Supporting Information

TRIFUNCTIONALIZED ALLENES. PART VI. SYNTHESIS OF 2,5-DIHYDRO-1,2-OXAPHOSPHOLES, FURAN-2(5H)-ONES AND 5,6-DIHYDRO-2H-PYRANS BY ELECTROPHILIC CYCLIZATION AND CYCLOISOMERIZATION OF 4-PHOSPHORYLATED 6-HYDROXY-2-METHYLHEPTA-2,3-DIENOATES

Ismail E. Ismailov, Ivaylo K. Ivanov and Valerij Ch. Christov*

Department of Chemistry, Faculty of Natural Sciences, Konstantin Preslavsky University of Shumen, 115, Universitetska str., BG-9712 Shumen, Bulgaria; E-Mail: vchristo@shu.bg

EXPERIMENTAL

All new synthesized compounds were purified by column chromatography and characterized based on NMR, IR, Mass, and microanalytical data. NMR spectra were recorded on Brucker Avance II+600 (^{1}H at 600.1 MHz, ^{13}C at 150.9 MHz, ^{31}P at 242.9 MHz) spectrometer for solutions in $CDCl_3$. All ^{1}H and ^{13}C NMR experiments were measured referring to the signal of internal TMS and ^{31}P NMR experiments were measured referring to the signal of external 85% H_3PO_4. *J* values are given in hertz. IR spectra were recorded with an FT-IRAfinity-1 Shimadzu spectrophotometer. Elemental analyses were carried out by the Microanalytical Service Laboratory using Vario EL*3* CHNS(O). HRMS were recorded on a Thermo Scientific Q Exactive hybrid quadrupole-orbitrap mass spectrometer. Column chromatography was performed on Kieselgel F_{254}60 (70-230 mesh ASTM, 0.063-0.200 nm, Merck). CH_2Cl_2 was distilled over CaH_2. Reactions were carried out in oven dried glassware under an argon atmosphere and exclusion of moisture. All compounds were checked for purity on TLC plates Kieselgel F_{254} 60 (Merck).

Diphenyl disulfide and sulfuryl chloride in dichloromethane were used to prepare benzenesulfenyl chloride which distilled *in vacuo* (bp 80-81 °C/20 mm Hg).[1] All other chemicals used in this study were commercially available and were used without additional purification unless otherwise noted. The starting 4-phosphorylated 5-hydroxyhexa-2,3-

dienoates **1-4** were prepared according to earlier reported procedure.[2]

General Procedure for the Reactions of the 4-Phosphorylated 5-Hydroxyhexa-2,3-dienoates 1–4 with Electrophilic Reagents.

To a solution of the 4-phosphorylated 5-hydroxyhexa-2,3-dienoates with protected (**1** or **2**) or unprotected (**3** or **4**) hydroxy group (3.0 mmol) in dry CH_2Cl_2 (10 mL) at -20 °C was added dropwise with stirring a solution of electrophilic reagent (sulfuryl chloride, bromine, benzenesulfenyl chloride or benzeneselenenyl chloride) (3.6 mmol) in the same solvent (10 mL). The reaction mixture was stirred at the same temperature for 3 h (**5** and **6**) and 5 h (**7** and **8**) at room temperature. After evaporation of the solvent, the residue was purified by column chromatography on a silica gel with EtOAc/hexane. The pure products **5** and **6** had the following properties:

Ethyl 2-methoxy-5-methyl-2-oxo-4-phenylselenenyl-3-(2-tetrahydro-2H-pyran-2-yloxypropyl)-2,5-dihydro-1,2-oxaphosphole-5-carboxylate 5a. Orange oil, yield: 44%. Eluent for TLC: EtOAc:hexane = 1:5, R_f 0.44; IR (neat, cm^{-1}): 1022 (C-O-P), 1125 (C-O-C), 1269 (P=O), 1438, 1491 (Ph), 1581 (C=C), 1726 (C=O). ^{1}H NMR (600.1 MHz): δ 1.10-1.27 (m, 6H, OTHP), 1.29 (t, *J*=6.8 Hz, 3H, MeCH$_2$O), 1.33 (d, *J*=6.3 Hz, 3H, MeCH), 1.76 (s, 3H, MeC=), 2.63-2.74 (m, 2H, CH_2), 3.50-3.65 (m, 2H, OTHP), 3.74 (d, *J*=11.4 Hz, 3H, MeO), 4.10-4.24 (m, 1H, MeCH), 4.16 (q, *J*=6.8 Hz, 2H, MeCH$_2$O), 4.56-4.63 (m, 1H, OTHP), 7.38-7.46 (m, 5H, Ph). ^{13}C NMR (150.9 MHz): δ 14.0 (CH_3), 20.1 (CH_2), 21.9 (*J*=7.8, CH_3), 22.9 (*J*=4.5, CH_3), 26.1 (CH_2), 32.2 (CH_2), 37.3 (*J*=5.8, CH_2), 52.0 (*J*=14.8, CH_3), 62.4 (CH_2), 64.1 (CH_2), 70.2 (*J*=8.2, CH), 91.5 (*J*=10.0 Hz, C), 96.2 (CH), 128.0 (*J*=101.5 Hz, C), 128.3-140.1 (Ph), 168.5 (*J*=15.3 Hz, C), 183.5 (*J*=8.2 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 33.4. Anal. Calcd for $C_{22}H_{31}O_7PSe$: C 51.07, H 6.04. Found: C 51.03, H 6.09.

Dimethyl [4-methyl-5-oxo-3-phenylselenenyl-2-(2-tetrahydro-2*H*-pyran-2-yloxypropyl)-2,5-dihydrofuran-2-yl]-phosphonate 6a. Light yellow oil, yield: 30%. Eluent for TLC: EtOAc:hexane = 1:5, R_f 0.65; IR (neat, cm^{-1}): 1125 (C-O-C), 1269 (P=O), 1439, 1490 (Ph), 1622 (C=C), 1747 (C=O). ^{1}H NMR (600.1 MHz): δ 1.11-1.25 (m, 6H, OTHP), 1.38 (d, *J*=5.9 Hz, 6H, MeCH), 2.11 (s, 3H, MeC=), 2.50-2.71 (m, 2H, CH_2), 3.64-3.77 (m, 2H, OTHP), 3.85 (d, *J*=10.5 Hz, 6H, MeO), 4.38-4.48 (m, 1H, MeCH), 4.54-4.59 (m, 1H, OTHP), 7.31-7.94 (m, 5H, Ph). ^{13}C NMR (150.9 MHz): δ 16.7 (*J*=5.3, CH_3), 20.1 (CH_2), 24.1 (*J*=5.2, CH_3), 26.0 (CH_2), 31.6 (CH_2), 38.1 (*J*=5.7, CH_2), 53.7 (*J*=5.9, 2CH_3), 63.4 (CH_2), 67.2 (*J*=7.8 Hz, CH), 96.0 (CH), 102.3 (*J*=126.5 Hz, C), 128.1 (*J*=7.9 Hz, C), 128.4-138.7 (Ph), 175.0 (*J*=8.0 Hz, C), 176.8 (*J*=15.0 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 15.3. Anal. Calcd for $C_{21}H_{29}O_7PSe$:

C 50.11, H 5.81. Found: C 50.17, H 5.85.

Ethyl 4-chloro-3-(2-hydroxypropyl)-2-methoxy-5-methyl-2-oxo-2,5-dihydro-1,2-oxaphosphole-5-carboxylate 5b. Colorless oil, yield: 41%. Eluent for TLC: EtOAc:hexane = 2:1, R_f 0.39; IR (neat, cm^{-1}): 1019 (C-O-P), 1262 (P=O), 1583 (C=C), 1728 (C=O), 3399 (OH). ^{1}H NMR (600.1 MHz): δ 1.24 (d, *J*=6.2 Hz, 3H, MeCHO), 1.29 (t, *J*=6.7 Hz, 3H, $MeCH_2O$), 1.80 (s, 3H, MeC=), 2.54-2.63 (m, 2H, CH_2), 3.21 (s, 1H, OH), 3.68 (d, *J*=11.5 Hz, MeO), 4.20 (q, *J*=6.7 Hz, 2H, $MeCH_2O$), 4.35-4.50 (m, 1H, MeCHO). ^{13}C NMR (150.9 MHz): δ 14.0 (CH_3), 23.0 (*J*=8.1, CH_3), 23.5 (*J*=4.5, CH_3), 38.3 (*J*=5.7, CH_2), 52.1 (*J*=15.1, CH_3), 62.2 (CH_2), 64.5 (*J*=7.8 Hz, CH), 88.4 (*J*=10.2 Hz, C), 127.6 (*J*=101.1 Hz, C), 156.3 (*J*=41.0 Hz, C), 174.0 (*J*=7.9 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 34.9. Anal. Calcd for $C_{11}H_{18}ClO_6P$: C 42.25, H 5.80. Found: C 42.31, H 5.77.

Dimethyl [3-chloro-2-(2-hydroxypropyl)-4-methyl-5-oxo-2,5-dihydrofuran-2-yl]-phosphonate 6b. Colorless oil, yield: 29%. Eluent for TLC: EtOAc:hexane = 2:1, R_f 0.67; IR (neat, cm^{-1}): 1117 (C-O-C), 1262 (P=O), 1624 (C=C), 1744 (C=O), 3420 (OH). ^{1}H NMR (600.1 MHz): δ 1.41 (d, *J*=6.4 Hz, 3H, MeCHO), 2.21 (s, 3H, MeC=), 2.38-2.61 (m, 2H, CH_2), 3.87 (d, *J*=10.5 Hz, 6H, 2MeO), 4.60-4.70 (m, 1H, MeCHO), 4.94 (s, 1H, OH). ^{13}C NMR (150.9 MHz): δ 16.1 (*J*=4.6, CH_3), 25.2 (*J*=5.1, CH_3), 40.6 (*J*=5.8, CH_2), 53.9 (*J*=14.4, $2CH_3$), 61.5 (*J*=8.1 Hz, CH), 99.8 (*J*=126.4 Hz, C), 130.5 (*J*=7.9 Hz, C), 163.4 (*J*=40.5 Hz, C), 171.8 (*J*=7.9 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 16.5. Anal. Calcd for $C_{10}H_{16}ClO_6P$: C 40.22, H 5.40. Found: C 40.26, H 5.46.

4-Bromo-5-ethoxycarbonyl-5-methyl-2,2-diphenyl-3-(2-tetrahydro-2H-pyran-2-yloxypropyl)-2,5-dihydro-1,2-oxaphosphol-2-ium Bromide 7a. Orange oil, yield: 48%. Eluent for TLC: EtOAc:hexane = 1:2, R_f 0.44; IR (neat, cm^{-1}): 1119 (C-O-C), 1439, 1487 (Ph), 1579 (C=C), 1727 (C=O). ^{1}H NMR (600.1 MHz): δ 1.14-1.26 (m, 6H, OTHP), 1.26 (t, *J*=6.8 Hz, 3H, $MeCH_2O$), 1.36 (d, *J*=5.9 Hz, 3H, MeCHO), 1.96 (s, 3H, MeC=), 2.84-3.00 (m, 2H, CH_2), 3.49-3.62 (m, 2H, OTHP), 4.11-4.21 (m, 2H, $MeCH_2O$), 4.18-4.26 (m, 1H, MeCHO), 4.54-4.62 (m, 1H, OTHP), 7.74-8.51 (m, 10H, 2Ph). ^{13}C NMR (150.9 MHz): δ 14.1 (CH_3), 20.0 (CH_2), 21.7 (*J*=5.1 Hz, CH_3), 26.1 (*J*=7.9 Hz, CH_3), 26.9 (CH_2), 31.9 (CH2), 34.1 (*J*=5.9 Hz, CH_2), 62.7 (CH_2), 63.7 (CH_2), 76.2 (*J*=8.1 Hz, CH), 91.4 (*J*=9.9 Hz, C), 96.1 (CH), 109.4-135.4 (2Ph), 132.4 (*J*=49.8 Hz, C), 143.7 (*J*=50.8 Hz, C), 171.3 (*J*=7.8 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 80.9. Anal. Calcd for $C_{27}H_{33}Br_2O_5P$: C 51.61, H 5.29. Found: C 51.68, H 5.33.

4-Bromo-5-(diphenylphosphinoyl)-3-methyl-5-(2-tetrahydro-2H-pyran-2-yloxypropyl)furan-2(5*H*)-one 8a. Yellow oil, yield: 27%. Eluent for TLC: EtOAc:hexane =

1:2, R_f 0.65; IR (neat, cm^{-1}): 1117 (C-O-C), 1177 (P=O), 1439, 1491 (Ph), 1628 (C=C), 1746 (C=O). ^{1}H NMR (600.1 MHz): δ 1.11-1.26 (m, 6H, OTHP), 1.37 (d, *J*=6.0 Hz, 3H, MeCH), 2.31 (s, 3H, MeC=), 2.35-2.55 (m, 2H, CH_2), 3.62-3.81 (m, 2H, OTHP), 4.56-4.62 (m, 1H, OTHP), 4.74-4.83 (m, 1H, MeCH), 7.53-7.96 (m, 10H, 2Ph). ^{13}C NMR (150.9 MHz): δ 17.0 (*J*=4.5 Hz, CH_3), 20.1 (CH_2), 23.9 (*J*=4.7 Hz, CH_3), 26.1 (CH_2), 31.5 (CH_2), 42.6 (*J*=5.9 Hz, CH_2), 63.7 (CH_2), 72.4 (*J*=8.1 Hz, CH), 96.2 (CH), 99.4 (*J*=126.6 Hz, C), 128.1-132.4 (2Ph), 134.0 (*J*=7.8 Hz, C), 149.2 (*J*=50.4 Hz, C), 174.8 (*J*=8.1 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 17.5. Anal. Calcd for $C_{25}H_{28}BrO_5P$: C 57.81, H 5.43. Found: C 57.85, H 5.48.

5-Ethoxycarbonyl-3-(2-hydroxypropyl)-5-methyl-2,2-diphenyl-4-phenylsulfenyl-2,5-dihydro-1,2-oxaphosphol-2-ium Chloride 7b. Yellow oil, yield: 47%. Eluent for TLC: EtOAc:hexane = 1:2, R_f 0.40; IR (neat, cm^{-1}): 1439, 1488 (Ph), 1583 (C=C), 1721 (C=O), 3422 (OH). ^{1}H NMR (600.1 MHz): δ 1.25 (t, *J*=6.7 Hz, 3H, MeCH$_2$O), 1.31 (d, *J*=6.0 Hz, 3H, MeCHO), 1.86 (s, 3H, Me), 2.60 (s, 1H, OH), 3.01-3.11 (m, 2H, CH_2), 3.49-3.59 (m, 1H, MeCHO), 4.12 (q, *J*=6.7 Hz, 2H, MeCH$_2$O), 6.84-8.62 (m, 15H, 3Ph). ^{13}C NMR (150.9 MHz): δ 14.2 (CH_3), 22.4 (*J*=4.5 Hz, CH_3), 29.1 (*J*=7.8 Hz, CH_3), 37.0 (*J*=5.9 Hz, CH_2), 62.1 (CH_2), 72.3 (*J*=8.1 Hz, CH), 89.1 (*J*=10.2 Hz, C), 113.0-139.4 (3Ph), 129.4 (*J*=50.3 Hz, C), 160.2 (*J*=14.6 Hz, C), 169.3 (*J*=7.9 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 83.8. HRMS (ESI): *m/z* calcd for $C_{28}H_{31}ClO_4PS$ $[M+H]^+$ 530.0358, found 530.0372. Anal. Calcd for $C_{28}H_{30}ClO_4PS$: C 63.57, H 5.72. Found: C 63.64, H 5.67.

5-(Diphenylphosphinoyl)-5-(2-hydroxypropyl)-3-methyl-4-phenylsulfenyl-furan-2(5*H*)-one 8b. Yellow oil, yield: 26%. Eluent for TLC: EtOAc:hexane = 1:2, R_f 0.67; IR (neat, cm^{-1}): 1123 (C-O-C), 1177 (P=O), 1439, 1490 (Ph), 1622 (C=C), 1746 (C=O), 3395 (OH). ^{1}H NMR (600.1 MHz): δ 1.41 (d, *J*=6.3 Hz, 3H, MeCH), 2.30 (s, 3H, MeC=), 2.42-2.66 (m, 2H, CH_2), 4.07-4.19 (m, 1H. MeCH), 5.01 (s, 1H, OH), 7.14-8.09 (m, 15H, 3Ph). ^{13}C NMR (150.9 MHz): δ 17.2 (*J*=4.6 Hz, CH_3), 25.2 (*J*=4.7 Hz, CH_3), 44.1 (*J*=8.8 Hz, CH_2), 67.2 (*J*=8.0 Hz, CH), 97.4 (*J*=127.0 Hz, C), 124.7 (*J*=8.2 Hz, C), 125.1-136.4 (3Ph), 173.4 (*J*=15.0 Hz, C), 174.7 (*J*=7.8 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 16.6. HRMS (ESI): *m/z* calcd for $C_{26}H_{26}O_4PS$ $[M+H]^+$ 465.5220, found 465.5209. Anal. Calcd for $C_{26}H_{25}O_4PS$: C 67.23, H 5.42. Found: C 67.16, H 5.36.

Procedure for Silver-catalyzed Cycloisomerization of the 4-Phosphorylated 6-Hydroxy-2-methylhepta-2,3-dienoates 3 and 4

Method A: Silver perchlorate (0.15 mmol) was added to a solution of the 4-phosphorylated 6-hydroxy-2-methylhepta-2,3-dienoates **3** or **4** (3.0 mmol) in dry CH_2Cl_2 (10 mL). The mixture was stirred at room temperature and in the dark for 7 h and 9 h. Saturated sodium chloride

solution was added to precipitate the silver ions. The product was extracted by $CHCl_3$. The organic layer was dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographed on a column with a mixture of EtOAc and hexane as an eluent to give the pure products **9** as oils.

Method B: The 4-phosphorylated 6-hydroxy-2-methylhepta-2,3-dienoates **3** or **4** (3.0 mmol) is dissolved in 40:60 water/acetone (10 mL) containing calcium carbonate (1 mmol) and silver nitrate (0.3 mmol). The mixture was stirred at room temperature and in the dark for 12 h and 15 h. The product is taken up in Et_2O and the ether solution is washed with saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate. After evaporation of the solvent, the residue was chromatographed on a column with a mixture of EtOAc and hexane as an eluent to give the pure products **9** as oils, which had the following properties:

Ethyl 4-(dimethylphosphoryl)-2,6-dimethyl-5,6-dihydro-2*H*-pyran-2-carboxylate 9a. Orange oil, yield: 74% (Method A), 51% (Method B). Eluent for TLC: EtOAc:hexane = 1:2, R_f 0.56; IR (neat, cm^{-1}): 1120 (C-O-C), 1259 (P=O), 1620 (C=C), 1726 (C=O). ^{1}H NMR (600.1 MHz): δ 1.25 (t, *J*=6.8 Hz, 3H, $\underline{Me}CH_2O$), 1.29-1.34 (m, 3H, $\underline{Me}CHO$), 1.57 (s, 3H, MeC), 2.30-2.57 (m, 2H, CH_2), 3.51-3.61 (m, 1H, $MeC\underline{H}O$), 3.73 (d, *J*=10.7 Hz, 6H, 2MeO), 4.18 (q, *J*=6.8 Hz, 2H, $MeC\underline{H_2}O$), 6.74-6.81 (m, 1H, =CH). ^{13}C NMR (150.9 MHz): δ 14.1 (CH_3), 22.5 (*J*=4.6 Hz, CH_3), 27.3 (*J*=5.0 Hz, CH_3), 36.4 (*J*=5.9 Hz, CH_2), 53.1 (*J*=15.1 Hz, $2CH_3$), 63.5 (CH_2), 66.0 (*J*=7.9 Hz, CH), 69.2 (*J*=7.9 Hz, C), 127.0 (*J*=173.5 Hz, C), 143.1 (*J*=8.1 Hz, CH), 176.1 (*J*=4.0 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 18.4. Anal. Calcd for $C_{12}H_{21}O_6P$: C 49.31, H 7.24. Found: C 49.43, H 7.22.

Ethyl 4-(diphenylphosphinoyl)-2,6-dimethyl-5,6-dihydro-2*H*-pyran-2-carboxylate 9b. Yellow oil, yield: 70% (Method A), 47% (Method B). Eluent for TLC: EtOAc:hexane = 1:2, R_f 0.48; IR (neat, cm^{-1}): 1124 (C-O-C), 1177 (P=O), 1440, 1494 (Ph), 1619 (C=C), 1724 (C=O). ^{1}H NMR (600.1 MHz): δ 1.25 (t, *J*=6.7 Hz, 3H, $\underline{Me}CH_2O$), 1.30-1.36 (m, 3H, $\underline{Me}CHO$), 1.59 (s, 3H, MeC), 2.33-2.58 (m, 2H, CH_2), 3.59-3.72 (m, 1H, $MeC\underline{H}O$), 4.15 (q, *J*=6.7 Hz, 2H, $MeC\underline{H_2}O$), 6.94-7.05 (m, 1H, =CH). 7.44-7.77 (m, 10H, 2Ph). ^{13}C NMR (150.9 MHz): δ 13.8 (CH_3), 21.8 (*J*=4.7 Hz, CH_3), 27.1 (*J*=5.2 Hz, CH_3), 39.2 (*J*=6.0 Hz, CH_2), 63.5 (CH_2), 70.5 (*J*=7.9 Hz, CH), 71.4 (*J*=7.8 Hz, C), 128.4-135.3 (2Ph), 132.7 (*J*=175.4 Hz, C), 144.5 (*J*=7.9 Hz, CH), 175.9 (*J*=4.6 Hz, C). ^{31}P NMR (242.9 MHz): δ_P 37.0. HRMS (ESI): *m/z* calcd for $C_{22}H_{26}O_4P$ $[M+H]^+$ 385.4132, found 385.4167. Anal. Calcd for $C_{22}H_{25}O_4P$: C 68.74, H 6.56. Found: C 68.89, H 6.71.

REFERENCES

1. H. Lecher, and F. Holschneider, *Ber. Dtsch. Chem. Ges.*, 1924, **57**, 755.
2. I. E. Ismailov, I. K. Ivanov, and V. C. Christov, *Bulg. Chem. Commun., Special Edition B*, 2017, **49**, 33.