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Trifunctionalized allenes. Part II. A practical regioselective synthesis of 4-phosphorylated β-hydroxyallenecarboxylates

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Dedicated to Prof. Dr. Toru Minami from Kyushu Institute of Technology, Tobata, Kitakyushu, Japan, on the occasion of his 80th anniversary

The paper discusses a practical regioselective synthesis of 4-phosphorylated 6-hydroxyhepta-2,3-dienoates by an atom-economical [2,3]-sigmatropic rearrangement of the mediated ethyl 2-(dimethoxyphosphanyl)oxy- or 2-(diphenylphosphino)oxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoates which can be easily prepared *via* reaction of the protected ethyl 2-hydroxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate with dimethyl chlorophosphite or chlorodiphenyl phosphine, respectively, in the presence of a base.

Keywords: synthesis, protection of hydroxy group, [2,3]-sigmatropic rearrangement, 4-phosphorylated 6-hydroxyhepta-2,3-dienoates.

INTRODUCTION

Allenes are considered to be unique compounds in organic chemistry due to their adjacent orthogonal π-bonds. During the last three decades synthesis and applications of allene derivatives have been increased in preparative organic chemistry. The availability of two π electron clouds that are separated by a single sp hybridized carbon atom is the main structural characteristic of allenes, and it is this unique structural and electronic arrangement that presupposes the extraordinary reactivity profile displayed by allenic compounds [1-5].

Functionalized allenes have provoked a growing interest because of their versatility as key building blocks for organic synthesis. Functionalized allenes could be used in a number of transformations due to their high reactive capacity. The synthetic capacity of functionalized allenes has been explored thoroughly in recent years, and this has led to the development of new methods in constructing a variety of functionalized heterocyclic and carbocyclic systems [6-11].

There are many methods which construct hydroxyallenes, including prototropic rearrangement of propargylic alcohols [12,13], metal-catalyzed nucleophilic addition of propargylic derivatives to aldehydes [14-18], Cu(I)-catalyzed reaction of propargylic chlorides with Grignard reagents [19,20], metal-catalyzed reaction of propargylic oxiranes with organometallic compounds [21-25] and ketones [26,27].

The most general methods for the synthesis of allenecarboxylates involve the Wittig [28-30], Wittig-Horner [31] or the Horner-Wadsworth-Emons [32] olefination of ketenes, iron-catalyzed olefination of ketenes with diazoacetate [33], etc. [34]. Also, there are methods for the synthesis of phosphorus-containing allenes (phosphonates [35-38], phosphinates [39,40], and phosphine oxides [41-46]) including reactions of α-alkynols with chloride-containing derivatives of phosphorus acids followed by [2,3]-sigmatropic rearrangement. Several diethylphosphono-substituted α-allenic alcohols were prepared by Brel [47,48] directly from alcohols by Horner-Mark rearrangement of unstable propargylic phosphites.

We have set in our research program on the chemistry of the trifunctionalized allenes to develop an efficient and regioselective method in order to introduce the phosphonate or phosphine oxide in the fourth-position, as well as the β-hydroxy group in the sixth position to the ester group of the allenecarboxylates. These groups provoke attention due to the useful functionalities in organic synthesis. More precisely, the focus is on the applications of these groups as temporary transformers of chemical reactivity of the allenic system in the synthesis of heterocyclic compounds.

Following our previous papers on the synthesis [49-52] and cyclization reactions [52-58] of bifunctionalized allenes, we have found a pragmatic synthesis of trifunctionalized allenes, namely the 4-phosphorylated β-hydroxyallenecarboxylates (4-phosphorylated 6-hydroxyhepta-2,3-dienoates).

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EXPERIMENTAL

General information

All newly synthesized compounds were purified by column chromatography and characterized on the basis of NMR, IR, and microanalytical data. NMR spectra were recorded on DRX Bruker Avance-250 (^{1}H at 250.1 MHz, ^{13}C at 62.9 MHz, ^{31}P at 101.2 MHz) and Bruker Avance II+600 (^{1}H at 600.1 MHz, ^{13}C at 150.9 MHz, ^{31}P at 242.9 MHz) spectrometers for solutions in $CDCl_3$. All ^{1}H and ^{13}C NMR experiments were performed referring to the signal of internal TMS and ^{31}P NMR experiments were performed referring to the signal of external 85% H_3PO_4. *J* values are given in Hertz. IR spectra were recorded with an FT-IR Afinity-1 Shimadzu spectrophotometer. Elemental analyses were carried out by the Microanalytical Service Laboratory using Vario EL*3* CHNS(O). Column chromatography was performed on Kieselgel F25460 (70–230 mesh ASTM, 0.063-0.200 nm, Merck). Et_2O and THF were distilled from Na wire/benzophenone, CH_2Cl_2 was distilled over CaH_2, and other organic solvents used in this study were dried over appropriate drying agents by standard methods and distilled prior to use. All other chemicals used in this study were commercially available and were used without additional purification unless otherwise noted. 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). Procedure for the synthesis of the 2-(1-methyl-but-3-ynyloxy)-tetrahydro-2*H*-pyran **2** (87% yield) by protection of the hydroxy-group in treatment of the pent-4-yn-2-ol **1** with DHP (3,4-dihydro-2*H*-pyran) in the presence of PPTS (pyridinium *p*-toluenesulfonate) as a catalyst is described in the literature [59-62].

Procedure for synthesis of ethyl 2-hydroxy-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hept-3-ynoate **5**

Ethylmagnesium bromide [prepared from magnesium (1.2 g, 50.0 mmol) and ethyl bromide (5.5 g, 50.0 mmol) in dry THF (50 mL)] was added dropwise under stirring to 2-(1-methyl-but-3-ynyloxy)-tetrahydro-2*H*-pyran **2** (50.0 mmol) and then the mixture was refluxed for 2 h. The solution of the prepared alkynyl magnesium bromides was added dropwise under stirring to ethyl 2-oxopropanoate **4** (100.0 mmol). The mixture was refluxed for 2 h and after cooling was hydrolyzed with a saturated aqueous solution of ammonium chloride. The organic layer was separated, washed with water, and dried over anhydrous sodium sulfate. Solvent and the excess of the ester were removed by distillation. Purification of the residue was achieved by column chromatography (silica gel, Kieselgel Merck 60 F254) with ethyl acetate-hexane. The pure product **5** had the following properties:

Ethyl 2-hydroxy-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hept-3-ynoate (**5**). Colourless oil, yield: 78%. Eluent for TLC: ethyl acetate:hexane = 1:9, R_f 0.48; IR (neat, cm^{-1}): 1123 (C-O-C), 1443, 1490 (Ph), 1723 (C=O), 2251 (C≡C), 3412 (OH). ^{1}H-NMR (250.1 MHz): δ_H 1.12-1.23, 3.64-3.74, 4.81-4.90 (overlapping multiplets, 9H, OTHP), 1.21 (t, *J*=6.4 Hz, 3H, MeCH_2O), 1.27 (d, *J*=6.9 Hz, 3H, MeCHO), 1.54 (s, 3H, MeC-OH), 2.64-2.73 (m, 2H, CH_2), 3.79-3.86 (m, 1H, OCHMe), 4.27-4.36 (m, 2H, OCH_2Me), 4.52 (s, 1H, OH). ^{13}C-NMR (62.9 MHz) δ_C 14.0 (CH_3), 19.1 (CH_2), 22.5 (CH_3), 25.7 (CH_3), 25.9 (CH_2), 26.2 (CH_3), 31.7 (CH_2), 62.5 (CH_2), 63.2 (CH_2), 72.1 (C), 76.2 (CH), 77.1 (C), 78.3 (C), 96.1 (CH), 165.8 (C). Anal. Calcd for $C_{15}H_{24}O_5$ requires: C 63.36, H 8.51. Found: C 63.42, H 8.55.

Procedure for synthesis of ethyl 4-(dimethylphosphoryl)-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hepta-2,3-dienoate **7**

To a solution of phosphorus trichloride (2.75 g, 20 mmol) and triethylamine (2.23 g, 22 mmol) in dry diethyl ether (60 mL) a solution of ethyl 2-hydroxy-2-methyl-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **5** (20 mmol) in the same solvent (20 mL) was added dropwise at -70^{o}C with stirring. After 30 min of stirring at the same conditions a solution of pyridine (3.16 g, 44 mmol) and of methanol (1.28 g, 40 mmol) in dry diethyl ether (50 mL) were added. The reaction mixture was stirred for an hour at the same temperature and for 4 h at room temperature. The mixture was then washed with water, 2N HCl, extracted with ether, washed with saturated NaCl, and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographied on a column (silica gel, Kieselgel Merck 60 F_{254}) with a mixture of ethyl acetate and hexane as an eluent to give the pure product **7** as oil, which had the following properties:

Ethyl 4-(dimethylphosphoryl)-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hepta-2,3-dienoate (**7**). Orange oil, yield: 70%. Eluent for TLC: ethyl acetate:hexane = 1:4, R_f 0.43; IR (neat, cm^{-1}): 1125 (C-O-C), 1260 (P=O), 1439, 1491 (Ph), 1727 (C=O), 1952 (C=C=C). ^{1}H-NMR (600.1 MHz): δ_H 1.12-1.25, 3.64-3.77, 4.54-4.61 (overlapping multiplets, 9H, OTHP), 1.27 (t, *J*=6.6 Hz, 3H, MeCH_2O), 1.26-1.29 (m, 3H, Me-CHO), 1.89-1.94 (m, 3H, Me-C=), 2.47-2.64 (m, 2H, CH_2), 3.80 (d,

J=12.7 Hz, 6H, 2MeO), 4.06-4.14 (m, 2H, MeC<u>H</u>$_2$O), 4.36-4.43 (m, 1H, MeC<u>H</u>O). ^{13}C-NMR (150.9 MHz) δ_C 14.1 (CH_3), 16.4 (*J*=4.7 Hz, CH_3), 19.0 (CH_2), 22.8 (CH_3), 24.6 (CH_2), 30.7 (CH_2), 37.5 (*J*=5.6 Hz, CH_2), 52.2 (*J*=14.7 Hz, CH_3), 59.8 (CH_2), 62.5 (CH_2), 69.2 (*J*=8.1 Hz, CH), 93.8 (*J*=182.7 Hz, C), 95.9 (CH), 97.1 (*J*=7.8 Hz, C), 166.9 (*J*=5.0 Hz, C), 218.0 (*J*=0.8 Hz, C). ^{31}P-NMR (242.9 MHz): δ_P 24.9. Anal. Calcd for $C_{17}H_{29}O_7P$ requires: C 54.25, H 7.77. Found: C 54.28, H 7.73.

Procedure for the synthesis of ethyl 4-(diphenylphosphinoyl)-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hepta-2,3-dienoate **9**

To a solution of ethyl 2-hydroxy-2-methyl-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **5** (20 mmol) and triethylamine (2.23 g, 22 mmol) in dry diethyl ether (60 mL) at -70°C, a solution of freshly distilled diphenylchloro phosphine (4.41 g, 20 mmol) in the same solvent (20 mL) was added dropwise with stirring. The reaction mixture was stirred for an hour at the same temperature and for 6 h at room temperature and then washed with water, 2N HCl, extracted with diethyl ether, and the extract was washed with saturated NaCl, and dried over anhydrous sodium sulfate. The solvent was removed using a rotatory evaporator, and the residue was purified by column chromatography on silica gel (Kieselgel Merck 60 F_{254}) with ethyl acetate-hexane to give the pure product **9** as oil, which had the following properties:

Ethyl 4-(diphenylphosphinoyl)-2-methyl-6-(tetrahydro-2H-pyran-2-yloxy)-hepta-2,3-dienoate (**9**). Colourless oil, yield: 76%. Eluent for TLC: ethyl acetate:hexane = 1:1, R_f 0.51; IR (neat, cm^{-1}): 1121 (C-O-C), 1178 (P=O), 1439, 1485 (Ph), 1715 (C=O), 1939 (C=C=C). ^{1}H-NMR (600.1 MHz): δ_H 1.11-1.24, 3.63-3.80, 4.56-4.63 (overlapping multiplets, 9H, OTHP), 1.24 (t, *J*=6.8 Hz, 3H, <u>Me</u>CH$_2$O), 1.28 (m, 3H, <u>Me</u>-CHO), 1.90-1.94 (m, 3H, Me-C=), 2.46-2.66 (m, 2H, CH_2), 4.11-4.22 (m, 2H, MeC<u>H</u>$_2$O), 4.27-4.37 (m, 1H, Me-C<u>H</u>), 7.46-7.94 (m, 10H, 2Ph). ^{13}C-NMR (150.9 MHz) δ_C 14.3 (CH_3), 16.3 (*J*=4.6 Hz, CH_3), 19.0 (CH_2), 23.0 (CH_3), 25.4 (CH_2), 30.8 (CH_2), 39.8 (*J*=6.0 Hz, CH_2), 60.0 (CH_2), 62.8 (CH_2), 72.8 (*J*=7.7 Hz, CH), 93.6 (*J*=183.2 Hz, C), 94.8 (CH), 101.5 (*J*=7.9 Hz, C), 128.9-135.1 (2Ph), 166.5 (*J*=5.0 Hz, C), 211.5 (*J*=0.6 Hz, C). ^{31}P-NMR (242.9 MHz): δ_P 31.3. Anal. Calcd for $C_{27}H_{33}O_5P$ requires: C 69.22, H 7.10. Found: C 69.28, H 7.15.

Procedure for the synthesis of ethyl 4-(dimethylphosphoryl)-6-hydroxy-2-methyl-hepta-2,3-dienoate **10** *and ethyl 4-(diphenylphosphinoyl)-6-hydroxy-2-methyl-hepta-2,3-dienoate* **11**

A solution of ethyl 4-(dimethylphosphoryl)-2-methyl-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **7** or ethyl 4-(diphenylphosphinoyl)-2-methyl-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **9** (5 mmol) and PPTS (0.5 mmol) in ethanol (10 mL) was stirred at room temperature for 5 h. The mixture was then washed with water, extracted with methylene chloride and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographied on a column (silica gel, Kieselgel Merck 60 F_{254}) with a mixture of ethyl acetate and hexane as an eluent to give the pure products **10** or **11** as oils, which had the following properties:

Ethyl 4-(dimethylphosphoryl)-6-hydroxy-2-methyl-hepta-2,3-dienoate (**10**). Yellow oil, yield: 85%. Eluent for TLC: ethyl acetate:hexane = 1:4, R_f 0.62; IR (neat, cm^{-1}): 1260 (P=O), 1437, 1490 (Ph), 1724 (C=O), 1949 (C=C=C), 3392 (OH). ^{1}H-NMR (600.1 MHz): δ_H 1.16 (d, *J*=6.1 Hz, 3H, <u>Me</u>CHO), 1.25 (t, *J*=6.2 Hz, 3H, <u>Me</u>CH$_2$O), 1.87-1.92 (m, 3H, Me-C=), 2.50-2.70 (m, 2H, CH_2), 2.92 (s, 1H, OH), 3.79 (d, *J*=12.9 Hz, 6H, 2MeO), 4.07-4.15 (m, 2H, MeC<u>H</u>$_2$O), 4.31-4.37 (m, 1H, Me-C<u>H</u>). ^{13}C-NMR (150.9 MHz) δ_C 14.3 (CH_3), 16.7 (*J*=4.6 Hz, CH_3), 23.2 (*J*=4.7 Hz, CH_3), 38.0 (*J*=5.6 Hz, CH_2), 52.1 (*J*=14.9 Hz, CH_3), 60.6 (CH_2), 61.5 (*J*=7.9 Hz, CH), 92.9 (*J*=182.5 Hz, C), 98.1 (*J*=7.9 Hz, C), 167.1 (*J*=4.8 Hz, C), 217.7 (*J*=0.7 Hz, C). ^{31}P-NMR (242.9 MHz): δ_P 24.3. Anal. Calcd for $C_{12}H_{21}O_6P$ requires: C 49.31, H 7.24. Found: C 49.26, H 7.20.

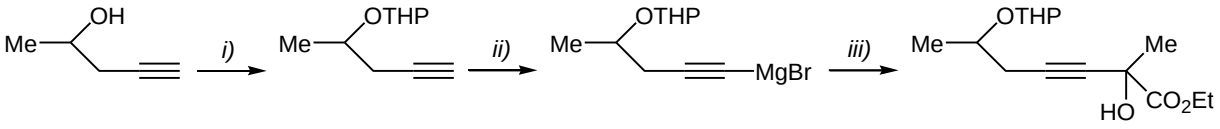
Ethyl 4-(diphenylphosphinoyl)-6-hydroxy-2-methyl-hepta-2,3-dienoate (**11**). Colourless oil, yield: 89%. Eluent for TLC: ethyl acetate:hexane = 1:2, R_f 0.62; IR (neat, cm^{-1}): 1179 (P=O), 1439, 1485 (Ph), 1719 (C=O), 1941 (C=C=C), 3389 (OH). ^{1}H-NMR (600.1 MHz): δ_H 1.20 (d, *J*=6.1 Hz, 3H, <u>Me</u>-CHO), 1.25 (t, *J*=6.7 Hz, 3H, <u>Me</u>CH$_2$O), 1.88-1.93 (m, 3H, Me-C=), 2.44-2.63 (m, 2H, CH_2), 2.84 (s, 1H, OH), 4.10-4.16 (m, 2H, MeC<u>H</u>$_2$O), 4.18-4.24 (m, 1H, Me-C<u>H</u>O), 7.43-7.88 (m, 10H, 2Ph). ^{13}C-NMR (150.9 MHz) δ_C 14.4 (CH_3), 16.0 (*J*=4.7 Hz, CH_3), 22.8 (*J*=4.6 Hz, CH_3), 40.0 (*J*=5.7 Hz, CH_2), 59.9 (CH_2), 71.5 (*J*=7.6 Hz, CH), 95.4 (*J*=183.4 Hz, C), 128.5-134.6 (2Ph), 165.8 (*J*=4.9 Hz, C), 167.2 (*J*=4.8 Hz, C), 210.5 (*J*=0.7 Hz, C). ^{31}P-NMR (242.9 MHz): δ_P 31.5. Anal. Calcd for $C_{22}H_{25}O_4P$ requires: C 68.74, H 6.56. Found: C 68.78, H 6.63.

RESULTS AND DISCUSSION

In order to assess the approach towards the target 1,1,3-trifunctionalized allenes, a range of 4-phosphorylated 6-hydroxy-allenecarboxylates **7**, **9**, **10**, and **11** were prepared by the following four-step

procedure including: i) protection of hydroxy group in pent-4-yn-2-ol; ii) subsequent reaction with Grignard reagent and ethyl 2-oxopropanoate to give ethyl 2,6-dihydroxy-hept-3-ynoate with protected hydroxy group at sixth position; iii) interaction with chloride of phosphorus acid in the presence of a base; and finally iv) [2,3]-sigmatropic rearrangement of the mediated protected ethyl 2-(dimethoxyphosphanyl)oxy- or 2-(diphenylphosphino)oxy-6-hydroxy-hept-3-ynoates.

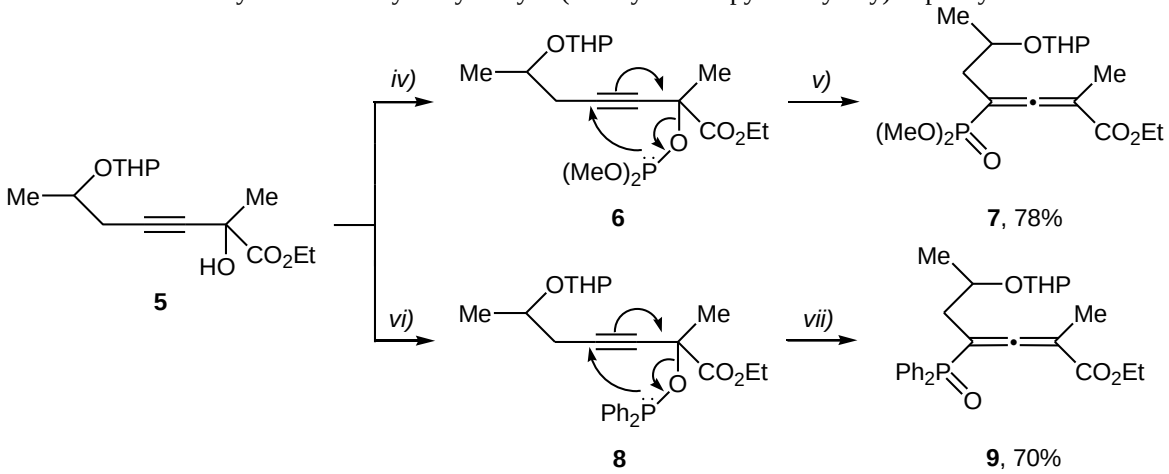
As a starting point for our investigation, we first examined the protection of hydroxy group in pent-4-yn-2-ol **1** with DHP in the presence of PPTS [59-62] (Scheme 1). Thus, the 2-(but-3-ynyloxy)-tetrahydro-2*H*-pyran formed **2** was isolated by column chromatography with very good yield (87%). Reaction of the protected alkynols **2** with ethyl magnesium bromide and subsequent dropwise addition of *in situ* generated alkynyl magnesium bromide **3** to ethyl 2-oxopropanoate **4** and reflux for 2 h gives the ethyl 2-hydroxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoates **5**, which are stable and were isolated by column chromatography in 78% yields as is shown in Scheme 1. With the required ethyl 2,6-dihydroxy-hept-3-ynoate **5** with protected hydroxy group at sixth position in hand, we were then able to investigate the proposed reactions with the corresponding chloro-containing phosphorus reagents such as dimethyl chlorophosphite and chlorodiphenyl phosphine in the presence of a base and subsequent [2,3]-sigmatropic rearrangement of the mediated phosphites **6** or phosphonites **8**.



1 **2**, 87% **3** **5**, 78%

Reagents and conditions: *i)* DHP (1.5 eq), PPTS (0.1 eq), CH_2Cl_2, rt, 2h, distillation; *ii)* EtMgBr (1 eq), THF, reflux, 2h; *iii)* dropwise addition of **3** to $MeC(O)CO_2Et$ (**4**) (2 eq), reflux, 2h, column chromatography.

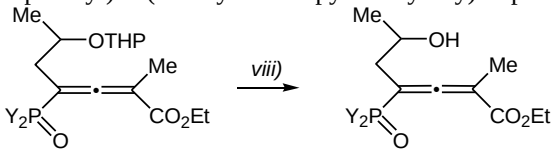
Scheme 1. Synthesis of ethyl 2-hydroxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **5**



5 **6** **7**, 78% **8** **9**, 70%

Reagents and conditions: *iv)* PCl_3 (1 eq), Et_3N (1.1 eq), Et_2O, -70 °C, 30 min stirring, pyridine (2.2 eq), MeOH (2 eq), Et_2O, -70 °C; *v)* [2,3-σ]-rearrangement, -70 °C, 1h, rt, 4h, column chromatography; *iv)* Ph_2PCl (1 eq), Et_3N (1.1 eq), Et_2O, -70 °C; *v)* [2,3-σ]-rearrangement, -70 °C, 1h, rt, 6h, column chromatography.

Scheme 2. Synthesis of ethyl 4-(dimethylphosphoryl)-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **7** and ethyl 4-(diphenylphosphinoyl)-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **9**



7, **9** **10**, Y=MeO, 85% **11**, Y=Ph, 89%

Reagents and conditions: *viii)* PPTS (0.1 eq), EtOH, rt, 6h, stirring, column chromatography.

Scheme 3. Synthesis of ethyl 4-(dimethylphosphoryl)-6-hydroxyhepta-2,3-dienoate **10** and ethyl 4-(diphenylphosphinoyl)-6-hydroxyhepta-2,3-dienoate **11**

In the first instance, the ethyl 4-(dimethylphosphoryl)-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **7** can be readily prepared *via* an atom-economical 2,3-sigmatropic rearrangement of the ethyl 2-(dimethoxyphosphanyl)oxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **6**, intermediate formed by reaction of the ethyl 2-hydroxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **5** with dimethyl chlorophosphite, prepared *in situ* from phosphorus trichloride and 2 *equiv* of methanol in the presence of triethylamine, and 2 *equiv* of pyridine, according to Scheme 2.

Next, the reaction of ethyl 2-hydroxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **5** with chlorodiphenyl phosphine in the presence of triethylamine at -70^{o}C gave the expected ethyl 4-(diphenylphosphinoyl)-2-methyl-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **9** in very good yield (70%) as a result of [2,3]-sigmatropic rearrangement of the ethyl 2-(diphenylphosphino)oxy-6-(tetrahydro-2*H*-pyran-2-yloxy)-hept-3-ynoate **8** for 6 h at room temperature, according to the reaction sequence outlined in Scheme 2.

A new family of 4-phosphorylated 6-hydroxyhepta-2,3-dienoates with protected hydroxy group **7** and **9** were synthesized *via* an atom-economical and regioselective [2,3]-sigmatropic rearrangement of the intermediate formed hydroxy- and carboxy-substituted propargyl phosphites **6** or phosphinites **8** in the reaction of protected hydroxy- and carboxy-substituted alkynols **5** with dimethylchloro phosphite or chlorodiphenyl phosphine in the presence of triethylamine. Compounds **7** and **9** were stable enough to be handled at ambient temperature. The hydroxy group was deprotected by stirring the ethanol solution of the protected ethyl 4-(dimethylphosphoryl)- or 4-(diphenylphosphinoyl)-6-(tetrahydro-2*H*-pyran-2-yloxy)-hepta-2,3-dienoate **7** or **9** in the presence of 0.1 *equiv* PPTS at room temperature for 6 h to give the ethyl 4-(dimethylphosphoryl)-6-hydroxy-hepta-2,3-dienoate **10** and the ethyl 4-(diphenylphosphinoyl)-6-hydroxy-hepta-2,3-dienoate **11**, according to Scheme 3.

After a conventional work-up, all allenic products **7**, **9**, **10**, and **11** were isolated by column chromatography as stable yellow, orange or colourless oils and identified by ^{1}H, ^{13}C, and ^{31}P NMR and IR spectra, as well as by elemental analysis.

A series of new 4-phosphorylated 6-hydroxyhepta-2,3-dienoates with protected **7** and **9** and unprotected hydroxy group **10** and **11** were synthesized by a convenient, expedient, atom-economical and regioselective method.

CONCLUSIONS

In conclusion, we could state that a convenient and practical regioselective synthesis of a new family of 1,1,3-trifunctionalized allenes has been explored. 4-Phosphorylated 6-hydroxyhepta-2,3-dienoates were derived from [2,3]-sigmatropic rearrangement of the intermediate hydroxy- and carboxy-substituted propargyl phosphites or phosphinites formed in the reaction of protected hydroxy- and carboxy-substituted alkynols with dimethylchloro phosphite or chlorodiphenyl phosphine in the presence of a base.

Currently, we are working on further progress of this potentially important synthetic methodology. At the same time, we are making research on the synthetic application of the prepared 4-phosphorylated 6-hydroxyhepta-2,3-dienoates with protected or unprotected hydroxy group for synthesis of different heterocyclic compounds in our laboratory as a part of our general synthetic strategy for studying the nature of the electrophilic cyclization and cycloisomerization reactions of trifunctionalized allenes. The results will be reported in due course. What could be emphasied on is that the results of the preliminary study of the biological activity of the compounds are encouraging. It is the antibacterial and antifungal activities of selected compounds, as well as the potential precursors of effective anticancer drugs that are currently analysed by our University researchers.

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REFERENCES

1. S. Patai (ed.), The Chemistry of Ketenes, Allenes and Related Compounds, John Wiley & Sons, New York, 1980.
2. S. R. Landor (ed.), The Chemistry of the Allenes, Vol. 1–3, Academic Press, London, 1982.
3. H. F. Schuster, G. M. Coppola, Allenes in Organic Synthesis, John Wiley & Sons, New York, 1988.
4. C. J. Elsevier, in: (Houben-Weyl) Methods of Organic Chemistry, R. W. Helmchen; J. Mulzer, E. Schaumann (eds.), Vol. E21a, Thieme, Stuttgart, 1995, p. 537.

5. N. Krause, A. S. K. Hashmi, (eds.), Modern Allene Chemistry, Vol. 1 and 2, Wiley-VCH, Weinheim, 2004.
6. R. W. Bates, V. Satcharoen, *Chem. Soc. Rev.*, **31**, 12 (2002).
7. N. Krause, A. S. K. Hashmi (eds.), Modern Allene Chemistry, Wiley-VCH, Weinheim, 2004, Vol. 1 & 2.
8. S. Ma, *Aldrichimica Acta*, **40**, 91 (2007).
9. K. M. Brummond, J. E. DeForrest, *Synthesis*, 795 (2007).
10. T. M. V. D. Pinho e Melo, *Curr. Org. Chem.*, **13**, 1406 (2009);
11. T. G. Back, K. N. Clary, D. Gao, *Chem. Rev.*, **110**, 4498 (2010).
12. S. Phadtare, J. Zemlicka, *J. Am. Chem. Soc.*, **111**, 5925 (1989).
13. S. Ma, H. Hou, S. Zhao, G. Wang, *Synthesis*, 1643 (2002).
14. P. Crabbé, H. Fillion, D. André, J.-L. Luche, *J. Chem. Soc. Chem. Commun.*, 859 (1979).
15. Y. Deng, X. Jin, S. Ma, *J. Org. Chem.*, **72**, 5901 (2007).
16. A. Alexakis, I. Marek, P. Mangeney, J. F. Normant, *Tetrahedron*, **47**, 1677 (1991).
17. J. A. Marshall, K. G. Pinney, *J. Org. Chem.*, **58**, 7180 (1993).
18. C. Deutsch, B. H. Lipshutz, N. Krause, *Angew. Chem. Int. Ed.*, **46**, 1650 (2007)
19. J. Ye, S. Li, B. Chen, W. Fan, J. Kuang, J. Liu, Y. Liu, B. Miao, B. Wan, Y. Wang, X. Xie, Q. Yu, W. Yuan, S. Ma, *Org. Lett.*, **14**, 1346 (2012).
20. G. P. Boldrini, L. Lodi, E. Tagliavini, C. Tarasco, C. Trombini, A. Umanl-Ronchi, *J. Org. Chem.*, **52**, 5447 (1987).
21. R. W. Hoffman, U. Weldmann, *Chem. Ber.*, **118**, 3966 (1985).
22. E. J. Corey, R. Imwinkelried, S. Pikul, Y. B. Xiang, *J. Am. Chem. Soc.*, **111**, 5493 (1989).
23. E. J. Corey, C.-M. Yu, D.-H. Lee, *J. Am. Chem. Soc.*, **112**, 878 (1990).
24. E. J. Corey, G. B. Jones, *Tetrahedron Lett.*, **32**, 5713 (1991).
25. J. Li, W. Kong, C. Fu, S. Ma, *J. Org. Chem.*, **74**, 5104 (2009).
26. J. Li, C. Zhou, C. Fu, S. Ma, *Tetrahedron*, **65**, 3695 (2009).
27. A. Alexakis, I. Marek, P. Mangeney, J. F. Normant, *Tetrahedron Lett.*, **30**, 2387 (1989).
28. H. J. Bestmann, H. Hartung, *Angew. Chem. Int. Ed. Engl.*, **2**, 214 (1963).
29. G. Aksnes, P. Froeyen, *Acta Chim. Scand.*, **22**, 2347 (1968).
30. R. W. Lang, H. -J. Hansen, *Helv. Chim. Acta*, **63**, 438 (1980).
31. H. Fillion, A. Hseine, M. -H. Pera, V. Dufaud, B. Refouvelet, *Synthesis*, 708 (1987).
32. K. Tanaka, K. Otsubo, K. Fuji, *Synlett*, 933 (1995).
33. C. -Y. Li, X. -B. Wang, X. -L. Sun, Y. Tang, J. -C. Zheng, Z. -H. Xu, Y. -G. Zhou, L. -X. Dai, *J. Am. Chem. Soc.*, **129**, 1494 (2007).
34. M. Miesch, Synthesis, 746 (2003) and references cited therein.
35. R. Zimmer, *Synthesis*, 165 (1993).
36. J. A. Marshall, Y. Tang, *J. Org. Chem.*, **58**, 3233 (1993).
37. V. Mark, The Uncatalyzed Rearrangements of Tervalent Phosphorus Esters, in: Selective Organic Transformations, B. S. Thyagarajan (ed.), John Wiley & Sons, New York, 1970, p. 319.
38. P. D. Landor, in: The Chemistry of the Allenes, Vol. 1, S. R. Landor (ed.), Academic Press, New York, 1982, p. 174.
39. R. W. Saalfrank, C.-J. Lurz, in: Methoden der Organischen Chemie (Houben Weyl), H. Kropf, E. Scheumann (eds.), Thieme, Stuttgart, 1993, p. 2959.
40. A. S. K. Hashmi, Synthesis of Allenes, in: Modern Allene Chemistry, Vol. 1, N. Krause, A. S. K. Hashmi (eds.), Wiley-VCH, Weinheim, 2004, p. 3.
41. R. S. Macomber, *J. Am. Chem. Soc.*, **99**, 3072 (1977).
42. S. E. Denmark, J. E. Marlin, *J. Org. Chem.*, **56**, 1003 (1991).
43. B. Cai, G. M. Blackburn, *Synth. Commun.*, **27**, 3943 (1997).
44. R. W. Saalfrank, M. Haubner, C. Deutscher, U. Bauer, *Eur. J. Org. Chem.*, 2367 (1999).
45. A. P. Boiselle, N. A. Meinhardt, *J. Org. Chem.*, **27**, 1828 (1962).
46. V. Mark, *Tetrahedron Lett.*, **3**, 281 (1962).
47. K. C. Nicolaou, P. Maligres, J. Shin, E. de Leon, D. Rideout, *J. Am. Chem. Soc.*, **112**, 7825 (1990).
48. M. L. Curfin, W. H. Okamura, *J. Org. Chem.*, **55**, 5278 (1990).
49. I. E. Ismailov, I. K. Ivanov, V. Ch. Christov, *Molecules*, **19**, 6309 (2014).
50. I. E. Ismailov, I. K. Ivanov, V. Ch. Christov, *Bulg. Chem. Commun.*, **46**, Special Issue A, 39 (2014).
51. I. E. Ismailov, I. K. Ivanov, V. Ch. Christov, *Bulg. Chem. Commun.*, **49**, Special Issue B, **49**, 25 (2017).
52. I. K. Ivanov, I. D. Parushev, V. Ch. Christov, *Heteroatom. Chem.*, **24**, 322 (2013).
53. I. E. Ismailov, I. K. Ivanov, V. Ch. Christov, *Molecules*, **19**, 11056 (2014).
54. V. Ch. Christov, I. E. Ismailov, I. K. Ivanov, *Molecules*, **20**, 7263 (2015).
55. I. K. Ivanov, I. D. Parushev, V. Ch. Christov, *Heteroatom. Chem.*, **25**, 60 (2014).
56. H. H. Hasanov, I. K. Ivanov, V. Ch. Christov, *Heteroatom. Chem.* **28**, e21357 (2017).
57. H. H. Hasanov, I. K. Ivanov, V. Ch. Christov, *Phosphorus, Sulfur, Silicon* **193**, 611 (2018).
58. H. H. Hasanov, I. K. Ivanov, V. Ch. Christov, *Phosphorus, Sulfur, Silicon* **193**, 797 (2018).
59. D. N. Robertson, *J. Org. Chem.*, **25**, 931 (1960).
60. M. Miyashita, A. Yoshikoshi, P. A. Griecolb, *J. Org. Chem.*, **42**, 3772 (1977).
61. M. C. Joshi, P. Joshi, D. S. Rawat, *ARKIVOC*, **xvi**, 65 (2006).
62. B. Partha, I. Pimkov, *US Patent 8378123 B2* (2011).