Synthesis of (–)-Berkelic Acid

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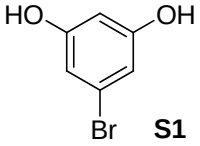
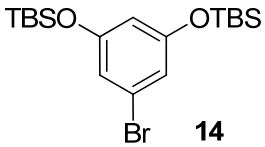
Experimental Section

General procedures. NMR spectra were recorded at 400 MHz in $CDCl_3$ with TMS as an internal standard unless otherwise indicated. Chemical shifts are reported in δ, coupling constants in Hz, and IR spectra in cm^{-1}. Spectra in CD_3OD are referenced to the residual solvent peaks at δ 3.30 (^1H) and δ 49.00 (^{13}C) to be consistent with the data for the natural product.[1] Spectra in acetone-d_6 are referenced to the residual solvent peaks at δ 2.05 (^1H). Spectra in benzene-d_6 are referenced to the residual solvent peaks at δ 7.16 (^1H) and δ 128.39 (^{13}C). The atom numbering used in the tabulation of all tetracyclic compounds (**22**, **27-30**, **S4-S5**, **33-36**) is that used in the isolation of berkelic acid[1] rather than that of the systematic name given in the procedure heading.



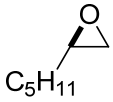
S1

5-Bromoresorcinol (S1) was prepared by the literature procedure.[9] To a solution of 1-bromo-3,5-dimethoxybenzene (**13**, 2 g, 9.2 mmol) in dry CH_2Cl_2 (25 mL) was added BBr_3 solution (19 mL, 1 M in CH_2Cl_2, 19 mmol) by syringe over 30 min under N_2 at -78 °C. The reaction mixture was stirred from -78 to 25 °C overnight. The brown solution was cooled to 0 °C and H_2O (50 mL) was added slowly. The aqueous layer was saturated with solid NaCl. The two layers were separated and the aqueous layer was extracted with EtOAc (4 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave 1.69 g (97%) of **S1** as a white solid: mp 86-87 °C (lit.[10a] mp 85-86.4 °C); ^1H NMR (acetone-d_6) 8.72 (s, 2, OH), 6.52 (d, 2, J = 2.1), 6.33 (t, 1, J = 2.1). The ^1H NMR (acetone-d_6) spectral data are identical to the literature data.[10a]



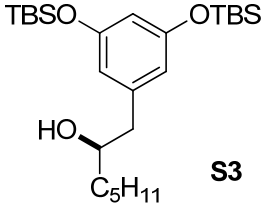
14

1-Bromo-3,5-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-benzene (14). A solution of **S1** (1.69 g, 8.94 mmol), imidazole (1.4 g, 20.6 mmol), and *tert*-butyldimethylsilyl chloride (2.83 g, 18.8 mmol) in anhydrous DMF (20 mL) was stirred under N_2 at 25 °C overnight. H_2O (20 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried ($MgSO_4$) and concentrated to yield 3.70 g of crude **14**. Flash chromatography on silica gel (hexanes) gave 3.50 g (94%) of **14** as a colorless liquid: ^{1}H NMR 6.63 (d, 2, J = 2.1), 6.25 (t, 1, J = 2.1), 0.97 (s, 18), 0.19 (s, 12); ^{13}C NMR 157.1 (2 C), 122.2, 116.9 (2 C), 111.1, 25.6 (6 C), 18.2 (2 C), -4.5 (4 C). After correction for improper referencing in the literature (TBS methyl group rather than TMS) our spectral data correspond to those reported.[11]



S2

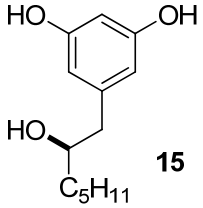
(2*R*)-(+)-2-Pentyloxirane (S2). To a mixture of (1*R*,2*R*)-(-)-*N*,*N*′-bis(3,5-di-*t*-butylsalicylidene)-1,2-cyclohexanediaminocobalt (II) (26 mg, 43 μmol, 0.005 equiv) and (±)-2-pentyloxirane (1.2 mL, 8.8 mmol) was added AcOH (18 μL, 189 μmol, 0.02 equiv), THF (100 μL, 1.23 mmol), and H_2O (86 μL, 4.8 mmol, 0.55 equiv) at 0 °C. The orange suspension warmed to 25 °C and stirred for 24 h. Flash chromatography on silica gel (30:1 pentane/ether) gave 376 mg (38%) of (2*R*)-(+)-2-pentyloxirane (**S2**) as a colorless liquid: $[\alpha]_D^{22}$ +9.7 (*c* 1.92, $CHCl_3$); {lit.[3] for the enantiomer: $[\alpha]_D^{21}$ - 10.6 (*c* 0.99, $CHCl_3$)}; ^{1}H NMR 2.94-2.88 (m, 1), 2.75 (dd, 1, J = 4.9, 4.3), 2.47 (dd, 1, J = 4.9, 2.4), 1.57-1.40 (m, 4), 1.39-1.27 (m, 4), 0.90 (t, 3, J = 6.7). The ^{1}H NMR spectral data are identical to the literature data.[3]



S3

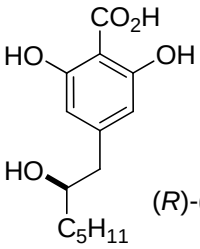
(α*R*)-3,5-Bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-α-pentylbenzeneethanol (S3). Bromobenzene **14** (427 mg, 1.02 mmol) in a flask was flame-dried under vacuum and dry THF (5 mL) was added. To the above solution was added *t*-BuLi (1.5 mL, 1.5 M in pentane, 2.25 mmol) over 5 min under N_2 at -78 °C and the solution was stirred at -78 °C for 30 min. (*R*)-

(+)-2-pentyloxirane (140 mg, 1.23 mmol) was added dropwise at -78 °C and the solution was stirred at -78 °C for 30 min and at -25 °C for 18 h. The resulting solution was warmed to 25 °C and quenched with saturated NH_4Cl (5 mL). The phases were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to yield 459.7 mg of crude **S3**. Flash chromatography on silica gel (80:1 to 30:1 hexanes/EtOAc) gave 340.7 mg (74%) of **S3** as a colorless liquid: $[\alpha]_D^{22}$ -4.7 (*c* 2.65, $CHCl_3$); ^{1}H NMR 6.33 (s, 2), 6.22 (s, 1), 3.79-3.70 (m, 1), 2.70 (dd, 1, *J* = 13.4, 4.3), 2.52 (dd, 1, *J* = 13.4, 7.9), 1.55 (d, 1, *J* = 3.7, OH), 1.54-1.21 (m, 8), 0.97 (s, 18), 0.89 (t, 3, *J* = 6.7), 0.19 (s, 12); ^{13}C NMR 156.6 (2 C), 140.4, 114.5 (2 C), 110.3, 72.5, 44.1, 36.6, 31.9, 25.7 (6 C), 25.4, 22.6, 18.2 (2 C), 14.1, -4.4 (4 C); IR (neat) 3373, 2957, 2931, 2859, 1588; HRMS (EI) calcd for $C_{25}H_{48}O_3Si_2$ (M^+) 452.3142, found 452.3142.



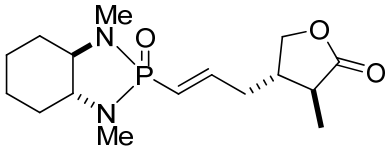
15

5-(2*R*)-2-Hydroxyheptyl-1,3-benzenediol (15). A solution of **S3** (892.2 mg, 1.97 mmol) in EtOH (25 mL) was treated with KOH (441 mg, 7.88 mmol) under N_2. The solution was heated at 55 °C for 8 h. EtOH was evaporated under reduced pressure and brine (10 mL) was added. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to yield 622 mg of crude **15**. Flash chromatography on silica gel (3:2 hexanes/EtOAc) gave 352.1 mg (80%) of pure **15**: mp 142-143 °C (lit.[3] mp 141.2-142.3 °C); $[\alpha]_D^{22}$ +4.1 (*c* 2.20, EtOH); {lit.[3] $[\alpha]_D^{21}$ +4.3 (*c* 2.21, EtOH)}; ^{1}H NMR (acetone-d_6) 8.09 (s, 2, OH), 6.22 (s, 2), 6.19 (s, 1), 3.77-3.68 (m, 1), 3.43 (d, 1, *J* = 4.9, OH), 2.56 (dd, 1, *J* = 13.4, 6.7), 2.54 (dd, 1, *J* = 13.4, 6.1), 1.55-1.20 (m, 8), 0.87 (t, 3, *J* = 7.0). The ^{1}H NMR (acetone-d_6) spectral data are identical to the literature data.[3]



(*R*)-(-)-**3**

2,6-Dihydroxy-4-[(2*R*)-2-hydroxyheptyl]-benzoic Acid ((*R*)-(–)-3). A mixture of **15** (60 mg, 267 μmol) and $KHCO_3$ (133 mg, 1.33 mmol) in dry glycerol (0.21 mL) was stirred under CO_2 (1 atm) at 150 °C for 5 h. After cooling, H_2O (6.7 mL) and $KHCO_3$ (645 mg) were added and the mixture was extracted with ether (3 × 6.7 mL). The aqueous layer was acidified with 10% HCl to pH 1 and extracted with EtOAc (3 × 11 mL). The combined EtOAc layers were washed with brine (3 × 6.7 mL), dried ($MgSO_4$), and concentrated to yield 42.1 mg (59%) of pure (*R*)-(–)-**3**. mp 127-129 °C (lit.[3] mp 127-130 °C); $[\alpha]_D^{22}$ –8.3 (*c* 1.29, EtOH); {lit.[3] $[\alpha]_D^{21}$ –8.4 (*c* 1.02, EtOH)}; ^{1}H NMR (acetone-d_6) 7.50-6.60 (br, 2, OH), 6.35 (s, 2), 3.84-3.75 (m, 1), 2.64 (dd, 1, *J* = 13.4, 5.5), 2.60 (dd, 1, *J* = 13.4, 7.3), 1.57-1.19 (m, 8), 0.87 (t, 3, *J* = 6.7). The ^{1}H NMR (acetone-d_6) spectral data are identical to the literature data. [3]

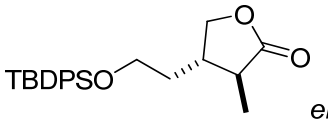


ent-**17**

(3*S*,4*S*)-Dihydro-4-[(2*E*)-3-[[(3a*R*,7a*R*)-octahydro-1,3-dimethyl-2-oxido-1*H*-1,3,2-benzodiazaphosphol-1-yl]phosphinyl]-2-propen-1-yl]-3-methyl-2(3*H*)-furanone (*ent*-17). To a solution of (*R*,*R*)-allyl phophonamide *ent*-**16**[14] (400 mg, 1.75 mmol) in THF (12 mL) was added *n*-BuLi (1.32 mL, 1.6 M in hexane, 2.11 mmol) by syringe over 5 min at -100 °C under N_2. The solution was stirred at this temperature for 10 min and at -78 °C for another 10 min. The solution was recooled to -100 °C and 2-butenolide (156 μL, 2.11mmol) was added dropwise. The mixture was stirred at -100 °C for 10 min and -78 °C for another 30 min. MeI (0.8 mL, 12.4 mmol) was added over 5 min at -78 °C. The solution was stirred from -78 to 25 °C for 4 h and quenched with saturated NH_4Cl (10 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried ($MgSO_4$)

and concentrated to yield 580 mg of crude *ent*-**17**. Flash chromatography on silica gel (100:5:1 EtOAc/MeOH/Et_3N) gave 415 mg (73%) of *ent*-**17** with >95:5 diastereoselectivity as determined by ^{1}H NMR spectroscopy: $[\alpha]_D^{22}$ – 29.6 (*c* 2.01, $CHCl_3$); ^{1}H NMR 6.72-6.57 (m, 1), 5.58 (dd, 1, *J* = 16.8, 20.5), 4.40 (dd, 1, *J* = 6.7, 9.1), 3.84 (dd, 1, *J* = 8.0, 9.1), 2.81-2.72 (m, 1), 2.63-2.23 (m, 5), 2.51 (d, 3, *J* = 12.2), 2.48 (d, 3, *J* = 12.2), 2.08-1.79 (m, 4), 1.41-1.20 (m, 3), 1.29 (d, 3, *J* = 6.7), 1.41-1.03 (m,1); ^{13}C NMR 179.0, 148.2 (d, *J* = 3.1), 123.0 (d, *J* = 151), 70.5, 64.5 (d, *J* = 7.6), 63.6 (d, *J* = 5.3), 42.3, 39.9, 36.2 (d, *J* = 19.8), 28.62-28.47 (2 C doublets), 28.0, 27.9, 24.1, 24.0, 14.0; IR (neat) 3445, 2935, 1777, 1770, 1633; HRMS (ES) calcd for $C_{16}H_{28}N_2O_3P$ (MH^+) 327.1838, found 327.1842.

An identical reaction with (*S*,*S*)-allyl phosphonamide **16** afforded **17**.



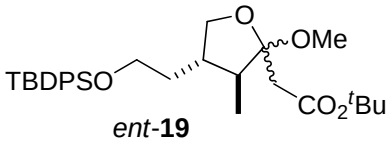
ent-**18**

(3*S*,4*S*)-Dihydro-4-[2-[(1,1-dimethylethyl)diphenylsilyloxy]ethyl]-3-methyl-2(3*H*)-furanone (*ent*-18). Ozone was bubbled through a solution of *ent*-**17** (830 mg, 2.55 mmol) in MeOH/CH_2Cl_2 (1:1, 50 mL) at -78 °C for a period of 20 min until the appearance of a persistent blue color. The excess ozone was replaced with oxygen (10 min) followed by nitrogen (30 min). $NaBH_4$ (670 mg, 17.2 mmol) was added and the solution was stirred from -78 to 25 °C for 3 h. The solvents were evaporated under reduced pressure at 25 °C and water (10 mL) was added to the residue. The aqueous solution was acidified with 10% HCl, saturated with solid NaCl, and extracted with CH_2Cl_2 (4 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to yield 445 mg of crude alcohol without further purification.

A solution of the above crude alcohol, imidazole (274 mg, 4.02 mmol), and TBDPSCl (0.97 mL, 3.79 mmol) in CH_2Cl_2 (25 mL) was stirred at 25 °C for 12 h under N_2. Saturated NH_4Cl (10 mL) and H_2O (10 mL) were added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (15:1 hexanes/EtOAc) 510.6 mg (52%) of *ent*-**18** as a colorless oil: $[\alpha]_D^{22}$ – 15.5 (*c* 2.73, $CHCl_3$); ^{1}H

NMR 7.64 (d, 4, *J* = 7.3), 7.47-7.36 (m, 6), 4.43 (dd, 1, *J* = 9.1, 7.9), 3.85 (dd, 1, *J* = 9.1, 8.1), 3.74-3.64 (m, 2), 2.34-2.22 (m, 1), 2.27-2.14 (m, 1), 1.90-1.80 (m, 1), 1.65-1.55 (m, 1), 1.23 (d, 3, *J* = 6.7), 1.06 (s, 9); ^{13}C NMR 179.5, 135.4 (4 C), 133.2, 133.1, 129.80, 129.78, 127.7 (4 C), 72.0, 62.0, 41.9, 40.2, 34.6, 26.8 (3 C), 19.0, 13.7; IR (neat) 2933, 2859, 1779; HRMS (Q-tof) calcd for $C_{23}H_{30}O_3SiNa$ (MNa^+) 405.1862, found 405.1871.

An identical reaction with **17** afforded **18**.



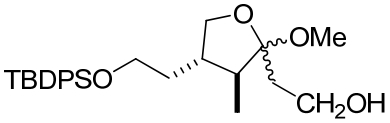
ent-**19**

1,1-Dimethylethyl (3*S*,4*S*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-tetrahydro-2-methoxyl-3-methyl-2-furanacetate (*ent*-19). To a solution of *tert*-butyl acetate (258 μL, 1.91 mmol) in THF (6 mL) was added LHMDS (1.90 mL, 1 M in THF, 1.90 mmol) over 5 min at -78 °C under N_2. The solution was stirred for 1 h at this temperature and a solution of *ent*-**18** (122.2 mg, 0.32 mmol) in THF (3 mL) was added dropwise by cannula to the reaction mixture. The reaction was stirred from -78 to 25 °C for 3 h and quenched with saturated NH_4Cl (8 mL). The two layers were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give 195.4 mg of crude adducts.

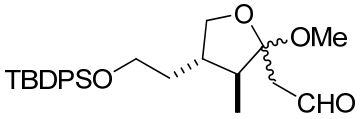
A solution of the crude adducts in anhydrous MeOH (12 mL) was treated with Dowex 50WX8-400-H^+ ion exchange resin (18 mg) at 25 °C. The reaction was stirred at 25 °C for 12 h. The reaction mixture was filtered through Celite to remove the catalyst and the filtrate was concentrated at 25 °C to give 137.6 mg of crude *ent*-**19**. Flash chromatography on MeOH-deactivated silica gel (50:1 hexanes/EtOAc) gave 128.3 mg (78%) of 90% pure *ent*-**19** (mainly one diastereomer of unknown stereochemistry at the ketal carbon) as a colorless oil: $[\alpha]_D^{22}$ – 36.2 (*c* 2.20, $CHCl_3$); ^{1}H NMR 7.65 (d, 4, *J* = 6.7), 7.46-7.34 (m, 6), 3.97 (dd, 1, *J* = 8.5, 7.9), 3.69-3.56 (m, 2), 3.49 (dd, 1, *J* = 8.5, 8.5), 3.23 (s, 3), 2.65 (d, 1, *J* = 13.4), 2.58 (d, 1, *J* = 13.4), 2.14-2.02 (m, 1), 2.02-1.91 (m, 1), 1.87-1.76 (m, 1), 1.48-1.38 (m, 1), 1.45 (s, 9), 1.04 (s, 9), 0.99

(d, 3, J = 6.7); ^{13}C NMR 169.0, 135.5 (4 C), 133.7, 133.6, 129.6 (2 C), 127.6 (4 C), 106.3, 80.5, 72.9, 63.2, 48.4, 47.1, 42.1, 39.6, 35.7, 28.0 (3 C), 26.8 (3 C), 19.1, 11.5; IR (neat) 2931, 2856, 1728; HRMS (Q-tof) calcd for $C_{29}H_{41}O_4Si$ (M^+-OCH_3) 481.2774, found 481.2758.

An identical reaction with **18** afforded **19**.



ent-**20**



ent-**21**

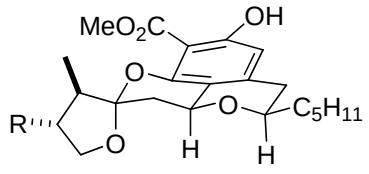
(3*S*,4*S*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-tetrahydro-2-methoxyl-3-methyl-2-furanethanol (*ent*-20) and (3*S*,4*S*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-tetrahydro-2-methoxyl-3-methyl-2-furanacetaldehyde (*ent*-21). DIBAL-H (0.82 mL, 1 M in hexane, 0.82 mmol) was added dropwise to a solution of *ent*-**19** (102.3 mg, 0.2 mmol) in ether (6 mL) at -78 °C under N_2. The reaction mixture was stirred at -78 °C for 1.5 h. The reaction was quenched with saturated Rochelle salt solution (8 mL) and allowed to warm to 25 °C. The resulting mixture was stirred at 25 °C for 1 h until clear separation of two layers was observed and extracted with ether (3 × 8 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated at 25 °C to give 84.7 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (30:1 to 5:1 hexanes/EtOAc) gave 37.8 mg (43%) of aldehyde *ent*-**21** followed by 34.4 mg (39%) of alcohol *ent*-**20**.

Data for *ent*-**21**: $[\alpha]_D^{22}$ – 74.7 (*c* 2.13, $CHCl_3$); ^{1}H NMR 9.69 (dd, 1, J = 3.7, 2.4), 7.65 (d, 4, J = 6.7), 7.47-7.33 (m, 6), 4.04 (dd, 1, J = 8.5, 8.5), 3.68-3.57 (m, 2), 3.55 (dd, 1, J = 8.5, 8.5), 3.26 (s, 3), 2.85 (dd, 1, J = 14.7, 2.4), 2.59 (dd, 1, J = 14.7, 3.7), 2.10-2.08 (m, 1), 1.84-1.74 (m, 1), 1.63-1.52 (m, 1), 1.48-1.37 (m, 1), 1.05 (s, 9), 0.98 (d, 3, J = 6.7); ^{13}C NMR 201.0, 135.5 (4 C), 133.6, 133.5, 129.6 (2 C), 127.7 (4 C), 106.0, 73.1, 63.1, 48.6, 48.5, 46.5, 41.9, 35.6, 26.8 (3 C), 19.1, 11.2; IR (neat) 2933, 2858, 1724; HRMS (Q-tof) calcd for $C_{26}H_{36}O_4SiNa$ (MNa^+) 463.2281, found 463.2270.

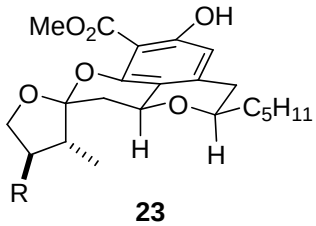
Data for *ent*-**20**: $[\alpha]_D^{22}$ – 51.0 (*c* 0.98, $CHCl_3$); ^{1}H NMR 7.65 (dd, 4, *J* =7.9, 1.8), 7.46-7.36 (m, 6), 3.99 (dd, 1, *J* = 8.5, 8.5), 3.73-3.59 (m, 4), 3.53 (dd, 1, *J* = 8.5, 8.5), 3.23 (s, 3), 2.96 (dd, 1, *J* = 7.3, 3.7, OH), 2.18-2.07 (m, 2), 1.86-1.67 (m, 3), 1.50-1.40 (m, 1), 1.05 (s, 9), 0.97 (d, 3, *J* = 6.7); ^{13}C NMR 135.5 (4 C), 133.65, 133.58, 129.6 (2 C), 127.7 (4 C), 109.1, 72.8, 63.2, 58.8, 48.3, 46.2, 41.9, 35.8, 33.5, 26.8 (3 C), 19.1, 11.6; IR (neat) 2931, 2856, 1728; HRMS (Q-tof) calcd for $C_{26}H_{38}O_4NaSi$ (MNa^+) 465.2437, found 465.2413.

An identical reaction with **19** afforded **21** and **20**.

Oxidation of *ent*-20 to Give *ent*-21. To a solution of oxalyl chloride (59 μL, 679 μmol) in dry CH_2Cl_2 (2 mL) was added a solution of DMSO (79 μL, 1.13 mmol) dropwise under N_2 at -78 °C. After 15 min, alcohol *ent*-**20** (100 mg, 226 μmol) in CH_2Cl_2 (2 mL) was added dropwise and the solution was stirred at -78 °C for 1 h. NEt_3 (0.47 mL, 226 μmol) was added dropwise and the solution was stirred at -78 °C for 2 h and warmed to -30 °C over a period of 1 h. The reaction mixture was quenched with 5% aqueous $NaHSO_3$ (6 mL) and warmed to 25 °C. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 6 mL). The combined organic layers were dried (Na_2SO_4) and concentrated at 25 °C. Flash chromatography on MeOH-deactivated silica gel (30:1 hexanes/EtOAc) gave 52.0 mg (52%) of aldehyde *ent*-**21**.

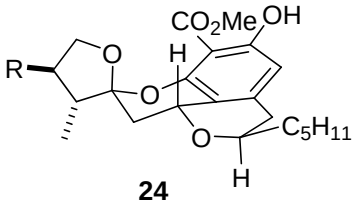


22

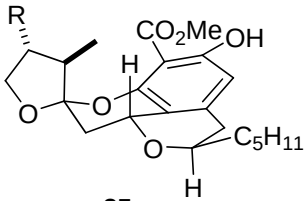


23

R = TBDPSO(CH$_2$)$_2$



24



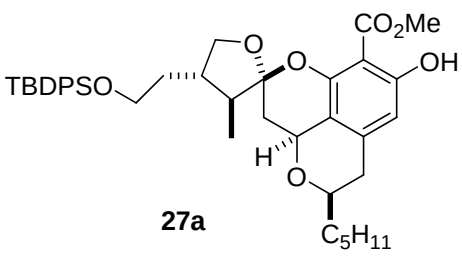
25

Methyl (2*S*,3*R*,3'a*S*,4*R*,5'*R*)-, (2*R*,3*R*,3'a*S*,4*R*,5'*R*)-, (2*R*,3*R*,3'a*R*,4*R*,5'*R*)-, and (2*S*,3*R*,3'a*R*,4*R*,5'*R*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-3',3'a,4,5,5',6'-hexahydro-8'-hydroxy-3-methyl-5'-pentyl-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (22, 23, 24, and 25, respectively). A solution of freshly prepared acid (*R*)-(–)-**3** (31.5 mg, 118 μmol) and freshly prepared ketal aldehyde **21** (40.4 mg, 92 μmol) was treated with Dowex 50WX8-400-H^+ ion exchange resin (30 mg) at 25 °C and stirred at 25 °C for 12 h. The reaction mixture was filtered through Celite to remove the catalyst and the filtrate was concentrated to give crude product.

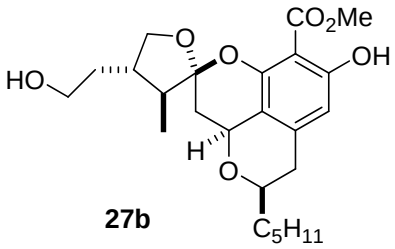
An ether solution (2 mL) of diazomethane (0.67 mmol) was added dropwise to an ether solution (2 mL) of the crude product at 25 °C. The resulting solution was stirred at 25 °C for 20 min and carefully concentrated to give crude tetracyclic diastereomers. Flash chromatography on silica gel (50:1 to 20:1 hexanes/EtOAc) gave 35.3 mg (57%) of a 4:1:3:0 mixture of **22**, **23**, **24**, and **25** as determined by integration of H-15 at δ 4.75 (dd, 1, *J* = 12.2, 5.2), 4.55 (dd, 1, *J* = 12.0, 5.6), and 4.85 (dd, 1, *J* = 11.3, 6.4), respectively. The structures were tentatively assigned by analogy to the peaks for **9-12** at δ 4.77 (dd, 1, *J* = 12.2, 5.4), 4.57 (dd, 1, *J* = 12.2, 5.3), 4.85 (dd, 1, *J* = 11.4, 6.5), and 4.68 (dd, 1, *J* = 10.3, 6.3).

TFA (2 μL) was added to a $CDCl_3$ solution (1 mL) of the above mixture. The reaction was stirred at 25 °C for 20 h and concentrated under reduced pressure. Flash chromatography on silica gel (30:1 hexanes/EtOAc) gave a 2:trace:1:0 mixture of **22-25**. The early fraction contained pure **22**.

Data for **22**: ^{1}H NMR 11.4 (s, 1, OH), 7.66 (d, 4, *J* = 6.3), 7.48-7.33 (m, 6), 6.32 (s, 1, H-4), 4.75 (dd, 1, *J* = 12.2, 5.2, H-15), 4.14 (dd, 1, *J* = 7.8, 7.8, H-26), 3.86 (s, 3, OMe), 3.84-3.77 (m, 1, H-9), 3.69 (dd, 1, *J* = 7.8, 7.8, H-26), 3.72-3.64 (m, 2, 2 H-21), 2.77 (dd, 1, *J* = 17.7, 4.3, H-8), 2.61 (dd, 1, *J* = 17.7, 11.0, H-8), 2.24 (dd, 1, *J* = 12.2, 5.2, H-16), 2.28-2.20 (m, 1, H-18), 2.04-1.86 (m, 3, 2 H-20, H-19), 1.81 (dd, 1, *J* = 12.2, 12.2, H-16), 1.68-1.60 (m, 1), 1.58-1.46 (m, 2), 1.45-1.26 (m, 5), 1.05 (s, 9), 1.05 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.7, 3 H-14).



27a



27b

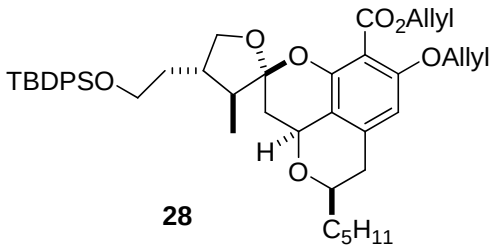
Methyl (2*S*,3*S*,3'a*S*,4*S*,5'*R*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-3',3'a,4,5,5',6'-hexahydro-8'-hydroxy-3-methyl-5'-pentyl-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (27a) and Methyl (2*S*,3*S*,3'a*S*,4*S*,5'*R*)-3',3'a,4,5,5',6'-Hexahydro-8'-hydroxy-4-[2-hydroxyethyl]-3-methyl-5'-pentyl-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (27b). A solution of freshly prepared acid (*R*)-(–)-**3** (37.8 mg, 141 μmol) and freshly prepared ketal aldehyde *ent*-**21** (48.0 mg, 109 μmol) was treated with Dowex 50WX8-400-H^+ ion exchange resin (25 mg) at 25 °C and stirred at 25 °C for 60 h. The reaction mixture was filtered through Celite to remove the catalyst and the filtrate was concentrated to give 79.1 mg of crude product.

An ether solution (2 mL) of diazomethane (0.67 mmol) was added dropwise to an ether solution (2 mL) of the 79 mg of crude product at 25 °C. The resulting solution was stirred at 25 °C for 20 min and carefully concentrated to give crude ester. Flash chromatography on silica gel (50:1 to 2:1 hexanes/EtOAc) gave 22.1 mg (30%) of **27a** followed by 10.6 mg (22%) of **27b**.

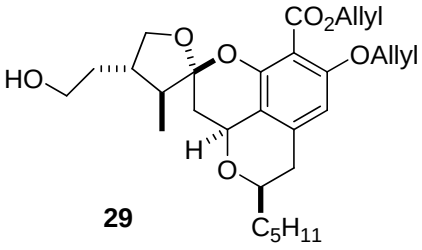
Data for **27a**: $[\alpha]_D^{22}$ –64.6 (*c* 1.11, $CHCl_3$); ^{1}H NMR 11.4 (s, 1, OH), 7.66 (d, 4, *J* = 7.8), 7.48-7.33 (m, 6), 6.31 (s, 1, H-4), 4.76 (dd, 1, *J* = 12.2, 5.4, H-15), 4.25 (dd, 1, *J* = 8.5, 8.5, H-26), 3.83-3.76 (m, 1, H-9), 3.82 (s, 3, OMe), 3.73-3.64 (m, 2, 2 H-21), 3.55 (dd, 1, *J* = 8.5, 8.5, H-26), 2.76 (dd, 1, *J* = 17.6, 3.9, H-8), 2.60 (dd, 1, *J* = 17.6, 10.7, H-8), 2.45-2.33 (m, 1, H-19), 2.16 (dd, 1, *J* = 12.2, 5.4, H-16), 1.95 (dd, 1, *J* = 12.2, 12.2, H-16), 1.95-1.87 (m, 1, H-20), 1.73 (dq, 1, *J* = 10.5, 6.7, H-18), 1.68-1.60 (m, 1, H-10), 1.58-1.46 (m, 3), 1.44-1.24 (m, 5), 1.06 (d, 3, *J* = 6.7, 3 H-25), 1.055 (s, 9), 0.90 (t, 3, *J* = 6.6); ^{13}C NMR 171.6, 162.1, 152.1, 141.3, 135.5 (4 C), 133.5 (2 C), 129.71, 129.69, 127.7 (4 C), 112.7, 108.9, 108.3, 99.9, 75.1, 73.5, 68.2, 63.2, 52.0, 49.0, 41.6, 36.3, 35.5, 34.5, 34.0, 31.8, 26.8 (3 C), 25.1, 22.6, 19.1, 14.0, 11.7; IR (neat)

3398, 2957, 2932, 2859, 1660; HRMS (EI) calcd for $C_{40}H_{52}O_7Si$ (M^+) 672.3482, found 672.3480.

Data for **27b**: $[\alpha]_D^{22}$ – 98.7 (*c* 0.53, $CHCl_3$); ^{1}H NMR 11.4 (s, 1, OH), 6.31 (s, 1, H-4), 4.76 (dd, 1, *J* = 12.2, 5.4, H-15), 4.25 (dd, 1, *J* = 8.5, 8.5, H-26), 3.91 (s, 3, OMe), 3.85-3.77 (m, 1, H-9), 3.72 (t, 2, *J* = 6.1, 2 H-21), 3.63 (dd, 1, *J* = 8.5, 8.5, H-26), 2.76 (dd, 1, *J* = 17.6, 3.9, H-8), 2.60 (dd, 1, *J* = 17.6, 10.7, H-8), 2.49-2.34 (m, 1, H-19), 2.18 (dd, 1, *J* = 12.2, 5.4, H-16), 1.96 (dd, 1, *J* = 12.2, 12.2, H-16), 1.99-1.90 (m, 1, H-20), 1.76 (dq, 1, *J* = 10.7, 6.3, H-18), 1.68-1.60 (m, 1, H-10), 1.60-1.46 (m, 3), 1.45-1.24 (m, 5), 1.09 (d, 3, *J* = 6.8, 3 H-25), 0.90 (t, 3, *J* = 6.6);^{13}C NMR 171.6, 162.1, 152.0, 141.3, 112.7, 109.1, 108.3, 99.9, 75.1, 73.1, 68.1, 61.9, 52.0, 48.9, 40.8, 36.3, 35.3, 34.5, 33.9, 31.8, 25.1, 22.6, 14.0, 11.7; IR (neat) 3406, 2953, 2933, 2860, 1660; HRMS (EI) calcd for $C_{24}H_{34}O_7$ (M^+) 434.2305, found 434.2305.



28



29

2-Propenyl (2*S*,3*S*,3'a*S*,4*S*,5'*R*)-4-[2-[(1,1-Dimethylethyl)diphenylsilyloxy]ethyl]-3',3'a,4,5,5',6'-hexahydro-3-methyl-5'-pentyl-8'-(2-propenyloxy)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (28) and 2-Propenyl (2*S*,3*S*,3'a*S*,4*S*,5'*R*)-3',3'a,4,5,5',6'-Hexahydro-4-[2-hydroxyethyl]-3-methyl-5'-pentyl-8'-(2-propenyloxy)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (29). A solution of freshly prepared acid (*R*)-(–)-**3** (42.0 mg, 157 μmol) and freshly prepared ketal aldehyde *ent*-**21** (43 mg, 97.7 μmol) was treated with Dowex 50WX8-400-H^+ ion exchange resin (23 mg) at 25 °C and the solution was stirred for 60 h. The reaction mixture was filtered through Celite to remove the catalyst and the filtrate was concentrated to give 78.8 mg of crude product.

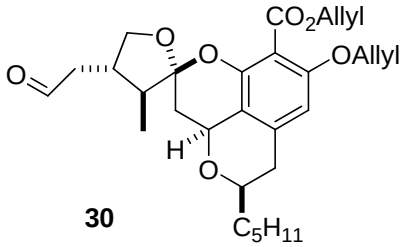
To a suspension of the above crude product and K_2CO_3 (108 mg, 784 μmol) in DMF (2 mL) was added allyl bromide (102 μL, 1.18 mmol) under N_2 at 25 °C. The reaction mixture

was stirred at 25 °C for 12 h. H_2O (4 mL) was added and the mixture was extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (30:1 to 2:1 hexanes/EtOAc) gave 23.1 mg (32%) of **28** followed by 10.0 mg (20%) of **29**.

Data for **28**: $[\alpha]_D^{22}$ –60.0 (*c* 2.31, $CHCl_3$); ^{1}H NMR 7.66 (d, 4, *J* = 6.7), 7.47-7.34 (m, 6), 6.23 (s, 1, H-4), 6.02-5.90 (m, 2), 5.36 (br d, 1, *J* = 17.7), 5.33 (br d, 1, *J* = 17.1), 5.22 (br d, 1, *J* = 10.4), 5.15 (br d, 1, *J* = 10.4), 4.84-4.65 (m, 2, H-15), 4.71 (dd, 1, *J* = 12.3, 5.2), 4.51 (d, 2, *J* = 4.9), 4.20 (dd, 1, *J* = 8.5, 8.5, H-26), 3.83-3.78 (m, 1, H-9), 3.72-3.60 (m, 2, 2 H-21), 3.62 (dd, 1, *J* = 8.5, 8.5, H-26), 2.75 (dd, 1, *J* = 17.1, 3.7, H-8), 2.60 (dd, 1, *J* = 17.1, 10.7, H-8), 2.30-2.18 (m, 1, H-19), 2.15 (dd, 1, *J* = 12.2, 4.9, H-16), 1.97 (dd, 1, *J* = 12.2, 12.2, H-16), 1.89-1.80 (m, 1, H-20), 1.73-1.59 (m, 2, H-18, H-10), 1.58-1.46 (m, 3), 1.43-1.25 (m, 5), 1.05 (s, 9), 1.01 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.4); ^{13}C NMR 165.5, 155.5, 149.0, 135.8, 135.5 (4 C), 133.55, 133.52, 132.9, 132.3, 129.7 (2 C), 127.7 (4 C), 118.1, 117.1, 114.6, 109.6, 108.7, 104.2, 75.3, 73.3, 69.4, 68.1, 65.6, 63.2, 49.0, 41.3, 36.3, 35.6, 34.5, 34.4, 31.8, 26.8 (3 C), 25.1, 22.6, 19.1, 14.0, 11.6; IR (neat) 2957, 2932, 2859, 1739, 1732; HRMS (EI) calcd for $C_{45}H_{58}O_7Si$ (M^+) 738.3952, found 738.3953.

Data for **29**: $[\alpha]_D^{22}$ –88.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR 6.23 (s, 1, H-4), 6.06-5.92 (m, 2), 5.39 (br d, 1, *J* = 17.1), 5.36 (br d, 1, *J* = 17.1), 5.24 (br d, 1, *J* = 9.8), 5.23 (br d, 1, *J* = 10.4), 4.86-4.76 (m, 2, H-15), 4.74 (dd, 1, *J* = 13.4, 5.5), 4.51 (d, 2, *J* = 4.9), 4.20 (dd, 1, *J* = 8.2, 8.2, H-26), 3.86-3.77 (m, 1, H-9), 3.72-3.58 (m, 2, 2 H-21), 3.59 (dd, 1, *J* = 8.2, 8.2, H-26), 2.75 (dd, 1, *J* = 16.5, 4.0, H-8), 2.60 (dd, 1, *J* = 16.5, 11.0, H-8), 2.30-2.19 (m, 1, H-19), 2.16 (dd, 1, *J* = 12.2, 5.5, H-16), 1.97 (dd, 1, *J* = 12.2, 12.2, H-16), 1.92-1.85 (m, 1, H-20), 1.71 (dq, 1, *J* = 10.5, 6.7, H-18), 1.70-1.60 (m, 1, H-10), 1.58-1.46 (m, 3), 1.45-1.25 (m, 5), 1.03 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.7); ^{13}C NMR 165.6, 155.5, 149.0, 135.9, 132.9, 132.3, 118.1, 117.1, 114.6, 109.5, 108.8, 104.3, 75.3, 72.9, 69.4, 68.1, 65.6, 61.8, 48.9, 40.6, 36.3, 35.7, 34.43, 34.40, 31.8, 25.1, 22.6, 14.0, 11.7; IR (neat) 3432, 2932, 2876, 1739, 1732, 1714; HRMS (EI) calcd for $C_{29}H_{40}O_7$ (M^+) 500.2774, found 500.2769.

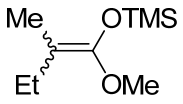
Deprotection of 28. To a solution of **28** (64.7 mg, 88 μmol) in THF (4 mL) was added TBAF (350 μL, 1 M in THF, 350 μmol) and AcOH (20 μL, 350 μmol). The solution was stirred at 25 °C for 12 h. The mixture was concentrated under reduced pressure at 25 °C. The residue was treated with brine (4 mL) and 45 drops of saturated $NaHCO_3$ to adjust the pH to 7 and the aqueous layer was extracted with distilled ether (6 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated to yield 73.6 mg of crude **29**. Flash chromatography on silica gel (2:1 hexanes/EtOAc) gave 37.7 mg (86%) of pure **29**.



30

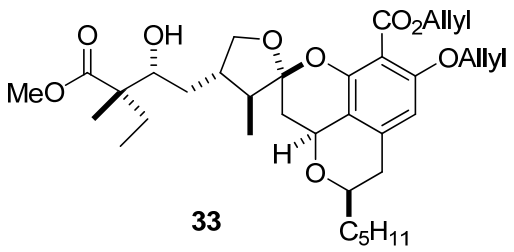
2-Propenyl (2*S*,3*S*,3'a*S*,4*S*,5'*R*)-3',3'a,4,5,5',6'-Hexahydro-3-methyl-4-[2-oxoethyl]-5'-pentyl-8'-(2-propenyloxy)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-9'-carboxylate (30). Dess-Martin periodinane (178 mg, 0.42 mmol) was added to a solution of alcohol **29** (105 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The suspension was allowed to warm to 25 °C and continued to stir for 1 h. The solvent was removed under reduced pressure at 25 °C. Flash chromatography on MeOH-deactivated silica gel (5:1 hexanes/EtOAc) gave 92.4 mg (88%) of pure **30**: $[\alpha]_D^{22}$ –103.9 (*c* 0.18, $CHCl_3$); ^{1}H NMR 9.81 (s, 1), 6.24 (s, 1, H-4), 6.08-5.92 (m, 2), 5.40 (br d, 1, *J* = 16.5), 5.36 (br d, 1, *J* = 15.9), 5.26 (br d, 1, *J* = 11.6), 5.23 (br d, 1, *J* = 11.0), 4.85 (dd, 1, *J* = 13.3, 6.1), 4.80 (dd, 1, *J* = 12.2, 5.5, H-15), 4.74 (dd, 1, *J* = 13.3, 5.8), 4.52 (d, 2, *J* = 4.9), 4.35 (dd, 1, *J* = 8.5, 8.5, H-26), 3.88-3.78 (m, 1, H-9), 3.51 (dd, 1, *J* = 8.5, 8.5, H-26), 2.80 (dd, 1, *J* = 17.7, 3.7, H-20), 2.75 (dd, 1, *J* = 16.5, 4.3, H-8), 2.61 (dd, 1, *J* = 16.5, 11.0, H-8), 2.66-2.57 (m, 1, H-19), 2.43 (dd, 1, *J* = 17.7, 9.8, H-20), 2.16 (dd, 1, *J* = 12.2, 5.5, H-16), 1.96 (dd, 1, *J* = 12.2, 12.2, H-16), 1.73 (dq, 1, *J* = 10.4, 6.7, H-18), 1.71-1.60 (m, 1, H-10), 1.58-1.46 (m, 2), 1.45-1.24 (m, 5), 1.04 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.7); ^{13}C NMR 200.5, 165.5, 155.6, 148.8, 135.9, 132.9, 132.3, 118.4, 117.2, 114.5, 109.6, 108.4, 104.5,

75.3, 72.2, 69.4, 68.0, 65.7, 48.5, 47.3, 37.6, 36.3, 34.4, 34.3, 31.8, 25.1, 22.6, 14.0, 11.5; IR (neat) 2957, 2932, 2860, 1738, 1732, 1716; HRMS (EI) calcd for $C_{29}H_{38}O_7$ (M^+) 498.2618, found 498.2611.

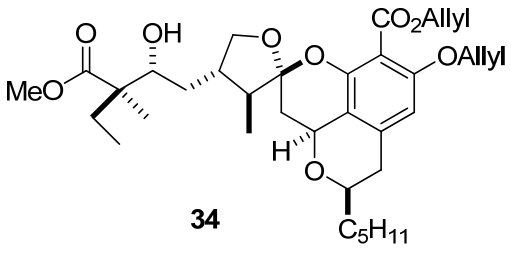


31

1-Methoxy-1-trimethylsiloxy-2-methyl-1-butene (31) was prepared by the literature procedure.[17] *n*-BuLi (12.6 mL, 1.6 M in hexane, 20 mmol) was added dropwise to a solution of diisopropylamine (2.82 mL, 20 mmol) in THF (15 mL) under N_2 at 0 °C. The resulting solution was stirred at 0 °C for 30 min and cooled to -78 °C. A solution of methyl 2-methylbutanoate (2.64 mL, 20 mmol) in THF (6 mL) was added dropwise to the reaction mixture and the reaction was stirred at -78 °C for 1 h. TMSCl (3 mL, 24 mmol) was added dropwise to the reaction mixture and the reaction was slowly warmed up to 25 °C over 3 h. The reaction was quenched with ice water (20 mL). The two layers were separated and the aqueous layer was extracted with hexanes (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated at 25 °C. The crude oil was purified by distillation (bp 95-97 °C/35 torr) to give 2.78 g (74%, 7:3 mixture of isomers) of **31** as a colorless oil: ^{1}H NMR 3.50 (s, 3), 1.99 (q, 0.3 × 2, J = 7.6), 1.94 (q, 0.7 × 2, J = 7.6), 1.55 (s, 0.7 × 3), 1.51 (s, 0.3 × 3), 0.94 (q, 0.3 × 2, J = 7.6), 0.93 (q, 0.7 × 2, J = 7.6), 0.208 (s, 0.3 × 3), 0.203 (s, 0.7 × 3). The ^{1}H NMR spectral data are identical to the literature data.[17]



33



34

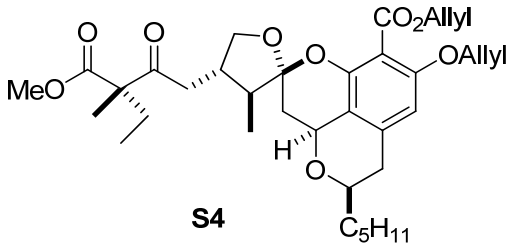
**Methyl (α*S*,β*R*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)- and (α*R*,β*R*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)- α,3-Dimethyl-α-ethyl-3',3'a,4,5,5',6'-hexahydro-β-hydroxyl-3-methyl-5'-pentyl-8'-(2-propenyloxy)-9'-(2-propenyloxycarbonyl)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-4-

butanoate (33 and 34). To a solution of *N*-Ts-(*S*)-valine (84 mg, 0.31 mmol)[19] in dry CH_2Cl_2 (2 mL) was added BH_3•THF (0.31 mL, 1 M solution in THF, 0.31 mmol) by syringe over 3 min under N_2 at 0 °C. The solution was stirred for 30 min at 0 °C and additionally for 30 min at 25 °C. The solution was cooled -78 °C and a solution of aldehyde **30** (44.0 mg, 88.4 μmol) in CH_2Cl_2 (0.5 mL) was added dropwise over 3 min. After stirring for 5 min, silyl ketene acetal **31** (49 mg, 0.31 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise over 3 min. The reaction mixture was stirred for 4 h at -78 °C and quenched with 1 M aqueous HCl (4 mL). The mixture was allowed to warm to 25 °C and the aqueous layer was extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 × 10 mL), dried ($MgSO_4$) and concentrated to yield 71.6 mg of crude aldol product. Preparative TLC (4:1 hexanes/EtOAc, developed four times) gave 21.5 mg (40%) of **33** followed with 21.9 mg (40%) of **34**.

Data for **33**: $[\alpha]_D^{22}$ –95.0 (*c* 0.22, $CHCl_3$); ^{1}H NMR 6.23 (s, 1, H-4), 6.07-5.92 (m, 2), 5.40 (br d, 1, *J* = 17.1), 5.36 (br d, 1, *J* = 16.5), 5.25 (br d, 1, *J* = 9.8), 5.22 (br d, 1, *J* = 9.2), 4.86-4.72 (m, 3, H-15), 4.51 (d, 2, *J* = 4.9), 4.28 (dd, 1, *J* = 8.5, 8.5, H-26), 3.86-3.78 (m, 1, H-9), 3.77-3.69 (m, 1, H-21), 3.709 (s, 3, OMe), 3.65 (dd, 1, *J* = 8.5, 8.5, H-26), 2.75 (dd, 1, *J* = 17.1, 3.4, H-8), 2.60 (dd, 1, *J* = 17.1, 11.0, H-8), 2.27-2.20 (m, 1, H-19), 2.22 (d, 1, *J* = 6.1, OH), 2.14 (dd, 1, *J* = 12.2, 5.5, H-16), 1.96 (dd, 1, *J* = 12.2, 12.2, H-16), 1.80 (dq, 1, *J* = 13.4, 7.3), 1.71-1.60 (m, 3), 1.59-1.46 (m, 3), 1.45-1.24 (m, 6), 1.14 (s, 3, 3 H-27), 1.03 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.7), 0.87 (t, 3, *J* = 7.3); ^{13}C NMR 176.94, 165.66, 155.55, 149.09, 135.89, 132.96, 132.40, 118.17, 117.13, 114.65, 109.52, 108.52, 104.23, 76.22, 75.31, 73.87, 69.38, 68.11, 65.64, 51.79, 51.23, 49.04, 42.48, 36.32, 35.31, 34.55, 34.41, 31.79, 28.38, 25.14, 22.61, 16.75, 14.04, 11.87, 8.99; IR (neat) 3508, 2953, 2933, 2860, 1739, 1732, 1715; HRMS (EI) calcd for $C_{35}H_{50}O_9$ (M^+) 614.3455, found 614.3451.

Data for **34**: $[\alpha]_D^{22}$ –96.3 (*c* 0.22, $CHCl_3$); ^{1}H NMR 6.23 (s, 1, H-4), 6.07-5.92 (m, 2), 5.40 (br d, 1, *J* = 17.1), 5.36 (br d, 1, *J* = 16.5), 5.25 (br d, 1, *J* = 9.8), 5.22 (br d, 1, *J* = 9.2), 4.86-4.72 (m, 3, H-15), 4.51 (d, 2, *J* = 4.9), 4.31 (dd, 1, *J* = 8.5, 8.5, H-26), 3.86-3.77 (m, 1, H-9), 3.726 (s, 3, OMe), 3.74-3.68 (m, 1, H-21), 3.66 (dd, 1, *J* = 8.5, 8.5, H-26), 2.75 (dd, 1, *J* =

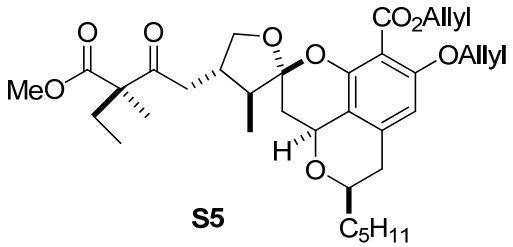
17.1, 3.4, H-8), 2.60 (dd, 1, *J* = 17.1, 11.0, H-8), 2.51 (d, 1, *J* = 7.3, OH), 2.30-2.21 (m, 1, H-19), 2.14 (dd, 1, *J* = 12.2, 4.9, H-16), 1.97 (dd, 1, *J* = 12.2, 12.2, H-16), 1.81-1.44 (m, 7), 1.43-1.17 (m, 6), 1.13 (s, 3, 3 H-27), 1.04 (d, 3, *J* = 6.1, 3 H-25), 0.90 (t, 3, *J* = 6.4), 0.85 (t, 3, *J* = 7.3); ^{13}C NMR 177.58, 165.63, 155.56, 149.10, 135.87, 132.96, 132.39, 118.11, 117.12, 114.64, 109.51, 108.43, 104.22, 75.49, 75.30, 74.00, 69.37, 68.11, 65.62, 51.86, 51.45, 49.07, 42.57, 36.31, 34.57, 34.49, 34.41, 31.78, 29.60, 25.13, 22.60, 16.94, 14.03, 11.87, 8.80; IR (neat) 3522, 2955, 2933, 2860, 1737, 1732, 1715; HRMS (EI) calcd for $C_{35}H_{50}O_9$ (M^+) 614.3455, found 614.3458.



S4

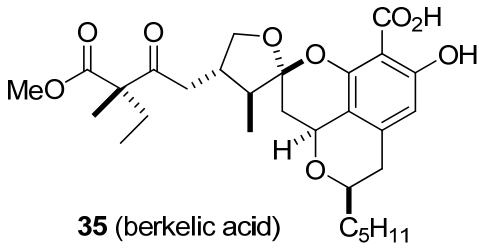
Methyl (α*S*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)-α,3-Dimethyl-α-ethyl-3',3'a,4,5,5',6'-hexahydro-3-methyl- β-oxo-5'-pentyl-8'-(2-propenyloxy)-9'-(2-propenyloxycarbonyl)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-4-butanoate (S4). The aldol product **33** (20 mg, 32.5 μmol) in CH_2Cl_2 (2 mL) was treated with Dess-Martin periodinane (28 mg, 66 μmol) at 0 °C. The suspension was allowed to warm to 25 °C and continued to stir for 12 h. The solvent was removed under reduced pressure at 25 °C. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 16.9 mg (85%) of **S4**: $[\alpha]_D^{22}$ –88.5 (*c* 0.73, $CHCl_3$); ^{1}H NMR 6.24 (s, 1, H-4), 6.08-5.92 (m, 2), 5.40 (br d, 1, *J* = 17.7), 5.36 (br d, 1, *J* = 17.1), 5.27 (br d, 1, *J* = 10.4), 5.23 (br d, 1, *J* = 10.4), 4.85 (dd, 1, *J* = 13.4, 6.1), 4.79 (dd, 1, *J* = 12.2, 5.5, H-15), 4.74 (dd, 1, *J* = 13.1, 5.8), 4.51 (d, 2, *J* = 4.9), 4.35 (dd, 1, *J* = 8.5, 8.5, H-26), 3.86-3.78 (m, 1, H-9), 3.74 (s, 3, OMe), 3.45 (dd, 1, *J* = 8.5, 8.5, H-26), 2.77 (dd, 1, *J* = 17.7, 3.4, H-20), 2.75 (dd, 1, *J* = 16.5, 3.7, H-8), 2.60 (dd, 1, *J* = 17.1, 11.0, H-8), 2.62-2.51 (m, 1, H-19), 2.43 (dd, 1, *J* = 17.7, 10.4, H-20), 2.14 (dd, 1, *J* = 12.2, 5.5, H-16), 1.96 (dd, 1, *J* = 12.2, 12.2, H-16), 2.02-1.91 (m, 1, H-23), 1.82 (dq, 1, *J* = 14.0, 7.3, H-23), 1.72-1.58 (m, 2), 1.58-1.46 (m, 2), 1.45-1.24 (m, 5), 1.33 (s, 3, H-27), 1.01 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.4), 0.84 (t, 3, *J* = 7.3); ^{13}C NMR 206.6, 173.5, 165.5, 155.6, 148.9, 135.8, 132.9, 132.2, 118.5, 117.1, 114.5, 109.7, 108.4, 104.4, 75.3,

72.8, 69.4, 68.0, 65.7, 59.7, 52.4, 48.4, 42.0, 38.9, 36.3, 34.42, 34.39, 31.8, 27.9, 25.1, 22.6, 18.4, 14.0, 11.6, 8.6; IR (neat) 2957, 2933, 2860, 1739, 1731, 1715; HRMS (EI) calcd for $C_{35}H_{48}O_9$ (M^+) 612.3298, found 612.3300.



S5

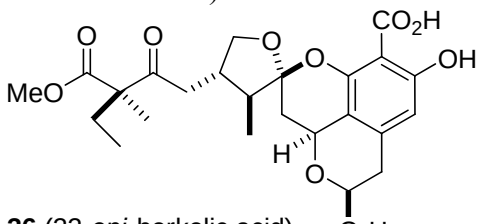
Methyl (α*R*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)-α,3-Dimethyl-α-ethyl-3',3'a,4,5,5',6'-hexahydro-3-methyl- β-oxo-5'-pentyl-8'-(2-propenyloxy)-9'-(2-propenyloxycarbonyl)-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-4-butanoate (S5). An identical reaction with **34** (20.2 mg, 32.9 μmol) afforded 15.6 mg (77%) of **S5**: $[\alpha]_D^{22}$ –91.9 (*c* 0.70, $CHCl_3$); ^{1}H NMR 6.23 (s, 1, H-4), 6.08-5.92 (m, 2), 5.40 (br d, 1, *J* = 17.7), 5.36 (br d, 1, *J* = 17.1), 5.27 (br d, 1, *J* = 10.4), 5.23 (d, 1, *J* = 10.4), 4.85 (dd, 1, *J* = 13.4, 6.1), 4.79 (dd, 1, *J* = 12.2, 5.5, H-15), 4.74 (dd, 1, *J* = 13.1, 5.8), 4.51 (d, 2, *J* = 4.9), 4.35 (dd, 1, *J* = 8.5, 8.5, H-26), 3.86-3.78 (m, 1, H-9), 3.74 (s, 3, OMe), 3.45 (dd, 1, *J* = 8.5, 8.5, H-26), 2.81 (dd, 1, *J* = 17.7, 3.1, H-20), 2.75 (dd, 1, *J* = 17.1, 3.7, H-8), 2.60 (dd, 1, *J* = 17.1, 11.0, H-8), 2.60-2.50 (m, 1, H-19), 2.35 (dd, 1, *J* = 17.7, 10.4, H-20), 2.14 (dd, 1, *J* = 12.2, 4.9, H-16), 1.96 (dd, 1, *J* = 12.2, 12.2, H-16), 2.02-1.91 (m, 1, H-23), 1.82 (dq, 1, *J* = 14.7, 7.3, H-23), 1.72-1.58 (m, 2), 1.58-1.46 (m, 2), 1.45-1.24 (m, 5), 1.34 (s, 3, H-27), 1.00 (d, 3, *J* = 6.7, 3 H-25), 0.90 (t, 3, *J* = 6.7), 0.83 (t, 3, *J* = 7.3); ^{13}C NMR 206.5, 173.5, 165.5, 155.6, 148.9, 135.8, 132.9, 132.2, 118.5, 117.2, 114.5, 109.7, 108.4, 104.4, 75.3, 72.8, 69.4, 68.0, 65.7, 59.7, 52.4, 48.5, 42.0, 38.9, 36.3, 34.42, 34.39, 31.8, 27.8, 25.1, 22.6, 18.3, 14.0, 11.6, 8.6; IR (neat) 2957, 2934, 2860, 1739, 1732, 1715; HRMS (EI) calcd for $C_{35}H_{48}O_9$ (M^+) 612.3298, found 612.3296.



35 (berkelic acid)

Methyl (α*S*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)-9'-Carboxy-α,3-dimethyl-α-ethyl-3',3'a,4,5,5',6'-hexahydro-8'-hydroxy-3-methyl- β-oxo-5'-pentyl-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-4-butanoate (35, berkelic acid). To a solution of $Pd(PPh_3)_4$ (6.1 mg, 5.3 μmol) and **S4** (16.2 mg, 26.4 μmol) in dry THF (2 mL) was added NEt_3 (148 μL, 1.06 mmol) and HCO_2H (40 μL, 1.06 mmol) under N_2 at 25 °C. The yellow solution was stirred at 25 °C for 15 h and quenched with saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with ether (4 × 5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel (80:1:0 to 200:1:1 CH_2Cl_2/MeOH/AcOH) gave 11.1 mg (78%) of berkelic acid (**35**): $[\alpha]_D^{22}$ –115.5 (*c* 0.55, MeOH); {lit.[1] $[\alpha]_D^{20}$ -83.5 (*c* 0.0113, MeOH)}; ^{1}H NMR ($CDCl_3$, the residual peak of solvent is referenced as δ 7.24 rather than 7.27 to facilitate comparison with the literature data[1]) 11.82 (s, 1, OH), 11.13-10.92 (br, 1, OH), 6.42 (s, 1, H-4), 4.76 (dd, 1, *J* = 12.2, 5.4, H-15), 4.44 (dd, 1, *J* = 8.5, 8.5, H-26), 3.84-3.76 (m, 1, H-9), 3.73 (s, 3, OMe), 3.59 (dd, 1, *J* = 8.5, 8.5, H-26), 2.85 (dd, 1, *J* = 17.0, 2.4, H-20), 2.78 (dd, 1, *J* = 17.7, 3.7, H-8), 2.60 (dd, 1, *J* = 17.7, 11.0, H-8), 2.54-2.45 (m, 1, H-19), 2.42 (dd, 1, *J* = 17.0, 9.8, H-20), 2.21 (dd, 1, *J* = 12.2, 5.4, H-16), 2.05 (dd, 1, *J* = 12.2, 12.2, H-16), 1.95 (dq, 1, *J* = 14.2, 7.3, H-23), 1.87 (dq, 1, *J* = 10.7, 6.8, H-18), 1.80 (dq, 1, *J* = 14.2, 7.3, H-23), 1.68-1.57 (m, 1), 1.58-1.43 (m, 2), 1.43-1.20 (m, 5), 1.32 (s, 3, H-27), 1.09 (d, 3, *J* = 6.8, 3 H-25), 0.88 (t, 3, *J* = 6.6), 0.83 (t, 3, *J* = 7.6); ^{1}H NMR (CD_3OD, 500 MHz) 6.27 (s, 1, H-4), 4.72 (dd, 1, *J* = 12.2, 5.4, H-15), 4.30 (dd, 1, *J* = 8.5, 8.5, H-26), 3.84-3.77 (m, 1, H-9), 3.73 (s, 3, OMe), 3.50 (dd, 1, *J* = 8.5, 8.5, H-26), 2.88 (dd, 1, *J* = 17.6, 3.1, H-20), 2.78 (dd, 1, *J* = 17.3, 3.7, H-8), 2.70-2.62 (m, 1, H-19), 2.54 (dd, 1, *J* = 17.3, 11.2, H-8), 2.53 (dd, 1, *J* = 17.6, 10.5, H-20), 2.14 (dd, 1, *J* = 12.2, 5.4, H-16), 1.94 (dq, 1, *J* = 14.2, 7.3, H-23), 1.91 (dd, 1, *J* = 12.2, 12.2, H-16), 1.88-1.78 (m, 2, H-23, H-18), 1.63-1.48 (m, 3), 1.46-1.27 (m, 5), 1.32 (s, 3, H-27), 1.08 (d, 3, *J* = 6.3, 3 H-25), 0.92 (t,

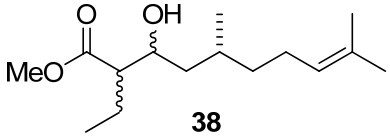
3, *J* = 6.8), 0.83 (t, 3, *J* = 7.6); ^{13}C NMR ($CDCl_3$) 206.0, 173.4, 170.5, 162.5, 149.8, 142.2, 112.2 (2 C), 110.5, 98.6, 75.2, 73.5, 67.2, 59.7, 52.5, 48.2, 41.6, 39.4, 36.2, 34.30, 34.29, 31.8, 27.9, 25.0, 22.6, 18.4, 14.0, 12.0, 8.7; ^{13}C NMR (CD_3OD, 400 MHz) 208.8, 174.8, 173.7, 163.4, 153.1, 142.3, 113.8, 110.7, 109.4, 101.1, 76.6, 74.2, 69.5, 61.0, 52.9, 42.6, 40.5, 37.4, 35.4, 35.0, 33.0, 28.9, 26.2, 23.7, 18.9, 14.4, 11.9, 9.0 (a peak near δ 49.2 is obscured by the solvent peak); IR (neat) 3238, 2957, 2933, 2860, 1713, 1694; HRMS (EI) calcd for $C_{29}H_{40}O_9$ (M^+) 532.2672, found 532.2659. The ^{1}H and ^{13}CNMR spectral data in both $CDCl_3$ and CD_3OD are identical to those of the natural product (see Tables S2-S5).[1]



36 (22-*epi*-berkelic acid)

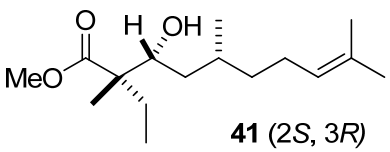
Methyl (α*R*,2*S*,3*S*,3'a*S*,4*S*,5'*R*)-9'-Carboxy-α,3-dimethyl-α-ethyl-3',3'a,4,5,5',6'-hexahydro-8'-hydroxy-3-methyl- β-oxo-5'-pentyl-spiro[furan-2(3*H*),2'-[2*H*]pyrano[2,3,4-*de*][1]benzopyran]-4-butanoate (36, 22-*epi*-berkelic acid). An identical reaction with **S5** (14.0 mg, 22.8 μmol) afforded 8.7 mg (72%) of 22-*epi*-berkelic acid (**36**): $[\alpha]_D^{22}$ –107.0 (*c* 0.43, MeOH); ^{1}H NMR ($CDCl_3$, the residual peak of solvent is referenced as δ 7.24 rather than 7.27 to facilitate comparison with the literature data[1]) 11.83 (s, 1, OH), 11.08-10.97 (br, 1, OH), 6.42 (s, 1, H-4), 4.77 (dd, 1, *J* = 12.2, 5.4, H-15), 4.45 (dd, 1, *J* = 8.5, 8.5, H-26), 3.84-3.76 (m, 1, H-9), 3.73 (s, 3, OMe), 3.59 (dd, 1, *J* = 8.5, 8.5, H-26), 2.90 (dd, 1, *J* = 17.6, 2.9, H-20), 2.79 (dd, 1, *J* = 17.6, 3.9, H-8), 2.60 (dd, 1, *J* = 17.6, 11.2, H-8), 2.54-2.44 (m, 1, H-19), 2.38 (dd, 1, *J* = 17.6, 10.0, H-20), 2.21 (dd, 1, *J* = 12.2, 5.4, H-16), 2.06 (dd, 1, *J* = 12.2, 12.2, H-16), 1.95 (dq, 1, *J* = 14.2, 7.3, H-23), 1.87 (dq, 1, *J* = 11.3, 6.8, H-18), 1.80 (dq, 1, *J* = 14.2, 7.3, H-23), 1.68-1.57 (m, 1), 1.58-1.43 (m, 2), 1.43-1.20 (m, 5), 1.33 (s, 3, H-27), 1.09 (d, 3, *J* = 6.8, 3 H-25), 0.88 (t, 3, *J* = 6.6), 0.81 (t, 3, *J* = 7.3); ^{1}H NMR (CD_3OD, 500 MHz) 6.27 (s, 1, H-4), 4.73 (dd, 1, *J* = 12.2, 5.4, H-15), 4.30 (dd, 1, *J* = 8.5, 8.5, H-26), 3.84-3.77 (m, 1, H-9), 3.73 (s, 3, OMe), 3.50 (dd, 1, *J* = 8.5, 8.5, H-26), 2.92 (dd, 1, *J* = 17.6, 3.0, H-20), 2.79 (dd, 1, *J* = 17.3, 3.6, H-8), 2.72-

2.62 (m, 1, H-19), 2.55 (dd, 1, *J* = 17.3, 10.3, H-8), 2.49 (dd, 1, *J* = 17.6, 10.5, H-20), 2.14 (dd, 1, *J* = 12.2, 5.4, H-16), 1.94 (dq, 1, *J* = 14.2, 7.3, H-23), 1.91 (dd, 1, *J* = 12.2, 12.2, H-16), 1.88-1.78 (m, 2, H-23, H-18), 1.64-1.49 (m, 3), 1.47-1.30 (m, 5), 1.33 (s, 3, H-27), 1.08 (d, 3, *J* = 6.3, 3 H-25), 0.92 (t, 3, *J* = 6.8), 0.82 (t, 3, *J* = 7.3); ^{13}C NMR ($CDCl_3$) 206.0, 173.4 (tiny), 170.5, 162.5, 149.8, 142.2, 112.17, 112.15, 110.5, 98.6, 75.2, 73.5, 67.2, 59.7, 52.5, 48.2, 41.5, 39.3, 36.2, 34.31, 34.29, 31.8, 27.9, 25.0, 22.6, 18.3, 14.0, 12.0, 8.6; ^{13}C NMR (CD_3OD, 400 MHz) 208.7, 174.8, 173.6, 163.4, 153.1, 142.3, 113.8, 110.7, 109.4, 101.1, 76.6, 74.1, 69.5, 61.0, 52.9, 42.6, 40.5, 37.4, 35.4, 35.0, 33.0, 28.8, 26.2, 23.7, 18.8, 14.4, 11.9, 8.9 (a peak near δ 49.2 is obscured by the solvent peak); IR (neat) 3233, 2957, 2933, 2860, 1713, 1694; HRMS (EI) calcd for $C_{29}H_{40}O_9$ (M^+) 532.2672, found 532.2667.

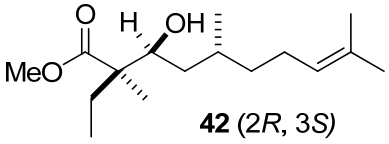


38

Methyl (5*R*)-5,9-Dimethyl-2-ethyl-3-hydroxy-8-decenoate (38). *n*-BuLi (6.3 mL, 1.6 M in hexane, 10 mmol) was added dropwise to a solution of diisopropylamine (1.41 mL, 10 mmol) in THF (4 mL) under N_2 at 0 °C. The resulting solution was stirred at 0 °C for 30 min and cooled to -78 °C. A solution of methyl butanoate (1.14 mL, 10 mmol) in THF (4 mL) was added dropwise to the reaction mixture and the reaction was stirred at -78 °C for 1 h. A solution of (*R*)-(+)-citronellal (**37**) (0.81 mL, 4 mmol) in THF (4 mL) was added dropwise to the reaction mixture and the reaction was slowly warmed up to 25 °C over 2 h. The reaction was quenched with saturated NH_4Cl (10 mL) and extracted with ether (3 × 15 mL). The combined ether extracts were dried (Na_2SO_4) and concentrated to give 1.23 g of crude **38**. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 0.89 g (86%) of **38** as a mixture of four diastereomers: ^{1}H NMR 5.14-5.02 (m, 1), 3.94-3.66 (m, 1), 3.72 (s, 3), 2.38-2.30 (m, 1), 2.06-1.88 (m, 3). 1.68 (s, 3), 1.60 (s, 3), 1.79-1.04 (m, 6), 0.98-0.80 (m, 6).

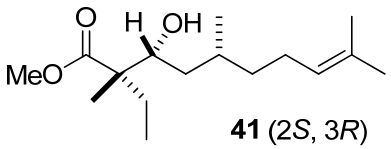


41 (2*S*, 3*R*)

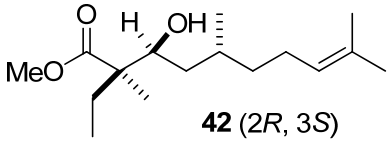


42 (2*R*, 3*S*)

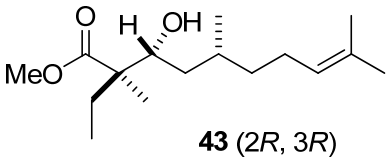
Methyl (2*S*,3*R*,5*R*)- and (2*R*,3*S*,5*R*)-2-Ethyl-3-hydroxy-2,5,9-trimethyl-8-decenoate (41 and 42). *n*-BuLi (0.275 mL, 1.6 M in hexane, 0.44 mmol) was added dropwise to a solution of diisopropylamine (62 μL, 0.44 mmol) in THF (0.5 mL) under N_2 at 0 °C. The resulting solution was stirred at 0 °C for 30 min and cooled to -50 °C. A solution of **38** (51 mg, 0.2 mmol) in THF (0.5 mL) was added dropwise to the reaction mixture. The resulting solution was stirred at -50 °C for 30 min and at -20 °C for 1 h. A solution of MeI (25 μL, 0.61 mmol) and HMPA (0.21 mL, 1.2 mmol) in THF (0.3 mL) was added dropwise to the reaction mixture. The solution was stirred at -20 °C for 2 h and slowly warmed up to 25 °C over 1 h. The reaction mixture was quenched with saturated NH_4Cl (4 mL) and extracted with ether (4 × 4 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel (25:1 hexanes/EtOAc) gave 8.8 mg (16%) of 1:1 mixture of **41** and **42**.



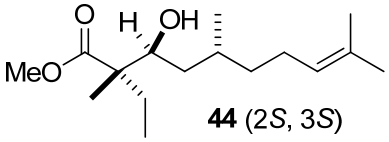
41 (2*S*, 3*R*)



42 (2*R*, 3*S*)



43 (2*R*, 3*R*)



44 (2*S*, 3*S*)

Methyl (2*S*,3*R*,5*R*)-, (2*R*,3*R*,5*R*)-, (2*R*,3*S*,5*R*)-, and (2*S*,3*S*,5*R*)-2-Ethyl-3-hydroxy-2,5,9-trimethyl-8-decenoate (41, 43, 42, and 44, respectively). To a solution of *N*-Ts-(*S*)-valine[19] (81 mg, 0.3 mmol) in dry CH_2Cl_2 (1 mL) was added BH_3•THF (0.3 mL, 1 M solution in THF, 0.3 mmol) by syringe over 3 min under N_2 at 0 °C. The solution was stirred for 30 min at 0 °C and additionally for 30 min at 25 °C. The solution was cooled -78 °C and a solution of *R*-(+)-citronellal (**37**) (16.3 μL, 90 μmol) in CH_2Cl_2 (0.5 mL) was added dropwise over 3 min. After stirring for 5 min, silyl ketene acetal **31** (47 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise over 3 min. The reaction mixture was stirred for 4 h at -78 °C and quenched with 1 M aqueous HCl (3 mL). The mixture was allowed to warm to 25 °C and the aqueous layer was

extracted with CH_2Cl_2 (4 × 3 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 × 6 mL), dried ($MgSO_4$) and concentrated to yield 21.9 mg of crude aldol product. Flash chromatography (25:1 hexanes/EtOAc) gave 9.1 mg (38%) of **41** contaminated with 15% of **42**, followed by 10.0 mg (41%) of **43** contaminated with 15% of **44**.

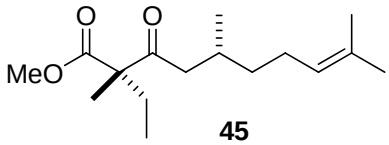
Data for **41**: ^{1}H NMR 5.13-5.06 (m, 1), 3.789 (br d, 1, *J* = 9.8), 3.685 (s, 3), 2.07-1.85 (m, 3, OH), 1.80 (dq, 1, *J* = 14.0, 7.3), 1.72-1.64 (m, 1), 1.68 (s, 3), 1.61 (s, 3), 1.54 (dq, 1, *J* = 13.4, 7.3), 1.52-1.42 (m, 1), 1.33-1.16 (m, 3), 1.113 (s, 3), 0.94 (d, 3, *J* = 6.7), 0.85 (t, 3, *J* = 7.3); ^{13}C NMR 177.05, 131.20, 124.78, 74.09, 51.62, 51.43, 40.16, 35.52, 29.60, 28.57, 25.72, 25.22, 20.76, 17.65, 16.22, 9.02.

Data for **43**: ^{1}H NMR 5.14-5.06 (m, 1), 3.755 (br, 1), 3.712 (s, 3), 2.34-2.26 (br, 1, OH), 2.09-1.96 (m, 1), 2.00-1.86 (m, 1), 1.74 (dq, 1, *J* = 14.0, 7.3), 1.76-1.68 (m, 1), 1.68 (s, 3), 1.61 (s, 3), 1.52 (dq, 1, *J* = 13.4, 7.3), 1.54-1.44 (m, 1), 1.37-1.22 (m, 2), 1.20-1.10 (m, 1), 1.095 (s, 3), 0.95 (d, 3, *J* = 6.7), 0.83 (t, 3, *J* = 7.3); ^{13}C NMR 177.72, 131.19, 124.79, 73.47, 51.73, 51.61, 39.23, 35.61, 29.50, 29.41, 25.72, 25.32, 20.82, 17.65, 16.53, 8.87.

An identical reaction from *N*-Ts-(*R*)-valine afforded 5.0 mg (21%) of **42** contaminated with 15% of **41** and 4.4 mg (18%) of **44** contaminated with 15% of **43**.

Data for **42**: ^{1}H NMR 5.13-5.06 (m, 1), 3.784 (br d, 1, *J* = 10.4), 3.687 (s, 3), 2.08-1.91 (m, 3, OH), 1.80 (dq, 1, *J* = 14.0, 7.3), 1.73-1.64 (m, 1), 1.68 (s, 3), 1.60 (s, 3), 1.55 (dq, 1, *J* = 14.0, 7.3), 1.47-1.38 (m, 1), 1.34-1.16 (m, 3), 1.119 (s, 3), 0.89 (d, 3, *J* = 6.7), 0.86 (t, 3, *J* = 7.3); ^{13}C NMR 177.07, 131.15, 124.70, 73.73, 51.60, 51.36, 39.82, 38.19, 29.10, 28.56, 25.70, 25.51, 18.68, 17.64, 16.25, 8.97.

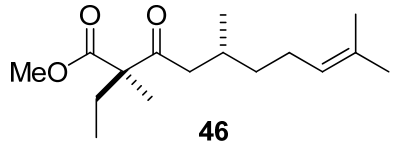
Data for **44**: ^{1}H NMR 5.13-5.06 (m, 1), 3.760 (br d, 1, *J* = 10.4), 3.712 (s, 3), 2.36-2.27 (m, 1, OH), 2.07-1.90 (m, 2), 1.74 (dq, 1, *J* = 14.0, 7.3), 1.78-1.68 (m, 1), 1.68 (s, 3), 1.60 (s, 3), 1.53 (dq, 1, *J* = 13.4, 7.3), 1.38-1.18 (m, 1), 1.18-1.06 (m, 3), 1.099 (s, 3), 0.90 (d, 3, *J* = 6.7), 0.83 (t, 3, *J* = 7.3); ^{13}C NMR 177.74, 131.14, 124.72, 73.05, 51.70, 51.49, 38.80, 38.29, 29.41, 28.92, 25.70, 25.54, 18.75, 17.64, 16.58, 8.82.



45

Methyl (2*S*,5*R*)-2-Ethyl-2,5,9-trimethyl-3-oxo-8-decenoate (45). Dess-Martin periodinane (15.7 mg, 37 μmol) was added to a solution of **41** (5.0 mg, 18.5 μmol) in CH_2Cl_2 (1 mL) at 25 °C. The suspension was stirred at 25 °C for 12 h. The solvent was removed under reduced pressure at 25 °C. Flash chromatography on silica gel (40:1 hexanes/EtOAc) gave 4.3 mg (87%) of **45**: ^{1}H NMR 5.10-5.04 (m, 1), 3.71 (s, 3), 2.37 (dd, 1, *J* = 17.1, 5.5), 2.26 (dd, 1, *J* = 17.7, 7.9), 2.10-2.00 (m, 1), 2.00-1.89 (m, 3), 1.79 (dq, 1, *J* = 14.0, 7.3), 1.68 (s, 3), 1.59 (s, 3), 1.32-1.24 (m, 1), 1.30 (s, 3), 1.20-1.08 (m, 1), 0.85 (d, 3, *J* = 6.7), 0.82 (t, 3, *J* = 7.3); ^{13}C NMR 207.2, 173.6, 131.4, 124.3, 60.2, 52.2, 45.6, 36.7, 28.2, 27.6, 25.7, 25.5, 19.5, 18.1, 17.6, 8.6.

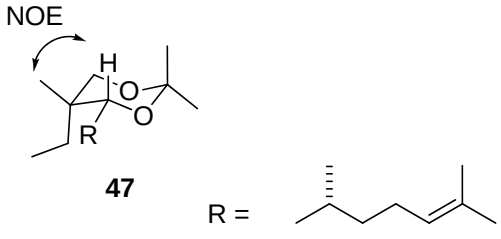
An identical reaction with **44** also afforded **45**.



46

Methyl (2*R*,5*R*)-2-Ethyl-2,5,9-trimethyl-3-oxo-8-decenoate (46). An identical reaction with **42** afforded **46**: ^{1}H NMR 5.11-5.04 (m, 1), 3.71 (s, 3), 2.41 (dd, 1, *J* = 17.1, 5.5), 2.24 (dd, 1, *J* = 17.7, 7.9), 2.11-2.00 (m, 1), 2.00-1.89 (m, 3), 1.78 (dq, 1, *J* = 14.0, 7.3), 1.68 (s, 3), 1.59 (s, 3), 1.33-1.24 (m, 1), 1.31 (s, 3), 1.19-1.08 (m, 1), 0.86 (d, 3, *J* = 6.7), 0.83 (t, 3, *J* = 7.3); ^{13}C NMR 207.2, 173.6, 131.4, 124.3, 60.1, 52.2, 45.6, 36.7, 28.1, 27.6, 25.7, 25.5, 19.5, 18.2, 17.6, 8.6.

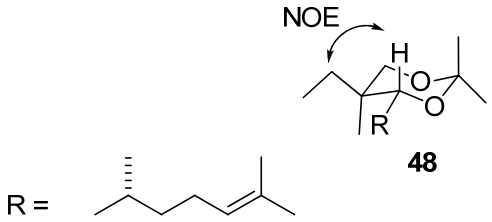
An identical reaction with **43** afforded **46**.



47

(4*R*,5*R*)-4-((2*R*)-2,6-Dimethyl-5-hepten-1-yl)-5-ethyl-2,2,5-trimethyl-1,3-dioxane (47). To a stirred suspension of lithium aluminum hydride (44.5 mg, 1.17 mmol) in ether (1.5 mL) was added a solution of β-hydroxy ester **41** (78.5 mg, 0.29 mmol) in ether (3 mL) under N_2 at 25 °C. The suspension was stirred for 3 h and quenched by slow addition of H_2O (1 mL). The white precipitate was filtered off through a pad of Celite and rinsed with EtOAc (6 × 5 mL). The organic layer was washed with brine (5 mL), dried ($MgSO_4$), and concentrated to give 63.2 mg of diol.

A solution of the diol and TsOH•H_2O (6.0 mg, 32 μmol) in 2,2-dimethoxypropane (2.5 mL) was stirred under N_2 for 40 min. The reaction mixture was diluted with ether (20 mL) and washed with saturated $NaHCO_3$ (3 × 5 mL). The organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography on silica gel (40:1 hexanes/EtOAc) gave 64.4 mg (79%) of **47**: ^{1}H NMR 5.13-5.06 (m, 1), 3.63 (dd, 1, *J* = 8.5, 2.4), 3.58 (d, 1, *J* = 11.6), 3.40 (d, 1, *J* = 11.6), 2.06-1.88 (m, 2), 1.93 (dq, 1, *J* = 14.0, 7.3), 1.69 (s, 3), 1.61 (s, 3), 1.63-1.51 (m, 1), 1.45-1.37 (m, 1), 1.42 (s, 3), 1.37 (s, 3), 1.32-1.21 (m, 2), 1.15 (dq, 1, *J* = 14.0, 6.7), 1.10-1.00 (m, 1), 0.91 (d, 3, *J* = 6.7), 0.85 (t, 3, *J* = 7.6), 0.62 (s, 3); ^{13}C NMR 131.1, 124.9, 98.3, 76.4, 67.2, 35.8, 35.7, 35.2, 29.6, 29.2, 25.7, 25.2, 21.4, 20.6, 18.9, 18.4, 17.6, 7.8. A 2D NOESY experiment showed NOEs from the three ring protons at δ 3.63, 3.58, and 3.40 to the methyl singlet at δ 0.62. Only the equatorial ring proton at δ 3.58 showed an NOE to the methyl triplet of the ethyl group at δ 0.91 and one methylene proton of the ethyl group at δ 1.93.

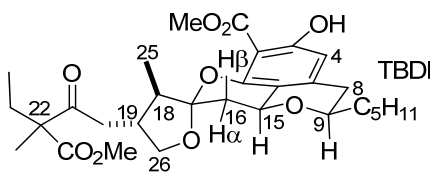


48

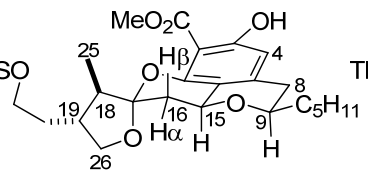
(4*R*,5*S*)-4-((2*R*)-2,6-Dimethyl-5-hepten-1-yl)-5-ethyl-2,2,5-trimethyl-1,3-dioxane (48). An identical series of reactions with **43** (63.5 mg, 0.24 mmol) afforded 53.7 mg (81%) of **48**: ^{1}H NMR 5.13-5.06 (m, 1), 3.69-3.62 (m, 2), 3.38 (d, 1, *J* = 11.6), 2.06-1.86 (m, 2), 1.68 (s, 3), 1.61 (s, 3), 1.64-1.55 (m, 1), 1.45-1.37 (m, 1), 1.40 (s, 3), 1.38 (s, 3), 1.30-1.19 (m, 3), 1.13

(dq, 1, J = 14.0, 7.3), 1.10-1.00 (m, 1), 0.97 (s, 3), 0.91 (d, 3, J = 6.7), 0.80 (t, 3, J = 7.3); ^{13}C NMR 131.1, 124.9, 98.2, 74.0, 69.9, 36.0, 35.7, 35.2, 29.4, 29.0, 28.4, 25.7, 25.2, 20.6, 19.1, 17.6, 15.7, 7.2; ^{1}H NMR (benzene-d_6) 5.29-5.20 (m, 1), 3.61 (br d, 1, J = 9.8), 3.52 (d, 1, J = 11.6), 3.38 (d, 1, J = 11.6), 2.16-1.99 (m, 2), 1.86-1.74 (m, 1), 1.70 (s, 3), 1.59 (s, 3), 1.59-1.49 (m, 1), 1.50 (s, 3), 1.39-1.29 (m, 1), 1.34 (s, 3), 1.23-1.10 (m, 2), 1.04 (s, 3), 0.97 (d, 3, J = 6.7), 1.09-0.99 (m, 1), 0.89 (dq, 1, J = 14.0, 7.3), 0.62 (t, 3, J = 7.6); ^{13}C NMR (benzene-d_6) 131.3, 125.9, 98.7, 74.8, 70.2, 36.9, 36.7, 35.7, 30.2, 29.9, 29.0, 26.3, 26.2, 21.3, 19.6, 18.1, 16.4, 7.7. A 2D NOESY (run in benzene-d_6 because two ring protons overlapped in $CDCl_3$) experiment showed NOEs from all three ring protons at δ 3.61, 3.52, and 3.38 to the methyl triplet of the ethyl group at δ 0.62, the ethyl methylene group multiplet at δ 0.89, and the ethyl methylene group multiplet at δ 1.09-0.99. Only the equatorial ring proton at δ 3.38 showed an NOE to the methyl singlet at δ 1.04.

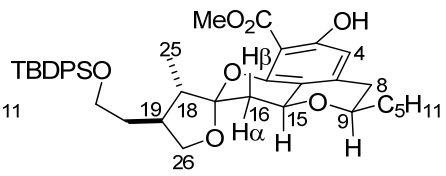
Table S1. Comparison of the ^{1}H NMR Spectral Data Reported for Berkelic Acid Methyl Ester in $CDCl_3$ with Those of Intermediates 22 and 27a.



literature data for natural berkelic acid methyl ester with proposed structure shown



22 with proposed stereochemistry

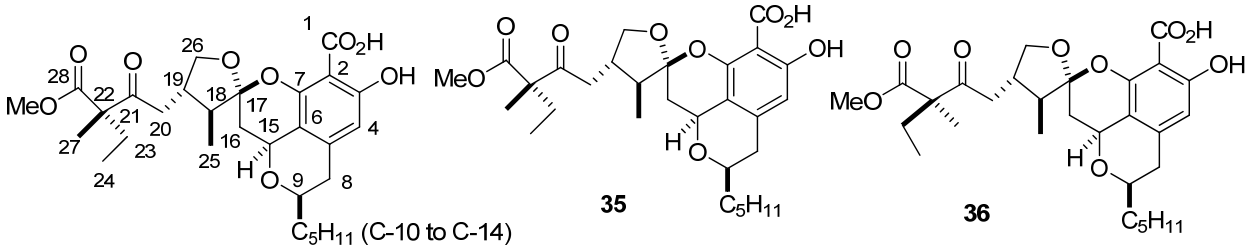


27a with revised stereochemistry at C-18 and C-19

Atom	Berkelic Acid Methyl Ester	**22**	**27a**
4	6.29 (s)	6.32 (s)	6.31 (s)
8α	2.77 (m)	2.77 (dd, 17.7, 4.3)	2.76 (dd, 17.6, 3.9)
8β	2.56 (dd, 17.4, 11.2)	2.61 (dd, 17.7, 11.0)	2.60 (dd, 17.6, 10.7)
9	3.79 (m)	3.79 (m)	3.79 (m)
15	4.73 (dd, 12.3, 5.2)	4.75 (dd, 12.2, 5.2)	4.76 (dd, 12.2, 5.4)
16α	**2.13 (dd, 12.3, 5.5)**	**2.24 (dd, 12.2, 5.2)**	**2.16 (dd, 12.2, 5.4)**
16β	**2.05 (dd, 12.3, 12.2)**	**1.81 (dd, 12.2, 12.2)**	**1.95 (dd, 12.2, 12.2)**
18	**1.83 (m)**	**2.24 (m)**	**1.73 (m)**
25	1.02 (d, 6.6)	1.05 (d, 6.7)	1.06 (d, 6.7)
26α	**4.31 (t, 8.5)**	**4.14 (t, 7.8)**	**4.25 (t, 8.5)**
26β	**3.44 (t, 8.5)**	**3.69 (t, 7.8)**	**3.55 (t, 8.5)**

Shifts in bold show significant differences in the ^{1}H NMR spectra of **22** and **27a**

Table S2. Comparison of the ^{1}H NMR Spectral Data Reported for Berkelic Acid in $CDCl_3$ with Those of 35 and 36.[a]

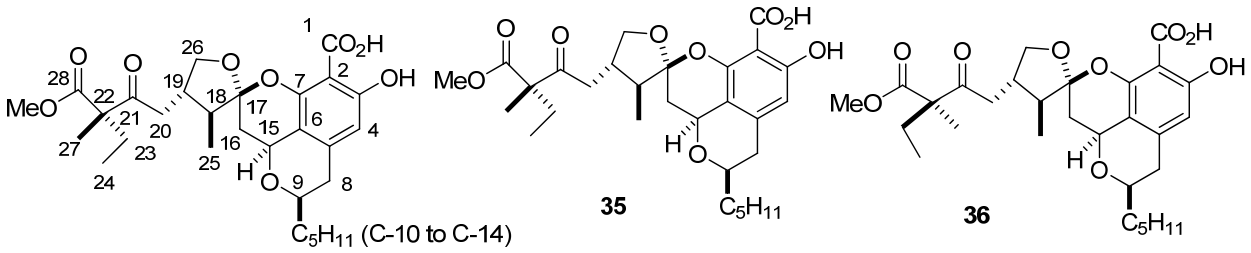


natural berkelic acid showing revised stereochemistry at C-18 and C-19 and assigned stereochemistry at C-22

Atom	Berkelic Acid	**35**	**36**
4	6.41 (s)	6.42 (s)	6.42 (s)
8α	2.77 (dd, 17.6, 4.0)	2.78 (dd, 17.7, 3.7)	2.79 (dd, 17.6, 3.9)
8β	2.59 (dd, 17.6, 11.0)	2.60 (dd, 17.7, 11.0)	2.60 (dd, 17.6, 11.2)
9	3.80 (m)	3.80 (m)	3.80 (m)
10	1.61 (m)	1.62 (m)	1.62 (m)
10	1.50 (m)	1.50 (m)	1.50 (m)
11	1.50 (m)	1.43 (m)	1.43 (m)
12	1.30 (m)	1.30 (m)	1.30 (m)
13	1.30 (m)	1.30 (m)	1.30 (m)
14	0.88 (t)	0.88 (t, 6.6)	0.88 (t, 6.6)
15	4.76 (dd, 12.2, 5.7)	4.76 (dd, 12.2, 5.4)	4.77 (dd, 12.2, 5.4)
16α	2.20 (dd, 12.2, 5.7)	2.21 (dd, 12.2, 5.4)	2.21 (dd, 12.2, 5.4)
16β	2.05 (dd, 12.2, 12.2)	2.05 (dd, 12.2, 12.2)	2.06 (dd, 12.2, 12.2)
18	1.87 (m)	1.87 (dq, 10.7, 6.8)	1.87 (dq, 11.3, 6.8)
19	2.50 (m)	2.50 (m)	2.49 (m)
20[b]	2.84 (dd, 17.0, 2.5)	2.85 (dd, 17.0, 2.4)	2.90 (dd, 17.6, 2.9)
20[b]	2.42 (dd, 17.0, 10.3)	2.42 (dd, 17.0, 9.8)	2.38 (dd, 17.6, 10.0)
23	1.94 (m)	1.95 (dq, 14.2, 7.3)	1.95 (dq, 14.2, 7.3)
23	1.80 (m)	1.80 (dq, 14.2, 7.3)	1.80 (dq, 14.2, 7.3)
24[b]	0.82 (t, 7.2)	0.83 (t, 7.3)	0.81 (t, 7.3)
25	1.08 (d, 6.8)	1.09 (d, 6.7)	1.09 (d, 6.7)
26α	4.43 (t, 8.8)	4.44 (t, 8.5)	4.45 (t, 8.5)
26β	3.58 (t, 8.8)	3.59 (t, 8.5)	3.59 (t, 8.5)
27[b]	1.31	1.32	1.33
OMe	3.73	3.73	3.73
OH	11.82	11.82	11.83

a) The spectra are referenced to the residual solvent peak at δ 7.24, not δ 7.27 to be consistent with the literature data. b) Bold hydrogens have different chemical shifts in **35** and **36**.

Table S3. Comparison of the ^{1}H NMR Spectral Data Reported for Berkelic Acid in CD_3OD with Those of 35 and 36.

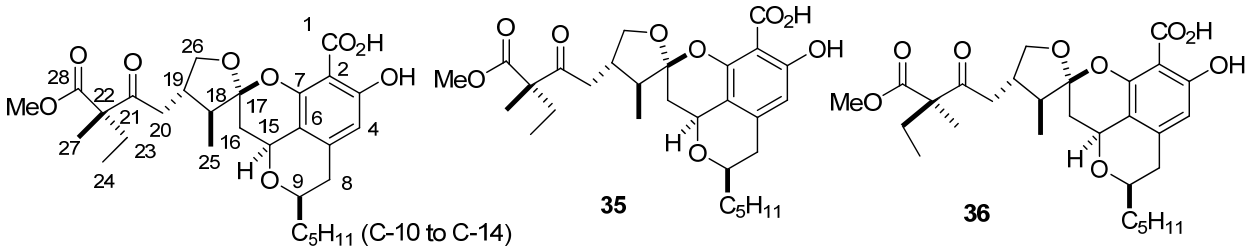


natural berkelic acid showing revised stereochemistry at C-18 and C-19 and assigned stereochemistry at C-22

Atom	Berkelic Acid	**35**	**36**
4	6.27 (s)	6.27 (s)	6.27 (s)
8α	2.77 (dd, 17.4, 5.3)	2.78 (dd, 17.3, 3.7)	2.79 (dd, 17.3, 3.6)
8β	2.54 (dd, 17.4, 11.0)	2.54 (dd, 17.3, 11.2)	2.55 (dd, 17.3, 10.3)
9	3.79 (m)	3.79 (m)	3.79 (m)
10	1.63 (m)	1.63 (m)	1.63 (m)
10	1.55 (m)	1.55 (m)	1.55 (m)
11	1.55 (m)	1.55 (m)	1.55 (m)
12	1.40 (m)	1.40 (m)	1.40 (m)
13	1.40 (m)	1.40 (m)	1.40 (m)
14	0.92 (t, 6.4)	0.92 (t, 6.8)	0.92 (t, 6.8)
15	4.72 (dd, 12.2, 5.4)	4.72 (dd, 12.2, 5.4)	4.73 (dd, 12.2, 5.4)
16α	2.16 (dd, 12.4, 5.4)	2.14 (dd, 12.2, 5.4)	2.14 (dd, 12.2, 5.4)
16β	1.9[a] (dd, 12.4, 12.4)	1.91 (dd, 12.2, 12.2)	1.91 (dd, 12.2, 12.2)
18	1.82 (m)	1.82 (m)	1.82 (m)
19	2.66 (m)	2.66 (m)	2.66 (m)
20[b]	2.87 (dd, 17.5, 3.0)	2.88 (dd, 17.6, 3.1)	2.92 (dd, 17.6, 3.0)
20[b]	2.53 (m)	2.53 (dd, 17.6, 10.5)	2.49 (dd, 17.6, 10.5
23	1.93 (m)	1.94 (dq, 14.2, 7.3)	1.94 (dq, 14.2, 7.3)
23	1.84 (m)	1.84 (m)	1.84 (m)
24[b]	0.83 (t, 7.7)	0.83 (t, 7.6)	0.82 (t, 7.3)
25	1.07 (d, 6.7)	1.08 (d, 6.3)	1.08 (d, 6.3)
26α	4.30 (t, 8.3)	4.30 (t, 8.5)	4.30 (t, 8.5)
26β	3.50 (t, 8.3)	3.50 (t, 8.5)	3.50 (t, 8.5)
27[b]	1.32	1.32	1.33
OMe	3.73	3.73	3.73

a) This peak is reported to absorb at δ 2.02.[1] However, examination of the supporting material indicate that there are no peaks between 2.0 and 2.1 and the COSY and HSQC indicate that this hydrogen absorbs at about δ 1.9. b) Bold hydrogens have different chemical shifts in **35** and **36**.

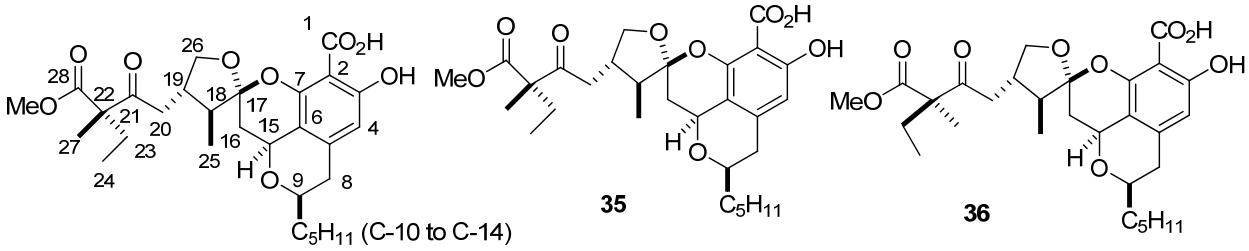
Table S4. Comparison of the ^{13}C NMR Spectral Data Reported for Berkelic Acid in $CDCl_3$ with Those of 35 and 36.



natural berkelic acid showing revised stereochemistry at C-18 and C-19 and assigned stereochemistry at C-22

Atom	Berkelic Acid	**35**	**36**
1	170.5	170.5	170.5
2	98.6	98.6	98.6
3	162.5	162.5	162.5
4	110.5	110.5	110.5
5	142.3	142.2	142.2
6	112.2	112.2	112.17 or 112.15
7	149.8	149.8	149.8
8	34.3	34.30 or 34.29	34.31 or 34.29
9	75.2	75.2	75.2
10	36.2	36.2	36.2
11	25.1	25.0	25.0
12	31.7	31.8	31.8
13	22.6	22.6	22.6
14	14.0	14.0	14.0
15	67.2	67.2	67.2
16	34.2	34.30 or 34.29	34.31 or 34.29
17	112.2	112.2	112.17 or 112.15
18	48.2	48.2	48.2
19	39.3	39.4	39.3
20	41.6	41.6	41.5
21	206.1	206.0	206.0
22	59.7	59.7	59.7
23	27.9	27.9	27.9
24	8.7	8.7	8.6
25	12.0	12.0	12.0
26	73.5	73.5	73.5
27	18.4	18.4	18.3
28	173.4	173.4	173.4
OMe	52.5	52.5	52.6

Table S5. Comparison of the ^{13}C NMR Spectral Data Reported for Berkelic Acid in CD_3OD with Those of 35 and 36.



natural berkelic acid showing revised stereochemistry at C-18 and C-19 and assigned stereochemistry at C-22

Atom	Berkelic Acid	**35**	**36**
1	173.6	173.7	173.6
2	101.0	101.1	101.1
3	163.4	163.4	163.4
4	109.4	109.4	109.4
5	142.3	142.3	142.3
6	113.7	113.8	113.8
7	153.0	153.1	153.1
8	35.4	35.4	35.4
9	76.5	76.6	76.6
10	37.4	37.4	37.4
11	26.2	26.2	26.2
12	33.0	33.0	33.0
13	23.7	23.7	23.7
14	14.4	14.4	14.4
15	69.4	69.5	69.5
16	35.0	35.0	35.0
17	110.7	110.7	110.7
18	49.2	obscured by CD_3OD	obscured by CD_3OD
19	40.4	40.5	40.5
20	42.6	42.6	42.6
21	208.7	208.8	208.7
22	61.0	61.0	61.0
23	28.9	28.9	28.8
24	9.0	9.0	8.9
25	11.9	11.9	11.9
26	74.1	74.2	74.1
27	19.0	18.9	18.8
28	174.8	174.8	174.8
OMe	52.9	52.9	52.9

Assignment of C-22 Stereochemistry

The Kiyooka aldol reaction leads to two, rather than four, aldol products making it possible to isolate pure **33** and **34**. Unfortunately, this reaction controls the stereochemistry at the alcohol center (C-21), which is lost in the Dess-Martin oxidation, rather than at C-22. Using reagent **32** derived from (*S*)-valine, the enol ether always approaches from the *Si*-face to afford adducts **33** and **34** with *R*-stereochemistry at C-21.[22] The ^{1}H and ^{13}C NMR spectra of alcohols **33** and **34** are slightly different, but these differences can't be used to assign their stereochemistry. We therefore prepared a series of analogues of known stereochemistry with the hope that the spectral differences between these analogues and compounds **33** and **34** were sufficiently consistent to permit us to assign the stereochemistry of **33** and **34** at C-22.

The analogues were prepared from (*R*)-citronellal (**37**) (see Scheme 8). Addition of **37** to the lithium enolate of methyl butyrate afforded **38**, which was converted to the alkoxy enolates **39** and **40**, which were treated with MeI as described by Fráter[23] to give 16% of a 1:1 mixture of **41** and **42**. Chelation in **39** and **40** controls the geometry so that methylation occurs primarily from the face opposite the alkyl group. This sequence typically proceeds with excellent relative stereocontrol, but in poor yield[24] so that it isn't practical to use it with aldehyde **30** to prepare berkelic acid. We also converted **37** and **31** by Kiyooka's procedure[19] to **41** (38%) and **43** (41%) using *N*-Ts-(*S*)-valine and to **42** (21%) and **44** (18%) using *N*-Ts-(*R*)-valine. Kiyooka's procedure controls the stereochemistry at C-3 well, but doesn't control C-2. The compound produced by both Fráter's procedure and Kiyooka's procedure using *N*-Ts-(*S*)-valine must be **41**. Therefore, the other isomer produced from Kiyooka's procedure using *N*-Ts-(*S*)-valine must be **43**. The compound produced by both Fráter's procedure and Kiyooka's procedure using *N*-Ts-(*R*)-valine must be **42**. Therefore, the other isomer produced from Kiyooka's procedure using *N*-Ts-(*R*)-valine must be **44**.

The structure assignments of **41**-**44** should be secure, but were confirmed by Dess-Martin oxidation of **41** and **44** to keto ester **45** and of **42** and **43** to keto ester **46**, and by conversion of **41**

and **43** to ketals **47** and **48**, respectively, whose stereochemistry was established by NOE studies.[25] At this point, the structures of **41**-**44** were secure. The only remaining assumption regards the face of the aldehyde that is attacked, which has been established by Kiyooka and others in numerous examples.[19,22]

We then compared the spectral data of **41**-**44** and **33** and **34**. The subtle differences in the ^{1}H and ^{13}C NMR spectra of (21*R*,22*S*)-**33**, (2*S*,3*R*)-**41**, (2*R*,3*S*)-**42** on the one hand and (21*R*,22*R*)-**34**, (2*R*,3*R*)-**43**, and (2*S*,3*S*)-**42** on the other hand are identical in all 10 features that we can distinguish as shown in Tables S6 and S7 suggesting that the stereochemistry of **33** and **34** can be assigned as shown by analogy to that of **41**-**44**. The chromatographic properties also support this assignment: **33** is less polar than **34**, **41** is less polar than **43**, and **42** is less polar than **44**.

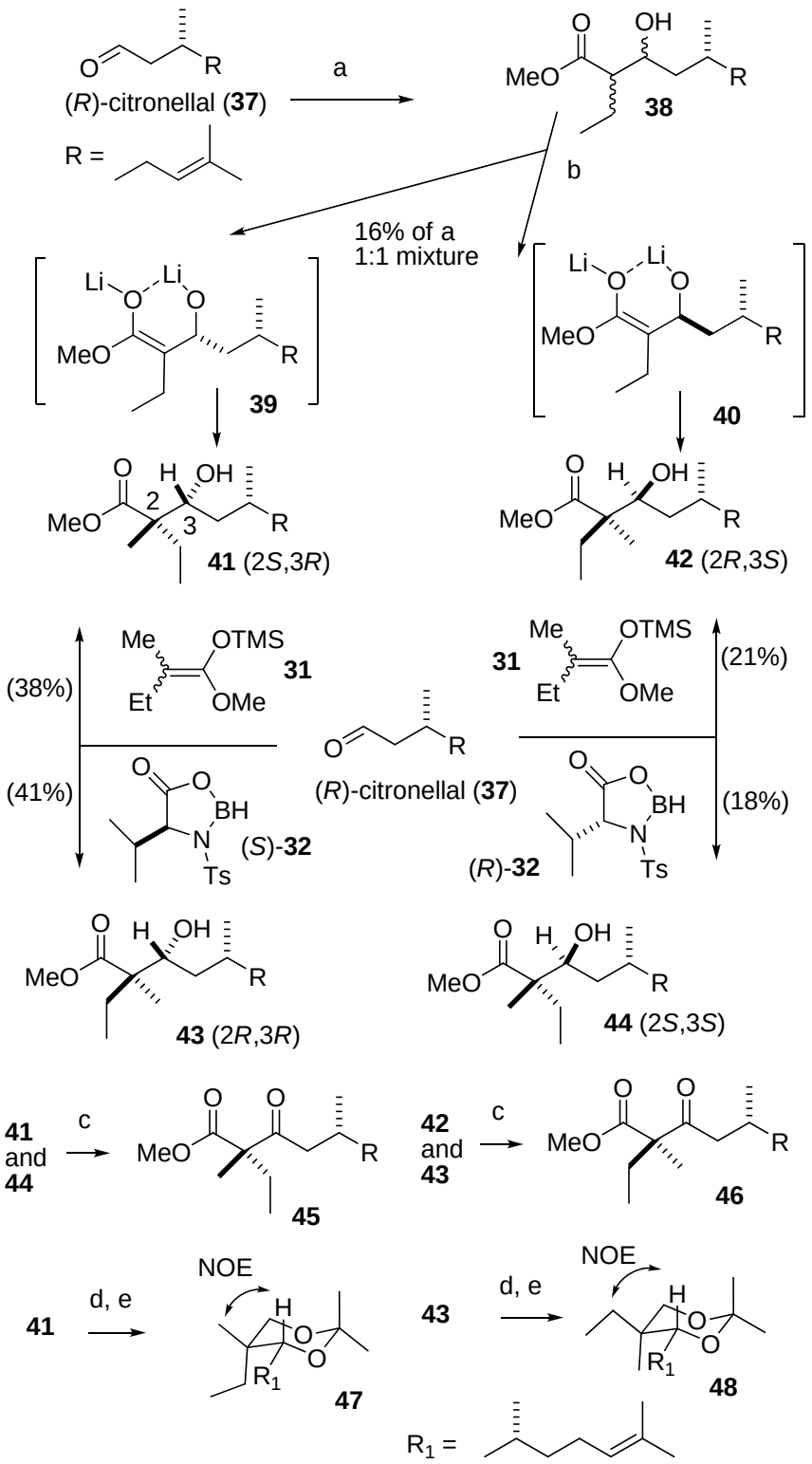
References

[22] K. Ishiwara and H. Yamamoto in *Modern Aldol Reactions, Vol. 2: Metal Catalysis* (Ed.; R. Mahrwald) Wiley-VCH, Weinheim, 2004, pp 25-68.

[23] a) G. Fráter, U. Müller, W. Günther, *Tetrahedron* **1984**, *40*, 1269-1277; b) G. Fráter, *Helv. Chem. Acta* **1979**, *62*, 2825-2828.

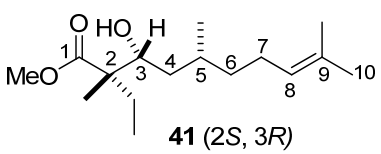
[24] E. Tayama, R. Hashimoto, *Tetrahedron Lett.* **2007**, *48*, 7950-7952.

[25] For analogous NOE studies on a related ketal, see: R. A. N. C. Crump, I. Fleming, J. H. M. Hill, D. Parker, N. L. Reddy, D. Waterson, *J. Chem. Soc. Perkin Trans. 1* **1992**, 3277-3294.

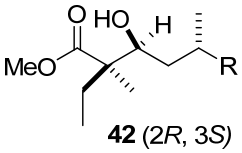


Scheme 8. Reagents and conditions: a) methyl butanoate, LDA, THF, –78 °C, 1 h, add **37**, –78 to –70 °C, 2 h (86%); b) 2 equiv LDA, THF, –50 to –20 °C, 90 min, then MeI, HMPA, –20 to 25 °C; c) Dess-Martin (87%); d) LAH, ether, 25 °C, 3 h; e) 2,2-dimethoxypropane, TsOH, 25 °C, 40 min (79% of **47** from **41**, 81% of **48** from **43**).

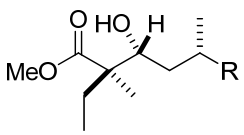
Table S6. Comparison of the ^{13}C and ^{1}H NMR Spectral Data Reported for Citronellal-derived Hydroxy Esters 41-44.



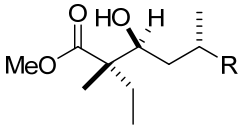
41 (2*S*, 3*R*)



42 (2*R*, 3*S*)



43 (2*R*, 3*R*)

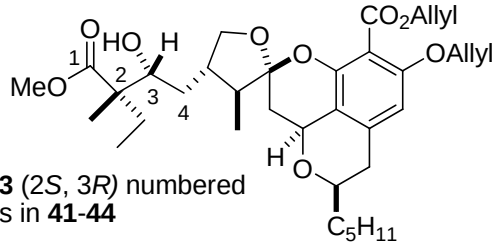


44 (2*S*, 3*S*)

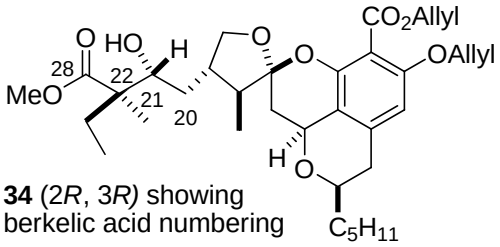
C (Roman)[a] *H(Italics)*[a]	**41** (2*S*,3*R*)	**42** (2*R*,3*S*)	**43** (2*R*,3*R*)	**44** (2*S*,3*S*)	
1	177.05	177.07	177.72	177.74	(2*R*,3*R*) and (2*S*,3*S*) 0.7 ppm downfield
2	51.6*	51.6*	51.73*	51.70*	
2-Me	16.21	16.25	16.53	16.58	(2*R*,3*R*) and (2*S*,3*S*) 0.3 ppm downfield
2-Me	*1.11*	*1.12*	*1.09*	*1.10*	*(2R,3R) and (2S,3S) 0.02 ppm upfield*
2-Et (CH_2)	28.57	28.56	29.41	29.41	(2*R*,3*R*) and (2*S*,3*S*) 0.85 ppm downfield
2-Et (CH_3)	9.0	9.0	8.87	8.82	(2*R*,3*R*) and (2*S*,3*S*) 0.15 ppm upfield
2-Et (CH_3)	*0.85*	*0.86*	*0.83*	*0.83*	*(2R,3R) and (2S,3S) 0.025 ppm upfield*
OMe	51.4*	51.4*	51.6*	51.5*	
OMe	*3.69*	*3.69*	*3.71*	*3.71*	*(2R,3R) and (2S,3S) 0.02 ppm downfield*
3	74.09	73.73	73.47	73.05	(2*R*,3*R*) and (2*S*,3*S*) 0.6-0.7 ppm upfield
3	*3.79*	*3.78*	*3.76*	*3.76*	*(2R,3R) and (2S,3S) 0.02 ppm upfield*
4	40.16	39.82	39.23	38.80	(2*R*,3*R*) and (2*S*,3*S*) 0.9-1.0 ppm upfield
5	29.60	29.10	29.50	28.92	(3*R*) 0.5 ppm downfield
5-Me	20.76	18.68	20.82	18.75	(3*R*) 2.1 ppm downfield
5-Me	*0.94*	*0.89*	*0.95*	*0.90*	*(3R) 0.05 ppm downfield*
6	35.52	38.19	35.61	38.29	(3*R*) 2.7 ppm upfield
7	25.2	25.5	25.3	25.5	
8	124.8	124.7	124.8	124.7	
9	131.2	131.2	131.2	131.1	
10	25.7	25.7	25.7	25.7	
9-Me	17.6	17.6	17.6	17.6	

* Data for C-2 and the OMe group may be switched. a) ^{13}C NMR data are in roman type and ^{1}H NMR data are in italic type.

Table S7. Comparison of the ^{13}C and ^{1}H NMR Spectral Data Reported for Berkelic Acid Intermediates 33 and 34.



33 (2*S*, 3*R)* numbered as in **41-44**



34 (2*R*, 3*R)* showing berkelic acid numbering

C (Roman)[a] *H (Italics)*[a]	**33** (2*S*,3*R*)	**34** (2*R*,3*R*)	
1	176.94	177.58	(2*R*,3*R*) 0.64 ppm downfield
2-Me	16.75	16.94	(2*R*,3*R*) 0.19 ppm downfield
2-Me	*1.14*	*1.13*	*(2R,3R) 0.01 ppm upfield*
2-Et (CH_2)	28.38	29.60	(2*R*,3*R*) 1.22 ppm downfield
2-Et (CH_3)	8.99	8.80	(2*R*,3*R*) 0.19 ppm upfield
2-Et (CH_3)	*0.87*	*0.85*	*(2R,3R) 0.02 ppm upfield*
OMe	*3.709*	*3.726*	*(2R,3R) 0.017 ppm downfield*
3	76.22	75.49	(2*R*,3*R*) 0.73 ppm upfield
3	*3.73*	*3.70*	*(2R,3R) 0.03 ppm upfield*
4	35.31	34.57	(2*R*,3*R*) 0.74 ppm upfield

a) ^{13}C NMR data are in roman type and ^{1}H NMR data are in italic type.

wxx-9-15-t33

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Ambient temperature
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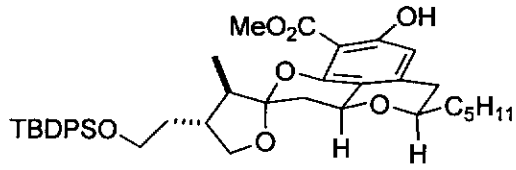

22
400 MHz ($CDCl_3$)

wxx-10-57-2

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Solvent: CDCl3
Ambient temperature
File: wxx-10-57-2
INOVA-500 "gamble"

Pulse 46.1 degrees
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Width 8000.0 Hz
27 repetitions
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DATA PROCESSING
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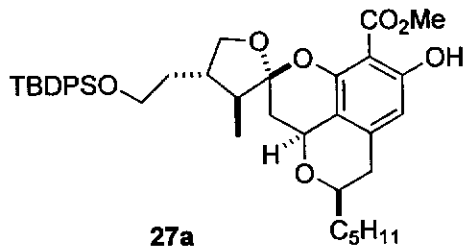
Total time 3 min, 31 sec



27a
400 MHz ($CDCl_3$)

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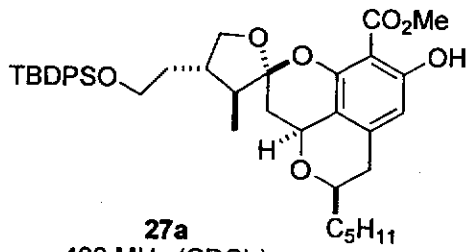
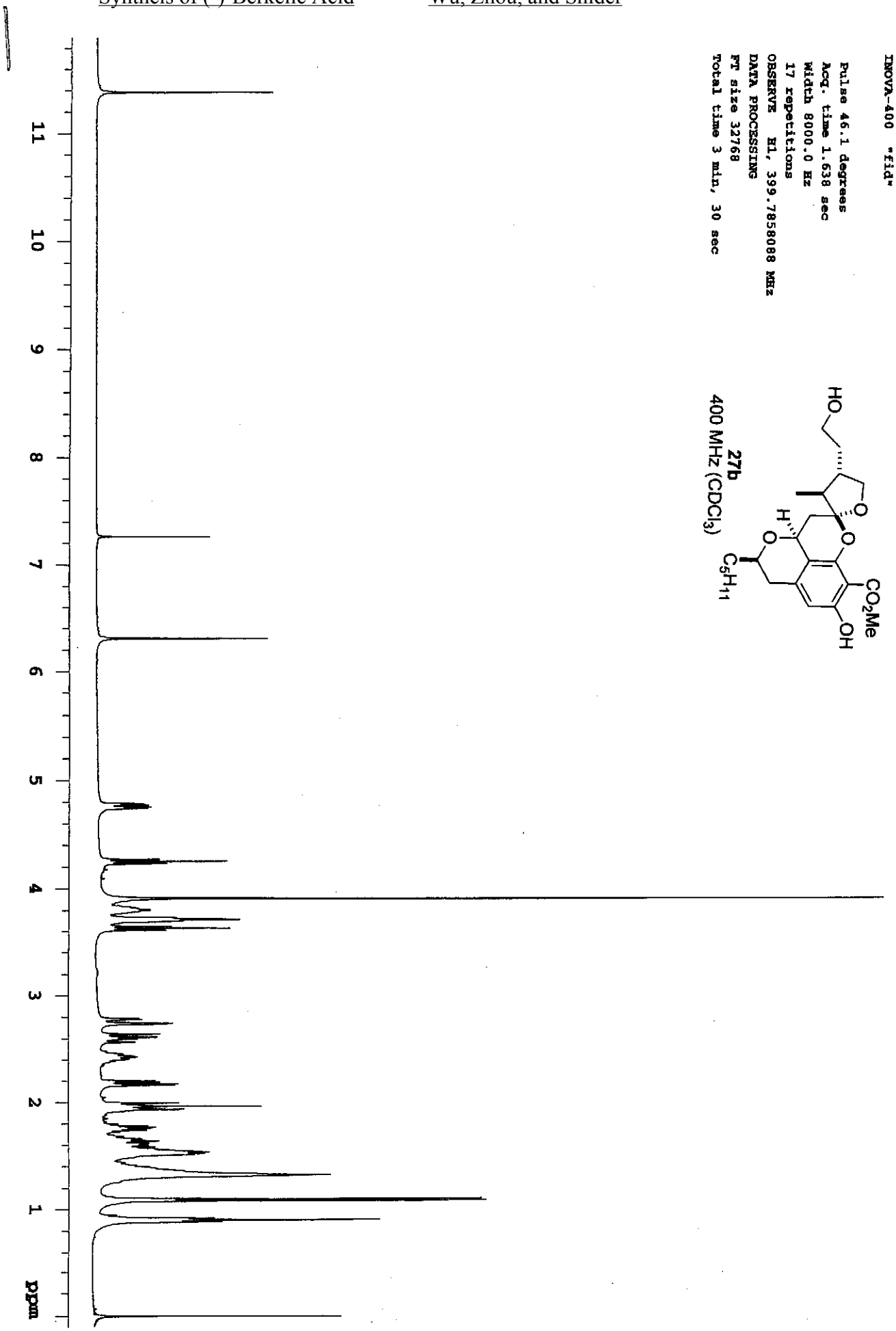
2	16294.597	162.093	24.5
3	15286.754	152.067	11.8
4	14202.617	141.283	21.3
5	13620.494	135.492	175.3
6	13422.130	133.519	32.6
7	13037.608	129.694	57.3
8	13039.134	129.709	58.8
9	12833.903	127.667	141.1
10	11327.861	112.686	16.7
11	10950.969	108.936	29.4
12	10887.645	108.307	33.8
13	10041.545	99.890	14.2
14	7772.563	77.319	43.0
15	7740.519	77.000	44.9
16	7708.476	76.681	44.1
17	7545.207	75.057	32.8
18	7386.516	73.478	30.3
19	6854.747	68.189	31.6
20	6357.310	63.240	33.3
21	5225.108	51.978	30.6
22	4922.221	48.965	40.6
23	4179.118	41.572	40.6
24	3651.164	36.321	40.4
25	3567.241	35.486	32.9
26	3469.584	34.514	32.5
27	3416.942	33.991	31.4
28	3193.400	31.767	46.3
29	2695.964	26.819	137.6
30	2522.014	25.088	43.0
31	2271.006	22.591	41.0
32	1921.580	19.115	27.7
33	1411.174	14.038	35.7
34	1173.137	11.670	34.0



27a
400 MHz ($CDCl_3$)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Width 8000.0 Hz
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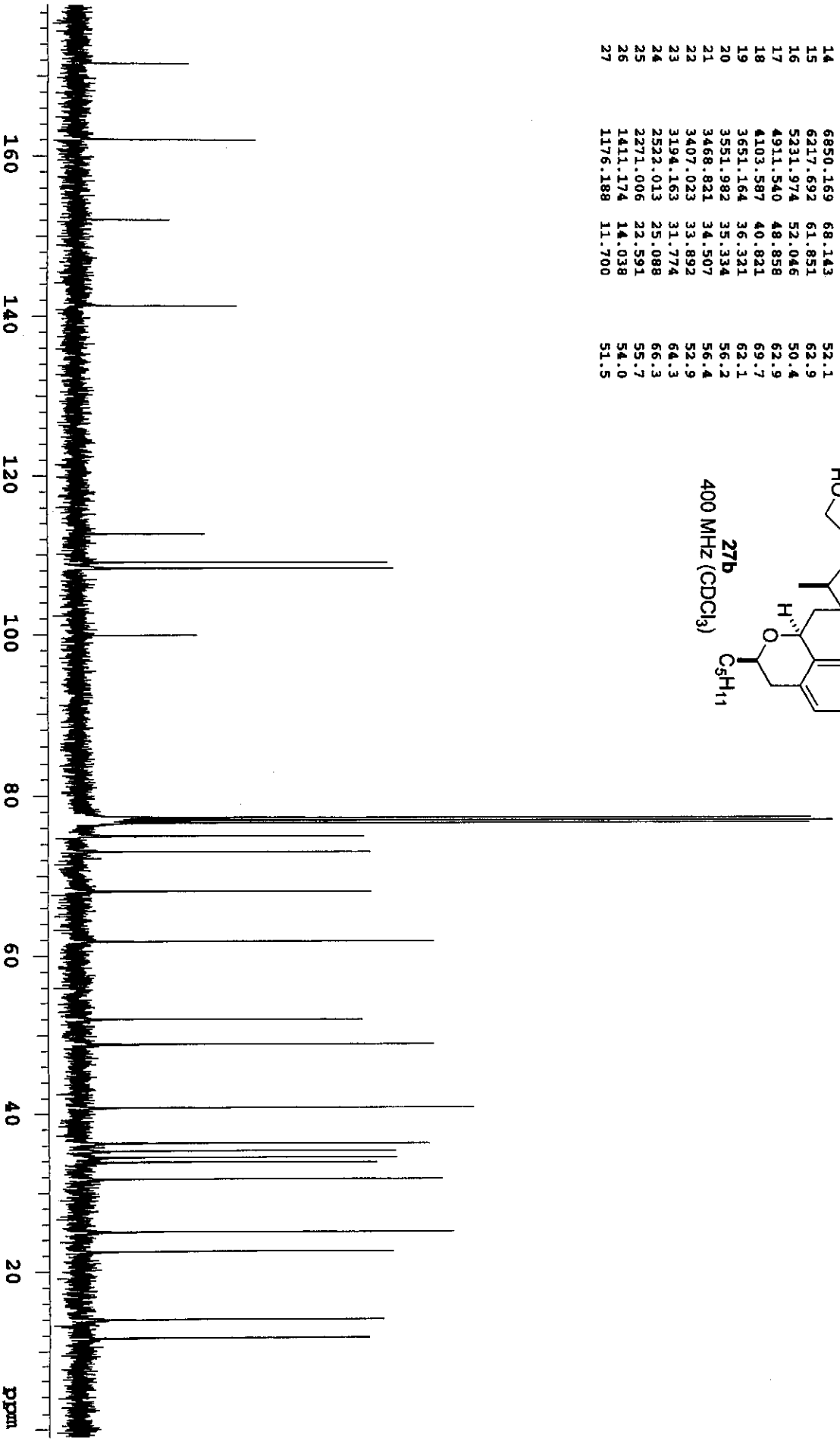
DATA PROCESSING
FT size 32768
Total time 3 min, 30 sec
27b
400 MHz (CDCl3)
HO
H
O
O
O
CO2Me
OH
C5H11
11
10
9
8
7
6
5
4
3
2
1
ppm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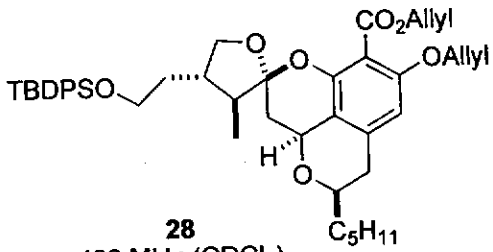
2 16292.308 162.070 32.0
3 15284.465 152.045 16.8
4 14204.142 141.298 28.6
5 11327.861 112.686 23.1
6 10963.938 109.065 54.9
7 10889.170 108.322 55.9
8 10040.782 99.882 21.6
9 7772.563 77.319 129.1
10 7740.519 77.000 132.9
11 7708.476 76.681 128.7
12 7546.733 75.072 50.8
13 7349.131 73.107 51.8
14 6850.169 68.143 52.1
15 6217.692 61.851 62.9
16 5231.974 52.046 50.4
17 4911.540 48.858 62.9
18 4103.587 40.821 69.7
19 3651.164 36.321 62.1
20 3551.982 35.334 56.2
21 3468.821 34.507 56.4
22 3407.023 33.892 52.9
23 3194.163 31.774 64.3
24 2522.013 25.088 66.3
25 2271.006 22.591 55.7
26 1411.174 14.038 54.0
27 1176.188 11.700 51.5
HO
O
O
H
O
CO2Me
OH
C5H11
27b
400 MHz (CDCl3)
160
140
120
100
80
60
40
20
ppm

wxx-10-143-10

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-10-143-10
INOVA-500 "gamble"

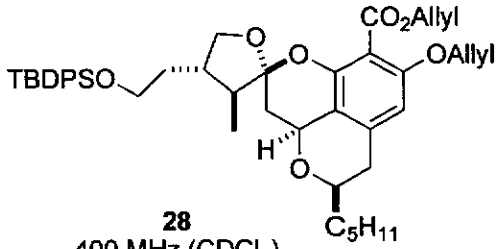
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
19 repetitions
OBSERVE H1, 399.7858276 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec



28
400 MHz ($CDCl_3$)

WXX-10-143-10C

INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	16640.971	165.539	18.2				
2	15636.180	155.543	21.1				
3	14983.104	149.047	16.6				
4	13656.352	135.849	26.6				
5	13622.020	135.507	172.8				
6	13425.181	133.549	15.4				
7	13422.130	133.519	16.9				
8	13364.909	132.949	26.7				
9	13297.007	132.274	20.2				
10	13033.793	129.656	86.7				
11	12834.666	127.675	170.0				
12	11871.837	118.097	32.8				
13	11772.654	117.110	33.9				
14	11522.410	114.621	22.1				
15	11015.818	109.582	14.5				
16	10925.029	108.678	29.8				
17	10479.472	104.246	29.0				
18	7772.563	77.319	71.7				
19	7740.519	77.000	75.4				
20	7708.476	76.681	74.7				
21	7571.147	75.315	34.2				
22	7372.020	73.334	29.1				
23	6972.239	69.357	41.4				
24	6850.169	68.143	31.5				
25	6590.007	65.555	40.3				
26	6355.021	63.218	34.3				
27	4922.221	48.965	38.5				
28	4153.941	41.322	39.3				
29	3649.638	36.305	36.3				
30	3583.262	35.645	30.9				
31	3470.347	34.522	29.5				
32	3460.429	34.423	31.4				
33	3194.163	31.774	46.1				
34	2694.438	26.803	136.9				
35	2527.354	25.141	44.3				
36	2272.532	22.606	48.1				
37	1915.477	19.054	29.4				
38	1411.174	14.038	40.3				
39	1167.033	11.609	38.6				



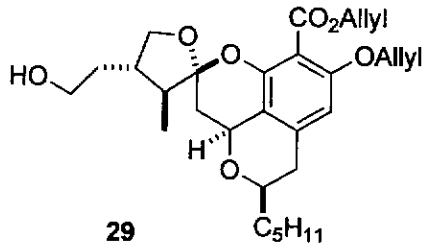
28
400 MHz ($CDCl_3$)

wxx-10-147-2

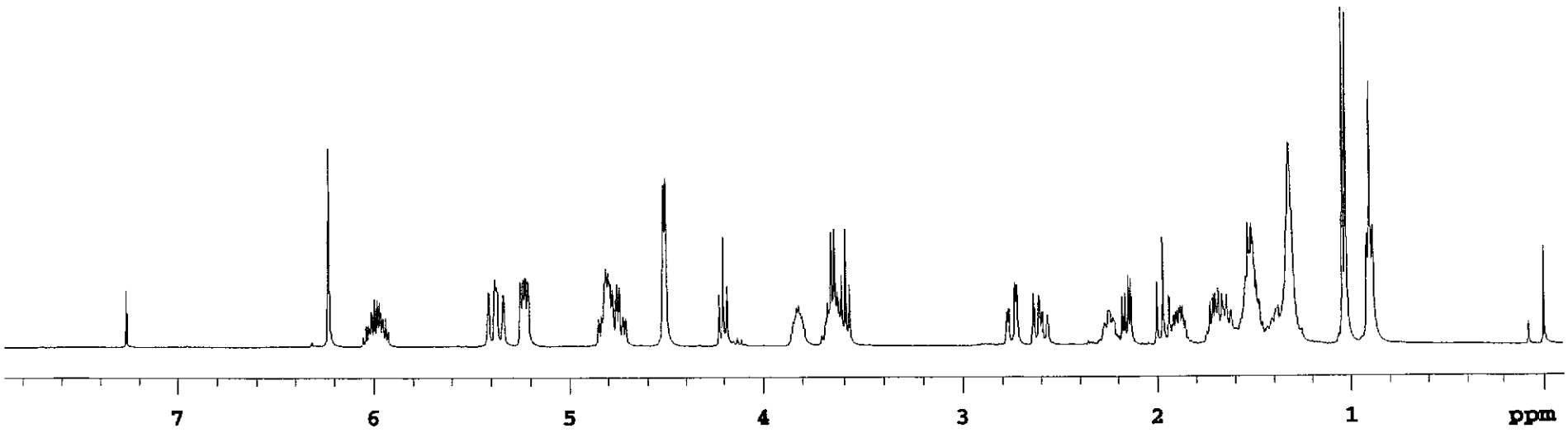
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-10-147-2
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
47 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec

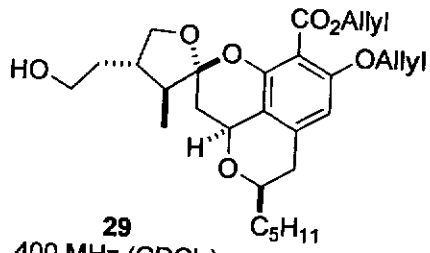


29
400 MHz ($CDCl_3$)

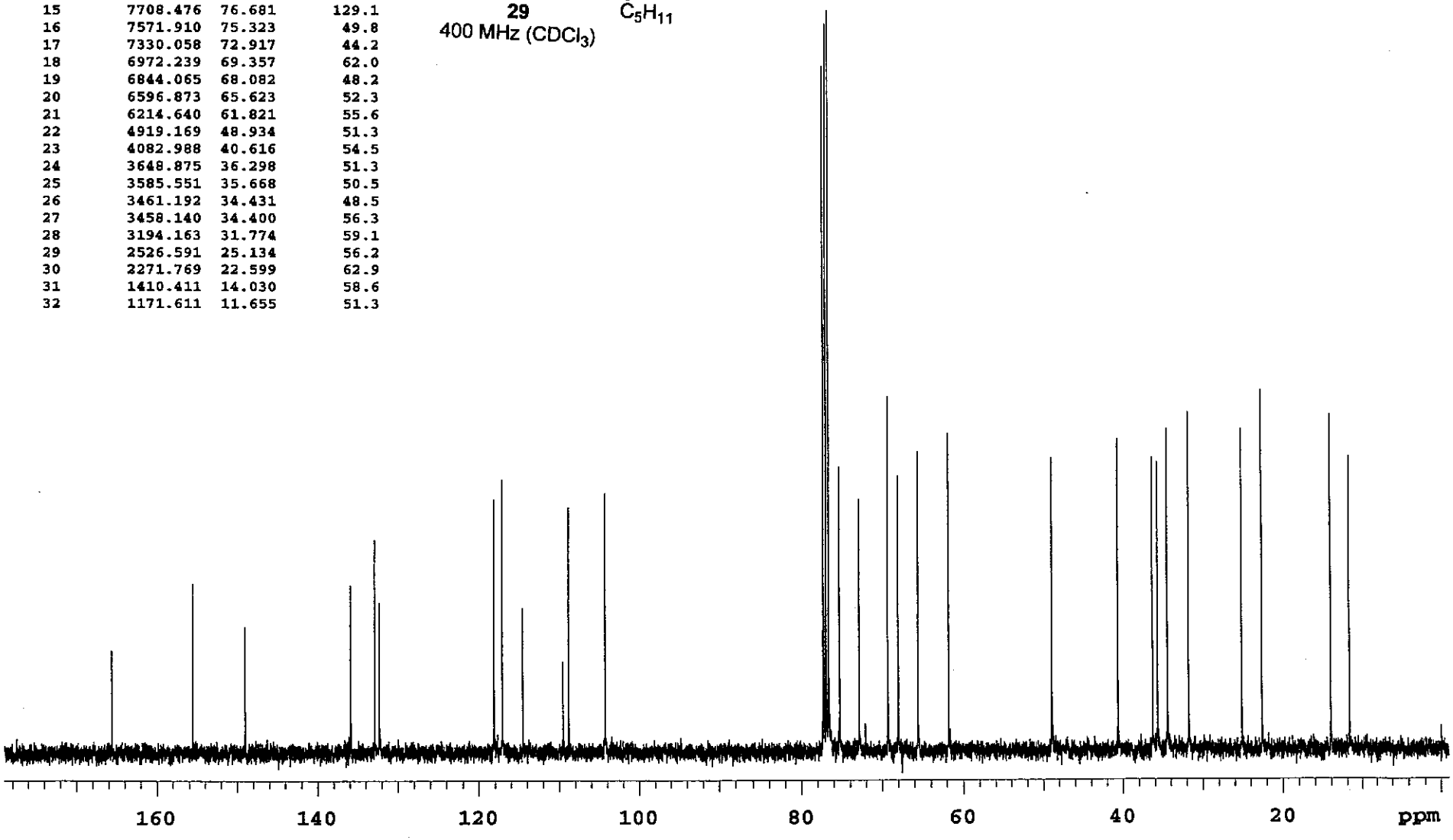


WXx-10-147-2C

INDEX	FREQUENCY	PPM	HEIGHT
1	16650.889	165.637	18.0
2	15636.180	155.543	29.7
3	14980.052	149.016	22.2
4	13662.455	135.909	29.4
5	13361.857	132.919	37.3
6	13302.348	132.327	26.4
7	11876.414	118.142	44.3
8	11775.706	117.141	47.6
9	11517.833	114.575	25.4
10	11007.426	109.498	16.0
11	10939.524	108.823	42.9
12	10481.761	104.269	45.2
13	7772.563	77.319	119.4
14	7740.519	77.000	126.8
15	7708.476	76.681	129.1
16	7571.910	75.323	49.8
17	7330.058	72.917	44.2
18	6972.239	69.357	62.0
19	6844.065	68.082	48.2
20	6596.873	65.623	52.3
21	6214.640	61.821	55.6
22	4919.169	48.934	51.3
23	4082.988	40.616	54.5
24	3648.875	36.298	51.3
25	3585.551	35.668	50.5
26	3461.192	34.431	48.5
27	3458.140	34.400	56.3
28	3194.163	31.774	59.1
29	2526.591	25.134	56.2
30	2271.769	22.599	62.9
31	1410.411	14.030	58.6
32	1171.611	11.655	51.3



29
400 MHz ($CDCl_3$)

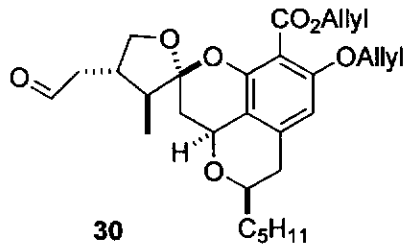


wxx-11-1-4

Pulse Sequence: s2pul

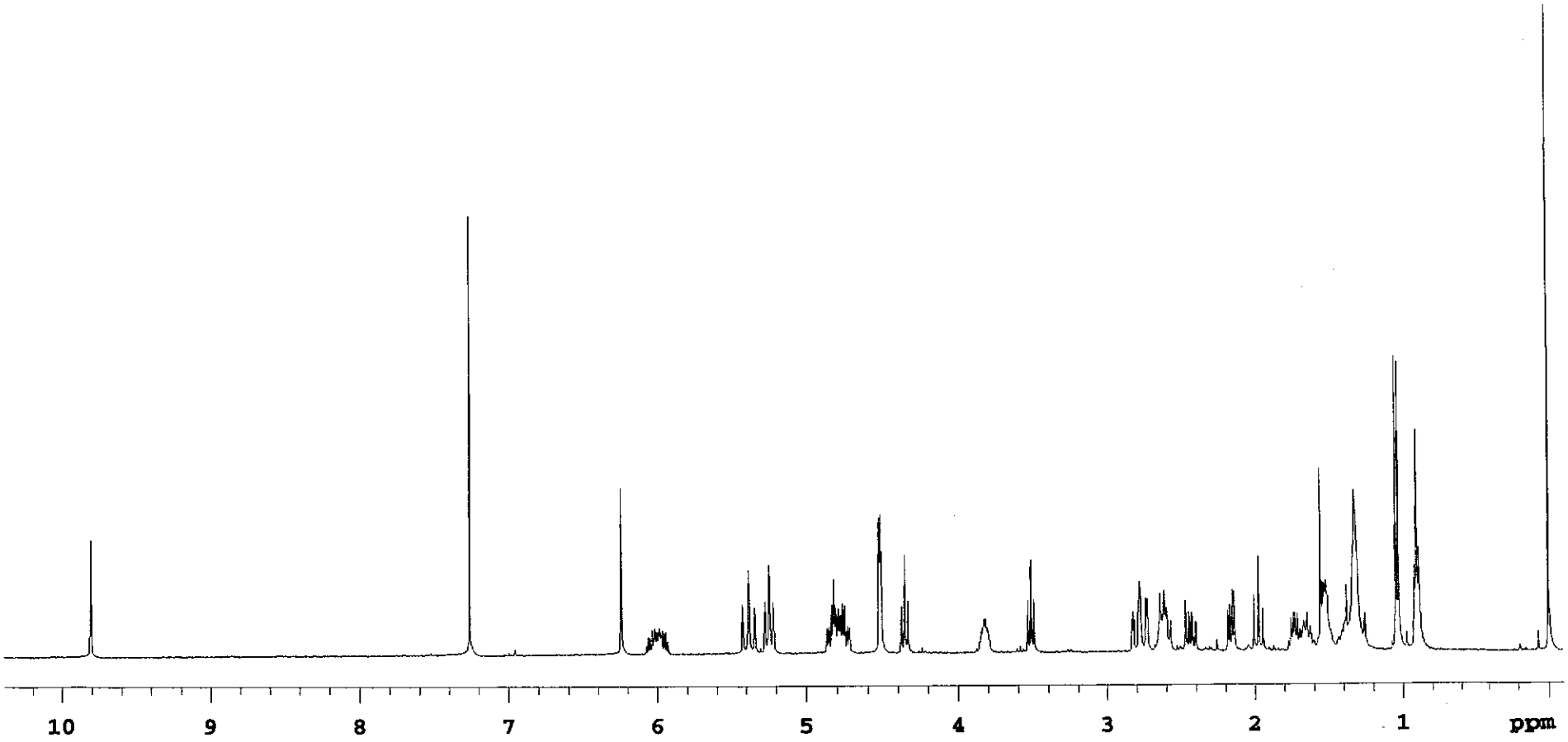
Solvent: CDCl3
Ambient temperature
File: wxx-11-1-4
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
21 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec



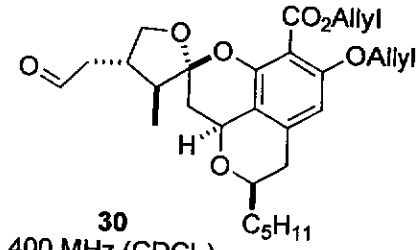
30

400 MHz ($CDCl_3$)



WX-11-1-3C

INDEX	FREQUENCY	PPM	HEIGHT
1	20159.648	200.541	48.1
2	16635.630	165.485	14.4
3	15640.757	155.589	25.0
4	14963.267	148.849	22.0
5	13663.981	135.925	31.7
6	13359.568	132.896	44.7
7	13294.719	132.251	29.5
8	11900.065	118.378	46.0
9	11778.758	117.171	54.8
10	11509.440	114.492	29.0
11	11015.818	109.582	15.8
12	10901.377	108.443	52.8
13	10500.071	104.451	57.0
14	7772.563	77.319	179.2
15	7740.519	77.000	188.7
16	7708.476	76.681	192.2
17	7574.198	75.345	50.9
18	7257.579	72.196	54.0
19	6974.528	69.380	66.7
20	6834.147	67.984	56.1
21	6602.214	65.677	60.4
22	4877.970	48.524	62.0
23	4752.085	47.272	65.3
24	3781.626	37.618	62.3
25	3648.875	36.298	61.2
26	3455.851	34.378	55.6
27	3448.985	34.309	53.3
28	3194.163	31.774	71.9
29	2525.828	25.126	70.8
30	2272.532	22.606	67.3
31	1411.174	14.038	64.3
32	1159.404	11.533	58.8



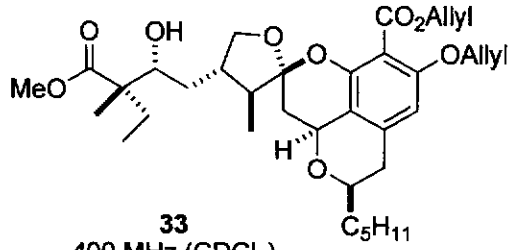
30
400 MHz ($CDCl_3$)

wxx-11-13-2

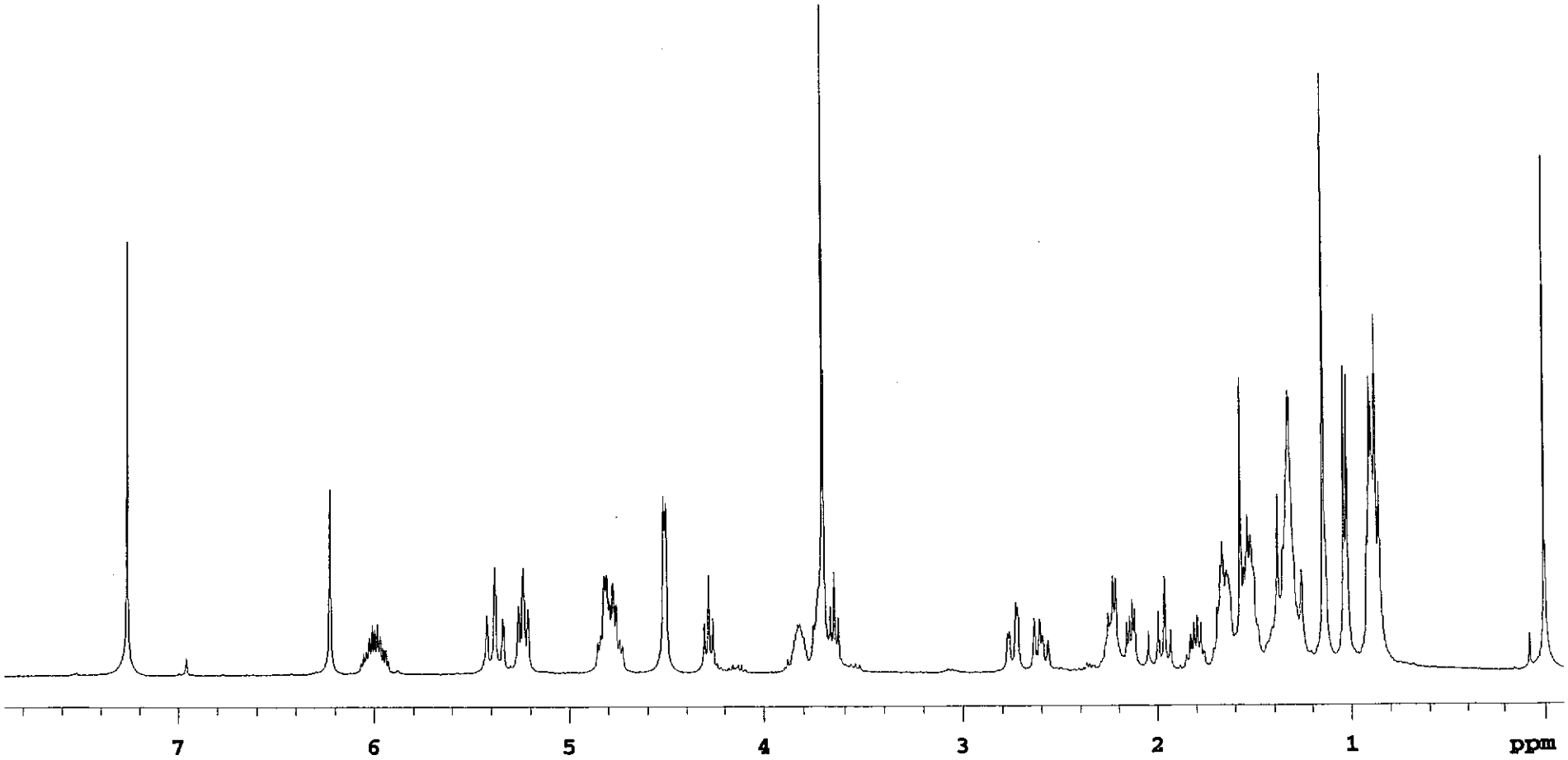
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-11-13-2
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
69 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec

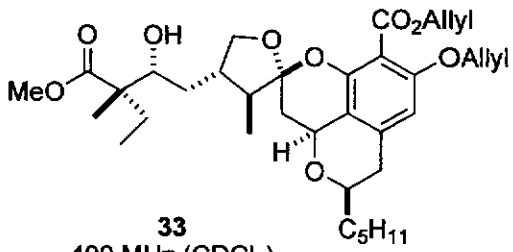


33
400 MHz ($CDCl_3$)



WXX-11-19-2C

INDEX	FREQUENCY	PPM	HEIGHT
1	17787.213	176.941	18.6
2	16653.449	165.663	18.0
3	15636.421	155.546	18.1
4	14987.140	149.087	17.8
5	13660.347	135.888	31.9
6	13365.844	132.959	37.6
7	13309.384	132.397	26.5
8	11878.829	118.166	37.9
9	11775.066	117.134	43.1
10	11524.814	114.645	25.6
11	11009.814	109.522	16.9
12	10909.104	108.520	33.7
13	10478.029	104.232	40.1
14	7772.563	77.319	133.2
15	7740.519	77.000	138.5
16	7708.475	76.681	133.9
17	7661.934	76.218	48.1
18	7570.378	75.308	45.9
19	7425.416	73.865	38.9
20	6974.504	69.380	52.0
21	6847.090	68.112	45.3
22	6598.364	65.638	49.4
23	5205.957	51.787	44.7
24	5149.498	51.225	41.7
25	4929.765	49.040	45.4
26	4269.802	42.475	51.8
27	3651.039	36.319	50.9
28	3549.565	35.310	41.3
29	3473.269	34.551	35.7
30	3459.535	34.414	43.2
31	3195.550	31.788	62.4
32	2852.980	28.380	42.1
33	2527.195	25.140	61.0
34	2272.365	22.605	69.4
35	1683.358	16.745	51.7
36	1410.980	14.036	61.1
37	1192.773	11.865	44.6
38	903.610	8.989	44.9



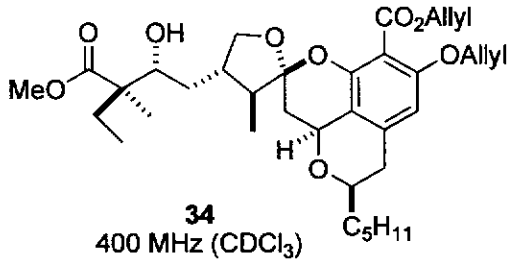
33
400 MHz ($CDCl_3$)

wxx-11-13-3

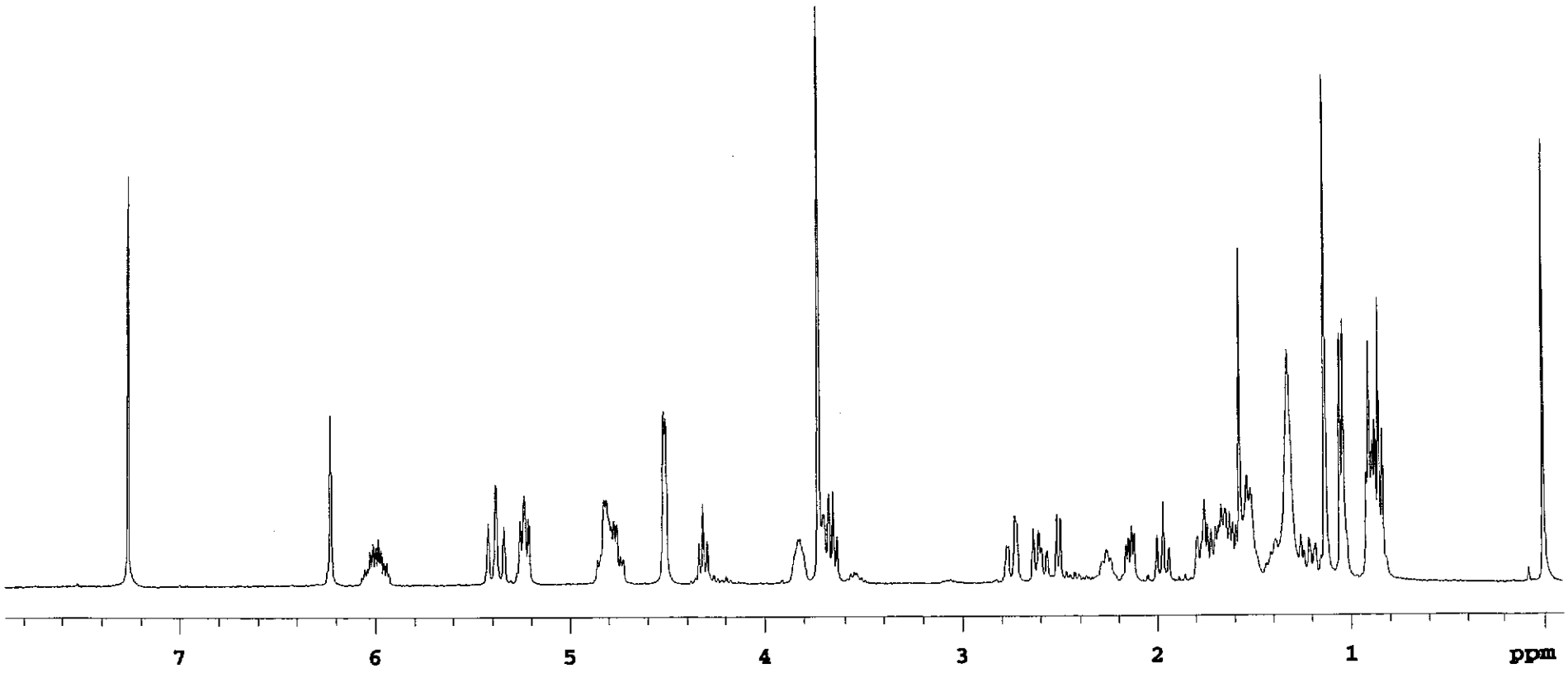
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-11-13-3
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
42 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec

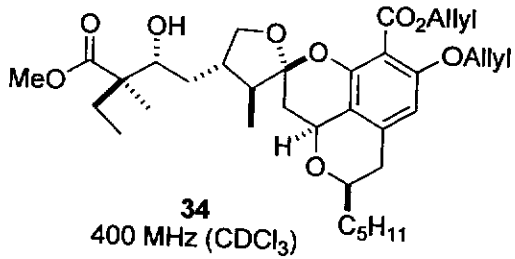


34
400 MHz ($CDCl_3$)

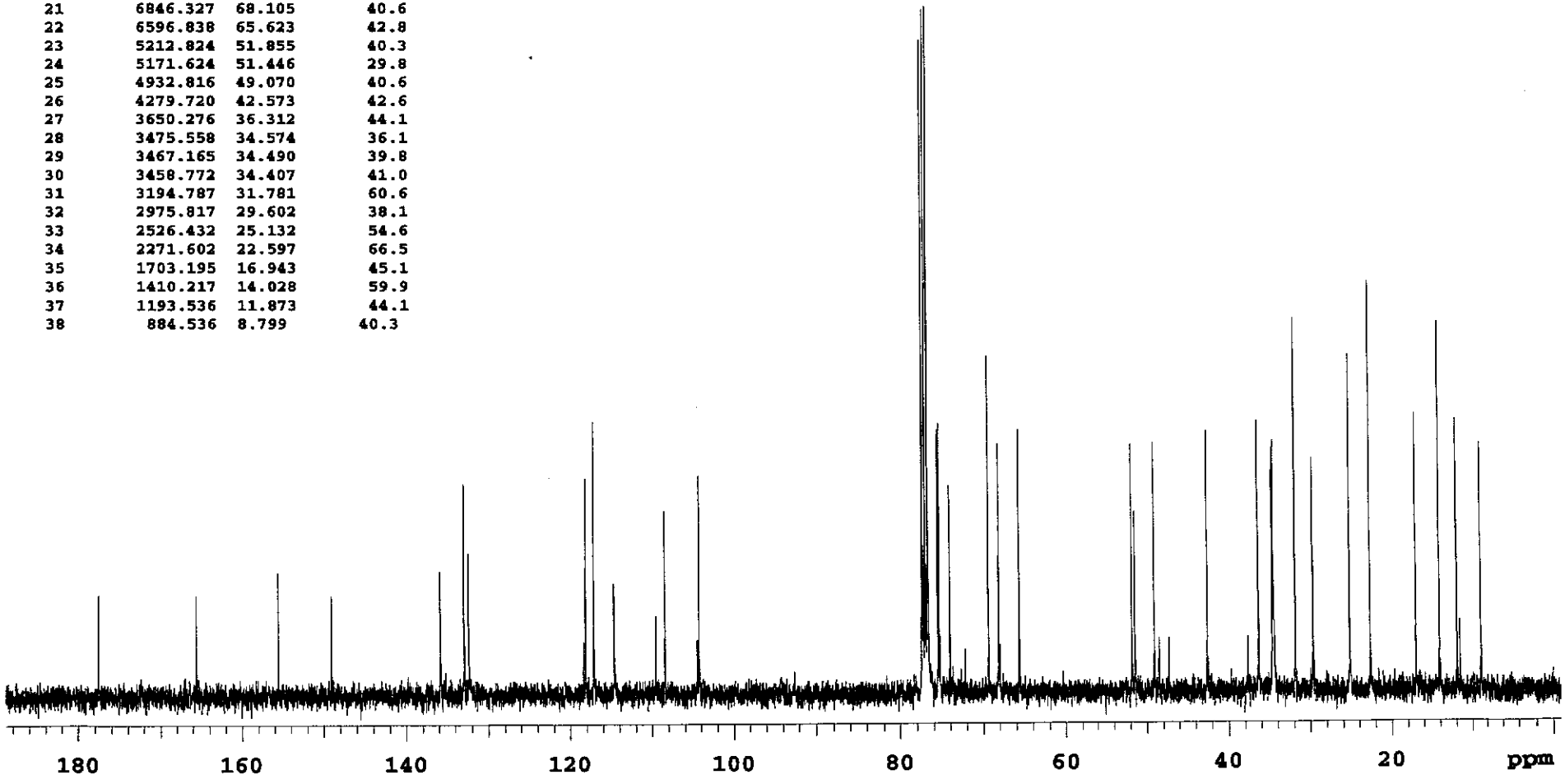


WXX-11-19-3C

INDEX	FREQUENCY	PPM	HEIGHT
1	17851.301	177.579	16.6
2	16650.398	165.632	16.4
3	15637.946	155.561	20.2
4	14988.665	149.102	16.4
5	13658.821	135.873	20.4
6	13365.844	132.959	34.3
7	13308.621	132.390	23.3
8	11873.488	118.113	35.3
9	11773.540	117.119	44.2
10	11524.052	114.637	18.3
11	11009.052	109.514	13.0
12	10899.948	108.429	30.1
13	10477.267	104.224	35.6
14	7772.563	77.319	105.9
15	7740.519	77.000	110.8
16	7708.475	76.681	111.3
17	7588.689	75.490	42.8
18	7569.616	75.300	43.8
19	7439.149	74.002	34.0
20	6973.742	69.372	54.6
21	6846.327	68.105	40.6
22	6596.838	65.623	42.8
23	5212.824	51.855	40.3
24	5171.624	51.446	29.8
25	4932.816	49.070	40.6
26	4279.720	42.573	42.6
27	3650.276	36.312	44.1
28	3475.558	34.574	36.1
29	3467.165	34.490	39.8
30	3458.772	34.407	41.0
31	3194.787	31.781	60.6
32	2975.817	29.602	38.1
33	2526.432	25.132	54.6
34	2271.602	22.597	66.5
35	1703.195	16.943	45.1
36	1410.217	14.028	59.9
37	1193.536	11.873	44.1
38	884.536	8.799	40.3



34
400 MHz ($CDCl_3$)

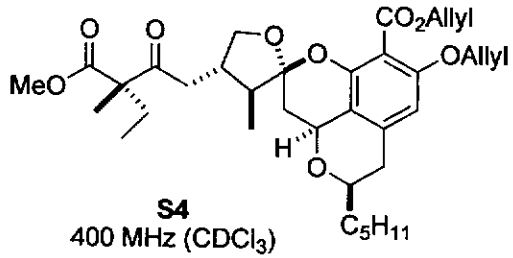


wxx-11-21-1

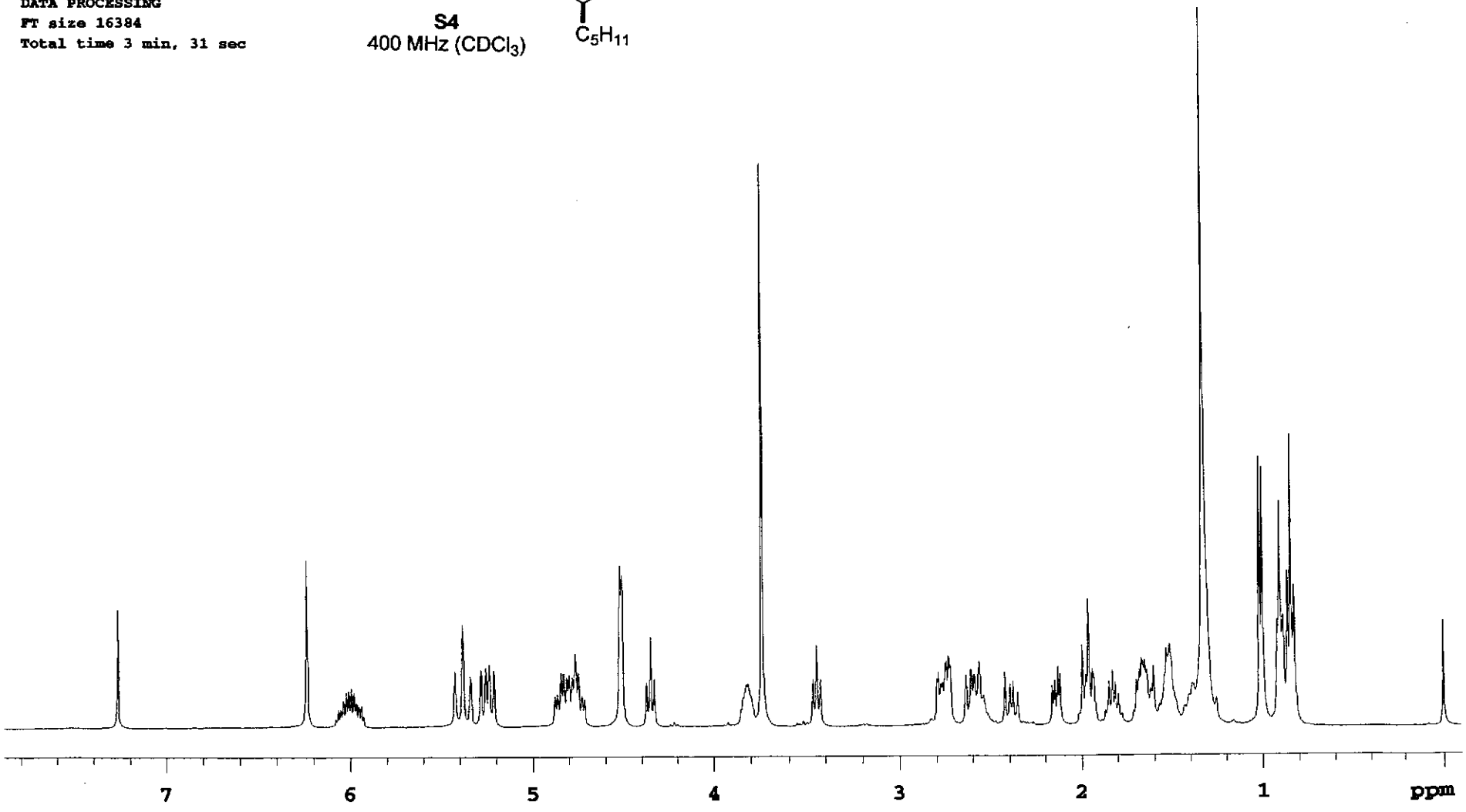
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-11-21-1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
39 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec

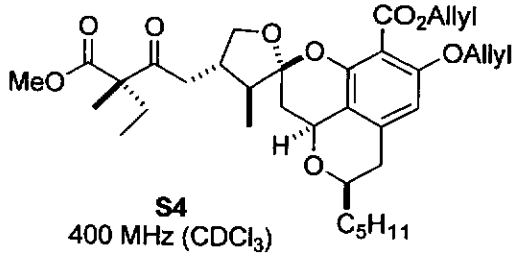


S4
400 MHz ($CDCl_3$)



WXX-11-21-1C

INDEX	FREQUENCY	PPM	HEIGHT
1	20763.896	206.552	29.9
2	17436.717	173.454	19.7
3	16637.919	165.508	20.1
4	15637.706	155.558	31.4
5	14970.896	148.925	23.5
6	13654.826	135.833	35.4
7	13363.383	132.934	46.3
8	13290.141	132.206	31.3
9	11913.035	118.507	50.6
10	11776.469	117.148	54.9
11	11511.729	114.515	29.3
12	11023.448	109.657	17.2
13	10899.852	108.428	52.5
14	10494.731	104.398	50.9
15	7772.563	77.319	225.1
16	7740.519	77.000	233.0
17	7708.476	76.681	229.0
18	7572.673	75.330	56.2
19	7316.325	72.780	49.3
20	6975.291	69.388	74.0
21	6837.962	68.022	56.0
22	6602.977	65.684	65.7
23	6004.832	59.734	36.9
24	5265.544	52.380	57.1
25	4868.052	48.426	60.6
26	4225.657	42.035	60.1
27	3907.511	38.871	69.4
28	3648.875	36.298	63.5
29	3459.666	34.416	59.1
30	3456.614	34.385	64.8
31	3194.163	31.774	67.9
32	2800.486	27.858	55.8
33	2525.828	25.126	72.2
34	2272.532	22.606	76.3
35	1849.101	18.394	64.4
36	1410.411	14.030	62.2
37	1167.033	11.609	60.4
38	867.198	8.627	49.7



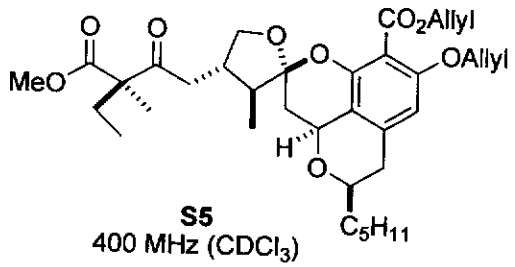
S4
400 MHz ($CDCl_3$)

wxx-11-21-2

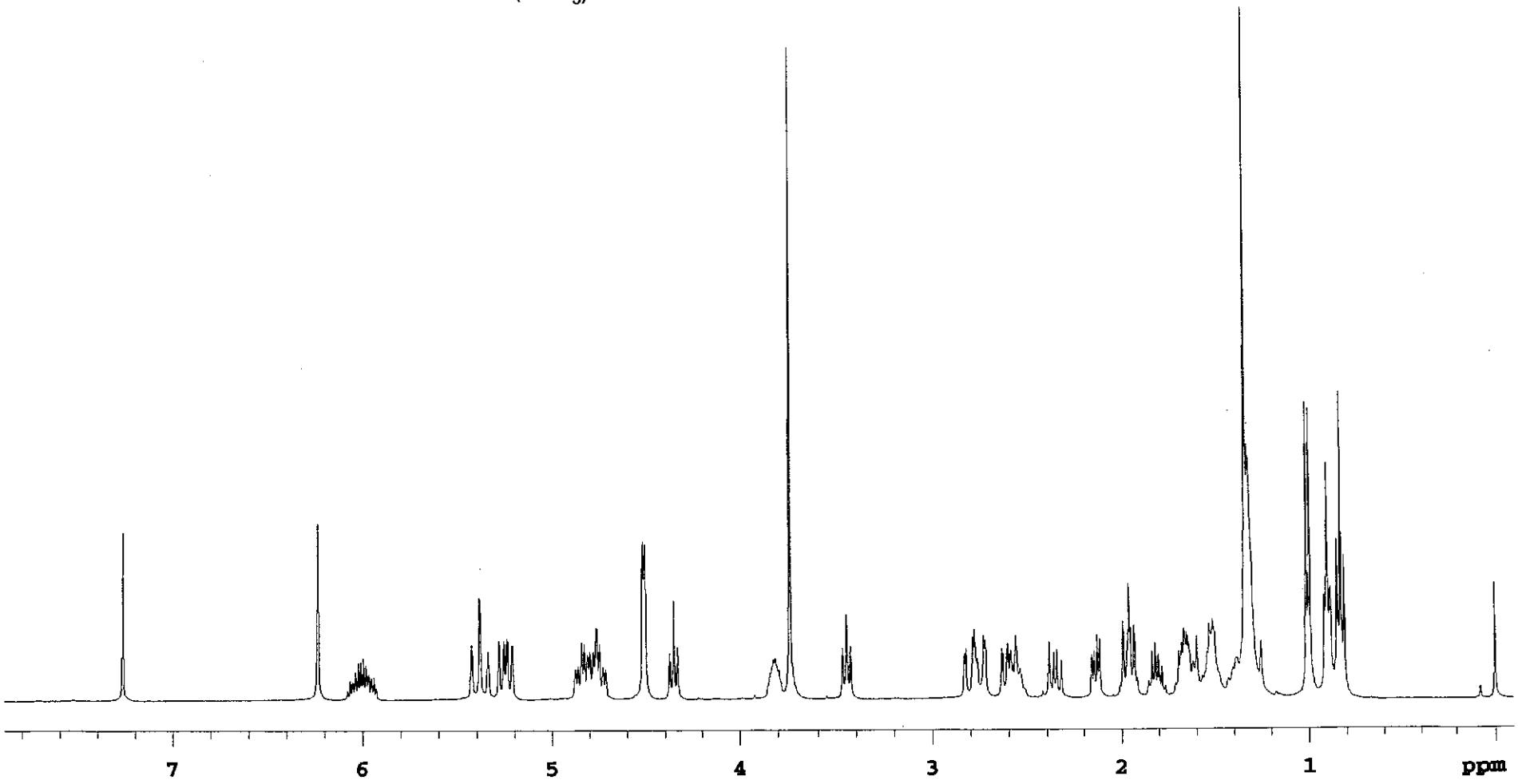
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wxx-11-21-2
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
29 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 16384
Total time 3 min, 31 sec

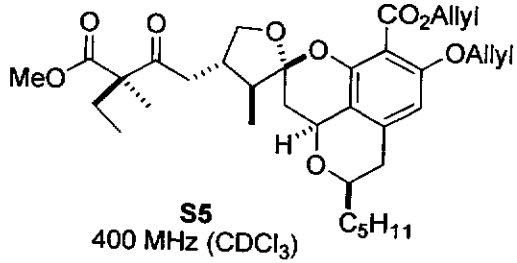


S5
400 MHz ($CDCl_3$)

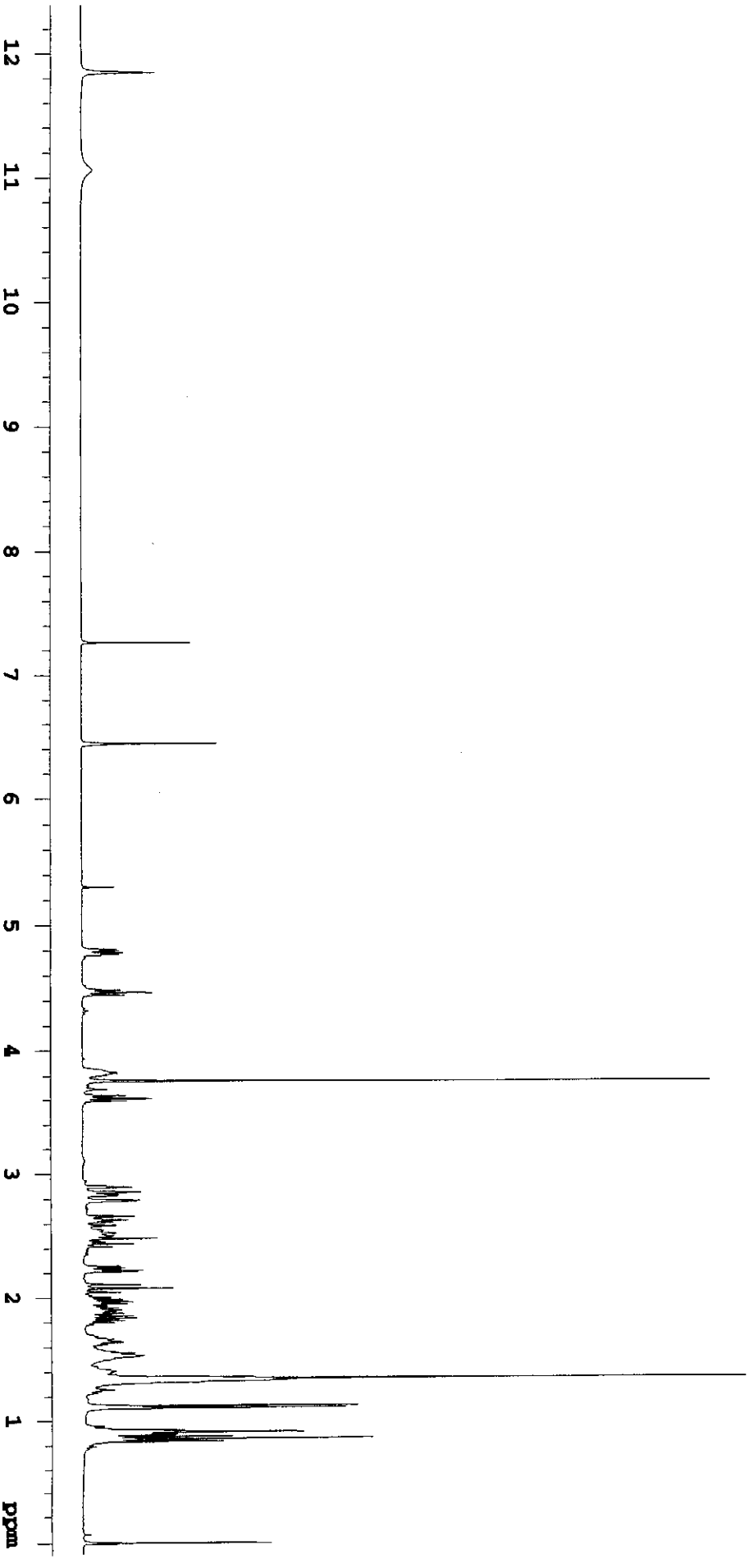


WX-11-21-2C

INDEX	FREQUENCY	PPM	HEIGHT
1	20758.555	206.499	23.6
2	17436.717	173.454	28.7
3	16638.682	165.516	21.1
4	15639.231	155.574	32.0
5	14971.659	148.933	23.6
6	13656.352	135.849	40.5
7	13364.909	132.949	39.3
8	13291.667	132.221	27.8
9	11912.272	118.499	49.6
10	11777.232	117.156	59.8
11	11513.255	114.530	32.4
12	11024.211	109.665	15.6
13	10899.851	108.428	49.8
14	10495.494	104.406	52.9
15	7772.563	77.319	206.3
16	7740.519	77.000	217.3
17	7708.476	76.681	209.6
18	7573.435	75.338	57.9
19	7314.799	72.765	50.3
20	6976.054	69.395	71.8
21	6839.488	68.037	52.2
22	6603.739	65.692	62.8
23	6004.832	59.734	47.7
24	5267.069	52.395	48.9
25	4871.867	48.464	60.4
26	4224.894	42.028	60.5
27	3907.511	38.871	67.1
28	3649.638	36.305	63.8
29	3457.377	34.393	69.1
30	3194.926	31.782	74.6
31	2793.620	27.790	52.8
32	2526.591	25.134	74.8
33	2273.295	22.614	69.4
34	1840.708	18.311	59.0
35	1411.173	14.038	62.4
36	1167.796	11.617	58.9
37	863.383	8.589	50.3

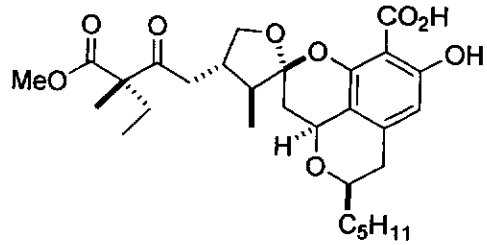


S5
400 MHz ($CDCl_3$)


wzx-11-23-5
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: wzx-11-23-5
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 8000.0 Hz
31 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 31 sec
MeO
O
O
O
H
O
O
C5H11
CO2H
OH
35 (berkelic acid)
400 MHz (CDCl3)
12
11
10
9
8
7
6
5
4
3
2
1
ppm

WXX-11-23-5C in $CDCl_3$

INDEX	FREQUENCY	PPM	HEIGHT
1	20712.779	206.044	22.0
2	17426.798	173.356	19.0
3	17139.170	170.495	27.5
4	16338.847	162.533	32.9
5	15055.583	149.768	20.4
6	14296.458	142.216	27.6
7	11275.981	112.170	59.2
8	11107.371	110.492	47.1
9	9914.897	98.630	23.0
10	7772.563	77.319	259.7
11	7740.519	77.000	265.4
12	7708.476	76.681	257.4
13	7560.465	75.209	48.6
14	7391.093	73.524	41.0
15	6759.379	67.240	45.8
16	6005.595	59.742	30.7
17	5276.225	52.486	45.7
18	4845.164	48.198	53.6
19	4178.355	41.565	50.6
20	3955.577	39.349	48.9
21	3643.534	36.245	56.7
22	3448.222	34.302	78.1
23	3191.874	31.752	69.2
24	2805.827	27.911	49.4
25	2515.147	25.020	53.4
26	2270.243	22.584	60.4
27	1850.627	18.409	50.3
28	1410.411	14.030	57.4
29	1205.943	11.996	50.9
30	871.775	8.672	42.4



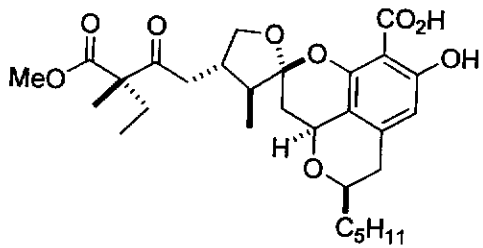
35 (berkelic acid)
400 MHz ($CDCl_3$)

wox-11-23-5-CD3OD – 500 M

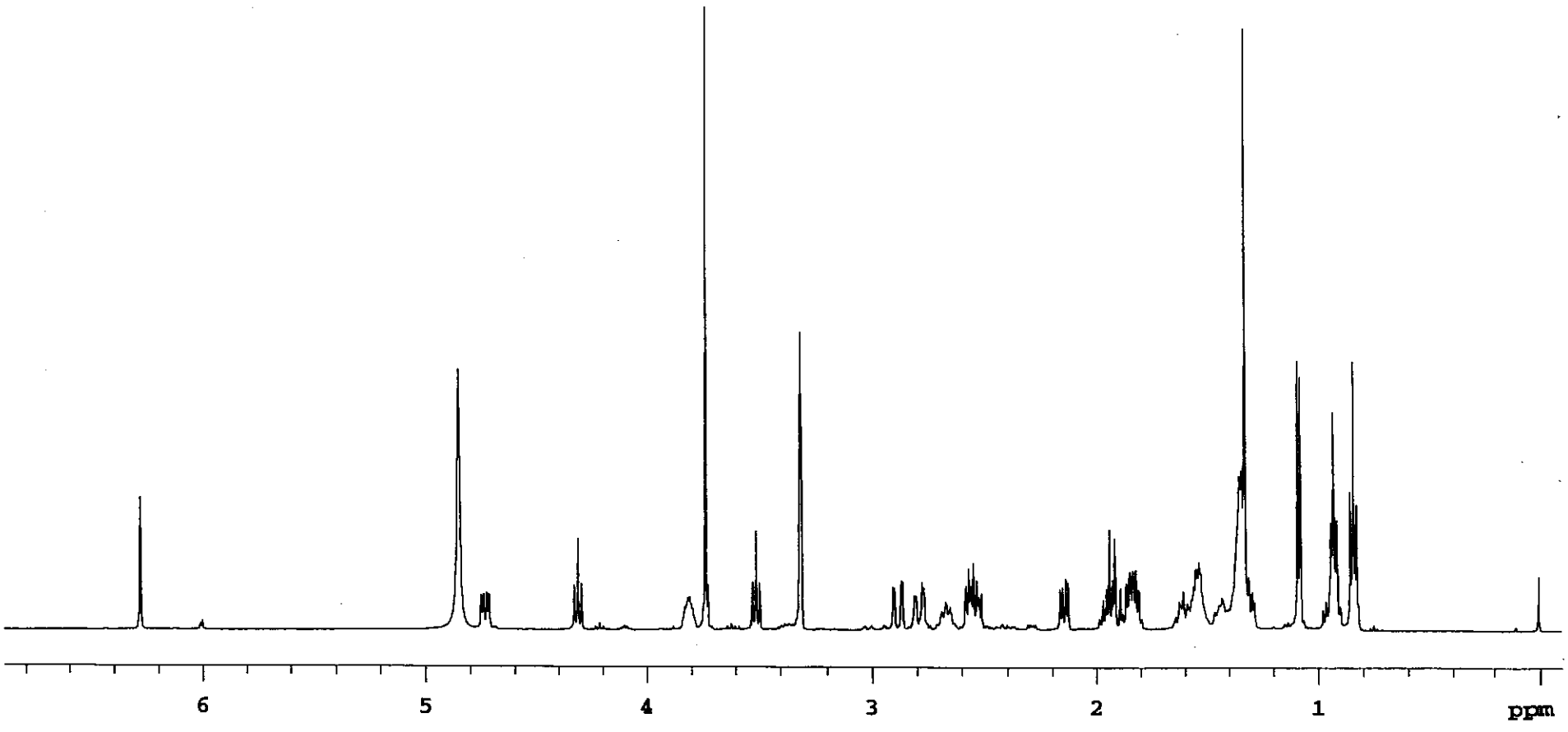
Pulse Sequence: s2pul

Solvent: CD3OD
Temp. 25.0 C / 298.1 K
File: wox-11-23-5-CD3OD
INOVA-500 "echo"

Pulse 47.4 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
66 repetitions
OBSERVE H1, 499.8040886 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 3 sec

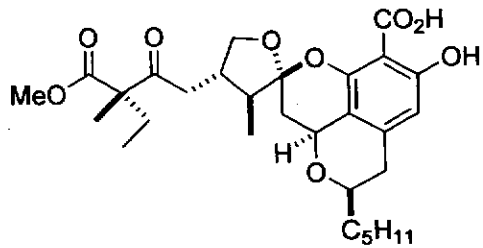


35 (berkelic acid)
500 MHz (CD_3OD)



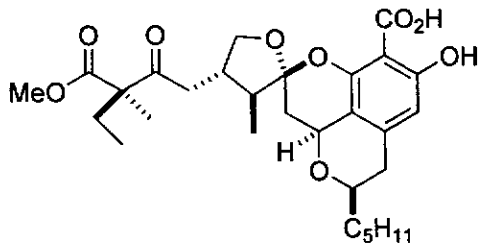
WXX-11-23-5- CD_3OD-C

INDEX	FREQUENCY	PPM	HEIGHT
1	20989.487	208.796	36.3
2	17575.333	174.833	31.6
3	17457.078	173.657	17.4
4	16424.058	163.380	37.6
5	15387.986	153.074	27.7
6	14303.086	142.282	40.9
7	11435.960	113.761	33.6
8	11131.547	110.732	52.2
9	10993.455	109.359	43.8
10	10167.954	101.147	14.3
11	7695.267	76.550	43.8
12	7455.705	74.167	40.4
13	6985.734	69.491	43.8
14	6135.056	61.029	57.1
15	5313.371	52.855	55.0
16	4989.884	49.638	349.0
17	4968.522	49.425	1186.2
18	4947.160	49.213	2434.1
19	4925.797	49.000	2529.8
20	4904.435	48.787	2206.7
21	4883.073	48.575	1207.1
22	4861.710	48.362	362.7
23	4284.165	42.617	49.7
24	4069.016	40.477	46.6
25	3762.315	37.426	49.0
26	3562.424	35.438	44.2
27	3521.226	35.028	37.7
28	3321.336	33.039	68.9
29	2904.771	28.896	49.1
30	2631.638	26.179	56.3
31	2382.920	23.704	74.7
32	1899.979	18.900	64.0
33	1449.082	14.415	67.4
34	1196.549	11.903	42.5
35	904.343	8.996	39.7

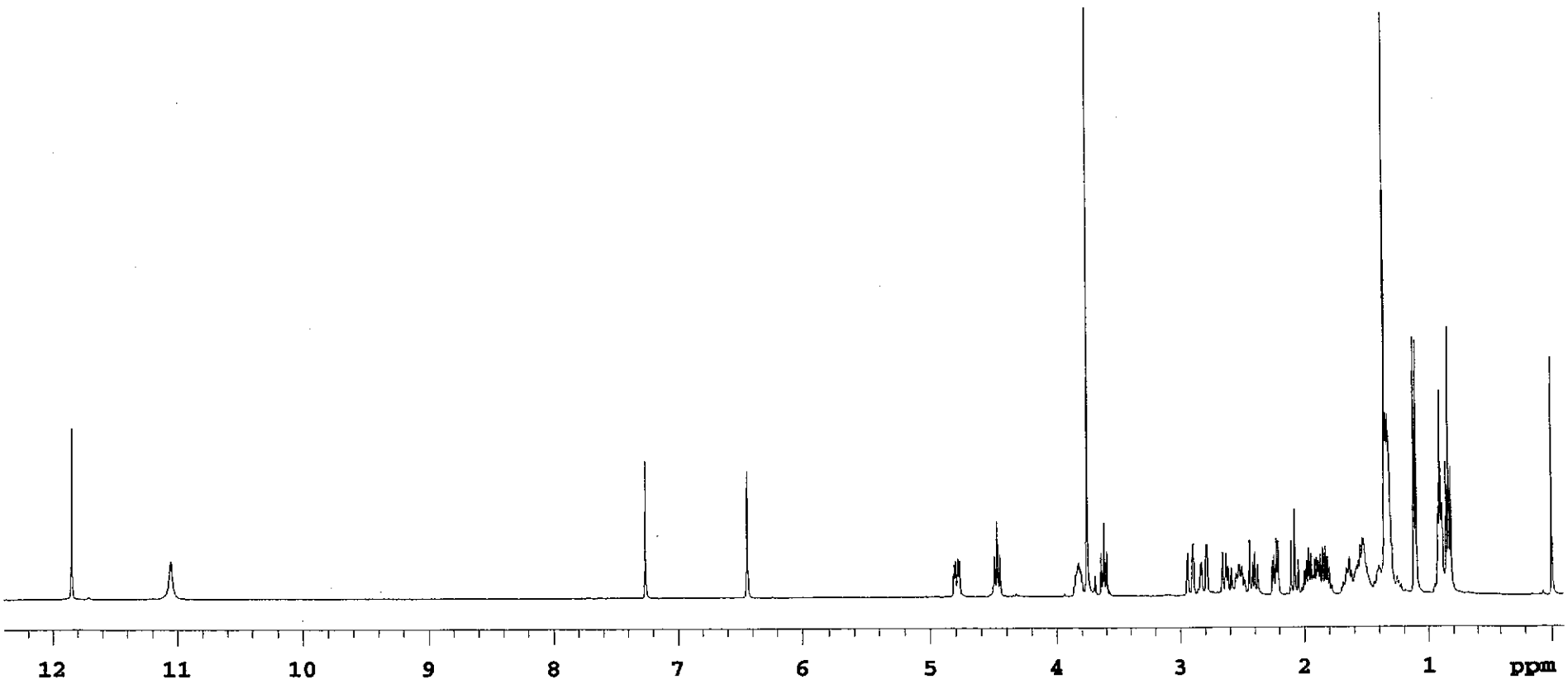


35 (berkelic acid)
400 MHz (CD_3OD)

```
wxx-11-23-6

Pulse Sequence: s2pul

 Solvent: CDCl3
 Ambient temperature
File: wxx-11-23-6
INOVA-500  "gamble"

 Pulse 46.1 degrees
 Acq. time 1.638 sec
 Width 8000.0 Hz
 18 repetitions
OBSERVE H1, 399.7857971 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 31 sec
```

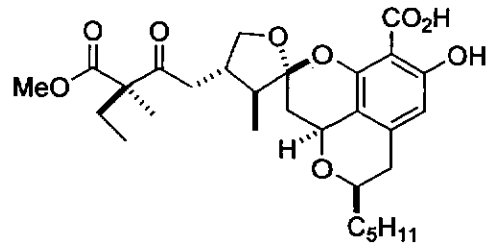


36 (22-*epi*-berkelic acid)
400 MHz ($CDCl_3$)



WXX-11-23-6C in $CDCl_3$

INDEX	FREQUENCY	PPM	HEIGHT
1	20705.149	205.968	14.9
2	17137.644	170.479	22.2
3	16338.847	162.533	26.9
4	15055.583	149.768	22.7
5	14295.695	142.209	30.5
6	11274.455	112.154	48.6
7	11108.134	110.500	53.2
8	9914.897	98.630	19.9
9	7772.563	77.319	331.6
10	7740.519	77.000	353.3
11	7708.476	76.681	350.7
12	7560.465	75.209	63.8
13	7389.567	73.509	48.9
14	6760.142	67.248	52.3
15	6004.069	59.726	34.9
16	5277.751	52.501	52.8
17	4846.690	48.213	63.1
18	4176.066	41.542	56.4
19	3954.814	39.341	63.2
20	3643.534	36.245	59.0
21	3448.222	34.302	88.3
22	3191.874	31.752	61.4
23	2799.723	27.851	49.3
24	2515.910	25.027	67.7
25	2271.006	22.591	63.5
26	1843.760	18.341	57.7
27	1411.173	14.038	58.4
28	1206.706	12.004	55.1
29	866.435	8.619	41.3
30	-1.790	-0.018	13.4



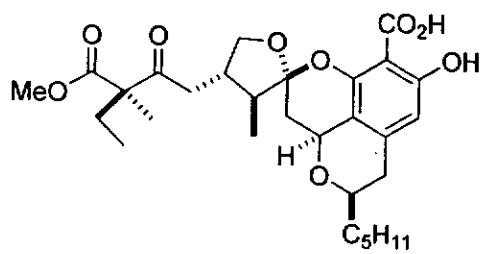
36 (22-*epi*-berkelic acid)
400 MHz ($CDCl_3$)

wxx-11-23-6-CD3OD - 500M

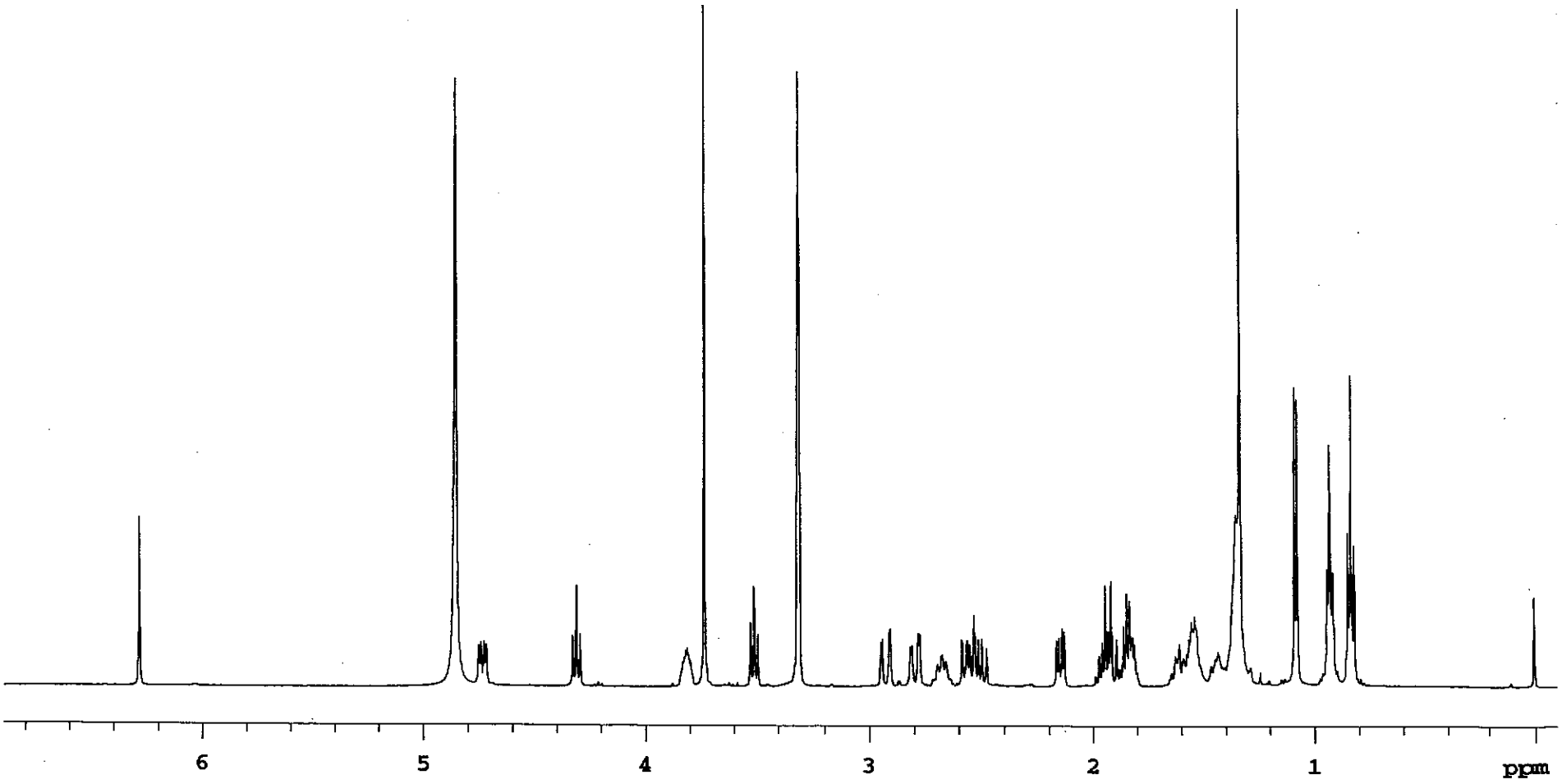
Pulse Sequence: s2pul

Solvent: CD3OD
Temp. 25.0 C / 298.1 K
INOVA-500 "echo"

Pulse 47.4 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
28 repetitions
OBSERVE H1, 499.8040901 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 3 sec

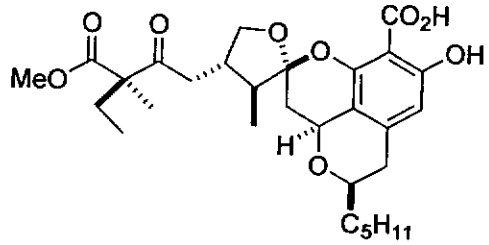


36 (22-*epi*-berkelic acid)
500 MHz (CD_3OD)



WXX-11-23-6-CD_3OD-C

INDEX	FREQUENCY	PPM	HEIGHT
1	20984.147	208.742	36.2
2	17576.096	174.840	32.8
3	17456.315	173.649	19.0
4	16424.058	163.380	28.1
5	15387.986	153.074	29.7
6	14303.849	142.289	39.0
7	11435.960	113.761	37.3
8	11132.310	110.740	49.6
9	10992.692	109.351	42.1
10	10167.191	101.139	17.1
11	7695.267	76.550	38.6
12	7452.653	74.136	33.7
13	6985.734	69.491	38.2
14	6135.056	61.029	54.6
15	5313.371	52.855	54.4
16	4989.884	49.638	474.1
17	4975.388	49.493	18.2
18	4968.522	49.425	1288.7
19	4947.160	49.213	2735.5
20	4925.797	49.000	3350.9
21	4904.435	48.787	2397.6
22	4882.310	48.567	1169.6
23	4860.947	48.355	431.6
24	4282.639	42.602	47.5
25	4066.727	40.454	51.2
26	3761.552	37.419	50.1
27	3561.662	35.430	45.6
28	3520.463	35.020	32.1
29	3320.573	33.032	70.5
30	2898.667	28.835	46.0
31	2631.638	26.179	54.7
32	2382.920	23.704	64.6
33	1887.009	18.771	50.9
34	1448.319	14.407	64.3
35	1195.786	11.895	48.6
36	899.003	8.943	39.4



36 (22-*epi*-berkelic acid)
400 MHz (CD_3OD)