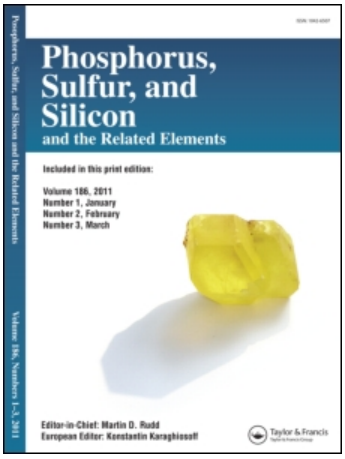

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Addition-Cyclization Reactions Of Alkylidene Phosphoranes With α-Benzoinoxime

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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,b**in 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.

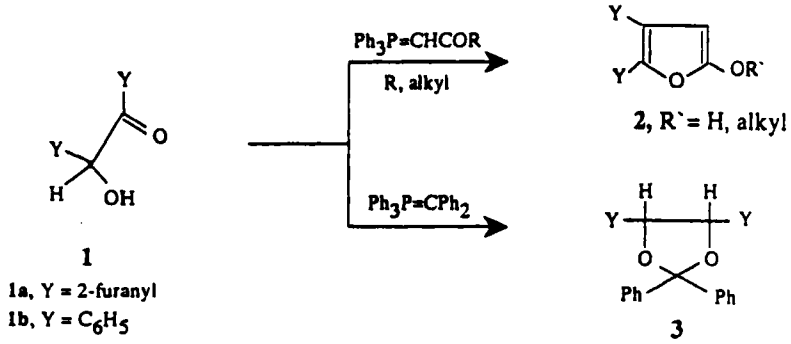
Keywords: Coumarins; isoquinolines; α-benzoinoxime; phosphorus ylides; oxazolines

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,

* corresponding author.



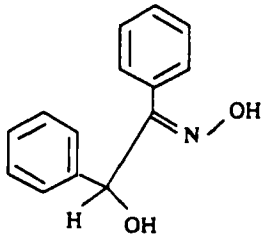
1

1a, Y = 2-furanyl

1b, Y = C_6H_5

SCHEME 1

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 ∝-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.



4

Ph_3P=CHCOR

5a, R= OCH_3

5b, R= OC_2H_5

Ph_3P^+- $CH_2R`$ Br^-

6a, R`= (-CH=CH_2)

6b, R`= H

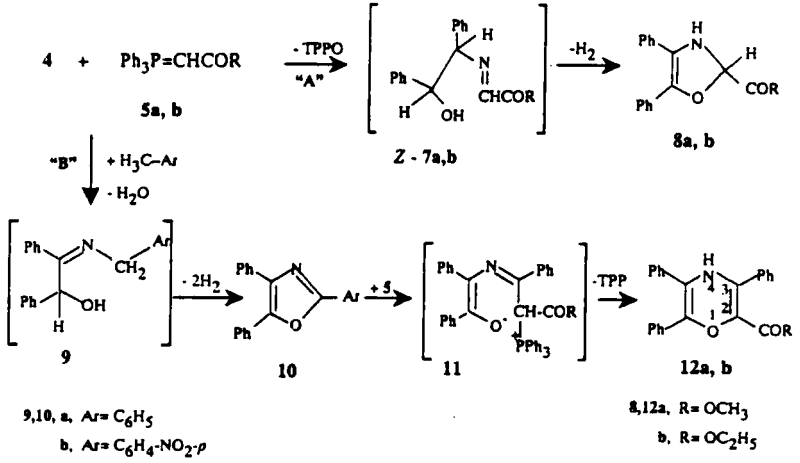
6c, R`= CH_3

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.

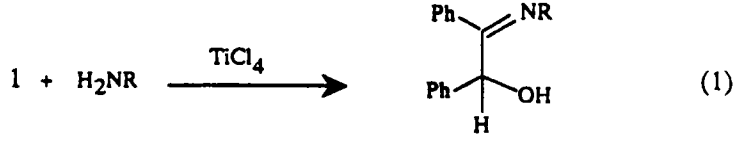


SCHEME 2

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 ∝-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.



(1)

Z-7Aa, R= CH_2COOCH_3

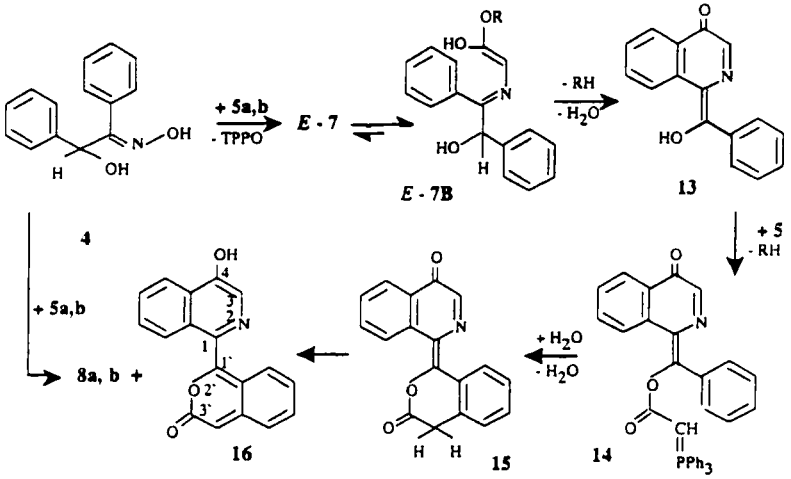
Z-9a, R= $CH_2C_6H_5$

29a, R= CH_3; **29b**, R= C_2H_5

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.

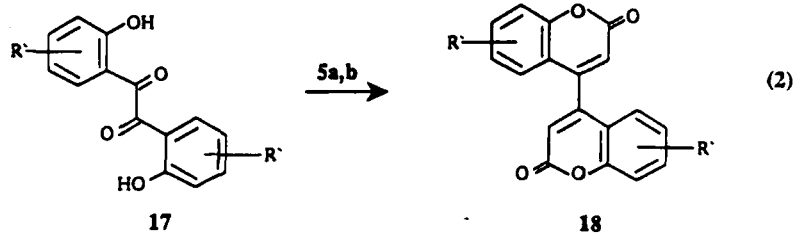
Repetition of the above reaction between the substrate **4** and two equivalents of **5a** in boiling benzene for two days furnished, 4′-hydroxy 1′(*3H*-[5,6]-3-oxo-benzopyran-1-yl) isoquinoline (**16**) (42%) along with the expected oxazoline **8a** (18%). Compounds **16** (37%) and **8b** (9%) were 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.



SCHEME 3

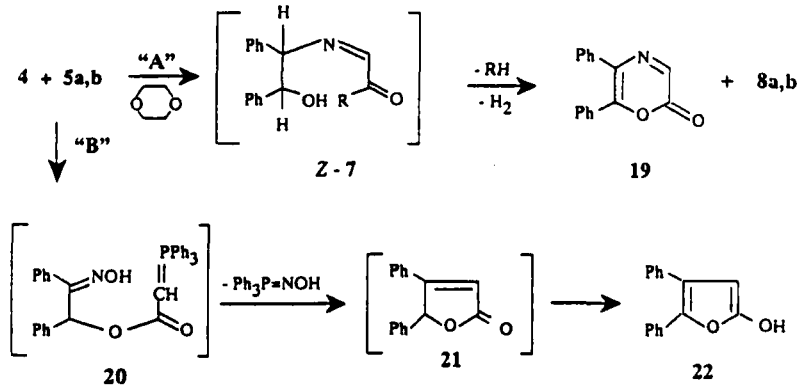
For the formation of compound **16**, an unusual [4+2] cycloelimination across the initial intermediate **7B** (*via* **7**, essentially in the *trans* form), extended from the exocyclic imino bond to the aromatic system, leading to the formation of the intermediate **13** can be proposed.[15a] Elimination of the H_2O 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 mecha-

nism 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).



17 **18** (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.



SCHEME 4

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 (Ph_3P=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]

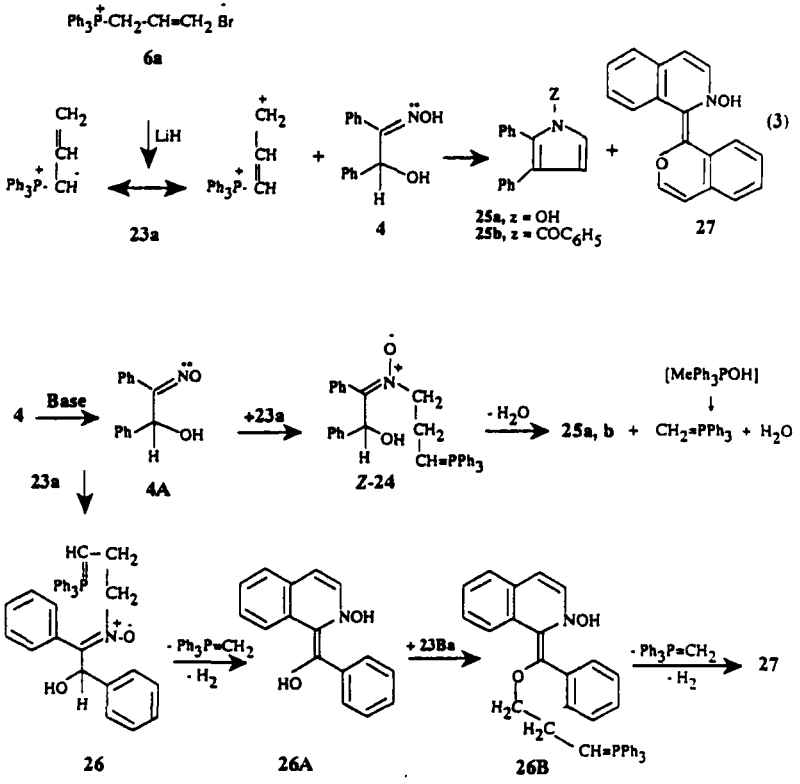
In a systemic study, we found that oxime **4** reacts similarly, with **5b** in dioxane whereby compounds **8b** (13%), **19** (27%) and **22** (26%) were formed.

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 aryl-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 ∝-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.



SCHEME 5

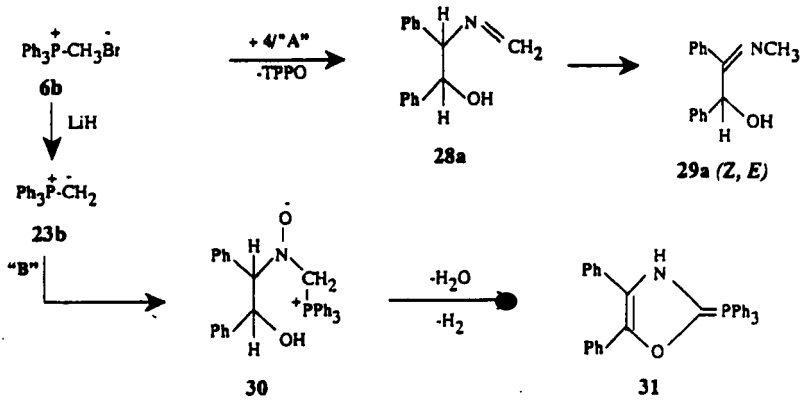
Apparently, formation of compound **25a** involves an initial attack of nitrogen on **23a** to give the ylide **24** (in the *cis* form) which readily cyclizes through [2+2] to give **25** upon displacement of a molecule of H_2O and elimination of the phosphorane moiety ($Ph_3P{=}CH_2$),[23] (Scheme 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 salicylaldehyde to vinyltriphenylphosponium bromide, in the presence of a base, led to an ylide intermediate (similar to **26B**) which cyclized to 3,4-chromene.

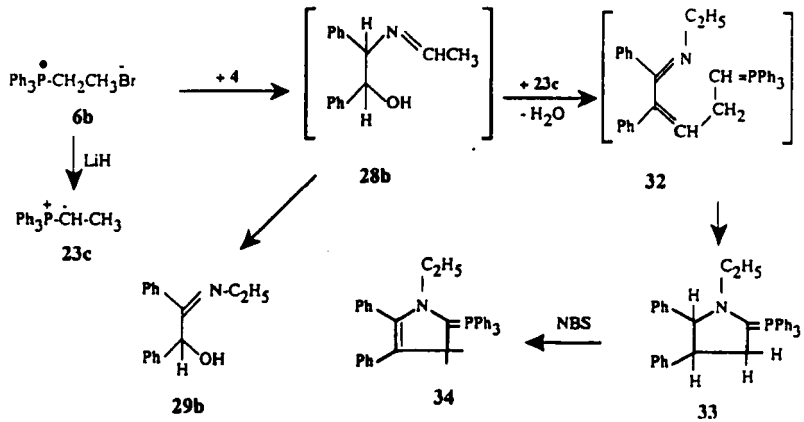
III. Reaction of ∝-Benzoinoxime (4) with Non-stabilized Ylides 23b,c

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**, *E* 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 ^{1}H-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]



SCHEME 6



SCHEME 7

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 ^{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 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 (d_6-DMSO): δ_H 3.38 (3H, s, OCH_3), 3.64 (1H, s, C-2-**H**), 7.25–7.78 (10H, m, Ar-**H**), 12.09 (1H, s, **NH**); δc 38.7 (**C**-2), 54.6 (OCH_3), 127.3 (**C**-5), 151.5 (**C**-4), 169.2 (**C**=O, ester). *m/z* (%): 381 [M^+. 100]. IR (KBr) cm^{-1}: υ 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 (d_6-DMSO): δ_H 3.53 (s, 3H, OCH_3), 7.17–7.88 (15 H, m, Ar-**H**), 9.35 (1H, br., **NH**); δ_c: 58.6 (OCH_3), 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}: υ 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 (CH_2Cl_2). Found: C, 73.26; H, 5.85; N, 4.63; $C_{18}H_{17}NO_3$ (295.34), requires: C, 73.2; H, 5.8; N, 4.74. NMR (d_6-DMSO): δ_H 1.52 (3H, t, J_{HH}= 7Hz, $OCCH_3$), 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**); δ_c 15.2 (-CH_3), 35.6 (C-2), 62.4 (OCH_2), 126.5 (**C**-4), 149.5 (**C**-5), 168.3 (**C**=O, ester). *m/z* (%): 295 [M^+, 100]. IR (KBr)cm^{-1}: υ 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, $OCCH_3$), 7.14–8.1 (15H, m, Ar-H), 9.12 (1H, s, NH); δc 16.5 (C-CH_3), 63.3 (OCH_2), 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}: υ 3191 (NH), 1718 (C=O, ester).

Reaction of ∝-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 (CH_2Cl_2) (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 $TiCl_4$ (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 ($MgSO_4$) 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 (CH_2Cl_2). Found: C, 71.85; H, 6.92; N, 4.78, $C_{17}H_{17}NO_3$ (383.33); requires: C, 72.07; H, 6.05; N, 4.94%. NMR ($CDCl_3$): δ_H 3.42 (3H, s, OCH_3), 4.17 (1H, d, J_{HH}=2.4 Hz, CHOH), 4.63 (2H, s, = NCH_2), 6.32 (1H, s, OH), 7.24–7.76 (10H, m, Ar-H); δc 48.3 (=N.CH_2), 54.5 (OCH_3), 63.8 (CHOH), 162.8 (C=N), 168.9 (C=O, ester). *m/z* (%): 383 [M^+, 100]. IR (KBr) cm^{-1}: υ 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 ($CDCl_3$): δ_H4.18 (1H, d, J_{HH}= 2.3 Hz, CHOH), 4.58 (2H, s, = N.CH_2), 6.27 (1H, s, OH), 7.25–7.86 (15H, m, Ar-H); δc 50.4 (CH_2), 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 (CH_2Cl_2) (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 (CH_2Cl_2) 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 ^{1}H 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 (d_6-DMSO): δ_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., O**H**), $\delta_C$ 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}: υ 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, ^{1}H- and ^{13}C 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 ($CHCl_3$/cyclohexane, 2:1, v/v). Found: C, 77.17; H, 4.36, N, 5.58, $C_{16}H_{11}NO_2$ (249.27), requires: C, 77.09; H, 4.45; N, 5.62. NMR (d_6-DMSO): δ_H 6.44 (1H, s, C-3-**H**), 7.13 – 7.88 (10H, m, Ar-**H**), δ_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}: υ 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 H_2O, and extracted with 2–100 mL portion of $CHCl_3$. The $CHCl_3$ extracts were combined, backwashed with 100 mL of H_2O, dried, and evaporated *in vacuo*. The residue was chromatographed on silica gel with hexane-$CHCl_3$ to give compounds **25** and **27**, respectively.

Fractions up to (8:2, v/v) yielded pale yellow crystals of *2,3-diphenyl 1-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 1([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, $C_{18}H_{13}NO_2$ (275.13), requires: C, 78.53, H, 4.76; N, 5.09%. NMR ($CDCl_3$): δ_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, NO**H**, exchangeable with D_2O), δc 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}; υ 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 reactiom 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, $C_{33}H_{26}NOP$ (483,56), requires: C, 81.97; H, 5.42; N, 2.89; P, 6.4%, NMR ($CDCl_3$): δ_H 7.25–7.75 (25H, m, Ar-**H**), 8.49 (1H, s, N**H**); δc 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}: υ 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%. $^1H(CDCl_3)$: δ_H 2.89, 2.9 (2^*3H, 2s, 2^*NCH_3), 4.24 (1H, d, diffused, CHOH), 6.18 (1H, s, OH), 7.25 – 8.23 (10H, m, Ar-H). δ_c 33.3 ($N.CH_3$), 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 ($CDCl_3$): δ_H 0.83 (3H, t, J_{HH} = 6.5 Hz, N-C-CH_3), 2.55 (2H, q, J_{HH}= 6.5 Hz, N-CH_2), 3.01 (2H, d of d, $^3J_{HP}$= 8.5 Hz, $^2J_{HH}$= 6.8 Hz, C-3-H_2), 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_c15.4 (N-C-CH_3), 28.4 (C-3-H_2), 35.8 (H-N-CH_2), 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}: υ 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 ($CDCl_3$): δ_H0.81 (3H, t, J_{HH} = 6.5 Hz, NC-CH_3), 2.68 (2H, q, J_{HH} = 6.5 Hz, N-CH_2), 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-CH_3), 37.7 (N-CH_2), 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 CCl_4. 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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