Asymmetric Synthesis of Horsfiline: Application of Palladium Asymmetric Allylic Alkylation

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Supplemental Information

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Experimental

General

All reactions were performed under an atmosphere of dry nitrogen in flame-dried glassware unless otherwise indicated. THF, DCM, DME, Et_3N, Et_2O, benzene, toluene, MeCN, pyridine, and DMF were purified by an alumina column purification system. Dichloroethane, HMDS, DIPEA, and diisopropylamine were distilled under a nitrogen atmosphere over CaH_2. Acetone was distilled over Dri-rite. Methanol was distilled from magnesium methoxide. Chiral ligands were prepared by the method of Trost.[1] All reagents were obtained from Aldrich, Fluka, or Acros unless otherwise noted.

Flash chromatography was performed with EM Science silica gel (0.040-0.063μm grade) according to the procedure of Still.[2] Solvents for chromatography are listed as volume/volume ratios. Analytical thin layer chromatography was performed using 0.2mm coated commercial silica gel plates (E.Merck, DC-Plastikfolien, Kieselgel 60 F_{254}). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected.

Infrared spectra were recorded on a Perkin Elmer Paragon 500 FT-IR spectrophotometer using 0.1mm path length sodium chloride cavity cells or sodium chloride plates. Absorbance frequencies are recorded in reciprocal centimeters (cm^{-1}). Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona. High resolution mass spectra (HRMS) were obtained from the Mass Spectrometry Resource, School of Pharmacy, University of California-San Francisco on a Kratos MS9 spectrometer. HRMS data are reported as a m/e (relative intensity), with accurate mass reported for the molecular ion (M^+) or suitable fragments.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were acquired at 300, 400, or 500 MHz on a Varian Gemini spectrometer. Chemical shifts are reported in delta (δ), units in parts per million (ppm) relative to the singlet (7.26 ppm) for the chloroform-*d* (residual $CHCl_3$) and the singlet (0.00 ppm) for TMS. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, quintet; m, multiplet; and br, broad. Coupling constants are recorded in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were acquired at 75, 100, or 125 MHz on a Varian Gemini, Mercury, and Unity spectrometer respectively. Chemical shifts are reported in ppm relative to the central line of the triplet at 77.0 ppm for chloroform-*d*. Routine ^{13}C NMR spectra were fully decoupled by broad-band decoupling.

Chiral HPLC analyses were performed on a Thermo Separation Products Spectraseries P100 amd UV100 or P200 and UV200 using Chrialcel® columns (AD, AS, OB-H, OC, OD, or OJ) with heptane/2-propanol mixtures with ratio of the eluent, flow rate, and column indicated. Retention times (τ_R) are reported in minutes (min). Chiral GC was performed on a Hewlett-Packard 6890 capillary gas chromatograph using a 30mx 0.252mm J&W CyclosilB column. Optical rotations were determined using a JASCO DIP-1000 digital polarimeter in 50-mm cells and the sodium D line (589 nm) at the temperature, solvent, and concentration indicated.

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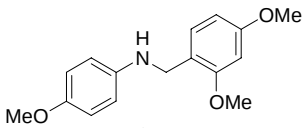
[1] (a) Trost, B.M.; Van Vranken, D.L. *Angew. Chem. Int. Ed.* **1992**, *31*, 228. (b). Trost, B.M.; Van Vranken, D.L. *J. Am. Chem. Soc.* **1992**, *114*, 9327.

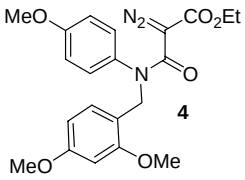
[2] Still, W.C.; Kahn, M.; Mitra, J.A. *J. Org. Chem.* **1978**, *48*, 2923.



3

(2,4-Dimethoxy-benzyl)-(4-methoxy-phenyl)-amine (3) A solution of 4-anisidine (10.33g, 82.5mmol) and 2,4-dimethoxybenzaldehyde (14.0 g, 84.2 mmol) in toluene (100 mL) in a 250 mL roundbottom flask with attached Dean Stark trap was stirred at 165^0 C for 18 h. The reaction mixture was then allowed to cool to rt. The solvent was then removed under reduced pressure resulting in a crude yellow solid. A crude ^{1}H NMR showed the desired imine. The crude solid was then dissolved in dichloromethane (50 mL) and EtOH (50 mL) and then cooled to 0^o C. Sodium borohydride (4.87 g, 128.7 mmol) was then slowly added to the cooled solution. The reaction mixture was then allowed to stir for 12 h before the reaction was poured onto ice and conc. HCl was added until the reaction was acidic. Then 5M NaOH was added until the reaction was basic. The reaction mixture was then transferred to a seperatory funnel and the layers separated. The aqueous portion was extracted dichloromethane (2 x 25mL). The combined organic fractions were then dried over $MgSO_4$, filtered and concentrate *in vacuo*. The crude white solid, **3** (22.5g, 100%) was carried on without further purification.

IR (neat): 3397, 2936, 2833, 1613, 1588, 1512, 1464, 1234, 1207 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (d, J=8.3 Hz, 1H), 6.74-6.78 (m, 2H), 6.60-6.64 (m, 2H), 6.46 (d, J=2.3 Hz, 1H), 6.41(dd, J=2.3, 5.9 Hz, 1H), 4.19 (s, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 158.4, 152.1, 142.6, 130.3, 129.8, 119.9, 114.8, 114.5, 103.8, 98.5, 55.7, 55.33, 55.31.

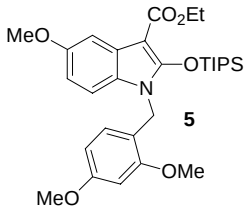


4

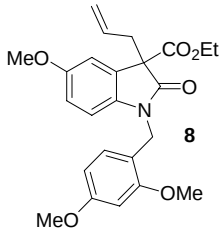
2-Diazo-N-(2,4-diethoxy-benzyl)-N-(4-methoxy-phenyl)-malonamic acid ethyl ester(4) To a solution of **3** (11.74g g, 42.95 mmol) in dichloromethane (120 mL) was added triethylamine (28 mL, 200.8 mmol) and chlorocarbonyl-diazo-acetic acid ethyl ester (7.59 g, 42.98 mmol) at 0^0C which resulted in a heterogeneous solution orange solution. The solution was warmed to rt and stirred under N_2 for 6 h. The reaction was then quenched with 1 M HCl (50 mL) and extracted with dichloromethane (3 x 25 mL). Combined dichloromethane portions were then dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a crude red oil. The crude material was then purified via silica gel chromatography (50% Et_2O / pet.ether) to yield **4** (15.98 g, 90%) as a yellow oil. R_F (50% EtOAc / pet.ether) = 0.63.

IR (neat): 3055, 2986, 2120, 1723, 1615, 1510, 1266, 739 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, J=8.3 Hz, 1H), 7.00 (d, J=8.7 Hz, 2H), 6.70 (d, J=8.7 Hz, 2H), 6.41 (dd, J=2.1, 8.3 Hz, 1H), 6.35 (d, J=2.1 Hz, 1H), 4.90 (s, 2H), 4.08 (q, J=7.1 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.60 (s, 3H), 1.17 (t, J=7.1 Hz, 3H). ^{13}C NMR (125 MHz,

$CDCl_3$): δ 162.2, 160.6, 160.1, 158.2, 158.1, 135.1, 130.6, 127.9, 117.4, 113.9, 103.9, 98.1, 61.1, 65.7, 55.2, 55.1, 54.9, 48.5, 14.1.
Anal. Calcd. for $C_{21}H_{23}N_3O_6$: C, 61.01; N, 10.16; H,5.61; Found: C, 61.16; N, 9.93; H, 5.55.

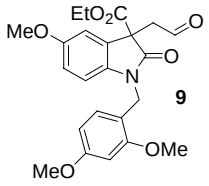


1-(2,4-Dimethoxy-benzyl)-5-methoxy-2-triisopropylsilanyloxy-1H-indole-3-carboxylic acid ethyl ester A solution of $Rh_2(acac)_4$ (462.7mg mg, 1.05 mmol) and trifluoroacetamide (2.37 g, 20.9 mmol) in dichloroethane (60 mL) was heated for 12 h at 86^0 C to perform the catalyst. The solution was then cooled to rt and a solution of **4** (13.7g, 33.1 mmol) in dichloromethane (100 mL) was added and the solution was stirred for 5 h. The green solution was concentrated down and a crude NMR was taken. The green oil than was dissolved in dichloromethane (60 mL). The solution was then cooled to 0^0 C and triethylamine (14 mL, 100.4 mmol) followed by TIPSOTf (12 mL, 20.9 mmol). The solution was allowed to stir at 0^0 C for 15 min before quenching with H_2O (150 mL) and extracted with dichloromethane (3 x 35 mL). The combined dichloromethane portions were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude oil was then purified *via* silica gel chromatography (5-10% Et_2O / pet. ether) to yield **5** (15.47 g, 86%) as a white solid. R_F (10% EtOAc / pet.ether) = 0.35. Melting point: 85-87^0 C.
IR (neat): 2945, 2867, 1694, 1619, 1591, 1538, 1456, 1376 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J=2.56 Hz, 1H), 6.93 (d, J=8.7 Hz, 1H), 6.69 (dd, J=2.56, 8.7Hz, 1H), 6.45-6.48 (m, 2H), 6.25 (dd, J=2.3, 8.5 Hz, 1H), 5.20 (s, 3H), 4.36 (q, J=7.1Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.72 (s, 3H), 1.42-1.49 (m, 6H), 1.06 (d, J=7.7 Hz, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.8, 160.0, 157.2, 155.5, 153.4, 127.3, 125.9, 125.8, 116.9, 109.9, 109.7, 104.1, 103.8, 98.2, 89.3, 58.9, 55.6, 55.2, 39.6, 17.8, 17.6, 14.7, 14.2.



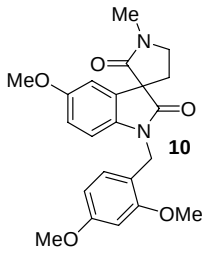
3-Allyl-1-(2,4-dimethoxy-benzyl)-5-methoxy-2-oxo-2,3-dihydro-1-H-indole-3-carboxylixacid ethyl ester (8)
Toluene was degassed via freeze-pump-thaw. **5** (5.03 g, 9.29 mmol), $[Pd(C_3H_5)Cl]_2$ (8.65 mg, 0.0235 mmol, 0.25% eq), standard Trost ligand, **2** (64.64 mg, 0.0935 mmol, 1.0% eq), and TBAT (759.9 mg, 1.40 mmol) was weighed into a 250 mL round bottom

flask and toluene (100 mL) was added. Freshly distilled allyl acetate (2.5 mL, 23.17 mmol, 2.5 eq) was then added. The solution was allowed to stir overnight (~12 h) before purification *via* silica gel chromatography (10%-30%Et_2O/pet.ether) to yield **8** (3.95g, 100%) as a clear oil. R_F (50% EtOAc / pet.ether) = 0.88. % ee = 84%, AD column (90:10 heptane / iPrOH), Retention times:13.24 min, 18.3 min.
IR (neat): 3077, 2938, 2836, 2837, 1740, 1713, 1614, 1509, 1496, 1458, 1437 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J=11.5 Hz, 1H), 6.86 (d, J=2.3 Hz, 1H), 6.65-6.74 (m, 2H), 6.46 (d, J=2.3 Hz, 1H), 6.33-6.37 (m, 1H), 5.36-5.48 (m, 1H), 5.10 (d, J=17.1 Hz, 1H), 4.79-4.96 (m, 3H), 4.05-4.24 (m, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 2.96-3.07 (m, 2H), 1.18 (t, J=7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ173.6, 169.1, 160.2, 157.9, 155.8, 136.9, 131.2, 128.8, 128.7, 119.7, 115.9, 113.3, 110.4, 109.8, 104.1, 98.2, 61.9, 59.6, 55.7, 55.35, 55.28, 38.0, 37.8, 13.9.
Anal. Calcd. for $C_{24}H_{27}NO_6$: C, 67.75; N, 3.29; H, 6.40; Found: C, 67.60; N, 3.25; H, 6.40. $[\alpha]_D$ ($CHCl_3$, c= 4.0)= -44.14^0 (98%ee)



1-(2,4-Dimethoxy-benzyl)-5-methoxy-2-oxo-3-(2-oxo-ethyl)-2,3-dihydro-1*H*-indole-3-carboxylic acid ethyl ester (9)
To a stirred solution of 3-allyl-1-(2,4-dimethoxy-benzyl)-5-methoxy-2-oxo-2,3-dihydro-1-H-indole-3-carboxylixacid ethyl ester, **8** (1.38 g, 3.24 mmol) in dichloromethane (40 mL) at rt was added *N*-methylmorpholine-*N*-oxide (0.761 g, 6.49 mmol). OsO_4 (0.82 ml, 0.129 mmol of a 4% solution in water) was added and a glass stopper was placed on the roundbottom flask. The solution was stirred for 6 h at rt. Reaction mixture was then quenched with 10% sodium thiosulfate (25 mL) and extracted with dichloromethane (3 x 10 ml). The combined dichloromethane portions were dried over magnesium sulfate, filtered and concentrated *in vacuo* to leave approximately 25 mL of dichloromethane remaining in the flask. $Pb(OAc)_4$ (1.64 g, 3.69 mmol) was carefully weighed in hood and then dissolved in dichloromethane (5 ml) and then added to the reaction mixture. The reaction was stirred for 15 min and then filtered through a silica gel plug with ethyl acetate. The ethyl acetate was then removed *in vacuo* to obtain **9** (1.35 g, 97%) as a white foam.
IR (neat): 2937, 2837, 1719, 1612, 1508, 1497 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, J=0.8 Hz, 1H), 7.14 (d, J=8.4 Hz, 1H), 6.85 (d, J=2.4 Hz, 1H), 6.71-6.76 (m, 2H), 6.47 (d, 2.4Hz, 1H), 6.38 (dd, J=2.4, 8.4 Hz, 1H), 4.96 (d, J=16 Hz, 1H), 4.84 (d, J=16 Hz, 1H), 4.09-4.23 (m, 2H), 3.87 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 3.27-3.40 (m, 2H), 1.18 (t, J=6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 173.2, 168.4, 160.3, 157.9, 155.9, 137.0, 128.8, 128.3, 115.7, 113.6, 110.4, 110.2, 104.2, 98.2, 62.4, 56.1, 55.6, 55.32, 55.25, 46.9, 38.3, 13.8.

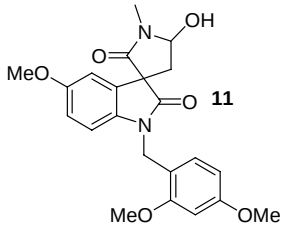
HRMS calculated for $C_{23}H_{25}NO_7$: 427.1631; found: 427.1631. $[\alpha]_D$ ($CHCl_3$, c=3.55] = -0.23^0 (98%ee)



1-(2,4-Dimethoxy-benzyl)-5-methoxy-1'-methyl-1*H*-spiro[indole-3,3'-pyrrolidine]-2,2'-dione (10)

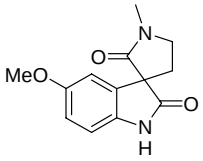
A solution of 1-(2,4-Dimethoxy-benzyl)-5-methoxy-2-oxo-3-(2-oxo-ethyl)-2,3-dihydro-1*H*-indole-3-carboxylic acid ethyl ester, **10** (0.935 g, 2.18 mmol) in THF (20 ml) was cooled to 0^o C. Then magnesium sulfate (4.05 g, 33.6 mmol) followed by methylamine (2.2 ml, 4.4 mmol of a 2.0 M solution in THF) was added. The reaction mixture was stirred for 1.5 h at rt. The solution was then filtered, concentrated *in vacuo* and dissolved in EtOH (20 ml). Then sodium borohydride (86.9 mg, 2.29 mmol) was added at 0^o C and then stirred at rt for 30min. The reaction mixture was then quenched with 1 M NaOH (20 ml) and extracted with DCM (3 x 10ml). The combined DCM portions were then dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude material was then purified via silica gel chromatography (25-100% EtOAc/pet. ether) to afford **10** (0.568 g, 66%) as a white foam.

IR (neat): 3399, 2939, 2836, 1690, 1612, 1590 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.12 (d, J=8.4 Hz, 1H), 6.62-6.76 (m, 3H), 6.44 (d, J=2.2 Hz, 1H), 6.39-6.42 (m, 1H), 4.91 (d, J=16 Hz, 1H), 4.77 (d, J=16 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H), 3.78-3.84 (m, 1H), 3.73 (s, 3H), 3.56-3.62 (m, 1H), 2.99 (s, 3H), 2.7-2.76 (m, 1H), 2.38-2.44 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.6, 170.6, 160.2, 157.9, 156.1, 137.3, 131.0, 128.8, 115.7, 113.0, 110.2, 109.9, 104.3, 98.3, 58.2, 55.7, 55.33, 55.27, 47.2, 38.3, 30.5, 29.4. HRMS calculated for $C_{22}H_{24}N_2O_5$: 396.1685. Found: 396.1688. $[\alpha]_D$ ($CHCl_3$, c=3.40] = 12.75^0 (98%ee)



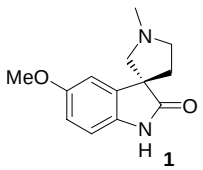
1-(2,4-Dimethoxy-benzyl)-5'-hydroxy-5-methoxy-1'-methyl-1*H*-spiro[indole-3,3'-pyrrolidine]-2,2'-dione(11)

Obtained as a side product (0.197g, 22% yield) in the formation of 1-(2,4-Dimethoxy-benzyl)-5-methoxy-1'-methyl-1*H*-spiro[indole-3,3'-pyrrolidine]-2,2'-dione **(**listed above as **10**).
IR (neat): 3354, 2940, 1682, 1614, 1590, 1509, 1496 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J=8 Hz, 1H), 6.74 (s, 3H), 6.38-6.44 (m, 2H), 5.33 (d, J=13 Hz, 1H), 5.16 (dd, J= 8.13 Hz, 1H), 4.89 (d, J=16 Hz, 1H), 4.78 (d, J=16 Hz, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.02 (s, 3H), 2.68 (dd, J=8,13 Hz, 1H), 2.38 (d, J=13 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 169.8, 160.4, 157.9, 156.5, 137.4, 128.9, 128.8, 114.9, 113.7, 110.5, 110.2, 104.3, 98.3, 82.8, 58.4, 55.6, 55.3, 55.2, 38.9, 38.4, 27.9.



12

5-Methoxy-1'-methyl-1*H*-spiro[indole-3,3'-pyrrolidine]-2,2'-dione(12)
To a solution of 1-(2,4-Dimethoxy-benzyl)-5-methoxy-1'-methyl-1*H*-spiro[indole-3,3'-pyrrolidine]-2,2'-dione, **11** (0.179 g, 0.452 mmol) in dichloromethane (30 ml) and water (3 ml) was added DDQ (0.515 g, 2.268 mmol) and trifluoroacetic acid (0.1mL, 1.34 mmol) at rt. The reaction was then refluxed for 2 d. The reaction mixture was then poured into saturated sodium bicarbonate (50 ml) and extracted with dichloromethane (3 x 15ml). The combined dichloromethane portions were dried over sodium sulfate, filtered and concentrated *in vacuo*. Crude material was then purified *via* silica gel chromatography (50-100% EtOAc / pet. ether) to yield **12** (67.1 mg, 60%) as a white foam.
IR (neat): 3240, 2943, 1721, 1682, 1603, 1491 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 6.70-6.80 (m, 3H), 3.7 (s, 3H), 3.72-3.80 (m, 1H), 3.53-3.60 (m, 1H), 2.90 (s, 3H), 2.66-2.74 (m, 1H), 2.30-2.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 170.7, 155.9, 135.2, 131.5, 113.4, 110.7, 110.2, 58.6, 55.8, 47.2, 30.5, 29.4.
HRMS calculated for $C_{13}H_{14}N_2O_3$: 246.1004. Found:246.1000. $[\alpha]_D$ ($CHCl_3$, c=2.30) = 6.05^0 (98%ee)



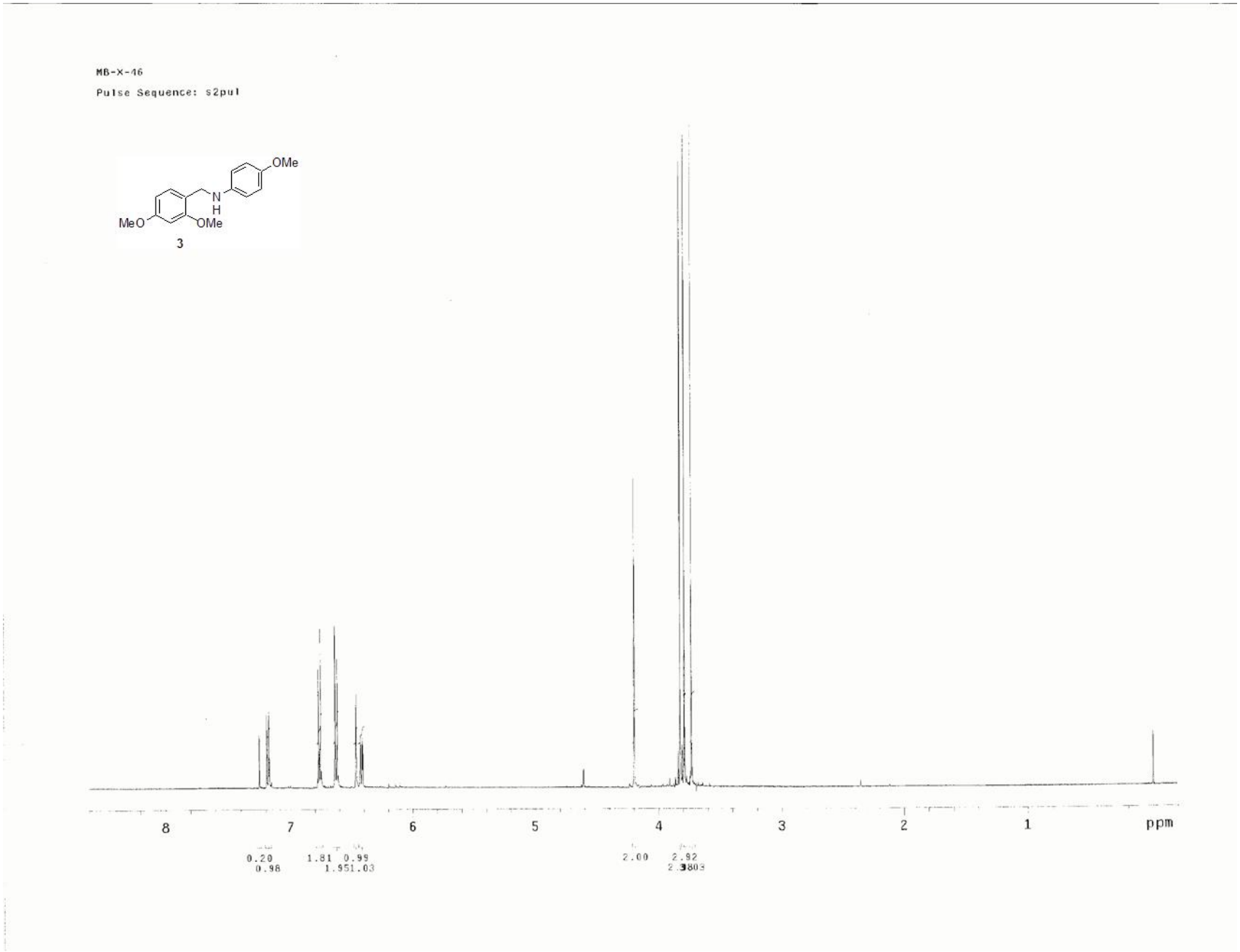
1

(+)-Horsfiline(1)
A solution of lithium aluminum hydride was prepared by dissolving LAH (0.25 g, 6.58 mmol) in of freshly distilled THF (20 mL) and stirring under nitrogen atmosphere for 30 min. The solution was then filtered using a Schlenk filter and the resulting clear solution

was titrated three times using a known procedure[3] and an average molarity used (0.206M in aluminum). Then trityllithium was prepared by dissolving triphenylmethane (0.3511 g, 1.44 mmol) in DME (3 mL). The resulting clear solution was cooled to 0^{o} C and then *n*BuLi (0.56 mL, 1.40 mmol, 2.5 M solution in hexanes) was added resulting in a deep red solution. Then 5-methoxy-1'-methyl-1*H*-spiro[indole-3,3-pyrrolidine]-2,2'-dione (**12**) (20.5 mg, 0.0832 mmol) in DME (1 mL) and cooled to 0^{o} C. Then trityllithium was added until a slight pink color persisted. Then the LAH solution (0.2 mL, 0.0412 mmol) was added at 0^{o}C and then warmed to rt and stirred for 1 h. The reaction was then quenched with H_2O (0.05 mL), 4M NaOH (0.05 mL) and H_2O (0.10 mL) and then filtered over Na_2SO_4 and concentrated *in vacuo*. The crude material was then purified via silica gel chromatography (100% EtOAc to 5% 9N NH_3 in MeOH / EtOAc) to yield horsfiline (9.3 mg, 48%) as a clear oil.

IR(neat): 3223, 2940, 2835, 1707, 1603, 1484 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ7.47 (bs, 1H), 7.04 (d, J=2.0 Hz, 1H), 6.76 (d, J=8.0 Hz, 1H), 6.72 (dd, J=2.0, 8.0Hz,1H), 3.80 (s, 3H), 2.98-3.03 (m, 1H), 2.86(s, 2H), 2.76 (dd, J=8.0, 9.0Hz, 1H), 2.45 (s, 3H), 2.40 (ddd, J=4.5, 7.5, 12Hz, 1H), 2.08 (dt, 7.5Hz, 13Hz, 1H) ^{13}C NMR (125 MHz, $CDCl_3$): δ 182.6, 156.1, 137.7, 133.3, 112.4, 110.3, 109.7, 66.4, 56.7, 55.9, 54.1, 41.8, 38.1.[$\alpha]^{23}_{D}$= 7.14^{0} (MeOH, c= 0.78) (Reported value for natural (-)-horsfiline: $[\alpha]^{23}_{D}$= -7.2 (c=1, MeOH ref. 1)

[3] Love, B.E.; Jones, E.C. *J. Org. Chem.* **1999**, *64*, 3755-3756.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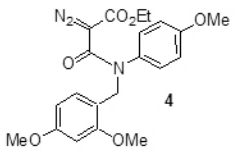
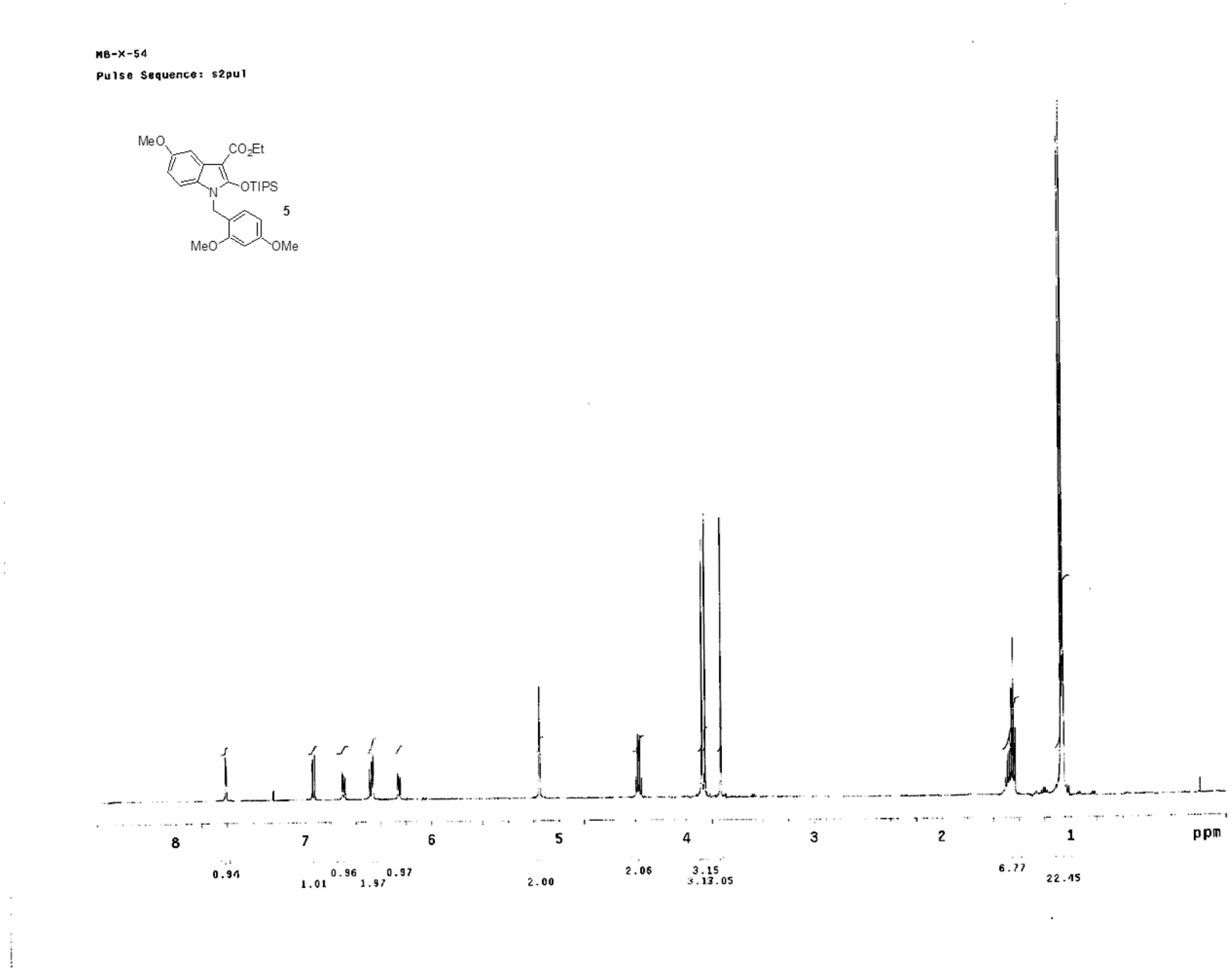
7
6
5
4
3
2
1
ppm
0.20
0.98
1.81
0.99
1.95
1.03
2.00
2.92

MB-X-40

Pulse Sequence: s2pul

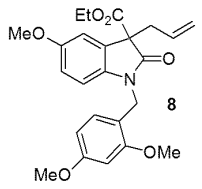


4


MB-X-54
Pulse Sequence: s2pul
MeO
CO2Et
OTIPS
N
5
MeO
OMe
8
7
6
5
4
3
2
1
ppm
0.94
1.01
0.96
1.97
0.97
2.00
2.06
3.15
3.13.05
6.77
22.45

MB-X-67

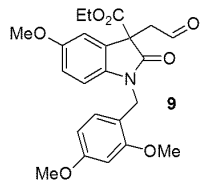
Pulse Sequence: s2pul



8

MB-XI-02

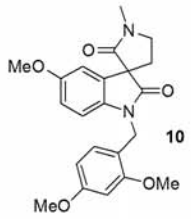
Pulse Sequence: s2pul



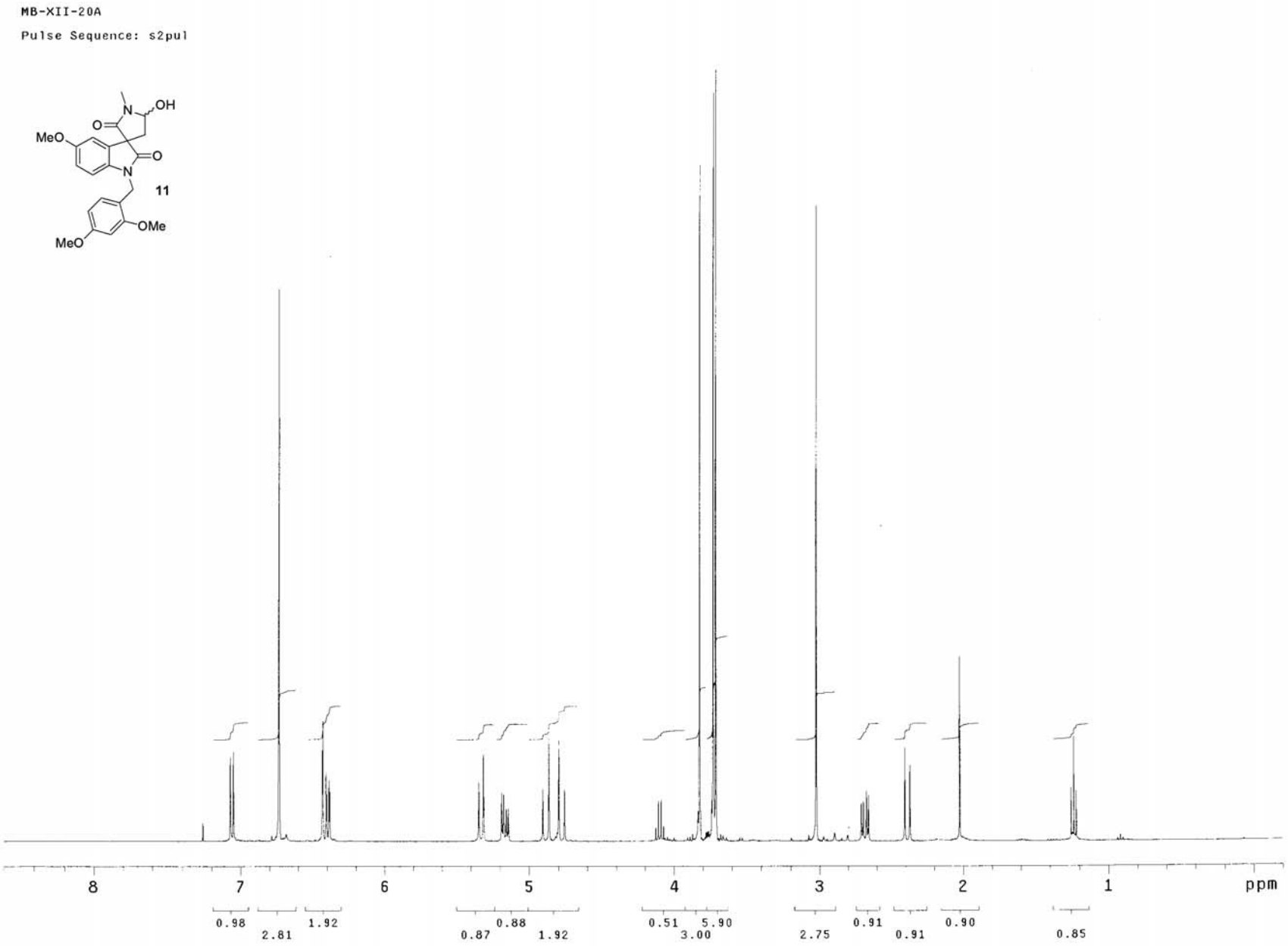
9

MB-XIII-01

Pulse Sequence: s2pul

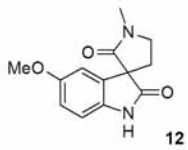


10

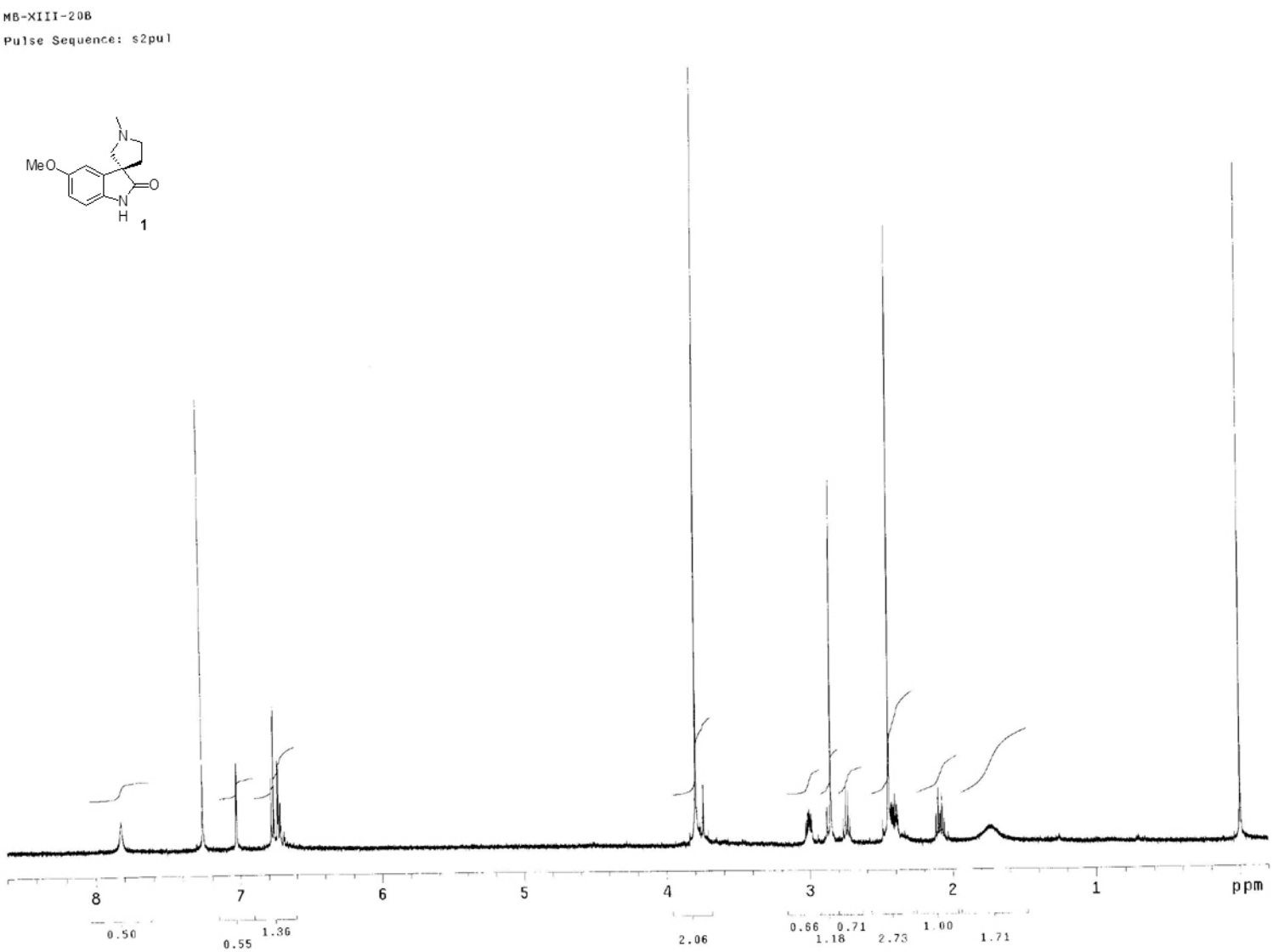

MB-XII-20A
Pulse Sequence: s2pul
MeO
OH
O
N
O
N
11
OMe
MeO
8
7
6
5
4
3
2
1
ppm
0.98
2.81
1.92
0.87
0.88
1.92
0.51
5.90
3.00
2.75
0.91
0.91
0.90
0.85

MB-XII-12B

Pulse Sequence: s2pul



12


MB-XIII-20B
Pulse Sequence: s2pul
MeO
N
O
N
H
1
8
7
6
5
4
3
2
1
ppm
0.50
0.55
1.36
2.06
0.66
1.18
0.71
2.73
1.00
1.71