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PHOSPHORUS HETEROCYCLE SYNTHESIS BY $RPX_2 \cdot AlX_3$ ADDITION TO [1,n]DIENES—IX. THE SYNTHESIS AND STRUCTURE OF SEVERAL OXAPHOSPHABICYCLIC COMPOUNDS

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Abstract—Several oxaphosphabicyclic compounds were synthesized by the reaction of methyl dihalophosphane under various conditions with 1,6-diketones and $\beta\gamma$-unsaturated ketones. The structure of one of the new compounds (**11**) was established by X-ray diffraction analysis. The ^{1}H- and ^{13}C-NMR spectra of the new compounds, which, except for **11**, served for their structure elucidation, are discussed.

The use of the $RPX_2 \cdot AlX_3$ complex (**1a**, R = Me; **1b**, R = Ph) for the synthesis of new phosphaheterocycles starting from [1,n] dienes has been recently reviewed.[1] The synthesis was found to be useful for the preparation of a whole variety of new phosphaheterocycles such as substituted phospholanes, phosphorinanes, phosphetanes, 3-phosphabicyclo[3.1.0]hexanes and other phosphabicyclic systems.[1] Moreover, it was demonstrated[1] that in the presence of small amounts of water the electrophilic addition of **1** takes another course and leads to a variety of phosphorylated compounds.

Furthermore, it could also be shown that $\beta\gamma$ and $\gamma\delta$-unsaturated ketones react with **1**; e.g. 2-methylhex-1-en-5-one gives with **1b** 2-oxo-2-phenyl-2-phospha-7-oxa-bicyclo[2.2.1]heptane (**2**).[2]

1,5-Diketones, on the other hand, failed to react with **1** but did react with RPX_2 in HOAc acid under Vysotskii's conditions[3] to afford a 2:1 adduct, e.g. 1,5-diphenylpentan-1,5-dione yielded with $MePCl_2$ in acetic acid two isomeric crystalline compounds.[4] The structure of one of the identified isomers (**3**), which was unequivocally established by an X-ray analysis, is shown in Scheme 1.

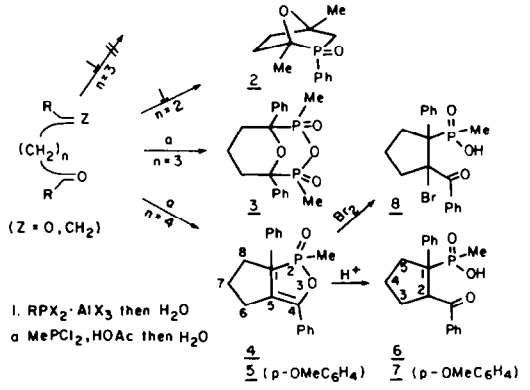
Studying the scope of the latter reaction brought us to examine the reaction between dibenzoylbutane, a 1,6-diketone, and $MePX_2$ in acetic acid. Following quenching of the reaction in water after 16 hr, a crystalline 1:1 adduct (**4**) m.p. 175°, *m/z* 310 (M^+, $C_{19}H_{19}PO_2$, 100%) was obtained.

Based on the NMR data of **4**: δ_H 1.25 d (3H, J_{PH} = 14.4 Hz), 1.94 m (1H), 2.18 m (1H), 2.40 m (2H), 2.50 m (1H), 2.65 dd (1H, J = 6, 9 Hz), δ_C 11.6 dq (J_{PC} = 95 Hz), 24.5 dt (J_{PC} = 7.3 Hz), 28.3 dt (J_{PC} = 13 Hz), 31.3 t, 62.9 d (J_{PC} = 81 Hz), we suggest for this compound the 1,4-diphenyl-2-methyl-2-oxo-3-oxa-2-phosphabicyclo[3.3.0]oct-4-ene structure **4** (Scheme 1). The NMR data point clearly to the following moieties: (a) a $>{}^1C—P(O)Me—O—{}^4C<$ functionality with coupling constants of J_{PC_1} = 81 and $J_{P\text{-}Me}$ = 95 Hz—characteristic for a phosphinate, (b) a $>{}^1CCH_2CH_2CH_2{}^5C<$ unit (the absence of vicinal protons to this segment was proved by double irradiations) and (c) two phenyl groups. The three unsaturations of **4** (in addition to the two phenyl and PO groups) together with the above mentioned functionalities are in full agreement with the proposed bicyclic enol–ether. As the C_4–C_5 double bond C signals overlap with the two phenyl group atoms, we have decided for clarification to synthesize the di-*p*-methoxyphenyl analog of **4** (**5** respectively). Indeed, in contrast to the spectrum of **4** each one of the sp^2 C atom signals in the ^{13}C-NMR spectrum of **5** was now resolved, δ 160.4 s & 160.3 s (C-4′ & 4″), 129.5 d (J_{PC} = 5, C-1′), 133.5 s (C-1″), 128.2 d & 131.4 d (C-2′ & 2″), 114.7 d & 114.0 d (C-3′ & 3″), and the enol–ether carbons 158.9 d (J_{PC4} = 43 Hz) and 126.0 s (C-5).†

This spectrum reveals clearly the former missing enol–ether (C_4 and C_5) atom signals. In order to confirm the latter functional group both **4** and **5** were treated with acid, under mild conditions, to give **6** and **7** respectively (Scheme 1).

As the acidity of regular unpurified $CDCl_3$ was sufficient to transform **4** into **6** it was easy to monitor the formation of the latter by NMR.

Most characteristic in the ^{1}H-NMR spectrum of **6** were the appearance of a doublet of doublets at δ 5.10 (J_{PH} = 13.5 and J_{HH} = 8 Hz) (and at δ 5.00 in **7**), an acidic proton at δ 8.30 (suggesting a P(O)OH group), and the low-field chemical shift of the *ortho* protons of the phenyl groups (Experimental).



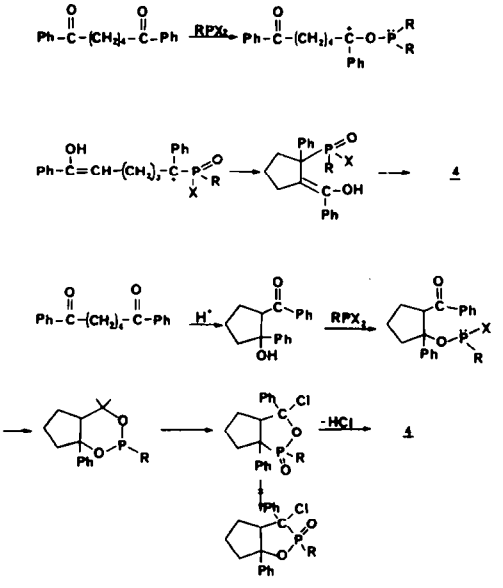
Scheme 1. Reaction of diones with dihalophosphanes.

† The carbons of the phenyl at C-1 are designated C-1′ to C-6′ and the ones of the C-4 phenyl as C-1″ to C-6″.

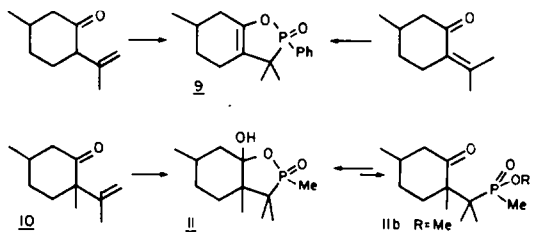
The suggested MeP(O)OH moiety of **6** (and **7**), was confirmed by its micro esterification with CH_2N_2 which furnished the methyl ester **6b** (δ_{POMe} = 3.80 d, J = 12 Hz). The ketone of **6** was confirmed by the ^{13}C-NMR spectrum (δ_C 201.2d, $^3J_{PC}$ = 15 Hz) as well as by the IR absorption at 1680 cm^{-1} and the expected UV shift (Experimental). A SFORD experiment correlated the low-field 5.10 ppm signal with the new appearing methine (δ_C 49.3 ppm) thereby confirming the sp^3 nature of this group. The outstanding low-field chemical shift of this α to CO proton is best rationalized by the vicinal phenyl and phosphinic acid. Furthermore, decomposing the enol–ether of **4** with DCl in $CDCl_3$, affording the 2-d_1-derivative of **6**, established unequivocally the 5.10 proton signal assignment. Bromination of **6** resulted as expected in the α-bromo ketone derivative (**8**).

The formation of **4** (or **5**) can be explained by either one of the routes described in Scheme 2. The first avenue starts with the attack of the RPK_2 on one of the carbonyls followed by ring cyclization. The second route, on the other hand, starts with the acid catalyst ring cyclisation followed in the second step by a P—O bond formation, phosphorylation of the alcohol, and then a P—O to P—C rearrangement.[5]

As mentioned above, unsaturated ketones also react with complex **1** to yield phosphaheterocycles. Thus, p-menth-8-en-3-one reacts with complex **1** to give **9** (Scheme 3).[2] The structure of **9**, *m/z* 276 (M^+, $C_{16}H_{21}PO_2$) was deduced from its ^{1}H-NMR spectrum, namely, from the appearance of a PhPO group (δ 7.0–7.5 m, 5H) and three methyls, at δ 1.05 d (J = 6 Hz) and a pair of methyls vicinal to the PO group at δ 1.38 d (J_{PH} = 16 Hz) and δ 0.84 dd (J_{PH} = 21, J_{HH} = 1 Hz). Further support for the structure came from the ^{13}C-NMR spectrum; δ_C 39.7 d (J_{PC} = 81 Hz)—a carbon adjacent to the PhP(O)O- group, *vide supra*, and 118.2 d (J_{PC} = 5 Hz) and 146.8 s—the enol–ether C atoms. The structure of **9** suggested that menthenone isomerizes under the acidic reaction conditions to pulegone which then



Scheme 2. Suggested mechanisms for production of compound **4**.



Scheme 3. Reaction of αβ-unsaturated ketones with RPX_2.

reacts with **1** to afford the product. Indeed, it was found that $AlCl_3$ isomerizes menthenone to pulegone and, secondly, that pulegone gives with **1b** the same product (**9**) as it gives with $PhPCl_2$ alone (without $AlCl_3$).

In order to avoid menthenone from isomerising it was alkylated to the 4-methyl derivative **10**.[6] Successively, reacting **10** with $MePCl_2 \cdot AlCl_3$ in CH_2Cl_2 under the usual conditions (1–2 hr at r.t.) gave no product. However, prolonging the reaction time for 5–6 days, afforded, although in low yield, after quenching in H_2O, a crystalline product (**11**); *m/z* 228 ($C_{12}H_{23}PO_3$–H_2O, 17%). The ^{1}H-NMR revealed five Me groups; δ 0.85 d (J_{HH} = 6 Hz), 1.08 s, 1.18 d (J_{PH} = 15 Hz), 1.43 d (J_{PH} = 14 Hz) and 1.65 d (J_{PH} = 11 Hz).

The ^{13}C-NMR spectrum of **11** showed only nine C atom signals. Even after applying a 10 sec delay between the RF pulses not more than two signals doubled in intensity. One C-atom was still missing and no structure could have been proposed. It was at this stage that it was decided to undertake an X-ray analysis.

An ORTEP view of the molecular structure of **11** is shown in Fig. 1. Table 1, summarizes the bond distances and bond angles of **11**.

The bicyclic framework is considerably strained, which is best reflected in the stretched C(sp^3)–C(sp^3) bonds around C6: 1.552, 1.553 and 1.578 Å (Table 1).

Table 1. Bond distances (Å) and bond angles (°) of **11**

C1—C2	1.518(3)	C6—C7	1.578(3)
C1—C6	1.552(3)	C6—C11	1.524(3)
C1—O9	1.470(3)	C7—P8	1.843(2)
C1—O16	1.389(3)	C7—C12	1.529(3)
C2—C3	1.518(3)	C7—C13	1.538(3)
C3—C4	1.522(3)	P8—O9	1.595(2)
C3—C10	1.522(4)	P8—C14	1.786(2)
C4—C5	1.526(3)	P8—O15	1.477(3)
C5—C6	1.553(3)		
O9—C1—O16	108.1(2)	C1—C6—C7	105.6(2)
C6—C1—O16	110.0(2)	C7—C6—C11	112.2(2)
C6—C1—O9	104.7(2)	C6—C7—C13	113.3(2)
C2—C1—O16	111.3(2)	C6—C7—C12	114.3(2)
C2—C1—O9	106.9(2)	C6—C7—P8	100.2(1)
C2—C1—C6	115.3(2)	C12—C7—C13	106.7(2)
C1—C2—C3	114.7(2)	P8—C7—C13	111.6(1)
C2—C3—C10	110.5(2)	P8—C7—C12	110.7(2)
C2—C3—C4	109.0(2)	C7—P8—O15	115.6(1)
C4—C3—C10	111.6(2)	C7—P8—C14	112.6(1)
C3—C4—C5	110.6(2)	C7—P8—O9	98.3(1)
C4—C5—C6	114.5(2)	C14—P8—O15	111.7(1)
C1—C6—C5	108.3(2)	O9—P8—O15	112.9(1)
C5—C6—C11	109.5(2)	O9—P8—C14	104.6(1)
C5—C6—C7	109.5(2)	C1—O9—P8	112.8(1)
C1—C6—C11	111.6(2)		

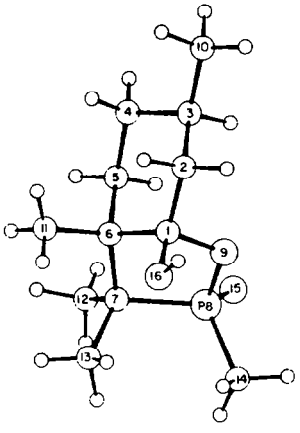


Fig. 1. ORTEP view of **11**.

Adjacent molecules displaced along *b* H-bond to each other through the OH donor and P = O acceptor, thus forming a continuous chain with the crystal lattice. Geometric parameters of this interaction are: 016-H16 = 0.90 Å, 016 ... 015 = 2.723(3) Å, H16 ... 015 = 1.85 Å and 016-H16 ... 015 = 163°.

The synthesis of **11** (Scheme 3) is anticipated to start by electrophilic attack of the $RPX_2 \cdot AlX_3 \cdot H_2O$ complex on the isopropylidene double bond of menthenone as described by us earlier.[1]

The absence of C-3 from the ^{13}C-NMR spectrum of **11** results most likely from a long relaxation time of the tert C-atom which can be further elongated by a possible equilibrium of **11** with its open keto form (Scheme 3). Finally, treatment of **11** with CH_2H_2 gave in low yield the methyl ester identified by its characteristic P—OMe group (δ3.80 d, J_{PH} = 12 Hz).

EXPERIMENTAL

For general directions see ref. 1.

1,4 - Diphenyl (and 1,4 - di - p - methoxyphenyl) - 2 - methyl - 2 - oxo - 3 - oxa - 2 - phosphabicyclo[3.3.0]oct - 4 - ene (**4** *and* **5**)

In the course of 5 min with stirring, 0.05 mol of the 1,6-diphenyl (or 1,6-di-*p*-methoxyphenyl)pentan-1,6-dione was added in small portions to 0.01 mol of CH_3PCl_2 at 60°. Then, at the same temp 3 ml of HOAc (gla) was added. The mixture was kept for 2 hr at 60°, then cooled down to r.t. and stirred for additional 16 hr. The mixture was then poured onto ice, extracted with $CHCl_3$ (3 × 30 ml), washed with $NaHCO_3$ aq, dried over $MgSO_4$, evaporated and finally submitted to a silica gel column for chromatography.

Compound **4** was obtained in 10% yield, m.p. (acetone) 175°; $\nu_{max}^{CHCl_3}$ 2960, 1630, 1590, 1480, 1440, 1300, 1050, 1040, 1030, 960, 880 cm^{-1}; ^{1}H-NMR (270 MHz), δ ($CDCl_3$): 1.25 d (3H, J_{PH} = 14.4 Hz), 1.94 m (1H), 2.18 m (1H), 2.40 m (2H), 2.50 m (1H), 2.65 dd (1H, J = 6, 9 Hz); ^{13}C-NMR: δ 11.6 dq (J_{PC} = 95 Hz), 24.5 dt (J_{PC} = 7.3 Hz), 28.3 dt (J_{PC} = 13 Hz), 31.3 t, 62.9 d (J_{PC} = 81 Hz); *m/z* 310 (M^+, 100%), suitable elemental analysis; λ_{max}^{MeOH} 264 (ε = 12,606).

Compound **5** was obtained in 10% yield; ^{1}H-NMR (300 MHz), δ($CDCl_3$): 1.25 d (3H, J_{PH} = 13.8 Hz), 2.00 m (1H), 2.14 m (1H), 2.34 m (1H), 2.48 dt (1H, J = 3, 11 Hz), 2.60 d (1H, J = 9 Hz), 2.57 d (1H, J = 9 Hz), 3.81 s (3H, OCH_3), 3.85 s (3H, OCH_3), 6.80, 7.52 ABquar (4H, J_{AB} = 9 Hz), 6.85 and 7.18 ABquar (4H, J_{AB} = 9 Hz, J_{BP} = 3 Hz). ^{13}C-NMR, δ ($CDCl_3$): 11.7 dq (J_{PC} = 97 Hz), 24.3 dt (J_{PC} = 8 Hz), 28.3 dt (J_{PC} = 13 Hz), 31.2 t, 55.2 q, 55.4 q, 55.9 d (J_{PC} = 85 Hz), 114.0 d, 123.6 s, 128.2 d, 129.5 d (J_{PC} = 5 Hz), 131.4 d, 133.5 s, 158.9 d (J_{PC} = 43 Hz), 160.3 s, 164.0 s; *m/z*: 370 (M^+, $C_{21}H_{23}PO_4$, 10%), 307 (28%), 291 (61%), 263 (30%), 235 (15%), 135 (50%).

Compound **6**. Compound **4** (20 mg) was left for 5 hr in acidic $CHCl_3$ (10 ml). The solvent was then removed by evaporation and the compound (20 mg) crystallized from acetone; m.p. 187°; $\nu_{max}^{CHCl_3}$ 2940, 1680, 1450, 1300, 1220, 980, 880 cm^{-1}. ^{1}H-NMR (270 MHz), δ ($CDCl_3$): 1.17 d (3H, J_{PH} = 13.5 Hz), 1.94 dd (1H, J = 10 Hz, J = 11 Hz), 1.86 bq (1H, J = 10 Hz), 2.00 m (1H), 2.35 m (2H), 2.65 m (1H), 5.10 dd (J_{PH} = 13.5, J_{HH} = 8 Hz). ^{13}C-NMR, δ ($CDCl_3$): 11.7 dq (J_{PC} = 97 Hz), 23.4 t, 30.9 t, 32.4 t, 49.3 d, 58.0 d (J_{PC} = 86 Hz), 201.2 d (J_{PC} = 15 Hz); *m/z* 310 ($M^+ - H_2O$, 5), 247 (26), 230 (62), 223 (M^+ – PhCO); λ_{max}^{MeOH} 264 (ε = 15,990), 258 (20,500), 252 (22,140).

Compound **6b** was obtained with CH_2N_2; *m/z* 342 (M^+, 5%), δ 3.80 d (J = 12 Hz).

Compound **7** was obtained in the same manner as **6**; ^{1}H-NMR (P-decoupled), δ ($CDCl_3$): 1.18 s (3H), 1.90–3.00 m (6H), 3.60 s (3H), 3.80 s (3H), 5.00 dd (1H, J_{PH} = 15 Hz, J_{HH} = 9 Hz, disappears when DCl in $CDCl_3$ is used), 6.55 and 7.85 two ABquart (8H, J_{AB} = 8 Hz), 9.4 s (1H); ^{13}C-NMR, δ ($CDCl_3$): 11.7 dq (J_{PC} = 97 Hz), 23.5 t, 28.6t, 32.7 t, 54.9 q, 55.3 q, 55.5 d (J_{PC} = 85 Hz), 200.4 d (J_{PC} = 12 Hz).

1 - Phenyl - 2 - bromo - 2 - benzoyl - cyclopentylmethyl phosphinic acid (**8**)

Compound **4** (30 mg) in CCl_4 (5 ml) was treated with a few drops of Br_2 in CCl_4 and left at r.t. for 30 min. The solution was then washed with $Na_2S_2O_4$ aq, dried over $MgSO_4$ and evaporated to give an oily material (35 mg); ^{1}H-NMR (300 MHz), δ($CDCl_3$): 1.32 d (3H, J_{PH} = 14.9 Hz), 2.16 m (2H), 2.60 ddt (1H, J_{PH} = 27 Hz, J = 5 Hz, J = 13 Hz), 3.00 dt (1H, J = 15 Hz, J = 8 Hz), 3.20 dt (1H, J = 15 Hz, J = 9.4 Hz), 3.38 tt (1H, J = 13 Hz, J = 5 Hz), 7.20–8.20 m (10H), 10.50 s (1H); ^{13}C-NMR, δ($CDCl_3$): 18.0 dq (J_{PC} = 108.7 Hz), 19.9 t, 35.1 t, 42.7 t, 65.3 d (J_{PC} = 76.9 Hz), 196.4 s.

1 - Hydroxy - 3,6,7,7,8 - pentamethyl - 8 - oxo - 8 - phospha - 9 - oxabicyclo[4.3.0]nonane (**11**)

Methyl pulegone[6] (0.83 g) in CH_2Cl_2 (2 ml) was added to a stirred soln of $AlCl_3$ (0.61 g) and $MePCl_2$ (0.58 g) in CH_2Cl_2 (20 ml) at 0°. After stirring for 5 days at r.t. the soln was poured over ice washed to neutral, dried over $MgSO_4$ and evaporated to give after chromatography pure **11** (100 mg): $\nu_{max}^{CHCl_3}$ 3200, 2950, 1500, 1380, 1300, 1220, 1190, 1150, 1100, 1040, 980, 950, 900, 880 cm^{-1}; ^{1}H-NMR (P-decoupled), δ: 0.85 d (3H, J = 6 Hz), 1.08 s (3H), 1.18 s (3H, J_{PH} = 15 Hz), 1.43 s (3H, J_{PH} = 14 Hz), 1.65 s (3H, J_{PH} = 11 Hz), 1.30–2.40 m (8H); ^{13}C-NMR, δ: 14.5 dq (J_{PC} = 89 Hz), 19.2 q, 21.5 q (2C), 23.4 q, 29.4 d, 30.5 t (2C), 34.4 t, 42.0 d (J_{PC} = 83 Hz), 44.3 s; *m/z* 228 ($M^+ - H_2O$, 17%), 213 (44%), 149 (24%).

Crystal structure analysis

X-ray diffraction measurements were carried on an Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator, employing MoKα radiation ($\bar{\lambda}$ = 0.7107 Å).

Crystal data. $C_{12}H_{23}PO_3$, M_r = 246.3, monoclinic, *a* = 6.898(1), *b* = 6.859(4), *c* = 13.993(3) Å, β = 96.52(2)°, *V* = 657.8 Å^3, *Z* = 2, d_c = 1.244 g cm^{-3}, μ(MoKα) = 1.94 cm^{-1}, F(000) = 268, space group $P2_1$.

Intensity data were collected in the $\omega - 2\theta$ mode with a scan width of 0.9 + 0.3 tan θ out to 2θ = 54°. The scan rate varied according to the detected intensity between 1.0 and 4.0° min^{-1}. Intensity-control reflections, monitored frequently, showed no decay of the crystal. The intensities were corrected for Lorentz and polarization effects and variable measuring time but not for absorption or secondary extinction.

The structure was solved by a combination of phase refinement, Karle recycling and weighted Fourier techniques, using the MULTAN 80 system of computer programs. Final anisotropic refinement of the nonhydrogen atoms converged at R = 0.032 and R_w = 0.034 for 1486 reflections with $I \geq 3\sigma(I)$. All hydrogen atoms were located in difference-Fourier maps, but neither their positions nor their isotropic

temp factors (set initially at $U = 0.05$ Å^2) were refined. Positional and thermal atomic parameters are available as supplementary material.

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