

New bicyclic phosphonates of unsymmetrical structure

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General procedure for the synthesis of unsymmetrical bicyclic phosphonates **3a,b**

(2-Ethoxyvinyl)phosphonic dichloride (5.3 mmol) in toluene (5 ml) was added dropwise to a boiled toluene (45 ml) solution of 2-methylresorcinol (5.3 mmol) with resorcinol (5.3 mmol for **3a**) or pyrogallol (5.3 mmol for **3b**) and trifluoroacetic acid (5.3 mmol). The mixture was refluxed for 6 h. The precipitate from reaction mixture was recrystallized from isopropyl alcohol to give symmetric derivative **4**, yield: ca. 0.7 g (~43%) after filtration. The filtrate was concentrated under vacuum. The white solid residue was washed with water, filtered, and dried to a constant weight.

4-Methyl-6,12-methano-12H-dibenzo[d,g][1,3,2]dioxaphosphocine-3,9-diol 6-oxide 3a Yield: 0.4 g (25%), m.p. 208 °C. ¹H NMR (400.1 MHz, DMSO-*d*₆) δ: 1.99 (s, 3H, CH₃), 2.63 (m, 2H, CH₂P), 4.57 (m, 1H, CH), 6.39 (m, 1H, ArH), 6.48 (m, 1H, ArH), 6.52 (dd, 1H, ArH), 7.06 (t, 1H, ArH), 7.22 (t, 1H, ArH), 9.55 (d, 1H, OH), 9.67 (d, 1H, OH). ¹³C NMR (100.6 MHz, DMSO-*d*₆) δ: 9.1 (d, C-18, ⁴J_{PC} 3.6 Hz), 20.6 (d, C-17, ¹J_{PC} 111.5 Hz), 40.1 (d, C-9, ²J_{PC} 10.2 Hz), 105.5 (d, C-14, J_{PC} 8.3 Hz), 110.8 (C-6), 111.9 (C-12), 113.8 (C-4), 119.7 (C-8, C-10), 125.7 (C-7), 129.6 (C-11), 149.8 (C-3, ²J_{PC} 7.6 Hz), 151.3 (d, C-15, ²J_{PC} 7.6 Hz), 155.9 (C-5), 158.1 (C-13). ³¹P NMR (162 MHz, DMSO-*d*₆) δ: 14.0. IR (KBr) ν/cm⁻¹: 1270 (P=O), 1618 (C=C_{Ar}), 3136 (CH₃), 3376, 3645 (OH). MS (MALDI), *m/z*: 305 [M+H]⁺, 327 [M+Na]⁺, 343 [M+K]⁺. Found (%): C, 59.16; H, 4.25; P, 10.15. Calc. for C₁₅H₁₃O₅P (%): C, 59.21; H, 4.27; P 10.19.

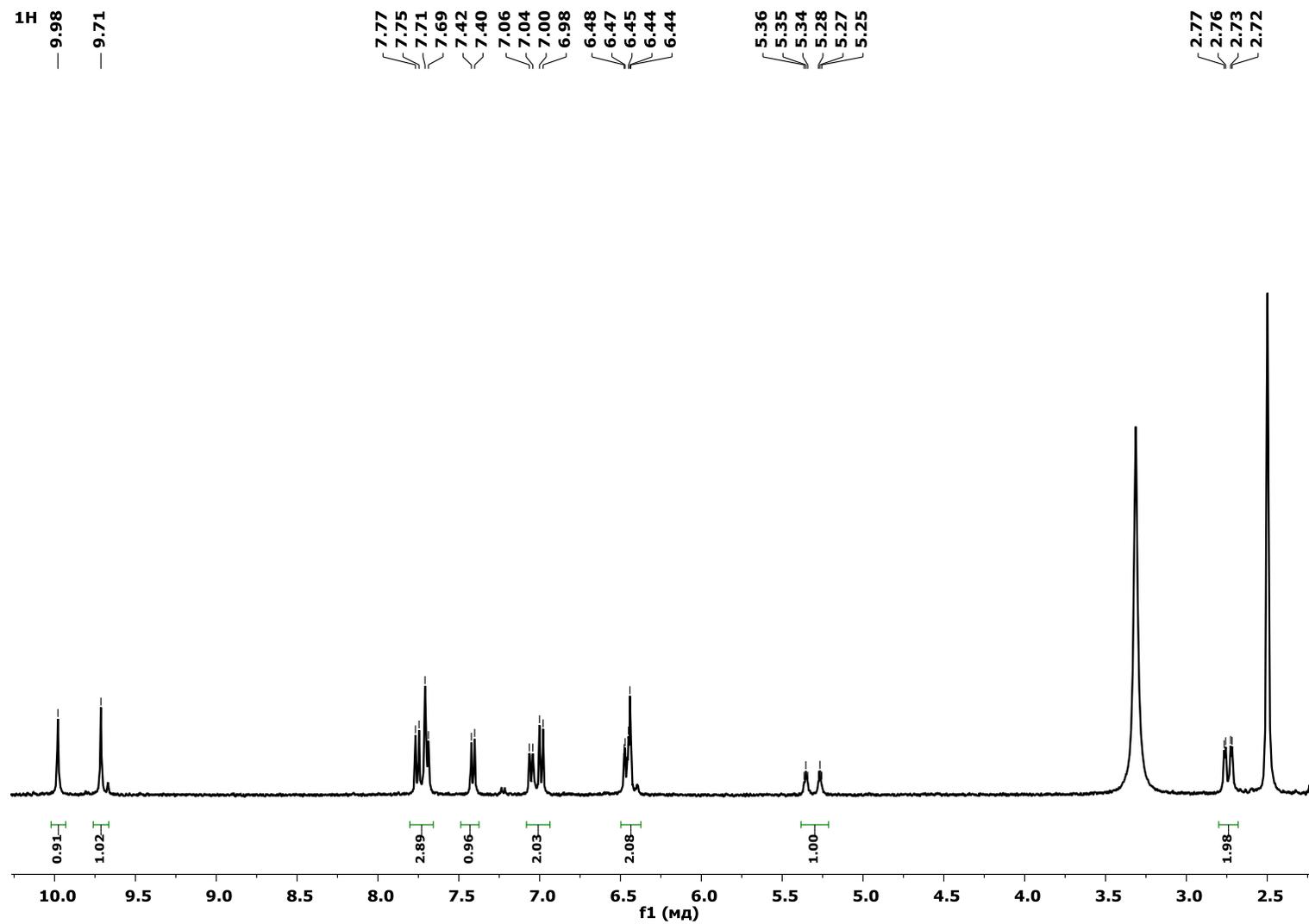
8-Methyl-6,12-methano-12H-dibenzo[d,g][1,3,2]dioxaphosphocine-3,4,9-triol 6-oxide 3b Yield: 0.35 g (21%), m.p. 285 °C. ¹H NMR (400.1 MHz, DMSO-*d*₆) δ: 2.00 (s, 3H, CH₃), 2.58 (dd, 2H, CH₂P, ³J_{HH} 3.6 Hz, ²J_{PH} 16.5 Hz), 4.53 (dt, 1H, CH, ³J_{HH} 3.2 Hz, ³J_{PH} 35.2 Hz), 6.46 (d, 1H, ArH, ³J_{HH} 8.4 Hz), 6.51 (d, 1H, ArH, ³J_{HH} 8.4 Hz), 6.65 (dd, 1H, ArH, ³J_{HH} 8.4 Hz, ⁴J_{HH} 4.3 Hz), 7.05 (dd, 1H, ArH, ³J_{HH} 8.4 Hz, ⁴J_{HH} 4.0 Hz), 8.83 (s, 1H, OH), 9.18 (s, 1H, OH), 9.54 (s, 1H, OH). ¹³C NMR (150.5 MHz, DMSO-*d*₆) δ: 8.98 (C-18), 20.58 (d, C-17, ¹J_{PC} 115.6 Hz), 40.2 (C-9), 110.8 (C-6), 111.3 (C-12), 113.7 (C-4), 117.6 (C-11), 119.6 (d, C-8, ³J_{PC} 10.9 Hz), 120.6 (C-10, ³J_{PC} 10.9 Hz), 125.8 (C-7), 134.9 (d, C-14, ³J_{PC} 7.9 Hz), 140.1 (d, C-3, ²J_{PC} 6.6 Hz), 146.4 (C-5), 149.8 (d, C-15, ²J_{PC} 7.9 Hz), 155.8 (C-13). ³¹P NMR (242.9 MHz, DMSO-*d*₆) δ: 14.0. IR (KBr) ν/cm⁻¹: 1235 (P=O), 1615 (C=C_{Ar}), 2925 (CH₃), 3415 (OH). MS (MALDI), *m/z*: [M]⁺ 320, [M+Na]⁺ 343. Found (%): C, 56.18; H, 4.01; P, 9.62. Calc. for C₁₅H₁₃O₆P (%): C 56.26; H 4.09; P 9.67.

General procedure for the synthesis of unsymmetrical bicyclic phosphonates **5a,b**

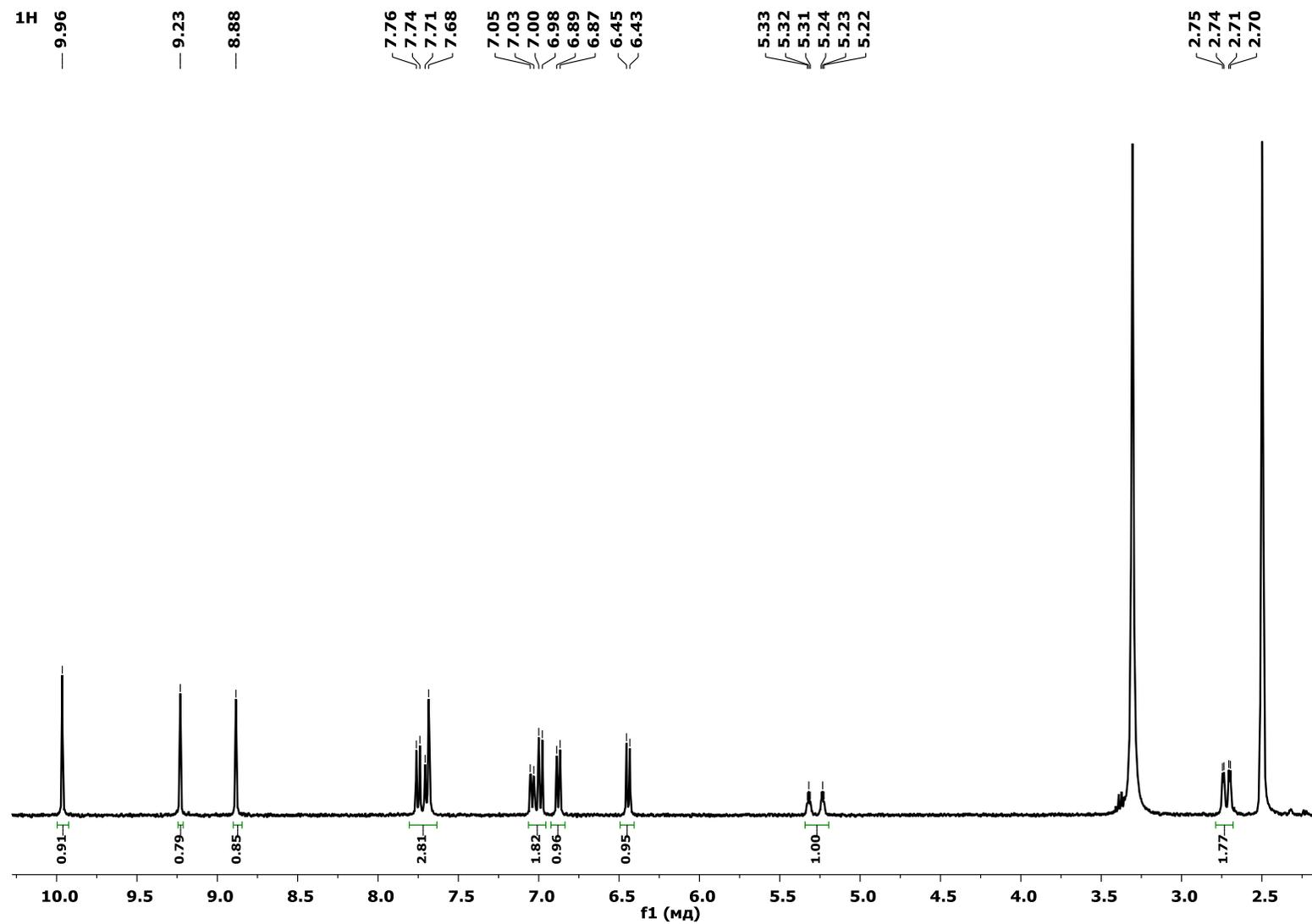
(2-Ethoxyvinyl)phosphonic dichloride (5.3 mmol) in toluene (5 ml) was added dropwise to a boiled toluene (35 ml) solution of naphthalene-2,7-diol (5.3 mmol) with resorcinol (5.3 mmol for **5a**) or pyrogallol (5.3 mmol for **5b**) and trifluoroacetic acid (5.3 mmol). The mixture was refluxed for 18 h. The precipitate from reaction mixture was washed with water and recrystallized in isopropyl alcohol to give symmetric derivative **6**, yield: ca. 0.7 g (~34%) after filtration. The filtrate was concentrated under vacuum. The white solid residue was washed with acetone, filtered, and dried up to a constant weight.

6,14-Methano-14H-benzo[d]naphtho[1,2-g][1,3,2]dioxaphosphocine-3,12-diol 6-oxide 5a.
Yield: 0.35 g (19%), m.p. >300 °C. ¹H NMR (400.1 MHz, DMSO-*d*₆) δ: 2.75 (dd, 2H, CH₂P, ²J_{PH} 16.1 Hz, ³J_{HH} 3.9 Hz), 5.32 (dt, 1H, CH, ³J_{PH} 34.6 Hz, ³J_{HH} 3.9 Hz), 6.45 (s, 1H, ArH), 6.47 (dd, 1H, ArH, ³J_{HH} 8.2 Hz, ⁴J_{HH} 2.3 Hz), 7.00 (d, 1H, ArH, ³J_{HH} 8.8 Hz), 7.06 (dd, 1H, ArH, ³J_{HH} 8.7 Hz, ⁴J_{HH} 1.7 Hz), 7.42 (d, 1H, ArH, ³J_{HH} 8.3 Hz), 7.71 (d, 1H, ArH, ³J_{HH} 8.6 Hz), 7.72 (s, 1H, ArH), 7.77 (d, 1H, ArH, ³J_{HH} 8.7 Hz), 9.72 (s, 1H, OH), 9.99 (s, 1H, OH). ¹³C NMR (150.5 MHz, DMSO-*d*₆) δ: 20.45 (d, C-21, ¹J_{PC} 107.6 Hz), 35.27 (d, C-9, ²J_{PC} 10.2 Hz), 105.75 (d, C-4, ³J_{PC} 8.4 Hz), 105.83 (C-12), 111.48 (C-6), 116.01 (d, C-18, ³J_{PC} 8.2 Hz), 117.79 (C-14), 118.21 (d, C-8, ³J_{PC} 10.2 Hz), 119.99 (d, C-10, ³J_{PC} 10.2 Hz), 125.35 (C-16), 129.28 (C-7), 129.74 (C-17), 130.98 (C-15), 132.40 (C-11), 149.28 (d, C-19, ²J_{PC} 8.4 Hz), 152.03 (d, C-3, ²J_{PC} 7.6 Hz), 157.31 (C-13), 158.20 (C-5). ³¹P NMR (242.9 MHz, DMSO-*d*₆) δ: 14.0. IR (KBr) ν/cm⁻¹: 1270 (P=O), 1597, 1624, 1697 (C=C_{Ar}), 3230, 3381 (OH). MS (MALDI), *m/z*: 341 [M+H]⁺, 363 [M+Na]⁺, 379 [M+K]⁺. Found (%): C, 63.49; H, 3.82; P, 9.13. Calc. for C₁₈H₁₃O₅P (%): C, 63.54; H, 3.85; P, 9.10.

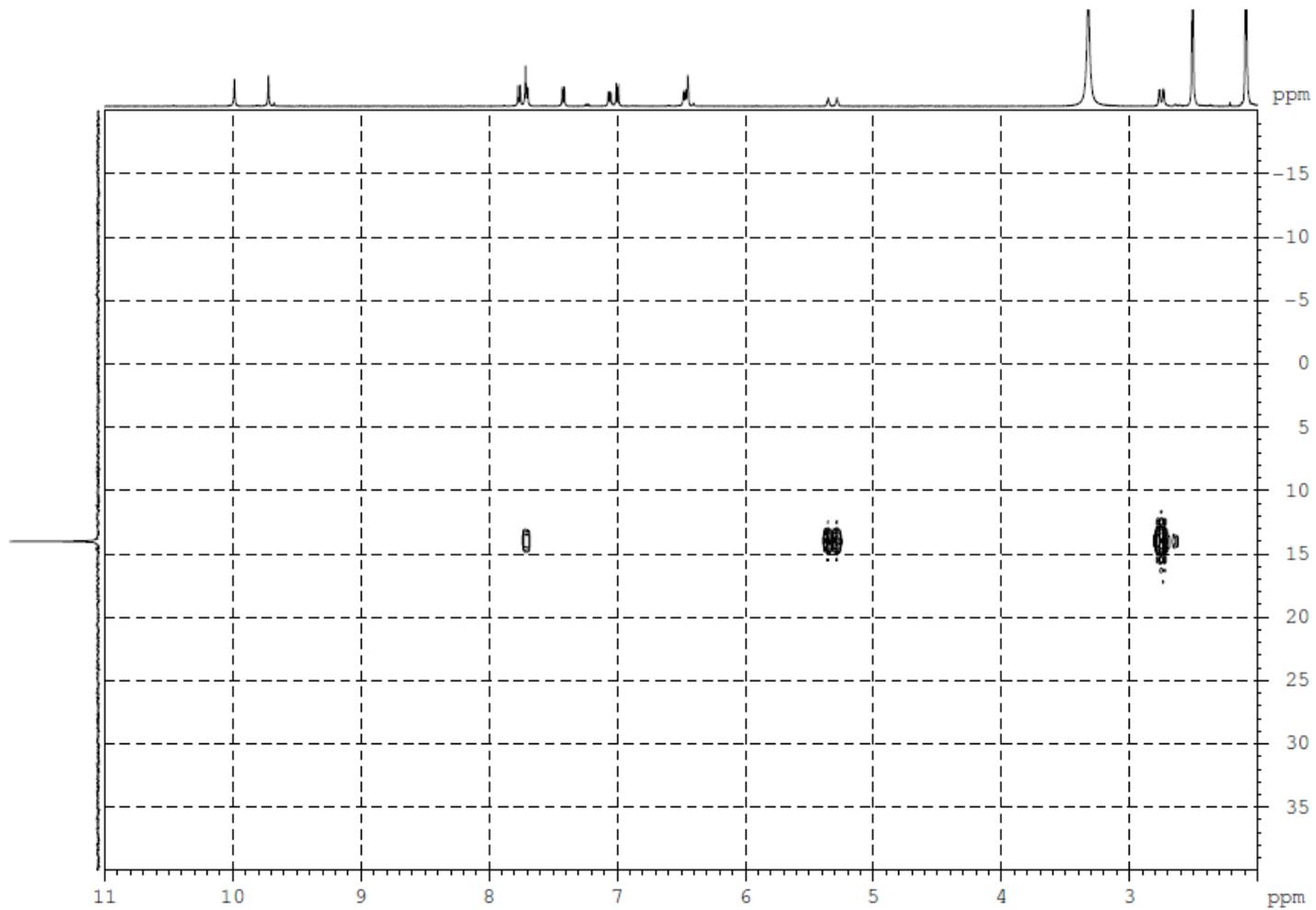
6,14-Methano-14H-benzo[d]naphtho[1,2-g][1,3,2]dioxaphosphocine-3,4,12-triol 6-oxide 5b.
Yield: 0.45 g (24%), m.p. >300 °C. ¹H NMR (600.1 MHz, DMSO-*d*₆) δ: 2.73 (dd, 2H, CH₂P, ²J_{PH} 15.8 Hz, ³J_{HH} 3.7 Hz), 5.28 (dt, 1H, CH, ³J_{PH} 34.3 Hz, ³J_{HH} 3.7 Hz), 6.44 (d, 1H, ArH, ³J_{HH} 8.3 Hz), 6.88 (d, 1H, ArH, ³J_{HH} 8.4 Hz), 6.99 (d, 1H, ArH, ³J_{HH} 8.8 Hz), 7.04 (dd, 1H, ArH, ³J_{HH} 8.7 Hz, ⁴J_{HH} 2.1 Hz), 7.68 (d, 1H, ArH, ³J_{HH} 8.3 Hz), 7.71 (d, 1H, ArH, ³J_{HH} 8.7 Hz), 7.75 (d, 1H, ArH, ³J_{HH} 8.8 Hz), 8.88 (s, 1H, OH), 9.23 (s, 1H, OH), 9.96 (s, 1H, OH). ¹³C NMR (150.5 MHz, DMSO-*d*₆) δ: 20.45 (d, C-21, ¹J_{PC} 111.3 Hz), 36.87 (d, C-9, ²J_{PC} 10.4 Hz), 105.98 (C-12), 110.96 (C-6), 116.01 (d, C-18, ³J_{PC} 8.6 Hz), 117.66 (C-7), 117.76 (C-14), 119.09 (d, C-8, ³J_{PC} 10.9 Hz), 120.01 (d, C-10, ³J_{PC} 10.3 Hz), 125.39 (C-16), 129.73 (C-17), 130.97 (C-15), 131.53 (C-11), 135.19 (d, C-4, ²J_{PC} 7.3 Hz), 140.79 (d, C-5, ²J_{PC} 7.3 Hz), 146.67 (C-3), 149.35 (d, C-19, ³J_{PC} 8.3 Hz), 157.25 (C-13). ³¹P NMR (242.9 MHz, DMSO-*d*₆) δ: 13.8. IR (KBr) ν/cm⁻¹: 1278 (P=O), 1587, 1604, 1634 (C=C_{Ar}), 3245, 3400 (OH). MS (MALDI), *m/z*: 357 [M+H]⁺, 379 [M+Na]⁺, 395 [M+K]⁺. Found (%): C 60.62; H 3.72; P 8.66. Calc. for C₁₈H₁₃O₆P (%): C, 60.68; H, 3.68; P, 8.69.



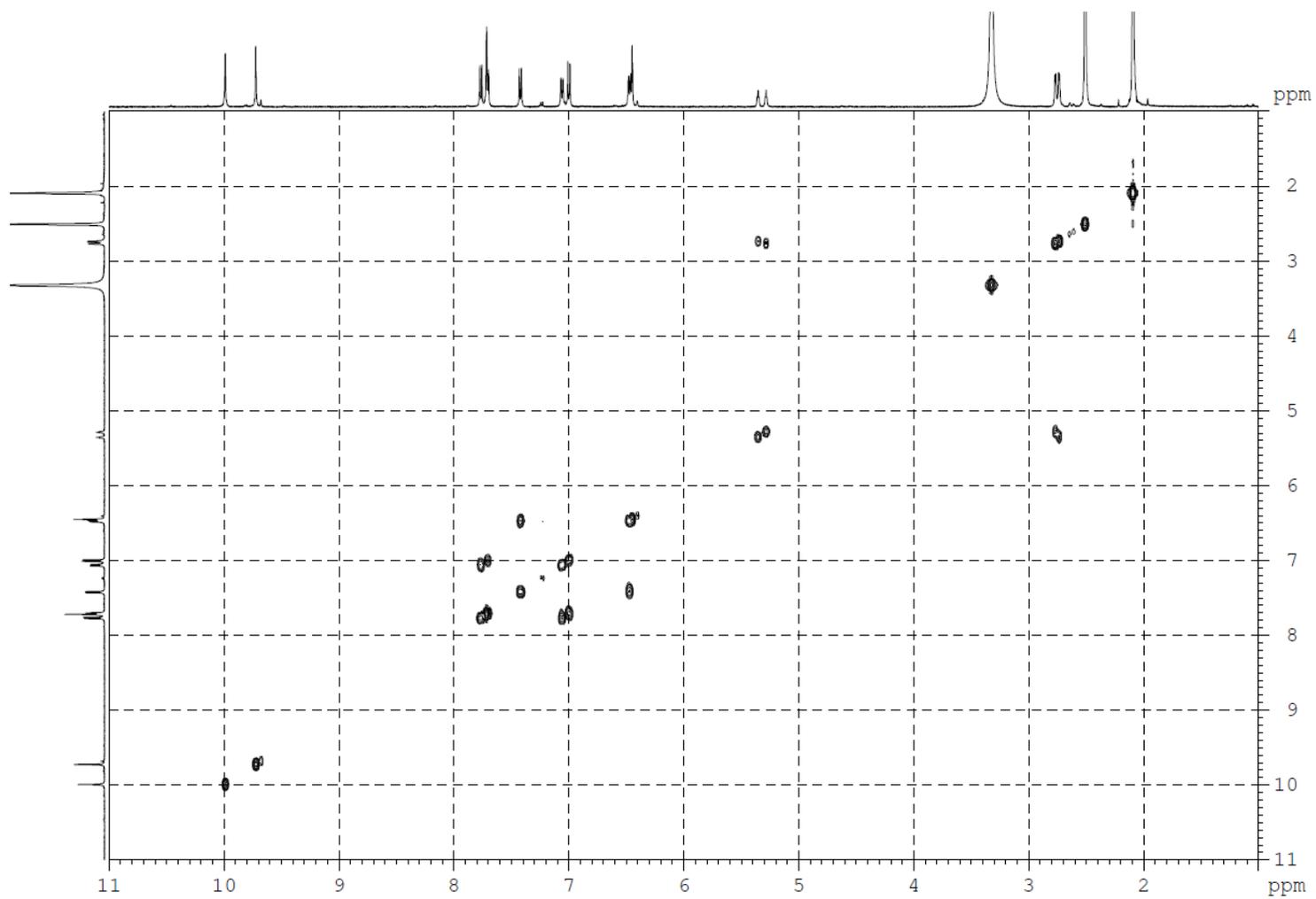
¹H NMR spectrum of compound 5a



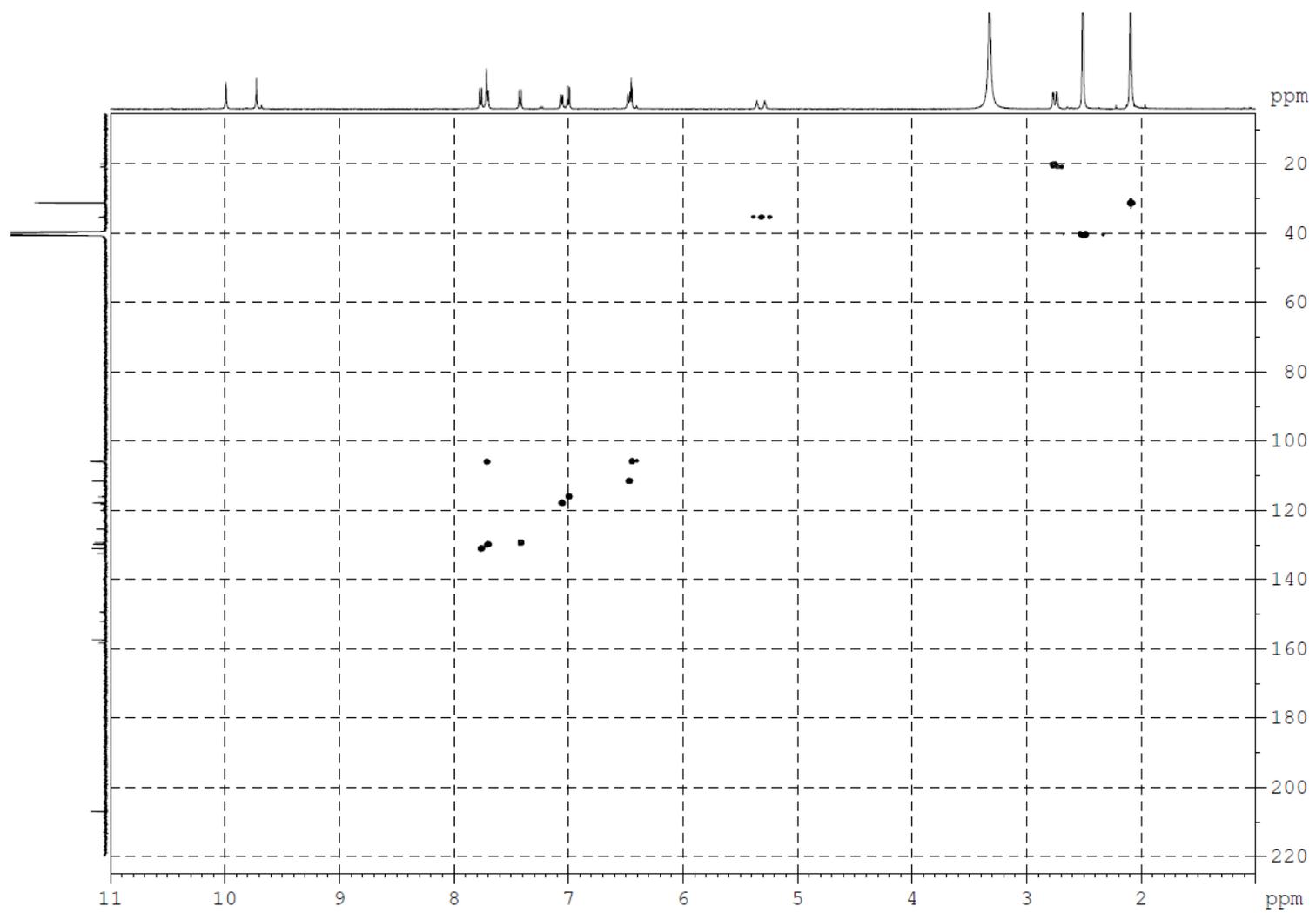
^1H NMR spectrum of compound **5b**



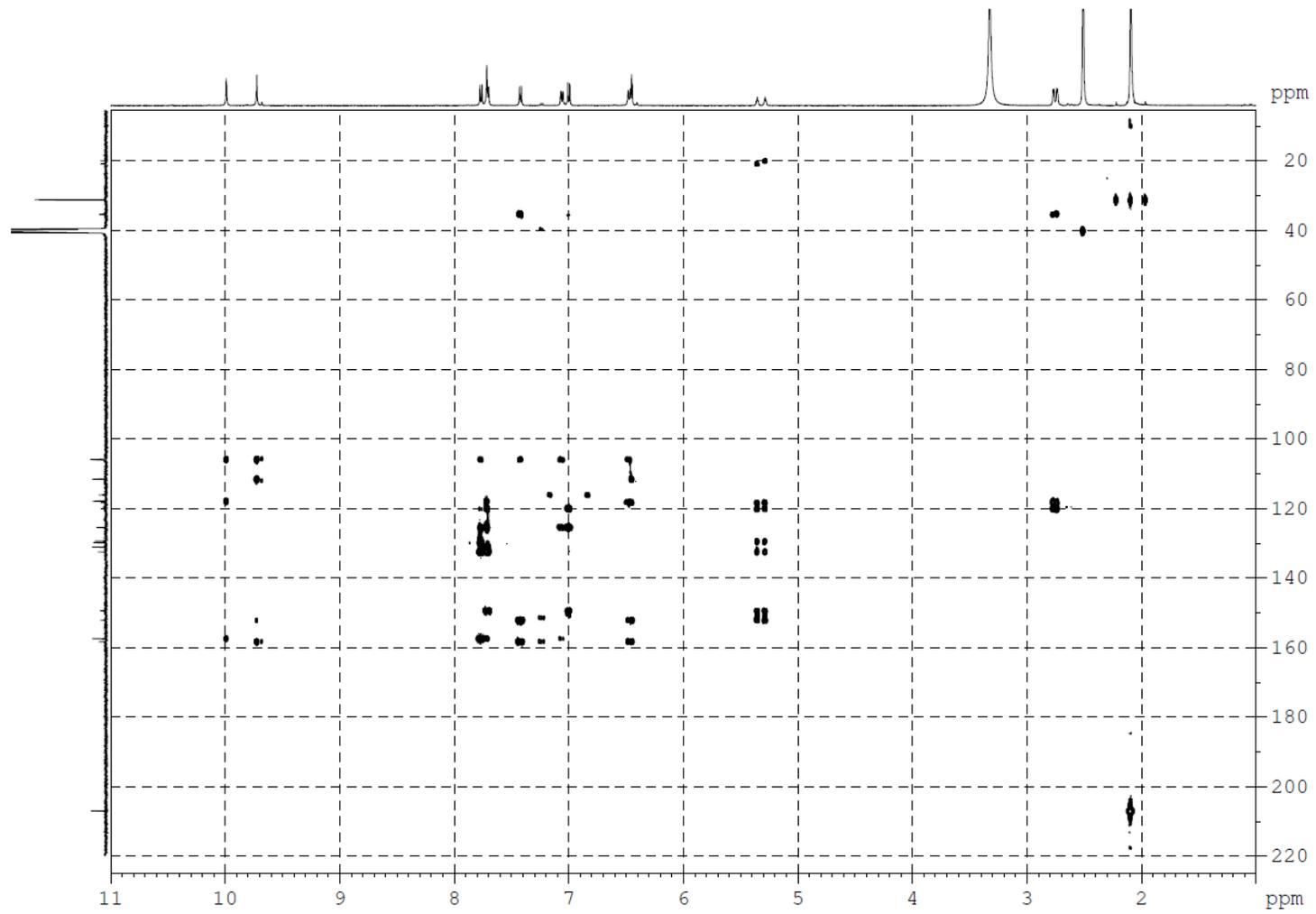
H-P HMBC spectrum of compound **5a**



H-H COSY spectrum of compound **5a**



H-C HSQC spectrum of compound **5a**



H-C HMBC spectrum of compound **5a**