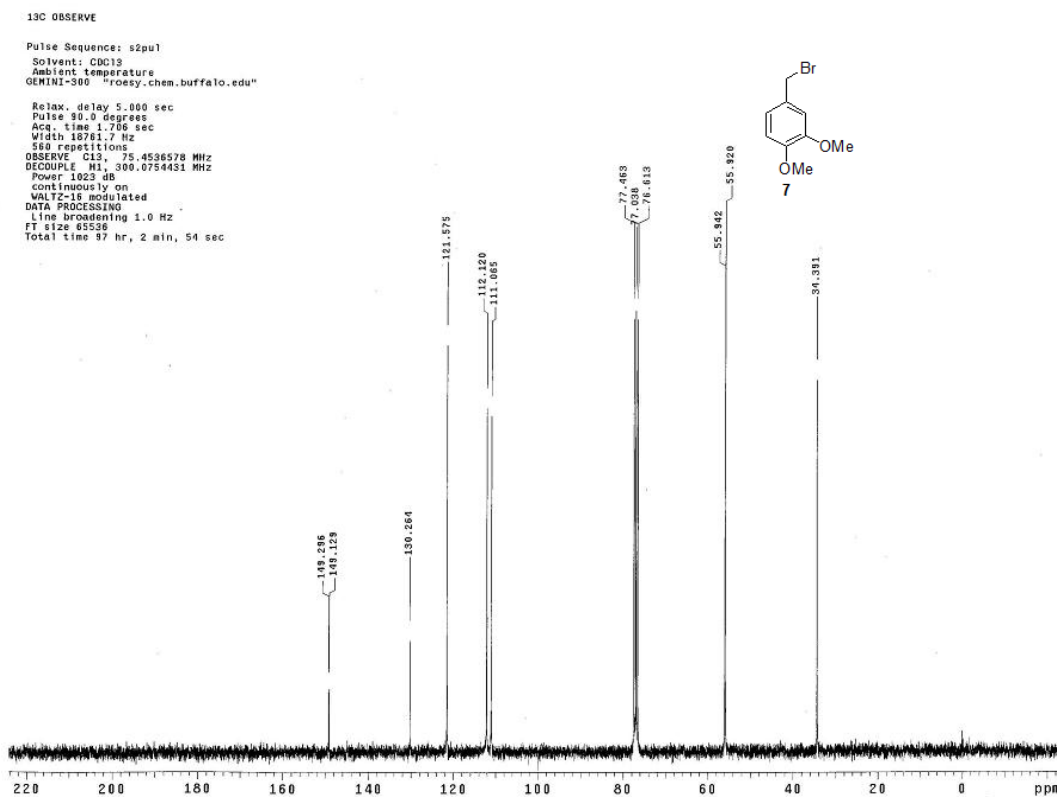
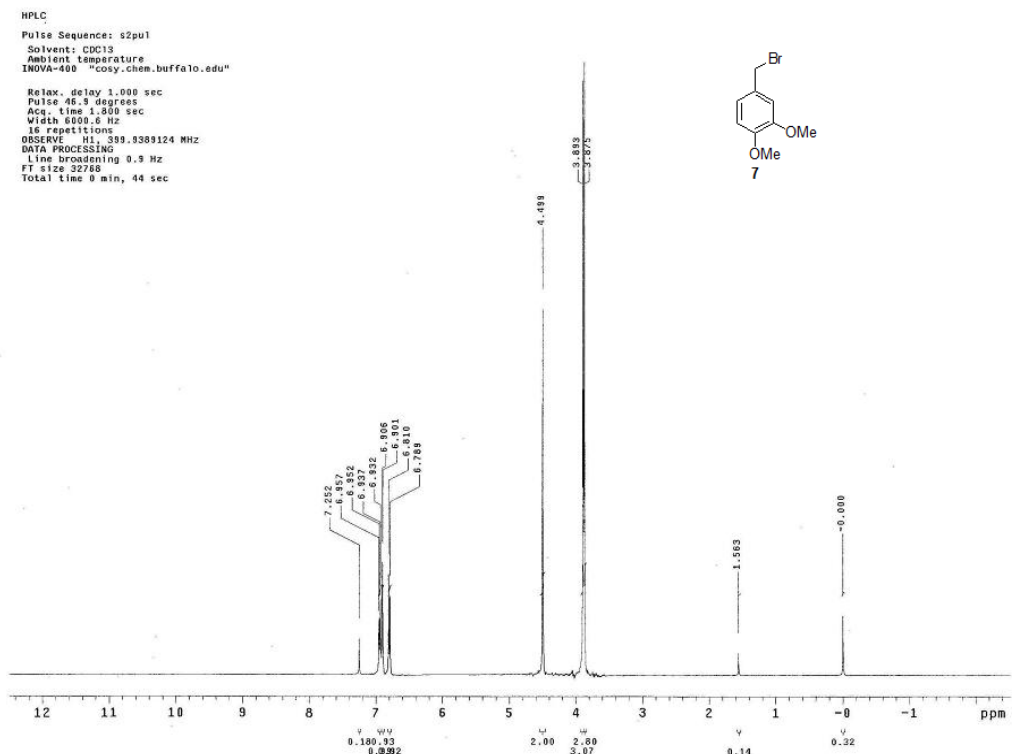
S-(+)-Tylophorine (1)

The Pictet-Spengler reaction was performed by modification of the procedure reported by Njoroge.¹⁰ To a solution of amine (7.3 mg, 0.02 mmol) in EtOH (0.50 mL) were added 37% formaldehyde (0.11 mL) and *conc.* HCl (11.0 μ L). The reaction mixture was refluxed for 2 days in the dark. Then the mixture was concentrated to dryness under reduced pressure, and the residue was treated with 1 mL of 20% KOH, the aqueous layer was extracted with CH₂Cl₂ (2 × 3 mL), and the combined organic layers were washed with water and brine and dried over Na₂SO₄. Filtration and concentration *in vacuo* afforded the crude which was purified by flash column chromatography on silica gel (CH₂Cl₂/MeOH, 20 : 1) to afford (S)-tylophorine (6.7 mg, 89%) as light yellow solid. Mp

283-285 °C (lit. mp 282-284 °C¹¹, 284-286 °C¹⁰). $[\alpha]_D^{23} = +62.1^\circ$ (c = 1.0 in CHCl₃). Lit¹⁰, $[\alpha]_D^{21} = +73^\circ$ (c = 0.7 in CHCl₃), ee = 81%, determined by HPLC analysis [Chiralcel AD-H, 15% IPA/hexane, 0.70 mL/min, λ = 254 nm, t (major) = 22.50 min, t(minor) = 34.54 min]; ¹H NMR (400 MHz, CDCl₃): δ 7.81 (s, 2 H), 7.29 (s, 1 H), 7.14 (s, 1 H), 4.60 (d, 1 H, J = 16 Hz), 4.11 (s, 6 H), 4.05 (s, 6 H), 3.66 (d, 1 H, J = 14.4 Hz), 3.48 (m, 1 H), 3.34 (d, 1 H, J = 17.2 Hz), 2.90 (t, 1 H, J = 11.2 Hz), 2.48-2.46 (m, 2 H), 2.31-2.20 (m, 1 H), 2.10-2.00 (m, 1 H), 2.10-2.00 (m, 1 H), 2.00-1.80 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 147.7, 147.5, 147.4, 125.3, 124.8, 123.3, 122.6, 122.4, 103.0, 102.5, 102.3, 102.1, 59.2, 55.0, 54.9, 54.1, 52.9, 32.7, 30.2, 20.6. IR (neat): 2957, 1717, 1602, 1535, 1515, 1472, 1441, 1425, 1416, 1262, 1249, 1213, 1195, 1150, 1016, 840, 770 cm⁻¹; HRMS (EI) calcd for [M]⁺ C₂₄H₂₇NO₄: 393.1935, found: 393.1933. These data were in agreement with those reported.¹⁰⁻¹³

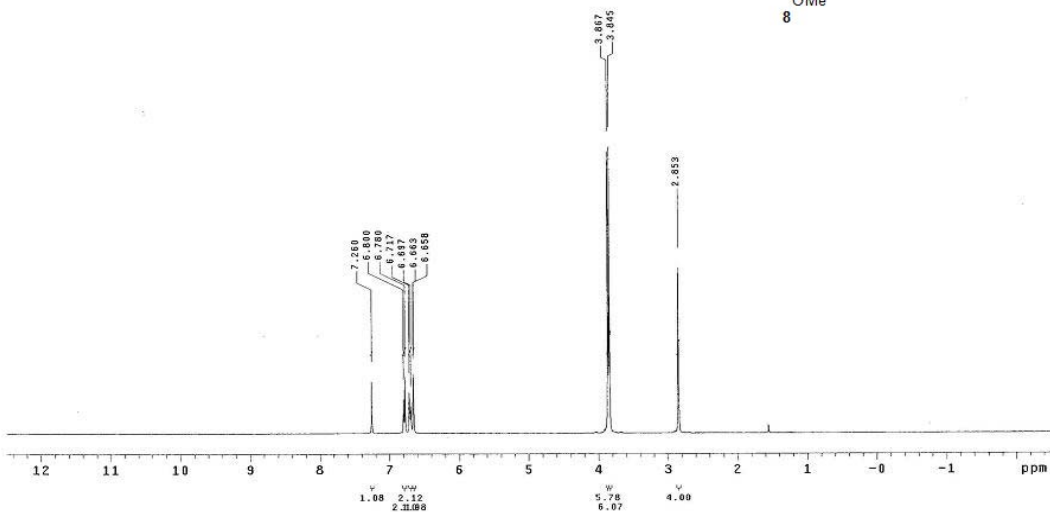
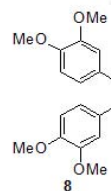
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^1H - and ^{13}C - NMR Spectra of Intermediate 3- 9, 12, 13 and Tylophorine 1

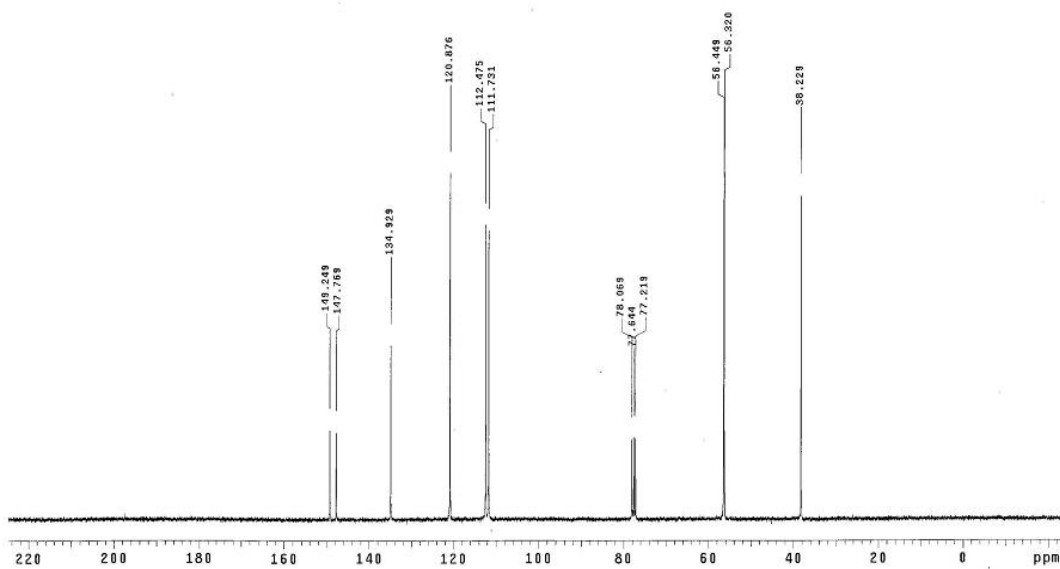
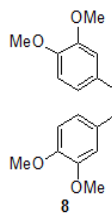
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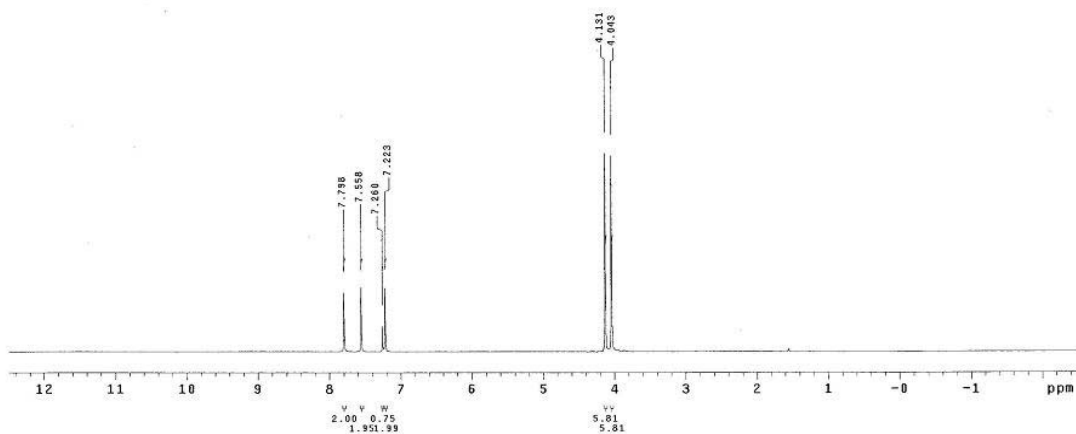
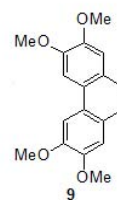


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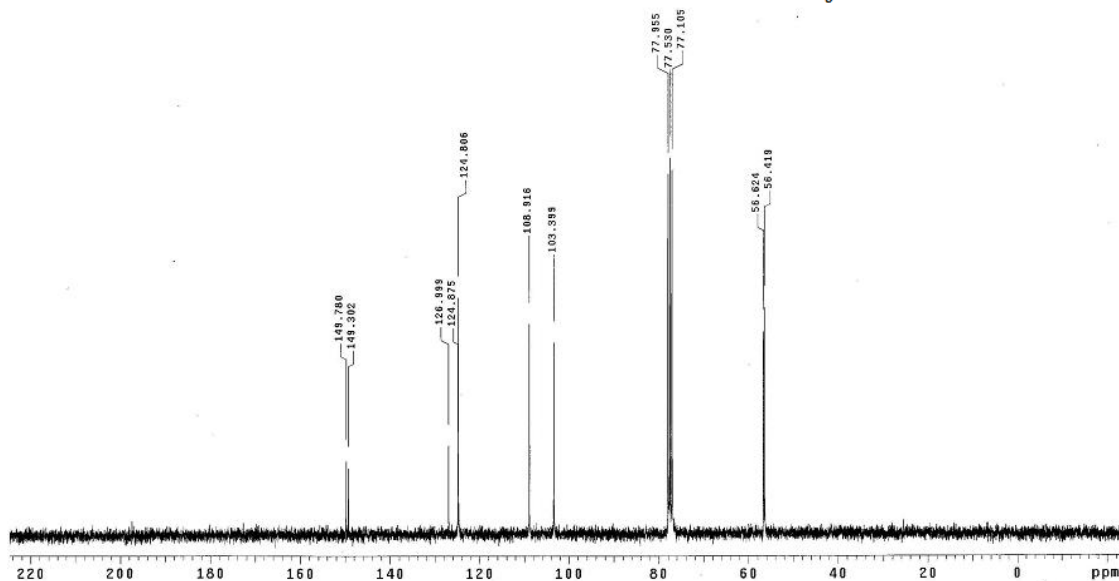
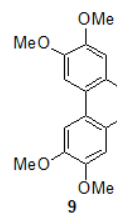
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12-18
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 Width 6000.6 Hz
 16 repetitions
 OBSERVE H1, 399.9389099 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec



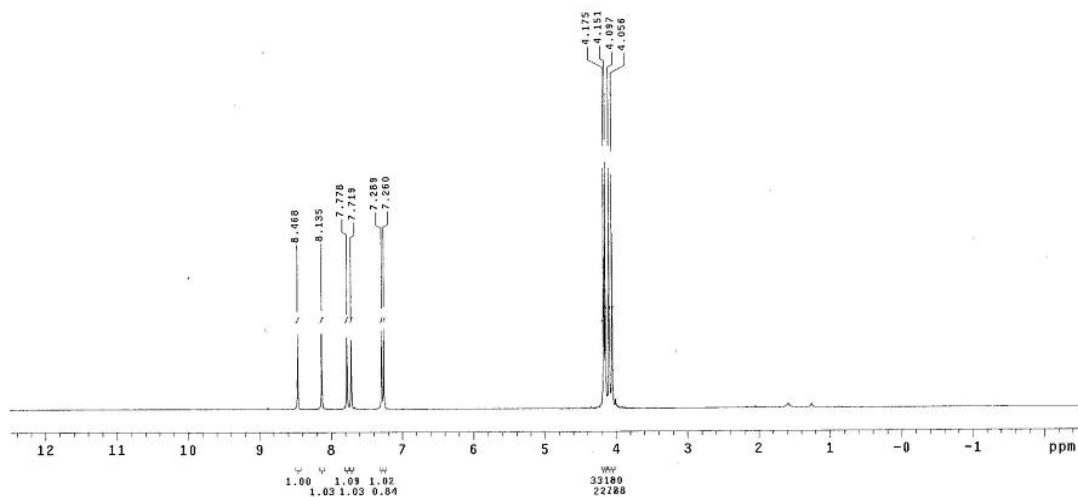
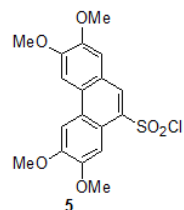
12-18
 Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 GEMINI-300 "rosy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.706 sec
 Width 18761.7 Hz
 560 repetitions
 OBSERVE C13, 75.4536195 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 0 min, 0 sec



12-21

Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"

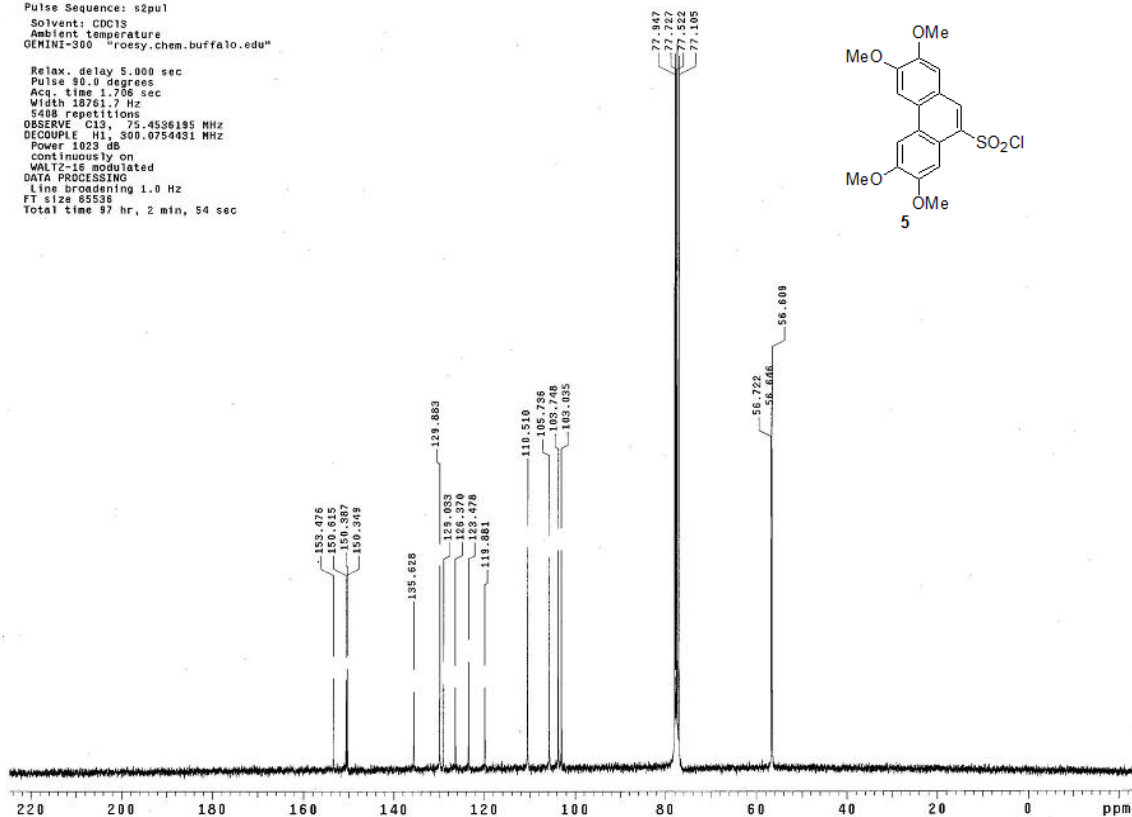
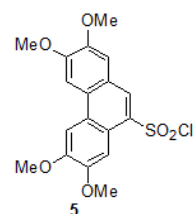
Relax. delay 1.000 sec
 Pulse 46.9 degrees
 Acq. time 1.000 sec
 Width 6000.6 Hz
 16 repetitions
 OBSERVE H1, 500.9389095 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec



12-21

Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 GENI-300 "roesy.chem.buffalo.edu"

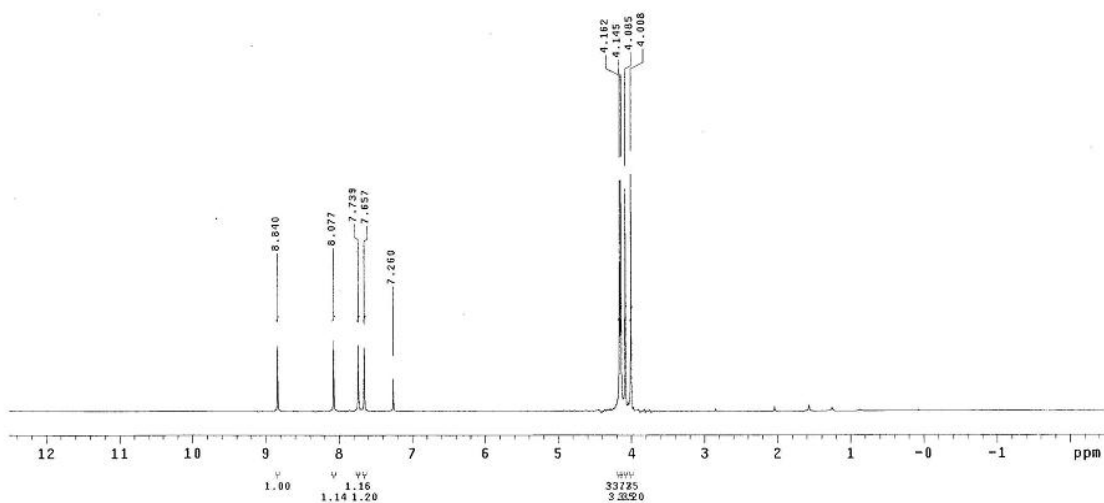
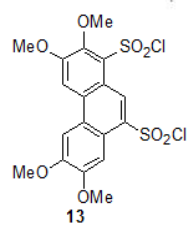
Relax. delay 5.000 sec
 Pulse 30.0 degrees
 Acq. time 1.706 sec
 Width 18761.7 Hz
 5408 repetitions
 OBSERVE C13, 75.4536195 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 Continuous on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 97 hr, 2 min, 54 sec



STANDARD 1H OBSERVE

Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"

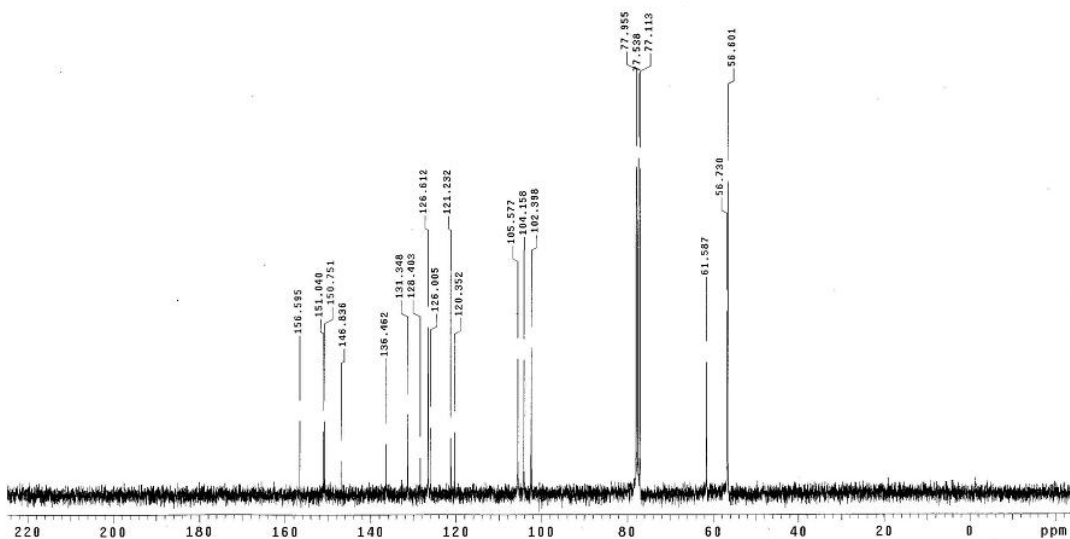
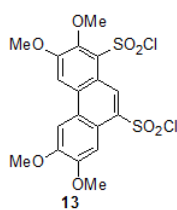
Relax. delay 1.000 sec
 Pulse 40.9 degrees
 Acq. time 1.800 sec
 Width 6000.6 Hz
 16 repetitions
 OBSERVE H1, 399.9389022 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec



diso2

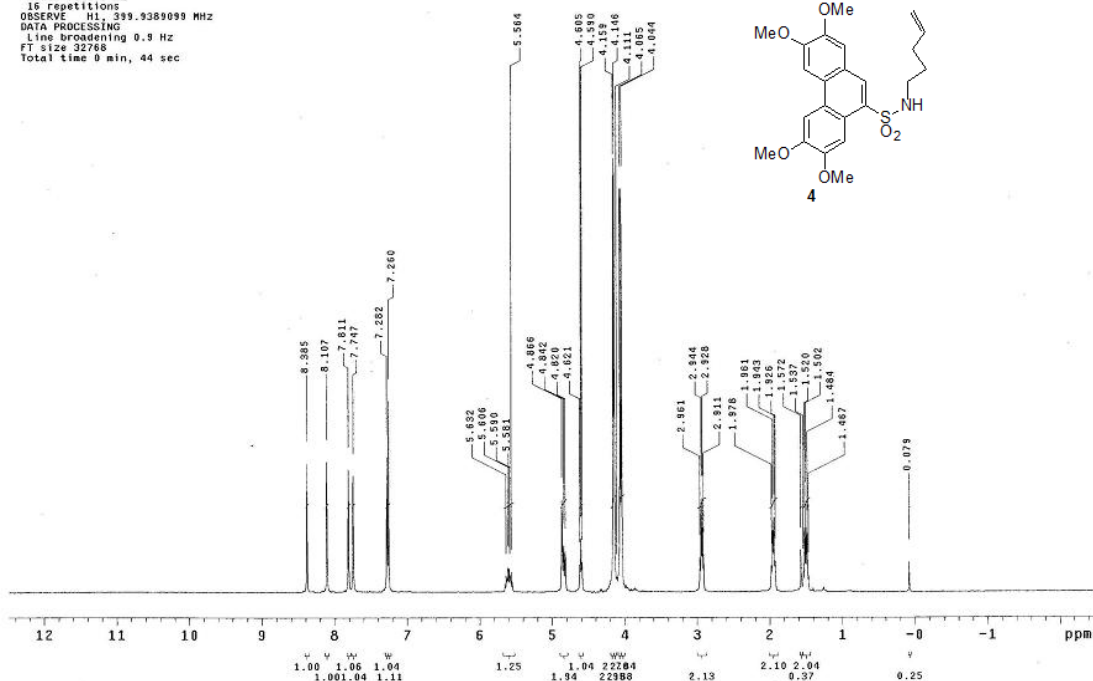
Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 GENI-300 "rossy.chem.buffalo.edu"

Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.700 sec
 Width 18761.7 Hz
 384 repetitions
 OBSERVE C13, 75.4536195 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1923 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 9 hr, 42 min, 58 sec



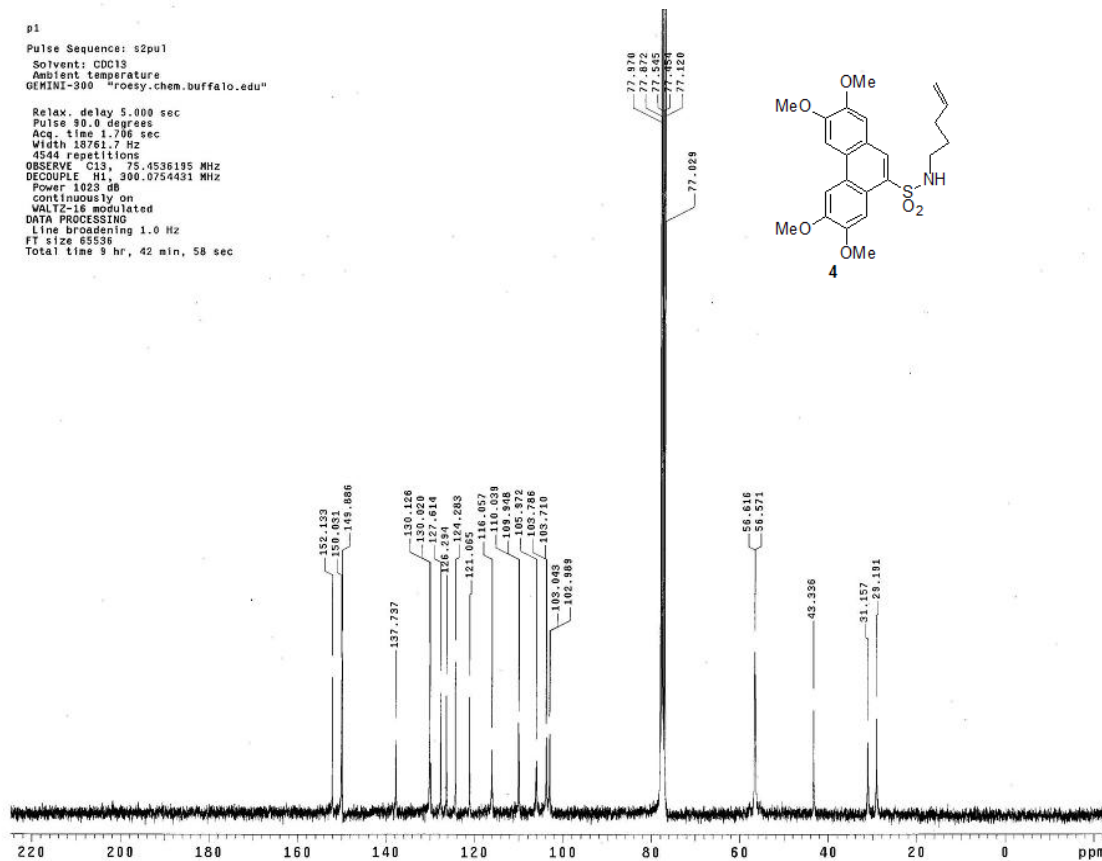
v1
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"

Relax. delay 1.000 sec
 Pulse 45.3 degrees
 Acq. time 1.800 sec
 Width 6800.6 Hz
 16 repetitions
 OBSERVE H1, 399.9389099 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 9 min, 44 sec



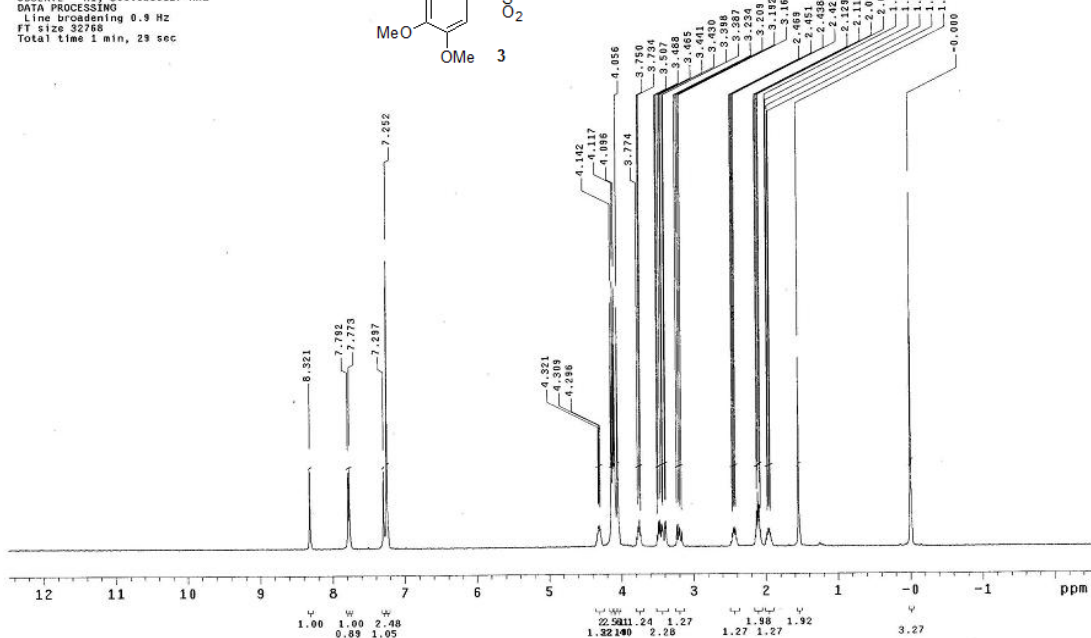
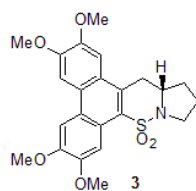
p1
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 GEKING-500 "prosy.chem.buffalo.edu"

Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.700 sec
 Width 18761.7 Hz
 4544 repetitions
 OBSERVE C13, 75.4536195 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 Continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 9 hr, 42 min, 58 sec



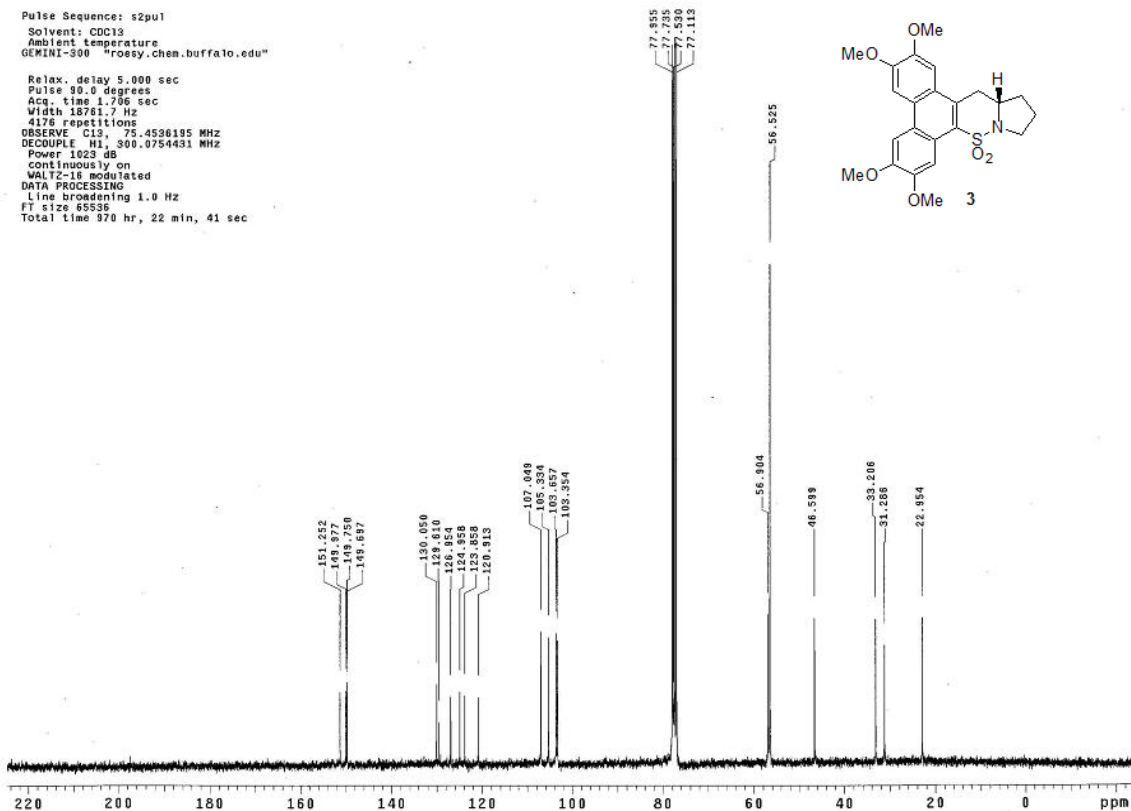
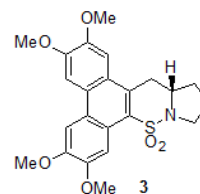
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 48.9 degrees
 Acq. time 1.800 sec
 Width 6000.5 Hz
 32 repetitions
 OBSERVE H1, 399.9389127 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 1 min, 29 sec



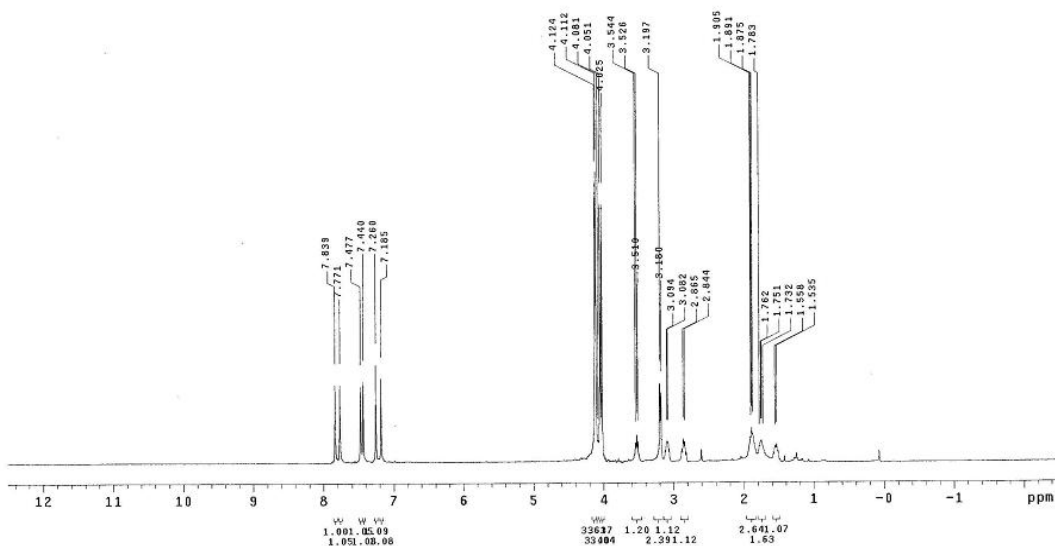
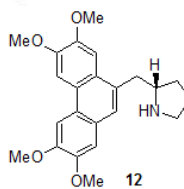
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 GEMINI-300 "roesy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.796 sec
 Width 18761.7 Hz
 4176 repetitions
 OBSERVE C13, 75.4536195 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 970 hr, 22 min, 41 sec



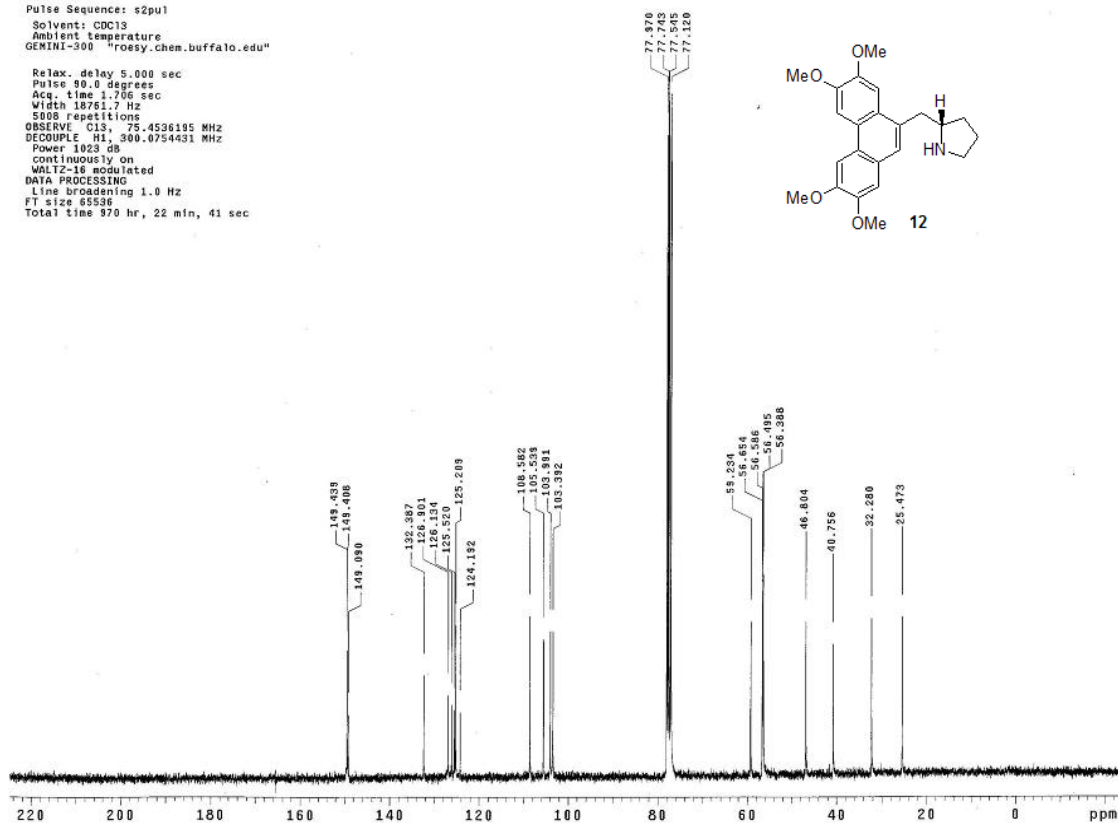
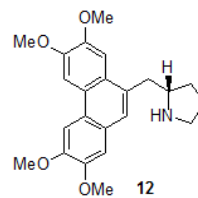
amino compound
Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
INNOVA-400 "cosy.chem.buffalo.edu"

Relax. delay 1.000 sec
Pulse 46.8 degrees
Acq. time 1.800 sec
Width 6000.6 Hz
16 repetitions
OBSERVE H1, 399.9389025 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 32768
Total time 0 min, 44 sec



amino compound
Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
GEMINI-300 "roesy.chem.buffalo.edu"

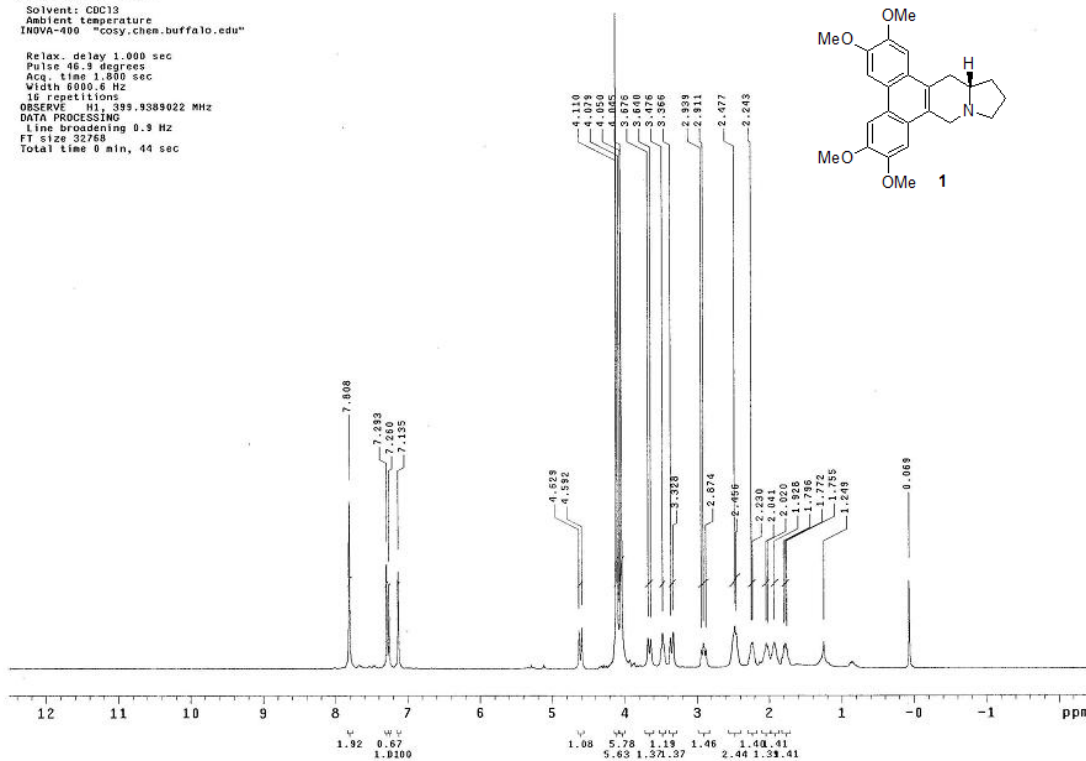
Relax. delay 5.000 sec
Pulse 90.0 degrees
Acq. time 1.706 sec
Width 18761.7 Hz
5808 repetitions
OBSERVE C13, 75.4536195 MHz
DECOUPLE H1, 300.0754431 MHz
Power 1023 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 870 hr, 22 min, 41 sec



STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDC13
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"

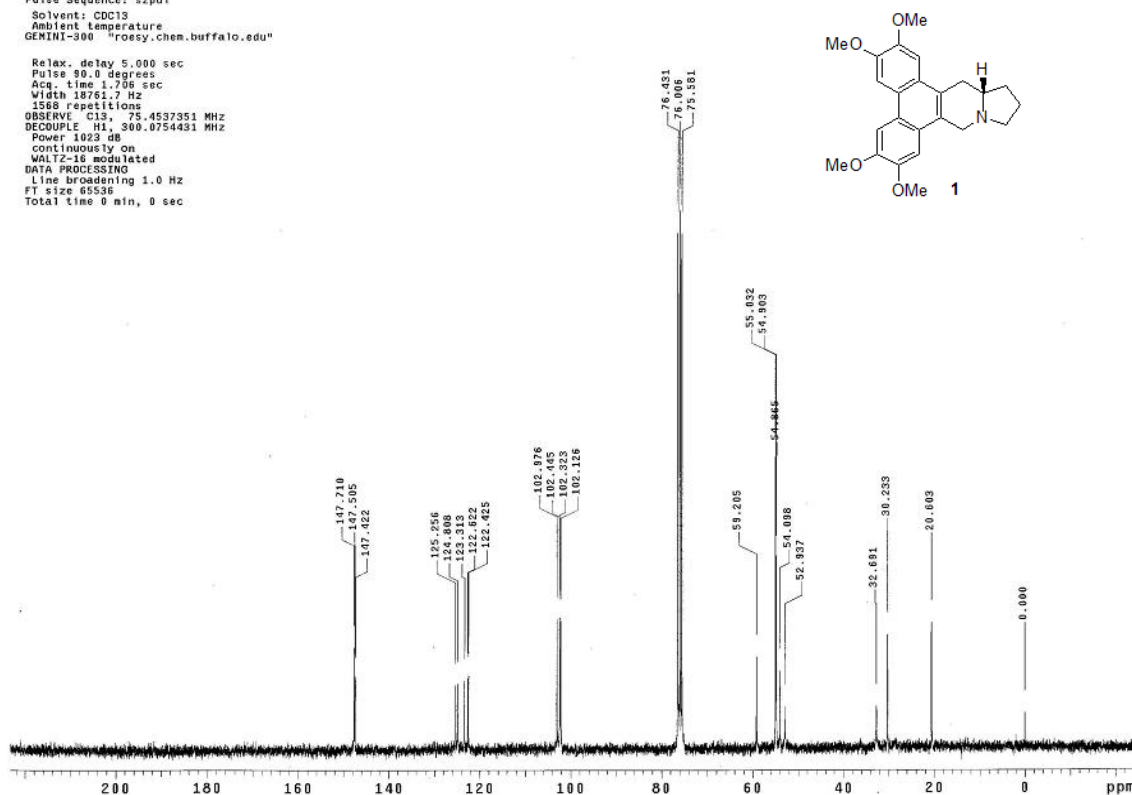
Relax. delay 1.000 sec
 Pulse 46.3 degrees
 Acq. time 1.800 sec
 Width 6000.6 Hz
 16 repetitions
 OBSERVE H1, 399.9389022 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec



13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDC13
 Ambient temperature
 GEMINI-300 "roesy.chem.buffalo.edu"

Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.708 sec
 Width 18761.7 Hz
 1568 repetitions
 OBSERVE C13, 75.4537351 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 0 min, 0 sec



Enantiomeric Excess Determination (HPLC traces) for Tylophorine 1

<div><chem>COc1cc2c(cc1OC)C3CCN(C3)Cc2</chem><div>1</div></div>	<div>HPLC Conditions: Chiral AD-H, 15% IPA/Hexane, 0.7mL/min flow</div>																																																																								
<div><div>HPLC spectra for racemic product 1</div></div>	<table><tr><th>Peak No</th><th>Peak Name</th><th>Result ()</th><th>Ret. Time (min)</th><th>Time Offset (min)</th><th>Area (counts)</th></tr><tr><td>1</td><td></td><td>1.6191</td><td>5.671</td><td>0.000</td><td>793962</td></tr><tr><td>2</td><td></td><td>0.8392</td><td>8.681</td><td>0.000</td><td>411508</td></tr><tr><td>3</td><td></td><td>0.0548</td><td>10.630</td><td>0.000</td><td>26859</td></tr><tr><td>4</td><td></td><td>0.0874</td><td>12.608</td><td>0.000</td><td>42882</td></tr><tr><td>5</td><td></td><td>0.1277</td><td>16.496</td><td>0.000</td><td>62606</td></tr><tr><td>6</td><td></td><td>0.0482</td><td>19.391</td><td>0.000</td><td>23623</td></tr><tr><td>7</td><td></td><td>0.0203</td><td>22.260</td><td>0.000</td><td>9974</td></tr><tr><td>8</td><td></td><td>43.7189</td><td>24.366</td><td>0.000</td><td>21438034</td></tr><tr><td>9</td><td></td><td>52.1528</td><td>31.966</td><td>0.000</td><td>25573668</td></tr><tr><td>10</td><td></td><td>1.3316</td><td>43.775</td><td>0.000</td><td>652950</td></tr><tr><td colspan="2">Totals</td><td>100.0000</td><td></td><td>0.000</td><td>49036064</td></tr></table>	Peak No	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	1		1.6191	5.671	0.000	793962	2		0.8392	8.681	0.000	411508	3		0.0548	10.630	0.000	26859	4		0.0874	12.608	0.000	42882	5		0.1277	16.496	0.000	62606	6		0.0482	19.391	0.000	23623	7		0.0203	22.260	0.000	9974	8		43.7189	24.366	0.000	21438034	9		52.1528	31.966	0.000	25573668	10		1.3316	43.775	0.000	652950	Totals		100.0000		0.000	49036064
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<div><div>HPLC spectra for reaction product 1</div></div>	<table><tr><th>Peak No</th><th>Ret. Time (min)</th><th>Area (counts)</th><th>Sep. Code</th><th>Result ()</th></tr><tr><td>1</td><td>5.22</td><td>192852</td><td>BV</td><td>0.17</td></tr><tr><td>2</td><td>5.57</td><td>191373</td><td>VV</td><td>0.17</td></tr><tr><td>3</td><td>5.98</td><td>600888</td><td>VP</td><td>0.54</td></tr><tr><td>4</td><td>7.10</td><td>72899</td><td>PB</td><td>0.07</td></tr><tr><td>5</td><td>22.50</td><td>99527008</td><td>BV</td><td>89.55</td></tr><tr><td>6</td><td>34.54</td><td>10561670</td><td>VB</td><td>9.50</td></tr><tr><td colspan="4">111146696</td><td>100.00</td></tr></table>	Peak No	Ret. Time (min)	Area (counts)	Sep. Code	Result ()	1	5.22	192852	BV	0.17	2	5.57	191373	VV	0.17	3	5.98	600888	VP	0.54	4	7.10	72899	PB	0.07	5	22.50	99527008	BV	89.55	6	34.54	10561670	VB	9.50	111146696				100.00																																
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