Total Synthesis of the Diazobenzofluorene Antibiotic (-)-Kinamycin C

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Supporting Information

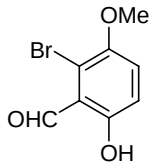
I) Experimental Section

a) General information:

^{1}H NMR spectra were recorded on a 400 MHz spectrometer at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded on a 300 MHz spectrometer (75 MHz) at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to chloroform (^{1}H, δ 7.24; ^{13}C, δ 77.00). Data for ^{1}H NMR are reported as follows: chemical shift, multiplicity (app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration and coupling constants. All ^{13}C NMR spectra were recorded with complete proton decoupling. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. Low and high-resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory using Finnegan MAT-90 or Waters Q-TOF API US spectrometers. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm and are recorded as $[\alpha]_D^{22}$ (concentration in grams/100 mL solvent). Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Chiral and analytical HPLC analysis was performed on a Agilent 1100 series utilizing Chiralcel OD and Agilent Zorba (4.6 x 75 mm) columns, respectively. Flash chromatography was performed using 200-400 mesh silica gel (Scientific Absorbents, Inc.). Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated. Methylene chloride, tetrahydrofuran, toluene, benzene were purified by passing through two packed columns of neutral alumina (Innovative Technology, Inc.). All reagents were used as supplied by Sigma-Aldrich, Fluka, and Strem Chemicals. Trityl hydroperoxide (Ph_3COOH)[S1] was prepared from trityl alcohol according to the literature procedure. 4Å MS was freshly activated at 150 ^oC *in vacuo* for 24 h. Natural kinamycin D was generously provided by Professor Philip Proteau (Oregon State University). Authentic kinamycin C was prepared from natural kinamycin D.[S2] All reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted. The Arthur™ Suite Reaction Planner (Symyx, Inc.) was used for experimental procedure planning.

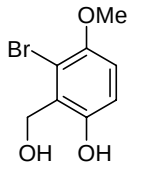
[S1] Bissing, D. E.; Matuszac, C. A.; McEwen, W. E. *J. Am. Chem. Soc.* **1964**, *86*, 3824.
[S2] For experimental details, see page S12.

b) Detailed experimental procedures:



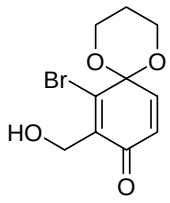
25

Bromobenzaldehyde 25. To hydroquinone **10** (15.5 g, 71.8 mmol), Me_3OBF_4 (11.2 g, 75.6 mmol), Proton Sponge (1,8-bis(dimethylamino)naphthalene) (16.2 g, 75.6 mmol), and activated 4Å MS (1.5 g, 10 *wt*. %) was added 300 mL of anhydrous CH_2Cl_2 and the reaction was stirred at rt under argon for 12 h. The reaction was quenched with water and extracted with CH_2Cl_2. The organic layers were combined, washed 4X with aqueous 1 N HCl and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 4:1) provided 14.0 g (61.0 mmol, 85 %) of bromobenzaldehyde **25** as a yellow solid. m.p. 73-74 ^oC; ^1H NMR (400 MHz, $CDCl_3$) 11.6 (s, 1H), 10.4 (s, 1H), 7.16 (d, 1H, J = 9.6 Hz), 6.92 (d, 1H, J = 9.6 Hz), 3.87 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 198.3, 158.1, 149.4, 122.4, 118.1, 117.8, 116.4, 57.8; IR (thin film) νmax 3741, 2960, 2838, 1649, 1580, 1468, 1270, 1180, 1063 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_8H_8BrO_3$: 230.9658, found: 230.9657.



11

4-Methoxyphenol 11. Bromobenzaldehyde **25** (14.0 g, 61.0 mmol) was dissolved in 100 mL of EtOH and cooled to 0 °C, $NaBH_4$ (2.8 g, 73.0 mmol) was added over 10 min and the reaction was stirred at 0 °C for a further 1 h. The reaction was quenched with acetic acid and extracted with EtOAc (600 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide 13.9 g (60.3 mmol, 99 %) of **11** as a white solid. m.p. 220-221 ^oC; ^1H NMR (400 MHz, $CDCl_3$) 7.80 (s, 1H), 6.78 (d, 1H, J = 8.0 Hz), 6.76 (d, 1H, J = 8.0 Hz), 5.11 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100.0 MHz, CD_3OD) δ 150.8, 148.5, 125.7, 116.2, 112.9, 109.6, 62.9, 56.4; IR (thin film) νmax 3225, 3007, 2940, 2838, 1473, 1436, 1256, 1062, 755 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_8H_{10}BrO_3$: 232.9813, found: 232.9828 .

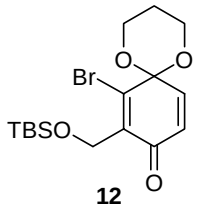


26

Cyclic ketal 26. Compound **11** (8.80 g, 37.8 mmol) was dissolved in 100 mL of MeOH and cooled to 0 °C, $PhI(OAc)_2$ (13.4 g, 41.6 mmol) was added over 10 min and the reaction was stirred at rt for a further 30 min. The reaction was quenched with sat. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product (9.93 g, 37.8 mmol), and 1,3-propanediol (18.0 g, 236.8 mmol) were placed in a round-bottomed flask and dissolved in 180 mL of anhydrous DME. To this solution was added $BF_3.Et_2O$ (5.0 mL, 39.7 mmol) dropwise at 0 °C over 0.5 h, and the reaction was stirred for a further 3 h at rt.[S3] The reaction was quenched by addition of 100 mL of sat. $NaHCO_3$ and extracted with 600 mL of EtOAc. The combined organic layers were washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 8.30 g (30.2 mmol, 80 %) of cyclic ketal **26** as a yellow solid. m.p. 112-113 ^oC; ^1H NMR (400 MHz, $CDCl_3$) 7.71 (d, 1H, J = 10.0 Hz), 6.29 (d, 1H, J = 10.0 Hz), 4.61 (s, 2H), 4.22 (m, 2H), 4.12 (m, 2H), 2.74 (s, 1H), 2.39 (m, 1H), 1.60 (m, 1H); ^{13}C NMR

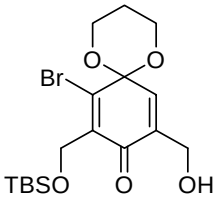
[S3] Pirrung, M. C.; Nunn, D.S. *Tetrahedron Lett*. **1992**, *33*, 6591-6594.

(100.0 MHz, $CDCl_3$) δ 214.3, 183.2, 146.9, 139.1, 138.6, 126.8, 89.7, 61.6, 61.3, 24.6; IR (thin film) νmax 3485, 3055, 2975, 2886, 1666, 1635, 1393, 1307, 1142, 1096, 1001, 928 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{10}H_{12}BrO_4$: 274.9920, found: 274.9932.



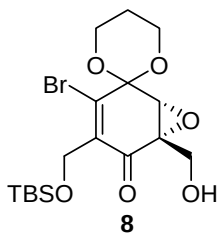
12

Quinone monoketal 12. Quinone monoketal **26** (8.30 g, 30.2 mmol), TBSCl (4.78 g, 31.7 mmol), and imidazole (2.16 g, 31.7 mmol) were dissolved in 50 mL of anhydrous of CH_2Cl_2, and the reaction was stirred at rt for 6 h. The reaction was quenched by addition of pH 7 buffer and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 4:1) provided 10.6 g (27.2 mmol, 90 %) of **12** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.66 (d, 1H, J = 10.4 Hz), 6.28 (d, 1H, J = 10.4 Hz), 4.56 (s, 2H), 4.25 (m, 2H), 4.13 (m, 2H), 2.37 (m, 1H), 1.58 (m, 1H), 0.88 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 181.3, 148.0, 139.1, 137.8, 127.1, 89.9, 61.5, 59.7, 26.1, 24.7, 18.6, -5.0; IR (thin film) νmax 2952, 2883, 1672, 1644, 1466, 1389, 1307, 1253, 1146, 1083, 1001, 835 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{16}H_{26}BrO_4$: 389.0784, found: 389.0744.



9

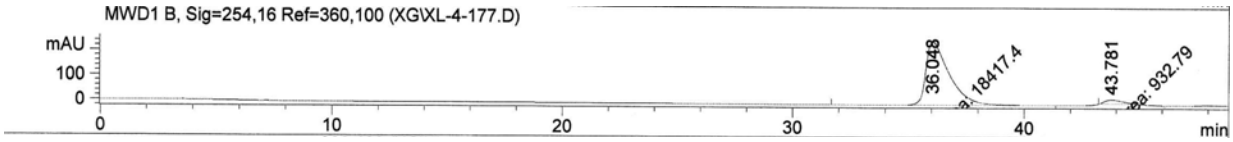
Quinone monoketal 9. Compound **12** (9.56 g, 24.6 mmol), $La(OTf)_3$ (720.0 mg, 1.23 mmol), and $N(CH_2CH_2OH)_3$ (1.84 g, 12.3 mmol) were placed in a 500 mL 2-necked round-bottomed flask and dissolved in 250 mL of anhydrous CH_2Cl_2. The reaction mixture was cooled to –78 °C. Another 50 mL round-bottomed flask containing paraformaldehyde (7.34 g, 246 mmol) was connected to the reaction flask *via* cannula and was heated at 150 °C to transfer the paraformaldehyde to the reaction flask as gaseous formaldehyde. Et_3P (3.6 mL, 24.6 mmol) was added dropwise to the reaction mixture at –78 °C for 30 min and the reaction was stirred at -20 °C. After 6 h, **12** was shown to be fully consumed by TLC analysis. The reaction mixture was filtered through a Celite pad, washed with CH_2Cl_2, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 7.22 g (17.2 mmol, 70 %) of quinone monoketal **9** as a yellow solid. m.p. 97-98 °C; ^1H NMR (400 MHz, $CDCl_3$) 7.58 (s, 1H), 4.48 (s, 2H), 4.36 (s, 2H), 4.18 (m, 2H), 4.00 (m, 2H), 2.25 (m, 1H), 1.48 (m, 1H), 0.79 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 214.3, 181.8, 148.7, 138.9, 136.1, 132.6, 90.0, 61.5, 60.4, 59.7, 26.1, 25.9, 24.7, 18.7, -5.0; IR (thin film) νmax 3424, 2932, 2883, 1651, 1464, 1388, 1252, 1086, 999, 840 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{17}H_{28}BrO_5Si$: 419.0889, found: 419.0849.



8

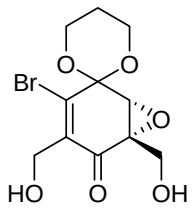
Epoxy ketone 8. Ph_3COOH (6.07 g, 22.0 mmol) and activated 4Å MS (400 mg) were dissolved in 60 mL of anhydrous toluene and 20.0 mL (20.0 mmol) of 1.0 M NaHMDS in THF was added at rt. After 20 min, (1.87 g, 8.0 mmol) *D*-DIPT in 40 mL of toluene was added, the reaction mixture was stirred for 20 min at rt, and then cooled to –78 °C. Compound **9** (1.68 g, 4.0 mmol) in 30 mL toluene was added dropwise and the reaction mixture was stirred at –65 °C for 72 h. The reaction was quenched with water and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*.

Purification on silica gel (hexane : EtOAc = 1:1) provided 1.64 g (3.8 mmol, 94 %) of epoxide **8** as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) 4.56 (d, 1H, *J* = 10.8 Hz), 4.49 (s, 1H), 4.45 (d, 1H, *J* = 10.8 Hz), 4.37 (m, 2H), 4.10 (m, 4H), 2.30 (m, 1H), 1.85 (1H, m), 1.66 (m, 1H), 0.85 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 190.4, 146.2, 137.3, 92.8, 61.6, 61.4, 60.6, 59.5, 58.2, 53.8, 26.1, 24.4, 21.2, 18.6, 14.4, -5.08, -5.10; IR (thin film) νmax 3433, 2929, 2857, 1684, 1622, 1464, 1250, 1143, 1086, 841 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{17}H_{28}BrO_6Si$: 435.0839 , found: 435.0827; $[\alpha]_D^{23}$ = -68^o (c = 0.1, $CHCl_3$). The ee was determined to be 90% by HPLC analysis using a Regis chiral HPLC column (R,R) whelk-O1 (25 cm × 4.0 mm (3 % isopropanol in hexane, retention times: 36.05 min (major enantiomer) and 43.78 min (minor enantiomer)).



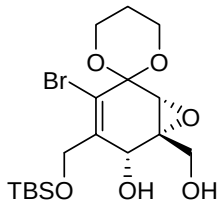
Signal 3: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.048	MM	1.1977	1.84174e4	256.28836	95.1794
2	43.781	MM	0.8890	932.79047	17.48836	4.8206
Totals :				1.93501e4	273.77672	



13

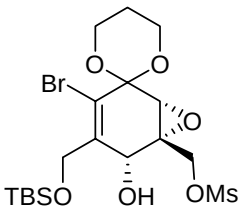
Epoxy alcohol 13. Epoxide **8** (43.5 mg, 0.1 mmol) was dissolved in 0.5 mL of anhydrous CH_3CN. To the reaction mixture was added triethylamine trihydrofluoride (Et_3N-3HF, 80 μL, 0.5 mmol). The reaction was stirred at rt for 12 h, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 1:3) provided 31.5 mg (0.098 mmol, 98 %) of **13** as a white solid. mp 174-175^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) 4.51 (s, 2H), 4.35 (m, 2H), 4.24 (m, 2H), 4.11 (m, 3H), 2.36 (s, 1H), 2.30 (m, 1H), 1.82 (s, 1H), 1.67 (1H, m); ^{13}C NMR (100.0 MHz, CD_3OD) δ 190.5, 146.1, 137.0, 133.1, 92.8, 61.2, 59.0, 58.3, 57.1, 53.7, 24.3; IR (thin film) νmax 3347, 2926, 2857, 1650, 1458, 1240, 1120, 1079 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{11}H_{14}BrO_6$: 320.9975 , found: 320.9989; $[\alpha]_D^{23}$ = -73^o (c = 0.15, CH_3OH). A suitable crystal of **13** for X-ray crystal structure analysis (see page S39) was obtained by slow evaporation from methanol.



27

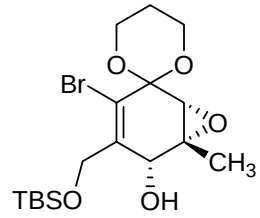
Diol 27. $Me_4NBH(OAc)_3$ (5.08 g, 19.3 mmol) and AcOH (3.0 mL, 49.0 mmol) were dissolved in 15 mL of anhydrous CH_3CN, and epoxide **8** (1.40 g, 3.2 mmol) in 15 mL of anhydrous CH_3CN was added dropwise at 0 ^{o}C. The reaction mixture was stirred at 0 ^{o}C for 24 h. The reaction was quenched with sat. $NaHCO_3$ and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and

concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 1:2) provided 1.27 g (2.9 mmol, 90 %) of diol **27** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) 4.68 (s, 1H), 4.61 (d, 1H, *J* = 10.0 Hz), 4.48 (d, 1H, *J* = 10.0 Hz), 4.27 (m, 3H), 4.12 (m, 2H), 3.87 (d, 1H, *J* = 13.2 Hz), 3.79 (s, 1H), 2.50 (s, 1H), 2.25 (m, 1H), 1.56 (m, 1H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 137.9, 121.8, 93.1, 67.1, 65.8, 62.3, 61.8, 61.3, 61.1, 52.8, 26.0, 24.5, 18.4, -5.2, -5.3; IR (thin film) νmax 3439, 2952, 2884, 1466, 1379, 1251, 1146, 1084, 1009, 838 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{17}H_{30}BrO_6Si$: 437.0995 , found: 437.0990; $[\alpha]_D^{23}$ = -75^o (c = 0.1, $CHCl_3$).



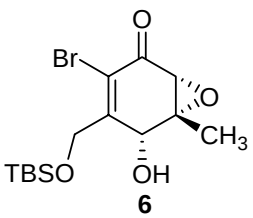
14

Epoxy mesylate 14. Diol **27** (1.27 g, 2.9 mmol) was dissolved in 60 mL of anhydrous CH_2Cl_2. To this mixture was added 2,4,6-collidine (3.8 mL, 29.0 mmol) at rt. The reaction mixture was cooled to 0 ^{o}C and MsCl (240 μL, 3.0 mmol) was added dropwise. The reaction mixture was stirred at 5 ^{o}C for 8 h, then quenched with water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 2:1) provided 1.26 g (2.5 mmol, 85%) of **14** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) 4.75 (s, 1H), 4.72 (d, 1H, *J* = 12.0 Hz), 4.58 (d, 1H, *J* = 14.0 Hz), 4.45 (d, 1H, *J* = 14.0 Hz), 4.35 (d, 1H, *J* = 12.0 Hz), 4.25 (m, 2H), 4.20 (s, 1H), 4.11 (m, 2H), 3.95 (d, 1H, *J* = 4.4 Hz), 3.06 (s, 3H), 2.24 (m, 1H), 1.56 (m, 1H), 0.86 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 137.3, 121.0, 93.0, 68.0, 66.6, 66.3, 61.8, 61.4, 60.0, 54.1, 38.1, 26.0, 24.4, 18.3, -5.2, -5.3; IR (thin film) νmax 3491, 2952, 2860, 1466, 1357, 1252, 1175, 1079, 1009, 837 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{18}H_{32}BrO_8SSi$: 515.0771 , found: 515.0803; $[\alpha]_D^{23}$ = -45^o (c = 0.1, $CHCl_3$).



15

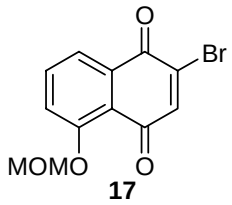
Epoxy alcohol 15. Compound **14 (**1.26 g, 2.5 mmol) was dissolved in 25 mL of anhydrous dichloroethane and 8.8 mL (8.8 mmol) of Super-Hydride (1.0 M in THF) was added at 60 °C. After stirring for 30 min at 60 °C, the reaction mixture was quenched with sat. aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 3:1) provided 980 mg (2.3 mmol, 95%) of **15** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) 4.60 (d, 1H, *J* = 13.6 Hz), 4.53 (s, 1H), 4.46 (d, 1H, *J* = 13.6 Hz), 4.26 (m, 2H), 4.12 (m, 2H), 3.88 (s, 1H), 2.25 (m, 1H), 1.60 (s, 3H), 1.56 (m, 1H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 138.5, 121.3, 93.3, 70.0, 65.9, 61.8, 61.2, 59.9, 56.7, 26.0, 25.8, 24.6, 20.2, 18.4, -5.2, -5.3; IR (thin film) νmax 3465, 2932, 2860, 1465, 1380, 1251, 1147, 1078, 1007, 837 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{17}H_{30}BrO_5Si$: 421.1046 , found: 421.1076; $[\alpha]_D^{23}$ = -70^o (c = 0.1, $CHCl_3$).



6

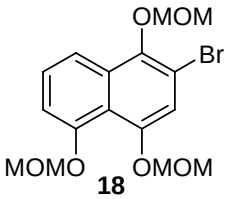
Epoxy ketone 6. Compound **15** (980.0 mg, 2.3 mmol) was dissolved in 45 mL of anhydrous CH_2Cl_2 and K-10 clay (2.3 g) was added in 3 portions at rt over 2 h. After stirring for an additional 2 h at rt, the reaction mixture was filtered through a Celite pad and washed with CH_2Cl_2. The combined

organic layers were washed with sat. $NaHCO_3$, brine, and dried over $MgSO_4$ and $KHCO_3$.[S4] The solution was filtered and concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 5:1) provided 740 mg (2.0 mmol, 90%) of **6** as a colorless oil. ^{1}H NMR 4.69 (d, 1H, J = 16.0 Hz), 4.64 (s, 1H), 4.56 (d, 1H, J = 16.0 Hz), 4.12 (s, 1H), 3.42 (s, 1H), 1.60 (s, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 187.2, 155.5, 116.8, 70.8, 66.8, 60.5, 58.9, 26.0, 25.7, 19.4, 18.3, -5.3, -5.4; IR (thin film) νmax 3492, 2934, 2860, 1694, 1609, 1464, 1382, 1256, 1178, 1099, 938, 837 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{14}H_{24}BrO_4Si$: 363.0627, found: 363.0647; $[\alpha]_D^{23}$ = -31^o (c = 0.08, $CHCl_3$).



17

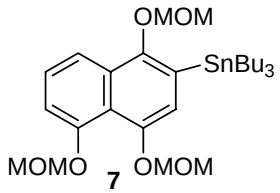
2-Bromo-5-hydroxy-1,4-naphthalenedione 17. Compound **16** [S5] (3.84 g, 15.2 mmol) was dissolved in 50 mL of anhydrous CH_2Cl_2. DIEA (5.3 mL, 30.4 mmol) was added at 0 ^{o}C, followed by MOMCl (1.7 mL, 22.8 mmol). The reaction mixture was stirred at rt for 3 h, then quenched with water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 3:1) provided 3.84 g (12.8 mmol, 85%) of **17** as a yellow solid. mp 145-146 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.89 (d, 1H, J = 8.0 Hz), 7.67 (t, 1H, J = 8.0 Hz), 7.57 (d, 1H, J = 8.0 Hz), 7.41 (s, 1H), 5.37 (s, 2H), 3.54 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 181.5, 178.3, 157.7, 142.5, 142.2, 137.3, 135.0, 133.2, 122.9, 122.1, 95.3, 56.9; IR (thin film) νmax 2965, 2862, 1675, 1655, 1604, 1582, 1461, 1236, 1156, 1087, 994, 881 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{12}H_{10}BrO_4$: 296.9762, found: 296.9786.



18

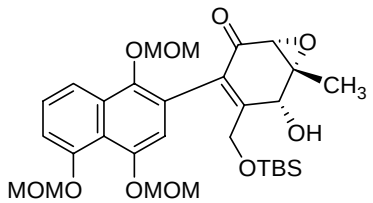
Bromonaphthalene 18. A suspension of **17** (3.84 g, 12.8 mmol) in 100 mL of Et_2O was shaken in a separatory funnel with a freshly prepared solution of sodium dithionate ($Na_2S_2O_4$, 11.1 g, 64.0 mmol) in 50 mL of water. After the mixture was shaken for 10 min, the organic layer was separated, washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide the desired hydroquinone intermediate as a grey solid.[S5] The crude product (3.84 g, 12.8 mmol) was dissolved in 50 mL of anhydrous CH_2Cl_2. DIEA (11.0 mL, 64.0 mmol) was added at 0 ^{o}C followed by MOMCl (3.9 mL, 51.2 mmol). The reaction mixture was stirred at rt for 24 h, then quenched with water, and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 2:1) provided 3.45 g (9.0 mmol, 70 %) of **17** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.85 (d, 1H, J = 8.0 Hz), 7.43 (t, 1H, J = 8.0 Hz), 7.21 (s, 1H), 7.13 (d, 1H, J = 8.0 Hz), 5.27 (s, 2H), 5.24 (s, 2H), 5.19 (s, 2H), 3.72 (s, 3H), 3.59 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 154.2, 150.8, 145.9, 132.7, 129.3, 128.4, 127.8, 117.5, 116.7, 113.5, 100.6, 97.0, 96.5, 58.8, 58.5, 56.8, ; IR (thin film) νmax 2944, 2829, 1580, 1459, 1369, 1253, 1157, 1051, 1001, 958, 810 cm^{-1}; CIHRMS $[M]^+$ calculated for $C_{16}H_{19}BrO_6$: 386.0365, found: 386.0317.

[S4] Shotwell, J. B.; Hu, S.; Medina, E.; Abe, M.; Cole, R.; Crews, C. M.; Wood, J. L. *Tetrahedron Lett.* **2000**, *41*, 9639.
[S5] Jung, M.; Hagenah, J. A. *J. Org. Chem.* **1987**, *52*, 1889



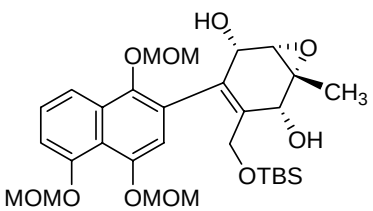
7

Stannane 7. $Pd(PPh_3)_4$ (560.0 mg, 0.48 mmol) was placed in a dry Schlenk flask, and compound **18** (1.86 g, 4.8 mmol) in 15 mL of anhydrous toluene was added to the flask at rt. The reaction mixture was degassed using three "freeze-pump-thaw" cycles. The reaction mixture was heated at 110 ^oC for 10 min, and bis(tributyltin) (3.1 mL, 6.0 mmol) was added. (Note: The order of addition of bis(tributyltin) was found to be critical for success of the stannylation). After stirring for 24 h at 110 ^oC, the reaction mixture was concentrated *in vacuo*. Purification on silica gel (hexane : Et_3N = 9:1, hexane : EtOAc = 5:1) provided 1.9 g (3.3 mmol, 70 %) of **7** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.86 (d, 1H, *J* = 8.0 Hz), 7.37 (t, 1H, *J* = 8.0 Hz), 7.10 (d, 1H, *J* = 8.0 Hz), 7.08 (s, 1H), 5.27 (s, 2H), 5.21 (s, 2H), 5.03 (s, 2H), 3.61 (s, 3H), 3.60 (s, 3H), 3.58 (s, 3H), 1.54 (m, 6H), 1.34 (m, 6H), 1.15 (t, 6H, *J* = 8.0 Hz), 0.90 (t, 9H, *J* = 8.0 Hz); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 154.7, 153.9, 149.7, 131.3, 131.1, 126.2, 121.7, 117.6, 113.2, 100.9, 97.8, 96.7, 57.9, 56.5, 56.2, 30.9, 30.6, 29.5, 29.4, 29.3, 29.1, 27.9, 27.7, 27.4, 13.9, 13.7, 10.7, 10.4, 10.2 ; IR (thin film) νmax 2954, 2923, 1579, 1458, 1357, 1252, 1156, 1047, 975 cm^{-1}; CIHRMS $[M]^+$ calculated for $C_{28}H_{46}O_6Sn$: 598.2316, found: 598.2345



19

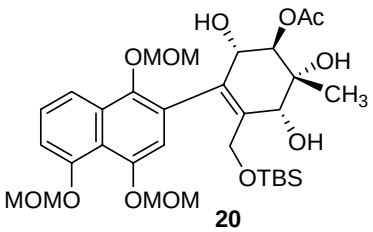
Epoxy ketone 19. $Pd_2(dba)_3$ (120 mg, 0.13 mmol), $AsPh_3$ (120 mg, 0.39 mmol), and CuCl (76 mg, 0.78 mmol) were placed in a dry Schlenk flask and dissolved in 5 mL of anhydrous CH_3CN. The mixture was stirred at rt for 10 min. Epoxyketone **6** (500 mg, 1.4 mmol) in 10 mL of anhydrous CH_3CN was added to the flask. The reaction mixture was degassed using three "freeze-pump-thaw" cycles. A pre-degassed solution of arylstannane **7** (1.0 g, 1.6 mmol) in 5 mL of anhydrous CH_3CN was added at 70 ^oC, followed by DIEA (250 μL, 1.6 mmol). After stirring for 4 h at 70 ^oC, the reaction mixture was concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 2:1) provided 570 mg (0.95 mmol, 70 %) of **19** as a yellow oil (2:1 mixture of rotamers by ^1H NMR at rt). ^1H NMR (400 MHz, $CDCl_3$, major rotamer reported) 7.86 (d, 1H, *J* = 8.0 Hz), 7.40 (t, 1H, *J* = 8.0 Hz), 7.14 (d, 1H, *J* = 8.0 Hz), 6.80 (s, 1H), 5.28 (m, 2H), 5.19 (m, 2H), 4.86 (m, 2H), 4.60 (d, 1H, *J* = 14.8 Hz), 4.42 (s, 1H), 4.23 (d, 1H, *J* = 14.8 Hz), 3.90 (s, 1H), 3.59 (s, 3H), 3.56 (s, 3H), 3.48 (s, 3H), 1.73 (s, 3H), 0.85 (s, 9 H), -0.04 (s, 6H); ^{13}C NMR (100.0 MHz, $CDCl_3$, both rotamers reported) δ 193.8, 154.2, 154.0, 150.0, 146.7, 132.0, 128.6, 126.9, 122.8, 117.7, 117.4, 114.5, 114.0, 113.9, 100.5, 100.3, 97.1, 96.7, 70.4, 69.9, 64.0, 63.5, 60.3, 58.3, 57.7, 56.6, 25.9, 25.6, 19.5, 18.3, -5.4; IR (thin film) νmax 3491, 2928, 2858, 1695, 1607, 1461, 1374, 1258, 1094, 834 cm^{-1}; CIHRMS $[M+Na]^+$ calculated for $C_{30}H_{42}O_{10}NaSi$: 613.2445, found: 613.2453. $[\alpha]_D^{23} = +10^o$ (c = 0.10, $CHCl_3$).



28

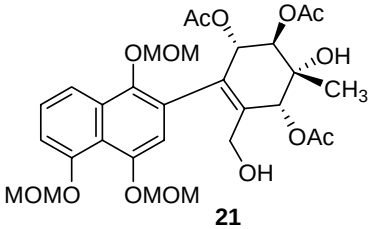
Epoxy alcohol 28. Compound **19** (405 mg, 0.69 mmol) was dissolved in 10.0 mL of anhydrous THF and 1.7 mL (1.7 mmol) Super-Hydride (1.0 M in THF) was slowly added at -78 °C. After stirring for 1 h min at -78 °C, the reaction mixture was quenched with sat. aqueous NH_4Cl and extracted with EtOAc. The combined organic layers were washed with brine, dried over

$MgSO_4$, filtered, and concentrated *in vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 325 mg (0.55 mmol, 80%) of **28** as a yellow oil (single rotamer by ^{1}H NMR at rt). ^{1}H NMR (400 MHz, $CDCl_3$) 7.62 (d, 1H, *J* = 8.0 Hz), 7.41 (t, 1H, *J* = 8.0 Hz), 7.13 (d, 1H, *J* = 8.0 Hz), 6.80 (s, 1H), 5.27 (m, 2H), 5.16 (m, 4H), 4.87 (d, 1H, *J* = 6.4 Hz), 4.67 (d, 1H, *J* = 11.2 Hz), 4.62 (d, 1H, *J* = 5.2 Hz), 4.39 (d, 1H, *J* = 12.4 Hz), 4.12 (d, 1H, *J* = 7.6 Hz), 3.93 (d, 1H, *J* = 12.4 Hz), 3.63 (s, 3H), 3.56 (s, 3H), 3.51 (s, 3H), 3.39 (d, 1H, *J* = 6.4 Hz), 1.62 (s, 3H), 0.79 (s, 9 H), -0.13 (s, 3H), -0.15 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 154.2, 150.8, 147.1, 134.5, 131.8, 129.5, 127.3, 127.2, 120.1, 117.1, 117.0, 113.7, 111.8, 100.2, 100.0, 97.0, 96.8, 96.7, 69.8, 67.6, 62.9, 62.4, 60.3, 58.8, 56.6, 56.5, 26.0, 20.2, 18.3, -5.4, -5.5; IR (thin film) νmax 3431, 2929, 2857, 1597, 1463, 1370, 1254, 1155, 1055, 979, 840 cm^{-1}; CIHRMS $[M+Na]^+$ calculated for $C_{30}H_{44}O_{10}NaSi$: 615.2601, found: 615.2635. $[\alpha]_D^{23}$ = +45^o (c = 0.10, $CHCl_3$).



20

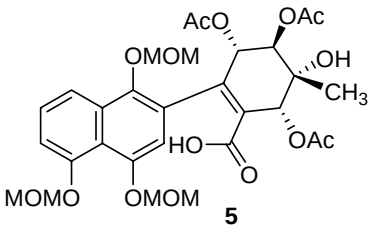
Triol 20. Compound **28** (240 mg, 0.40 mmol) and activated 4Å MS (60 mg) were dissolved in 2.0 mL of anhydrous CH_2Cl_2 and Ti(^{i}PrO)$_4$ (240.0 μL, 0.80 mmol) was added slowly at rt. After stirring for 30 min at rt, a solution of Bu_4NOAc (360 mg, 1.2 mmol) in 2.0 mL of anhydrous CH_2Cl_2 was added to the reaction mixture dropwise at 0 ^{o}C. Stirring was continued for 10 h at rt, at which time the reaction was diluted with EtOAc and quenched with 0.3 N solution of aqueous acetic acid. The mixture was filtered through a Celite pad and washed with EtOAc. The combined organic layer was washed with sat. aqueous $NaHCO_3$, brine, and dried over $MgSO_4$ and $KHCO_3$. The solution was filtered and concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 156 mg (0.24 mmol, 60%) of **20** as a yellow oil (8:1 mixture of rotamers by ^{1}H NMR at rt). ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer reported) 7.64 (d, 1H, *J* = 8.0 Hz), 7.43 (t, 1H, *J* = 8.0 Hz), 7.14 (d, 1H, *J* = 8.0 Hz), 6.69 (s, 1H), 5.41 (d, 1H, *J* = 8.4 Hz), 5.29 (m, 2H), 5.20 (m, 2H), 5.12 (d, 1H, *J* = 6.8 Hz), 4.96 (d, 1H, *J* = 6.8 Hz), 4.30 (d, 1H, *J* = 6.4 Hz), 4.25 (s, 1H), 3.96 (d, 1H, *J* = 12.0 Hz), 3.78 (d, 1H, *J* = 12.0 Hz), 3.70 (s, 3H), 3.59 (s, 3H), 3.57 (s, 3H), 3.20 (s, 1H), 2.19 (s, 3H), 1.29 (s, 3H), 0.85 (s, 9 H), -0.04 (s, 3H), -0.07 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$, both rotamers reported) δ 154.2, 150.8, 147.1, 134.5, 131.8, 129.5, 127.3, 127.2, 120.1, 117.1, 117.0, 113.7, 111.8, 100.2, 100.0, 97.0, 96.8, 96.7, 69.8, 67.6, 62.9, 62.4, 60.3, 58.8, 56.6, 56.5, 26.0, 20.2, 18.3, -5.4, -5.5; IR (thin film) νmax 3431, 2929, 2857, 1597, 1463, 1370, 1254, 1155, 1055, 979, 840 cm^{-1}; CIHRMS $[M+Na]^+$ calculated for $C_{32}H_{48}O_{12}NaSi$: 675.2813, found: 675.2846. $[\alpha]_D^{23}$ = -18^o (c = 0.10, $CHCl_3$).



21

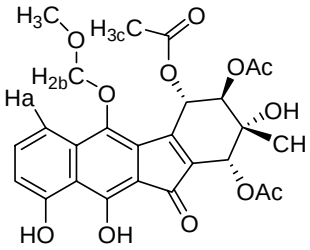
Alcohol 21. Compound **20** (120 mg, 0.18 mmol) was dissolved in 1.0 mL of anhydrous pyridine and acetic anhydride (0.5 mL) was added at rt. After stirring for 2 h at rt, the reaction mixture was quenched with sat. aqueous $NaHCO_3$ and extracted with EtOAc. The combined organic layers were washed with sat. $NaHCO_3$, brine, and dried over $MgSO_4$. The solution was filtered and concentrated in *vacuo* to provide 140 mg of the intermediate triacetate silyl ether as a yellow oil. The crude compound (140 mg, 0.18 mmol) was dissolved in 1.0 mL of anhydrous CH_3CN and Et_3N-3HF (90 μL, 0.57

mmol) was added at rt. After stirring for 12 h at rt, the reaction mixture was concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 1:2) provided 78 mg (0.12 mmol, 67%) of **21** as a yellow oil (1.3:1 mixture of rotamers by ^{1}H NMR at rt). ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer reported) 7.89 (d, 1H, *J* = 8.0 Hz), 7.44 (t, 1H, *J* = 8.0 Hz), 7.15 (d, 1H, *J* = 8.0 Hz), 6.71 (s, 1H), 6.10 (d, 1H, *J* = 8.0 Hz), 5.69 (s, 1H), 5.51 (d, 1H, *J* = 8.0 Hz), 5.29 (m, 2H), 5.20 (m, 2H), 4.98 (m, 2H), 4.14 (m, 1H), 3.90 (s, 1H), 3.60 (s, 3H), 3.58 (s, 3H), 3.54 (s, 3H), 2.95 (s, 1H), 2.43 (s, 1H), 2.22 (s, 3H), 2.13 (s, 3H), 1.64 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$, both rotamers reported) δ 171.6, 171.0, 169.8, 154.0, 136.1, 135.4, 132.1, 131.7, 130.0, 127.1, 123.8, 117.7, 116.2, 113.9, 113.2, 112.2, 111.5, 101.0, 100.0, 97.2, 97.0, 96.7, 75.0, 72.8, 72.5, 72.1, 61.1, 60.5, 58.1, 56.7, 56.6, 25.9, 25.7, 21.5, 21.2, 20.6; IR (thin film) νmax 3473, 2929, 2857, 1738, 1650, 1597, 1459, 1372, 1231, 1156, 1044 cm^{-1}; CIHRMS $[M+H]^+$ calculated for $C_{30}H_{39}O_{14}$: 623.2340, found: 623.2312. $[\alpha]_D^{23}$ = -5^o (c = 0.20, $CHCl_3$).



5

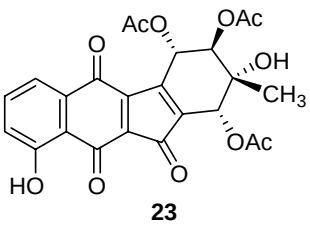
Acid 5. Compound **21** (72 mg, 0.11 mmol) and *N*-methylmorpholine *N*-oxide (20 mg, 0.18 mmol) were dissolved in 1.0 mL of anhydrous CH_2Cl_2 and tetrapropylammonium perruthenate (8 mg, 0.02 mmol) was added at 0 ^{o}C. After stirring for 20 min at rt, the reaction mixture was filtered through a short silica pad to provided 72 mg of the desired aldehyde as a yellow oil. The crude aldehyde was directly used for the next step. Aldehyde (72 mg, 0.11 mmol) was dissolved in 1.0 mL of *tert*-butyl alcohol and 0.2 mL of 2-methyl-2-butene. A solution of $NaClO_2$ (96 mg, 1.1 mmol) and NaH_2PO_4 (96 mg, 1.1 mmol) in 0.5 mL of water was slowly added to the reaction mixture at 0 ^{o}C. After stirring at rt for 12 h, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic layers were washed with brine and dried over $MgSO_4$. The solution was filtered and concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 64 mg (0.09 mmol, 88%) of carboxylic acid **5** as a yellow oil (8:1 mixture of rotamers by ^{1}H NMR at rt). ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer reported) 7.64 (m, 2H), 7.32 (d, 1H, *J* = 8.0 Hz), 6.31 (s, 1H), 6.09 (s, 1H), 5.98 (d, 1H, *J* = 7.2 Hz), 5.53 (d, 1H, *J* = 7.2 Hz), 5.27 (m, 4H), 4.59 (d, 1H, *J* = 8.0 Hz), 4.49 (d, 1H, *J* = 8.0 Hz), 3.51 (s, 6H), 3.20 (s, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$, both rotamers reported) δ 181.6, 170.7, 170.0, 167.5, 159.5, 157.3, 142.5, 140.1, 137.1, 134.9, 132.2, 130.7, 127.6, 120.4, 119.3, 117.9, 95.3, 95.1, 92.5, 73.6, 71.5, 69.8, 67.5, 56.6, 56.4, 20.8, 20.5, 20.0; IR (thin film) νmax 3466, 2925, 2854, 1748, 1661, 1594, 1460, 1372, 1229, 1156, 1032, 980 cm^{-1}; CIHRMS $[M+Na]^+$ calculated for $C_{30}H_{36}O_{14}Na$: 659.1952, found: 659.1937. $[\alpha]_D^{23}$ = +44^o (c = 0.10, $CHCl_3$).



22

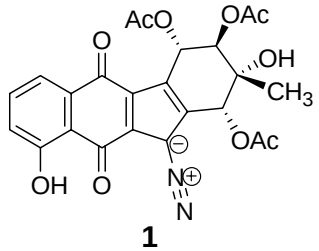
MOM-protected hydroquinone 22. Compound **5** (40 mg, 0.06 mmol) and activated 4Å MS (10 mg) were dissolved in 1.0 mL of anhydrous DCE and TFAA (18.0 μL, 0.12 mmol) was slowly added at 0 ^{o}C. After stirring for 1 h at rt, the reaction mixture was quenched with pH 7 buffer and extracted with EtOAc. The combined organic layers were washed with sat. pH 7 buffer, brine, and dried over $MgSO_4$. The solution was filtered and concentrated in *vacuo*. Purification on silica

gel ($CHCl_3$: MeOH = 10:1) provided 30 mg (0.057 mmol, 90%) of MOM-protected hydroquinone **22** as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) 11.9 (s, 1H), 7.63 (t, 1H, *J* = 8.0 Hz), 7.46 (d, 1H, *J* = 8.0 Hz), 7.08 (d, 1H, *J* = 8.0 Hz), 6.41 (s, 1H), 6.10 (s, 1H), 6.01 (d, 1H, *J* = 7.2 Hz), 5.53 (d, 1H, *J* = 7.2 Hz), 4.61 (d, 1H, *J* = 8.0 Hz), 4.47 (d, 1H, *J* = 8.0 Hz), 3.22 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 2.11 (s, 3H), 1.32 (s, 3H); NOED (400 MHz, $CDCl_3$) irrd. δ4.61 (H_b), 3.0 % enhancement at H_a, 2.0 % enhancement at $–CH_{3c}$; irrd. δ7.46 (H_a), 3.0 % enhancement at H_b. For nOe spectra, see page S36. ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 187.3, 170.7, 170.0, 161.9, 142.0, 141.6, 137.9, 137.0, 128.5, 128.3, 119.7, 118.5, 95.2, 95.0, 92.5, 92.0, 73.5, 71.5, 69.7, 67.4, 66.0, 56.6, 20.8, 20.6, 20.1; IR (thin film) νmax 3473, 2925, 2855, 1747, 1650, 1613, 1457, 1371, 1226, 1171, 1031, 979 cm^{-1}; CIHRMS $[M+Na]^+$ calculated for $C_{26}H_{26}O_{12}Na$: 553.1322, found: 553.1340. $[\alpha]_D^{23}$ = +37^o (c = 0.10, $CHCl_3$).



23

Quinone 23. Compound **22** (30 mg, 0.057 mmol) and CBr_4 (4.0 mg, 0.012 mmol) were dissolved in 0.5 mL of anhydrous isopropyl alcohol. The reaction mixture was gently heated to reflux at 84 ^{o}C. After stirring for 1 h at 84 ^{o}C, the reaction mixture was cooled to rt and concentrated *in vacuo*. The crude MOM-deprotected hydroquinone product was dissolved in 1.0 mL of anhydrous EtOAc, and Pd/C (15.0 mg, 50 *wt* %) was added to the solution. The reaction mixture was exposed to air and stirred at rt for 30 min before being filtered and concentrated in *vacuo*. Purification on silica gel ($CHCl_3$: MeOH = 10:1) provided 18 mg (0.039 mmol, 70%) of ketoquinone **23** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) 11.50 (s, 1H), 7.71 (d, 1H, *J* = 8.0 Hz), 7.66 (t, 1H, *J* = 8.0 Hz), 7.32 (d, 1H, *J* = 8.0 Hz), 6.46 (d, 1H, *J* = 6.0 Hz), 6.09 (s, 1H), 5.47 (d, 1H, *J* = 6.0 Hz), 2.16 (s, 3H), 2.14 (s, 3H), 1.93 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 180.4, 179.7, 178.5, 171.0, 170.4, 169.1, 162.5, 156.2, 154.9, 146.3, 142.6, 138.4, 132.0, 128.2, 125.3, 120.4, 75.2, 73.2, 71.0, 69.9, 21.2, 20.9, 20.8, 20.7; IR (thin film) νmax 3472, 2933, 1750, 1652, 1621, 1568, 1456, 1372, 1226, 1164, 1036 cm^{-1}; HRTOFMS $[M+H]^+$ calculated for $C_{24}H_{21}O_{11}$: 485.1084, found: 485.1070; $[\alpha]_D^{23}$ = -80^o (c = 0.1, $CHCl_3$).



1

Synthetic Kinamycin C 1. A freshly prepared solution of scandium trifluoromethanesulfonate in anhydrous CH_3CN (0.01 M, 6 μL, 0.01 equiv.) was transferred to a 5 mL round-bottom flask. The solvent was evaporated by argon, and the flask was further evacuated *in vacuo* for 15 min. Keto quinone **23** (3.0 mg, 0.0062 mmol) in 0.1 mL of anhydrous CH_2Cl_2 was added to the reaction flask. The reaction mixture was cooled to -78 ^{o}C, and 1,2-Bis(*tert*-butyldimethylsilyl)hydrazine[S6](2.0 μL, 0.0063 mmol, 1.05 equiv.) in 0.1 mL of anhydrous CH_2Cl_2 was slowly added. The reaction was allowed to slowly warm to rt, and carefully monitored by TLC, at which time the quinone **23** was consumed. One portion of 0.5 mL of cold anhydrous hexane was added, and the mixture was quickly filtered through a pipette column with cotton. The solution was

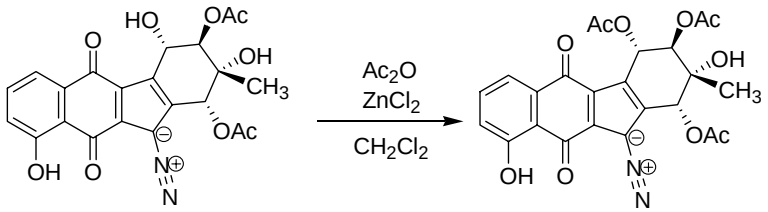
[S6] For the preparation of 1,2-bis(*tert*-butyldimethylsilyl)hydrazine, see: Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 5436.

collected and concentrated *in vacuo*. The corresponding *N*-*tert*-butyldimethylsilylhydrazone was directly used for the next step without further purification. The crude hydrazone and activated 4Å MS (3.0 mg) were dissolved in 0.1 mL of anhydrous CH_2Cl_2, and the mixture was cooled to -78 ^oC. To this solution was added 2-chloropyridine (4.0 mL, 0.038 mmol, 6.0 equiv.), followed by freshly prepared 0.1 M solution of iodobenzenedifluoride ($PhIF_2$)[S7] in CH_2Cl_2 (180 mL, 0.018 mmol, 3.0 equiv.) dropwise. The reaction mixture was stirred at -78 ^oC for 4 h, at which point the cooling bath was allowed to warmed gradually to rt over 3 h. After stirring for 2 h at rt, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, and dried over $MgSO_4$. The solution was filtered and concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 1.1 mg (0.0022 mmol, 35 %) of kinamycin C **1** as an orange solid. mp 149-150 ^oC. ^1H NMR (400 MHz, $CDCl_3$) 12.09 (s, 1H), 7.63 (d, 1H, *J* = 8.4 Hz), 7.52 (t, 1H, *J* = 8.4 Hz), 7.15 (d, 1H, *J* = 8.4 Hz), 6.19 (d, 1H, *J* = 7.2 Hz), 5.57 (d, 1H, *J* = 7.2 Hz), 5.46 (s, 1H), 2.66 (bs, 1H), 2.18 (s, 3H), 2.16 (s, 3H), 2.08 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 184.2, 178.2, 172.1, 171.1, 170.3, 162.2, 136.4, 134.5, 132.7, 130.1, 129.2, 126.8, 123.9, 120.1, 115.7, 78.0, 75.6, 73.6, 71.1, 68.2, 21.2, 21.0, 20.8, 18.7; IR (thin film) νmax 3461, 2977, 2936, 2150, 1742, 1659, 1621, 1458, 1370, 1232, 1158, 1075, 1039 cm^{-1}; HRTOFMS $[M+Na]^+$ calculated for $C_{24}H_{20}N_2NaO_{10}$: 519.1016, found: 519.1055; $[\alpha]_D^{23}$ = -26^o (c = 0.1, $CHCl_3$).

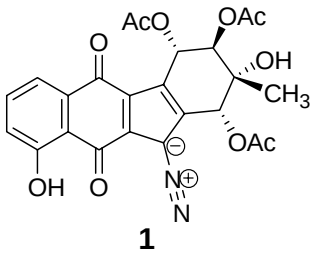
[S7] For the preparation of $PhIF_2$ in CH_2Cl_2, see: Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 12222.

c) Detailed procedure for the preparation of kinamycin C from natural kinamycin D:

Kinamycin C (1) was obtained by acylation of natural kinamycin D with acetic anhydride using the procedure [S8] reported for acylation of kinamycin D using *S*-2-methylbutyric anhydride.



kinamycin D **kinamycin C**



1

Natural Kinamycin C 1. In a 5 mL round bottom flask was placed anhydrous $ZnCl_2$ (30.0 mg, 0.22 mmol) and acetic acid (24.0 mL, 0.15 mmol) in 0.5 mL of anhydrous CH_2Cl_2 was added at rt. After stirring for 1 h at rt, the reaction mixture was cooled to -78 ^oC, and natural kinamycin D (6.0 mg, 0.013 mmol) in 0.2 mL of anhydrous CH_2Cl_2 was slowly added. The reaction was slowly warmed to 0 ^oC, and stirred for an additional 1 h. The reaction was diluted with anhydrous CH_2Cl_2, washed with water, dried over $MgSO_4$, filtered and concentrated in *vacuo*. Purification on silica gel (hexane : EtOAc = 1:1) provided 3.0 mg (0.06 mmol, 50%) of kinamycin C as an orange solid. mp 151-153 ^oC. ^1H NMR (400 MHz, $CDCl_3$) 12.09 (s, 1H), 7.63 (d, 1H, J = 8.4 Hz), 7.52 (t, 1H, J = 8.4 Hz), 7.15 (d, 1H, J = 8.4 Hz), 6.19 (d, 1H, J = 7.2 Hz), 5.57 (d, 1H, J = 7.2 Hz), 5.46 (s, 1H), 2.66 (bs, 1H), 2.18 (s, 3H), 2.16 (s, 3H), 2.08 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 184.2, 178.2, 172.1, 171.1, 170.3, 162.2, 136.4, 134.5, 132.7, 130.1, 129.2, 126.8, 123.9, 120.1, 115.7, 78.0, 75.6, 73.6, 71.1, 68.2, 21.2, 21.0, 20.8, 18.7; IR (thin film) νmax 3461, 2977, 2936, 2150, 1742, 1659, 1621, 1458, 1370, 1232, 1158, 1075, 1039 cm^{-1}; HRTOFMS $[M+Na]^+$ calculated for $C_{24}H_{20}N_2NaO_{10}$: 519.1016, found: 519.1022; $[\alpha]_D^{23}$ = -24^o (c = 0.1, $CDCl_3$).

Synthetic and natural kinamycin C gave the same R_f value in the following three solvent systems: R_f = 0.50 ($CHCl_3$: MeOH = 10:1), R_f = 0.23 (hexane : EtOAc = 1:1), R_f = 0.16 ($CHCl_3$: EtOAc = 5:1).

[S8] Gould, S. J.; Tamayo, N.; Melville, C. R.; Cone, M. C. *J. Am. Chem. Soc*. **1994**,*116*, 2207

II) Comparison of natural and synthetic kinamycin C

NMR data (in $CDCl_3$) comparison of natural and synthetic kinamycin C

^{1}H NMR (Hz)		^{13}C NMR (Hz)	
Natural (400 MHz)	Synthetic (400 MHz)	Natural (100 MHz)	Synthetic (100.0 MHz)
12.09 (s, 1H)	12.09 (s, 1H)	184.0	184.2
7.63 (d, 1H, *J* = 8.4 Hz)	7.63 (d, 1H, *J* = 8.4 Hz)	178.0	178.2
7.52 (t, 1H, *J* = 8.4 Hz)	7.52 (t, 1H, *J* = 8.4 Hz)	172.0	172.1
7.15 (d, 1H, *J* = 8.4 Hz)	7.15 (d, 1H, *J* = 8.4 Hz)	171.1	171.1
6.19 (d, 1H, *J* = 7.2 Hz)	6.19 (d, 1H, *J* = 7.2 Hz)	170.2	170.3
5.57 (d, 1H, *J* = 7.2 Hz)	5.57 (d, 1H, *J* = 7.2 Hz)	162.0	162.2
5.46 (s, 1H)	5.46 (s, 1H)	136.2	136.4
2.66 (bs, 1H)	2.66 (bs, 1H)	134.2	134.5
2.18 (s, 3H)	2.18 (s, 3H)	132.5	132.7
2.16 (s, 3H)	2.16 (s, 3H)	130.1	130.1
2.08 (s, 3H)	2.08 (s, 3H)	128.9	129.2
1.24 (s, 3H)	1.24 (s, 3H)	126.6	126.8
		123.7	123.9
		119.9	120.1
		115.5	115.7
		78.5[S9]	78.0
		75.4	75.6
		73.5	73.6
		70.9	71.1
		68.1	68.2
		21.1	21.2
		21.0	21.0
		20.9	20.8
		18.6	18.7

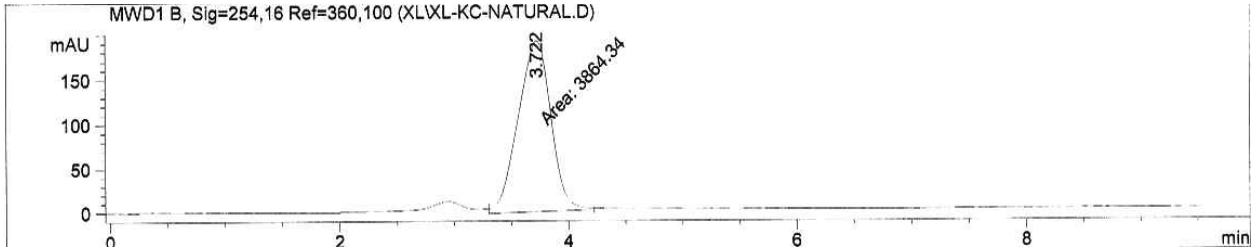
$[\alpha]_D$ for Natural and Synthetic kinamycin C:

	Natural kinamycin C	Synthetic kinamycin C
$[\alpha]_D$	-24^o (*c*=0.1, $CHCl_3$)	-26^o (*c*=0.1, $CHCl_3$)

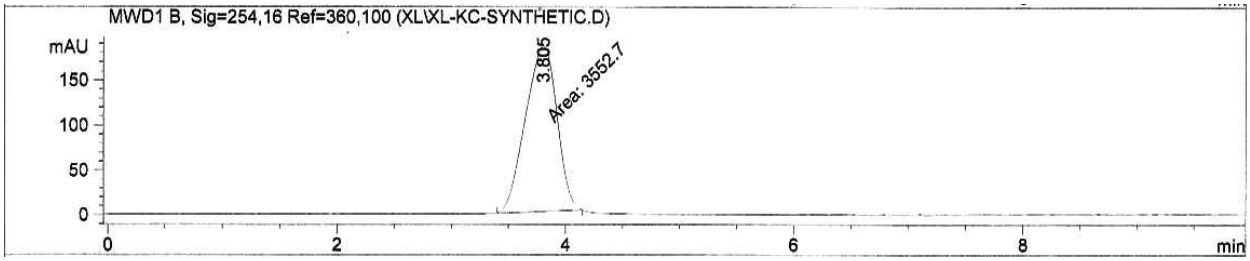
[S9] The diazo-bearing carbon (formerly cyanamide) has a ^{13}C chemical shift of δ78.5 ppm in $CDCl_3$, see: (a). Sato, Y.; Gould, S. J. *J. Am. Chem. Soc.* **1986**, *108*, 4625. (b). Seaton, P. J.; Gould, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 5912.

HPLC data for natural and synthetic kinamycin C[a]

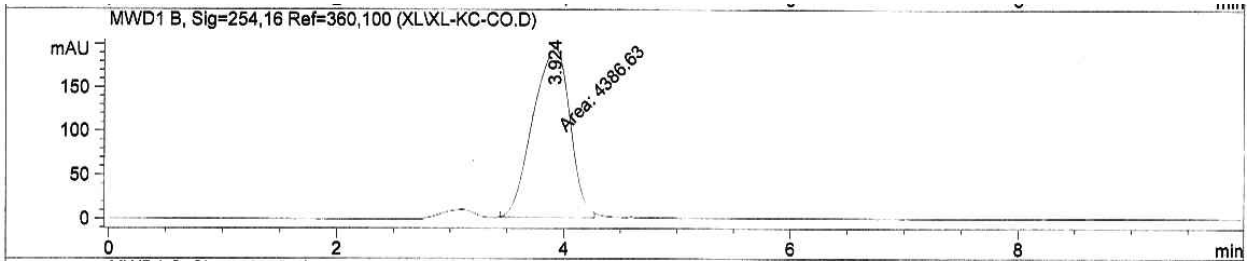
Natural:



Synthetic:



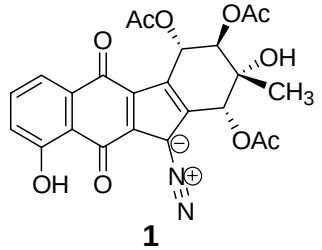
Natural+Synthetic:



Sample Name	r_t (min)
Natural kinamycin C	3.722
Synthetic kinamycin C	3.805
Natural and synthetic kinamycin C (co-injection)	3.924

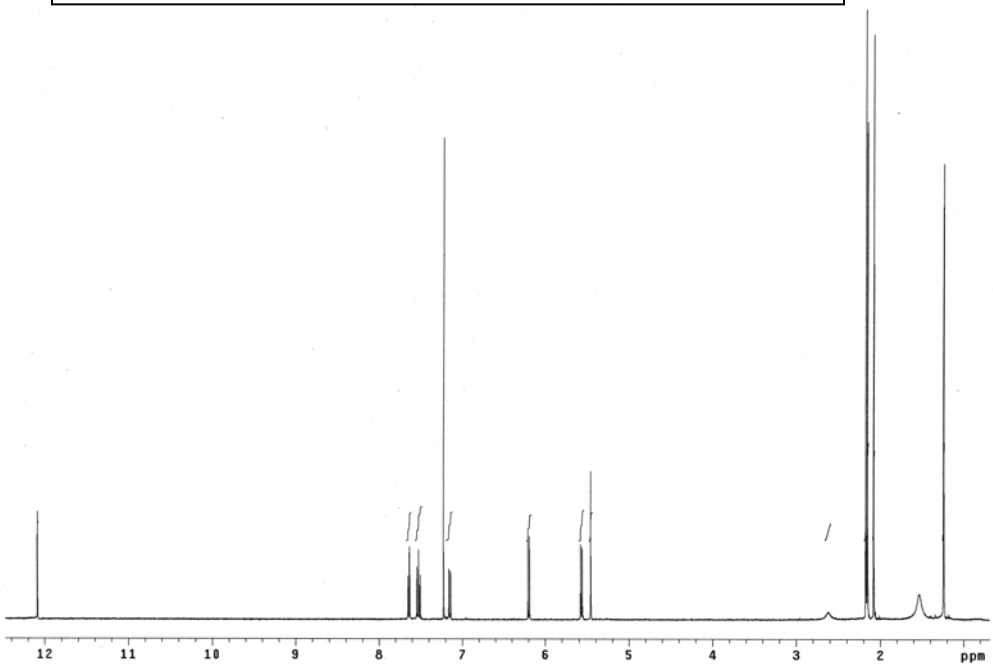
[a] Experimental condition:
Column: Agilent Zorbax SB-C18 (4.6mm ID x 7.5cm) 3.5μL
Eluent: 35% MeCN, 65% water
Detector wavelength: 254 nm
Flow rate: 1.0 mL/min.

^{1}H NMR (400 MHz, $CDCl_3$) of natural kinamycin C

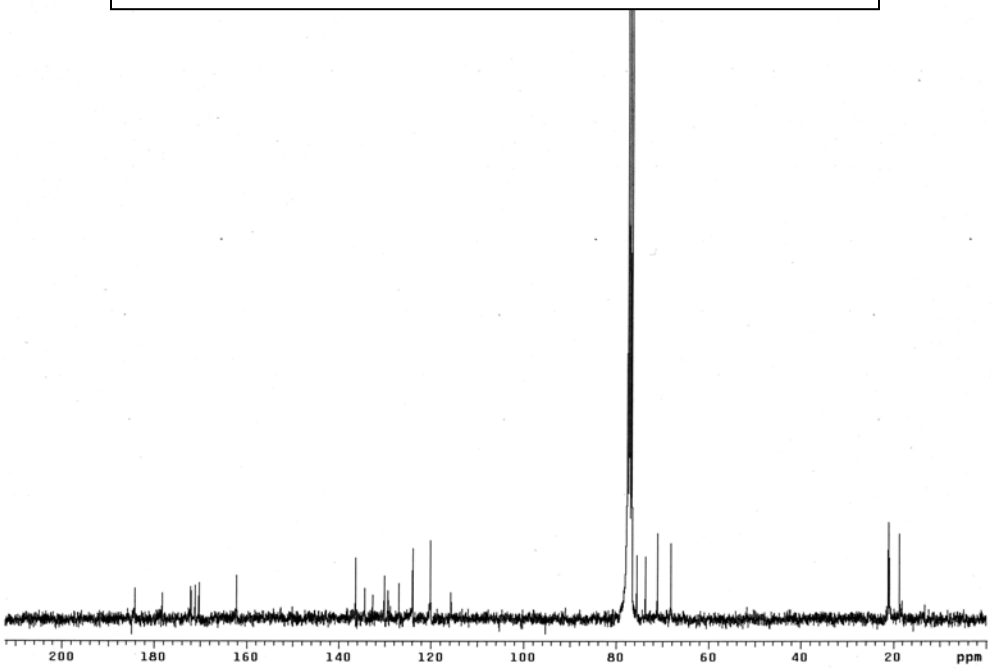


1

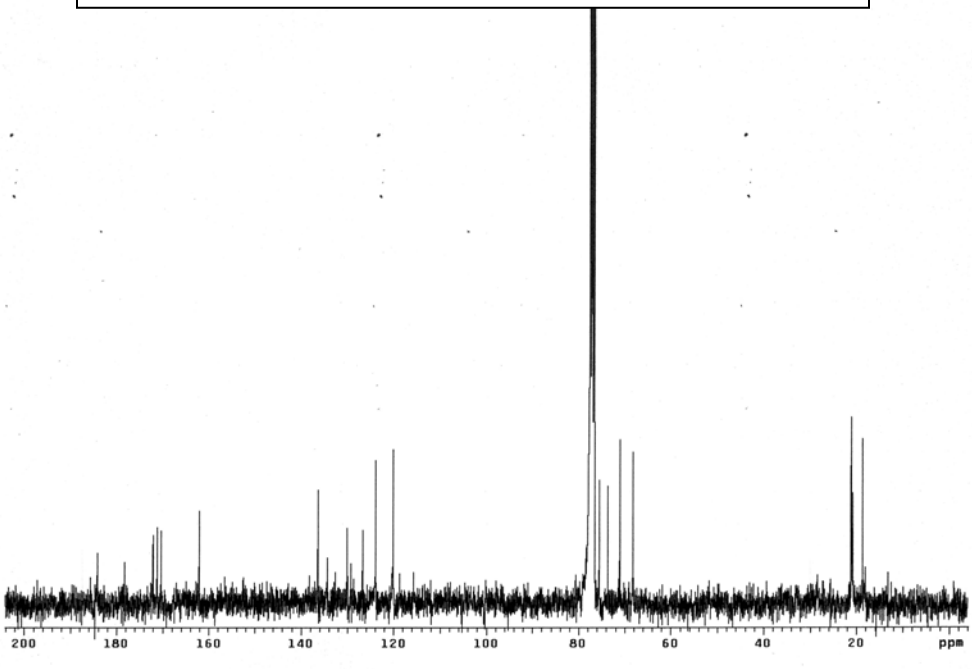
^{1}H NMR (400 MHz, $CDCl_3$) of synthetic kinamycin C



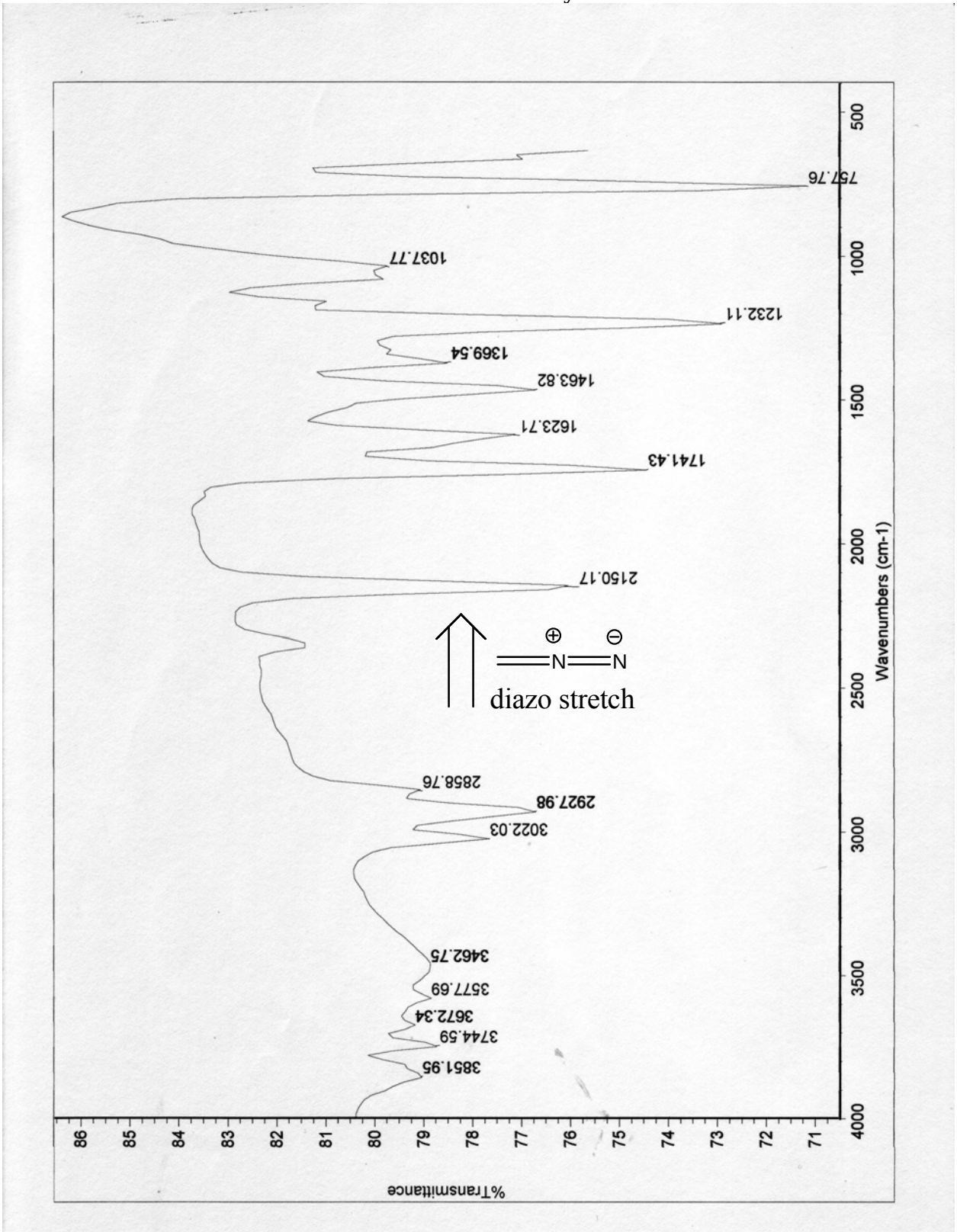
^{13}C NMR (100 MHz, $CDCl_3$) of natural kinamycin C



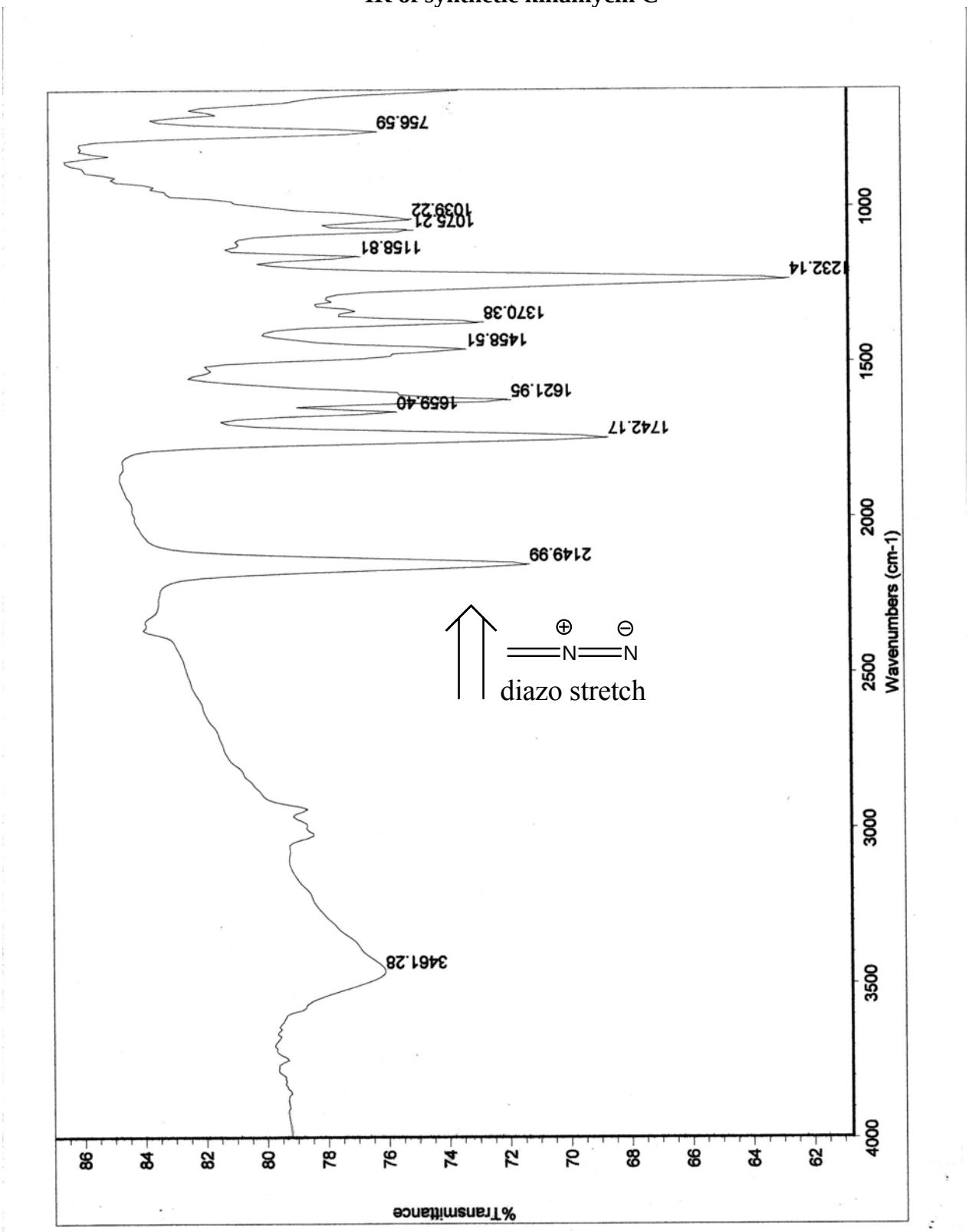
^{13}C NMR (100 MHz, $CDCl_3$) of synthetic kinamycin C



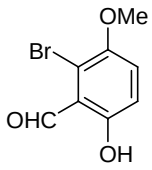
IR of natural kinamycin C



IR of synthetic kinamycin C



III) ^{1}H and ^{13}C NMR spectra



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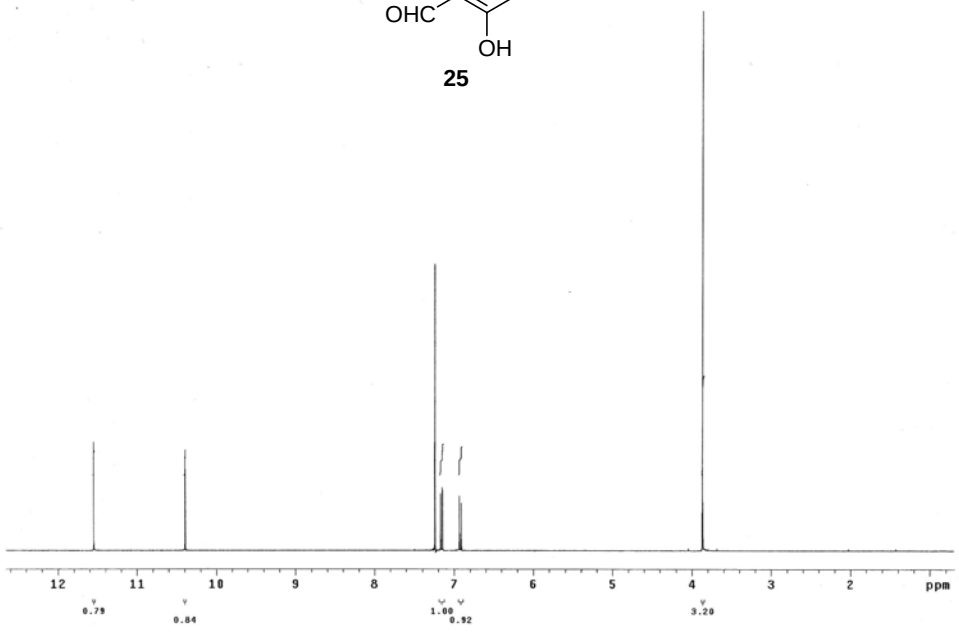

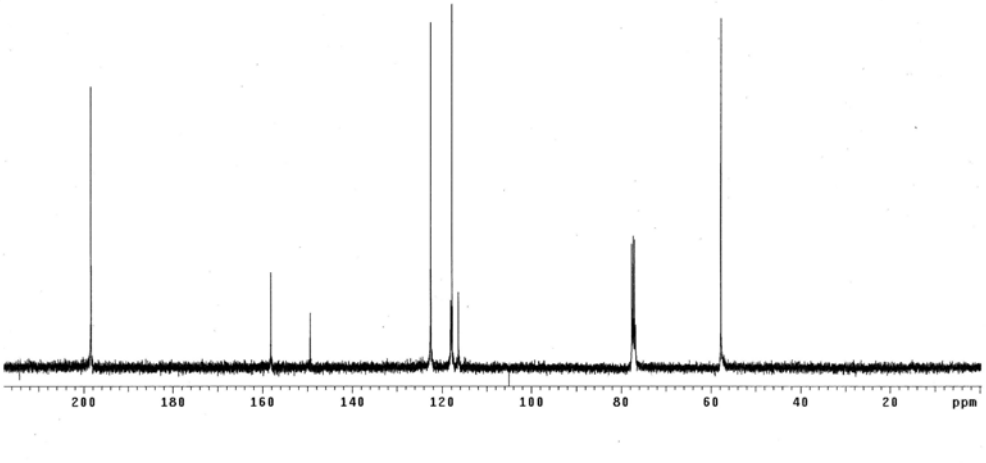

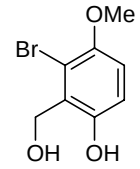
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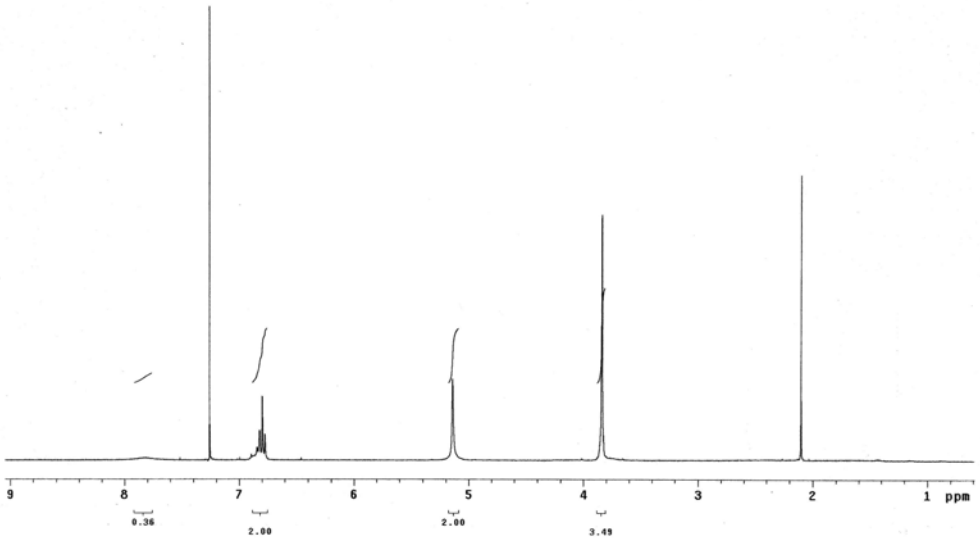
OH

11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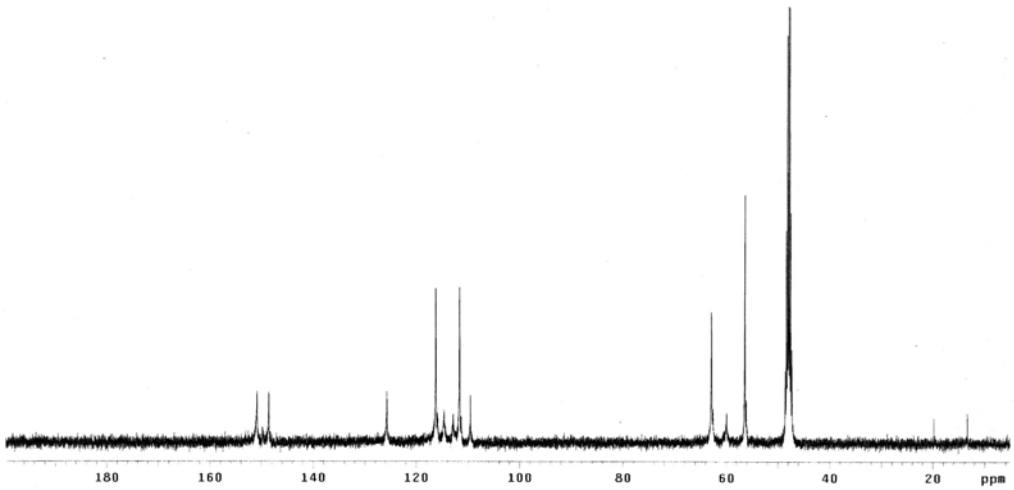
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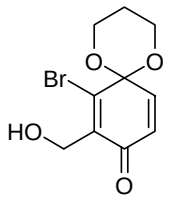
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O
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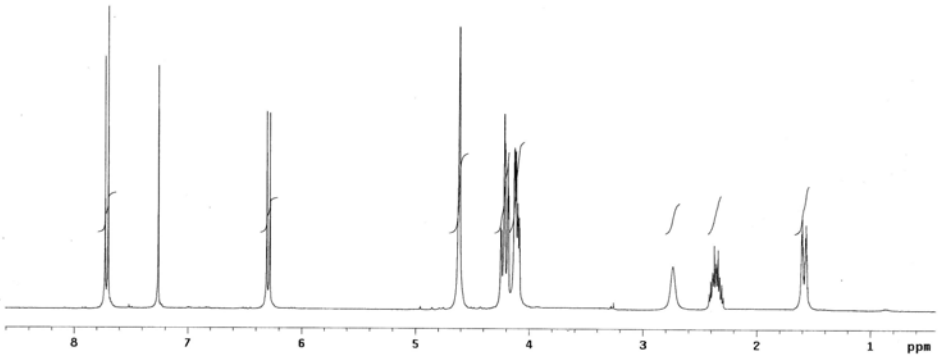
O

26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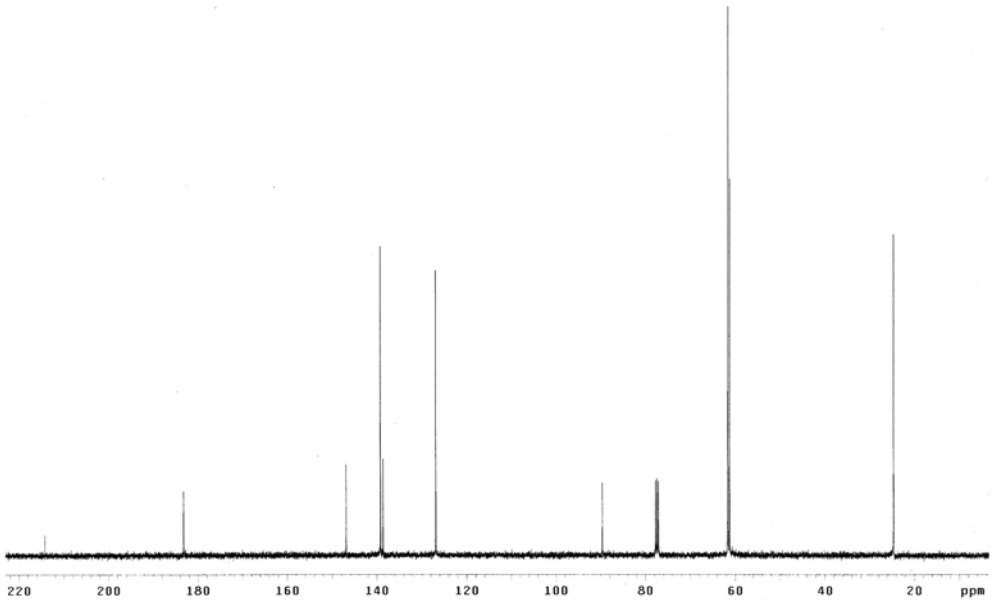
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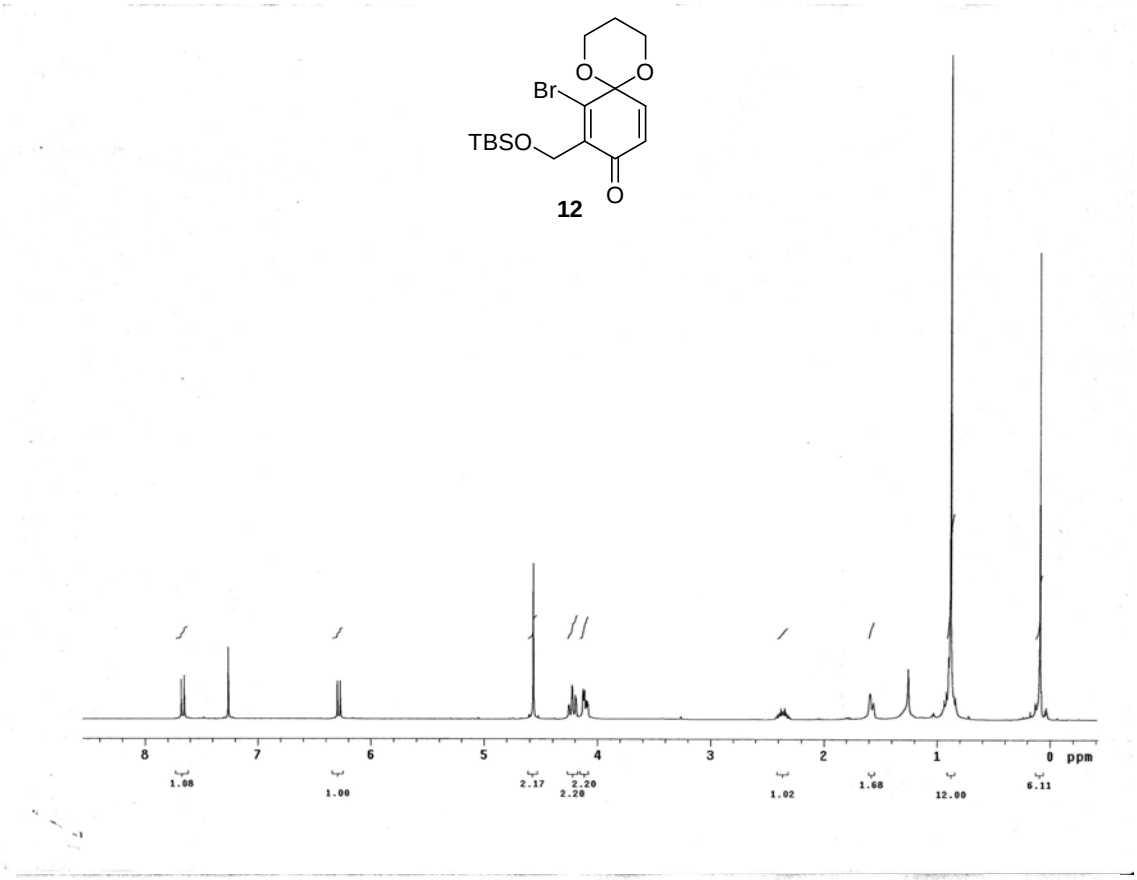
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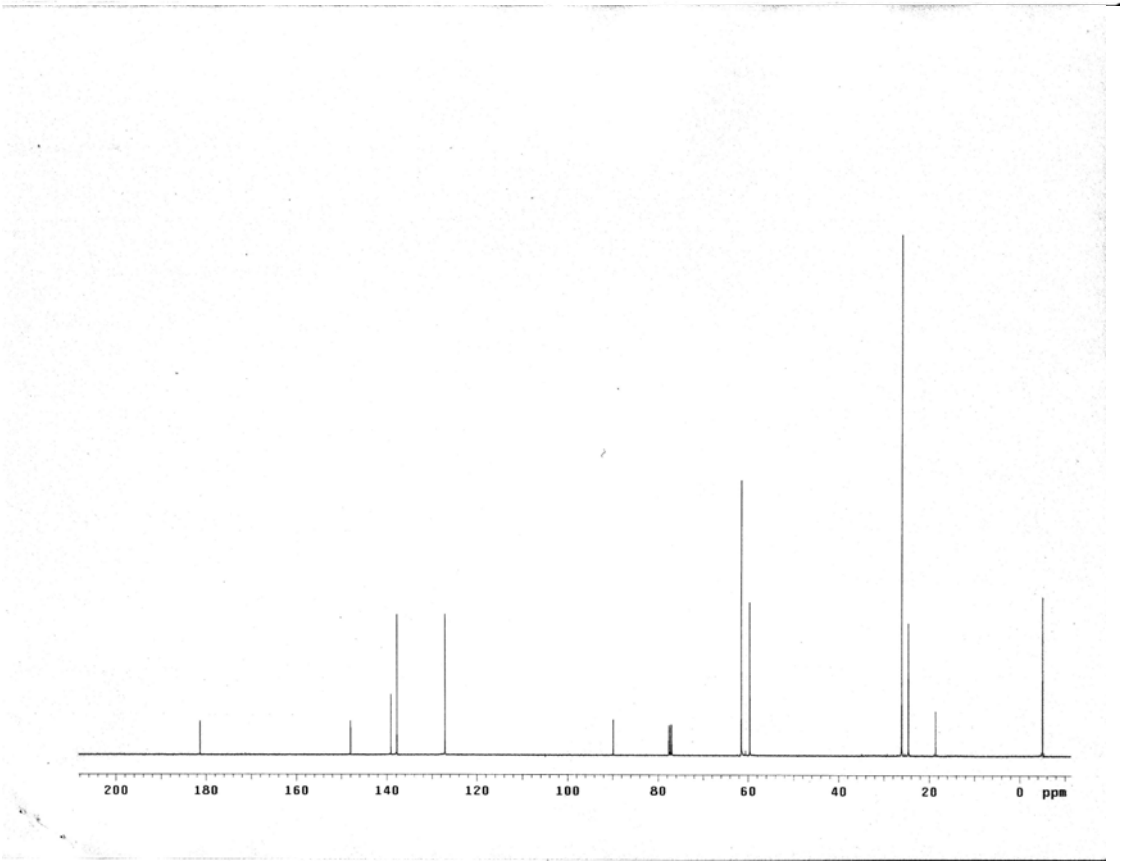
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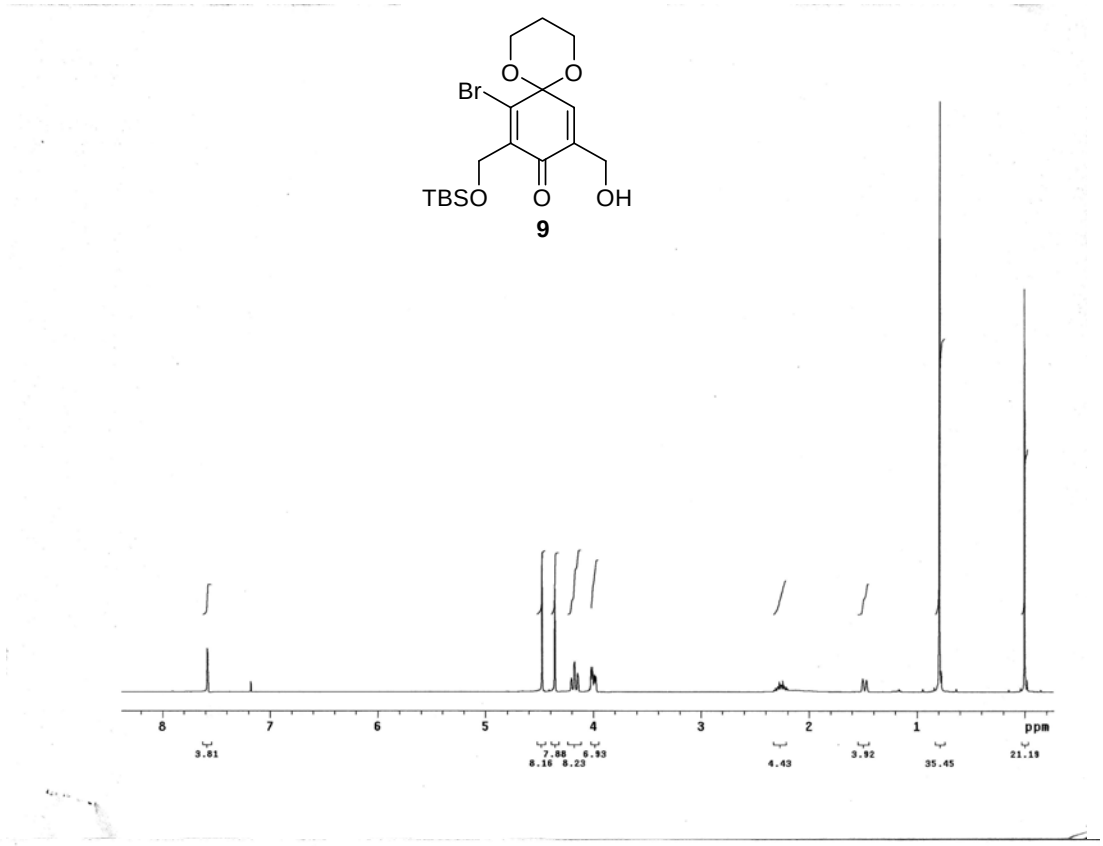
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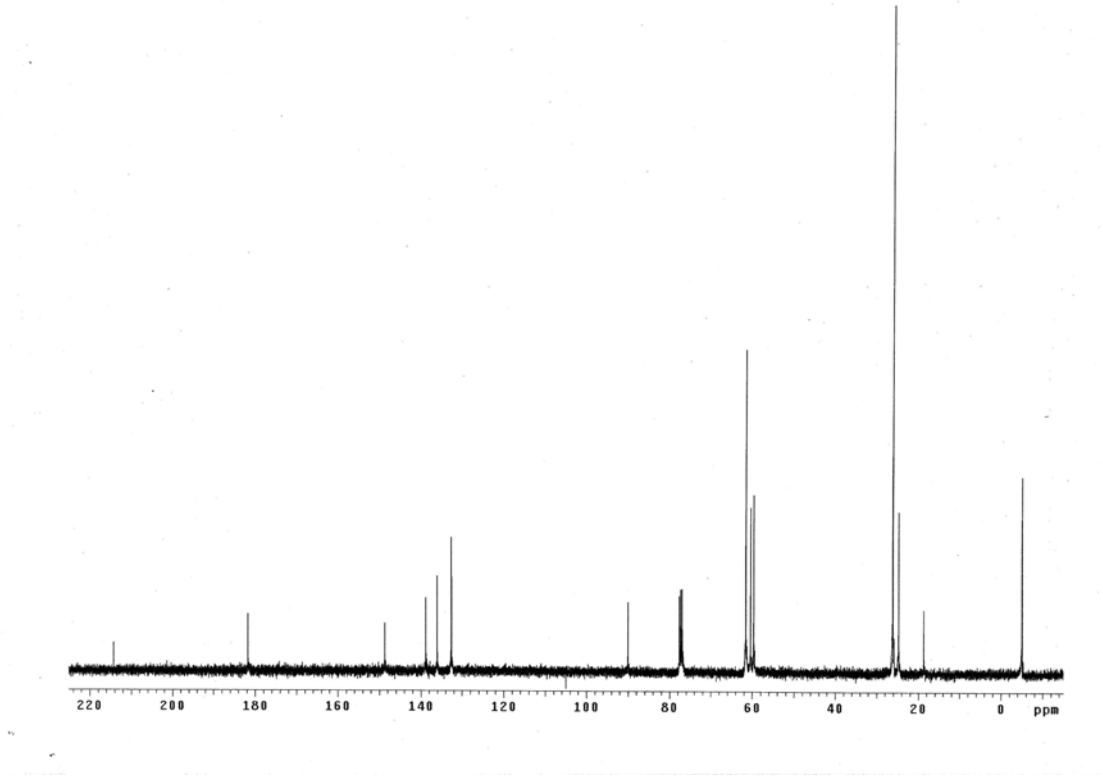
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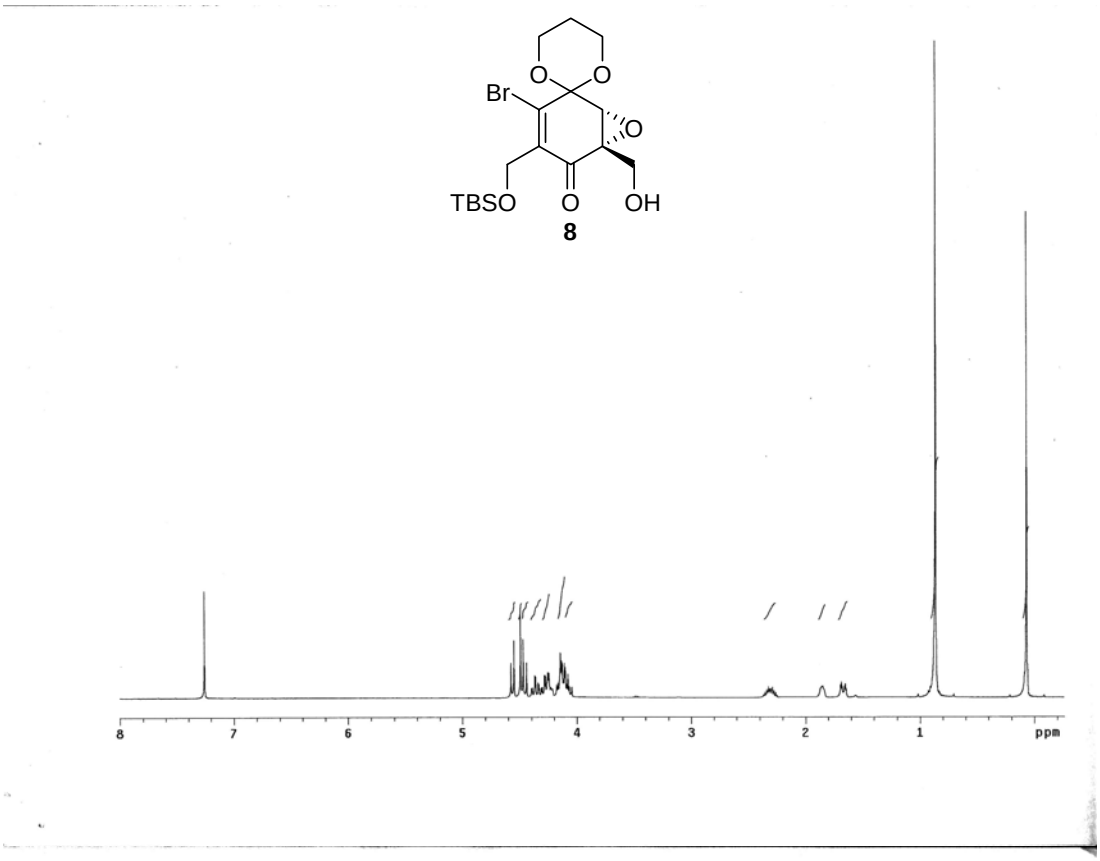
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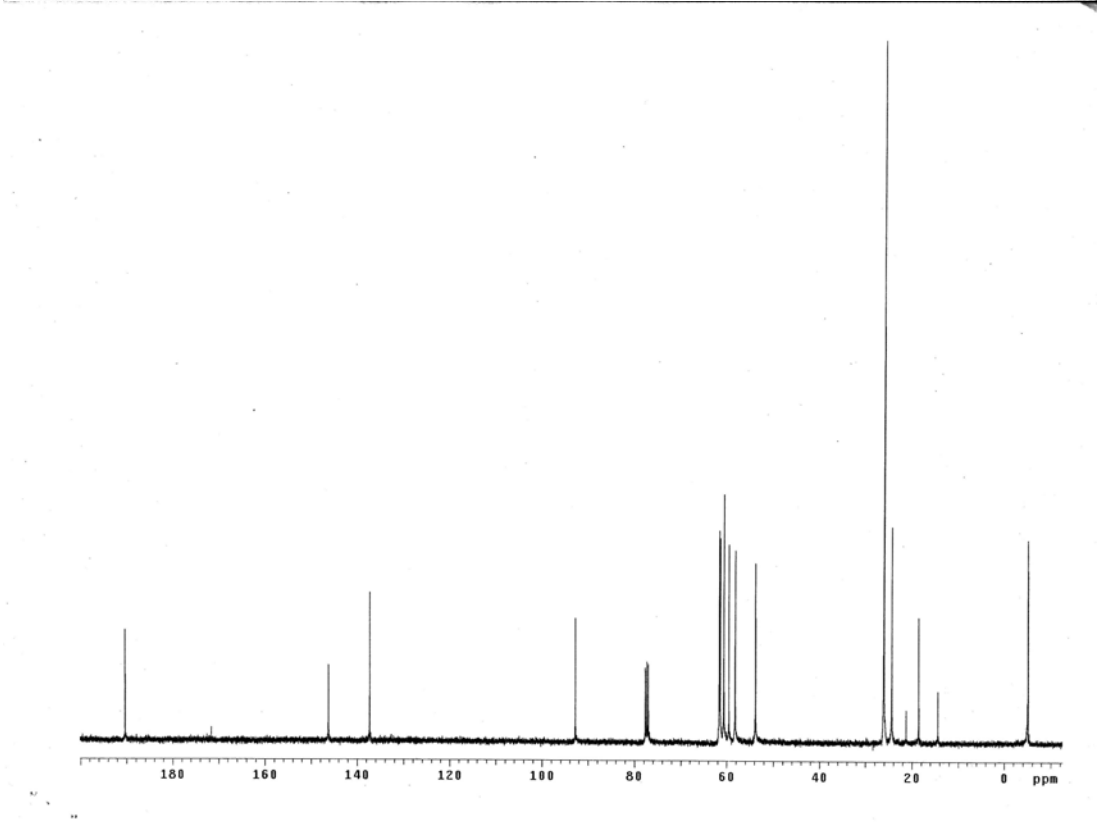
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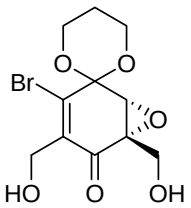
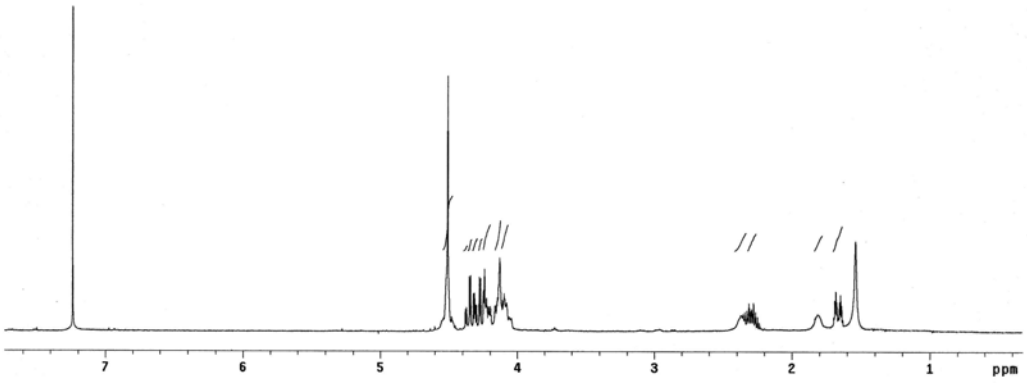
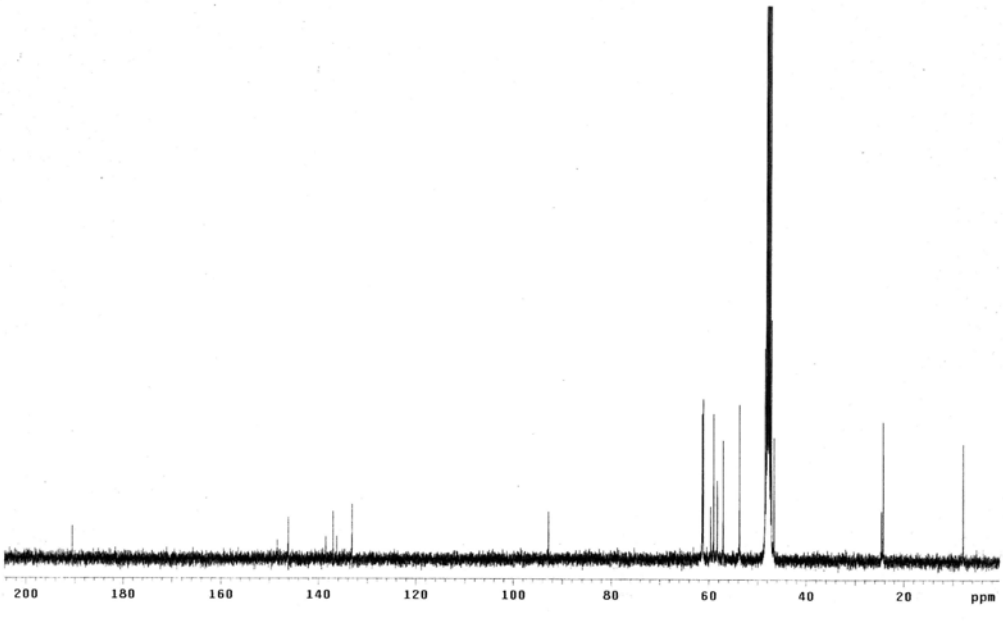
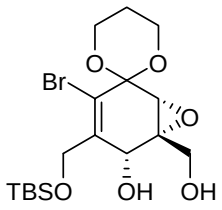


13

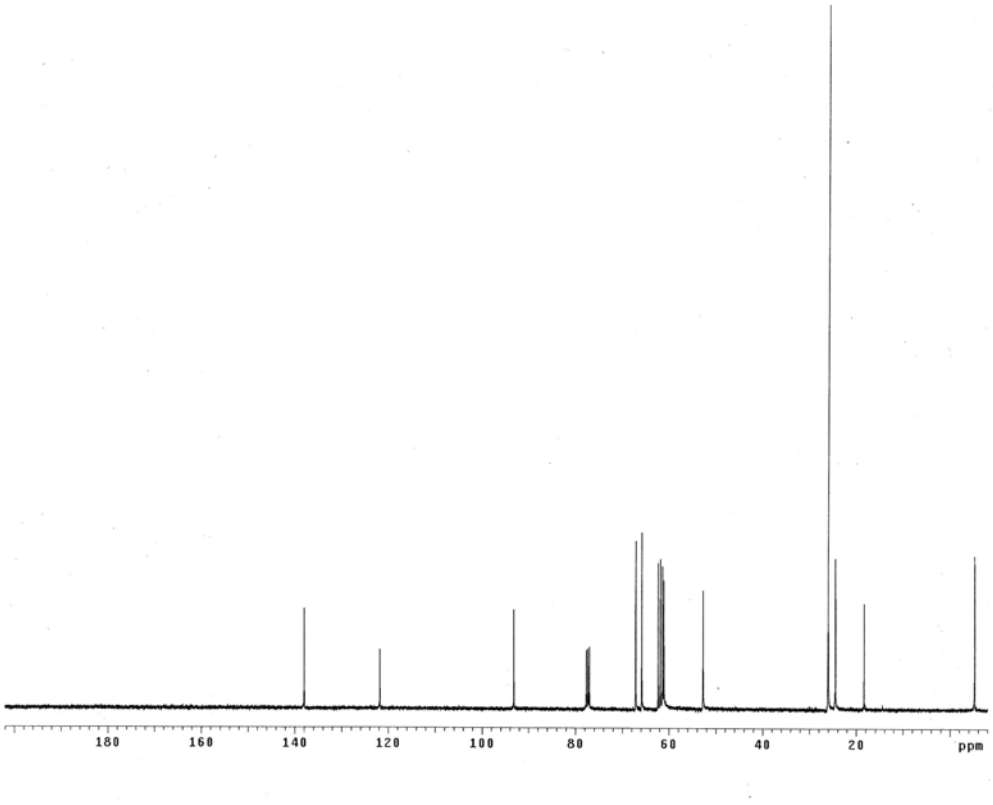


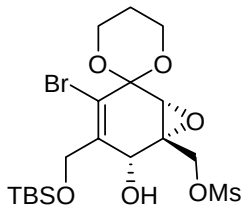



Br
O
O
O
TBSO
OH
OH

27

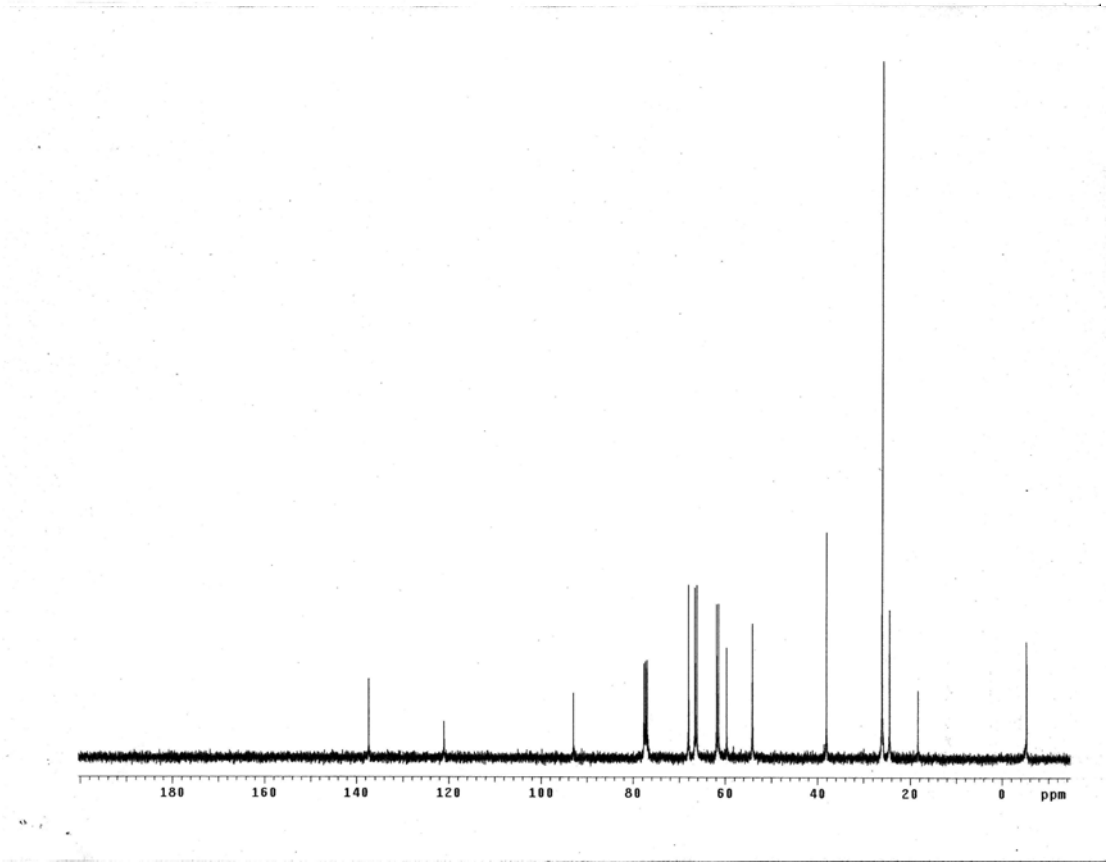
8
7
6
5
4
3
2
1
ppm
0.600.83 1.74 1.00
0.94 1.842.16
0.46 1.30
0.98
6.72
4.19

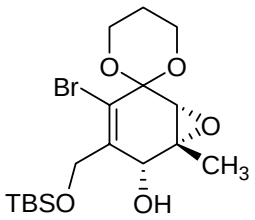

180
160
140
120
100
80
60
40
20
ppm


O
O
Br
O
TBSO
OH
OMs

14

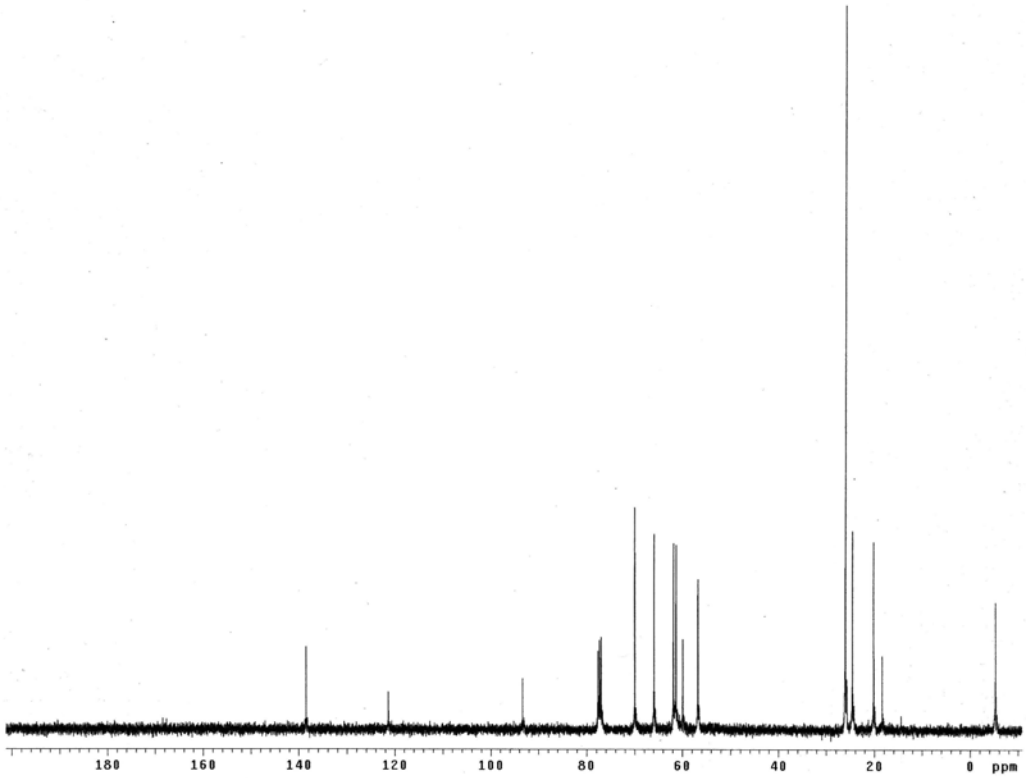
8
7
6
5
4
3
2
1
ppm
2.19 1.28 2.86 2.95
1.22 1.25 3.81 1.05
3.00
1.37
2.02
10.59
5.69

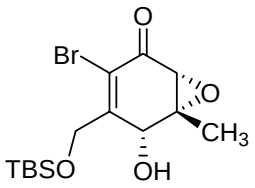

180
160
140
120
100
80
60
40
20
0
ppm


O
O
Br
O
CH3
TBSO
OH

15

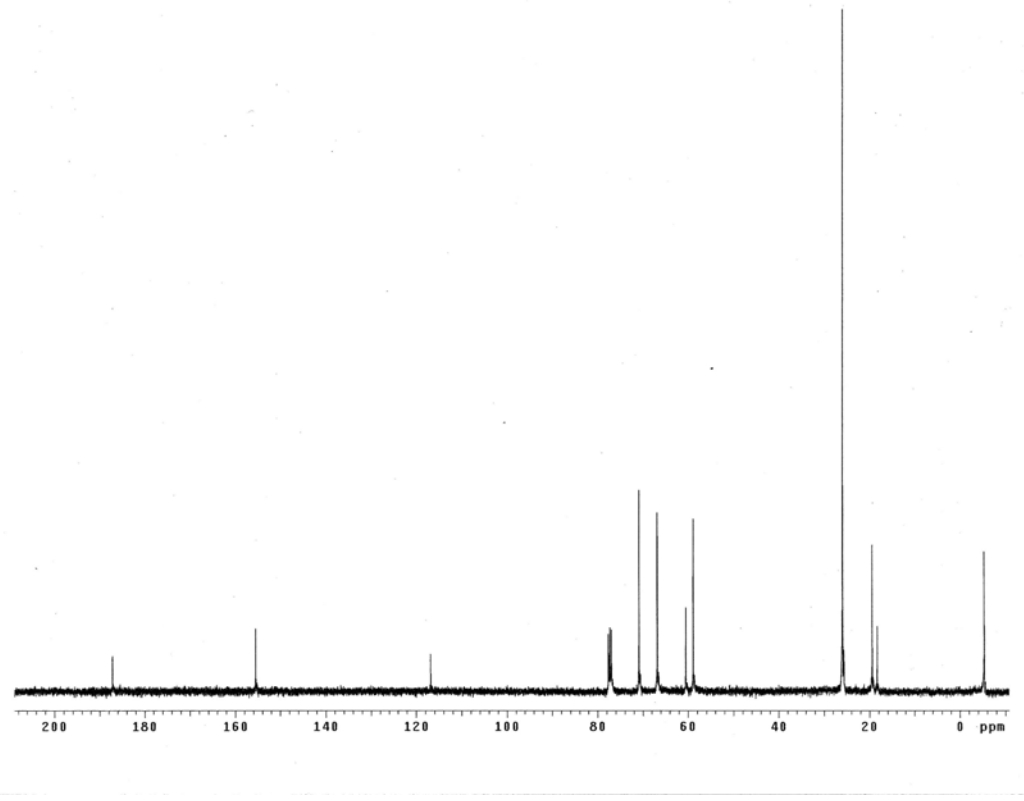
8
7
6
5
4
3
2
1
ppm
1.00
0.10
3.20
0.90
2.56
1.09
1.13
2.26
3.17
10.63
6.00

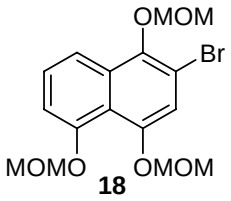

180
160
140
120
100
80
60
40
20
0
ppm


O
Br
O
CH3
TBSO
OH

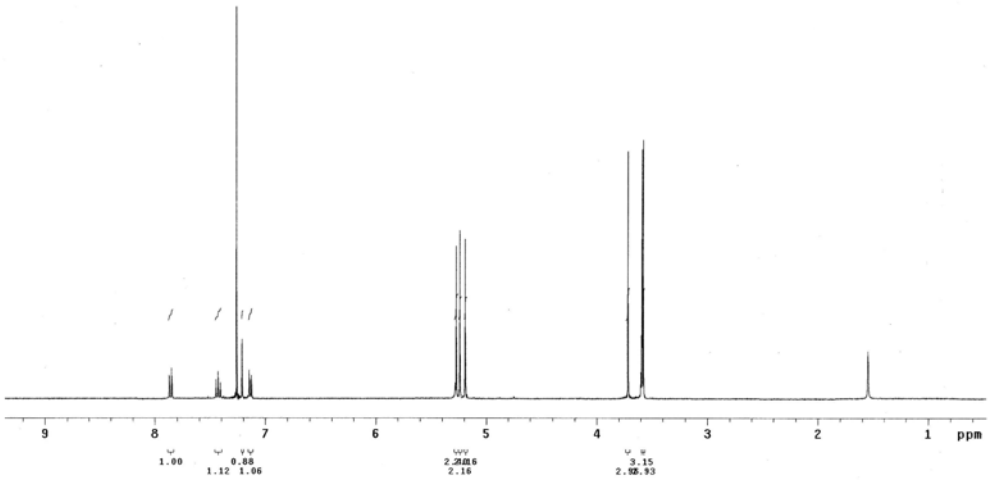
6

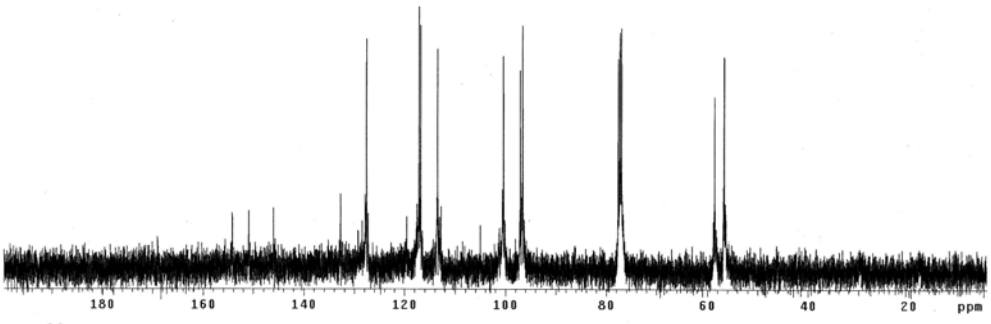
7
6
5
4
3
2
1
0 ppm
1.25
1.25
1.16
0.94
1.00
3.68
11.80
6.44

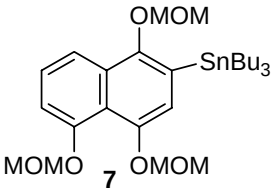

200
180
160
140
120
100
80
60
40
20
0 ppm


OMOM
Br
MOMO
OMOM

18

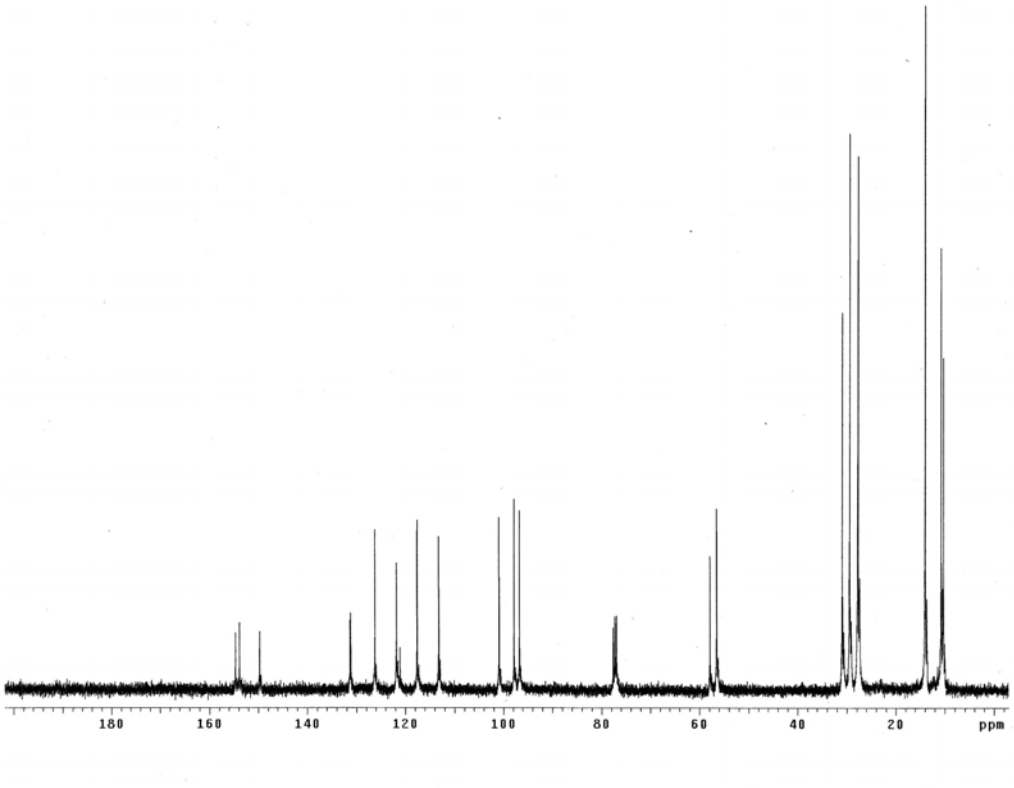

9
8
7
6
5
4
3
2
1
ppm
1.00
0.88
1.12
1.06
2.16
3.15


180
160
140
120
100
80
60
40
20
ppm

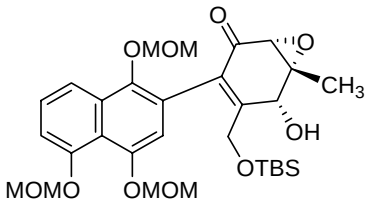

OMOM
SnBu3
MOMO
OMOM

7

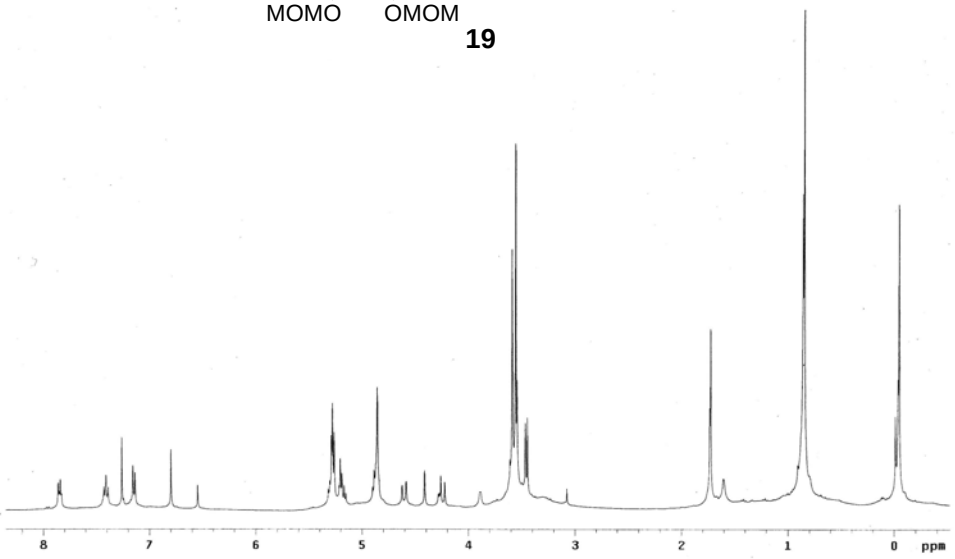
8
7
6
5
4
3
2
1
ppm

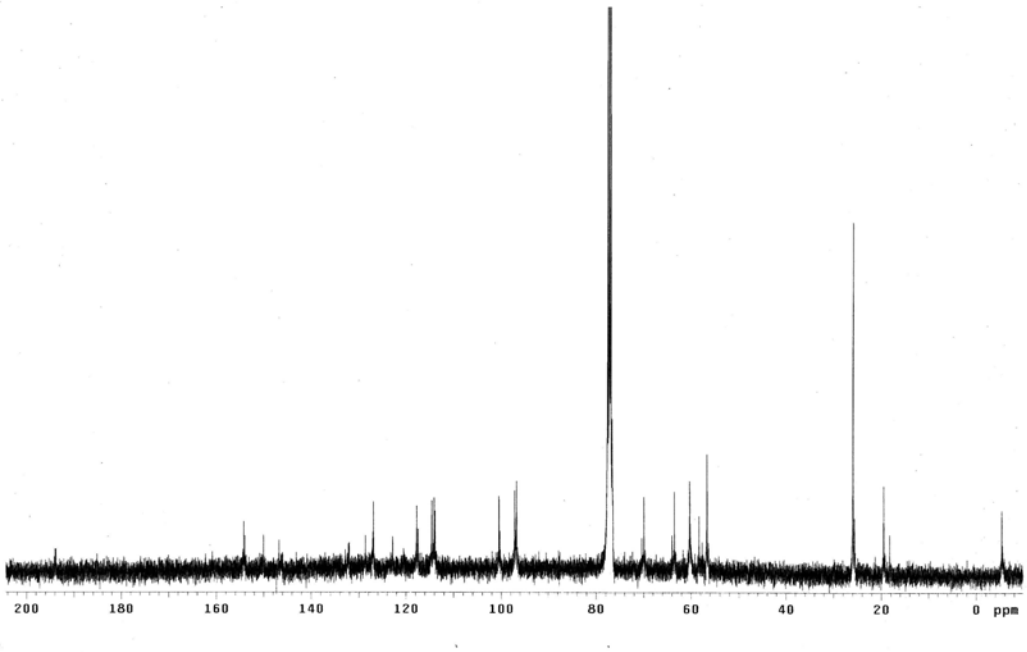

180
160
140
120
100
80
60
40
20
ppm

2:1 mixture of rotamers

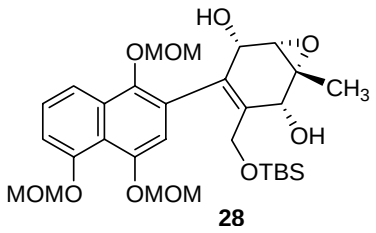


19

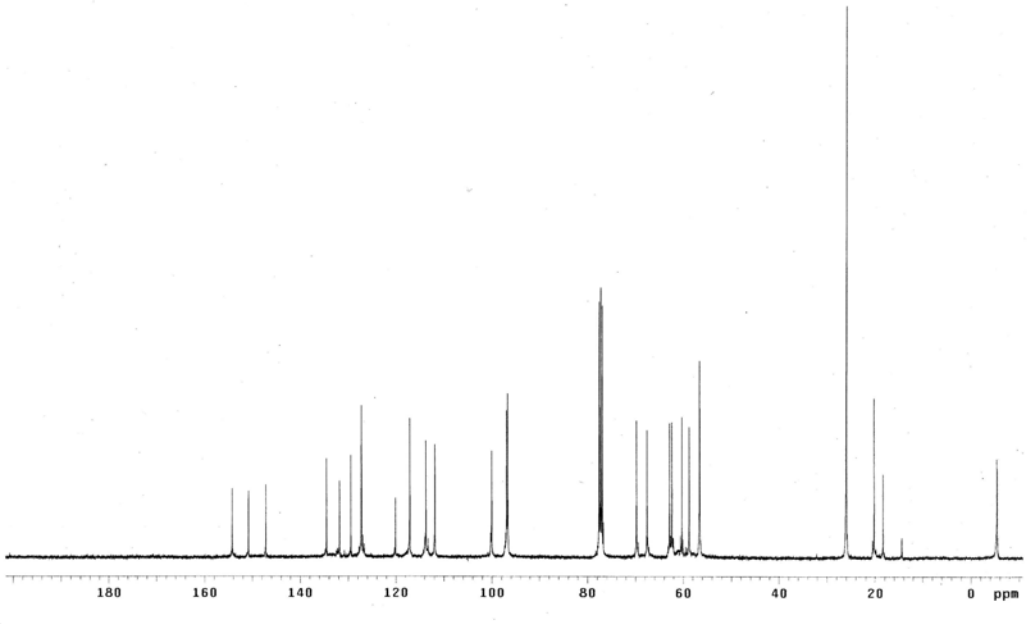




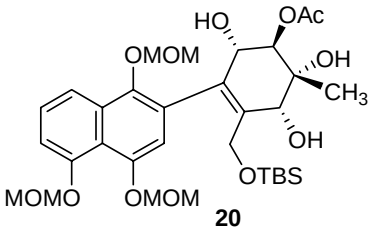
single rotamer



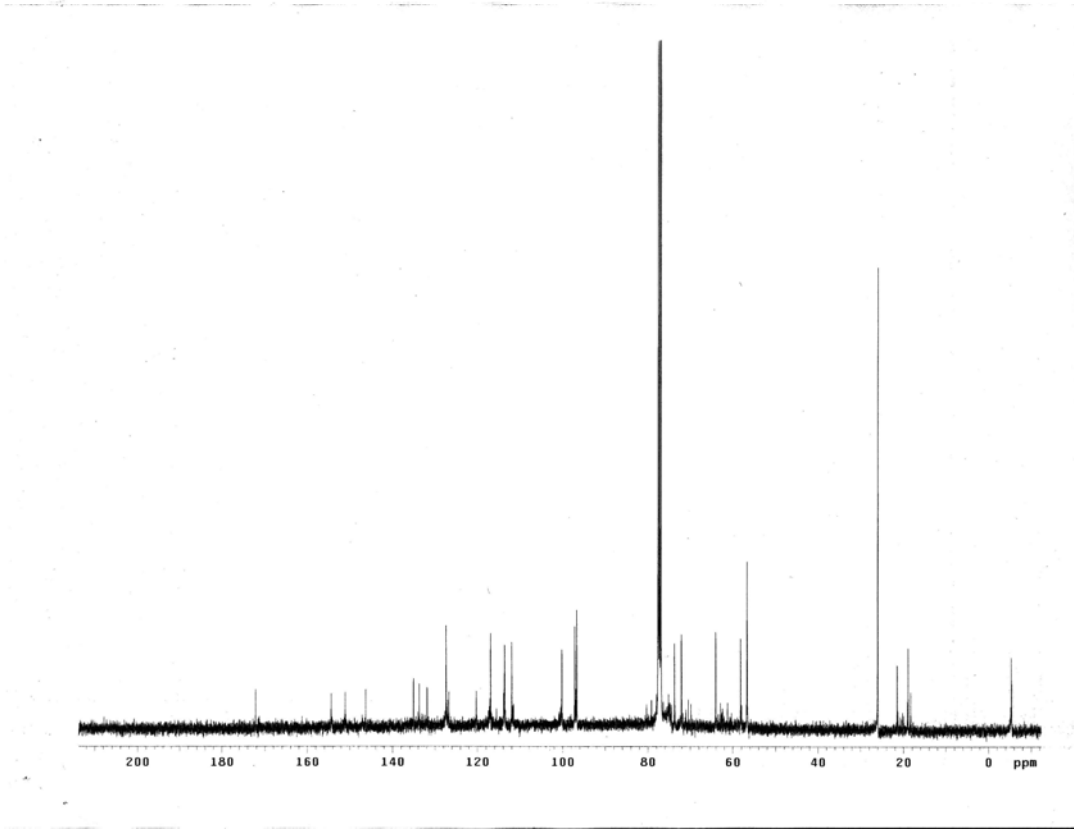
28



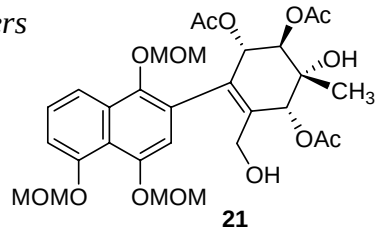
8:1 mixture of rotamers



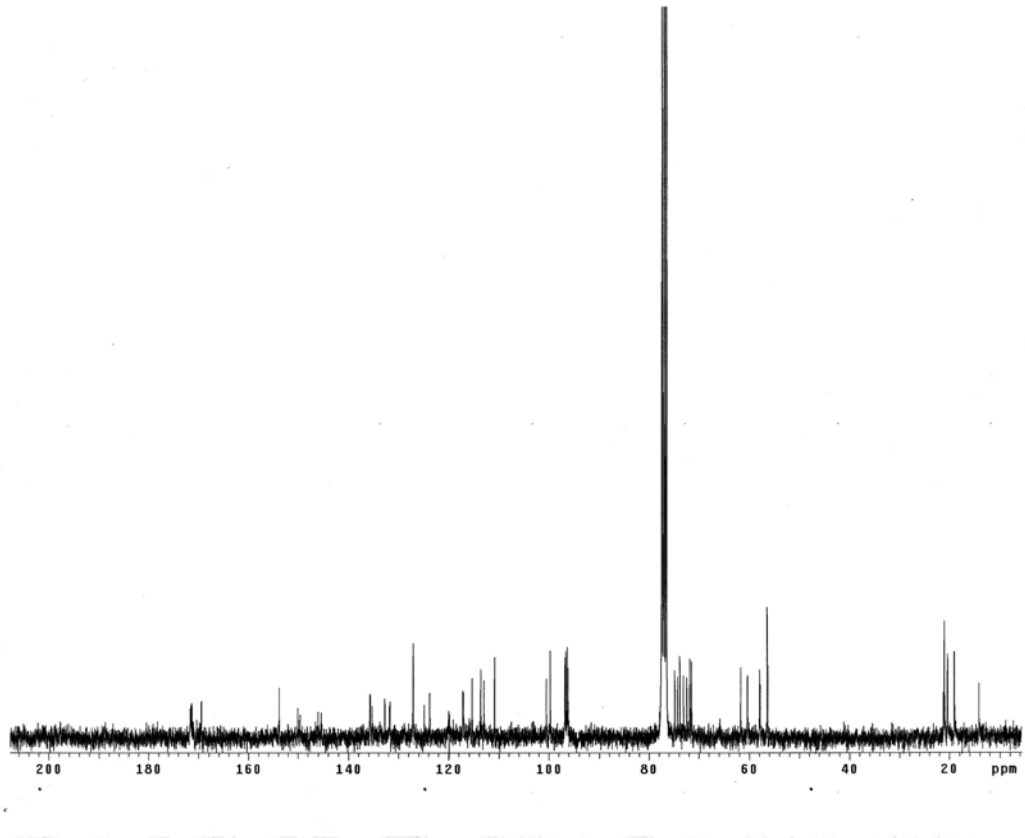
20

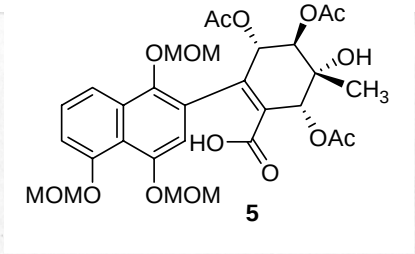


1.2:1 mixture of rotamers

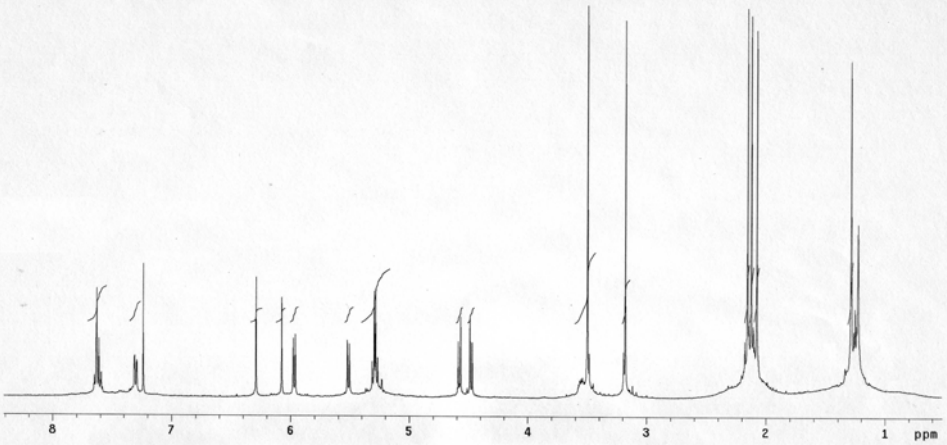


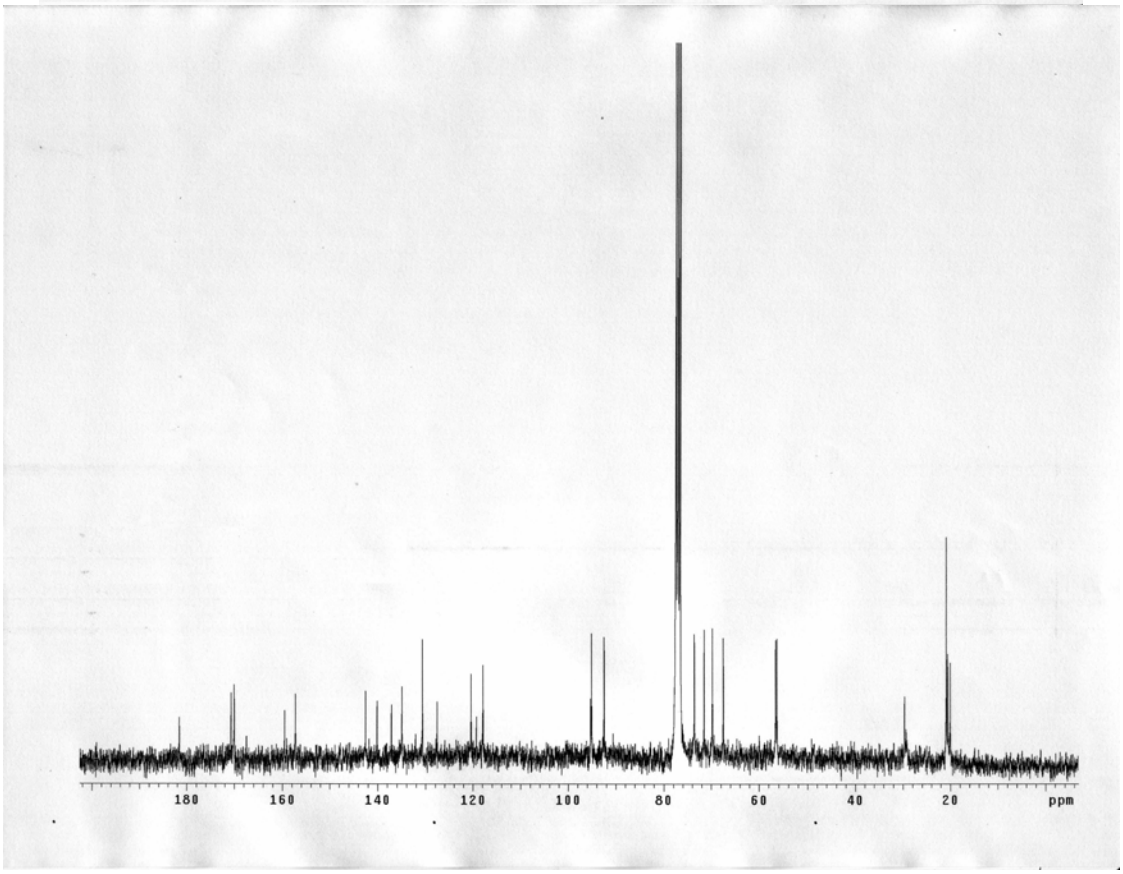
21

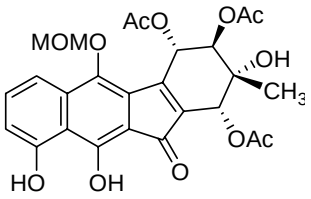



AcO
OAc
OMOM
OH
CH3
HO
OAc
O
MOMO
OMOM

5

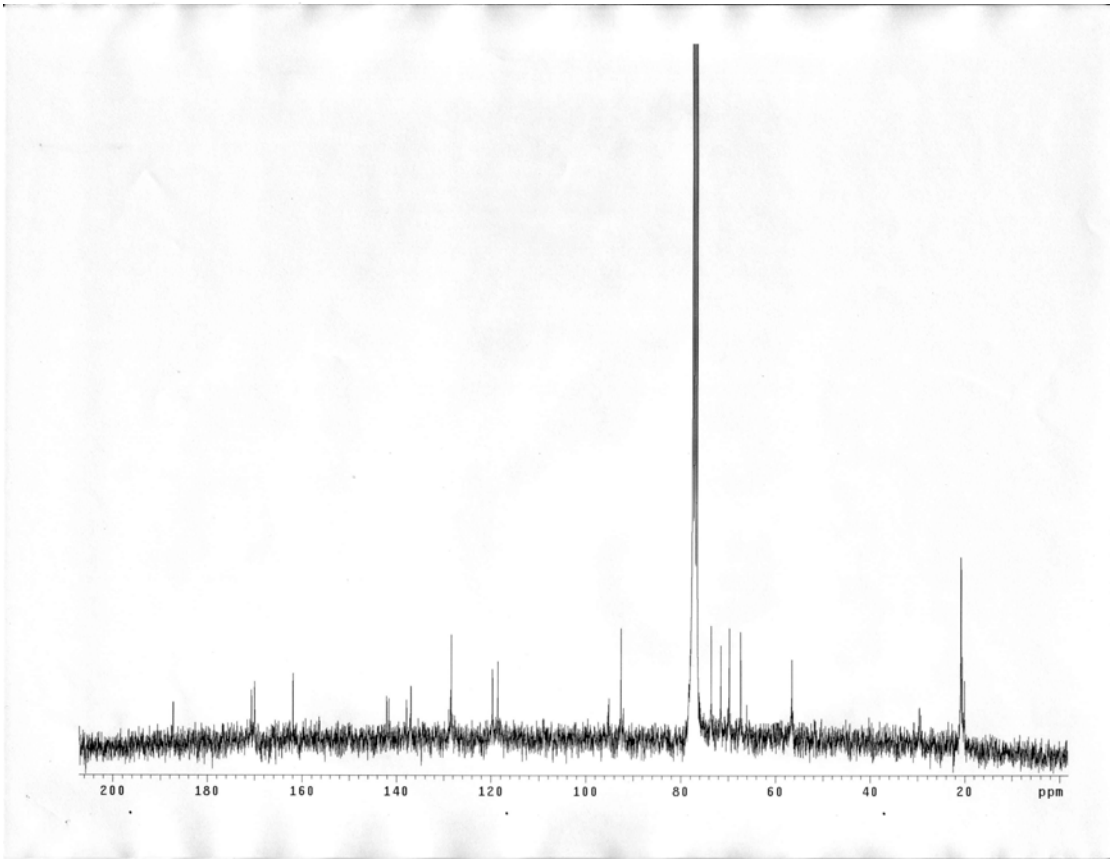

8
7
6
5
4
3
2
1
ppm

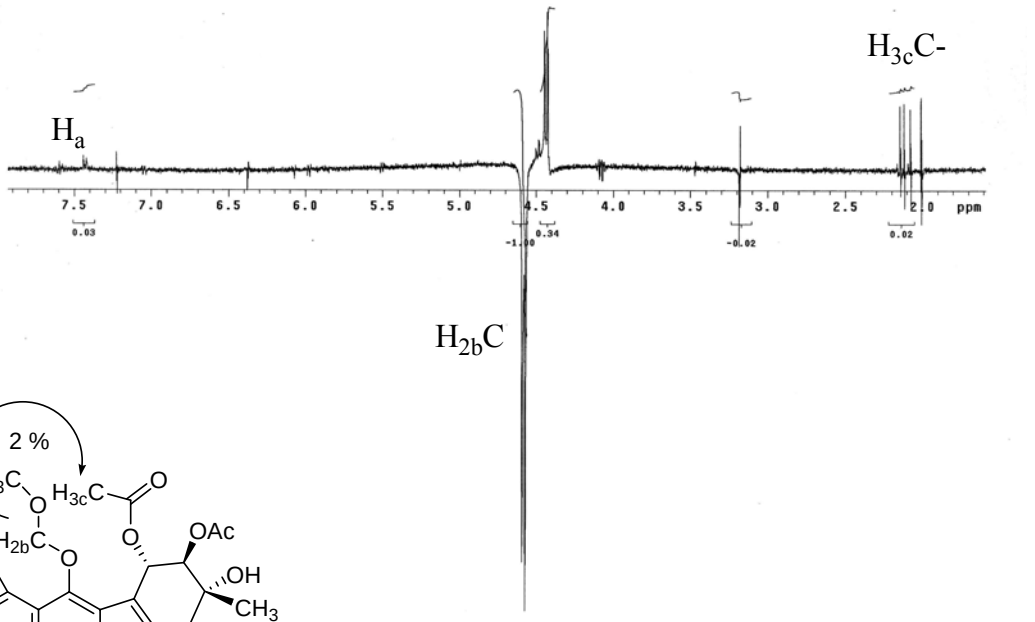

180
160
140
120
100
80
60
40
20
ppm

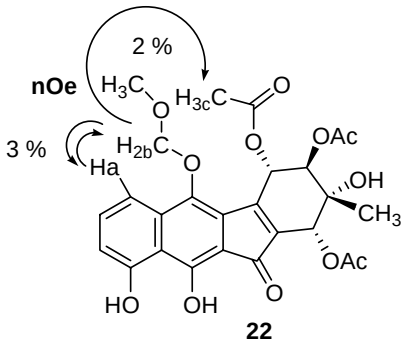

MOMO
AcO
OAc
OH
CH3
OAc
HO
OH
O

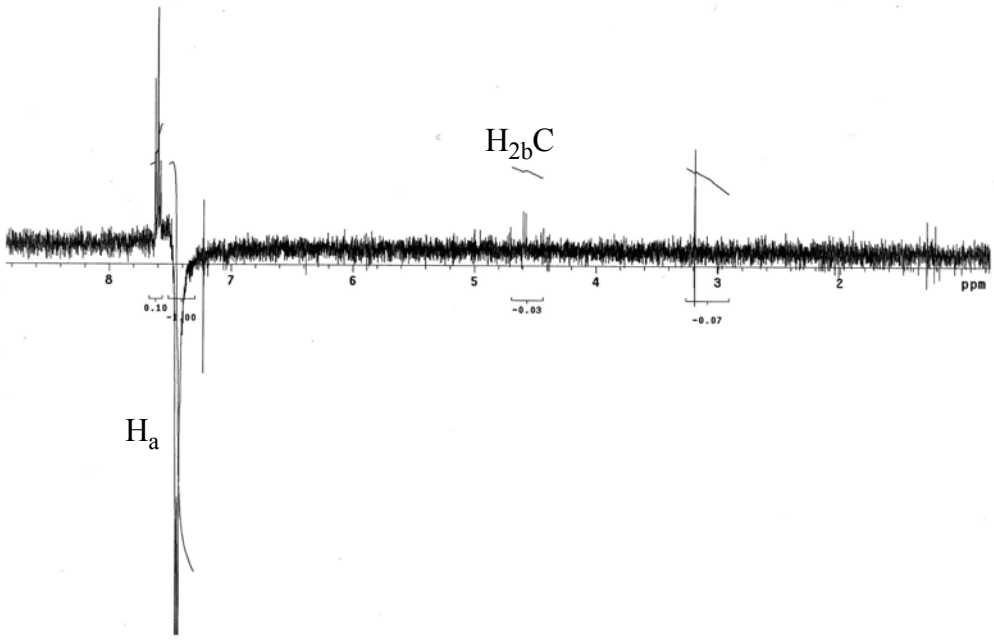
22

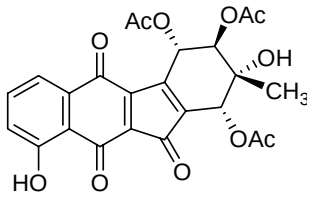
12
11
10
9
8
7
6
5
4
3
2
1
ppm


200
180
160
140
120
100
80
60
40
20
ppm

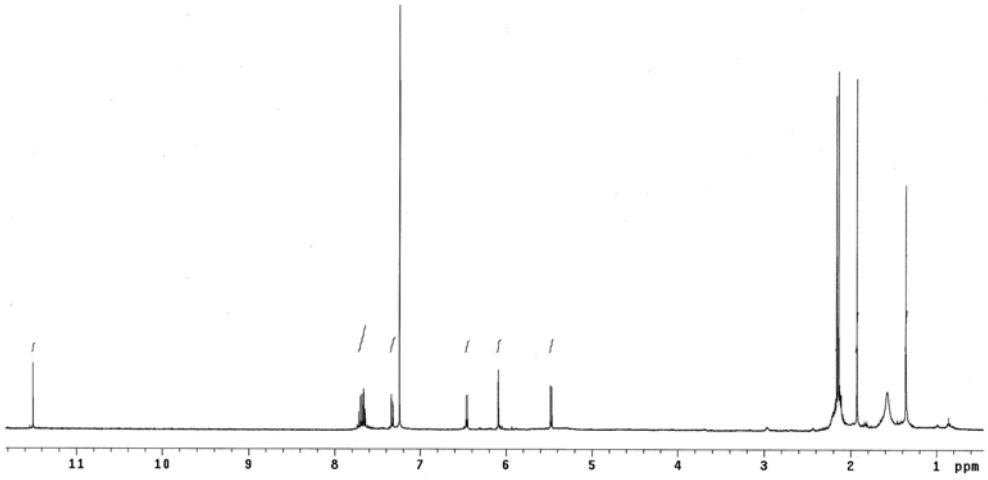

H_a
$H_{3c}C$-
$H_{2b}C$
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

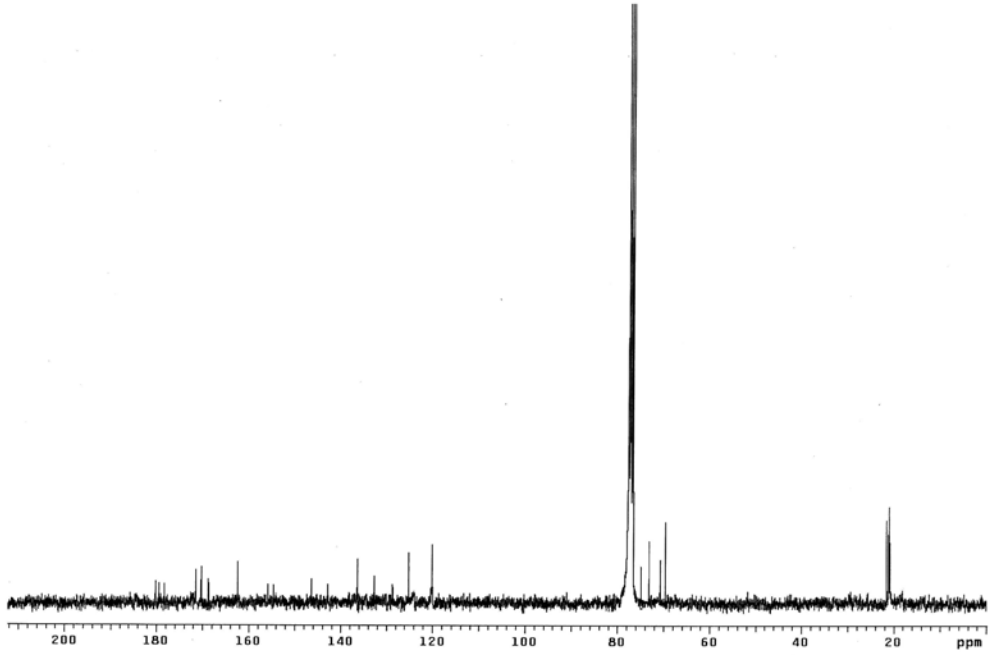

nOe
2 %
3 %
H_3C
$H_{3c}C$
O
$H_{2b}C$
Ha
OAc
OH
CH_3
HO
OH
22


$H_{2b}C$
H_a
8
7
6
5
4
3
2
ppm

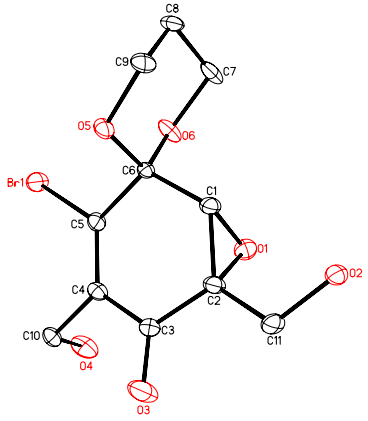

AcO
OAc
O
OH
CH3
OAc
HO
O
O

23


11
10
9
8
7
6
5
4
3
2
1 ppm


200
180
160
140
120
100
80
60
40
20
ppm

IV) X-ray crystallographic data for 13



Crystals of compound **13** suitable for x-ray analysis were obtained by slow evaporation from methanol. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 606400). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for **13**.

Identification code	**13 (CCDC 606400)**	
Empirical formula	C22 H26 Br2 O12	
Formula weight	642.25	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.2717(6) Å	α= 72.459(3)°.
	b = 8.2798(5) Å	β= 88.762(4)°.
	c = 9.1507(7) Å	γ = 75.142(3)°.
Volume	576.54(7) $Å^3$	
Z	1	
Density (calculated)	1.850 Mg/m^3	
Absorption coefficient	3.583 mm^{-1}	
F(000)	324	
Crystal size	0.45 x 0.30 x 0.15 mm^3	

Theta range for data collection	2.34 to 30.51°.
Index ranges	-11<=h<=11, -11<=k<=11, -13<=l<=13
Reflections collected	13320
Independent reflections	6044 [R(int) = 0.0232]
Completeness to theta = 30.51°	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6155 and 0.2954
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6044 / 3 / 429
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0257, wR2 = 0.0650
R indices (all data)	R1 = 0.0286, wR2 = 0.0658
Absolute structure parameter	0.047(6)
Largest diff. peak and hole	0.453 and -0.430 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **13**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1394(1)	18976(1)	6546(1)	26(1)
Br(2)	-5692(1)	19119(1)	9459(1)	27(1)
O(1)	-2073(2)	17885(2)	3343(2)	23(1)
O(2)	-4278(3)	15744(3)	3491(3)	20(1)
O(3)	-4915(3)	19784(4)	5520(4)	38(1)
O(4)	-2191(4)	22515(3)	4719(3)	30(1)
O(5)	372(3)	15353(3)	7027(2)	21(1)
O(6)	1263(3)	16702(3)	4630(3)	23(1)
O(7)	-1489(2)	22258(2)	9546(2)	21(1)
O(8)	3(3)	22319(4)	12419(3)	25(1)
O(9)	624(3)	18035(3)	10704(3)	33(1)
O(10)	-2106(4)	15624(3)	11122(3)	31(1)
O(11)	-5169(3)	21179(3)	11583(3)	22(1)
O(12)	-5025(3)	22725(3)	9005(3)	23(1)
C(1)	-1510(3)	16456(4)	4754(4)	21(1)
C(2)	-3225(3)	17611(4)	4600(3)	20(1)

C(3)	-3518(4)	19030(4)	5334(4)	17(1)
C(4)	-2032(4)	19502(4)	5822(4)	17(1)
C(5)	-500(4)	18399(4)	5952(4)	17(1)
C(6)	-74(4)	16684(4)	5597(4)	15(1)
C(7)	1946(4)	15057(5)	4330(4)	24(1)
C(8)	2500(4)	13637(5)	5818(4)	29(1)
C(9)	1075(5)	13611(4)	6886(4)	26(1)
C(10)	-2384(4)	21257(4)	6097(4)	18(1)
C(11)	-4718(4)	17132(5)	4151(5)	23(1)
C(12)	-2629(4)	21904(4)	10738(3)	19(1)
C(13)	-958(4)	20723(4)	10916(3)	19(1)
C(14)	-749(4)	19038(4)	10546(4)	19(1)
C(15)	-2244(4)	18663(4)	9995(3)	15(1)
C(16)	-3762(4)	19716(4)	9944(3)	15(1)
C(17)	-4166(4)	21461(4)	10304(3)	15(1)
C(18)	-5750(5)	24391(4)	9257(5)	28(1)
C(19)	-6925(5)	24157(5)	10539(5)	34(1)
C(20)	-6011(5)	22757(5)	11943(4)	27(1)
C(21)	-1907(4)	16886(4)	9711(4)	19(1)
C(22)	419(4)	20811(5)	11911(4)	20(1)