

A CONVENIENT SYNTHETIC ROUTE TO 2-DIPHENYLPHOSPHINOYL- 3-HYDROXY, AMINO AND ALKYL INDOLE DERIVATIVES

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(Received in Belgium 19 November 1992)

Abstract: *A series of 2-diphenylphosphinoyl-3-hydroxy, amino and alkyl indole derivatives have been efficiently prepared by base-induced intramolecular cyclization of aromatic Horner-Wittig reagents containing carboxamido, cyano and oxo groups, respectively.*

The incorporation of the diphenylphosphino and diphenylphosphinoyl groups in aromatic and heteroaromatic systems continues to represent a challenge for organic chemists owing to the importance of this class of compounds, both as ligands in transition metal complexes and as intermediates in organic synthesis.¹⁻⁵ The synthetic methodologies employed for the elaboration of such systems, albeit adequately described in the literature, remain limited in scope. They generally involve the reaction of an anion generated at a specific site in the heterocyclic substrate with chlorodiphenylphosphine.⁶ Photostimulated substitution of halogenated derivatives by lithium or potassium diphenylphosphide under $S_{RN}1$ conditions^{7,8} has also been shown to be effective. A major problem in

both these techniques is the necessity to fully protect base sensitive groups. These multistep reaction sequences usually result in decrease of overall yield.

For these different reasons it is necessary to further develop new routes to versatile functionally substituted aryl and heteroarylphosphine oxides.⁹ We wish to report in this paper a simple, convenient and general synthetic methodology for the elaboration of phosphorylated heterocyclic systems which also contain sensitive functional groups such as hydroxy and amino groups. The synthetic potential of the procedure has been further demonstrated by its extension to the preparation of alkyl substituted derivatives. Our investigation has been focused in particular on the construction of the indole nucleus, as this entity has been extensively studied by organic chemists in view of its presence in a large variety of alkaloids and biologically active compounds.¹⁰⁻¹²

Our strategy which permits an efficient access to a wide variety of 2-phosphorylated-3-hydroxy, amino and also 3-alkyl indole derivatives is based upon the base-induced intramolecular cyclization of aromatic Horner-Wittig reagents substituted with carboxamido, cyano and oxo groups respectively.

Synthesis of 2-diphenylphosphinoyl-3-hydroxy indole derivatives 2a,b :

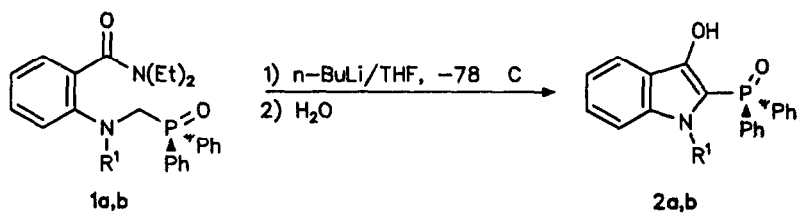
The 3-hydroxy-2-phosphorylated indole derivatives **2a,b** are easily obtained by treatment of the Horner-Wittig reagents **1a,b** (scheme 1) readily accessible from the corresponding amines **3a,b** with *n*-butyllithium in tetrahydrofuran at -78°C. These amines were prepared according to two different procedures depending on the nature of the substituent. The aromatic isopropylamine **3a** was obtained by reduction of the imine **5** obtained from the condensation of *N,N*-diethylantranilamide¹³ with acetone (scheme 2, Table 1). Amine **3b** was prepared by reacting the sodium salt of commercial isatoic anhydride with propargyl bromide followed by the base-induced ring-opening of the intermediate anhydride **6**.¹⁴ Treatment of the ester **7** with lithium diethylamide **13** gave the expected aromatic amine **3b** in good overall yield (scheme 3, Table 1).

The Horner-Wittig reagents **1a,b** are readily accessible according to the general procedure outlined in scheme 4 ((A) = CONEt₂). This involves reaction of chlorodiphenylphosphine with the *N,O*-acetals obtained by treatment of the corresponding amines **3a,b** with paraformaldehyde in ethanol (Table 2).^{15,26}

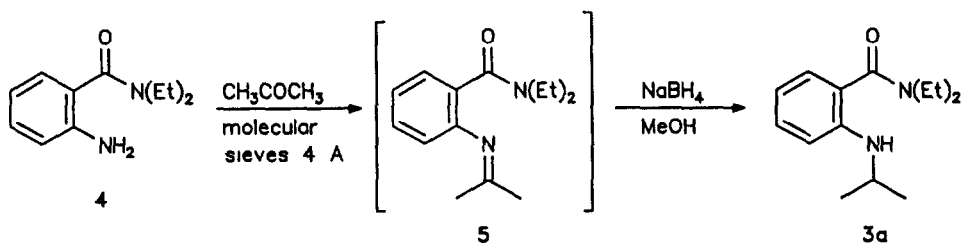
Table 1. Analytical Data of the Starting Amides, Nitriles and Ketones Prepared

Prod- uct	Yield ^a (%)	mp ^{b,c} (°C)	¹ H-NMR (CDCl ₃ /TMS) ^d δppm, J(Hz)	MS (70 eV) ^e m/z (%)
3a	58	45-46	1.14 (t, J = 7.1, 6H, CH ₃), 1.17 (d, J = 6.2, 6H, CH(CH ₃) ₂), 3.40 (q, J = 7.0, 4H, CH ₂), 3.52 (m, 1H, CH), 4.36 (br. s, 1H, NH), 6.42-7.37 (m, 4H _{arom})	234 (M ⁺ , 25), 188 (53), 161 (100), 130 (66)
3b	65	63-64	1.15 (t, J = 7.0, 6H, CH ₃), 2.17 (t, J = 2.4, 1H, HC≡), 3.40 (q, J = 7.0, 4H, CH ₂), 3.89 (dd, J = 2.4, 5.4, 2H, CH ₂ -C≡), 5.03 (br. s, 1H, NH), 6.53-7.43 (m, 4H _{arom})	230 (M ⁺ , 33), 188 (42), 156 (81), 130 (100)
12	62	-	1.26 (d, J = 6.2, 6H, CH(CH ₃) ₂), 3.72 (m, 1H, CH), 4.33 (br. s, 1H, NH), 6.42-7.58 (m, 4H _{arom})	160 (M ⁺ , 26), 145 (100), 118 (19)
13	77	117-118 (117-11929)	4.44 (d, J = 5.3, 2H, NCH ₂), 5.01 (br. s, 1H, NH), 6.55-7.67 (m, 9H _{arom})	208 (M ⁺ , 40), 91 (100)
14	60	68-69 (6929)	2.91 (d, J = 4.0, 3H, NCH ₃), 4.68 (br. s, 1H, NH), 6.47-7.89 (m, 4H _{arom})	132 (M ⁺ , 100), 104 (51)
20	71	-	1.15 (d, J = 7.1, 3H, CH(CH ₃) ₂), 1.18 (d, J = 6.8, 3H, CH(CH ₃) ₂), 2.91 (s, 3H, NCH ₃), 3.49 (m, 1H, CH), 6.42-7.87 (m, 4H _{arom}), 9.17 (br. s, 1H, NH)	177 (M ⁺ , 52), 134 (100)
21	68	-	0.94 (t, J = 7.3, 3H, CH ₃), 1.39 (m, 2H, CH ₂), 1.69 (m, 2H, CH ₂), 2.88 (s, 3H, NCH ₃), 2.92 (t, J = 7.5, 2H, COCH ₂), 6.55-7.76 (m, 4H _{arom}), 8.83 (br. s, 1H, NH)	191 (M ⁺ , 56), 134 (100)

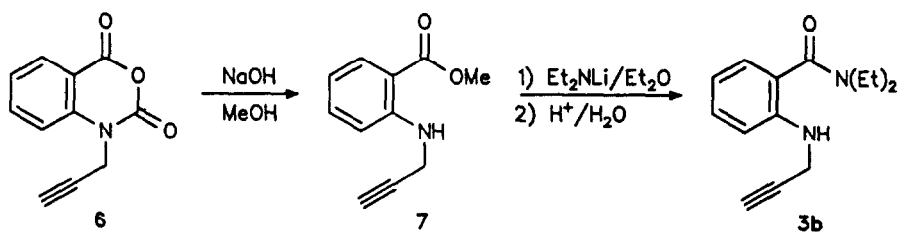
^a Overall yield. ^b Uncorrected. ^c Satisfactory microanalysis obtained for new compounds: C ± 0.35, H ± 0.20, N ± 0.29, O ± 0.31. ^d Recorded on a Bruker AM 400 WB. ^e Obtained on a Ribier 10-10 spectrometer.



scheme 1



scheme 2

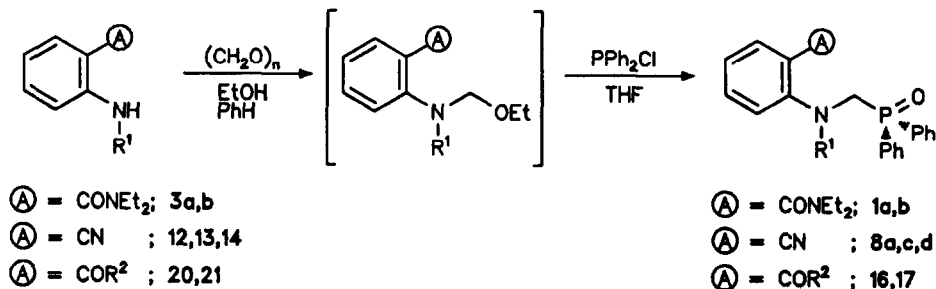


scheme 3

Table 2. Analytical Data for the Phosphorylated Compounds 1a,b, 8a,c,d, 16, 17 Prepared

Prod- uct	R ¹	R ²	Yield ^a (%)	mp ^{b,c} (°C)	¹ H-NMR (CDCl ₃ /TMS) ^{d,e} δppm, J(Hz)	MS (70 eV) ^f m/z (%)
1a	i-Pr	-	72	75-76	0.93 and 1.13 (two t, J = 7.1, 6H, CH ₃), 0.93 and 1.28 (two br. s, 6H, CH(CH ₃) ₂), 2.71, 3.14 and 3.78 (three br. s, 4H, CH ₂), 3.88 and 4.66 (two br. s, 2H, NCH ₂ P), 4.19 (m, 1H, CH), 6.84-7.71 (m, 14H _{arom})	448 (M ⁺ , 2), 247 (100), 201 (16)
1b	HC≡CCH ₂	-	68	141-142	0.85 and 1.13 (two t, J = 7.1, 6H, CH ₃), 2.15 (t, J = 2.4, HC≡), 2.68, 2.96, 3.24 and 3.65 (four br. s, 4H, CH ₂), 4.10 (br. s, 1H, NCH ₂ C≡), 4.30 (br. s, 3H, NCH ₂ C≡ + NCH ₂ P), 6.91-7.78 (m, 14H _{arom})	444 (M ⁺ , 2), 402 (7), 243 (25), 201 (22), 86 (100)
8a	i-Pr	-	75	120-121	1.05 and 1.36 (two d, J = 6.7, 6H, CH(CH ₃) ₂), 3.67 (m, 1H, CH), 4.15 (d, J = 7.5, 2H, NCH ₂ P), 6.87-8.02 (m, 14H _{arom})	374 (M ⁺ , 45), 201 (17), 173 (100)
8c	PhCH ₂	-	73	101-102	4.31 (d, J = 2.9, 2H, NCH ₂ P), 4.74 (s, 2H, NCH ₂ Ph), 6.85-7.87 (m, 19H _{arom})	422 (M ⁺ , 43), 221 (18), 173 (100)
8d	Me	-	78	115-116	3.20 (s, 3H, NCH ₃), 4.45 (d, J = 3.7, 2H, NCH ₂ P), 6.65-7.93 (m, 14H _{arom})	346 (M ⁺ , 45), 201 (92), 145 (100)
16	Me	i-Pr	55	-	0.65 (d, J = 7.0, 6H, CH(CH ₃) ₂), 2.90 (s, 3H, NCH ₃), 3.10 (m, 1H, CH), 3.90 (d, J = 4.0, 2H, NCH ₂ P), 6.85-7.65 (m, 14H _{arom})	391 (M ⁺ , 1), 348 (2), 190 (75), 91 (100)
17	Me	n-Bu	52	62-63	0.93 (t, J = 7.2, 3H, CH ₃), 1.13 (m, 2H, CH ₂), 1.33 (m, 2H, CH ₂), 2.65 (t, J = 7.0, 2H, COCH ₂), 3.06 (s, 3H, NCH ₃), 3.98 (d, J = 4.8, 2H, NCH ₂ P), 6.87-7.95 (m, 14H _{arom})	405 (M ⁺ , 1), 387 (2)

^a Overall yield. ^b Uncorrected. ^c Satisfactory microanalysis obtained: C ± 0.31, H ± 0.24, N ± 0.25, O ± 0.31, P ± 0.27. ^d Recorded on a Bruker AM 400 WB. ^e IR (KBr or neat) 1a,b $\nu_{\text{CO}} = 1620$, $\nu_{\text{PO}} = 1180$ cm⁻¹; 8a,c,d $\nu_{\text{CN}} = 2215$, $\nu_{\text{PO}} = 1180$ cm⁻¹; 16, 17 $\nu_{\text{CO}} = 1680$, $\nu_{\text{PO}} = 1180$ cm⁻¹. ^f Obtained on a Ruber 10-10 spectrometer.



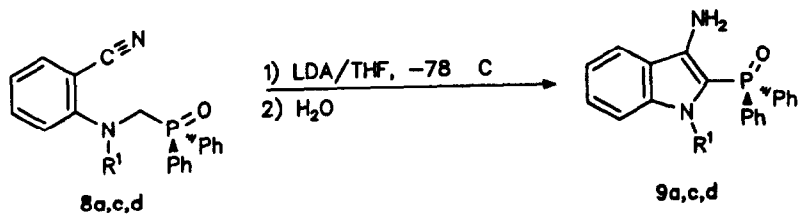
scheme 4

The formation of the heteroaromatic β -hydroxydiphenylphosphine oxides **2a,b** obtained by basic treatment of the open systems **1a,b** is actually the combined result of the nucleophilicity of the transient carbanions of **1a,b**, a property mainly used thusfar for enamines synthesis,¹⁶ and of the sensitivity of the carboxamido group with respect to nucleophilic attacks^{27,28}. Representative examples of compounds which have been prepared by this method are presented in Table 3. It can be seen that this simple procedure furnishes the cyclocondensation products **2a,b** in excellent yields.

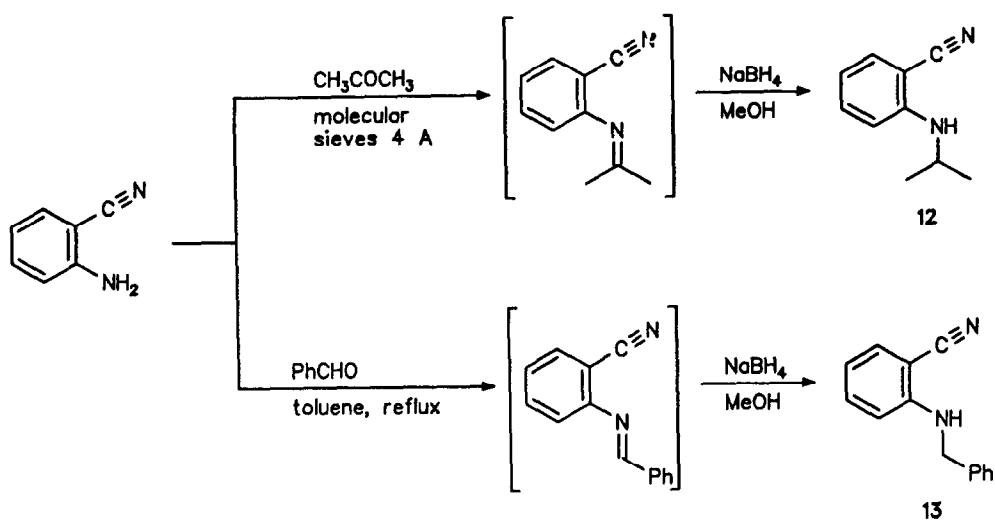
Synthesis of 3-amino-2-diphenylphosphinoyl indole derivatives **9a,c,d** :

The presence of the cyano group in the parent models **8a,c,d** (scheme 5) requires use of lithium diisopropylamide as the base for the annelation reaction. The intramolecular attack of the prealably generated carbanion of the Horner-Wittig reagents **8a,c,d** on the cyano group gives rise almost quantitatively to the indolic β -amino-diphenylphosphine oxides **9a,c,d** (Table 3). This type of reaction has been already applied for the construction of various aminated heterocyclic systems.^{19,20}

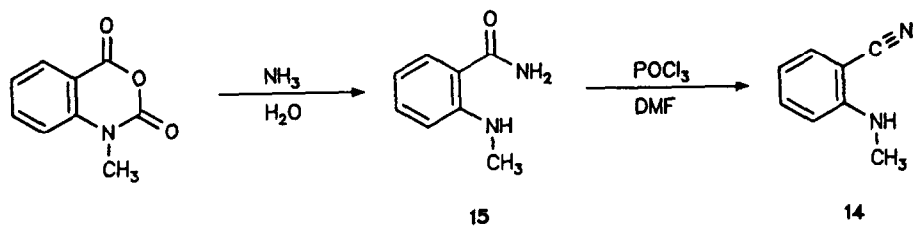
The starting compounds **8a,c,d** were readily prepared from the corresponding aromatic amines **12, 13, 14** according to the general protocol described for carboxamides **1a,b** in scheme 4 ((A) = CN) (Table 2). Initially *N*-isopropyl and *N*-benzylanthranilonitrile, **12** and **13** respectively, were obtained by reduction with NaBH₄ of the imines resulting from the condensation between anthranilonitrile and acetone or benzaldehyde (scheme 6, Table 1). *N*-methylanthranilonitrile **14** was obtained by dehydration of the primary amide **15**¹⁷ (scheme 7) arising from ring opening of *N*-methylisatoic anhydride upon treatment with ammonia.¹⁸



scheme 5



scheme 6



scheme 7

Table 3. Analytical Data for the Phosphorylated Indoles 2a,b, 9a,c,d, 18, 19 Prepared

Prod- uct	R ¹	R ²	Yield (%)	mp ^{a,b} (°C)	¹ H-NMR (CDCl ₃ or d ₆ -DMSO/TMS) ^{c,d} δppm, J(Hz)	MS (70 eV) ^e m/z (%)
2a	i-Pr	-	91	200-201	1.16 (d, J = 7.2, 6H, CH(CH ₃) ₂), 3.97 (m, 1H, CH), 6.92-8.12 (m, 14H _{arom}), 10.21 (br. s, 1H, OH)	375 (M ⁺ , 48), 332 (21), 201 (29), 185 (100)
2b	HC≡CCH ₂	-	85	185-186	2.00 (t, J = 2.5, HC≡), 4.38 (d, J = 2.5, 2H, CH ₂ C≡), 6.82-8.14 (m, 14H _{arom}), 10.10 (br. s, 1H, OH)	371 (M ⁺ , 31), 332 (10), 201 (72), 185 (100)
9a	i-Pr	-	91	110-111	1.22 (d, J = 8.4, 6H, CH(CH ₃) ₂), 4.14 (br. s, 2H, NH ₂), 4.48 (m, 1H, CH), 7.03-8.07 (m, 14H _{arom})	374 (M ⁺ , 73), 201 (36), 173 (47), 86 (100)
9c	PhCH ₂	-	92	123-124	4.10 (br. s, 2H, NH ₂), 5.27 (s, 2H, NCH ₂ Ph), 6.53-7.88 (m, 19H _{arom})	422 (M ⁺ , 84), 331 (100), 221 (36), 201 (22)
9d	Me	-	93	138-139	3.43 (s, 3H, NCH ₃), 4.00 (br. s, 2H, NH ₂), 7.02-7.97 (m, 14H _{arom})	346 (M ⁺ , 41), 201 (11), 145 (20), 91 (100)
18	Me	i-Pr	90	174-175	0.54 (d, J = 6.6, 3H, CH(CH ₃) ₂), 0.60 (d, J = 6.6, 3H, CH(CH ₃) ₂), 1.97 (m, 1H, CH), 3.20 (s, 3H, NCH ₃), 6.62-7.90 (m, 14H _{arom})	373 (M ⁺ , 38), 358 (26), 201 (100), 172 (28)
19	Me	n-Bu	87	113-114	0.75 (t, J = 7.4, 3H, CH ₃), 1.09 (m, 2H, CH ₂), 1.45 (m, 2H, CH ₂), 2.13 (t, J = 8.2, 2H, COCH ₂), 3.82 (s, 3H, NCH ₃), 6.97-7.99 (m, 14H _{arom})	387 (M ⁺ , 75), 344 (95), 201 (75), 144 (100)

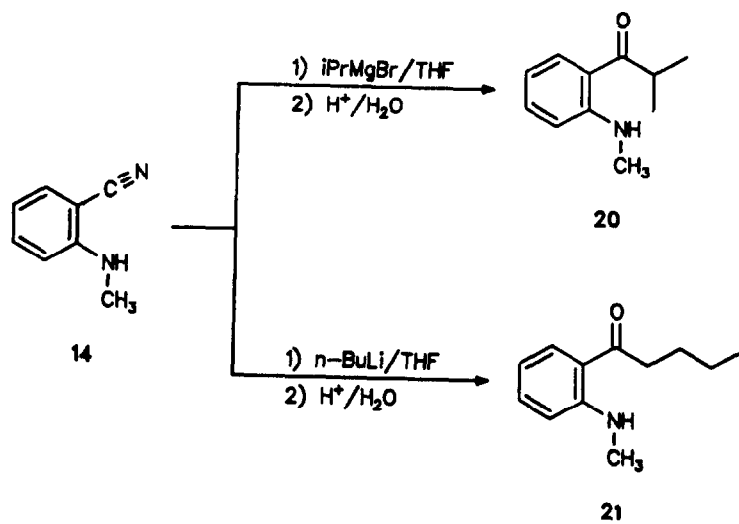
^a Uncorrected. ^b Satisfactory microanalysis obtained: C ± 0.35, H ± 0.34, N ± 0.32, O ± 0.23, P ± 0.29. ^c Recorded on a Bruker AM 400 WB in CDCl₃ for 2a,b and 9a,c,d; in d₆-DMSO for 18 and 19. ^d IR (KBr) 2a,b ν_{OH} = 1620, ν_{PO} = 1160 cm⁻¹; 9a,c,d ν_{NH} = 3450, 3315, 3210, ν_{PO} = 1160 cm⁻¹; 18, 19 ν_{PO} = 1160 cm⁻¹. ^e Obtained on a Ribet 10-10 spectrometer.

Synthesis of 3-alkyl-2-diphenylphosphinoyl indole derivatives 18, 19 :

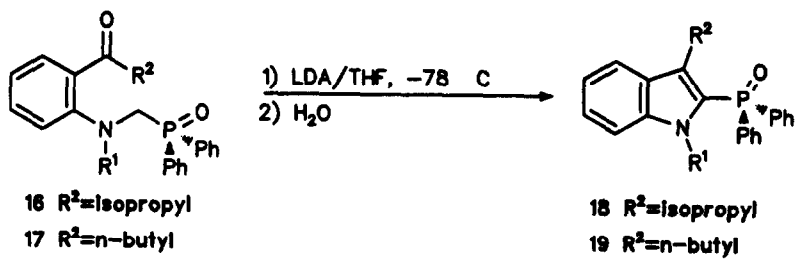
The elaboration of precursors 16, 17 (Table 2) required the preliminary synthesis of the corresponding aromatic ketones 20, 21 respectively. These compounds were prepared by treatment of *N*-methylantranilonitrile 15 with isopropylmagnesium bromide or with *n*-butyllithium in ether (scheme 8, Table 1).

The incorporation of the diphenylphosphinoylmethyl group in the parent ketones 20, 21 was achieved according to the general reaction pathway (scheme 4, (A) = COR). However, the yields were appreciably lower than for the carboxamido and cyano derivatives (Table 2). This may be the consequence of secondary interactions due to the enolisation character of the parent ketones. On the other hand the base-induced intramolecular cyclization of the diphenylphosphine oxides 16 and 17 (scheme 9) was accomplished with lithium diisopropylamide in THF at low temperature and was shown to be remarkably efficient. The 2-diphenylphosphinoyl-3-isopropyl and 3-butyl indoles, 18 and 19 respectively, were indeed obtained with yields superior to 85% after recrystallization (Table 3).

These reactions illustrate the versatility and the synthetic potential of the procedure described in this paper. First it constitutes a conceptually and experimentally simple new approach to the indole skeleton. It also represents a method of choice for the simultaneous introduction in the heterocyclic nucleus of versatile functionally substituents, namely hydroxy and amino, with the diphenylphosphinoyl group. The presence of these two entities in the heterocyclic framework can be undoubtedly interesting for further synthetic planning both in the field of organic^{21,22} and organometallic chemistry.^{9,23,24} Furthermore the scope of these reactions can be broadened to include the preparation of 2-phosphorylated-3-alkyl indole derivatives. The easy availability of the starting materials, the simplicity of this short and clean procedure and the high yields of annelation products render this process particularly attractive and should be undoubtedly extended to other heterocyclic systems.



scheme 8



scheme 9

EXPERIMENTAL**2-N-isopropylamino-N',N'-diethylbenzamide 3a**

A solution of 2-amino-N,N-diethylbenzamide¹³ (1.92 g, 10 mmol) in acetone (50 mL) with molecular sieves 4Å was kept in the refrigerator for 2 days. The reaction mixture was filtered on Celite^R and evaporated *in vacuo* to dryness. The crude imine **5** thus obtained was dissolved in absolute methanol (50 mL) and subsequently treated with NaBH₄ (760 mg, 20 mmol) under N₂ in an ice-cooled flask. After stirring the mixture for an hour, water (50 mL) was added and the reaction product extracted several times with CH₂Cl₂ (3 x 50 mL), then dried (MgSO₄). Evaporation of the solvent furnished the crude oily amine **3a** which was finally purified by column chromatography on silica using a mixture acetone-hexane as eluent (Table 1).

2-N-propargylamino-N',N'-diethylbenzamide 3b

N-propargylisatoic anhydride **6** was prepared according to a reported procedure.¹⁴ The ring opening of this compound with NaOH in methanol²⁵ led to the ester **7** which was distilled *in vacuo* (5.10⁻³ torr). The ester **7** was subsequently treated with lithium diethylamide in tetrahydrofuran following a procedure already described by us for the synthesis of N,N-diethylantranilamide **4** (Table 1).¹³

2-N-isopropylaminobenzonitrile 12

This compound was obtained from the commercial 2-aminobenzonitrile (antranilonitrile) by condensation with acetone in the presence of molecular sieves 4Å. The mixture was worked up and the crude imine treated with NaBH₄ as previously described for **3a**. The product **12** was purified by vacuum distillation (Table 1).

2-N-benzylaminobenzonitrile 13

A mixture of antranilonitrile (1.18 g, 10 mmol), benzaldehyde (1.17 g, 11 mmol) in toluene (100 mL) was refluxed for 2 h in a Dean-Stark apparatus in the presence of a catalytic amount of *p*-toluenesulfonic acid. The solvent was evaporated *in vacuo* and the crude product was subsequently treated with NaBH₄ (760 mg, 20 mmol) in MeOH as described above for **3a**. The classical work-up furnished an oily product which slowly solidified on standing and was finally recrystallized from hexane-toluene (Table 1).

2-N-methylaminobenzonitrile 14

Initially, 2-N-methylaminobenzamide 15 was prepared by treatment of commercial N-methylisatoic anhydride with ammonia.¹⁸ Subsequent dehydration of 15 with POCl₃ in pyridine was carried out by adapting an already reported procedure (Table 1).¹⁷

2-N-methylaminophenyl isopropyl ketone 20

To a cold (0°C) solution of N-methylantranilonitrile (5.7 g, 28 mmol) in dry Et₂O (20 mL) was added dropwise *i*-PrMgCl (2 M in Et₂O, 39 mL, 78 mmol) with stirring under argon. The mixture was warmed to room temperature and stirring was continued for 5 h. The solution was recooled (0°C) and 50 mL of 10% HCl was slowly added. The reaction mixture was stirred for an additional 3 hours and then made basic by addition of solid NaOH. The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL) and the combined extracts were dried (MgSO₄). Evaporation of the solvent furnished an oily product which was finally purified by flash column chromatography on silica gel using 15% EtOAc in hexane as eluent. The ketone 20 could be used directly for the next step but an analytical sample of 20 was obtained by bulb to bulb distillation (Table 1).

2-N-methylaminophenyl butyl ketone 21

This compound was prepared as described above for the isopropyl derivative 20, starting from N-methylantranilonitrile (5.7 g, 28 mmol) and a commercial solution of *n*-BuLi (1.6 M in hexane, 52.5 mL, 84 mmol) (Table 1).

General procedure for the preparation of the phosphorylated carboxamides, nitriles and ketones 1a,b, 8a,c,d, 16, 17 respectively

A solution of the appropriate carboxamides²⁶, nitriles or ketones 3a,b, 12, 13, 14, 20, 21 (30 mmol) and paraformaldehyde (1.35 g) in a mixture of EtOH (20 mL) and toluene (50 mL) was refluxed overnight. The solvent and the excess paraformaldehyde were removed *in vacuo* (5.10⁻² torr). The mixture was dissolved in THF (10 mL) and chlorodiphenylphosphine (7.2 g, 30 mmol) was slowly added in an atmosphere of dry N₂. The solution was stirred at room temperature for 1 h, K₂CO₃ (7 g) was added and stirring was maintained for 15 mn. The reaction mixture was filtered on Celite^R and then poured on petroleum ether (500 mL) with vigorous stirring. The product was collected by suction, then dissolved in CH₂Cl₂ and purified by column chromatography on silica gel using 50%

acetone in hexane as eluent. The solids were usually recrystallized from hexane-toluene (Table 2).

General procedure for the preparation of the 2-diphenylphosphinoyl-3-hydroxyindole derivatives 2a,b

A solution of *n*-BuLi in hexane (1.6 M, 3.4 mL, 5.5 mmol) was slowly added, with stirring under Ar, to a solution of 1a,b (5 mmol) in anhydrous THF (20 mL) at -78°C. The deep-red colored solution was stirred for 0.5 h at the same temperature, warmed to -30°C and then quenched with water (30 mL). The aqueous layer was extracted several times with CH₂Cl₂ and the combined organic extracts were washed with brine, then dried over MgSO₄ and evaporated *in vacuo* to give the phosphorylated hydroxyindole derivatives 2a,b. Trituration of the crude oily products with Et₂O induced solidification and recrystallization of the solids in hexane-toluene furnished analytically pure samples of 2a,b. Yields reported in Table 3 have been evaluated after recrystallization.

General procedure for the preparation of the 2-diphenylphosphinoyl-3-amino and 3-alkyl indole derivatives 9a,c,d and 18, 19

A solution of lithium diisopropylamide (LDA) was prepared at -78°C by the slow addition under Ar of *n*-BuLi in hexane (1.6 M, 3.4 mL, 5.5 mmol) to a solution of diisopropylamine (560 mg, 5.5 mmol) in THF (10 mL). The mixture was stirred for 15 mn and a solution of the compounds 8a,c,d or 16, 17 (5 mmol) in THF (10 mL) was added dropwise. The solution was stirred for 0.5 h, then warmed to -30°C. Work-up and isolation of the reaction products were carried out as described above for compounds 2a,b (Table 3).

REFERENCES

1. Lampin, J.P.; Mathey, F. *Fr Demande* 2 242 398/1975 (*Chem. Abstr.* 1975, 83, 164369s).
2. Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* 1986, 51, 629.
3. Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* 1992, 503.
4. Badener, A.; Lindner, E. *Coord. Chem. Rev.* 1991, 108, 27.
5. Southern, T.G. *Polyhedron* 1989, 8, 407.
6. Brown, J.M.; Canning, L.R. *J. Chem. Soc., Chem. Commun.* 1983, 460.

7. Swartz, J.E.; Bunnet, J.F. *J. Org. Chem.* **1979**, *44*, 340.
8. Rossi, R.A.; de Rossi, R.H. *Aromatic Substitution by the S_{RN}¹ Mechanism*; Caserio, M.C. Ed.; ACS Monograph 178: Washington D.C., 1983.
9. Ravindar, V.; Hemling, H.; Schumann, H.; Blum, J. *Synth. Commun.* **1992**, 841 and 1453.
10. Sundberg, J.R. in *The Chemistry of Indoles*; Academic Press: New York and London, 1970; p. 164.
11. Dumas, D.J.; Bradford, J.C.; Rozitis, J. *J. Med. Chem.* **1977**, *20*, 537.
12. Ho, C.Y.; Haegman, W.E.; Persico, F. *J. Med. Chem.* **1986**, *29*, 118.
13. Couture, A.; Cornet, H.; Grandclaoudon, P. *Synthesis* **1991**, 1009.
14. Hardtmann, G.E.; Koletar, G.; Pfister, O.R. *J. Heterocycl. Chem.* **1975**, *12*, 565.
15. Broekhof, N.L.J.M.; van der Gen, A. *Recl. Trav. Chim. Pays Bas* **1984**, *103*, 305 and references cited therein.
16. Broekhof, N.L.J.M.; Jonkers, F.L.; van der Gen, A. *Tetrahedron Lett.* **1981**, 2671.
17. Taylor, E.C.; Ravindranathan, R.V. *J. Org. Chem.* **1962**, *27*, 2622.
18. Staiger, R.P.; Miller, E.B. *J. Org. Chem.* **1959**, *24*, 1214.
19. Strekowski, L.; Suk-Bin, K.; Cegla, M.T.; Harden, D.B. *Heterocycles* **1989**, *29*, 538.
20. Vinick, F.J.; Desai, M.C.; Yung, S.; Thadeio, P. *Tetrahedron Lett.* **1989**, 787.
21. Cavalla, D.; Warren, S. *Tetrahedron Lett.* **1983**, 285.
22. Cavalla, D.; Cruse, W.B.; Warren, S. *J. Chem. Soc., Perkin Trans I* **1987**, 1883.
23. Schvets, A.A.; Popov, L.D.; Kogan, V.A.; Litvinov, V.V.; Etmetchenko, L.N. *Zh. Obshch. Khim.* **1988**, *58*, 104.
24. Bhattacharya, A.K.; Roy, N.K. in *The Chemistry of Organophosphorus Compounds*; Hartley, F.R. Ed.; John Wiley and Sons Ltd: Chichester, 1992; vol. 2, pp. 195-285.
25. Staiger, R.P.; Moyer, C.L.; Pitcher, G.R. *J. Chem. and Eng. Data* **1963**, *8*, 454.
26. Couture, A.; Deniau, E.; Grandclaoudon, P. *Synthesis*, in press.
27. Jahangir; Clark, R.D. *J. Org. Chem.* **1987**, *52*, 5378.
28. Date, M.; Watanabe, M.; Furukawa, S. *Chem. Pharm. Bull.* **1990**, *38*, 902
29. Bergman, J.; Brynolf, A.; Vuorinen, E. *Tetrahedron* **1986**, *42*, 3869.