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Supporting Information

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Total Synthesis of Efomycine M

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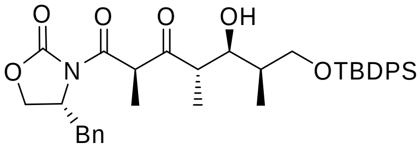
General Experimental Procedures

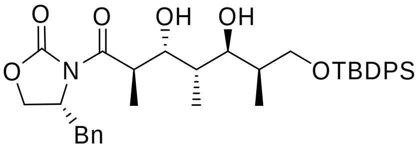
^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 K on a Bruker Avance DRX 400 or DRX 600 at 400.1 MHz (100.6 MHz) or 600.1 MHz (150.9 MHz), respectively. Chemical shifts were referenced to residual $CHCl_3$ (δ_H = 7.26) and $CDCl_3$ (δ_C = 77.0). All chemical shifts are given in ppm, all coupling constants in Hertz. Assignment of proton resonances were confirmed by correlated spectroscopy. IR spectra were recorded as thin films on a silicon disc on a Perkin-Elmer 1600 FT-IR spectrometer. Mass spectra were measured on a Micro mass, trio 200 Fisions Instruments. High resolution mass spectra (HRMS) were performed with a Finnigan MAT 8230 with a resolution of 10000. Optical rotations were measured at 20°C on a Perkin-Elmer 351 polarimeter in a 1 dm cell. Melting points were measured on a Reichert Thermovar instrument and were uncorrected.
The reaction progress was checked on precoated TLC plates (Merck Kieselgel 60 F_{254}). Spots were visualised under 254 nm UV light and/or by dipping the TLC plate into a solution of 20 g $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ and 0.5 g $CeSO_4\cdot 7H_2O$ in 400 ml 10% H_2SO_4 followed by heating with a hot gun. Column chromatography was performed with Merck silica gel 60 (230-400 mesh).
Analytical HPLC was performed on a Jasco System (PU-980 pump, UV 975 and RI 930) using a Nucleosil 50 column (5µm, Ø 4mm x 241 mm) at ambient temperature. Preparative HPLC was performed on a Dynamix Model SD-1 equipped with a Model UV-1 absorbance detector using a Supershere (60 Å pore size, 4µm particle size, Ø 25mm x 250 mm) at ambient temperature.
All solvents (hexane, ethyl acetate, CH_2Cl_2, Et_2O) were distilled prior to use. All reactions were performed under an atmosphere of argon using oven-dried glassware and standard syringe/septa techniques. THF and Et_2O were distilled from sodium-benzophenone, toluene from sodium. CH_2Cl_2 was dried over P_2O_5. CH_3CN, DMF, NEt_3, Me_2NEt, *i*Pr_2NH, *i*Pr_2NEt and 2,6-lutidine were distilled from CaH_2.



(2*R*,4*S*,5*S*,6*R*)-1-[(*R*)-4-Phenylmethyl-2-oxo-oxazolidin-3-yl)]-7-(*tert*-butyl-diphenyl-silanyloxy)-5-hydroxy-2,4,6-trimethyl-heptane-1,3-dione (10b):

To a stirred solution of *β*-keto imide **8** (5.77 g, 19.94 mmol) in 95 mL Et_2O was added a solution of chlorodicyclohexylborane (1.0 M in hexane, 23.0 mL, 23.0 mmol) at 0 °C. Me_2NEt (3.05 ml, 28.15 mmol) was added dropwise and the resulting yellow suspension was stirred at 0 °C for 90 minutes. After cooling to -78 °C a solution of freshly prepared aldehyde **9b**[1] (6.46 g, 19.78 mmol) in 12 mL Et_2O was added dropwise. The reaction mixture was stirred at -78 °C for 6 hours and then allowed to warm up to +4 °C within 12 hours. The reaction was quenched with 80 mL of a saturated solution of NH_4Cl. The organic phase was separated and concentrated under reduced pressure. The remaining yellow oil was dissolved in 80 mL of MeOH and 80 mL of pH 7 phosphate buffer and cooled to 0 °C. 16 mL H_2O_2 (30%) was added cautiously and the reaction mixture was stirred for 60 minutes at 0 °C. After dilution with CH_2Cl_2 the organic phase was separated and the aqueous phase was extracted four times with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography (hexane:ethyl acetate, 3:1) provided ß-hydroxy ketone **10b** (10.83 g, 89%, d.r. = 95:5) as a colourless, highly viscous oil which still contained 9% of β-keto imide **8** as determined by ^{1}H NMR. An analytical sample was additionally purified by preparative HPLC (hexane:*i*PrOH, 97.5:2.5, flow: 80 mL min^{-1}, **R$_t$** = 7.0 min).

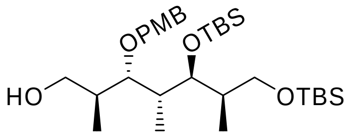
R$_f$ = 0.28 (hexane:ethyl acetate, 3:1).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 – 7.67 (m, 4H, H_{arom}), 7.18 – 7.45 (m, 11H, H_{arom}) 4.91 (q, *J* = 7.3 Hz, 1H, $\underline{CH}CH_3$), 4.75 (m, 1H, NCH), 4.22 (dd ~ t, *J* = 9.1 Hz, 1H, $\underline{CH_A}H_BPh$), 4.16 (dd, *J* = 9.1, 2.9 Hz, 1H, $\underline{CH_B}H_APh$), 4.07 (ddd, *J* = 9.5, 3.0, 2.0 Hz, 1H, $\underline{CH}OH$), 3.75 (dd, *J* = 10.1, 4.2 Hz, 1H, $\underline{CH_A}H_BOSi$), 3.65 (dd, *J* = 10.1, 5.9 Hz, 1H, $\underline{CH_B}H_AOSi$), 3.31 (dd, *J* = 13.3, 3.0 Hz, $\underline{CH_A}H_BO$), 2.92 (dq, *J* = 9.5, 7.0 Hz, 1H, $\underline{CH}CH_3$), 2.79 (dd, *J* = 13.3, 9.6 Hz, 1H, $\underline{CH_B}H_AO$), 2.59 (d, *J* = 3.1 Hz, 1H, OH), 1.76 (m, 1H, $\underline{CH}CH_3$), 1.49 (d, *J* = 7.3 Hz, 3H, $\underline{CH_3}CH$), 1.05 (s, 12H, *t*Bu, $\underline{CH_3}CH$), 0.90 (d, *J* = 7.0 Hz, 3H, $\underline{CH_3}CH$).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 211.1 (C), 170.9 (C), 153.4 (C), 135.7 (CH), 135.6 (CH), 135.2 (C), 133.2 (C), 133.0 (C), 129.8 (CH), 129.7 (CH), 129.4 (CH), 129.0 (CH), 127.8 (2x CH), 127.4 (CH), 75.0 (CH), 68.3 (CH_2), 66.3 (CH_2), 55.4 (CH), 53.0 (CH), 47.4 (CH), 38.0 (CH_2), 35.9 (CH), 26.9 (3x CH_3), 19.2 (C), 13.8 (CH_3), 12.8 (CH_3), 8.9 (CH_3).
IR (thin film): 3503, 2931, 2858, 1780, 1718, 1696, 1359, 702 cm^{-1}.
HRMS: [MNa^+] calcd.: 638.2914, found: 638.2922.
Optical Rotation: $[\alpha]_D^{20}$ = -51.6 (*c*=1.13, CH_2Cl_2).



(*R*)-4-Methylphenyl-3-[(2*R*,3*R*,4*S*,5*S*,6*R*)-7-(*tert*-butyl-diphenyl-silanyloxy)-3,5-dihydroxy-2,4,6-trimethyl-heptanoyl]-oxazolidin-2-one (**11b**):

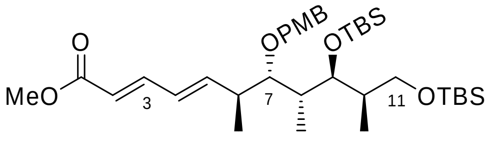
R$_f$ = 0.23 (hexane:ethyl acetate, 2:1).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (m, 4H, H_{arom}), 7.21 – 7.47 (series of m, 11H, H_{arom}), 4.74 (m, 1H, NCH), 4.27 (m, 1H, $\underline{CH}OH$), 4.21 (dd ~ t, *J* = 9.1 Hz, 1H, $\underline{CH_A}H_BPh$), 4.16 (dd, J = 9.1, 3.0 Hz, 1H, $\underline{CH_B}H_APh$), 4.04 (dq, *J* = 9.5, 6.9 Hz, 1H, $\underline{CH}CH_3$), 3.87 (br d, *J* = 7.5 Hz, 1H, $\underline{CH}OH$), 3.78 (dd, *J* = 10.1, 3.9 Hz, 1H, $\underline{CH_A}H_BOSi$), 3.69 (dd, *J* = 10.1, 4.5 Hz, 1H, $\underline{CH_B}H_AOSi$), 3.27 (dd, *J* = 13.4, 3.3 Hz, 1H, $\underline{CH_A}H_BO$), 3.00 (br s, 1H, OH), 2.81 (br s, 1H, OH), 2.80 (dd, *J* = 13.3, 9.6 Hz, 1H, $\underline{CH_B}H_AO$), 1.74 – 1.87 (m, 2H, 2x $\underline{CH}CH_3$), 1.12 (d, *J* = 6.9 Hz, 3H, $\underline{CH_3}CH$), 1.07 (s, 9H, *t*Bu), 1.04 (d, *J* = 7.0 Hz, 3H, $\underline{CH_3}CH$), 0.90 (d, *J* = 7.0 Hz, 3H, $\underline{CH_3}CH$).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.8 (C), 153.5 (C), 135.7 (CH), 135.6 (CH), 135.3 (C), 133.1 (C), 132.9 (C), 129.8 (CH), 129.8 (CH), 129.4 (CH), 128.9 (CH), 127.8 (2x CH), 127.3 (CH), 75.8 (CH), 73.5 (CH), 68.9 (CH_2), 66.1 (CH_2), 55.3 (CH), 40.0 (CH), 38.0 (CH_2), 36.7 (CH), 36.7 (CH), 26.9 (3x CH_3), 19.2 (C), 14.3 (CH_3), 10.3 (CH_3), 10.0 (CH_3).

IR: (thin film) 3480 (br), 2963, 1931, 2858, 1783, 1699, 1472, 1455, 1428, 1390, 1350, 1212, 1112, 1019, 972, 738, 702 cm^{-1}.
HRMS: [M$^+$-*t*Bu] calcd.: 560.7327, found: 560.7321.
Optical Rotation: $[\alpha]_D^{20}$ = -52.7 (*c*=0.77, CH_2Cl_2).



(2*S*,3*S*,4*R*,5*S*,6*R*)-5,7-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-(4-methoxy-benzyloxy)-2,4,6-trimethyl-heptan-1-ol (**14**):

R*$_f$* = 0.26 (hexane:ethyl acetate, 7:1).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (m, 2H, H_{arom}), 6.87 (m, 2H, H_{arom}), 4.60, 4.54 (AB system, *J* = 10.2 Hz, 2H, OCH_2Ph), 4.00 (br d, *J* = 6.3 Hz, 1H, CHO), 3.83 (ddd ~ dt, 11.0, 3.9 Hz, 1H, $\underline{CH_A}H_BOH$), 3.80 (s, 3H, OCH_3), 3.59 (ddd ~ dt, *J* = 11.0, 5.8 Hz, 1H, $\underline{CH_B}H_AOH$), 3.47 (dd ~ t, *J* = 5.4 Hz, 1H, CHOSi), 3.42 (dd ~ t, *J* = 9.6 Hz, 1H, $\underline{CH_A}H_BOSi$), 3.34 (dd, *J* = 9.6, 5.6 Hz, 1H, $\underline{CH_B}H_AOSi$), 2.90 (dd, *J* = 6.2, 5.1 Hz, 1H, OH), 1.91 – 2.02 (m, 2H, 2x $\underline{CH}CH_3$), 1.75 (m, 1H, $\underline{CH}CH_3$), 1.08 (d, *J* = 7.3 Hz, 3H, $\underline{CH_3}CH$), 1.06 (d, *J* = 7.3 Hz, 3H, $\underline{CH_3}CH$), 0.91 (s, 9H, *t*Bu), 0.89 (s, 9H, *t*Bu), 0.84 (d, *J* = 6.8 Hz, 3H, $\underline{CH_3}CH$), 0.10, (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si), 0.04 (s, 6H, 2x CH_3Si).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (C), 130.5 (C), 129.3 (CH), 113.9 (CH), 86.6 (CH), 75.3 (CH_2), 71.5 (CH), 66.0 (CH_2), 65.5 (CH_2), 55.3 (CH_3), 42.8 (CH), 37.7 (CH), 37.2 (CH), 26.1 (3x CH_3), 25.9 (3x CH_3), 18.5 (C), 18.2 (C), 15.6 (CH_3), 11.7 (CH_3), 10.7 (CH_3), -3.4 (CH_3), -4.4 (CH_3), -5.4 (2x CH_3).
IR: (thin film) 3448 (br), 2956, 2929, 2857, 1515, 1473, 1465, 1251, 1086, 1043, 836, 774 cm^{-1}.
HRMS: [M$^+$] calcd.: 554.3823, found: 554.3814.
Optical Rotation: $[\alpha]_D^{20}$ = - 6.2 (*c*=1.10, CH_2Cl_2).

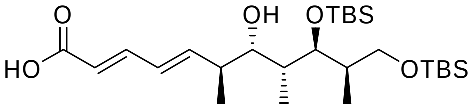


(2*E*,4*E*)-(6*S*,7*S*,8*R*,9*S*,10*R*)-9,11-Bis-(*tert*-butyl-dimethyl-silanyloxy)-7-(4-methoxy-benzyloxy)-6,8,10-trimethyl-undeca-2,4-dienoic acid methyl ester (**15**):

Dess-Martin periodinane (3.54 g, 8.35 mmol) was added in one portion to a stirred solution of alcohol **14** (2.57 g, 4.63 mmol) in 50 mL CH_2Cl_2 under argon atmosphere at 0 °C. The reaction mixture was stirred at 0 °C for 30 minutes and for 4 hours at room temperature. The reaction was quenched by the addition of 20 mL of a 1.0 M solution of $Na_2S_2O_3$ and neutralised with 30 mL of a saturated solution of $NaHCO_3$. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered over a short column of silica gel and concentrated *in vacuo*. The crude product (2.56 g) was used in the next step without further purification.

A solution of LDA was prepared by adding a solution of *n*BuLi (2.5 M in hexane, 2.65 mL, 6.63 mmol) to a solution of *i*Pr$_2$NH (0.93 mL, 6.64 mmol) in 15 mL THF under argon atmosphere at 0 °C and stirring for 30 minutes. Phosphonate **7b** (1.55 g, 6.56 mmol) was dissolved in 30 mL THF and cooled to -78 °C under argon atmosphere. The freshly prepared solution of LDA was added dropwise at -78 °C and the reaction mixture was allowed to warm up to -20 °C within 3 hours. The reaction mixture was re-cooled to -78 °C and a solution of the freshly prepared aldehyde (2.56 g, 4.63 mmol) in 15 mL THF was added dropwise. The reaction mixture was allowed to warm up to room temperature over night and was quenched by the addition of 40 mL of a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted three times with Et_2O. The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash column chromatography (hexane:ethyl acetate, 15:1) gave 2*E*,4*E*-dienoate **15** (2.61 g, 89% over two steps, 4*E*:4*Z* > 50:1) as a colourless viscous oil.

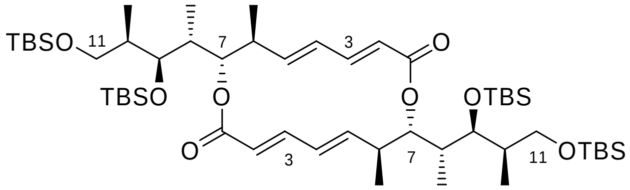
R_f = 0.29 (hexane:ethyl acetate, 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.24 – 7.31 (m, 3H, H$_{arom}$, C$_3$-H), 6.88 (m, 2H, H$_{arom}$), 6.24 (m, 2H, C$_4$-H, C$_5$-H), 5.78 (d, *J* = 15.4, 1H, C$_2$-H), 4.57, 4.52 (AB system, *J* = 10.4 Hz, 2H, OCH_2Ph), 4.01 (br d, *J* = 5.6 Hz, 1H, C$_9$-H), 3.81 (s, 3H, OCH_3), 3.74 (s, 3H, C$_1$-OCH_3), 3.41 (dd ~ t, *J* = 9.6 Hz, 1H, C$_{11}$-H$_A$), 3.32 (dd, *J* = 9.6, 5.3 Hz, 1H, C$_{11}$-H$_B$), 3.25 (dd, *J* = 7.5, 3.3 Hz, 1H, C$_7$-H), 2.71 (m, 1H, C$_6$-H), 1.84 (m, 1H, C$_8$-H), 1.72 (m, 1H, C$_{10}$-H), 1.13 (d, *J* = 6.8 Hz, 3H, C$_6$-CH_3), 1.05 (d, *J* = 7.1 Hz, 3H, C$_8$-CH_3), 0.93 (s, 9H, *t*Bu), 0.88 (s, 9H, *t*Bu), 0.84 (d, *J* = 6.8 Hz, 3H, C$_{10}$-CH_3), 0.08 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si), -0.03 (s, 3H, CH_3Si).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6 (C), 159.1 (C), 146.5 (CH), 145.3 (CH), 131.0 (CH), 129.1 (CH), 128.7 (CH), 119.1 (CH), 113.8 (CH), 85.2 (CH), 75.0 (CH_2), 70.0 (CH), 66.4 (CH_2), 55.3 (CH_3), 51.4 (CH_3), 43.4 (CH), 40.5 (CH), 37.4 (CH), 26.0 (6x CH_3), 18.3 (C), 18.3 (C), 18.2 (CH_3), 11.8 (CH_3), 11.2 (CH_3), -3.7 (CH_3), -4.7 (CH_3), -5.2 (CH_3), -5.3 (CH_3).
IR: (thin film) 2955, 2930, 2857, 1722 (br), 1516, 1250, 1142, 1072, 1042, 836, 774 cm^{-1}.
HRMS: [M$^+$-*t*Bu] calcd.: 577.3381, found: 577.3394.
Optical Rotation: $[\alpha]_D^{20}$ = - 2.0 (*c*=0.82, CH_2Cl_2).



(2*E*,4*E*)-(6*S*,7*S*,8*R*,9*S*,10*R*)-9,11-Bis-(*tert*-butyl-dimethyl-silanyloxy)-7-hydroxy-6,8,10-trimethyl-undeca-2,4-dienoic acid (**6**):

R_f = 0.17 (hexane:ethyl acetate, 3:1).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (m, 1H, C$_3$-H), 6.27 (m, 2H, C$_4$-H, C$_5$-H), 5.79 (d, *J* = 15.3 Hz, 1H, C$_2$-H), 3.87 (dd ~ t, *J* = 4.1 Hz, 1H, C$_9$-H), 3.74 (dd, *J* = 8.7, 2.1 Hz, 1H, C$_7$-H), 3.51 (dd, *J* = 9.8, 6.4 Hz, 1H, C$_{11}$-H$_A$), 3.46 (dd, *J* = 9.8, 5.9 Hz, 1H, C$_{11}$-H$_B$), 2.43 (m, 1H, C$_6$-H), 1.90 (m, 1H, C$_{10}$-H), 1.78 (m, 1H, C$_8$-H), 0.98 (d, *J* = 6.9 Hz, C$_8$-CH_3), 0.97 (d, *J* =6.6 Hz, C$_6$-CH_3), 0.94 (d, *J* = 6.9 Hz, C$_{10}$-CH_3), 0.91 (s, 9H, *t*Bu), 0.89 (s, 9H, *t*Bu), 0.10 (CH_3Si), 0.09 (CH_3Si), 0.04 (CH_3Si), 0.04 (CH_3Si).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1 (C), 148.9 (CH), 147.4 (CH), 128.1 (CH), 118.8 (CH), 77.9 (CH), 75.0 (CH), 66.0 (CH_2), 40.8 (CH), 39.5 (CH), 37.8 (CH), 26.2 (3x CH_3), 25.9 (3x CH_3), 18.4 (C), 18.2 (C), 16.4 (CH_3), 13.1 (CH_3), 11.2 (CH_3), -3.8 (CH_3), -4.0 (CH_3), -5.4 (2x CH_3).
IR: (thin film) 3470 (br), 2956, 2929, 2858, 1691, 1639, 1257, 1089, 1048, 1004, 836, 774 cm^{-1}.
HRMS: [M$^+$-*t*Bu] calcd.:443.2649, found: 443.2657.

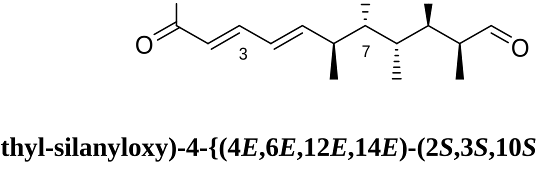
Optical Rotation: $[\alpha]_D^{20}$ = -24.3 (c=1.08, CH_2Cl_2).



(3*E*,5*E*,11*E*,13*E*)-(7*S*,8*S*,15*S*,16*S*)-8,16-Bis-[(1*R*,2*S*,3*R*)-2,4-bis-(*tert*-butyl-dimethyl-silanyloxy)-1,3-dimethyl-butyl]-7,15-dimethyl-1,9-dioxa-cyclohexadeca-3,5,11,13-tetraene-2,10-dione (**18**):

NEt_3 (160 µL, 1.148 mmol) and 2,4,6-trichlorobenzoylchloride (110 µL, 0.704 mmol) were added to a stirred solution of *seco*-acid **6** (285 mg, 0.569 mmol) in 35 mL toluene and the cloudy solution was stirred at room temperature for 4 hours. A solution of *N,N*-dimethylaminopyridine (140 mg, 1.146 mmol) in 6 mL toluene was added over a periode of 8 hours with a syringe pump and stirring was continued over night. The resulting slightly yellow suspension was quenched with 10 mL of a 1.0 M solution of $KHSO_4$. The organic phase was separated and the aqueous phase was extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification with flash column chromatography (hexane:ethyl acetate, 30:1) gave macrodiolide **18** (163 mg, 59%) as colourless thin needles together with the corresponding monomer (60 mg, 22%).

18: R_f = 0.22 (hexane:ethyl acetate, 15:1). **18** (monomer): R_f = 0.17 (hexane:ethyl acetate, 15:1)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93 (dd, J = 15.3, 11.1 Hz, 2H, C_3-H), 5.98 (dd, J = 15.0, 11.1 Hz, 2H, C_4-H), 5.63 (dd, J = 15.0, 9.9 Hz, 2H, C_5-H), 5.58 (d, J = 15.3 Hz, 2H, C_2-H), 4.94 (br d, J = 10.1 Hz, 2H, C_7-H), 3.74 (dd, J = 6.8, 1.7 Hz, 2H, C_9-H), 3.47 (dd, J = 9.8, 7.6 Hz, 2H, C_{11}-H_A), 3.38 (dd, J = 9.8, 6.9 Hz, 2H, C_{11}-H_B), 2.42 (m, 2H, C_6-H), 1.93 (m, 2H, C_8-H), 1.76 (m, 2H, C_{10}-H), 1.05 (d, J = 6.6 Hz, 6H, C_6-CH_3), 0.96 (d, J = 7.2 Hz, 6H, C_8-CH_3), 0.91 (s, 18H, *t*Bu), 0.86 (s, 18H, *t*Bu), 0.84 (d, J = 6.8 Hz, 6H, C_{10}-CH_3), 0.15 (s, 6H, CH_3Si), 0.05 (s, 6H, CH_3Si), 0.02 (s, 6H, CH_3Si), 0.01 (s, 6H, CH_3Si).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6 (C), 145.2 (CH), 144.5 (CH), 130.7 (CH), 121.3 (CH), 76.9 (CH), 73.7 (CH), 66.0 (CH_2), 42.5 (CH), 39.0 (CH), 38.7 (CH), 26.3 (3x CH_3), 25.9 (3x CH_3), 18.7 (C), 18.2 (C), 16.3 (CH_3), 10.4 (CH_3), 10.2 (CH_3), -3.6 (CH_3), -4.3 (CH_3), -5.3 (CH_3), -5.3 (CH_3).
IR: (thin film) 2956, 2943, 2930, 2885, 2856, 1709 (br), 1643, 1472, 1385, 1251, 1225, 1150, 1123, 1118, 1106, 1044, 1006, 849, 837, 776 cm^{-1}.
HRMS: [MNa^+] calcd.: 987.6393, found: 987.6381.
Optical Rotation: $[\alpha]_D^{20}$ = + 46.4 (c=1.30, CH_2Cl_2).
m.p.: 174 – 175 °C.



(2*S*,3*R*,4*R*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-4-{(4*E*,6*E*,12*E*,14*E*)-(2*S*,3*S*,10*S*,11*S*)-10-[(1*R*,2*R*,3*S*)-2-(*tert*-butyl-dimethyl-silanyloxy)-1,3-dimethyl-4-oxo-butyl]-3,11-dimethyl-8,16-dioxo-1,9dioxa-cyclohexadeca-4,6,12,14-tetraen-2-yl}-2-methyl-pentanal (**3**):

R$_f$ = 0.23 (hexane:ethyl acetate, 5:1).

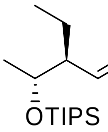
^{1}H NMR (250 MHz, CDCl$_3$): δ = 9.70 (s, 2H, C$_{11}$-H), 6.95 (dd, *J* = 15.3, 11.1 Hz, 2H, C$_3$-H), 6.00 (dd, *J* = 15.1, 11.1 Hz, 2H, C$_4$-H), 5.63 (dd, *J* = 15.0, 10.0 Hz, 2H, C$_5$-H), 5.60 (d, *J* = 15.4 Hz, 2H, C$_2$-H), 4.99 (d, *J* = 10.2 Hz, 2H, C$_7$-H), 4.17 (dd, *J* = 7.1, 2.1 Hz, 2H, C$_9$-H), 2.42 (m, 4H, C$_6$-H, C$_{10}$-H), 2.00 (m, 2H, C$_8$-H), 1.14 (d, *J* = 7.0 Hz, 6H, C$_{10}$-CH$_3$), 1.06 (d, *J* = 6.6 Hz, 6H, C$_6$-CH$_3$), 0.98 (d, *J* = 7.1 Hz, 6H, C$_8$-CH$_3$), 0.87 (s, 18H, *t*Bu), 1.14 (s, 6H, CH$_3$Si), -0.03 (s, 6H, CH$_3$Si).

^{13}C NMR (63 MHz, CDCl$_3$): δ = 204.9 (CH), 167.6 (C), 145.6 (CH), 144.5 (CH), 130.9 (CH), 121.2 (CH), 76.5 (CH), 72.8 (CH), 50.1 (CH), 42.4 (CH), 38.8 (CH), 26.1 (3x CH$_3$), 18.4 (C), 16.2 (CH$_3$), 10.0 (CH$_3$), 7.4 (CH$_3$), -4.2 (2x CH$_3$).

IR: (thin film) 2930, 2885, 2857, 1721, 1717, 1642, 1258, 1220, 1146, 1107, 1028, 999, 838.

Optical Rotation: $[\alpha]_D^{20}$ = + 124.8 (*c*=0.99, CH$_2$Cl$_2$).

m.p.: 126 °C.



((*E*)-(1*R*,2*S*)-2-Ethyl-4-iodo-1-methyl-but-3-enyloxy)-triisopropyl-silane (**4**):

R$_f$ = 0.78 (hexane).

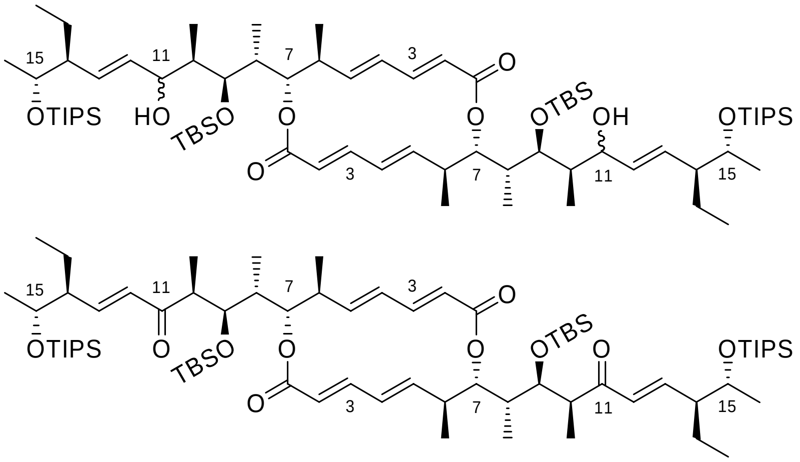
^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.38 (dd, *J* = 14.4, 9.7 Hz, 1H, $\underline{\text{CH}}$=CHI), 5.97 (d, *J* = 14.4 Hz, 1H, $\underline{\text{CHI}}$=CH), 3.94 (dq, *J* = 6.2, 3.6 Hz, 1H, CHOSi), 1.95 (ddt, *J* = 9.8, 6.1, 3.8 Hz, 1H, $\underline{\text{CH}}$CH$_2$), 1.54 – 1.64 (m, 1H, $\underline{\text{CH}_\text{A}}H_\text{B}CH_3$), 1.29 – 1.40 (m, 1H, $\underline{\text{CH}_\text{B}}H_\text{A}CH_3$), 1.11 (d, *J* = 6.2 Hz, 3H, $\underline{\text{CH}_3}$CH), 1.06 (s, 21H, 3x *i*Pr), 0.86 (t, *J* = 7.4 Hz, 3H, CH$_3$CH$_2$).

^{13}C NMR (100 MHz, CDCl$_3$): δ = 147.5 (CH), 75.3 (CH), 70.6 (CH), 56.8 (CH), 22.4 (CH$_2$), 21.1 (CH$_3$), 18.2 (3x *i*Pr), 12.7 (CH$_3$).

IR (thin film): 2961, 2943, 2866, 1463, 1155, 1131, 1108, 1054, 998, 951, 882, 677 cm^{-1}.

HRMS: [M$^+$-*i*Pr] calcd.: 353.0798, found: 353.0807.

Optical Rotation: $[\alpha]_D^{20}$ = + 3.7 (*c*=1.84, CH$_2$Cl$_2$).



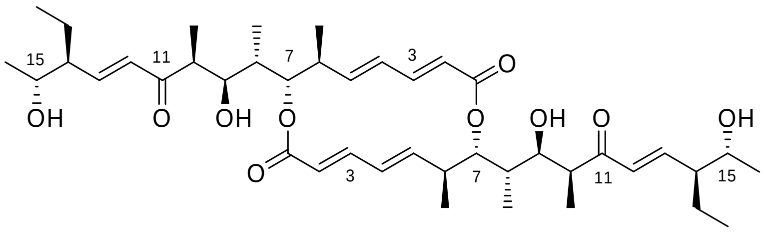
Bis-allylic alcohol **23** and oxidation to enone **24**:

(3*E*,5*E*,11*E*,13*E*)-(7*S*,8*S*,15*S*,16*S*)-8,16-Bis-[(*E*)-(1*R*,2*S*,3*R*,7*S*,8*R*)-2-(*tert*-butyl-dimethyl-silanyloxy)-7-ethyl-4-hydroxy-1,3-dimethyl-8-triisopropylsilanyloxy-non-5-enyl]-7,15-dimethyl-1,9-dioxa-cyclohexadeca-3,5,11,13-tetraene-2,10-dione (**23**):
(3*E*,5*E*,11*E*,13*E*)-(7*S*,8*S*,15*S*,16*S*)-8,16-Bis-[(*E*)-(1*R*,2*R*,3*S*,7*S*,8*R*)-2-(*tert*-butyl-dimethyl-silanyloxy)-7-ethyl-1,3-dimethyl-4-oxo-8-triisopropylsilanyloxy-non-5-enyl]-7,15-dimethyl-1,9-dioxa-cyclohexadeca-3,5,11,13-tetraene-2,10-dione (**24**):

*t*BuLi (1.7 M in pentane, 0.54 mL, 0.918 mmol) was added dropwise to a stirred solution of vinyliodide **4** (180 mg, 0.454 mmol) in 4.5 mL Et_2O at -78 °C. The reaction mixture was stirred at -78 °C for 20 minutes and at 0 °C for 10 minutes before being re-cooled to -78 °C. A solution of dialdehyde **3** (128 mg, 0.175 mmol) in 6.0 mL Et_2O was added dropwise and the reaction mixture was stirred at -78 °C for 20 minutes and at 0 °C for 20 minutes. The reaction was quenched with 5.0 mL of a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted four times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash column chromatography (hexane:ethyl acetate, 10:1) gave bis-allylic alcohol **23** (198 mg, 89%) as an inseparable mixture of diastereomers (d.r. = 2:1:1). $\mathbf{R_f}$ = 0.27 (hexane:ethyl acetate, 10:1).

Dess-Martin periodinane (362 mg, 0.854 mmol) was added in one portion to a stirred solution of the diastereomeric mixture of bis-allylic alcohol **23** (198 mg, 0.155 mmol) in 10 mL CH_2Cl_2 at 0 °C. The reaction was stirred at room temperature for 6 hours before being quenched with 4 mL of a 1.0 M solution of $Na_2S_3O_3$ and 10 mL of a saturated solution of $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (hexane:ethyl acetate, 15:1) gave the enone **24** (162 mg, 82%) as a highly viscous gum.

$\mathbf{R_f}$ = 0.20 (hexane:ethyl acetate, 15:1).
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.90 (dd, *J* = 15.3, 11.2 Hz, 2H, C_3-H), 6.79 (dd, *J* = 15.9, 9.4 Hz, 2H, C_{13}-H), 6.16 (d, *J* = 15.9 Hz, 2H, C_{12}-H), 5.97 (dd, *J* = 15.0, 11.2 Hz, 2H, C_4-H), 5.57 (d, *J* = 15.3 Hz, 2H, C_2-H), 5.56 (dd, *J* = 15.1, 11.3 Hz, 2H, C_5-H), 4.96 (d, *J* = 10.0 Hz, 2H, C_7-H), 4.03 (m, 4H, C_9-H, C_{15}-H), 3.11 (m, 2H, C_{10}-H), 2.38 (m, 2H, C_6-H), 2.12 (m, 2H, C_{14}-H), 1.96 (m, 2H, C_8-H), 1.74 (m, 2H, C_{14}-$\underline{CH_A}H_B$), 1.45 (m, 2H, C_{14}-$\underline{CH_B}H_A$), 1.12 (d, *J* = 7.0 Hz, 6H, C_{10}-CH_3), 1.10 (d, *J* = 6.3 Hz, C_{15}-CH_3), 1.06 (s, 42H, 6x *i*Pr), 1.03 (d, *J*= 7.2 Hz, 6H, C_8-CH_3), 0.95 (d, *J* = 6.6 Hz, 6H, C_6-CH_3), 0.86 (s, 18H, 2x *t*Bu), 0.86 (t, *J* = 7.3 Hz, 6H, C_{14}-$CH_2\underline{CH_3}$), 0.09 (s, 6H, 2x CH_3Si), -0.02 (s, 6H, 2x CH_3Si).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 202.4 (C), 167.3 (C), 148.7 (CH), 145.0 (CH), 144.1 (CH), 131.0 (CH), 130.8 (CH), 121.6 (CH), 76.0 (CH), 75.9 (CH), 70.9 (CH), 53.1 (CH), 47.3 (CH), 42.4 (CH), 37.8 (CH), 26.2 (3x CH_3), 22.2 (CH_2), 21.0 (CH_3), 18.4 (C), 18.2 (6x CH_3), 16.1 (CH_3), 13.1 (CH_3), 12.6 (3x CH), 12.5 (CH_3), 10.9 (CH_3), -3.7 (CH_3), -3.9 (CH_3).
IR (thin film): 2963, 2951, 2944, 2867, 1717, 1109, 1085, 1056, 998 cm^{-1}.
HRMS: [M^+] calcd.: 1268.8898, found: 1268.8904.
Optical Rotation: $[\alpha]_D^{20}$ = + 96.6 (*c*=0.65, CH_2Cl_2).



Efomycine M (1)

Enone **24** (57 mg, 44.8 µmol) was dissolved in 2.0 mL of THF and 3.0 mL of MeCN in a polyethylene vessel and the solution was cooled to 0 °C. HF·pyridine-complex (70%, 0.15 mL, 5.77 mmol) was added dropwise and the reaction mixture was allowed to warm up to room temperature. Stirring was continued for 72 hours. The reaction was quenched by the addition of 0.5 mL of a saturated solution of $NaHCO_3$ and one spatula of solid $NaHCO_3$. The participate was filtered off over Celite and washed excessively with CH_2Cl_2. The crude product was concentrated *in vacuo*. Purification by flash column chromatography (hexane:ethyl acetate, 1:6) gave 23 mg (70%) efomycine M (**1**) as a colourless solid.

R*f* = 0.33 (ethyl acetate).
^{1}H NMR (600 MHz, $CDCl_3$, 7 mg): δ = 6.95 (dd, *J* = 15.3, 11.2 Hz, 2H, C_3-H), 6.72 (dd, *J* = 15.8 9.6 Hz, 2H, C_{13}-H), 6.23 (d, *J* = 15.8 Hz, 2H, C_{12}-H), 6.04 (dd, *J* = 15.0, 11.2 Hz, 2H, C_4-H), 5.64 (dd, *J* = 15.0, 9.8 Hz, 2H, C_5-H), 5.60 (d, *J* = 15.5 Hz, 2H, C_2-H), 5.08 (dd, *J* = 10.3, 1.6 Hz, 2H, C_7-H), 3.81 (m, 2H, C_{15}-H), 3.74 (br. dd, *J* = 9.3, 2.6 Hz, 2H, C_9-H), 3.31 (br. s, 2H, C_9-OH), 2.89 (dq, *J* = 7.1, 2.7 Hz, 2H, C_{10}-H), 2.48 (ddq ~ tq, *J* = 10.0, 6.6 Hz, 2H, C_6-H), 2.03 (m, 2H, C_{14}-H), 1.94 (m, 2H, C_8-H), 1.61 (m, 2H, C_{14}-$\underline{CH_A}H_B$), 1.42 (br. m, 2H, C_{14}-$\underline{CH_B}H_A$), 1.17 (d, *J* = 6.3 Hz, 6H, C_{15}-CH_3), 1.16 (d, *J* = 7.1 Hz, 6H, C_{10}-CH_3), 1.03 (d, *J* = 6.7 Hz, 6H, C_6-CH_3), 0.92 (d, *J* = 7.0 Hz, 6H, C_8-CH_3), 0.86 (t, *J* = 7.4 Hz, 6H, C_{14}-CH_2CH_3).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 203.2 (C), 168.4 (C), 147.6 (CH), 145.2 (CH), 144.5 (CH), 131.3 (CH), 131.0 (CH), 121.1 (CH), 76.6 (CH), 71.5 (CH), 69.5 (CH), 52.4 (CH), 45.5 (CH), 41.5 (CH), 36.0 (CH), 23.5 (CH_2), 21.3 (CH_3), 15.3 (CH_3), 11.9 (CH_3), 9.3 (CH_3), 9.2 (CH_3).
IR: (thin film) 3470 (br), 2963, 1703, 1699, 1695, 1683, 1652, 1634, 1222, 1183, 1145, 997 cm^{-1}.
HRMS: [$M+Na^+$] calcd.: 751.4397, found: 751.4405.
Optical Rotation: $[\alpha]_D^{20}$ = + 104.8 (*c*=1.1, MeOH).
Lit.: **Optical Rotation**: $[\alpha]_D^{20}$ = + 107 (*c*=1, MeOH).[2]

Efomycine M (authentic sample)

^{1}H NMR (600 MHz, $CDCl_3$, 3 mg): δ = 6.96 (dd, *J* = 15.4, 11.2 Hz, 2H, C_3-H), 6.73 (dd, *J* = 15.8, 9.6 Hz, 2H, C_{13}-H), 6.24 (dd, *J* = 15.8, 0.7 Hz, 2H, C_{12}-H), 6.05 (dd, *J* = 15.1, 11.2, 2H, C_9-H), 5.64 (dd, *J* = 15.1, 9.8 Hz, 2H, C_5-H), 5.61 (d, *J* = 15.4 Hz, 2H, C_2-H), 5.09 (dd, *J* = 10.3, 1.7 Hz, 2H, C_7-H), 3.82 (m, 2H, C_{15}-H), 3.74 (ddd ~ dt, *J* = 9.3, 3.1 Hz, 2H, C_9-H), 2.90 (dq, *J* = 7.1, 2.8 Hz, 2H, C_{10}-H), 3.30 (d, *J* = 3.8 Hz, 2H, C_9-OH), 2.49 (ddq ~ tq, *J* = 10.0, 6.6 Hz, 2H, C_6-H), 2.04 (m, 2H, C_{14}-H), 1.94 (m, 2H, C_8-H), 1.61 (m, 2H, C_{14}-$\underline{CH_A}H_B$), 1.42 (br. m, 2H, C_{14}-$\underline{CH_B}H_A$), 1.18 (d, *J* = 6.3 Hz, 6H, C_{15}-CH_3), 1.17 (d, *J* = 7.1 Hz, 6H, C_{10}-CH_3), 1.03 (d, *J* = 6.7 Hz, 6H, C_6-CH_3), 0.92 (d, *J* = 7.0 Hz, 6H, C_8-CH_3), 0.86 (t, J = 7.4 Hz, 6H, C_{14}-CH_2CH_3).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 203.1 (C), 168.4 (C), 147.6 (CH), 145.2 (CH), 144.5 (CH), 131.4 (CH), 131.0 (CH), 121.1 (CH), 76.6 (CH), 71.6 (CH), 69.6 (CH), 52.4 (CH), 45.5 (CH), 41.5 (CH), 36.0 (CH), 23.5 (CH_2), 21.4 (CH_3), 15.3 (CH_3), 11.9 (CH_3), 9.3 (CH_3), 9.2 (CH_3).

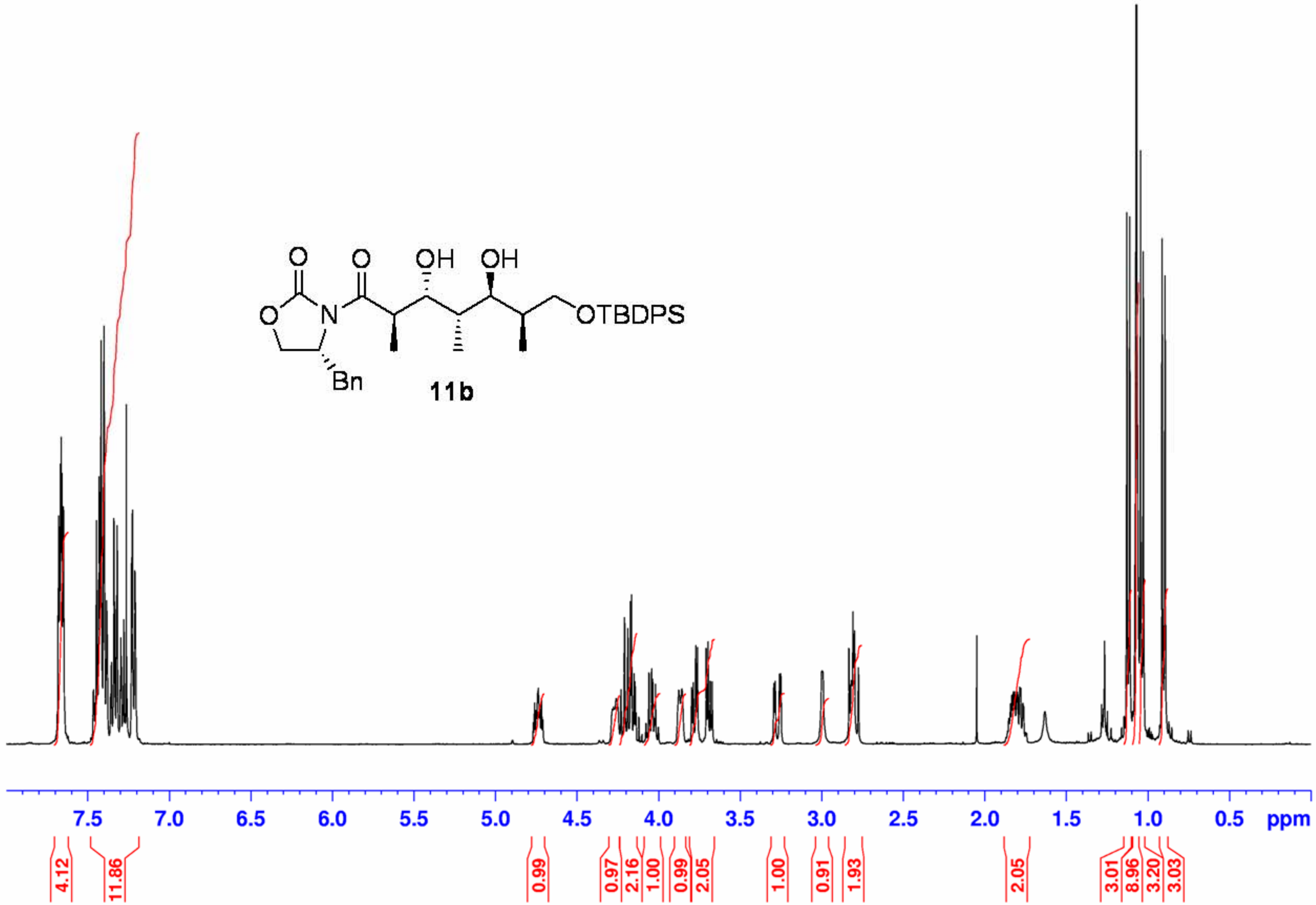
Table 1: ^{1}H NMR Data (600.1 MHz): Comparison of Efomycine M (**1**) in $CDCl_3$ for synthetic material (7 mg) and an authentic sample (3 mg):

	Synthetic compound	Authentic Sample
Atom	δH (ppm), multiplicity, *J* (Hz)	δH (ppm), multiplicity, *J* (Hz)
2	5.60, d, 15.5 Hz	5.61, d, 15.4 Hz
3	6.95, dd, 15.3, 11.2 Hz	6.96, dd, 15.4, 11.2 Hz
4	6.04, dd, 15.0, 11.2 Hz	6.05, dd, 15.1, 11.2 Hz
5	5.64, dd, 15.0, 9.8 Hz	5.64, dd, 15.1, 9.8 Hz
6	2.48, ddq ~ tq, 10.0, 6.6 Hz	2.49, ddq ~ tq, 10.0, 6.6 Hz
6-CH_3	1.03, d, 6.7 Hz	1.03, d, 6.7 Hz
7	5.08, dd, 10.3, 1.6 Hz	5.09, dd, 10.3, 1.7 Hz
8	1.94, m	1.94, m
8-CH_3	0.92, d, 7.0 Hz	0.92, d, 7.0 Hz
9	3.74, br. dd, 9.3, 2.6 Hz	3.74, dt, 9.3, 3.1 Hz
9-OH	3.31, br. s	3.30, d, 3.8 Hz
10	2.89, dq, 7.1, 2.7 Hz	2.90, dq, 7.1, 2.8 Hz
10-CH_3	1.16, d, 7.1 Hz	1.17, d, 7.1 Hz
12	6.23, d, 15.8 Hz	6.24, d, 15.8, 0.7 Hz
13	6.72, dd, 15.8, 9.6 Hz	6.73, dd, 15.8, 9.6 Hz
14	2.03, m	2.04, m
14-CH_A	1.61, m	1.61, m
14-CH_B	1.42, m	1.42, m
14-$CH_2\underline{CH_3}$	0.86, t, 7.4 Hz	0.86, t, 7.4 Hz
15	3.81, m	3.82, m
15-CH_3	1.17, d, 6.3 Hz	1.18, d, 6.3 Hz
15-OH	1.40 – 1.60, br. s	1.40 – 1.60, br. s

Table 2: ^{13}C NMR Data (150.9 MHz): Comparison of Efomycine M (**1**) in $CDCl_3$ for synthetic material (7 mg) and an authentic sample (3 mg):

	Synthetic compound	Authentic Sample
Atom	δC (ppm)	δC (ppm)
1	168.4	168.4
2	121.1	121.1
3	145.2	145.2
4	131.3	131.4
5	144.5	144.5
6	41.5	41.5
6-CH_3	15.3	15.3
7	76.6	76.6
8	36.0	36.0
8-CH_3	9.2	9.2
9	71.5	71.6
10	45.5	45.5
10-CH_3	9.3	9.3
11	203.2	203.1
12	131.0	131.0
13	147.6	147.6
14	52.4	52.4
14-CH_2	23.5	23.5
14-$CH_2\underline{CH_3}$	11.9	11.9
15	69.5	69.6
15-CH_3	21.3	21.4

[1] P. R. R. Meira, L. C. Diaz, *J. Org. Chem*. **2005**, *70*, 4762-4773.
[2] P. Hammann, G. Kretzschmar, *Z. Naturforsch*. **1990**, *45b*, 515-517.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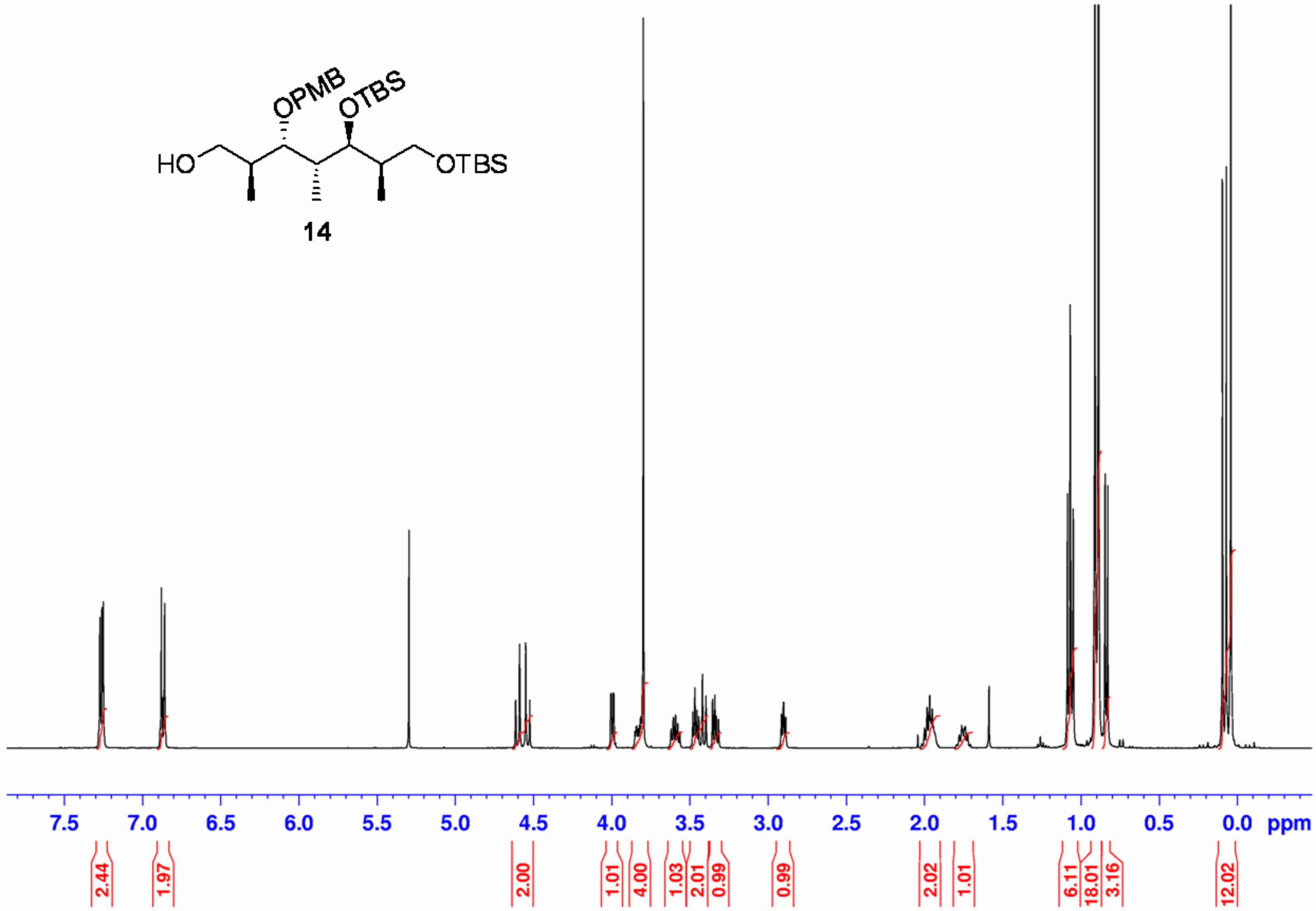
11b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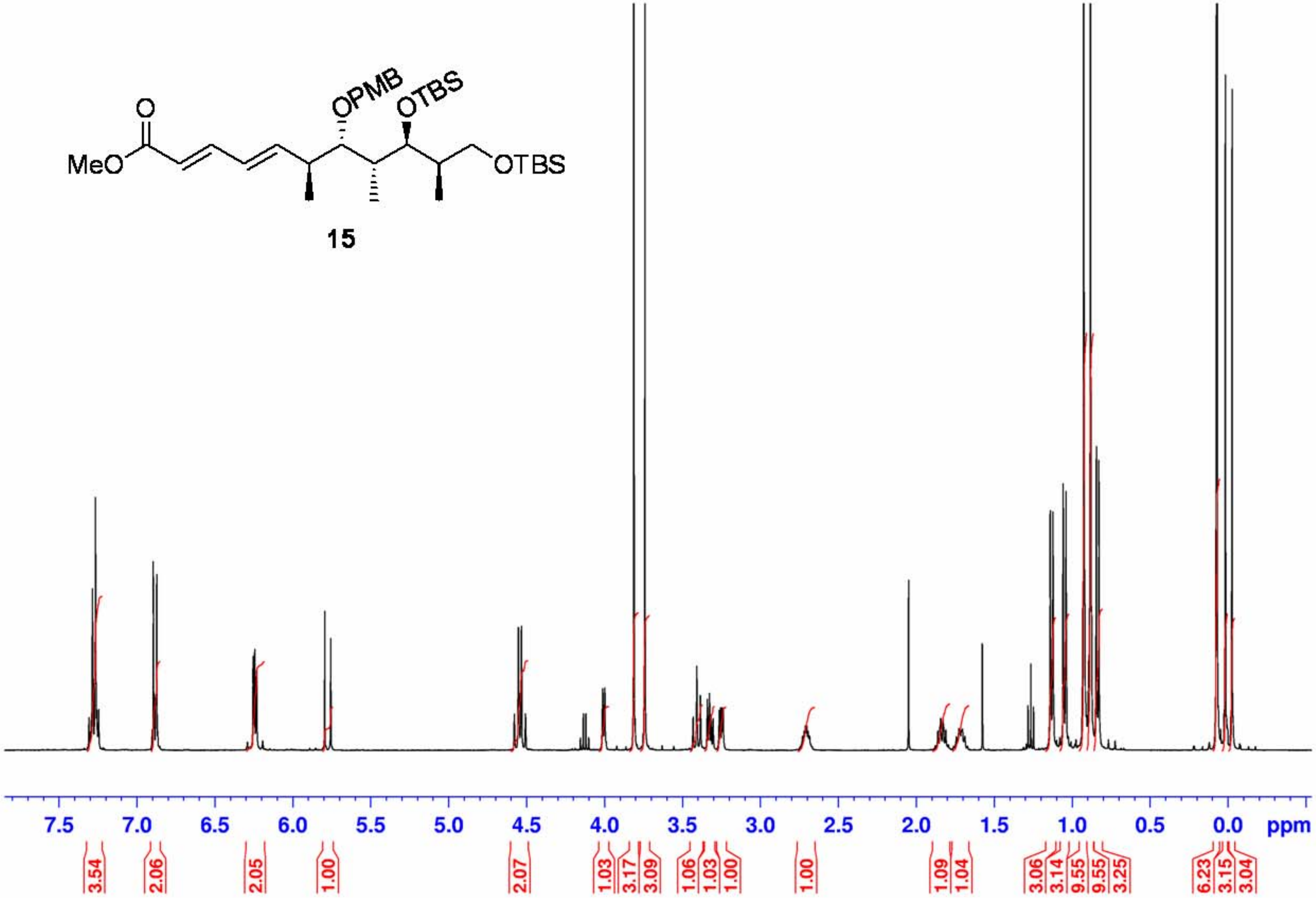
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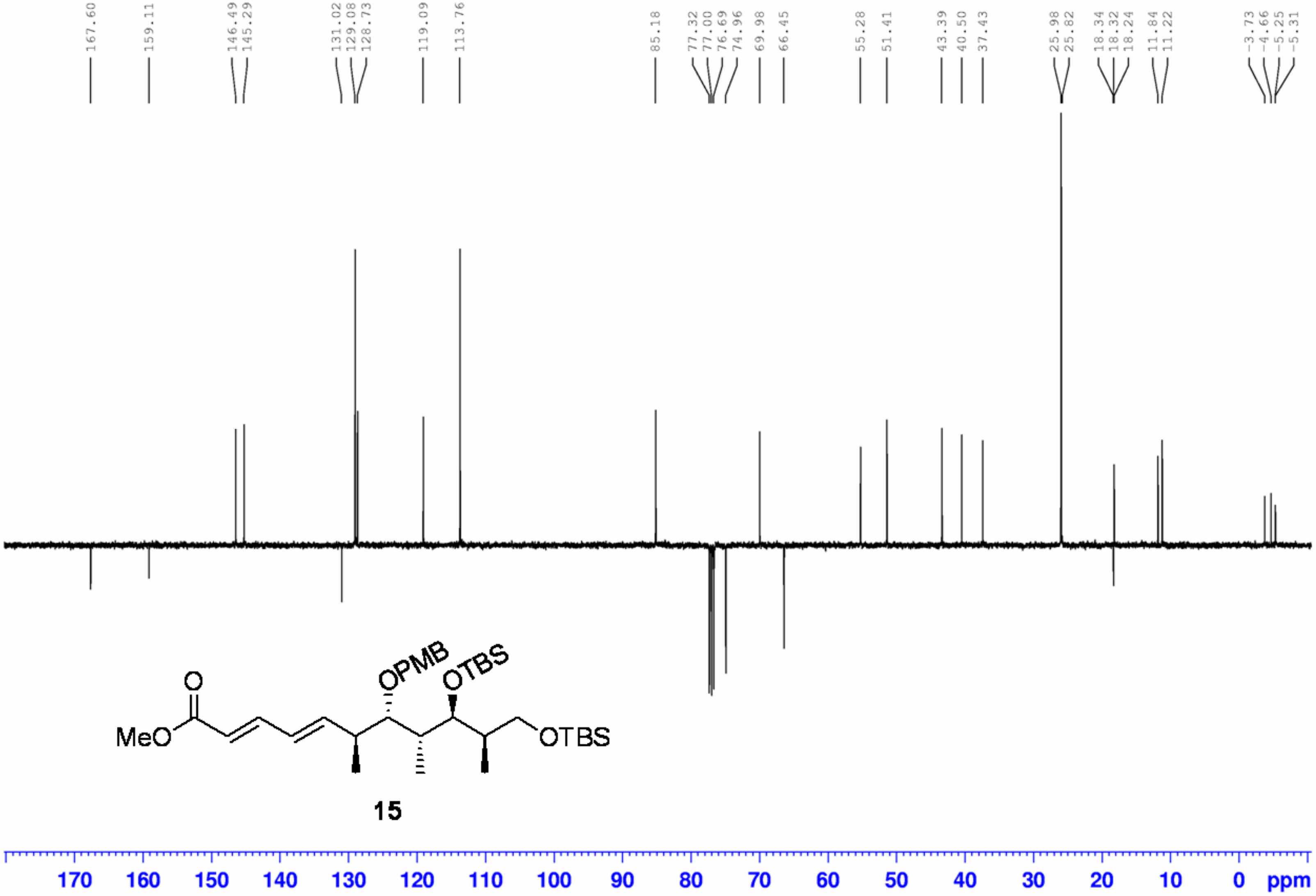
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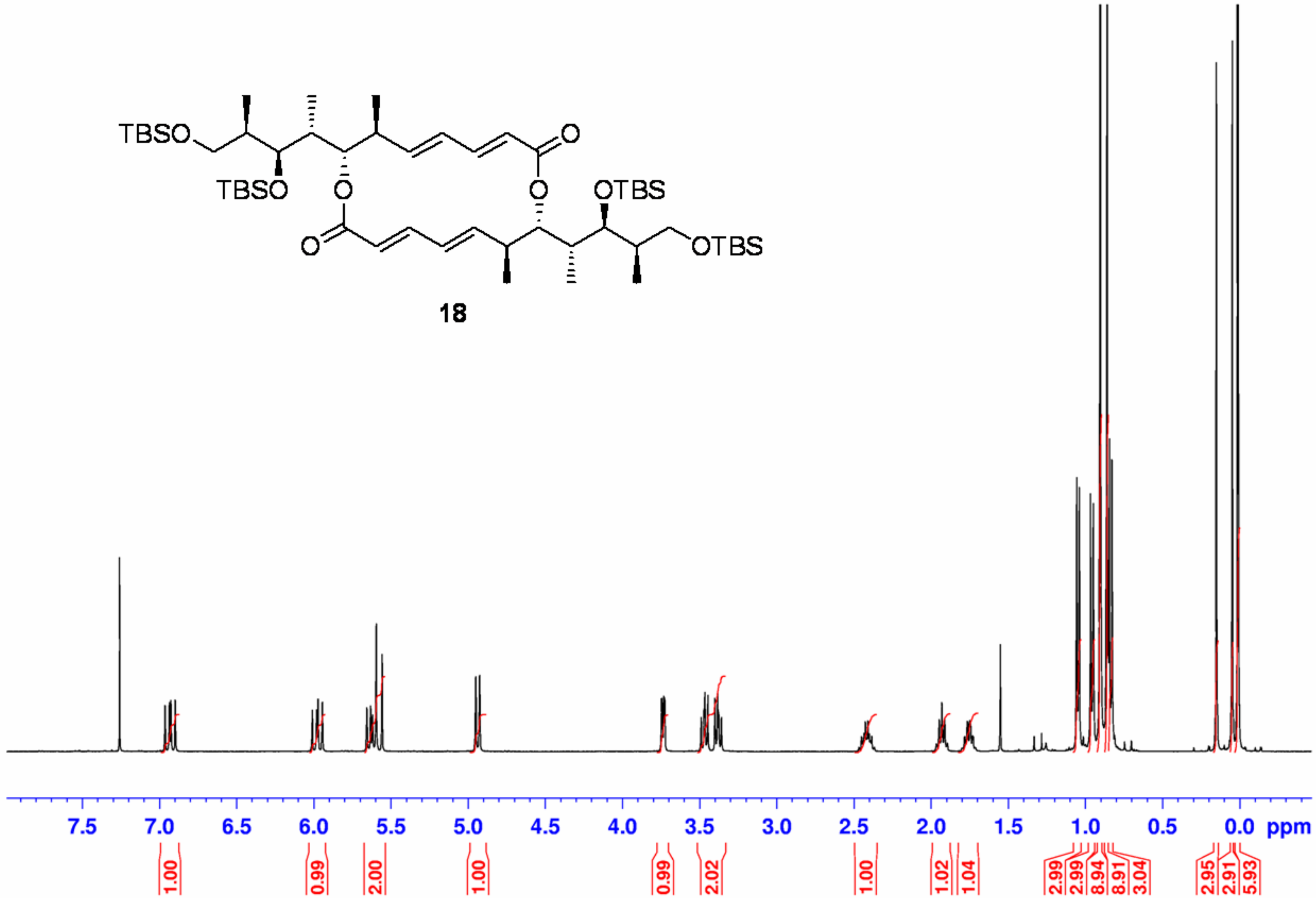
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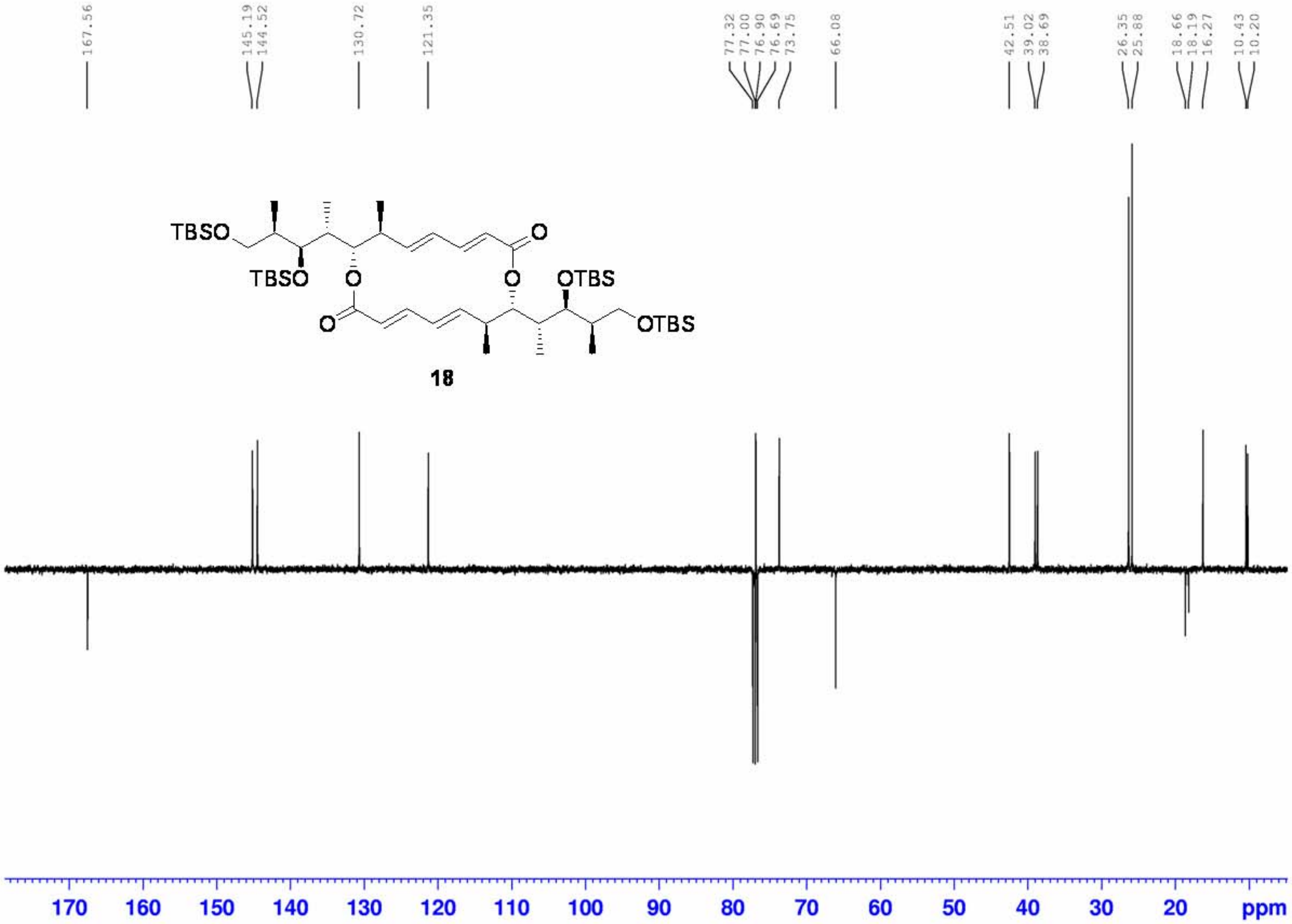
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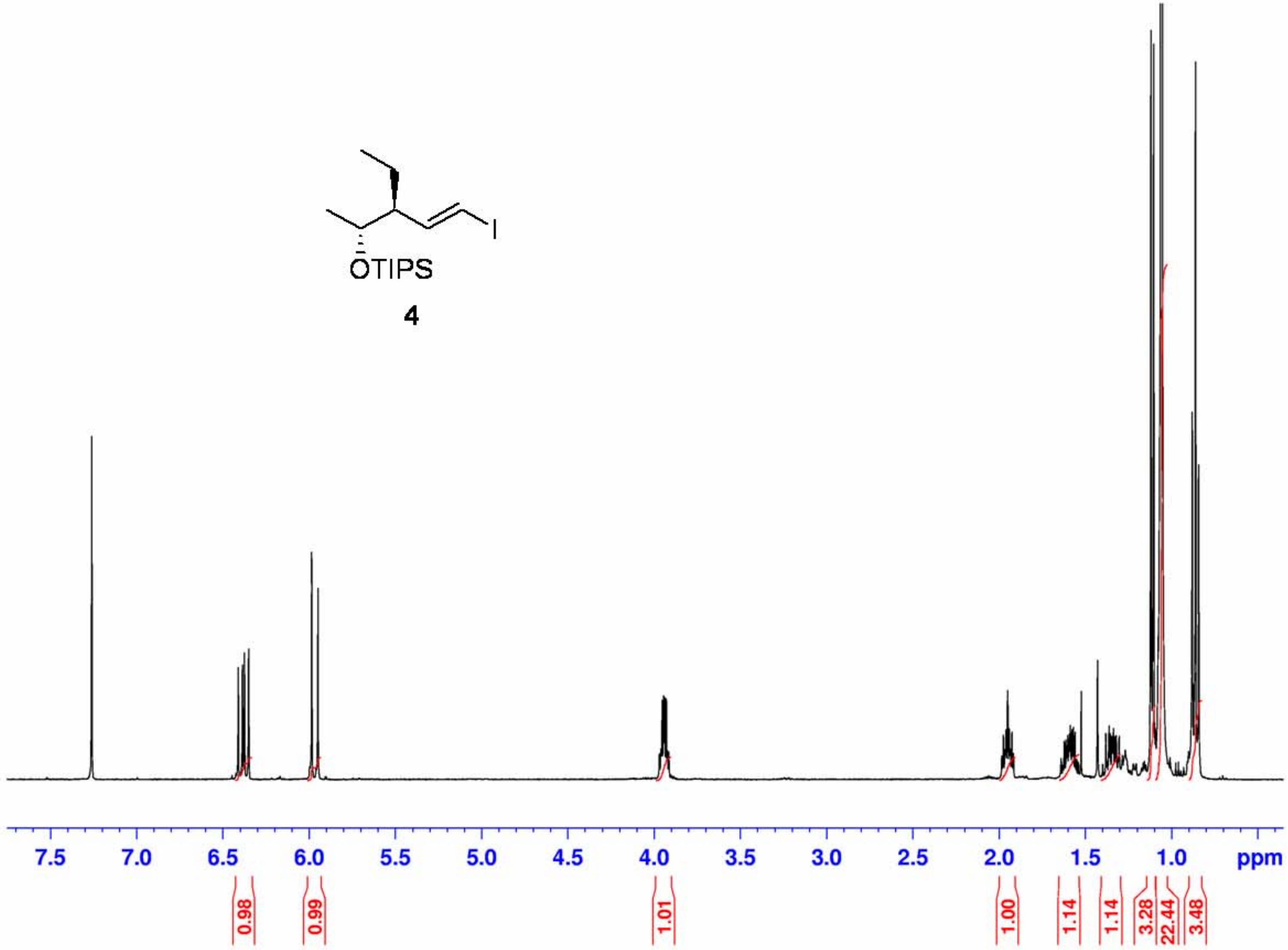
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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
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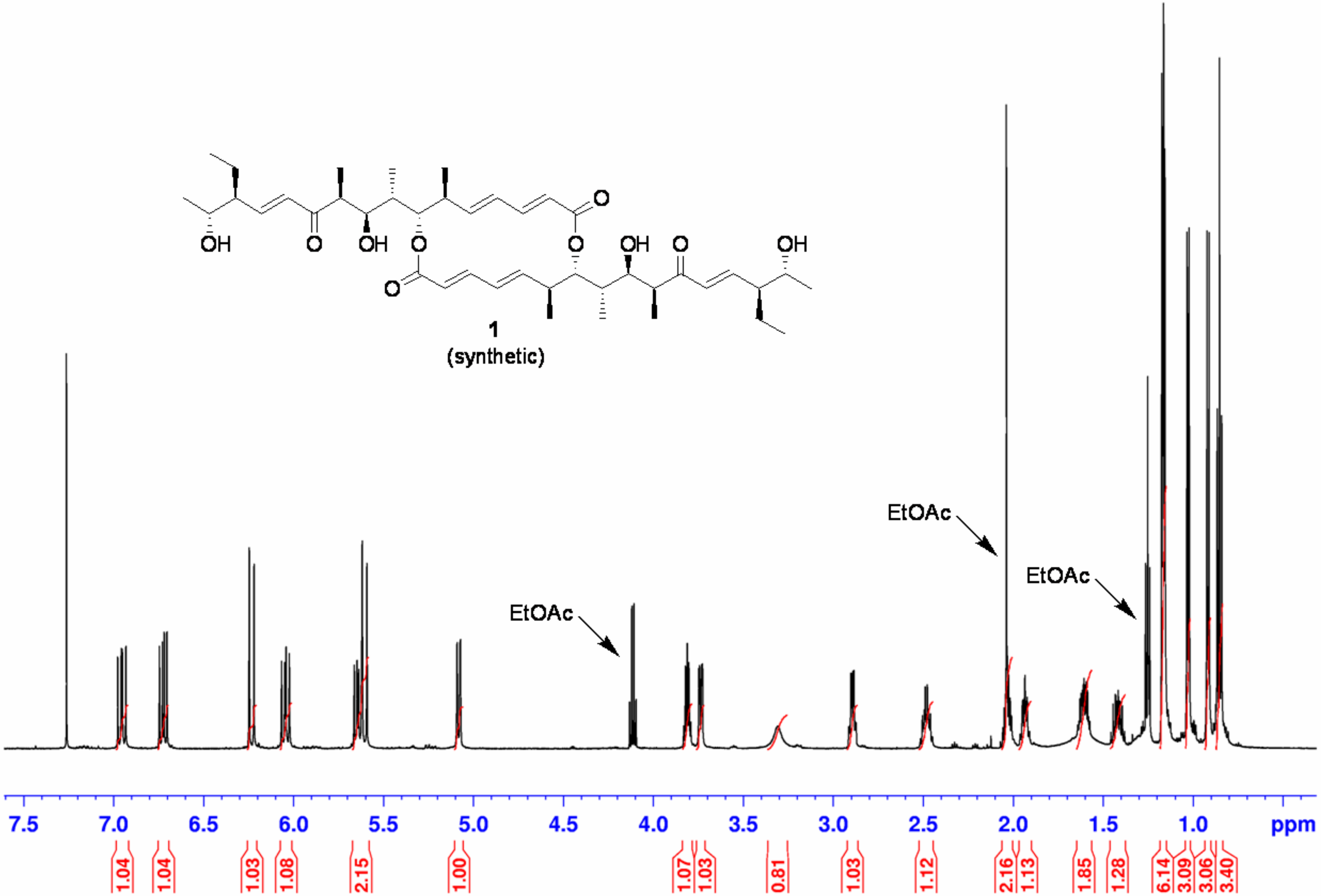
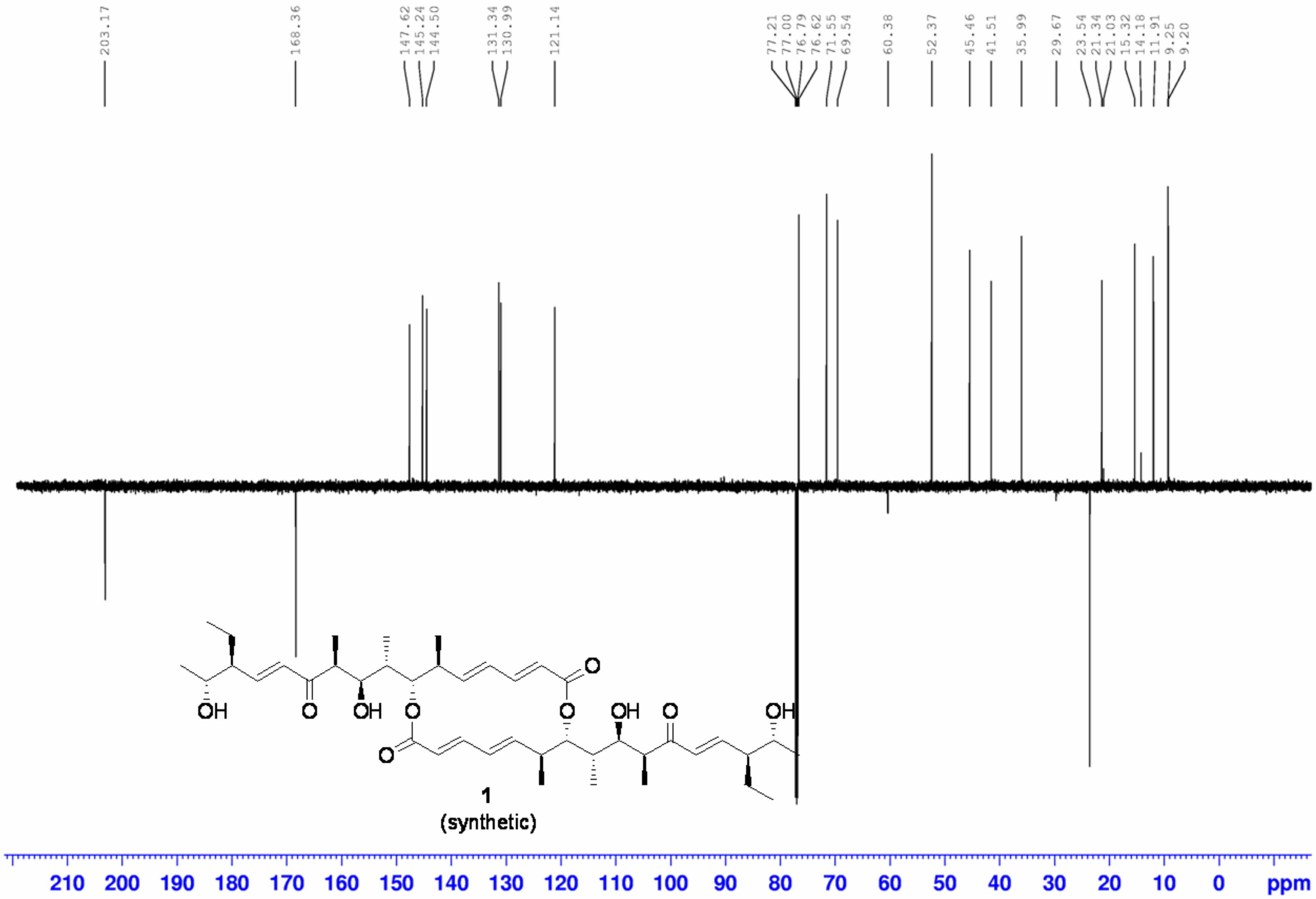
0.99
1.01
1.00
1.14
1.14
3.28
22.44
3.48



1
(synthetic)

EtOAc
EtOAc
EtOAc
OH
O
OH
O
O
O
OH
O
OH
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.04
1.04
1.03
1.08
2.15
1.00
1.07
1.03
0.81
1.03
1.12
2.16
1.13
1.85
1.28
6.14
3.09
3.06
3.40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147.62
145.24
144.50
131.34
130.99
121.14
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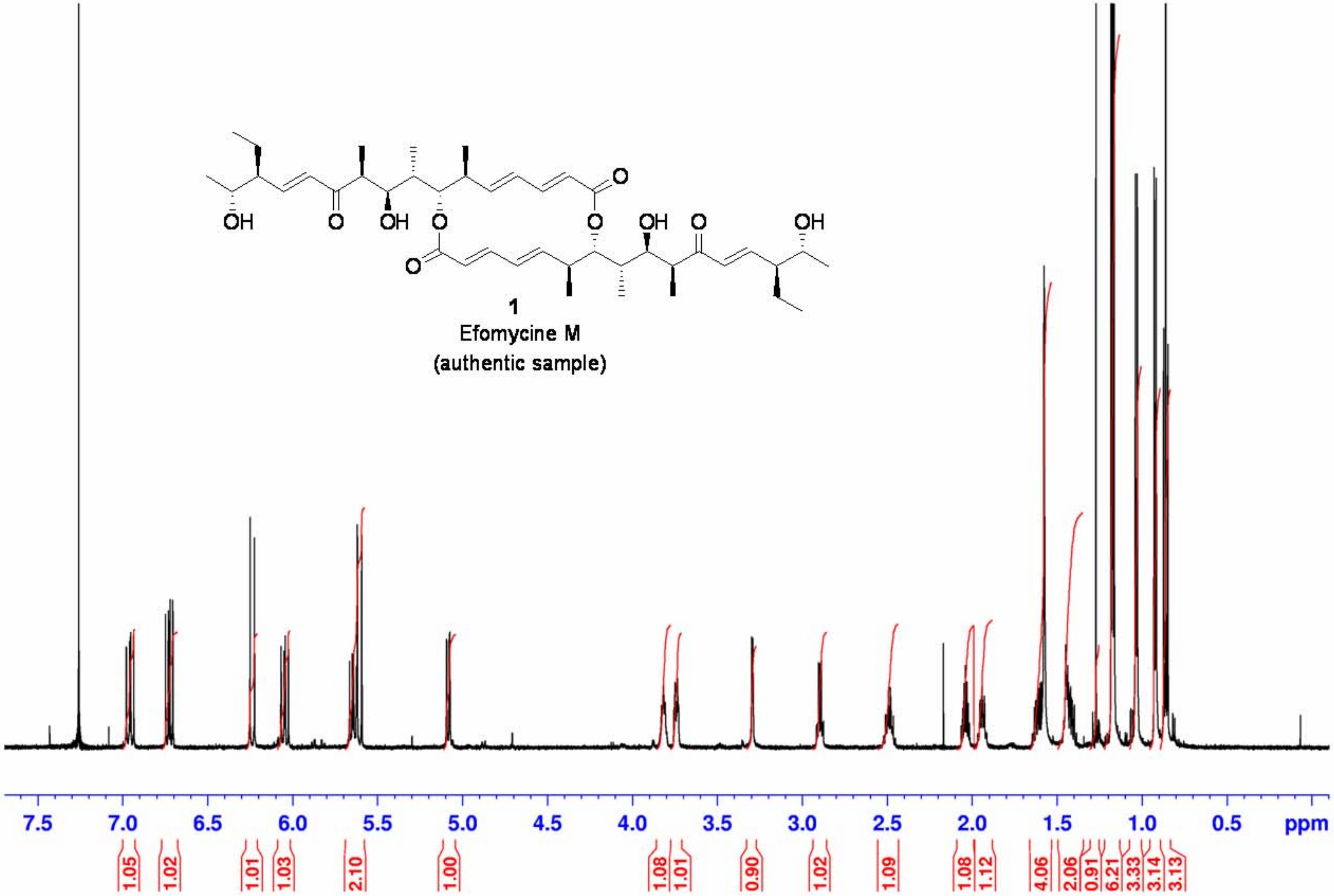
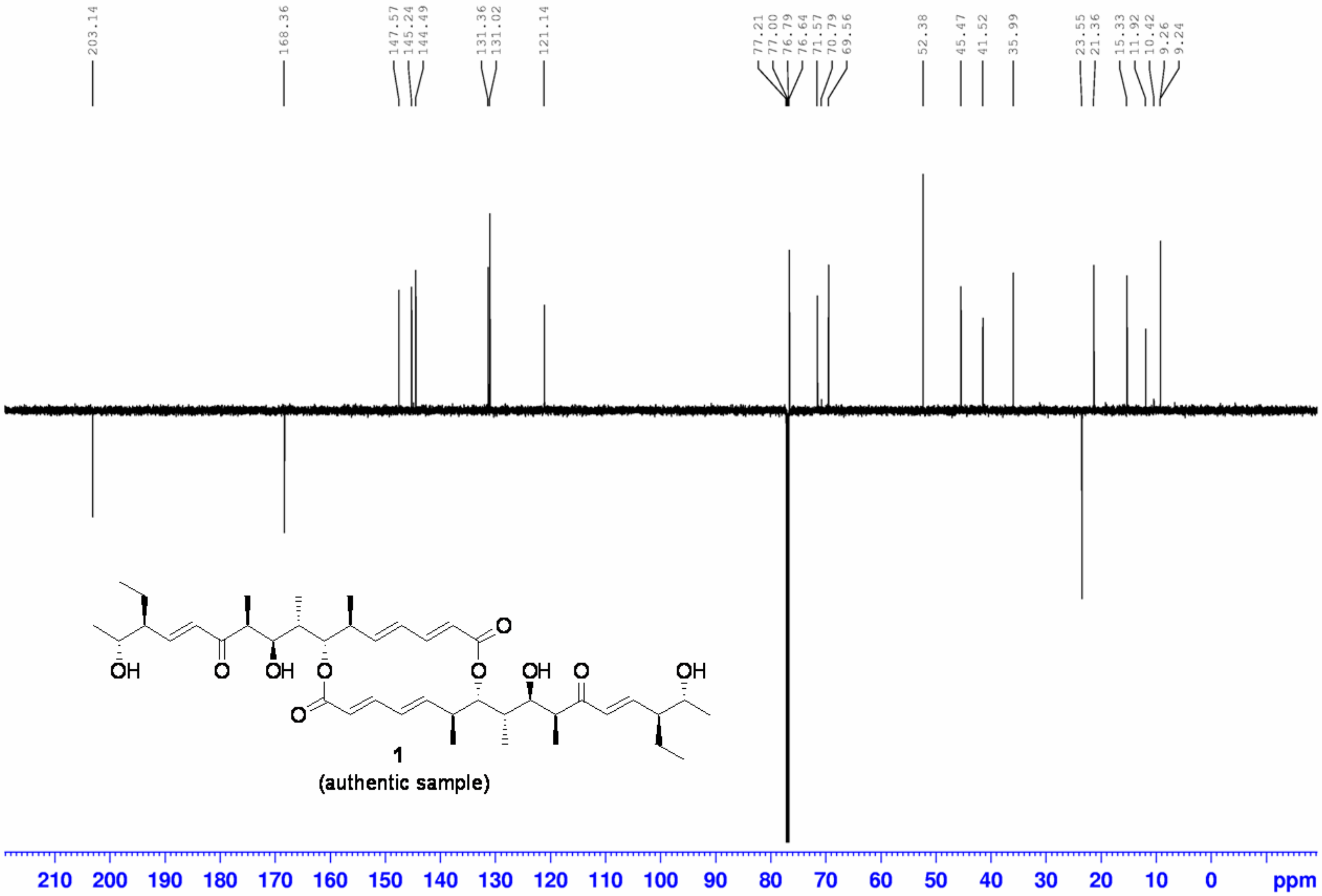
77.00
76.79
76.62
71.55
69.54
60.38
52.37
45.46
41.51
35.99
29.67
23.54
21.34
21.03
15.32
14.18
11.91
9.25
9.20
OH
O
OH
O
O
O
OH
O
OH
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

1
(synthetic)


OH
O
OH
O
O
O
OH
O
OH
O
1
Efomycine M
(authentic sample)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.05
1.02
1.01
1.03
2.10
1.00
1.08
1.01
0.90
1.02
1.09
1.08
1.12
4.06
2.06
0.91
6.21
3.33
3.14
3.13



1

(authentic sample)