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Condensation of α-Hydroxy Ketones with Phosphorus Ylides: A Convenient Synthesis of Linear Heterocyclic Formation

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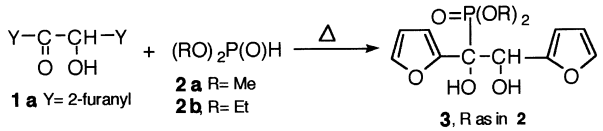
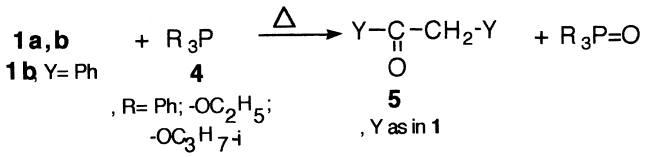
ABSTRACT: *Reaction of α-hydroxy ketones, furoin (***1a***) and/or benzoin (***1b***), with an appropriate phosphorus ylide (***6a–d***) provides access to new alkenes E-***8a–d, 15, 16** *and/or furan derivatives* **11a,b** *and* **21**. *Furthermore, reaction of* **1a,b** *with arylidenephosphorane* **7** *led to the formation of the respective dioxolo compound* **22a,b**. © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 481–487, 1999

INTRODUCTION

In one of our previous studies [1–5] of the synthesis of phosphono-substituted heterocycles for biological/pharmacological evaluation, we reported that dialkyl phosphonates **2** phosphorylate furoin [also known as 1,2-di-(2-furanyl)-2-hydroxyethanone, **1a**] to yield adducts of type **3** (eqn. 1) [5]. Conversely, both triphenylphosphine and trialkyl phosphites **4** deoxygenate the α-hydroxy ketones **1a,b** to afford the respective deoxy-derivative **5** (eqn. 2) [5].

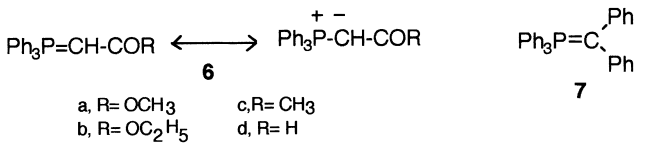


(1)



(2)

In the area of the application of the reaction of Wittig reagents with α-hydroxy ketones, only a few studies are known [6,7]. However, none of these studies have covered the reaction of **1** with phosphorus ylides. In order to fill this gap, we studied the behavior of **1** with stabilized phosphorus ylides **6a–d** and **7**. The incentive for this direction is based on recorded potencies of the Wittig reagents for the synthesis of a wide variety of new ring systems and fused heterocycles [8,9]. Furthermore, furoin has been used in the crosslinking of polyesters with styrene and in the polymerization of chloroethylene [10]. It has also been used in the photographic development of a diffusion-transfer process [11].



RESULTS AND DISCUSSION

Reactions of Phosphorus Ylides **6a,b** *with* **1a,b.**

The reaction of furoin (**1a**) with carbomethoxymethylenetriphenylphosphorane (**6a**) proceeded in

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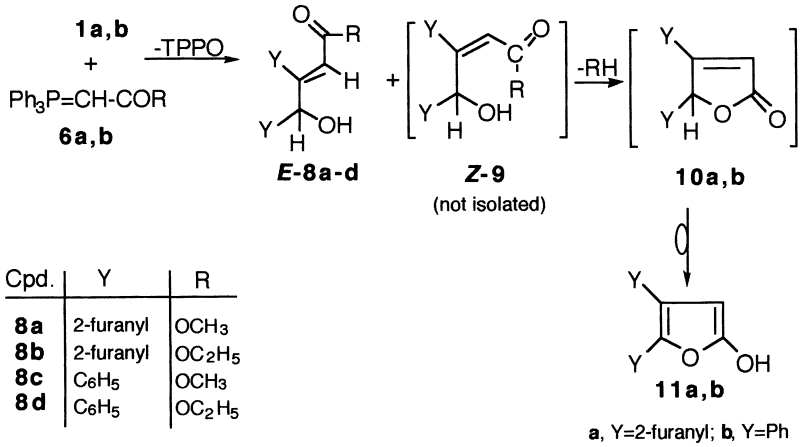


Cpd.	Y	R
8a	2-furanyl	OCH_3
8b	2-furanyl	OC_2H_5
8c	C_6H_5	OCH_3
8d	C_6H_5	OC_2H_5

SCHEME 1

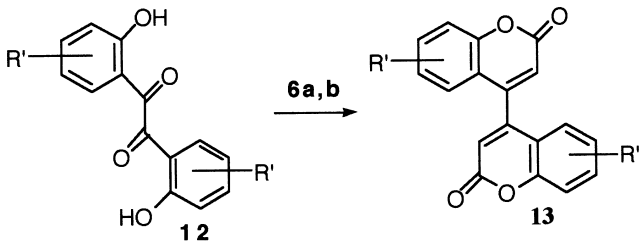
boiling toluene that contained a catalytic amount of benzoic acid. Chromatographic separation of the product mixture produced two main products, **8a** (58%) and **11a** (12%). When the same reaction was performed in boiling ethyl acetate that contained triethylamine (TEA), only the cyclic product **11a** (in 72% yield) was obtained (Scheme 1).

The first product was formulated as methyl 3,4-di-(2-furanyl)-4-hydroxy-but-2-enoate (**8a**, *trans* form). Its elemental analysis and molecular weight determination (MS) agreed with the molecular formula $C_{13}H_{12}O_5$ (248.2). Its IR (KBr) spectrum showed strong absorption bands at 3425 (OH), 1695 (C=O, ester), 1642 (C=CH, exocyclic), and 1610 cm^{-1} (C=C, furanyl). Its ^{1}H-NMR ($CDCl_3$, δ) spectrum showed the exocyclic methine proton (HO–**CH**–C=CH) as a diffused doublet of doublets due to its coupling with the hydroxyl- and the olefinic protons (long allylic coupling) [12] at 4.99–5.01. The protons of the $COOCH_3$ group gave a singlet at 3.62, the vinyl proton (C=C**H**) appeared as a doublet (J_{HH} = 2.4 Hz, long allylic coupling) at 6.14, and the **OH** proton was shown as a doublet (J_{HH} = 4 Hz) at 3.37 (exchangeable with D_2O). The ^{13}C-NMR [12,13] spectrum of **8a** showed signals at 51.6 (OCH_3), 63.3 (**C**HOH), 124.6 (C=**C**H) and 171.9 (**C**=O, ester).

The second product was assigned the structure of 4,5-di-(2-furanyl)-2-hydroxyfuran (**11a**) for various reasons. Its IR spectrum showed an absorption band at 3377 (hydroxyl) and lacked a signal due to the lactone-carbonyl in the range ~1700 cm^{-1} (**cf. 10**). Also, the ^{1}H-NMR (δ) spectrum of **11a** showed the furanyl protons as a multiplet in the range 6.48–7.05 and a singlet at 3.65 (**OH**). Its ^{13}C-NMR(δ) spectrum also furnished strong evidence in support of the structure **11a** because it showed signals at 149.7 (=**C**–OH) and at 106.4 (**C**H=C–OH). The presence of a signal due to the hydroxyl group in the IR and PMR spectra of **11a**, the absence of a signal due to the lactone-carbonyl in its ^{13}C-NMR and IR spectra, and the absence of a signal ($\delta \sim 4 \rightarrow 5$) due to a saturated methine proton (Y-C-5-**H**, **cf. 10**) in its PMR spectrum confirm the assigned structure **11a** and rule out the other alternative structure **10a**.

Compounds *E*-**8b–d** (~48%) and **11a,b** (~11%) were similarly obtained by reacting **1a,b** with an appropriate phosphorus ylide **6a,b** in boiling toluene that contained benzoic acid. Meanwhile, only the furan derivatives **11a,b** were isolated (~70% yield) when the reactions were performed in refluxing ethyl acetate (TEA) (see the Experimental section).

From a mechanistic point of view, the formation of compounds **11** involves the intermediate formation of the Wittig product **9** (essentially in the *cis* form [14]), which readily lactonizes to give **10** upon displacement of an RH molecule. Prototropic rearrangement of **10** results in the formation of its tautomeric form **11**. Concurrent with formation of compounds **9**, the *trans* analogs **8** are also produced, which would not lactonize to give **10** (Scheme 1). Because stereochemical factors are essential for the ring closure to heterocyclic precursors [14,15], it appears that conversion of **9** to **10** is a stereoselective process. The discovery that **8a** (which is assumed to be the *trans* analog of **9a**) is recovered practically unchanged when heated alone in boiling toluene, even for 15 hours, supports this idea. It is worthwhile to mention that a similar lactonization process was observed previously [16] for the Wittig reaction of dihydroxybenzils (**12**) with **6a** or **6b**, whereby biscoumarins **13** were produced in each case.

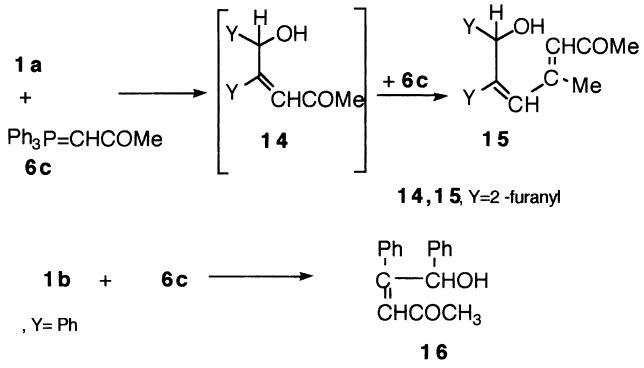


Moreover, the directing effect of the neighboring hydroxyl group is proposed to account for the enhanced rate and *E* regioselectivity in the initial olefination process and formation of **8** and **9** [7,17]. Conversely, with respect to the problem posed by the effect of the polarity of the medium on the final products in the reactions of **1a,b** with **6a,b**, the reported observations are consistent with the assigned mechanism (Scheme 1) because it is established [18] that the use of polar solvents enhance the formation of the *cis* isomer.

Reaction of Phosphorus Ylide **6c** *with* **1a,b.**

Treatment of furoin (**1a**) with two equivalents of acetylmethylene-triphenylphosphorane (**6c**) in the presence of benzoic acid in boiling toluene for 15 hours gave, after separation by column chromatography, the conjugated diene **15** in 66% yield according to the mechanism proposed in Scheme 2. Obviously, the olefin intermediate **14** which initially formed gives, by further Wittig olefination of the acetyl carbonyl in **14**, the final product **15** (Scheme 2).

However, benzoin (**1b**) reacts with **6c** in the presence of benzoic acid in boiling toluene for 28 hours to give, instead of the expected analog of **15**, 3-acetyl-1,2-diphenylprop-2-en-1-ol (**16**) in 58% yield. Obviously, in this case, the initial Wittig product **16** does not undergo any further reaction. Structures of **15** and **16** were confirmed by a thorough study of their spectroscopic data.



SCHEME 2

Reaction of Phosphorus Ylide **6d** *with* **1a,b.**

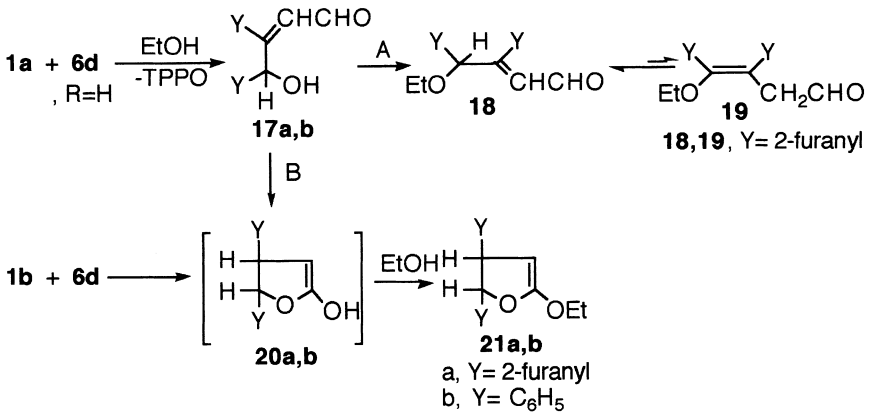
Treatment of furoin (**1a**) with an equimolar amount of formyl-methylenetriphenylphosphorane (**6d**, R = H), obtained from the chloride salt in the presence of triethylamine in ethanol, led to the formation of the olefin **18** (20%) and the dihydrofuran derivative **21a** (25%), as depicted in Scheme 3. The proposed structures **18** and **21a** were confirmed by elemental analyses and spectral data. The ^{1}H-NMR spectrum of **18** revealed the presence of signals at δ 1.05 (t, 3H, C**H**$_3$, J_{HH} = 7 Hz), 4.15 (d of q, 2H, O**CH**$_2$, J_{HH} = 7 Hz, 2.4 Hz), 4.76 (t, 1H, $-\overset{|}{\underset{|}{C}}$-H, J_{HH} = 3.4 Hz), 5.58 (d of d, 1H, -CH–C = C**H**–C(O)H, distorted) and 8.52 (d, 1H, **CHO**, J_{HH} = 4.5 Hz), and its IR spectrum showed the absence of the OH absorption band but showed stretching frequencies at 1707 [C(O)H] and 1635 cm^{-1} (C = CH). However, the structure **19** cannot be excluded, because the ^{1}H-NMR spectrum of **18** revealed a signal at δ 2.4 (d, 2H, J_{HH} = 4.8 Hz), which was attributed to the methylene protons (cf. **19**). The ^{1}H-NMR spectrum of **21a** showed two signals due to the dihydrofuran protons at 5.28 (d of d, 1H, C-4-**H**, J_{HH} = 5.5 Hz), 5.42 (d, 1H, C-5-**H**, J_{HH} = 5.5 Hz) and two signals due to the ethyl group protons at δ 1.75 (t, 3H,-C**H**$_3$) and 3.74 (q, 2H, -O**CH**$_2$).

The formation of **18** and **21a** is believed to occur via the Wittig condensation of **1a** with **6d** to produce the aldehyde **17**, which by or concurrent with further *O*-alkylation due to the presence of the ethanol medium, yields the adduct **18** (Scheme 3, A). Moreover, compound **18** may be present in an equilibrium **18** ⇄ **19** via prototropic rearrangement. On the other hand, internal hemiacetalization of **17** affords compound **21**, probably via **20** (Scheme 3, "B").

Conversely, no reaction was observed when benzoin (**1b**) was treated with **6d** under the previous experimental conditions. When the same reaction was carried out in the presence of a strong base sodium ethoxide (NaOEt) in ethyl alcohol, only the dihydrofuran derivative **21b** (42%) was isolated, along with other unidentified products of high melting points (Scheme 3, B).

Reaction of Phosphorus Ylide **7** *with* **1a,b.**

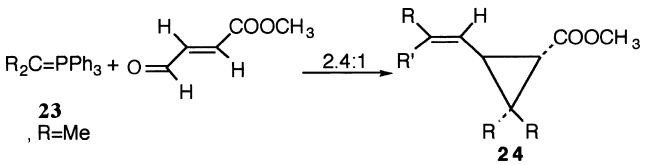
Contrary to the previously described behavior of the Wittig reagents **6a–d,** which undergo several competing processes with **1a,b** leading to different products, diphenylmethylene-triphenylphosphorane (**7**) that was prepared in situ from the corresponding bromo-phosphonium salts by addition of sodium ethoxide in absolute ethyl alcohol reacted smoothly with α-hydroxy ketones **1a,b** through one reaction



SCHEME 3

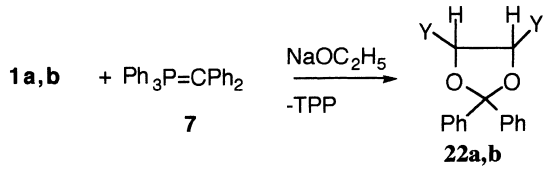
pathway and gave the dioxolo compounds **22a,b** in high yields (~64%). No Wittig products or the reduced form of **1** (i.e., the corresponding diol) were obtained from the reactions of the reagent depicted in Scheme 4. An analogous reaction has been reported to proceed between the same phosphorus ylide and *o*-quinones, with elimination of triphenylphosphine, whereby 1,3-dioxolo compounds were obtained [19,20].

In view of the latter observations (**1a,b** + **7**), the results are not fully in agreement with the information found in the literature regarding the behavior of dialkyl- and diarylmethylenetriphenylphosphoranes in reactions with both ketones and hydroxy ketones. According to a report by Olah and Krishnamurthy [21], one observes either no reaction under the usual Wittig conditions between **7** or **23** and the ketones (or hydroxy ketones) or else a reduction of the carbonyl group becomes the major pathway. It is of interest that Devos et al. [22] reported that *trans*-methyl chrysanthemate **24** was obtained by the reaction of methyl *trans* 4-oxobutenoate (one equivalent) with isopropylidenetriphenyl-phosphorane (2.4 equivalent).



CONCLUSION

In contrast to a previous report [7] that the reaction of both cyclic and acyclic α-hydroxy ketones (e.g., 1,2-dimethyl-2-hydroxyethanone) with stabilized ylide phosphoranes of type **6** afford only the respective Wittig products, the results of the present investigation indicate that the final products obtained from the reactions of **1a,b** with Wittig reagents depend on the electronic nature of the substituents (*R*) in the α-position of the methylenephosphoranes and on the reaction conditions. Wittig olefination products were formed either as stable compounds (**cf. 8a–d, 16,** and **18**) or as intermediates, which were further transformed to stable linear heterocyclic derivatives (cf. **11** and **21**). However, in some cases, for example, with ylide **7,** a conjugate-addition process leading to the formation of dioxolo derivatives **22a,b** was observed. In addition, some concluding remarks should be cited: (a) the results showed again (cf. Equations 1 and 2 [5]) a marked resemblance between **1a** and **1b** in their chemical behavior toward phosphorus ylides under investigation; (b) the polarity and the pH (basicity) of the medium play a crucial role in the reaction pathways; and (c) these findings can be used to join more than two heterocyclic moieties of anticipated biological activities in one molecule via application of the Wittig reaction to the appropriate α-hydroxy ketones.



SCHEME 4

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were measured in KBr on a Perkin-Elmer Infracord Spectrometer model 197 (Grating). The ^{1}H- and ^{13}C-

NMR spectra were recorded on a Varian Gemini 200 (200 MHz) instrument using TMS as an internal reference. The mass spectra (MS) were run at 70 eV on Kratos MS-50 equipment and/or Varian MAT 311A spectrometer. Elemental analyses were carried out at the Microanalysis Laboratory, Cairo University. MS refers to mass spectroscopy, NaOEt refers to sodium ethoxide, TEA refers to triethylamine, TPPO refers to triphenylphosphine oxide and AcOEt refers to ethyl acetate.

Action of Phosphorus Ylides **6a** *and* **6b** *on Furoin* (**1a**)

General procedure. A stirred solution of furoin (**1a**) (1.9 g, 0.01 mol) and carbomethoxy-methylenetriphenylphosphorane (**6a**) (3.7 g, 0.011 mol) in dry toluene (50 mL) that contained benzoic acid (0.3 g) was boiled under reflux for 15 hours. The product mixture was evaporated on silica gel under reduced pressure and applied to a silica gel column using chloroform that contained increasing amounts of ethyl acetate as eluents whereby the olefin **8a**, the furan derivative **11a**, and triphenylphosphine oxide were eluted, respectively; TPPO was eluted (6:4, v/v, $CHCl_3$/AcOEt), m.p. 156°C (ca. 85%).

Methyl 3,4-di-(2-furanyl)-4-hydroxybut-2-enoate (**8a**) was eluted (8:2, v/v) as yellow needles (1.4 g, 58%), m.p. 142°C ($CHCl_3$-pentane, 1:2, v/v). Anal. calcd. for $C_{13}H_{12}O_5$ (248.2): C, 62.9; H, 4.87. Found: C, 63.05; H, 4.78%. IR (KBr) cm^{-1}: 3425 (OH), 1695 (C=O, ester), 1642 (C=CH, exocyclic), and 1610 (furan). NMR ($CDCl_3$): δ_H 3.37 (d, 1H, **OH**, J_{HH} = 4 Hz, exchangeable with D_2O), 3.62 (s, 3H,-CH_3), 4.99–5.01 (d of d, diffused, 1H, OH–C**H**), 6.14 (d, 1H, HC–C=C**H**, J_{HH} = 2.4 Hz), and 6.42–7.05 ppm (m, 6H, furan-**H**); δ_c 51.6 (O**C**H_3), 63.3 (CHOH), 124.6 (C=CH), and 171.9 ppm (C=O, ester). MS: *m/z* = 248 (M^+, 22%).

4,5-Di-(2-furanyl)-2-hydroxyfuran (**11a**) was eluted (7:3, v/v) as colorless crystals (0.26 g, 12%), m.p. 175°C (benzene). Anal. calcd. for $C_{12}H_8O_4$ (216.2): C, 66.67; H, 3.73. Found: C, 66.75; H, 3.66%. IR (KBr) cm^{-1}: 3377 (OH), 1608 (C=C, furan) and 1265 (C–O, stretching). NMR ($CDCl_3$) δppm: δ_H 3.65 (s, 1H, **OH**) and 6.48–7.05 (m, 7H, furan-**H**), δc: 106.4 (CH=C–OH) and 149.7 (=C–OH). MS: *m/z* = 216 (M^+, 44%).

Similarly, the reaction of carboethoxymethylenetriphenylphosphorane (**6b**) and furoin (**1a**) was performed under reflux for 15 hours in toluene that contained benzoic acid, whereas the procedure and the workup are the same (with **6a**) using the same amounts. The product residue was chromatographed with $CHCl_3$-ethyl acetate to give **8b, 11a**, and TPPO.

Ethyl 3,4-di-(2-furanyl)-4-hydroxybut-2-enoate (**8b**) was eluted (8:2 v/v) as yellow crystals (1.2 g, 47%), m.p. 140.5°C (AcOEt-ether, 1:3 v/v). Anal. calcd. for $C_{14}H_{14}O_5$ (262.26): C, 64.12; H, 5.38. Found: C, 64.28; H, 5.22%. IR (KBr) cm^{-1}: 3355 (OH), 1700 (C=O, ester), 1635 (C=CH, exocyclic), and 1610 (C=C, furan). ^{1}H-NMR ($CDCl_3$): δ_H 1.13 (t, 3H, OC–**C**H_3), J_{HH} = 6.4 Hz), 3.85 (d, 1H, -**OH**, J_{HH} = 4.5 Hz), 4.08 (q, 2H, O**C**H_2, J_{HH} = 6.2 Hz), 4.63–4.75 (d of d, 1H, HO–C–**H**, J_{HH} = 1.8 Hz), 6.22 (d, 1H, C=C**H**, J_{HH} = 2.4 Hz) and 6.64–7.12 (m, 6H, furan-**H**). MS: *m/z* = 262 (M^+, 39%).

The furan derivative **11a** (0.35 g, 16%) was again eluted (7:3, v/v) and characterized (m.p., mixed m.p.s, and comparative spectra).

A mixture of **1a** (1.9 g, 0.01 mol) and **6a** or **6b** (0.011 mol) in ethyl acetate containing triethylamine (1 mL) was refluxed for 22 hours. After the usual workup, we obtained, in each case, only the product **11a** in ~70% yield (m.p. and mixed m.p.s and comparative spectra) along with triphenylphosphine oxide.

Action of Phosphorus Ylides **6a** *and* **6b** *on Benzoin* (**1b**)

A mixture of α-hydroxy ketone **1b** (1g, 0.005 mol) and methoxy- **6a** or ethoxy-**6b**-carbonylmethylenetriphenylphosphorane (0.0057 mol) in 50 mL of dry toluene containing benzoic acid (0.3 g) was refluxed for 18 hours. After evaporation of the solvent, the residual material was subjected to column chromatography on silica gel. The column was then developed with chloroform that contained increasing amounts of ethyl acetate to give, besides TPPO, compounds **8c** and **11b**, or **8d** and **11b**, respectively.

With **6a**, methyl 3,4-diphenyl-4-hydroxybut-2-enoate (**8c**) was eluted (8:2, v/v) as pale yellow crystals (0.65 g, 48%), m.p. 98°C (benzene). Anal. calcd. for $C_{17}H_{16}O_3$ (268.32): C, 76.1; H, 6.01. Found: C, 76.17; H, 5.93%. IR (KBr) cm^{-1}: 3410 (OH), 1722 (C=O, ester), 1645 (C=CH, exocyclic) and 1535, 1495 (C=C, aromatic). ^{1}H-NMR ($CDCl_3$): δppm 3.42 (d, 1H, -**OH**, J_{HH} = 4.4 Hz), 3.65 (s, 3H, -O**C**H_3), 4.98 (d of d, 1H, OH-C**H**-C=CH, J_{HH} = 4.2 Hz, 1.5 Hz), 6.17 (d, 1H, C=C**H**, J_{HH} = 2.5 Hz), 6.53–7.87 (m, 10H, Ar-**H**). MS: *m/z* = 268 (M^+, 16%).

4,5-Diphenyl-2-hydroxyfuran (**11b**) was eluted (7:3, v/v) as colorless crystals (110 mg, 10%), m.p. 182°C (ethyl alcohol). Anal. calcd. for $C_{16}H_{12}O_2$ (236.27): C, 81.34; H, 5.12. Found: C, 81.44; H, 5.05%. IR (KBr) cm^{-1}: 3303 (OH), 1610 (C=C, fu-

ran), 1538, 1444 (C=C, aromatic) and 1255 (-C-O, stretching). NMR ($CDCl_3$): δ_H 3.62 (br., 1H, **OH**), 6.46 (s, 1H, furanyl-**H**) and 7.36–7.94 ppm (m, 10H, Ar-**H**); δc: 111.8 (CH=C-OH) and 148.6 (=**C**-OH). MS: m/z = 236 (M^+, 25%).

With **6b**, ethyl 3,4-diphenyl-4-hydroxybut-2-enoate (**8d**) was eluted ($CHCl_3$-AcOEt, 8:2, v/v) as pale yellow crystals (0.62 g, 47%), m.p. 139°C (cyclohexane). Anal. calcd. for $C_{18}H_{18}O_3$ (282.34): C, 76.57; H, 6.42. Found: C, 76.52; H, 6.35%. IR (KBr) cm^{-1}: 3330 (OH), 1705 (C=O, ester), 1628 (-C=CH, exocyclic), 1570, 1480 (C=C, aromatic). ^{1}H-NMR ($CDCl_3$): δ_H: 1.05 (t, 3H, OC-C**H**$_3$, J_{HH} = 6.2 Hz), 3.95 (q, 2H, O**CH**$_2$, J_{HH} = 6.2 Hz), 4.15, 4.2 (d of d, 1H, OH-C**H**-C=CH, J_{HH} = 1.5 Hz), 5.48 (d, 1H, C=C**H**, J_{HH} = 2.4 Hz), and 7.17–7.92 (m, 10H, Ar-**H**). MS: m/z = 282 (M^+, 12%).

Compound **11b** was obtained as a sole product (in ~72% yield) from the reaction of **1b** and **6a** or **6b** in refluxing ethyl acetate containing TEA for 25 hours (m.p., mixed mp, and comparative IR and mass spectra).

Action of Heat on Compounds **8a–d**

Compound **8a**, taken as a representative example (0.5 g), was refluxed in dry toluene (30 mL) for 15 hours. After evaporation of the solvent to dryness *in vacuo*, the residual substance was recrystallized from $CHCl_3$-pentane to give yellow needles (ca. 0.45 g, 93%) and proved to be unchanged (m.p. mixed m.p.s, and comparative IR spectra).

Action of Phosphorus Ylide **6c** *on* **1a** *and* **1b**

A mixture of acetylmethylenetriphenylphosphorane (**6c**) (3.2 g, 0.01 mol) and furoin (**1a**) (0.96 g, 5 mmol) was refluxed in toluene containing 0.3 g of benzoic acid for 18 hours. The solvent was evaporated under reduced pressure and chromatography was performed on the residue on silica gel using hexane containing increasing amounts of chloroform.

1,2-Di(2-furanyl)-4-methyl-5-acetyl-penta-2,4-diene-1-ol (**15**) was eluted (1:1, v/v) as yellow needles (0.74 g, 66%), m.p. 152°C (acetonitrile). Anal. calcd. for $C_{16}H_{16}O_4$ (272.3): C, 70.57; H, 5.92. Found: C, 70.63; H, 5.85%. IR (KBr) cm^{-1}: 3385 (OH), 1695 (C=O). NMR ($CDCl_3$), δppm: δ_H 1.76, 2.19 (2s, 6H, 2-C**H**$_3$), 3.49 (d, 1H, O**H**, J_{HH} = 4.2 HZ), 4.15 (d of d, diffused, 1H, -C**H**OH), 6.34–7.52 (m, 8H, furanyl-**H** and 2=C**H**); δc: 18.6, 27.3 (2-**C**H$_3$), 46.4 (-**C**HOH), 148.4 (-**C**-CH$_3$), 196.7 (**C**=O). MS: m/z = 254 (M^+, 38%).

1,2-Di(2-furanyl)-4-methyl-5-acetylpenta-2,4-dien-1-ol (**16**) was likewise produced upon reacting **1b** (1 g, 5 mmol) with **6c** (1.6 g, 5 mmol) in boiling toluene (50 mL) that contained benzoic acid (0.3 g) for 30 hours. Elution with hexane-$CHCl_3$ (7:3, v/v) afforded **16** as colorless crystals (0.7 g, 58%), m.p. 92°C (cyclohexane). Anal. calcd. for $C_{17}H_{16}O_2$ (252.3): C, 80.93; H, 6.39. Found: C, 80.87; H, 6.32%. IR (KBr) cm^{-1}: 3422 (OH), 1690 (C=O), 1647 (C=CH). ^{1}H-NMR ($CDCl_3$): δ_{ppm} 2.61 (s, 3H, C**H**$_3$), 4.24 (d of d, diffused, C**H**OH), 6.19 (d, 1H, J_{HH} = 2.5 Hz, CH-C=C**H**), 7.45–8.0 (m, 10H, Ar-**H**), 11.64 (d, 1H, CHO**H**, J_{HH} = 4.5 Hz). MS: m/z = 252 (M^+, 29%).

Action of Phosphorus Ylide **6d** *on* **1a,b**

A mixture of furion (**1a**) (1 g, 5 mmol) and formylmethylenetriphenyl-phosphonium chloride (1.8 g, 5.5 mmol) in ethyl alcohol (50 mL) that contained triethylamine (2 mL) was refluxed for 2 days. The product mixture was separated by column chromatography on silica gel. Elution with $CHCl_3$-AcOEt (1:1, v/v) afforded yellow crystals of 3,4-di-(2-furanyl)-4-ethoxyprop-2-en-1-al (**18**) (0.25 g, 20%), m.p. 187°C (alcohol/charcoal). Anal. calcd. for $C_{14}H_{14}O_4$ (246.3): C, 68.28; H, 5.73. Found: C, 68.22; H, 5.65%. IR (KBr) cm^{-1}: 1707 [C(O)H], 1635 (=CH), 1605 (C=C, furan). ^{1}H-NMR (DMSO): δ_{ppm} 1.05 (t, 3H, C**H**$_3$, J_{HH} = 7 Hz), 2.4 (d, 2H, C**H**$_2$, J_{HH} = 4.5 Hz), 4.15 (d of q, 2H, OC**H**$_2$, J_{HH} = 7 Hz, J_{HH} = 2.2 Hz), 4.76 (t, 1H, $-\overset{|}{\underset{|}{C}}$**H**, J_{HH} = 3.4 Hz), 5.58 [d of d, 1H, -CH-C=C**H**-C(O)H, distorted], 6.83–7.58 (6H, m, furanyl-**H**) and 8.52 (d, 1H, -C**H**O, J_{HH} = 4.8 Hz). MS: m/z = 246 (M^+, 46%).

4,5-Di-(2-furanyl)-2-ethoxy-4,5-dihydrofuran (**21a**) was eluted (3:7, v/v, $CHCl_3$-AcOEt) as colorless crystals (0.3 g, 25%), m.p. 172°C (alcohol/charcoal). Anal. calcd. for $C_{14}H_{14}O_4$ (246.3): C, 68.28; H, 5.73. Found: C, 68.36; H, 5.64%. ^{1}H-NMR (DMSO): δ_{ppm} 1.75 (t, 3H, C**H**$_3$, J_{HH} = 7 Hz), 3.74 (q, 2H, -C**H**$_2$, J_{HH} = 7 Hz), 5.32 (d, 1H, -O-C**H**, J_{HH} = 5.5 Hz), 5.28 (d of d, 1H, -C-4-**H**, J_{HH} = 5.5 Hz), 7.28 (m, 7H, furanyl-**H**). MS: m/z = 246 (M^+, 66%).

No reaction was observed when equimolar amounts of **1b** and **6d** were refluxed in ethyl alcohol containing TEA, even after 2 days.

Into a well dried, three-necked flask that contained the product of the dissolution of 0.5 g of sodium metal dissolved in 30 mL absolute ethyl alcohol, formymlethylene-triphenylphosphonium chloride (1.8 g, 5.5 mmol) was added portionwise. The reaction mixture was stirred at room temperature for 1 hour followed by addition of **1b** (1 g, 5 mmol) and then was refluxed for 20 hours. The product mixture was concentrated to 10 mL, diluted with 20 mL of distilled water, acidified with concentrated HCl, and then extracted with two-100 portions of

$CHCl_3$. The chloroform extracts were combined, backwashed with 100 mL of H_2O, dried over anhydrous $MgSO_4$, and evaporated **in vacuo** under reduced pressure. Chromatography was performed on the residue on silica gel with hexane that contained increasing amounts of chloroform.

4,5-Diphenyl-2-ethoxy-4,5-dihydrofuran (**21b**) was eluted with pure chloroform as a white substance (525 mg, 42%), m.p. 180°C (ethyl alcohol). Anal. calcd. for $C_{18}H_{18}O_2$ (266.34): C, 81.17; H, 6.81. Found: C, 81.22; H, 6.72%. IR (KBr) cm^{-1}: 1628 (C=C), 1605 (aryl C=C) and 1022 (-C=C-O-). ^{1}H-NMR (DMSO): δ_{ppm} 1.53 (t, 3H, CH_2CH_3), 3.73 (q, 2H, OCH_2), 5.22 (d, 1H, -O-CH, J_{HH} = 8.3 Hz), 5.45 (d of d, 1H, benzyl-H), 6.65–7.82 (m, 11H, aryl-H and furanyl-H). MS: m/z = 266 (M^+, 100%).

Action of Phosphorus Ylide **7** *on* **1a,b**

A mixture of **1a** or **1b** and diphenylmethylenephosphonium bromide in ethyl alcohol that contained sodium ethoxide was caused to react, whereas the procedure and the work up are the same (with **1b** and **6d**), using the same amounts. Chromatography was performed on the product residue, whereby elution with pure chloroform afforded **22a** or **22b**, respectively.

The dioxole **22a** was obtained as colorless crystals (1.2 g, 66%), m.p. 123°C (CH_2Cl_2). Anal. calcd. for $C_{23}H_{18}O_4$ (358.4): C, 77.08; H, 5.06. Found: C, 77.18; H, 4.99%. ^{1}H-NMR ($CDCl_3$): δ_{ppm} 4.43, 4.55 (2d, 2H, CH–CH, J_{HH} = 6.8 Hz), 6.48–7.8 (m, 16H, aryl-H and furanyl-H). MS: m/z = 358 (M^+, 55%).

The dioxole **22b** was obtained as white material (1 g, 60%), m.p. 165.5°C (acetonitrile). Anal. calcd. for $C_{27}H_{22}O_2$ (378.5): C, 85.68; H, 5.86. Found: C, 85.73; H, 5.8%. ^{1}H-NMR ($CDCl_3$): δ_{ppm} 4.37, 4.53 (2d, 2H, CH–CH, J_{HH} = 6.8 Hz), 7.33–7.88 (m, 20H, aryl-H). MS: m/z = 378 (M^+, 50%).

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