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ADDITION-CYCLIZATION REACTIONS OF ALKYLIDENE PHOSPHORANES WITH ∝-BENZOINOXIME

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Treatment of ∞ -benzoinoxime (4) with stable phosphorus ylides 5a,bin dioxane gives oxazolines 8a,b, oxazinone-19 and hydroxyfuran 22, whereas in benzene besides 8a,b, the isoquinoline 16 is obtained. Performing the reaction of 4 and 5a,b in toluene, besides 8a,b, the oxazole 10a and the oxazines 12a,b are obtained. Compound 4, on treatment with a phosphonium salt of the semi-stabilized allylic ylide 23a affords 1-hydroxypyrrole 25a and 2-hydroxy isoquinolidene 27, while with phosphonium salts of the reactive ylides 23b,c gives the imines 29a,b along with the ylides 31 or 33, respectively.

Keywords: Coumarins; isoquinolines; a-benzoinoxime; phosphorus ylides; oxazolines

INTRODUCTION

In relation to previous studies about phosphorus ylides as inexpensive and easily accessible synthons for many different heterocycles,^[1] we described in a very recent communication^[2] the syntheses of furanyl- and dioxolo substituted-furan or phenyl species 2 and 3, respectively, which were prepared from the appropriate ylides and furion or benzoin (**1a,b**) (Scheme 1). Several compounds which incorporate furan moieties are known to be biologically active materials^[3,4] besides having many other uses and applications, such as effective photo-reactive cross-linkage reagents for nucleic acid.^[5]

As a sequel to the preceding work^[2] we herein report the construction of several different nitrogen-containing heterocycles such as oxazolines,

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oxazines, isoquinolines and pyrroles for biological evaluation. The chemistry of the quinoline group and its related compounds has been of increasing interest since a wide range of these compounds showed therapeutic activity, especially against malaria, cancer and micro-organisms.^[6-8] Also the attention paid to oxazole- and oxazine derivatives was attributed to otherwise similar reasons.^[9] Synthesis of the desired compounds was achieved by allowing \propto -benzoinoxime (4) to react with the stabilized ylides **5a,b** and the salts **6a-c** of semi-stabilized and reactive ylides as depicted in Schemes 2–7.



RESULTS AND DISCUSSION

I. Reaction of ~-Benzoinoxime (4) with Stable Phosphorus Ylides 5a,b

Treatment of 4 with equimolar carbomethoxymethylenetriphenylphosphorane (5a) in boiling toluene for two days gave, after separation on column

chromatography, methyl 4,5-diphenyl (3*H*)oxazoline-2-carboxylate (8a) (11%) along with the known 2,4,5-triphenyl-oxazole (10a)^[10] (18%) and methyl 3,5,6-triphenyl(4H)1,4-oxazine-2-carboxylate (12a) (25%). By similar treatment of 4 with carboethoxymethylenetriphenylphosphorane (5b) analogous that described for 5a, compounds 8b (15%), 10a (18%) and 12b (30%) were obtained (Scheme 2). Structures of the above products were substantiated by elemental analyses and spectral data.



Formation of 8 might involve an initial nucleophilic attack by the ylide carbanion 5 on 4 in its tautomeric nitrosa form to give the intermediates Z-7, followed by ring closure (of OH on C=N) and dehydrogenation by a radical process^[11] (pathway A). On the other hand, formation of the unexpected products 10a and 12a,b indicates that participation of the solvent toluene must be involved. Consequently, it can be assumed that a homolytic bond scissions and bond formations between 4 and toluene lead originally to water elimination and formation of the intermediate 9 (pathway B). Intramolecular cyclization of 9 and dehydrogenation afford the oxazole 10a.^[11,12] Both MS and NMR spectra of the oxazole in question, however, favour structure 10a instead of the expected hydro-derivative. Meanwhile, compounds 12a,b are produced by the addition of ylide species 5a,b to the oxazole 10a initially formed, to give the resonance hybrids 11 which by elimination of triphenylphosphine afford compounds 12a,b

through [4+2] cycloaddition. Another possibility involves nucleophilic attack of 5 to the imine-derivative 9 followed by dehydrogenation and elimination of triphenylphosphine can also account for the formation of 12. Interaction of the solvent toluene in the above reaction was proved by refluxing a solution of 4 in toluene (or *p*-nitrotoluene) for 2 days. From the latter reaction only the corresponding oxazole 10 was isolated in ~27% yield. Analogous thermal condensations were also observed during photolysis of phenanthraquinone- 9,10-monoimine in the presence of substituted toluenes which leads to phenanthro-[9,10-*d*]oxazoles. It is assumed that intermediates arising from homolytic scission of aryl-C-H bond are involved in these transformations.^[13] Subsequently, the same mechanism was adopted by Nicolaides *et al*^[12,14] for the reactions of *o*-quinone monoximes with some dienophiles in refluxing toluene as well as for the reactions of monoximes with several methyl substituted aromatic systems.^[12b]

In order to support the mechanism that outlined in Scheme 2, the intermediates methyl benzoiniminoacetate (Z-7Aa, the tautomeric form of Z-7a) and \propto -benzyliminobenzoin (9a) were independently synthesized and characterized (see experimental section). The route involves titanium (IV) chloride catalyzed condensation of amine to the readily available benzoin (equation 1). Subjecting compounds Z-7Aa and 9a to the reaction conditions (heating in toluene for two days), oxazoles 8a (17%) and 10a (55%) were obtained, respectively. However, addition of a catalytic amount of triethylamine to the reaction mixture in the first case (Z-7Aa). affords 8a in 43% yield. In this respect, phosphorus ylides is considered to be acting as a weak base.



Furthermore, treating of 9a with an equimolar amount of 5a in boiling toluene for two days gave 12a (33%) and 10a (22%). The products 8a, 10a

and 12a were confirmed by m.p., mixed m.ps. and comparative IR and NMR spectra with the reference samples.

Repetition of the above reaction between the substrate 4 and two equivalents of 5a in boiling benzene for two days furnished, 4'-hydroxy 1'(3H-[5,6]-3-oxo-benzopyran-1-yl) isoquinoline (16) (42%) along with the expected oxazoline 8a (18%). Compounds 16 (37%) and 8b (9%) were likewise obtained by refluxing 4 and 5b (2 equiv.) in benzene for two days (Scheme 3). The proposed structure 16 has been confirmed by elemental analysis and spectral data.



For the formation of compound 16, an unusual [4+2] cycloelimination across the initial intermediate 7B (via 7, essentially in the trans form), extended from the exocyclic imino bond to the aromatic system, leading to the formation of the intermediate 13 can be proposed.^[15a] Elimination of the H₂O molecule and the appropriate alcohol (RH) moiety might arise, however, by an electrocyclic process.^[11] Further condensation of 13 with a second ylide species **5a,b** leads to extrusion of RH and formation of the phosphonium intermediate 14. A behaviour which recalls that of other hydroxy compounds toward the phosphorus ylides **5a,b**.^[15b] Hydrolysis of 14, followed by an intramolecular cyclization, dehydration and rearomatization affords the final product 16 via the intermediate 15. Such a mechanism was previously reported^[15a] for the formation of biscoumarin 18 from the reaction of dihydroxybenzils 17 with stabilized Wittig reagents 5a,b whereupon 18 was produced in each case (eqn. 2).



The anomalous results of the above two reactions prompted us to study the same reaction in dioxane. When equimolar amounts of oxime 4 and ylide 5a were heated in dioxane at reflux temperature for two days and then the reaction mixture was subjected to chromatographic separation, the oxazoline 8a (21%), the known^[2] 4,5-diphenyl 2-hydroxyfuran (22) (16%) and 5,6-diphenyl 2*H*-1,4-oxazin-2-one (19) (29%) were obtained and identified (Scheme 4). No trace of compound 16 could be observed in the product mixture.



According to the mechanism has been proposed in Scheme 4, the formation of compound 19 involves the previously suggested intermediate $Z-7^{[16]}$ which readily lactonizes to give 19 by loss of alcohol and radical

induced dehydrogenation. Concurrunt with formation of 7, the ylide 20 is also formed from the condensation of 5a with the hydroxyl group in $4^{[15b]}$ (pathway B). Intramolecular elimination of (hydroxyimino)triphenylphosphorane species (Ph₃P=NOH) from 20 results in the formation of 21 from which compound 22 was formed by a prototropic rearangement. An analogous reaction has been reported to proceed between phosphorus ylides and Manich bases^[17] or oximes.^[17,18]

In a systemic study, we found that oxime 4 reacts similarly, with 5b in dioxane whereby compounds 8b (13%), 19 (27%) and 22 (26%) were formed.

Turning now to the scope of the above three reactions of oxime 4 with the stable phosphorus ylides 5a,b some concluding remarks should be cited: (1) even though Schemes 2-4 describe competition reactions between two options available to ylides 5a,b in their reactions with oxime 4, i.e., an attack of the ylide on the imino group and/or on the hydroxyl function, it is obvious that addition-elimination reaction of 5 on the oximino-group in 4 is predominantly observed (cf. compounds 8, 16 and 19); (2) it is safe to state that both the type and the polarity of the solvent play significant roles in the reaction pathways. Considering the first reaction, participation of the solvent toluene in formation of the final products 10 and 12 occured wherein intermediates arising from homolytic scission of the arvl-H bond are involved. With respect to the problem posed by the effect of the polarity of the medium (benzene or dioxane), on the final products, it seems that the reported observations, however, are consistent with assigned mechanisms since it is established^[19] that the use of polar solvents (e.g., dioxane) enhance the formation of cis-isomer (see Scheme 4), while generation of E-7 in benzene is evoked by the non-polar medium^[19] and by the presence of the exocyclic \propto -hydroxyl group;^[20] (3) since stereochemical factors are essential requisites for the ring closure of heterocyclic precursors.^[21] it appears that conversion of 7 either to 8 and 19 or to 16 is a stereoselective process.^[21] Furthermore, transformation of 9 to oxazole product 10 through dehydrogenation can be explained by the prolonged time of heating (> 48 h) through radical processes.^[11]

II. Reaction of ∞ -Benzoinoxime (4) with the Semi-stabilized Allylic Ylide 23a

When a mixture of oxime 4 and allyltriphenylphosphonium bromide (6a) (two equivalents) in dimethylformamide (DMF) is treated with lithium

hydride (LiH), N-hydroxy 1([5',6']benzopyran-1'-ylidene)isoquinoline (27) and the known^[22] 2,3-diphenyl 1-hydroxy-pyrrole (25a) are isolated in 32 and 28% yield, respectively, (equation 3). The pyrrole derivative 25a has also been obtained previously^[22a] by treatment of *E*-benzil monoxime with vinyltriphenylphosphonium bromide in DMF containing sodium hydride (NaH). The structure of compound 27 has been substantiated on the basis of elemental analysis and spectral data.



Apparently, formation of compound 25a involves an initial attack of nitrogen on 23a to give the ylide 24 (in the *cis* form) which readily cyclizes through [2+2] to give 25 upon displacement of a molecule of H_2O and elimination of the phosphorane moiety ($Ph_3P=CH_2$),^[23] (Scheme 5, A). Concurrent with formation of the betaine Z-24, its *trans* analog of type

E-24 is also produced followed by elimination of the phosphorane moiety $(Ph_3P=CH_2)$ and dehydrogenation to give the highly instable intermediate 26A. Stabilization of 26A was attained, however, by the addition of a second ylide species 23a in an identical way to give the coumarin 27 via 26B (Scheme 5, B). The reaction at the central carbon of the allyl group in 23a is a documented process,^[23] subsequently, formation of an intermediate such as 24 is also reported.^[22a] Furthermore, it is assumed that the ready elimination of methylidenetriphenylphosphorane occurs through a carbanion mechanism driven by the resulting gain in aromaticity. Moreover, it is evident that a competitive formation of the *cis* and *trans* isomers is evoked by the presence of the protonic solvent DMF^[24] and the neighbouring hydroxyl group,^[20] respectively. Moreover, generation of the intermediate 26B is not surprising since it is reported^[22b] that addition of salicylalde-hyde to vinyltriphenylphosponium bromide, in the presence of a base, led to an ylide intermediate (similar to 26B) which cyclized to 3,4-chromene.

III. Reaction of ∝-Benzoinoxime (4) with Non-stabilized Ylides 23b,c

Furthermore, we have studied the behaviour of oxime 4 with reactive ylides 23b,c (Schemes 6 and 7). A mixture of compound 4 and methylidenetriphenylphosphorane (23b), prepared in situ from the corresponding bromide salt 6b, in dimethylformamide containing LiH was heated under reflux for 18 h. The product mixture was then separated by column chromatography to give the stereoisomers 1-hydroxy 1,2-diphenyl-2-N-methyliminoethane (29a. Ε and Z) (38%)and 4.5-diphenyl (3H-oxazol-2-ylidene)triphenylphosphorane (31) (23%)(Scheme 6). Efforts made to separate the stereomers of 29 were unsuccessful.

Obviously, an initial nucleophilic attack by the ylide carbanion on the nitroso group (pathway A) leads to the imine 28a which can readily isomerizes to the imine 29a. Meanwhile, the addition of 23b to 4 leads to the betaine 30 which by further intramolecular cyclization, dehydration and dehydrogenation gives the phosphorane product 31 (pathway B). Formation of 31 instead of the expected 4,5-dihydro-derivative is based on the ¹H-NMR spectroscopy of the compound in question which was consistent with structure 31. Furthermore, the formation of the intermediate 30 by the action of non-stabilized Wittig reagent 23b recalls that of other ∞ -keto-oximes toward unstabilized ylides.^[22a]



Finally, the reaction of 4 with ethyltriphenylphosphonium bromide (6c) under phase-transfer catalysis condition, as described for salts 6a,b, affords the ethyl analog 29b (*E* and *Z*) (42%) along with (4,5-diphenyl-3,4,5-trihydro-1-ethylpyrrole-2-ylidene)triphenylphosphorane (33) in 33% yield, most probably by means of a condensation of a second ylide species 23c to the intermediate 28b which is initially formed according to Scheme 7. When 33 was treated with N-bromosuccinimide, 34 (88%) was

isolated. Moreover, structure 29 was rigorously attested by unequivocal routes by reacting benzoin either with methyl or ethylamine (anhydrous) (see experimental). Nevertheless, no conversion for 29b to 33 was observed in a parallel experiment when 29b was allowed to react with 6c under the same reaction conditions. This result can be explained in terms of both intermediates 28b and 32 are formed concurrently in the reaction.

CONCLUSION

The results of the previous^[2] and the present work showed a marked resemblence between 1 and 4 in their chemical behaviour toward triphenylmethylenephosphoranes. Firstly, either the carbonyl function in 1 or the imino-moiety in 4 is the most vulnerable site of attack by the nucleophilic Wittig reagents. The initial product is usually followed by variable transformations leading to the construction of different heterocyclic products. Secondly, the hydroxyl function in 1 and 4 can also occasionally envolve in the reactions. The structure of the final products depends upon the electronic and the characteristics of both reactants and the experimental conditions.

EXPERIMENTAL

All mps are uncorrected. IR spectra were measured in KBr, on a Perkin-Elmer infrared spectrometer model 197 (Grating). The ¹H- and ¹³C-NMR spectra were recorded on a Varian Gemini 200 (200 MHz) instrument using TMS as an internal reference. The mass spectra were run at 70 eV on Kratos MS-50 equipment and/or Varian MAT 311 A spectrometer. Elemental analyses were carried out at the Microanalysis Laboratory, Cairo University. Light petroleum refers to the fraction of 40–60°C. ∞ -Benzoinoxime and reagents were purchased from Aldrich.

I. Reaction of ∞ -Benzoinoxime (4) with Phosphorus Ylides 5a,b. General procedure

A solution of compound 4 (1 g, 4.4 mmol) and the appropriate ylide (5a,b) (4.6 mmol) in toluene or dioxane (or 8.8 mmol in benzene) 20 mL was heated at reflux untill all the oxime was consumed (-2 days; the reactions

were monitored by TLC). After removal of the solvent, the residue was chromatographed on silica gel with hexane containing increasing amounts of chloroform as eluent. According to this general procedure the following products were obtained:

A. Using the solvent toluene

Methyl 4,5-diphenyl-3H-oxazoline-2-carboxylate (**8a**) was obtained from **5a** (8:2, v/v) as pale yellow crystals (140 mg, 11%), m.p. 180–182 °C (ethyl alcohol-ether, 1:3, v/v). Found: C, 72.65; H, 5.29; N, 4.88; $C_{17}H_{15}NO_3$ (381.32), requires: C, 72.58; H, 5.37; N, 4.98%. NMR (d₆-DMSO): δ_H 3.38 (3H, s, OCH₃), 3.64 (1H, s, C-2-H), 7.25–7.78 (10H, m, Ar-H), 12.09 (1H, s, NH); δ_C 38.7 (C-2), 54.6 (OCH₃), 127.3 (C-5), 151.5 (C-4), 169.2 (C=O, ester). *m/z* (%): 381 [M⁺. 100]. IR (KBr) cm⁻¹: v 3416 (NH), 1715 (C=O, ester), 1262 (C-O-C-stretching).

2,4,5-Triphenyl oxazole (10a) was obtained from 5a (7:3, v/v) as yellow crystals (230 mg, 18%), m.p. 113–115°C (lit.^[10], m.p. 114.5°C) (dichloromethane). The reaction between equimolar amounts of 4 and 5b under the same conditions also gave compound 10a (220 mg, 18%). The identity of 10 (MS, IR and ¹H NMR) is exactly the same as previously described: [10]

Methyl 3,5,6-triphenyl-(4H)-1,4-oxazine-2-carboxylate (12a) was also obtained (1:1, v/v) as yellow crystals (410 mg, 25%), m.p. 192–193°C (acetonitrile). Found: C, 78.92; H, 5.1; N, 3.72, $C_{24}H_{19}NO_3$ (369.42), requires: C, 78.03; H, 5.18; N, 3.79%. NMR (d₆-DMSO): δ_H 3.53 (s, 3H, OCH₃), 7.17–7.88 (15 H, m, Ar-H), 9.35 (1H, br., NH); δ_c : 58.6 (OCH₃), 126.1 (C-5), 150.2 (C-6), 154.4 (C-2), 166.8 (C=O, ester). *m/z* (%): 369 [M⁺, 100]. IR (KBr) cm⁻¹: v 3410 (NH), 1710 (C=O, ester).

Ethyl 4,5-diphenyl-3H-oxazoline-2-carboxylate (**8b**) was obtained from **5b** (8:2, v/v) as pale yellow crystals (190 mg, 15%), m.p. 167–169°C (CH₂Cl₂). Found: C, 73.26; H, 5.85; N, 4.63; C₁₈H₁₇NO₃ (295.34), requires: C, 73.2; H, 5.8; N, 4.74. NMR (d₆-DMSO): $\delta_{\rm H}$ 1.52 (3H, t, J_{HH}= 7Hz, OCCH₃), 3.84 (1H, s, C-2-H); 4.15 (2H, q, J_{HH} = 7 Hz), 7.13 – 8.05 (10 H, m, Ar-H), 11.83 (1 H, s, NH); $\delta_{\rm c}$ 15.2 (-CH₃), 35.6 (C-2), 62.4 (OCH₂), 126.5 (C-4), 149.5 (C-5), 168.3 (C=O, ester). *m/z* (%): 295 [M⁺, 100]. IR (KBr)cm⁻¹: v 3390 (NH), 1705 (C=O, ester), 1260 (C-O-C).

Ethyl 3,5,6-triphenyl-4H-oxazine-2-carboxylate (12b) was also obtained from **5b**, (1:1, v/v) as yellow crystals (500 mg, 30%), m.p 180–182 °C (acetonitrile). Found: C, 78.26; H, 5.48; N, 3.57, $C_{25}H_{21}NO_3$ (383.45),

requires: C, 78.31; H, 5.52; N, 3.65%. NMR (d_6 -DMSO): δ_H 1.48 (3H, t, J_{HH} = 7 Hz, OCCH₃), 7.14–8.1 (15H, m, Ar-H), 9.12 (1H, s, NH); δc 16.5 (C-CH₃), 63.3 (OCH₂), 118.3 (C-3), 128.2 (C-5), 144.7 (C-6), 168.4 (C=O, ester). *m/z* (%): 383 [M⁺, 100]. IR (KBr) cm⁻¹: v 3191 (NH), 1718 (C=O, ester).

Reaction of \propto -Benzoinoxime (4) with Toluenes

A solution of 4 (0.3 g, 1.3 mmol) in toluene (or *p*-nitrotoluene) (5 ml) was refluxed for two days. The solvent was evaporated and the residue was separated by fractional crystallization to give compound **10a** (100 mg, 27%), m.p. 113–115°C (CH₂Cl₂) (lit. ^[10], m.p. 114.5°C or **10b** (126 mg, 28%), m.p. 143–145°C (ethanol) (lit^[25], m.p. 145–146°C).

Synthesis of Imino Benzoins Z-7Aa and 9a

The procedure reported^[26] by Armesto *et al.* for the preparation of ∞ -imino oximes (Z, Z-configuration) from 1,2-dicarbonyl compounds was modified as follows:

to a solution of 2 g (9 mmol) of benzoin and glycine methyl ester hydrochloride (or benzylamine) (266 mmol) in 200 mL of dry benzene at 5°C was added dropwise a solution of TiCl₄ (1.47 mL, 13 mmol) in 150 mL of benzene. The reaction mixture was further stirred at room temperature for 3 days. The product mixture was then filtered, the solid residue is washed repeatedly with benzene (6×50 mL), and the solvent removed by distillation under reduced pressure. The crude product is dissolved in ether (200 mL) and the excess amine is then removed by repeated extraction with 10% dil HCl (3×100 mL). The ethereal layer is dried (MgSO₄) and evaporated to dryness under reduced pressure to give Z-7Aa and 9a, respectively.

Compound Z-7Aa was obtained as colorless crystals (0.9 g, 35%), m.p. 147–149°C (CH₂Cl₂). Found: C, 71.85; H, 6.92; N, 4.78, C₁₇H₁₇NO₃ (383.33); requires: C, 72.07; H, 6.05; N, 4.94%. NMR (CDCl₃): $\delta_{\rm H}$ 3.42 (3H, s, OCH₃), 4.17 (1H, d, J_{HH}=2.4 Hz, CHOH), 4.63 (2H, s, = NCH₂), 6.32 (1H, s, OH), 7.24–7.76 (10H, m, Ar-H); $\delta_{\rm C}$ 48.3 (=N.CH₂), 54.5 (OCH₃), 63.8 (CHOH), 162.8 (C=N), 168.9 (C=O, ester). *m/z* (%): 383 [M⁺, 100]. IR (KBr) cm⁻¹: v 3440 (OH), 1710 (C=O, ester), 1628 (C=N).

Compound 9a was obtained as colorless crystals (1.2 g, 42%), m.p. 106–108°C (n-hexane). Found: C, 83.53; H, 6.28; N, 4.41; $C_{21}H_{19}NO$ (301.39), requires: C, 83.69; H, 6.35; N, 4.65%. NMR (CDCl₃): $\delta_{H}4.18$ (1H, d, $J_{HH}=2.3$ Hz, CHOH), 4.58 (2H, s, = N.CH₂), 6.27 (1H, s, OH), 7.25–7.86 (15H, m, Ar-H); δc 50.4 (CH₂), 63.6 (CHOH), 160.8 (C=N). *m/z* (%): 301 [M⁺, 100]. IR (KBr) cm⁻¹: υ 3425 (OH), 1620 (C=N).

Conversion of Z-7Aa into 8a

A solution of 0.5 g (1.8 mmol) of Z-7Aa in 15 mL of dry toluene (best yield in the presence of 0.5 mL TEA) was heated under reflux for 2 days. The solvent was evaporated and the residue was crystallized from dichloromethane to give the oxazole 8a (210 mg 43%), m.p. 182°C. The identity of 8a is established by comparison of the m.ps. and spectroscopic data with the corresponding reference sample.

Conversion of 9a into 10a

A solution of **9a** (0.5 g, 1.6 mmol) in toluene (10 mL) was refluxed for two days. The solvent was evaporated and the residue was separated by fractional crystallization to give compound **10a** (270 mg, 55%), m.p. 115°C (CH₂Cl₂) (m.p., mixed m.ps. and comparative IR and NMR spectra).

Reaction of 9a with 5a

The reaction of **9a** (0.5 g, 1.6 mmol) with **5a** (0.57 g, 1.7 mmol) in refluxing toluene for two days as described in the general procedure and the same working up afforded compounds **10a** (110 mg, 22%), m.p. 115°C (CH₂Cl₂) and **12a** (200 mg, 33%), m.p. 190–193°C (acetonitrile). **10a** and **12a** were proved by admixed melting points and by study of their infrared and ¹H NMR spectra as well as by elemental analyses.

B. using the solvent benzene

The reaction of 4 (1 g, 4.4 mmol) with 5a,b (8.8 mmol) in refluxing benzene for two days as described above afforded the products 8a and 16 or 8b and 16, respectively. Compounds 8a and 8b were obtained (8:2, v/v) in 18 and 9% yield, respectively.

4'-Hydroxy 1'(3H-[5,6]-3-oxo-benzopyran-1'-yl) isoquinoline(16) was obtained from 5a (4:6, v/v) as yellow crystals (530 mg, 42%), m.p. 172–174°C (acetone). Found: C, 74.68; H, 3.76; N, 4.77; $C_{18}H_{11}NO_3$ (289.29), requires: C, 74.73; H, 3.83; N, 4.84%. NMR (d₆-DMSO): $\delta_{\rm H}$ 6.42 (1H, d, J_{HH}= 2.6 Hz, C-4`-H), 7.13–7.89 (9H, m, Ar-H), 9.45 (1H, br., OH), $\delta_{\rm C}$ 129.3 (C-4`), 144.6 (C-4), 153.5, 154.2 (C-1`) and C-1), 177.4 [C-3` (O)]. m/z (%): 289 [M⁺, 22]. IR (KBr) cm⁻¹: v 3450 (OH), 1720 (C=O, pyrone). Compound 16 was also obtained from 5b (470 mg, 37%).

C. using the solvent dioxane

The reaction of 4(1 g, 4.4 mmol) with 5a,b (4.6 mmol) in refluxing dioxane for two days (TLC) as described in the general procedure, the following products were chromatographically separated:

Compounds 8a and 8b were obtained (8:2, v/v) in 21 and 13% yield, respectively.

4,5-Diphenyl-2-hydroxyfuran (22) was separated (7:3, v/v) from both reactions of 4 with 5a and with 5b in 16 and 26% yield, respectively. compound 22 was obtained as colourless crystals, m.p. 180–182 °C (benzene) (lit^[2], m.p. 182 °C). IR, ¹H- and ¹³C NMR of 22 are consistent with the literature.^[2]

5,6-Diphenyl (2H)1,4-oxazin-2-one (19) was also separated (2:8, v/v) from both reactions with 5a and 5b in 29 and 27% yield, respectively. Compound 19 was obtained as yellow crystals, m.p. 167–168 °C (CHCl₃/cyclohexane, 2:1, v/v). Found: C, 77.17; H, 4.36, N, 5.58, C₁₆H₁₁NO₂ (249.27), requires: C, 77.09; H, 4.45; N, 5.62. NMR (d₆-DMSO): $\delta_{\rm H}$ 6.44 (1H, s, C-3-H), 7.13 – 7.88 (10H, m, Ar-H), $\delta_{\rm C}$ 131.1 (C-3), 143.4 (C-5), 153.8 (C-6), 176.2 [C-2(O)]. *m/z* (%): 249 [M⁺, 100]. IR (KBr) cm⁻¹: v 1755 (C=O, pyrone), 1595 (C=N), 1235 (C-O-C).

II. Reaction of ∞ -Benzoinoxime (4) with Allyltriphenylphosphonium Bromide (6a)

To a slurry of 93 mg of lithium hydride (LiH) dispersion (57% in mineral oil) in 10 mL of dry dimethylformamide (DMF) was added dropwise 1 g (4.4 mol) of the oxime 4 in 20 mL of DMF. The reaction mixture was

stirred at room temperature until all hydrogen evolution had ceased, and the salt **6a** (8.8 mmol) was introduced all at once. The reaction was allowed to remain at room temperature for further 2 h and then refluxed for 14 h. The product mixture was poured into 300 mL of H₂O, and extracted with 2–100 mL portion of CHCl₃. The CHCl₃ extracts were combined, backwashed with 100 mL of H₂O, dried, and evaporated *in vacuo*. The residue was chromatographed on silica gel with hexane-CHCl₃ to give compounds **25** and **27**, respectively.

Fractions up to (8:2, v/v) yielded pale yellow crystals of 2,3-diphenyl *l*-hydroxypyrrole (**25a**) (280 mg, 28%), m.p. 50–52 °C (light petroleum 40–60°) (m.p. is not recorded in the literature ^[22a]). Benzoylation of **25a**, as previously described by Schweizer *et al*^[22] yielded *N*-benzoyl derivative **25b**, m.p. 82–84 °C (light petroleum, b.r. 40–60°) (lit.^[22a], m.p. 80–83 °C). IR and ¹H NMR of **25a,b** are consistent with the literature.^[22a]

Fractions up to (7:3, v/v) afforded yellow crystals of *N*-hydroxy $l([5,6]benzopyran-1-ylidene)isoquinoline (27) (385 mg, 32%), m.p. 111–112°C (diethyl ether). Found: C 78.5; H, 4.71, N, 5.03, C₁₈H₁₃NO₂ (275.13), requires: C, 78.53, H, 4.76; N, 5.09%. NMR (CDCl₃): <math>\delta_{\rm H}$ 6.42, 6.44 (2^{*} 1H, 2d, J_{HH}= 3.3 Hz, C-3'-H & C-3-H), 6.77, 6.8 (2^{*}1H, 2d, J_{HH}= 3.3 Hz, C-4'-H & C-4-H), 7.35–7.83 (8H, m, Ar-H), 11.65 (1H, s, NOH, exchangeable with D₂O), $\delta_{\rm C}$ 108.6 (C-4), 114.6 (C-4'), 125.2 (C-3), 136 (C-1), 146.2 (C-1'), 148.8 (C-3'), m/z (%): 275 [M⁺, 100]. IR (KBr) cm⁻¹; v 3393 (NOH), 1634 (C=C, exocyclic), 1465 (C-O-C).

III. Reaction of ∝-Benzoinoxime (4) with Non-stabilized Ylides 23b,c

A solution of the appropriate salt **6b** (4.6 mmol) or **6c** (8.2 mmol) and the oxime **4** (1 g, 4.4 mmol) in dry dimethylformamide (DMF, 40 mL) was treated with lithium hydride (LiH) under the experimental conditions described for the salt **6a**. The reaction mixture was heated under reflux for 20 h and then worked up as described for the reaction of **6a** and separated by column chromatography using n-hexane/chloroform (8:2 up to 1:1) as the eluent.

(4,5-Diphenyl-3H-oxazol-2-ylidene)triphenylphosphorane (31) (490 mg, 23%) was obtained from (4 + 6b) as pale yellow crystals, m.p. 125 °C (light petroleum). Found: C, 81.89; H, 5.34; N, 2.83; P, 6.33, C₃₃H₂₆NOP (483,56), requires: C, 81.97; H, 5.42; N, 2.89; P, 6.4%, NMR (CDCl₃): $\delta_{\rm H}$ 7.25–7.75 (25H, m, Ar-H), 8.49 (1H, s, NH); $\delta_{\rm C}$ 85 (d, ²J_{cp}= 105 Hz, C-2),

128.3 (C-5), 151.7 (C-4); δ_p = 16.35 ppm. *m/z* (%)= 483 [M⁺, 8]. IR (KBr) cm⁻¹: v 3340 (NH), 1628 (C=C), 1672, 1505 (C=P).

1-Hydroxy 1,2-diphenyl-2-N-methyliminoethane (**29a, E, Z**) (370 mg, 38%) was obtained from (**4** + **6b**) as yellow leaflets, m.p. 96–98 °C (pentane). Found: C, 79.86; H, 6.66; N, 6.28, $C_{15}H_{15}NO$ (225.29), requires: C, 79.97; H, 6.71; N, 6.22%. ¹H(CDCl₃): $\delta_{\rm H}$ 2.89, 2.9 (2*3H, 2s, 2*NCH₃), 4.24 (1H, d, diffused, CHOH), 6.18 (1H, s, OH), 7.25 - 8.23 (10H, m, Ar-H). $\delta_{\rm c}$ 33.3 (N.CH₃), 63.6 (CHOH), 146.3, 153.4 (C-NOH, *E* & *Z* isomers). *m/z* (%)= 225 [M⁺, 18]. IR (KBr)cm⁻¹: υ 3446 (OH), 1620 (C=N).

Triphenylphosphine oxide was also obtained from (4 + 6b and/or 6c) and identified.

(4.5-Diphenyl-3,4,5-trihydro-1-ethylpyrrole-2-ylidene)triphenylphosphorane (33) (33%) was obtained from (4 + 6c) as pale yellow needles, m.p. 139–140°C (ether/cyclohexane). Found: C, 84.43, H, 6.65; N, 2.64; P, 6.15, $C_{36}H_{34}NP$ (511.66), requires: C, 84.51; H, 6.7; N, 2.74, P, 6.05%. NMR (CDCl₃): δ_{H} 0.83 (3H, t, J_{HH} = 6.5 Hz, N-C-CH₃), 2.55 (2H, q, J_{HH}= 6.5 Hz, N-CH₂), 3.01 (2H, d of d, ³J_{HP}= 8.5 Hz, ²J_{HH}= 6.8 Hz, C-3-H₂), 4.15 (1H, d of t, broad, C-4-H), 4.48 (1H, d of d, ²J_{HH}= 6.6 Hz, ⁴J_{HH}= 1.7 Hz, C-5-H), 6.83–7.85 (25H, m, Ar-H); δ_{c} 15.4 (N-C-CH₃), 28.4 (C-3-H₂), 35.8 (H-N-CH₂), 36.2, 37.5 (C-4 and C-5), 54.3 (d, J_{cp} = 183.5 Hz, C=P); δ_{p} = 17.3 ppm. *m*/z (%): 511 [M⁺, < 6]. IR (KBr)cm⁻¹: v 1677, 1515 (C=P).

1-Hydroxy 1,2-diphenyl-2-ethylaminoethylene (**29b**) (42%) was obtained from (**4** + **6c**) as yellow crystals, m.p. 76–78 °C (light petroleum). Found: C, 80.22; H, 7.1; N, 5.78; $C_{16}H_{17}NO$ (239.32), requires: C, 80.3; H, 7.16; N. 5.85%. NMR (CDCl₃): $\delta_{H}0.81$ (3H, t, $J_{HH} = 6.5$ Hz, NC-CH₃), 2.68 (2H, q, $J_{HH} = 6.5$ Hz, N-CH₂), 4.05 (1H, d, diffused, CHOH), 5.74 (1H, s, OH), 6.93–7.72 (10H, m, Ar-H), δ_c 16.3 (N-C-CH₃). 37.7 (N-CH₂), 64.2 (HC.OH), 143.5, 155.2 (C=NOH, *E* & Z isomers). *m*/z (%): 239 [M⁺, 22]. IR: 3438 (OH), 1625 (C=N).

Reaction of 33 with NBS

N-Bromosuccinimide (NBS) (27 mg, 0.15 mmol) and benzoyl peroxide (3.6 mg, 0.02 mmol) were added to a solution of ylide **33** (76 mg, 0.15 mmol) in 15 mL of dry CCl₄. The mixture was heated under reflux for 2 h and filtered while hot. Evaporation of the solvent left an oil, which was chromatographed (silica gel, 8:2 n-hexane/ethyl acetate) to give **34**

(67 mg, 88%), m.p. 108 °C (cyclohexane). Found: C, 84.74; H, 6.25; N, 2.67; P, 6.15, $C_{36}H_{32}NP$ (509.64), requires: C, 84.84; H, 6.33; N, 2.75; P, 6.08%. m/z (%): 509 [M⁺, 27]. IR: 1618 (C=C), 1680, 1510 (C=P).

Preparation of the Imines 29a,b

Methylamine or ethylamine (unhydrous) (150 mmol) was bubbled within an hour into a stirred solution of benzoin (1 g, 4.5 mmol) in absolute ethyl alcohol (15 mL) at -35° C. The reaction mixture was allowed to warm till room temperature and further stirred for 3 h. Evaporation of the volatile materials, *in a vacuo*, resulted in the isolation and identification (comparative m.ps., MS and IR spectra) of compounds **29a,b** in ~ 68% yield.

Reaction of 29b with 23c

A mixture of **29b** (0.5 g, 2.1 mmol) and ethyltriphenylphosphonium bromide (**6c**) (0.6 g, 2.3 mmol) in dimethylformamide (20 mL) containing LiH (0.2 g) whereby the procedure and the working up are the same (with 4 + 6c). The product residue was chromatographed whereupon **29b** and unidentified compounds were the isolated products. **29b** was confirmed by comparative m.ps., MS and IR spectra).

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