Stereoselective Construction of the Tetracyclic Core of Cryptotrione

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Supporting Information

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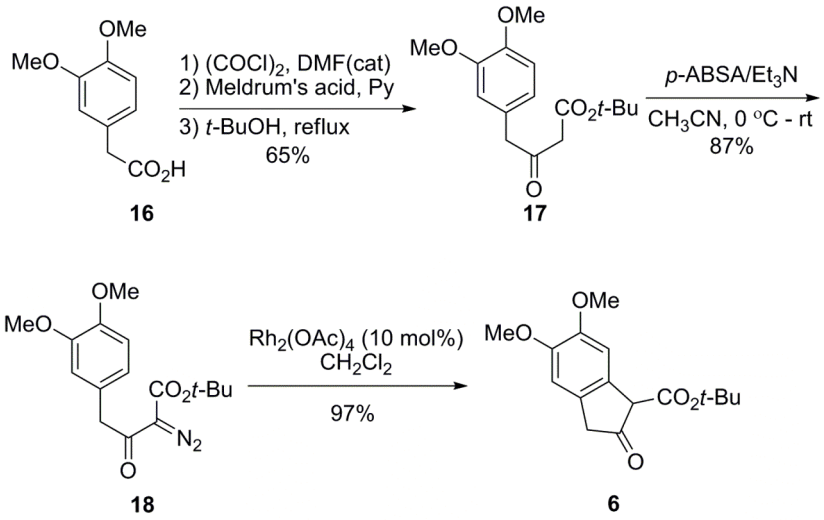
General Methods. All commercially available reagents were used without further purification. All solvents were freshly distilled under nitrogen from appropriate drying agents before use. Tetrahydrofuran was distilled from sodium-benzophenone. Dichloromethane and acetonitrile were distilled from CaH_2. *N*,*N*-Dimethylformamide and dimethylsulfoxide were dried over 4 Å molecular sieves (activated at 180 °C in vacuo over 8 h). Column chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on a 400 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected.

Experimental Procedures and Spectroscopic Data



***Tert*-buyl 4-(3,4-dimethoxyphenyl)-3-oxobutanoate (17).** To a solution of homoveratric acid **16** (3.92 g, 20.0 mmol) in CH_2Cl_2 (40 mL) were added $(COCl)_2$ (10.15 g, 6.8 mL, 80.0 mmol) and DMF (0.05 mL) at 0 °C under N_2. Upon stirring at 0 °C for 2 h and at rt for 4 h, the reaction mixture was concentrated. The residue was dissolved in CH_2Cl_2 (5 mL) and was added to a solution of Meldrum's acid (3.17 g, 22.0 mmol) and pyridine (3.16 g, 3.2 mL, 40.0 mmol) in CH_2Cl_2 (35 mL) at 0 °C. Upon stirring at 0 °C for 2 h and at rt overnight, the reaction mixture was washed with

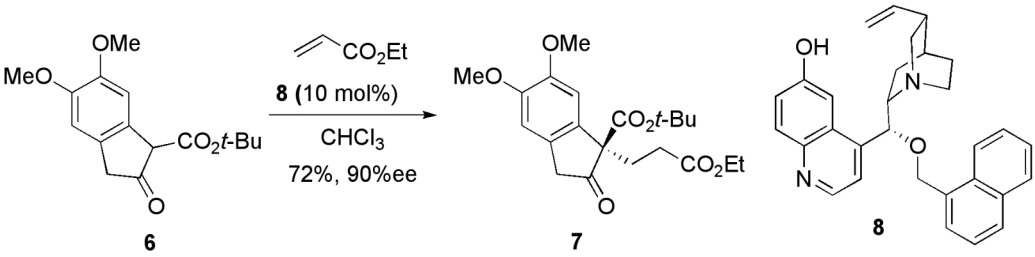
aqueous 3N HCl (20 mL), extracted with CH_2Cl_2 (20 mL x 3). The combined organic phases were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. The crude mixture was dissolved in *t*-BuOH (20 mL), refluxed overnight, cooled, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 5/1) to give compound **17** as yellow solid (3.82 g; 65%). mp. 38-40 ^oC; IR (film): 1734, 1716, 1517, 1261 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.82 (d, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 3.85 (s, 6H), 3.74 (s, 2H), 3.35 (s, 2H), 1.45 (s, 9H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 201.5, 166.6, 149.3, 148.5, 126.0, 122.0, 112.7, 111.6, 82.2, 56.1, 56.0, 49.7, 49.5, 28.1; HRMS Calcd for $C_{16}H_{23}O_5$ (M+H): 295.1540; Found: 295.1542.

***Tert*-butyl 2-diazo-4-(3,4-dimethoxyphenyl)-3-oxobutanoate (18).** To a solution of **17** (2.94 g, 10.0 mmol) in MeCN (50 mL) were added 4-acetamidobenzenesulfonyl azide (2.64 g, 11.0 mmol) and Et_3N (4.05 g, 5.6 mL, 40.0 mmol) at 0 ^oC under N_2. Upon stirring at rt for 3 h, the reaction mixture was quenched with saturated $NaHCO_3$ (25 mL), extracted with EtOAc (25 mL x 3), dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 5/1) to give compound **18** as white solid (2.78 g, 87%). mp. 92-94 ^oC; IR (film): 2134, 1709, 1652, 1262 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.88-6.82 (m, 2H), 6.80 (d, *J* =8.4 Hz, 1H), 4.10 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 1.53 (s, 9H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 191.1, 160.6, 149.0, 148.2, 126.9, 122.0, 113.0, 111.3, 83.4, 56.05, 55.96, 45.3, 28.5; Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74; Found: C, 59.85; H, 6.26; N, 8.84.

***Tert*-butyl 5,6-dimethoxy-2-oxo-2,3-dihydro-1H-indene-1-carboxylate (6).** A solution of **18** (23.12 g, 72.0 mmol) in CH_2Cl_2 (200 mL) was slowly added to a solution of $Rh_2(Ac)_4$ (0.32 g, 0.72 mmol) in CH_2Cl_2 (280 mL) via syringe pump over 1.5 h. Upon stirring at rt for 1 h, the reaction mixture was passed through a pad of silic gel, eluted with CH_2Cl_2 (100 mL), and concentrated to give compound **6** as light

yellow solid (20.37 g, 97%). mp. 74-76 °C; IR (film): 1649, 1596, 1493, 1156 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 10.97 (br, 1H), 7.23 (s, 1H), 6.90 (s, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.47 (s, 2H), 1.64 (s, 9H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 179.6, 168.4, 148.7, 146.2, 133.1, 124.9, 108.8, 106.1, 104.9, 82.0, 56.6, 56.0, 37.6, 28.6; HRMS Calcd for $C_{16}H_{21}O_5$ (M+H): 293.1384. Found: 293.1389.

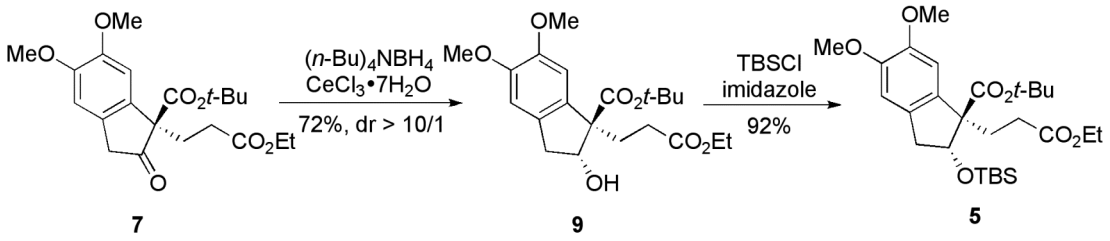
U. K. Tambar, D. C. Ebner and B. M. Stoltz, *J. Am. Chem. Soc.*, 2006, **128**, 11752.



(*R*)-*tert*-butyl 1-(3-ethoxy-3-oxopropyl)-5,6-dimethoxy-2-oxo-2,3-dihydro-1H-indene-1-carboxylate (7). To a solution of **6** (5.85 g, 20.0 mmol) and ethyl acrylate (6.01 g, 6.5 mL, 60.0 mmol) in $CHCl_3$ (40 mL) was added catalyst **8** (0.90 g, 2.0 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 60 h, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 5/1) to give compound **7** as colorless oil (5.62 g, 72%, 90% ee) (the ee was determined by chiral HPLC, chiralcel OD-H column, *i*-PrOH/hexane = 7/93, 0.5 mL/min, λ = 210 nm). $[\alpha]^{20}_D$ = -24.1 (*c* 1.16, $CHCl_3$); IR (film): 1757, 1731, 1506, 1252 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.73 (s, 1H), 4.07-3.92 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.66 (d, *J* = 22.4 Hz, 1H), 3.38 (d, *J* = 22.4 Hz, 1H), 2.52-2.41 (m, 1H), 2.39-2.28 (m, 1H), 2.06 (t, *J* = 8.0 Hz, 2H), 1.30 (s, 9H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 212.4, 172.8, 169.4, 149.9, 149.5, 132.1, 129.5, 107.9, 106.6, 82.5, 65.2, 60.6, 56.3, 56.2, 43.5, 29.6, 28.5, 27.9, 14.3; HRMS Calcd for $C_{21}H_{29}O_7$ (M+H): 393.1908. Found: 393.1912.

(*a*) C. L. Rigby and D. J. Dixon, *Chem. Commun.*, 2008, 3798.

(*b*) F. Wu, H. Li, R. Hong and L. Deng, *Angew. Chem., Int. Ed.*, 2006, **45**, 947.



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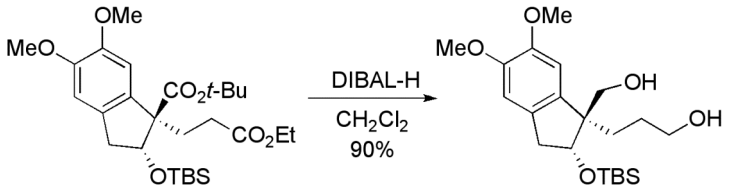
(*1R*,*2R*)-*tert*-butyl 1-(3-ethoxy-3-oxopropyl)-2-hydroxy-5,6-dimethoxy-2,3-dihydro-1H-ind-ene-1-carboxylate (9). To a mixture of **7** (4.86 g, 12.4 mmol) and $CeCl_3 \cdot 7H_2O$ (6.93 g, 18.6 mmol) in EtOH (62 mL) was added $(n\text{-}Bu)_4NBH_4$ (4.14 g, 16.1 mmol) at -78 °C. Upon stirring at -78 °C for 2 h and warming to rt, the reaction mixture was quenched with saturated NH_4Cl (20 mL), extracted with CH_2Cl_2 (50 mL x 3), washed with brine (20 mL), dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 5/1 to 2/1) to give **9** as colorless oil (3.54 g, 72%). $[\alpha]^{20}_D = +30.3$ (*c* 0.99, $CHCl_3$); IR (film): 3515, 1719, 1504, 1251 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.99 (s, 1H), 6.73 (s, 1H), 4.80 (dt, *J* = 4.8, 6.8 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2 H), 3.88 (s, 3H), 3.85 (s, 3H), 3.19 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.81 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.48 (d, *J* = 4.8 Hz, 1H), 2.31-2.42 (m, 2H), 2.10-2.26 (m, 2H), 1.47 (s, 9H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 173.7, 173.6, 149.4, 148.4, 133.3, 131.7, 109.1, 108.0, 81.7, 76.8, 61.3, 60.6, 56.2, 56.1, 38.6, 30.3, 28.2, 27.6, 14.3; HRMS Calcd for $C_{21}H_{31}O_7$ (M+H): 395.2064; Found: 395.2056.

(*a*) M. Taniguchi, H. Fujii, K. Oshima and K. Utimoto, *Tetrahedron*, 1993, **49**, 11169

(*d*) J. Gong, G. Lin, W. Sun, C.-C. Li and Z. Yang, *J. Am. Chem. Soc.*, 2010, **132**, 16745

(*1R*,*2R*)-*tert*-butyl 2-(tert-butyldimethylsilyloxy)-1-(3-ethoxy-3-oxopropyl)-5,6-dimethoxy-2,3-dihydro-1H-indene-1-carboxylate (5). To a solution of **9** (8.01 g, 20.0 mmol) in DMF (40 mL) were added imidazole (5.45 g, 80.0 mmol) and TBSCl (4.52 g, 30.0 mmol) under N_2. Upon stirring at rt for 11 h, the reaction mixture was quenched with water (20 mL), extracted with Et_2O (50 mL x 3), washed with brine (20 mL), dried over Na_2SO_4, filtered, concentrated, and purified by flash

column chromatography (silica gel, eluent: PE/EtOAc = 8/1) to give compound **5** as colorless oil (9.37 g, 92%). $[\alpha]^{20}_{D}$ = -15.8 (*c* 1.20, $CHCl_3$); IR (film): 1724, 1504, 1252, 1155 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.76 (s, 1H), 6.66 (s, 1H), 5.05 (t, *J* = 7.6 Hz, 1H), 4.04 (q, *J* = 7.2, 2H), 3.84 (s, 6H), 3.11 (dd, *J* = 15.6, 7.6 Hz, 1H), 2.77 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.42-2.33 (m, 1H), 2.32-2.21 (m, 2H), 2.20-2.10 (m, 1H), 1.46 (s, 9H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 174.0, 173.6, 149.4, 148.5, 134.4, 131.8, 108.1, 107.8, 81.1, 77.4, 61.9, 60.3, 56.2, 56.1, 40.6, 30.6, 28.3, 27.9, 26.0, 18.2, 14.4, -4.4, -4.7; HRMS Calcd for $C_{27}H_{45}O_7Si$ (M+H): 509.2929; Found: 509.2933.



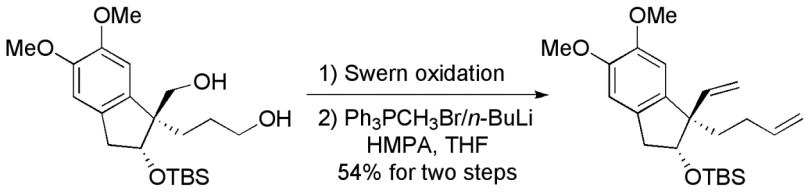
5 **10**

3-((*1S*,*2R*)-2-(*tert*-butyldimethylsilyloxy)-1-(hydroxymethyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-yl)propan-1-ol (10). To a solution of **5** (3.28 g, 6.5 mmol) in CH_2Cl_2 (65 mL) was added DIBAL-H (1 M in hexane) (32.5 mL, 32.5 mmol) at -78 ^{o}C under N_2. Upon stirring at -78 ^{o}C for 15 min and at 0 ^{o}C for 1 h, the reaction mixture was quenched with MeOH (2 mL) and saturated sodium potassium tartrate (40 mL), stirred at rt for 0.5 h, extracted with CH_2Cl_2 (50 mL x 3), washed with brine (50 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 1/5) to give compound **10** as white solid (2.32 g, 90%). mp. 76-78 ^{o}C; $[\alpha]^{20}_{D}$ = -26.4 (*c* 1.00, $CHCl_3$); IR (film): 3414, 1503, 1252, 1099 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.62 (s, 1H), 4.60 (t, *J* = 8.4 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.78 (d, *J* = 10.8 Hz, 1H), 3.62 (d, *J* = 11.2 Hz, 1H), 3.49 (t, *J* = 6.4 Hz, 2H), 3.01 (dd, *J* = 15.2, 8.0 Hz, 1H), 2.80 (dd, *J* = 15.2, 8.4 Hz, 1H), 1.69-1.42 (m, 5H), 1.38-1.12 (m, 1H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 149.0, 148.7, 135.3, 132.6, 108.5, 107.0, 76.4, 66.9, 63.8, 56.4, 56.1, 55.2, 40.1, 28.3, 27.8, 26.0, 18.1, -4.2, -4.8; HRMS

Calcd for $C_{21}H_{37}O_5Si$ (M+H): 397.2405; Found: 397.2410.

(*a*) D. L. J. Clive, M. Yu and M. Sannigrahi, *J. Org. Chem.*, 2004, **69**, 4116

(*b*) K.Okura, S. Matsuoka, R. Goto and M. Inoue, *Angew. Chem., Int. Ed.*, 2010, **49**, 329



10 **4**

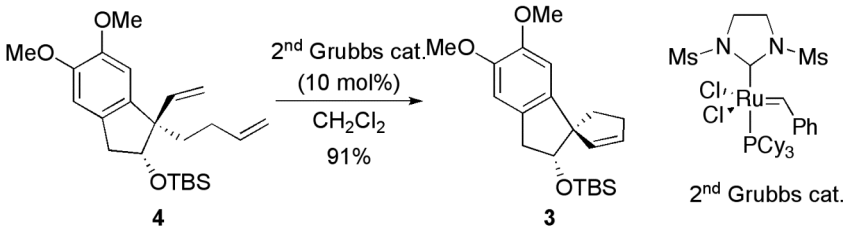
((*1R*,*2R*)-1-(but-3-enyl)-5,6-dimethoxy-1-vinyl-2,3-dihydro-1H-inden-2-yloxy) (*tert*-butyl)diethylsilane (4). To a solution of $(COCl)_2$ (3.34 g, 2.6 mL, 26.3 mmol) in CH_2Cl_2 (100 mL) was slowly added DMSO (4.11 g, 3.7 mL, 52.6 mmol) at -78 ^oC under N_2. After the reaction mixture was stirred at -78 ^oC for 15 min, a solution of **10** (2.61 g, 6.58 mmol) in CH_2Cl_2 (16 mL) was added. The resulting mixture was stirred at -78 ^oC for another 45 min. Upon addition of Et_3N (5.86 g, 8.1 mL, 57.9 mmol), the reaction mixture was warmed to rt over 2 h, quenched with water (50 mL), extracted with CH_2Cl_2 (50 mL x 3), washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in anhydrous Et_2O (50 mL) and filtered to remove white solids. The filtrate was concentrated to give the aldehyde as yellow oil.

To a suspension of Ph_3PCH_3Br (10.34 g, 28.9 mmol) in THF (200 mL) was added *n*-BuLi (2.5 M in hexane) (10.5 mL, 26.3 mmol) at 0 ^oC under N_2. Upon stiiring at 0 ^oC for 1 h and subsequent addition of HMPA (9.43 g, 9.2 mL, 52.6 mmol), the reaction mixture was stirred at 0 ^oC for additional 15 min. At this point, a solution of the above aldehyde in THF (127 mL) was slowly added via syringe pump over 1 h. The resulting reaction mixture was stirred at 0 ^oC for 0.5 h, quenched with saturated NH_4Cl (50 mL), extracted with EtOAc (50 mL x 3), washed with brine (50 mL), dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 50/1) to give compound **4** as light

yellow oil (1.37 g, 54% for two steps). $[\alpha]^{20}_D$ = +1.13 (*c* 1.06, $CHCl_3$); IR (film): 1499, 1252, 1142 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.72 (s, 1H), 6.60 (s, 1H), 5.97 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.35-5.20 (m, 1H), 5.16 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.11 (dd, *J* = 17.6, 1.2 Hz, 1H), 4.94 (dd, *J* = 16.8, 1.6 Hz, 1H), 4.90-4.83 (m, 1H), 4.33 (t, *J* = 8.4 Hz, 1H), 3.85 (s, 6H), 2.98 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.82 (dd, *J* = 15.2, 8.4 Hz, 1H), 2.11-1.97 (m, 1H), 1.96-1.82 (m, 1H), 1.81-1.65 (m, 2H), 0.92 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 148.6, 148.2, 144.8, 139.8, 137.7, 131.6, 114.2, 113.9, 109.0, 108.0, 82.0, 56.7, 56.3, 56.1, 39.7, 32.1, 29.2, 26.0, 18.2, -4.3, -4.5; HRMS Calcd for $C_{23}H_{37}O_3Si$ (M+H): 389.2507; Found: 389.2517.

(*a*) D. Crich, H. Xu and F. Kenig, *J. Org. Chem.*, 2006, **71**, 5016

(*b*) H. Toya, K. Okano, K. Takasu, M. Ihara, A. Takahashi, H. Tanaka and H. Tokuyama, *Org. Lett.*, 2010, **12**, 5196.

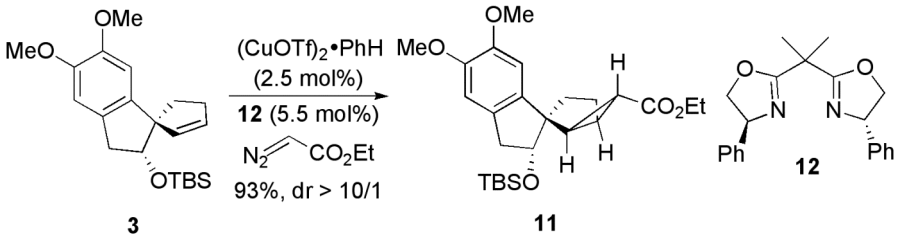


***Tert*-butyl((*1R*,*2'R*)-5',6'-dimethoxy-2',3'-dihydrospiro[cyclopent[2]ene-1,1'-indene]-2'-yloxy)dimethylsilane (3).** To a solution of **4** (0.389 g, 1.0 mmol) in CH_2Cl_2 (110 mL) was added the second-generation Grubbs catalyst (0.085 g, 0.1 mmol) at rt. The reaction mixture was stirred at rt for 4.5 h, passed through a pad of silica gel, eluted with CH_2Cl_2 (50 mL), concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 50/1) to give compound **3** as white solid (0.326 g, 91%). mp. 71-73 °C; $[\alpha]^{20}_D$ = -66.9 (*c* 0.81, $CHCl_3$); IR (film): 1499, 1252, 1115 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.58 (s, 1H), 6.06-5.98 (m, 1H), 5.55-5.49 (m, 1H), 4.33 (dd, *J* = 8.8, 7.2 Hz, 1H), 3.85 (s, 6H), 2.93 (dd, *J* = 14.8, 7.2 Hz, 1H), 2.79 (dd, *J* = 14.4, 8.8 Hz, 1H), 2.74-2.62 (m, 1H), 2.51-2.35 (m, 2H), 1.53-1.42 (m, 1H), 0.92 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H);

^{13}CNMR (100 MHz, $CDCl_3$) δ 148.7, 148.5, 140.9, 135.8, 133.9, 130.2, 108.0, 106.7, 80.1, 65.0, 56.1, 39.6, 32.7, 30.3, 25.9, 18.2, -4.60, -4.64; HRMS Calcd for $C_{21}H_{32}NaO_3Si$ (M+Na): 383.2013; Found: 383.2020.

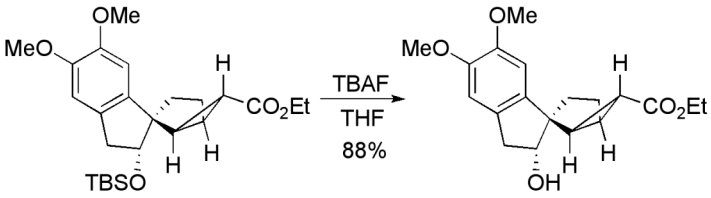
(*a*) M. Scholl, T. M. Trnka, J. P. Morgan and R. H. Grubbs, *Tetrahedron Lett.*, 1999, **40**, 2247

(*b*) B. Biswas, P. K. Sen and R. V. Venkateswaran, *Tetrahedron*, 2007, **63**, 12026

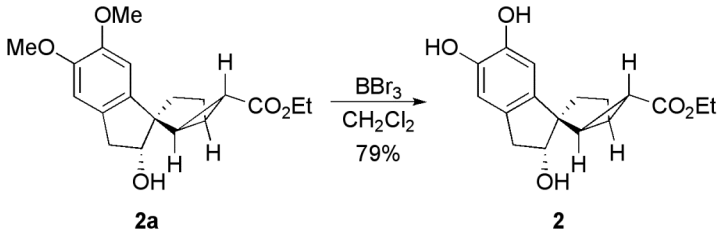


(*1'R,2'R,5R,6S*)-ethyl 2'-(*tert*-butyldimethylsilyloxy)-5',6'-dimethoxy-2',3'-dihydrospiro[bicyclo[3.1.0]hexane-2,1'-indene]-6-carboxylate (11). A solution of $(CuOTf)_2$·PhH (0.0063 g, 0.0125 mmol) and ligand **12** (0.0092 g, 0.0275 mmol) in CH_2Cl_2 (0.5 mL) was stirred at 25 °C for 1 h, followed by the addition of compound **3** (0.1803 g, 0.5 mmol). At this point, a solution of ethyl diazoacetate (containing 15% CH_2Cl_2) (0.6712 g, 5.0 mmol) in CH_2Cl_2 (1 mL) was slowly added via syringe pump over 10 h. The reaction mixture was stirred at 25 °C for another 1 h, passed though a pad of silica gel, eluted with CH_2Cl_2 (20 mL), concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 20/1 to 10/1) to give compound **11** as colorless oil (0.2071 g, 93%). $[\alpha]^{20}_D$ = -36.8 (*c* 0.57, $CHCl_3$); IR (film): 1724, 1500, 1252, 1178 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.94 (s, 1H), 6.67 (s, 1H), 4.38 (t, *J* = 7.2 Hz, 1H), 4.20-4.06 (m, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 2.95 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.75 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.28-2.09 (m, 2H), 2.06-1.92 (m, 2H), 1.87-1.75 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.09-0.09 (m, 1H), 0.92 (s, 9H), 0.11 (s, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 173.6, 148.8, 148.6, 138.3, 131.1, 108.1, 106.2, 81.7, 60.4, 58.7, 56.1, 39.3, 38.0, 28.22, 28.18, 27.2, 26.02, 25.99, 22.0, 18.2, 14.5, -4.5, -4.7; HRMS Calcd for $C_{25}H_{42}NO_5Si$ (M+NH_4): 464.2827; Found: 464.2820.

D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul, *J. Am. Chem. Soc.*, 1991, **113**, 726



(*1'R,2'R,5R,6S*)-ethyl-2'-hydroxy-5',6'-dimethoxy-2',3'-dihydrospiro[bicycle-[3.1.0]hexane- 2,1'-indene]-6-carboxylate (2a). To a solution of **11** (0.622 g, 1.39 mmol) in THF (30 mL) was added TBAF (1 M in THF) (2.8 mL, 2.8 mmol). The reaction mixture was stirred at rt for 3 h, quenched with water (10 mL), extracted with EtOAc (20 mL x 3), washed with brine (10 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 1/1) to give compound **2a** as colorless oil (0.405 g, 88%). $[\alpha]^{20}_{D}$ = -31.9 (*c* 1.00, $CHCl_3$); IR (film): 3481, 1718, 1499, 1180 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.80 (s, 1H), 6.74 (s, 1H), 4.41-4.30 (m, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.18 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.79 (dd, *J* = 15.6, 4.8 Hz, 1H), 2.22-2.02 (m, 3H), 2.01-1.91 (m, 2H), 1.90-1.79 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.31-1.15 (m, 1H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 173.6, 149.0, 148.7, 137.3, 131.5, 108.5, 106.6, 80.4, 60.5, 59.4, 56.3, 56.1, 39.1, 37.4, 27.5, 27.4, 26.5, 21.5, 14.4; HRMS Calcd for $C_{23}H_{37}O_3Si$ (M+H): 333.1697; Found: 333.1698.

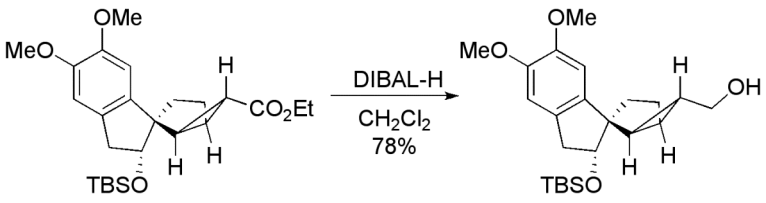


(*1'R,2'R,5R,6S*)-ethyl 2',5',6'-trihydroxy-2',3'-dihydrospiro[bicyclo[3.1.0]-hexane-2,1'-indene] -6-carboxylate (2). To a solution of **2a** (0.405 g, 1.22 mol) in

CH_2Cl_2 (9 mL) was added a solution of BBr_3 (0.917g, 0.33 mL, 3.7 mmol) in CH_2Cl_2 (3 mL) at -78 ^oC under N_2. The reaction mixture was warmed to rt and stirred at rt for 1 h, poured to ice-water (10 mL), extracted with $CHCl_3$ (10 mL x 10), dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 1/1) to give compound **2** as white solid (0.293 g, 79 %). mp. 94-96 ^oC; $[\alpha]^{20}_D$ = -42.6 (*c* 0.74, $CHCl_3$); IR (film): 3372, 1694, 1307, 1276 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.69 (s, 1H), 6.64 (s, 1H), 6.38 (br, 1H), 6.19 (br, 1H), 4.31-4.19 (m, 1H), 4.17-3.95 (m, 2H), 3.19-3.04 (m, 1H), 2.76-2.64 (m, 1H), 2.57 (br, 1H), 2.15-1.86 (m, 4H), 1.85-1.74 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.09-1.07 (m, 1H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 174.5, 143.7, 143.3, 137.4, 131.8, 112.3, 110.4, 80.4, 61.0, 59.6, 39.1, 37.3, 28.1, 27.4, 26.1, 21.6, 14.4; HRMS Calcd for $C_{17}H_{21}O_5$ (M+H): 305.1384; Found: 305.1384.

(*a*) C.-C. Lin, T.-M. Teng, C.-C. Tsai, H.-Y. Liao and R.-S. Liu, *J. Am. Chem. Soc.*, 2008, **130**, 16417

(*b*) C. Pan, X. Zeng, Y. Guan, X. Jiang, L. Li and H. Zhang, *Synlett*, 2011, 425



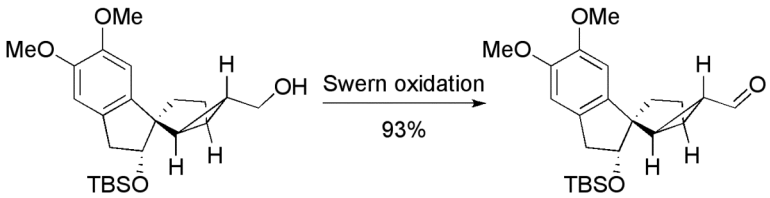
11 **13a**

((*1'R*,*2'R*,*5R*,*6S*)-2'-(*tert*-butyldimethylsilyloxy)-5',6'-dimethoxy-2',3'-dihydr -ospiro[bicycle- [3.1.0]hexane-2,1'-indene]-6-yl)methanol (13a). To a solution of **11** (0.495 g, 1.1 mmol) in CH_2Cl_2 (11 mL) was added DIBAL-H (1 M in hexane) (2.8 mL, 2.8 mmol) at -78 ^oC under N_2. Upon stirring at -78 ^oC for 15 min and at 0 ^oC for 1 h, the reaction mixture was quenched with MeOH (0.5 mL) and saturated sodium potassium tartrate (20 mL), stirred at rt for 0.5 h, extracted with CH_2Cl_2 (10 mL x 3), washed with brine (10 mL), dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 2/1) to give compound **13a** as colorless oil (0.346 g, 78%). $[\alpha]^{20}_D$ = -52.8 (*c* 0.48, $CHCl_3$);

IR (film): 3497, 1498, 1252, 1104 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.66 (s, 1H), 4.34 (t, *J* = 7.2 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.67-3.55 (m, 1H), 3.46-3.32 (m, 1H), 2.92 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.74 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.24-2.12 (m, 1H), 2.11-2.00 (m, 1H), 1.80-1.66 (m, 2H), 1.54-1.43 (m, 1H), 1.35-1.25 (m, 1H), 1.18-0.99 (m, 2H), 0.92 (s, 9H), 0.11 (s, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 148.6, 148.5, 139.5, 130.9, 108.0, 106.3, 82.2, 66.0, 58.0, 56.2, 56.1, 39.2, 32.8, 29.2, 28.1, 26.0, 22.6, 22.0, 18.2, -4.6, -4.7; HRMS Calcd for $C_{23}H_{40}NO_4Si$ (M+NH_4): 422.2721; Found: 422.2718.

(*a*) D. L. J. Clive, M. Yu and M. Sannigrahi, *J. Org. Chem.*, 2004, **69**, 4116

(*b*) K.Okura, S. Matsuoka, R. Goto and M. Inoue, *Angew. Chem., Int. Ed.*, 2010, **49**, 329.

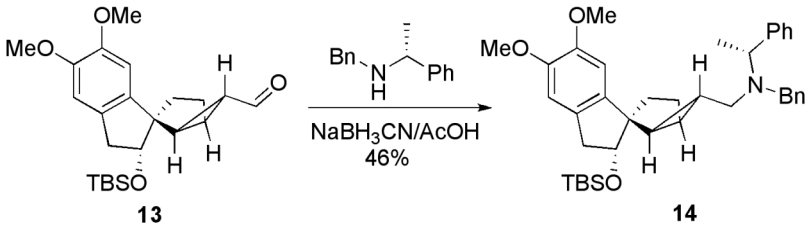


13a **13**

(*1'R,2'R,5R,6S*)-2'-(*tert*-butyldimethylsilyloxy)-5',6'-dimethoxy-2',3'-dihydro -spiro[bicycle- [3.1.0]hexane-2,1'-indene]-6-carbaldehyde (13). To a solution of $(COCl)_2$ (0.123 g, 0.095 mL, 0.97 mmol) in CH_2Cl_2 (8 mL) was slowly added DMSO (0.126 g, 0.115 mL, 1.62 mmol) at -78 °C under N_2. After the reaction mixture was stirred at -78 °C for 15 min, a solution of **13a** (0.327 g, 0.81 mmol) in CH_2Cl_2 (1 mL) was added. The resulting mixture was stirred at -78 °C for another 45 min. Upon addition of Et_3N (0.328 g, 0.451 mL, 3.24 mmol), the reaction mixture was warmed to rt over 2 h, quenched with water (5 mL), extracted with CH_2Cl_2 (10 mL x 3), washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 5/1) to give compound **13** as white solid (0.304 g, 93%). mp. 91-93 °C; $[\alpha]^{20}_{D}$ = -70.3 (*c* 0.76, $CHCl_3$); IR (film): 1706, 1499, 1252, 1107 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 4.8 Hz, 1H), 6.83 (s, 1H), 6.68 (s, 1H), 4.11 (t, *J* = 7.2 Hz, 1H), 3.85 (s, 3H), 3.83 (s,

3H), 2.96 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.76 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.30-2.15 (m, 3H), 2.14-2.03 (m, 1H), 1.95-1.92 (m, 1H), 1.90-1.79 (m, 1H), 1.01-1.12 (m, 1H), 0.93 (s, 9H), 0.12 (s, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 199.9, 149.0, 148.8, 137.6, 131.1, 108.2, 106.2, 81.9, 58.7, 56.4, 56.2, 39.2, 37.2, 32.5, 28.14, 28.09, 27.3, 26.0, 18.3, -4.4, -4.6; HRMS Calcd for $C_{23}H_{34}O_4Si$ (M^+): 402.2226; Found: 402.2221.

S. F. Martin, J. M. Humphrey, A. Ali and M. C. Hillier, *J. Am. Chem. Soc.*, 1999, **121**, 866.

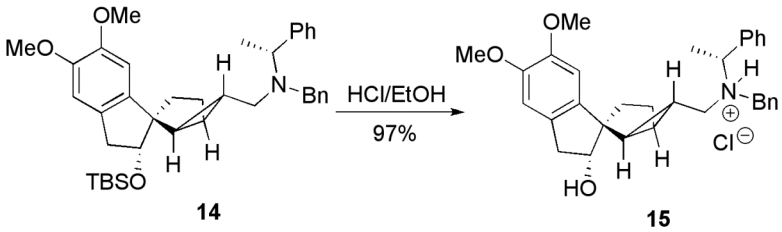


13 **14**

(*1R*)-*N*-benzyl-*N*-(((*1'R*,*2'R*,*5R*,*6S*)-2'-(*tert*-butyldimethylsilyloxy)-5',6'-dime -thoxy-2',3'-dihydrospiro[bicyclo[3.1.0]hexane-2,1'-indene]-6-yl)methyl)-1-pheny l-ethanamine (14). To a solution of **13** (0.271 g, 0.67 mmol), (*R*)-(+)-*N*-benzyl-1-phenylethylamine (0.171 g, 0.17 mL, 0.81 mmol), AcOH (0.089 g, 0.86 mL, 1.48 mmol) in MeOH (11 mL) was added $NaBH_3CN$ (0.0758 g, 1.20 mmol) under N_2. The reaction mixture was stirred at rt overnight, quenched with aqueous NaOH (5 mL, 1M), concentrated, extracted with EtOAc (10 mL x 3), washed with brine (5 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 15/1) to give compound **14** as colorless oil (0.185 g, 46%). $[\alpha]^{20}_D$ = -61.0 (*c* 0.92, $CHCl_3$); IR (film) 1496, 1251, 1104 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.44-7.13 (m, 10H), 6.74 (s, 1H), 6.67 (s, 1H), 4.24 (t, *J* = 6.8 Hz, 1H), 4.13-4.03 (m, 1H), 3.81 (s, 3H), 3.72 (d, *J* = 14.4 Hz, 1H), 3.61 (s, 3H), 3.50 (d, *J* = 14.4 Hz, 1H), 2.94 (dd, *J* = 14.8, 6.4 Hz, 1H), 2.71 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.59-2.49 (m, 1H), 2.28-2.17 (m, 1H), 2.16-2.05 (m, 1H), 2.02-1.90 (m, 1H), 1.72-1.60 (m, 1H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.21-1.02 (m, 3H), 0.90 (s, 9H), 0.86-0.79 (m, 1H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}CNMR (100 MHz,

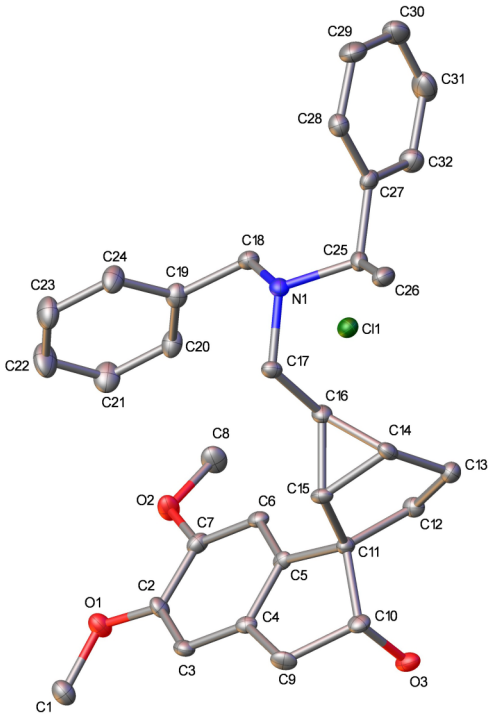
$CDCl_3$) δ 148.5, 144.7, 141.2, 139.7, 131.1, 128.7, 128.3, 128.1, 127.9, 126.73, 126.66, 108.1, 106.4, 82.1, 58.9, 57.4, 56.2, 56.1, 54.4, 52.2, 39.5, 32.7, 28.8, 28.2, 26.1, 24.6, 18.5, 18.4, 13.6, -4.5, -4.6; HRMS Calcd for $C_{38}H_{52}NO_3Si$ (M+H): 598.3711; Found: 598.3718.

N. T. Hatzenbuhler, R. Baudy, D. A. Evrard, A. Failli, B. L. Harrison, S. Lenicek, R. E. Mewshaw, A. Saab, U. Shah, J. Sze, M. Zhang, D. Zhou, M. Chlenov, M. Kagan, J. Golembieski, G. Hornby, M. Lai, D. L. Smith, K. M. Sullivan, L. E. Schechter and T. H. Andree, *J. Med. Chem.*, 2008, **51**, 6980.



(*1R*)-*N*-benzyl-*N*-(((*1'R*,*2'R*,*5R*,*6S*)-2'-hydroxy-5',6'-dimethoxy-2',3'-dihydrospiro[bicycle-[3.1.0]hexane-2,1'-indene]-6-yl)methyl)-1-phenylethanaminium chloride (15). To a solution of **14** (0.0794 g, 0.13 mmol) in EtOAc (20 mL) was added a solution of HCl in EtOH (5 mL). The reaction mixture was stirred at rt for 0.5 h, concentrated, and washed with EtOAc (20 mL) to give compound **15** as white solid (0.065 g, 97%), which was crystallized from MeOH/Et_2O/EtOAc for the X-ray structure. HRMS Calcd for $C_{32}H_{38}NO_3$ (M-Cl): 484.2846; Found: 484.2839.

The X-ray Structure of Compound 15



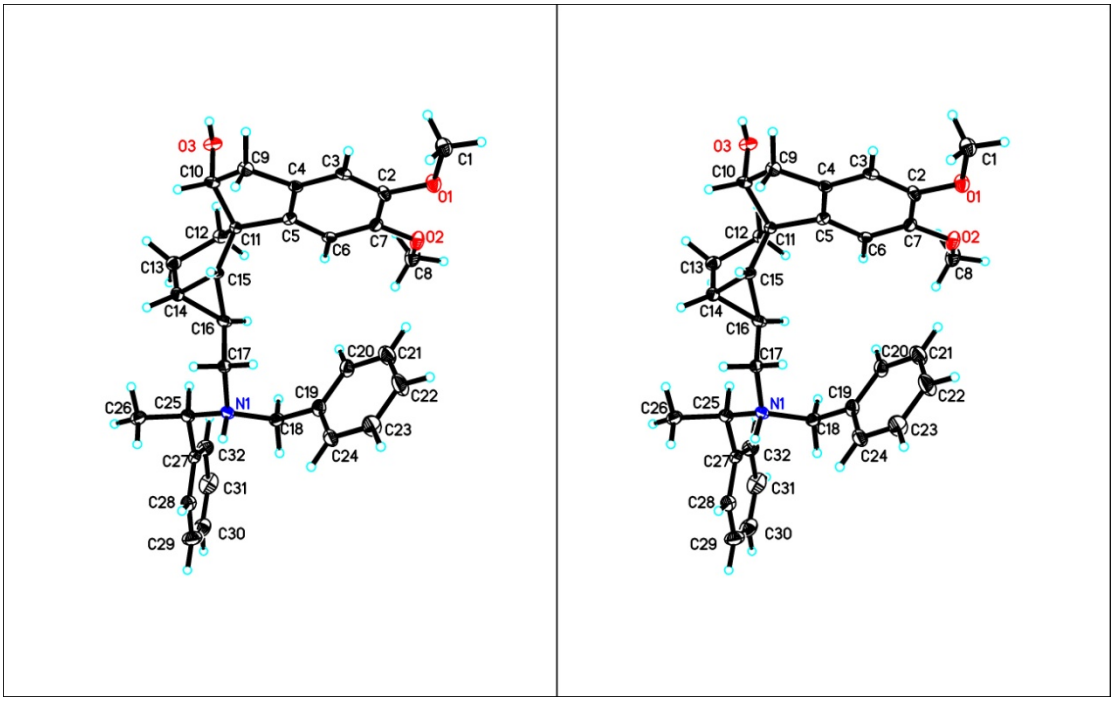


Table 1. Crystal data and structure refinement for a.

Identification code	a
Empirical formula	C33 H42 Cl N O4
Formula weight	552.13
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Tetragonal, P4(1)2(1)2
Unit cell dimensions	a = 12.3304(17) A alpha = 90 deg.
	b = 12.3304(17) A beta = 90 deg.
	c = 38.821(8) A gamma = 90 deg.
Volume	5902.3(17) A^3
Z, Calculated density	8, 1.243 Mg/m^3
Absorption coefficient	0.167 mm^-1
F(000)	2368
Crystal size	0.25 x 0.19 x 0.05 mm
Theta range for data collection	1.73 to 25.00 deg.
Limiting indices	-14<=h<=14, -14<=k<=14, -45<=l<=45
Reflections collected / unique	34943 / 5205 [R(int) = 0.0990]
Completeness to theta = 25.00	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.6720
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5205 / 0 / 356
Goodness-of-fit on F^2	1.321
Final R indices [I>2sigma(I)]	R1 = 0.0906, wR2 = 0.1577
R indices (all data)	R1 = 0.0932, wR2 = 0.1587
Absolute structure parameter	0.06(13)
Largest diff. peak and hole	0.227 and -0.224 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for a.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Cl(1)	6941(1)	4424(1)	3727(1)	27(1)
O(1)	9424(3)	7082(3)	2328(1)	33(1)
O(2)	7954(3)	6098(3)	2680(1)	33(1)
O(3)	10573(3)	8408(3)	3861(1)	31(1)
O(4)	3693(4)	5540(4)	3906(1)	57(1)
N(1)	10193(3)	2376(3)	3893(1)	24(1)
C(1)	10196(4)	7685(5)	2131(1)	35(1)
C(2)	9651(4)	6960(4)	2671(1)	26(1)
C(3)	10588(4)	7333(4)	2833(1)	25(1)
C(4)	10719(4)	7170(4)	3186(1)	21(1)
C(5)	9937(4)	6619(4)	3374(1)	20(1)
C(6)	8994(4)	6243(4)	3215(1)	23(1)
C(7)	8843(4)	6429(4)	2865(1)	27(1)
C(8)	6998(4)	5888(5)	2860(1)	39(1)
C(9)	11643(4)	7522(4)	3414(1)	27(1)
C(10)	11147(4)	7431(4)	3775(1)	27(1)
C(11)	10308(4)	6499(4)	3748(1)	21(1)
C(12)	9450(4)	6490(4)	4030(1)	26(1)
C(13)	9982(4)	5914(4)	4337(1)	29(1)
C(14)	10723(4)	5083(4)	4173(1)	24(1)
C(15)	10941(4)	5430(4)	3807(1)	23(1)
C(16)	10285(4)	4424(4)	3874(1)	26(1)
C(17)	10834(4)	3361(4)	3789(1)	23(1)
C(18)	9188(4)	2210(4)	3670(1)	27(1)
C(19)	9402(4)	2389(4)	3291(1)	30(1)
C(20)	8959(4)	3262(4)	3126(1)	33(1)
C(21)	9145(5)	3453(5)	2779(2)	45(2)
C(22)	9765(6)	2734(5)	2599(2)	53(2)
C(23)	10226(5)	1862(5)	2758(1)	47(2)
C(24)	10047(5)	1669(5)	3105(1)	39(1)
C(25)	9890(4)	2394(4)	4280(1)	25(1)
C(26)	10924(5)	2353(4)	4498(1)	34(1)
C(27)	9123(4)	1488(4)	4378(1)	27(1)
C(28)	9468(5)	412(4)	4380(1)	32(1)
C(29)	8774(5)	-389(5)	4492(2)	47(2)

C(30)	7734(5)	−146(5)	4599(2)	49(2)
C(31)	7389(5)	907(6)	4589(2)	52(2)
C(32)	8081(5)	1728(5)	4481(1)	37(1)
C(33)	3624(5)	5756(5)	4262(2)	49(2)

Table 3. Bond lengths [A] and angles [deg] for a.

O(1)-C(2)	1.368(5)
O(1)-C(1)	1.429(6)
O(2)-C(7)	1.373(6)
O(2)-C(8)	1.397(6)
O(3)-C(10)	1.437(6)
O(3)-H(3)	0.8401
O(4)-C(33)	1.411(7)
O(4)-H(4)	0.8402
N(1)-C(17)	1.505(6)
N(1)-C(18)	1.526(6)
N(1)-C(25)	1.547(6)
N(1)-H(1)	0.9300
C(1)-H(1C)	0.9800
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(2)-C(3)	1.393(7)
C(2)-C(7)	1.411(7)
C(3)-C(4)	1.394(6)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.387(6)
C(4)-C(9)	1.508(7)
C(5)-C(6)	1.395(6)
C(5)-C(11)	1.530(7)
C(6)-C(7)	1.390(7)
C(6)-H(6)	0.9500
C(8)-H(8C)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8A)	0.9800
C(9)-C(10)	1.531(7)
C(9)-H(9B)	0.9900
C(9)-H(9A)	0.9900
C(10)-C(11)	1.549(7)
C(10)-H(10)	1.0000
C(11)-C(12)	1.523(7)
C(11)-C(15)	1.550(6)
C(12)-C(13)	1.533(7)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.512(7)
C(13)-H(13B)	0.9900
C(13)-H(13A)	0.9900

C(14)-C(15)	1.508(6)
C(14)-C(16)	1.517(7)
C(14)-H(14)	1.0000
C(15)-C(16)	1.503(6)
C(15)-H(15)	1.0000
C(16)-C(17)	1.512(6)
C(16)-H(16)	1.0000
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.510(7)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(20)	1.368(7)
C(19)-C(24)	1.394(7)
C(20)-C(21)	1.384(8)
C(20)-H(20)	0.9500
C(21)-C(22)	1.363(8)
C(21)-H(21)	0.9500
C(22)-C(23)	1.364(8)
C(22)-H(22)	0.9500
C(23)-C(24)	1.385(7)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(25)-C(27)	1.513(7)
C(25)-C(26)	1.532(7)
C(25)-H(25)	1.0000
C(26)-H(26A)	0.9800
C(26)-H(26C)	0.9800
C(26)-H(26B)	0.9800
C(27)-C(32)	1.378(7)
C(27)-C(28)	1.394(7)
C(28)-C(29)	1.378(8)
C(28)-H(28)	0.9500
C(29)-C(30)	1.381(9)
C(29)-H(29)	0.9500
C(30)-C(31)	1.368(9)
C(30)-H(30)	0.9500
C(31)-C(32)	1.389(8)
C(31)-H(31)	0.9500
C(32)-H(32)	0.9500
C(33)-H(33A)	0.9800
C(33)-H(33B)	0.9800
C(33)-H(33C)	0.9800

C(2)-O(1)-C(1)	116.2(4)
C(7)-O(2)-C(8)	117.7(4)
C(10)-O(3)-H(3)	94.0
C(33)-O(4)-H(4)	111.6
C(17)-N(1)-C(18)	112.4(3)
C(17)-N(1)-C(25)	112.1(4)
C(18)-N(1)-C(25)	111.0(4)
C(17)-N(1)-H(1)	107.0
C(18)-N(1)-H(1)	107.0
C(25)-N(1)-H(1)	107.0
O(1)-C(1)-H(1C)	109.5
O(1)-C(1)-H(1A)	109.5
H(1C)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1C)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(2)-C(3)	124.8(4)
O(1)-C(2)-C(7)	115.3(4)
C(3)-C(2)-C(7)	119.9(4)
C(2)-C(3)-C(4)	119.4(5)
C(2)-C(3)-H(3A)	120.3
C(4)-C(3)-H(3A)	120.3
C(5)-C(4)-C(3)	120.5(5)
C(5)-C(4)-C(9)	110.9(4)
C(3)-C(4)-C(9)	128.6(4)
C(4)-C(5)-C(6)	120.7(4)
C(4)-C(5)-C(11)	109.8(4)
C(6)-C(5)-C(11)	129.4(4)
C(7)-C(6)-C(5)	119.1(5)
C(7)-C(6)-H(6)	120.4
C(5)-C(6)-H(6)	120.4
O(2)-C(7)-C(6)	124.8(5)
O(2)-C(7)-C(2)	114.9(4)
C(6)-C(7)-C(2)	120.3(5)
O(2)-C(8)-H(8C)	109.5
O(2)-C(8)-H(8B)	109.5
H(8C)-C(8)-H(8B)	109.5
O(2)-C(8)-H(8A)	109.5
H(8C)-C(8)-H(8A)	109.5
H(8B)-C(8)-H(8A)	109.5
C(4)-C(9)-C(10)	102.4(4)
C(4)-C(9)-H(9B)	111.3
C(10)-C(9)-H(9B)	111.3
C(4)-C(9)-H(9A)	111.3

C(10)-C(9)-H(9A)	111.3
H(9B)-C(9)-H(9A)	109.2
O(3)-C(10)-C(9)	110.4(4)
O(3)-C(10)-C(11)	108.0(4)
C(9)-C(10)-C(11)	105.0(4)
O(3)-C(10)-H(10)	111.1
C(9)-C(10)-H(10)	111.1
C(11)-C(10)-H(10)	111.1
C(12)-C(11)-C(5)	118.5(4)
C(12)-C(11)-C(10)	114.9(4)
C(5)-C(11)-C(10)	101.1(4)
C(12)-C(11)-C(15)	103.7(4)
C(5)-C(11)-C(15)	112.0(4)
C(10)-C(11)-C(15)	106.5(4)
C(11)-C(12)-C(13)	105.4(4)
C(11)-C(12)-H(12A)	110.7
C(13)-C(12)-H(12A)	110.7
C(11)-C(12)-H(12B)	110.7
C(13)-C(12)-H(12B)	110.7
H(12A)-C(12)-H(12B)	108.8
C(14)-C(13)-C(12)	104.3(4)
C(14)-C(13)-H(13B)	110.9
C(12)-C(13)-H(13B)	110.9
C(14)-C(13)-H(13A)	110.9
C(12)-C(13)-H(13A)	110.9
H(13B)-C(13)-H(13A)	108.9
C(15)-C(14)-C(13)	108.1(4)
C(15)-C(14)-C(16)	59.6(3)
C(13)-C(14)-C(16)	117.9(4)
C(15)-C(14)-H(14)	118.8
C(13)-C(14)-H(14)	118.8
C(16)-C(14)-H(14)	118.8
C(16)-C(15)-C(14)	60.5(3)
C(16)-C(15)-C(11)	117.1(4)
C(14)-C(15)-C(11)	107.0(4)
C(16)-C(15)-H(15)	119.2
C(14)-C(15)-H(15)	119.2
C(11)-C(15)-H(15)	119.2
C(15)-C(16)-C(17)	115.9(4)
C(15)-C(16)-C(14)	59.9(3)
C(17)-C(16)-C(14)	118.3(4)
C(15)-C(16)-H(16)	116.9
C(17)-C(16)-H(16)	116.9
C(14)-C(16)-H(16)	116.9

N(1)-C(17)-C(16)	113.9(4)
N(1)-C(17)-H(17A)	108.8
C(16)-C(17)-H(17A)	108.8
N(1)-C(17)-H(17B)	108.8
C(16)-C(17)-H(17B)	108.8
H(17A)-C(17)-H(17B)	107.7
C(19)-C(18)-N(1)	113.0(4)
C(19)-C(18)-H(18A)	109.0
N(1)-C(18)-H(18A)	109.0
C(19)-C(18)-H(18B)	109.0
N(1)-C(18)-H(18B)	109.0
H(18A)-C(18)-H(18B)	107.8
C(20)-C(19)-C(24)	119.0(5)
C(20)-C(19)-C(18)	120.2(5)
C(24)-C(19)-C(18)	120.8(5)
C(19)-C(20)-C(21)	121.6(5)
C(19)-C(20)-H(20)	119.2
C(21)-C(20)-H(20)	119.2
C(22)-C(21)-C(20)	118.7(5)
C(22)-C(21)-H(21)	120.6
C(20)-C(21)-H(21)	120.6
C(21)-C(22)-C(23)	121.0(5)
C(21)-C(22)-H(22)	119.5
C(23)-C(22)-H(22)	119.5
C(22)-C(23)-C(24)	120.5(5)
C(22)-C(23)-H(23)	119.8
C(24)-C(23)-H(23)	119.8
C(23)-C(24)-C(19)	119.1(5)
C(23)-C(24)-H(24)	120.4
C(19)-C(24)-H(24)	120.4
C(27)-C(25)-C(26)	110.9(4)
C(27)-C(25)-N(1)	112.6(4)
C(26)-C(25)-N(1)	109.7(4)
C(27)-C(25)-H(25)	107.8
C(26)-C(25)-H(25)	107.8
N(1)-C(25)-H(25)	107.8
C(25)-C(26)-H(26A)	109.5
C(25)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
C(25)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
H(26C)-C(26)-H(26B)	109.5
C(32)-C(27)-C(28)	119.2(5)
C(32)-C(27)-C(25)	119.9(5)

C(28)-C(27)-C(25)	120.9(5)
C(29)-C(28)-C(27)	119.6(5)
C(29)-C(28)-H(28)	120.2
C(27)-C(28)-H(28)	120.2
C(28)-C(29)-C(30)	121.2(6)
C(28)-C(29)-H(29)	119.4
C(30)-C(29)-H(29)	119.4
C(31)-C(30)-C(29)	119.1(6)
C(31)-C(30)-H(30)	120.5
C(29)-C(30)-H(30)	120.5
C(30)-C(31)-C(32)	120.6(6)
C(30)-C(31)-H(31)	119.7
C(32)-C(31)-H(31)	119.7
C(27)-C(32)-C(31)	120.3(6)
C(27)-C(32)-H(32)	119.8
C(31)-C(32)-H(32)	119.8
O(4)-C(33)-H(33A)	109.5
O(4)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
O(4)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for a.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Cl(1)	29(1)	23(1)	28(1)	-2(1)	1(1)	0(1)
O(1)	29(2)	42(2)	28(2)	5(2)	0(2)	-5(2)
O(2)	23(2)	49(2)	27(2)	-4(2)	-2(2)	-9(2)
O(3)	30(2)	21(2)	44(2)	-1(2)	5(2)	-2(2)
O(4)	47(3)	70(3)	55(3)	-12(2)	13(2)	-18(2)
N(1)	28(2)	20(2)	23(2)	3(2)	1(2)	2(2)
C(1)	32(3)	44(4)	30(3)	5(3)	3(2)	-1(2)
C(2)	30(3)	31(3)	18(2)	7(2)	1(2)	0(2)
C(3)	27(3)	19(2)	28(3)	5(2)	3(2)	-2(2)
C(4)	18(2)	16(2)	29(3)	3(2)	-2(2)	3(2)
C(5)	15(2)	19(3)	27(3)	-4(2)	2(2)	2(2)
C(6)	23(3)	15(2)	30(3)	1(2)	0(2)	0(2)
C(7)	28(3)	23(3)	30(3)	-4(2)	-7(2)	1(2)
C(8)	24(3)	54(4)	38(3)	-2(3)	-5(3)	-9(3)
C(9)	12(2)	30(3)	39(3)	7(2)	-2(2)	-5(2)
C(10)	33(3)	16(2)	32(3)	2(2)	-2(2)	3(2)
C(11)	25(3)	18(2)	20(2)	1(2)	-2(2)	-1(2)
C(12)	22(3)	24(3)	31(3)	1(2)	2(2)	1(2)
C(13)	34(3)	26(3)	28(3)	-2(2)	3(2)	-2(2)
C(14)	26(3)	27(3)	20(2)	6(2)	0(2)	-7(2)
C(15)	20(2)	17(2)	32(3)	2(2)	1(2)	-4(2)
C(16)	33(3)	18(2)	25(3)	3(2)	2(2)	2(2)
C(17)	24(3)	22(3)	24(3)	3(2)	-2(2)	-5(2)
C(18)	29(3)	23(3)	29(3)	-1(2)	0(2)	-4(2)
C(19)	26(3)	36(3)	29(3)	-3(2)	-3(2)	2(2)
C(20)	32(3)	38(3)	28(3)	-6(3)	-5(2)	11(2)
C(21)	52(4)	44(4)	40(3)	3(3)	-7(3)	17(3)
C(22)	75(5)	58(4)	26(3)	7(3)	-2(3)	21(4)
C(23)	55(4)	51(4)	36(3)	-5(3)	4(3)	18(3)
C(24)	54(4)	35(3)	26(3)	1(3)	-8(3)	11(3)
C(25)	34(3)	22(3)	20(2)	-1(2)	3(2)	3(2)
C(26)	46(4)	25(3)	31(3)	-1(2)	-2(3)	-7(2)
C(27)	34(3)	25(3)	22(3)	-4(2)	-4(2)	-2(2)
C(28)	34(3)	33(3)	28(3)	-1(2)	3(2)	-1(2)
C(29)	64(4)	27(3)	49(4)	0(3)	3(3)	-10(3)

C(30)	52(4)	51(4)	44(4)	-1(3)	2(3)	-22(3)
C(31)	42(4)	67(5)	46(4)	-8(3)	12(3)	-12(3)
C(32)	33(3)	37(3)	41(3)	-2(3)	2(3)	-3(3)
C(33)	45(4)	47(4)	57(4)	-1(3)	7(3)	-11(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for a.

	x	y	z	U(eq)
H(3)	11072	8818	3793	38
H(4)	4255	5811	3819	69
H(1)	10638	1777	3859	29
H(1C)	10270	8414	2228	53
H(1A)	9948	7737	1892	53
H(1B)	10900	7315	2138	53
H(3A)	11133	7695	2704	30
H(6)	8461	5864	3345	27
H(8C)	6836	6500	3013	58
H(8B)	7086	5227	2998	58
H(8A)	6400	5791	2697	58
H(9B)	11865	8277	3363	32
H(9A)	12277	7037	3389	32
H(10)	11715	7262	3951	32
H(12A)	8796	6093	3953	31
H(12B)	9240	7240	4093	31
H(13B)	10400	6433	4479	35
H(13A)	9429	5559	4483	35
H(14)	11334	4780	4313	29
H(15)	11692	5357	3712	28
H(16)	9488	4471	3830	31
H(17A)	10965	3331	3537	28
H(17B)	11548	3339	3905	28
H(18A)	8915	1462	3704	32
H(18B)	8614	2717	3746	32
H(20)	8511	3749	3251	39
H(21)	8847	4073	2669	54
H(22)	9877	2843	2360	64
H(23)	10674	1383	2629	57
H(24)	10359	1055	3214	46
H(25)	9518	3098	4329	30
H(26A)	11370	1736	4426	51
H(26C)	10730	2269	4742	51
H(26B)	11334	3027	4468	51
H(28)	10178	231	4303	38
H(29)	9015	-1120	4497	56

H(30)	7264	-704	4679	59
H(31)	6669	1080	4657	62
H(32)	7834	2458	4477	44
H(33A)	3355	5111	4382	74
H(33B)	3125	6363	4301	74
H(33C)	4345	5945	4350	74

Table 6. Torsion angles [deg] for a.

C(1)-O(1)-C(2)-C(3)	-3.1(7)
C(1)-O(1)-C(2)-C(7)	175.7(4)
O(1)-C(2)-C(3)-C(4)	179.2(5)
C(7)-C(2)-C(3)-C(4)	0.4(7)
C(2)-C(3)-C(4)-C(5)	1.5(7)
C(2)-C(3)-C(4)-C(9)	-178.4(5)
C(3)-C(4)-C(5)-C(6)	-1.6(7)
C(9)-C(4)-C(5)-C(6)	178.3(4)
C(3)-C(4)-C(5)-C(11)	176.9(4)
C(9)-C(4)-C(5)-C(11)	-3.2(5)
C(4)-C(5)-C(6)-C(7)	-0.2(7)
C(11)-C(5)-C(6)-C(7)	-178.4(5)
C(8)-O(2)-C(7)-C(6)	22.0(7)
C(8)-O(2)-C(7)-C(2)	-160.2(5)
C(5)-C(6)-C(7)-O(2)	179.8(4)
C(5)-C(6)-C(7)-C(2)	2.1(7)
O(1)-C(2)-C(7)-O(2)	1.0(7)
C(3)-C(2)-C(7)-O(2)	179.9(4)
O(1)-C(2)-C(7)-C(6)	178.9(4)
C(3)-C(2)-C(7)-C(6)	-2.2(8)
C(5)-C(4)-C(9)-C(10)	-17.3(5)
C(3)-C(4)-C(9)-C(10)	162.6(5)
C(4)-C(9)-C(10)-O(3)	-85.8(5)
C(4)-C(9)-C(10)-C(11)	30.4(5)
C(4)-C(5)-C(11)-C(12)	148.3(4)
C(6)-C(5)-C(11)-C(12)	-33.3(7)
C(4)-C(5)-C(11)-C(10)	21.9(5)
C(6)-C(5)-C(11)-C(10)	-159.8(5)
C(4)-C(5)-C(11)-C(15)	-91.1(5)
C(6)-C(5)-C(11)-C(15)	87.2(6)
O(3)-C(10)-C(11)-C(12)	-42.7(6)
C(9)-C(10)-C(11)-C(12)	-160.6(4)
O(3)-C(10)-C(11)-C(5)	86.0(4)
C(9)-C(10)-C(11)-C(5)	-31.8(5)
O(3)-C(10)-C(11)-C(15)	-156.9(4)
C(9)-C(10)-C(11)-C(15)	85.3(5)
C(5)-C(11)-C(12)-C(13)	157.5(4)
C(10)-C(11)-C(12)-C(13)	-83.0(5)
C(15)-C(11)-C(12)-C(13)	32.7(5)
C(11)-C(12)-C(13)-C(14)	-33.2(5)
C(12)-C(13)-C(14)-C(15)	20.4(5)

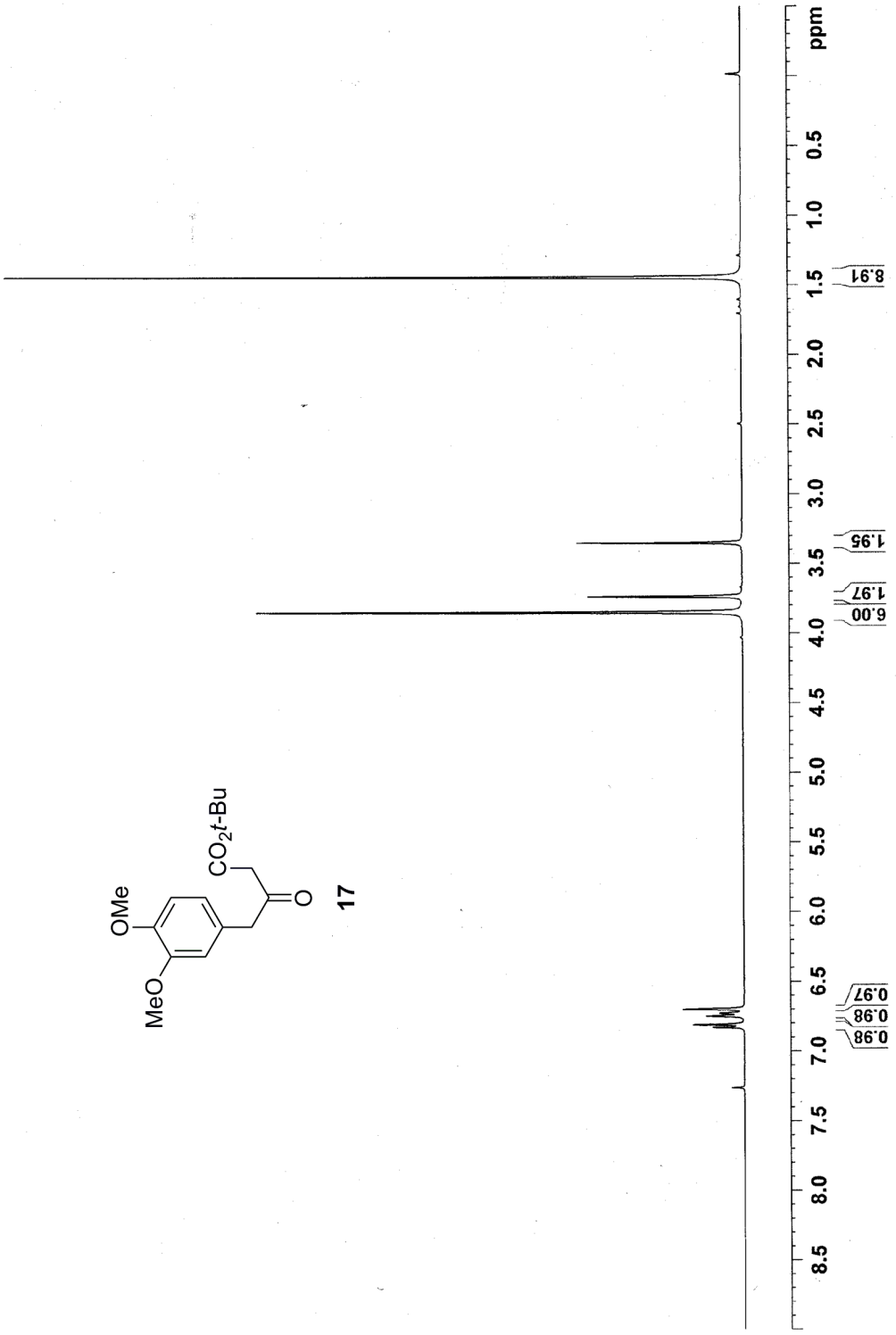
C(12)-C(13)-C(14)-C(16)	-44.1(6)
C(13)-C(14)-C(15)-C(16)	-112.3(5)
C(13)-C(14)-C(15)-C(11)	-0.3(5)
C(16)-C(14)-C(15)-C(11)	112.0(4)
C(12)-C(11)-C(15)-C(16)	45.0(5)
C(5)-C(11)-C(15)-C(16)	-83.9(5)
C(10)-C(11)-C(15)-C(16)	166.5(4)
C(12)-C(11)-C(15)-C(14)	-20.0(5)
C(5)-C(11)-C(15)-C(14)	-148.9(4)
C(10)-C(11)-C(15)-C(14)	101.5(4)
C(14)-C(15)-C(16)-C(17)	-109.1(5)
C(11)-C(15)-C(16)-C(17)	155.9(4)
C(11)-C(15)-C(16)-C(14)	-95.0(5)
C(13)-C(14)-C(16)-C(15)	95.5(5)
C(15)-C(14)-C(16)-C(17)	105.2(5)
C(13)-C(14)-C(16)-C(17)	-159.3(4)
C(18)-N(1)-C(17)-C(16)	70.9(5)
C(25)-N(1)-C(17)-C(16)	-55.0(5)
C(15)-C(16)-C(17)-N(1)	174.1(4)
C(14)-C(16)-C(17)-N(1)	105.9(5)
C(17)-N(1)-C(18)-C(19)	43.0(5)
C(25)-N(1)-C(18)-C(19)	169.5(4)
N(1)-C(18)-C(19)-C(20)	-111.3(5)
N(1)-C(18)-C(19)-C(24)	69.0(6)
C(24)-C(19)-C(20)-C(21)	-0.8(9)
C(18)-C(19)-C(20)-C(21)	179.6(5)
C(19)-C(20)-C(21)-C(22)	1.7(10)
C(20)-C(21)-C(22)-C(23)	-2.3(11)
C(21)-C(22)-C(23)-C(24)	2.0(11)
C(22)-C(23)-C(24)-C(19)	-1.1(10)
C(20)-C(19)-C(24)-C(23)	0.5(9)
C(18)-C(19)-C(24)-C(23)	-179.9(5)
C(17)-N(1)-C(25)-C(27)	172.4(4)
C(18)-N(1)-C(25)-C(27)	45.8(5)
C(17)-N(1)-C(25)-C(26)	-63.6(5)
C(18)-N(1)-C(25)-C(26)	169.7(4)
C(26)-C(25)-C(27)-C(32)	123.4(5)
N(1)-C(25)-C(27)-C(32)	-113.3(5)
C(26)-C(25)-C(27)-C(28)	-54.1(6)
N(1)-C(25)-C(27)-C(28)	69.2(6)
C(32)-C(27)-C(28)-C(29)	-1.9(8)
C(25)-C(27)-C(28)-C(29)	175.6(5)
C(27)-C(28)-C(29)-C(30)	1.0(9)
C(28)-C(29)-C(30)-C(31)	0.6(10)

C(29)-C(30)-C(31)-C(32)	-1.4(10)
C(28)-C(27)-C(32)-C(31)	1.1(8)
C(25)-C(27)-C(32)-C(31)	-176.5(5)
C(30)-C(31)-C(32)-C(27)	0.6(9)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for a [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)



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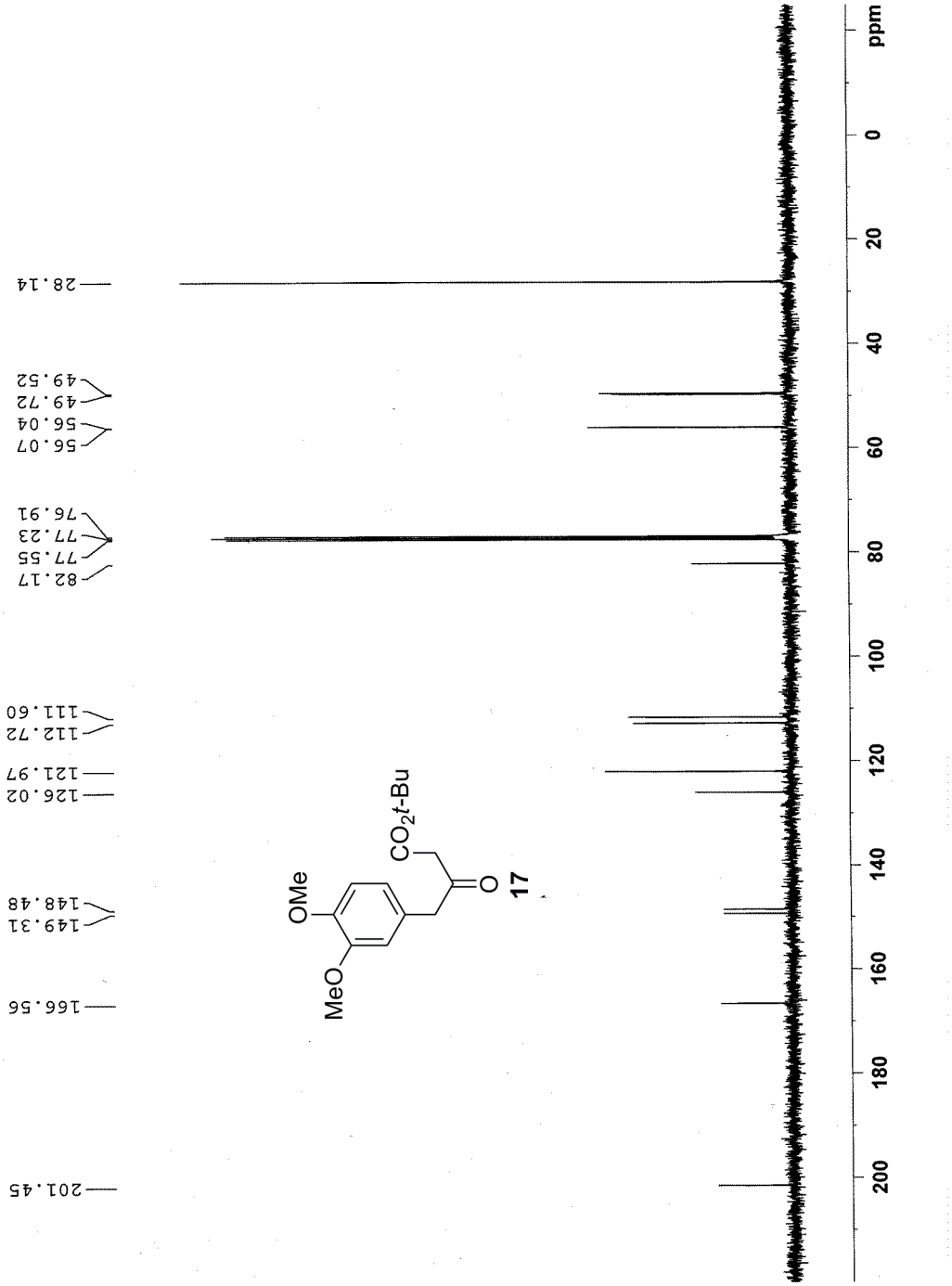

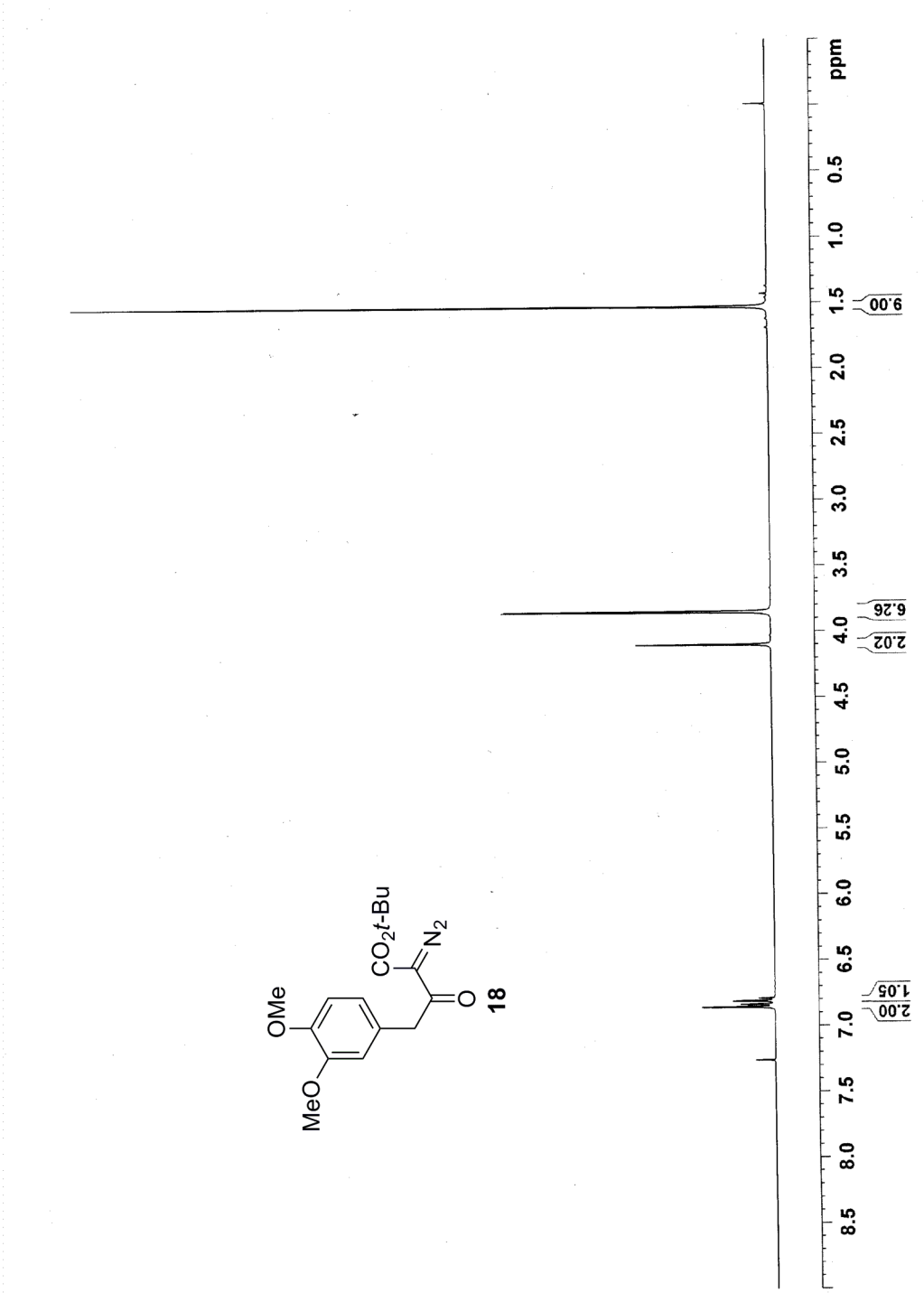

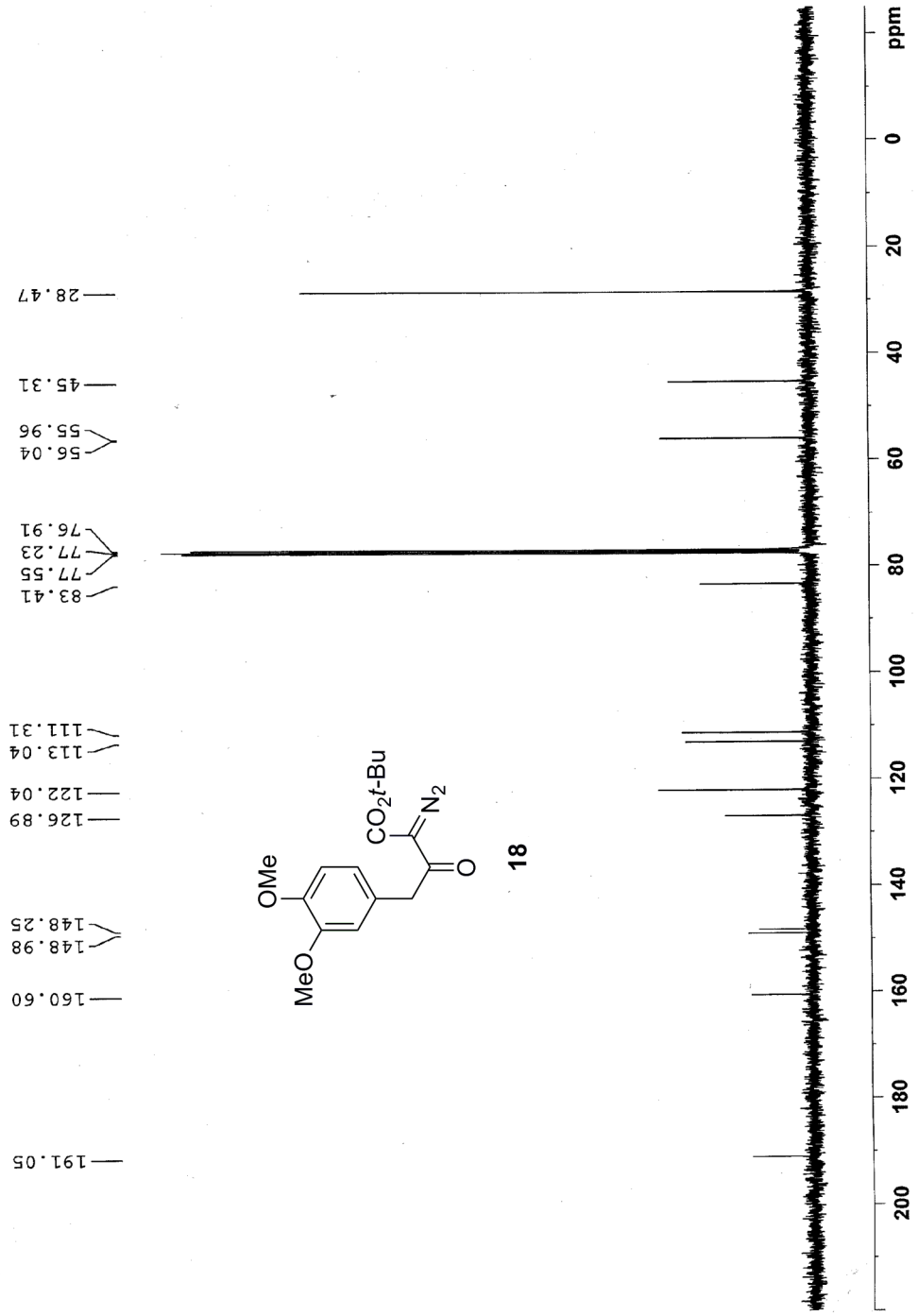

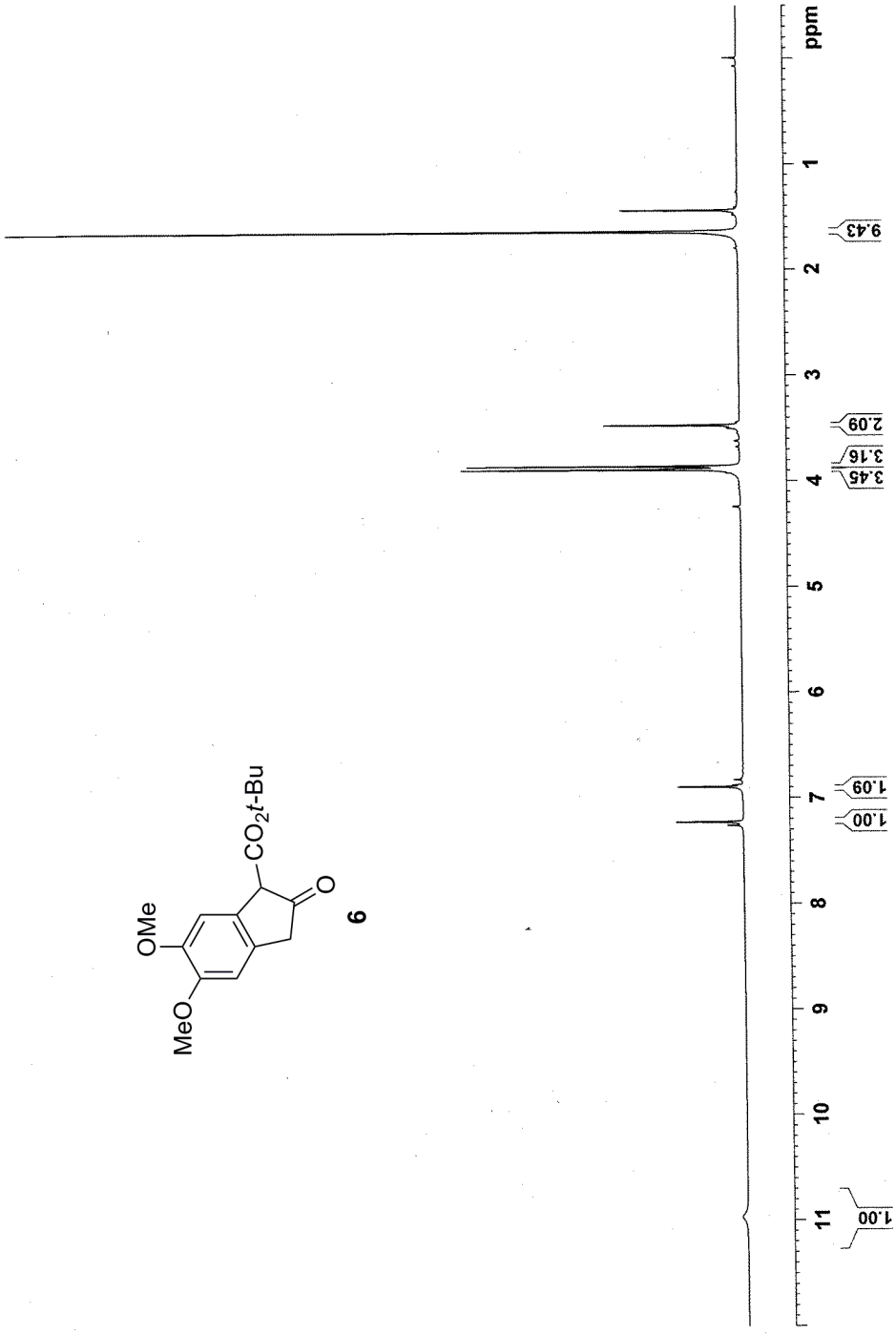

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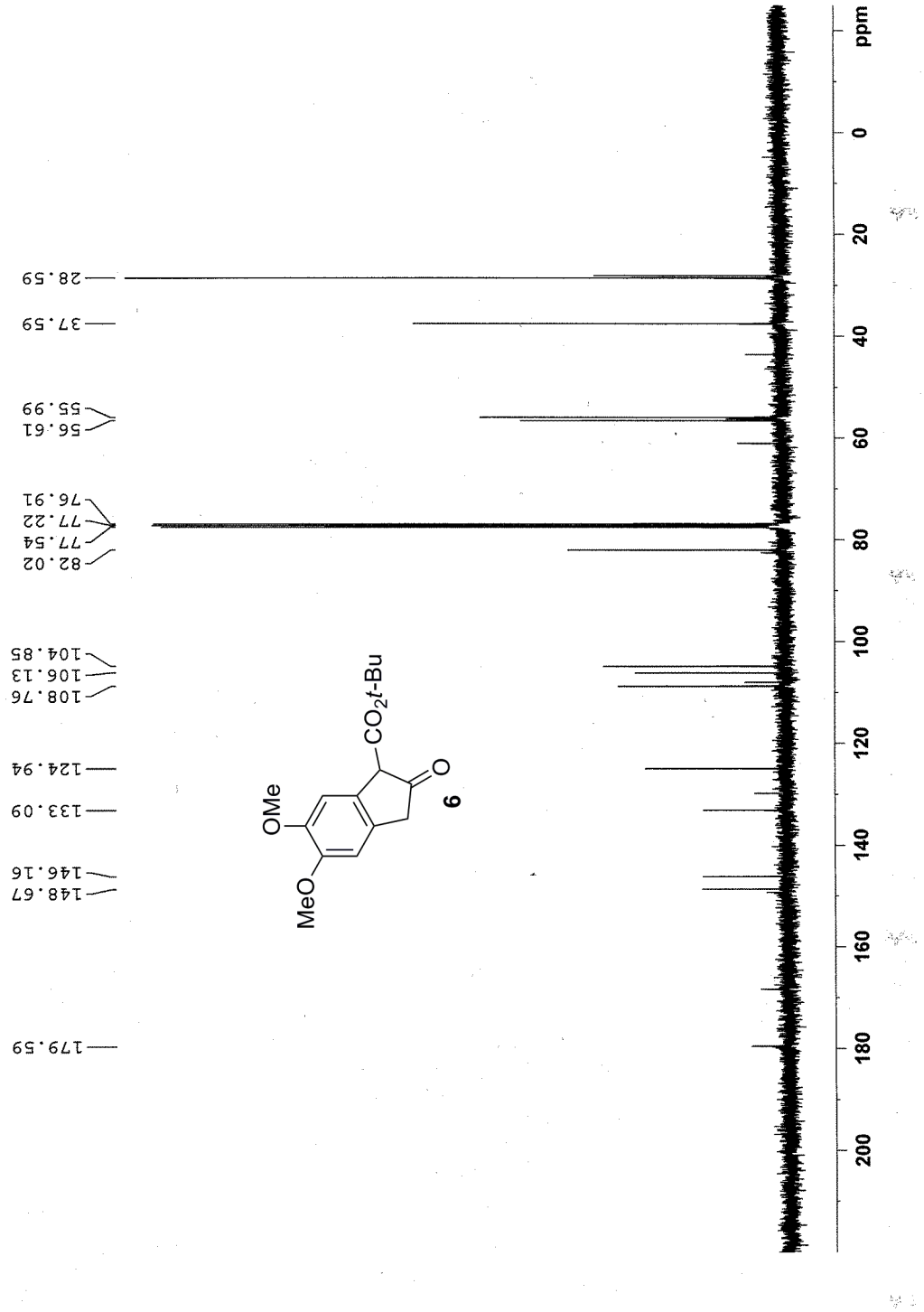

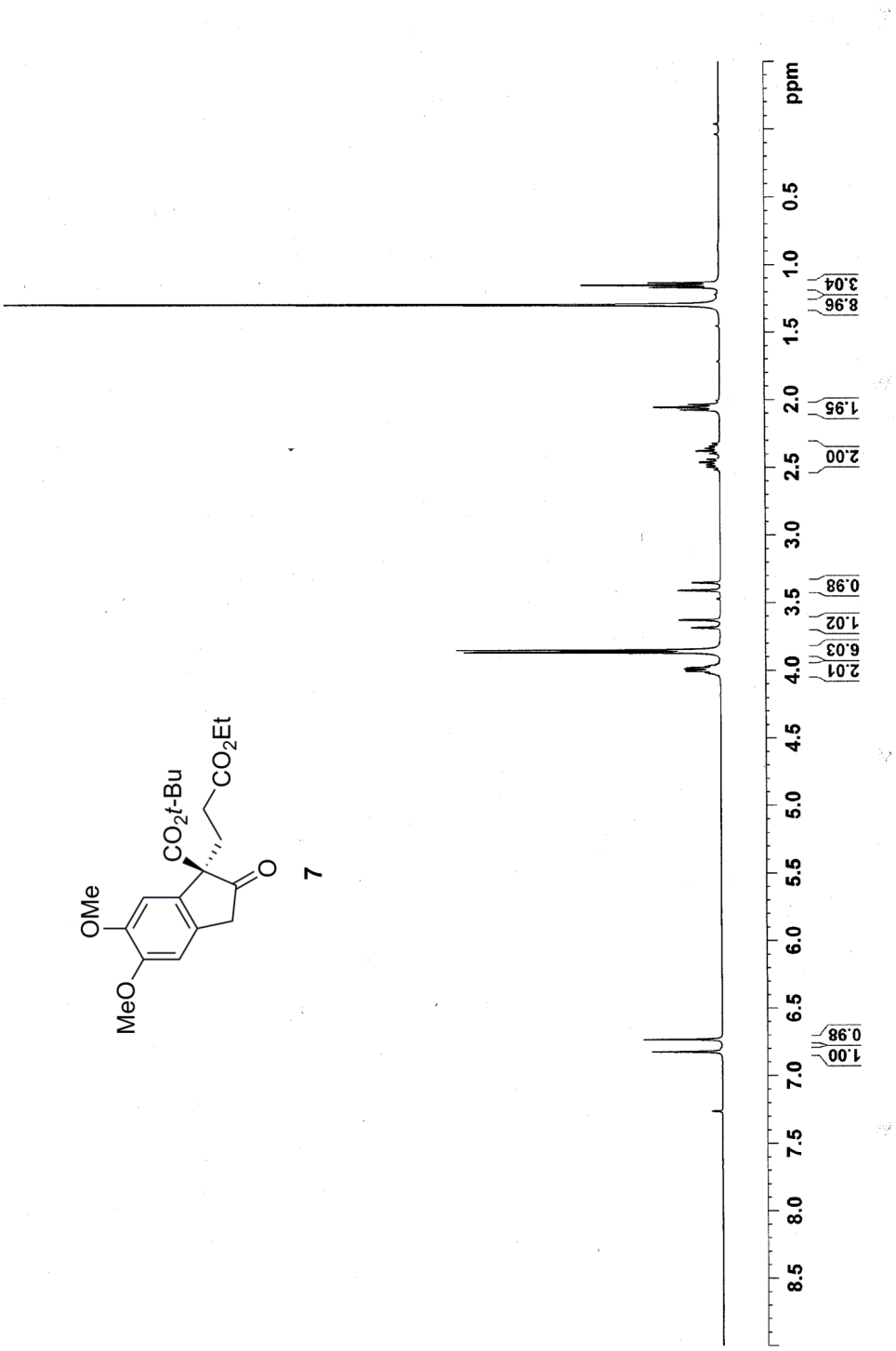

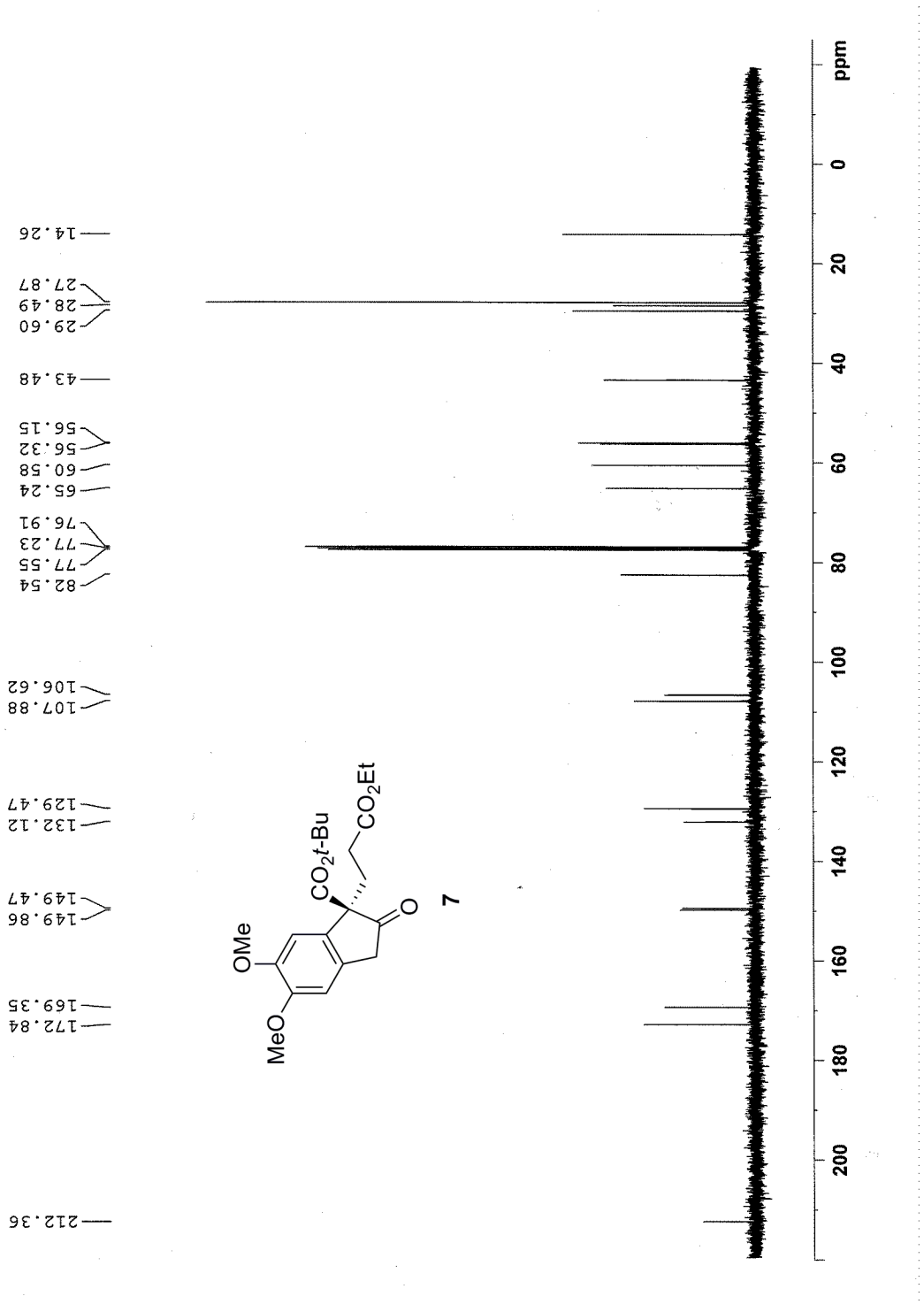

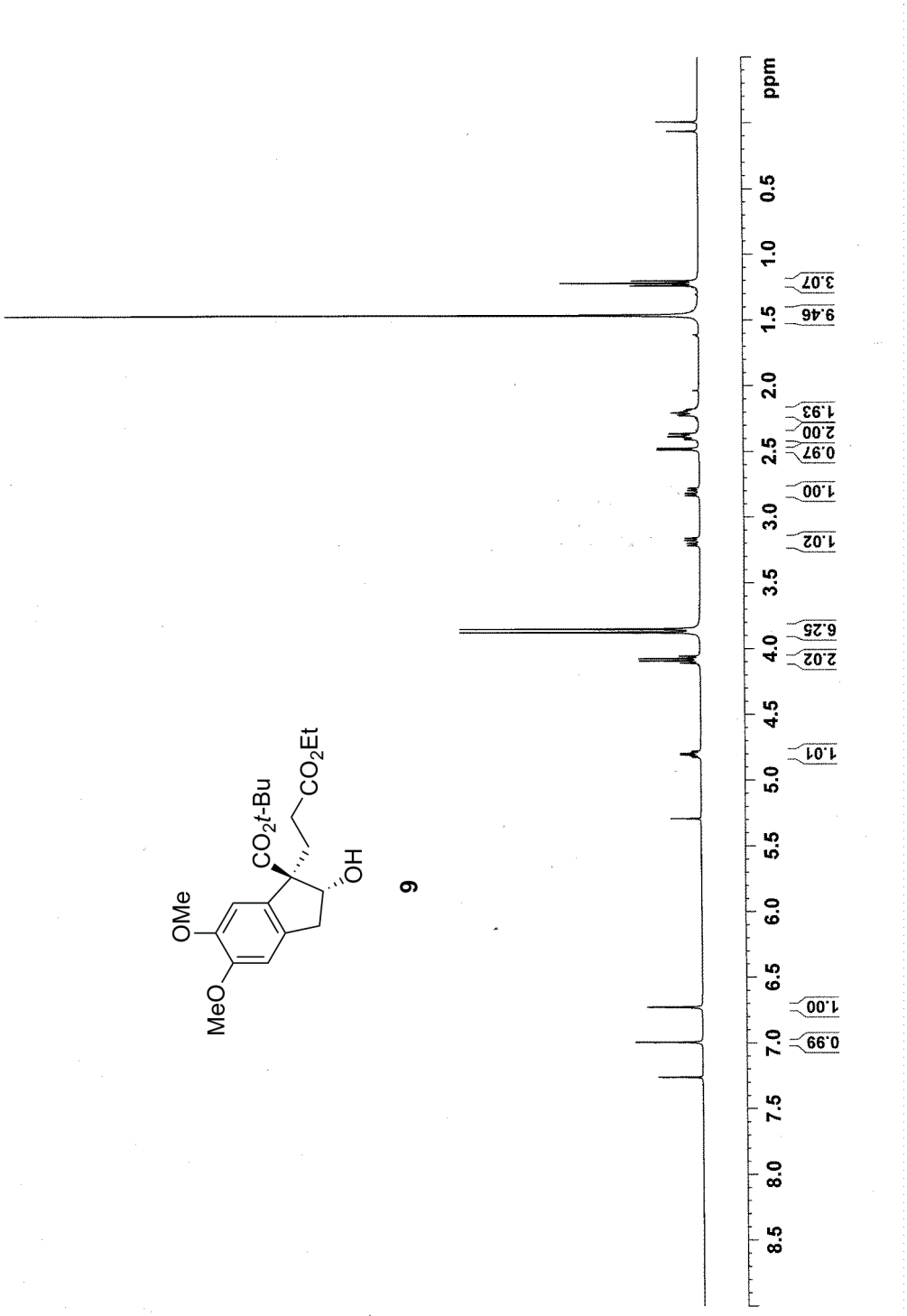

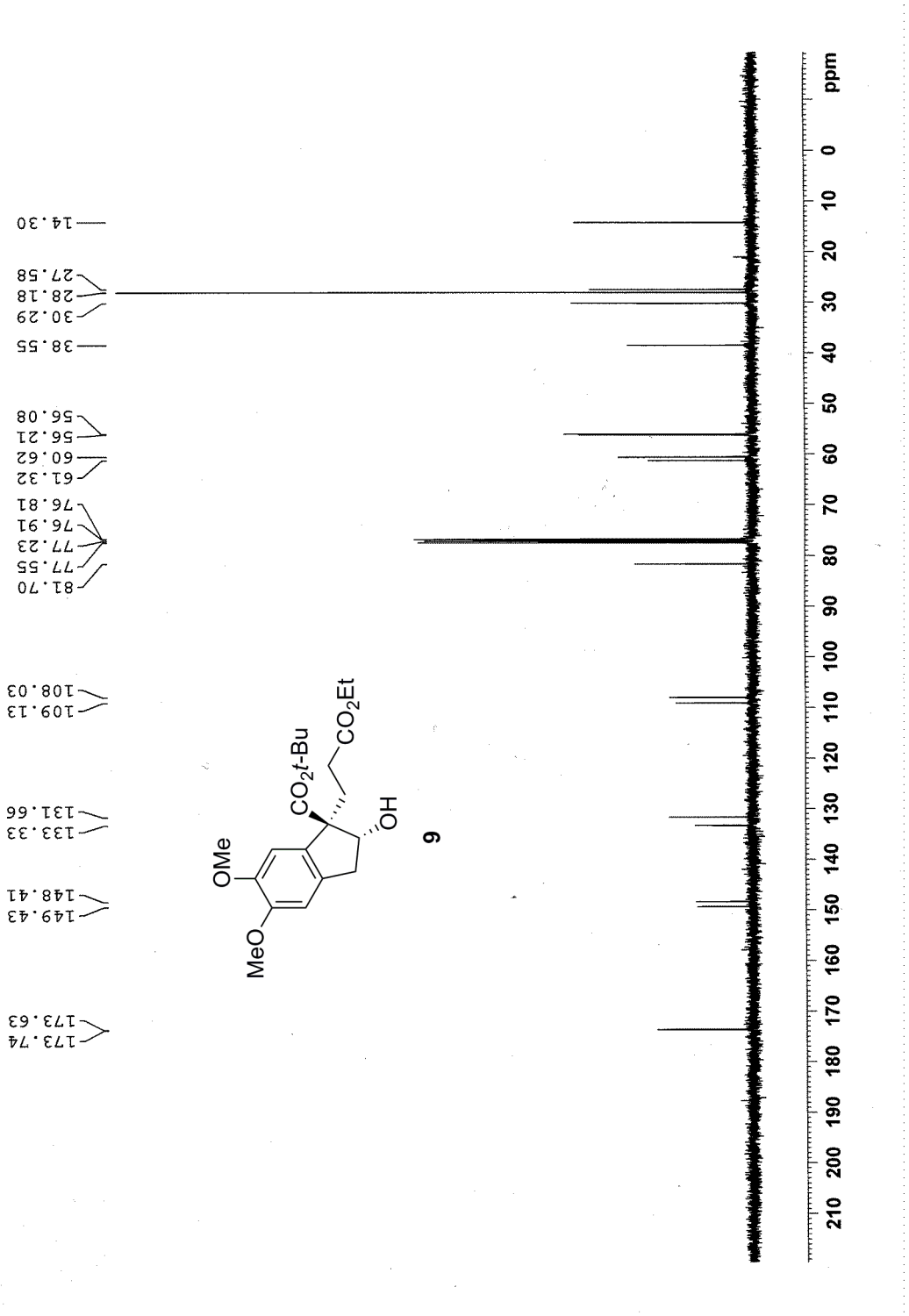

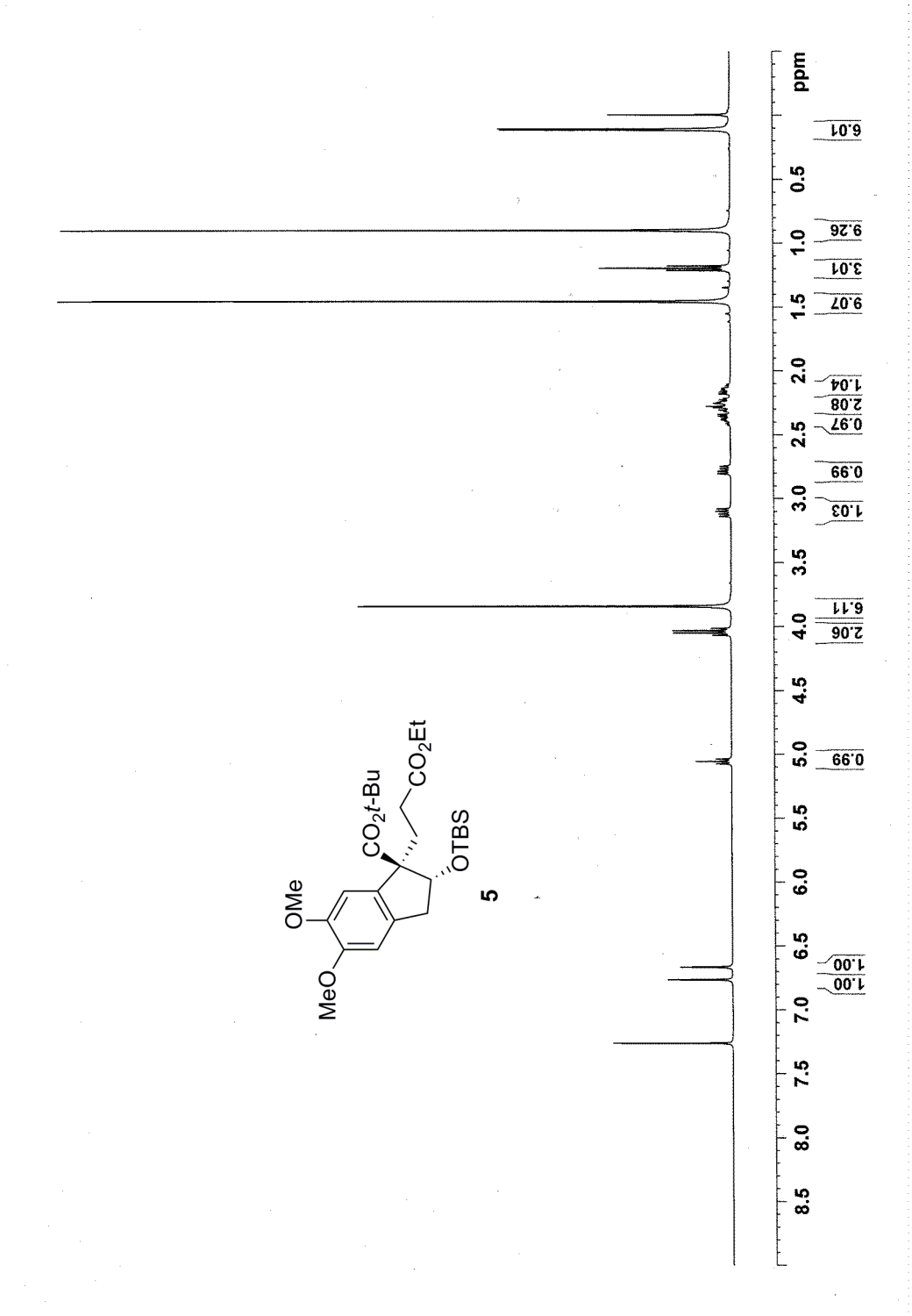

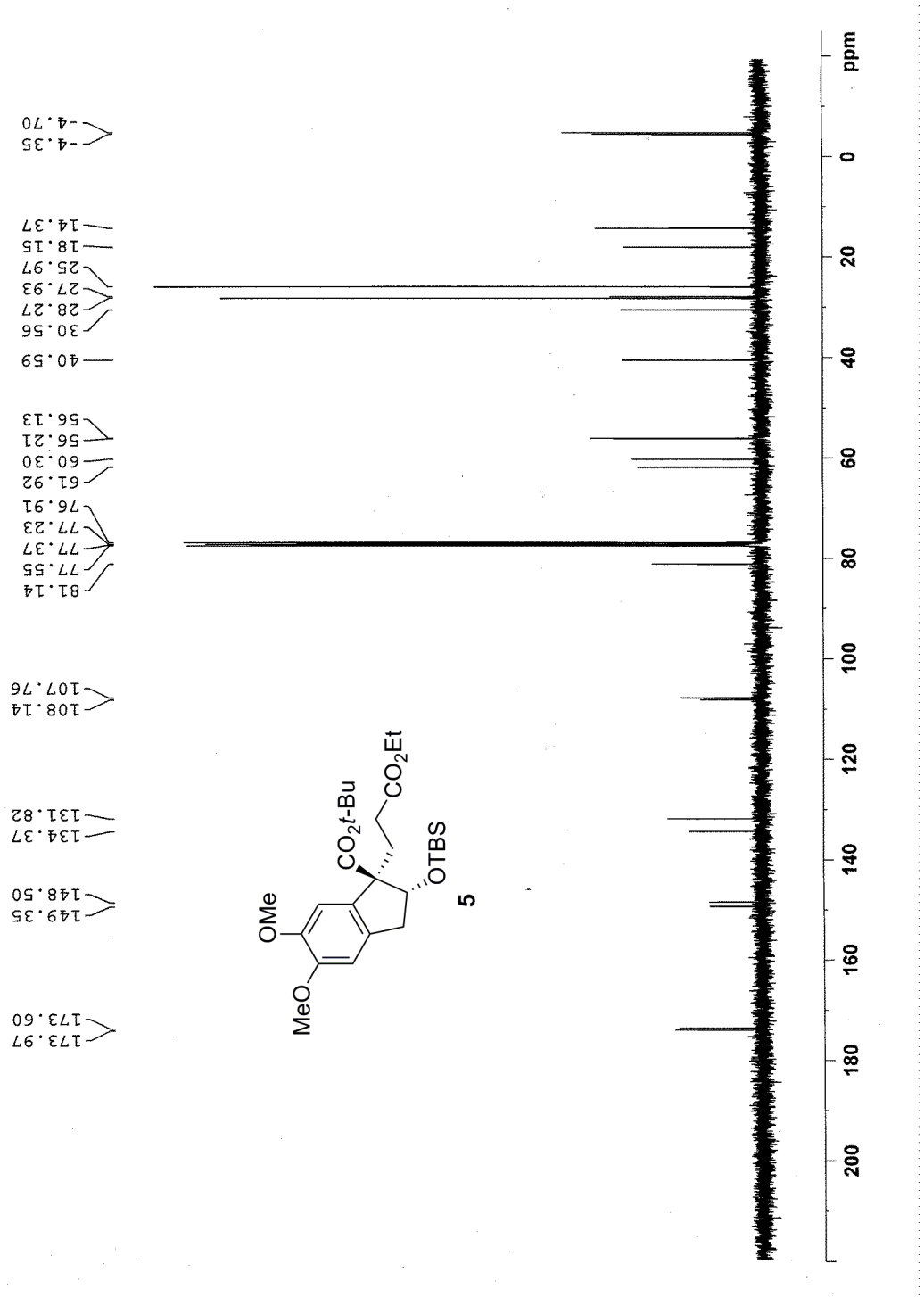

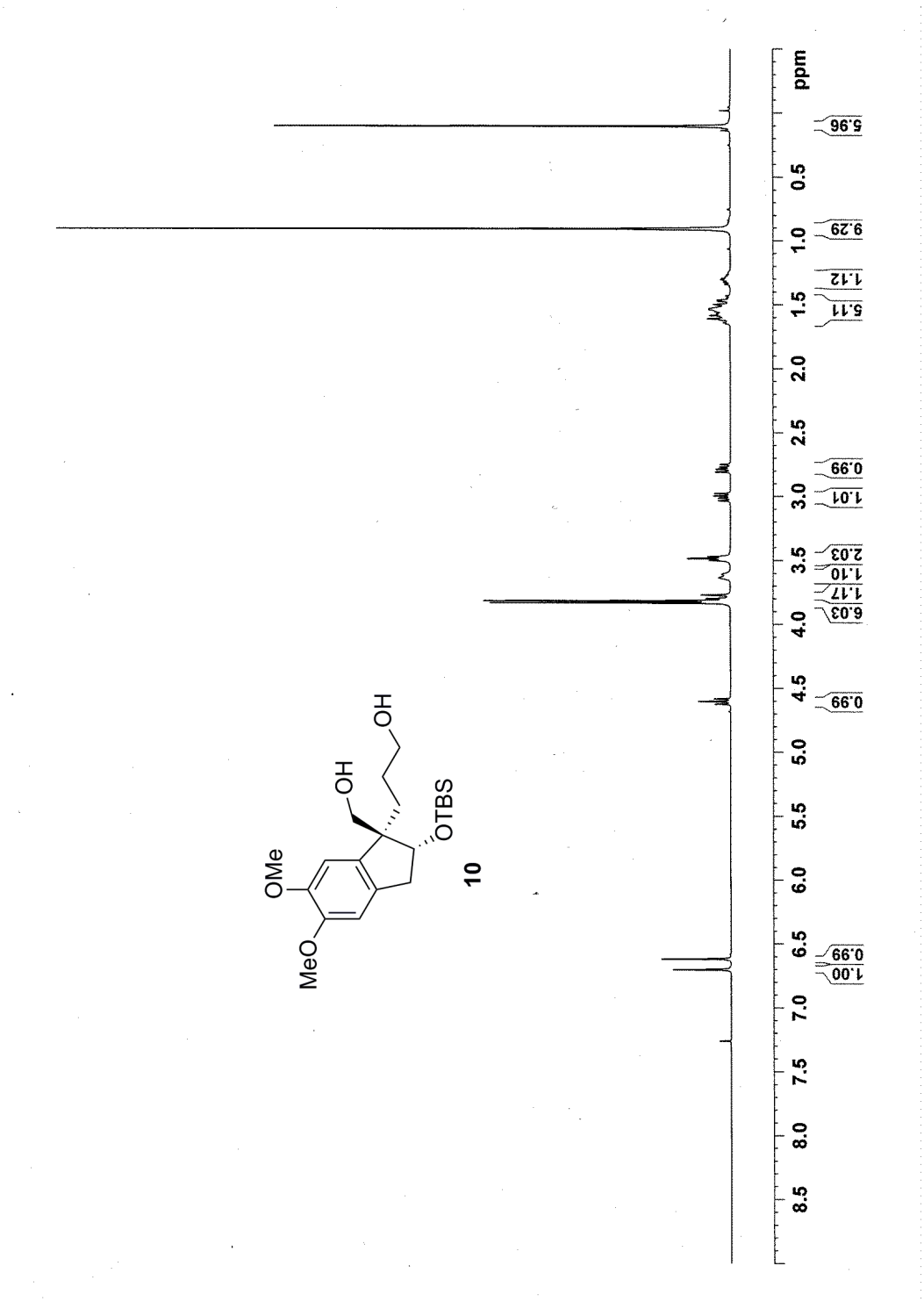

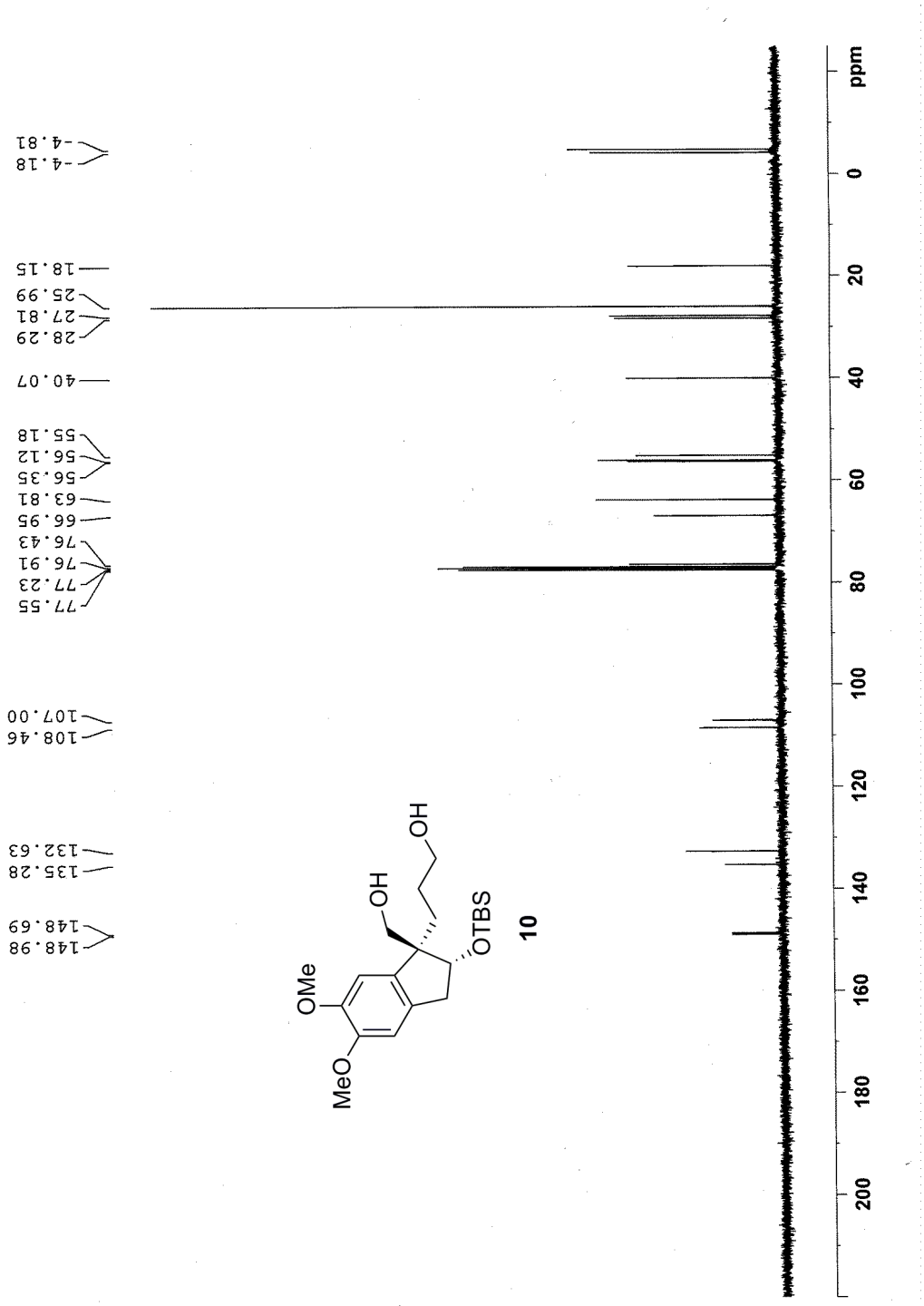

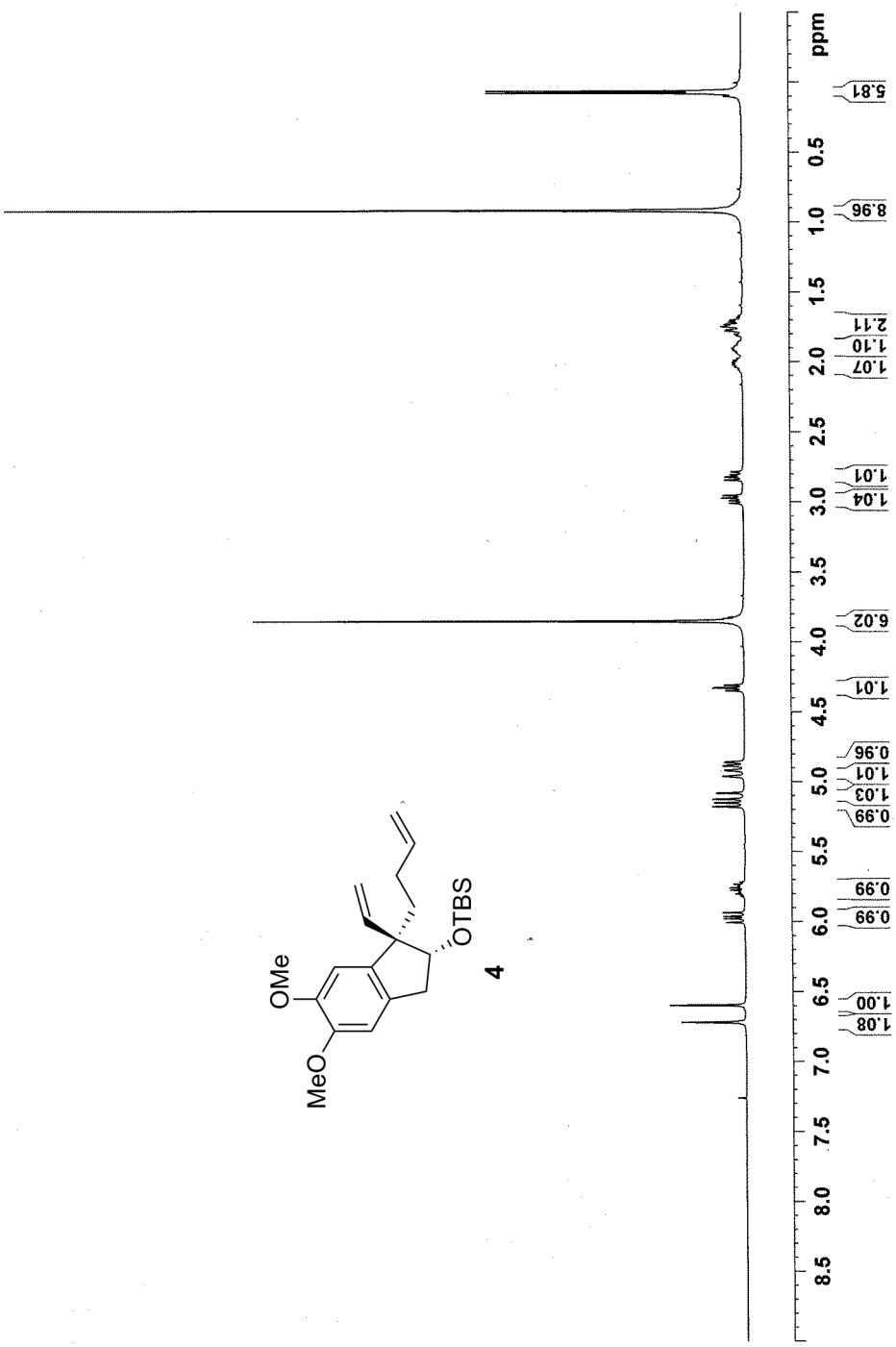

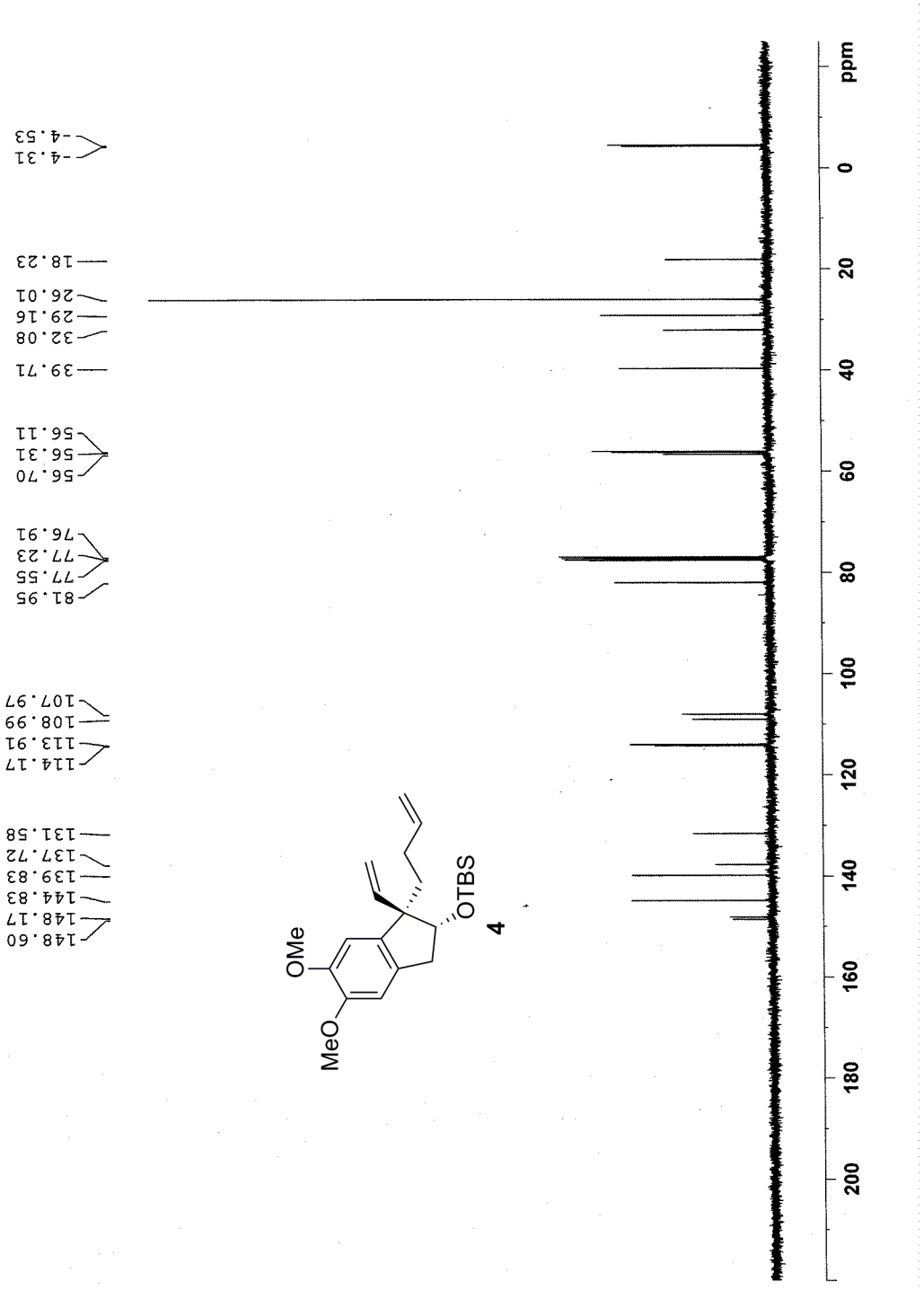

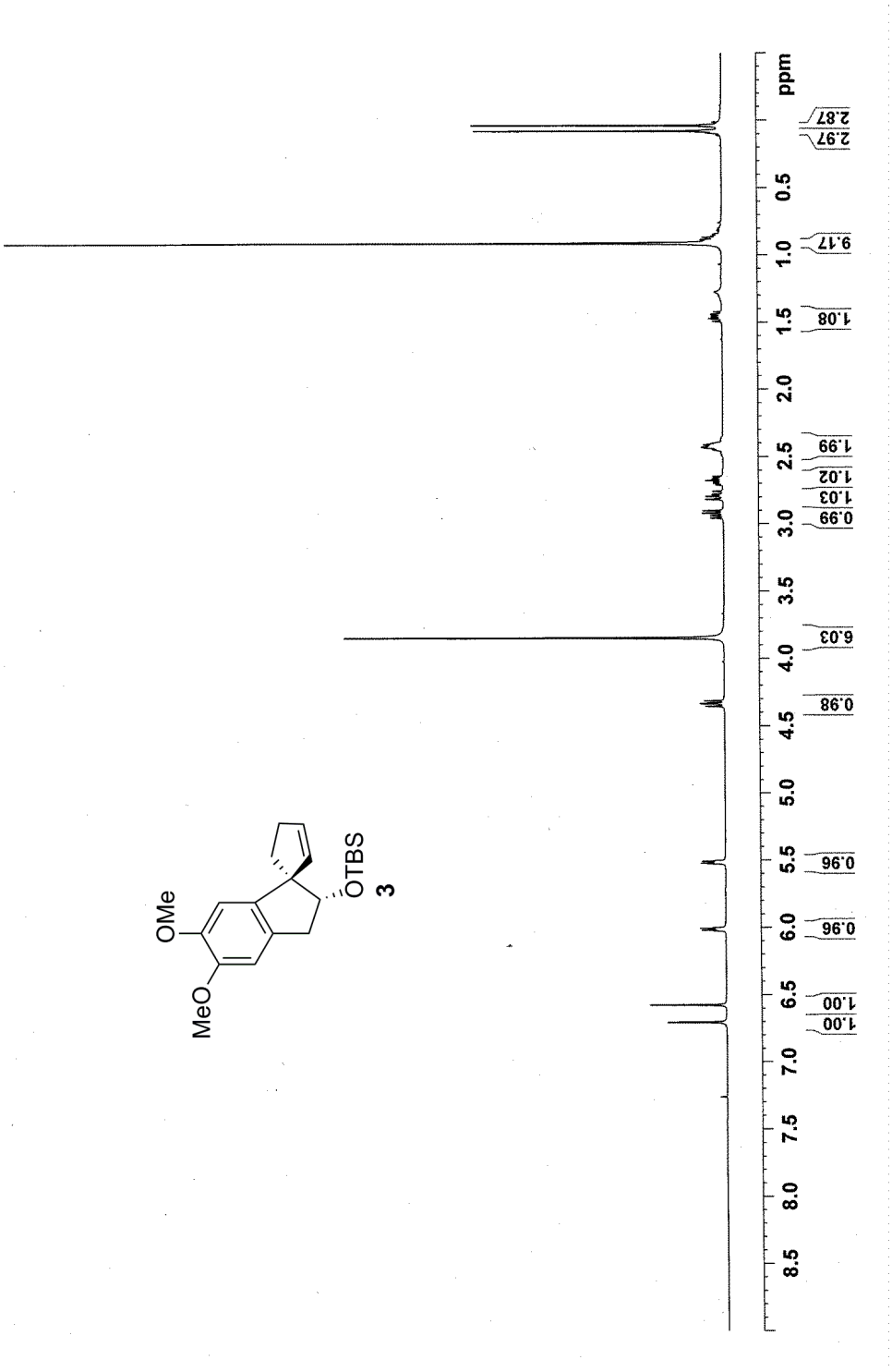

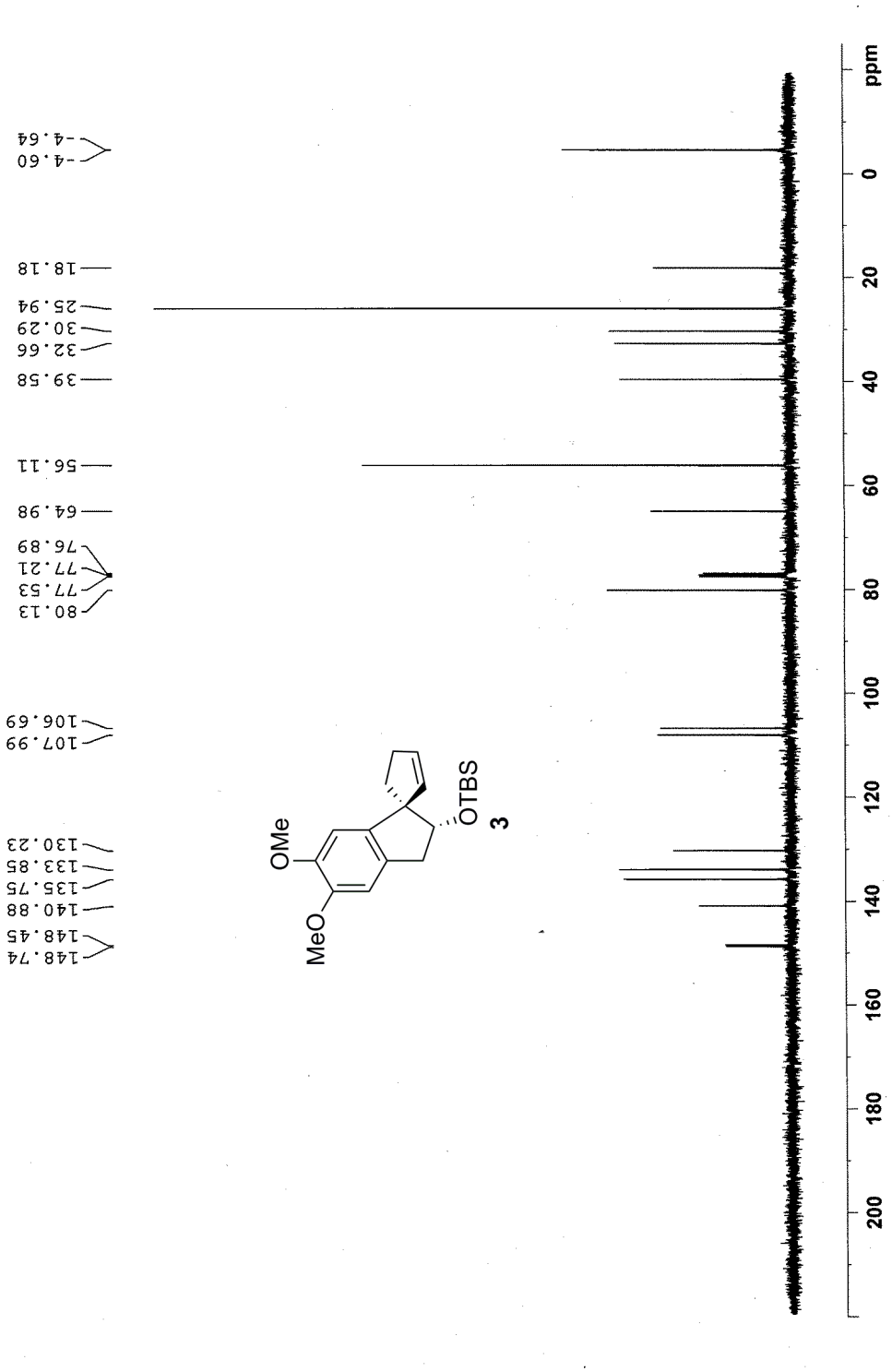

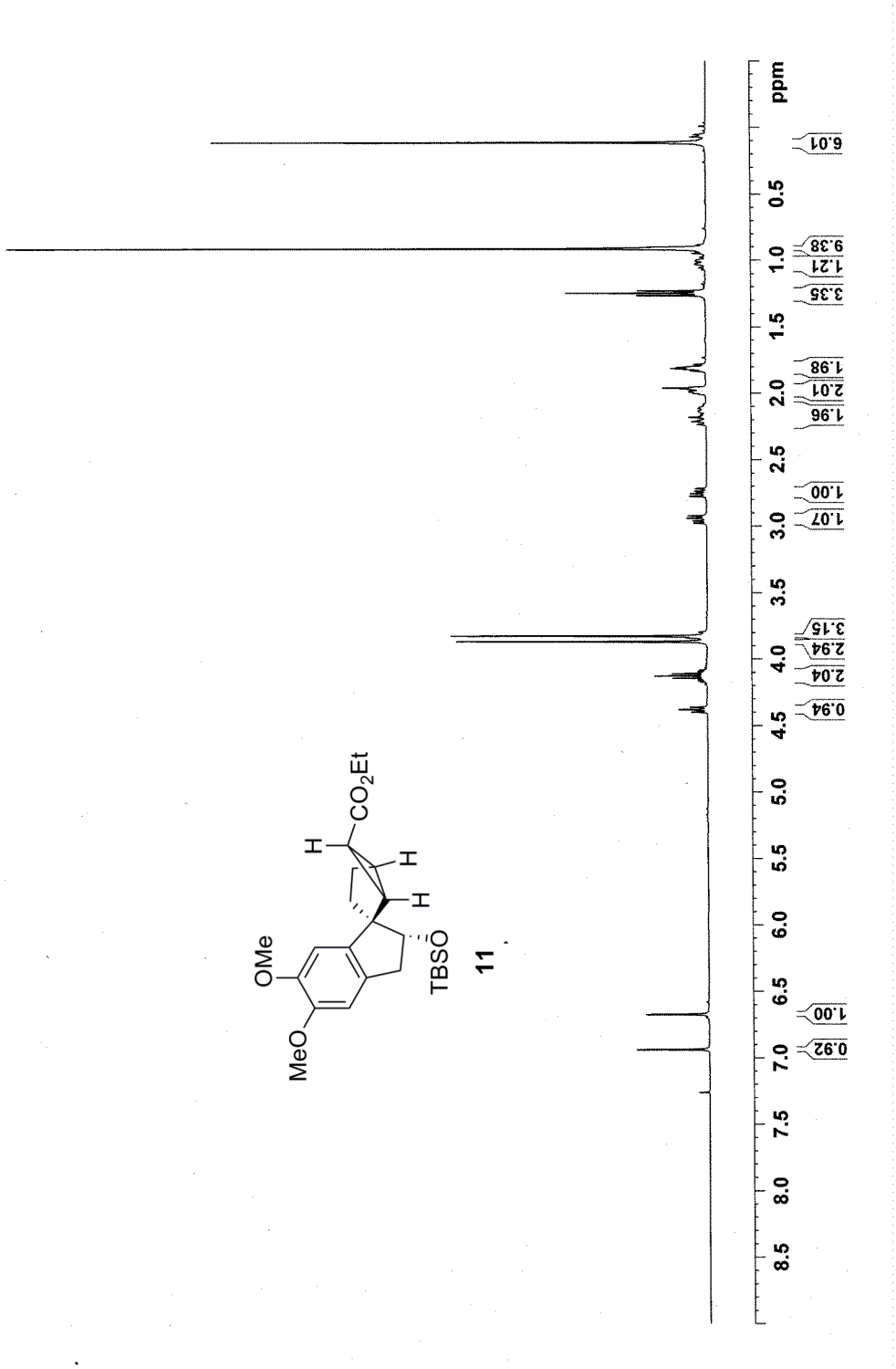

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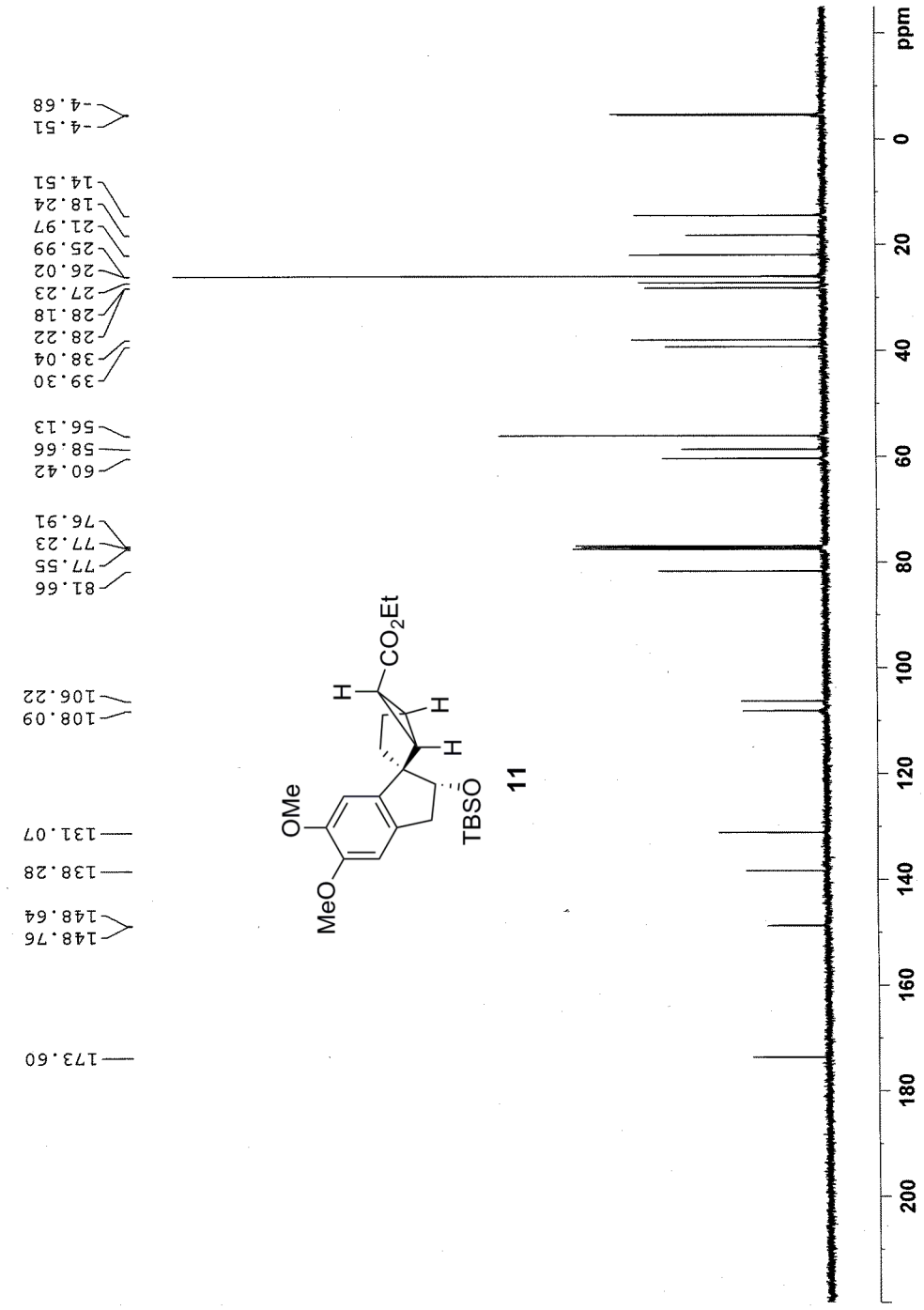

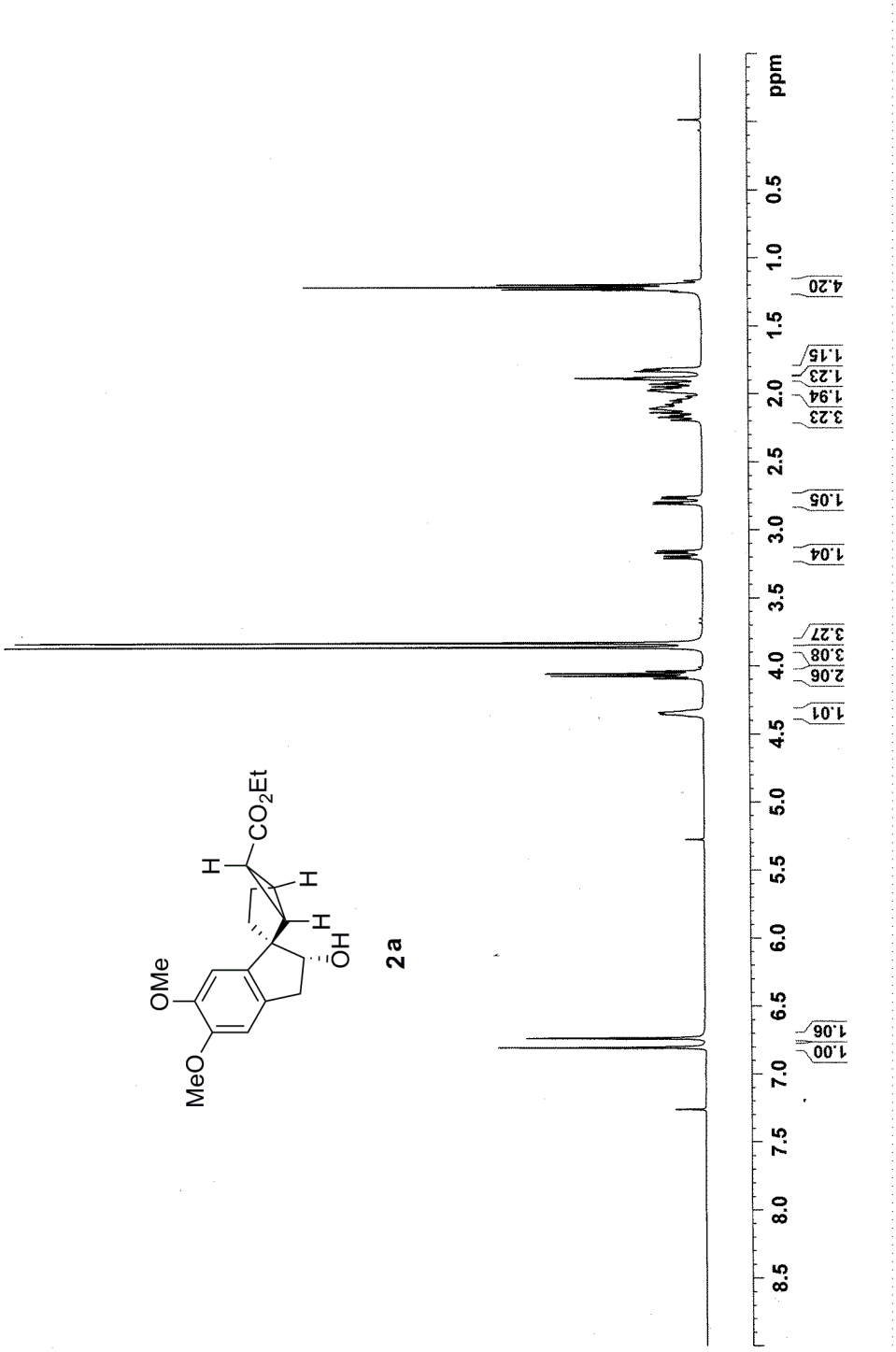

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