Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Stereodivergent Synthesis of 17-α and 17-β–Aryl Steroids: Application and Biological Evaluation of D-Ring Cortistatin Analogs

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SUPPORTING INFORMATION

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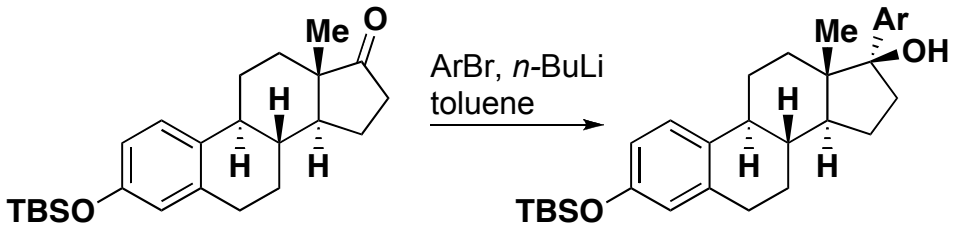
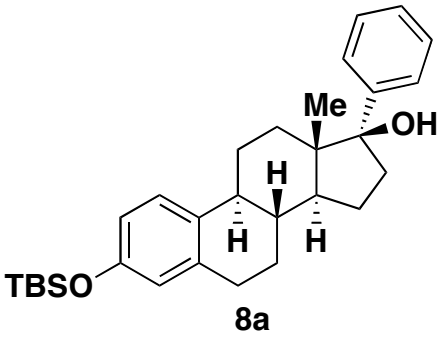
General procedures. All reactions were carried out under a nitrogen atmosphere with dry solvents using anhydrous conditions unless otherwise stated. Dry tetrahydrofuran (THF), diethyl ether, dichloromethane (CH_2Cl_2), benzene, toluene, methanol (MeOH), acetonitrile, 1,2-dimethoxyethane (DME), *N,N*-dimethylformamide (DMF), and triethylamine (Et_3N) were obtained by passing these previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as the visualizing agent and an acidic mixture of anisaldehyde, phosphomolybdic acid, or ceric ammonium molybdate, or basic aqueous potassium permangante ($KMnO_4$), and heat as developing agents. E. Merck silica gel (60, particle size 0.043–0.063 mm) was used for flash column chromatography. Preparative thin layer chromatography (PTLC) separations were carried out on 0.25 or 0.5 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 or Varian Inova-400 instruments and calibrated using residual undeuterated solvent as an internal reference ($CHCl_3$ @ 7.26 ppm ^{1}H NMR, 77.0 ppm ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. High-resolution mass spectra (HRMS) were recorded on Agilent LC/MSD TOF time-of-flight mass spectrometer by electrospray ionization time of flight reflectron experiments. IR spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus. Optical rotations were obtained on a Pekin-Elmer 431 Polarimeter.



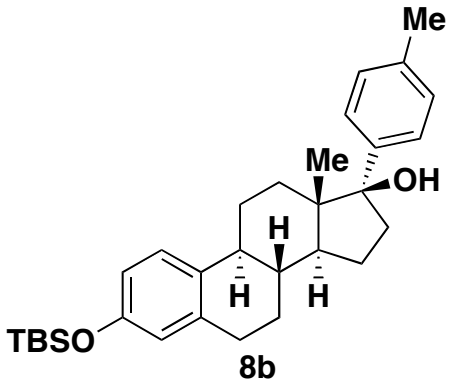
General Procedure A: ArBr (3 equiv) was dissolved in Et_2O (0.63 *M*) and cooled to –78 °C. *n*-BuLi (2.5 *M*, 3.0 equiv) was added dropwise. After 40 minutes, the mixture was warmed up to room temperature and cannulated into a toluene solution of O-TBS-estrone[1] (0.1 *M*, 1.0 equiv) at room temperature and stirred at that temperature for 40 minutes. The reaction was then quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc (3 times). The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by flash chromatography on silica.[2]



8a

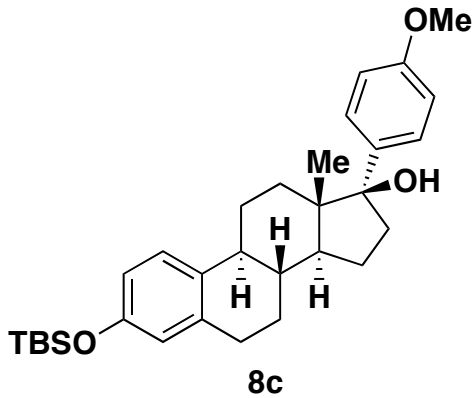
Alcohol 8a: Prepared from O-TBS-estrone (50 mg, 0.129 mmol) according to general procedure A. Purification by flash chromatography (1:2 hexanes:CH_2Cl_2) afforded alcohol **8a** (39 mg, 0.084 mmol, 65%) as a white solid (mp 156-159°C): R_f = 0.53 (1:4 pentanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +46.8° (*c* = 0.95, CH_2Cl_2); IR (neat) ν_{max} = 3459, 2929, 2360, 1495, 1252 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.7 Hz, 2 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.36 (dd, *J* = 13.0, 6.1Hz, 1 H), 7.09 (d, *J* = 8.5 Hz, 1 H), 6.65 (d, *J* = 8.4 Hz, 1 H), 6.63 (s, *J* = 2.6 Hz, 1 H), 2.96 – 2.84 (m, 2 H), 2.54 (ddd, *J* = 14.5, 9.7, 5.0 Hz, 1 H), 2.26 (dd, *J* =, 13.1, 4.3 Hz, 1H), 2.22 – 2.12 (m, 1 H), 2.05 – 1.98 (m, 3 H), 1.98 – 1.91 (m, 1 H), 1.77 – 1.69 (m, 2 H), 1.61 – 1.46 (m, 3 H), 1.43 – 1.32 (m, 1 H), 1.19 (s, 3 H), 1.07 (s, 9 H), 0.71 (dt, *J* = 12.9 , 4.0 Hz, 1H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 146.1, 137.8, 133.2, 127.5 (2 C), 127.4 (2 C), 127.0, 126.1, 120.0, 117.2, 86.1, 48.3, 47.1, 43.5, 39.6, 38.8, 33.8, 29.8, 27.6, 26.4, 25.9 (3 C), 24.3, 18.3, 15.0, -4.2 (2 C);

HRMS (ESI-TOF) calcd for $C_{30}H_{43}O_2Si$ $[M+H]^+$: 463.3027; found: 463.3020.



8b

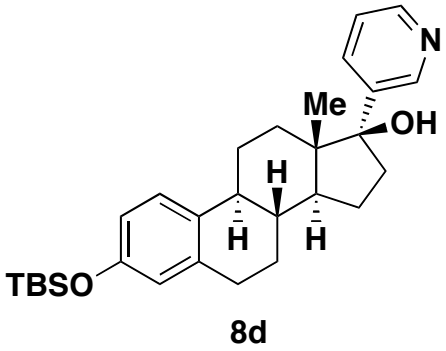
Alcohol 8b: Prepared from O-TBS-estrone (48 mg, 0.125 mmol) according to general procedure A. Purification by flash chromatography (1:2 hexanes:CH_2Cl_2) afforded alcohol **8b** (35 mg, 0.070 mmol, 56%) as a white solid (mp 120-123°C): R_f = 0.36 (1:5 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +38.2° (*c* = 0.45, CH_2Cl_2); IR (neat) ν_{max} = 3476, 2931, 1496, 1253 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.2 Hz, 2 H), 7.16 (d, *J* = 7.9 Hz, 2 H), 7.00 (d, *J* = 8.5 Hz, 1 H), 6.56 (dd, *J* = 8.4 , 2.6 Hz, 1 H), 6.53 (d, *J* = 2.5, 1 H), 2.86 – 2.74 (m, 2 H), 2.42 (ddd, *J* = 14.6, 9.8, 5.1 Hz, 1 H), 2.36 (s, 3 H), 2.17 – 2.08 (m, 2 H), 1.93 – 1.83 (m, 4 H), 1.66 – 1.57 (m, 2 H), 1.51 – 1.35 (m, 3 H), 1.33 – 1.24 (m, 1 H), 1.09 (s, 3 H), 0.97 (s, 9 H), 0.65 (dt, *J* = 12.9 , 4.1 Hz, 1H), 0.18 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 143.2, 137.9, 136.5, 133.3, 128.2 (2 C), 127.4 (2 C), 126.2, 120.0, 117.2, 86.0, 48.3, 47.1, 43.5, 39.6, 38.8, 33.8, 29.8, 27.6, 26.4, 25.9 (3 C), 24.2, 21.1, 18.3, 14.9, -4.2 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{44}O_2SiNa$ $[M+Na]^+$: 499.3003; found: 499.2988.



8c

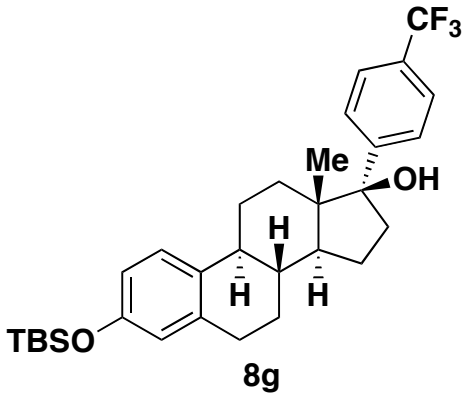
Alcohol 8c: Prepared from O-TBS-estrone (49 mg, 0.127 mmol) according to general procedure A. Purification by flash chromatography (1:2 hexanes:CH_2Cl_2) afforded alcohol **8c** (25 mg, 0.051 mmol, 40%) as a white foam: R_f = 0.30 (1:5 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +38.2° (*c* = 0.3, CH_2Cl_2); IR (neat) ν_{max} = 3463, 2928, 1607, 1497, 1251 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.5 Hz, 2 H), 7.01 (d, *J* = 8.4 Hz, 1 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 6.57 (dd, *J*

= 8.4, 2.3 Hz, 1 H), 6.54 (d, *J* = 2.0 Hz, 1 H), 3.83 (s, 3 H), 2.87 – 2.75 (m, 2 H), 2.41 (ddd, *J* = 14.4, 9.7, 4.9 Hz, 1 H), 2.18 – 2.10 (m, 2 H), 1.93 – 1.83 (m, 4 H), 1.66 – 1.57 (m, 2 H), 1.51 – 1.21 (m, 4 H), 1.09 (s, 3 H), 0.98 (s, 9 H), 0.67 (dt, *J* = 12.9, 4.0 Hz, 1H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3, 153.3, 138.2, 137.9, 133.2, 128.6 (2 C), 126.1, 120.0, 117.2, 112.8 (2 C), 85.8, 55.4, 48.3, 47.0, 43.5, 39.6, 38.8, 33.7, 29.8, 27.6, 26.4, 25.8 (3 C), 24.2, 18.3, 14.9, -4.3 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{45}O_3Si$ $[M+H]^+$: 493.3132; found: 493.3130.



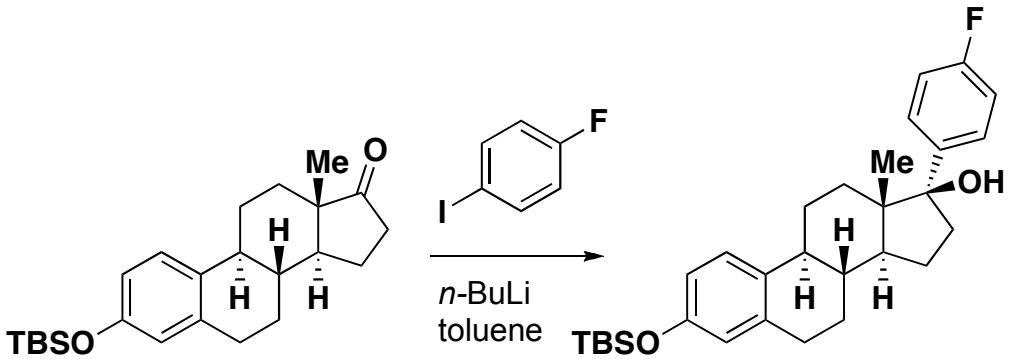
8d

Alcohol 8d: Prepared from O-TBS-estrone (50 mg, 0.131 mmol) according to general procedure A. Purification by flash chromatography (2:3 hexanes:EtOAc) afforded alcohol **8d** (34 mg, 0.073 mmol, 56%) as a white foam: R_f = 0.3 (1:2 hexanes:EtOAc); $[\alpha]^D_{20}$ = +39.0° (*c* = 0.41, CH_2Cl_2); IR (neat) ν_{max} = 3237, 2929, 1496, 1252 cm^{-1}; ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.56 (s, 1 H), 8.41 (d, *J* = 3.8 Hz, 1 H), 7.79 (d, *J* = 7.9 Hz 1 H), 7.27 – 7.25 (m, 1 H), 7.02 (d, *J* = 8.4 Hz, 1 H), 6.59 (dd, *J* = 8.4, 2.5 Hz, 1 H), 6.55 (d, *J* = 2.4, 1 H), 3.65 – 3.35 (b, 1 H), 2.89 – 2.76 (m, 2 H), 2.39 (ddd, *J* = 14.5, 9.6, 5.1 Hz, 1 H), 2.23 – 2.11 (m, 2 H), 1.93 – 1.83 (m, 3 H), 1.72 – 1.63 (m, 2 H), 1.55 – 1.39 (m, 2 H), 1.36 – 1.24 (m, 2 H), 1.13 (s, 3 H), 0.99 (s, 9 H), 0.56 (dt, *J* = 12.7, 3.9 Hz, 1H), 0.20 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 148.5, 147.74, 141.8, 137.7, 135.4, 132.9, 126.1, 122.4, 120.0, 117.2, 84.6, 48.3, 47.2, 43.4, 39.5, 38.5, 33.5, 29.7, 27.5, 26.2, 25.8 (3 C), 24.1, 18.2, 14.8, -4.3 (2 C); HRMS (ESI-TOF) calcd for $C_{29}H_{42}NO_2Si$ $[M+H]^+$: 464.2979; found: 464.2984.



8g

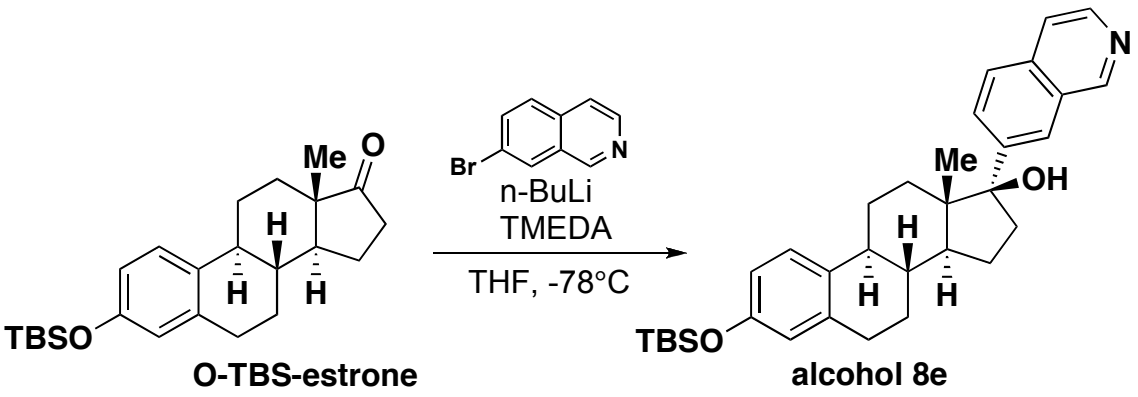
Alcohol 8g: Prepared from O-TBS-estrone (202 mg, 0.527 mmol) according to general procedure A. Purification by flash chromatography (1:2 hexanes:CH_2Cl_2) afforded alcohol **8g** (190 mg, 0.358 mmol, 68%) as a white foam: R_f = 0.6 (1:4 pentanes:CH_2Cl_2); $[\alpha]^{D}_{20}$ = +40.2° (*c* = 0.51, CH_2Cl_2); IR (neat) ν_{max} = 3443, 2927, 1496, 1328 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 6.57 (dd, *J* = 8.4, 2.2 Hz, 1 H), 6.54 (s, 1 H), 2.88 – 2.75 (m, 2 H), 2.44 (ddd, *J* = 14.3, 9.6, 4.9 Hz, 1 H), 2.21 – 2.10 (m, 2 H), 1.96 – 1.83 (m, 4 H), 1.73 – 1.59 (m, 2 H), 1.55 – 1.20 (m, 4 H), 1.11 (s, 3 H), 0.98 (s, 9 H), 0.55 (dt, *J* = 12.7, 3.7 Hz, 1H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 150.1, 137.7, 132.9, 129.1 (q, J_{CF} = 32.2 Hz), 127.85 (2 C), 124.4 (q, J_{CF} = 271.8 Hz), 124.3 (q, J_{CF} = 3.57 Hz, 2 C), 126.1, 120.0, 117.2, 86.1, 48.4, 47.3, 43.4, 39.6, 38.9, 33.6, 29.7, 27.5, 26.2, 25.8 (3 C), 24.2, 18.3, 14.9, -4.3 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{42}F_3O_2Si$ $[M+H]^+$: 531.2901; found: 531.2905.



O-TBS-estrone alcohol 8f

Alcohol 8f: 4-FC_6H_4I (0.78 mmol, 173 mg, 90 µl, 1.1 equiv) was dissolved in toluene (8.1 mL, 0.96 *M*) and cooled to –78 °C, after which *n*-BuLi (2.27 *M*, 0.78 mmol, 378 µl, 1.1 equiv) was added dropwise. After 40 minutes, the ArLi solution was warmed up to room temperature and cannulated into O-TBS-

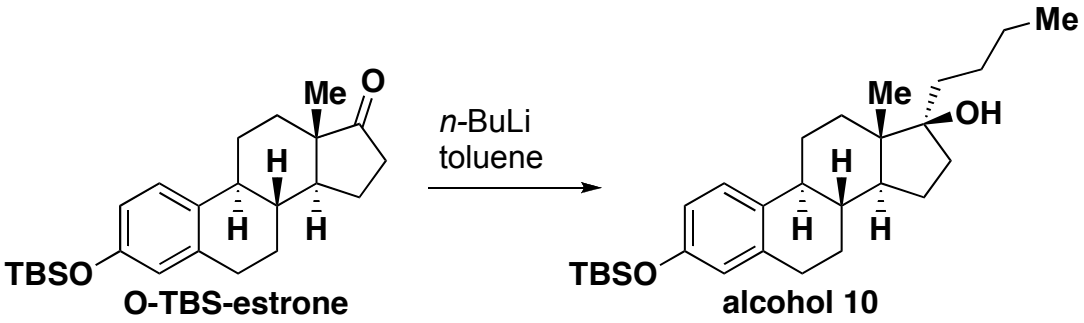
estrone (300 mg, 0.781 mmol, 1 equiv) in toluene (3.9 mL, 0.2 *M*) and the mixture was stirred for 30 minutes. The reaction was then quenched with sat. aq. $NaHCO_3$ (10 ml). The aqueous layer was extracted with EtOAc (20 ml × 4). The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Chromatography on silica (6% EtOAc in hexanes) afforded alcohol **8f** (263.5 mg, 0.549 mmol, 70%) as a white solid (mp 155-159°C): R_f = 0.32 (1:4 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +55.1° (*c* = 1.45, CH_2Cl_2); IR (neat) ν_{max} = 3462, 2928, 1605, 1496, 1252 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 7.5, 5.2 Hz, 2 H), 7.08 – 7.00 (m, 3 H), 6.57 (d, *J* = 8.5 Hz, 1 H), 6.54 (s, 1 H), 2.86 – 2.75 (m, 2 H), 2.44 (ddd, *J* = 14.5, 9.7, 5.0 Hz, 1 H), 2.17 – 2.10 (m, 2 H), 1.92 – 1.83 (m, 4 H), 1.67 – 1.58 (m, 2 H), 1.51 – 1.38 (m, 2 H), 1.35 – 1.25 (m, 2 H), 1.09 (s, 3 H), 0.98 (s, 9 H), 0.60 (dt, *J* = 12.8, 3.8 Hz, 1H), 0.18 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6 (d, J_{CF} = 245.3 Hz), 154.1, 142.5 (d, J_{CF} = 3.0 Hz), 138.6, 133.8, 129.9 (d, J_{CF} = 7.7 Hz, 2 C), 126.9, 120.7, 118.0, 114.9 (d, J_{CF} = 21.0 Hz, 2 C), 86.6, 49.0, 47.8, 44.3, 40.3, 39.7, 34.4, 30.5, 28.3, 27.1, 26.6 (3 C), 24.9, 19.1, 15.6, -4.3 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{42}FO_2Si$ $[M+H]^+$: 481.2932; found: 481.2944.



O-TBS-estrone **alcohol 8e**

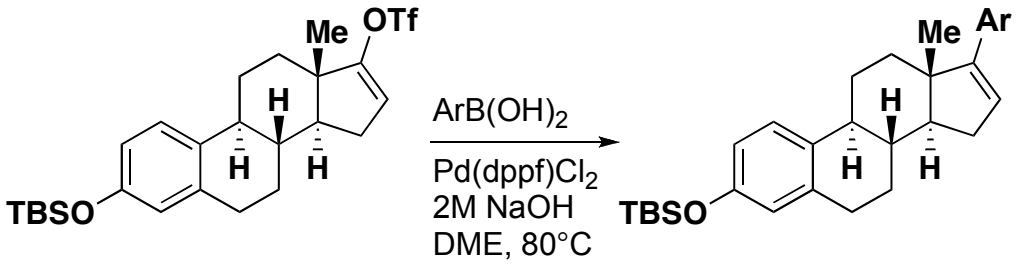
Alcohol 8e: To a THF solution of 7-bromoisoquinoline (40 mg, 0.193 mmol, 1 mL, 0.19 *M*, 3 equiv) was added *n*-BuLi (88μL, 2.3 *M*, 0.19 mmol, 3 equiv) dropwise at –78 °C. After 40 minutes, TMEDA (88μL, 0.58 mmol, 9 equiv) was added and the mixture was stirred at –78 °C for 10 minutes.[3] A THF solution of

O-TBS-estrone (25 mg, 0.065 mmol, 1 equiv, 0.3 mL, 0.22 *M*) was added and the reaction mixture was stirred for 40 minutes at –78 °C. The reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The aqueous layer was extracted with EtOAc (20 mL × 4). The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Chromatography on silica (30% EtOAc in hexanes) afforded alcohol **8e** (25 mg, 0.049 mmol, 74%) as a yellow solid (mp 183-185°C): R_f = 0.31 (1:1 EtOAc:CH_2Cl_2); $[\alpha]^D_{20}$ = +16.9° (*c* = 0.54, CH_2Cl_2); IR (neat) ν_{max} = 3210, 1496, 1285, 1251, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.28 (s, 1 H), 8.51 (d, *J* = 4.8 Hz, 1 H), 7.88 (d, *J* = 7.8 Hz, 2 H), 7.79 (d, *J* = 8.9 Hz, 1 H), 7.65 (d, *J* = 5.6 Hz, 1 H), 6.95 (d, *J* = 8.3 Hz, 1 H), 6.55 – 6.50 (m, 2 H), 2.73 – 2.87 (m, 2 H), 2.59 (ddd, *J* = 14.8, 9.8, 5.1 Hz, 1 H), 2.25 (ddd, *J* = 17.1, 12.5, 4.4 Hz, 1 H), 2.10 – 2.00 (m, 2 H), 1.96 – 1.91 (m, 1 H), 1.79 (td, *J* = 11.2, 4.0 Hz, 1 H), 1.75 – 1.65 (m, 2 H), 1.55 – 1.45 (m, 1 H), 1.47 – 1.32 (m, 1 H), 1.33 – 1.22 (m, 2 H), 1.15 (s, 3 H), 0.95 (s, 9 H), 0.57 (td, *J* = 12.8, 4.1 Hz, 1 H), 0.16 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 152.8, 145.2, 142.9, 137.6, 134.6, 132.8, 130.8, 127.9, 125.9, 125.3, 125.2, 120.0, 119.8, 117.0, 86.1, 48.3, 47.4, 43.3, 39.5, 38.9, 33.7, 29.6, 27.4, 26.1, 25.7 (3 C), 24.2, 18.1, 14.8, -4.4 (2 C) ; HRMS (ESI-TOF) calcd for $C_{33}H_{44}NO_2Si$ $[M+H]^+$: 514.3136; found: 514.3140.

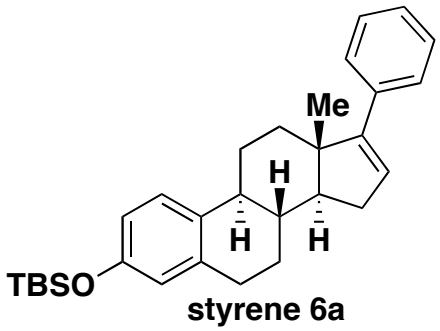


Alcohol 10: O-TBS-estrone (30 mg, 0.078 mmol, 1 equiv) was dissolved in toluene (0.78 mL, 0.1 *M*). *n*-BuLi (2.5 *M*, 0.23 mL, 3 equiv) was added dropwise at room temperature and stirred for 40 minutes. The reaction was then quenched with sat. aq. $NaHCO_3$ (5 mL). The aqueous layer was extracted with EtOAc

(3 × 10 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Chromatography on silica (10% EtOAc in hexanes) afforded alcohol **10** (22.5 mg, 0.051 mmol, 65 %) as a white solid (mp 85-89°C): R_f = 0.30 (1:4 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +26.9° (*c* = 0.84, CH_2Cl_2); IR (neat) ν_{max} = 3443, 2930, 1605, 1496, 1286, 1252, 954 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.5 Hz, 1 H), 6.61 (dd, *J* = 8.4, 2.5 Hz, 1 H), 7.08 – 7.00 (m, 3 H), 6.55 (d, *J* = 2.4 Hz, 1 H), 2.86 – 2.75 (m, 2 H), 2.34 – 2.26 (m, 1 H), 2.18 – 2.13 (m, 1 H), 2.05 – 1.99 (m, 1 H), 1.90 – 1.85 (m, 1 H), 1.66 – 1.51 (m, 6 H), 1.51 – 1.49 (m, 4 H), 1.43 – 1.23 (m, 6 H), 0.98 (s, 9 H), 0.95 (t, *J* = 7.1 Hz, 3H), 0.91 (s, 3 H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 137.9, 133.1, 126.1, 126.1, 119.9, 117.1, 83.5, 49.5, 46.7, 43.9, 39.6, 36.5, 34.4, 31.6, 29.7, 27.6, 26.3, 25.9, 25.7 (3 C), 23.6, 23.4, 18.2, 14.4, 14.3, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{28}H_{47}O_2Si$ $[M+H]^+$: 443.3340; found: 443.3324.

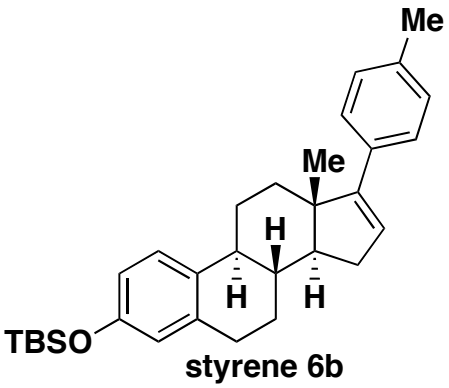


General Procedure B: Vinyl triflate[4] (1.0 equiv), $ArB(OH)_2$ (1.3 equiv) and $Pd(dppf)Cl_2$ (10 mmol%) were dissolved in DME (0.1 *M*) and 2 *M* NaOH (1.3 equiv) was added. The solution was degassed for 10 minutes by bubbling with Ar under sonication. The reaction was then immersed in an oil bath preheated to 80°C for 1 hour. The reaction was allowed to cool to ambient temperature, diluted with EtOAc, and washed with sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc (3 times). The combined organic portions were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by flash chromatography on silica. (**Note: vinyl triflate was prepared according to ref. 4 and 90% yield from O-TBS-Estrone**)



styrene 6a

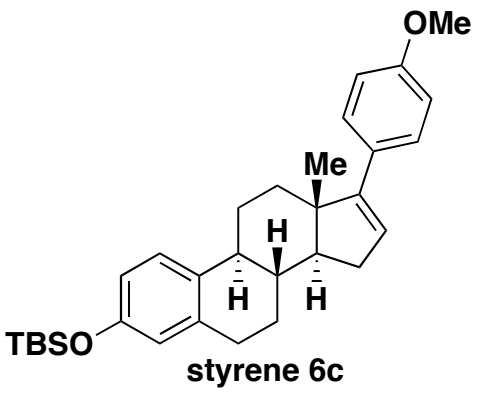
Stryrene 6a: Prepared from vinyl triflate (48 mg, 0.093 mmol) according to general procedure B. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded stryrene **6a** (34 mg, 0.076 mmol, 82%) as a white solid (mp 108-111°C): R_f = 0.27 (9:1 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +29.7° (*c* = 0.4, CH_2Cl_2); IR (neat) ν_{max} = 2932, 1495, 1258 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.33 – 7.28 (m, 2 H), 7.25 – 7.21 (m, 1 H), 7.12 (d, *J* = 8.4 Hz, 1 H), 6.62 (dd, *J* = 8.4, 2.6 Hz, 1 H), 6.58 (d, *J* = 2.6 Hz, 1 H), 5.94 (dd, *J* = 3.2, 1.8 Hz, 1 H), 2.94 – 2.80 (m, 2 H), 2.38 – 2.27 (m, 3 H), 2.20 (dd, *J* = 8.5, 2.3 Hz, 1H), 2.12 (ddd, *J* = 15.5, 11.4, 1.7 Hz, 1 H), 1.98 – 1.92 (m, 1 H), 1.80 (dt, *J* = 11.3, 6.5 Hz, 1 H), 1.72 – 1.61 (m, 3 H), 1.52 – 1.41 (m, 1 H), 1.07 (s, 3 H), 0.98 (s, 9 H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 153.5, 138.0, 137.5, 133.5, 128.3 (2 C), 127.4, 126.9, 126.8 (2 C), 126.0, 120.1, 117.2, 57.0, 47.7, 44.3, 37.4, 35.7, 31.5, 29.7, 27.9, 26.7, 25.9 (3 C), 18.3, 16.9, -4.2 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{41}OSi$ $[M+H]^+$: 445.2921; found: 445.2903.



styrene 6b

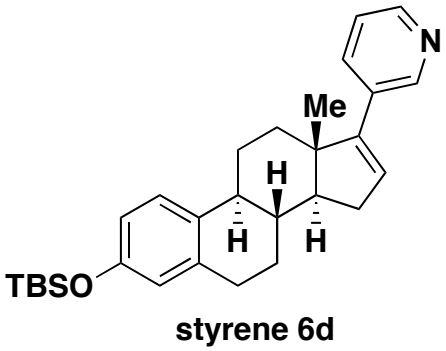
Styrene 6b: Prepared from vinyl triflate (49 mg, 0.095 mmol) according to general procedure B. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded styrene **6b** (37 mg, 0.081 mmol, 85%) as a white solid (mp 103-107°C): R_f = 0.31(10% CH_2Cl_2 in hexanes); $[\alpha]^D_{20}$ = +24.2° (*c* = 0.75, CH_2Cl_2); IR (neat) ν_{max} = 2931, 1738, 1494, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.1 Hz, 2 H), 7.14 (d, *J* = 8.0 Hz, 3 H), 6.63 (dd, *J* = 8.4, 2.6 Hz, 1 H), 6.59 (d, *J* = 2.5 Hz, 1 H), 5.91 (dd, *J* = 3.2, 1.7 Hz, 1 H), 2.95 – 2.81 (m, 2 H), 2.40 (s, 1 H), 2.36 (s, 3 H), 2.34 – 2.28 (m, 2 H), 2.21 (dd, *J* = 8.4 , 2.4 Hz, 1 H), 2.11 (ddd, *J* = 15.4, 11.3, 1.6 Hz, 1 H), 1.99 – 1.93 (m, 1 H), 1.79 (dt, *J* =

11.3, 6.4 Hz, 1 H), 1.73 – 1.62 (m, 3 H), 1.54 – 1.42 (m, 1 H), 1.07 (s, 3 H), 1.00 (s, 9 H), 0.21 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 153.3, 137.9, 136.4, 134.4, 128.8 (2 H), 126.6 (2 H), 126.3, 125.8, 120.0, 117.2, 56.8, 47.5, 44.2, 37.3, 35.3, 31.3, 29.6, 27.8, 26.6, 25.7 (3 H), 21.1, 18.2, 16.7, -4.4 (2 H); HRMS (ESI-TOF) calcd for $C_{31}H_{43}OSi$ $[M+H]^+$: 459.3078; found: 459.3087.



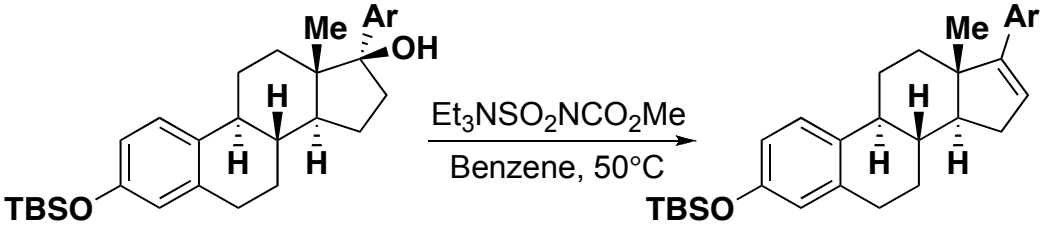
styrene 6c

Styrene 6c: Prepared from vinyl triflate (51 mg, 0.099 mmol) according to general procedure B. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded styrene **6c** (38 mg, 0.080 mmol, 81%) as a white solid (mp 96-101°C): R_f = 0.28 (4:1 hexanes:CH_2Cl_2); $[\alpha]^D_{20}$ = +25.8° (*c* = 0.31, CH_2Cl_2); IR (neat) ν_{max} = 2928, 1497, 1251 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2 H), 7.13 (d, *J* = 8.4 Hz, 1 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 6.62 (dd, *J* = 8.4, 2.6 Hz, 1 H), 6.58 (d, *J* = 2.5 Hz, 1 H), 5.85 (dd, *J* = 3.1, 1.7 Hz, 1 H), 3.82 (s, 3 H), 2.95 – 2.81 (m, 2 H), 2.39 – 2.27 (m, 3 H), 2.19 (dd, *J* = 8.5, 2.3 Hz, 1 H), 2.10 (ddd, *J* = 15.4, 11.3, 1.6 Hz, 1 H), 1.98 – 1.92 (m, 1 H), 1.78 (dt, *J* = 11.3, 6.5 Hz, 1 H), 1.72 – 1.61 (m, 3 H), 1.47 (ddd, *J* = 24.1, 11.7, 6.8 Hz, 1 H), 1.05 (s, 3 H), 0.99 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 154.4, 153.3, 137.9, 133.3, 129.9, 127.8 (2 C), 125.8, 125.4, 120.0, 117.1, 113.5 (2 C), 56.8, 55.2, 47.5, 44.2, 37.3, 35.6, 31.2, 29.6, 27.8, 26.6, 25.7 (3 C), 18.2, 16.7, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{43}O_2Si$ $[M+H]^+$: 475.3027; found: 475.3010.

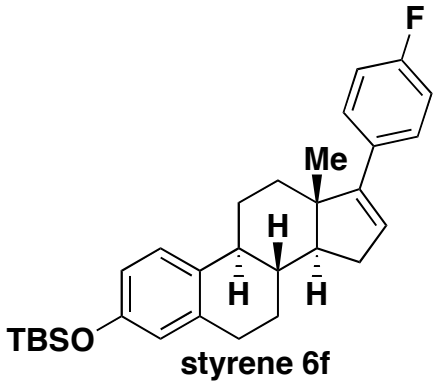


styrene 6d

Styrene 6d: Prepared from vinyl triflate (49 mg, 0.094 mmol) according to general procedure B. Purification by flash chromatography (2:1 EtOAc:hexanes) afforded styrene **6d** (26 mg, 0.058 mmol, 62%) as a white foam: R_f = 0.5 (1:1 hexanes:EtOAc); $[\alpha]^{D}_{20}$ = +24.1° (*c* = 0.85, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1496, 1380, 1253, 1188 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1 H), 8.48 (s, 1 H), 7.71(d, *J* = 7.88 Hz, 1 H), 7.71 – 7.69 (m, 1 H), 7.12 (d, *J* = 8.42 Hz, 1 H), 6.62 (dd, *J* = 8.4, 2.6 Hz, 1 H), 6.58 (d, *J* = 2.6 Hz, 1 H), 6.03 (dd, *J* = 3.2, 1.8 Hz, 1 H), 2.94 – 2.82 (m, 2 H), 2.39 – 2.27 (m, 3 H), 2.18 – 2.10 (m, 2 H), 1.98 – 1.92 (m, 1 H), 1.81 (dt, *J* = 11.5, 6.5 Hz, 1 H), 1.72 – 1.60 (m, 3 H), 1.48 (ddd, *J* = 17.7, 11.8, 6.0 Hz, 1 H), 1.05 (s, 3 H), 0.98 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 151.7, 147.3, 147.2, 137.9, 133.2, 129.6, 126.9, 125.9, 123.6, 120.1, 117.3, 113.5, 56.9, 47.9, 44.2, 37.3, 35.5, 31.7, 29.6, 27.9, 26.6, 25.9 (3 C), 18.3, 16.9, -4.2 (2 C); HRMS (ESI-TOF) calcd for $C_{29}H_{40}NOSi$ $[M+H]^+$: 446.2874; found: 446.2863.

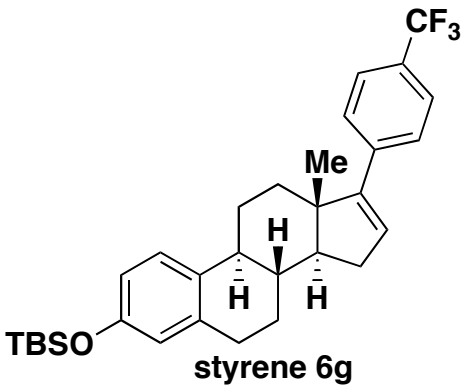


General procedure C: To a solution of alcohol (1.0 equiv) in benzene (0.03 *M*) was added N-(trimethylammoniumsulphonyl)carbamate (5.0 equiv). The reaction was then immersed in a preheated oil bath at 50°C. After 2 hours, the reaction was allowed to cool to ambient temperature and diluted with EtOAc. The reaction was washed with H_2O and sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by flash chromatography on silica.



styrene 6f

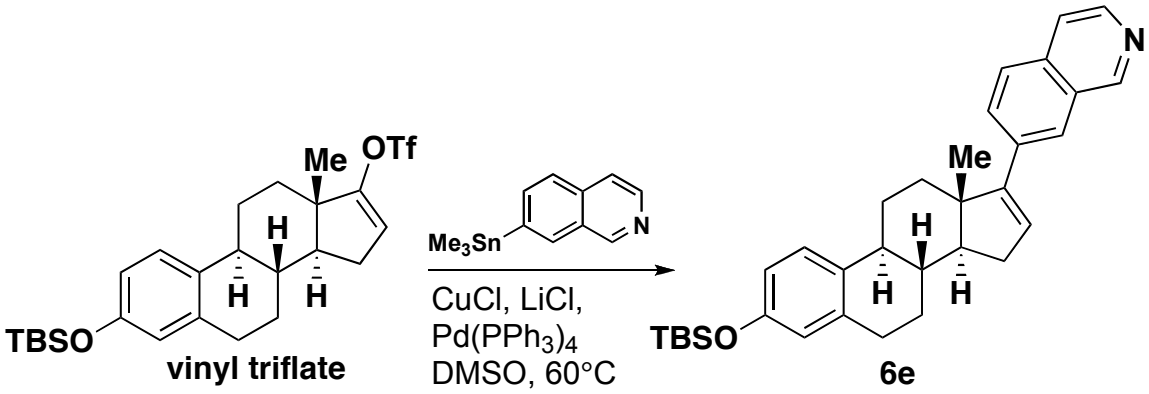
Styrene 6f: Prepared from alcohol **8f** (117 mg, 0.243 mmol) according to general procedure C. Purification by flash chromatography (1:6 CH_2Cl_2:hexanes) afforded styrene **6f** (92 mg, 0.197 mmol, 81%) as a white solid (mp 140-144°C): R_f = 0.33 (1:6 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +32.5° (*c* = 0.54, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1497, 1255 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.7, 5.5 Hz, 2 H), 7.17 (d, *J* = 8.4 Hz, 1 H), 7.03 (t, *J* = 8.8 Hz, 2 H), 6.68 (dd, *J* = 8.4, 2.5 Hz, 1 H), 6.63 (d, *J* = 2.2 Hz, 1 H), 5.92 (dd, *J* = 2.8, 1.5 Hz, 1 H), 2.99 – 2.85 (m, 2 H), 2.42 – 2.31 (m, 3 H), 2.19 – 2.11 (m, 2 H), 2.05 – 1.97 (m, 1 H), 1.82 (dt, *J* = 11.3, 6.5 Hz, 1 H), 1.76 – 1.66 (m, 3 H), 1.51 (dq, *J* = 12.2, 11.8, 6.8 Hz, 1 H), 1.05 (s, 3 H), 1.04 (s, 9 H), 0.25 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (d, J_{CF} = 245.7 Hz) 154.2, 153.5, 138.0, 133.5 (d, J_{CF} = 3.3 Hz), 128.4 (d, J_{CF} = 7.7 Hz, 2 C), 127.1, 126.0, 120.2, 117.3, 115.1 (d, J_{CF} = 21.1 Hz, 2 C), 57.0, 47.8, 44.3, 37.5, 35.7, 31.4, 29.7, 27.9, 26.7, 25.9 (3 C), 18.3, 16.8, -4.2 (2 C) ; HRMS (ESI-TOF) calcd for $C_{30}H_{41}FOSi$ $[M+H]^+$: 463.2872; found: 463.2835.



styrene 6g

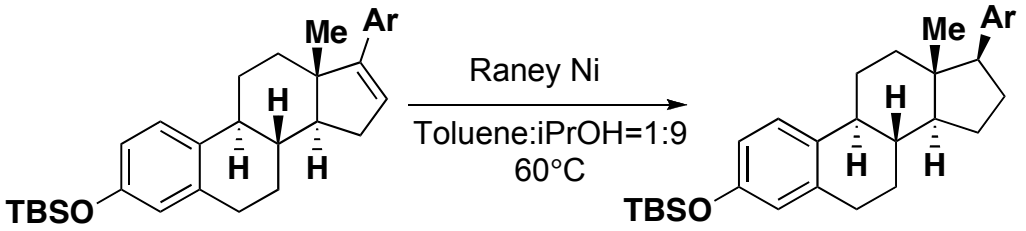
Styrene 6g: Prepared from alcohol **8g** (100 mg, 0.188 mmol) according to general procedure C. Purification by flash chromatography (1:5 CH_2Cl_2:hexanes) afforded styrene **6g** (82 mg, 0.160 mmol, 85%) as a white solid (mp 75-81°C): R_f = 0.32 (1:6 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +18.8° (*c* = 0.67, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1497, 1325, 1125 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 26.4, 8.3 Hz, 4 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.69 (dd, *J* = 8.4, 2.6 Hz, 1 H), 6.65 (d, *J* = 2.4 Hz, 1 H), 6.09 (dd, *J* = 3.1, 1.7 Hz, 1 H), 3.00 – 2.81 (m, 2 H), 2.46 – 2.32 (m, 3 H), 2.32 –

2.26 (m, 2 H), 2.05 – 1.98 (m, 1 H), 1.85 (dt, J = 11.4, 6.5 Hz, 1 H), 1.78 – 1.65 (m, 3 H), 1.56 – 1.43 (m, 1 H), 1.13 (s, 3 H), 1.05 (s, 9 H), 0.26 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 153.5, 141.0, 137.9, 133.2, 129.5, 128.7 (q, J_{CF} = 32.3 Hz), 126.9, 126.5 (q, J_{CF} = 32.3 Hz), 125.9, 125.1 (q, J_{CF} = 3.7 Hz, 2 C), 121.7 (q, J_{CF} = 269.7 Hz), 120.1, 117.3, 56.9, 47.8, 44.2, 37.3, 35.5, 31.6, 29.6, 27.8, 26.6, 25.8 (3 C), 18.2, 16.9, -4.3 (2 C) ; HRMS (ESI-TOF) calcd for $C_{31}H_{41}F_3OSi$ $[M+H]^+$: 513.2795; found: 513.2805.



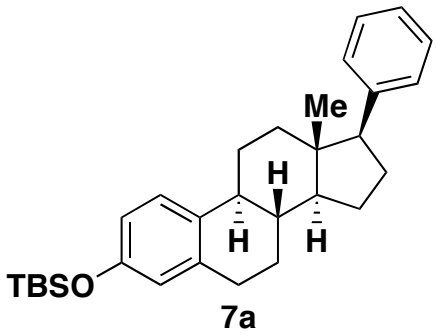
Stryene 6e: To a solution of vinyl triflate (134 mg, 0.26 mmol, 1.0 equiv) in DMSO (2.6 mL, 0.1 *M*) was added 7-trimethylstannylisoquinoline (152 mg, 0.52 mmol, 2.0 equiv), CuCl (254 mg, 2.6 mmol, 10 equiv), LiCl(110 mg, 2.6 mmol, 10 equiv) and $Pd(PPh_3)_4$ (300 mg, 0.26 mmol, 0.1 equiv). The solution was bubbled with Ar under sonication for 10 minutes. The reaction was then immersed in a preheated oil bath at 60°C. After 2 hours, the reaction was allowed to cool to ambient temperature and diluted with EtOAc (10 mL) and washed with 5% NH_4OH (10 mL). The aqueous layer was extracted with EtOAc (10 mL × 4). The combined organic portions were washed with sat. aq. NaCl (20 mL), dired over $MgSO_4$, filtered, and concentrated *in vacuo*. Chromatography on silica (1:4 EtOAc:hexanes) afforded Styrene **6e** (103 mg, 0.208 mmol, 79%) as a white foam: R_f = 0.35 (1:3 EtOAc:hexanes); $[\alpha]^D_{20}$ = +22.5° (c = 0.08, CH_2Cl_2); IR (neat) ν_{max} = 2925, 2854, 1604, 1496, 1250, 954, 840, 781 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$)

δ 9.23 (s, 1 H), 8.48 (d, *J* = 5.6 Hz, 1 H), 7.95 (s, 1 H), 7.77 (dd, *J* = 15.8, 8.5 Hz, 2 H), 7.62 (d, *J* = 5.5 Hz, 1 H), 7.14 (d, *J* = 8.4 Hz, 1 H), 6.63 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.59 (s, 1 H), 6.15 (d, *J* = 1.2 Hz, 1 H), 2.95 – 2.81 (m, 2 H), 2.43 – 2.35 (m, 1 H), 2.03 – 1.94 (m, 1 H), 1.86 (ddd, *J* = 17.9, 11.4, 6.5 Hz ,1 H), 1.78 – 1.66 (m, 2 H), 1.53 – 1.46 (m, 1 H), 1.40 – 1.28 (m, 2 H), 1.15 (s, 3 H), 0.98 (s, 9 H), 0.88 (t, *J* = 6.8 Hz, 1 H), 0.20 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.1, 153.3, 152.6, 142.7, 137.8, 136.2, 134.7, 133.1, 130.2, 129.1, 128.8, 126.2, 125.8, 123.8, 124.0, 120.2, 120.0, 117.0, 56.9, 47.8, 44.1, 37.2, 35.6, 31.5, 27.7, 26.5, 25.7 (3 C), 18.2, 16.8, 1.0, -4.4 (2 C) ; HRMS (ESI-TOF) calcd for $C_{33}H_{42}NO_2Si$ $[M+H]^+$: 496.3030; found: 496.3036.



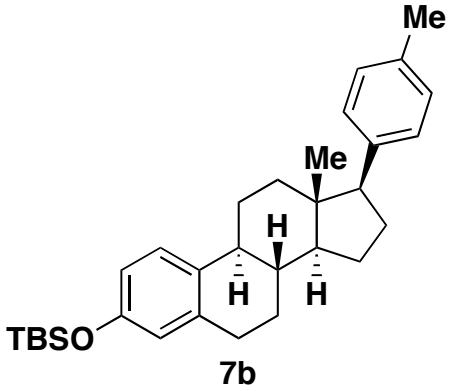
General Procedure for the Standardization of Raney Nickel (Ra-Ni): Raney® 2800 Nickel (*ca.* 1 g of a 1g/mL slurry in H_2O, pH = 9, Sigma-Aldrich) was placed in a vial. The water was removed by pipette, and the Ra-Ni was washed by 5 seconds of shaking, followed by removal of the supernatant: first H_2O (2 x 2 mL), then sat. aq. Rochelle's salt (2 × 2 mL), then H_2O (10 × 2 mL). After all washes, the Ra-Ni aqueous solution (pH = 7) was stored under H_2O (1 mL).

General Procedure D: To a solution of styrene in *i*-PrOH/toluene (9:1, 0.01 *M*), was added the suspension of Ra-Ni prepared above (the Ra-Ni suspension was removed by 5.75' pipette from the thick bottom layer of the vial; 1 drop suspension per 0.1 mL solution). The reaction flask was immersed in an oil bath preheated to 60 °C and stirred vigorously for 120 minutes. After cooling to ambient temperature, the reaction mixture was passed through Celite, the Ra-Ni washed by CH_2Cl_2, and the combined filtrates were concentrated *in vacuo*. The product was purified by flash column chromatography.



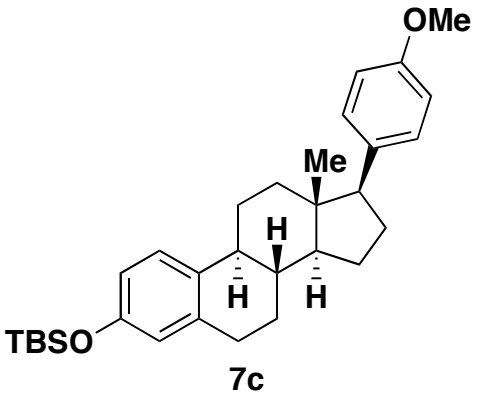
7a

7a: Prepared from Styrene **6a** (15 mg, 0.033 mmol) according to general procedure D. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7a** (14.3 mg, 0.032 mmol, 97%) as a white solid (mp 110-113°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +3.1° (c = 0.48, CH_2Cl_2); IR (neat) ν_{max} = 2925, 1495, 1253 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 5 H), 7.11 (d, J = 8.5 Hz, 1 H), 6.60 (dd, J = 8.5, 2.5 Hz, 1 H), 6.55 (d, J = 2.5 Hz, 1 H), 2.85 – 2.82 (m, 3 H), 2.78 (t, J = 10.0 Hz, 1 H), 2.28 – 2.24 (m, 2 H), 2.19 – 2.12 (m, 1 H), 2.05 – 1.87 (m, 3 H), 1.72 – 1.70 (m, 1 H), 1.48 – 1.42 (m, 6 H), 0.98 (s, 9 H), 0.51 (s, 3 H), 0.18 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.2, 141.1, 137.9, 133.3, 128.7 (2 C), 127.7 (2 C), 126.1, 126.0, 119.0, 57.1, 55.3, 44.6, 39.2, 37.7, 29.7 (2 C), 27.9, 26.3, 26.1, 25.7 (3 C), 24.2, 18.2, 12.8, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{43}OSi$ $[M+H]^+$: 447.3078; found: 447.3078.



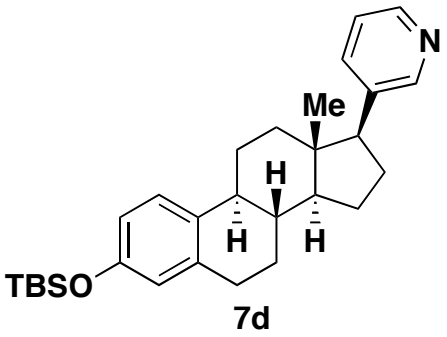
7b

7b: Prepared from Styrene **6b** (17 mg, 0.037 mmol) according to general procedure D. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7b** (16.7 mg, 0.036 mmol, 98%) as a white solid (mp 108-112°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +5.1° (c = 0.82, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1497, 1254 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.10 (m, 5 H), 6.60 (dd, J = 8.5 , 2.5 Hz, 1 H), 6.55 (d, J = 2.5 Hz, 1 H), 2.87 – 2.78 (m, 3 H), 2.74 (t, J = 10.0 Hz, 1 H), 2.33 (s, 3 H), 2.27 – 2.24 (m, 2 H), 2.14 – 2.09 (m, 1 H), 2.05 – 1.86 (m, 3 H), 1.71 – 1.69 (m, 1 H), 1.46 – 1.40 (m, 6 H), 0.98 (s, 9 H), 0.51 (s, 3 H), 0.19 (s, 6 H); ^{13}C NMR δ 153.2, 138.0, 137.9, 135.4, 133.4, 128.6 (2 C), 128.4 (2 C), 126.1, 119.9, 117.1, 56.8, 55.3, 44.4, 44.1, 39.2, 37.8, 29.7, 26.33, 26.29, 25.7 (3 C), 24.2, 21.0, 18.2, 12.8, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{43}OSi[M+H]^+$: 461.3234; found: 461.3236.



7c

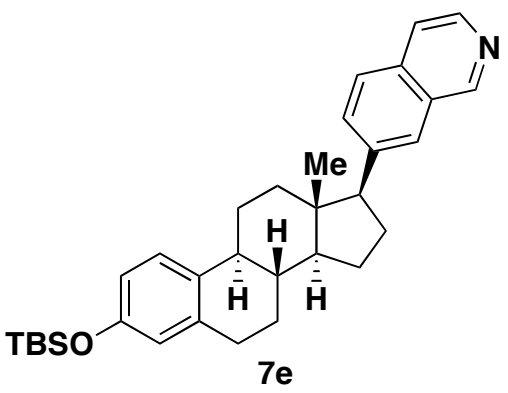
7c: Prepared from Styrene **6c** (15 mg, 0.031 mmol) according to general procedure D. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7c** (14.0 mg, 0.029 mmol, 93%) as a white solid (mp 110-113°C): R_f = 0.26 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +1.8° (*c* = 0.33, CH_2Cl_2); IR (neat) ν_{max} = 2924, 1258 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 9.0 Hz, 2 H), 7.10 (d, *J* = 8.5 Hz, 1 H), 6.84 (d, *J* = 9.0 Hz, 2 H), 6.59 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.51 (d, *J* = 2.5 Hz, 1 H), 2.86 – 2.78 (m, 2 H), 2.72 (t, *J* = 9.5 Hz, 1 H), 2.29 – 2.23 (m, 2 H), 2.12– 1.85 (m, 4 H), 1.70 – 1.67 (m, 1 H), 1.43 – 1.40 (m, 6 H), 0.98 (s, 9 H), 0.50 (s, 3 H), 0.18 (s, 6 H); ^{13}C NMR δ 157.9, 153.2, 137.9, 133.3, 133.1, 129.5 (2 C), 126.1, 119.9, 117.1, 113.1 (2 C), 56.3, 55.2, 44.4, 44.1, 39.2, 37.7, 29.74, 29.71, 27.8, 26.3, 26.3, 25.7 (3 C), 24.2, 21.0, 18.2, 12.7, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{45}O_2Si$ $[M+H]^+$: 477.3183; found: 477.3193.



7d

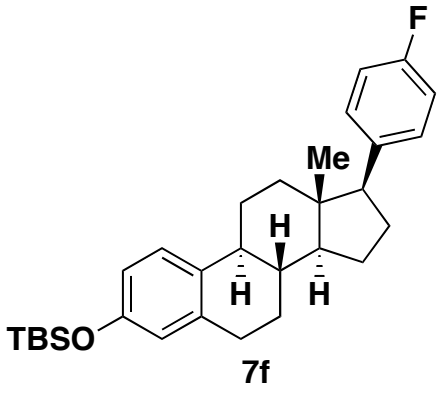
7d: Prepared from Styrene **6d** (6.3 mg, 0.014 mmol) according to general procedure D. Purification by flash chromatography (2:1 hexanes:EtOAc) afforded **7d** (4.5mg, 0.010 mmol, 72%) as a white solid (mp 168-170°C): R_f = 0.15 (1:3 EtOAc:hexanes); $[\alpha]^D_{20}$ = +2.1° (*c* = 0.52, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1495, 1258 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.49 (brs, 1 H), 7.56 (d, *J* = 7.5 Hz, 1 H), 7.23 (brs, 1 H), 7.10 (d, *J* = 8.5 Hz, 1 H), 6.60 (dd, *J* = 8.5, 2.5Hz, 1 H), 6.56 (d, *J* = 2.5 Hz, 1 H), 2.86 – 2.80 (m, 2 H), 2.78 (t, *J* = 9.5 Hz, 1 H), 2.30 – 2.24 (m, 2 H), 2.15 – 1.92 (m, 4 H), 1.70 – 1.60 (m, 1 H), 1.43 – 1.40 (m, 6 H), 0.97 (s, 9H), 0.53 (s, 3 H), 0.18 (s, 6 H); ^{13}C NMR δ 153.3, 150.3, 147.5, 137.8, 135.7, 133.0, 126.1, 119.9,

117.0, 55.3, 54.6, 44.7, 44.0, 39.2, 37.5, 29.7 (2 C), 27.8, 26.2, 25.9, 25.7 (3 C), 24.2, 18.2, 12.8, 1.0, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{29}H_{42}NOSi$ $[M+H]^+$: 448.3030; found: 448.3034.



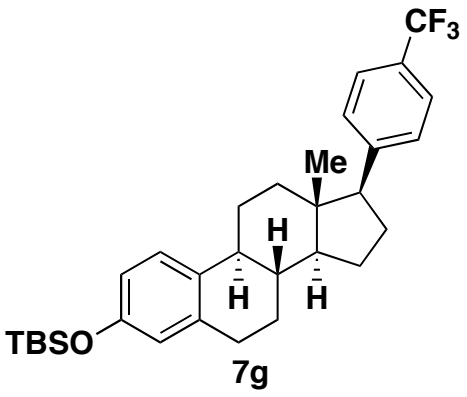
7e

7e: Prepared from Styrene **6e** (4.3 mg, 0.008 mmol) according to general procedure D. Purification by flash chromatography (2:1 hexanes:EtOAc) afforded **7e** (2.5 mg, 0.005 mmol, 58%) as a colorless oil: R_f = 0.56 (1:1 EtOAc: hexanes); $[\alpha]^{D}_{20}$ = –2.0° (*c* = 0.10, CH_2Cl_2); IR (neat) ν_{max} = 2925, 2855, 1653, 1559, 1539, 1507, 1496, 1472, 1457, 1284, 1254, 947, 843 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.22 (s, 1 H), 8.47 (d, *J* = 5.4 Hz, 1 H), 7.80 (s, 1 H), 7.75 (d, *J* = 8.4 Hz, 1 H), 7.62 (s, 1 H), 7.61 (d, *J* = 12.4 Hz, 1 H), 7.11 (d, *J* = 8.5 Hz, 1 H), 6.60 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.56 (d, *J* = 2.2 Hz, 1 H), 2.98 (t, *J* = 9.8 Hz, 1 H), 2.90 – 2.78 (m, 2 H), 2.34 – 2.24 (m, 3 H), 2.15 – 2.07 (m, 1 H), 2.02 – 1.94 (m, 2 H), 1.73 (dt, *J* = 12.9, 2.9 Hz, 1 H), 1.57 – 1.38 (m, 6 H), 0.97 (s, 9 H), 0.54 (s, 3 H), 0.18 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3, 152.3, 142.3, 140.7, 137.8, 134.6, 133.1, 132.4, 128.6, 126.1, 126.0, 125.5, 120.1, 120.0, 117.1, 57.2, 55.3, 45.1, 44.0, 39.2, 37.8, 29.7, 27.8, 26.3, 26.2, 25.7 (3 C), 24.3, 18.2, 12.9, –4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{33}H_{43}NOSi$ $[M+H]^+$: 498.3187; found: 498.3195.



7f

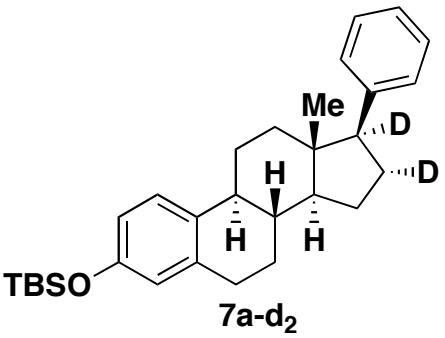
7f: Prepared from Styrene **6f** (10 mg, 0.022 mmol) according to general procedure D. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7f** (9.3 mg, 0.020 mmol, 93%) as a white solid (mp 117-121°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +1.6° (*c* = 0.37, CH_2Cl_2); IR (neat) ν_{max} = 2928, 1508, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.8 Hz, 1 H), 7.19 (d, *J* = 8.8 Hz, 1 H), 7.11 (d, *J* = 8.4Hz, 1 H), 6.99 (d, *J* = 8.8 Hz, 1 H), 6.97 (d, *J* = 8.8 Hz, 1 H), 6.61 (dd, *J* = 8.4, 2.4 Hz, 1 H), 6.57 (d, *J* = 2.4 Hz, 1 H), 2.86 – 2.82 (m, 2 H), 2.75 (t, *J* = 10.0 Hz, 1 H), 2.24 – 2.30 (m, 2 H), 2.10 – 1.89 (m, 4 H), 1.67 (dd, *J* = 8.4, 2.4Hz, 1 H), 1.45 – 1.42 (m, 6 H), 0.98 (s, 9 H), 0.50 (s, 3 H), 0.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5 (d, J_{CF} = 242.1 Hz), 153.3, 137.9, 136.7 (d, J_{CF} = 3.1 Hz), 133.2, 129.9 (d, J_{CF} = 7.5 Hz, 2 C), 126.1, 119.9, 117.1, 114.4 (d, J_{CF} = 20.6 Hz, 2 C), 56.4, 55.2, 44.4, 44.1, 39.2, 37.7, 29.7, 27.8, 26.5, 26.3, 25.7 (3 C), 24.2, 18.2, 18.2, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{42}OFSi$ $[M+H]^+$: 465.2983; found: 465.2972.



7g

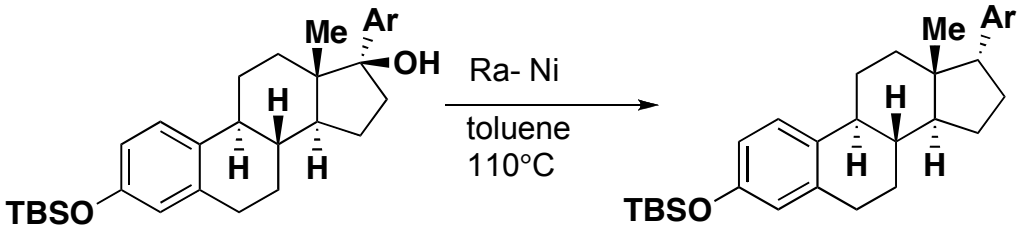
7g: Prepared from Styrene **6g** (17 mg, 0.030 mmol) according to general procedure D. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7g** (15.0 mg, 0.029 mmol, 96%) as a white solid (mp 129-131°C): R_f = 0.65 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +5.1° (*c* = 0.71, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1497, 1327, 1123 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 2 H), 7.35 (d, *J* = 8.3 Hz, 2 H), 7.11 (d, *J* = 8.5Hz, 1 H), 6.61 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.56 (d, *J* = 2.5 Hz, 1 H), 2.86 – 2.82 (m, 3 H), 2.30 – 2.25 (m, 2 H), 2.18 – 2.12 (m, 1 H), 2.08 – 2.00 (m, 1 H), 1.95 – 1.90 (m, 2 H), 1.71 – 1.68 (m, 1 H), 1.54 – 1.40 (m, 6 H), 0.98 (s, 9 H), 0.51 (s, 3 H), 0.19 (s, 6 H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 153.3, 145.4, 137.8, 133.1, 128.9 (2 C), 128.3 (q, J_{CF} = 32.2 Hz), 124.6 (q, J_{CF} = 3.8 Hz, 2C), 121.7 (q, J_{CF} = 394.1 Hz), 120.0, 117.1, 57.0, 55.4, 44.9, 44.0, 39.2, 37.7, 29.7, 26.3, 26.2, 25.7 (3 C), 24.2, 18.2, 12.8, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{42}OF_3Si$ $[M+H]^+$: 515.2951; found: 515.2959.



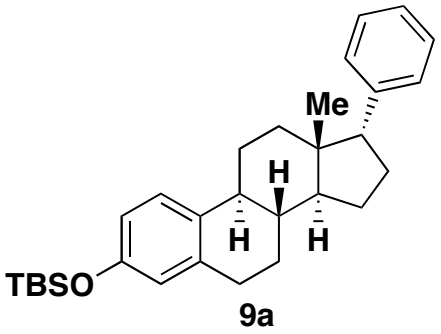
7a-d$_2$

7a-d$_2$: Prepared from Styrene **6a** (13 mg, 0.029 mmol) according to general procedure D, except Ra-Ni was washed with D_2O and isopropanol-*d*8 and toluene-*d*8 were used as solvent. Purification by flash chromatography (15:1 hexanes:CH_2Cl_2) afforded **7a-d$_2$** (12.3 mg, 0.027 mmol, 95%) as a white solid (mp 135-138°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +3.1° (c = 0.19, CH_2Cl_2); IR (neat) ν_{max} = 2925, 1495, 1253 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 5 H), 7.11 (d, *J* = 8.5 Hz, 1 H), 6.60 (dd, *J* = 2.5, 8.5 Hz, 1 H), 6.55 (d, *J* = 2.5 Hz, 1 H), 2.85 – 2.82 (m, 2 H), 2.78 (t, *J* = 10.0 Hz, 1 H), 2.28 – 2.24 (m, 2 H), 2.19 – 2.12 (m, 1 H), 2.05 – 1.87 (m, 2 H), 1.72 – 1.70 (m, 1 H), 1.48 – 1.42 (m, 6 H), 0.98 (s, 9 H), 0.51 (s, 3 H), 0.18 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.2, 141.1, 137.9, 133.3, 128.7 (2 C), 127.7 (2 C), 126.1, 126.0, 119.9, 57.1 (t, J_{CD} = 26.0 Hz), 55.3, 44.6, 44.1, 39.2, 37.7, 29.8, 29.7, 27.9, 26.3, 25.7 (3 C), 24.2, 23.7 (t, J_{CD} = 26.6 Hz), 18.2, 12.8, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{40}D_2OSi$ $[M+H]^+$: 449.3201; found: 449.3191.



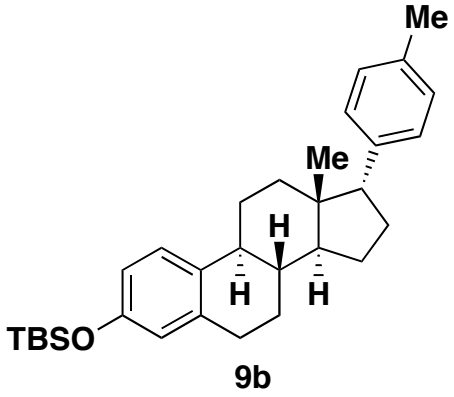
General procedure E: To a solution of alcohol in toluene (0.01 *M*), was added the suspension of Ra-Ni

prepared above (the Ra-Ni suspension was removed by 5.75' pipette from the thick bottom layer of the vial; 1 drop suspension per 0.1 mL solution). The reaction flask was immersed in an oil bath preheated to 110°C and stirred vigorously for 5 hours. After cooling to ambient temperature, the reaction mixture was passed through Celite, the Ra-Ni washed by CH_2Cl_2, and the combined filtrates were concentrated *in vacuo*. The product was purified by flash column chromatography.



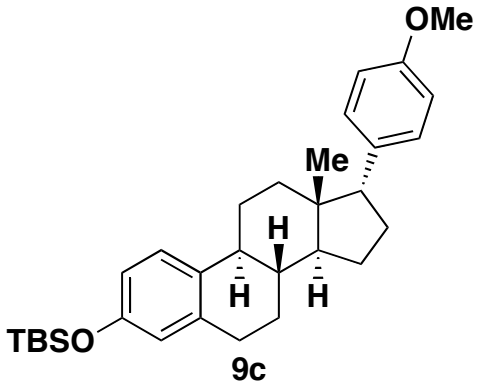
9a

9a: Prepared from alcohol **8a** (36 mg, 0.081 mmol) according to general procedure E. Purification by flash chromatography (5:1 hexanes:CH_2Cl_2) afforded **9a** and **7a** (dr = 6.6:1) as an unseperable mixture (35.0 mg, 0.080 mmol, 98%) (white solid) (mp 113-118°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +41.7° (*c* = 0.93, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1496, 1255 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31– 7.19 (m, 3 H), 7.14 – 7.11 (m, 2 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.56 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.54 (d, *J* = 2.5 Hz, 1 H), 3.00 (dd, *J* = 9.0, 1.5 Hz, 1 H), 2.88 – 2.76 (m, 2 H), 2.37– 2.24 (m, 1 H), 2.11 – 1.94 (m, 5 H), 1.55 – 1.37 (m, 6 H) , 0.99 (s, 3 H), 0.97 (s, 9 H), 0.62 (dt, *J* = 15.0, 5.0 Hz, 1 H), 0.18 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 145.0, 137.8, 133.3, 128.7 (2 C), 127.6 (2 C), 126.1, 125.6, 119.8, 117.0, 55.8, 48.8, 45.4, 43.4, 39.3, 35.3, 29.8, 28.4, 26.4, 25.7 (3 C), 21. 4, 18.2, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{43}OSi$ $[M+H]^+$: 447.3078; found: 447.3083.



9b

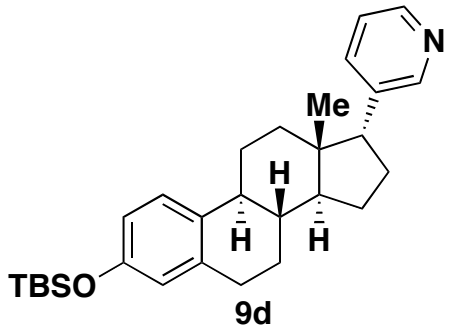
9b: Prepared from Alcohol **8b** (12 mg, 0.026 mmol) according to general procedure E. Purification by flash chromatography (5:1 hexanes:CH_2Cl_2) afforded **9b** and **7b** (dr = 26:1) as an unseperable mixture (10.3 mg, 0.023 mmol, 88%) (colorless oil): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +39.6° (*c* = 1.14, CH_2Cl_2); IR (neat) ν_{max} = 2928, 1496, 1288, 1256 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.0 Hz, 2 H), 7.03 (d, *J* = 8.0 Hz, 2 H), 7.02 (d, *J* = 8.0 Hz, 1 H), 6.56 (dd, *J* =8.0, 2.5 Hz, 1 H), 6.54 (d, *J* = 2.5 Hz, 1 H), 2.97 (dd, *J* = 8.5, 1.5 Hz, 1 H), 2.88 – 2.77 (m, 2 H), 2.34 (s, 3 H), 2.56 – 2.29 (m, 1H), 2.12 – 1.89 (m, 5 H), 1.54 – 1.38 (m, 1 H), 0.98 (s, 3 H), 0.97 (s, 9 H), 0.65 (brdt, 1 H), 0.18 (s, 6 H) ;^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 142.0. 137.8, 135.0, 133.3, 128.6, 128.3 (2 C), 126.1 (2 C), 119.8, 117.0, 55.3, 48.8, 45.3, 39.3, 35.3, 29.8, 28.5, 28.3, 26.4, 25.7 (3 C), 21.4, 21.0, 18.1, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{43}OSi$ $[M+H]^+$: 461.3234; found: 461.3231.



9c

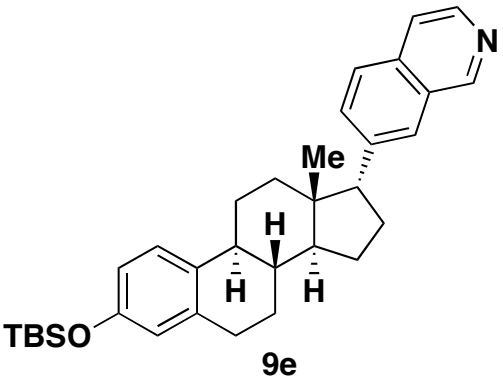
9c: Prepared from Alcohol **8c** (19 mg, 0.038 mmol) according to general procedure E. Purification by flash chromatography (5:1 hexanes:CH_2Cl_2) afforded **9c** and styrene **7c** (dr = 4.2:1) as an unseperable mixture (12.0 mg, 0.025 mmol, 68%) (white solid) (mp 78-83°C); $[\alpha]^D_{20}$ = +10.9° (*c* = 0.42, CH_2Cl_2); IR (neat) ν_{max} = 2925, 1498, 1252 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.6 Hz, 2 H), 7.09 – 6.96 (m, 2 H), 6.84 (dd, *J* = 8.4, 6.0 Hz, 2 H), 6.57 – 6.53 (m, 2 H), 3.80 (s, 3 H), 2.95 (dd, *J* = 8.9, 1.5 Hz, 1 H), 2.88 – 2.77 (m, 2 H), 2.35 – 2.20 (m, 2 H), 2.11 – 2.06 (m, 1 H), 2.02 – 1.85 (m, 3 H), 1.69 – 1.37 (m, 6 H), 0.98 (s, 3 H), 0.97 (s, 9 H), 0.65 (dt, *J* = 13.6, 13.3, 4.1 Hz 1 H), 0.18 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.6, 153.1, 137.8, 137.1, 133.3, 129.5 (2 C), 126.1, 119.8,

113.0 (2 C), 55.1, 54.8, 48.7, 45.3, 39.3, 35.3, 29.8, 28.6, 28.3, 25.7 (3 C), 24.2, 21.3, 18.1, 12.7, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{31}H_{44}O_2Si$ $[M+H]^+$: 477.3183; found: 477.3181.



9d

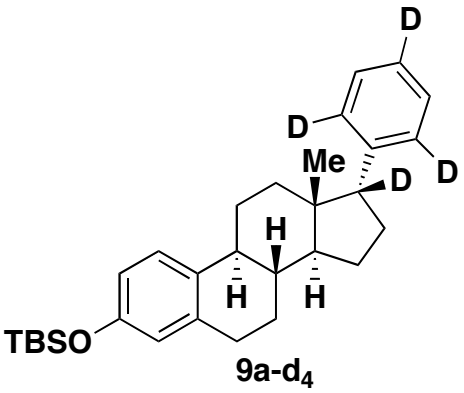
9d: Prepared Alcohol **8d** (12 mg, 0.025 mmol) according to general procedure E. Purification by flash chromatography (3:1 hexanes:EtOAc) afforded **9d** and **7d** (dr = 13:1) as an unseperable mixture (8.4 mg, 0.019 mmol, 72%) (white solid) (mp 82-84°C): R_f = 0.15 (3:1 hexanes: EtOAc); $[\alpha]^D_{20}$ = +34.5° (c = 0.55, CH_2Cl_2); IR (neat) ν_{max} = 2931,1498, 1220 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.43 (brd, 2 H), 7.44 (brd, 1 H), 7.24 (brt, 1 H), 7.00 (d, J = 8.5 Hz, 1 H), 6.56 (dd, J = 8.5 , 2.0 Hz, 1 H), 6.53 (d, J = 2.0 Hz, 1 H), 3.00 (dd, J = 8.5, 1.5 Hz, 1 H), 2.87 – 2.76 (m, 2 H), 2.41 – 2.33 (m, 1 H), 2.13 – 1.88 (m, 5 H), 1.57 – 1.37 (m, 6 H), 1.01 (s, 3 H), 0.96 (s, 9 H), 0.59 (brdt, 1 H), 0.17 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.2, 150.2, 147.2, 137.7, 135.8, 133.0, 126.0, 119.8, 117.1, 53.2, 49.0, 45.5, 43.4, 39.3, 35.2, 29.7, 28.2, 28.1, 26.3, 25.7 (3 C), 25.6, 21.2, 18.2, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{29}H_{42}NOSi$ $[M+H]^+$: 448.3030; found: 448.3028.



9e

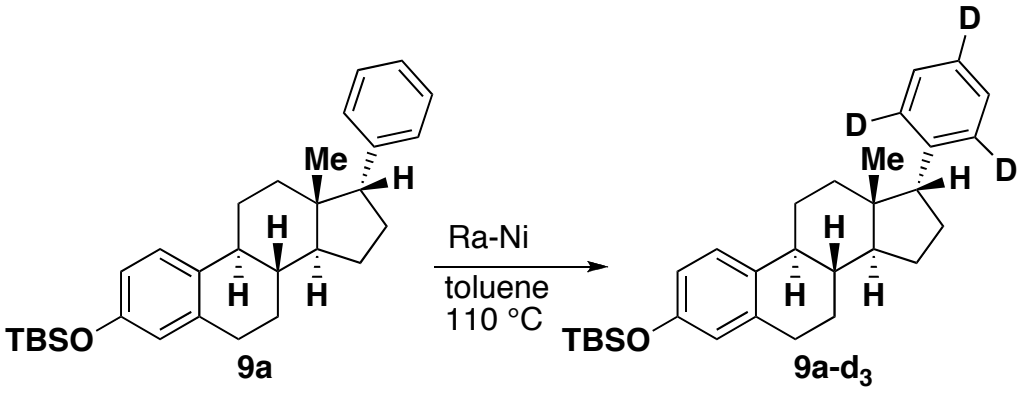
9e: Prepared from Alcohol **8e** (5.6 mmol, 0.011 mmol) according to general procedure E. Purification by flash chromatography (2:1 hexanes:EtOAc) afforded **9e** and **7e** (dr = 4.3:1) as an unseperable mixture (4.1 mg, 0.007 mmol, 71%) (white solid) (mp 153-157°C): R_f = 0.39 (3:1 hexanes: EtOAc); $[\alpha]^D_{20}$ = +18.3° (c = 0.18, CH_2Cl_2); IR (neat) ν_{max} = 2925, 2855, 1653, 1559, 1254.0, 1284, 1254, 947, 843 cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$) δ 9.25 (bs, 1 H), 8.48 (bs, 1 H),

7.74 (d, *J* = 14.4 Hz, 1 H), 7.67 (s, 1H), 7.58 – 7.54 (m, 2 H), 7.51 (d, *J* = 8.8 Hz, 1 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 3.20 (d, *J* = 8.1 Hz, 1 H), 2.89 – 2.75 (m, 2 H), 2.48 – 2.39 (m, 1 H), 2.17 – 2.03 (m, 2 H), 2.01 – 1.88 (m, 2 H), 1.64 – 1.48 (m, 3 H), 1.48 – 1.38 (m, 2 H), 1.06 (s, 3 H), 0.95 (s, 9 H), 0.91 – 0.81 (m, 2 H), 0.58 (dd, *J* = 12.7, 4.1 Hz, 1 H), 0.16 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ153.2, 144.5, 142.3, 137.8, 134.3, 133.0, 132.8, 126.0, 125.7, 125.5, 119.8, 117.0, 55.9, 49.0, 45.8, 43.4, 39.3, 35.4, 29.7 (2 C), 28.4, 28.3, 26.4, 25.8, 25.7 (3 C), 21.5, 18.1, –4.4 (2 C); HRMS (ESI-MS) calcd for $C_{33}H_{43}NOSi$ [M + H]$^+$ 498.3187, found 498.3195.

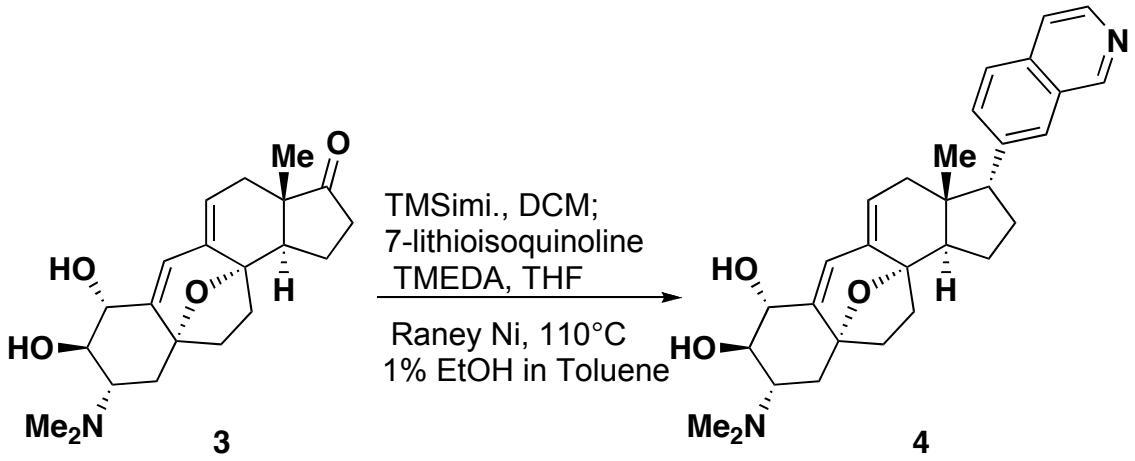


9a-d$_4$

9a-d$_4$: Prepared from Alcohol **8a** (18 mg, 0.039 mmol) according to general procedure E, except Ra-Ni was washed with D_2O and toluene-d_8 was used as solvent. Purification by flash chromatography (5:1 hexanes:CH_2Cl_2) afforded **9a-d$_4$** and **9a** (dr = 10:1) as an unseperable mixture (white solid) (17.0 mg, 0.037 mmol, 96%) (mp 110-115°C): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +43.4° (*c* = 1.63, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1496, 1255 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 2 H), 7.02 (d, *J* = 8.0 Hz, 1 H), 6.57 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.54 (d, *J* = 2.5 Hz, 1 H), 2.88 – 2.77 (m, 2 H), 2.36 – 2.34 (m, 1 H), 2.11 – 1.94 (m, 5 H), 1.55 – 1.37 (m, 6 H) , 1.00 (s, 3 H), 0.98 (s, 9 H), 0.63 (dt, *J* = 15.0, 5.0 Hz, 1 H), 0.19 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 145.0, 137.8, 133.3, 128.7, 127.5 (t, J_{CD} = 32.0 Hz, 2 C), 126.1 (2 C), 125.4 (t, J_{CD} = 24.3 Hz), 119.8, 117.0, 55.3 (t, J_{CD} = 26.6 Hz), 48.9, 45.3, 43.4, 39.3, 35.3, 29.8, 28.4, 26.4, 25.7 (3 C), 21. 4, 18.2, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{39}D_4OSi$ [M+H]$^+$: 451.3325; found: 451.3320.



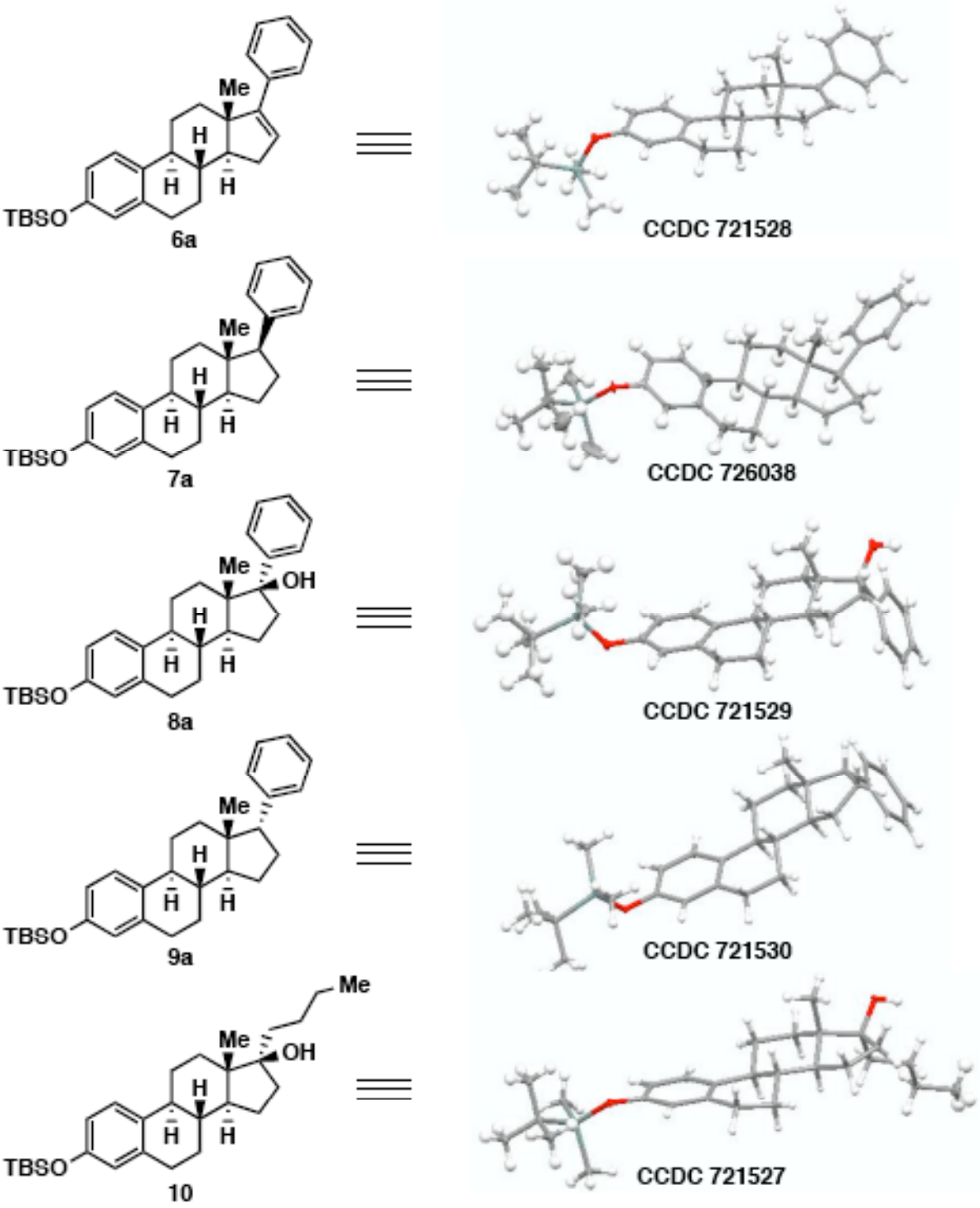
9a-d$_3$: Prepared from **9a** (14 mg, 0.031 mmol) according to general procedure E, except Ra-Ni was washed with D_2O and toluene-*d*8 was used as solvent. Purification by preparative TLC (10:1 hexanes:CH_2Cl_2) afforded **9a-d$_3$** (dr = 10:1) and its diasteroisomer as an unseperable mixture (10 mg, 0.023 mmol, 75%) (white foam): R_f = 0.60 (1:3 CH_2Cl_2:hexanes); $[\alpha]^D_{20}$ = +45.8° (*c* = 0.31, CH_2Cl_2); IR (neat) ν_{max} = 2930, 1496, 1255 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 (s, 2 H), 7.02 (d, *J* = 8.0 Hz, 1 H), 6.57 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.54 (d, *J* = 2.5 Hz, 1 H), 3.00 (dd, *J* = 9.0, 1.5 Hz, 1 H), 2.88 – 2.77 (m, 2 H), 2.36 – 2.34 (m, 1 H), 2.11 – 1.94 (m, 5 H), 1.55 – 1.37 (m, 6 H) , 1.00 (s, 3 H), 0.98 (s, 9 H), 0.63 (dt, *J* = 15.0, 5.0 Hz, 1 H), 0.19 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 145.0, 137.8, 133.3, 128.7, 127.5 (t, J_{CD} = 32.0 Hz, 2 C), 126.1 (2 C), 125.4 (t, J_{CD} = 24.3 Hz), 119.8, 117.0, 55.3, 48.9, 45.3, 43.4, 39.3, 35.3, 29.8, 28.4, 26.4, 25.7 (3 C), 21. 4, 18.2, -4.4 (2 C); HRMS (ESI-TOF) calcd for $C_{30}H_{40}D_3OSi$ $[M+H]^+$: 450.3263; found: 450.3251.



17-*epi*-cortistatin A (**4**): To cortistatinone (5 mg, 0.014 mmol, 1.0 equiv) in CH_2Cl_2 (1.4 mL, 0.001 *M*) was added TMSimidazole (5.8 mg, 6.1 μl, 0.042 mmol, 3.0 equiv). After 5 hours, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with by sat. aq. $NaHCO_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL) and these portions were added to the organic layer, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by chromatography (EtOAc) and then dissolved into THF (28 μl, 0.5 *M*) (solution A). To 7-bromoisoquinoline (8.6 mg, 0.042 mmol, 3.0 eqiv) in THF (0.21 mL, 0.2 *M*) was added *n*-BuLi (17 μL, 2.5 *M*, 0.042 mmol, 3.0 equiv) dropwise at -78 °C. After 40 minutes, TMEDA was added (19 μL, 0.13 mmol, 9.0 equiv). After 10 minutes, solution A was added into the reaction mixture. After another 10 minutes, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The aqueous layer was extracted with EtOAc (4 × 10 mL). The combined organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in 1% EtOH in toluene (2.8 ml, 0.005 *M*) and Ra-Ni (prepared by procedure above, 28 drops) was added. The reaction was immersed in an oil bath preheated to 110°C and stirred vigorously for 30 minutes, at which point the reaction had progressed to approximately 70% conversion, as judged by LCMS. Removal of the supernatant, followed by washing of the Raney nickel catalyst with 1:1 MeOH:EtOAc (10 mL), and concentration of the combined filtrates produced a residue that was stirred in 10% aq. AcOH (1 mL) for

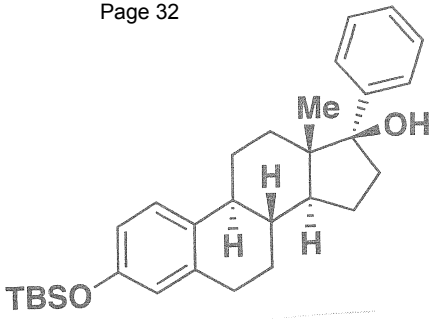
10 mintues and concentrated *in vacuo*. The residue was then purified by HPLC, yielding 17-*epi*-cortistatin A (**4**) (1.1 mg, 0.002 mmol, 16%) as a colorless oil and cortistatin A (**1**) (0.3 mg, 0.0006 mmol, 5%) as a white solid. 17-*epi*-cortistatin A: $[\alpha]^{D}_{20}$ = +45.5° (*c* = 0.068, CD_3OD); IR (neat) ν_{max} = 3355, 3039, 1679, 1295, 1202, 897, 887 cm^{-1}; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.27 (s, 1 H), 8.32 (d, *J* = 6.0 Hz, 1 H), 7.95 – 7.85 (m, 3 H), 7.69 (d, *J* = 8.1 Hz,1 H), 6.01 (d, *J* = 2.4 Hz, 1 H), 5.15 (dd, *J* = 5.1. 2.5 Hz, 1 H), 3.9 (d, *J* = 9.0 Hz, 1 H), 3.36 (t, *J* = 9.8 Hz, 1 H), 3.28 – 3.25 (m, 1 H), 3.12 (t, *J* = 7.2 Hz, 1 H), 2.84 (s, 3 H), 2.69 (s, 3 H), 2.50 – 2.44 (m, 1 H), 2.40 – 2.31 (m, 2 H), 2.18 – 2.16 (m, 1 H), 2.11 – 2.03 (m, 3 H), 1.95 – 1.88 (m, 3 H), 1.75 – 1.64 (m, 3 H), 1.04 (s, 3 H); HRMS (ESI-MS) calcd for $C_{30}H_{36}N_2O_3$ $[M + H]^+$ 473.2799, found 473.2786.

Figure S1: X-ray structures of compound 6a, compound 7a, compound 8a, compound 9a, and compound 10.



Reference:

1. T. L. Fevig, J. A. Katzenellenbogen, *J. Org. Chem.* **1987**, *52*, 247 – 251.
2. V. Lecomte, E. Stéphan, F. L. Bideau, G. Jaouen, *Tetrahedron* **2003**, *59*, 2169 – 2176.
3. N. Foy, E. Stéphan, A. Vessières, E. Salomon, J. –M. Heldt, M. Huché, G. Jaouen, *Chembiochem* **2003,** *4,* 494 – 503.
4. Z. Liu, J. Meinwald, *J. Org. Chem.* **1996**, *61*, 6693 – 6699.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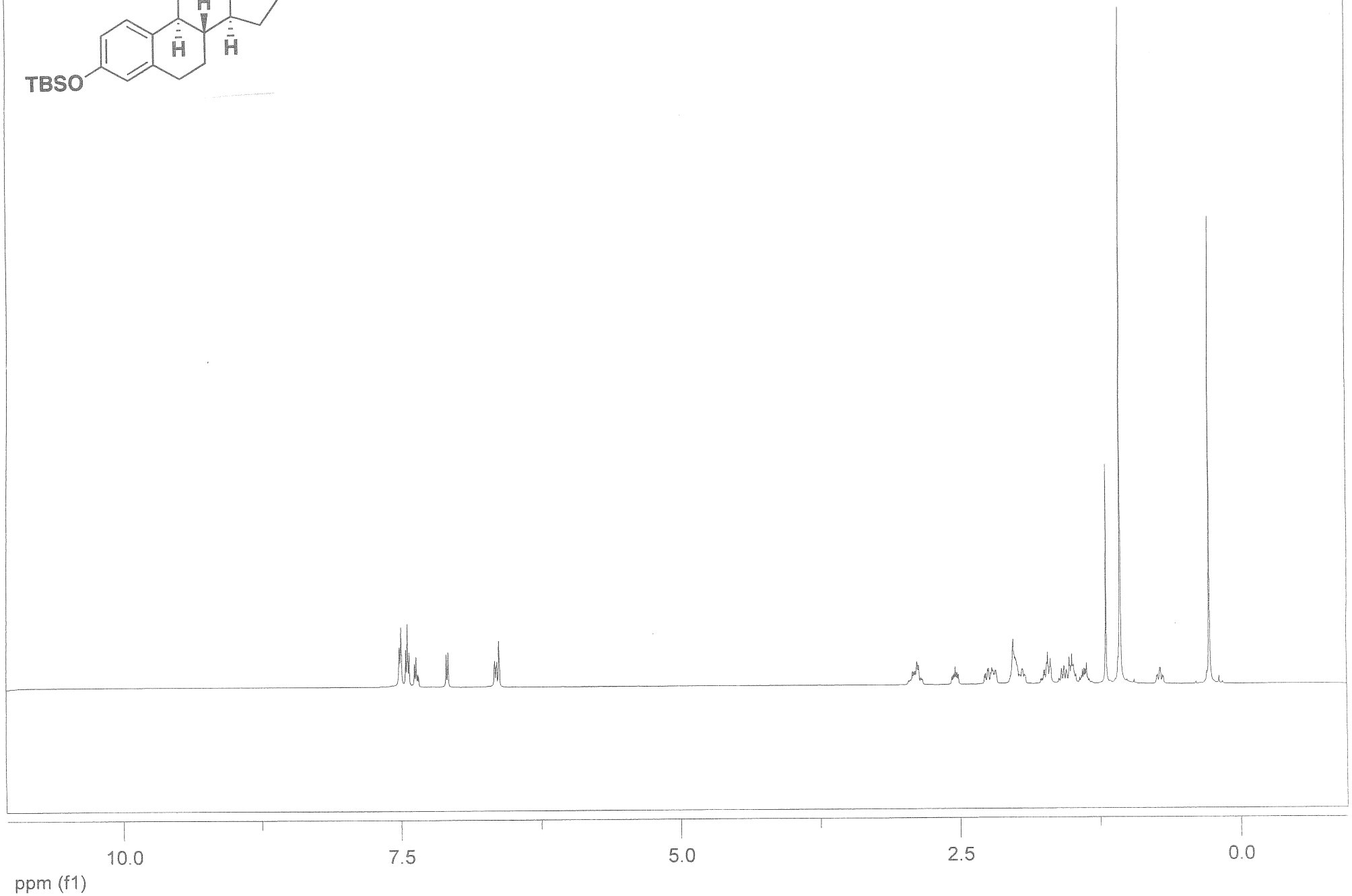
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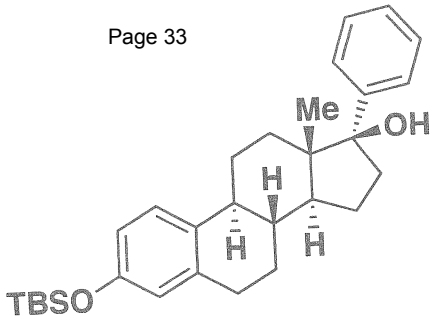
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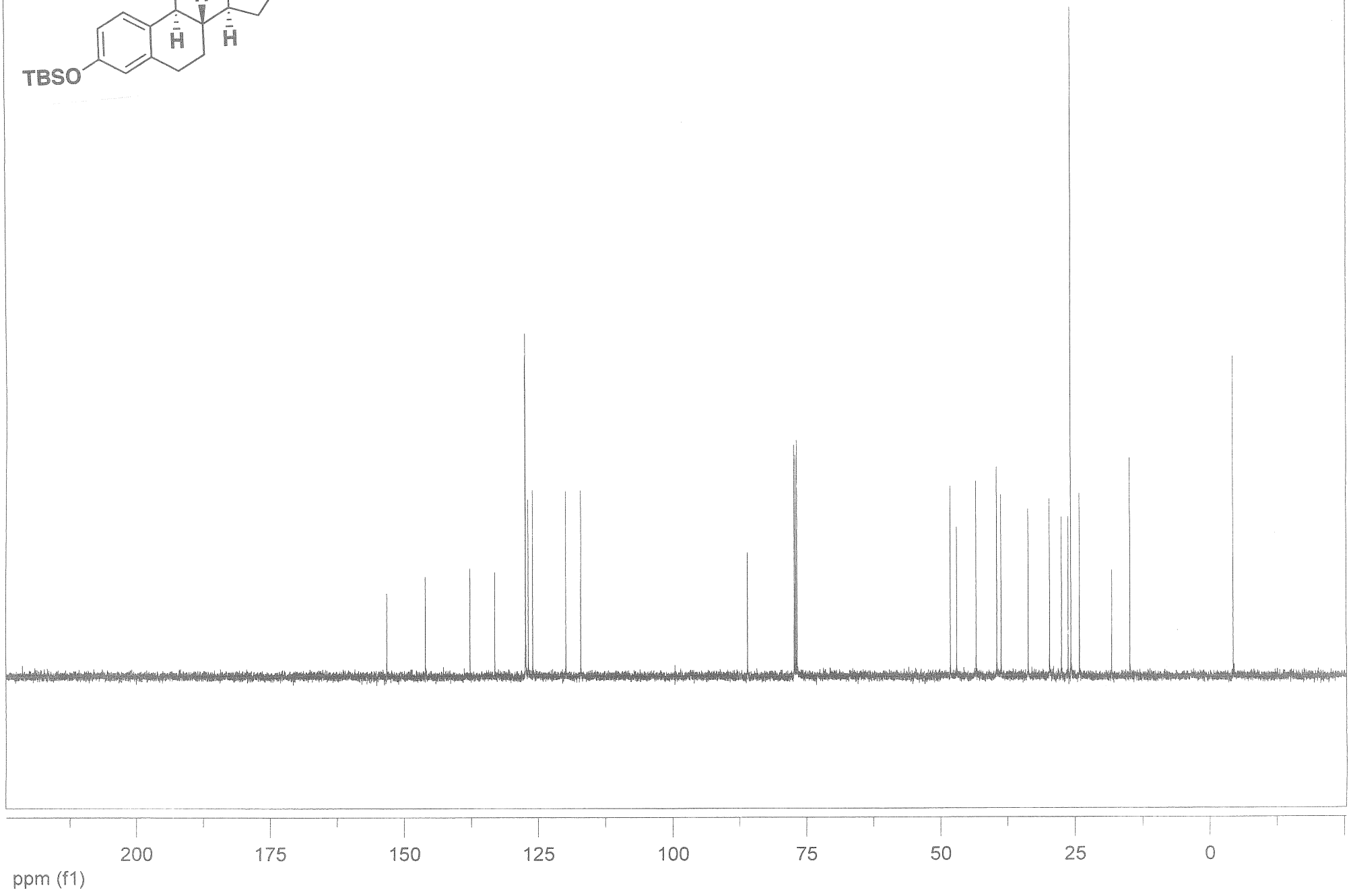
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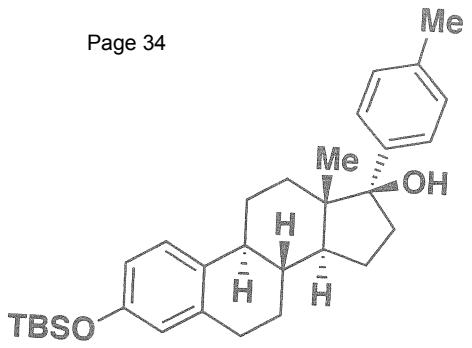
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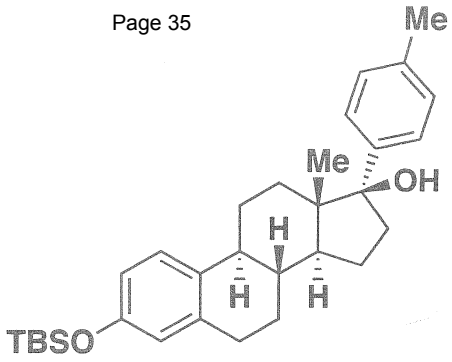
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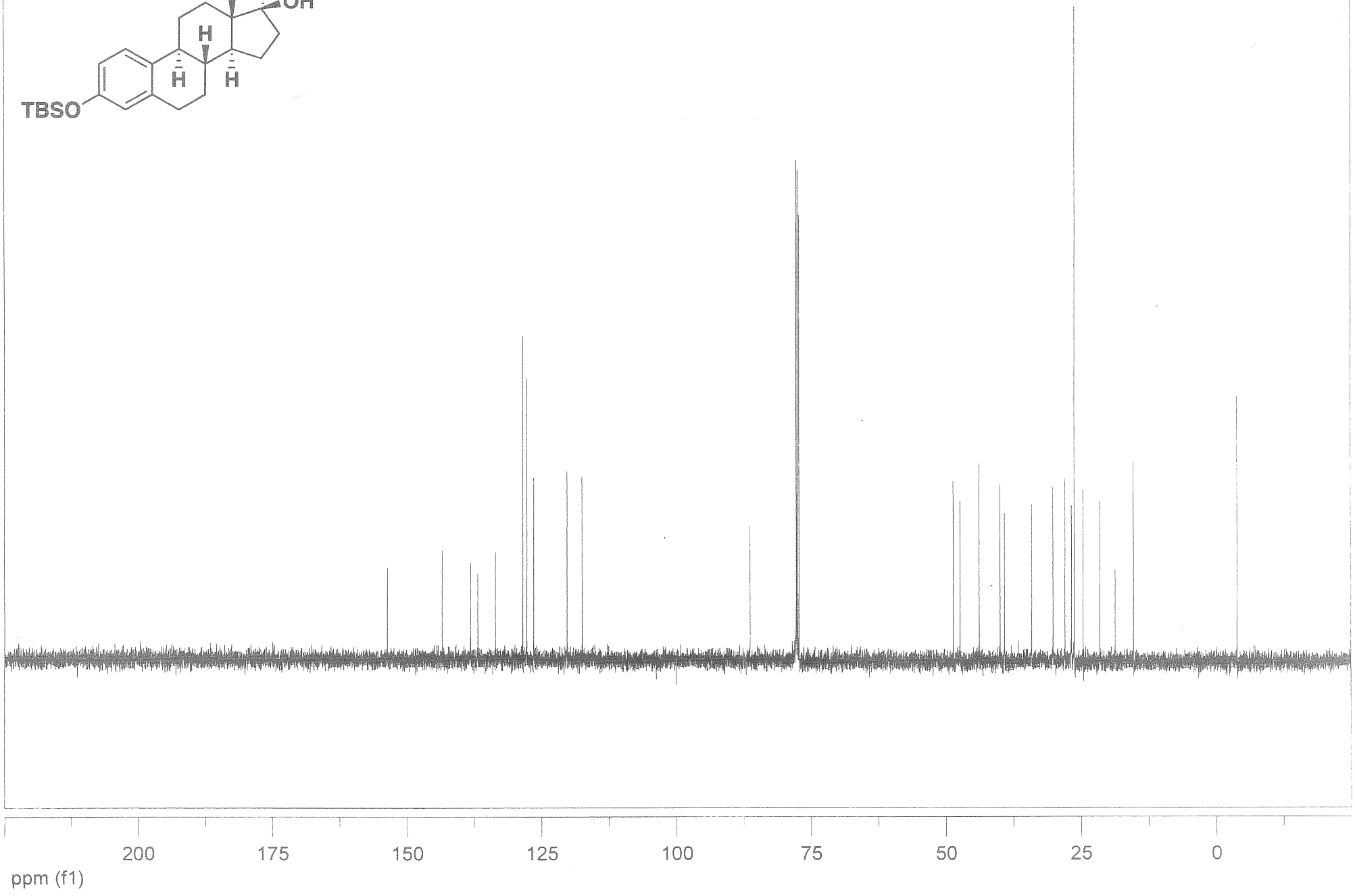
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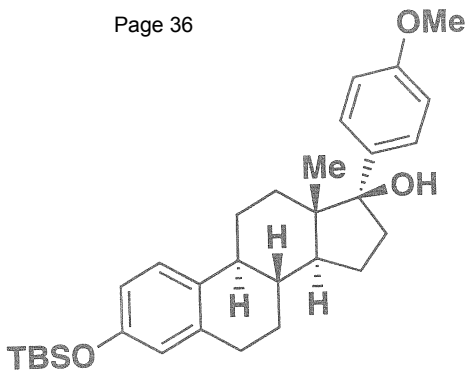
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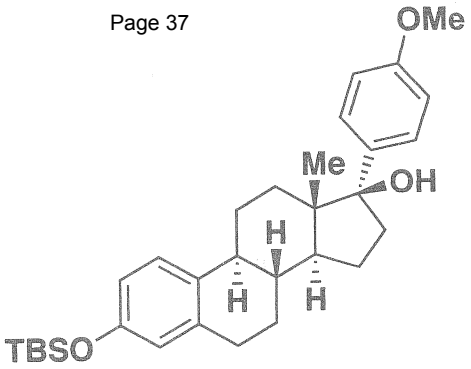
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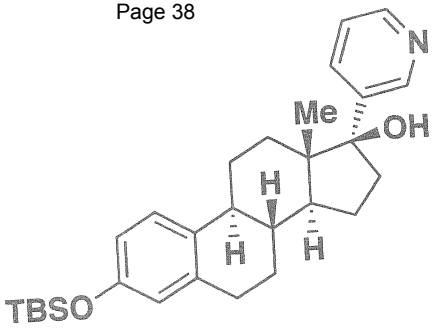
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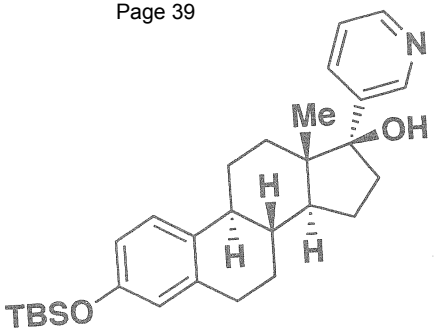
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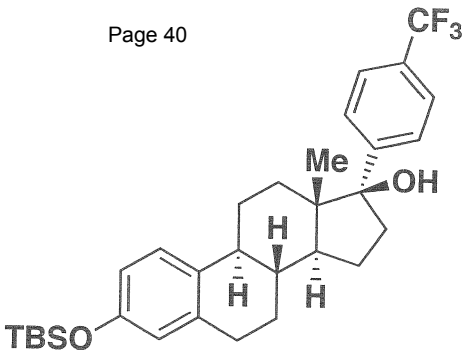
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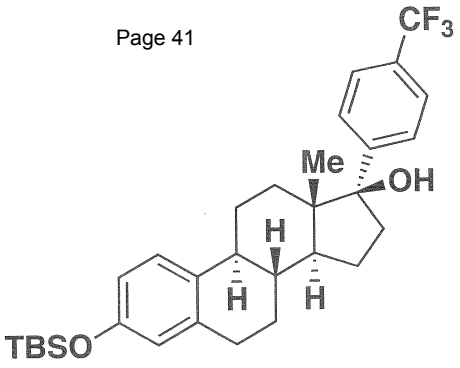
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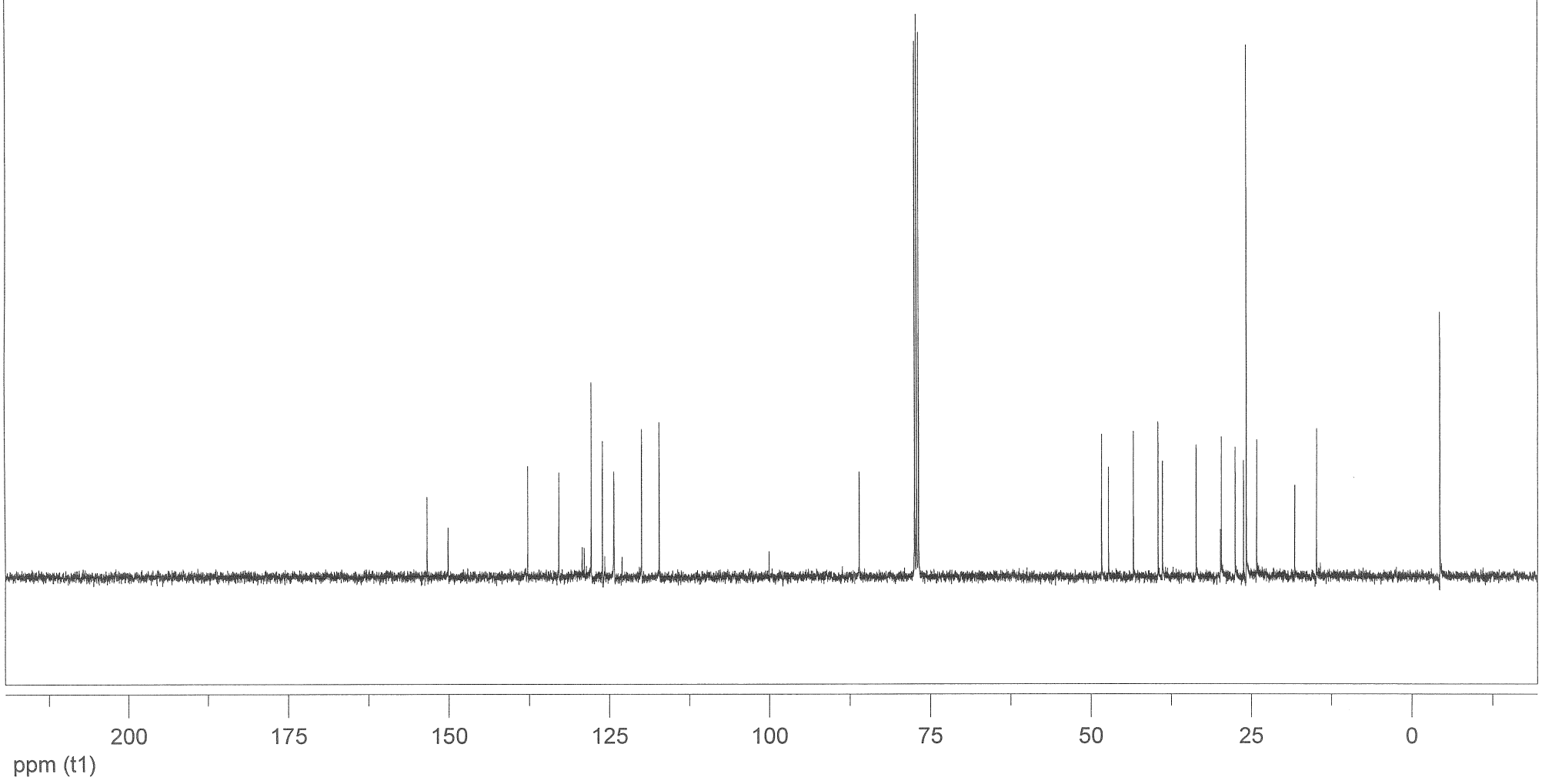
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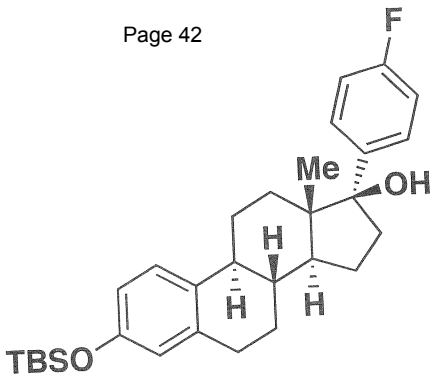
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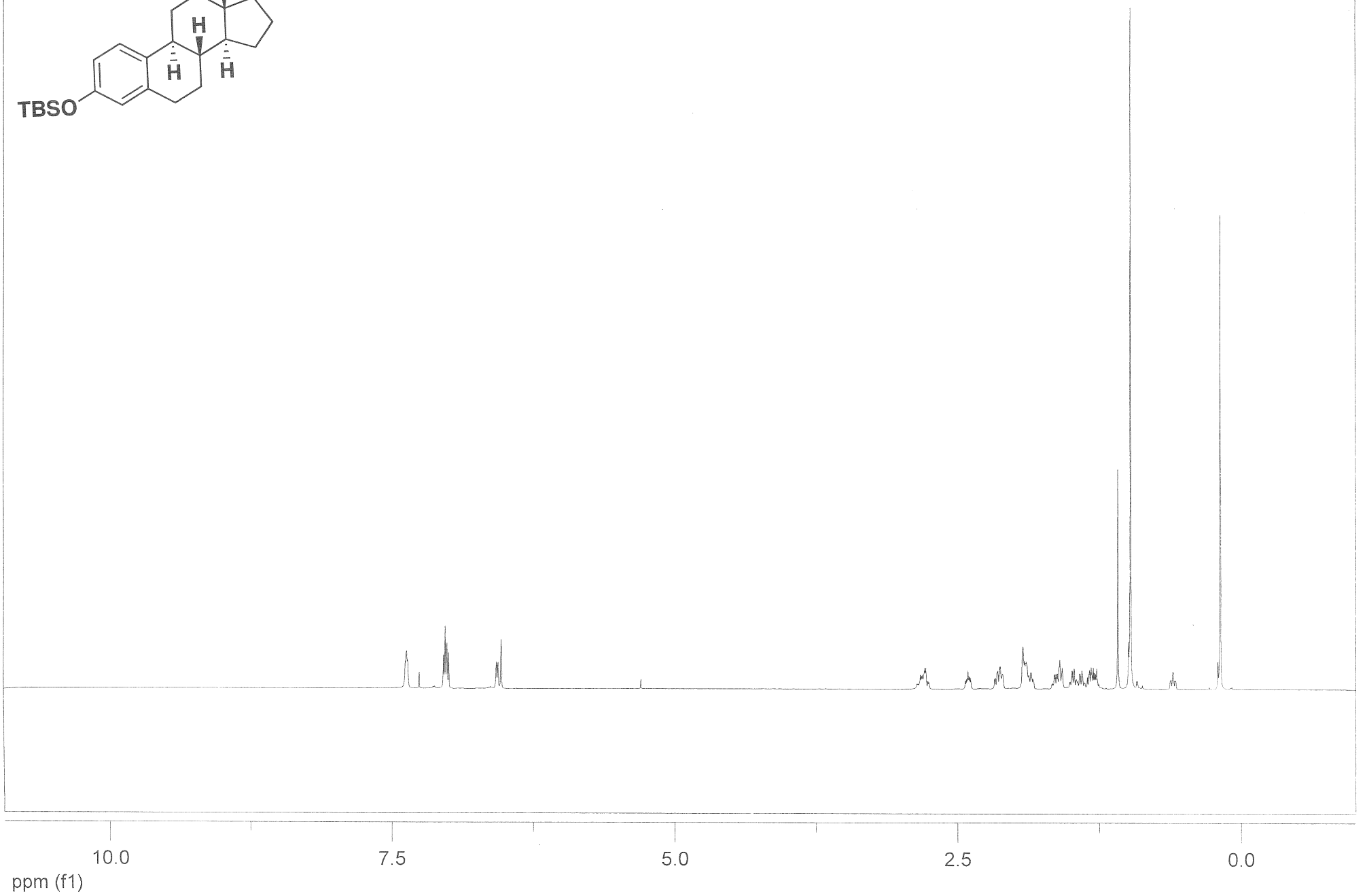
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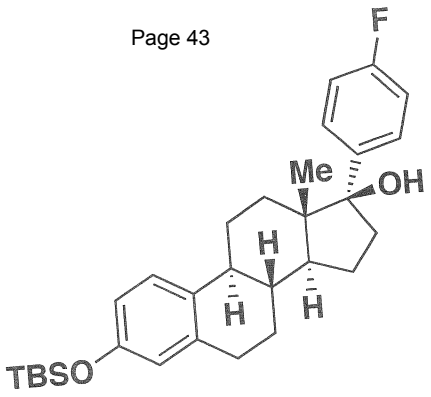
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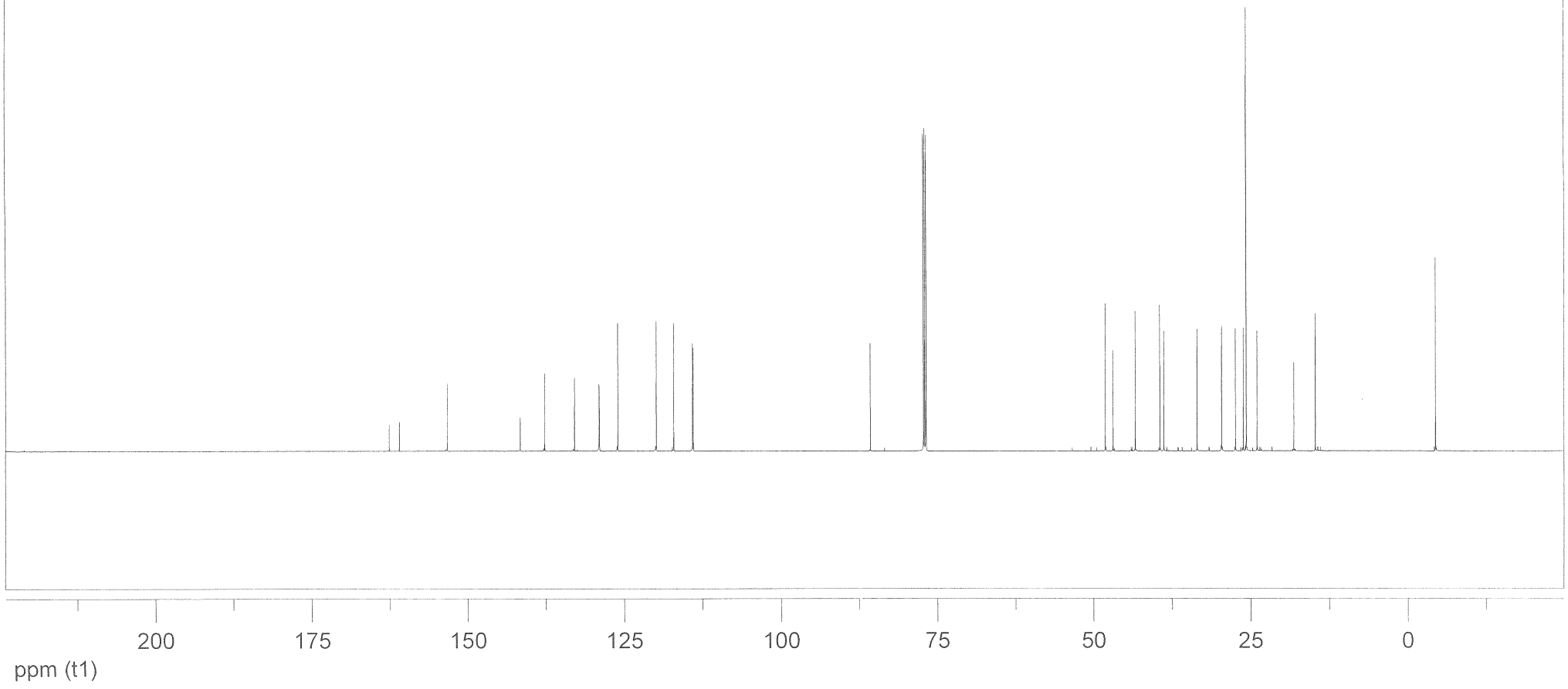
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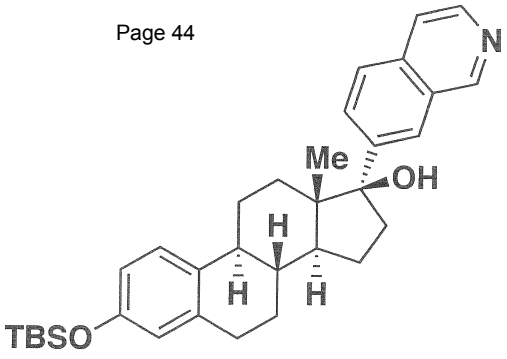
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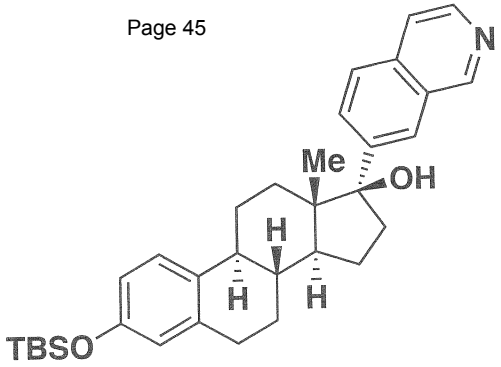
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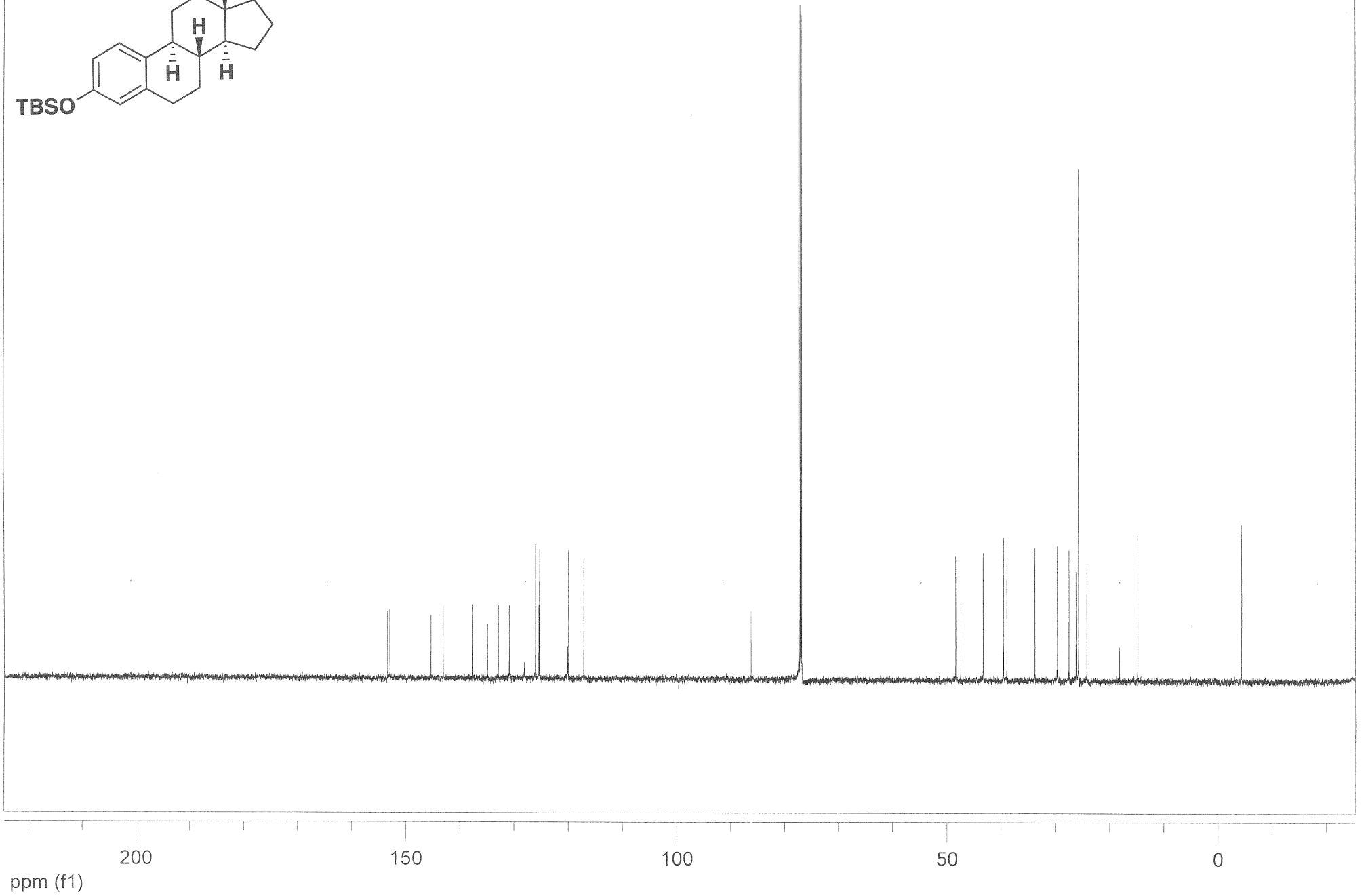
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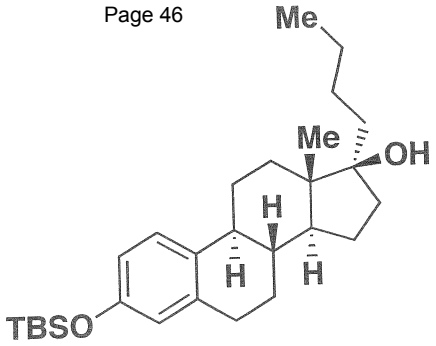
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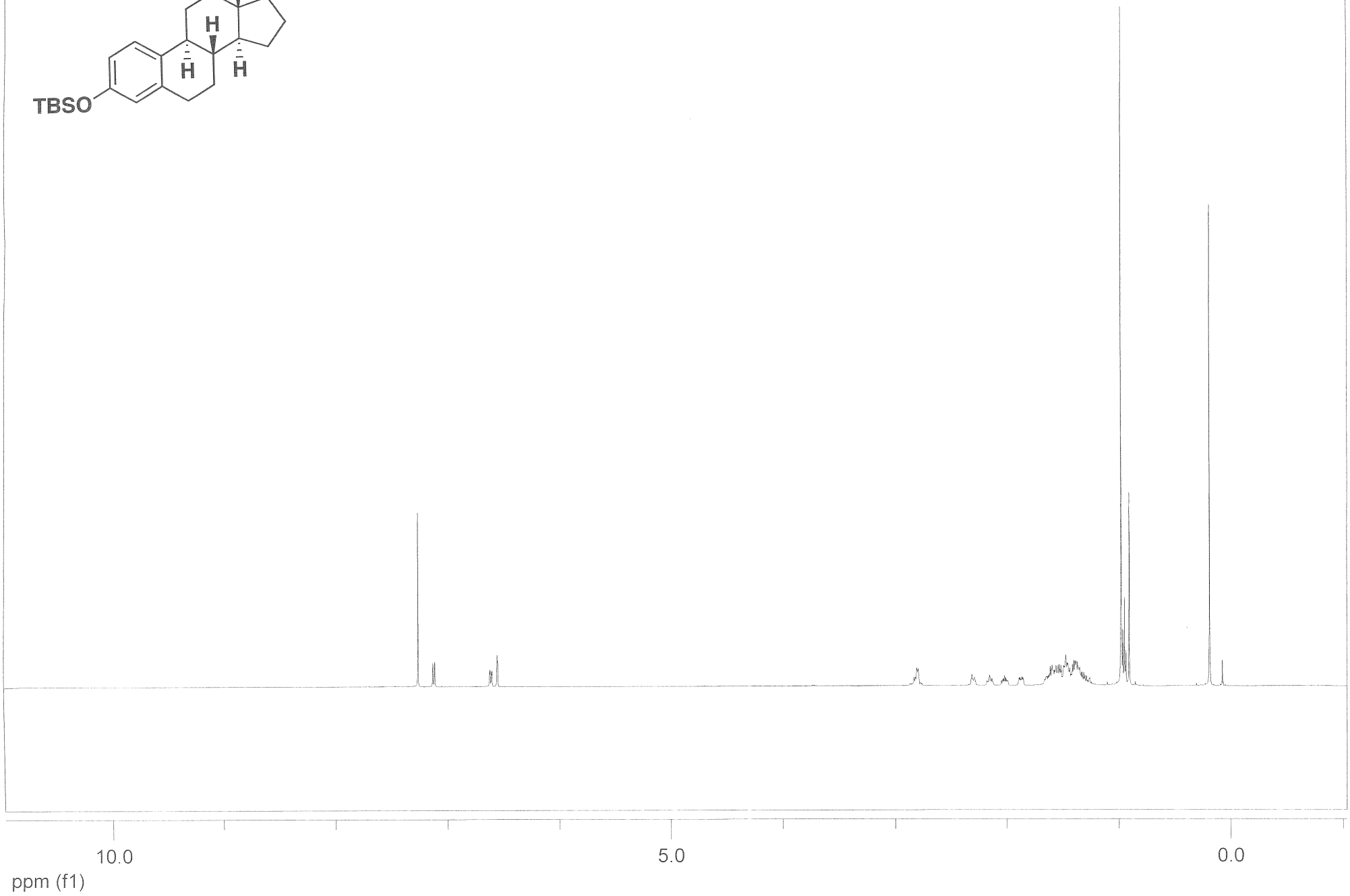
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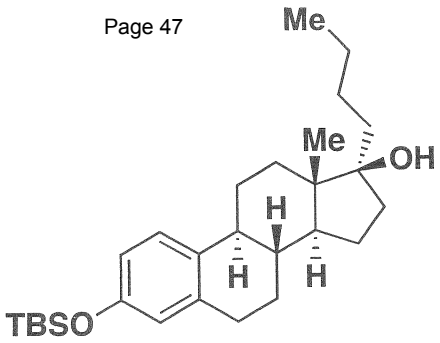
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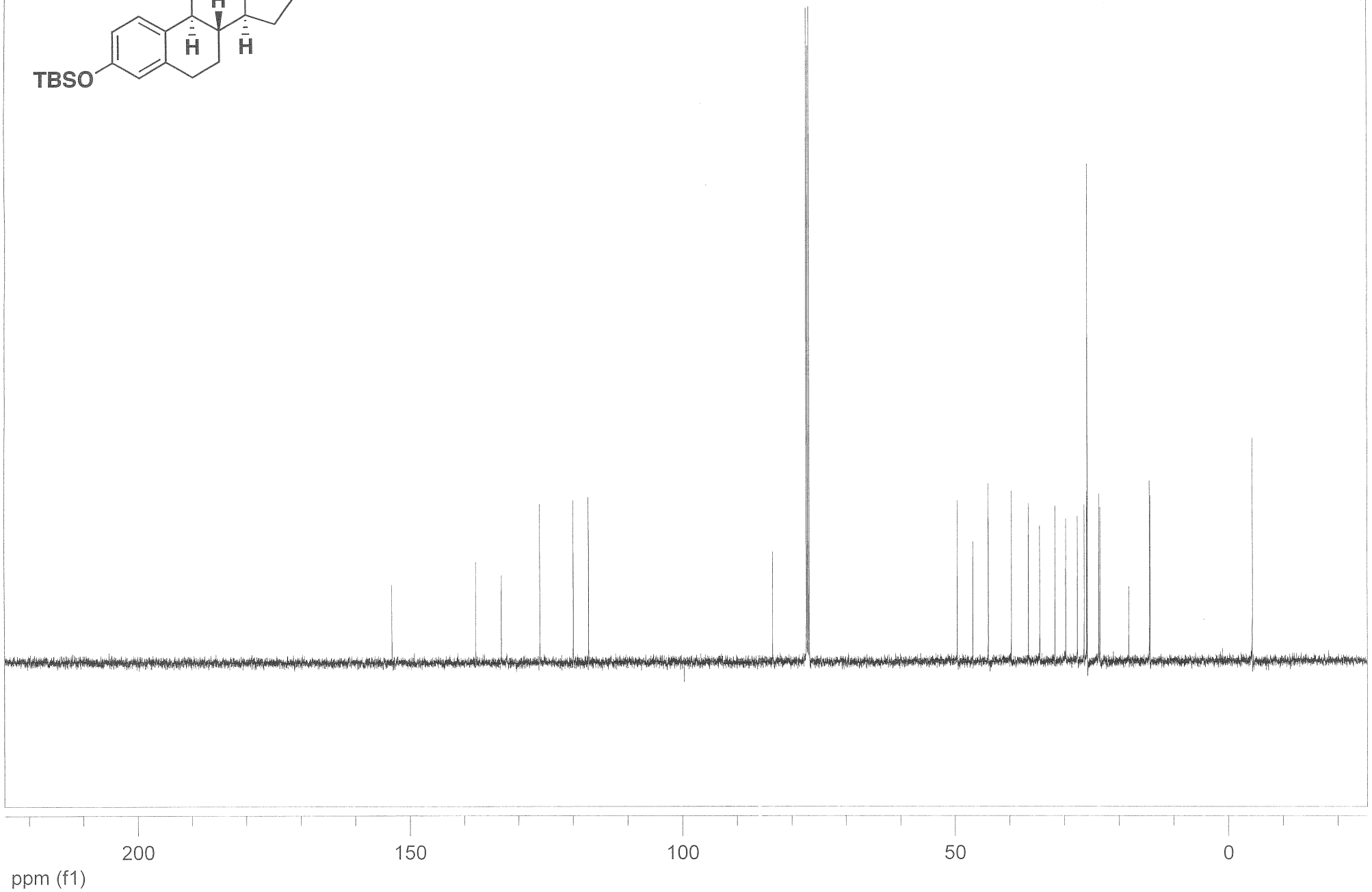
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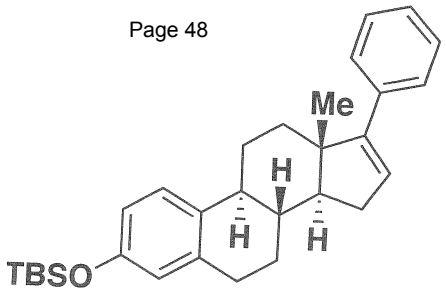
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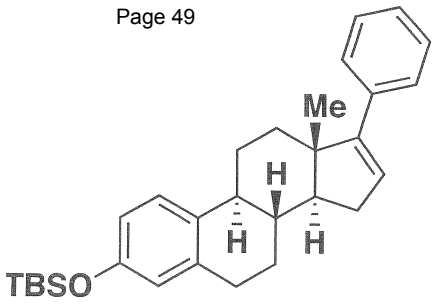
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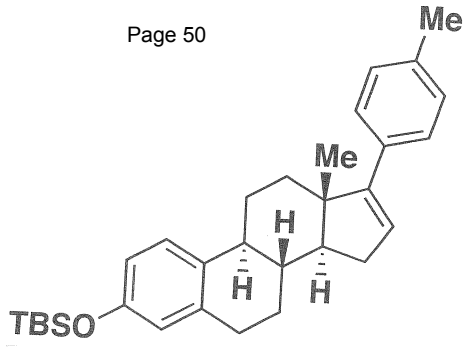
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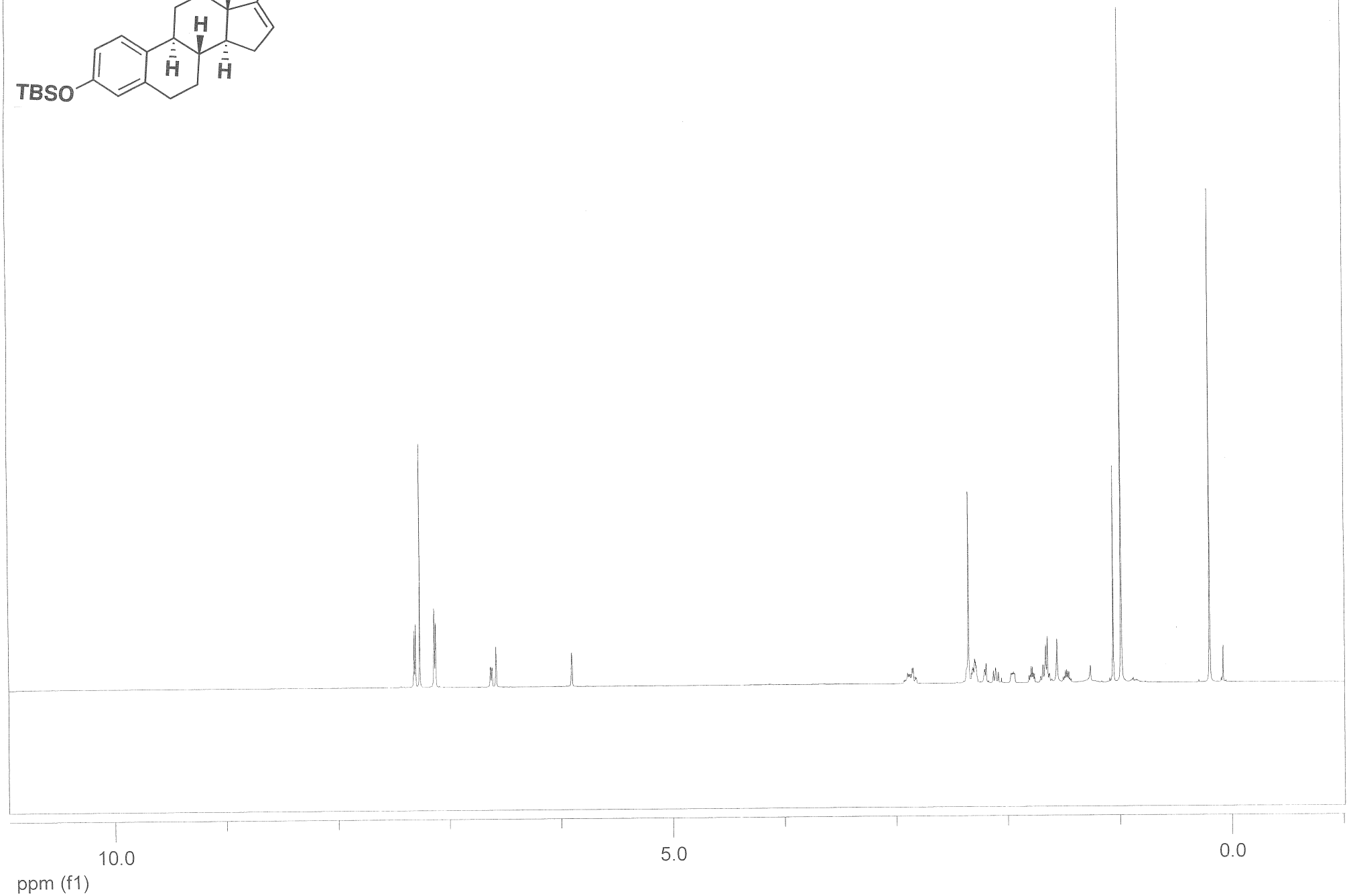
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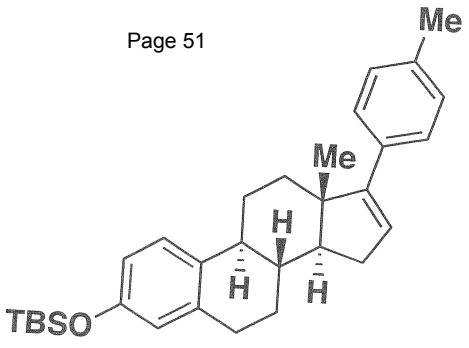
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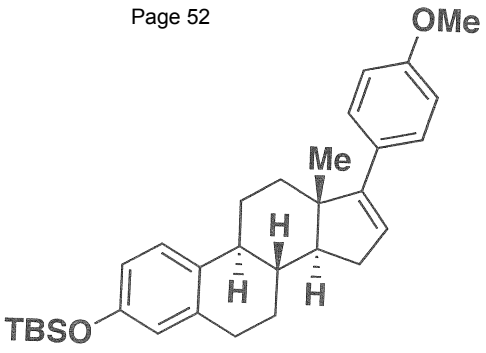
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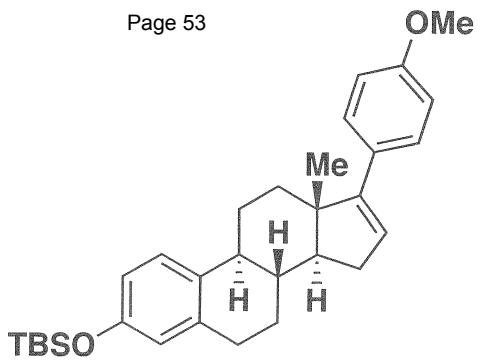
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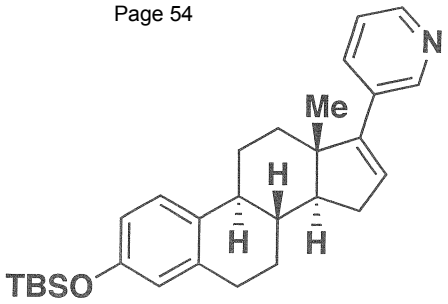
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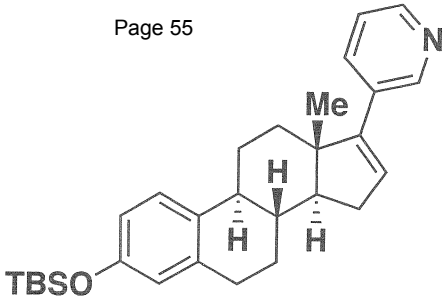
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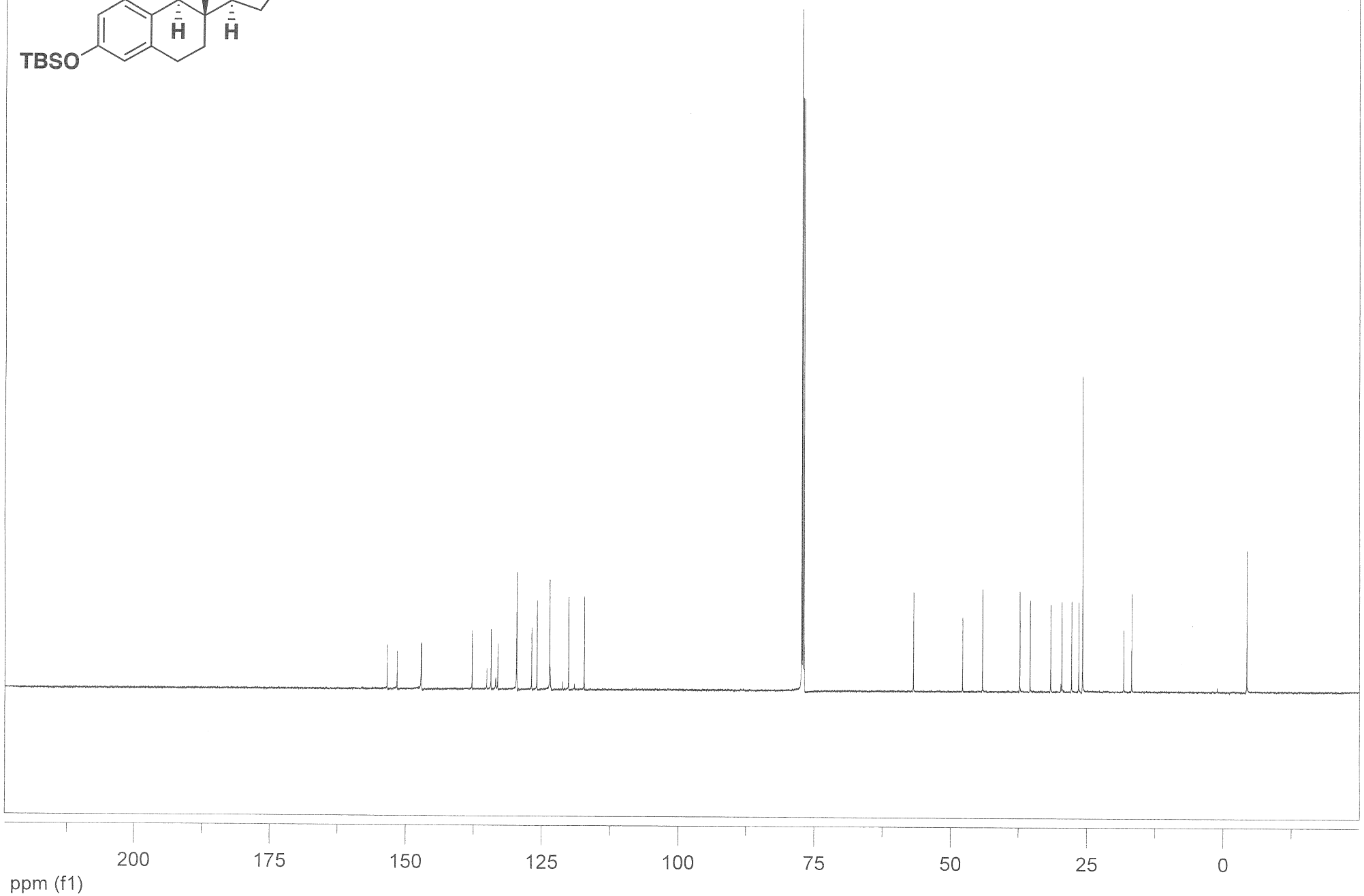
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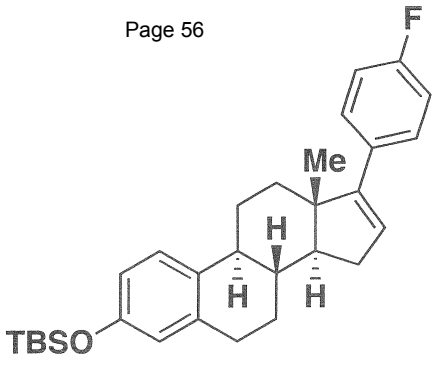
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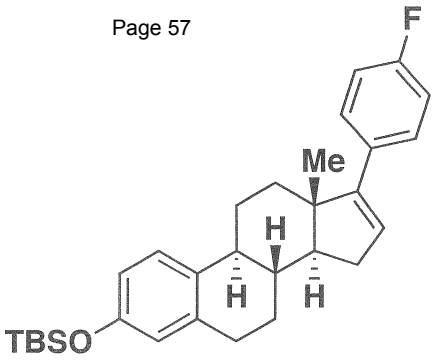
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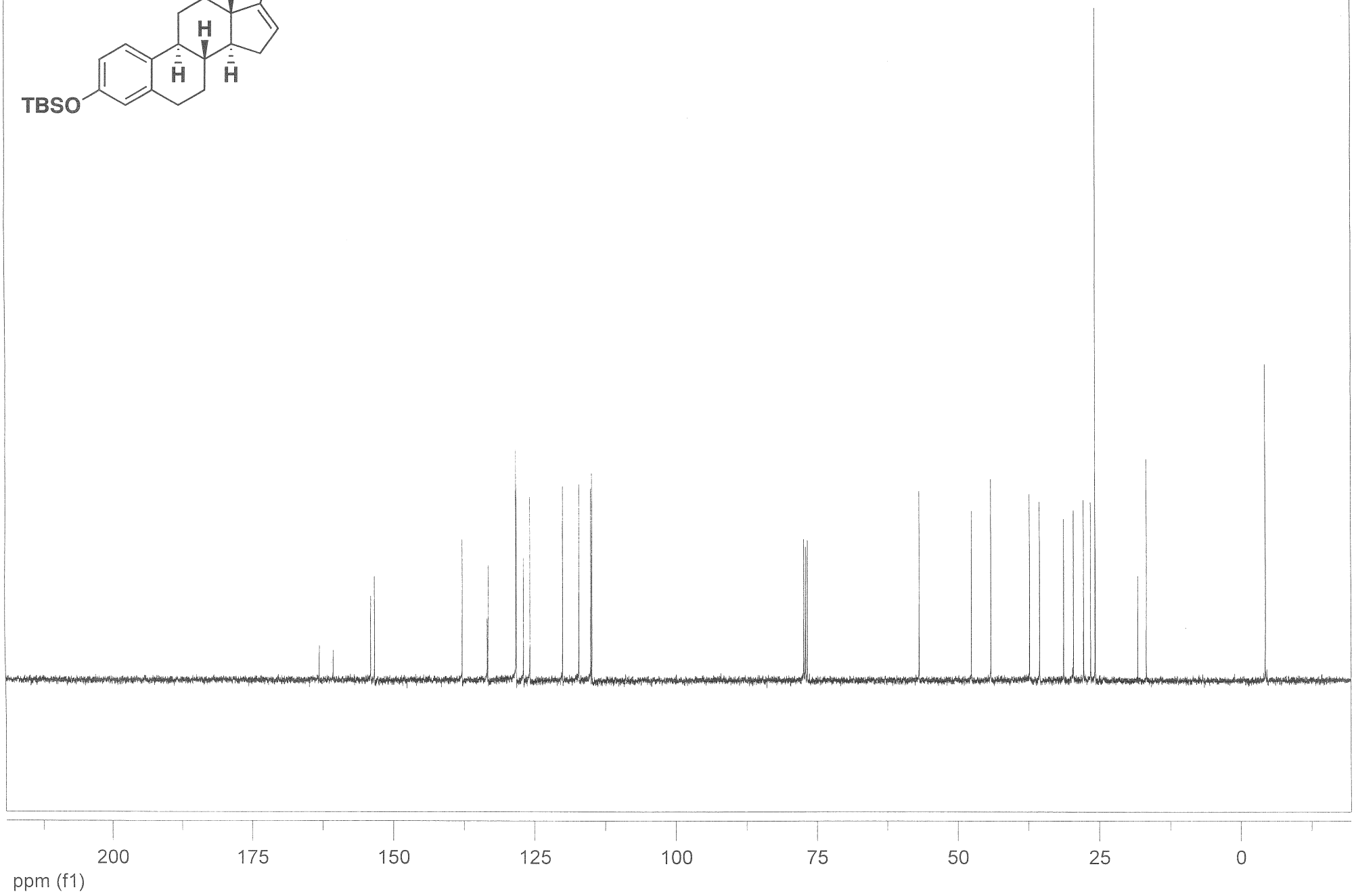
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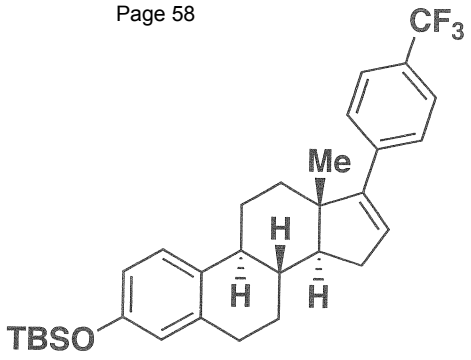
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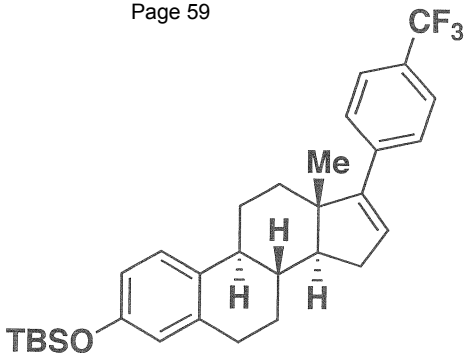
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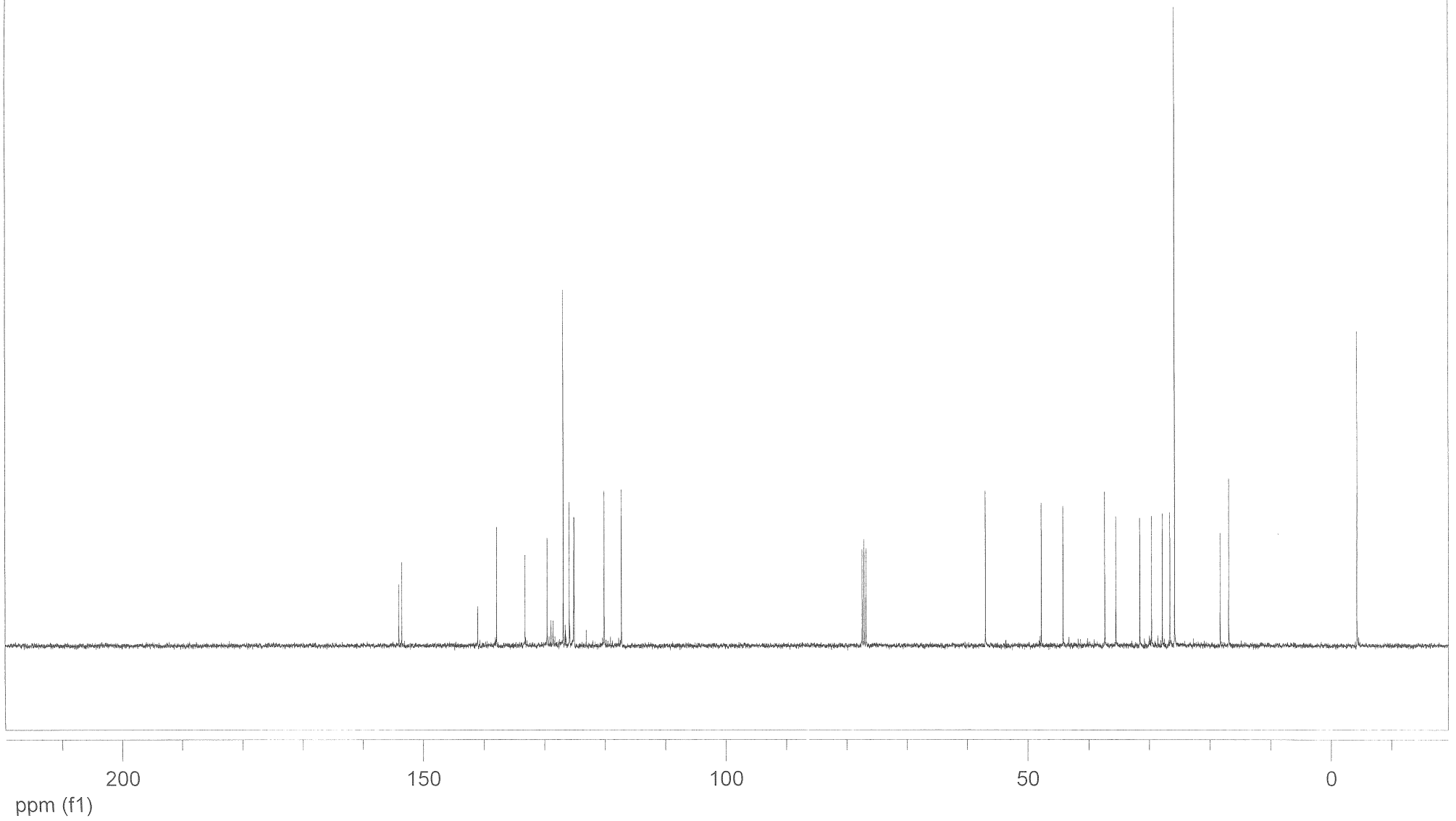
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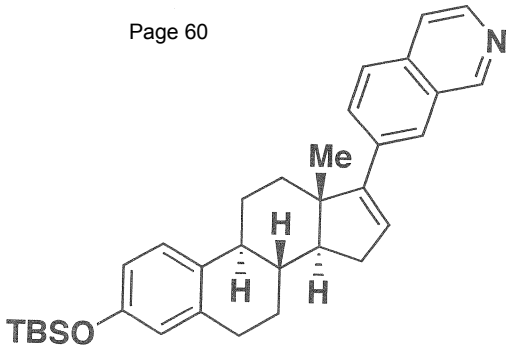
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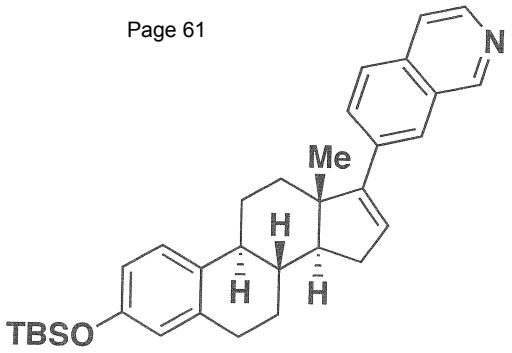
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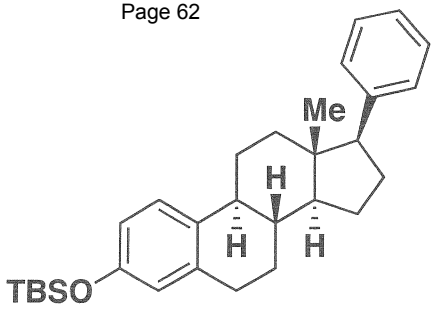
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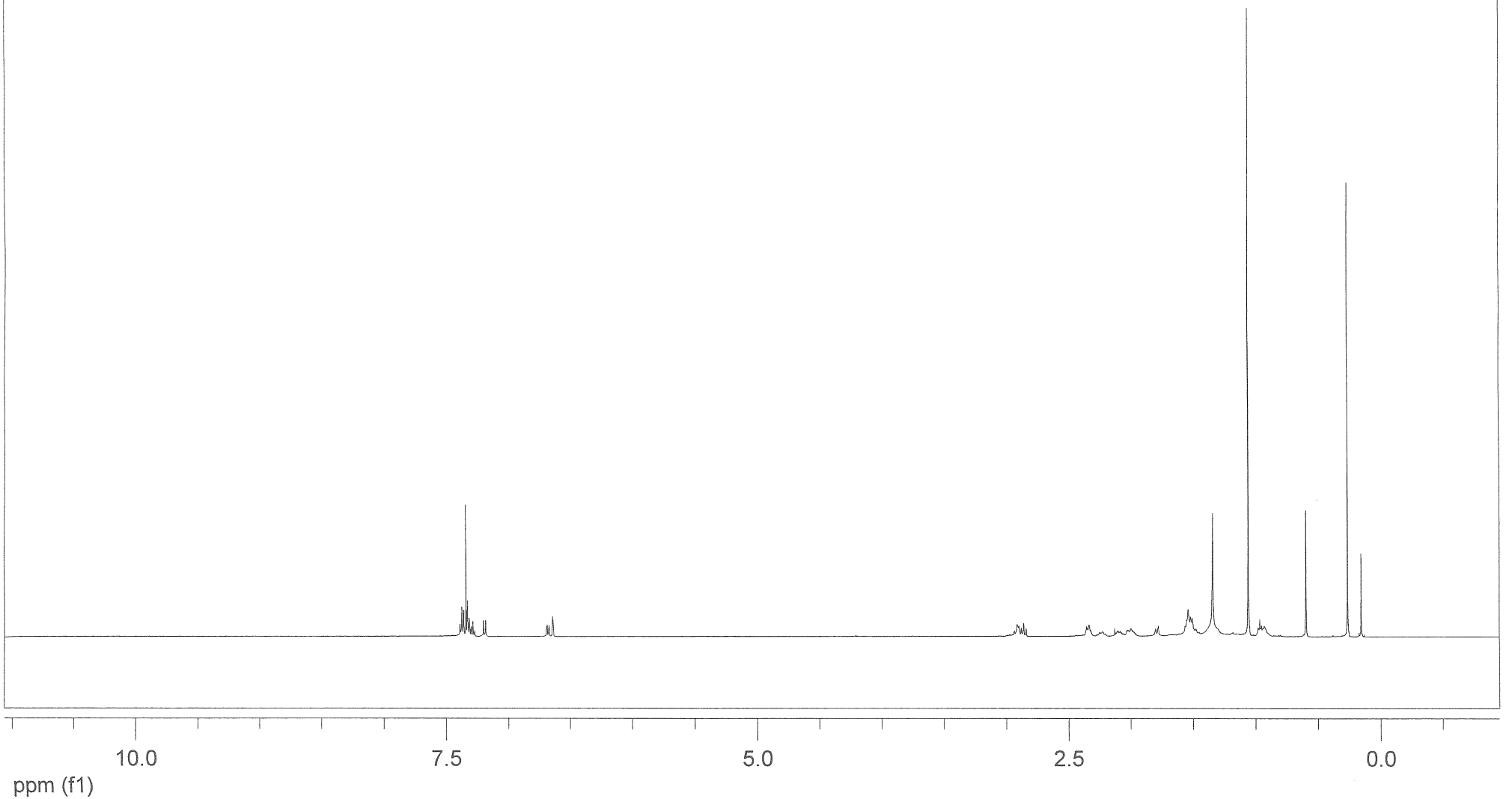
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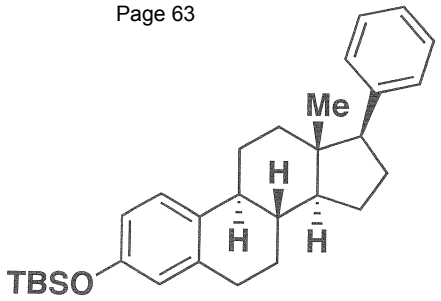
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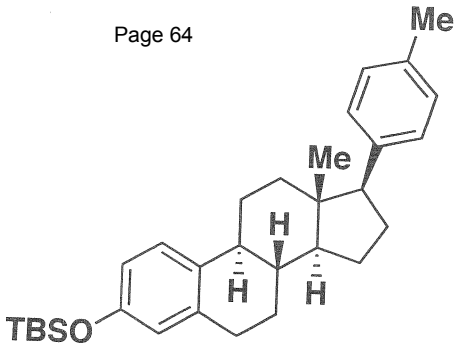
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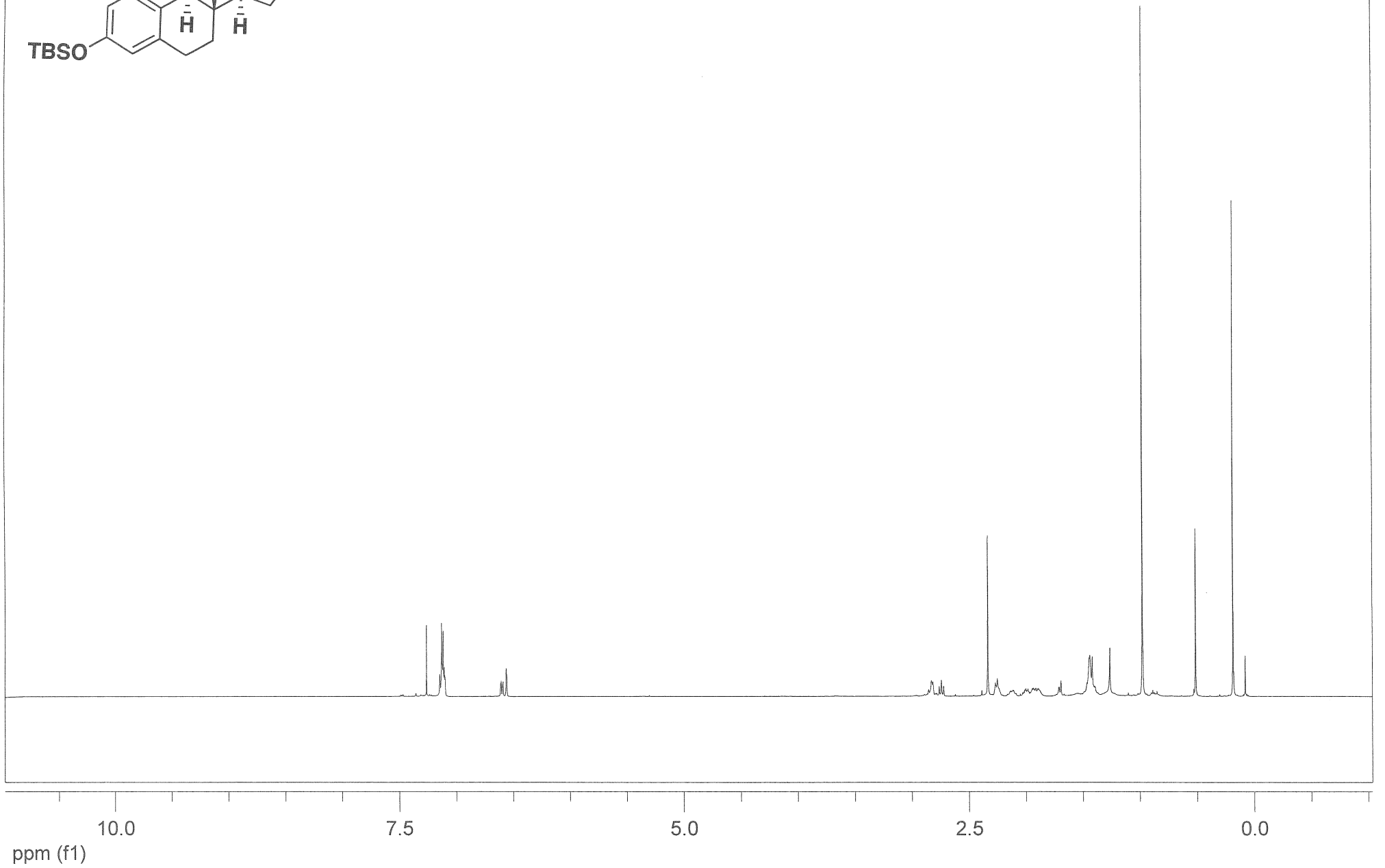
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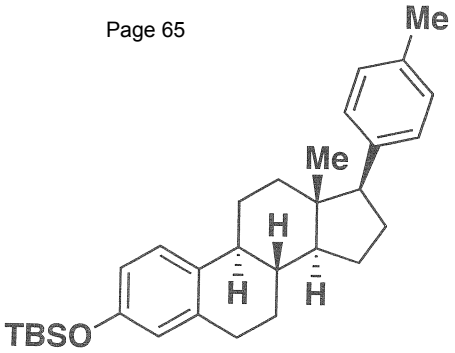
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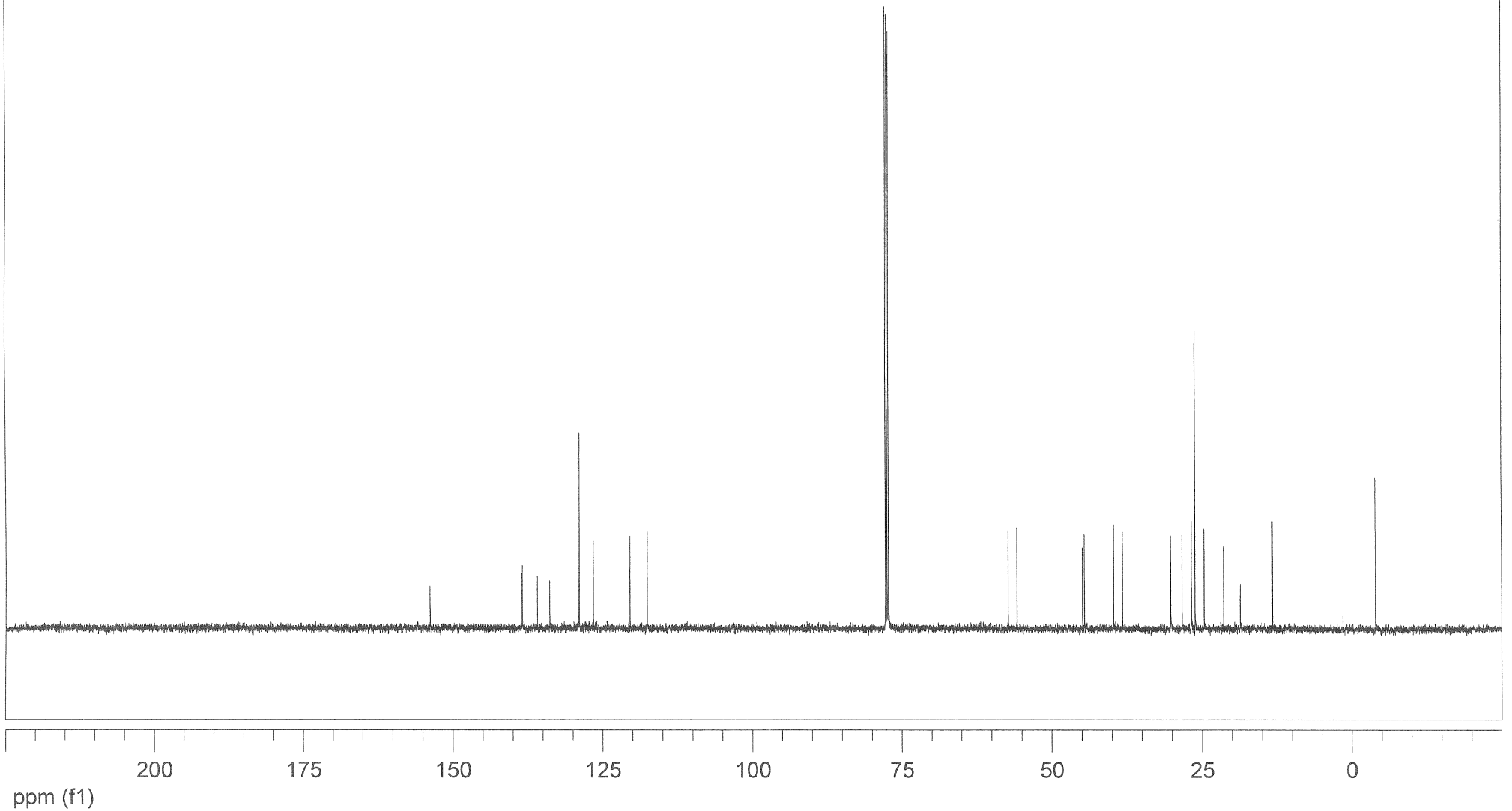
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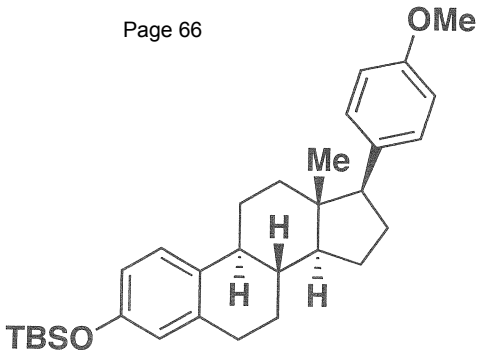
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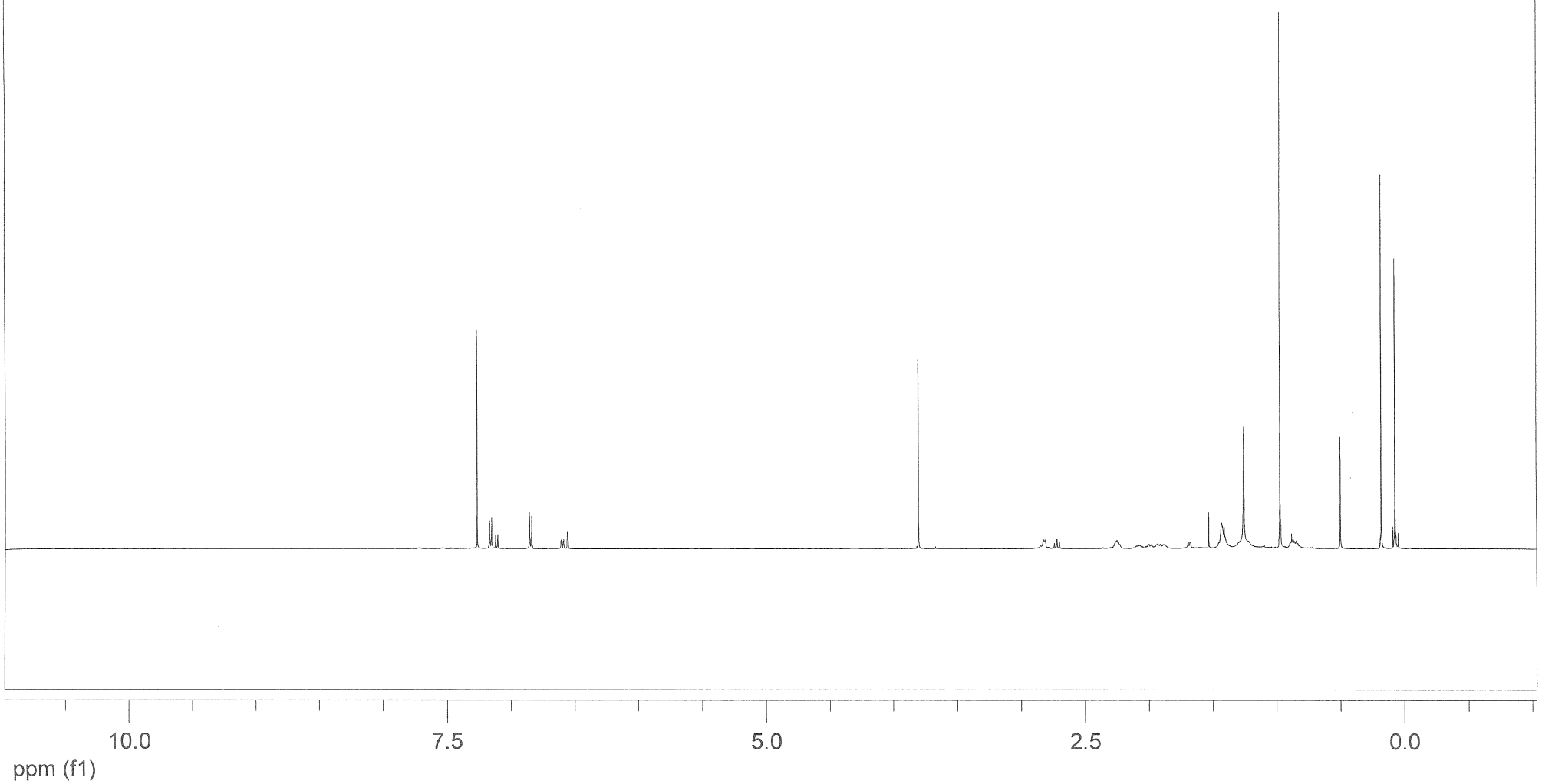
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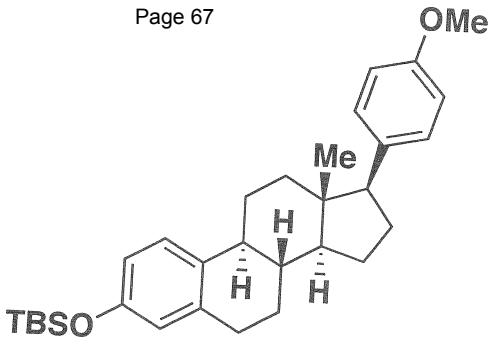
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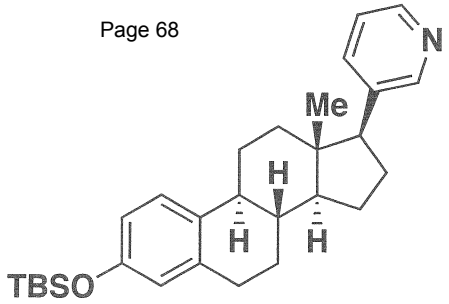
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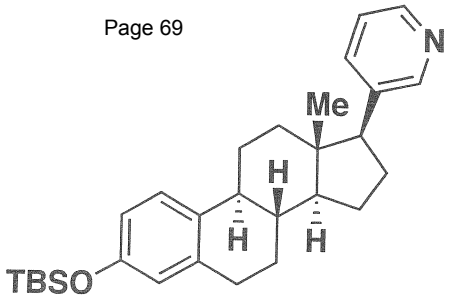
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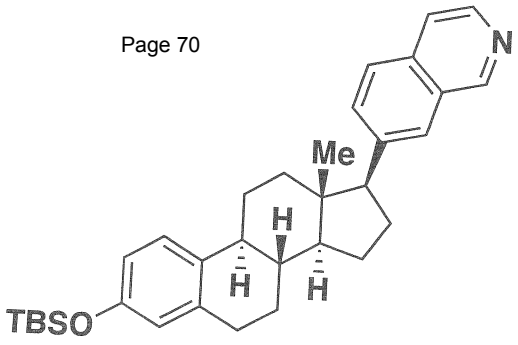
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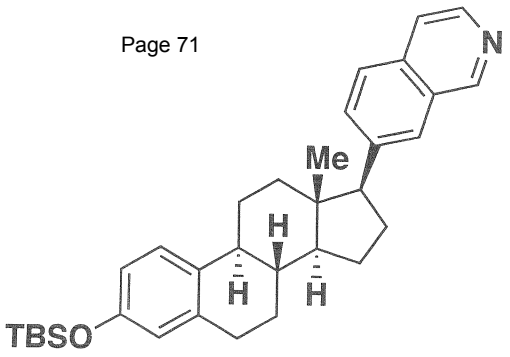
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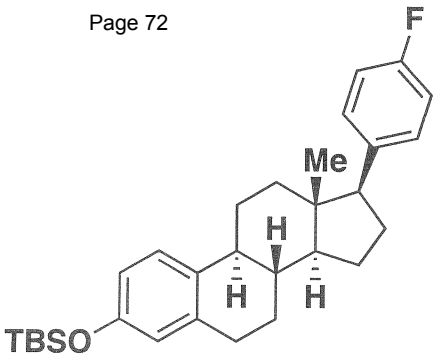
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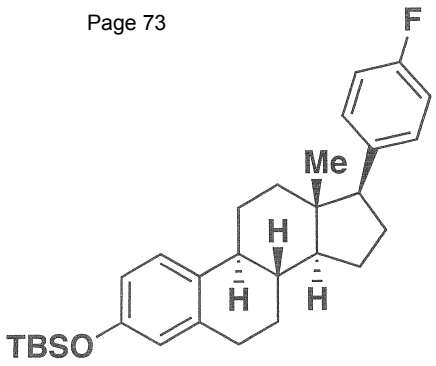
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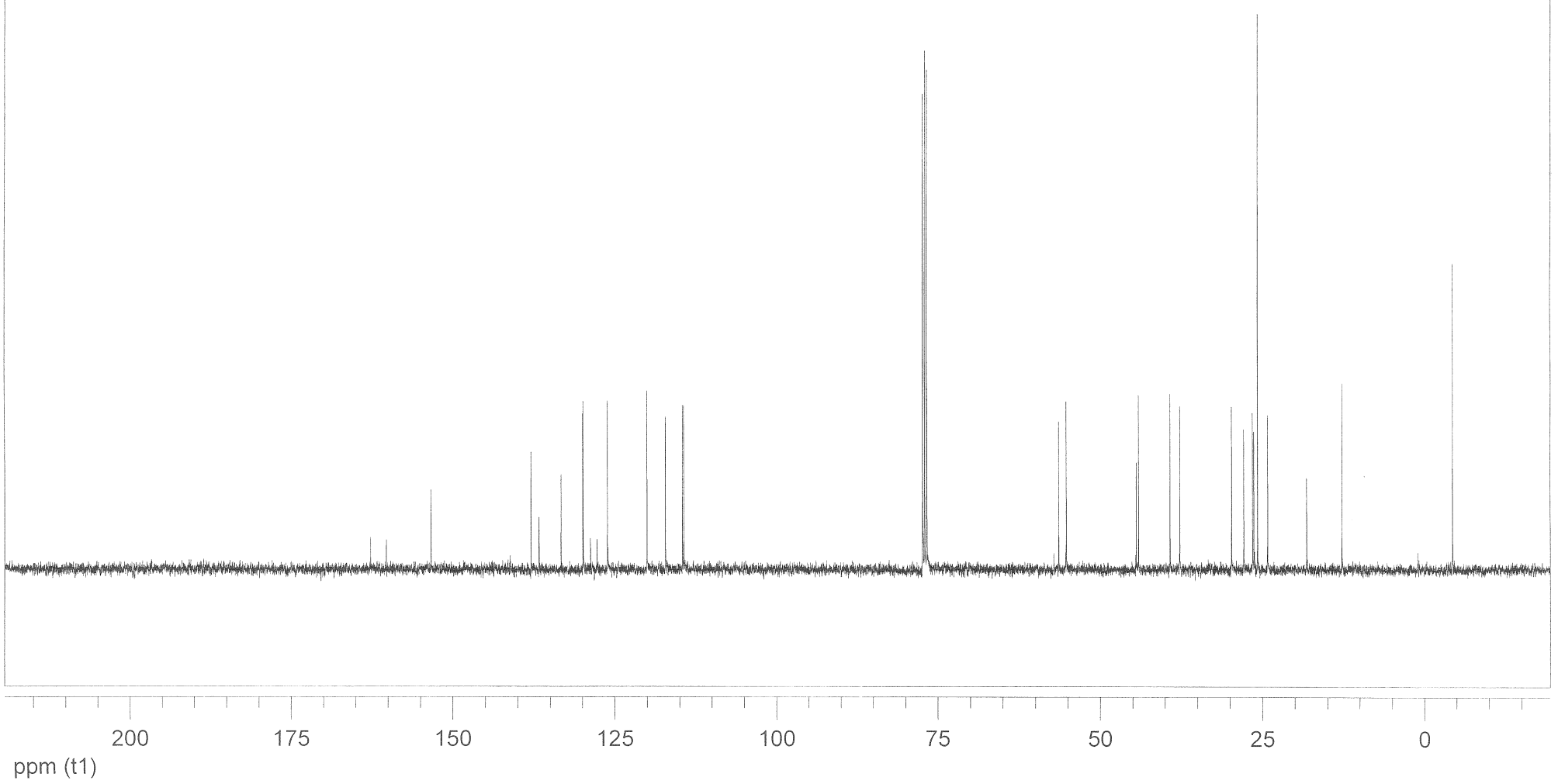
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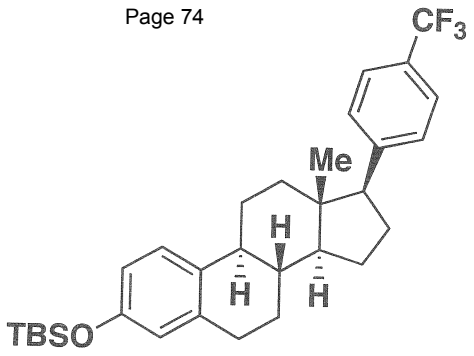
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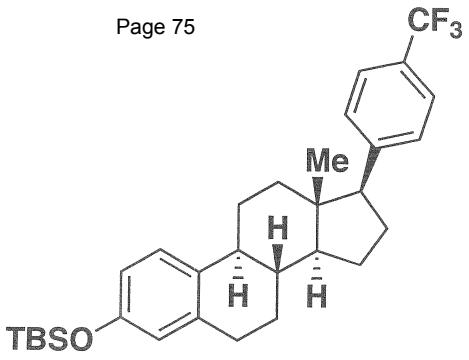
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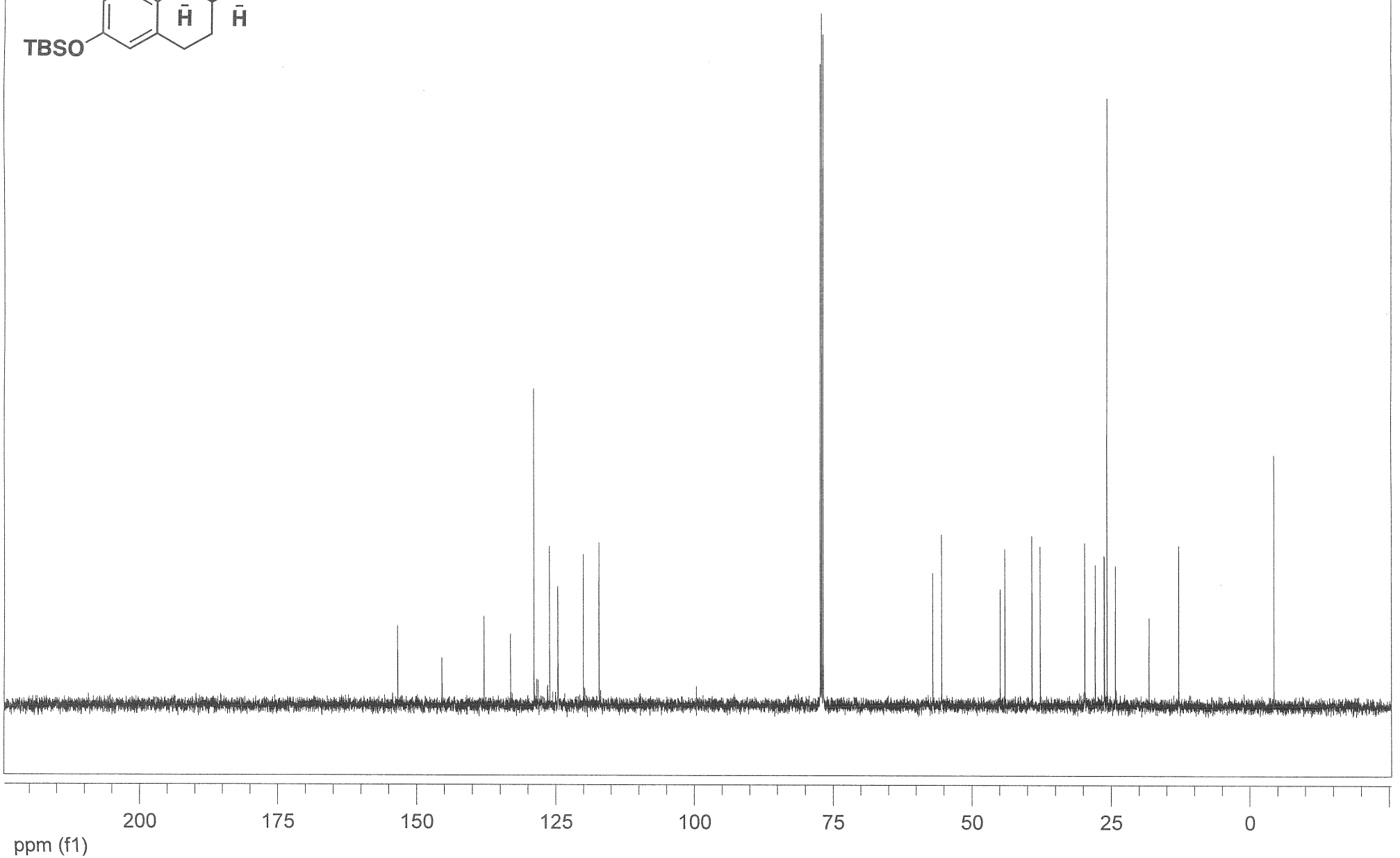
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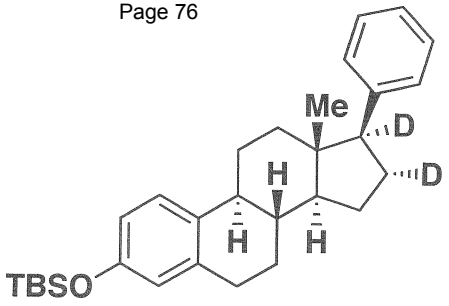
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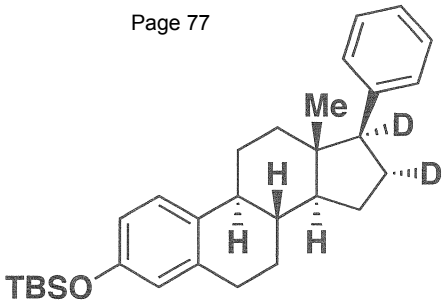
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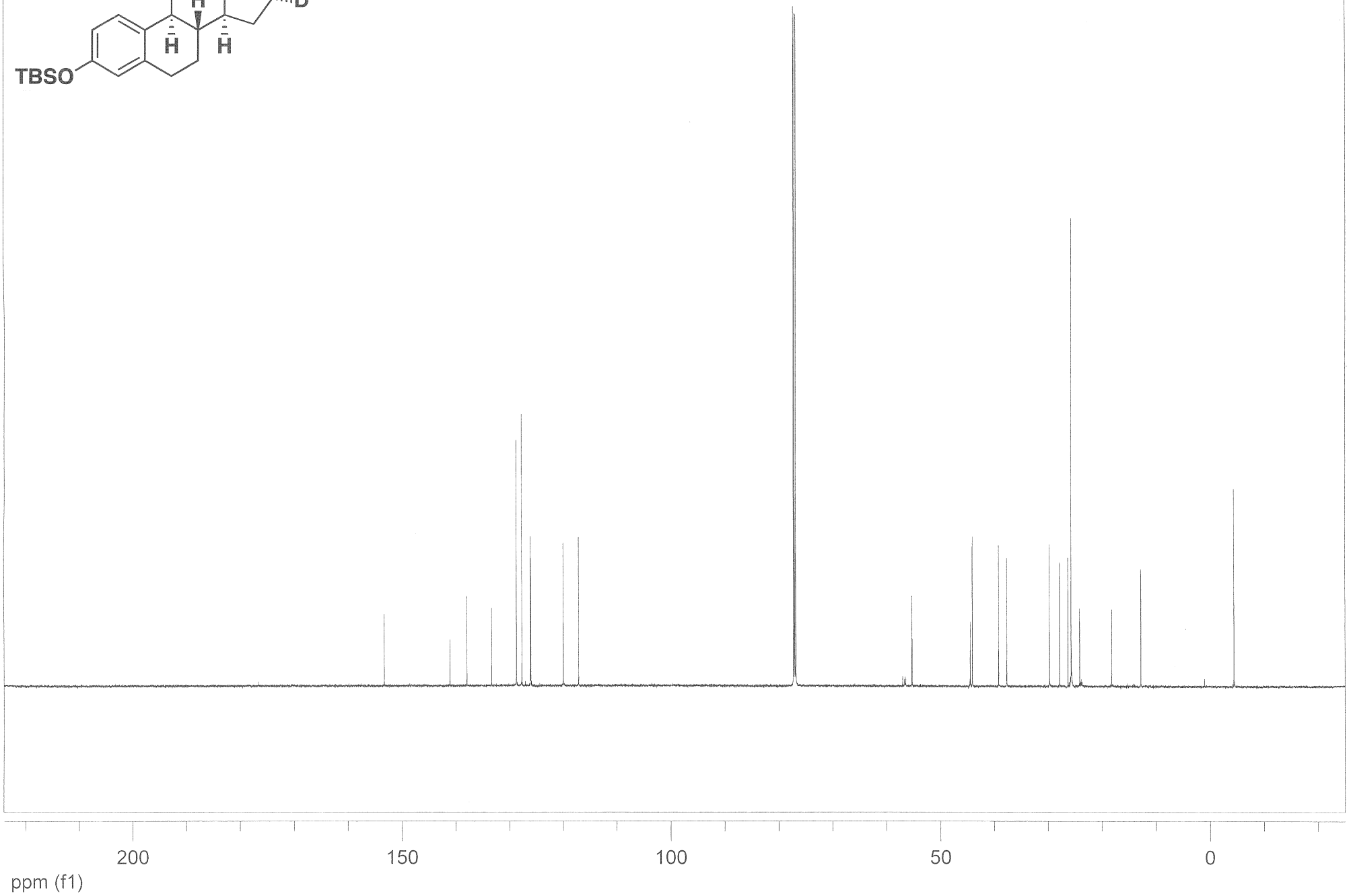
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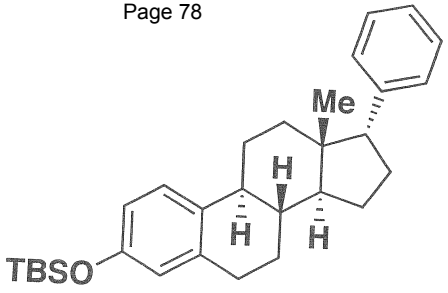
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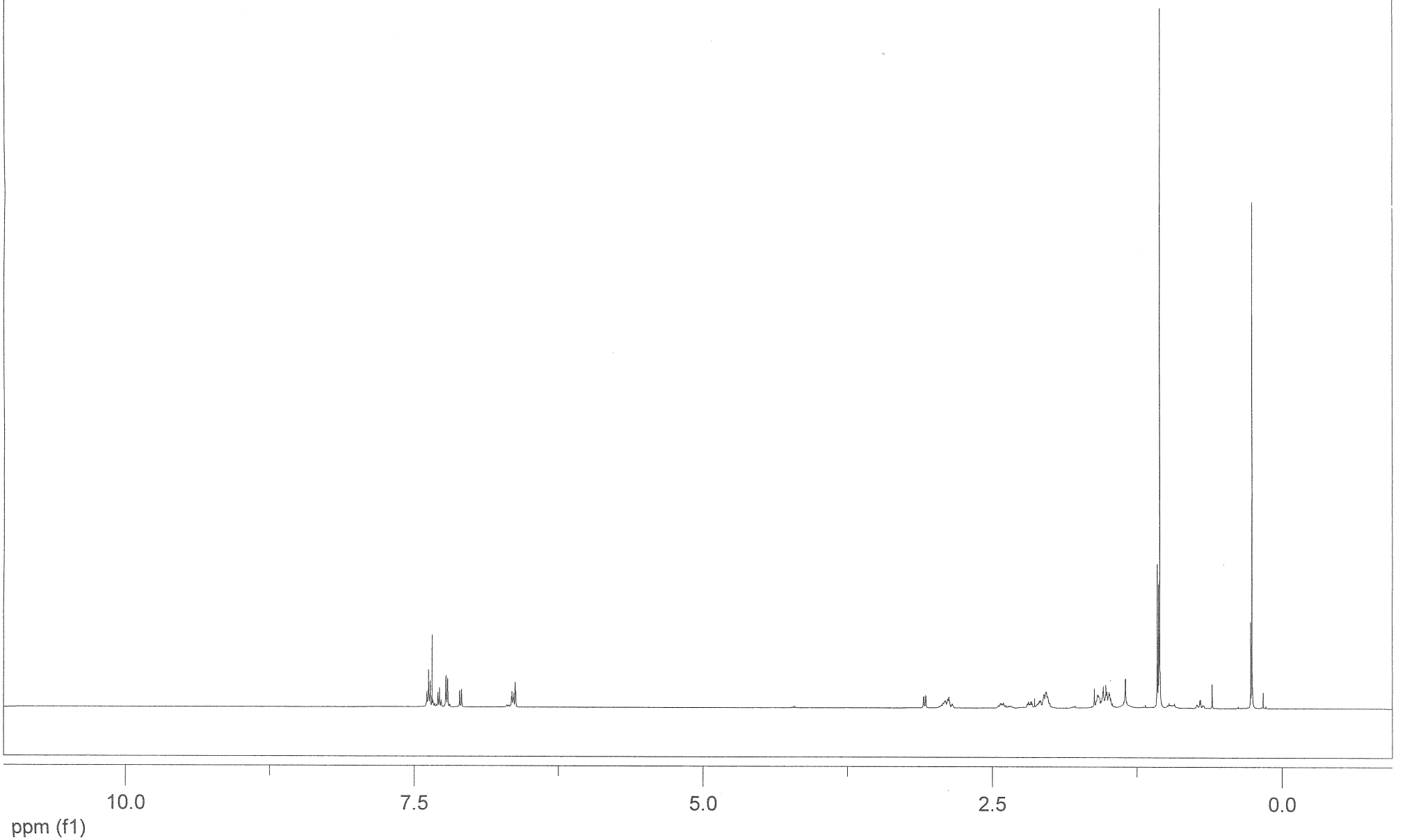
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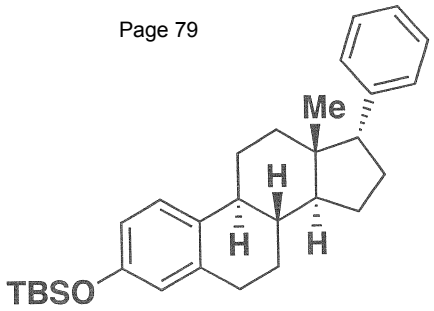
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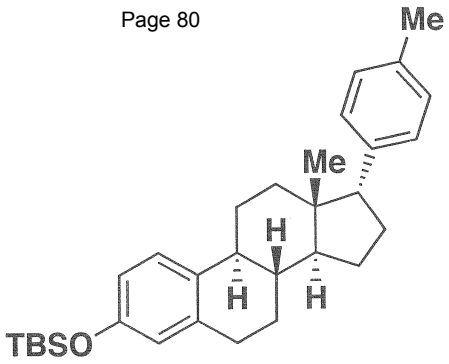
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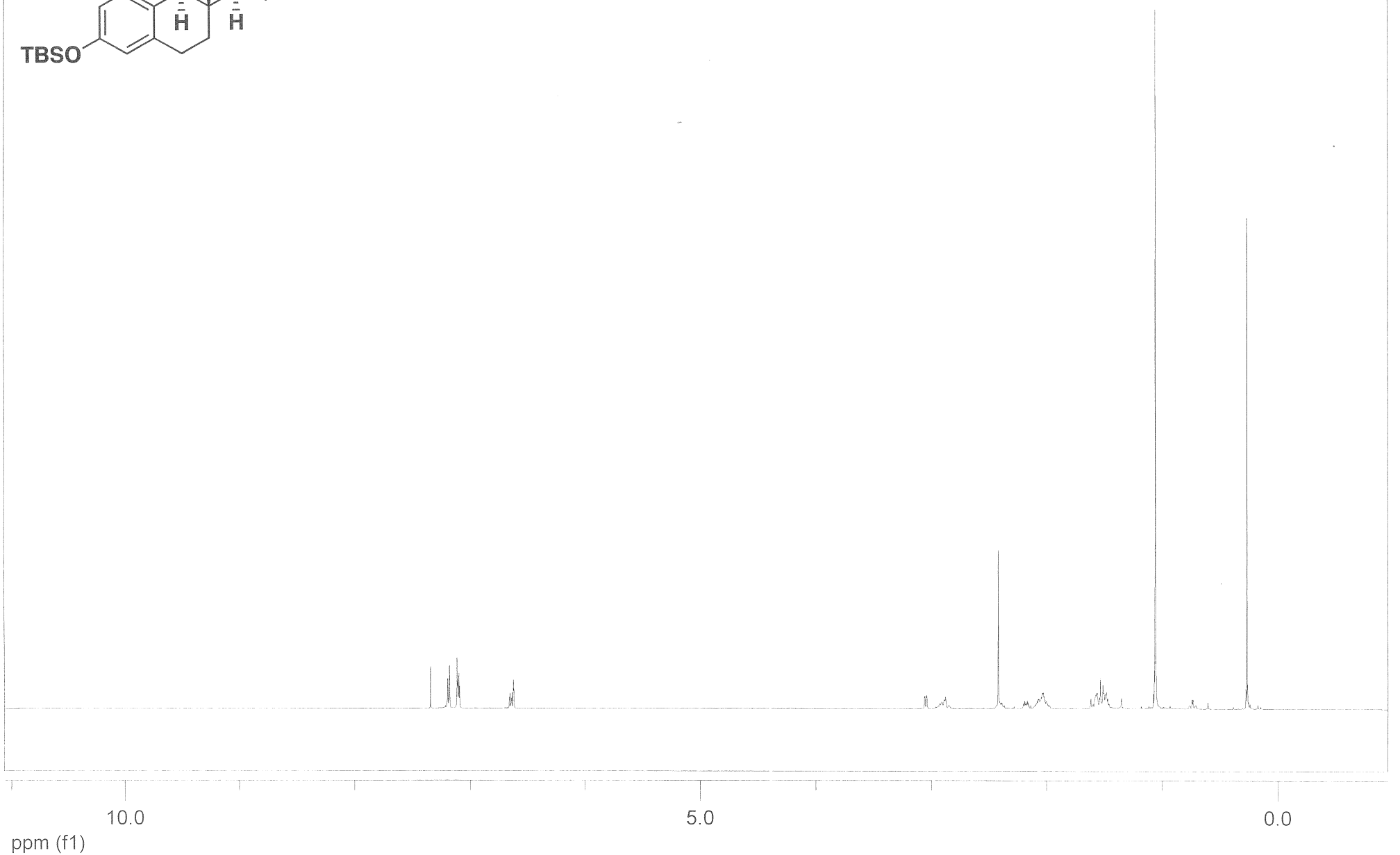
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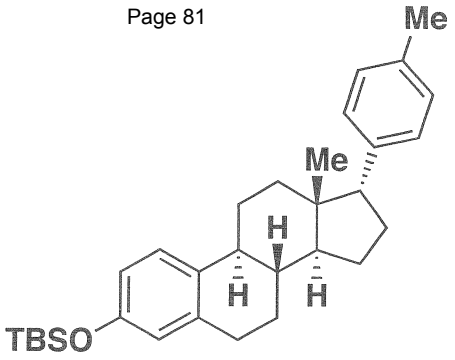
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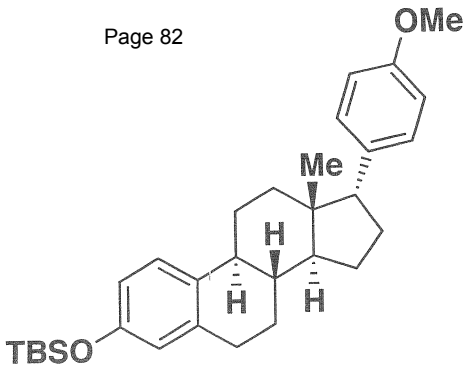
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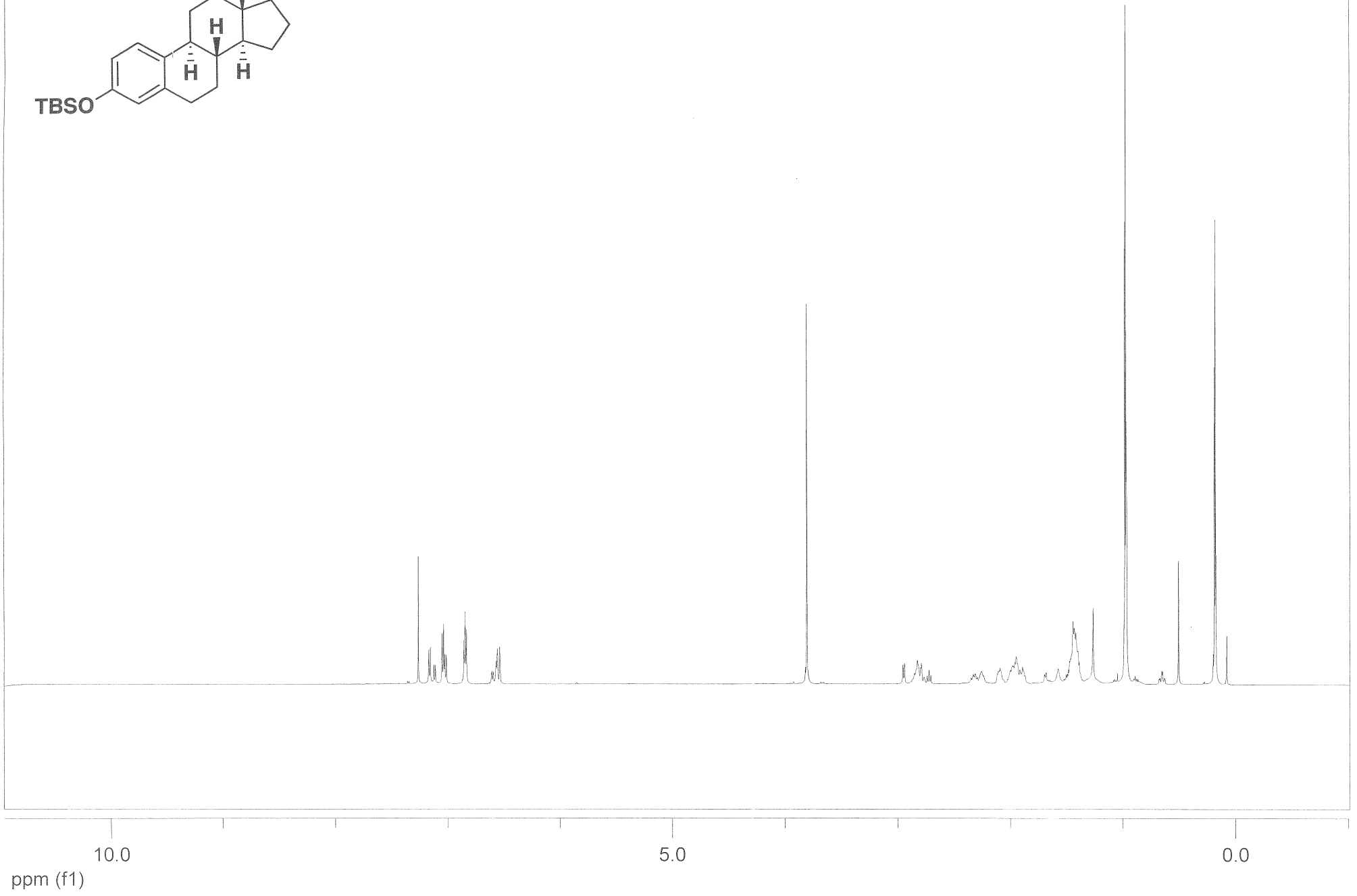
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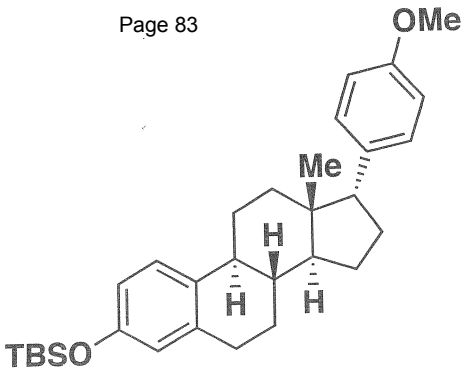
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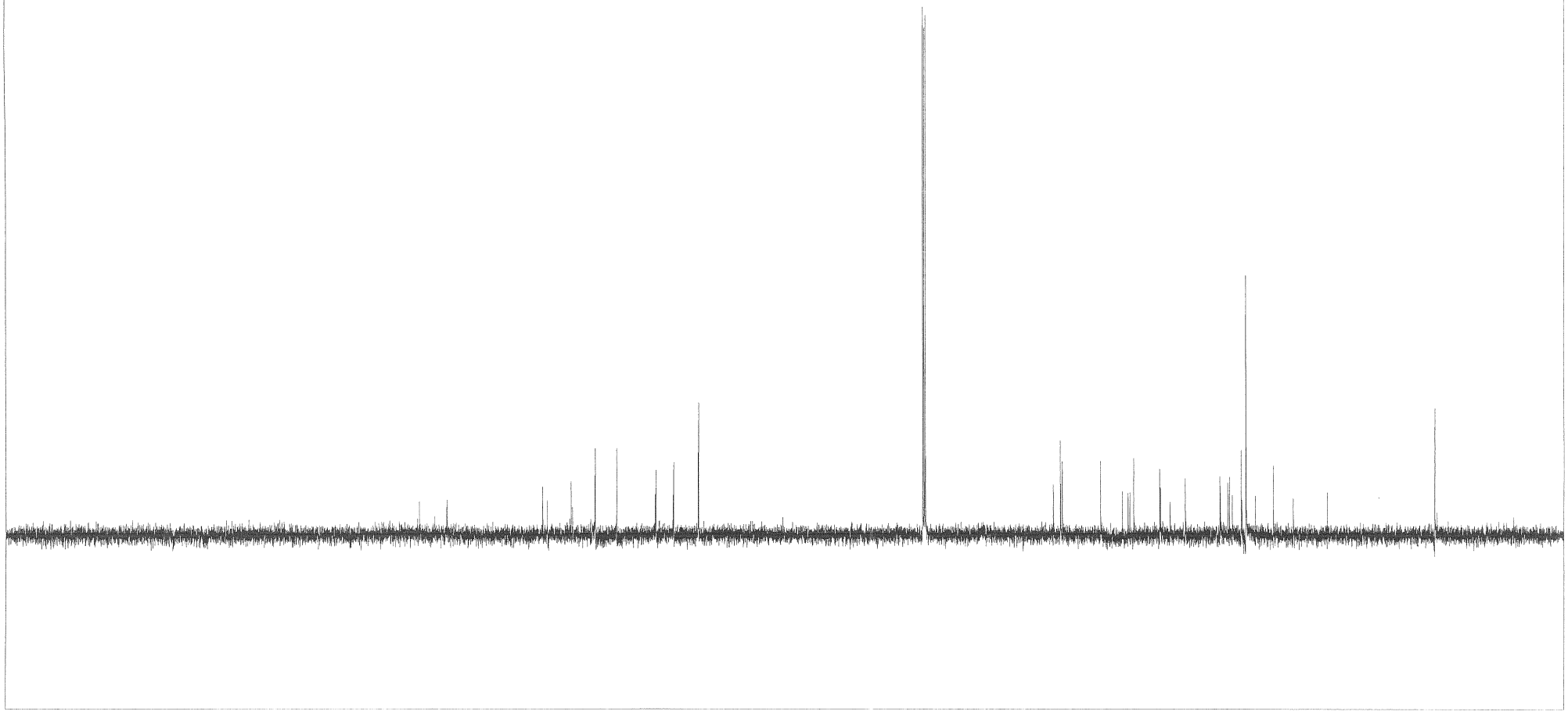
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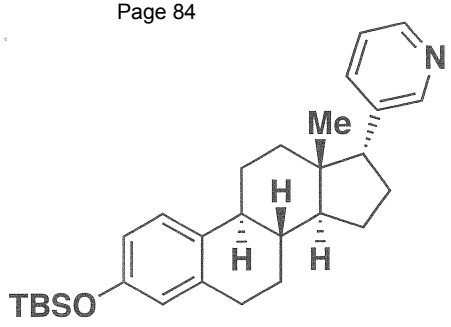
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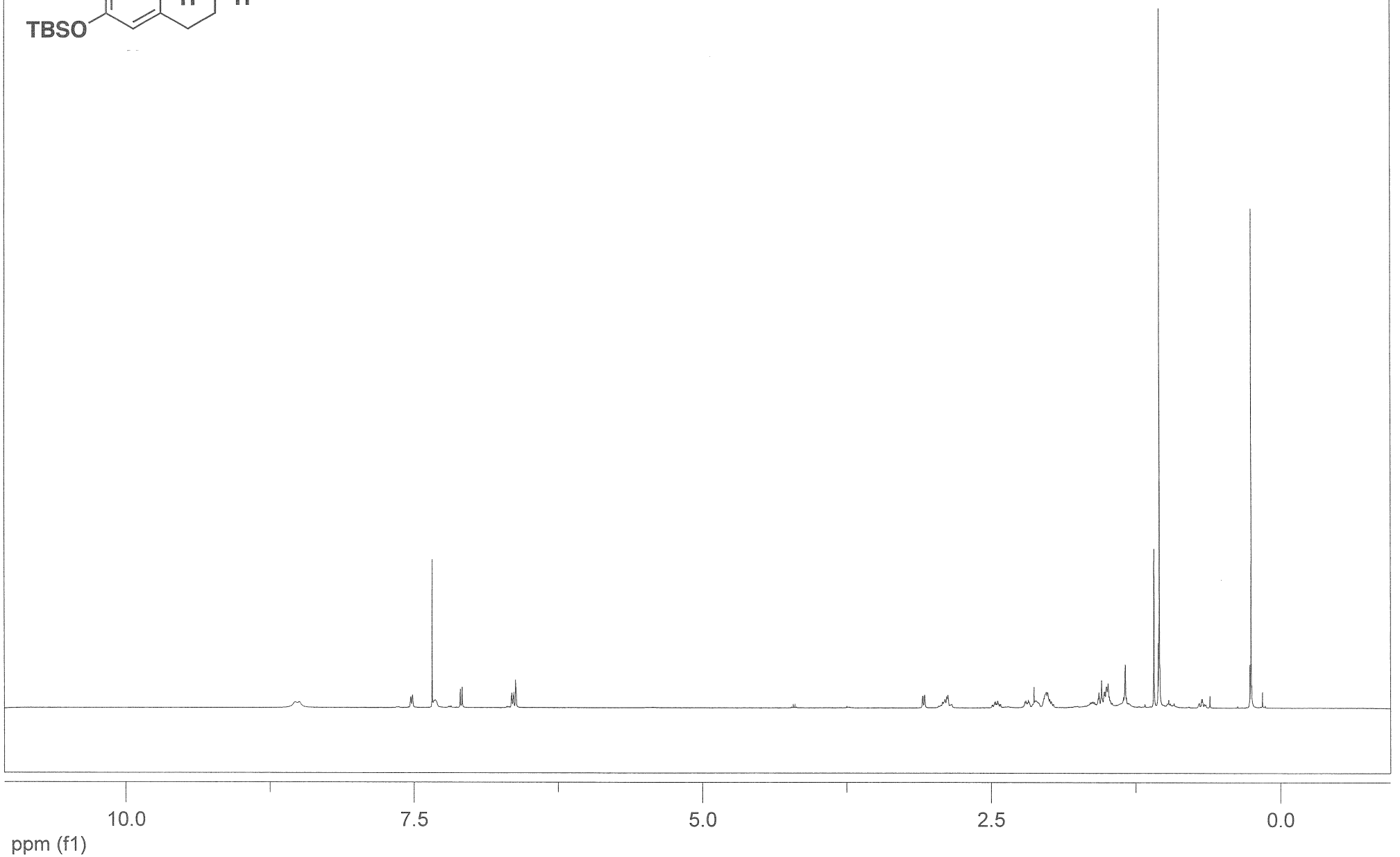
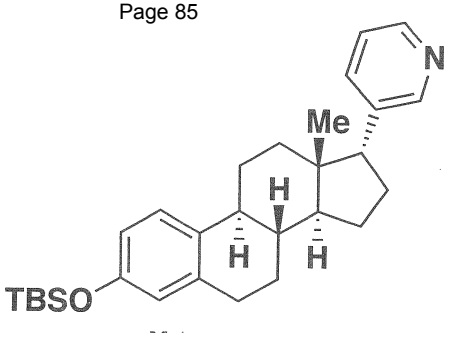
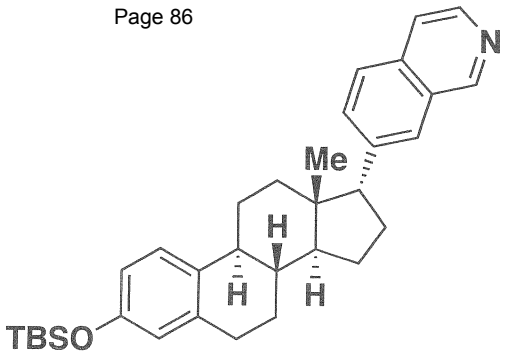
H
TBSO

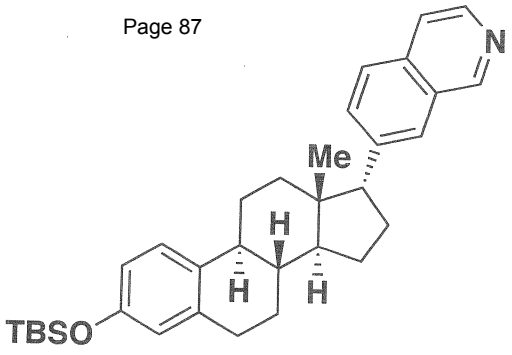

10.0
7.5
5.0
2.5
0.0
ppm (f1)


N
Me
H
H
H
TBSO

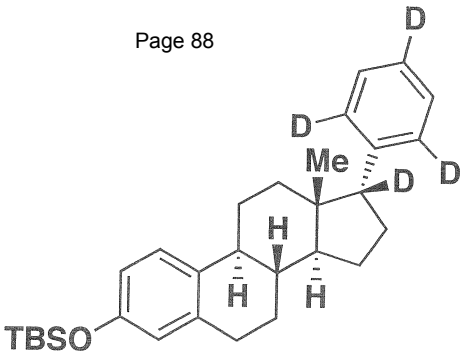
200
175
150
125
100
75
50
25
0
ppm (f1)

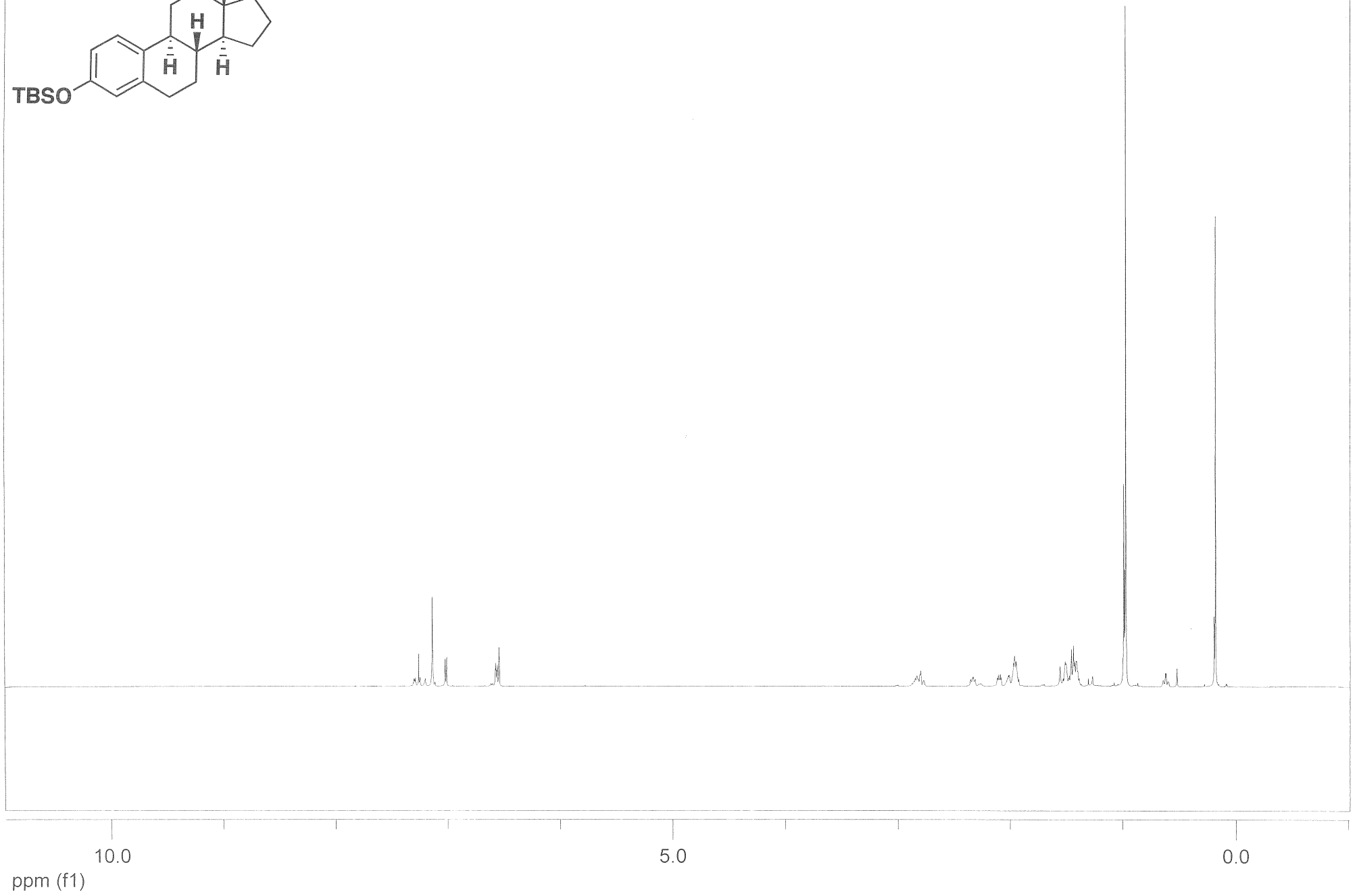

N
Me
H
H
H
TBSO

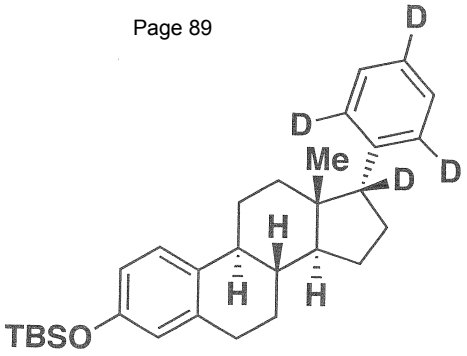
10.0
7.5
5.0
2.5
0.0
ppm (f1)


N
Me
H
H
H
TBSO

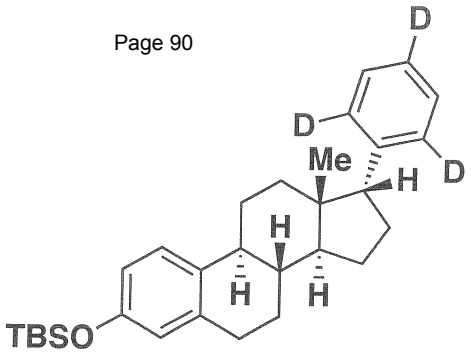
200
175
150
125
100
75
50
25
0
ppm (f1)

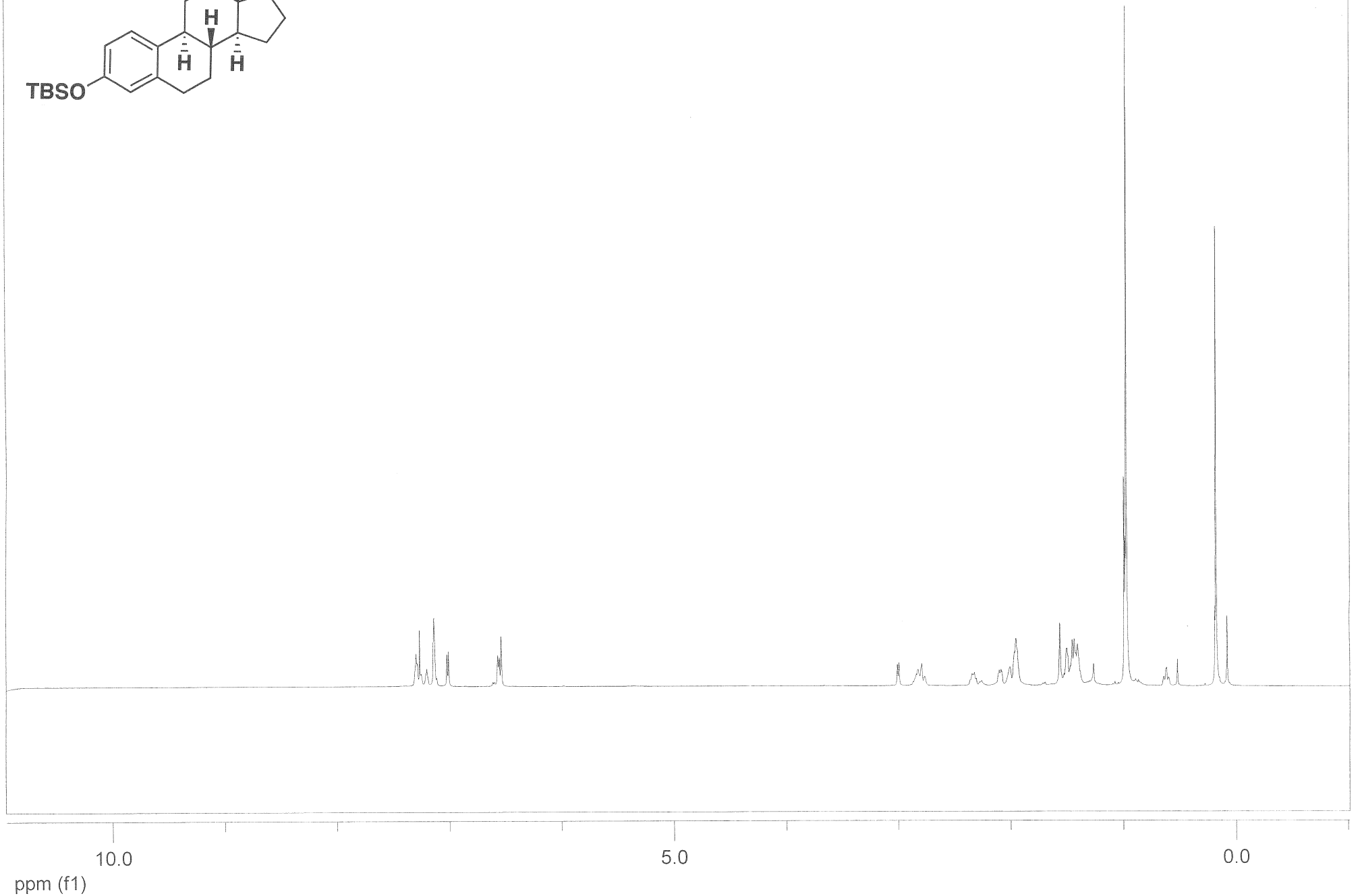

D
D
Me
D
D
H
H
H
TBSO

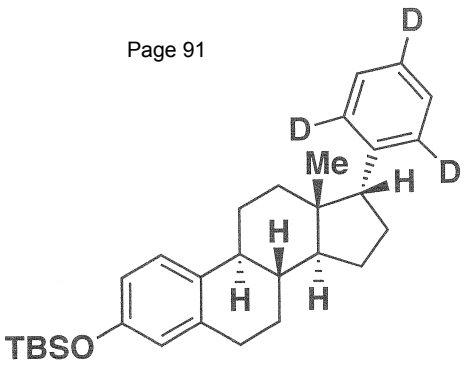

10.0
5.0
0.0
ppm (f1)


D
D
Me
D
D
H
H
H
TBSO

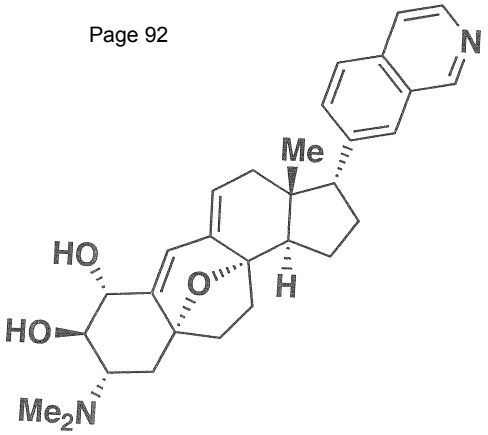
200
150
100
50
0
ppm (f1)


D
D
Me
H
D
H
H
H
TBSO


10.0
5.0
0.0
ppm (f1)


D
D
Me
H
D
H
H
H
TBSO

200
150
100
50
0
ppm (f1)


N
Me
HO
O
H
HO
Me2N

10.0
5.0
0.0
ppm (t1)