Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Dramatic influence of the substitution of alkylidene-5*H*-furan-2-ones in Diels-Alder cycloadditions with *o*-quinonedimethide as diene partner:

En route to the CDEF polycyclic ring system of lactonamycin

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General Experimental Methods.

All reactions sensitive to oxygen and moisture were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted.

^{1}H NMR and ^{13}C NMR spectra were recorded on a AC300, AC400 or AC500 using the deuterated solvent as internal deuterium lock. Chemical shift data are given in units δ relative to residual protic solvents where δ (chloroform) = 7.26 ppm and δ (benzene) = 7.16 ppm. The multiplicity of a signal is indicated as: br - broad, s - singlet, d - doublet, t - triplet, q - quartet, m - multiplet, dd - doublet of doublets, dt - doublet of triplets, etc. Coupling constants (*J*) are quoted in Hz and recorded to the nearest 0.1 Hz. ^{13}C NMR Spectra were recorded on a AC300, AC400 or AC500 spectrometer using the deuterated solvents as internal deuterium lock. Chemical shift data are given in units δ relative to residual protic solvents where δ (chloroform) = 77.16 ppm, δ (benzene) = 128.06 ppm and δ (acetonitrile) = 1.32 ppm. NMR Spectra were assigned using information ascertained from DEPT, HMQC and NOE experiments.

Reagents and solventss were commercial grades and were used as supplied. Benzene was distilled from calcium hydride and stored over molecular sieves 4 Å. Commercially available C_6D_6 was used without further purification.

Mass spectra (MS) were performed with a triple quadrupole system with a pneumatically assisted electrospray interface. High resolution mass spectra (HRMS) have been performed using a mass spectrometer equipped with a pneumatically assisted atmospheric pressure ionization. The sample was ionized in positive mode electrospray in the following conditions: electrospray voltage (ISV): 5500 V; orifice voltage (OR): 70 V; nebulising gas flow pressure (air): 0.6 psi. The mass spectrum was obtained using a time of flight analyzer (TOF). The measure was realized in triplicate. The sample was dissolved in methanol (500 µL) then diluted (dilution factor 4/10000) in a methanolic solution of ammonium acetate (3 mM). The sample solution was infused in the ionization source at a 5 µL/min flow rate.

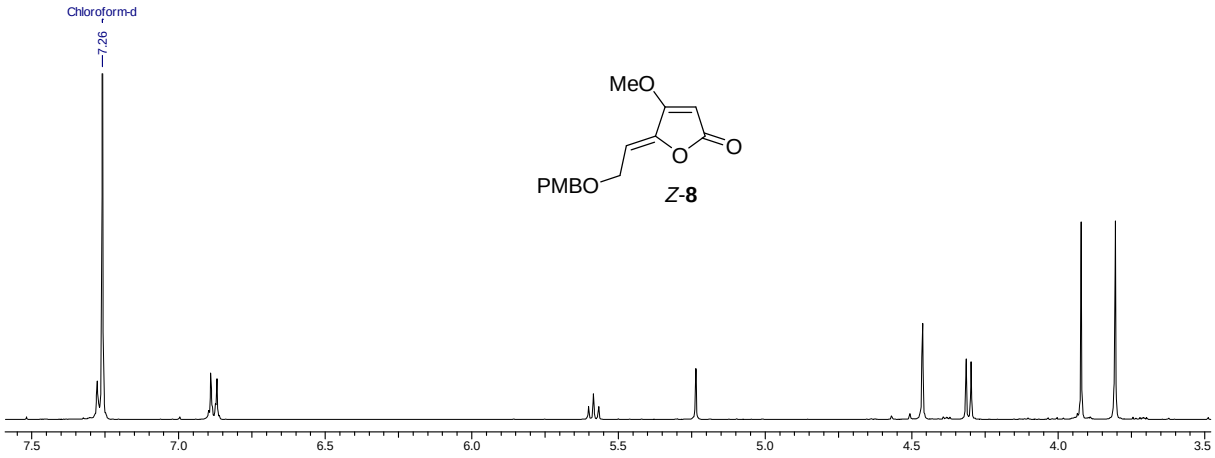
Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F254. Flash column chromatography was performed on Merck Kieselgel 60 (230–400 mesh).

Infrared spectra were recorded on a Bruker VERTEX70 Fourier transform infrared spectrometer equipped with a single reflection diamond ATR Bruker A222 accessory. The measurements were done for pure samples. For each individual spectrum, about 30 scans were averaged at 4 cm^{-1} resolution. The diamond crystal without sample served as reference. All the system was purged with dry air. The identification of peaks was done with the standard method proposed in OPUS 6.0 software.

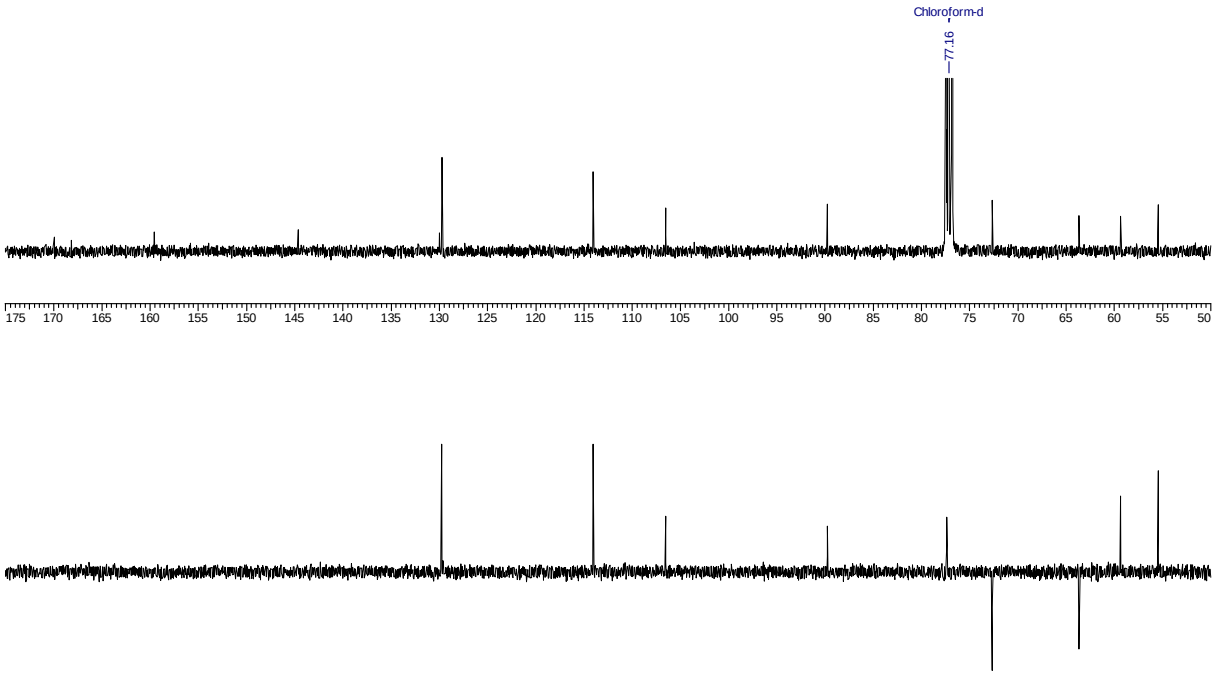
Melting point were performed with Buchï Melting Point B-540

Compounds (*Z*)-8 and (*E*)-8. To a stirred solution of THF at -80°C was added a solution of *n*-BuLi (7.7 mL, 193 mmol, 1.1 equiv, 2.5 M in hexane). A precooled solution of methyltetronate **9**[1] (2g, 175 mmol, 1 equiv) in THF (35 mL) was then added dropwise at -80°C. After 20 min at -80°C, a precooled solution of aldehyde **10**[2] (3.4 g, 175 mmol, 1 equiv) in THF (17 mL) was added to the mixture and allowed to warm at room temperature. After 2h, ice crish followed by diluted aqueous HCl were added to the mixture. The aqueous phase was extracted with Et_2O. The combined organic phases were dried over Na_2SO_4 and concentrated under vacuum. The crude product was then purified by flash chromatography (3:7 petroleum ether:ethyl acetate) to afford a inseparable 52/48 mixture of alcohol **11** (3.2 g) in 74% yield. To a stirred solution of alcohol **11** (1.14 g, 3.87 mmol, 1equiv) in CH_2Cl_2 (7 mL), was added triethylamine (1.61 mL, 11.6 mmol, 3eq) followed by mesylchloride (0.419 mL, 5.43 mmol, 1.4 equiv) were added dropwise. The mixture was heated at reflux overnight. The reaction was then quenched by addition of saturated aqueous solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and concentrated under vacuum. The crude material was finally purified by flash chromatography (8:2 petroleum ether:ether) to afford (56% yield) (*Z*)-**8** (404 mg) and (*E*)-**8** (194 mg) in 67/33 ratio.

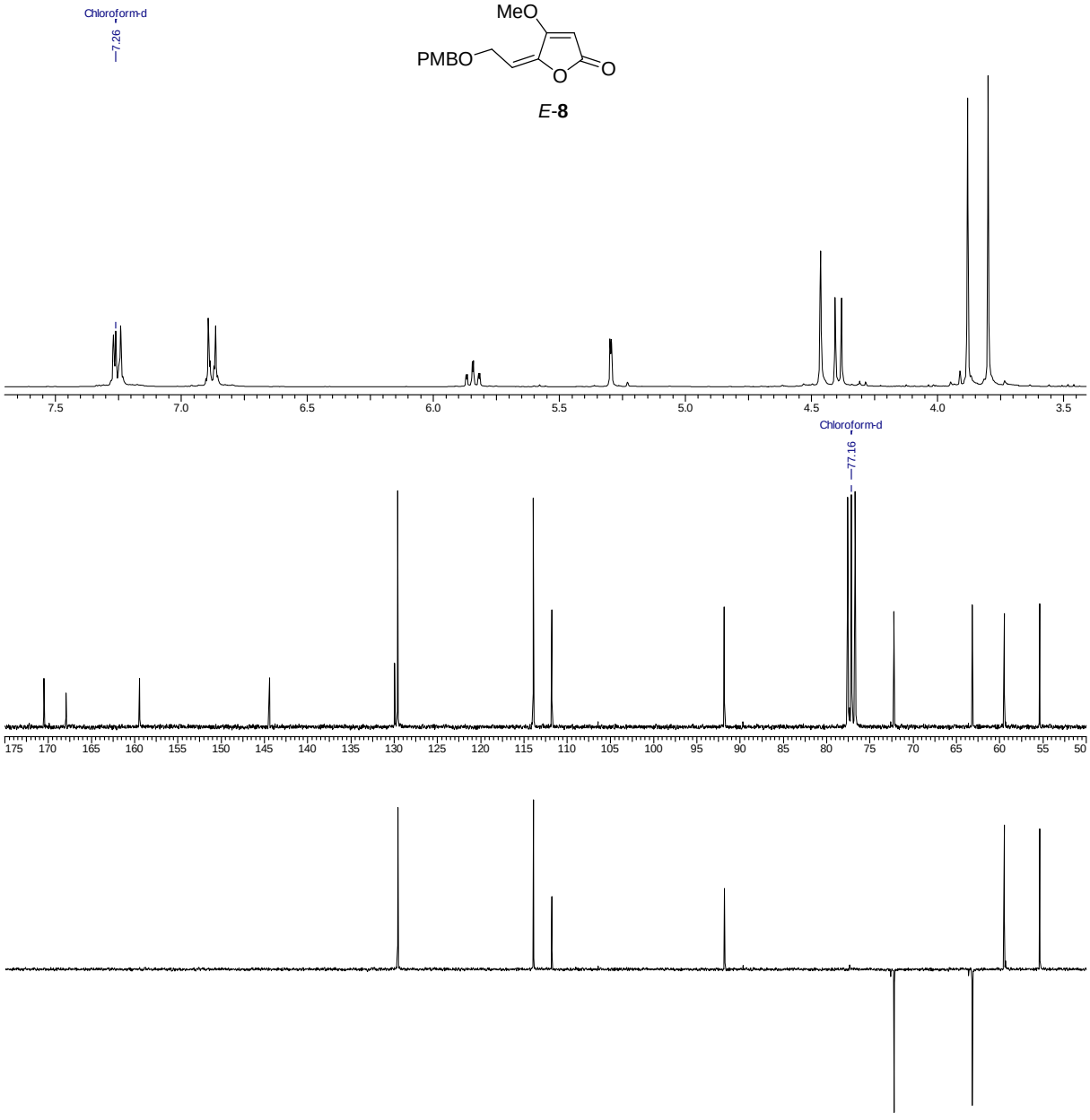
(Z)-**8**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.81 (3H, CH_3), 3.92 (3H, CH_3), 4.30 (2H, d, J = 6.8 Hz, CH_2), 4.46 (2H, s, CH_2), 5.24 (1H, br s, CH), 5.59 (1H, t, J = 6.8 Hz, CH), 6.88 (2H, d, J = 8.5, 2 x CH_{Ar}), 7.27 (2H, d, J = 8.5 Hz, 2 x CH_{Ar}); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 55.4 (CH_3), 59.3 (CH_3), 63.7 (CH_2), 72.7 (CH_2), 89.8 (CH), 106.5 (CH), 114.0 (2 x CH_{Ar}), 129.7 (2 x CH_{Ar}), 130.0 (C), 144.6 (C), 159.5 (C), 168.2 (C), 169.9 (C); **HRMS** found 277.1074 $[M + H]^+$, $C_{15}H_{17}O_5$ requires 277.1071.



[1] a) T. Momose, N. Toyooka and Y. Takeuchi, *Heterocycles*, 1986, **24**, 1429-1431; b) S. Gelin and P. Pollet, *Synth. Commun.*, 1980, **10**, 805-812.
[2] A. B. Smith III and R. J. Fox, *Org. Lett.*, 2004, **6**, 1477-1480.

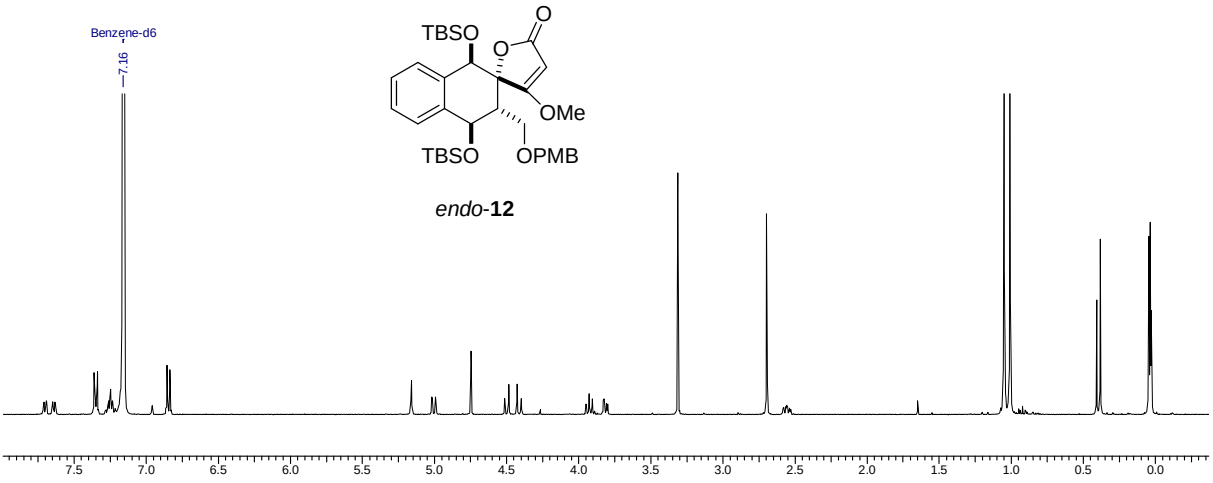


(E)-**8**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.80 (3H, s, CH_3), 3,88 (3H, s, CH_3), 4.39 (2H, d, J = 7.6, CH_2), 4.46 (2H, s, 1H, CH_2), 5.30 (1H, br d, J = 1.3 Hz, CH), 5.84 (1H, dt, J = 7.6 and 1.3 Hz, CH), 6.88 (2H, d, J = 8.7 Hz, 2 x CH_{Ar}), 7.27 (2H, d, J = 8.7 Hz, 2 x CH_{Ar}); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.4 (CH_3), 59.5 (CH_3), 63.2 (CH_2), 72.2 (CH_2), 91.8 (CH), 111.8 (CH), 113.9 (2 x CH_{Ar}), 129.6 (2 x CH_{Ar}), 130.0 (C), 144.4 (C), 159.5 (C), 167.9 (C), 170.5 (C); **HRMS** found 277.1074 $[M + H]^+$, $C_{15}H_{17}O_5$ requires 277.1071.

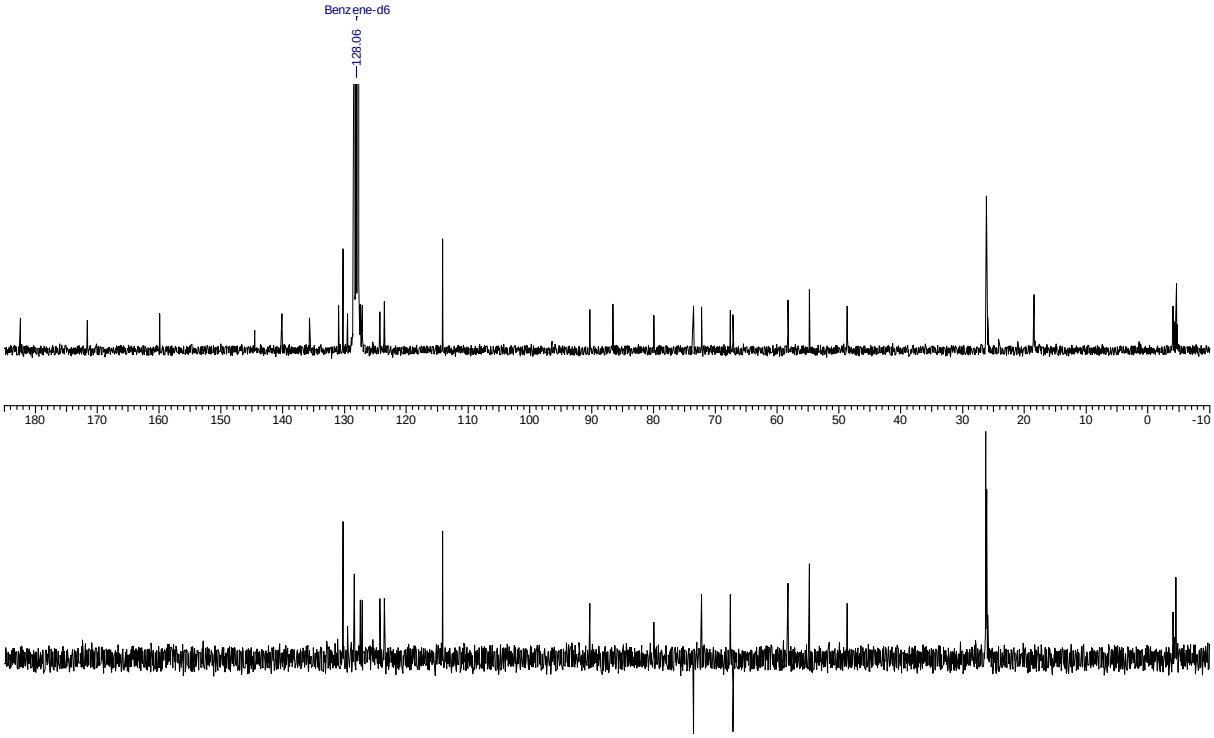


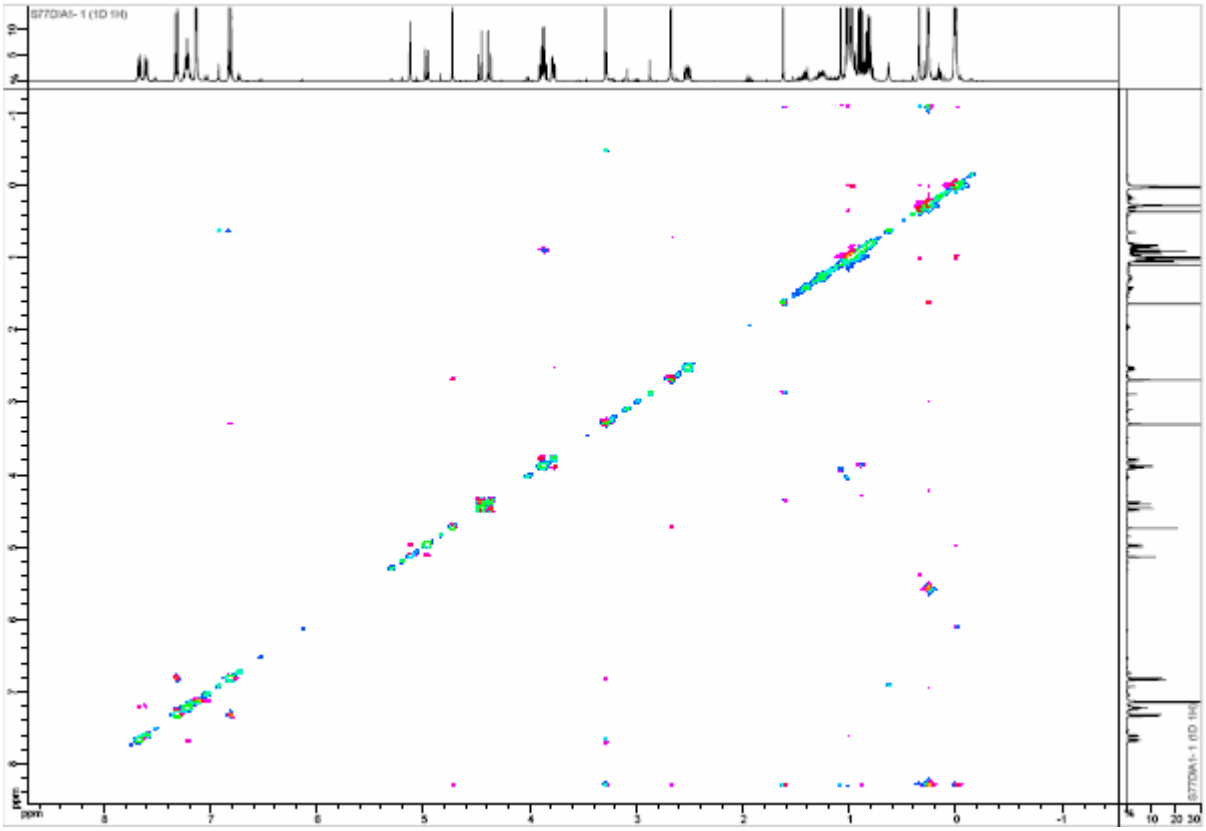
Compound 12. In a oven-dried Schlenk tube, *trans*-1,2-bis(*tert*-butyldimethylsilyloxy)-1,2-benzocyclobutene **1**[3] (326 mg, 0.89 mmol, 1.5 equiv) and butenolide (*Z*)-**8** (164 mg, 0.59 mmol, 1 equiv) were dissolved in benzene-D_6 (3.3 mL). The solution was degassed for 10 min at -80°C three times. The mixture was then heated at 55°C. The reaction was followed by ^{1}H NMR and after disappearance of (*Z*)-**8** (3 days), the solvent was removed under vacuum. The crude product was purified by flash chromatography (8:2 petroleum ether:ethyl acetate) to give a separable 1/1 mixture (374 mg) of *exo*-**12** and *endo*-**12** in quantitative yield.

endo-**12**: **^{1}H NMR** (400 MHz, C_6D_6) δ 0.03 (6H, s, 2 x CH_3), 0.04 (3H, s, CH_3), 0.37 (3H, s, CH_3), 1.00 (9H, s, 3 x CH_3), 1.04 (9H, s, 3 x CH_3), 2.52-2.58 (1H, m, CH), 2.71 (3H, s, CH_3), 3.32 (3H, s, CH_3), 3.81 (3H, dd, *J* = 9 and 3.0 Hz, CH_2), 3.89-3.94 (1H, m, CH_2), 4.40 (1H, d, CH_2, *J* = 11.1 Hz), 4.49 (1H, d, CH_2, *J* = 11.1 Hz), 4.75 (1H, s, C), 5.00 (1H, d, *J* = 10 Hz, CH), 5.15 (1H, s, CH), 6.84 (2H, d, *J* = 8.7 Hz, 2 x CH_{Ar}), 7.21-7.28 (2H, m, 2 x CH_{Ar}), 7.35 (2H, d, *J* = 8.7 Hz, 2 x CH_{Ar}), 7.62-7.63 (1H, m, CH_{Ar}), 7.68-7.70 (1H, m, CH_{Ar}); **^{13}C NMR** (100 MHz, C_6D_6) δ -4.7 (CH_3), -4.6 (2 x CH_3), -4.1 (CH_3), 18.4 (C), 18.5 (C), 26.1 (3 x CH_3), 26.2 (3 x CH_3), 48.6 (CH), 54.8 (CH_3), 58.3 (CH_3), 67.1 (CH_2), 67.5 (CH), 72.1 (CH), 73.5 (CH_2), 86.6 (C), 90.3 (CH), 114.1 (2 x CH_{Ar}), 123.5 (CH), 124.2 (CH), 127.1 (CH), 127.4 (CH), 130.2 (2 x CH_{Ar}), 130.9 (C), 135.6 (C), 140.1 (C), 159.9 (C), 171.6 (C), 182.4 (C); **IR** (ν_{max}): 2956, 2930, 2889, 2856, 1759, 1637, 1613, 1510, 1460, 1366, 1247, 1173, 1131, 1098, 1070, 1036 cm^{-1}; **MS**: *m/z* (ESI+) 663 (M + Na)$^+$; **HRMS** found 658.3588 [M + NH_4]$^+$, $C_{35}H_{56}NO_7Si_2$ requires 658.3590.

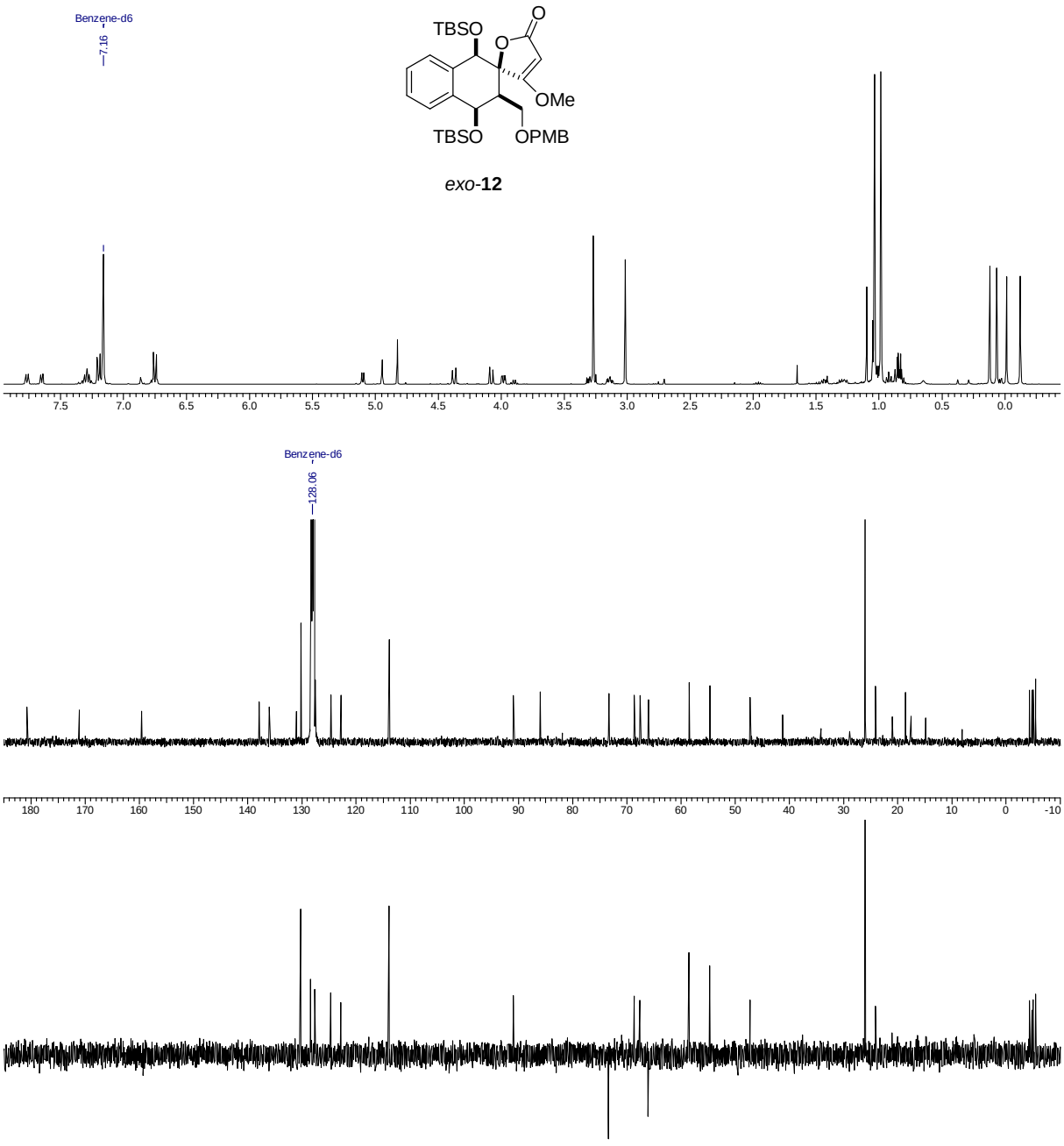


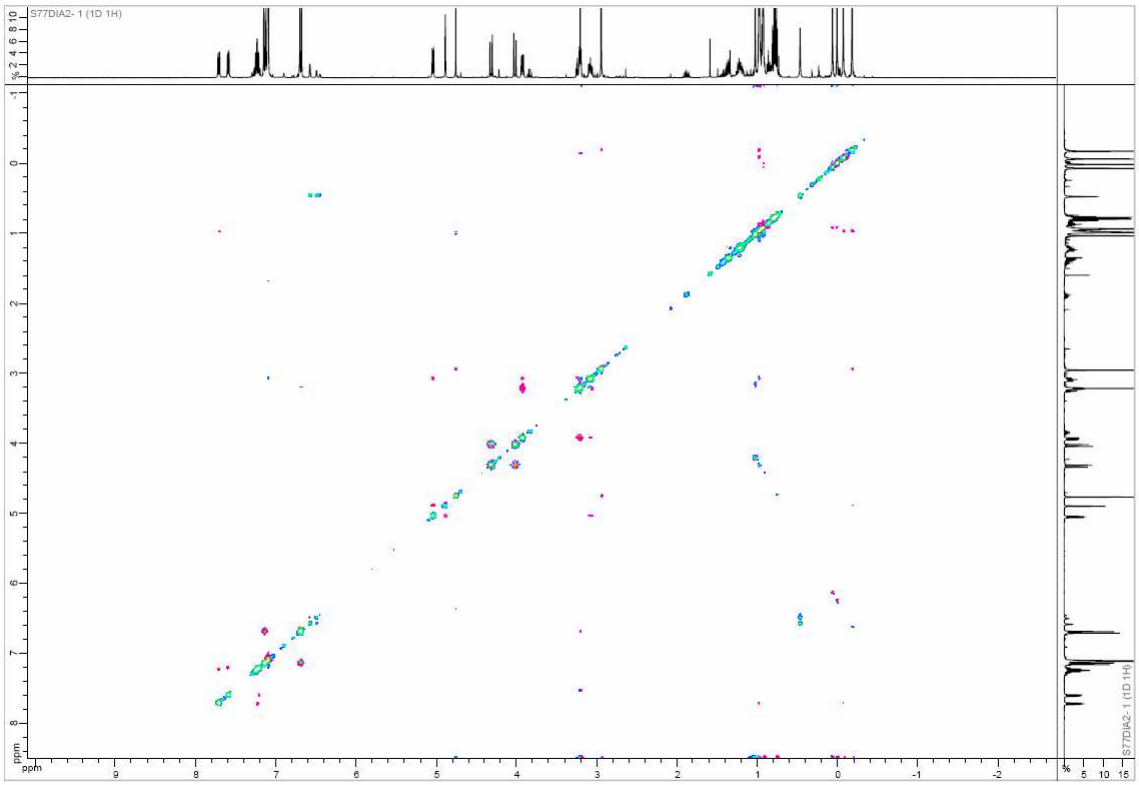
[3] a) M. S. South and L. S. Liebeskind, *J. Org. Chem.*, 1982, **47**, 3815-3821; b) J. G. Allen, M. F. Hentemann and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2000, **122**, 571-573.





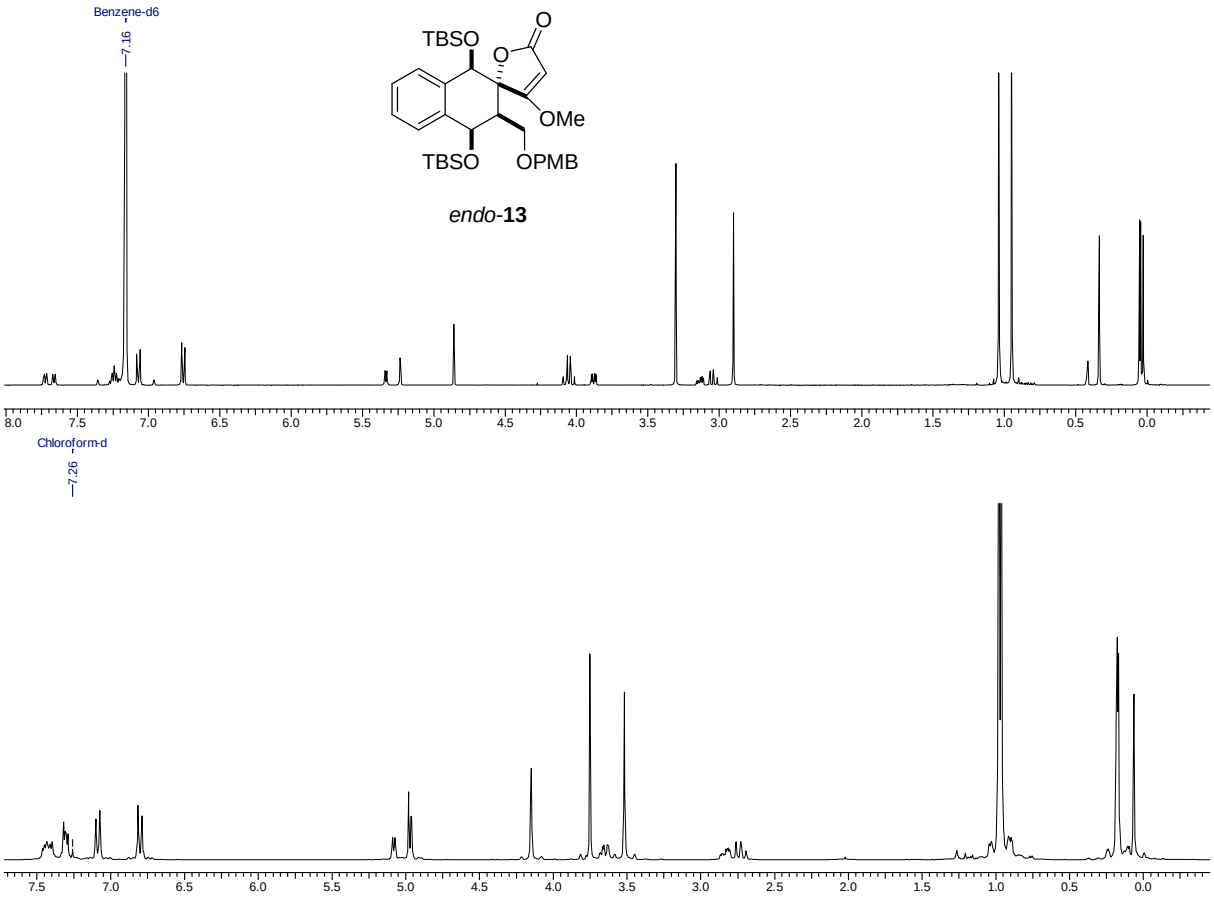
exo-**12:** **^{1}H NMR** (400 MHz, C_6D_6) δ -0.12 (3H, s, CH_3), -0.01 (3H, s, CH_3), 0.06 (3H, s, CH_3), 0.12 (3H, s, CH_3), 0.99 (9H, s, 3 x CH_3), 1.04 (9H, s, 3 x CH_3), 3.02 (3H, s, CH_3), 3.11-3.16 (1H, m, CH), 3.25-3.32 (2H, m, CH_2), 3.27 (3H, s, CH_3), 3.98 (1H, dd, J = 8.9 and 3 Hz, CH_2), 4.08 (1H, d, CH_2, J = 11 Hz, H9), 4.38 (1H, d, CH_2, J = 11 Hz), 4.82 (1H, s, CH), 4.94 (1H, s, CH), 5.11 (1H, d, J = 6.8 Hz, CH), 6.75 (2H, d, J = 8.7 Hz, 2 x CH_{Ar}), 7.20 (2H, d, J = 8.7 Hz, 2 x CH_{Ar}), 7.26-7.37 (2H, m, CH_{Ar}), 7.64 (1H, br d, J = 6.8 Hz, CH_{Ar}), 7.77 (1H, br d, J = 7.5 Hz, CH_{Ar}); **^{13}C NMR** (100 MHz, C_6D_6) δ -5.5 (CH_3), -5.0 (CH_3), -4.8 (CH_3), -4.3 (CH_3), 18.4 (C), 18.6 (C), 26.0 (6 x CH_3), 47.3 (CH), 54.7 (CH_3), 58.5 (CH_3), 66.1 (CH_2), 67.6 (CH), 68.7 (CH), 73.4 (CH_2), 86.0 (C), 91.0 (CH), 113.9 (2 x CH_{Ar}), 122.8 (CH), 124.7 (CH), 127.5 (CH), 127.6 (CH), 130.2 (2 x CH_{Ar}), 131.1 (C), 136.0 (C), 137.9 (C), 159.6 (C), 171.1 (C), 180.8 (C, C2); **IR** (ν_{max}): 2952, 2930, 2888, 2857, 1756, 1641, 1515, 1471, 1461, 1360, 1247, 1192, 1171, 1131, 1071, 1031 cm^{-1}; **MS**: *m/z* (ESI+) 663 (M + Na)$^{+}$; **HRMS** found 658.3589 $[M + NH_4]^{+}$, $C_{35}H_{56}NO_7Si_2$ requires 658.3590.

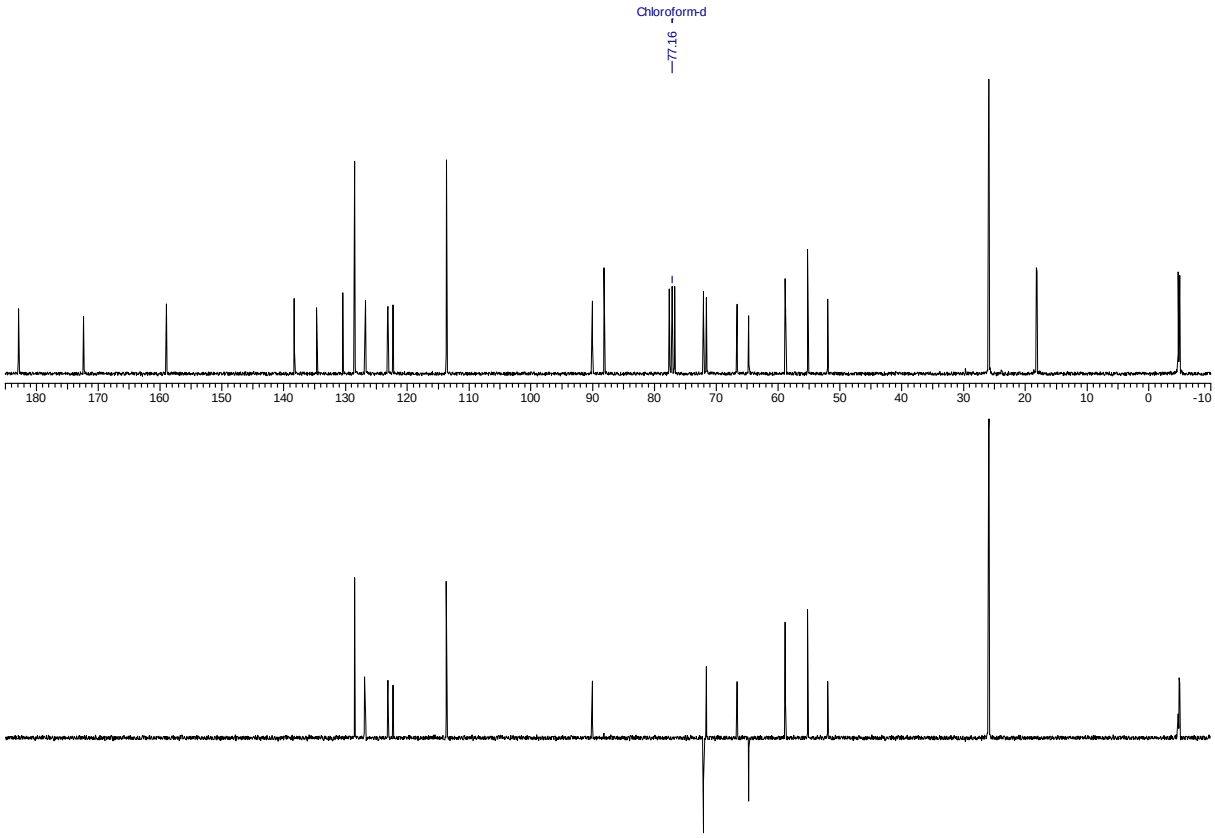


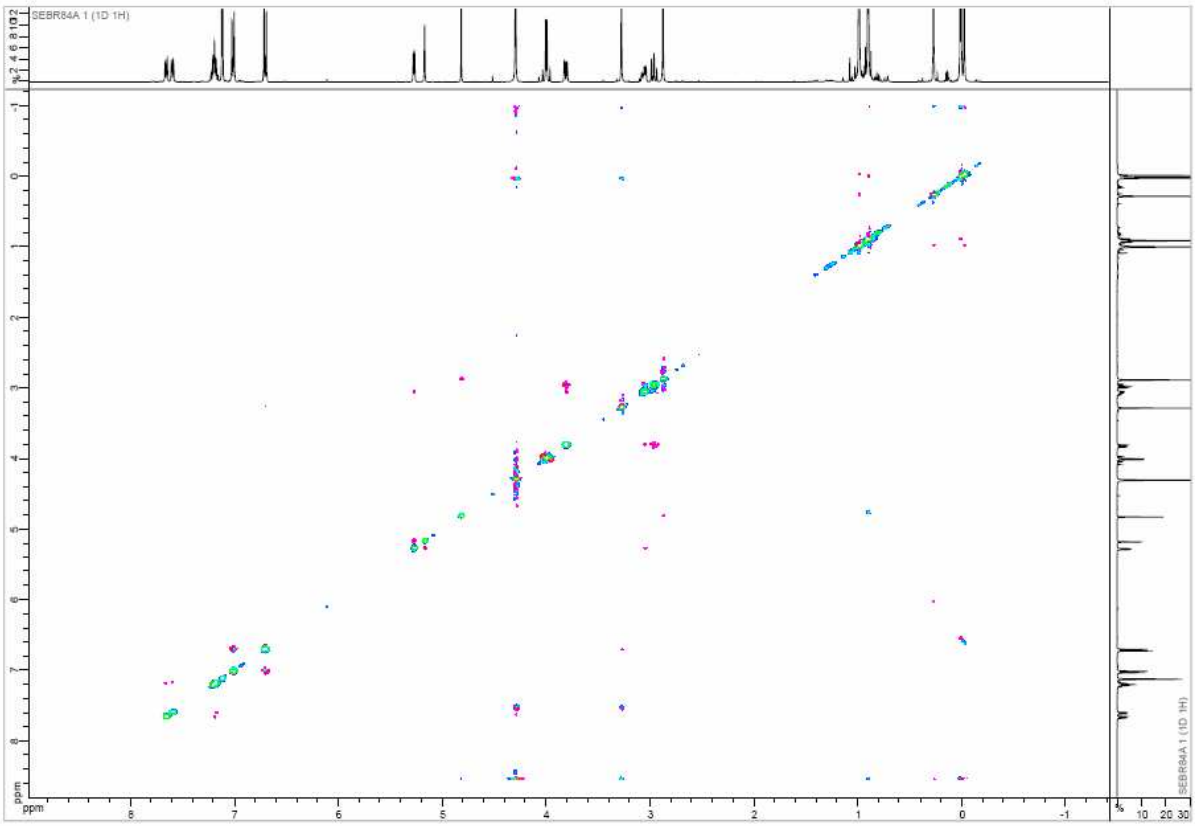


Compound *endo*-**13**. In a oven-dried Schlenk tube, *trans*-1,2-bis(*tert*-butyldimethylsilyloxy)-1,2-benzocyclobutene **1** (253 mg, 0.69 mmol, 1.5 equiv) and butenolide (*E*)-**8** (128 mg, 0.46 mmol, 1 equiv) were dissolved in benzene-*d*6 (2.6 mL). The solution was degassed for 10 min at -80°C three times. The mixture was then heated at 55°C. The reaction was followed by ^{1}H NMR and after disappearance of (*E*)-**8** (3 days), the solvent was removed under vacuum. The crude product was purified by flash chromatography (9:1 petroleum ether:ethyl acetate) to give *endo*-**13** (269 mg) in quantitative yield.

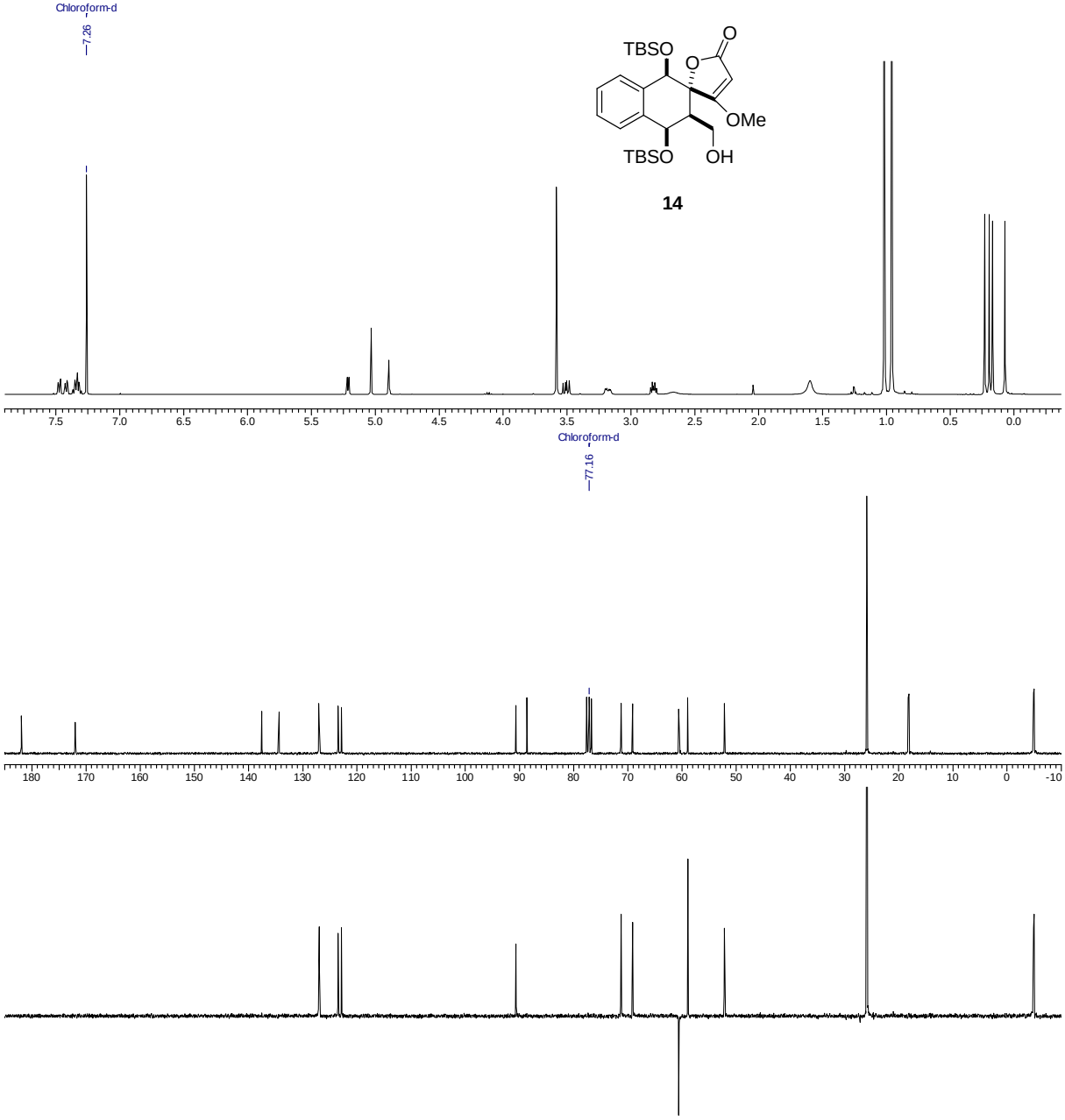
^{1}H NMR (400 MHz, C_6D_6) δ 0.03 (3H, s, CH_3), 0.05 (3H, s, CH_3), 0.6 (3H, s, CH_3), 0.34 (3H, s, CH_3), 0.95 (9H, s, 3 x CH_3), 1.04 (9H, s, 3 x CH_3), 2.9 (3H, s, CH_3), 3.01-3.06 (1H, m, CH_2), 3.11-3.16 (1H, m, CH), 3.30 (3H, s, CH_3), 3.88 (1H, dd, J = 9.8 and 3.5 Hz, CH_2), 4.02 (1H, d, CH_2, J = 11.8 Hz), 4.07 (1H, d, CH_2, J = 11.8 Hz), 4.86 (1H, s, CH), 5.24 (1H, br s, CH), 5.32 (1H, d, J = 5.3 Hz, CH), 6.76 (2H, d, J = 8.5 Hz, 2 x CH_{Ar}), 7.07 (2H, d, J = 8.5 Hz, 2 x CH_{Ar}), 7.20-7.27 (2H, m, 2 x CH_{Ar}), 7.66 (1H, br d, J = 5.5 Hz, CH_{Ar}), 7.72 (1H, br d, J = 5.8 Hz, CH_{Ar}); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (3H, s, CH_3), 0.17 (3H, s, CH_3), 0.18 (3H, s, CH_3), 0.19 (3H, s, CH_3), 0.96 (9H, s, 3 x CH_3), 0.98 (9H, s, 3 x CH_3), 2.69-2.76 (1H, m, CH_2), 2.81-2.87 (1H, m, CH), 3.52 (3H, s, CH_3), 3.65 (1H, dd, J = 9.6 and 2.8 Hz, CH_2), 4.15 (3H, s, CH_3), 4.15 (2H, s, CH_2), 4.96 (1H, br s, CH), 4.98 (1H, br s, CH), 5.08 (1H, d, J = 5.1 Hz, CH), 6.80 (2H, d, J = 8.5 Hz, 2 x CH_{Ar}), 7.08 (2H, d, J = 8.5 Hz, 2 x CH_{Ar}), 7.29-7.32 (2H, m, 2 x CH_{Ar}), 7.40-7.46 (2H, m, 2 x CH_{Ar}); **^{13}C NMR** (75 MHz, $CDCl_3$) δ -5.0 (CH_3), -4.9 (CH_3), -4.8 (CH_3), -4.7 (CH_3), 18.1 (C), 18.2 (C), 25.8 (3 x CH_3), 25.9 (3 x CH_3), 52.0 (CH), 55.2 (CH_3), 58.8 (CH_3), 64.7 (CH_2), 66.6 (CH,), 71.6 (CH), 72.1 (CH_2), 88.1 (C), 90.0 (CH), 113.6 (2 x CH_{Ar}), 122.3 (CH), 123.1 (CH), 126.7 (CH), 126.8 (CH), 128.5 (2 x CH_{Ar}), 130.4 (C), 134.6 (C), 138.3 (C), 158.9 (C), 172.3 (C), 182.9 (C); **MS**: *m/z* (ESI+) 664 $(M + Na)^+$; **HRMS** found 641.3327 $[M + H]^+$, $C_{35}H_{53}O_7Si_2$ requires 641.3324



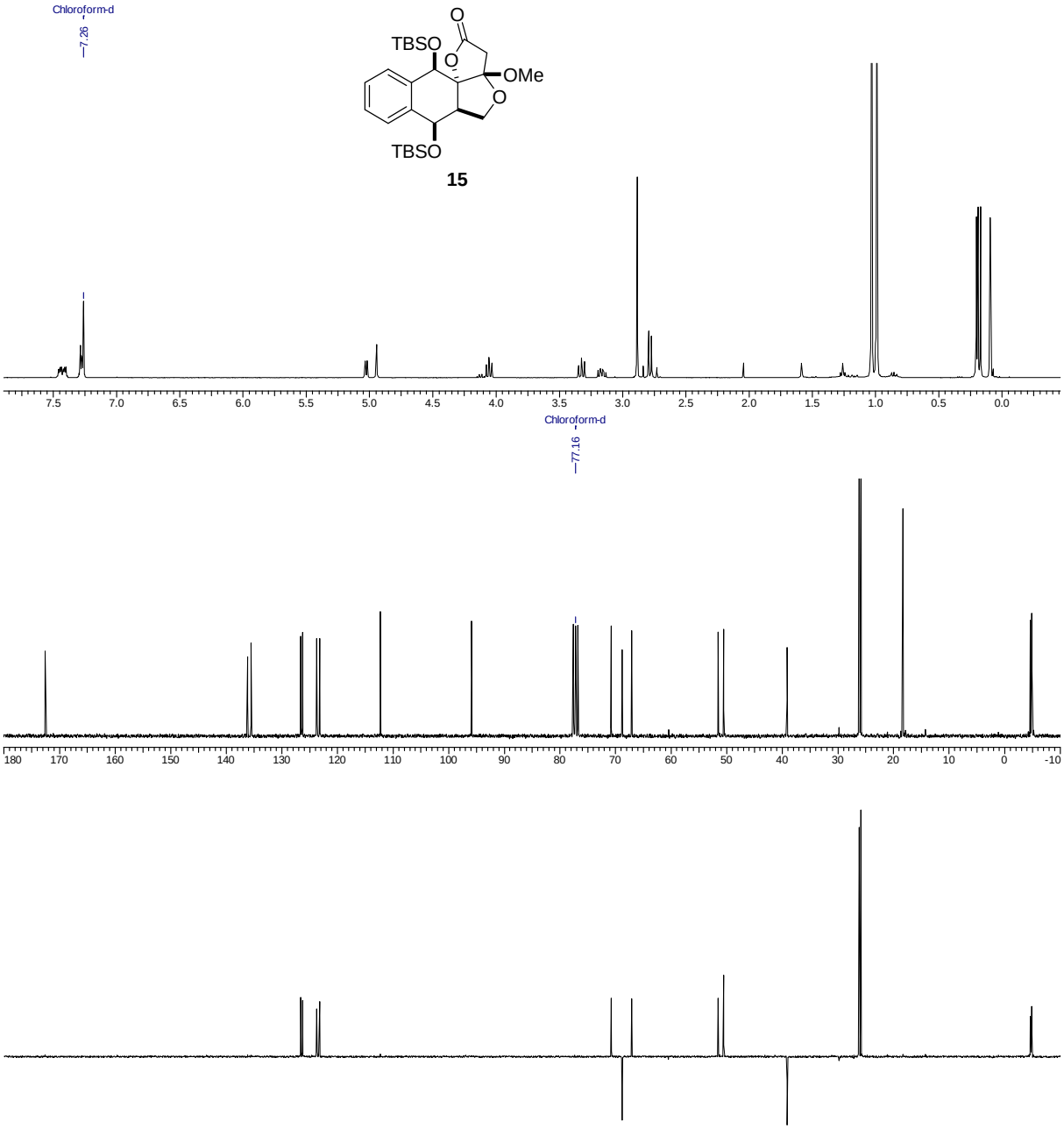




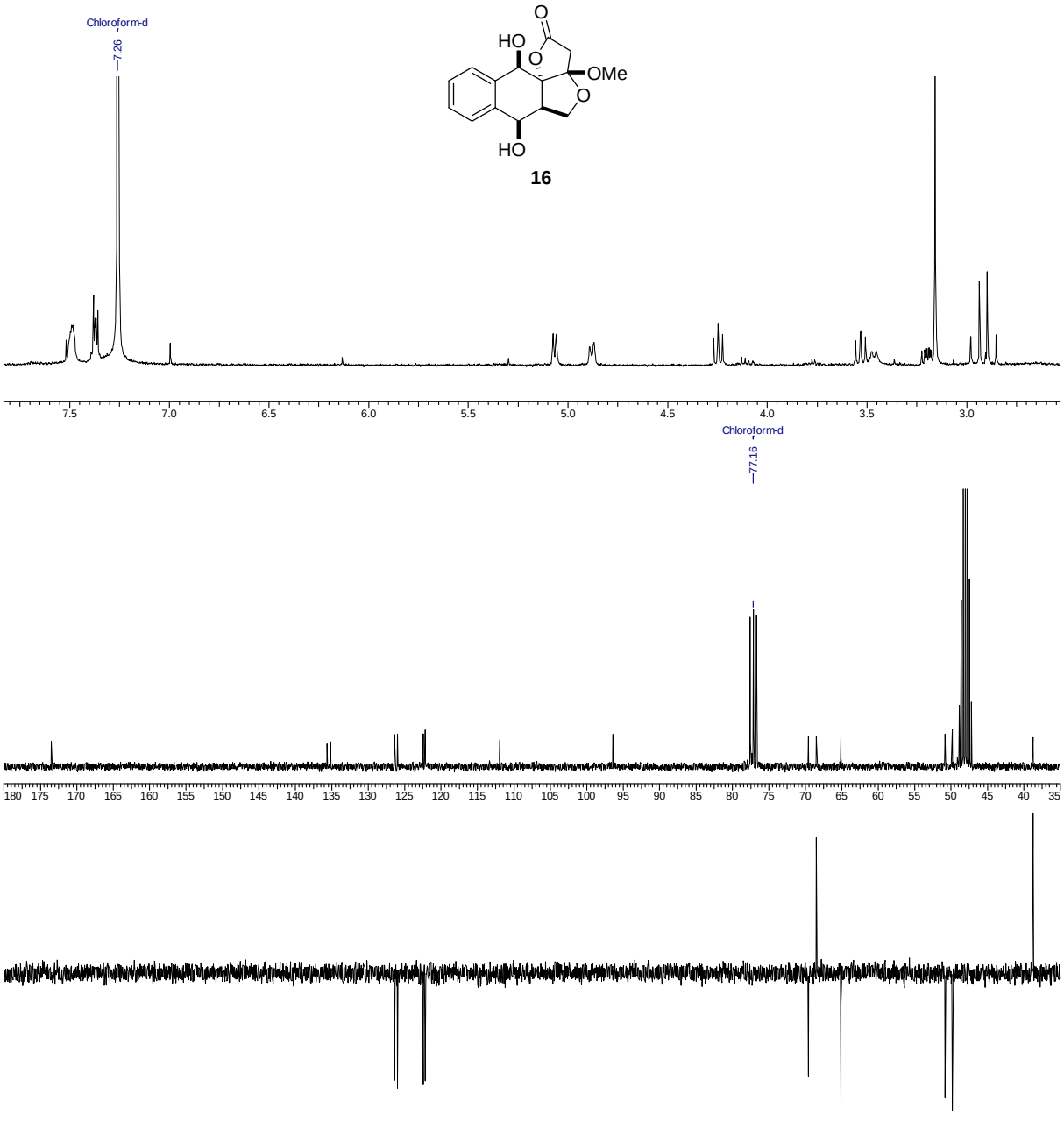
Compound 14. To a stirred solution of *endo*-**13** (260 mg, 0.405 mmol, 1equiv) in 10.5 mL of 5% aqueous CH_2Cl_2 was added at 0°C DDQ(102 mg, 0.446 mmol, 1.1 equiv). After 1h at 0°C the solution was stirred at room temperature until disappearance of starting material (1 hour) then filtered throught a pad of florosil and celite then concentrated. The crude product was purified by flash chromatography (8:2 petroleum ether:ethyl acetate) to give **14** (199 mg) in 94% yield; **Mp** = 209 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.07 (3H, s, CH_3), 0.17 (3H, s, CH_3), 0.19 (3H, s, CH_3), 0.23 (3H, s, CH_3), 0.96 (9H, s, 3 x CH_3), 1.02 (9H, s, 3 x CH_3), 2.67 (1H, m, OH), 2.82 (1H, dt, *J* = 8.3 and 5.5 Hz, CH), 3.18 (1H, dd, *J* = 11.6 and 4.8 Hz, CH_2), 3.50 (1H, dd, *J* = 11.6 and 8.3 Hz, CH_2), 3.58 (3H, s, CH_3), 4.89 (1H, s, CH), 5.03 (1H, s, CH), 5.21 (1H, d, CH, *J* = 5.5 Hz, H7), 7.30-7.37 (2H, m, 2 x CH_{Ar}), 7.41-7.48 (2H, m, 2 x CH_{Ar}); **^{13}C NMR** (75 MHz, $CDCl_3$) δ -5.0 (CH_3), -4.9$_3$ (CH_3), -4.8$_7$ (CH_3), -4.8 (CH_3), 18.1 (C), 18.3 (C), 25.9 (6 x CH_3), 52.8 (CH), 58.9 (CH_3), 60.6 (CH_2), 69.1 (CH), 71.3 (CH), 88.6 (C), 90.6 (CH), 122.8 (CH_{Ar}), 123.5 (CH_{Ar}), 126.9 (CH_{Ar}), 127.0 (CH_{Ar}), 134.3 (C_{Ar}), 137.5 (C_{Ar}), 171.9 (C), 181.9 (C); **IR** (ν_{max}): 3451, 2952, 2929, 2888, 2857, 1738, 1628, 1471, 1459, 1252, 1185, 1130, 1068, 1049 cm^{-1}; **MS**: *m/z* (ESI+) 543 (M + Na)$^+$; **HRMS** found 521.2747 [M + H]$^+$, $C_{27}H_{45}O_6Si_2$ requires 521.2749.



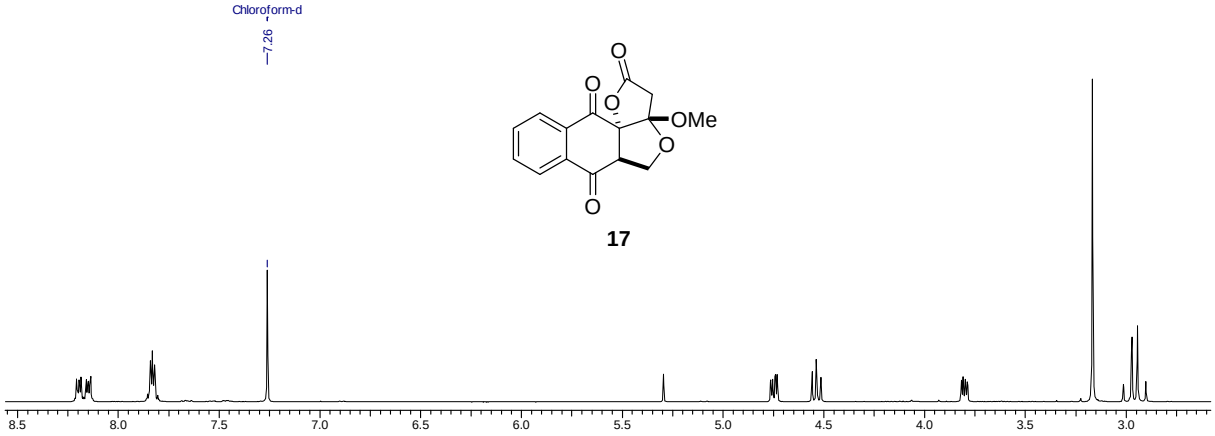
Compound 15. A solution of **14** (145 mg, 0.279 mmol, 1 equiv), NEt_3 (116 µL, 0.837 mmol, 3 equiv) in $CHCl_3$ (15 mL) was stirred at room temperature. After disappearance of the starting material (3 days), the solvent was removed under vacuum and the crude product was purified by flash chromatography (9:1 petroleum ether:ethyl acetate) to afford **15** (131 mg) in 90% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.09 (3H, s, CH_3), 0.17 (3H, s, CH_3), 0.19 (3H, s, CH_3), 0.20 (3H, s, CH_3), 0.99 (9H, s, 3 x CH_3), 1.03 (9H, s, 3 x CH_3), 2.75 (1H, d, J = 16.8 Hz, CH_2), 2.81 (1H, d, J = 16.8 Hz, CH_2), 2.88 (3H, s, CH_3), 3.13-3.19 (1H, m, CH), 3.30-3.35 (1H, m, CH_2), 4.03-4.08 (1H, m, CH_2), 4.94 (1H, br s, CH), 5.02 (1H, d, J = 6.5 Hz, CH), 7.26-7.39 (2H, m, 2 x CH_{Ar}), 7.39-7.46 (2H, m, 2 x CH_{Ar}), **^{13}C NMR** (75 MHz, $CDCl_3$) δ -4.9 (CH_3), -4.8$_3$ (CH_3), -4.7$_7$ (CH_3), -4.6 (CH_3), 18.3 (2 x C), 25.9 (3 x CH_3), 26.2 (3 x CH_3), 39.1 (CH_2), 50.5 (CH_3), 51.5 (CH), 67.1 (CH), 68.8 (CH_2), 70.8 (CH), 95.9 (C), 112.3 (C), 123.2 (CH_{Ar}), 123.7 (CH_{Ar}), 126.3 (CH_{Ar}), 126.6 (CH_{Ar}), 135.6 (C_{Ar}), 136.2 (C_{Ar}), 172.6 (C); **IR** (ν_{max}): 2954, 2930, 2888, 2857, 1791, 1472, 1461, 1251, 1211, 1182, 1126, 1076, 1061, 1013 cm^{-1}; **MS**: *m/z* (ESI+) 543 (M + Na)$^+$; **HRMS** found 538.3011 [M + NH_4]$^+$, $C_{27}H_{48}NO_6Si_2$ requires 538.3015.

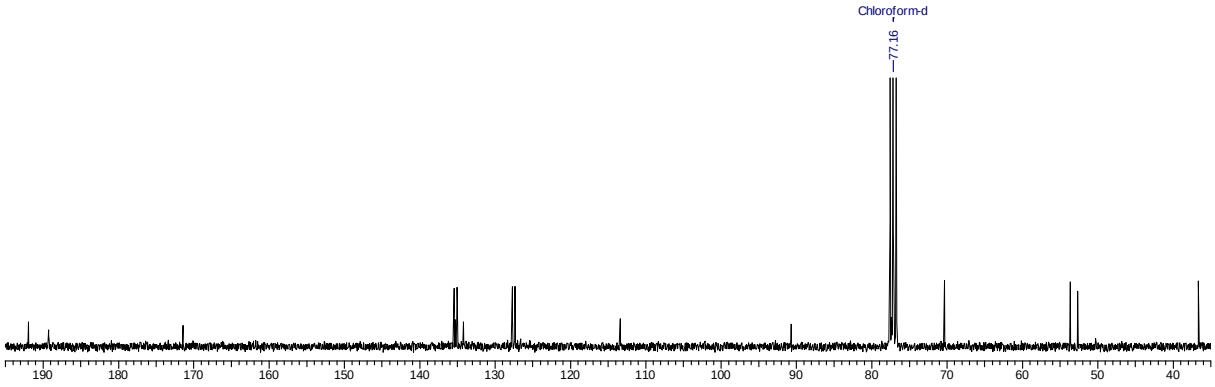


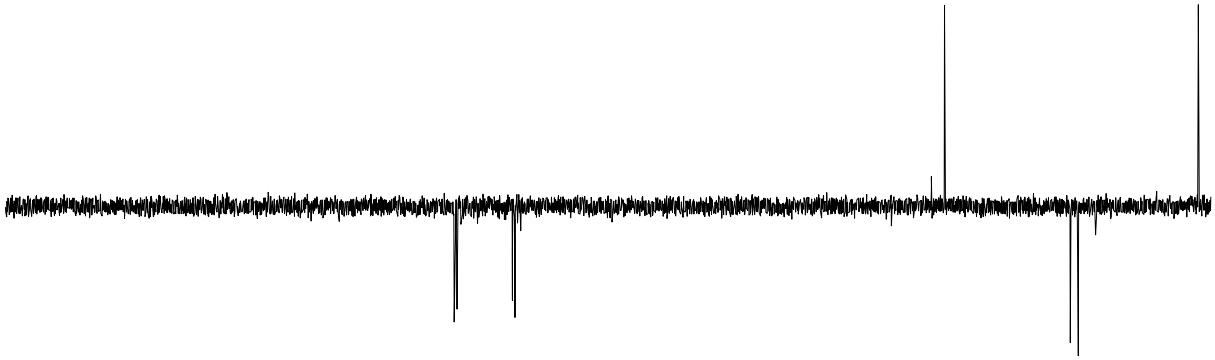
Compound 16. In an oven dry flask, **15** (130 mg, 0.25 mmol, 1 equiv) was dissolved in THF (8 mL). At 0°C, a TBAF solution (0.625 mL, 0.625 mmol, 1M in THF, 2.5 equiv) was added dropwise. The solution was stirred at room temperature and after completion of the reaction (1 hour), the mixture was quenched with aqueous saturated $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc. The combined organic phases were dried over Na_2SO_4 then concentrated under vacuum. The crude product was purified by flash chromatography (1:1 petroleum ether:ethyl acetate) to give the diol **16** (53 mg) in 73% yield. **Mp** = 251 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.87 (1H, d, *J* = 17.6 Hz, C*H*$_2$), 2.96 (1H, d, *J* = 17.6 Hz, C*H*$_2$), 3.16 (3H, s, CH_3), 3.18-3.21 (1H, m, CH), 3.46 (1H, br d, *J* = 8.3 Hz, OH), 3.51-3.56 (1H, m, C*H*$_2$), 4.23-4.27 (1H, m, C*H*$_2$), 4.88 (1H, br d, *J* = 8.3 Hz) 5.07 (1H, d, *J* = 6.3 Hz, CH), 7.36-7.38 (2H, m, 2 x CH_{Ar}), 7.48-7.52 (2H, m, 2 x CH_{Ar}); **^{13}C NMR** (75 MHz, $CDCl_3$/MeOD) δ 38.8 (CH_2), 49.8 (CH_3), 50.8 (CH), 65.1 (CH), 68.5 (CH_2), 69.6 (CH), 96.5 (C), 112.0 (C), 122.2 (CH_{Ar}), 122.5 (CH_{Ar}), 126.0 (CH_{Ar}), 126.4 (CH_{Ar}), 135.2 (C_{Ar}), 135.7 (C_{Ar}), 173.5 (C); **IR** (ν_{max}): 3484, 3411, 2988, 2934, 2892, 1768, 1458, 1412, 1281, 1262, 1249, 1228, 1188, 1140, 1099, 1063, 1048, 1033, 1007 cm^{-1}; **MS**: *m/z* (ESI+) 315 $(M + Na)^+$; **HRMS** found 293.1019 $[M + H]^+$, $C_{15}H_{17}O_6$ requires 293.1020.



Compound 17. To a solution of diol **16** (16 mg, 0.055 mmol, 1 equiv) in CH_2Cl_2 (7 mL), under argon, at 0 °C, was added Dess-Martin periodinane (232 mg, 0.55 mmol, 10 equiv). The reaction mixture was stirred at room temperature and monitored by TLC. After disappearance of the starting material, the mixture was poured into (1/1) mixture of saturated aqueous solution of $Na_2S_2O_3$and saturated aqueous solution of $NaHCO_3$ (25 mL) and shaken vigorously for 5 min. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution, saturated aqueous NaCl, dried over Na_2SO_4, dried over Na_2SO_4 and concentrated under vacuum to give the crude product **17** (16 mg) in quantitative yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.92 (1H, d, J = 16.8 Hz, CH_2), 2.99 (1H, d, J = 16.8 Hz, CH_2), 3.17 (3H, s, CH_3), 3.80 (1H, dd, J = 8.0 and 3.8 Hz, CH), 4.54 (1H, m, CH_2), 4.75 (1H, dd, J = 9.0 and 3.8 Hz, CH_2), 7.80-7.85 (2H, m, 2 x CH_{Ar}), 8.14-8.21 (2H, m, 2 x CH_{Ar}); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 36.6 (CH_2), 52.6 (CH), 53.7 (CH_3), 70.4 (CH_2), 90.7 (C), 113.4 (C), 127.4 (CH_{Ar}), 127.7 (CH_{Ar}), 134.2 (C_{Ar}), 135.0 (CH_{Ar}), 135.3 (C_{Ar}), 135.4 (CH_{Ar}), 171.4 (C), 189.3 (C), 191.9 (C); **IR** (ν_{max}): 2958, 2919, 2850, 1730, 1711, 1668, 1641, 1591, 1563, 1437, 1340, 1328, 1306, 1258, 1245, 1175, 1140, 1087, 1015 cm^{-1}; **HRMS** found 306.0971 $[M + NH_4]^+$, $C_{15}H_{16}NO_6$ requires 306.0972.

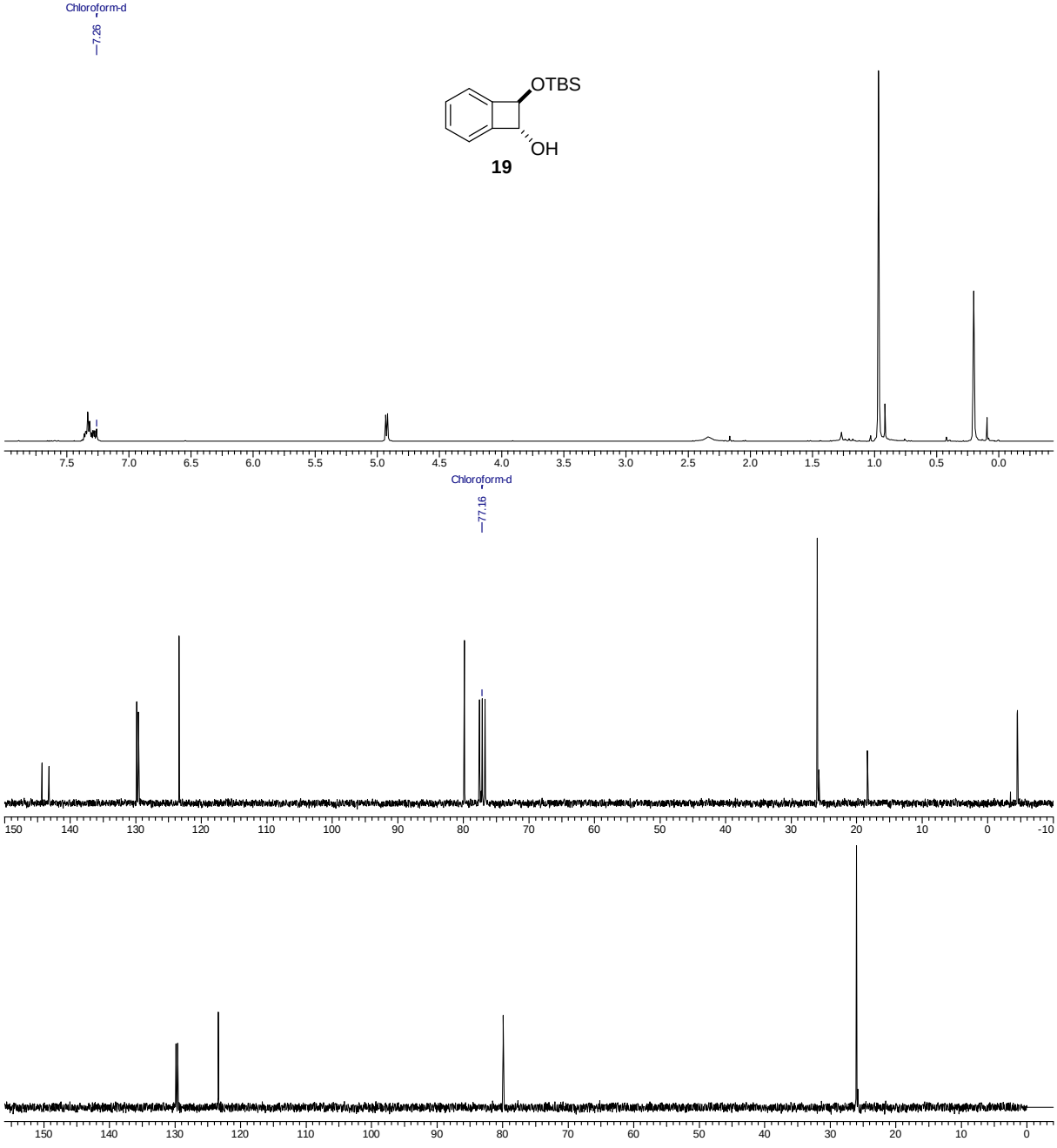




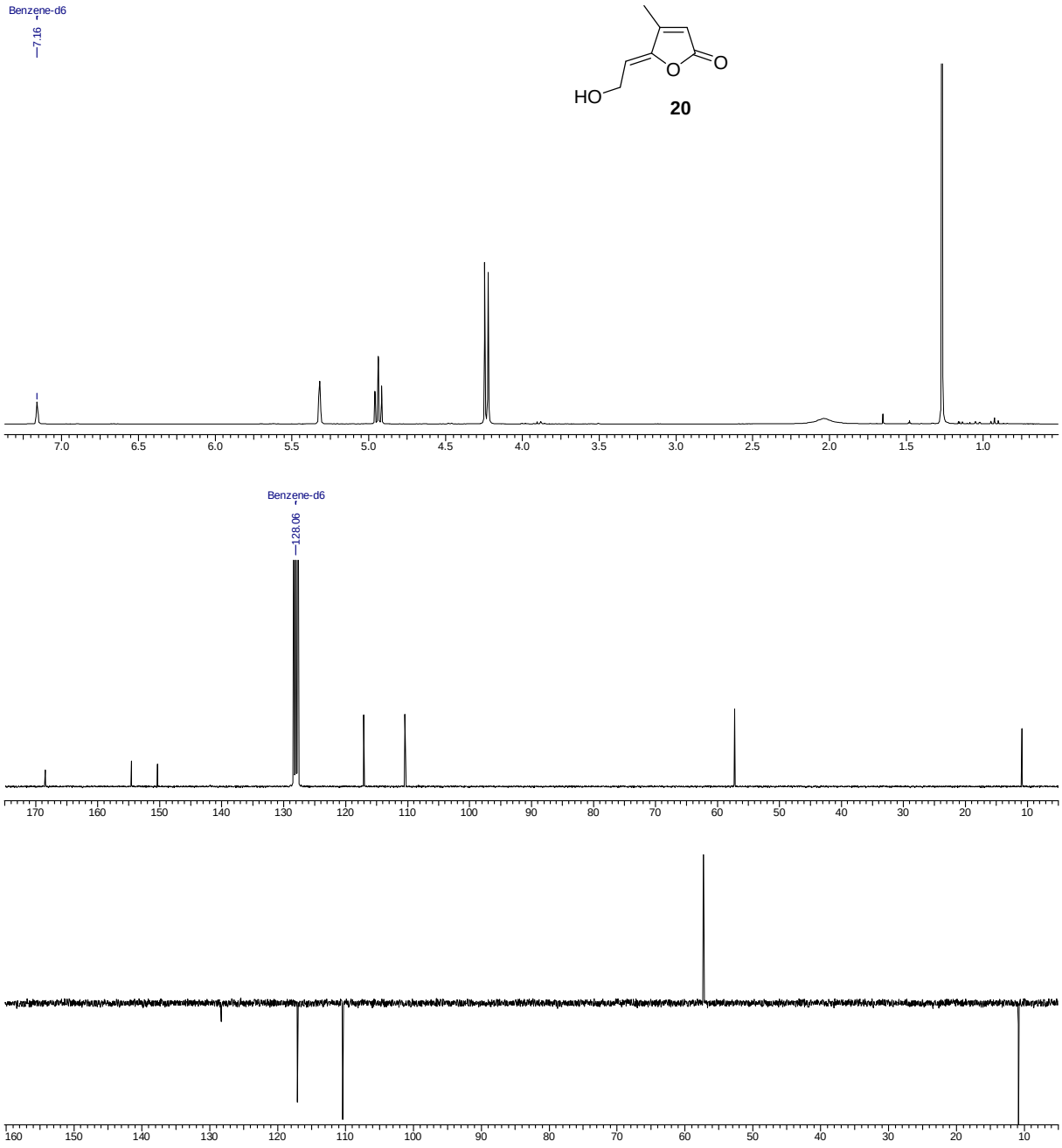


Compound 19.

To a stirred solution of diketone (500 mg, 3.78 mmol) in methanol (50 mL) at 0°C was added sodium borohydride (143 mg, 3.78 mmol) portionwise (10 mg / 10 min). After 1h, the solvent was removed under vacuum at 0°C. The crude product (370 mg) was dissolved in DCM (0.1 M) and cooled to 0°C. Imidazole (157 mg, 2.312 mmol, 0.85 equiv) was added to the mixture and TBSCl (369 mg, 2.45 mmol, 0.9 equiv) dissolved in 20 mL of DCM was added *via* a seringe pump (3.6 mL/h). After one night at 0°C, the reaction was quenched by adding water. The aqueous layer was extracted with DCM and the organic phases were dried over Na_2SO_4 and the solvent removed under high vaccum. The crude product was purified by flash chromatography (7/3 : EP/Et_2O) to give the monoprotected benzocyclobutenediol **19** in variable amount (33% - 76%). **RMN ^{1}H** (300MHz, $CDCl_3$) δ = 0.2 (6H, s, 2 x CH_3), 0.97 (9H, s, 3 x CH_3), 2.33 (1H, OH), 4.92 (1H, s, CH), 4.93 (1H, s, CH), 7.27-7.36 (4H, m, 4 x CH_{Ar}); **RMN ^{13}C** (75MHz, $CDCl_3$) δ = -4.5 (2 x CH_3), 18.4 (C), 26.0 (3 x CH_3), 79.9 (2 x CH), 123.4 (2 x CH_{Ar}), 129.6 (CH_{Ar}), 129.9 (CH_{Ar}), 143.3 (C_{Ar}), 144.3 (C_{Ar})**; MS**: *m/z* 273 $[M+Na]^+$



Compound 20. To a stirred solution of the γ-butenolide[4] (400 mg, 1.57 mmol, 1 equiv) in anhydrous THF (8.2 mL) at 0°C was added a solution of HF-pyridine (121 µL, 70% in pyridine, 4.72 mmol, 3 equiv). The reaction was stirred at room temperature and followed by TLC. After disappearance of the starting material, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The aqueous phase was extracted with ether and the combined organics layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in-vacuo*. The resulting crude product was purified by flash chromatography on silica gel (petroleum ether:ethyl acetate 1:1) to give **20** (157 mg) in 71% yield. **^{1}H RMN** (400 MHz, C_6D_6) δ = 1.27 (3H, d, J = 1.3 Hz, CH_3), 4.23 (2H, d, J = 6.8 Hz, CH_2), 4.94 (1H, CH, td, J = 6.8 and 0.8 Hz, CH), 5.32 (1H, m, CH); **^{13}C RMN** (100 MHz, C_6D_6) δ = 10.9 (CH_3), 57.3 (CH_2), 110.5 (CH), 117.1 (CH), 150.4 (C), 154.6 (C), 168.5 (C); **MS**: *m/z* (ESI+) 163 $(M + Na)^{+\cdot}$.

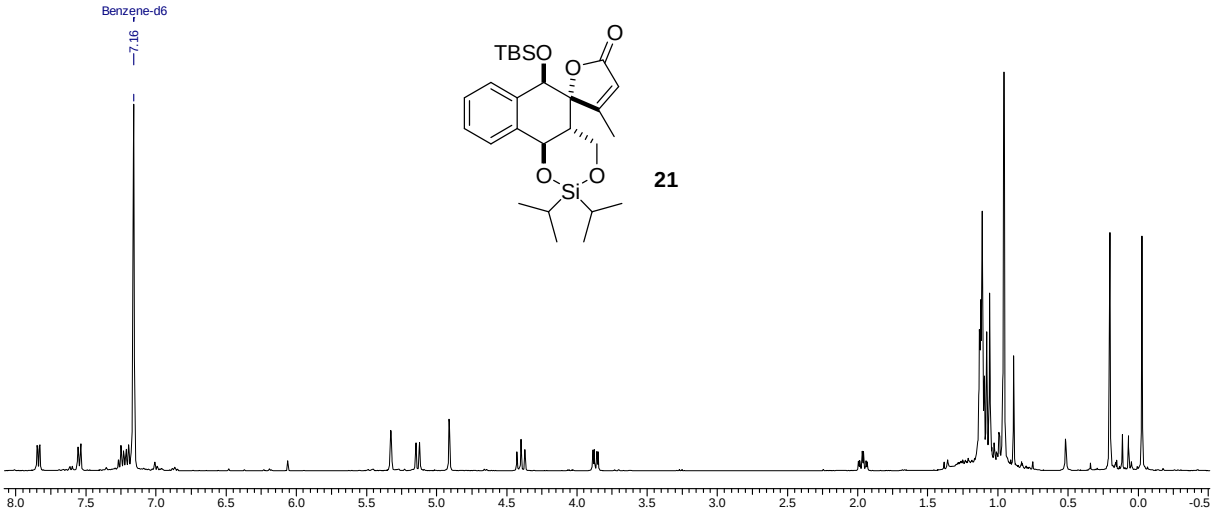


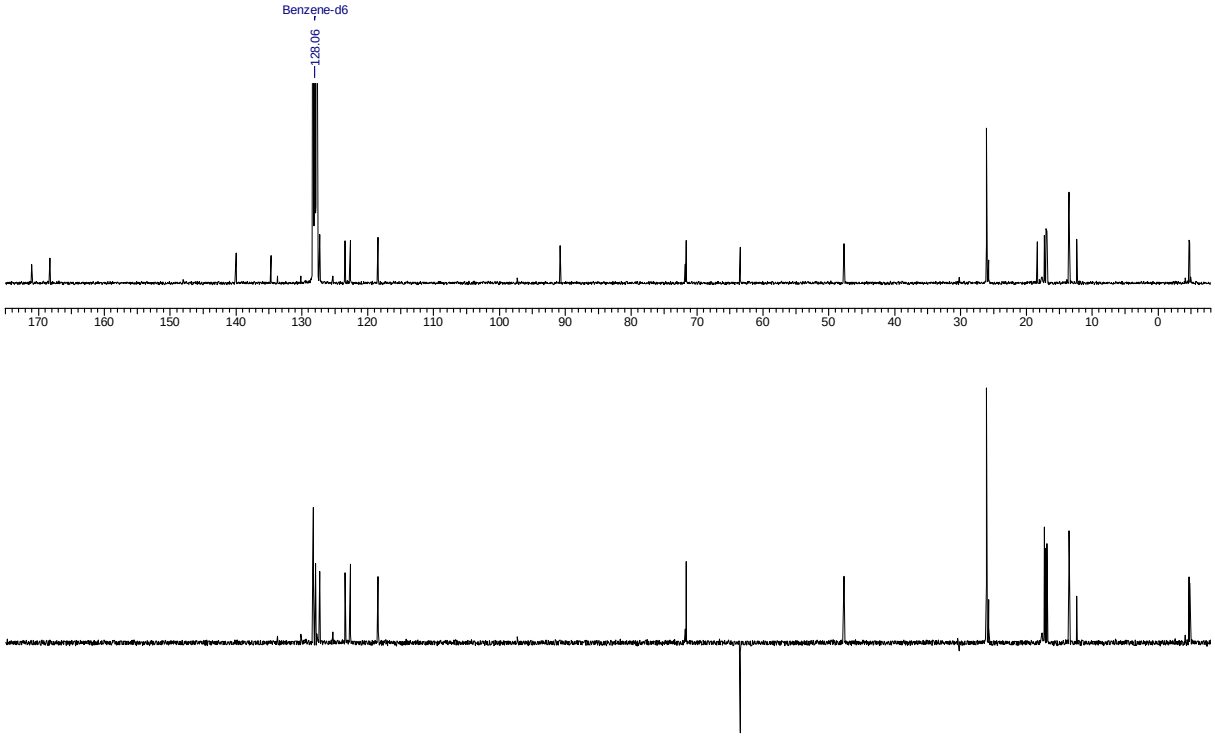
[4] S. Inack-Ngi, R. Rahmani, L. Commeiras, G. Chouraqui, J. Thibonnet, A. Duchêne, M. Abarbri and J.-L. Parrain, *Adv. Synth. Catal.*, 2009, **351**, 779-788.

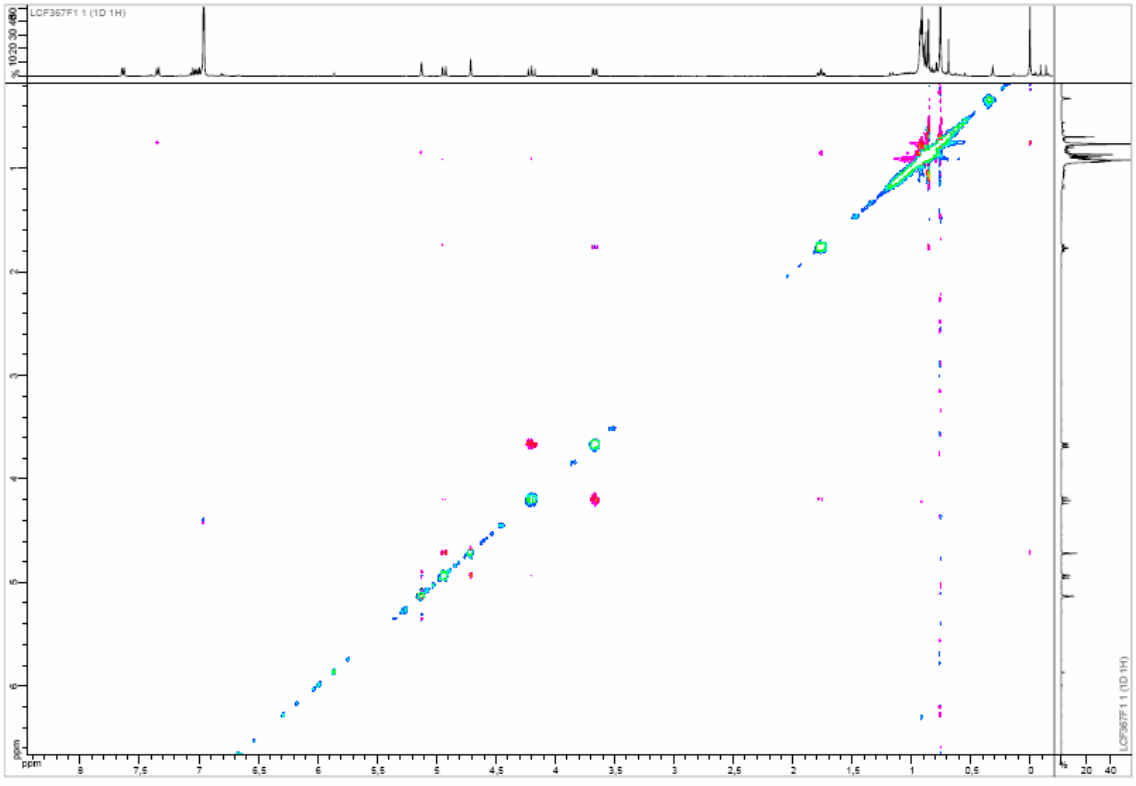
Compound 21. To a stirred solution of CH_2Cl_2 (0.6 mL), imidazole (38 mg, 0.56 mmol, 5 equiv) and iPr$_2$SiCl$_2$ (20 µL, 0.11 mmol, 1 equiv) was added dropwise and at room temperature **19** (28 mg, 0.11 mmol, 1 equiv) in CH_2Cl_2 (0.35 mL). After disappearance of **20** (5 mn), lactone **20** (16 mg, 0.11 mmol, 1 equiv) was added to the mixture. The reaction was stirred for 15 mn, then quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2. The combined organic phase were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether:diethylether 85:15) to give **18** (40 mg) in 71% yield. **^{1}H RMN** (300MHz, $CDCl_3$) δ = 0.19 (6H, s, 2 x CH_3), 0.94 (9H, s, 2 x CH_3), 1.02-1.06 (3H, m, CH_3), 1.09-1.16 (11H, m, 3 x CH_3 and CH), 2.10 (3H, br s, CH_3), 4.69 (2H, d, J = 6.3 Hz, CH_2), 5.00 (1H, br s, CH), 5.11 (1H, br s, CH_3), 5.40 (1H, t, J = 6.3 Hz, CH), 5.93 (1H, br s, CH_3), 7.24-7.34 (4H, m, CH_{Ar}); **MS** *m/z* (ESI+) 525 $[M+Na]^+$.

The ^{1}H RMN revealed the formation of the cycloadduct **18** Thus, no more characterisation was made on this kind of product.

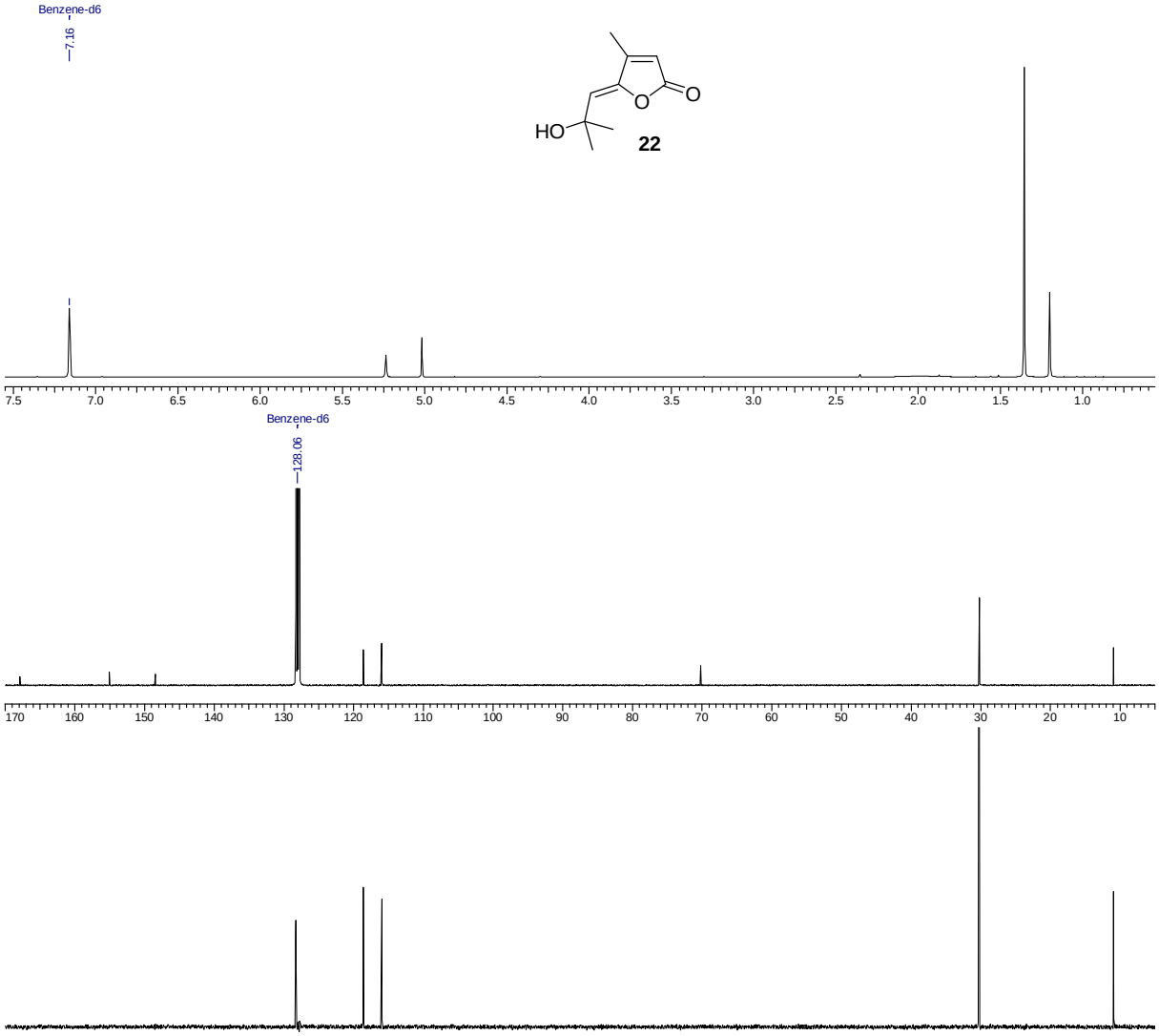
In Schlenk tube, **18** (40 mg) was heated (55 °C) in degazed C_6D_6 (2 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether:diethylether 85:15:) to give **21** (23 mg) in 57% yield. **^{1}H RMN** (400MHz, C_6D_6) δ = -0.03 (3H, s, CH_3), 0.20 (3H, s, CH_3), 0.96 (9H, s, 3 x CH_3), 1.06 (3H, br s, CH_3), 1.08-1.13 (14H, m, 4 x CH_3 and 2 x CH), 1.96 (1H, td, J = 10.5 and 3.5 Hz, CH), 3.87 (1H, dd, J = 11.5 and 3.5 Hz, CH_2), 4.40 (1H, t, J = 11.5 Hz, CH_2), 4.91 (1H, s, CH), 5.13 (1H, d, J = 10.5 Hz, CH), 5.33 (1H, br s, CH), 7.17-7.27 (2H, m, 2 x CH_{Ar}), 7.55 (1H, d, J = 7.5 Hz, CH_{Ar}), 7.84 (1H, d, J = 7.5 Hz, CH_{Ar}); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = -4.8 (CH_3), -4.7 (CH_3), 12.4 (CH_3), 13.5 (2 x CH), 16.9 (CH_3), 17.0 (CH_3), 17.2 (CH_3), 17.3 (CH_3), 18.4 (C), 21.1 (3 x CH_3), 47.7 (CH), 63.4 (CH_2), 71.2 (CH), 71.7 (CH), 77.8 (CH), 90.9 (C), 118.5 (CH), 122.7 (CH), 123.5 (CH), 127.4 (CH), 127.8 (CH), 127.9 (CH), 134.7 (C), 140.1 (C), 168.3 (C), 171.0 (C); **IR** (ν_{max}): 2953, 2928, 2861, 1771, 1463, 1261, 1133, 1071 cm^{-1}; **MS** *m/z* (ESI+) 525 $[M+Na]^+$; **HRMS** found 520.2907 $[M + NH_4^+]$, $C_{27}H_{46}NO_5Si_2$ requires 520.2909.



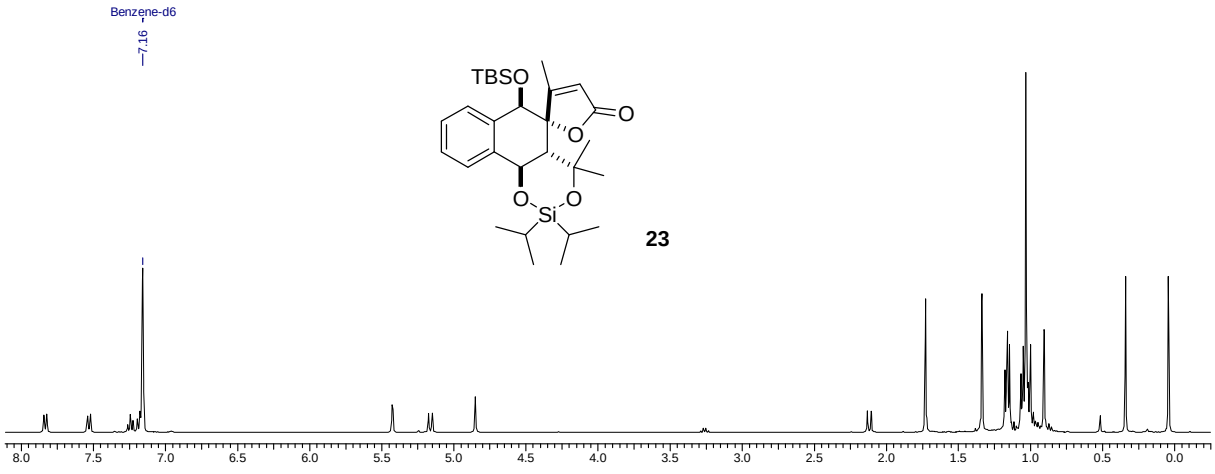


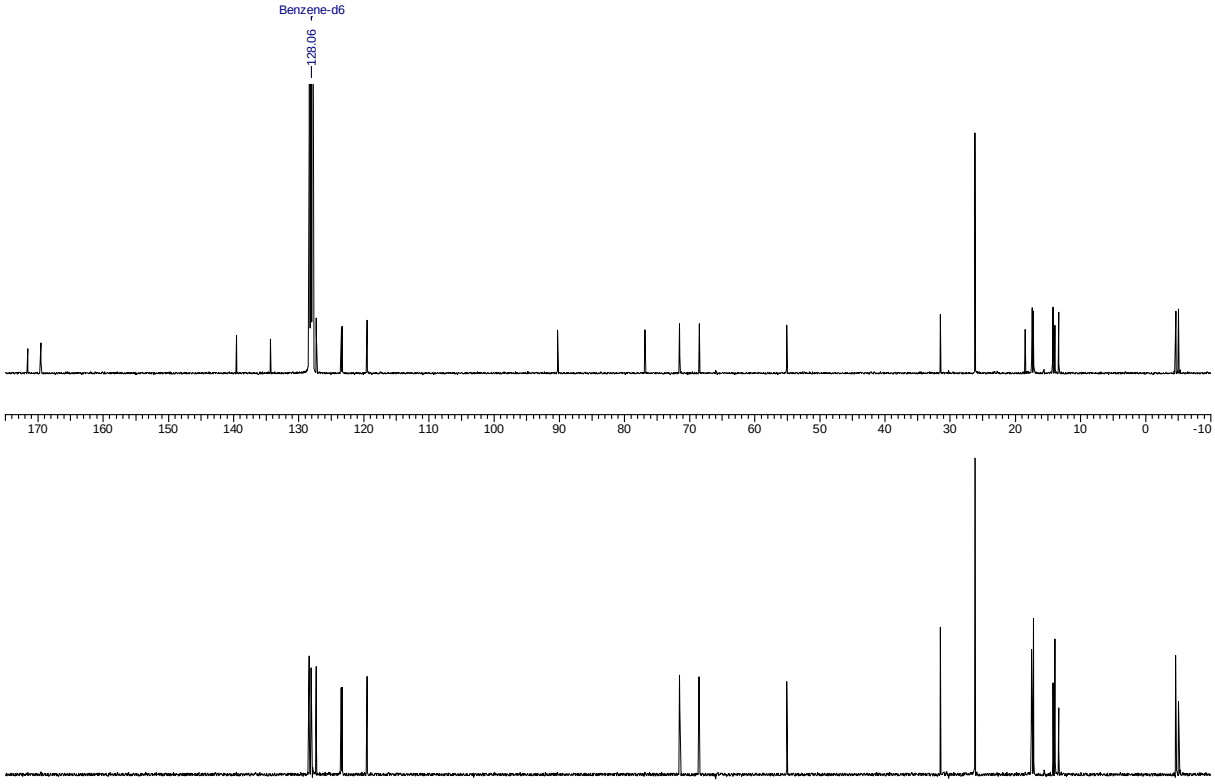


Compound 22. A dry schlenk tube equipped with a Teflon-coated magnetic stirrer was charged with anhydrous K_2CO_3 (1.3 g, 9.40 mmol, 2 equiv) and (Z)-α,β-insaturated-β-iodide acid (1 g, 4.70 mmol, 1 equiv). The mixture vessel was evacuated and backfilled with argon. Then freshly distilled DMF (15 mL) was added and the suspension was stirred for 15 min at room temperature. The mixture was degassed at 0°C for 5 min and backfilled with argon. After reaching room temperature, the alkyne (0.461 g, 4.70 mmol, 1 equiv) and CuI (0.9 g, 4.70 mmol, 1 equiv) were added. The schlenk tube was sealed and then placed in a preheated oil bath at 55°C. Stirring was allowed for 4 hours. Then, the mixture was placed in an ice bath and a saturated aqueous solution of NH_4Cl was added. Stirring at 0°C was allowed for 10 min at which time the reactionnal mixture was diluted with ether and filtered through a short pad of celite. The filtrate was washed with brine and the organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in-vacuo* to yield the expecting γ-butyrolactone **22** (700 mg, 88% yield) which was engaged in the next step without further purifications. **^{1}H RMN** (400 MHz, C_6D_6) δ = 1.20 (3H, br d, J =1.0 Hz, CH_3), 1.36 (6H, s, 2 x CH_3), 5.02 (1H, s, CH), 5.24 (1H, m, CH); **^{13}C RMN** (100 MHz, C_6D_6) δ = 11.0 (CH_3), 30.2 (2 x CH_3), 70.3 (C), 116.0 (CH), 118.7 (CH), 148.5 (C), 155.1 (C), 168.0 (C); **IR** (ν_{max}): 3429, 2976, 2932, 2873, 1745, 1664, 1608, 1362, 1341, 1310, 1220, 1135, 1037 cm^{-1}; **HRMS** found 186.1129 [M + NH_4^+], $C_9H_{16}NO_3$ requires 186.1125.

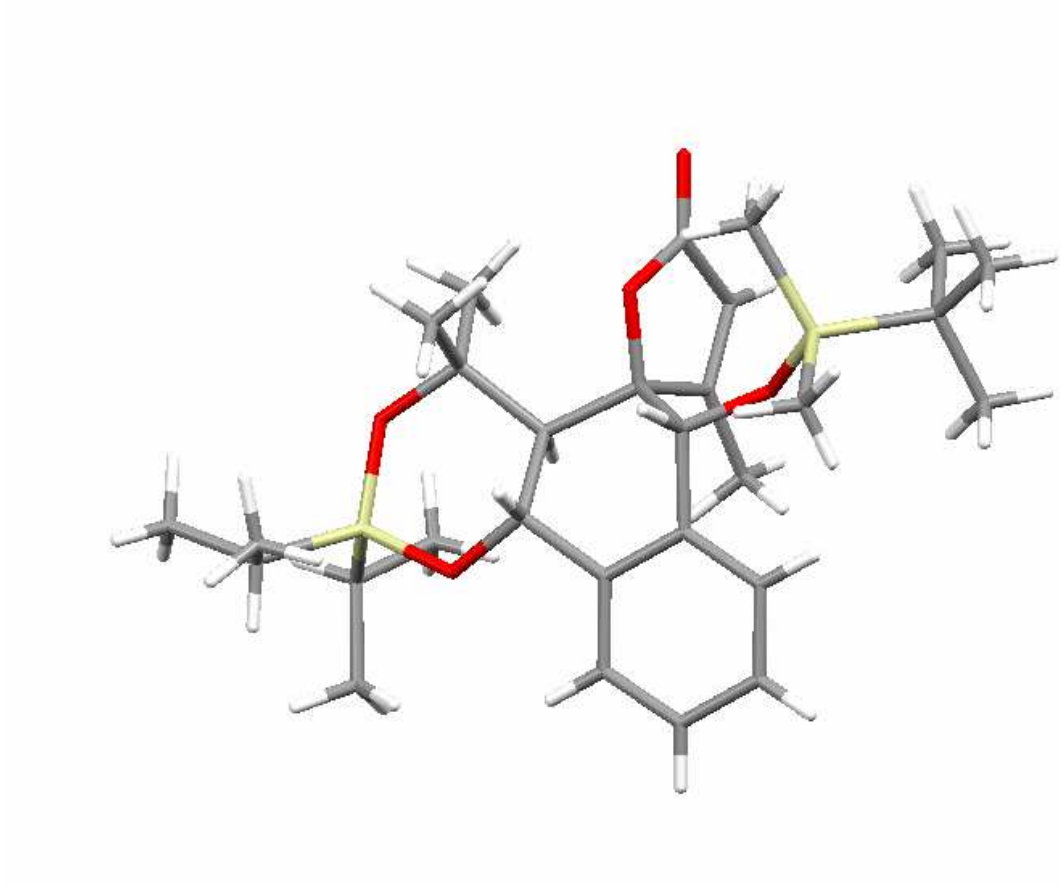


Compound 23. To a stirred solution of **22** (17 mg, 0.1 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL) was added at room temperature imidazole (34 mg, 0.5 mmol, 5 equiv) followed by $i Pr_2SiCl_2$ (17.4 µL, 0.1 mmol, 1 equiv) after complete dissolution of imidazole. After disappearance of **22** (2 hours), **19** (25 mg, 0.1 mmol, 1 equiv) in CH_2Cl_2 (0.3 mL)was added to the mixture. The reaction was stirred for 15 mn, then quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2. The combined organic phase were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether:diethylether 8:2) to give the silicon tethered (23 mg) in 43% yield. In Schlenk tube, the silicon tethered (23 mg) was heated (55 °C) in degazed C_6D_6 (1 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether:diethylether 85:15:) to give **23** (17 mg) in 74% yield. **Mp**= 161 °C; **^{1}H RMN** (400 MHz, C_6D_6) δ = 0.04 (3H, s, CH_3), 0.34 (3H, s, CH_3), 0.91 (3H, br s, CH_3), 1.00-1.07 (7H, m, 2 x CH_3 and CH), 1.03 (9H, s, 3 x CH_3), 1.15-1.18 (7H, m, 2 x CH_3 and CH),), 1.34 (3H, s, CH_3), 1.73 (3H, s, CH_3), 2.12 (1H, d, J = 10.5 Hz, CH), 4.85 (1H, s, CH), 5.16 (1H, d, J = 10.5 Hz, CH), 5.43 (1H, br s, CH), 7.18 (1H, t, J = 7.5 Hz, CH_{Ar}), 7.24 (1H, t, J = 7.5 Hz, CH_{Ar}), 7.53 (1H, d, J = 7.5 Hz, CH_{Ar}), 7.84 (1H, d, J = 7.5 Hz, CH_{Ar}); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = -5.02 (CH_3), -4.6 (CH_3), 13.3 (CH), 13.9 (CH_3), 14.2 (CH), 17.1$_6$ (CH_3), 17.2 (CH_3), 17.4 (CH_3), 17.5 (CH_3), 18.5 (C), 26.2 (4 x CH_3), 31.5 (CH_3), 55.0 (CH), 68.5 (CH), 71.5 (CH), 76.8 (CH), 90.2 (C), 119.5 (CH), 123.3 (CH), 123.4 (CH), 127.3 (CH), 128.1 (CH), 134.3 (C), 139.5 (C), 169.5 (C), 171.6 (C); **IR** (ν_{max}): 2933, 2891, 2863, 1756, 1645, 1465, 1348, 1253, 1201, 1133, 1073, 1028, 1016 cm^{-1}; **MS** *m/z* (ESI+) 553 $[M+Na]^+$; **HRMS** found 531.2957 $[M + H^+]$, $C_{29}H_{47}O_5Si_2$ requires 531.2957.

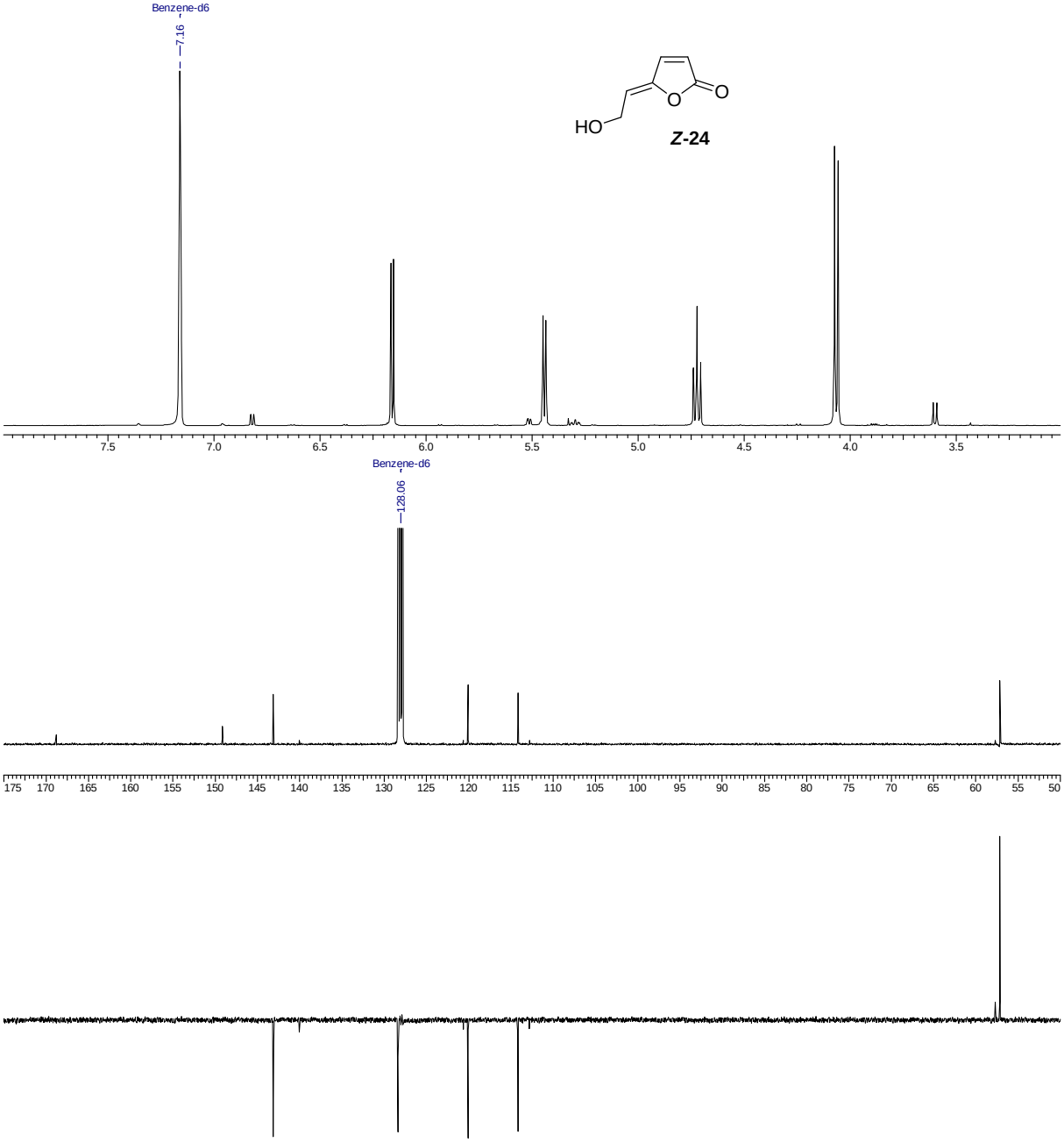




X-Ray analysis



Compound 24. To a stirred solution of the γ-butenolide[27] (500 mg, 2.08 mmol, 1 equiv) in anhydrous THF (11 mL) at 0°C was added a solution of HF-pyridine (76 µL, 70% in pyridine, 4.17 mmol, 2 equiv). The reaction was stirred at room temperature and followed by TLC. After disappearance of the starting material, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The aqueous phase was extracted with ether and the combined organics layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in-vacuo*. The resulting crude product was purified by flash chromatography on silica gel (petroleum ether:ethyl acetate 1:1) to give **24** (200 mg) in 76% yield as a 9:1 mixture of diastereomers. **^{1}H RMN** (400 MHz, C_6D_6) δ = 4.06 (2H, d, *J* = 6.8 Hz, CH_2), 4.72 (1H, t, *J* = 6.8 Hz, CH), 5.44 (1H, d, *J* = 5.3 Hz, CH), 6.16 (1H, d, *J* = 5.3 Hz, CH); **^{13}C RMN** (100 MHz, C_6D_6) δ = 57.2 (CH_2), 114.2 (CH), 120.1 (CH), 143.1 (C), 149.2 (C), 168.8 (C); **IR** (ν_{max}): 3347, 2954, 2922, 2854, 1774, 1747, 1677, 1463, 1118, 1065 cm^{-1}; **HRMS** found 127.0389 $[M + H]^+$, $C_6H_7O_3$ requires 127.0390.



Compound 25. To a stirred solution of CH_2Cl_2 (1.6 mL), imidazole (108 mg, 2.55 mmol, 5 equiv) and iPr$_2$SiCl$_2$ (58 µL, 0.32 mmol, 1 equiv) was added dropwise and at room temperature **19** (80 mg, 0.32 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL). After disappearance of **19** (5 mn), lactone **24** (40 mg, 0.32 mmol, 1 equiv) in CH_2Cl_2 (1.5 mL) was added to the mixture. The reaction was stirred for 15 mn, then quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2. The combined organic phase were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether:diethylether 8:2) to give the silicon tethered (109 mg) in 70% yield. In Schlenk tube, the silicon tethered (109 mg) was heated (55 °C) in degazed C_6D_6 (6 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether:diethylether 85:15:) to give **25** (44 mg) in 40% yield. **^{1}H RMN** (400MHz, C_6D_6) δ = -0.17 (3H, s, CH_3), 0.01 (3H, s, CH_3), 0.87 (9H, s, 3 x CH_3), 1.08-1.12 (14H, m, 4 x CH_3 and 2 x CH), 2.63 (1H, td, J = 10 and 4 Hz, CH), 3.84 (1H, dd, J = 11 and 4 Hz, CH_2), 4.01-4.07 (1H, m, CH_2), 4.43 (1H, s, CH), 5.24 (1H, d, J = 10 Hz, CH), 5.33 (1H, d, J = 5.5 Hz, CH), 5.33 (1H, d, J = 5.5 Hz, CH), 7.10-7.24 (3H, m, 3 x CH_{Ar}), 7.82 (1H, d, J = 7.5 Hz, CH_{Ar}); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = -4.5 (CH_3), -4.2 (CH_3), 12.4 (CH), 13.6 (CH), 16.9 (CH_3), 17.0 (CH_3), 17.2 (CH_3), 17.2$_4$ (CH_3), 18.3 (C), 25.9 (3 x CH_3), 44.2 (CH), 64.1 (CH_2), 72.3 (CH), 73.8 (CH), 89.8 (C), 121.8 (CH), 125.6 (CH), 127.4 (CH), 127.5 (CH), 128.9 (CH), 134.3 (C), 139.1 (C), 156.7 (CH), 171.9 (C); **IR** (ν_{max}): 2953, 2928, 2896, 2860, 1767, 1463, 1254, 1134, 1081, 1027 cm^{-1}; **MS** *m/z* (ESI+) 511 $[M+Na]^+$; **HRMS** found 506.2751 $[M + NH_4^+]$, $C_{26}H_{44}NO_5Si_2$ requires 506.2753.