BIFUNCTIONALIZED ALLENES. PART IV. 1,2λ^5-OXAPHOSPHOLE-3-CARBOXYLATES AND 3-PHOSPHORYL-2(5*H*)-FURANONES FROM 2-PHOSPHORYL-2,3-ALKADIENOATES

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Abstract. 2,5-Dihydro-2-oxo-1,2λ^5-oxaphosphole-3-carboxylates 3 and 3-phosphoryl-2(5*H*)-furanones 4 and 5 were synthesized in very good yields *via* electrophile-induced cyclization reactions of 2-phosphoryl-2,3-alkadienoates 1 and 2. Bromination of ethyl 2-(dimethoxyphosphoryl)-2,3-alkadienoates 1 led to formation of mixtures of 4-bromo-2,5-dihydro-2-oxo-1,2λ^5-oxaphosphole-3-carboxylates 3 and 4-bromo-3-(dimethoxyphosphoryl)-2(5*H*)-furanones 4, while the reaction with ethyl 2-(diphenylphosphoryl)-2,3-alkadienoates 2 afforded 4-bromo-3-(diphenylphosphoryl)-2(5*H*)-furanones 5 only.

INTRODUCTION

In the past three decades, synthesis and use of allene derivatives have been expanded in preparative organic chemistry.(1) Reactions of electrophilic addition to allenes,(2) in which the double bonds are differently substituted, presents the possibility of formation of eight different monoaddition products(2f) depending on i) which double bond is attacked; ii) whether electrophile or nucleophile becomes attached to the central carbon; and iii) whether substituents on the remained double bond are *E* or *Z*. Moreover, the electrophilic addition to allenes can occur, as it does for alkenes, stereospecifically *syn* (suprafacial) or *anti* (antarafacial) and regioselectively with Markovnikov or anti-Markovnikov orientation.(2g)

An impressive number of heterocyclic systems has been prepared from allenic starting materials. The electrophile-induced cyclization of a variety of monofunctionalized allenes such as alcohols,(3) carboxylic acids and their esters,(4) sulfoxides,(5a) sulfinates,(5b) sulfones,(5b,5c,5d) phosphonates,(5b,6), phosphinates(5b,6) and phosphine oxides,(6) to heterocyclic systems has received considerable attention due to its synthetic utility and remarkable stereoselectivity.(3a,3f,4b,4f,5c,5d,6c) α-Allenecarboxylic acids and their esters, disubstituted on the γ-carbon atom, underwent electrophilic attack on the central atom and ring closure to 2(5*H*)-furanones (γ-lactones) when treated with strong acids and bromine.(4) On the other hand, the reactions of phosphorylated allenes with electrophilic reagents have been intensively investigated in the past 20 years. It has been shown(6) that depending on the structure of the starting allenic compound as well as the type of the electrophilic reagent, the reactions proceed with cyclization of the allenic system bearing phosphoryl group (O=P-C=C=C) to give heterocyclic compounds in most cases. Thus, the reaction of electrophilic reagents with allenephosphonic dialkyl esters leads to 2,5-dihydro-1,2-oxaphospholes or/and 2,1- or/and 2,3-adducts or a mixture of them, depending on the degree of substitution at the C^1 and C^3 atoms of the allenic system, on the nature of these substituents, and on the type of the reagents.(6a,6c)

In a continuation to our previous reports on the synthesis(7a,7b) and electrophile-induced cyclization reactions (7c) of bifunctionalized allenes, we have investigated the bromine-promoted heterocyclization of 2-phosphoryl-2,3-alkadienoates. It must be noted that conceptually there exist two distinct modes of cyclization of the phosphorylated 2,3-alkadienoates (phosphonates and phosphine oxides) if the bromine atom forms a new bond with the central carbon of the allenic system, which seems likely.(4,6) It is evident that these pathways are closely connected with the intramolecular participation of the carbonyl and/or the phosphoryl groups as internal nucleophile(s) in the final step of the heterocyclization.

EXPERIMENTAL

Method of analysis.

^1H and ^{13}C NMR spectra were obtained on a BRUCKER DRX-250 spectrometer for solutions in $CDCl_3$. Chemical shifts are in parts per million downfield from internal TMS. IR spectra were recorded with an IR-72 spectrophotometer (Carl Zeiss, Jena). Elemental analyses were carried out by the University of Shoumen Microanalytical Service Laboratory. The melting points were measured in open capillary tubes and are uncorrected. The solvents were purified by standard methods. Reactions were carried out in oven-dried glassware under an argon atmosphere and exclusion of moisture. All compounds were checked for their purify on TLC plates.

Starting materials.

The substrates 2-(dimethoxyphosphoryl)-2,3-alkadienoates 1 and 2-(diphenylphosphoryl)-2,3-alkadienoates 2 were synthesized according to the established procedure.(7b)

Bromination of the 2-phosphoryl-2,3-alkadienoates 1 and 2. *General procedure.*

To a solution of the 2-phosphoryl-2,3-alkadienoates 1 or 2 (10 mmol) in dry dichloromethane (15 ml) was added dropwise with stirring a solution of bromine (10 mmol) in the same solvent (10 ml) at -20 °C. The reaction mixture was stirred at the same temperature for 1 h and then at room temperature for 3 h. The solvent was removed using a rotatory evaporator and the residue was chromatographied on column (silica gel, Kieselgel Merck 60 F_{254}), a mixture of ethyl acetate and hexane being used as elution solvent, and from which the heterocyclic products 3-5 were isolated.

Ethyl 4-bromo-2-methoxy-5,5-dimethyl-2-oxo-2,5-dihydro-1,2λ^5-oxaphosphole-3-carboxylate 3a and 4-bromo-3-(dimethoxyphosphoryl)-5,5-dimethyl-2(5*H*)-furanone 4a.

Oxaphosphole 3a: yield: 54 %, oil, *Anal.* Calcd for $C_9H_{14}O_5PBr$: P 9.89, Br 25.52. Found: P 9.98, Br 25.71. IR (neat): 1254, 1586, 1741 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.22 (t, *J* 7.04 Hz, 3H),1.57, 1.66 (ss, 6H), 3.8 (d, *J* 11.4 Hz, 3H), 4.24 (q, *J* 7.04 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 14.05, 25.1, 28.3, 52.45 *J* 15.0 Hz, 58.62 *J* 5.1 Hz, 82.14 *J* 15.1 Hz, 123.25 *J* 127.7 Hz, 139.5 *J* 31.6 Hz, 153.64 *J* 15.2 Hz).

Furanone 4a: yield: 23 %, oil, *Anal.* Calcd for $C_8H_{12}O_5PBr$: P 10.46, Br 26.72. Found: P 10.53, Br 26.85. IR (neat): 1245, 1618, 1768 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.71, 1.83 (ss, 6H), 3.74 (d, *J* 12.0 Hz, 6H). ^{13}C NMR ($CDCl_3$), δ: 24.75 *J* 4.6 Hz, 26.18 *J* 4.6 Hz, 51.05, 82.43 *J* 8.1 Hz, 120.7 *J* 157.47 Hz, 160.5 *J* 52.4 Hz, 169.4 *J* 4.6 Hz).

Ethyl 4-bromo-2-methoxy-1-oxa-2-oxo-2λ^5-phosphaspiro[4,5]dec-3-en-3-carboxylate 3b and 4-bromo-3-(dimethoxyphosphoryl)-1-oxaspiro[4,5]dec-3-en-2-one 4b.

Oxaphosphole 3b: yield: 50 %, mp 95-96 °C, *Anal.* Calcd for $C_{12}H_{18}O_5PBr$: P 8.77, Br 22.63. Found: P 8.86, Br 22.78. IR (nujol): 1263, 1594, 1748 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.23 (t, *J* 7.06 Hz, 3H), 1.54 and 2.52 (bsbs, 10H), 3.79 (d, *J* 11.4 Hz, 3H), 4.29 (q, *J* 7.07 Hz, 2H). ^{13}C NMR ($CDCl_3$), δ: 11.12, 20.18 *J* 4.6 Hz, 23.1, 34.15 *J* 7.8 Hz, 50.85 *J* 5.1 Hz, 58.16 *J* 5.1 Hz, 85.45 *J* 14.9 Hz, 117.35 *J* 126.8 Hz, 140.26 *J* 32.7 Hz, 156.74 *J* 15.2 Hz.

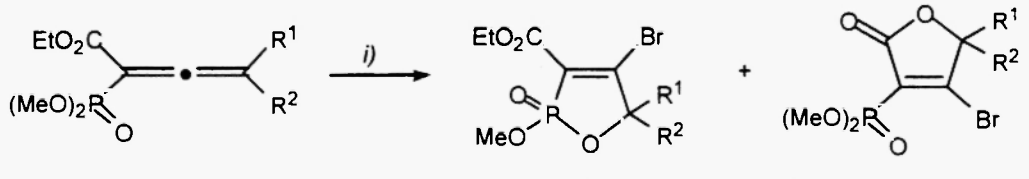
Furanone 4b: yield: 22 %, oil, *Anal.* Calcd for $C_{11}H_{16}O_5PBr$: P 9.13, Br 23.56. Found: P 9.25, Br 23.71. IR (neat): 1238, 1620, 1766 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.51 and 2.61 (bsbs, 10H), 3.72 (d, *J* 12.4 Hz, 3H). ^{13}C NMR ($CDCl_3$), δ: 21.15, 24.74, 34.2, 50.84 *J* 4.6 Hz, 88.25 *J* 8.2 Hz, 124.54 *J* 156.4 Hz, 164.23 *J* 51.4 Hz, 168.7 *J* 15.0 Hz.

4-Bromo-5,5-dimethyl-3-(diphenylphosphoryl)-2(5*H*)-furanone 5a: yield: 69 %, mp 108-109 °C, *Anal.* Calcd for $C_{18}H_{16}O_3PBr$: P 7.92, Br 20.43. Found: P 7.99, Br 20.60. IR (nujol): 1193, 1605, 1761 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.73 and 1.82 (ss, 6H), 7.44-8.38 (m, 10H). ^{13}C NMR ($CDCl_3$), δ: 24.13 *J* 4.6 Hz, 26.3 *J* 4.6 Hz, 88.74 *J* 8.1 Hz), 125.64 *J* 157.18 Hz, 128.15-132.06, 163.82 *J* 50.6 Hz, 167.54 *J* 14.9 Hz.

4-Bromo-3-(diphenylphosphoryl)-1-oxaspiro[4,5]dec-3-en-2-one 5b: yield: 71 %, mp 100-101 °C, *Anal.* Calcd for $C_{21}H_{20}O_3PBr$: P 7.18, Br 18.53. Found: P 7.3, Br 18.71. IR (nujol) 1188, 1602, 1764 cm^{-1}. ^1H NMR ($CDCl_3$), δ: 1.59 and 2.60 (bsbs, 10H), 7.47-8.39 (m, 10H). ^{13}C NMR ($CDCl_3$), δ: 23.18, 25.44, 35.8, 87.66 *J* 8.1 Hz, 128.34 *J* 156.15 Hz, 130.2-132.6, 165.74 *J* 51.0 Hz, 168.26 *J* 15.3 Hz.

RESULTS AND DISCUSSION

In order to establish the preferred pathway, we treated the ethyl 2-(dimethoxyphosphoryl)-2,3-alkadienoates 1 with bromine ir dichloromethane at -20 °C and found that the reaction took place with electrophile-induced cyclization by neighboring participation of both dimethoxyphosphoryl and ethoxycarbonyl groups as internal nucleophiles to give *ca.* 2.3:1 mixtures of 4-bromo-2,5-dihydro-2-oxo-1,2λ^5-oxaphosphole-3-carboxylates 3 and 4-bromo-3-(dimethoxyphosphoryl)-2(5*H*)-furanones 4 in 72 and 75% overyields as shown in **Scheme 1**:



1 3 4

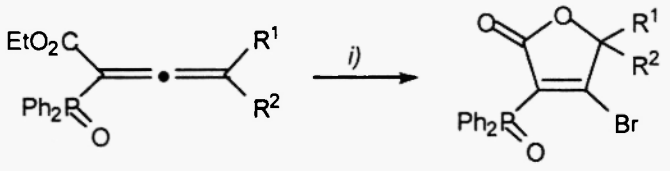
1,3,4	R^1	R^2
a	Me	Me
b	$-(CH_2)_5-$	

Reagents and Conditions:
i) Br_2, CH_2Cl_2, -20 °C, 1h, rt, 2-3h.

Scheme 1

On the other hand, the bromination reaction of the ethyl 2-(diphenylphosphoryl)-2,3-alkadienoates 2 in the same conditions afforded the 4-bromo-3-(diphenylphosphoryl)-2(5*H*)-furanones 5 only, i. e. the electrophile-induced cyclization

proceeded by neighboring participation of ethoxycarbonyl groups as internal nucleophile only, according to the following sequence outlined in **Scheme 2**:



2 5

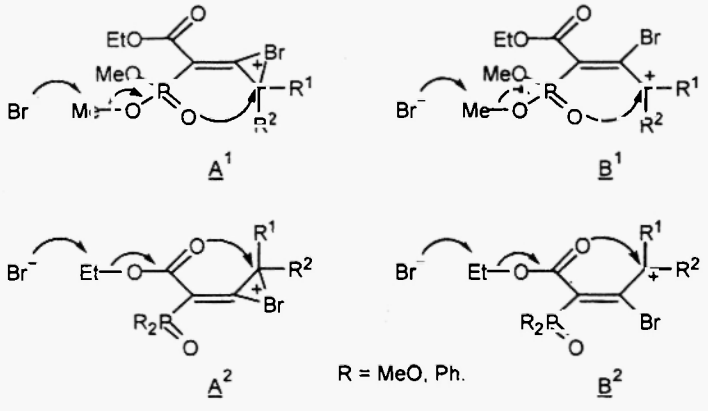
2,5	R^1	R^2
a	Me	Me
b	-$(CH_2)_5$-	

Reagents and Conditions: i) as in **Scheme 1**

Scheme 2

The resulting heterocyclic compounds 3-5 were isolated by column chromatography as light yellow oils or white crystals in good yields (22-71 %). Compounds 3-5 exhibited correct spectroscopic properties which are in good agreement with IR, ^1H and ^{13}C NMR data reported for similar structures.(4,6) The data from elemental analysis confirm the structure of compounds prepared.

In addition to the above, we observe second order kinetics, first-order in electrophile (bromine) and first order in substrate (2-phosphoryl-2,3-alkadienoate), which establishes the composition of the rate determining transition state as containing one equivalent of each reactant. Similar observations have been reported by D. G. Garratt and co-workers (3f) in the cyclization reaction of allenic alcohols with electrophile. These data are indicative of a reaction hypersurface containing the cyclic bromonium ions, A^1 and/or A^2, or the open carbenium ions, B^1 and/or B^2, which collapse to the products 3-5 after attack of internal nucleophile [dimethoxy(diphenyl)phosphoryl and/or ethoxycarbonyl groups].



These are presumed to arise from attack on the allenic C^2-C^3 double bond *anti* to the functional group which assisted in the heterocyclization by neighboring group participation as an internal nucleophile. On the other hand, a possible explanation of the occurred two types cyclization consists in the following. In the first case (**Scheme 1**), the reason for the predominant participation of the phosphonate group as an internal nucleophile is the higher nucleophilicity of the

phosphoryl oxygen in comparison with carboxylic one, which is in connection with the more polarization of the phosphoryl group. In the second case (**Scheme 2**), this reaction pathway is probably favourable from energetic point of view. If the phosphine oxide group takes place as an internal nucleophile in the cyclization, the prepared cyclic compounds should be phosphonium salts,(8) since in this case the stabilization by the elimination of an alkyl bromide (second stage of an Arbuzov type rearrangement) and formation of stable products with tetracoordinated phosphorus is impossible.

The above mentioned explanation should be corroborated or refuted from the results on the study of the bromination reactions of other functionalized phosphorylated allenes and specially their stereochemistry. Further work in this area is being focused on exploiting and extending the synthetic utility of the bifunctionalized allenes for the preparation of different heterocyclic systems using the electrophile-induced cyclization methodology.

CONCLUSIONS

Our results indicate that the 2-phosphoryl-2,3-alkadienoates 1 and 2 are efficient synthons for the synthesis of 2,5-dihydro-2-oxo-1,2λ^5-oxaphosphole-3-carboxylates 3 and 3-phosphoryl-2(5*H*)-furanones 4 and 5 *via* electrophile-induced intramolecular ring closure. Whereas the intramolecular cyclizations are also possible for other monofunctionalized allenes,(3-6) the nature of the electrophile-induced cyclization opens new synthetic routes for several classes of heterocyclic compounds from the bifunctionalized allenes(7a,7b) as precursors. Studies in this area are currently in progress and the results of them will be reported in the near future.

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