Cyclohexenones as Michael Acceptors in the Staunton-Weinreb Annulation: A Simple Stannane Modification for the Synthesis of Polycyclic Systems

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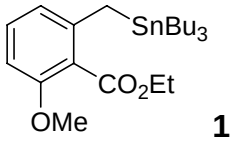
Supporting Information

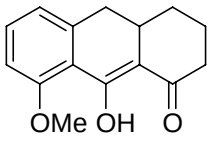
General Information: Tetrahyrofuran (THF) was dried and distilled over Na/benzophenone and diisopropylamine was dried and distilled over CaH_2. All other reagents were purchased and used as obtained from commercial sources. All glassware was dried in a oven and stored in a dry box prior to use. All NMR spectra were recorded in $CDCl_3$ on a Bruker 300 Avance spectrometer and reported at δ 7.24 and δ 77.0 for the ^1H and ^{13}C respectively.



1

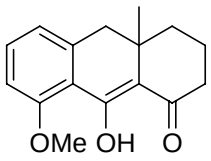
Stannane 1: To a solution of *i*-Pr_2NH (3.24 mL, 23.2 mmole) and THF (90 mL) at 0°C was added *n*-BuLi (2.0 M, 10.8 mL, 21.6 mmole). After 15 mins the solution was cooled to –78°C and a solution of ethyl-2-methoxy-6-methyl benzoate[1] (3.00 g, 15.45 mmole) and THF (30 mL) was added *via* cannula. The resulting red solution was stirred for 2 hrs at –78°C before Bu_3SnCl (5.44 mL, 20.1 mmole) was added *via* a syringe. The resulting yellow solution was warmed to room temperature and quenched with aq NH_4Cl. The product was extracted with Et_2O (x3), washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by flash chromatography (25:1 Hexanes:EtOAc) yielded 4.57 g, (61%) of stannane as a clear colourless liquid. ^1H NMR (300 MHz) δ 7.10 (1H, t, *J* = 8.0 Hz), 6.58 (1H, d, *J* = 7.8 Hz), 6.51 (1H, d, *J* = 8.3 Hz), 4.34 (2H, q, *J* = 7.1 Hz), 3.76 (3H, s), 2.22 (2H, s), 1.43-1.16 (15H, m), 0.92-0.72 (15H, m); ^{13}C NMR (75 MHz) δ 168.5, 156.6, 142.9, 129.8, 121.2, 120.5, 120.4, 105.5, 60.7, 55.6, 28.8 (t, *J* = 10 Hz), 27.2 (t, *J* = 27.6 and 34.6 Hz), 17.4, 16.2, 13.6, 9.8 (t, *J* = 153.6 and 160.3 Hz); LR-EIMS *m/z*: 427 (M^+-C_4H_9, 100), 425 (M^+-C_4H_9, 75); LR-CIMS (NH_3): 485 (MH^+, 100); HR-EIMS calculated for $C_{19}H_{31}{}^{116}SnO_3$ (M^+-C_4H_9): 423.1285 found 423.1284

General Ring Annulation Protocol: To a cooled (–78°C) solution of stannane (1.4 eq) in THF was added *n*-BuLi (1.4 eq) resulting in a deep red colour. The mixture was stirred for 30 mins before a solution of enone (1.0 eq) and THF was added *via* cannula. The solution was stirred at –78°C for 1 hr before being warmed to room temperature and stirred for a further 3 hrs (the red colour disappears resulting in a yellow solution). The reaction was quenched with aq. NH_4Cl, extracted with Et_2O (x3), washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by flash chromatography (8:1 Hexanes: EtOAc) yielded pure products.



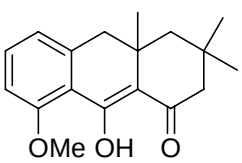
2

Compound 2: Stannane (500 mg, 1.03 mmole) in THF (8 mL), *n*-BuLi (2.0 M, 520 μL, 1.03 mmole), cyclohex-1-en-one (71 μL, 0.739 mmole) in THF (2 mL) yielded 135.4 mg (75%) of product as a pale yellow solid. ^{1}H NMR (300 MHz) δ 7.30 (1H, t, *J* = 8.0 Hz), 6.82 (1H, d, *J* = 8.5 Hz), 6.73 (1H, d, *J* = 7.6 Hz), 3.87 (3H, s), 2.69 (1H, dd, *J* = 13.2, 3.0 Hz), 2.62-2.53 (1H, m), 2.59 (1H, d, *J* = 13.2 Hz), 2.42-2.36 (2H, m), 1.99-1.83 (2H, m), 1.62-1.52 (1H, m), 1.32-1.19 (1H, m); ^{13}C NMR (75 MHz) δ 186.9, 182.7, 159.9, 144.6, 133.3, 120.6, 120.0, 110.4, 109.3, 55.9, 37.5, 32.9, 31.2, 29.9, 20.7; LR-EIMS *m/z*: 244 (M^+, 100), 216 (37), 188 (42); HR-EIMS: calculated for $C_{15}H_{16}O_3$: 244.1099 found 244.1099.



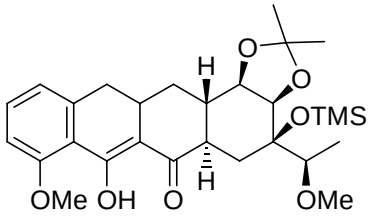
4

Compound 4: Stannane (500 mg, 1.03 mmole) in THF (8 mL), *n*-BuLi (2.0 M, 520 μL, 1.03 mmole), 3-methyl-cyclohex-1-en-one (83 μL, 0.735 mmole) in THF (2 mL) yielded 140 mg (74%) of product as a pale yellow solid. ^{1}H NMR (300 MHz) δ 7.32 (1H, t, *J* = 8.0 Hz), 6.84 (1H, d, *J* = 8.5 Hz), 6.73 (1H, d, *J* = 7.4 Hz), 3.89 (3H, s), 2.80 (1H, d, *J* = 15.0 Hz), 2.55 (1H, d, *J* = 15.0 Hz), 2.43-2.38 (2H, m), 1.86-1.66 (3H, m), 1.51 (1H, dt, *J* = 13.0, 3.8 Hz), 0.95 (3H, s); ^{13}C NMR (75 MHz) δ 186.3, 182.8, 159.9, 143.4, 133.5, 120.8, 119.9, 112.8, 110.4, 55.8, 45.1, 37.2, 32.8, 31.0, 24.7, 17.2; LR-EIMS *m/z*: 258 (M^+, 20), 243 (M^+-CH_3, 100); HR-EIMS: calculated for $C_{16}H_{18}O_3$: 258.1256 found 258.1252.



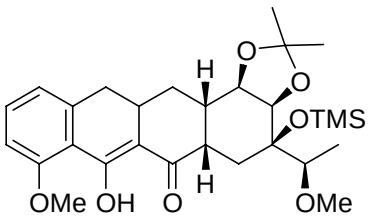
5

Compound 5: Stannane (500 mg, 1.03 mmole) in THF (8 mL), *n*-BuLi (2.0 M, 520 μL, 1.03 mmole), isophorone (110 μL, 0.735 mmole) in THF (2 mL) yielded 175.3 mg (83%) of product as a white solid. ^{1}H NMR (300 MHz) δ 7.27 (1H, t, *J* = 8.0 Hz), 6.79 (1H, d, *J* = 8.4 Hz), 6.68 (1H, d, *J* = 7.4 Hz), 3.85 (3H, s), 2.86 (1H, d, *J* = 15.2 Hz), 2.47 (1H, d, *J* = 15.2 Hz), 2.17 (2H, d, *J* = 2.17 Hz), 1.50 (2H, ABq, *J* = 4.0 Hz), 1.02 (3H, s), 0.98 (3H, s), 0.97 (3H, s); ^{13}C NMR (75 MHz) δ 185.1, 183.4, 159.9, 143.5, 133.4, 121.0, 120.1, 111.1, 110.3, 55.8, 50.5, 46.4, 45.7, 33.1, 30.8, 30.5, 30.0, 27.2; LR-EIMS *m/z*: 286 (M^+, 15), 271 (100); HR-EIMS: calculated for $C_{18}H_{22}O_3$: 286.1569 found 286.1569.



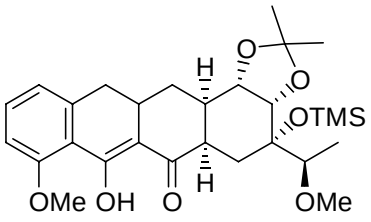
6a

Compound 6a: Stannane (244 mg, 0.505 mmole) in THF (5 mL), *n*-BuLi (2.0 M, 252 μL, 0.505 mmole), enone (133 mg, 0.361 mmole) in THF (5 mL) yielded 132.9 mg (71%) of tetracycle as an amorphous solid. ^{1}H NMR (300 MHz) δ 7.34 (1H, t, *J* = 8.0 Hz), 6.86 (1H, d, *J* = 8.4 Hz), 6.78 (1H, d, *J* = 7.4 Hz), 3.95-3.91 (2H, m), 3.91 (3H, s), 3.28 (3H, s), 3.28-3.24 (1H, m), 2.78-2.47 (5H, m), 2.27-2.22 (1H, m), 1.59-1.53 (2H, m), 1.47 (3H, s), 1.39 (3H, s), 1.27 (3H, d, *J* = 6.2 Hz), 1.04 (1H, q, *J* = 11.1 Hz), 0.12 (9H, s); ^{13}C NMR (75 MHz) δ 186.1, 185.4, 159.8, 144.5, 133.2, 120.6, 120.0, 110.5, 108.4, 107.5, 107.3, 85.3, 80.5, 80.4, 77.8, 57.2, 56.0, 40.3, 38.9, 37.6, 33.3, 32.3, 30.6, 28.7, 26.3, 12.5, 2.7; LR-EIMS *m/z*: 516 (M^+, 75), 399 (M^+-$C_6H_{13}O_2$, 100), 457 (M^+-C_3H_7O, 90); HR-EIMS calculated for $C_{28}H_{40}O_7Si$: 516.2543 found 516.2555.



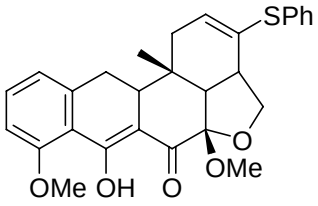
6b

Compound 6b: Stannane (354 mg, 0.732 mmole) in THF (7.5 mL), *n*-BuLi (2.0 M, 370 μL, 0.732 mmole), enone (192.7 mg, 0.523 mmole) in THF (7.5 mL) yielded 167.7 mg (62%) of tetracycle as an amorphous solid. ^{1}H NMR (300 MHz) δ 7.31 (1H, t, *J* = 8.0 Hz), 6.83 (1H, d, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 7.4 Hz), 4.03 (1H, d, *J* = 7.1 Hz), 3.98-3.90 (1H, m), 3.88 (3H, s), 3.24-3.17 (1H, m), 3.22 (3H, s), 2.85-2.66 (3H, m), 2.52 (1H, d, *J* = 14.1 Hz), 2.45-2.29 (2H, m), 2.16-2.12 (1H, m), 1.49 (3H, s), 1.45-1.35 (2H, m), 1.29 (3H, s), 1.17 (3H, d, *J* = 6.2 Hz), 0.12 (9H, s); ^{13}C NMR (75 MHz) δ 186.3, 185.9, 159.8, 144.5, 133.3, 120.8, 120.0, 110.5, 108.5, 108.3, 81.0, 77.7, 75.7, 74.5, 56.2, 56.0, 37.5, 36.5, 33.0, 29.6, 29.5, 28.0, 27.4, 25.2, 12.3, 2.7; LR-EIMS *m/z*: 516 (M^+, 10), 457 (M^+-C_3H_7O, 100), 399 (M^+-$C_6H_{13}O_2$, 35); HR-EIMS: calculated for $C_{28}H_{40}O_7Si$: 516.2543 found 516.2531.



7

Compound 7: Stannane (228 mg, 0.472 mmole) in THF (5 mL), *n*-BuLi (2.0 M, 240 μL, 0.472 mmole), enone (124.3 mg, 0.337 mmole) in THF (5 mL) yielded 89.6 mg (51%) of tetracycle as an amorphous solid. ^{1}H NMR (300 MHz) δ 7.31 (1H, t, *J* = 8.0 Hz), 6.83 (1H, d, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 7.4 Hz), 4.04-3.92 (2H, m), 3.88 (3H, s), 3.26-3.22 (1H, m), 3.24 (3H, s), 2.85-2.66 (3H, m), 2.55-2.46 (2H, m), 2.23-2.13 (2H, m), 1.65 (1H, dd, *J* = 14.9, 8.9 Hz), 1.45-1.40 (1H, m), 1.44 (3H, s), 1.27 (3H, s), 1.15 (3H, d, *J* = 6.2 Hz), 0.13 (9H, s); ^{13}C NMR (75 HMz) δ 187.1, 184.8, 159.8, 144.7, 135.5, 120.8, 120.0, 110.4, 108.6, 108.5, 81.4, 77.9, 74.5, 74.4, 56.3, 56.0, 37.5, 36.3, 33.2, 31.2, 29.7, 28.0, 27.6, 25.6, 13.7, 2.4; LR-EIMS *m/z*: 516 (M^+, 5), 457 (100), 399 (25), 367 (20); HR-EIMS: calculated for $C_{28}H_{40}O_7Si$ 516.2543 found 516.2548.



8

Compound 8: Stannane (62 mg, 0.128 mmole), in THF (5 mL), *n*-BuLi (2.0 M, 65 μL, 0.128 mmole), enone (30.1 mg, 0.0916 mmole) in THF (1 mL) yielded 20.6 mg (47%) of pentacycle as a film. ^{1}H NMR (300 MHz) δ 7.40-7.22 (6H, m), 6.87 (1H, d, *J* = 8.5 Hz), 6.77 (1H, d, *J* = 8.5 Hz), 6.05 (1H, d, *J* = 6.7 Hz), 4.04 (1H, t, *J* = 8.5 Hz), 3.92 (3H, s), 3.42 (3H, s), 3.31-3.28 (2H, m), 2.94-2.88 (2H, m), 2.64-2.53 (2H, m), 2.42 (1H, dd, *J* = 17.5, 6.9 Hz), 2.12-2.02 (1H, m), 1.09 (3H, s); LR-EIMS *m/z*: 476 (M^+, 42), 444 (100), 416 (65), 367 (33), 307 (70), 201 (32); HR-EIMS calculated for $C_{28}H_{28}O_5S$ 476.1657 found 476.1656.

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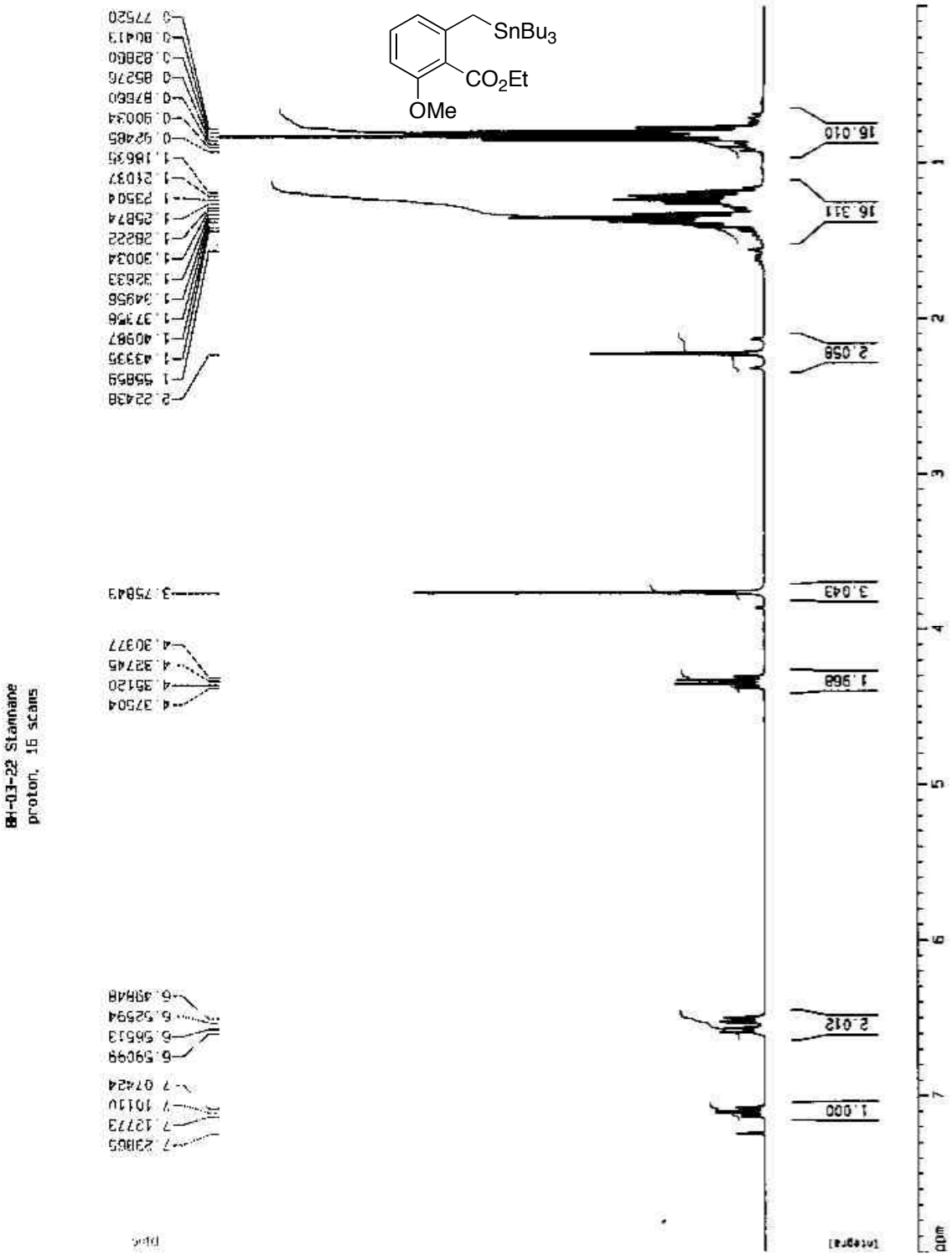
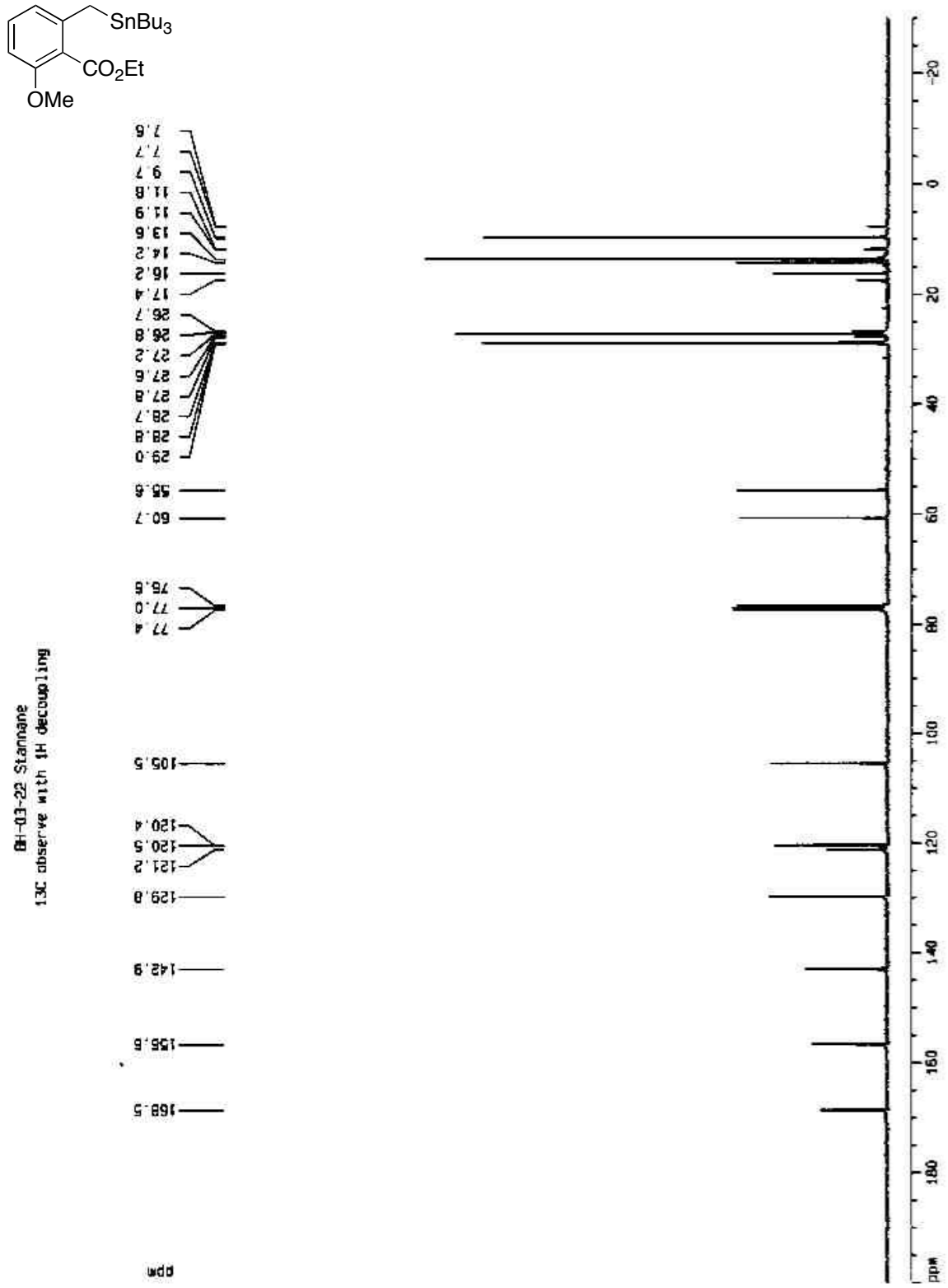
[1] Hauser, F.M.; Pogany, S.A. *Synthesis*, **1980**, 814 and Hamada, Y.; Hara, O.; Kawai, A.; Kohno, Y.; Shioiri, T. *Tetrahedron*, **1991**, *47*, 8635

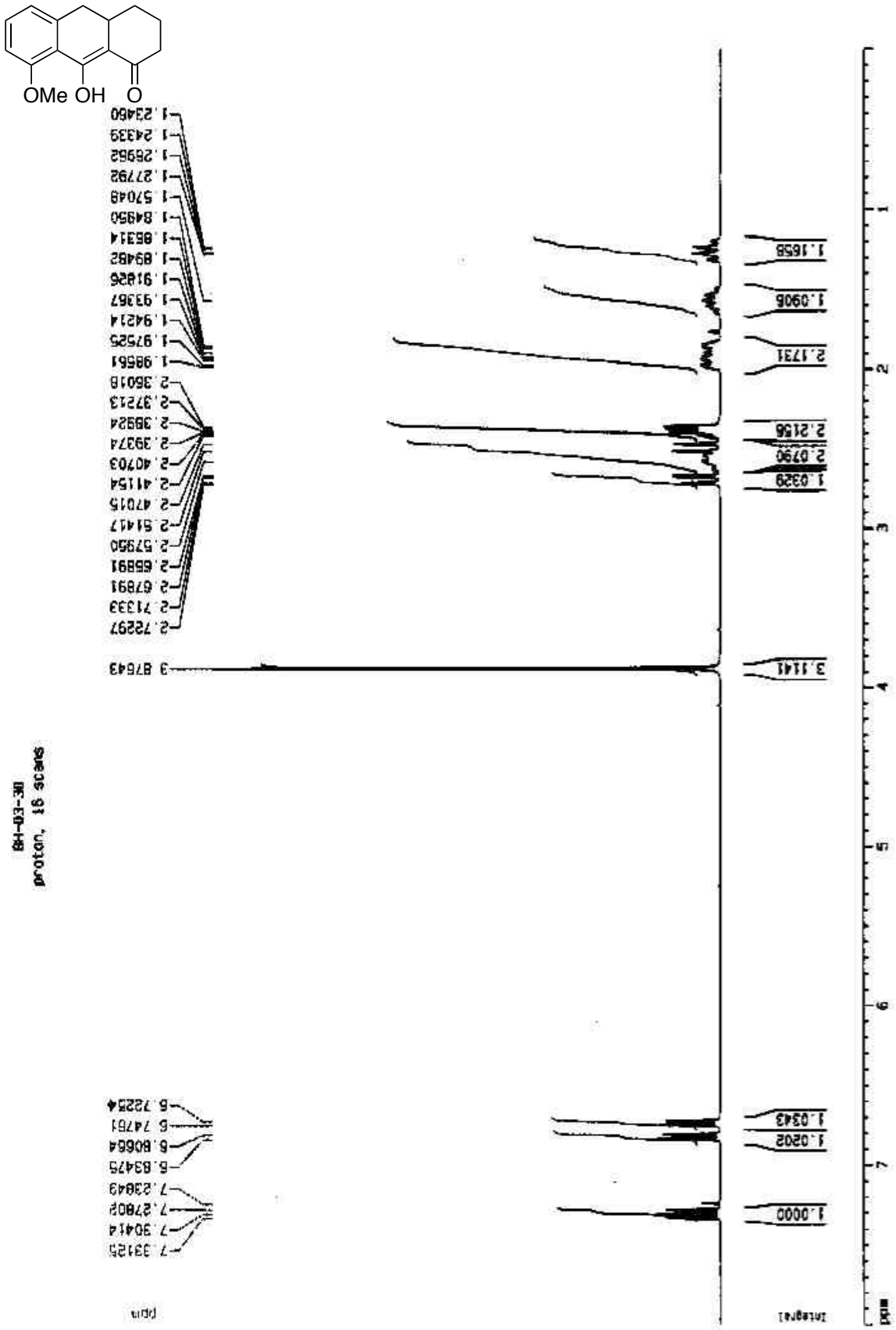
Stannane 1, 300 MHz ^{1}H NMR ($CDCl_3$)



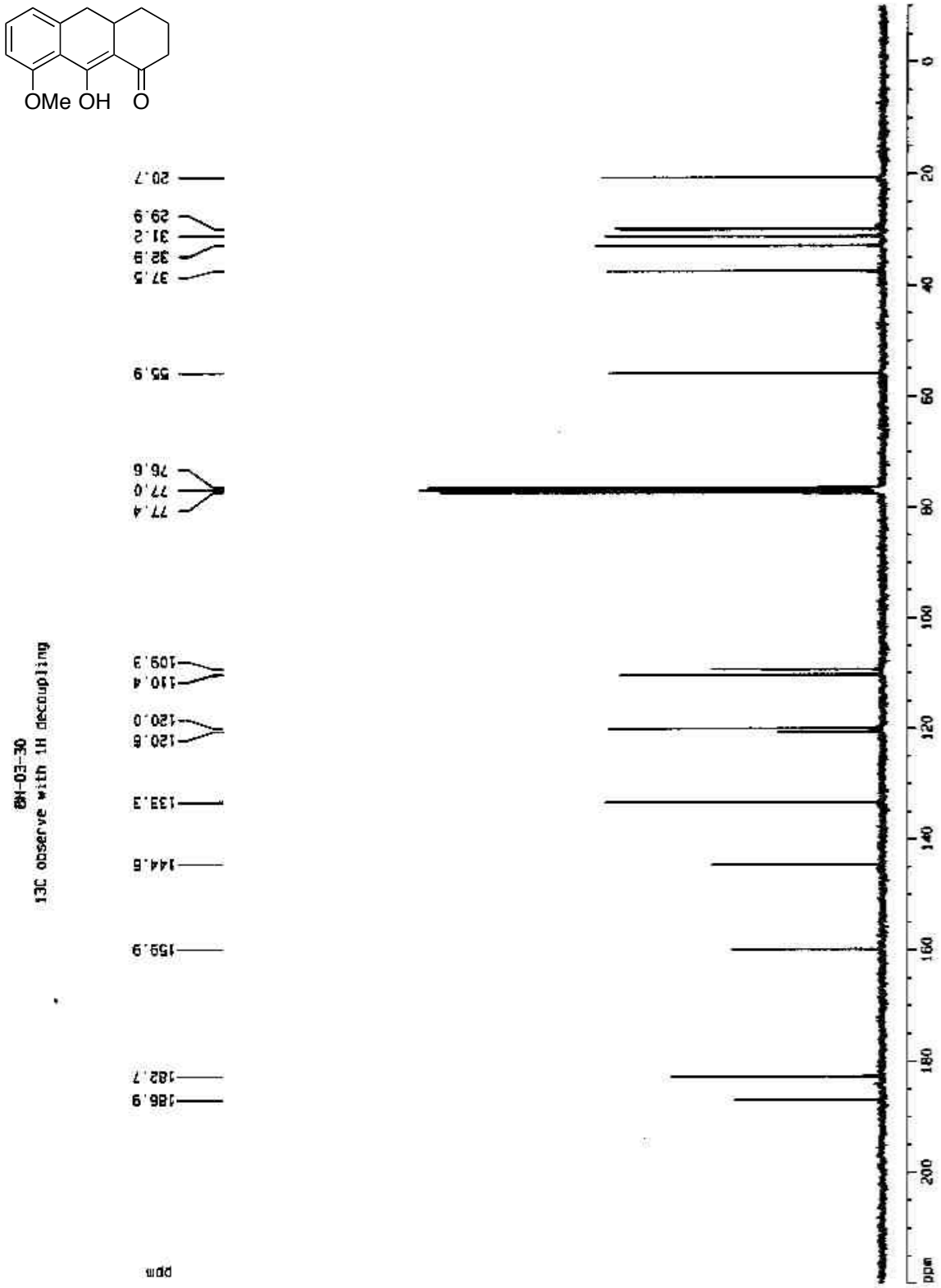
Stannane 1, 75 MHz ^{13}C NMR ($CDCl_3$)



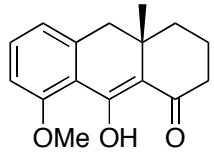
Compound 2, 300 MHz ^{1}H NMR ($CDCl_3$)

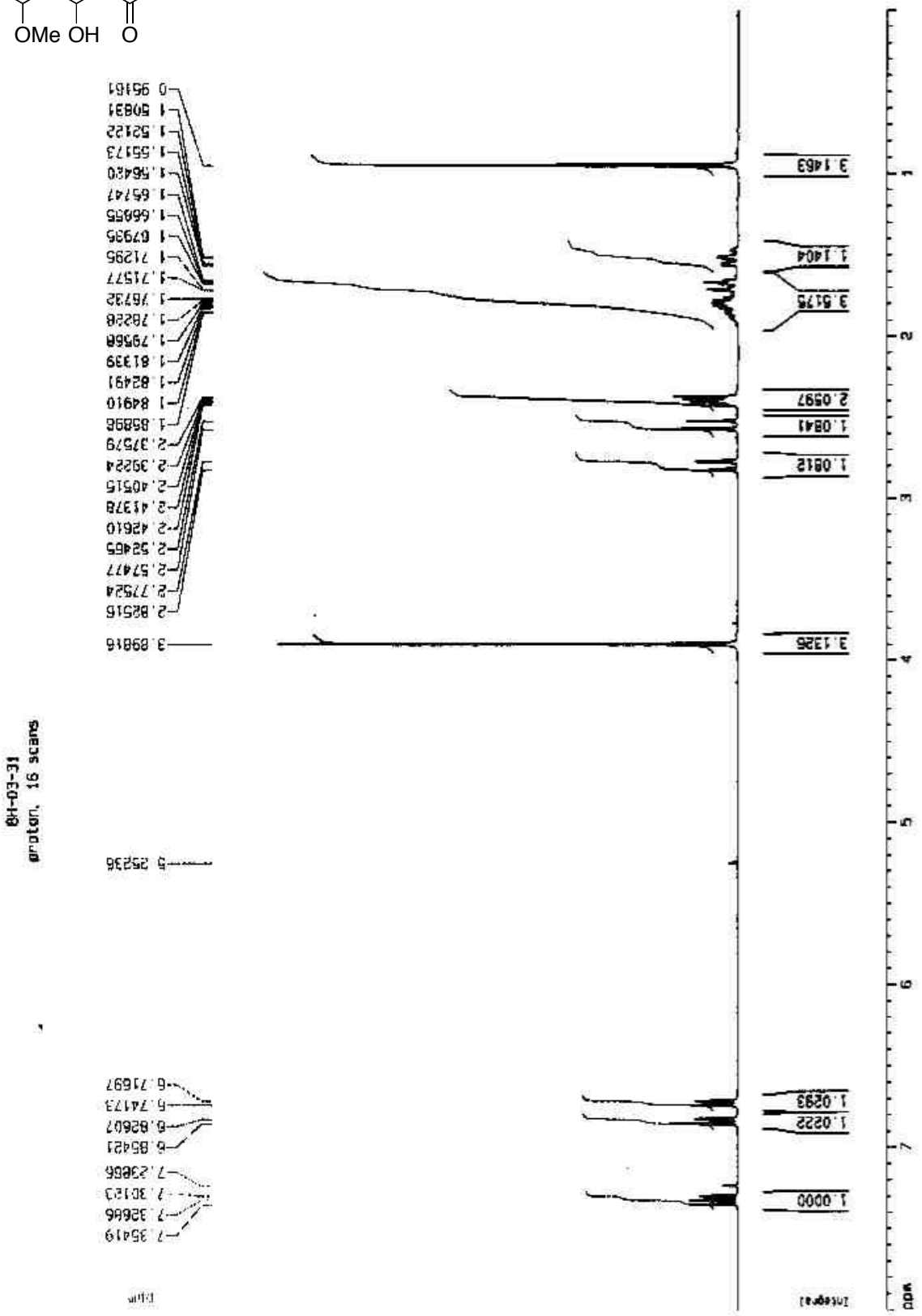


Compound 2, 75 MHz ^{13}C NMR ($CDCl_3$)

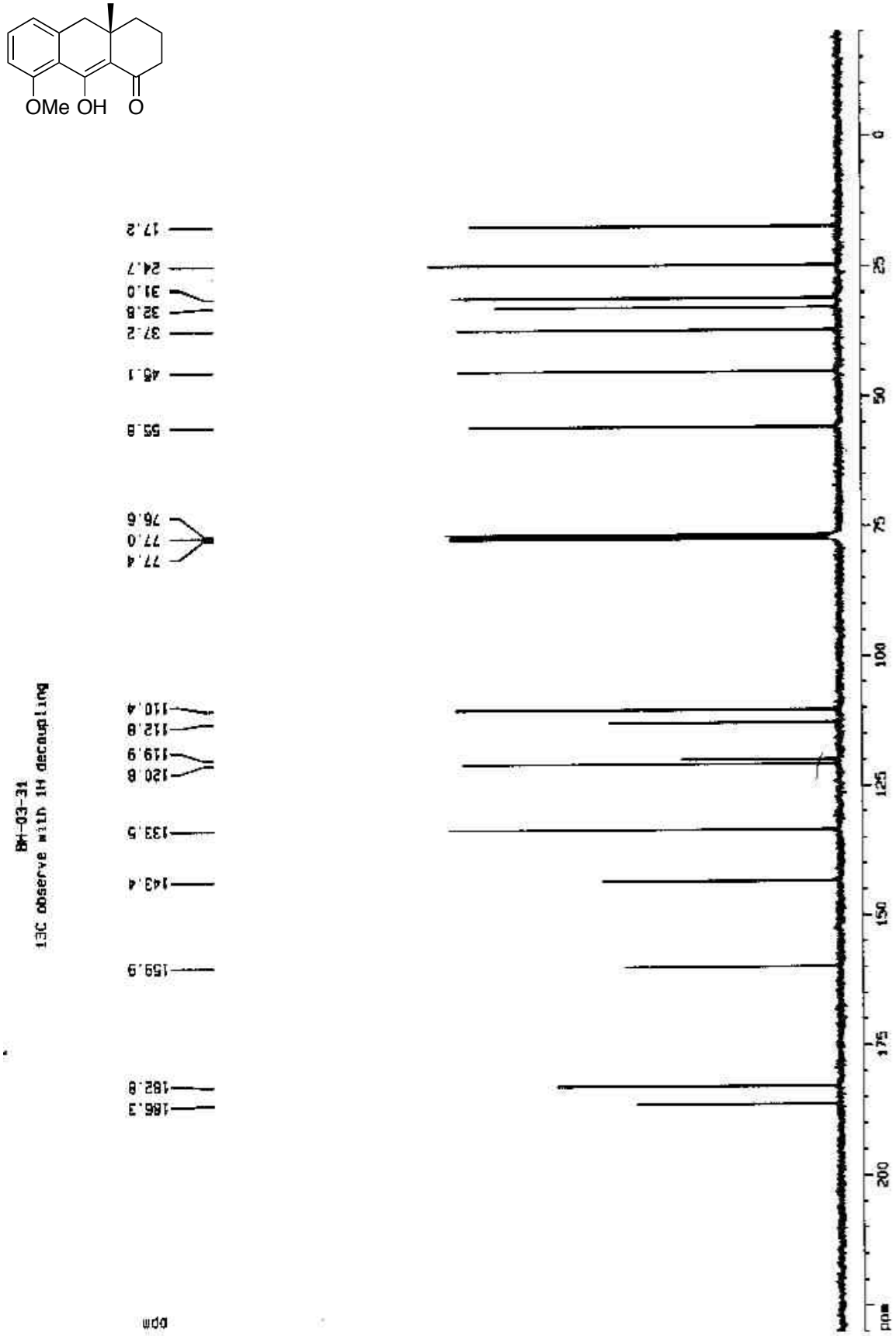


Compound 4, 300 MHz ^{1}H NMR ($CDCl_3$)

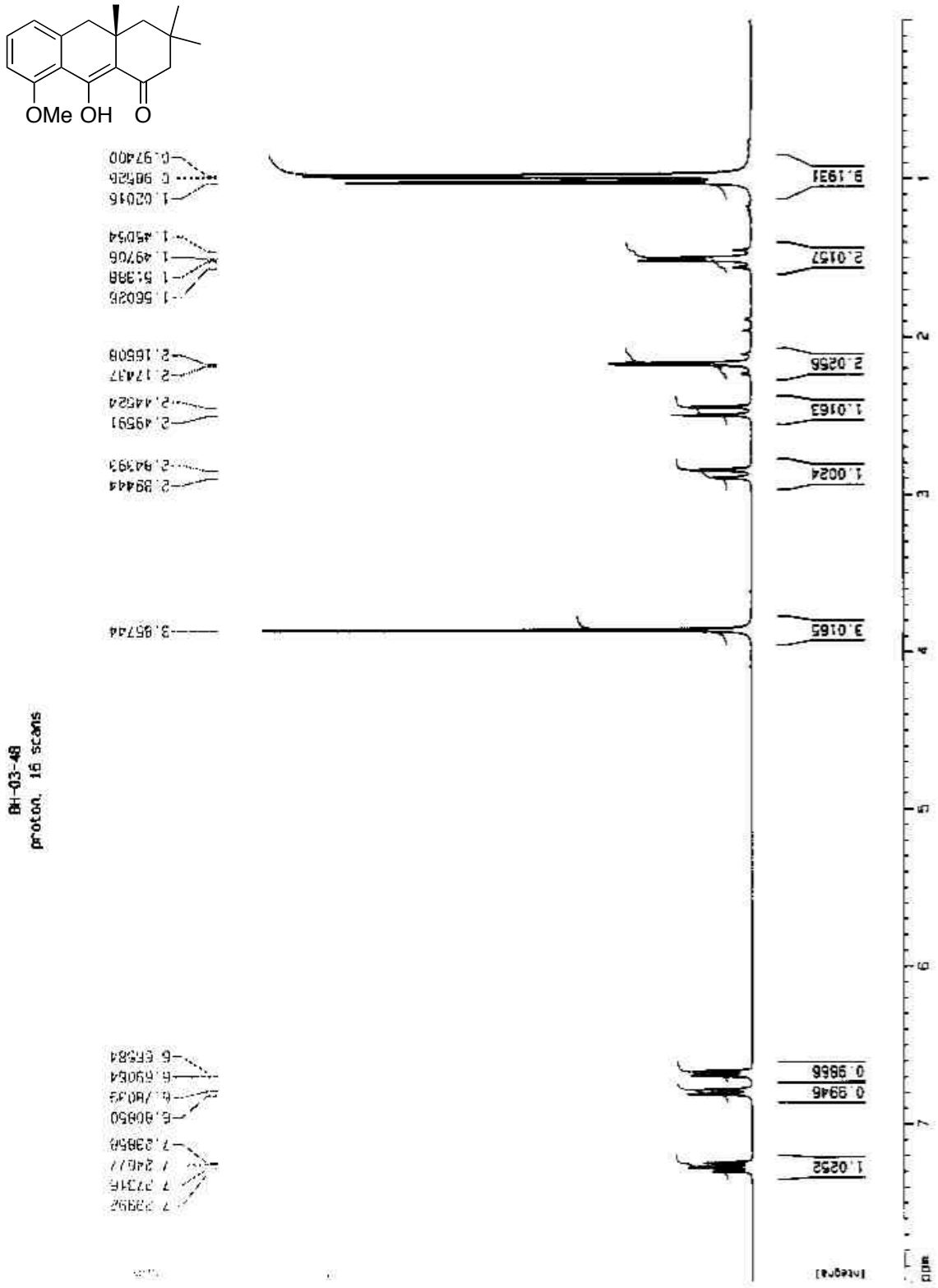




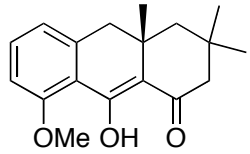
Compound 4, 75 MHz ^{13}C NMR ($CDCl_3$)



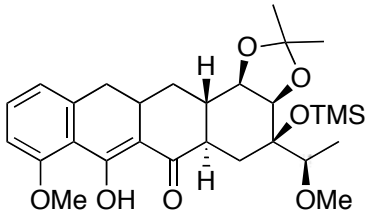
Compound 5, 300 MHz ^{1}H NMR ($CDCl_3$)

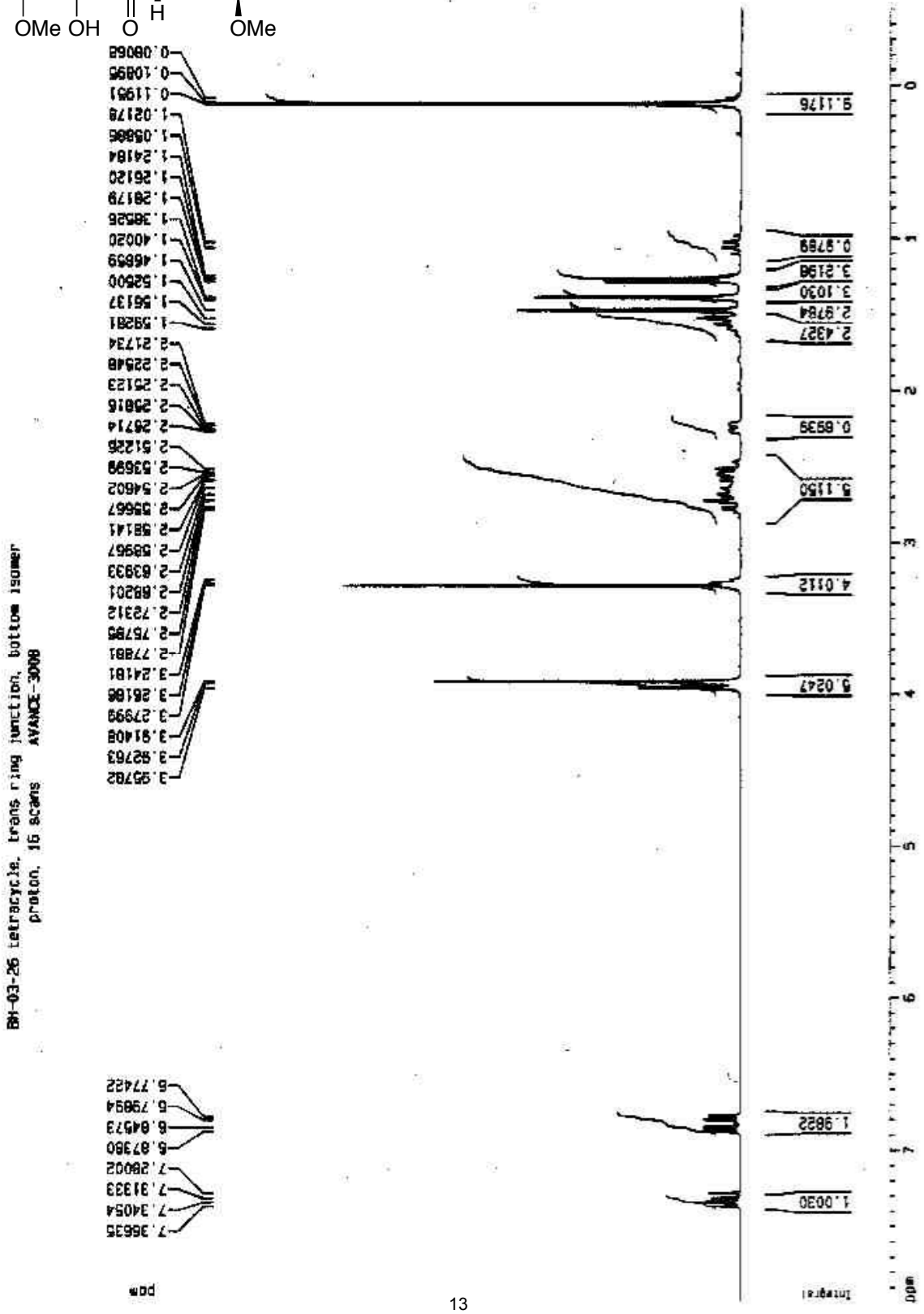


Compound 5, 75 MHz ^{13}C NMR ($CDCl_3$)

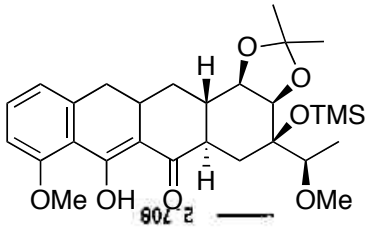


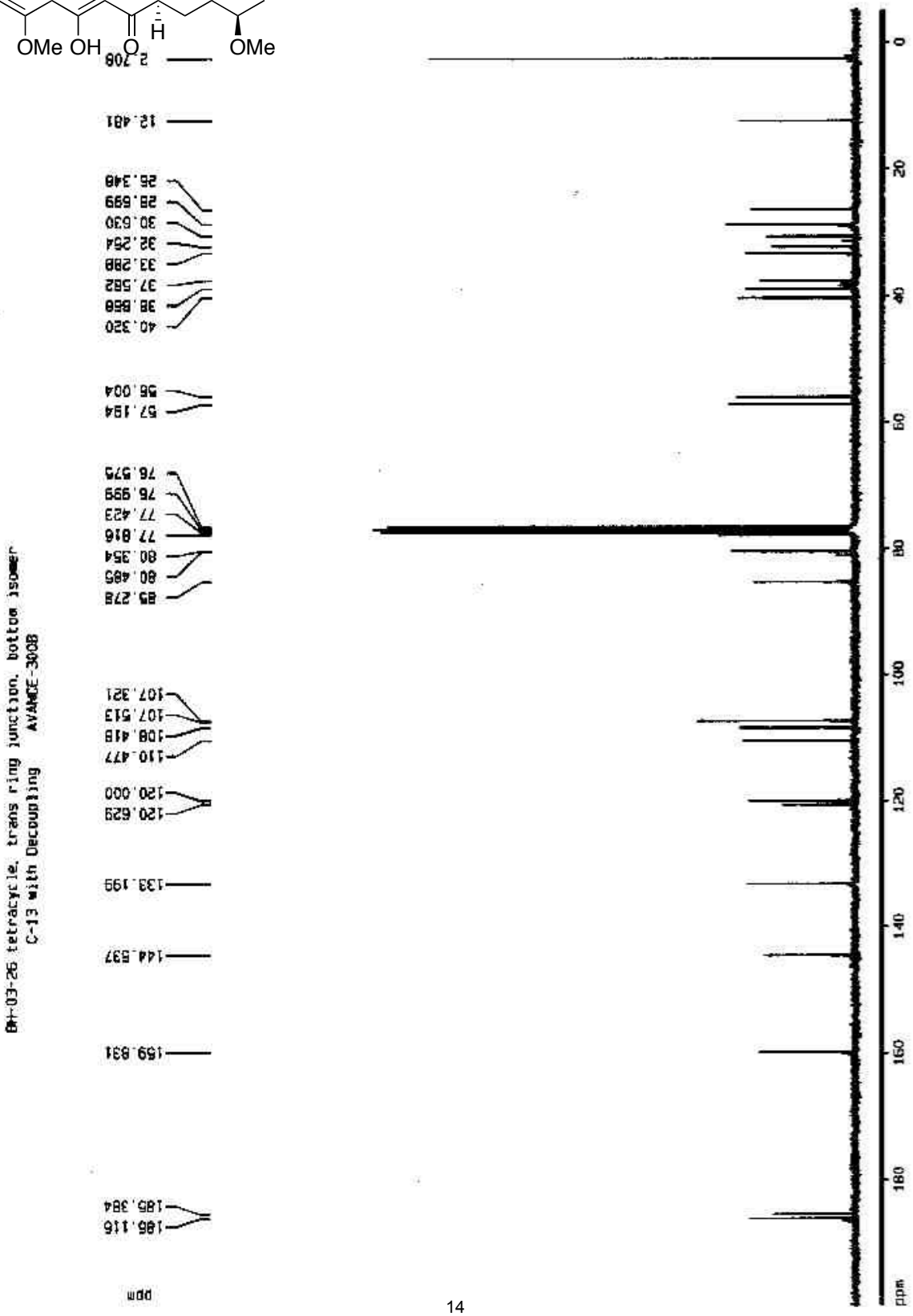
Compound 6a, 300 MHz ^{1}H NMR ($CDCl_3$)



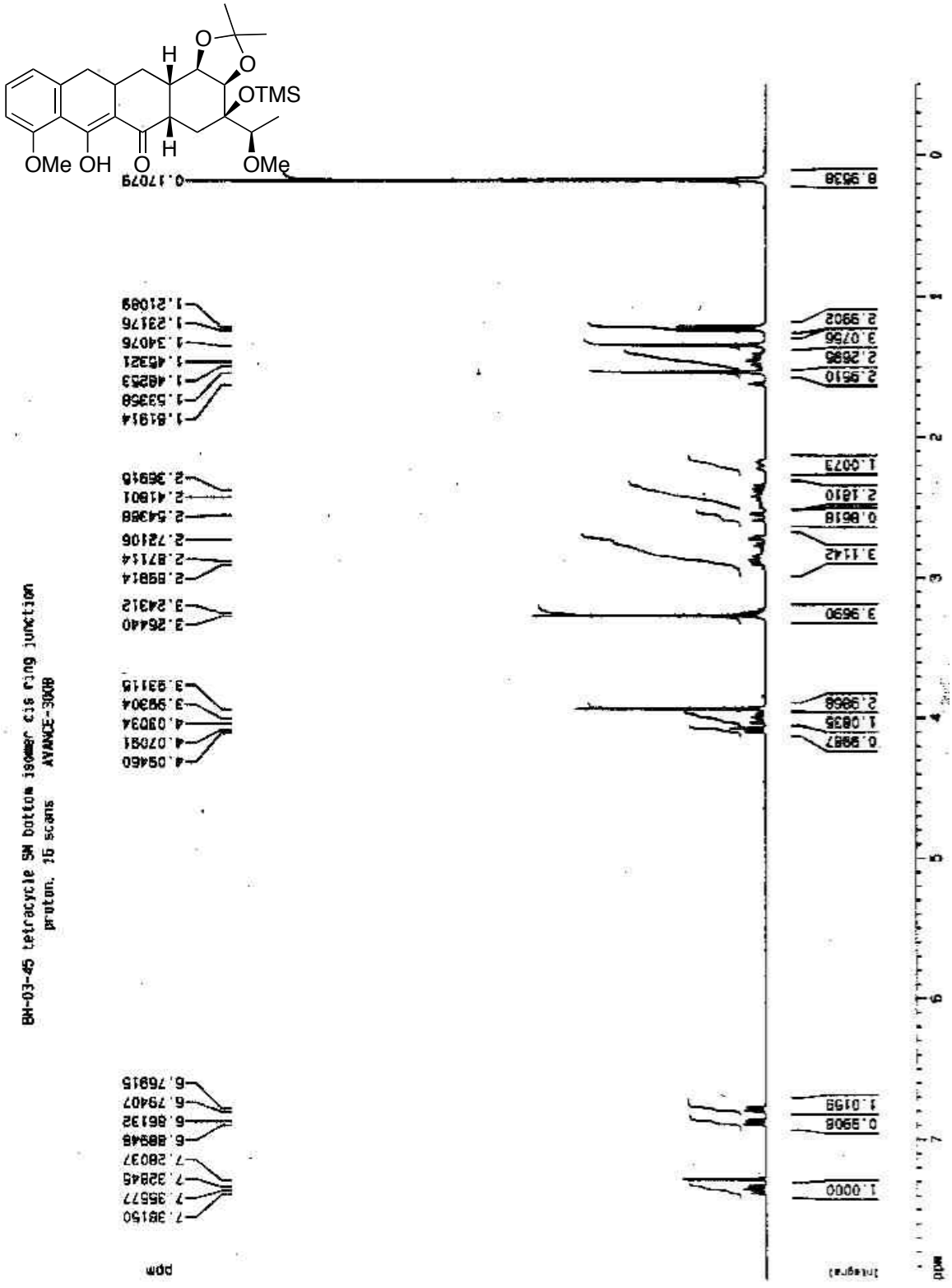


Compound 6a, 75 MHz ^{13}C NMR ($CDCl_3$)

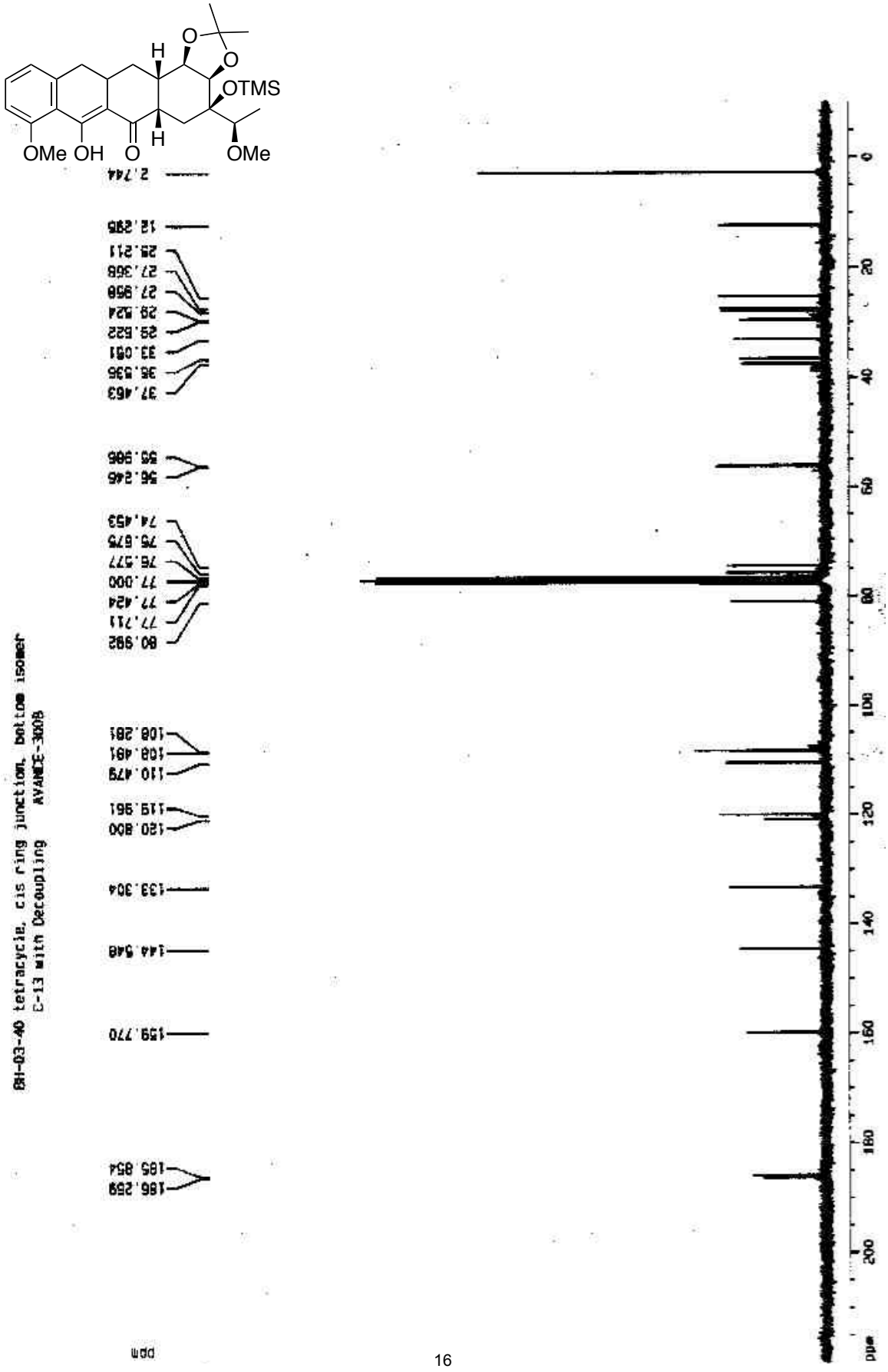




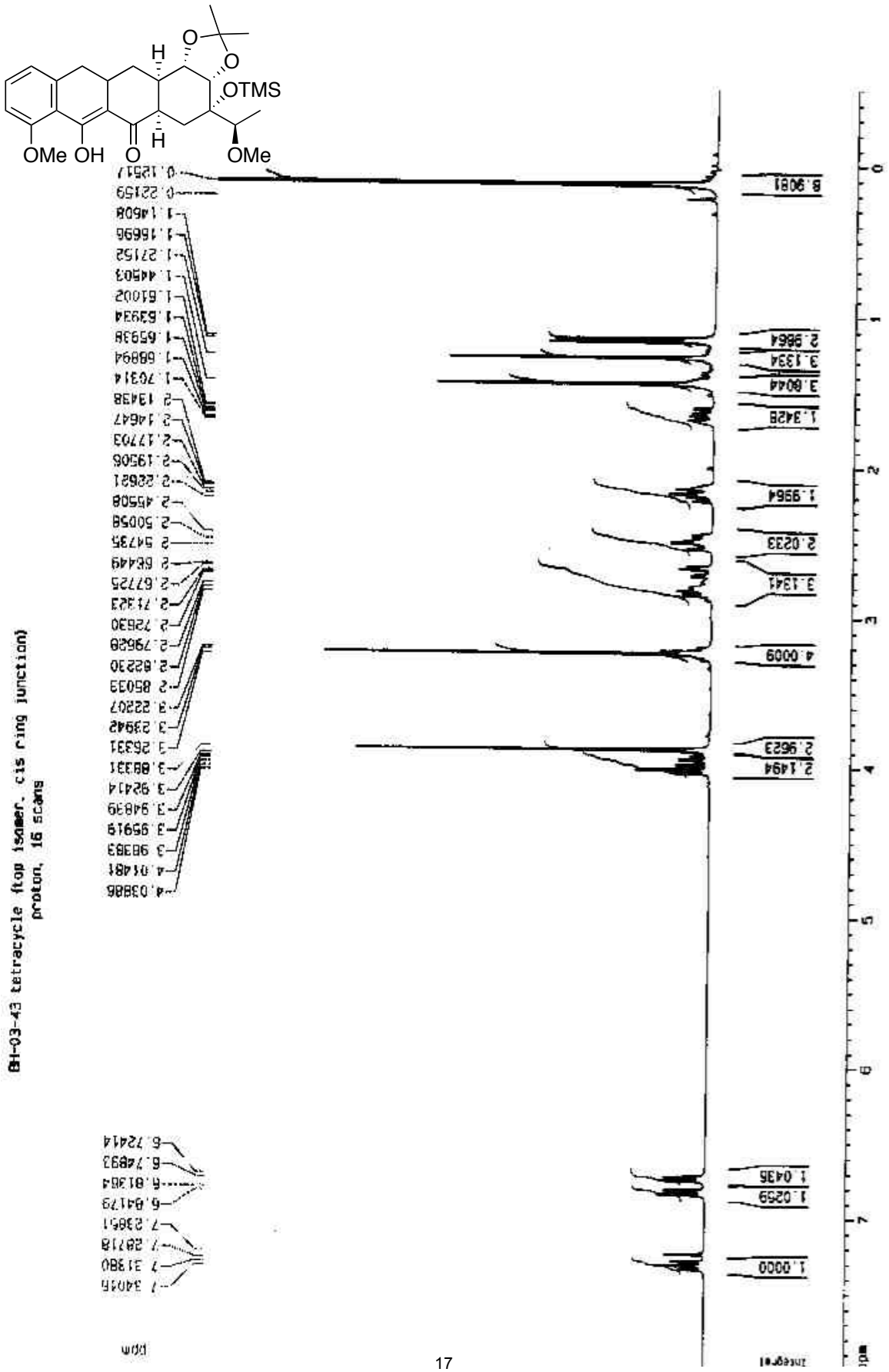
Compound 6b, 300 MHz ^{1}H NMR ($CDCl_3$)



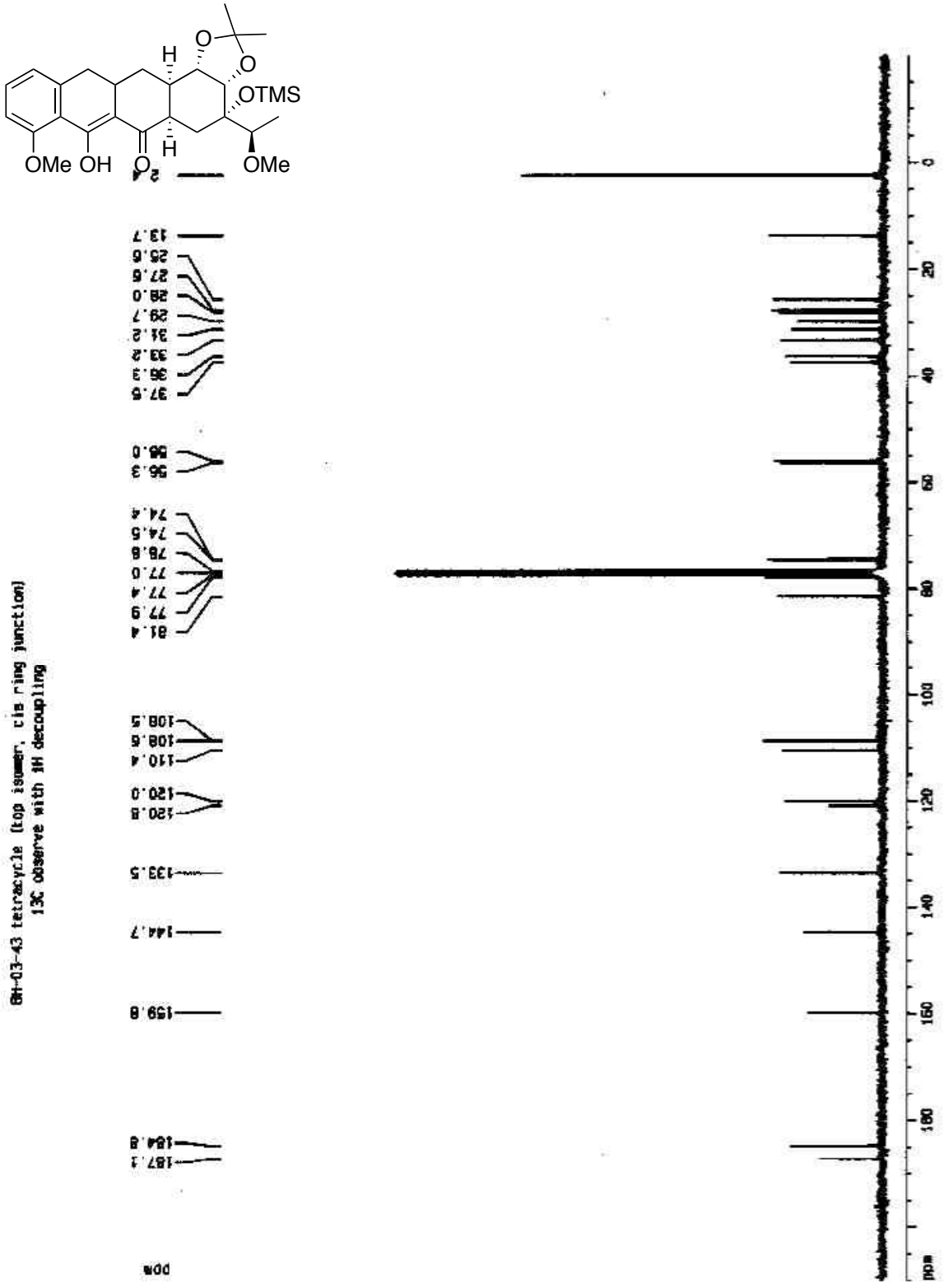
Compound 6b, 75 MHz ^{13}C NMR ($CDCl_3$)



Compound 7, 300 MHz ^{1}H NMR ($CDCl_3$)



Compound 7, 75 MHz ^{13}C NMR ($CDCl_3$)



Compound 8, 300 MHz ^{1}H NMR ($CDCl_3$)