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Organophosphorus Chemistry, XII [1]. Reaction of Furil with Alkyl Phosphites and Ylide-Phosphoranes**

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Summary. The reaction of furil (**1**) with trialkyl phosphites **2** yielded caged phosphorane derivatives of types **3a–c**. Dry hydrogen chloride gas converted **3a–c** into the respective *α*-hydroxyvinyl-phosphates **8a–c** which are equally produced by reacting furil with the appropriate dialkyl phosphite **7**. The reaction of furil with ylide-phosphoranes **10** proceeded according to the Wittig reaction mechanism to give the respective ethylenes **11a–c**. The new compounds have been characterized by their spectroscopic data (IR, PMR, ^{31}P-NMR, MS) and elementary analyses.

Keywords. Furil; *α*-Diketones; Alkyl phosphites; Caged phosphoranes; Ylide-phosphoranes.

Organophosphor-Chemie, 12. Mitt.: Reaktionen von Furil mit Alkylphosphiten und Ylid-Phosphoranen

Zusammenfassung. Die Reaktion von Furil (**1**) mit Trialkylphosphiten **2** ergab Phosphoranderivate des Typs **3a–c**. Trockenes Chlorwasserstoffgas setzte **3a–c** zu den entsprechenden *α*-Hydroxyvinyl-phosphaten **8a–c** um, die auch bei der Reaktion von Furil mit dem entsprechenden Dialkylphosphit **7** entstehen. Die Reaktion der Ylid-Phosphorane **10** verlief nach dem Mechanismus der Wittig-Reaktion und ergab die entsprechenden Ethylene **11a–c**. Die neuen Verbindungen wurden mittels spektroskopischer Daten (IR, PMR, ^{31}P-NMR, MS) und der Elementaranalysen charakterisiert.

Introduction

The reactivity of alkyl phosphites towards dialkyl-, diaryl-, and aralkyl-*α*-diketones [2–4] has attracted the interest of several groups of investigators. To the best of our knowledge, however, studies including *α*-diketones bearing heterocyclic substituents have not appeared in the literature. Therefore, we have now studied the reaction of furil (**1**) with alkyl phosphites. This would clarify whether the dione system in **1** will be preferentially attacked by the phosphorus nucleophiles or it will facilitate their approach to the furan ring(s) as do 2-furyl ketones in their reactions with certain nitrogen nucleophiles [5]. A comparative study on the reactivity of furil towards stable ylide-phosphoranes (Wittig reagents) is also undertaken.

Results and Discussion

It has been found that furil (**1**) reacts with trialkyl phosphites **2** in absence of solvent at 100°C to give brown 1 : 1 adducts (yield ca. 60%) which could be obtained in

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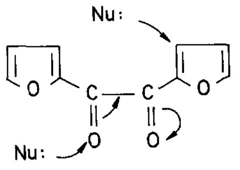
** Dedicated to Prof. M. Sidky on the occasion of his 60th birthday crystalline form (Scheme 1). They are reasonably stable in absence of both air and moisture. The adducts were formulated as 4,5-di-(2-furyl)-2,2,2-trialkoxy-1,3-2-dioxaphospholanes (**3 a–c**) for the following reasons: a) Correct elemental analyses



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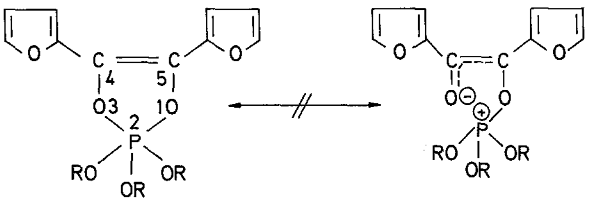
and molecular weight measurements (MS) were obtained for all new compounds. b) The adducts showed negative shifts around $\delta - 58$ ppm (vs. 85% H_3PO_4) in their ^{31}P-NMR spectra which indicated that the phosphorus atom of **2** was covalently bound to five oxygen atoms in the adducts [6]. c) The strong carbonyl band present in the IR spectrum of furil (**1**) at 1675 cm^{-1} was absent in the IR spectra of **3 a–c**. d) The PMR spectrum of adduct **3 a**, taken as an example, showed protons of the methoxyl groups (9 H) as a doublet, at δ 3.23 ppm due to P – O – CH coupling (J_{HP} = 13.5 Hz). This shows that the OCH_3 groups are magnetically equivalent and occupy positions in the molecule which are readily interchangeable without rupture of the P – O bond [7]. The afore-mentioned spectral data not only offer strong evidence for structure **3** but also exclude other alternative structures like **4**–**6** from further considerations (Scheme 2).

Adducts **3** react readily with dry hydrogen chloride gas, in CH_2Cl_2, to give products assigned the α-hydroxyvinyl phosphate structure **8** for the following reasons: a) Compounds **8 a–c** are freely soluble in dilute aqueous alkali. b) Elemental analyses and molecular weight determination (MS) for **8 a**, taken as a representative

$\underline{1} + \underset{\underline{2}}{(RO)_3P} \longrightarrow$

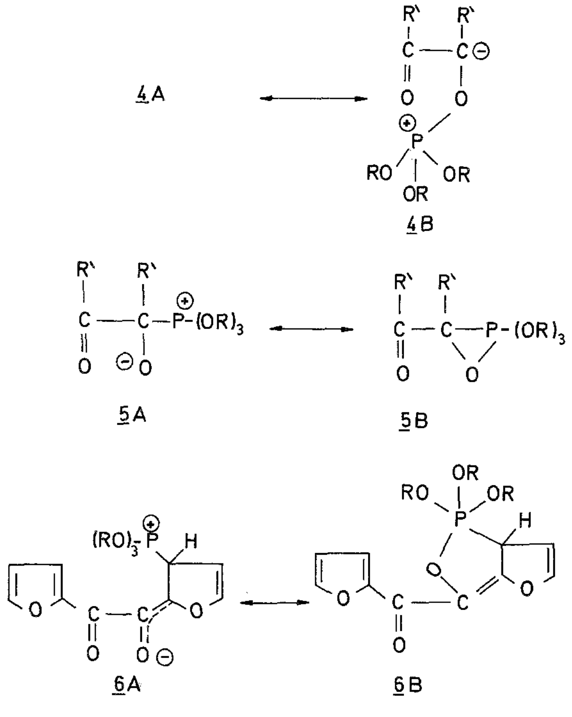
$\underline{2}$ a, R = CH_3, TMP
b, R = C_2H_5, TEP
c, R = C_3H_7-i, TiPP



$\underline{4}$A

$\underline{3}$ a, R = CH_3
b, R = C_2H_5
c, R = C_3H_7-i

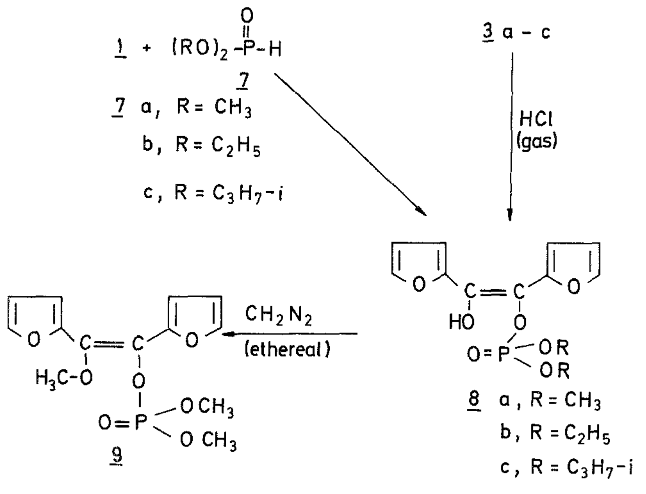
Scheme 1



R = alkyl;
R' = 2-furyl

Scheme 2

example, corresponded to $C_{12}H_{13}O_7P$. c) It showed negative chemical shift (δ −10 ppm, vs. 85% H_3PO_4) in the ^{31}P-NMR spectrum which is in good accord with phosphate shifts [6]. d) The PMR spectrum of **8a** (in $CDCl_3$) disclosed the presence of signals at δ 4.06 (6 H, d, $J_{HP} = 11.5$ Hz) due to the methoxyl groups attached to phosphorus and at δ 5.65 ppm (1 H, broad singlet, exchangeable with D_2O) due to the acidic −OH proton. The furan ring protons (6 H) gave a multiplet in the δ 6.3–7.5 region. e) The IR spectrum of **8a** revealed the presence of absorption bands at 3 430 (−OH), 1 230 ($\geqslant$P=O, bonded) and at 1 020 cm^{-1} (P−O−CH_3) [8]. Moreover, compounds **8a–c** could be prepared by an unequivocal route which

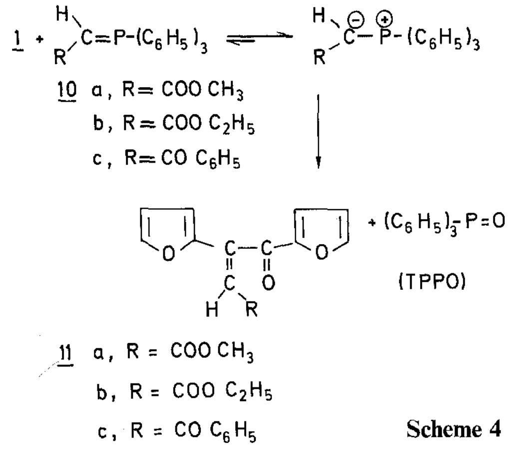


Scheme 3

comprised reacting furil (**1**) with the appropriate dialkyl phosphite **7** in absence of solvent at 100°C (Scheme 3).

On the other hand, when compound **8a** was treated with an ethereal diazomethane solution, it yielded a product which was isomeric but not identical with **3a** ($C_{13}H_{15}O_7P$, MS: m/z 314, M^+). We assigned structure **9** (Scheme 3). The PMR spectrum of **9** showed a doublet ($J_{HP} = 12\,Hz$) at $\delta\,3.34$ for the methoxyl groups attached to phosphorus (6 H) and a singlet at $\delta\,3.77$ (3 H) which is assignable for the $-OCH_3$ group on an ethylenic linkage [8].

We have also found that furil (**1**) reacts with stabilized methylenetriphenylphosphoranes **10a–c** in boiling toluene to give colorless crystalline products formulated as **11a–c**, respectively. Triphenylphosphine oxide (*TPPO*) was also isolated and identified in each case. Compounds **11** are chromatographically pure and possess sharp melting points. Structure **11** was attested by the following evidence: a) Compatible elemental analyses and molecular weight determinations (MS) were obtained for all products. b) The IR spectrum of methyl β-2-furyl-γ-oxo-2-furancrotonate (**11a**), taken as a representative example, revealed the presence of strong absorption bands at 1700 ($C=O$, ester) and at 1660 cm^{-1} ($C=O$, furoyl). c) The exocyclic olefinic proton in compounds **11a–c** resonated in their PMR spectra around $\delta\,6.5$ ppm. Moreover, the $^{13}C-H$ coupling constant between the α-furylcarbonyl group and the vinyl proton (5.5 Hz) recorded for **11a** coincides with the assigned *cis*-configuration **11a** [8b]. Analytical and spectroscopic measurements for ethyl β-2-furyl-γ-oxo-2-furancrotonate **11b** and benzoyl β-2-furyl-γ-oxo-2-furanilidene (**11c**) were also in good accord with the assigned structures (Scheme 4).



Scheme 4

From the present study, it is safe to state that furil (**1**) behaves as an α-diketone toward alkyl phosphites [2–4] and stabilized ylide-phosphoranes (Wittig reagents) [9] at least under the prevailing experimental conditions. Despite the presence of different sites in **1** susceptible for nucleophilic attack, furil is preferentially attacked at the dione system by trialkyl phosphites to give pentaoxyphosphorane structures like **3a–c**. This represents a simple and direct approach for preparing ring structures incorporating phosphorus and contributes to the expanded interest in the chemistry of caged phosophoranes [10–16]. Under the influence of dry HCl gas, the newly prepared caged phosphoranes **3** are easily transformed into the respective α-hydroxyvinyl phosphates **8**. This also represents a convenient preparation of a type of compounds of interest in biological chemistry [17].

Experimental Part

All melting points are uncorrected. The IR spectra were run on a Perkin-Elmer Infracord Spectrometer 197 (grating) in KBr. The PMR and ^{13}C-NMR spectra were recorded on a Bruker Spectrometer Model-WH 90. The chemical shifts are recorded in ppm relative to *TMS*. The ^{31}P-NMR spectra were taken on a Varian CFT-20 (vs. 85% H_3PO_4). The mass spectra were performed at 70 eV on MS-50 Kratos (A.E.I.) Spectrometer. Elemental analyses were carried out by "Microanalysis Lab., National Research Centre (Cairo)". All reactions were carried out under N_2 atmosphere.

Trialkyl phosphites (*TAP*) were purified by treatment with sodium wire followed by fractional distillation. Dialkyl phosphites (*DAP*) were freshly distilled. Furil was prepared by an established method [18].

Action of Trialkyl Phosphites (TAP, **2***) on Furil* (**1**)*. General Procedure*

A mixture of furil (**1**, 1 g, 0.005 mol) and *TAP* (**2**, 4 ml) was heated in absence of solvent on a steam bath for 8–10 h. The excess of *TAP* was removed under vacuum, and the residue was washed several times with light petroleum, then recrystallized from the appropriate solvent to give **3 a–c**.

4,5-Di(2-furyl)-2,2,2-trimethoxy-1,3,2-dioxaphospholane (**3 a**)

Brown crystals (1.88 g, 60%), m.p. 120°C (acetonitrile). $C_{13}H_{15}O_7P$ (314.243). Calcd. C 49.69, H 4.81, P 9.85; found C 49.67, H 4.77, P 9.82. IR (KBr) cm^{-1}: 1 635 (C=C), 1 020 (P−O−CH_3). ^1H-NMR (δ ppm): 3.23 (9 H, P−O−CH_3, d, $J_{HP} = 13.5$ Hz), 6.45–7.8 (6 H, furans, m). ^{31}P-NMR: δ −59.28 ppm. MS: *m/z* 314 (M^+).

4,5-Di(2-furyl)-2,2,2-triethoxy-1,3,2-dioxaphospholane (**3 b**)

Brown crystals (2.33 g, 65%), m.p. 145°C (acetonitrile). $C_{16}H_{21}O_7P$ (356.324). Calcd. C 53.93, H 5.94, P 8.69; found C 53.88, H 5.92, P 8.56. IR (KBr) cm^{-1}: 1 630 (C=C), 1 025 (POC_2H_5). ^1H-NMR (δ ppm): 1.28 (9 H, P−O−CH_2CH_3, t, $J_{HP} = 12$ Hz, 3.5 (6 H, P−O−CH_2, qt, $J_{HP} = 12$ Hz), 6.05–7.7 (6 H, furans, m). ^{31}P-NMR: δ −58.6 ppm. MS: *m/z* 356 (M^+).

4,5-Di(2-furyl)-2,2,2-tri-iso-propoxy-1,3,2-dioxaphospholane (**3 c**)

Brown crystals (2.74, 69%), m.p. 130°C (cyclohexane). $C_{19}H_{27}O_7P$ (398.405). Calcd. C 57.28, H 6.83, P 7.77; found C 57.16, H 6.81, P 7.75. IR (KBr) cm^{-1}: 1 630 (C=C), 1 000 (P−O−C). ^1H-NMR (δ ppm): 1.33 (18 H, P−O−CH $(CH_3)_2$, d, $J_{HP} = 11.5$ Hz), 3.74 (3 H, P−O−CH, sept, $J_{HP} = 11.5$ Hz), 6.15–7.6 (6 H, furans, m). ^{31}P-NMR: δ −53.0 ppm. MS: *m/z* 398 (M^+).

Action of Dry Hydrogen Chloride on **3**

A solution of compound **3 a** (**3 b** and/or **3 c**, 1.5 g) in CH_2Cl_2 (30 ml) was treated with an excess of hydrogen chloride gas at 10–15°C. The solution was filtered and the precipitate was shaken with a solution of $NaHCO_3$ (10%). The substance that collected was recrystallized from the appropriate solvent to give **8 a–c**.

Dimethoxy[1,2(di-2-furanyl)-2-hydroxyethylene]phosphate (**8a**)

Brown crystals (2.34 g, 78%), m.p. 185°C (chloroform – light petroleum (1 : 2 *v*/*v*). $C_{12}H_{13}O_7P$ (300.20). Calcd. C 48.01, H 4.36, P 10.31; found C 47.88, H 4.25, P 9.96. IR (KBr) cm^{-1}: 3430 (OH), 1230 (P=O), 1020 (P–O–C). ^{1}H-NMR (δ ppm): 4.06 (6 H, P–O–CH_3, d of d, J_{HP} = 11.5 Hz), 5.65 (1 H, –OH, s, br), 6.3–7.5 (6 H, furans, m). ^{31}P-NMR: δ –10.00 ppm. MS: *m*/*z* 300 (M^+).

Diethoxy[1,2(di-2-furanyl)-2-hydroxyethylene]phosphate (**8b**)

Brown crystals (2.46 g, 75%), m.p. 165°C (acetone-ether, 1 : 1 *v*/*v*). $C_{14}H_{17}O_7P$ (328.26). Calcd. C 51.22, H 5.22, P 9.42; found C 51.09, H 5.18, P 9.40. IR (KBr) cm^{-1}: 3420 (–OH), 1225 (P=O), 1025 (P–O–C). ^{1}H-NMR (δ ppm): 1.37 (6 H, P–O–C–CH_3, d of t, J_{HP} = 12 Hz, J_{HH} = 3 Hz), 4.22 (4 H, P–O–CH_2, qt, J_{HP} = 12 Hz), 5.4 (1 H, –OH, s, br), 6.6–7.7 (6 H, furans, m). ^{31}P-NMR: δ –10.00 ppm. MS: *m*/*z* 328 (M^+).

Diiso-propoxy[1,2(di-2-furanyl)-2-hydroxyethylene]phosphate (**8c**)

Brown crystals (2.7 g, 76%), m.p. 190°C (ethanol). $C_{16}H_{21}O_7P$ (356.31). Calcd. C 53.93, H 5.94, P 8.69; found C 53.78, H 5.67, P 8.67. IR (KBr) cm^{-1}: 3435 (–OH), 1220 (P=O), 1010 (P–O–C). ^{1}H-NMR (δ ppm): 1.28 (12 H, P–O–CH (CH_3), d, J_{HP} = 11.5 Hz), (1 H, –OH, s, br), 6.7–7.88 (6 H, furans, m). MS: *m*/*z* 356 (M^+).

Action of Diazomethane on **8a**

A solution of **8a** (0.8 g) in methanol (20 ml) was treated with an ethereal diazomethane solution (from 5 g N-nitrosomethylurea), then kept at 5°C for 6 h. After removal of ether, the residue was crystallized from ether to give **9**, brown crystals (0.66 g, 80%), m.p. 110°C (acetonitrile). $C_{13}H_{15}O_7P$ (314.24). Calcd. C 49.69, H 4.81, P 9.85; found C 49.58, H 4.65, P 9.76. IR (KBr) cm^{-1}: 1280 (P=O), 1050 (P–O–C). ^{1}H-NMR (ppm): 3.34 (6 H, P–O–CH_3, d, J_{HP} = 12 Hz), 3.77 (3 H, –OCH_3, s), 6.14–7.65 (6 H, furans, m). ^{31}P-NMR: δ –4.75 ppm.

Action of Dialkyl Phosphites (*DAP*, **7**) *on* **1**. *General Procedure*

A mixture of furil (**1**, 1 g, 0.005 mol) and dimethyl phosphite (*DMP*, **7a**, 0.05 mol) was heated at 100°C for 10 h. After removal of the volatile materials in vacuo, the residual oily material was triturated with ether (5 ml), then left to cool in the refrigerator. The solid product was collected (85%) and recrystallized from acetone-petroleum ether (b.r. 40–60°C) to give brown crystals of the phosphate **8a** (m.p., mixed m.p. and comparative IR spectra).

Similarly, phosphates **8b** and **8c** were isolated (yield ca. 80%) and identified (mixed m.p. and comparative IR spectra) upon reacting furil (**1**) with diethyl- and diisopropyl-phosphites, respectively.

Action of Wittig Reagents **10** *on Furil* (**1**). *General Procedure*

A mixture of **1** (1.9 g, 0.01 mol) and ylide **10a** [19] (**10b** [19] and/or **10c** [20], 0.01 mol) in toluene (100 ml) was refluxed for 18 h. The reaction mixture was then concentrated at 60°C under reduced pressure. The solid product was redissolved in methanol (100 ml) and evaporated to dryness in the presence of silica gel (8 g). The mixture was then added to a column previously charged with silica gel in cyclohexane. The column was developed with cyclohexane containing increasing amounts of diethyl ether. Fraction (up to 8 : 2 *v*/*v*): eluted 1.5 g (60%) of a colorless substance, recrystallized from the suitable solvent to give **11a–c**.

Compound **11a**, colorless crystals (2.0 g, 82%), m.p. 95°C (acetone – ether, 1 : 1 *v*/*v*). $C_{13}H_{10}O_5$ (246.223). Calcd. C 63.41, H 4.09; found C 63.38, H 4.06. IR (KBr) cm^{-1}: 1700 (C=O, ester), 1660

(C=O, furoyl). ^{1}H-NMR (δppm): 3.66 (3H, $C-CH_3$, s), 6.55 (1H, C=CH, s), 6.5–7.6 (6H, furans, m). MS: *m/z* 246 (M^+).

Compound **11b**, colorless crystals (2.1 g, 80%), m.p. 85°C (cyclohexane). $C_{14}H_{12}O_5$ (260.25). Calcd. C 64.61, H 4.64; found C 64.55, H 4.61. IR (KBr) cm^{-1}: 1700 (C=O, ester), 1650 (C=O, furoyl). ^{1}H-NMR (δppm): 1.11 (3H, $-CH_2-CH_3$, t, J_{HH} = 7 Hz), 4.04 (2H, q, J_{HH} = 7 Hz), 6.4 (1H, =CH, s), 6.5–7.5 (6H, furans, m). MS: *m/z* 260 (M^+).

Compound **11c**, colorless crystals (2.39 g, 82%), m.p. 130°C (chloroform – light petroleum, 1:2 *v/v*). $C_{18}H_{12}O_4$ (192.294). Calcd. C 73.96, H 4.14; found C 73.94, H 4.05. IR (KBr) cm^{-1}: 1710 (C=O, aroyl), 1670 (C=O, furoyl). MS: *m/z* 292 (M^+).

The fraction up to 6:4 *v/v* afforded colorless needles, m.p. 156°C (ca. 82% yield) of triphenylphosphine oxide [21] (m.p., mixed m.p. and comparative IR spectra).

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