Total synthesis of (±)-epithuriferic acid methyl ester via Diels-Alder reaction

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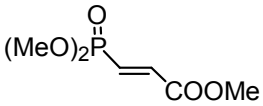
^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Brucker AV 200 or DRX 500 spectrometers. Coupling constants J are given in hertz (Hz). MS spectra were recorded on a Finnigan MAT 95 spectrometer. Microanalyses were carried out on EA1108 apparatus. Melting points were measured with a PHMK Boetius (VEB Analytik Dresden) apparatus. All reactions were performed using anhydrous conditions under argon atmosphere, unless otherwise noted. Purification with column chromatography was performed on silica gel (Merck, Kieselgel 70 – 230 mesh). TLC was carried out on silica gel plates (Merck F_{254}). Chemicals and solvents were obtained from commercial sources and distilled or dried according to standard procedures.



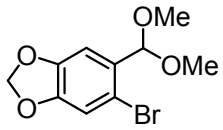
(E)-methyl 3-(dimethoxyphosphoryl)acrylate ((E)-5)

The title (*E*) isomer was synthesized according to the literature procedure via the Arbuzov reaction (Procedure **A**) as mixture of (*E*) and (*Z*) isomers and separated from (*Z*) isomer by column chromatography on silica gel using a mixture of ethyl acetate/acetone in gradient as eluent. The title compound was also synthesized stereospecifically according to another literature procedure via sillyl ether (Procedure **B**) as a pure (*E*) isomer.

Procedure **A**: (a) H. W. Coover, Marvin A. McCall, J. B. Dickey *J. Am. Chem. Soc.* **1957**, *79*, 1963-1967; (b) G. Pattenden, B. J. Walker *J. Chem. Soc.* **1969**, 531.

Procedure **B**: K. Afarinkia, M. Evans, J. C. H. Graham, G. Jimenez-Bueno, *Tetrahedron Lett.* **1998**, *39*, 433-434.

A colorless oil: b.p. (0.2 mmHg): 115-120 °C; yield: 57% (Procedure A) or 88% (Procedure B); R_f = 0.36 (AcOEt); R_f = 0.51 (AcOEt:acetone 5:1 v/v). ^{31}P-NMR (C_6D_6): 16.77. ^{31}P-NMR ($CDCl_3$): 17.39. ^{1}H-NMR (500 MHz) (acetone-d_6): 17.52. ^{1}H (C_6D_6): 3.23 (s, 3H, C(O)OCH$_3$); 3.23 (d, $^{3}J_{PH}$ = 11.1, 6H, P(O)(OCH$_3$)$_2$); 6.82 (dd$_{AB}$, $^{3}J_{HH}$ = 17.2, $^{2}J_{PH}$ = 20.0, 1H, =CH-C(O)O); 6.90 (dd$_{AB}$, $^{3}J_{HH}$ = 17.2, $^{3}J_{PH}$ = 18.4, 1H, =CH-P(O)). ^{1}H ($CDCl_3$): 3.77 (d, $^{3}J_{PH}$ = 11.4, 6H, P(O)(OCH$_3$)$_2$); 3.80 (s, 3H, C(O)OCH$_3$); 6.72 (dd$_{AB}$, $^{3}J_{HH}$ = 17.2, $^{3}J_{PH}$ = 20.4, 1H, =CH-C(O)O); 6.85 (dd$_{AB}$, $^{3}J_{HH}$ = 17.2, $^{3}J_{PH}$ = 17.2, 1H, =CH-P(O)). ^{1}H-NMR (500MHz) (acetone-d_6): 3.74 (d, $^{3}J_{PH}$ = 11.1, 6H, P(O)(OCH$_3$)$_2$); 3.78 (s, 3H, COOCH$_3$); 6.64 (dd, $^{3}J_{HH}$ = 17.2, $^{3}J_{PH}$ = 20.5, 1H, =CH-COO); 6.86 (dd, $^{3}J_{HH}$ = 17.2, $^{2}J_{PH}$ = 17.7, 1H, =CH-P(O)). ^{13}C-NMR ($CDCl_3$): 52.13 (s, C(O)OCH$_3$); 52.58 (d, $^{2}J_{PC}$ = 5.9, P(O)(OCH$_3$)); 130.51 (d, $^{1}J_{PC}$ = 184.9, =CHP(O)); 137.40 (d, $^{2}J_{PC}$ = 7.0, =CHC(O)O); 164.41 (d, $^{3}J_{PC}$ = 28.4, C(O)O). ^{13}C-NMR (acetone-d_6): 53.24 (s, COOCH$_3$); 53.74 (d, $^{2}J_{PC}$ = 5.5, P(O)(OCH$_3$)$_2$); 132.84 (d, $^{1}J_{PC}$ = 182.1, =CH-P(O)); 138.60 (d, $^{2}J_{PC}$ = 6.7, =CH-COO); 165.94 (d, $^{3}J_{PC}$ = 27.8, O-C=O).



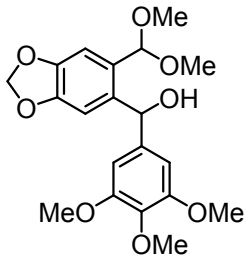
5-Bromo-6-dimethoxymethyl-benzo[1,3]dioxole (7)

2-Bromopiperonal (10.00 g, 43.66 mmol) was dissolved in benzene (20 mL), and then anhydrous methanol (5 mL) and trimethyl orthoformate (10.0 mL, 91.41 mmol) were added. The mixture was vigorously stirred in a Schlenk tube at 80 °C in an inert atmosphere (argon) for 8 h. Then, the benzene and an excess of orthoformate were removed in vacuo. Column chromatography on silica gel (*n*-hexane/ethyl acetate/Et_3N – 50:50:1 v/v) of the residue gave 12.01 g (100%) of the protected aldehyde as a pale yellow oil.

Spectroscopic data of **7** were consistent with the literature data.[1]

1) Tetsutaro Hattori, Hideyuki Tanaka, Yoshikazu Okaishi and Sotaro Miyano *J. Chem. Soc Perkin Trans. 1*, **1995**, 235-241; Michael E. Jung, Patrick Yuk-Sun Lam, Muzzamil M. Mansuri, and Laurine M. Speltz *J.* Org. *Chem.* **1985**, *50*, 1087-1105.

(6-Dimethoxymethyl-benzo[1,3]dioxol-5-yl)-(3,4,5-trimethoxy-phenyl)-methanol (8)



To a stirred solution of 5-bromo-6-dimethoxymethyl-benzo[1,3]dioxole **7** (5.00 g, 18.18 mmol) in dry THF (200 mL), *n*-BuLi (1.2 eq., 10.9 mL, 2.0 M in hexane) was added at -78˚C and the resulting solution was stirred at the same temperature for 10 minutes. Then, 3,4,5-trimethoxybenzaldehyde (1.2 eq., 4.28 g) in THF (30 mL) was added and the resulting solution was stirred at -78˚C for the next hour. Then, the reaction mixture was warmed to room temperature and aqueous saturated NH_4Cl solution was added (20 mL). The reaction mixture was concentrated under reduced pressure, then ethyl acetate (200 mL) was added and the layers were separated. The organic layer was washed with water (3x50 mL), dried ($MgSO_4$), filtered and evaporated. The crude product was purified by column chromatography (hexane/ethyl acetate) to afford **8** (5.56 g, 78%).

Pale yellow crystals, m.p. = 113-115 ˚C; R_f = 0.27 (*n*-hexane/ethyl acetate 1:1 v/v); ^{1}H-NMR (C_6D_6): 3.11 (s, 6H, 2xOCH_3), 3.33 (bs, 1H, OH), 3.46 (s, 6H, 2xOCH_3), 3.91 (s, 3H, OCH_3), 5.32 (s, 1H, OCH_2O), 5.35 (s, 1H, OCH_2O), 5.59 (s, 1H, CH-OH), 6.34 (s, 1H, OCHO), 6.92 (s, 2H, 2,6-H_2Ar'), 7.16 (s, 1H, ArH), 7.39 (s, 1H, ArH); ^{13}C-NMR (CD_2Cl_2): 54.60 (s, 2xOCH_3), 59.10 (s, 2xOCH_3), 69.49 (s, OCH_3), 100.14 (s, OCH_2O), 100.37 (s, =CH), 102.11 (s, 2x=CH), 105.88 (s, =CH), 107.18 (s, =CH), 128.21 (s, >C<), 135.50 (s, >C<), 137.71 (s, >C<), 145.41 (s, =C-OCH_2), 146.46 (s, =C-OCH_2), 151.85 (s, 2x >C<); HRMS (EI) (*m/z*): calcd. for $C_{20}H_{24}O_8$: 392.1471; found: 392.1491.

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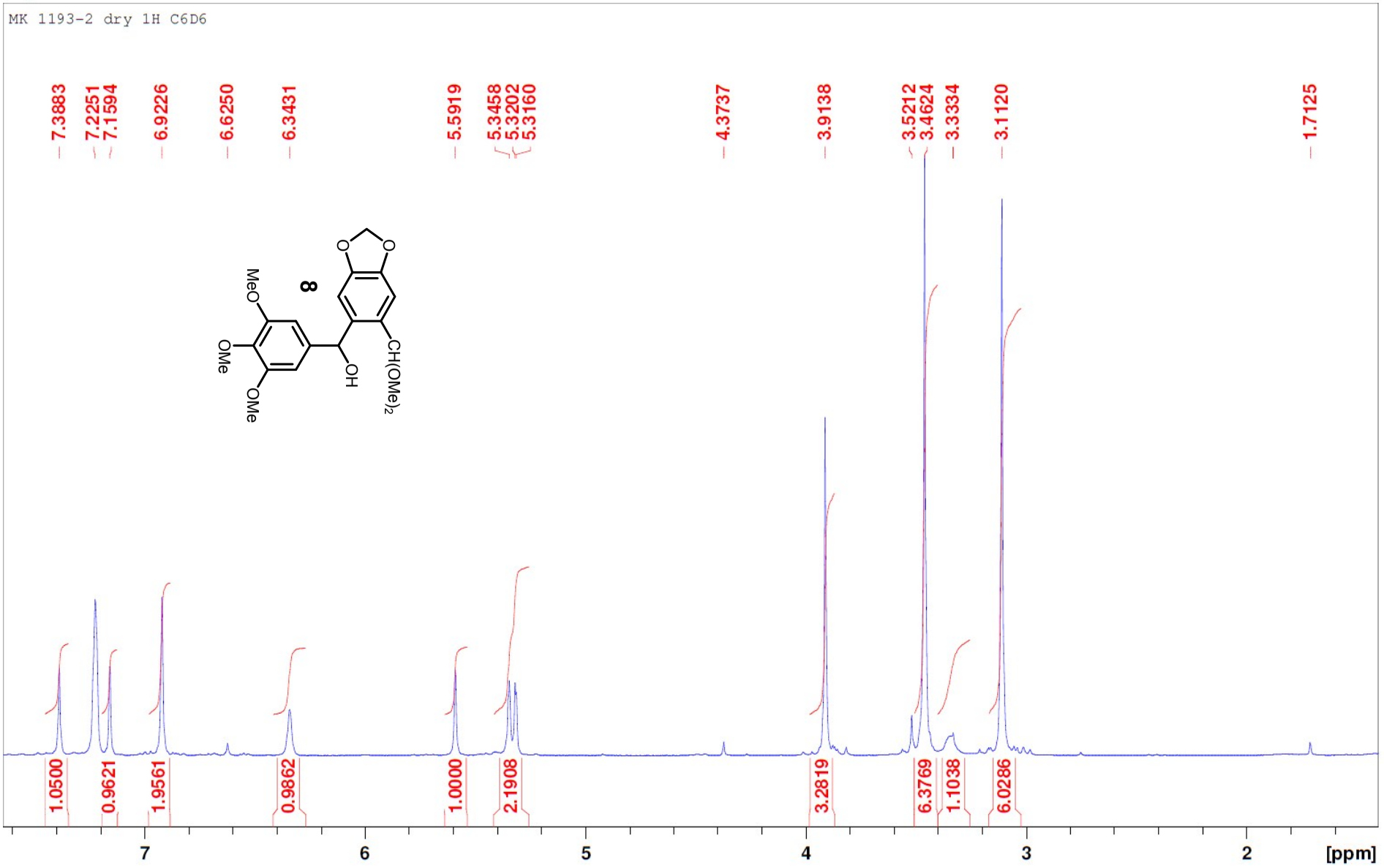
MK 1193-2 dry 1H C6D6



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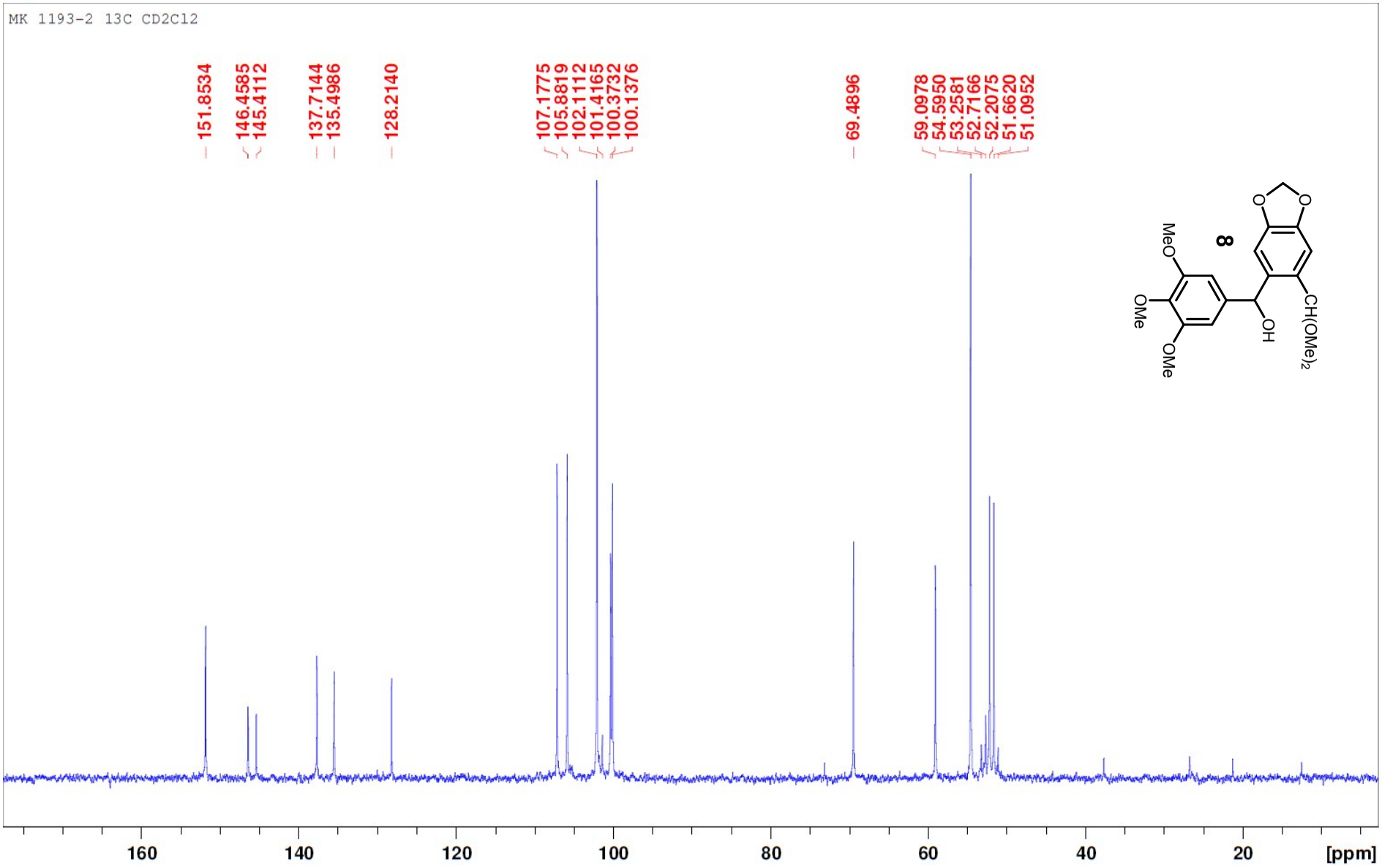

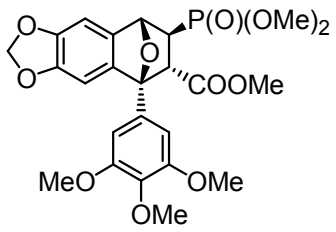

(5R,6R,7S,8R)-rel-5,6,7,8-tetrahydro-7-(dimethoxyphosphoryl)-5-(3,4,5-trimethoxyphenyl)-5,8-epoxynaphtho[2,3-d]-1,3-dioxole-6-carboxylic acid methyl ester (9)

(6-(dimethoxymethyl)benzo[*d*][1,3]dioxol-5-yl)(3,4,5-trimethoxyphenyl) methanol **8** (1.500 g, 3.83 mmol), *p*-TSA (2 mg) and (*E*)-methyl 3-(dimethoxyphosphoryl) acrylate ((*E*)-**5**) (0.891 g, 4.59 mmol, 1.2 eq.) were stirred and heated in dry toluene (5 mL) for 3 h at 110 °C under argon atmosphere in the Schlenk tube. After cooling of the reaction mixture to -10 °C, a spontaneous crystallization gave a white solid. Recrystallization from EtOH led to 0.959 g (48%) of the major cycloadduct **9** as a single diastereoisomer. The second, minor diastereoisomer **10** was isolated by column chromatography (ethyl acetate/acetone) from evaporated mother liquor in 30% yield (0.600 g).

White crystals, yield: 48 %; R_f = 0.26 (AcOEt); R_f = 0.37 (AcOEt/acetone 5:1 v/v); mp.: = 158-161 °C (MeOH/benzene). ^{31}P-NMR (C_6D_6): 30.73. ^{1}H-NMR (acetone-d_6): 2.57 (dd, $^3J_{HH}$ = 4.8, $^2J_{PH}$ = 13.7, 1H, CHP(O)) {in ^{1}H {^{31}P}-NMR spectrum: d, J = 4.8}; 3.59 (s, 3H, C(O)OCH_3); 3.74 (d, $^3J_{PH}$ = 10.8, 3H, P(O)OCH_3); 3.76 (d, $^3J_{PH}$ = 10.8, 3H, P(O)OCH_3); 3.75-3.90 (m; 1H, CHC(O)O); 3.78 (s, 3H, *p*-CH_3OAr'); 3.86 (s, 6H, 3,5-(CH_3O)$_2$Ar'); 5.65 (d; $^3J_{PH}$ = 7.7, 1H, CH-O-) {in ^{1}H {^{31}P}-NMR spectrum - singlet}; 6.00 (s, 1H, OCH_2O); 6.03 (s, 1H, OCH_2O); 6.61 (s, 1H, Ar-H); 7.03 (s, 2H, 2,6-H$_2$-Ar'); 7.06 (s, 1H, Ar-H). ^{1}H (C_6D_6): 3.03 (dd, $^3J_{HH}$ = 4.7, $^2J_{PH}$ = 15.0, 1H, CHP(O)); 3.07 (s, 3H, C(O)OCH_3); 3.39 (s, 6H, 3,5-(CH_3O)$_2$Ar'); 3.46 (d, $^3J_{PH}$ = 10.9, 3H, P(O)OCH_3); 3.52 (d, $^3J_{PH}$ = 10.7, 3H, P(O)OCH_3); 3.87 (s, 3H, 4-CH_3OAr'); 4.29 (dd, $^3J_{HH}$ = 4.7, $^3J_{PH}$ = 20.2, 1H, CHC(O)O); 5.20 (s, 1H, OCH_2O); 5.25 (s, 1H, OCH_2O); 5.83 (d, $^3J_{PH}$ = 7.7, CH-O); 6.40 (s, 1H, Ar-H); 6.66 (s, 1H, Ar-H); 7.25 (s, 2H, 2,6-H$_2$-Ar'). ^{13}C-NMR (CD_2Cl_2): 45.21 (d, $^1J_{PC}$ = 146.2, CHP(O)); 50.88 (s, C(O)OCH_3); 52.58 (d, $^2J_{PC}$ = 6.6, P(O)(OCH_3)$_2$); 52.98 (s, CHC(O)O); 56.36 (s, 3,5-(CH_3O)$_2$Ar'); 60.71 (s, 4-CH_3OAr'); 79.06 (s, CH-O-); 92.86 (s, Ar'-C-O-); 101.04 (s, OCH_2O); 102.02 (s, C$_{Ar}$-H); 103.50 (s, C$_{Ar}$-H); 105.68 (s, 2,4-Ar'-H); 131.56 (s, 4-Ar'); 138.33 (s, *ipso*-Ar'); 138.76 (s, Ar); 139.69 (d, $^3J_{PC}$ = 14.0, Ar); 147.32 (s, =C-O-); 147.71 (s, =C-O-); 153.43 (s, 3,5-Ar'); 170.73 (d, $^3J_{PC}$ = 5.6, C=O). MS (CI) (*m/z*): 523 (4, M$^+$ (+H)); 473 (12); 329 (92, (-(CH_3O)$_2$P(O)-CH=CH-C(O)OCH_3, +H)); 328 (100, M$^+$ (-(CH_3O)$_2$P(O)-CH=CH-C(O)OCH_3)); 313 (18), 195 (36, ((CH_3O)$_2$P(O)-CH=CH-C(O)OCH_3)$^+$); HRMS (EI) (*m/z*): calcd. for $C_{24}H_{27}O_{11}P$: 522.1291; found: 522.1273.

X-Ray analysis of the crystal **9** shows that the torsion angle of 85.36˚ between C-H-8 and C-H-7 bonds was close to the right angle (90˚), therefore the observed coupling constant was zero Hz. The torsion angle between C-H-8 and C-7-P bonds was only 36.47˚ and according to the Karplus curve, the corresponding coupling constant should be larger than zero (7.7 Hz). The protons H-7 and H-6 are in the *trans* configuration but the observed torsion angle of 129.87˚ between C-H-7 and C-H-6 bonds was far from 180˚, therefore the coupling constant was not too large (4.7 Hz) (Scheme 1).

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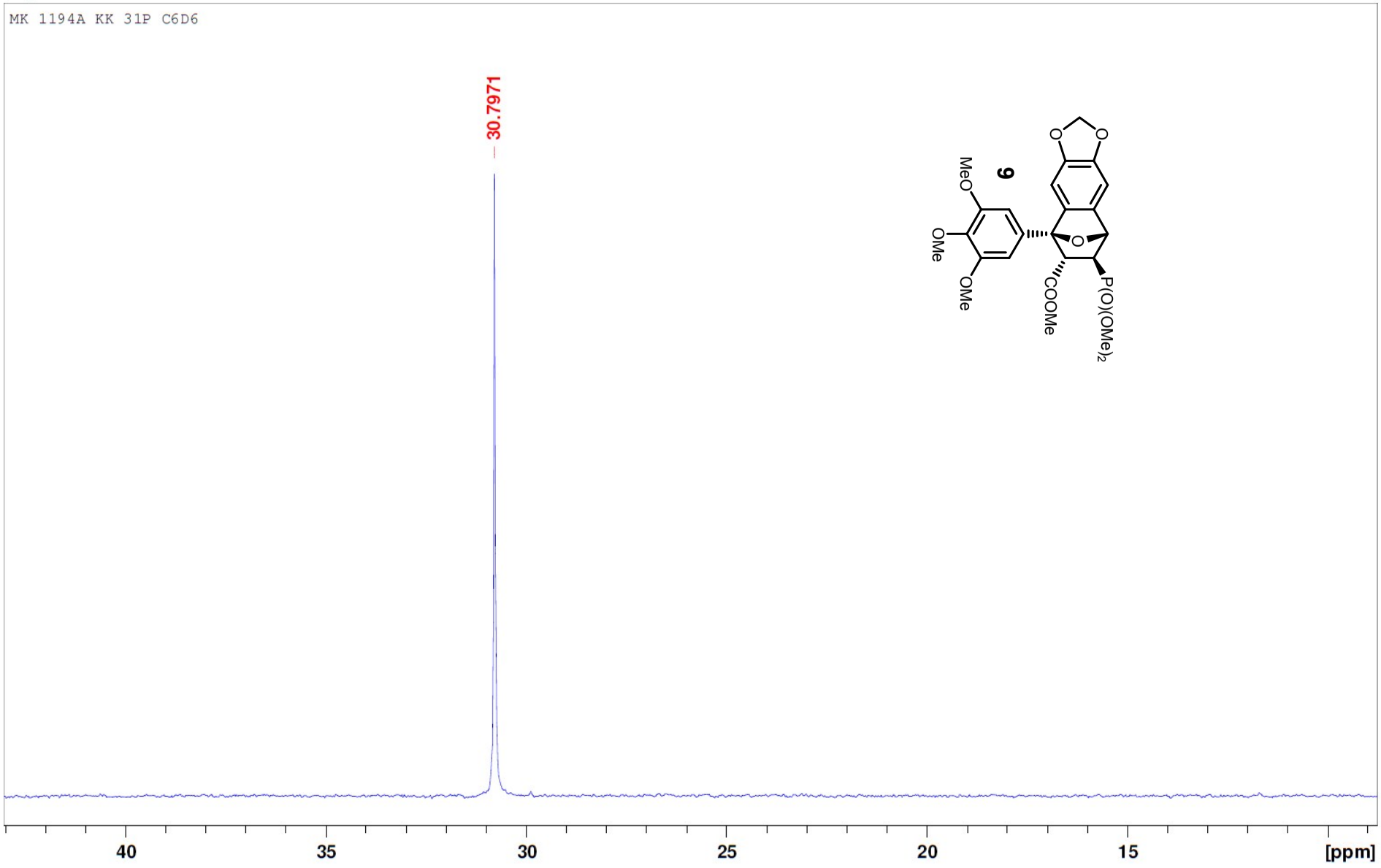
MK 1194A KK 31P C6D6



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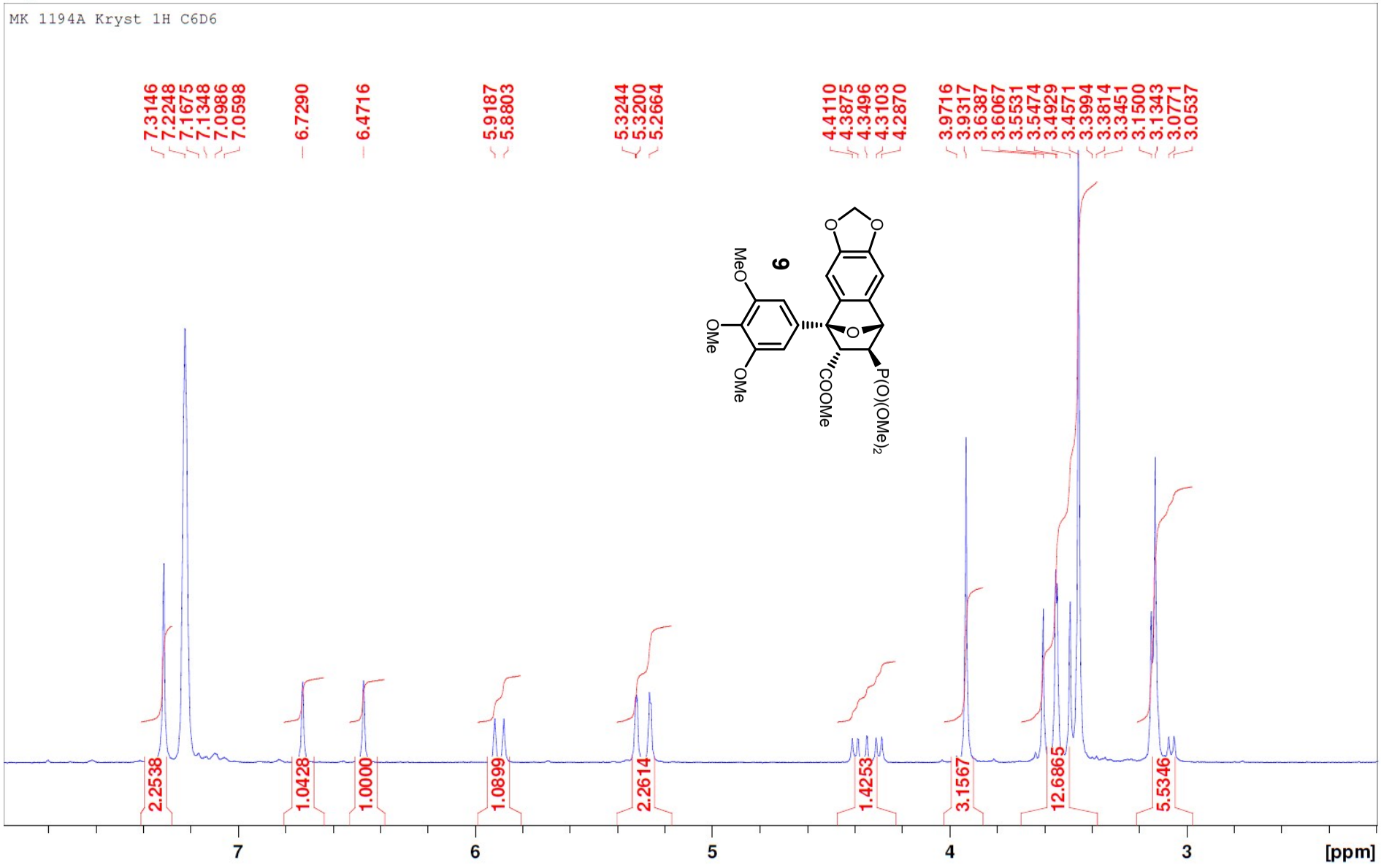

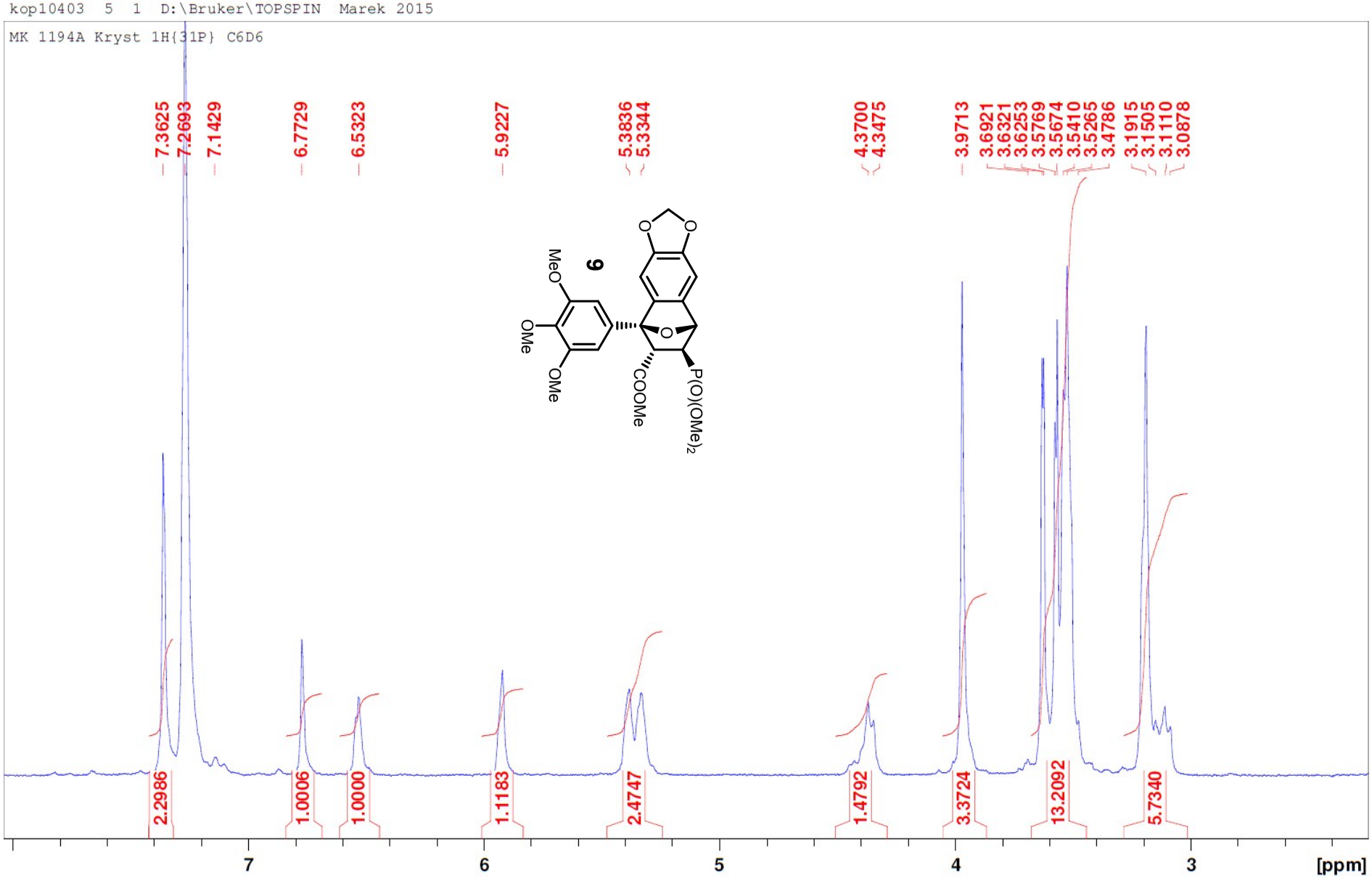
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OMe
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5
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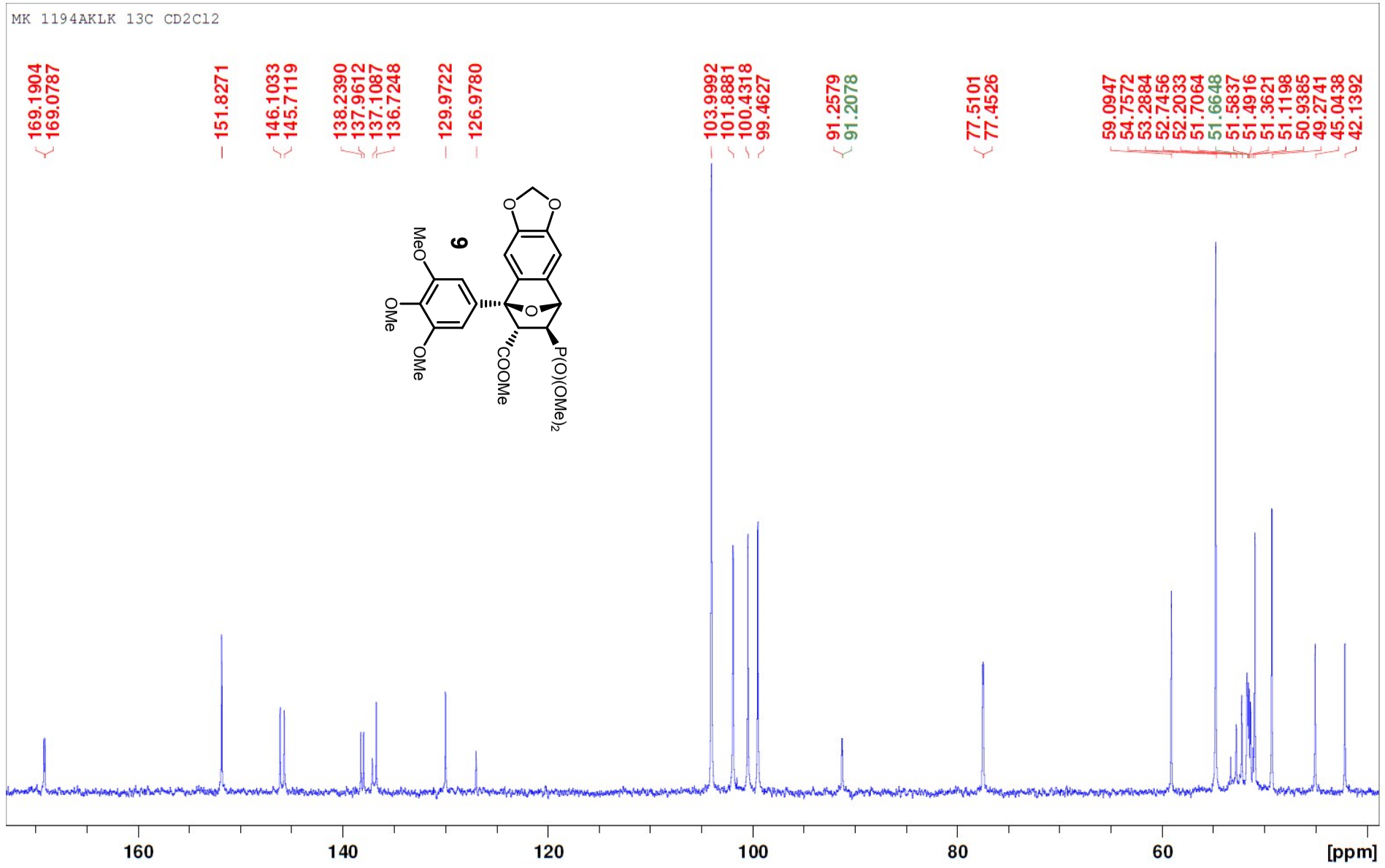
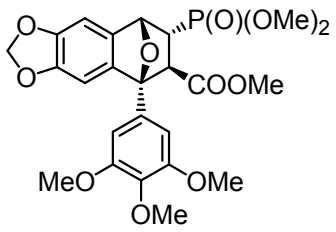
MK 1194AKLK 13C CD2Cl2





(5R,6S,7R,8R)-rel-5,6,7,8-tetrahydro-7-(dimethoxyphosphoryl)-5-(3,4,5-trimethoxyphenyl) 5,8-epoxynaphtho[2,3-3]-1,3-dioxole-6-carboxylic acid methyl ester (10)

Colorless oil, yield: 30%; R_f = 0.24 (AcOEt); R_f = 0.35 (AcOEt:acetone 5:1 v/v). ^{31}P-NMR (C_6D_6): 27.07. ^{1}H-NMR (C_6D_6): 3.07 (s, 3H, $COOCH_3$); 3.18 (d, $^3J_{PH}$ = 10.7, 3H, $P(O)OCH_3$); 3.23 (d, $^3J_{PH}$ = 10.9, 3H, $P(O)OCH_3$); 3.37 (s, 6H, 3,5-$(CH_3O)_2$Ar'); 3.58-3.76 (m, 2H, CHCOO, CHP(O)); 3.85 (s, 3H, 4-CH_3O-Ar'); 5.28 (s, 1H, OCH_2O); 5.33 (s, 1H, OCH_2O); 5.65 (d, $^3J_{HH}$ = 4.2, O-CH); 6.84 (s, 1H, Ar-H); 6.94 (s, 2H, 2,6-H_2Ar'); 6.97 (s, 1H, Ar-H). ^{1}H-NMR (C_6D_6, 500 MHz): 3.07 (s, 3H, $COOCH_3$); 3.17 (d, $^3J_{PH}$ = 10.7, 3H, $P(O)OCH_3$); 3.23 (d, $^3J_{PH}$ = 10.9, 3H, $P(O)OCH_3$); 3.36 (s, 6H, 3,5-$(CH_3O)_2$Ar'); 3.61 (dd, $^3J_{HH}$ = 5.6, $^3J_{PH}$ = 14.8, 1H, CHCOO) {in ^{1}H {^{31}P} d, J = 5.6}; 3.70 (ddd, $^3J_{HH}$ = 4.6, $^3J_{HH}$ = 5.6, $^2J_{PH}$ = 14.3, 1H, CHP(O)) {in ^{1}H {^{31}P}-NMR spectrum: dd, J = 5.6, J = 4.6}; 3.85 (s, 3H, 4-CH_3O-Ar'); 5.26 (s, 1H, OCH_2O); 5.31 (s, 1H, OCH_2O); 5.65 (d, $^3J_{HH}$ = 4.6, O-CH) {in ^{1}H {^{31}P} d, J = 4.6}; 6.84 (s, 1H, Ar-H); 6.94 (s, 2H, 2,6-H_2Ar'); 6.93 (s, 1H, Ar-H). ^{1}H (acetone-d_6): 3.15-3.33 (m, 2H, CHCOO, CHP(O)); 3.38 (s, 3H, $COOCH_3$); 3.47 (d, $^3J_{PH}$ = 10.8, 3H, $P(O)OCH_3$); 3.64 (d, $^3J_{PH}$ = 10.9, 3H, $P(O)OCH_3$); 3.74 (s, 3H, 4-CH_3O-Ar'); 3.87 (s, 6H, 3,5-$(CH_3O)_2$Ar'); 5.68 (d, $^3J_{HH}$ = 1.8, 1H, -O-CH); {in ^{1}H {^{31}P}-NMR spectrum: d, J = 1.8} 5.98 (s, 2H, OCH_2O); 6.75 (s, 1H, Ar-H); 6.85 (s, 2H, 2,6-H_2Ar'); 6.98 (s, 1H, Ar-H). ^{13}C-NMR (C_6D_6): 45.78 (d, $^1J_{PC}$ = 150.3, CHP(O)); 52.32 (s, $C(O)OCH_3$); 52.55 (d, $^2J_{PC}$ = 6.5, $P(O)OCH_3$); 52.80 (d, $^2J_{PC}$ = 6.3, $P(O)OCH_3$); 53.47 (s, CHC(O)O); 56.46 (s, 3,5-$(CH_3O)_2$Ar'); 61.19 (s, 4-CH_3OAr'); 80.24 (d, $^2J_{PC}$ = 4.0, CH-O-); 94.59 (d, $^3J_{PC}$ = 7.6, Ar'-C-O-); 102.20 (s, OCH_2O); 104.62 (s, 2,6-H_2Ar'); 104.63 (s, Ar-H); 106.97 (s, Ar-H); 131.52 (s, 4-Ar'); 138.10 (s, Ar); 139.47 (s, Ar); 142.52 (s, *ipso*-Ar'); 147.97 (s, =C-O-); 148.22 (s, =C-O-); 154.68 (s, 3,5-Ar'); 172.63 (d, $^3J_{PC}$ = 3.9, C(O)O). MS (CI) (*m/z*): 523 (7, M^+ (+H)); 473 (16); 329 (87, (-$(CH_3O)_2$P(O)-CH=CH-C(O)OCH_3, +H)); 328 (100, M^+ (-$(CH_3O)_2$P(O)-CH=CH-C(O)OCH_3)); 195 (44, ($(CH_3O)_2$P(O)-CH=CH-C(O)OCH_3)$^+$). HRMS (EI) (*m/z*): calcd for $C_{24}H_{27}O_{11}P$: 522.1291; found: 522.1276.

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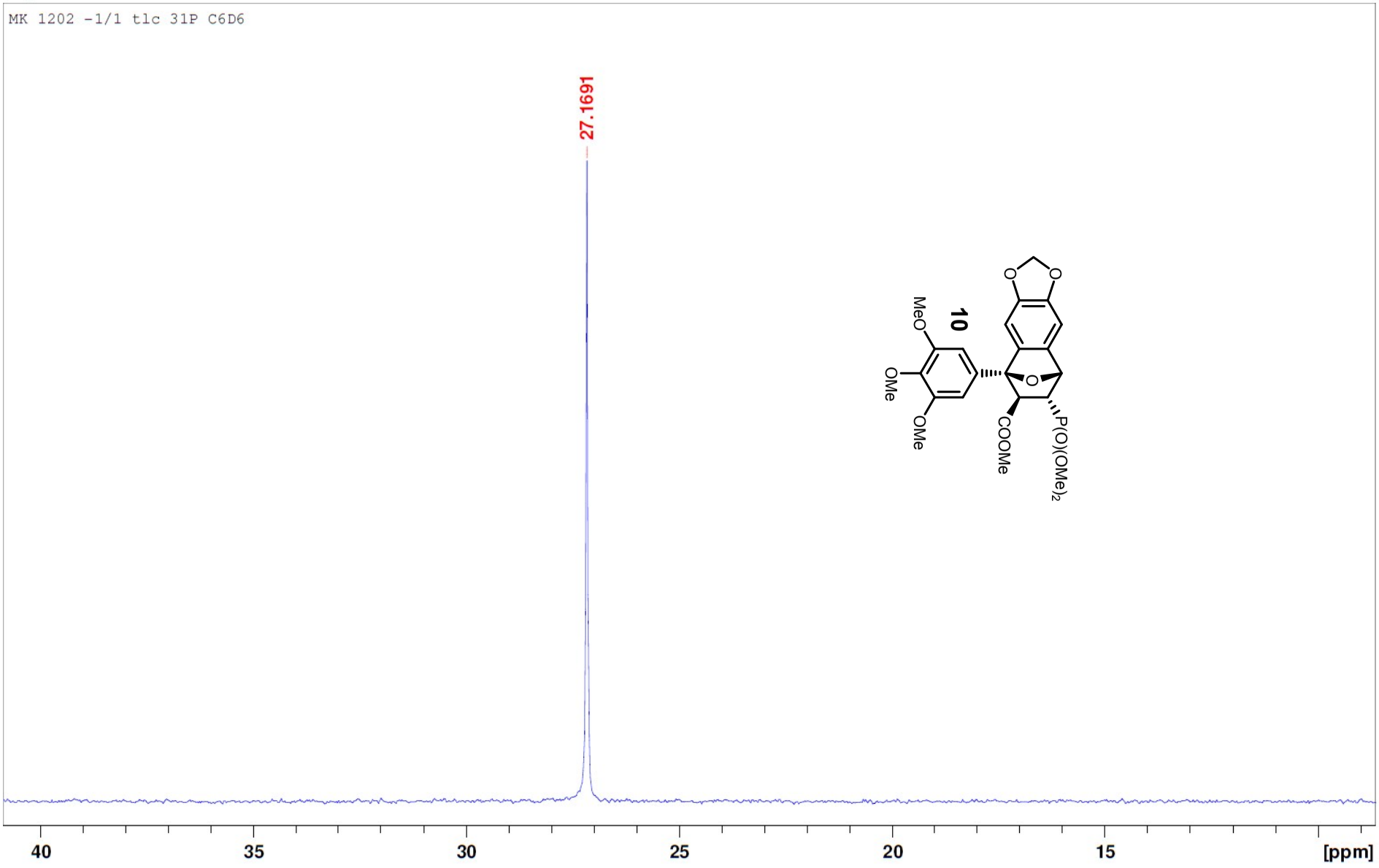

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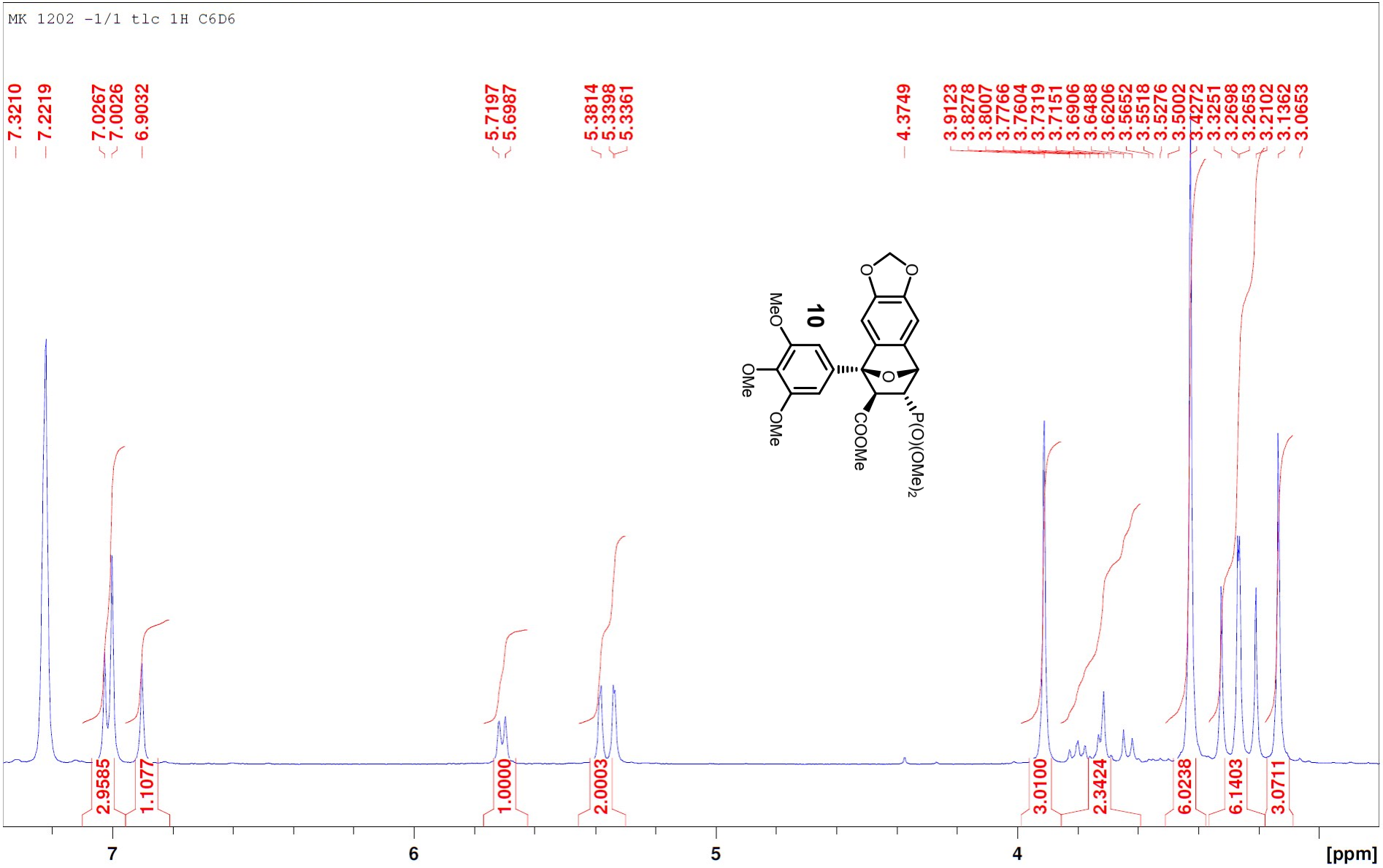

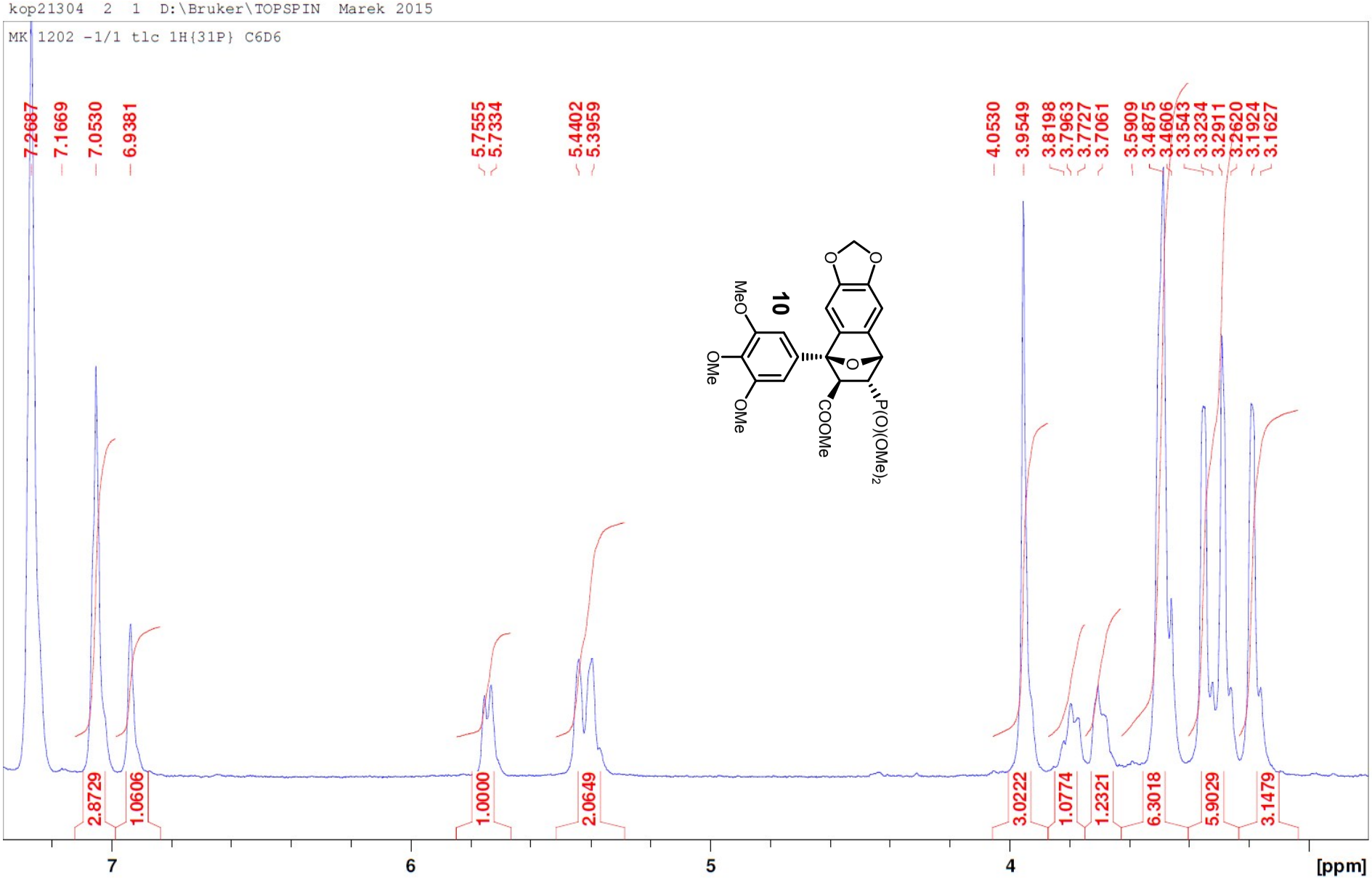
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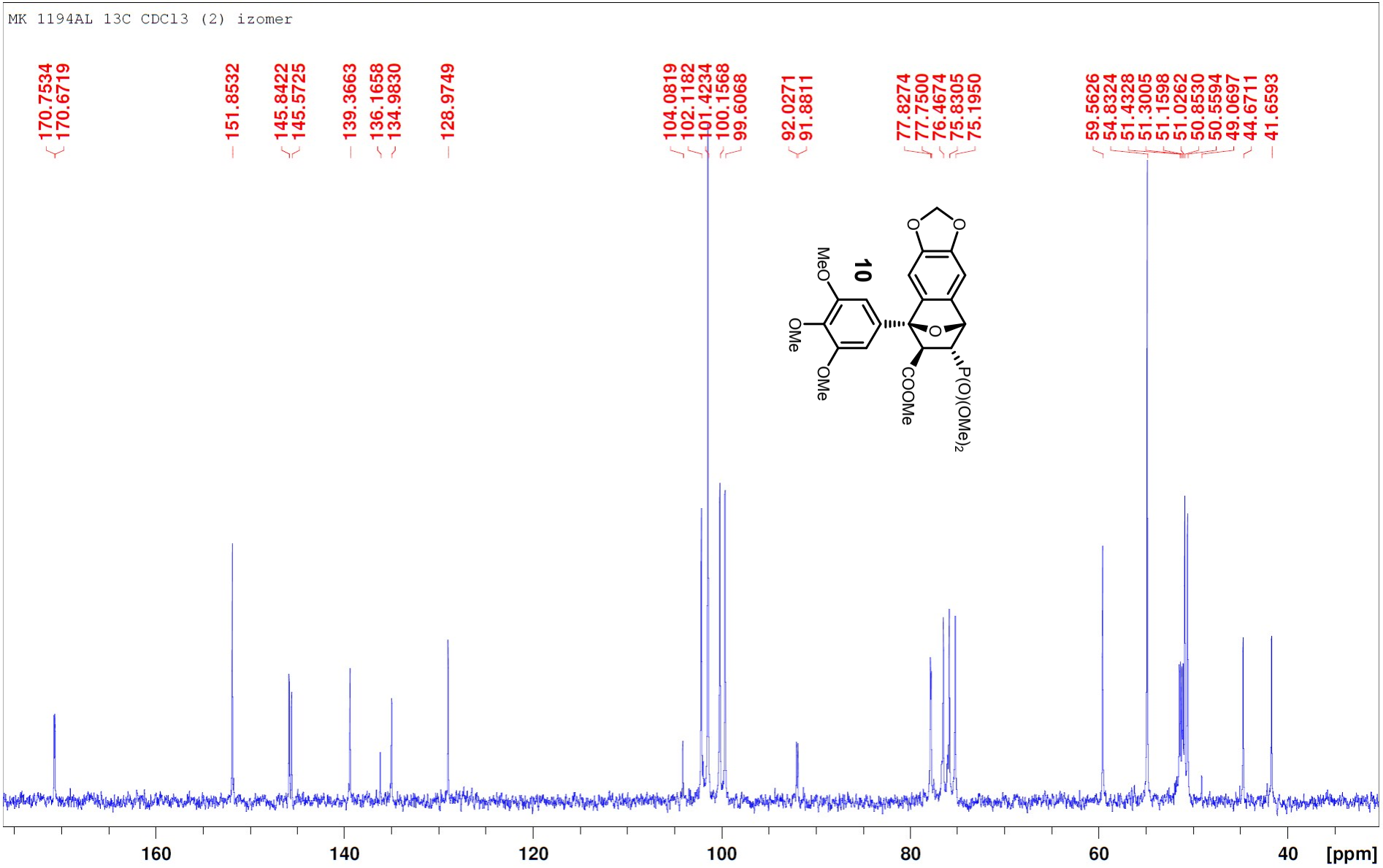
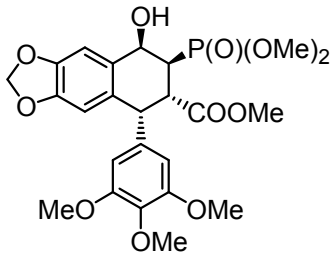
3.2911
3.2620
3.1924
3.1627
10
MeO
OMe
OMe
COOMe
P(O)(OMe)2
2.8729
1.0606
1.0000
2.0649
3.0222
1.0774
1.2321
6.3018
5.9029
3.1479
7
6
5
4
[ppm]

kop11303 1 1 D:\Bruker\TOPSPIN Marek 2015

MK 1194AL 13C CDCl3 (2) izomer





(5S,6S,7S,8R)-5,6,7,8-tetrahydro-8-hydroxy-5-(3,4,5-trimethoxyphenyl)-7-(dimethoxyphosphoryl)-naphtho[2,3-d]-1,3-dioxole-6-carboxylic acid methyl ester (12)

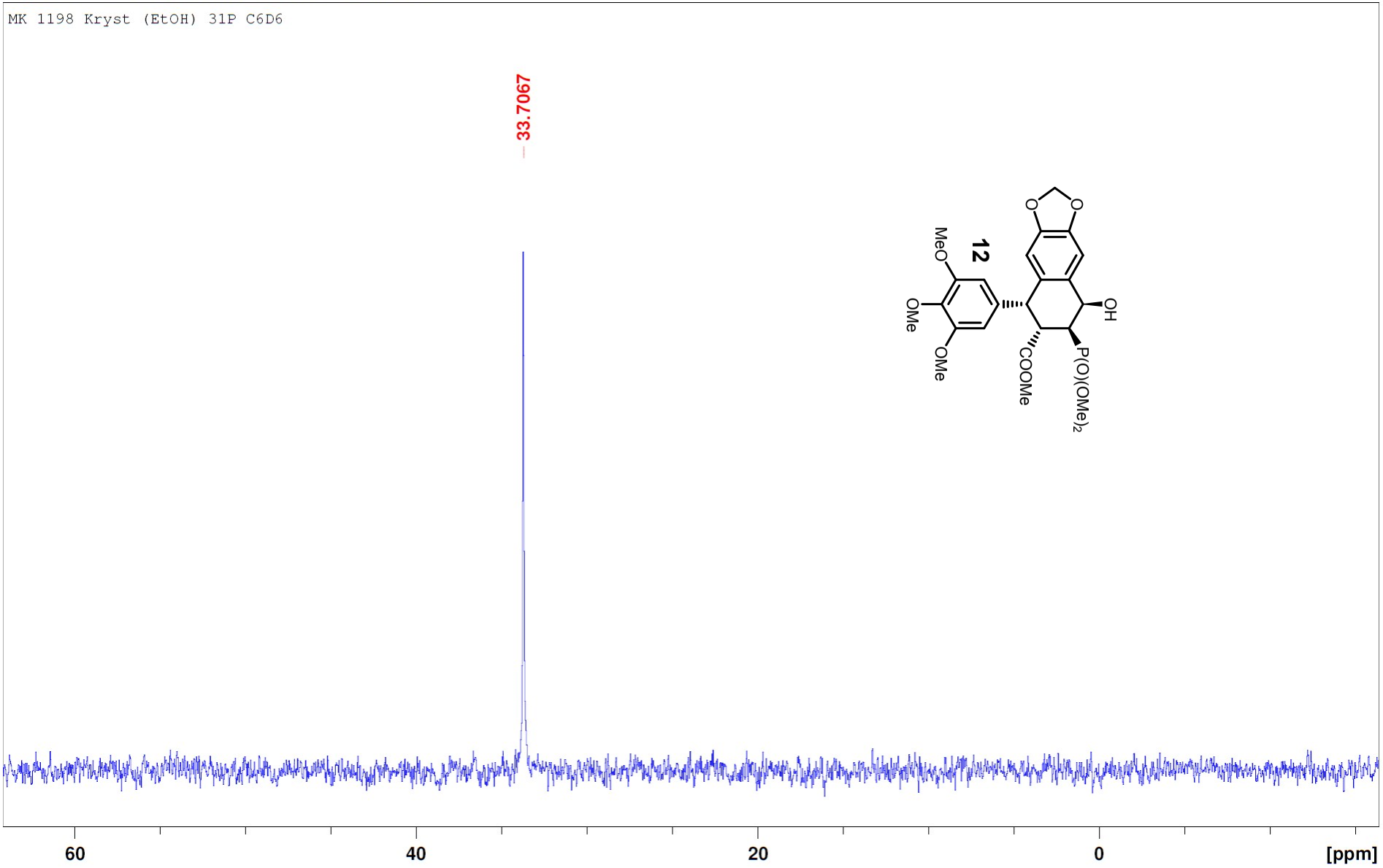
A solution of the cycloadduct **9** (0.200 g, 0.383 mmol) in EtOH (10 mL) in the presence of Raney-Nickel (W-2) was heated for 5h at reflux under hydrogen atmosphere. The catalyst was filtered through Celite® and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate) to give the product **12** – 0.165 g (82%).

White crystals, yield: 82 %; R_f = 0.06 AcOEt); R_f = 0.11 (AcOEt:acetone 5:1 v/v); mp.: 183-188 °C (heptane/benzene); ^{31}P-NMR (C_6D_6): 33.71; ^{31}P-NMR ($CDCl_3$): 33.43; ^{1}H-NMR (C_6D_6): 3.24 (s, 3H, $COOCH_3$), 3.30 (ddd, $^{2}J_{PH}$ = 19.7, $^{3}J_{HH}$ = 3.5, $^{3}J_{HH}$ = 7.1, 1H, CHP(O)), 3.39 (s, 6H, 3,5-$(CH_3O)_2$Ar'), 3.37 (d, $^{3}J_{PH}$ = 10.6, 3H, P(O)$(OCH_3)_2$), 3.49 (d, $^{3}J_{PH}$ = 10.6, 3H, P(O)$(OCH_3)_2$), 3.85 (s, 3H, 4-CH_3OAr'), 4.13 (ddd, $^{3}J_{HH}$ = 6.6, $^{3}J_{HH}$ =7.1, $^{3}J_{PH}$ = 11.6, 1H, CHCOO), 4.63 (dd, $^{3}J_{HH}$ = 6.6, $^{4}J_{PH}$ = 1.6, 1H, CHAr'), 4.87 (d, $^{3}J_{HH}$ = 3.5, 1H, CH-OH), 5.31 (s, 2H, OCH_2O), 5.42 (ddd, $^{3}J_{HH}$ = 3.5, $^{3}J_{PH}$ = 3.5, $^{3}J_{HH}$ = 3.5, 1H, CH-OH), 6.31 (s, 2H, 2,6-H_2Ar'), 6.63 (s, 1H, =CH), 7.03 (s, 1H, =CH). ^{1}H-NMR (CD_2Cl_2): 2.87 (ddd, $^{2}J_{PH}$ = 19.7, $^{3}J_{HH}$ = 3.0, $^{3}J_{HH}$ = 7.1, 1H, CHP(O)), 3.41 (s, 3H, $COOCH_3$), 3.64-3.77 (m, 2H, CHCOO, OH), 3.71 (d, $^{3}J_{PH}$ = 10.6, 3H, P(O)$(OCH_3)_2$), 3.72 (d, $^{3}J_{PH}$ = 10.6, 3H, P(O)$(OCH_3)_2$), 3.72 (s, 6H, 3,5-$(CH_3O)_2$Ar'), 3.79 (s, 3H, 4-CH_3OAr'), 4.45 (dd, $^{3}J_{HH}$ = 6.6, $^{4}J_{PH}$ = 2.0, 1H, CHAr'), 5.17 (dd, $^{3}J_{HH}$ = 3.0, $^{3}J_{PH}$ = 3.6, 1H, CH-OH), 5.88 (d, $^{2}J_{HH}$ = 1.0, 1H, OCH_2O), 5.91 (d, $^{2}J_{HH}$ = 1.0, 1H, OCH_2O), 6.07 (s, 2H, 2,6-H_2Ar'), 6.39 (s, 1H, =CH), 6.84 (s, 1H, =CH). ^{13}C-NMR (CD_2Cl_2): 36.82 (d, $^{1}J_{PC}$ = 141.9, CHP(O)); 41.76 (d, $^{2}J_{PC}$ = 2.8, CHC(O)); 45.38 (d, $^{3}J_{PC}$ = 11.9, CHAr'); 50.02 (s, C(O)OCH_3); 52.75 (d, $^{2}J_{PC}$ = 7.0, P(O)OCH_3); 53.25 (d, $^{2}J_{PC}$ = 7.0, P(O)OCH_3); 54.71 (s, 3,5-$(CH_3)_2$OAr'), 59.06 (s, 4-CH_3OAr'); 65.74 (d, $^{2}J_{PC}$ = 5.9, CH-OH); 100.01 (s, OCH_2O); 105.48 (s, 2,6-H_2Ar'); 107.11 (s, Ar-H); 107.50 (s, Ar-H); 128.68 (d, $^{3}J_{PC}$ = 13.6, Ar); 129.01 (s, Ar); 135.34 (s, 4-Ar'); 135.92 (s, *ipso*-Ar'); 145.44 (s, =C-O-); 146.65 (s, =C-O-); 151.70 (s, 3,5-Ar'); 171.07 (d, $^{3}J_{PC}$ = 3.8, C=O). MS (CI) (*m/z*): 507 (100, M^+ (+H) (-H_2O)); 475 (35, M^+ (-H_2O, -OCH_3)); 447 (18, M^+ (-H_2O, -$COOCH_3$)); Anal. for $C_{24}H_{29}O_{11}P$ requires: C, 54.96%; H, 5.57%; found: C, 55.01%; H, 5.55%.

X-ray analysis of **12** showed the torsion angle of 53.67˚ between C-H-8 and C-H-7 bonds was similar to the torsion angle of 60.01˚ between C-H-8 and C-7-P bonds, therefore H-8 proton was observed as doublet of doublets with a small coupling constants (3.5 Hz and 3.5 Hz). The protons H-7 and H-6 were in *trans* configuration and the observed torsion angle of 169.29˚ between C-H-7 and C-H-6 was near to 180˚, therefore the coupling constant H-7/H-6 was relatively high (7.1 Hz). The protons H-6 and H-5 were in *cis* configuration with the coupling constant of 6.6 Hz due to the small torsion angle of 39.20˚ between C-H-6 and C-H-5 bonds (Scheme 2).

kop21203 3 1 D:\Bruker\TOPSPIN Marek 2015

MK 1198 Kryst (EtOH) 31P C6D6



kop21203 1 1 D:\Bruker\TOPSPIN Marek 2015

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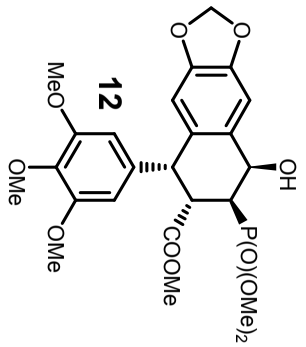

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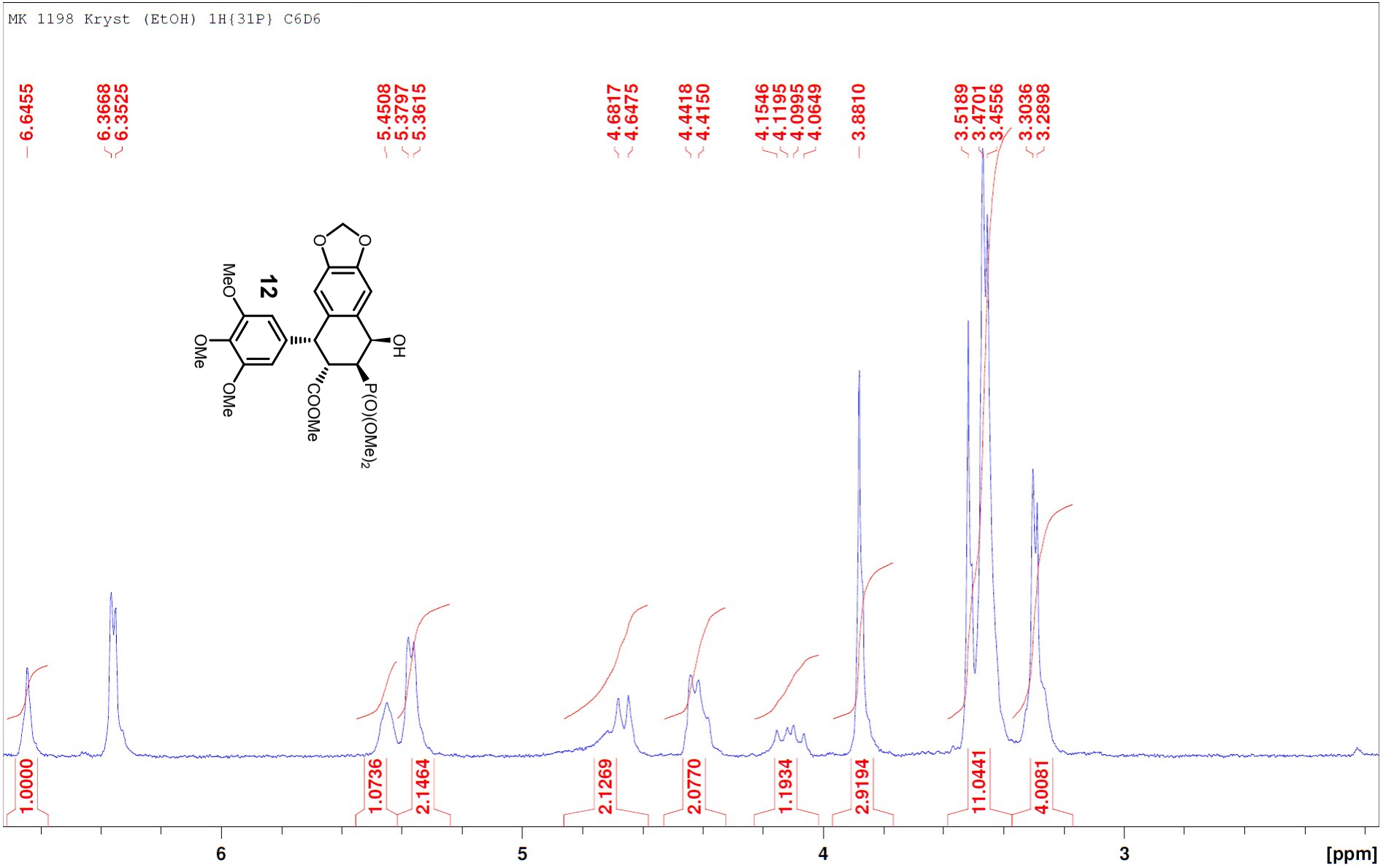
1.0263 1.2046 2.0000 1.0965 1.1082 2.1441 1.2271 2.7819 4.3402 6.9636 3.8197

6 5 4 3 [ppm]

kop21203 2 1 D:\Bruker\TOPSPIN Marek 2015

MK 1198 Kryst (EtOH) 1H{31P} C6D6



kop31603 3 1 D:\Bruker\TOPSPIN Marek 2015

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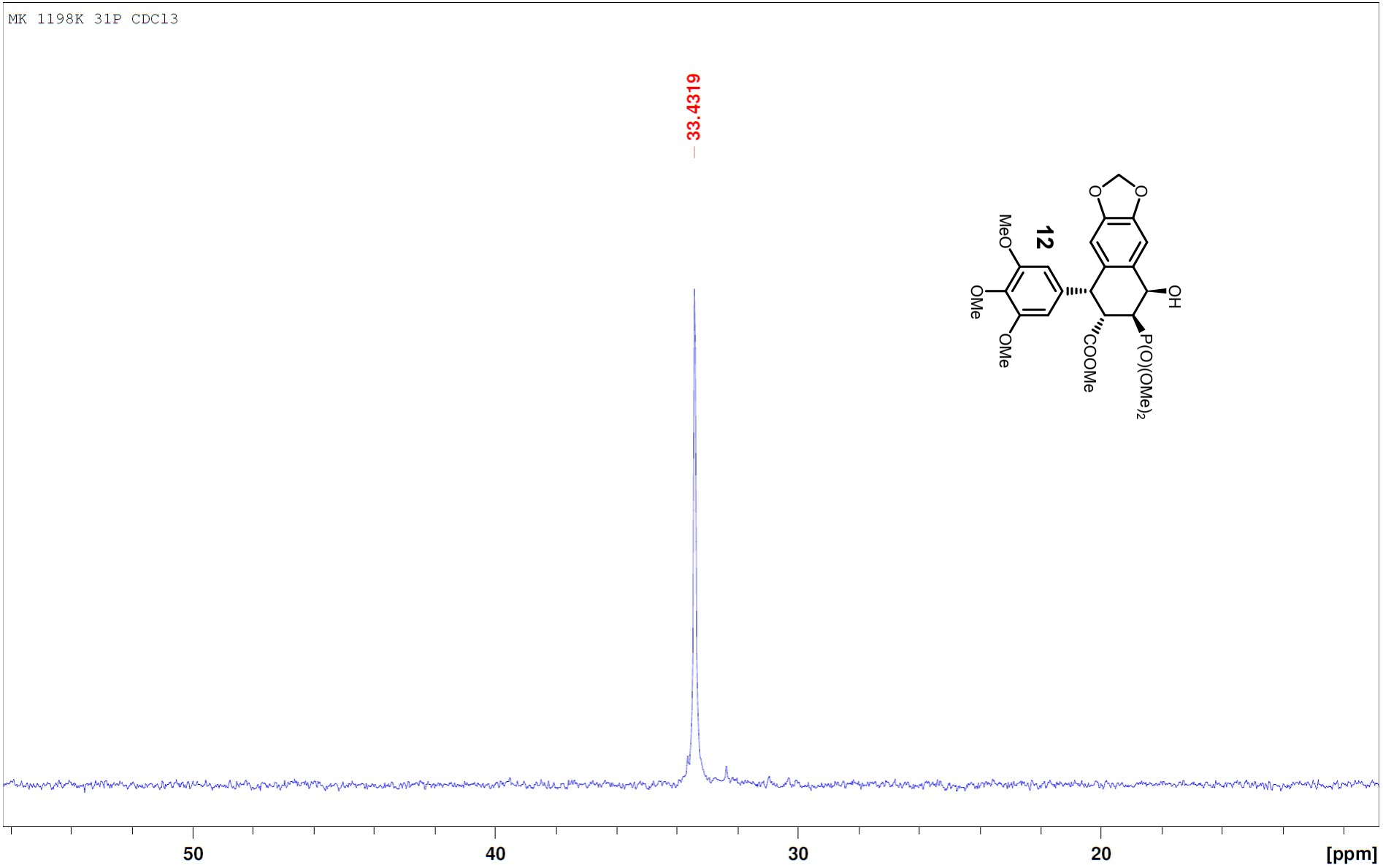

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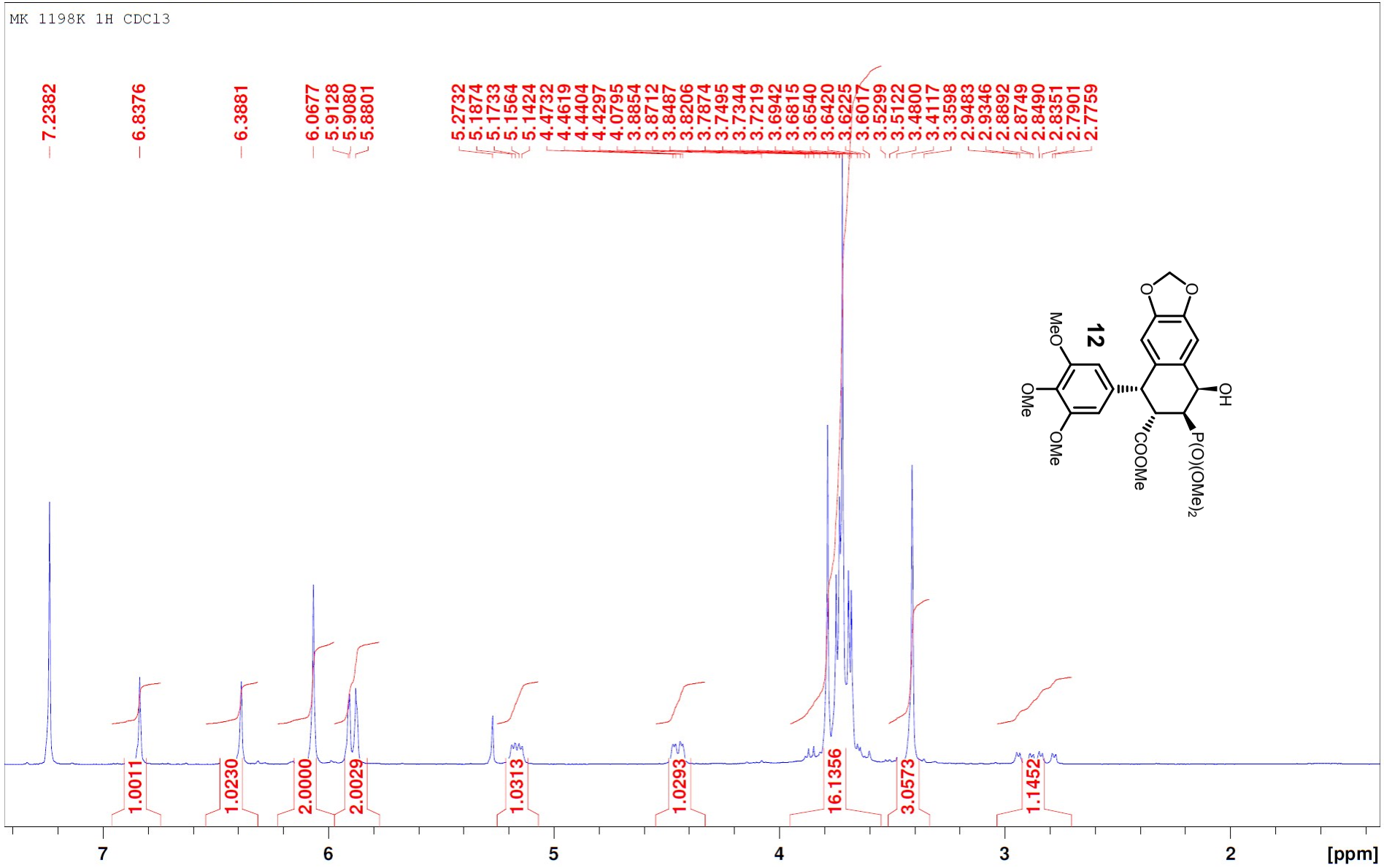

kop31603 2 1 D:\Bruker\TOPSPIN Marek 2015

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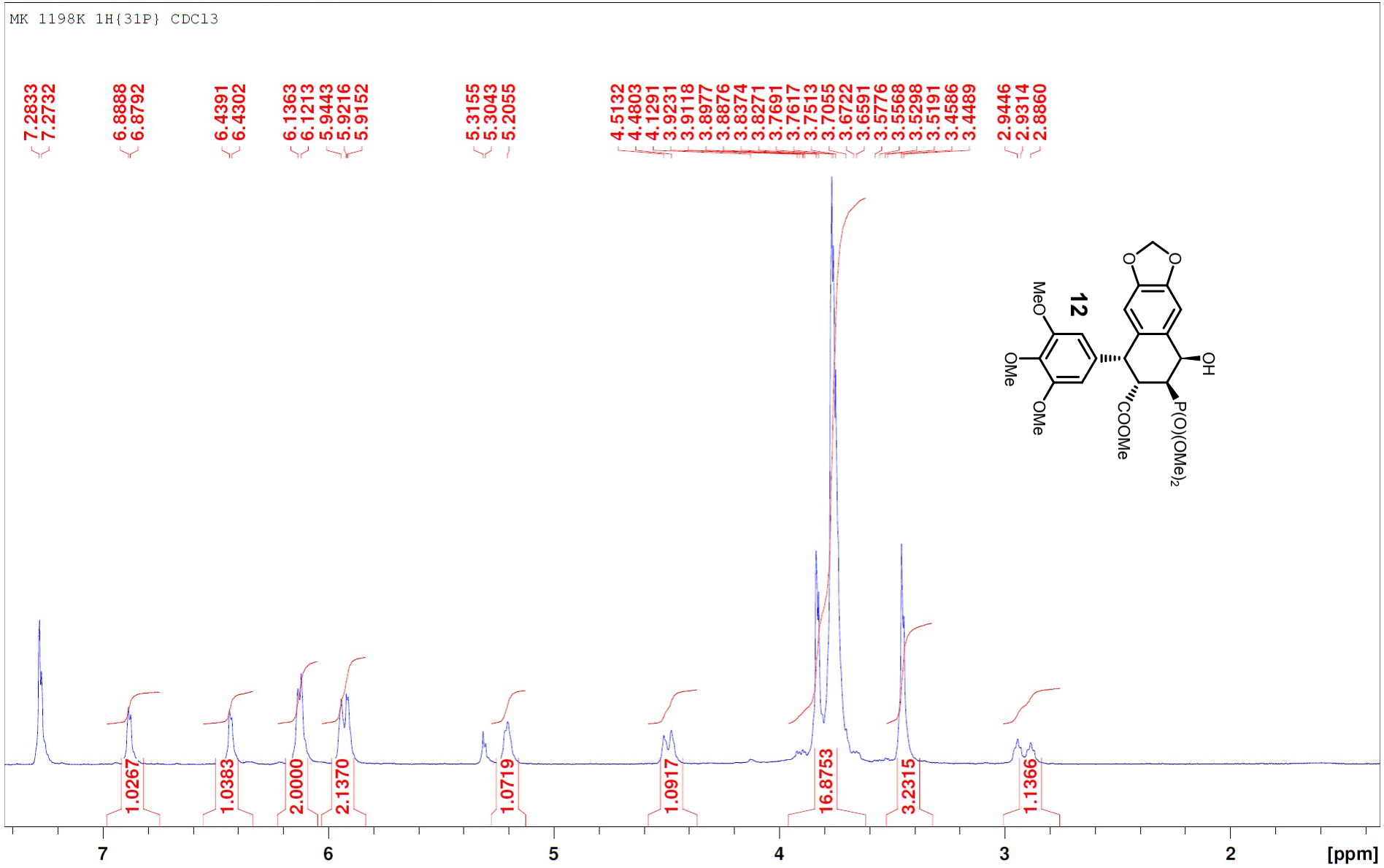

kop11703 1 1 D:\Bruker\TOPSPIN Marek 2015

MK 1198K 13C CD2Cl2

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128.5465
107.5035
107.1138
105.4781
100.0123
65.8010
65.6832
59.0612
54.7079
53.2417
52.7048
52.1628
51.8082
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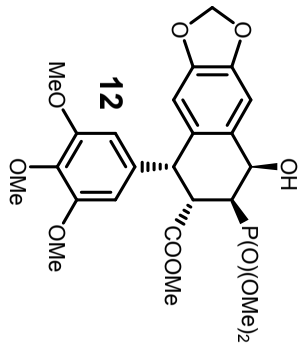
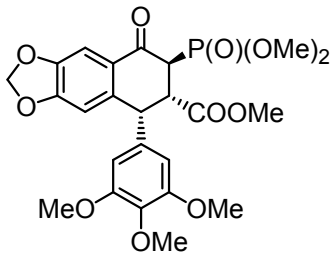
38.2277
35.4082



160 140 120 100 80 60 40 [ppm]



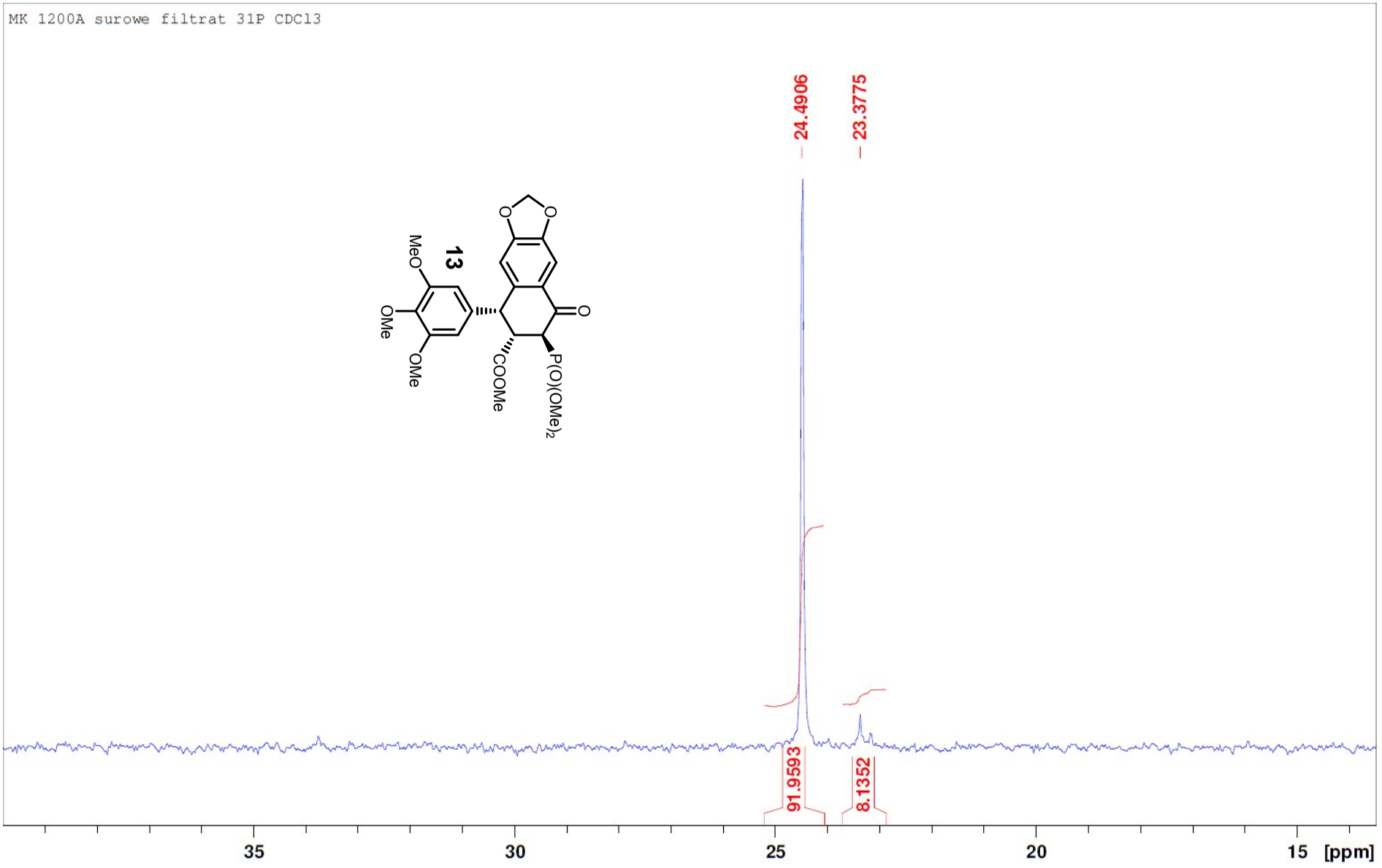
(5S,6S,7S)-5,6,7,8-tetrahydro-8-oxo-5-(3,4,5-trimethoxyphenyl)-7-(dimethoxyphosphoryl)-naphtho[2,3-d]-1,3-dioxole-6-carboxylic acid methyl ester **(*13*)**

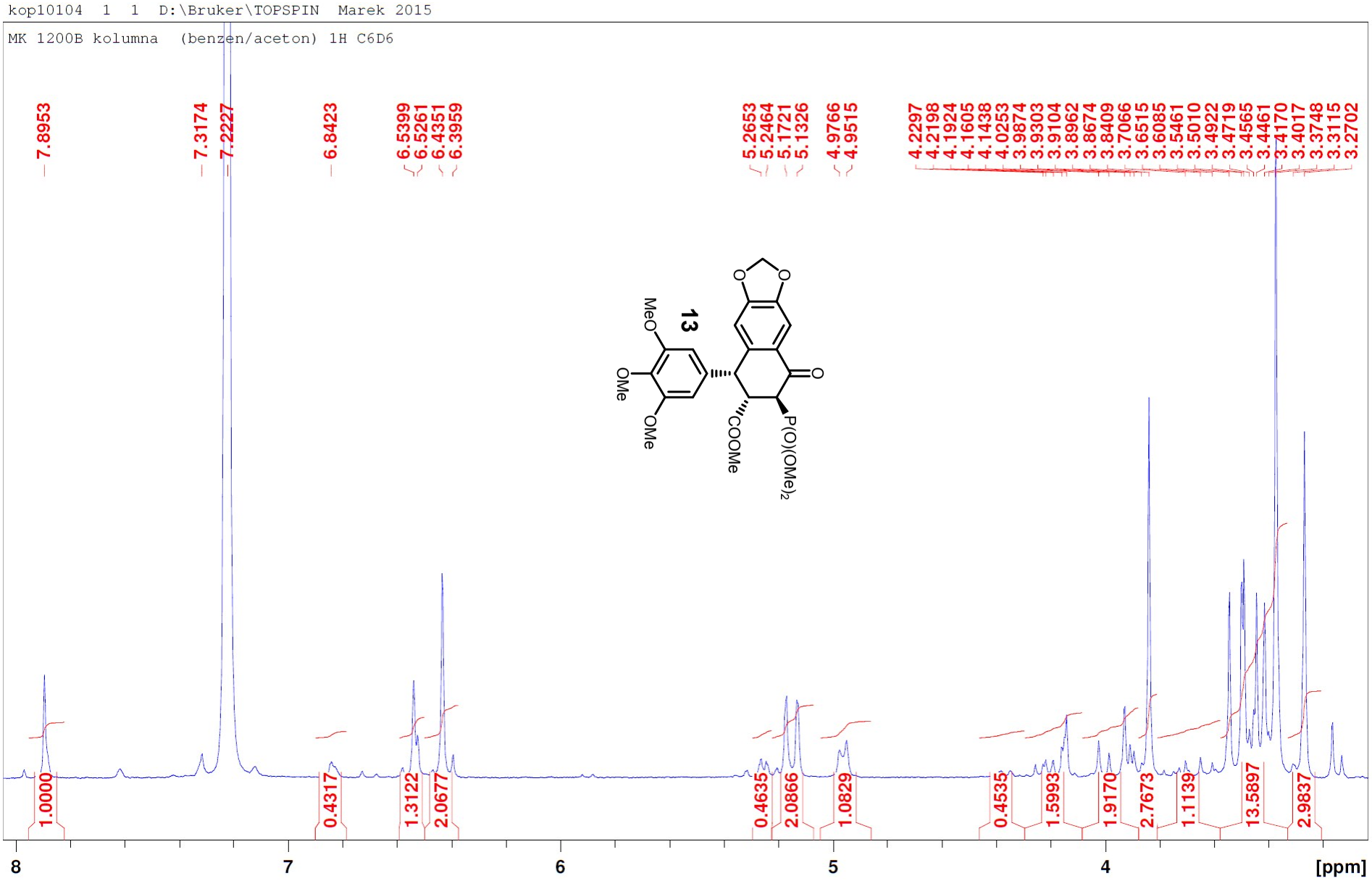
To a solution of alcohol **12** (0.358 g, 0.683 mmol) in CH_2Cl_2 (10 mL), the Dess-Martin reagent (1.2 eq., 0.347 g, 0.820 mmol) was added and the mixture was stirred for 2 h at 0 °C under argon atmosphere. Then the reaction mixture was filtered off and evaporated in vacuo and the residue was purified on silica gel to give β-ketophosphonate **13** in 88% yield (0.314 g).

Pale yellow viscous oil, yield: 88 %; R_f = 0.25 (AcOEt); R_f = 0.46 (AcOEt:acetone 5:1 v/v); ^{31}P-NMR (C_6D_6): 24.51. ^{1}H-NMR (C_6D_6) (500 MHz): 3.22 (s, 3H, C(O)OCH_3); 3.32 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.42 (d, $^3J_{PH}$ = 11.1, 3H, P(O)OCH_3); 3.46 (d, $^3J_{PH}$ = 10.9, 3H, P(O)OCH_3); 3.77 (s, 3H, 4-CH_3O-Ar'); 4.01 (dd, $^2J_{PH}$ = 26.8, $^3J_{HH}$ = 7.6, 1H, CHP(O)) {in ^{1}H{^{31}P}-NMR spectrum: d, J = 7.6}; 4.12 (ddd, $^3J_{HH}$ = 5.4, $^3J_{HH}$ = 7.6, $^3J_{PH}$ = 13.1, 1H, CHC(O)O) {in ^{1}H{^{31}P} dd, J = 5.4, J = 7.6}; 4.89 (d, $^3J_{HH}$ = 5.4, 1H, CHAr'); 5.12 (s, 1H, OCH_2O); 5.17 (s, 1H, OCH_2O); 6.37 (s, 2H, 2,6-H_2-Ar'); 6.49 (s, 1H, Ar-H); 7.81 (s, 1H, Ar-H). ^{1}H-NMR (acetone-d_6): 3.56 (s, 3H, C(O)OCH_3); 3.68 (d, $^3J_{PH}$ = 11.1, 3H, P(O)OCH_3); 3.69 (s, 3H, 4-CH_3OAr'); 3.69-3.75 (m, 2H, CHP(O), CHC(O)O); 3.71 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.74 (d, $^3J_{PH}$ = 10.5, 3H, P(O)OCH_3); 4.81 (d, $_3J_{HH}$ = 5.5, 1H, CHAr'); 6.10 (s, 1H, OCH_2O); 6.11 (s, 1H, OCH_2O); 6.28 (s, 2H, 2,6-H_2-Ar'); 6.68 (s, 1H, Ar-H); 7.36 (s, 1H, Ar-H). ^{13}C-NMR (CD_2Cl_2): 46.60 (d, $^1J_{PC}$ = 129.9, CHP(O)); 46.63 (d, $^1J_{PC}$ = 7.8, CHP(O)); 47.56 (s, CH-Ar'); the signals due to P(O)$(OCH_3)_2$ are covered by CD_2Cl_2; 56.27 (s, 3,5-$(CH_3O)_2$Ar'); 60.66 (s, 4-CH_3OAr'); 102.56 (s, OCH_2O); 106.09 (s, Ar-H); 106.31 (s, 2,6-Ar'); 108.52 (s, Ar-H); 127.89 (s, 4-Ar'); 128.56 (s, Ar); 134.88 (s, 3,5-Ar'); 137.82 (s, Ar); 139.55 (s, *ipso*-Ar'); 148.18 (s, =C-O-); 153.28 (s, =C-O-); 153.66 (s, 2,6-Ar'); 171.92 (d, $^3J_{PC}$ = 3.0, O-C=O); 189.69 (d, $^2J_{PC}$ = 3.0, C=O). MS (CI) (*m/z*): 524 (82, M^+ ($+H_2$)); 523 (100, M^+ (+H)); 522 (74, M^+); 483 (52, M^+ (-C(O)OCH_3)); 412 (10, M^+ (-HP(O)(OCH_3))); 353 (9, M^+ (HP(O)(OCH_3), -C(O)OCH_3)). HRMS (CI) (*m/z*): calcd for $C_{24}H_{27}O_{11}P$: 522.1291, found: 522.1300.

kop12303 3 1 D:\Bruker\TOPSPIN Marek 2015

MK 1200A surowe filtrat 31P CDCl3




kop10104 1 1 D:\Bruker\TOPSPIN Marek 2015
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5.2653
5.2464
5.1721
5.1326
4.9766
4.9515
4.2297
4.2198
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4.1605
4.1438
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3.6085
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3.5010
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13
MeO
OMe
OMe
COOMe
P(O)(OMe)2
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O
O
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1.9170
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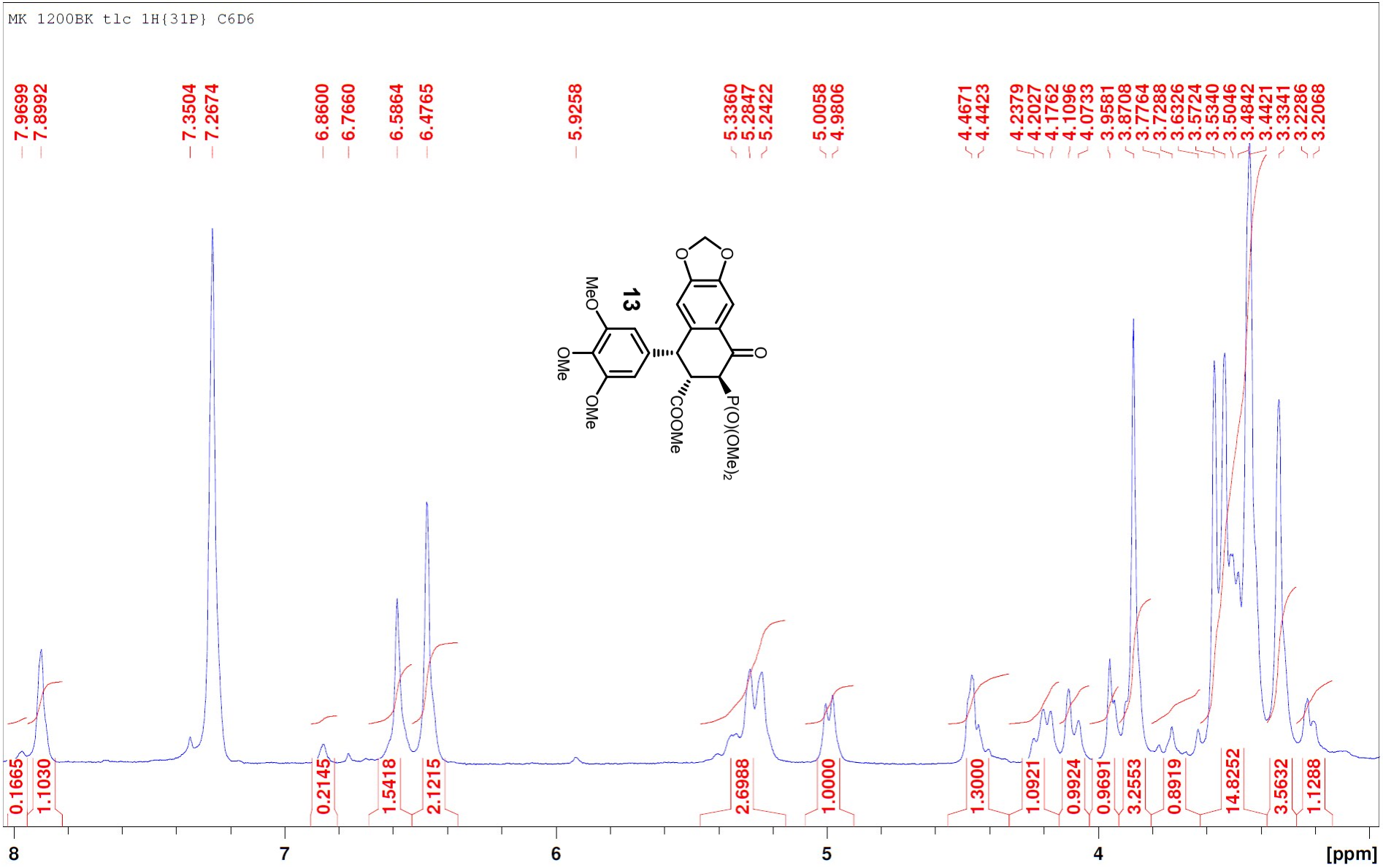
1.1139
13.5897
2.9837
8
7
6
5
4
[ppm]

kop11304 5 1 D:\Bruker\TOPSPIN Marek 2015

MK 1200BK tlc 1H{31P} C6D6



kop20104 1 1 D:\Bruker\TOPSPIN Marek 2015

MK 1200 Kolumna CD2Cl2

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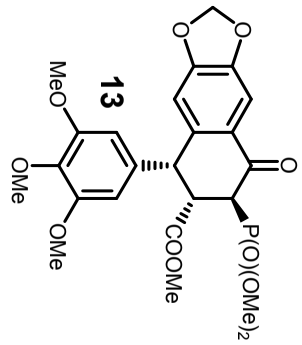

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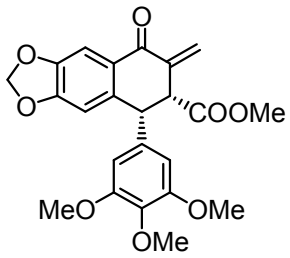


Methyl 7-methylene-8-oxo-5-(3,4,5- trimethoxyphenyl)- 5,6,7,8- tetrahydronaphtho [2,3-d] [1,3] dioxole-6-carboxylate (4b), (rac)-epithuriferic acid methyl ester (4b)

To β-ketophosphonate **13** (174 mg, 0.333 mmol) dissolved in dry THF (2 mL), NaH was added (1.2 eq., 15 mg). The resulting mixture was stirred for 1 h at 0 °C and then a suspension of paraformaldehyde (4.0 eq., 42 mg) in THF (2 mL) was added and stirred for additional 2 h at 0 °C. To the crude mixture, aqueous saturated NH_4Cl (2 mL) was added and then ethyl acetate (10 mL). Organic layer was washed with water (2 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The solid residue was chromatographed on silica gel using AcOEt/hexane as eluent to give the pure product **4b** in 58% yield (82 mg).

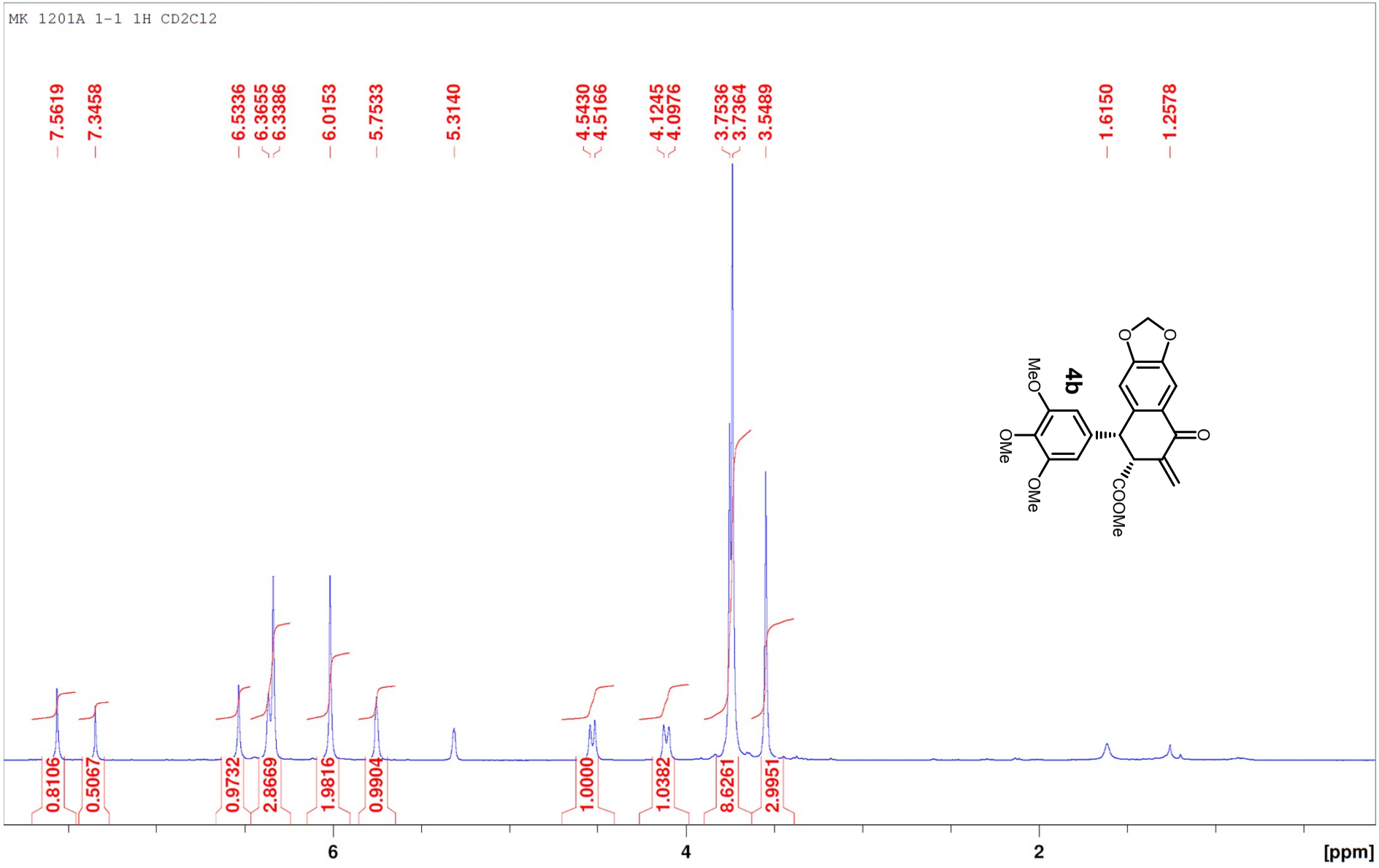
White crystals, yield: 58%; R_f = 0.60 (AcOEt); m.p. = 130-135 °C (benzene); ^{1}H-NMR ($CDCl_3$): 3.57 (s, 3H, $COOCH_3$); 3.77 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.83 (s, 3H, 4-CH_3O-Ar'); 4.11 (d, $^3J_{HH}$ = 5.2, 1H, CHCOO); 4.51 (d, $^3J_{HH}$ = 5.2, 1H, CHAr'); 5.78 (s, 1H, =CH); 6.02 (s, 2H; OCH_2O); 6.35 (s, 2H, 2,6-H_2-Ar'); 6.45 (s, 1H, =CH); 6.54 (s, 1H, Ar-H); 7.63 (s, 1H, Ar-H). ^{1}H (C_6D_6): 3.11 (s, 3H, $COOCH_3$); 3.38 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.79 (s, 3H, 4-CH_3O-Ar'); 3.93 (d, $^3J_{HH}$ = 5.2, 1H, CHCOO); 4.21 (d, $^3J_{HH}$ = 5.2, 1H, CHAr'); 5.07 (s, 1H; OCH_2O); 5.14 (s, 1H; OCH_2O); 5.61 (s, 1H, =CH); 6.39 (s, 2H, 2,6-H_2-Ar'); 6.53 (s, 1H, Ar-H); 6.63 (s, 1H, =CH); 8.04 (s, 1H, Ar-H). ^{1}H-NMR (C_6D_6): 3.18 (s, 3H, $COOCH_3$), 3.44 (s, 6H, 3,5-$(CH_3O)_2$-Ar'), 3.86 (s, 3H, 4-CH_3O-Ar'), 4.01 (d, $^3J_{HH}$ = 5.2, 1H, CHCOO), 4.28 (d, $^3J_{HH}$ = 5.2, 1H, CH-Ar), 5.15 (s, 1H, OCH_2O), 5.22 (s, 1H, OCH_2O), 5.68 (bs, 1H, O=C-C=CH), 6.46 (s, 2H, 2,6-H_2-Ar'), 6.61 (s, 1H, Ar-H), 6.70 (bs, 1H, O=C-C=CH), 8.11 (s, 1H, Ar-H). ^{1}H-NMR (CD_2Cl_2): 3.55 (s, 3H, $COOCH_3$); 3.74 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.75 (s, 3H, 4-CH_3O-Ar'); 4.11 (d, $^3J_{HH}$ = 5.4, 1H, CHCOO); 4.53 (d, $^3J_{HH}$ = 5.4, 1H, CHAr'); 5.75 (s, 1H, =CH); 6.02 (s, 2H; OCH_2O); 6.34 (s, 2H, 2,6-H_2-Ar'); 6.37 (s, 1H, =CH); 6.53 (s, 1H, Ar-H); 7.56 (s, 1H, Ar-H). ^{13}C-NMR (CD_2Cl_2): 47.52 (COOCH3), 50.40 (CHAr), 54.65 (2xOCH3), 56.07 (CHCOO), 59.08 (1xOCH3), 100.87 (OCH_2O), 103.31, 104.94 (2x=CH), 106.91 (=CH), 123.02 (=CH), 126.27, 126.98, 133.82, 138.30, 138.97, 146.34, 151.24, 151.99, 169.69 (C(O)O), 183.07 (C=O); HRMS (CI) (*m/z*): calcd for $C_{23}H_{22}O_8$: 426.1315, found: 426.1316.

Spectroscopic data of **4b** are consistent with the literature data: R. Höfert, P. H. Matusch, *Helv. Chim. Acta* **1994**, *77*, 771-777.

See also spectroscopic data for **4a**: Lopez-Perez, J.; del Olmo, E.; de Pascual-Teresa, B.; Merino, M.; Martin, S.; San Feliciano, A. *Tetrahedron* **1995**, *51*, 6343– 6348. Jackson, D. E.; Dewick, P. M. *Phytochemistry* **1981**, *20*, 2277–2280.

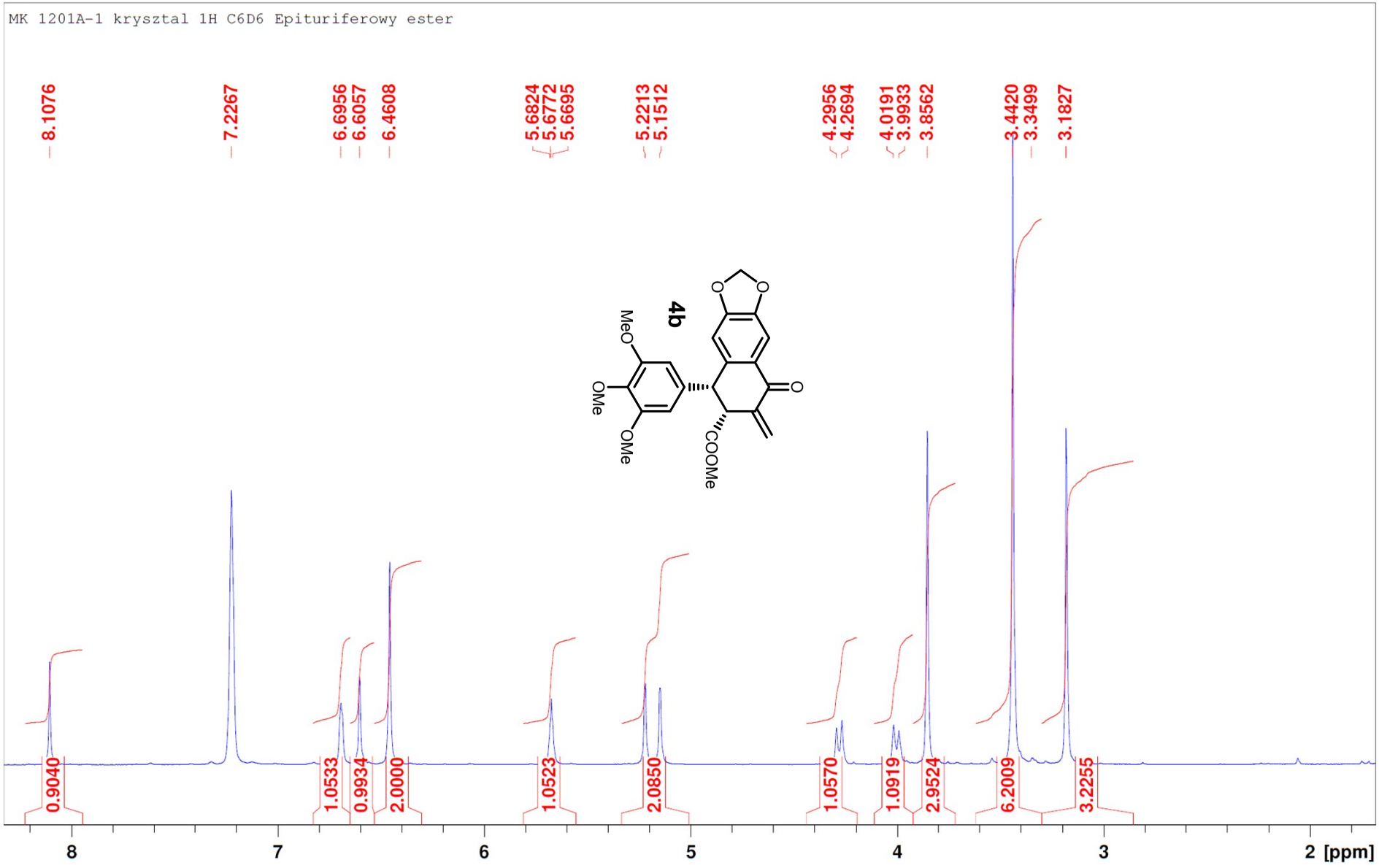
kop20705 2 1 D:\Bruker\TOPSPIN Marek 2015

MK 1201A 1-1 1H CD2Cl2



kop12304 1 1 D:\Bruker\TOPSPIN Marek 2015

MK 1201A-1 krysztal 1H C6D6 Epituriferowy ester



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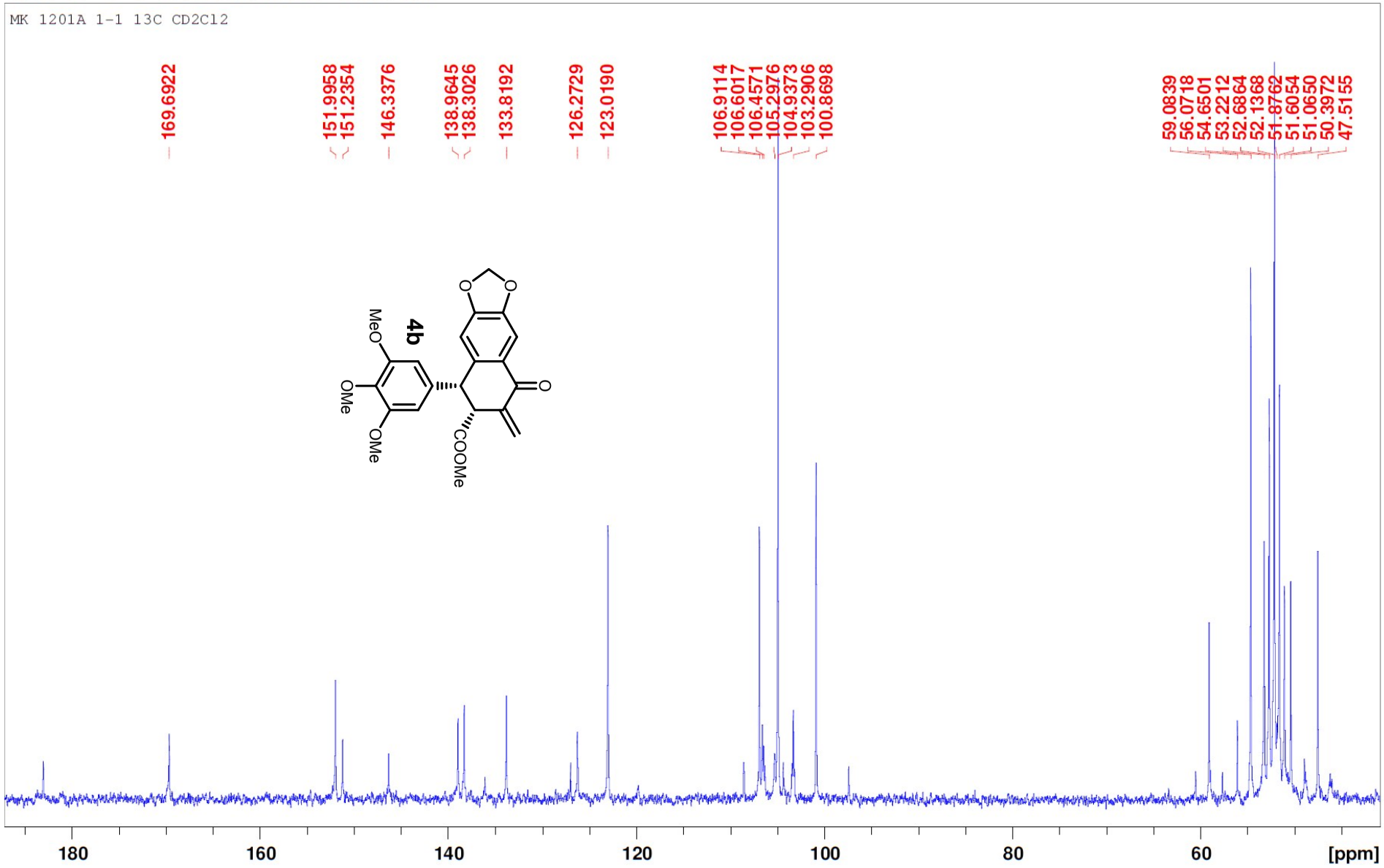
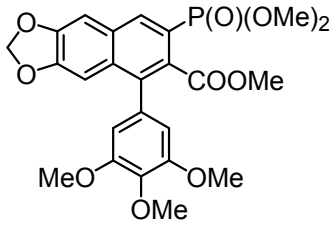




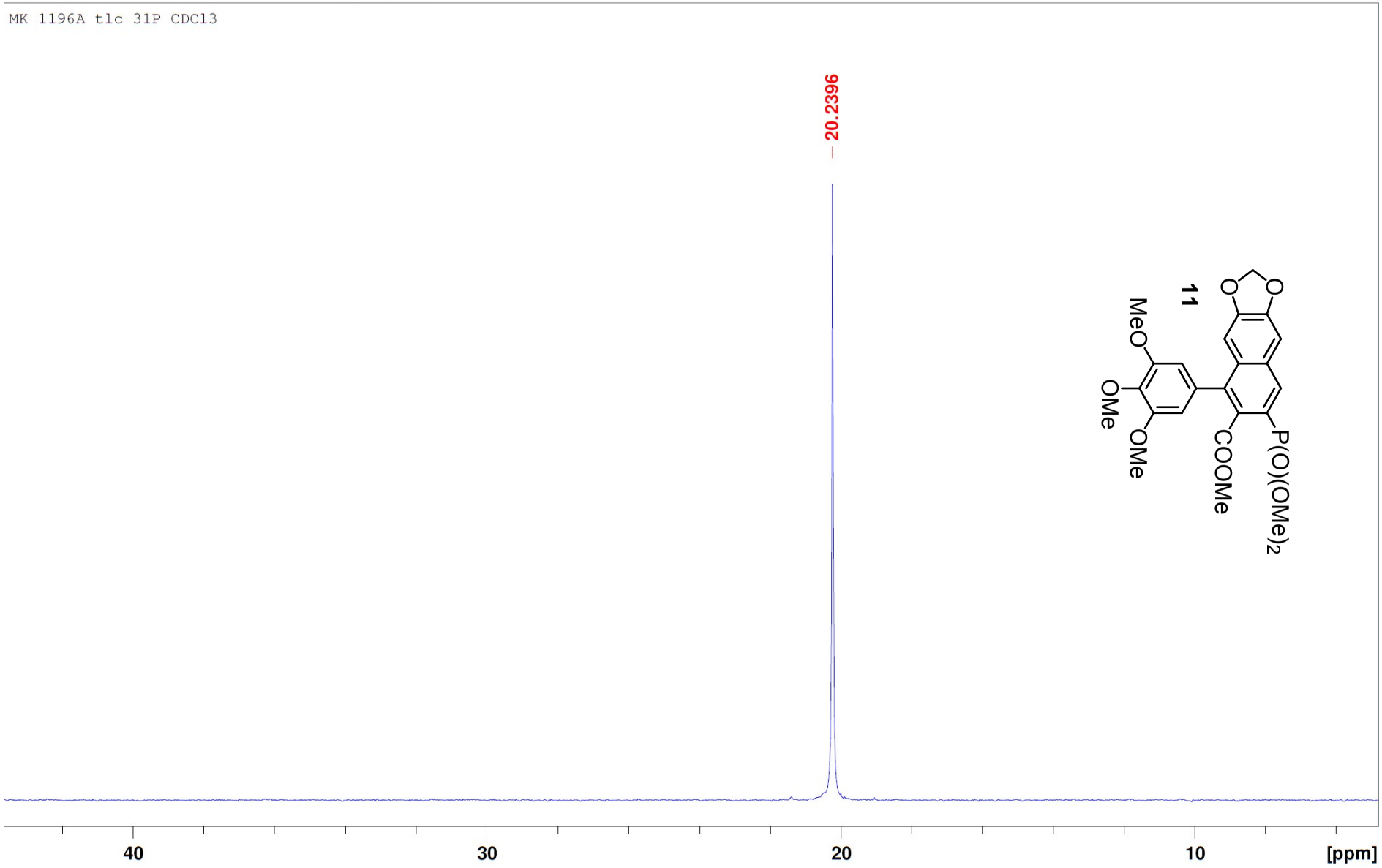
Methyl 7-(dimethoxyphosphoryl)- 5- (3,4,5-trimethoxyphenyl)naphtho [2,3-d] [1,3] dioxole-6-carboxylate (11)

A mixture of the cycloadduct **9** or **10** (200 mg, 0.383 mmol) and *p*-TSA (1 eq. 73 mg) dissolved in dry toluene (5 mL) was stirred and heated for 1h at 100 °C. Then, the crude mixture was washed with water (2 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The solid residue was chromatographed on silica gel using AcOEt/hexane as eluent to give the pure product **11** in 100% yield (193 mg).

White crystals; yield: 100% (from (**6**) and (**7**)); R_f = 0.21 (EtOAc). ^{31}P-NMR (C_6D_6): 19.76. ^{31}P-NMR (Acetone-d_6): 19.18. ^{1}H-NMR (C_6D_6): 3.33 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 3.47 (s, 3H, $COOCH_3$); 3.58 (d, $^{3}J_{PH}$ = 11.2, 6H, $P(O)(OCH_3)_2$); 3.88 (s, 3H, 4-CH_3O-Ar'); 5.11 (s, 2H, OCH_2O); 6.62 (s, 2H, 2,6-H_2-Ar'); 6.83 (s, 1H, Ar-H); 7.23 (s, 1H, Ar-H); 8.52 (d, $^{3}J_{PH}$ = 15.3, 1H, H-C=C-P(O)). ^{1}H-NMR (Acetone-d_6): 3.58 (s, 3H, $COOCH_3$); 3.75 (d, $^{3}J_{PH}$ = 11.2, 6H, $P(O)(OCH_3)_2$); 3.81 (s, 3H, 4-CH_3O-Ar'); 3.83 (s, 6H, 3,5-$(CH_3O)_2$-Ar'); 6.18 (s, 2H, OCH_2O); 6.58 (s, 2H, 2,6-H_2-Ar'); 6.91 (s, 1H, Ar-H); 7.49 (s, 1H, Ar-H); 8.31 (d, $^{3}J_{PH}$ = 15.4, 1H, H-C=C-P(O)). ^{13}C-NMR ($CDCl_3$): 52.17 (s, $C(O)OCH_3$); 52.95 (d, $^{2}J_{PC}$ = 5.4, $P(O)OCH_3$); 56,06 (s, 3,5-$(CH_3O)_2$Ar'); 60.84 (s, 4-CH_3OAr'); 101.71 (s, OCH_2O); 103.15 (s, Ar-H); 104.57 (s, Ar-H); 107.27 (s, 2,6-Ar'); 119.14 (d, $^{1}J_{PC}$ = 189.8, =C-P(O)); 129.73 (d, J_{PC} = 16.4), 131.00 (d, J_{PC} = 10.4); 131.56 (s); 132.44 (s); 133.80 (d, J_{PC} = 8.8); 137.43 (s); 137.59 (s); 148.76 (s, =C-O-); 150.23 (s, =C-O-); 152.77 (s, 3,5-Ar'); 168.85 (d, $^{3}J_{PC}$ = 3.5, C=O). ^{13}C (C_6D_6): 52.75 (s, $C(O)OCH_3$); 53.21 (d, $^{2}J_{PC}$ = 5.1, $P(O)OCH_3$); 56,44 (s, 3,5-$(CH_3O)_2$Ar'); 61.26 (s, 4-CH_3OAr'); 102.35 (s, OCH_2O); 104.08 (s, Ar-H); 105.64 (s, Ar-H); 108.97 (s, 2,6-Ar'); 121.99 (d, $^{1}J_{PC}$ = 186.9, =C-P(O)); 131.10 (d, J_{PC} = 15.9), 132.86 (d, J_{PC} = 4.0); 132.86 (s); 133.67 (d, J_{PC} = 10.6); 134.90 (d, J_{PC} = 8.5); 138.74 (d, J_{PC} = 13.1); 139.68 (s); 149.79 (s, =C-O-); 151.31 (s, =C-O-); 154.54 (s, 3,5-Ar'); 169.60 (d, $^{3}J_{PC}$ = 3.5, C=O). MS (CI) (*m/z*): 505 (58, M^+ (+H)); 473 (100, M^+ (+H, - CH_3OH)). HRMS (CI) (*m/z*): calcd for $C_{24}H_{25}O_{10}P$: 504.1185, found: 504.1192.

kop10903 3 1 D:\Bruker\TOPSPIN Marek 2015

MK 1196A tlc 31P CDCl3



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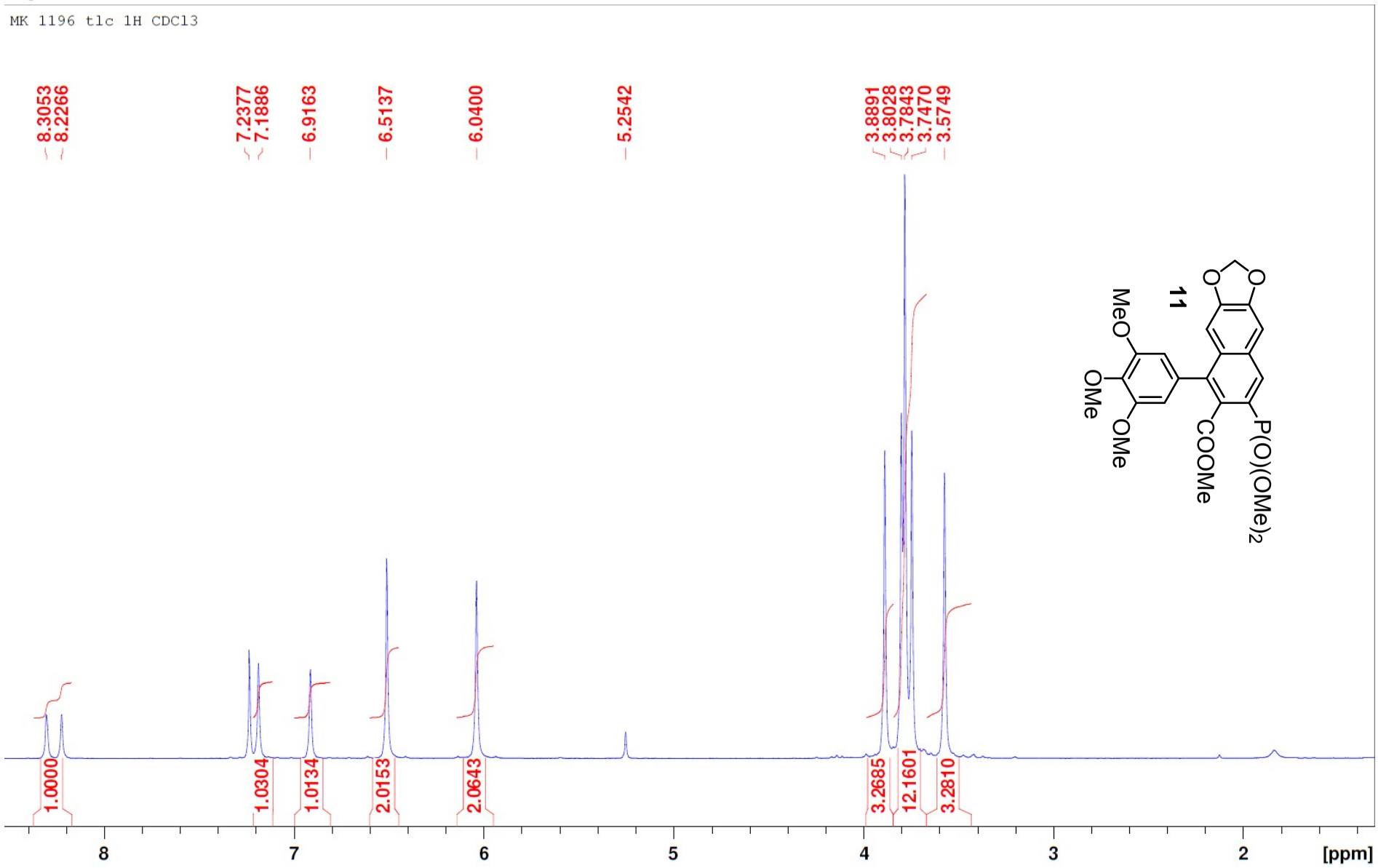

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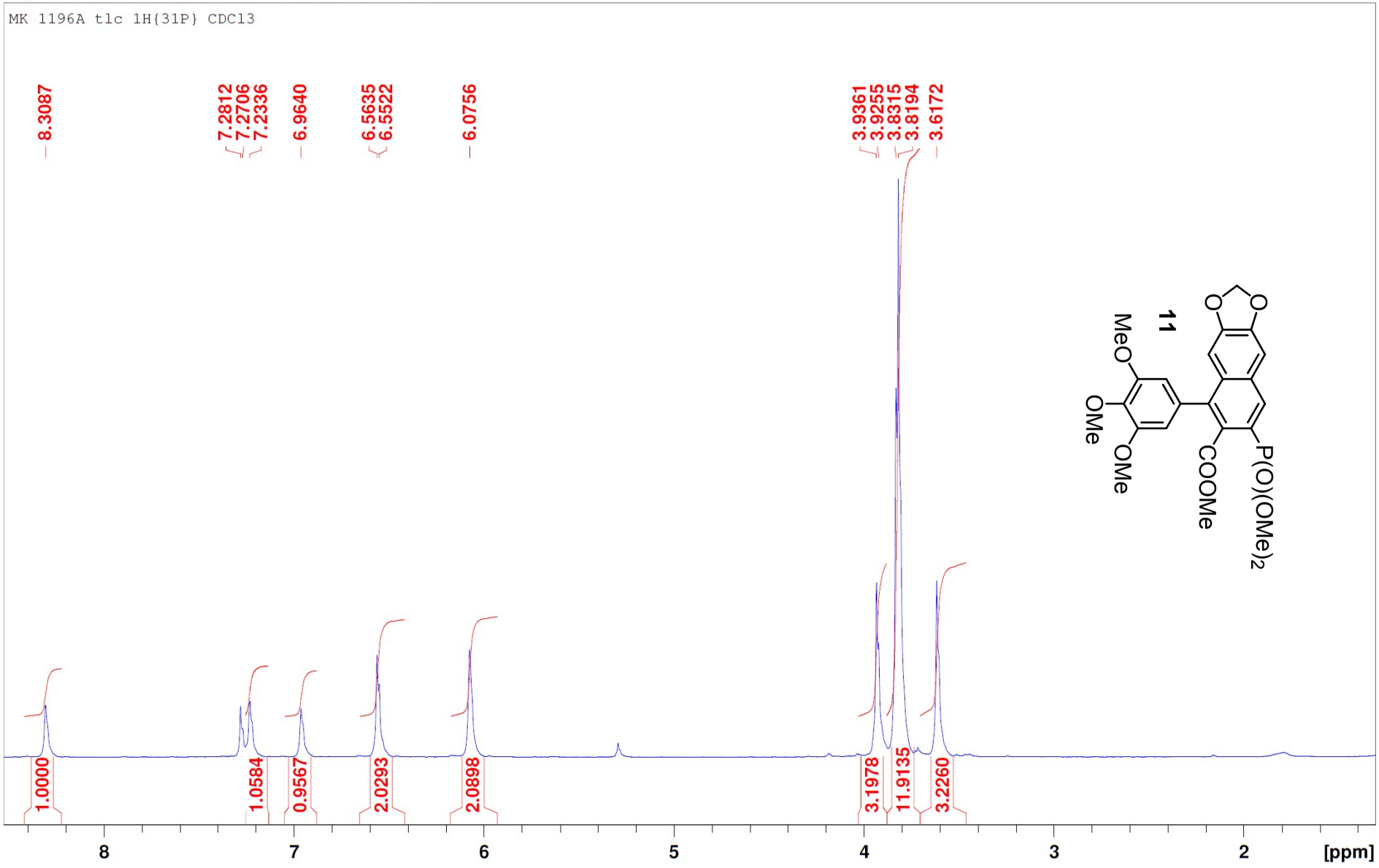

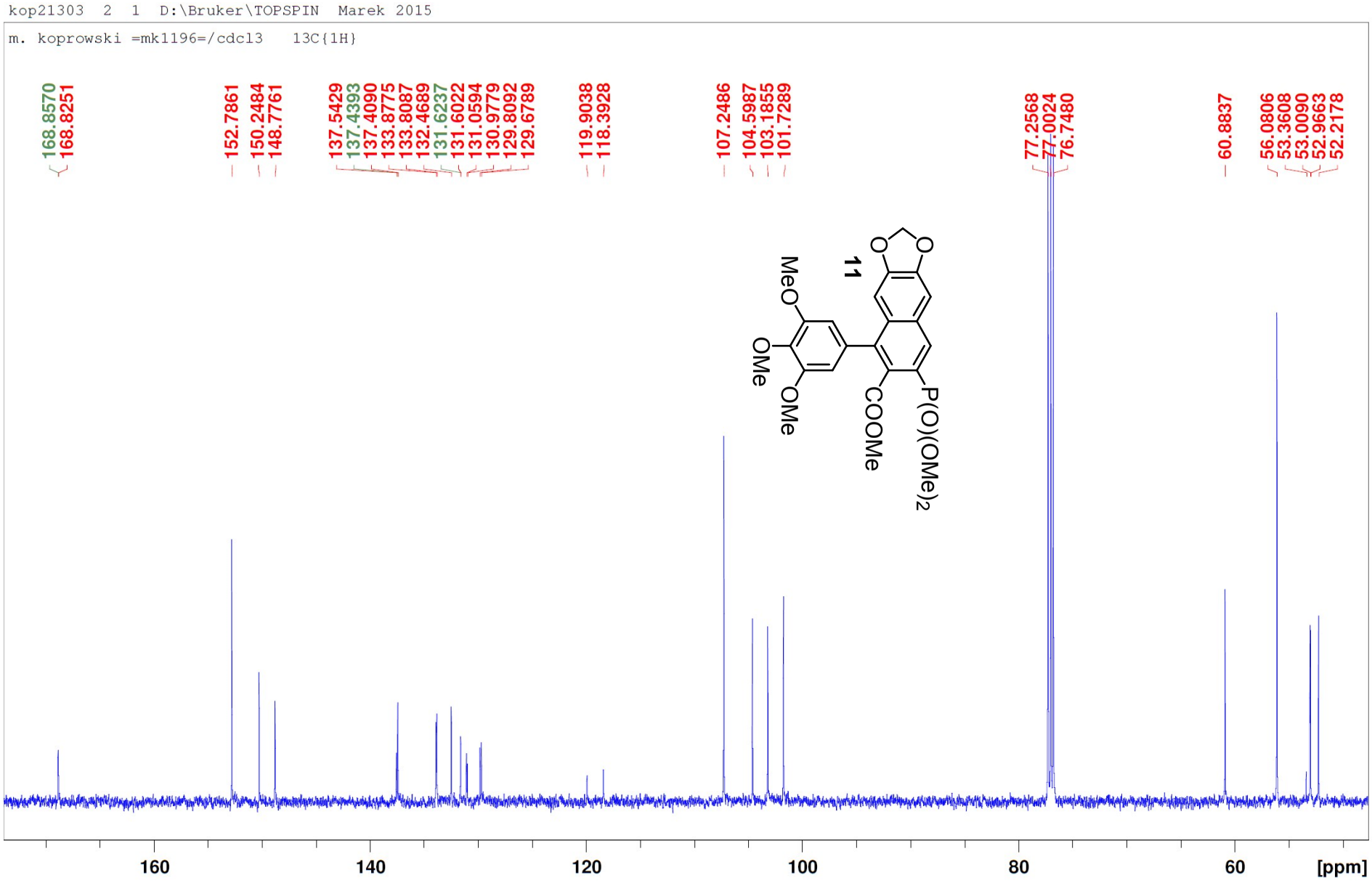
kop21303 2 1 D:\Bruker\TOPSPIN Marek 2015
m. koprowski =mk1196=/cdcl3 13C{1H}
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168.8251
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150.2484
148.7761
137.5429
137.4393
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132.4689
131.6237
131.6022
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129.8092
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104.5987
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77.2568
77.0024
76.7480
60.8837
56.0806
53.3608
53.0090
52.9663
52.2178
11
MeO
OMe
OMe
COOMe
P(O)(OMe)2
160
140
120
100
80
60
[ppm]

X-ray crystal structure determination and Hirshfeld surface analysis

Crystal structure data for **9**: $C_{24}H_{27}O_{11}P$, M = 522.43, colorless column, 0.43×0.15×0.12 mm^3, monoclinic, space group P21/c (No. 14), a = 10.9953(4) Å, b = 27.3594(8) Å, c = 9.1869(4) Å, β = 111.321(4) °, V = 2574.5(2) $Å^3$, Z = 4, T = 290(2) K, D_{calc} = 1.348 $g \cdot cm^{-3}$, MoKα radiation, $2\theta_{max}$ = 50.24 °, 4574 reflections collected, 4574 reflections unique and 3921 reflections with $I > 2\sigma(I)$. Final GooF = 1.076, R1 = 0.0599 and wR2 = 0.1806 for 3921 reflections and 354 parameters.

Crystal structure data for **12**: $C_{24}H_{29}O_{11}P$, M = 524.44, colourless tablet, 0.52×0.48×0.22 mm^3, triclinic, space group $P\bar{1}$ (No. 2), a = 10.0529(7) Å, b = 10.0781(8) Å, c = 13.2162(9) Å, α = 79.723(5) °, β = 74.590(6) °, γ = 72.609(7) °, V = 1224.69(15) $Å^3$, Z = 2, T = 290(2) K, D_{calc} = 1.422 $g \cdot cm^{-3}$, CuKα radiation, $2\theta_{max}$ = 134.12 °, 18102 reflections collected, 4331 reflections unique and 3651 reflections with $I > 2\sigma(I)$. Final GooF = 1.156, R1 = 0.0589 and wR2 = 0.1887 for 3651 reflections and 353 parameters.

Diffraction data were collected using an Oxford Diffraction Xcalibur™ 3 diffractometer. The structures were solved by direct methods and refined by full-matrix least-squares on F^2 with SHELXL-97.[1] During refinement, one methoxy groups in **9** were found to be disordered over two sites with occupancies of 0.61(1) and 0.39(1). In the crystal structure of this compound there are solvent accessible voids with an overall volume of 146 $Å^3$ and with a total electron count per cell of 24. The single void has a volume of 73 $Å^3$, i.e. 50% of the overall void volume and about 4% of the unit-cell volume. Because the electron density in the voids could not be modeled, the remaining electron densities resulting from the residual solvent molecules were removed from the data set using the SQUEEZE routine[2] of PLATON,[3] and the structure was refined further using the data generated.

The non-hydrogen atoms were refined anisotropically. All aromatic and methyl H atoms were positioned geometrically and constrained to ride on their parent atoms, with C-H distances of 0.93 and 0.96 Å, respectively, and with U_{iso}(H) values of 1.2 $U_{eq}(C_{aromatic})$ and 1.5 $U_{eq}(C_{methyl})$. Other H atoms were located in difference maps and refined with U_{iso}(H) set at 1.5 Ueq(C), giving C-H distances in the range 0.93(3)–0.99(3) Å and 0.91(5)–1.04(4) Å in (**9**) and (**12**), respectively, and with U_{iso}(H) set at 1.5 Ueq(O), giving O-H distance of 0.90(4) Å in (**9**). Further details on the crystal structure investigations have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1426547 and CCDC 1426546.

The three-dimensional Hirshfeld surfaces of molecules in crystals,[4] which illustrate the interatomic contacts with distances equal to the sum of the van der Waals radii (represented as white) and with distances shorter (red) and longer (blue) than the values of this sum, were constructed by using the CrystalExplorer 3.1 program.[5]

References

1. G.M. Sheldrick, *Acta Cryst. A*, 2008, **64**, 112.
2. A.L. Speck, *Acta Cryst. C*, 2015, **71**, 9.
3. A.L. Speck, *J. Appl. Cryst.* 2003, **36**, 7.
4. M. A. Spackman, D. Jayatilaka, *Cryst. Eng. Comm.,* 2009, **11**, 19.
5. S. K. Wolff, D. J. Grimwood, J. J. McKinnon, M. J. Turner, D. Jayatilaka, M. A. Spackman, *Crystal Explorer* (Version **3.1**). University of Western Australia, 2012.

Table 1. Geometry of intra- and intermolecular contacts [Å, °].

D-H···A	D-H	H···A	D···A	D-H···A
compound (**9**)				
C11-H11···O22	0.98(3)	2.48(3)	2.899(3)	105(2)
C20-H20A···O16	0.96	2.50	2.960(9)	110
C26-H26···O23	0.93	2.38	3.246(3)	155
C10-H10···O16$^{(i)}$	0.99(3)	2.37(3)	3.224(3)	143(3)
C20-H20B···O22$^{(ii)}$	0.96	2.36	3.295(9)	164
C18-H18A···O33$^{(iii)}$	0.96	2.58	3.295(6)	131
Symmetry codes: (i) 2-x, -y, 1-z; (ii) x, y, -1+z; (iii) 1+x, 1/2-y, 1/2+z.				
compound (**12**)				
C12-H12···O14	0.97(3)	2.52(4)	2.890(3)	102(3)
C18-H18C···O14	0.96	2.59	3.414(4)	144
C24-H24A···O22	0.96	2.33	2.698(5)	102
O14-H14A···O16$^{(i)}$	0.90(4)	1.89(4)	2.792(3)	174(3)
C36-H36B···O33$^{(ii)}$	0.96	2.43	3.352(3)	160
C2-H2A···O31$^{(iii)}$	0.96(5)	2.54(5)	3.456(4)	160(4)
Symmetry codes: (i) -x, -y, -z; (ii) -x, 1-y, 1+z; (iii) 1-x, 1-y, -z.				

Table 2. Selected geometric parameters for molecules (**9**) and (**12**) [Å, °].

Bond	**9**	**12**	Bond	**9**	**12**
O1-C8	1.375(3)	1.383(3)	C13-C25	1.505(3)	1.533(3)
O1-C2	1.426(4)	1.413(4)	C13-H13	-	0.95(3)
C2-O3	1.422(5)	1.418(4)	O14-H14A	-	0.90(4)
C2-H2A	0.987(19)	0.96(5)	P15-O16	1.4640(18)	1.461(2)
C2-H2B	0.983(19)	0.91(5)	P15-O19	1.629(8)	1.5639(19)
O3-C9	1.380(3)	1.379(3)	P15-O17	1.556(2)	1.582(2)
C4-C9	1.375(4)	1.365(4)	O17-C18	1.419(5)	1.433(4)
C4-C5	1.400(3)	1.399(4)	O19-C20	1.337(11)	1.423(4)
C5-C6	1.391(3)	1.389(3)	C21-O22	1.190(3)	1.197(3)
C5-C10	1.507(3)	1.516(3)	C21-O23	1.339(3)	1.332(3)
C6-C7	1.385(3)	1.412(3)	O23-C24	1.450(3)	1.451(4)
C6-C13	1.521(3)	1.506(3)	C25-C26	1.389(3)	1.381(3)
C7-C8	1.378(3)	1.359(4)	C25-C30	1.392(3)	1.393(3)
C8-C9	1.383(4)	1.374(4)	C26-C27	1.394(3)	1.397(3)
C10-O14	1.445(2)	1.431(3)	C27-O31	1.368(3)	1.364(3)
C10-C11	1.561(3)	1.544(3)	C27-C28	1.393(3)	1.384(4)
C10-H10	0.99(3)	1.04(4)	C28-O33	1.374(3)	1.378(3)
C11-C12	1.556(3)	1.536(3)	C28-C29	1.393(4)	1.394(3)
C11-P15	1.797(2)	1.822(2)	C29-O35	1.362(3)	1.367(3)
C11-H11	0.99(3)	0.96(4)	C29-C30	1.388(3)	1.385(3)
C12-C21	1.515(3)	1.512(3)	O31-C32	1.404(4)	1.420(4)
C12-C13	1.595(3)	1.563(3)	O33-C34	1.419(4)	1.428(4)
C12-H12	0.93(3)	0.97(3)	O35-C36	1.416(4)	1.412(3)
C13-O14	1.447(2)	-			
Angle	**9**	**12**	Angle	**9**	**12**
C8-O1-C2	105.8(2)	105.3(2)	C6-C13-C12	107.61(15)	112.76(18)
O3-C2-O1	108.6(3)	109.6(3)	C10-O14-C13	97.72(14)	-
C9-O3-C2	105.8(2)	105.4(2)	O16-P15-O17	115.57(12)	115.18(12)
C9-C4-C5	114.2(2)	117.7(2)	O16-P15-O19A	109.5(3)	112.93(12)
C6-C5-C4	121.8(2)	120.6(2)	O17-P15-O19A	108.8(3)	102.68(11)
C6-C5-C10	105.23(18)	121.4(2)	O16-P15-C11	114.59(11)	114.25(11)
C4-C5-C10	132.8(2)	117.9(2)	C20-O19-P15	125.2(7)	123.8(2)
C7-C6-C5	123.1(2)	120.4(2)	O17-P15-C11	101.30(12)	108.60(11)
C7-C6-C13	131.81(19)	116.4(2)	O19A-P15-C11	106.4(3)	101.80(10)
C5-C6-C13	104.91(18)	122.9(2)	C18-O17-P15	123.0(3)	122.6(2)
C8-C7-C6	114.6(2)	117.3(2)	O22-C21-O23	123.4(2)	124.6(2)
O1-C8-C7	127.7(2)	127.8(2)	O22-C21-C12	124.9(2)	126.0(2)
O1-C8-C9	109.8(2)	109.9(2)	O23-C21-C12	111.68(19)	109.3(2)
C7-C8-C9	122.5(2)	122.3(2)	C21-O23-C24	115.1(2)	117.4(2)
C4-C9-O3	126.7(2)	128.5(3)	C30-C25-C26	120.62(19)	120.00(19)
C4-C9-C8	123.7(2)	121.7(3)	C30-C25-C13	117.76(19)	119.9(2)
O3-C9-C8	109.6(2)	109.9(2)	C26-C25-C13	121.58(18)	120.1(2)
O14-C10-C5	101.94(16)	111.04(19)	C25-C26-C27	119.4(2)	119.9(2)
O14-C10-C11	100.29(15)	107.0(2)	O31-C27-C28	115.9(2)	115.1(2)
C5-C10-C11	107.40(17)	111.19(19)	O31-C27-C26	123.9(2)	124.6(2)
C12-C11-C10	101.87(15)	108.17(19)	C28-C27-C26	120.2(2)	120.2(2)
C12-C11-P15	114.05(14)	117.67(18)	O33-C28-C27	120.0(2)	120.2(2)
C10-C11-P15	113.16(15)	109.78(16)	O33-C28-C29	120.2(2)	120.0(2)
C21-C12-C11	111.44(16)	116.3(2)	C27-C28-C29	119.7(2)	119.7(2)
C21-C12-C13	115.56(17)	107.18(18)	O35-C29-C30	124.7(2)	124.3(2)
C11-C12-C13	100.85(15)	110.56(19)	O35-C29-C28	115.0(2)	115.7(2)
O14-C13-C25	110.49(15)	-	C30-C29-C28	120.3(2)	120.0(2)
O14-C13-C6	101.31(16)	-	C29-C30-C25	119.7(2)	120.1(2)
C25-C13-C6	116.77(17)	109.06(18)	C27-O31-C32	117.79(19)	117.8(2)
O14-C13-C12	99.14(15)	-	C28-O33-C34	112.9(2)	112.3(2)
C25-C13-C12	118.71(17)	112.94(17)	C29-O35-C36	117.7(2)	117.62(19)