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Bifunctionalized allenes. Part XIV. A convenient and efficient regioselective synthesis of phosphorylated β-hydroxyallenes with protected and unprotected hydroxy group

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Dedicated to Acad. Dimiter Ivanov on the occasion of his 120th birth anniversary

A convenient and efficient regioselective synthesis of phosphorylated β-hydroxyallenes by an atom economical [2,3]-sigmatropic rearrangement of the mediated propargyl phosphite or phosphinite which can be readily prepared *via* reaction of protected 5-methyl-dec-6-yn-5-ol with dimethyl chlorophosphite or chlorodiphenyl phosphine respectively in the presence of a base is described.

Key words: synthesis, protection of hydroxy group, [2,3]-sigmatropic rearrangement, phosphorylated β-hydroxyallenes

INTRODUCTION

In the past three decades, synthesis and use of allene derivatives have been expanded in preparative organic chemistry. The presence of two π electron clouds separated by a single sp hybridized carbon atom is the identifying structural characteristic of allenes, and it is this unique structural and electronic arrangement that is responsible for the extraordinary reactivity profile displayed by allenic compounds [1-8].

Functionalized allenes have attracted a growing attention because of their versatility as key building blocks for organic synthesis. The synthetic potential of functionalized allenes has been explored extensively in recent years, and this has led to the development of novel methods for the construction of a variety of functionalized heterocyclic and carbocyclic systems [9-13].

A plethora of methods exists for the construction of hydroxyallenes, including prototropic rearrangement of propargylic alcohols [14,15], metal-catalyzed nucleophilic addition of propargylic derivatives to aldehydes [16-22], Cu(I)-catalyzed reaction of propargylic chlorides with Grignard reagents [23,24], metal-catalyzed reaction of propargylic oxiranes with organometallic compounds [25-29] and ketones [30,31], reduction of alcohols, ethers, oxiranes etc. with aluminium reagents [32-34], Pd(0)-catalyzed reaction of cyclic carbonates with acetylenic compounds [35,36], S_N2'[37,38] and A_N [39-41] reactions of metalled alkoxy-allenes with oxiranes and ketones [5], and by other methods [42].

There are methods [43-46] for the synthesis of phosphorus-containing allenes (phosphonates [47-50], phosphinates [51,52], and phosphine oxides [53-58]) 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 [59,60] directly from alcohols by Horner-Mark rearrangement of unstable propargylic phosphites.

Since its discovery five decades ago [51,52], the reversible interconversion of propargylic phosphites, phosphonites and phosphinites to allenyl phosphonates, phosphinates and phosphine oxides has become one of the most studied and synthetically useful [2,3]-sigmatropic rearrangement. Numerous synthetic applications of the rearrangement have been reported, including its use in the synthesis of allenic steroids as substrate-induced inactivation of aromatase [61], in the efficient synthesis of (2*R*)-2-amino-5-phosphonopentanoic acid (AP5) as a powerful and selective N-methyl-*D*-aspartate (NM*D*A) antagonist [62], in the preparation of the phosphonate analogues of phosphatidyl derivatives [63,64], and in the synthesis of new acyclic analogues of nucleotides containing a purine or pyrimidine moiety and an allenic skeleton [65,66].

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As a part of our research program on the chemistry of the bifunctionalized allenes, we required a convenient method to introduce a phosphorus-containing group such as phosphonate or phosphine oxide group as well as a β-hydroxy-alkyl group in the first position to the allenic system of double bonds. The above mentioned groups attract increasing attention as useful functionalities in organic synthesis. Of particular interest are the applications of these groups as temporary transformers of chemical reactivity of the allenic system in the synthesis of eventually heterocyclic compounds.

In a continuation to our previous reports on the synthesis [67] and electrophilic cyclization reactions [68] of bifunctionalized allenes, we have found a convenient and efficient method for regioselective synthesis of phosphorylated β-hydroxy-allenes by an atom economical [2,3]-sigmatropic rearrangement of the mediated 4-(tetrahydro-2*H*-pyran-2-yloxy)-propargyl phosphite or phosphinite.

EXPERIMENTAL

General information

All new synthesized compounds were purified by column chromatography and characterized on the basis of NMR, IR, and microanalytical data. NMR spectra were recorded on DRX Brucker Avance-250 (Bruker BioSpin, Karlsruhe, Germany) (^{1}H at 250.1 MHz, ^{13}C at 62.9 MHz, ^{31}P at 101.2 MHz) and Brucker Avance II+600 (Bruker BioSpin GmbH, Karlsruhe, Germany) (^{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 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 (Shimadzu, Tokyo, Japan). Elemental analyses were carried out by the Microanalytical Service Laboratory of Faculty of Chemistry and Pharmacy, University of Sofia, Bulgaria, using Vario EL*3* CHNS(O) (Elementar Analysensysteme, Hanau, Germany). Column chromatography was performed on Kieselgel F_{254}60 (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, other commercially available chemicals 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 [21] *for synthesis of 2-(1-methyl-but-3-yn-1-yloxy)-tetrahydro-2H-pyran* **2**

A solution of the pent-4-yn-2-ol **1** (60 mmol) and DHP (3,4-dihydro-2*H*-pyran) (7.57 g, 90 mmol) in dry methylene chloride (50 ml) containning PPTS (pyridinium *p*-toluenesulfonate) (1.50 g, 6 mmol) is stirred for 4 h at room temperature. Then the reaction was quenched with saturated $NaHCO_3$ end extracted with methylene chloride. The organic layer was dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographed on a column (silica gel, Kieselgel Merck 60 F_{254}) with a mixture of ethyl acetate and hexane (3:1) as an eluent. The pure product **2** had the following properties:

2-(1-Methyl-but-3-ynyloxy)-tetrahydro-2H-pyran (**2**). Colourless oil, yield: 87%. R_f 0.55. IR (neat, cm^{-1}): 1125 (C-O-C), 2106 (C≡C), 3292 (≡C-H). ^{1}H-NMR (250.1 MHz): δ = 1.09-1.25, 3.65-3.77, 4.74-4.81 (mmm, 9H, OTHP), 1.27 (d, *J* = 7.2 Hz, 3H, Me-CHO), 2.02 (m, 1H, H-C≡), 2.38, 2.59 (mm, 2H, CH-C≡), 3.80-3.89 (m, 1H, Me-CHO). ^{13}C-NMR (62.9 MHz) δ = 20.1 (CH_2), 22.7 (CH_3), 25.8 (CH_2), 26.4 (CH_2), 31.9 (CH_2), 63.8 (CH_2), 67.0 (CH), 75.2 (CH), 81.2 (C), 95.9 (CH). Anal. Calcd. for $C_{10}H_{16}O_2$ (168.23): C 71.39; H 9.59; found: C 71.32; H 9.65.

Synthesis of the 5-methyl-9-(tetrahydro-2H-pyran-2-yloxy)-dec-6-yn-5-ol **5**

Ethylmagnesium bromide [prepared from magnesium (1.22 g, 50 mmol) and ethyl bromide (5.50 g, 50 mmol) in dry THF (50 ml)] is added dropwise under stirring to substituted alkynyloxy-tetrahydro-2*H*-pyran **2** (50 mmol) and then the mixture is refluxed for 2 h. The solution of the prepared pentynyl magnesium bromide **3** is added dropwise under stirring to the hexan-2-one **4** (100 mmol). The mixture is refluxed for 24 h and after cooling is hydrolyzed with a saturated aqueous solution of ammonium chloride. The organic layer is separated, washed with water, and dried over anhydrous sodium sulfate. Solvent and the excess of ketone are removed by distillation. Purification of the residue is achieved by column chromatography (silica gel, Kieselgel Merck 60 F_{254}) with ethyl acetate and hexane (5:1). The pure product **5** had the following properties:

5-Methyl-9-(tetrahydro-2H-pyran-2-yloxy)-dec-6-yn-5-ol (**5**). Colourless oil, yield: 55%. R_f 0.51.

IR (neat, cm^{-1}): 1122 (C-O-C), 3408 (OH). ^{1}H-NMR (250.1 MHz): δ = 0.88 (t, *J* = 6.5 Hz, 3H, Me-$(CH_2)_3$), 1.15-1.37, 3.60-3.81, 4.73-4.81 (mmm, 9H, OTHP), 1.28 (d, *J* = 7.1 Hz, 3H, Me-CHO), 1.30-1.58 (m, 2H, Me-$(CH_2)_2$), 1.37 (s, 3H, Me-C), 2.54 (s, 1H, OH), 2.57-2.64 (m, 2H, O-CH-CH_2-C≡), 3.83-3.88 (m, 1H, Me-CHO). ^{13}C-NMR (62.9 MHz) δ = 14.7 (CH_3), 20.1 (CH_2), 22.7 (CH_3), 24.3 (CH_2), 24.7 (CH_2), 25.1 (CH_2), 25.6 (CH_2), 30.0 (CH_3), 31.8 (CH_2), 45.3 (CH_2), 63.9 (CH_2), 68.1 (C), 75.7 (CH), 78.4 (C), 82.3 (C), 96.1 (CH). Anal. Calcd. for $C_{16}H_{28}O_3$ (268.39): C 71.60; H 10.52; found: C 71.66; H 10.44.

Synthesis of dimethyl 3-methyl-1-[2-(tetrahydro-2H-pyran-2-yloxy)-propyl]-hepta-1,2-diene-phosphonate **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) at -70°C was added dropwise with stirring a solution of the 5-methyl-9-(tetrahydro-2*H*-pyran-2-yloxy)-dec-6-yn-5-ol **5** (20 mmol) in the same solvent (20 ml). After 30 min 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 10 hours 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 chromatographed on a column (silica gel, Kieselgel Merck 60 F_{254}) with a mixture of ethyl acetate and hexane (10:1) as an eluent to give the pure product **7** as an oil, which had the following properties:

Dimethyl 3-methyl-1-[2-(tetrahydro-2H-pyran-2-yloxy)-propyl]-hepta-1,2-dienephosphonate (**7**). Orange oil, yield: 71%. R_f 0.45. IR (neat, cm^{-1}): 1118 (C-O-C), 1258 (P=O), 1955 (C=C=C). ^{1}H-NMR (600.1 MHz): δ = 0.90 (t, *J* = 7.3 Hz, 3H, Me-$(CH_2)_3$), 1.17 (d, *J* = 6.0 Hz, 3H, Me-CHO), 1.20-1.23, 1.24-1.29, 1.42-1.47, 3.84-3.95, 4.90-4.94 (mmmmm, 9H, OTHP), 1.32-1.38 (m, 2H, Me-CH_2(CH_2)$_2$), 1.51-1.57 (m, 2H, Me-CH_2C$H_2$$CH_2$), 1.76 (d, *J* = 7.0 Hz, 3H, Me-C=), 2.14-2.42 (m, 2H, O-CH-CH_2-C=), 2.35-2.42 (m, 2H, Me-$(CH_2)_2$CH_2), 3.73 (d, *J* = 11.1 Hz, 3H, MeO), 4.67-4.71 (m, 1H, Me-CHO). ^{13}C-NMR (150.9 MHz) δ = 13.9 (CH_3), 18.8 (*J* = 5.3 Hz, CH_3), 19.7 (CH_2), 20.0 (*J* = 7.8 Hz, CH_3), 20.4 (CH_2), 25.3 (CH_2), 29.4 (CH_2), 32.0 (CH_2), 36.1 (*J* = 6.7 Hz, CH_2), 36.9 (*J* = 8.9 Hz, CH_2), 52.8 (*J* = 6.4 Hz, CH_3), 62.9 (*J* = 12.1 Hz, CH), 63.7 (CH_2), 88.4 (*J* = 191.8 Hz, C), 96.2 (CH), 102.4 (*J* = 13.2 Hz, C), 208.3 (*J* = 5.1 Hz, C). ^{31}P-NMR (242.9 MHz): δ 21.9. Anal. Calcd. for $C_{18}H_{33}O_5P$ (360.43): C 59.98; H 9.23. Found: C 59.93; H 9.16.

Synthesis of 2-(3-diphenyl-phosphinoyl-1,5-dimethyl-nona-3,4-dienyloxy)-tetrahydro-2H-pyran **9**

To a solution of the 5-methyl-9-(tetrahydro-2*H*-pyran-2-yloxy)-dec-6-yn-5-ol **5** (20 mmol) and triethylamine (2.23 g, 22 mmol) in dry diethyl ether (60 ml) at -70°C, a solution of freshly distilled diphenylchlorophosphine (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 8 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 rotary evaporator, and the residue was purified by column chromatography on a silica gel (Kieselgel Merck 60 F_{254}) with ethyl acetate-hexane (10:1) to give the pure product **9** as an oil, which had the following properties:

2-(3-Diphenylphosphinoyl-1,5-dimethyl-nona-3,4-dienyloxy)-tetrahydro-2H-pyran (**9**). Yellow oil, yield: 79%. R_f 0.43. IR (neat, cm^{-1}): 1122 (C-O-C), 1156 (P=O), 1436, 1490 (Ph), 1951 (C=C=C). ^{1}H-NMR (600.1 MHz): δ = 0.81 (t, *J* = 7.3 Hz, 3H, Me-$(CH_2)_3$), 1.11-1.16, 1.23-1.28, 1.44-1.49, 3.86-3.94, 4.88-4.93 (mmmmm, 9H, OTHP), 1.17 (d, *J* = 6.1 Hz, 3H, Me-CHO), 1.35-1.39 (m, 2H, Me-CH_2(CH_2)$_2$), 1.49-1.55 (m, 2H, Me-CH_2C$H_2$$CH_2$), 1.79 (d, *J* = 7.1 Hz, 3H, Me-C=), 2.04-2.16 (m, 2H, O-CH-CH_2-C=), 2.29-2.36 (m, 2H, Me-$(CH_2)_2$CH_2), 4.66-4.70 (m, 1H, Me-CHO), 7.37-7.88 (m, 10H, 2Ph). ^{13}C-NMR (150.9 MHz) δ = 13.9 (CH_3), 19.1 (*J* = 5.4 Hz, CH_3), 19.8 (*J* = 8.0 Hz, CH_3), 21.1 (CH_2), 21.3 (CH_2), 25.4 (CH_2), 29.3 (CH_2), 32.1 (CH_2), 35.1 (*J* = 6.2 Hz, CH_2), 35.6 (*J* = 8.7 Hz, CH_2), 62.7 (*J* = 12.2 Hz, CH), 62.9 (CH_2), 93.8 (*J* = 103.6 Hz, C), 96.2 (CH), 102.9 (*J* = 13.2 Hz, C), 127.7-133.2 (2Ph), 207.9 (*J* = 6.6 Hz, C). ^{31}P-NMR (242.9 MHz): δ 32.6. Anal. Calcd. for $C_{28}H_{37}O_3P$ (452.57): C 74.31; H 8.24; found: C 74.39; H 8.20.

Synthesis of dimethyl [1-(2-hydroxypropyl)-3-methyl-hepta-1,2-dienyl]-phosphonate **10** *and 4-diphenylphosphinoyl-6-methyl-deca-4,5-dien-2-ol* **11**

A solution of the dimethyl 3-methyl-1-[2-(tetrahydro-2*H*-pyran-2-yloxy)-propyl]-hepta-1,2-diene-phosphonate **7** or the 2-(3-diphenyl-phosphinoyl-

1,5-dimethyl-nona-3,4-dienyloxy)-tetrahydro-2*H*-pyran **9** (5 mmol) and PPTS (0.5 mmol) in ethanol (10 ml) was stirred at room temperature for 6 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 chromatographed on a column (silica gel, Kieselgel Merck 60 F_{254}) with a mixture of ethyl acetate and hexane (10:1) as an eluent to give the pure products **10** or **11** as oils, which had the following properties:

Dimethyl 1-(2-hydroxypropyl)-3-methyl-hepta-1,2-dienephosphonate (**10**). Yellow oil, yield: 83%. R_f 0.59. IR (neat, cm^{-1}): 1259 (P=O), 1951 (C=C=C), 3420 (OH). ^{1}H-NMR (600.1 MHz): δ = 0.91 (t, *J* = 7.3 Hz, 3H, Me-$(CH_2)_3$), 1.22 (d, *J* = 6.4 Hz, 3H, Me-CHO), 1.33-1.38 (m, 2H, Me-C$H_2$$(CH_2)_2$), 1.41-1.47 (m, 2H, Me-$CH_2CH_2$$CH_2$), 1.78 (d, *J* = 6.9 Hz, 3H, Me-C=), 2.03-2.06 (m, 2H, O-CH-CH_2-C=), 2.27-2.33 (m, 2H, Me-$(CH_2)_2$CH_2), 2.88 (s, 1H, OH), 3.74 (d, *J* = 11.1 Hz, 3H, MeO), 4.59-4.62 (m, 1H, Me-CHO). ^{13}C-NMR (150.9 MHz) δ = 13.8 (CH_3), 18.0 (*J* = 5.8 Hz, CH_3), 22.2 (CH_2), 22.7 (*J* = 7.9 Hz, CH_3), 29.3 (CH_2), 33.0 (*J* = 6.6 Hz, CH_2), 39.4 (*J* = 12.1 Hz, CH_2), 52.9 (*J* = 6.3 Hz, CH_3), 66.9 (*J* = 9.7 Hz, CH), 88.6 (*J* = 190.3 Hz, C), 102.3 (*J* = 15.9 Hz, C), 208.1 (*J* = 5.2 Hz, C). ^{31}P-NMR (242.9 MHz): δ 22.6. Anal. Calcd. for $C_{13}H_{25}O_4P$ (276.31): C 56.51; H 9.12; found: C 56.43; H 9.19.

4-Diphenylphosphinoyl-6-methyl-deca-4,5-dien-2-ol (**11**). Orange oil, yield: 88%. R_f 0.58. IR (neat, cm^{-1}): 1167 (P=O), 1436, 1491 (Ph), 1949 (C=C=C), 3401 (OH). ^{1}H-NMR (600.1 MHz): δ = 0.82 (t, *J* = 7.2 Hz, 3H, Me-$(CH_2)_3$), 1.20 (d, *J* = 6.4 Hz, 3H, Me-CHO), 1.40-1.44 (m, 2H, Me-C$H_2$$(CH_2)_2$), 1.46-1.51 (m, 2H, Me-$CH_2CH_2$$CH_2$), 1.80 (d, *J* = 7.1 Hz, 3H, Me-C=), 2.04-2.10 (m, 2H, O-CH-CH_2-C=), 2.30-2.36 (m, 2H, Me-$(CH_2)_2$CH_2), 2.90 (s, 1H, OH), 4.58-4.61 (m, 1H, Me-CHO), 7.35-7.89 (m, 10H, 2Ph). ^{13}C-NMR (150.9 MHz) δ = 13.9 (CH_3), 18.7 (*J* = 5.9 Hz, CH_3), 21.1 (CH_2), 22.9 (*J* = 8.0 Hz, CH_3), 29.2 (CH_2), 32.9 (*J* = 6.4 Hz, CH_2), 39.5 (*J* = 12.4 Hz, CH_2), 67.3 (*J* = 9.8 Hz, CH), 94.6 (*J* = 102.4 Hz, C), 102.2 (*J* = 15.7 Hz, C), 128.0-132.5 (2Ph), 209.0 (*J* = 5.4 Hz, C). ^{31}P-NMR (242.9 MHz): δ 34.5. Anal. Calcd. for $C_{23}H_{29}O_2P$ (368.45): C 74.98; H 7.93; found: C 75.04; H 7.88.

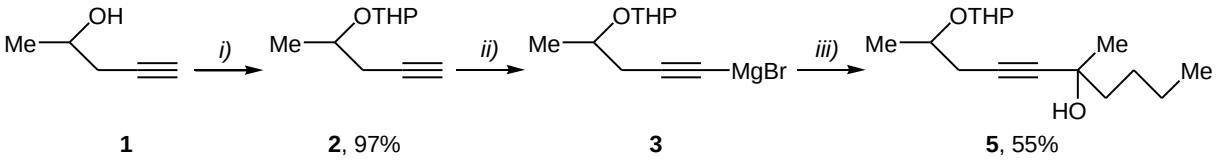
RESULTS AND DISCUSSION

Our strategy for the synthesis of the phosphorylated α-hydroxyallenes, using our experience on the preparation of the 4-heteroatom-functionalized allenecarboxylates [67], relies on the well-precedented [2,3]-sigmatropic shift of propergylic phosphites to allenephosphonates [47-50] and propargylic phosphinites to allenyl phosphine oxides [53-58]. Precedent exists for such an approach to the synthesis of the diethylphosphono-substituted α-allenic alcohols [59,60] only. However, to the best of our knowledge, synthesis of phosphorylated (phosphonates and phosphine oxides) β-hydroxyallenes with protected or unprotected hydroxy group has not been reported.

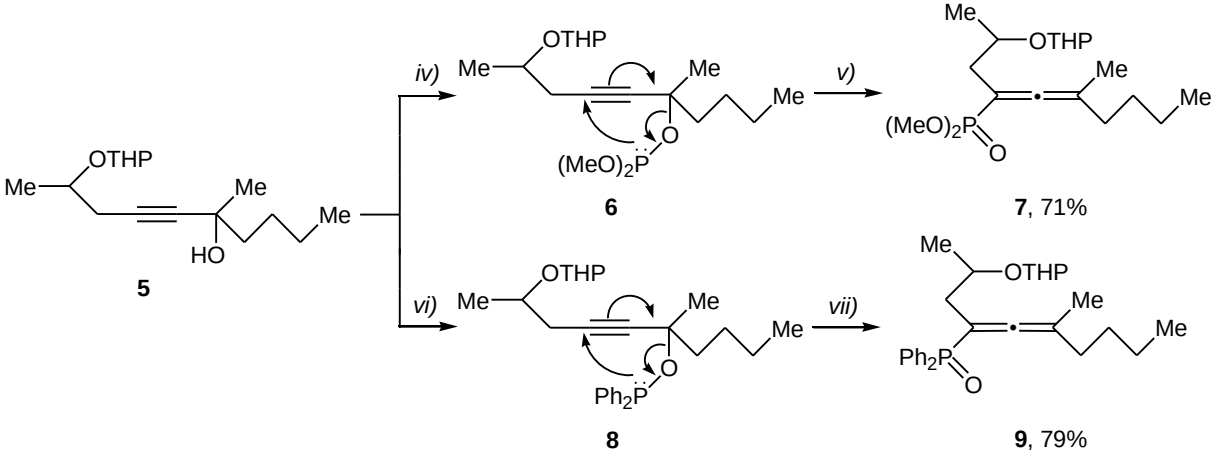
In order to assess this approach towards the target 1,1-bifunctionalized allenes, a range of the phosphorylated β-hydroxyallenes **7**, **9**, **10**, and **11**, was prepared by the following four-step procedure including i) protection of hydroxy group in the pent-4-yn-2-ol **1**; ii) subsequent reaction with Grignard reagent and butylmethyl ketone to give the 6-methyl-dec-4-yne-2,6-diol **5** with protected hydroxy group at 2 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 propargyl phosphite or phosphinite.

As a starting point for our investigation, we first examined the protection of hydroxy group in the pent-4-yn-2-ol **1** with DHP in the presence of PPTS [69-72] (Scheme 1). Thus, the formed 2-(1-methyl-but-3-ynyloxy)-tetrahydro-2*H*-pyran **2** was isolated by column chromatography with excellent yield (87%). Reaction of the protected pent-4-yn-2-ol **2** with ethyl magnesium bromide and subsequent dropwise addition of *in situ* the generated pentynyl magnesium bromide **3** to the hexan-2-one **4** and reflux for 24 hours gave the 5-methyl-9-(tetrahydro-2*H*-pyran-2-yloxy)-dec-6-yn-5-ol **5**, which was stable and was isolated by column chromatography in 55% yield.

With the required dec-4-yne-2,6-diol **5** with protected hydroxy group at 2 position in hand, we were then able to investigate the proposed reactions with the corresponding chlorocontaining phosphorus reagents such as dimethyl chlorophosphite and chlorodiphenyl phosphine in the presence of a base and subsequent [2,3]-sigmatropic rearrangement of the mediated 4-(tetrahydro-2*H*-pyran-2-yloxy)-propargyl phosphite **6** or phosphinite **8**. In the first instance, the dimethyl 1-(tetrahydro-2*H*-pyran-2-yloxy)-alka-1,2-dienephosphonates **7** can be readily prepared *via* an atom economical 2,3-sigmatropic rearrangement of the 4-(tetrahydro-2*H*-pyran-2-yloxy)-propargyl phosphite **6**, intermediate formed by reaction of the (tetrahydro-2*H*-pyran-2-yloxy)-alkynol **5** with dimethyl chlorophosphite, prepared *in situ* from phosphorus trichloride and 2 *equiv* of



Scheme 1. Synthesis of the 5-methyl-9-(tetrahydro-2*H*-pyran-2-yloxy)-dec-6-yn-5-ol **5**. Reagents and Conditions: i) DHP (1.5 eq), PPTS (0.1 eq), CH_2Cl_2, rt, 4 h, distillation; ii) EtMgBr (1 eq), THF, reflux, 2 h; iii) dropwise addition of **3** to MeC(O)Bu **4** (2 eq), reflux, 24 h, column chromatography.



Scheme 2. Synthesis of the dimethyl-3-methyl-1-[2-(tetrahydro-2*H*-pyran-2-yloxy)-propyl]-hepta-1,2-dienephosphonate **7** and 2-(3-diphenylphosphinoyl-1,5-dimethyl-nona-3,4-dienyloxy)-tetrahydro-2*H*-pyran **9**. 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, 1 h, rt, 10 h; vi) Ph_2PCl (1 eq), Et_3N (1.1 eq), Et_2O, -70°C, 1 h, rt, 10 h, column chromatography; vii) [2,3-σ]-rearrangement, -70°C, 1 h, rt, 8 h, column chromatography.

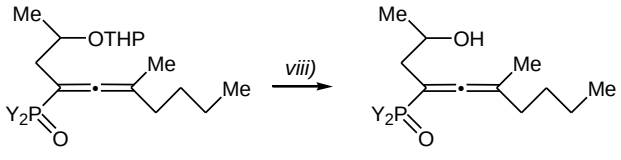
pyridine, according to Scheme 2.

Pleasingly, the reaction of the (tetrahydro-2*H*-pyran-2-yloxy)-alkynol **5** with chlorodiphenyl phosphine in the presence of triethylamine at -70°C gave the expected 2-(2-(diphenylphosphinoyl-alka-2,3-dienyloxy)-tetrahydro-2*H*-pyrans **9** in very good yield (79%) as a result of [2,3]-sigmatropic rearrangement of the 4-(tetrahydro-2*H*-pyran-2-yloxy)-propargyl phosphinite **8** for 8 hours at room temperature, according to the reaction sequence outlined in Scheme 2.

A new family of phosphorylated β-hydroxy-allenes with protected hydroxyl group **7** and **9** was synthesized *via* an atom economical and regio-selective [2,3]-sigmatropic rearrangement of the intermediate formed propargyl phosphite **6** or phosphinite **8** in the reaction of protected alkynol **5** with dimethylchloro phosphite or chlorodiphenyl phosphine in the presence of triethylamine.

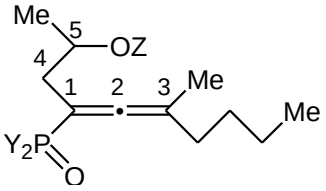
Compounds **7** and **9** were stable enough to be handled at ambient temperature. The hydroxy group was deprotected by stirring the ethanol solution of the protected hydroxypropyl-allenephosphonate **7** and hydroxypropyl-allenyl phosphine oxide **9** in the presence of 0.1 *equiv* PPTS at room temperature for 6 hours, according to Scheme 3.

After a conventional work-up, all allenic products **7**, **9**, **10**, and **11** were isolated as stable yellow or orange oils by column chromatography and identified by ^1H, ^{13}C, and ^{31}P NMR and IR spectra as well as by elemental analysis. Some characteristic chemical shifts and coupling constants in the ^{13}C and ^{31}P NMR spectra of the prepared phosphorylated β-hydroxyallenes **7**, **9**, **10**, and **11** are summarized in Table 1.



Scheme 3. Synthesis of the dimethyl [1-(2-hydroxy-propyl)-3-methyl-hepta-1,2-dienyl]-phosphonate **10** and the 4-(diphenylphosphinoyl)-6-methyl-deca-4,5-dien-2-ol **11**. *Reagents and Conditions*: *viii)* PPTS (0.1 eq), EtOH, rt, 6h, stirring, column chromatography.

Table 1. Some characteristic ^{13}C and ^{31}P NMR spectral data of the prepared phosphorylated β-hydroxyallenes **7**, **9**, **10**, and **11**.



7, Y=MeO, Z=THP
9, Y=Ph, Z=THP
10, Y=MeO, Z=H
11, Y=Ph, Z=H

Allene	δ_{C-1} ($^1J_{P-C-1}$)	δ_{C-2} ($^2J_{P-C-2}$)	δ_{C-3} ($^2J_{P-C-4}$)	δ_{C-4} ($^3J_{P-C-3}$)	δ_{C-5} ($^3J_{P-C-5}$)	δ^{31}_P
7	88.4 (191.8)	208.3 (5.1)	102.4 (13.2)	36.9 (8.9)	62.9 (12.1)	21.9
9	93.8 (103.6)	207.9 (6.6)	102.9 (13.2)	35.6 (8.7)	62.7 (12.2)	32.6
10	88.6 (190.3)	208.1 (5.2)	102.3 (15.9)	39.4 (12.1)	66.9 (9.7)	22.6
11	94.6 (102.4)	209.0 (5.4)	102.2 (15.7)	39.5 (12.4)	67.3 (9.8)	34.5

A series of new phosphorylated β-hydroxyallenes with protected **7** and **9** and unprotected hydroxy group **10** and **11** were synthesized by a convenient, efficient, atom economical and regioselective method.

CONCLUSION

In conclusion, a convenient and efficient method for regioselective synthesis of a new family of 1,1-bifunctionalized allenes has been explored. Phosphorylated α-hydroxyallenes prepared were derived from [2,3]-sigmatropic rearrangement of the intermediate propargyl phosphites or phosphinites formed in the reaction of protected alkynols with dimethylchloro phosphite or chlorodiphenyl phosphine in the presence of a base.

Further investigations on this potentially important synthetic methodology are currently in progress. At the same time, the synthetic application of the prepared phosphorylated β-hydroxyallenes with protected or unprotected hydroxy group for synthesis of different heterocyclic compounds is now under investigation in our laboratory as a part of our general synthetic strategy for investigation of the scope and limitations of the electrophilic cyclization and cycloisomerization reactions of bifunctionalized allenes. Results of these investigations will be reported in due course.

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БИФУНКЦИОНАЛИЗИРАНИ АЛЕНИ. ЧАСТ XIV. УДОБЕН И ЕФИКАСЕН РЕГИОСЕЛЕКТИВЕН СИНТЕЗ НА ФОСФОРИЛИРАНИ β-ХИДРОКСИАЛЕНИ СЪС ЗАЩИТЕНА И НЕЗАЩИТЕНА ХИДРОКСИ ГРУПА

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(Резюме)

Описан е удобен и ефикасен региоселективен синтез на фосфорилирани β-хидроксиалени чрез атом-икономична [2,3]-сигматропна прегрупировка на междинно образуваните пропаргилови фосфити или фосфонити, които лесно се получават чрез реакция на защитения 5-метил-дец-6-ин-5-ол с диметил хлорофосфит или хлородифенил фосфин съответно в присъствие на база.