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Synthetic Applications of Functionalized Phosphoranylideneamino-1,4-Benzoquinones: Preparation of Oxazolo[5,4-*b*]phenoxazine, 4*H*-[3,1]Benzoxazino-5,8-quinone and Benzoxazole Derivatives.†

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Abstract: The aza-Wittig reaction of the triphenylphosphoranylideneamino-1,4-benzoquinone **1** with aryl isocyanates and aroyl chlorides allows the preparation of oxazolo[5,4-*b*]phenoxazine and benzoxazole derivatives. The same reaction using **7** as iminophosphoranoquinone provides substituted benzoxazoles and the previously unreported 4*H*-[3,1]benzoxazino-5,8-quinones.

The chemistry of iminophosphoranes has attracted considerable interest in the last two decades, since the imination of carbonyl compounds with these phosphorus ylides is a powerful tool for the preparation of different nitrogen-containing functionalities such as amines, imines, nitrocompounds, amides or aziridines, among others.[1] Heterocyclic synthesis *via* intramolecular aza-Wittig, tandem aza-Wittig ring closure or consecutive aza-Wittig cyclization processes, is one of the most expanding methodologies in heterocyclic chemistry.[2-4] Therefore, the preparation of novel substituted iminophosphoranes bearing an additional moiety able to react intramolecularly with that functionality, free or as an aza-Wittig derivative, allowing potential further cyclizations to different new heterocyclic systems, has focused the attention of many synthetic chemists.[3,4]

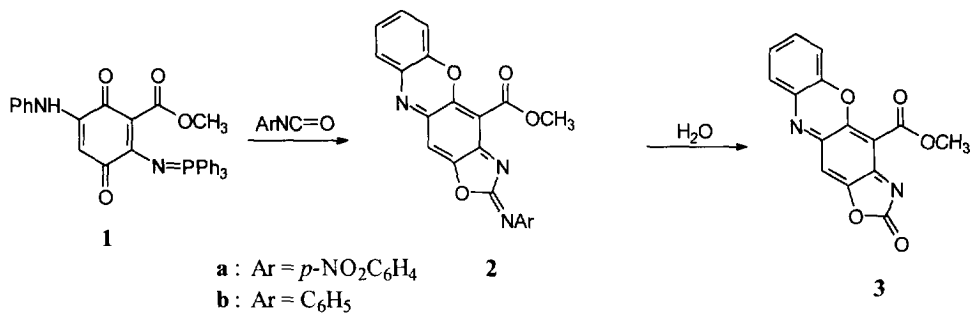
Despite the wide range of organic compounds with an attached iminophosphorane subunit that have been described, there are very few examples where a quinonic and an iminophosphorane functionalities are incorporated in one entity.[5-7] One of the two examples of phosphoranylideneaminobenzoquinones reported,[6,7] was developed by us and represents a facile and efficient method for the synthesis of highly functionalized phosphoranylideneaminoquinones starting from benzisoxazolequinone derivatives.[7]

Continuing our interest in quinone chemistry,[8,9] we describe here the first studies of reactivity of iminophosphoranequinones as the key intermediates for the synthesis of heterocycles by tandem aza-Wittig/cyclization reactions with aryl isocianates and aroyl chlorides as carbonylic compounds reagents.

† This paper is dedicated to Professor Wolfram Schäfer on the occasion of his 65th birthday celebration.

Reaction of phosphoranylideneamino-1,4-benzoquinones with aryl isocyanates.

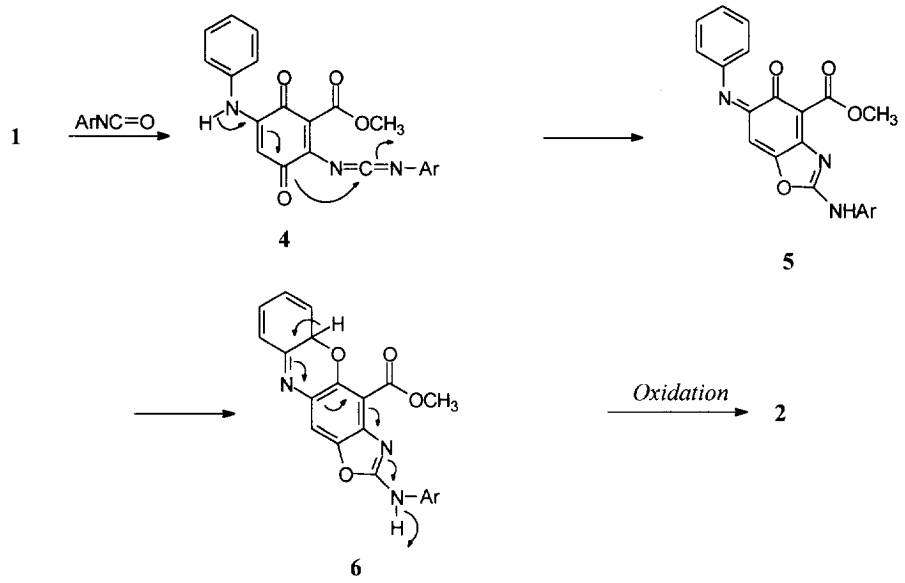
The iminophosphoranoquinone **1** was reacted with an excess of *p*-nitrophenyl isocyanate in toluene at 60 °C to give the oxazolophenoxazine **2a** in good yield. However, reaction of **1** with phenyl isocyanate under the same reaction conditions afforded the oxazolone derivative **3** as major product and traces of the corresponding phenoxazine **2b**, which was detected by MS (Scheme 1). Compound **3** was also obtained by acid hydrolytic cleavage of **2a**. According to these results it seems likely that the hydrolysis of the exocyclic imino group of compounds **2** is slowed down by the presence of substituents on the benzene ring, able to delocalize the iminic double bond such as the nitro group.



Scheme 1

The structures of **2** and **3** were established by comparison of their spectroscopical data with those of related derivatives that had been previously reported in the literature. Thus, compound **2a** shows in MS the expected molecular ion peak at *m/z* 416. Its IR spectrum exhibits signals corresponding to a vinylous ester group (1770 cm^{-1}) and to an iminic moiety (1675 cm^{-1}) in addition to the bands due to the nitro group. The ^{1}H NMR spectrum of **2a** showed signals due to both aromatic systems. The four aromatic protons of the *ortho* substituted ring appear at δ 7.7-8.2 ppm, and the pattern of a *para* disubstituted aromatic system can be also observed. In accordance with bibliographical data,[10,11] the proton closest to the nitrogen atom of the fused oxazine ring appears as a double doublet at δ 8.2 ppm. The ^{13}C NMR spectrum showed the azaquinonic carbon (C^{11}-H) at δ 98 ppm. The isolation of compound **2b** was not possible, but its molecular ion peak was found in the mass spectrum of the corresponding reaction crude at *m/z* 371. The isolated product in this case was compound **3**, whose spectroscopical data are in good agreement with the proposed structure. Its MS spectrum showed the expected molecular ion peak at *m/z* 296. The IR spectrum exhibits a new band in relation to compound **2a** at 1800 cm^{-1} that indicates the presence of a new O-CO-N moiety in **3**. In ^{13}C NMR, the azaquinonic carbon appeared at δ 105 ppm, whereas it showed the four signals corresponding to the fused benzene ring. Attempts to produce the same reaction by using less reactive isocyanates like ethyl isocyanate failed, and the starting material was recovered unchanged. The formation of the oxazolophenoxazine could be

explained by a mechanism that is depicted in Scheme 2 in accordance with the structures of the obtained products.

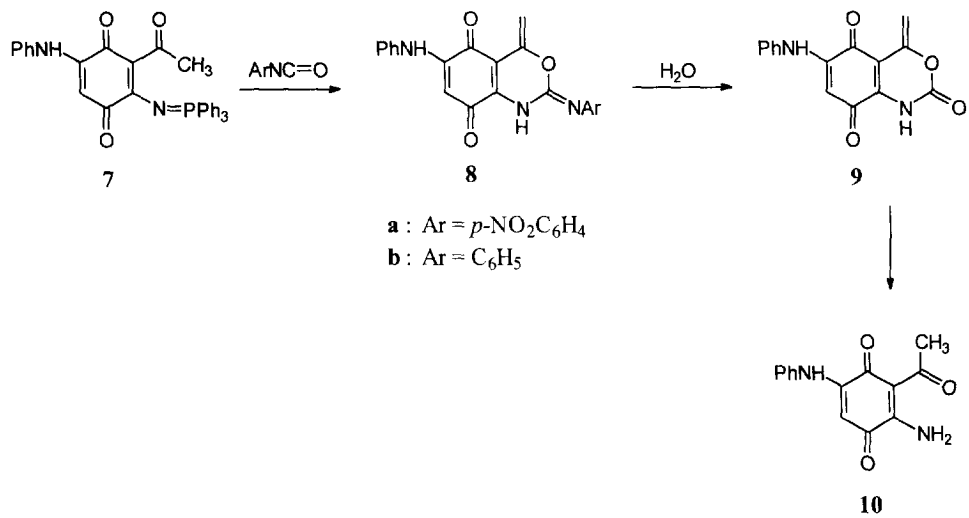


Scheme 2

It would involve the formation of the carbodiimide intermediate **4** in the first step, by an aza-Wittig reaction type between the iminophosphorane and the isocyanate. This intermediate would cyclize through the enolic form of the quinonic carbonyl function, giving the benzoxazole **5**. Similar heterocyclizations have been reported in the literature.[12,13] The tendency of azaquinonic systems, like **5**, to undergo aromatization processes, was described previously.[14,15] It might be the driving force of an electrocyclic reaction that would promote ring closure, thus affording the phenoxazine derivative **6,** followed by oxidative aromatization to provide the corresponding compound **2**. Compound **2b** undergoes a hydrolytic cleavage during work-up to give **3**.

When the iminophosphoranequinone employed was **7,** the reaction with aryl isocyanates in dry toluene at room temperature afforded the previously unreported heterocyclic system of [3,1]benzoxazino-5,8-quinone derivatives **8a,b** in good yields (Scheme 3). These compounds underwent a further partial hydrolysis of the imine group during the work-up, providing the corresponding carbamates **9**. However, after isolation, they proved to be very stable under dry and low temperature storing conditions. The reaction of **7** with less reactive isocyanates, like ethyl isocyanate, did not give the expected products and afforded the unreacted starting materials. The structures of compounds **8a,b** and **9** were established from the spectroscopic (^{1}H- ^{13}C NMR, IR and MS) data. The IR spectra reveals the presence in **8** of an iminic group [-NH-C(OR)=N-] at 1710 cm^{-1}, in addition to a broad band at 3300 cm^{-1} corresponding to the amino groups. The carbonylic stretch of the quinone moieties appears at 1630 cm^{-1} in **8a** and 1650 cm^{-1} in **8b**, whilst in the former case the absorptions

corresponding to the nitro group are clearly observed at 1570 and 1350 cm^{-1}. The MS spectra of benzoxazinic derivatives **8a,b** showed molecular ion peaks at *m/z* 402 and *m/z* 357 respectively, as the base peaks of these spectra. The most informative data about these structures were obtained from their NMR spectra. Thus, the ^1H NMR spectra of compounds **8** in DMSO-d_6 show the quinonic proton at δ 5.7 ppm, whilst the exocyclic methylenic protons appear as two doublets at δ 3.6 and 5.6 ppm, with a characteristic olefinic geminal coupling constant of *J* 1.6 Hz.[16] Moreover, two N-H protons at δ 9.6 ppm and *ca.* 11 ppm are observed. Likewise, in the spectrum of **8a** two different aromatic systems can be distinguished, one of them with a typical pattern of a *para* disubstituted aromatic system. In the ^{13}C NMR spectrum the quinonic (C-H) carbon appears at δ 95.8 ppm, while the exocyclic methylenic carbon is found at δ 92 ppm,[16] revealed by a DEPT experiment.

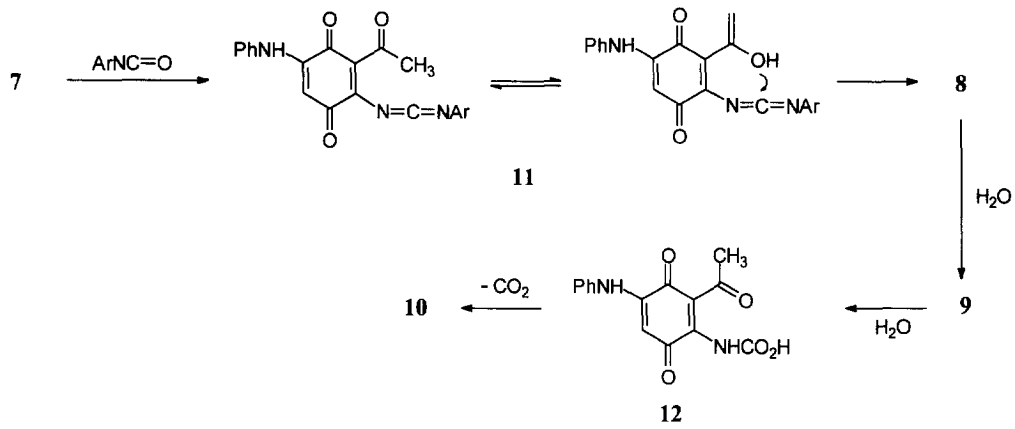


Scheme 3

The spectroscopical data corresponding to compound **9** are in good agreement with the proposed structure. The mass spectrum shows the expected molecular ion peak at *m/z* 282. In ^1H NMR the N-H moieties of the anilino and the carbamic groups appear at δ 9.6 and 11.0 ppm respectively.[17-19] The quinonic proton appears at δ 5.7 ppm, whilst two doublets due to the exocyclic olefinic protons are observed at δ 5.6 and 4.6 ppm. DEPT and 2D-NMR HMQC spectra show the quinonic (C-H) and methylenic carbons at δ 96.3 and 94.8 ppm respectively. In the IR spectrum a double band corresponding to the N-H lactamic moiety appears at 3260 and 3160 cm^{-1}, and a new carbonylic band is observed at 1780 cm^{-1}. Compound **9** was purified by recrystallization from ethyl acetate, since it undergoes hydrolytic cleavage on silica gel or in aqueous DMSO to give aminoquinone **10**.

The formation of **8** can be rationalized in terms of an initial aza-Wittig type reaction between the iminophosphorane **7** and the isocyanate, to afford a highly reactive intermediate carbodiimide **11** (Scheme 4). The latter would then undergo a cyclization, by intramolecular nucleophilic attack of the ketone moiety, through its enol form, at the activated central carbon atom of the carbodiimide moiety, thus originating the

oxazine ring of **8**. Similar processes were reported previously.[16,20] Finally, partial hydrolysis of **8** during work-up would lead to the cyclic carbamate **9**. Nucleophilic attack of traces of water at the carbamate carbonyl group of **9** during the purification process would lead to the carbamic acid **12** (Scheme 4), which by decarboxylation at room temperature would give **10**.



Scheme 4

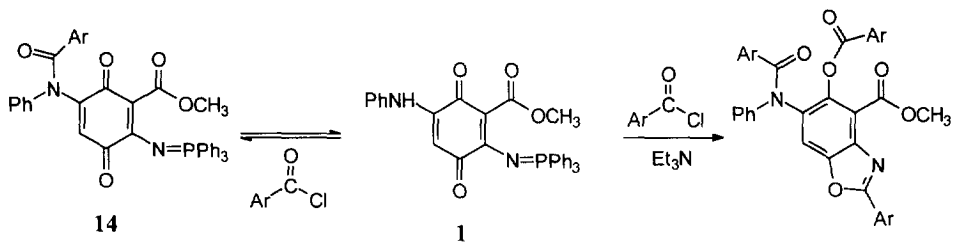
Reaction of phosphoranylideneamino-1,4-benzoquinones with aroyl chlorides.

The reaction of iminophosphoranes **1** and **7** with aroyl chlorides afforded benzoxazoles in good yields. Compound **1** was reacted with an excess of *p*-nitrobenzoyl chloride and benzoyl chloride, respectively in dry toluene, in the presence of triethylamine, at reflux temperature to give the benzoxazoles **13a,b** (Scheme 5). The structures of these reaction products were established by comparison of their spectroscopical data with those of other related derivatives that had been previously reported in the literature.[14,15] The MS spectra showed the molecular ion peaks at *m/z* 703 in **13a** and *m/z* 568 in **13b**. The ^{1}H NMR spectra indicated the presence of different aromatic rings, while in ^{13}C NMR the quinonic carbonyl groups (*ca.* δ 180 ppm) disappeared, and the former quinonic carbon (C-H) in **1**, which in these compounds is part of the central aromatic ring, appeared at δ 117.5 ppm in **13a** and δ 113.8 ppm in **13b**.

When this reaction was carried out in the absence of triethylamine, an equilibrium between **1** and its monoacylated derivative **14** was established, and the process to give **13** did not take place under these conditions (Scheme 5). The triethylamine was found necessary to produce **13**, since it facilitates the equilibrium displacement to form the benzoxazole derivative. Thus, the monoacylated derivative **14b** was reacted with the aroyl chloride in the presence of triethylamine to afford **13b** in good yield. Iminophosphorane **14b** showed in ^{13}C NMR a new signal in relation to the iminophosphorane **1** at δ 161.6 ppm, belonging to the carbonyl group of the amide moiety.

The formation of **13** can be explained by an aza Wittig reaction of **1** to give the intermediate imidoyl chloride **15** (depicted in Scheme 6),[21-24] which would undergo an intramolecular nucleophilic attack by the

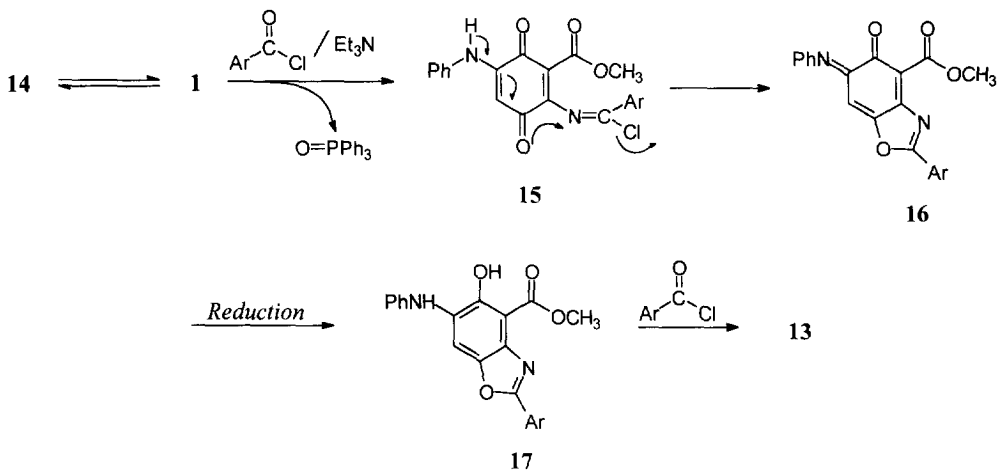
activated oxygen atom of the quinonic carbonyl moiety (C-1) through its enol form, at the haloiminic carbon in **15** to give the oxazole derivative **16**.



a : Ar = *p*-$NO_2C_6H_4$
b : Ar = C_6H_5

Scheme 5

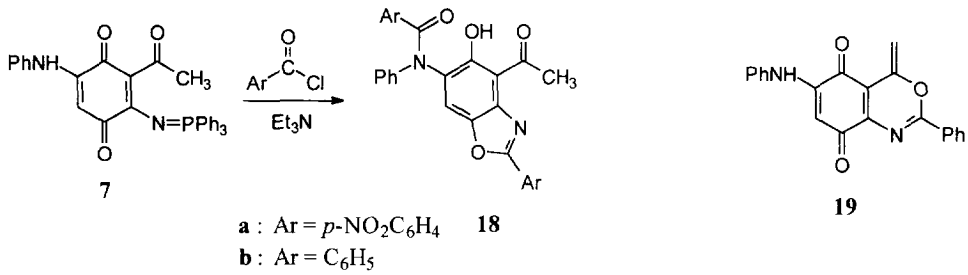
Similar processes of formation of benzoxazoles from related quinonic derivatives have been previously described.[14] Likewise, cyclizations to afford oxazole rings from α-iminophosphoranoketones with an available proton on the α position to the ketone function have also been reported.[25,26] Iminobenzoxazoles **16** would undergo a reduction process in the reaction conditions to give the benzoxazoles **17**. This kind of reduction is reasonable under these conditions, taking into account the tendency of azaquinonic systems to undergo aromatization processes.[14,15] Compounds **17** would react with further equivalents of remaining aroyl chloride to give the observed reaction products **13**.



Scheme 6

However, acetyliminophosphorane **7** reacted with an excess of benzoyl chloride in the presence of triethylamine to give a mixture of the corresponding benzoxazole **18b** and small amounts (4% by NMR) of the

benzoxazinic derivative **19** (Scheme 7). When the same reaction was carried out using *p*-nitrobenzoyl chloride as aroyl chloride, only the benzoxazole **18a** was detected (Scheme 7).



7 **18** **19**

a : Ar = *p*-$NO_2C_6H_4$
b : Ar = C_6H_5

Scheme 7

The structural characterization of compounds **18** was achieved by their spectroscopical data. In the ^1H NMR spectra, the OH proton appeared at low field, which may be a consequence of an hydrogen bonding that forms a six-membered ring chelate between the OH and the carbonyl oxygen, while the two *ortho* protons of the phenyl group attached to the benzoxazole ring in **8b** appeared as a double doublet at δ 8.2 ppm.[14,15] In the MS spectra the molecular ion peaks of **18a,b** are found at *m/z* 538 and *m/z* 448 respectively. Compound **19**, which was not isolated, exhibits in the ^1H NMR spectrum a quinonic proton at δ 6.1 ppm, in addition to two doublets at δ 5.8 and 5.4 ppm with an olefinic geminal coupling constant corresponding to the exocyclic methylene moiety. Presumably, the conversion **7** —> **18** involves a similar pathway to that proposed for the formation of **13** (Scheme 6). In this case, the greater association of the phenolic group with the neighbouring ketonic carbonyl function could be responsible for the isolation of only monoacylated products instead of the diacylated derivatives. On the other hand, the conversion **7** —> **19** would have a mechanism comparable to that proposed for the formation of benzoxazinoquinones **8**, where the imidoyl chloride formed by aza-Wittig reaction cyclizes through the enol form of the ketonic carbonyl function.

In conclusion, we have developed a simple and highly reliable phosphoranylideneamino-1,4-benzoquinone-mediated synthesis of a variety of new nitrogen heterocyclic compounds by intermolecular aza-Wittig reaction, depending on the carbonylic compound used as well as on the substituents that the quinone nucleus bears. The easy access to the starting materials, together with the different possibilities of functionalization of these quinonic compounds, make these systems promising tools for heterocyclic synthesis.

EXPERIMENTAL

Melting points were determined on a Büchi 504392 (S) apparatus and are uncorrected. IR spectra were obtained on a Phillips PU-9716 spectrophotometer. NMR spectra were recorded on a Bruker WP-200-SY (200 MHz) or a Bruker AMX 300 (300 MHz) spectrometers. Mass spectra were recorded on a VG Autospec spectrometer.

Reaction of 5-Anilino-3-methoxycarbonyl-2-(triphenylphosphoranylidene)amino-1,4-benzoquinone (1) with *p*-Nitrophenyl Isocyanate. 4-Methoxycarbonyl-2-(p-nitrophenylimino)oxazolo [5,4-b]-phenoxazine (2a).

To a stirred suspension of *p*-nitrophenyl isocyanate (328 mg, 2 mmol) in dry toluene (10 ml) under argon, a solution of the iminophosphorane **1** (532 mg, 1 mmol) in the same solvent (25 ml) was added at room temperature. The reaction mixture was heated at 60 °C for 20 h. and the precipitate was then collected by filtration. The crude product was washed repeatedly with hot acetone, and the residue was recrystallized from ethyl acetate to give 262 mg of **2a** (63 %) as a crystalline green solid, m.p. 288 °C. (Found: C, 60.60; H, 2.93; N, 13.24. $C_{21}H_{12}N_4O_6$ requires: C, 60.58; H, 2.90; N, 13.45); ^{1}H n.m.r. δ (DMSO-d_6): 8.20, 7.45 (AA'XX', 4H, arom.), 7.8-7.5 (m, 4H, arom.), 7.40 (s, 1H, H-11) and 3.97 ppm (s, 3H, OCH_3); ^{13}C n.m.r. δ (DMSO-d_6): 164.0 ($\underline{C}OOCH_3$), 162.4 (C-11a), 154.8, 152.8, 150.0 (C-3a, C-4a, C-5a), 142.4, 140.6, 140.0 (C-2, C-9a, C-1', C-4'), 133.6, 130.0 (C-7, C-8), 129.4 (C-10a), 126.7 (C-9), 124.7, 124.0 (C-2', C-3'), 112.6 (C-6), 98.5 (C-4), 97.3 (C-11) and 52.7 ppm ($COO\underline{C}H_3$); i.r. (KBr): 1770 (COOMe), 1720 (C=N), 1675 [N-C(OR)=N], 1570 (NO_2), 1595, 1460, 1440, 1330 (NO_2) and 1100 cm^{-1}; MS [EI, 70eV, *m/z* (%)]: 416 (M^+, 12), 414 (16), 358 (15), 210 (100), 194 (11), 166 (13), 144 (19), 138 (13), 90 (22) and 77 (21).

Reaction of 5-Anilino-3-methoxycarbonyl-2-(triphenylphosphoranylidene)amino-1,4-benzoquinone (1) with Phenyl Isocyanate. 4-Methoxycarbonyloxazolo[5,4-b]phenoxazine-2-one (3).

To a solution of freshly distilled phenyl isocyanate (1.6 ml, 5 mmol) in dry toluene (5 ml), a solution of the iminophosphorane **1** (532 mg, 1 mmol) in the same solvent (25 ml) was added at room temperature under argon. The reaction mixture was heated at 60 °C for 4 days. After cooling at 0 °C in a ice bath, the precipitate was collected by filtration and it was washed repeatedly with diethyl ether. The violet solid thus obtained was recrystallized from toluene to give 180 mg (61%) of **3** as green needles, m.p. 253 °C (dec. at 238 °C). (Found: C, 60.81; H, 2.73; N, 9.53. $C_{15}H_8N_2O_5$ requires: C, 60.82; H, 2.72; N, 9.45);^{1}H n.m.r. δ ($CDCl_3$): 8.08 (dd, 1H, H-9), 7.9-7.6 (m, 3H, arom.), 7.19 (s, 1H, H-11) and 4.09 ppm (s, 3H, OCH_3); ^{1}H n.m.r. δ (DMSO-d_6): 8.14 (dd, 1H, H-9), 8.0-7.7 (m, 3H, arom.), 7.59 (s, 1H, =CH) and 3.97 ppm (s, 3H, OCH_3); ^{13}C n.m.r. δ (DMSO-d_6): 170.7 (C-2), 164.0 ($\underline{C}OOCH_3$), 162.1 (C-11a), 151.6, 148.4, 146.5, 143.2 (C-3a, C-4a, C-5a, C-9a), 134.7, 134.6, 130.3 (C-7, C-8, C-10a), 128.0 (C-9), 117.2 (C-6), 105.1 (C-11), 102.2 (C-4) and 52.8 ppm ($COO\underline{C}H_3$); i.r. (KBr): 1800 (O-CO-N), 1770 (COOMe), 1720 (C=N), 1515, 1455, 1400, 1245, 1210, 1150, 1125 and 1080 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 298 $[M+2H]^+$ (95), 296 M^+ (63), 266 (77), 265 (57), 238 (56), 237 (67), 210 (100) and 181 (20).

The filtrate of the preceding reaction was concentrated to dryness under reduced pressure, and the excess of phenyl isocyanate was removed by distillation at 40 °C/0.1 mm Hg. The residue was washed with diethyl ether, to give 5 mg of a mixture of **3** and 4-methoxycarbonyl-3-phenyliminooxazolo[5,4-*b*]phenoxazine (**2b**), deduced from the MS spectrum (*m/z* 371, M^+).

*Hydrolysis of **2a**.*

10 mg of **2a** were dissolved in 5 ml of hydrochloric acid (5%), and the solution was stirred at room temperature for 5 min. After evaporation to dryness, the residue was analyzed by ^{1}H NMR and shown to be a mixture of **2a** and **3** as major products.

Reaction of 3-Acetyl-5-anilino-2-(triphenylphosphoranyliden)amino-1,4-benzoquinone (7) with *p*-Nitrophenyl Isocyanate. 6-Anilino-4-methylene-3-(*p*-nitroanilino)[3,1]benzoxazine-5,8-quinone (8a).

To a stirred suspension of *p*-nitrophenyl isocyanate (328 mg, 2 mmol) in dry toluene (10 ml), a solution of the iminophosphorane **7** (516 mg, 1 mmol) in the same solvent (20 ml) was added under argon. The reaction mixture was stirred protected from light at room temperature for 24 h. After evaporation of solvent to dryness, the residue was triturated with hot acetone. The ^{1}H NMR spectrum of the crude showed a mixture of **8a** and **9**. These compounds were isolated as follows:

The crude was extracted with cold ethyl acetate, and the layers were concentrated to dryness under reduced pressure. The residue was chromatographed on a silica gel column with dichloromethane/acetone (10:1) as eluent. The first eluted component gave 8 mg (3%) of the aminoquinone **10**. The polar component was recrystallized from chloroform/hexane affording 221 mg (55%) of **8a** as a dark-orange solid, m.p. 224 °C. (Found: C, 62.77; H, 3.63; N, 14.14. $C_{21}H_{14}N_4O_5$ requires: C, 62.69; H, 3.51; N, 13.92); ^{1}H n.m.r. δ (DMSO-d_6): 10.55 (broad s, exchangeable with D_2O, 1H, NH), 9.59 (broad s, exchangeable with D_2O, 1H, NH), 8.39, 7.62 (AA'XX', 4H, arom.), 7.5-7.2 (m, 5H, arom.), 5.77 (s, 1H, =CH), 5.64 (d, $^{H\text{-}H}J$= 1.6 Hz, 1H, =CH_2) and 3.60 ppm (d, $^{H\text{-}H}J$= 1.6 Hz, 1H, =CH_2); ^{13}C n.m.r. δ (DMSO-d_6): 178.1, 176.4 (C-5, C-8), 148.2, 147.4 (C-2, C-8a), 143.8 (C-6), 139.0 (C-4, C-1"), 137.7 (C-1'), 131.3 (C-3"), 129.6, (C-3'), 126.2 (C-4'), 128.6 (C-4"), 125.5 (C-2"), 124.3 (C-2'), 95.8 (C-7) and 94.0 ppm (=CH_2); i.r. (KBr): 3300 (broad, NH), 1710 [NHC(OR)=N], 1650 (C=O), 1610, 1580 (NO_2), 1525, 1500, 1470, 1450, 1385, 1370, 1350 (NO_2), 1280, 1180, 1115, 1090, 860, 760, 750 and 700 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 402 M^+ (100), 356 (18), 355 (21), 144 (18), 138 (11), 117 (10), 90 (12) and 77 (26).

The residue of the preceding extraction with cold ethyl acetate was recrystallized from hot ethyl acetate to give 16 mg (6%) of 6-anilino-4-methylene[3,1]benzoxazine-3-one-5,8-quinone (**9**) as a green crystalline solid, m.p. 215 °C. (Found: C, 63.74; H, 3.63; N, 10.12. $C_{15}H_{10}N_2O_4$ requires: C, 63.83; H, 3.57; N, 9.92); ^{1}H n.m.r. δ (DMSO-d_6): 11.01 (broad s, exchangeable with D_2O, 1H, NH), 9.58 (broad s, exchangeable with D_2O, 1H, NH), 7.5-7.2 (m, 5H, arom.), 5.74 (s, 1H, =CH), 5.57 (d, $^{H\text{-}H}J$= 1.6 Hz, 1H, =CH_2) and 4.87 ppm (d, $^{H\text{-}H}J$= 1.6 Hz, 1H, =CH_2); ^{13}C n.m.r. δ (DMSO-d_6): 177.6, 176.3 (C-5, C-8), 147.6 (C-6), 146.7, 146.0 (C-2, C-8a), 140.6 (C-4), 137.7 (C-1'), 129.6 (C-3'), 126.2 (C-4'), 124.3 (C-2'), 104.8 (C-4a), 96.3 (C-7) and 94.7 ppm (=CH_2); i.r. (KBr): 3260, 3160 (NH), 1780 (-O-CO-NH), 1650 (C=O), 1565, 1510, 1470, 1450, 1380, 1260, 750 and 700 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 284 $[M+2H]^+$ (74), 282 M^+ (81), 266 (17), 256 (10), 149 (57), 144 (17), 117 (13), 105 (15), 104 (12), 93 (10), 91 (10), 77 (41), 71 (19) and 69 (100).

10 mg (0.03 mmol) of pure **9** were chromatographed on a short silica gel column with acetone as eluent, and 5 mg of aminoquinone **10** were obtained; m.p. 282 °C (Lit.[8] 282 °C).

On the other hand a solution of 10 mg of **9** in DMSO (0.5 ml) was allowed to stand for 3 days, affording aminoquinone **10** in quantitative yield.

Reaction of 3-Acetyl-5-anilino-2-(triphenylphosphoranyliden)amino-1,4-benzoquinone (7) with Phenyl Isocyanate. 3,6-Bis(anilino)-4-methylene[3,1]benzoxazine-5,8-quinone (8b).

To a solution of freshly distilled phenyl isocyanate (1.6 ml, 15 mmol) in dry toluene (5 ml), a solution of the iminophosphorane **7** (516 mg, 1 mmol) in the same solvent (25 ml) was added under argon and protected from light. The reaction mixture was stirred at room temperature for 4 days. The solvent was evaporated to dryness under reduced pressure and the excess of phenyl isocyanate was removed at 40 °C/0.1 mm Hg. After trituration of the residue with diethyl ether at room temperature, the ^{1}H NMR spectrum of the crude showed a mixture of benzoxazines **8b** and **9**. These compounds were isolated as follows:

The crude was extracted with cold ethyl acetate. The organic extracts were evaporated under reduced pressure and the residual material was chromatographed on a silica gel column using dichloromethane/acetone (15:1) as eluent. From the first red eluted component, 10 mg (4%) of aminoquinone **10** were obtained. The second eluted component was recrystallized from ethyl acetate/hexane to give 171 mg (48%) of **8b** as a dark-orange solid, m.p. 252 °C (dec.). (Found: C, 70.81; H, 4.43; N, 11.87. $C_{21}H_{15}N_3O_3$ requires: C, 70.58; H, 4.23; N, 11.75); ^{1}H n.m.r. δ ($CDCl_3$): 8.18 (broad s, exchangeable with D_2O, 1H, NH), 8.03 (broad s, exchangeable with D_2O, 1H, NH), 7.6-7.2 (m, 10H, arom.), 6.09 (s, 1H, =CH), 5.74 (d, ^{H-H}J= 1.6 Hz, 1H, =CH_2) and 3.93 ppm (d, ^{H-H}J= 1.6 Hz, 1H, =CH_2); ^{1}H n.m.r. δ (DMSO-d_6): 10.37 (broad s, exchangeable with D_2O, 1H, NH), 7.60 (broad s, exchangeable with D_2O, 1H, NH), 7.7-7.2 (m, 10H, arom.), 5.88 (s, 1H, =CH), 5.62 (broad s, 1H, =CH_2) and 3.60 ppm (broad s, 1H, =CH_2); ^{13}C n.m.r. δ (DMSO-d_6): 178.0, 176.5 (C-5, C-8), 148.8, 148.2 (C-2, C-8a), 147.3 (C-6), 141.1 (C-4), 139.4 (C-1"), 137.7 (C-1'), 130.2, 129.6, 129.3 (C-3', C-2", C-3"), 128.6 (C-4"), 126.2 (C-4'), 124.3 (C-2'), 105.6 (C-4a), 95.4 (C-7) and 92.0 ppm (=CH_2); i.r. (KBr): 3300 (broad, NH), 1710 (-NH-C(OR)=N-), 1650 (C=O), 1610, 1585, 1575, 1550, 1470, 1450, 1380, 1260, 750 and 700 cm $^{-1}$; MS [EI, 70 eV, *m/z* (%)]: 357 M^+ (100), 280 (14) and 77 (29).

The residue of the preceding extraction with cold ethyl acetate was recrystallized from hot ethyl acetate to give 28 mg (10%) of **9**.

Reaction of 5-Anilino-3-methoxycarbonyl-2-(triphenylphosphoranylidene)amino-1,4-benzo-quinone (1) with *p*-Nitrobenzoyl Chloride. 4-Methoxycarbonyl-5-(*p*-nitrobenzoyloxy)-3-(*p*-nitrophenyl)-6-[N-phenyl-(*p*-nitrobenzamido)] benzoxazole (13a).

To a suspension of iminophosphorane **1** (532 mg, 1 mmol) in dry toluene (12 ml), *p*-nitrobenzoyl chloride (928 mg, 5 mmol) and triethylamine (0.01 ml, 0.07 mmol) in the same solvent (12 ml) was added under argon at room temperature. The reaction mixture was heated at reflux temperature for 2 days. After evaporation of the solvent at reduced pressure, the crude was resuspended in 50 ml of toluene and then filtered. The solvent was evaporated and the residue was purified by chromatography on a silica gel column using dichloromethane/acetone

(50:1) as eluent. The orange solid was recrystallized from chloroform/hexane affording 417 mg (68%) of **13a** as an orange solid., m.p. 170-2 °C. (Found: C, 59.82; H, 2.89; N, 10.15. $C_{35}H_{21}N_5O_{12}$ requires: C, 59.75; H, 3.01; N, 9.95);.^{1}H n.m.r. δ ($CDCl_3$): 8.4-7.2 (m, 18H, arom.) and 3.93 ppm (s, 3H, OCH_3); ^{13}C n.m.r. δ ($CDCl_3$): 170.6 (N-CO-), 166.4, 165.6, 164.0 (ArCOO-, COOCH$_3$, C-7a), 151.2, 150.1, 145.5, 141.8 (C-2, C-3a, C-5, C-6), 131.6, 131.3, 129.9, 129.1, 128.4, 128.3, 125.3, 124.4, 124.1, 124.0, 123.9, 123.7, 122.3, 122.2, 120.3 (C-arom.), 118.3 (C-4), 117.5 (C-7) and 53.4 ppm (COOCH$_3$); i.r. (KBr): 1740, 1680 (CON, COOR), 1580, 1530 (NO_2), 1510, 1490, 1335 (NO_2), 1310, 1240, 1220, 1080, and 700 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 703 M^+ (10), 657 (11), 581 (100) 553 (40) and 77 (40).

Reaction of 5-Anilino-3-methoxycarbonyl-2-(triphenylphosphoranylidene)amino-1,4-benzoquinone (1) with Benzoyl Chloride. 5-Benzoyloxy-4-methoxycarbonyl-3-phenyl-6-(N-phenylbenzamido)-benzoxazole (13b).

To a suspension of iminophosphorane **1** (532 mg, 1 mmol) in dry toluene (6 ml), a solution of freshly purified benzoyl chloride (1.86 ml, 16 mmol) and triethylamine (0.28 ml, 2 mmol) in the same solvent (6 ml) was added under argon at room temperature. The reaction mixture was heated at reflux temperature for 7 days. After evaporation of the solvent at reduced pressure, the excess of benzoyl chloride was removed by distillation at 60 °C/0.1 mm Hg. The crude was resuspended in 50 ml of toluene and triethylammonium chloride was removed by filtration. The layers were concentrated to dryness and the solid thus obtained was purified by chromatography on a silica gel column using dichloromethane/acetone (50:1) as eluent. The yellow solid was recrystallized from benzene/hexane or hot hexane affording 437 mg (77%) of **13b** as a yellow crystalline solid., m.p. 152 °C. (Found: C, 74.05; H, 4.23; N, 4.93. $C_{35}H_{24}N_2O_6$ requires: C, 73.94; H, 4.25; N, 4.92);.^{1}H n.m.r. δ ($CDCl_3$): 8.26 (dd, 2H, arom.), 8.05 (dd, 2H, arom.), 7.7-7.0 (m, 17H, arom.) and 3.87 ppm (s, 3H, OCH_3); ^{13}C n.m.r. δ ($CDCl_3$): 170.7 (N-CO-), 165.7, 165.0, 163.2 (ArCOO-, COOCH$_3$, C-7a), 148.5 (C-5), 143.4, 143.3, 140.9 (C-2, C-3a, C-6), 135.1, 134.8, 133.7, 132.3, 130.7, 130.4, 129.2, 128.9, 128.4, 128.2, 127.9, 127.0, 126.4, 126.2 (C-arom.), 118.0 (C-4), 113.9 (C-7) and 52.6 ppm (COOCH$_3$); i.r. (KBr): 1740, 1670 (CON, COOR), 1600, 1555, 1490, 1455, 1430, 1355, 1330, 1305, 1275, 1245, 1210, 1180, 1100, 1080, 1060, 1030, 780 and 705 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 568 M^+ (14), 448 (26), 447 (69), 105 (100) and 77 (50).

*Isolation of **14b**.*

When the preceding reaction was carried out under the same reaction conditions but by heating for 8 h, the ^{1}H NMR spectrum of the crude showed the presence of 3-methoxycarbonyl-5-(N-phenylbenzamido)-2-(triphenylphosphoranylidene)amino-1,4-benzoquinone (**14b**) as major product. After chromatography using dichloromethane/acetone (50:1) as eluent, the solid was recrystallized from ethyl ether/hexane to yield 413 mg (65%) of **14b** as a dark red solid, m.p. 128 °C. (Found: C, 73.75; H, 4.36; N, 4.58. $C_{39}H_{29}N_2O_5P$ requires: C, 73.58; H, 4.59; N, 4.40);.^{1}H n.m.r. δ ($CDCl_3$): 7.9-7.0 (m, 25H, arom.), 5.89 (s, 1H, =CH) and 3.92 ppm (s, 3H, OCH_3); ^{13}C n.m.r. δ ($CDCl_3$): 181.4 ($^{P\text{-}C}J$= 8.9 Hz, C-1), 175.4 ($^{P\text{-}C}J$= 4.2 Hz, C-4), 171.6 (N-CO-), 167.2

($\underline{C}OOCH_3$), 153.2 (C-5), 152.9 ($^{P\text{-}C}J$= 6.8 Hz, C-2), 141.9, 134.3 (C-arom.), 132.2 ($^{P\text{-}C2}J$= 10.1 Hz), 131.7 ($^{P\text{-}C4}J$= 2.3 Hz), 131.3 (C-arom.), 129.6 ($^{P\text{-}C1}J$= 107.6 Hz), 129.5 ($^{P\text{-}C3}J$= 11.1 Hz), 128.5, 128.2, 127.9, 127.2, 127.1 (C-arom.), 121.3 (C-6), 117.3 ($^{P\text{-}C}J$= 22.6 Hz, C-3) and 51.8 ppm (OCH_3); ^{31}P n.m.r. δ ($CDCl_3$): 14.56 ppm; i.r. (KBr): 1730 (C=O), 1660 (broad C=O), 1540, 1440, 1420, 1310, 1235, 1200, 1170 , 1110, 730 and 710; EM (FAB): 639 [M+3H$^+$] and 637 [M+H$^+$];

Iminophosphorane **14b** was also obtained when the reaction was carried out under the same conditions but in the absence of triethylamine. After 5 days heating, a mixture of iminophosphoranes **1** and **14b** in the ratio 3:7 respectively, was obtained.

*Reaction of **14b** with benzoyl chloride.*

To a suspension of iminophosphorane **14b** (64 mg, 0.1 mmol) in dry toluene (3 ml), a solution of freshly purified benzoyl chloride (0.2 ml, 1.6 mmol) and triethylamine (0.03 ml, 0.2 mmol) in the same solvent (3 ml) was added under argon at room temperature. The reaction mixture was heated at reflux temperature for 6 days. After evaporation of the solvent at reduced pressure, the excess of benzoyl chloride was removed by distillation at 60 °C/0.1 mm Hg. The crude was resuspended in 10 ml of toluene and triethylammonium chloride was removed by filtration. The layers were concentrated to dryness and the residue was purified by chromatography on a silica gel column using dichloromethane/acetone (50:1) as eluent. After recrystallization from benzene/hexane 35 mg (62%) of **13b** were obtained.

Reaction of 3-Acetyl-5-anilino-3-(triphenylphosphoranylidene)amino-1,4-benzoquinone (7) with *p*-Nitrobenzoyl Chloride. 4-Acetyl-6-(N-*p*-nitrophenylbenzamido)-3-*p*-nitrophenylbenzoxazole (18a).

To a suspension of **7** (516 mg, 1 mmol) in dry toluene (12 ml), a solution of *p*-nitrobenzoyl chloride (928 mg, 5 mmol) and triethylamine (0.01 ml, 0.07 mmol) in the same solvent (12 ml) was added under argon. The reaction mixture was heated at reflux temperature (110 °C) for 24 h. After evaporation of the solvent at reduced pressure, the crude was resuspended in 50 ml of toluene and then filtered. The solution was evaporated to dryness and the residue was chromatographed on a silica gel column with dichloromethane/acetone (50:1) as eluent. The product thus obtained was recrystallized from chloroform/hexane, affording 306 mg (62%) of **18a** as a yellow solid, m.p. 112 °C. (Found: C,62.61; H, 3.28; N, 10.57. $C_{28}H_{18}N_4O_8$ requires: C, 62.45; H, 3.37; N, 10.40); ^{1}H n.m.r. δ ($CDCl_3$): 13.57 (s, 1H, OH), 8.4-7.2 (m, 14H, arom.) and 3.14 ppm (s, 3H, CH_3); ^{13}C n.m.r. δ ($CDCl_3$): 204.2 ($\underline{C}OCH_3$), 162.4 (N-CO), 157.7, 149.7, 148.4, 143.7, 141.5 (C-2, C-3a, C-5, C-6, C-7a), 131.7, 129.5, 129.2, 128.6, 128.3, 127.4, 126.8, 125.2, 124.3, 123.9, 123.2, 120.3 (C-arom.), 118.1 (C-7), 111.5 (C-4) and 31.8 ppm ($CO\underline{C}H_3$); i.r. (KBr): 1670, 1640 (CON, -CO-), 1605, 1555, 1530 (NO_2), 1500, 1435, 1415, 1350, 1330 (NO_2), 1300, 860 and 715 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]: 538 M$^+$ (30), 492 (10), 416 (100) and 77 (61).

Reaction of 3-Acetyl-5-anilino-3-(triphenylphosphoranylidene)amino-1,4-benzoquinone (7) with Benzoyl Chloride. 4-Acetyl-6-(N-phenylbenzamido)-3-phenylbenzoxazole (18b).

To a suspension of **7** (516 mg, 1 mmol) in dry toluene (6 ml), a solution of freshly purified benzoyl chloride (0.93 ml, 8 mmol) and triethylamine (0.28 ml, 2 mmol) in the same solvent (6 ml) was added under argon. The reaction mixture was heated at reflux temperature (110 °C) for 24 h. After evaporation of the solvent at reduced pressure, the excess of benzoyl chloride was removed at 65 °C/0.1 mm Hg. The crude was dissolved in toluene and the triethylammonium chloride was removed by filtration. The solvent was evaporated to dryness at reduced pressure and the solid thus obtained was analysed by ^{1}H NMR. The spectrum showed a mixture of the benzoxazole **18b** and the benzoxazine 6-anilino-4-methylene-3-phenyl[3,1]benzoxazine-5,8-quinone (**19**). Characteristic spectroscopical data of **19** (taken from the mixture of **18b** and **19**): ^{1}H n.m.r. δ ($CDCl_3$): 6.10 (s, 1H, =CH), 5.78 (d, ^{H-H}J= 1.6, 1H, =CH_2) and 5.39 ppm (d, ^{H-H}J=1.6, 1H, =CH_2).

The crude was chromatographed on a silica gel column with dichloromethane/acetone (50:1) as eluent. The eluted component was recrystallized from benzene/hexane, affording 331 mg (74%) of **18b** as a yellow crystalline solid, m.p. 210 °C. (Found: C, 74.85; H, 4.37; N, 6.13. $C_{28}H_{20}N_2O_4$ requires: C, 74.99; H, 4.49; N, 6.24); ^{1}H n.m.r. δ ($CDCl_3$): 13.37 (s, 1H, OH), 8.22 (dd, 2H, arom.), 7.65 (s, 1H, H-7), 7.6-7.1 (m, 13H, arom.) and 3.12 ppm (s, 3H, CH_3); ^{13}C n.m.r. δ ($CDCl_3$): 204.5 (C=OCH_3), 171.0 (N-CO-), 164.5 (C-7a), 157.4 (C-5), 143.4, 141.7 (C-2, C-3a, C-6), 135.6, 132.9, 132.1, 130.3, 130.0, 129.0, 128.9, 127.9, 127.8, 126.8, 126.3 (C-arom.), 118.2 (C-7), 111.3 (C-4) and 31.8 ppm (COCH_3); i.r. (KBr): 1670, 1630 (CON, -CO-), 1610, 1600, 1550, 1490, 1450, 1430, 1375, 1350, 1335, 1290, 780 and 700 cm^{-1}; MS [EI, 70 eV, *m/z* (%)]:448 M^+ (32), 406 (13), 326 (16), 198 (11), 105 (100) and 77 (50).

REFERENCES

1. Murahashi, S.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, 54, 3292. Barluenga, J.; Ferrero, M.; Palacios, F. *Tetrahedron Lett.* **1988**, 29, 4863. Corey, E. J.; Samuelson, B.; Luzzio, F. A.; *J. Am. Chem. Soc.* **1984**, 106, 3682. Garcí, J.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **1984**, 25, 4841. Legters, J.; Thijs. L.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, 30, 4881.
2. Bohn, T.; Kramer, R.; Neidlein, R.; Suschitzky, *J. Chem. Soc., Perkin Trans 1* **1994**, 947. Peinador, C; Moreira, M. J.; Quintela, J. M. *Tetrahedron* **1994**, 50, 6705. Molina, P.; Aller, E.; López-Lázaro, A.; Alajarín, M. *Tetrahedron Lett.* **1994**, 35, 3817. Molina, P.; Alajarín, M.; Vidal, M. *J. Chem. Soc., Chem. Commun.* **1992**, 295. Molina, P.; Fresneda, P. M.; Garcíazafra, S.; Almendros, P. *Tetrahedron Lett.* **1994**, 35, 9951.
3. Gusar. N. Y. *Russian Chem. Rev.* **1991**, 60, 146. Eguchi, S.; Masuschita, Y.; Yamashita, Y. *Org. Prep. Proced. Int.* **1992**, 24, 209. Barluenga, J; Palacios, F.; *Ibid* **1991**, 23, 1.
4. For recent reviews see Nitta, M. in *Reviews on Heteratom* Chemistry, Vol. 9; Oae, S., Ed.; MYU: Tokyo, **1993**, p. 87. Molina, P.; Vilaplana, M. J. *Synthesis* **1994**, 1197.
5. Mosby, W. L.; Silva, M. L. *J. Chem. Soc.* **1965**, 1003. Mosby, W. L. ; Silva, M. L. *ibid* **1965**, 2727. Molina, P.; Pastor, A.; Vilaplana, M. J. *Tetrahedron* **1995**, 51, 1265.

6. Stegmann, H. B.; Bauer, G.; Breitmaier, E.; Herrmann, E.; Scheffler, K. *Phosphorus* **1975**, 207.
7. Rodríguez-Morgade, S.; Torres, T.; Vázquez, P. *Synthesis* **1993**, 1235.
8. Torres, T.; Eswaran, S. V.; Schäfer, W. *J. Heterocyclic Chem.* **1985**, *22*, 697. Torres, T.; Eswaran, S.; Schäfer, W. *J. Heterocyclic Chem.* **1985**, *22*, 701. Torres, T.; Eswaran, S.; Schäfer, W. *J. Heterocyclic Chem.* **1985**, *22*, 705.
9 Torres, T.; Schäfer, W. *Tetrahedron Lett.* **1991**, *32*, 5825. Martínez-Díaz, M. V.; Rodríguez-Morgade, S.; Schäfer, W.; Torres, T. *Tetrahedron* **1993**, *11*, 2261
10. Agarwal, N. L.; Schäfer, W. *J. Org. Chem.* **1980**, 45, 2155.
11. Agarwal, N. L.; Schäfer, W. *J. Org. Chem.* **1980**, 45, 5144.
12. Molina, P.; Arques, A.; Vinader, M. V. *J. Org. Chem.* **1988**, 53, 4654; Molina, P.; Alajarín, A.; Vidal, A. *Tetrahedron Lett.* **1988**, 29, 3849; Molina, P.; Alajarín, A.; Vidal, A. *Tetrahedron* **1989**, 45, 4263.
13. Rossi, E.; Calabrese, D.; Farma, F. *Tetrahedron* **1991**, 47, 5819; Molina, P.; Arques, A.; Alias, A.; Foces-Foces, M. C.; Llamas-Saiz, A. L. *J. Chem. Soc., Chem. Commun.* **1992**, 424; Wamhoff, H.; Wintersohl, H.; Stolben, S.; Paasch, J.; -jue, Z. N.; Fang, G. *Ann.* **1990**, 901; Molina, P.; Alajarín, A.; Vidal, A. *Tetrahedron* **1990**, 46, 1063; Molina, P.; Conesa, C.; Velasco, M. D. *Tetrahedron Lett.* **1993**, 34, 175.
14. Schäfer, W.; Falkner, C. *Liebigs Ann. Chem.* **1977**, 177, 1445.
15. Schäfer, W.; Terdic, M.; Bartl, P. *Synthesis* **1975**, 438.
16. Molina, P.; Conesa, C.; Alias, A.; Arques, A.; Velasco, M. D.; Llamasaiz, A. L.; Foces-Foces, C. *Tetrahedron* **1993**, 49, 7599.
17. Kuo, S. -C; Lee, H. -Z.; Juang, J. P. ; Ling, Y. -T.; Wu, -S.; Chang, J. -J.; Lecnicer, K.; Paull, D.; Lin, C. M.; Hamel, E.; Lee, K. -H. *J. Med. Chem.* **1993**, 36, 1146.
18. Torii, S.; Okumoto, H.; Xu, L. H. *Tetrahedron Lett.* **1991**, 32, 237.
19. Staskun, B.; van Es, T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 511.
20. Molina, P.; Arques, A.; Molina, A. *Synthesis* **1991**, 21.
21. Masriera, M. *An. Real Soc. Esp. Quím.* **1923**, 21, 418.
22. Zbiral, E.; Bauer, E. *Phosphorus* **1972**, 2, 35.
23. Bruché, L.; Garanti, L.; Zecchi, G. *Synthesis* **1986**, 772.
24. Molina, P.; Arques, A.; Alías, A.; Vinader, M. V. *Tetrahedron Lett.* **1991**, 32, 4401; Molina, P.; Arques, A.; Alías, A. *Tetrahedron* **1992**, 48, 1285; *ibid, J. Org. Chem.* **1993**, 58, 5264.
25. Wolloch, A.; Zbiral, E. *Tetrahedron* **1976** 32, 1289.
26. Zbiral, E.; Penz, G. *Chem.Ber.* **1985**, 118, 4131.

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