

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

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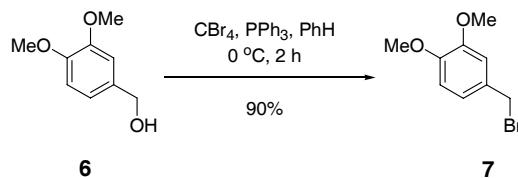
Supplementary Material

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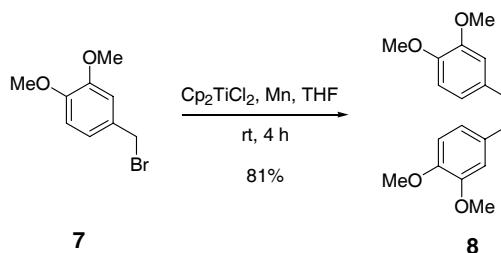
General Information:

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 ¹³C 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

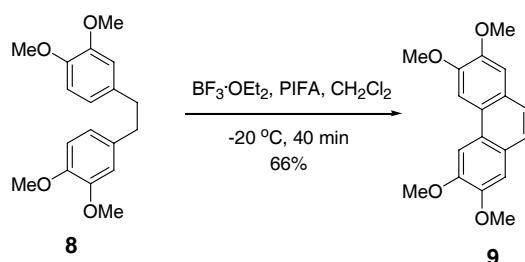
3, 4-Dimethoxybenzyl bromide (**7**) was prepared as described by Barrero.^{1a} CBr₄ (0.66 g, 2.0 mmol) and Ph₃P (0.53 g, 2.0 mmol) at 0 °C under Ar atmosphere were added to a stirred solution of 3, 4-dimethoxybenzylic alcohol (0.17 g, 1.0 mmol) in benzene (7 mL). The solution was stirred at the same 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, CDCl₃): 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); ¹³C NMR (75 MHz, CDCl₃): 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)

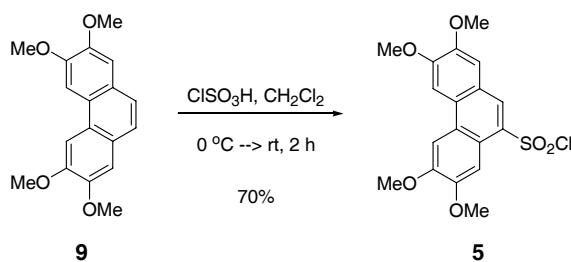
1, 2-Bis (3, 4-dimethoxyphenyl) ethane (**8**) was prepared as described by Barrero.^{1a} A mixture of Cp₂TiCl₂ (69.7 mg, 0.280 mmol) and Mn dust (0.610 g, 11.1 mmol) in thoroughly deoxygenate THF (20 mL) was stirred under an Ar atmosphere at room

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 $BF_3\cdot OEt_2$ (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.

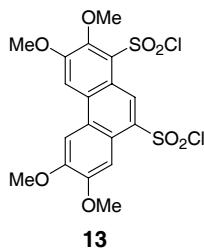


2, 3, 6, 7-Tetramethoxy-phenanthrene-9-sulfonyl chloride (**5**)

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 × 2 mL), and the combined organic layer was

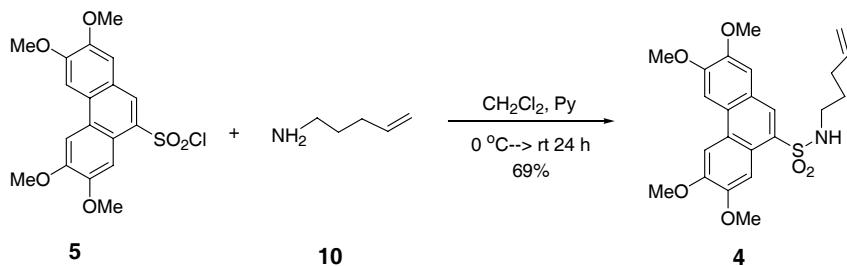
washed with H_2O (2 mL), then dried over MgSO_4 , filtered and concentrated in *vacuo*. The crude residue was purified by flash chromatography on silica gel (EtOAc / hexane, 1 : 1.5) to afford 2, 3, 6, 7-tetramethoxyphenanthrene-9-sulfonyl chloride (**5**) (93.3 mg, 70%) as yellow solid. Mp 207- 209 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3): 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); ^{13}C NMR (75 MHz, CDCl_3): 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 $[\text{M}]^+$ $\text{C}_{18}\text{H}_{17}\text{ClO}_6\text{S}$: 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)

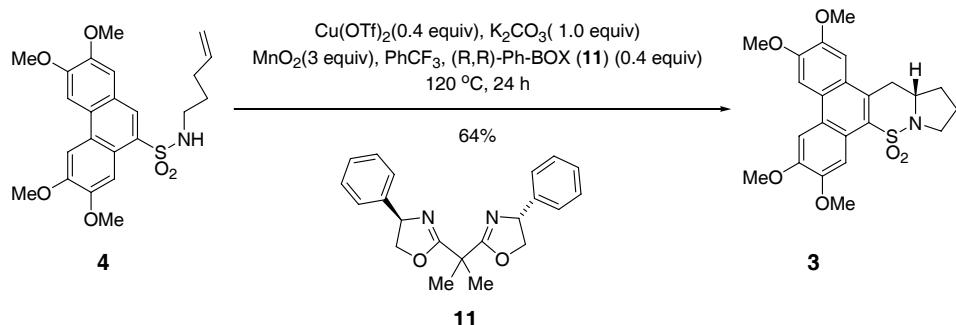
Data for **13**: Yellow solid, Mp 205- 208 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3): δ 8.84 (s, 1 H), 8.08 (s, 1 H), 7.74 (s, 1 H), 7.66 (s, 1 H), 4.16 (s, 3 H), 4.15 (s, 3 H), 4.09 (s, 3 H), 4.01 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 156.6, 151.0, 150.8, 146.8, 136.5, 131.3, 128.4, 126.6, 126.0, 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 $[\text{M}]^+$ $\text{C}_{18}\text{H}_{16}\text{Cl}_2\text{O}_8\text{S}_2$: 430.0039, found: 430.0028.



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

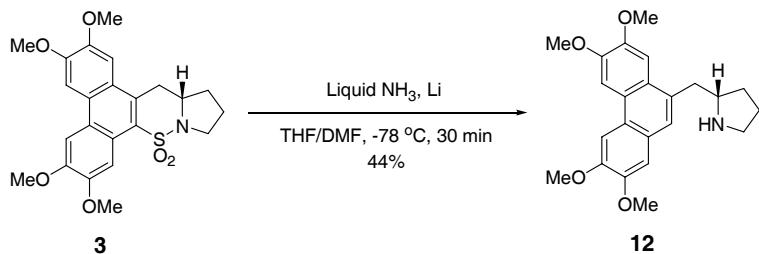
Dry pyridine (158 mg, 2.00 mmol) and 2,3,6,7-tetramethoxy-phenanthrene-9-sulfonyl chloride (**5**) (475.8 mg, 1.20 mmol) were added to a solution of pent-4-enylamine⁸ (**10**) (85 mg, 1.0 mmol) in dry CH_2Cl_2 (8 mL) at 0 $^{\circ}\text{C}$. The mixture was then warmed to room temperature and allowed to stir for 24 h (monitoring by TLC). 1N HCl (10 mL) was added and the mixture was extracted with Et_2O (3×20 mL). The combined organic layers were dried over Na_2SO_4 , 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 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3): 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.



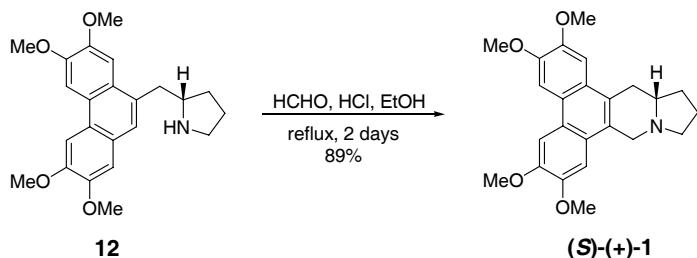
(S)-2, 3, 6, 7-Tetramethoxy-11, 12, 12a, 13-tetrahydro-10H-9-thia-9-a-azacyclopenta[b]triphenylene-9, 9-dioxide (3)

$\text{Cu}(\text{OTf})_2$ (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 ($\text{EtOAc}/\text{hexane}$, 3: 1; $\text{CHCl}_3/\text{EtOAc}$, 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); $[\alpha]_D^{23} = +47.1^\circ$ ($c = 2$ 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, 1 H), 4.31 (m, 1 H), 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, 2 H), 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 desulfonylation 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)

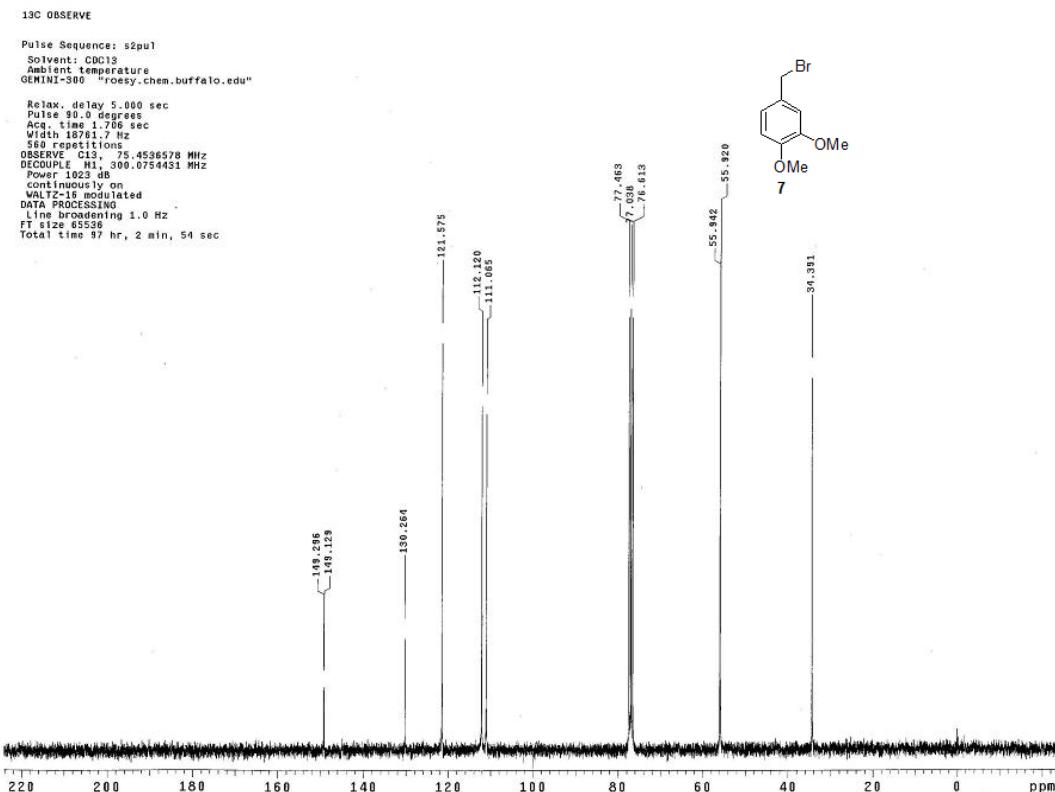
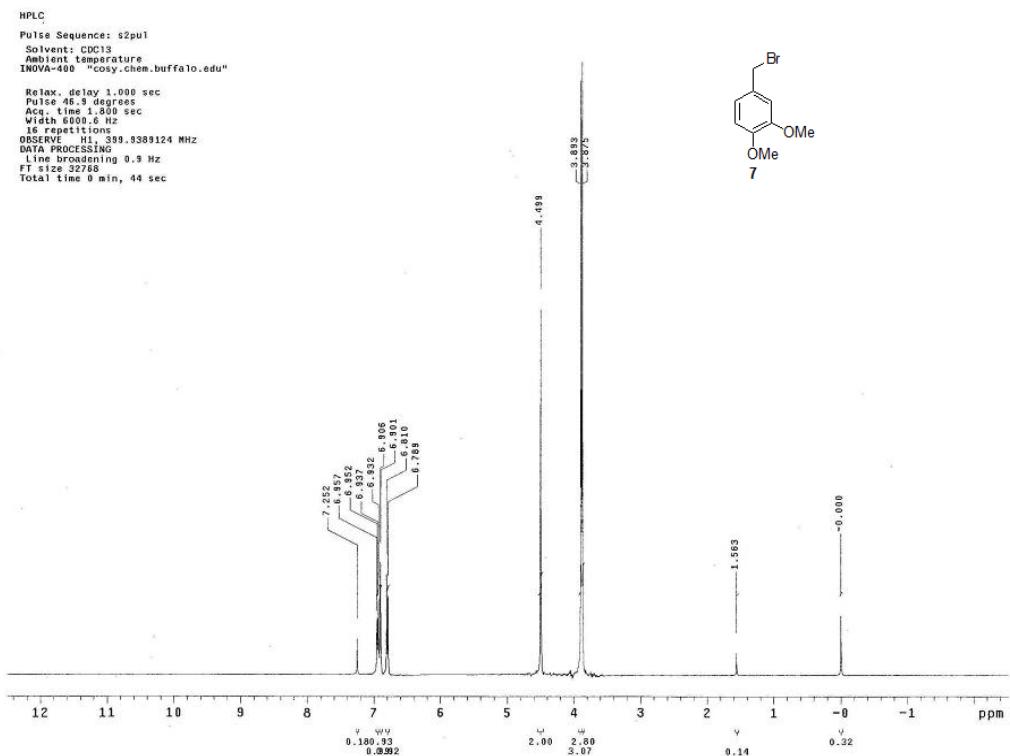
The Pictet-Spengler reaction was performed by modification of the procedure reported by Njoroge.¹⁰ To a solution of amine (7.3 mg, 0.02 mmol) in EtOH (0.50 mL) were added 37% formaldehyde (0.11 mL) and *conc.* HCl (11.0 μL). The reaction mixture was refluxed for 2 days in the dark. Then the mixture was 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, $\lambda = 254$ 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

References

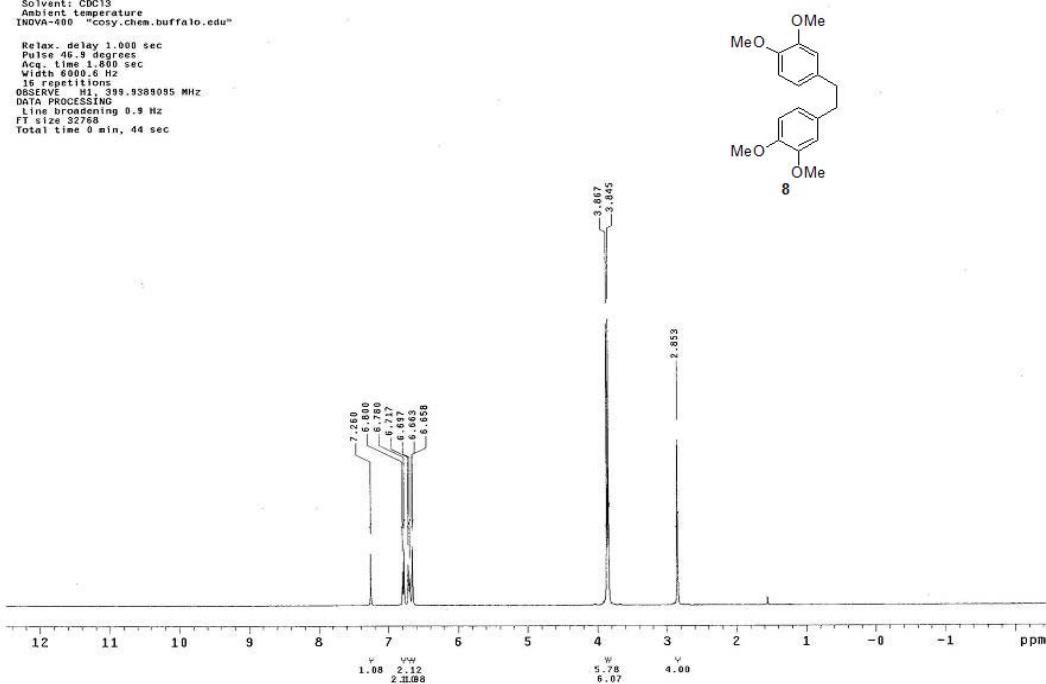
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¹H- and ¹³C- NMR Spectra of Intermediate 3- 9, 12, 13 and Tylophorine 1



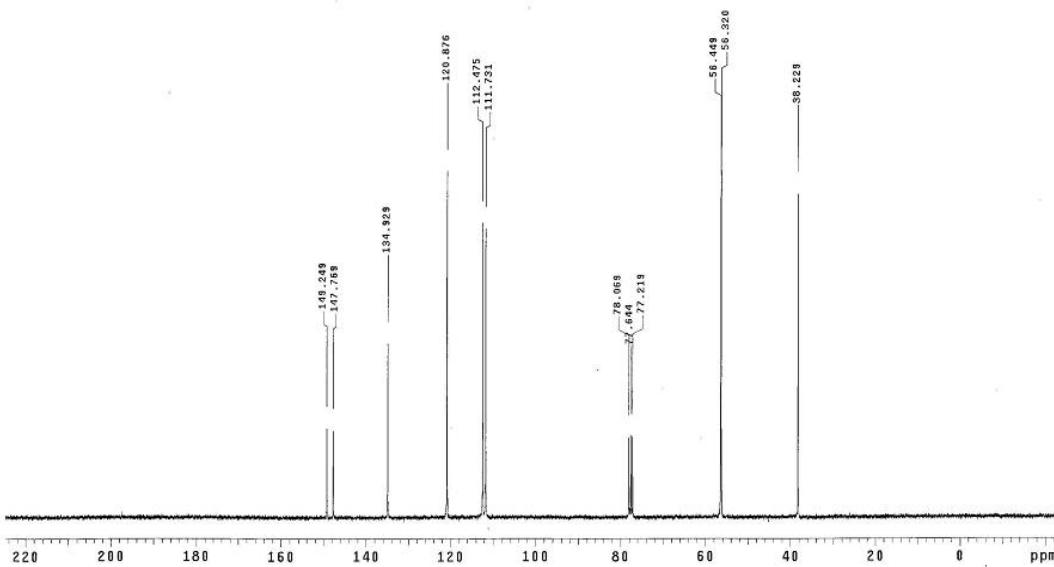
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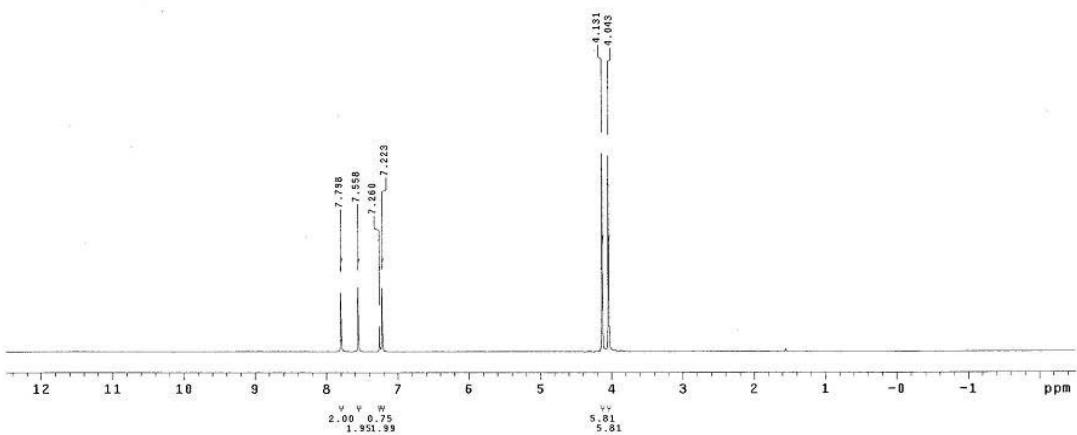
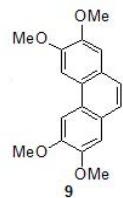


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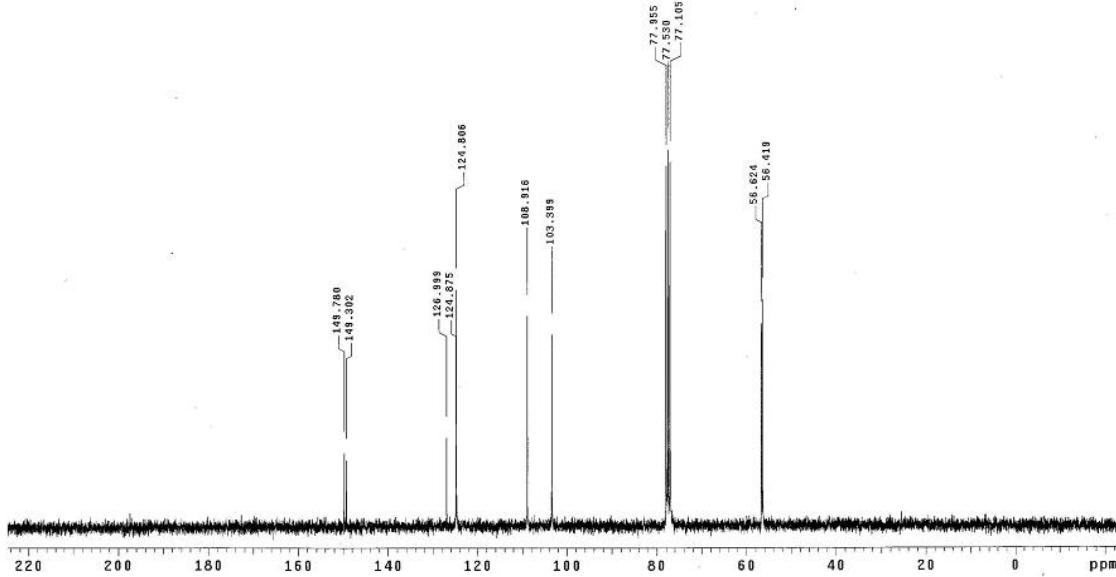
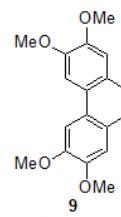
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 Total time 8 hr, 42 min, 58 sec



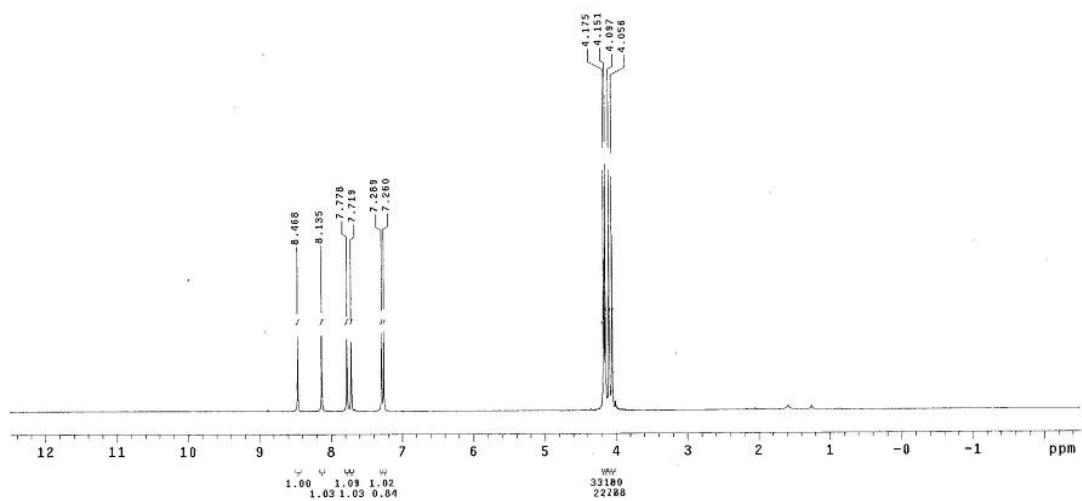
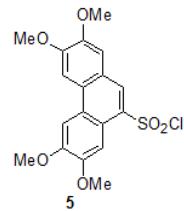
12-18
 Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INNOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 46.3 degrees
 Acq. time 1.800 sec
 W1 8000.0 Hz
 16 repetitions
 OBSERVE ¹H, 399.9389098 MHz
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 32768
 Total time 0 min, 44 sec



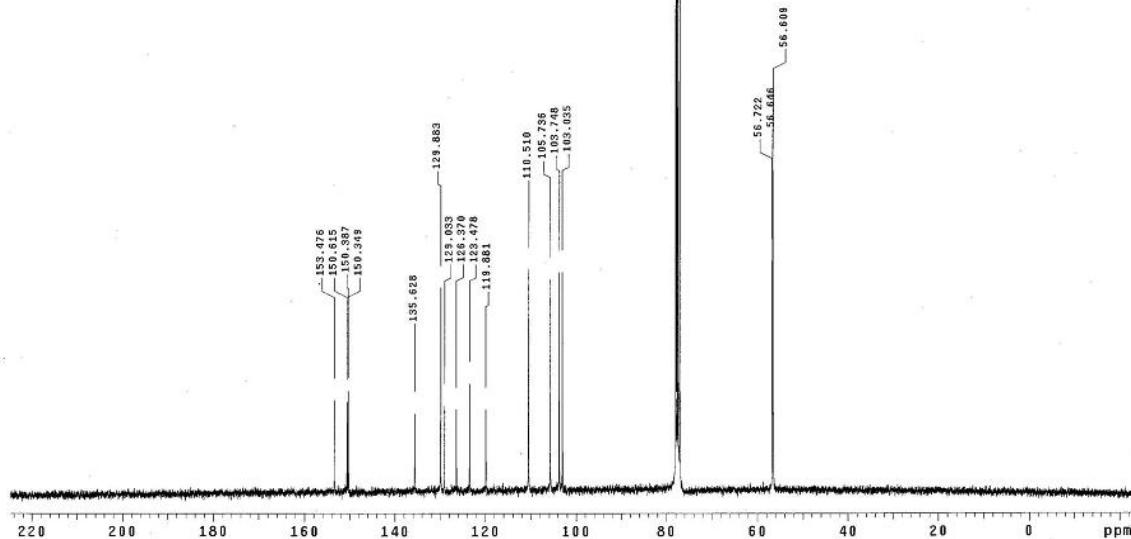
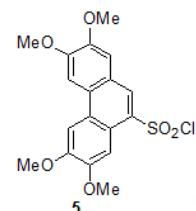
12-18
 Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 GEMINI-300 "rosy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.708 sec
 W1 7500.0 Hz
 560 repetitions
 OBSERVE ¹³C, 75.4536195 MHz
 DECOUPLE ¹H, 300.0754451 MHz
 Power 100% dB
 continuously on
 WALTZ-16 modulated
 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
 INNOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 46.9 degrees
 Acq. time 1.800 sec
 Width 6000.6 Hz
 16321 tics
 OBSERVE = H1, 399.9389095 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec

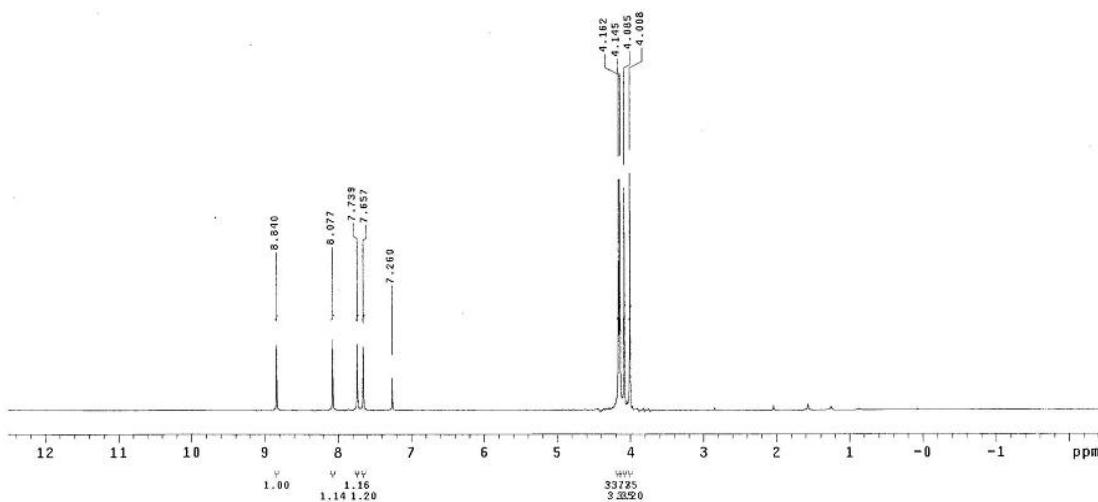
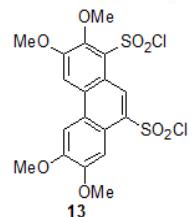


12-21
 Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 GEMINI-300 "rosy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.706 sec
 Width 18761.7 Hz
 54992 tics
 OBSERVE = C13, 75.4536195 MHz
 DECOUPLE = H1, 300.0754431 MHz
 Power 1023 dB
 Complexes on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 97 hr, 2 min, 54 sec



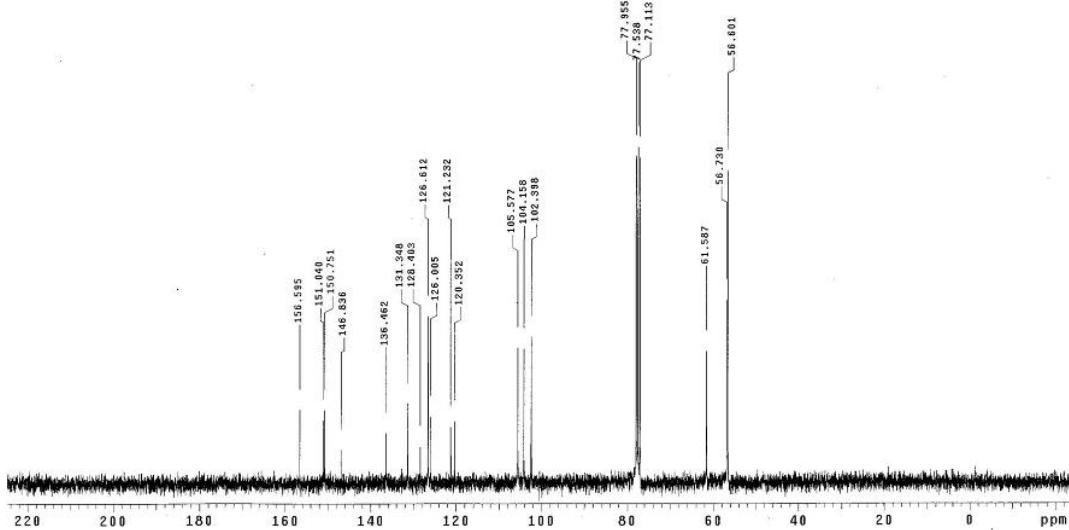
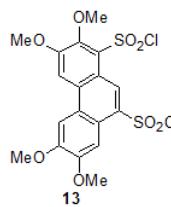
STANDARD 1H OBSERVE

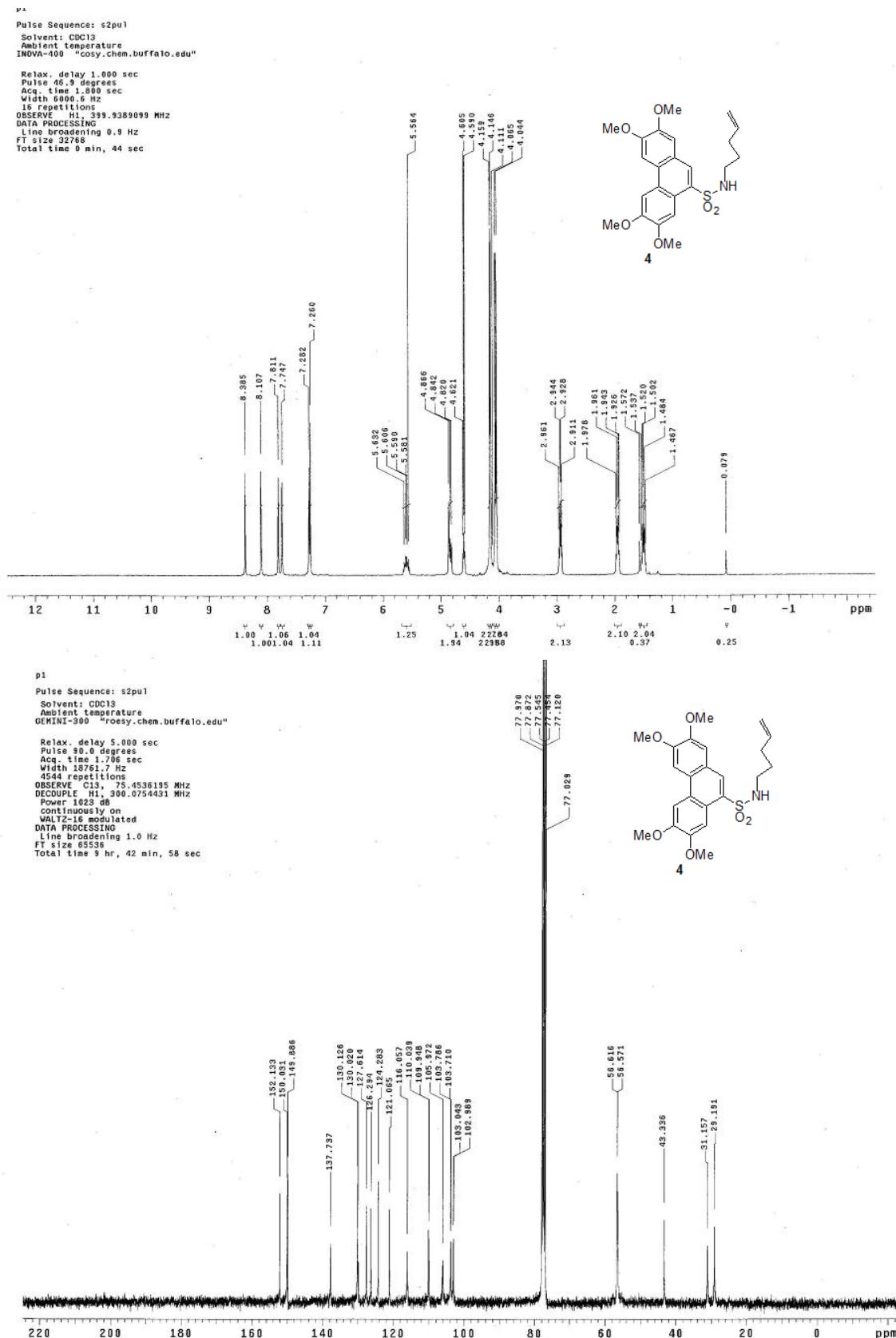
Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 46.9 degrees
 Acq. time 1.800 sec
 Width 601.6 Hz
 16 repetitions
 OBSERVE: H1, 399.9389022 MHz
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 32768
 Total time 0 min, 44 sec



d1502

Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 GEMINI-300 "troesy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 30 degrees
 Acq. time 1.795 sec
 Width 18761.7 Hz
 304 repetitions
 OBSERVE: H1, 399.4536195 MHz
 DECOUPLE: H1, 300.4534431 MHz
 Power 1023 dB
 Convoluted 1.000 sec
 WALTZ-16 simulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 9 hr, 42 min, 58 sec





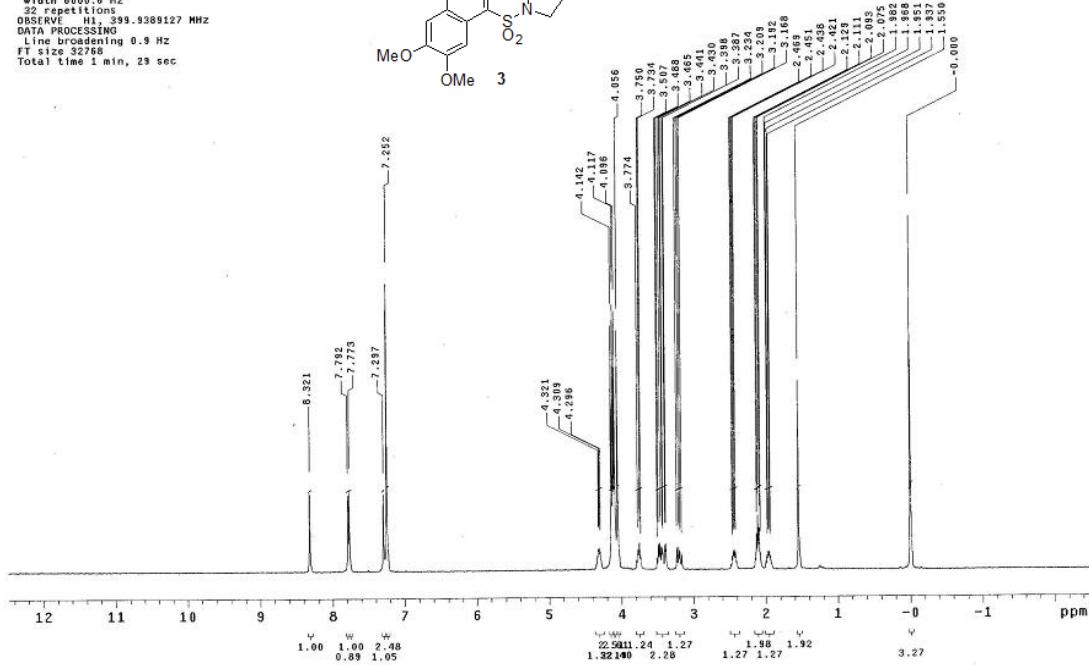
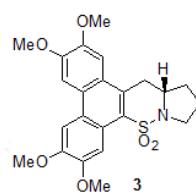
STANDARD 1H OBSERVE

```

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

Relax. delay 1.000 SEC
Pulse 45.8 degrees
Acq. time 1.800 sec
Width 6000.6 Hz
32 repetitions
OBSTIME 1.000000399.93889127 MHZ
DQF PROCESSING
Line broadening 0.9 Hz
FT size 32768
Total time 1 min, 23 sec

```



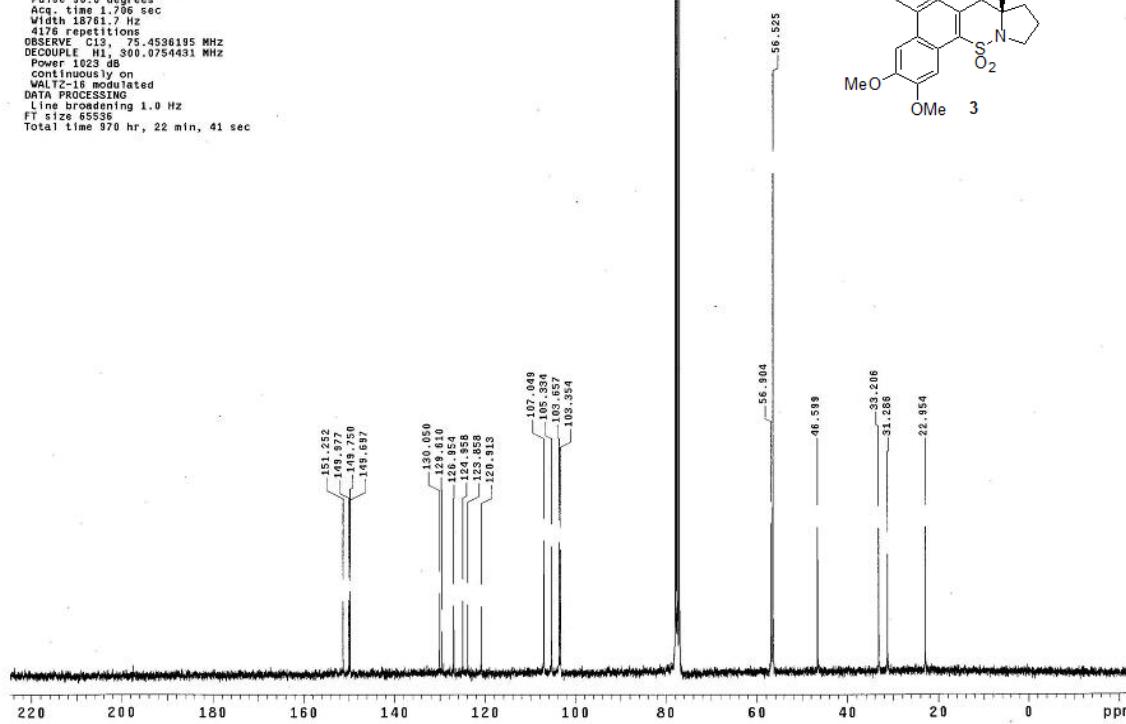
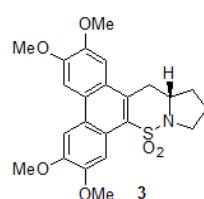
13C OBSERVE

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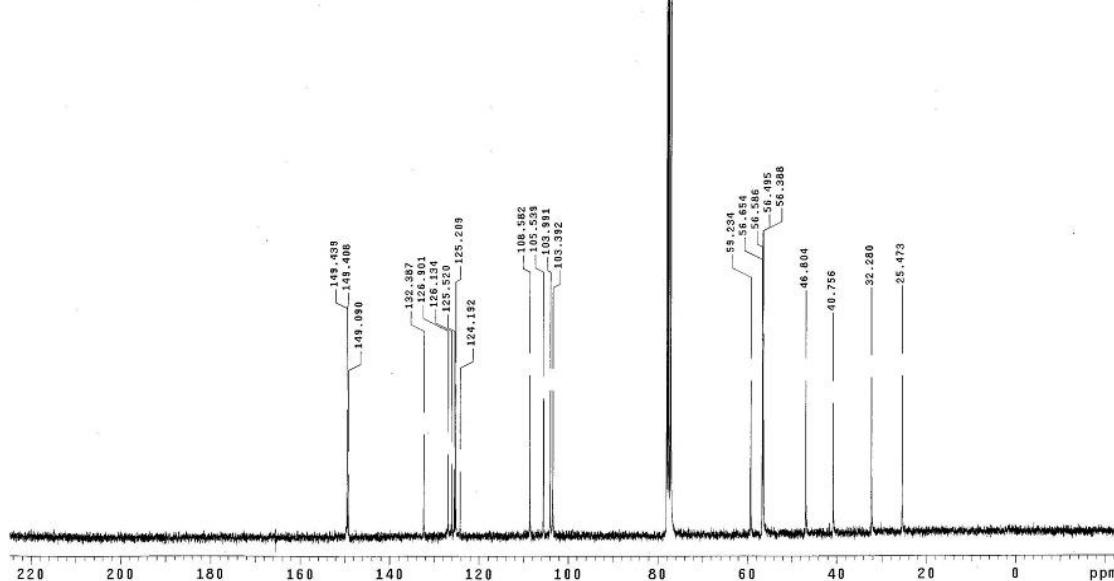
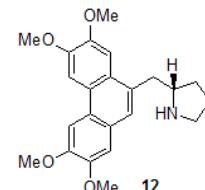
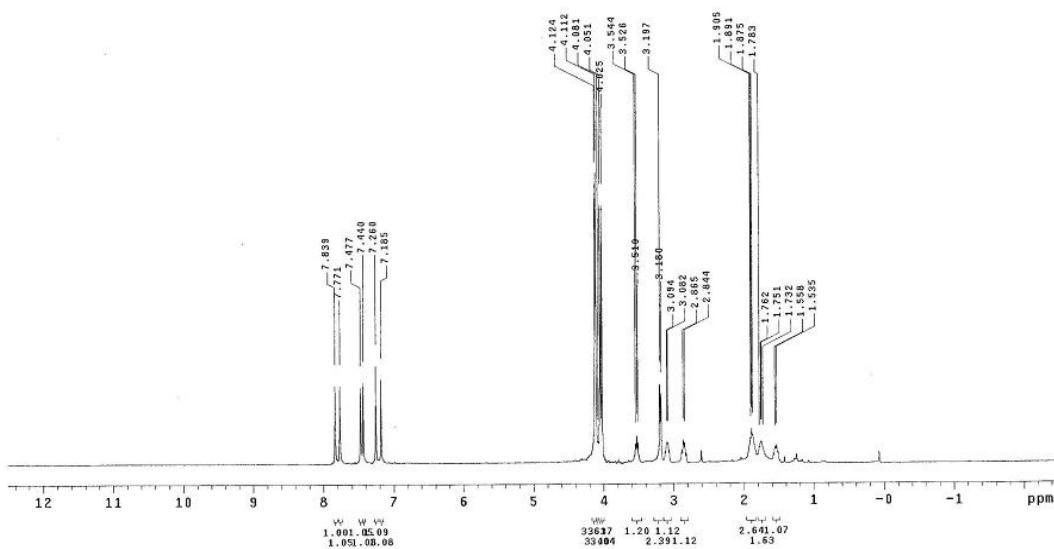
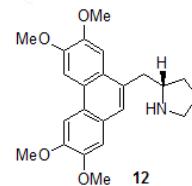
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
GEMINI-300 "chem.chem.buffalo.edu"

Relax, delay 5.000 sec
Pulse 0 degrees
Acc time 1.000 sec
Width 18761.1 Hz
4176 repetitions
OBSERVE C13, 75.4536195 MHz
DETECTOR FID, 0.000 0.0544311 MHz
Power 1023 dB
continuously on
WALTZ-18 modulated
DPPG 1.000 sec
Line broadening 1.0 Hz
FT size 65536
Total time 870 hr, 22 min, 41 sec

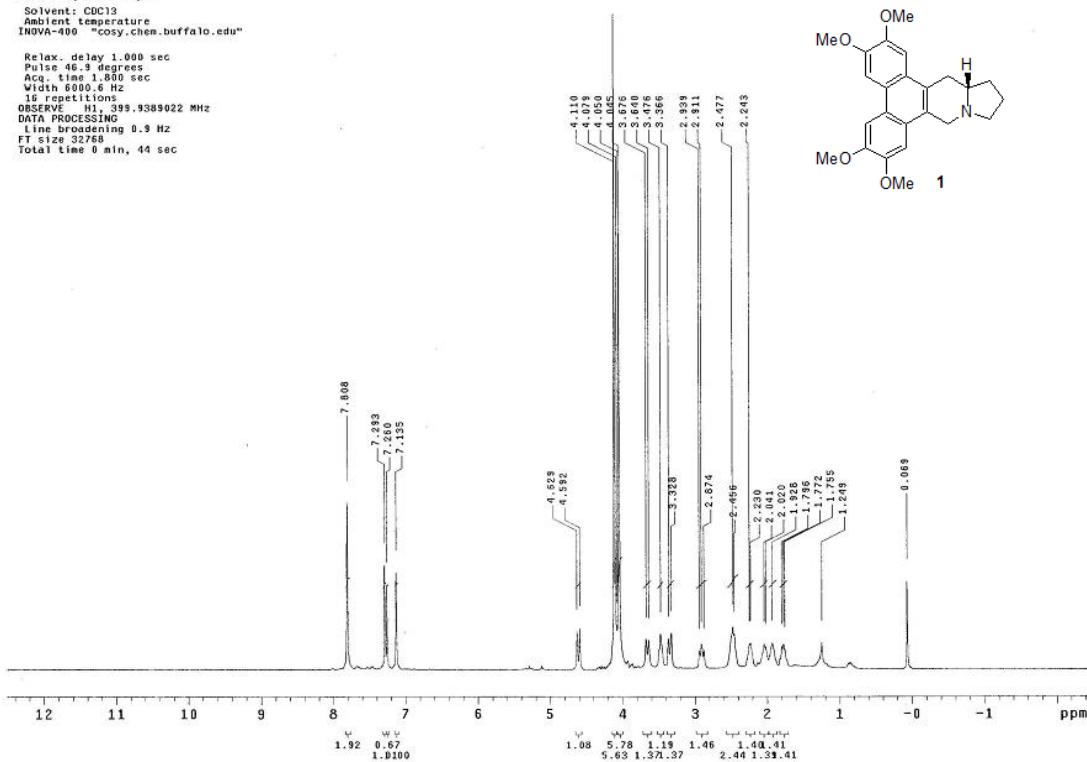
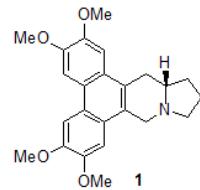
```



amino compound
 Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.800 sec
 Width 6000.6 Hz
 16 repetitions
 OBSERVE: CDCl₃, 75.3899025 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec



STANDARD 1H OBSERVE



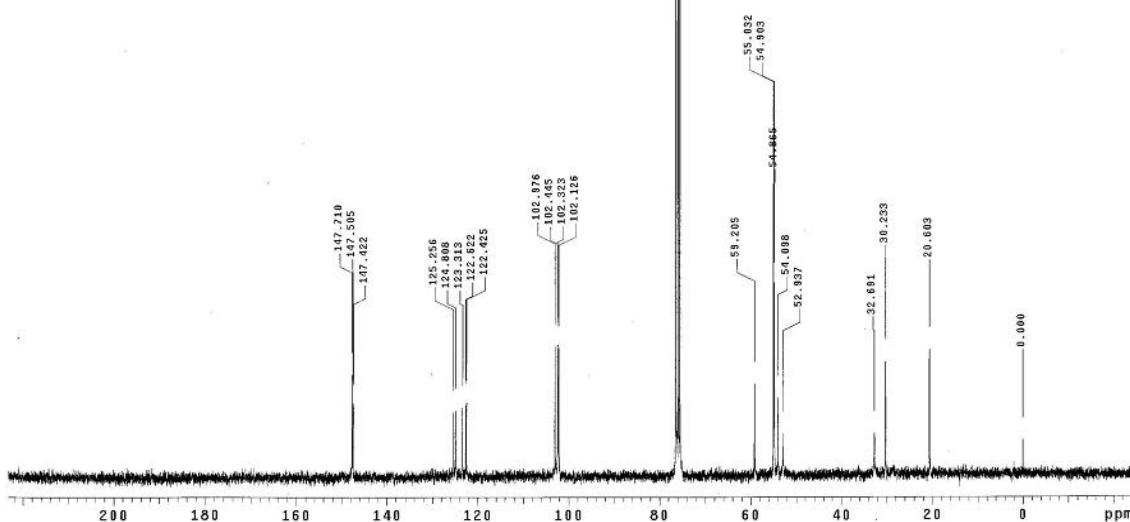
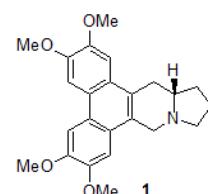
13C OBSERVE

```

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
GENIN-300 "roses.chem.buffalo.edu"

Relax. delay 5.000 sec
Pulse 90.0 degrees
Acc. time 1.67 sec
W1 1076.8 Hz
1588 repetitions
OBSERVE C13, 75.4557351 MHz
DECOUPLE H1, 0.030.0544311 MHz
power 100.0 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
DATA binning 1.0 Hz
FT size 65536
TOT1,16.0_min,0 sec

```



Enantiomeric Excess Determination (HPLC traces) for Tylophorine 1

