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Vilsmeier Formylation and Glyoxylation Reactions of Nucleophilic Aromatic Compounds Using Pyrophosphoryl Chloride

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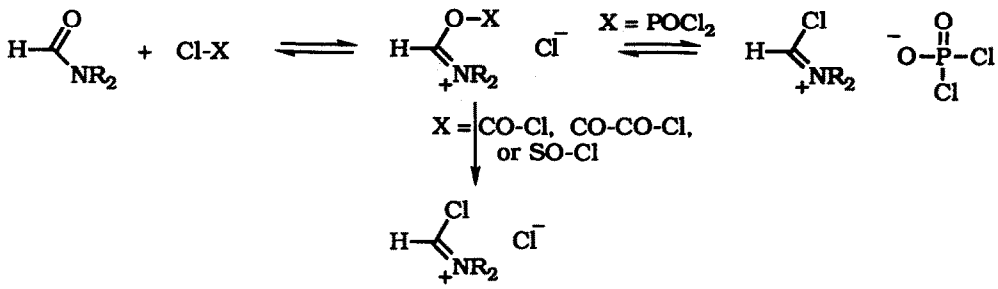
Abstract: *Reactions of N,N-dimethylformamide and N-methylformanilide with pyrophosphoryl chloride lead to the formation of reagents that undergo reactions with a wide range of nucleophilic aromatic substrates, including indoles, pyrroles, thiophenes, furans, and methoxy-substituted carbocyclic arenes to afford, after hydrolysis of the initial products, good to excellent yields of the expected aldehydes; reactions with methyl oxamates allow the preparation of methyl arylglyoxylates.*

Although formanilide and phosphoryl chloride was used as a formylating agent for resorcinol and pyrogallol in the early years of the century, the reaction failed with *N,N*-dialkylanilines.[1] It was only when Vilsmeier used formamides such as *N*-methylformanilide (NMFA) and *N,N*-dimethylformamide (DMF) that the generality of the formylation reaction was established.[2] A limited number of reactions, which lead to the formation of ketones, have been carried out using other secondary amides such as *N*-methylbenzamide.[3] Reviews have been published which summarise earlier work.[4,5,6] Although it is frequently assumed that the reagent involved, when using a range of acid chlorides, is an *N,N*-disubstituted chloromethyleneiminium chloride, it has also been suggested that a series of equilibria are involved in reactions of *N,N*-disubstituted formamides with acid chlorides such as phosphoryl chloride.[5] On the other hand it is clear that reactions involving thionyl chloride, phosgene, and oxalyl chloride lead irreversibly to the related *N,N*-disubstituted chloromethyleneiminium chloride after the loss of small thermodynamically stable gases.[5] It is also appropriate to note that whereas the attempted formylation of 2-phenyl-6a-thiathiopthene using DMF and phosphoryl chloride gave 4-formyl-2-phenyl-6a-thiathiopthene in only 4% yield a similar reaction in which *N,N*-dimethylthioformamide was substituted for the DMF resulted in an improvement of the yield to 62%.[7]

In the proposed sequence, the reaction of a formamide derivative with phosphoryl chloride leads initially to a mixed amide-phosphorodichloridate cationic anhydride which is converted into the eventual reagent, an *N,N*-disubstituted chloromethyleneiminium chloride. If a series of equilibria are involved it may be concluded that the differences that have been reported when using different electrophiles and solvent systems relate either to the position of the equilibria or to the irreversible formation of the low energy *N,N*-disubstituted chloromethyleneiminium chloride. The use of an electrophilic anhydride should lead to a cationic mixed amidic anhydride which cannot react with a nucleophile to form a lower energy species. This type of strategy has been used recently in generating a good formylating agent from DMF and trifluoromethanesulfonic anhydride.[8]



Our interest in acylating agents[9] led us to consider alternative electrophiles that should lead to more powerful formylating agents. In particular we considered the use of pyrophosphoryl chloride. We reasoned that the cationic intermediate that would be formed in the reaction between pyrophosphoryl chloride and an *N,N*-disubstituted formamide would be identical to the first formed intermediate involved in reactions of an *N,N*-disubstituted formamide with phosphoryl chloride. However, whereas in the latter reactions the first formed intermediate can afford a lower energy species by the displacement of the phosphorodichloridate ion by chloride ion, this should not be possible when using pyrophosphoryl chloride. The reagents (**1**) would be expected to be more electrophilic and more sterically demanding than, for example *N,N*-dimethylchloromethyleneiminium chloride. A study of the reactions of pyrophosphoryl chloride and a comparison with reactions using phosphoryl chloride and *N,N*-dimethylchloromethyleneiminium chloride also allows some conclusions to be drawn with respect to the reagent or reagents involved in the classical reactions which used phosphoryl chloride as the activating acid chloride. If phosphoryl chloride and pyrophosphoryl chloride were to give identical results then this would be strong evidence that the phosphorus containing reagent is the reacting species in the classical reaction. Similarly if reactions involving the use of pre-formed *N,N*-dimethylchloromethyleneiminium chloride give the same results as those obtained when using DMF and phosphoryl chloride then the alternative and most frequently suggested reagent is involved. However, if all three reagent systems give different results then one may conclude that the suggestion concerning equilibration is reasonable. We have recorded our preliminary findings of reactions using both NMFA and DMF and now report the full details of that study.[10]

(**1**)

The reactions that we have carried out using carbocyclic compounds have been restricted to methoxyarenes, *N,N*-dimethylaniline, and resorcinol, while the heterocyclic systems include pyrrole, indole, thiophene, and furan derivatives. Different experimental procedures were used depending on the nature of the aromatic compound and also on the ease with which the arylformiminium salt is hydrolysed to the corresponding aldehyde. We also carried out some reactions using phosphoryl chloride and pre-formed *N,N*-dimethylchloromethyleneiminium chloride where we decided that it was necessary to check previously reported results. Our results involving reactions of carbocyclic aromatic compounds are collected together in ***Table 1***.

A reaction of anisole with DMF and pyrophosphoryl chloride gave, after hydrolysis, a mixture of 4-methoxybenzaldehyde and 2-methoxybenzaldehyde in 70.5% and 4.5% isolated yields respectively. Previous reports of Vilsmeier formylation reactions involving anisole have not reported the formation of 2-methoxybenzaldehyde.[11] However, it is possible that the availability of high field nmr spectroscopy makes it easier to detect minor products We repeated the reaction of anisole with DMF and phosphoryl chloride and obtained a mixture of 4-methoxybenzaldehyde (34%) and 2-methoxybenzaldehyde (4%) but, as compared with the previous report, our yield was much reduced. We also carried out a reaction of anisole with pre-formed *N,N*-dimethylchloromethyleneiminium chloride but we only isolated 4-methoxybenzaldehyde in less than a 5% yield and, probably because of the low yield, we did not detect the 2-isomer. We may also note that the reaction of anisole with NMFA and pyrophosphoryl chloride gave, after hydrolysis, a mixture of 4-methoxybenzaldehyde and 2-methoxybenzaldehyde in 72% and <1% isolated yields respectively. The greater bulk of the reagent (**1**, R^1 =Ph, R^2 = Me) as compared with (**1**, $R^1 = R^2$ = Me) evidently biases attack to the less hindered position.

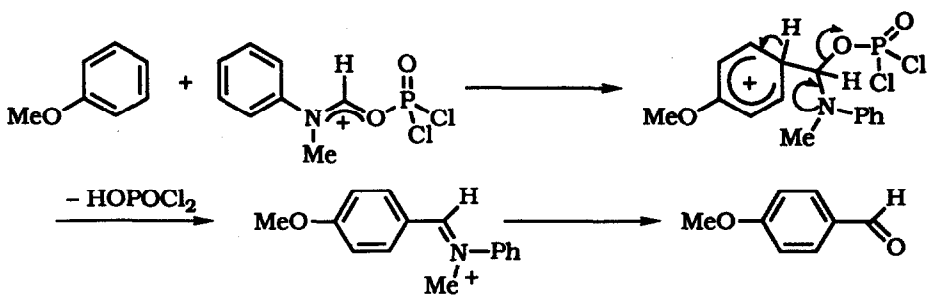


Table 1

Preparation of Aldehydes from Carbocyclic Aromatic Compounds

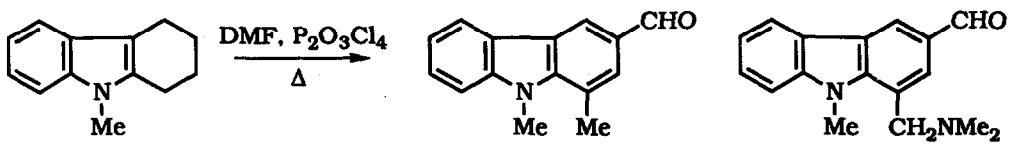
Aromatic Compound	Reagents	Temperature (°C) / Time (h)	Products	% Yield
N,N-dimethylaniline	$P_2O_3Cl_4$/DMF	65 / 15	4-$Me_2NC_6H_4CHO$	99
anisole	$P_2O_3Cl_4$/DMF	100 / 24	4-$MeOC_6H_4CHO$	70.5
			2-$MeOC_6H_4CHO$	4.5
anisole	$P_2O_3Cl_4$/NMFA	100 / 24	4-$MeOC_6H_4CHO$	72
			2-$MeOC_6H_4CHO$	< 1
anisole	$POCl_3$/DMF	100 / 24	4-$MeOC_6H_4CHO$	34
			2-$MeOC_6H_4CHO$	4
anisole	$Me_2NCHCl^+ Cl^-$	100 / 24	4-$MeOC_6H_4CHO$	< 5
o-dimethoxybenzene	$P_2O_3Cl_4$/DMF	95 / 24	3,4-$(MeO)_2C_6H_3CHO$	52
o-dimethoxybenzene	$P_2O_3Cl_4$/NMFA	115 / 1; 100 / 18	3,4-$(MeO)_2C_6H_3CHO$	83
m-dimethoxybenzene	$P_2O_3Cl_4$/DMF	100 / 4	2,4-$(MeO)_2C_6H_3CHO$	99
p-dimethoxybenzene	$P_2O_3Cl_4$/DMF	100 / 48	2,5-$(MeO)_2C_6H_3CHO$	40
1-methoxynaphthalene	$P_2O_3Cl_4$/DMF	100 / 28	4-MeO-$C_{10}H_6CHO$	96
2-methoxynaphthalene	$P_2O_3Cl_4$/DMF	100 / 28	2-MeO-$C_{10}H_6CHO$	90
resorcinol	$P_2O_3Cl_4$/DMF	20 / 5	2,4-$(OH)_2C_6H_3CHO$	88

These results also suggest that the proposals[5] concerning possible equilibria do have some validity and that the improved yields obtained using pyrophosphoryl chloride result from the greater electrophilicity of the cationic mixed amidic anhydride (1, $R^1 = R^2 = Me$) as compared with *N,N*-dimethylmethyleneiminium chloride. Reactions with the majority of the other methoxyarenes are also higher when using pyrophosphoryl chloride than when using phosphoryl chloride. Thus for example the most nucleophilic of the dimethoxybenzenes, *m*-dimethoxybenzene, is reported to afford 2,4-dimethoxybenzaldehyde in 85% yield using either DMF[12] or NMFA.[13] The reactions of phosphoryl chloride with NMFA and DMF afford the expected aldehydes in reactions with the other dimethoxybenzenes but in lower yields than those obtained in the present study. The reported yields were with *o*-dimethoxybenzene (NMFA) 38%[13] and 52%[14] (DMF) 11%[14] and with *p*-dimethoxybenzene (NMFA) 16%[13] and 7%[14] and (DMF) 0%[14]. We believe that a combination of reasons account for the greatly improved yields obtained in reactions of the methoxybenzenes involving pyrophosphoryl chloride. We have already argued that the reagents (1) produced from pyrophosphoryl chloride will be more electrophilic than the equilibrium reagents generated using phosphoryl chloride. In addition, our results obtained in the reactions of anisole indicate that the position of the equilibrium may be temperature dependent. The position of the equilibrium when using phosphoryl chloride may also depend on the amount of phosphoryl chloride used. Thus higher yields are frequently obtained when an excess of phosphoryl chloride is used.[15] We also noted that *N,N*-dimethylchloromethyleneiminium chloride is relatively unstable at high temperatures which would account for the very low yield obtained when using that reagent in the reaction with anisole. As a result of the increased stability of the reagents (1) we were able to carry out reactions, for example with *o*- and *p*-dimethoxybenzene, at temperatures significantly higher than those reported earlier,[13,14] and this factor may also be partly responsible for our higher yields. The yields obtained using our reagent system in reactions of both α– and β–methoxynaphthalene were also higher than those reported earlier.[16,17] The result that we obtained in a reaction with resorcinol was significantly better than that previously recorded,[18] possibly because we used a different experimental procedure. The reported yield in the reaction using resorcinol was 46% but in our experiment where we pre-formed the reagent we obtained 2,4-dihydroxybenzaldehyde in 88% yield.

In the majority of the reactions involving heterocyclic aromatic compounds we anticipated that the results that had been reported previously would not be markedly improved by using our reagent systems. However, there are some points to which we should draw attention. For example, indole and simple alkyl- and arylindoles are formylated in the 3-position in excellent yields using phosphoryl chloride and DMF and so there is little advantage in using the pyrophosphoryl chloride-DMF system. 1,3-Dimethylindole also affords the 2-formyl- derivative in an excellent yield when using our reagent system.

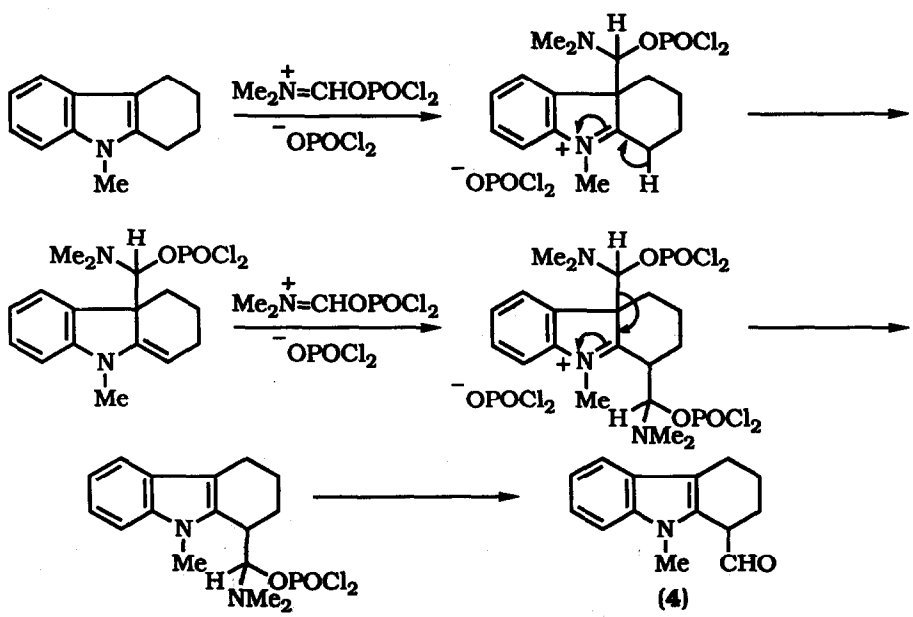
We also decided to carry out reactions with 1,2,3,4-tetrahydrocarbazole and 9-methyl-1,2,3,4-tetrahydrocarbazole as examples of 2,3-dialkylindoles. We expected that, like the reactions of other 2,3-dialkylindoles with electrophiles, reactions would occur initially at the 4a-position but could be controlled and lead to good yields of 9-formyl-1,2,3,4-tetrahydrocarbazole or, in the case of a 9-alkyl-1,2,3,4-tetrahydrocarbazole, replacement of a hydrogen by a formyl group at the 1-position. The formylation of 1,2,3,4-tetrahydrocarbazole using DMF and phosphoryl chloride affords a mixture of 9-formyl-1,2,3,4-tetrahydrocarbazole and the unstable 4a,9-diformyl-2,3,4,4a-tetrahydrocarbazole in 36.6% and 17.7% yields respectively.[19] In our hands using a ratio of pyrophosphoryl chloride : 1,2,3,4-tetrahydrocarbazole (1.3:1) at 80° C and a relatively brief reaction time (20min) we obtained a mixture of 9-formyl-1,2,3,4-tetrahydrocarbazole and the unstable 4a,9-diformyl-2,3,4,4a-tetrahydrocarbazole in 17% and 21% yields respectively. However, when we heated the reaction mixture at 100° C for 5h we obtained 9-formyl-1,2,3,4-tetrahydrocarbazole in 70% yield. Vilsmeier reactions of 9-alkyl-1,2,3,4-tetrahydrocarbazole derivatives have also been reported on a number of occasions.[20] However, it is only recently that the conflicting reports have been partially rationalised.[21] The major reason for the difference between our results and those reported in the previous studies probably relates to different molar ratios of reagents being used. Temperature and anion differences are also important. We have concentrated in

our study on reactions of 9-methyl-1,2,3,4-tetrahydrocarbazole. Reactions carried out at high temperatures afforded mixtures in which the major products were 1,9-dimethyl-3-formylcarbazole (**2**) and 1-*N*,*N*-dimethylaminomethyl-3-formyl-9-methylcarbazole (**3**). The yields of the two products were shown to vary with the amount of pyrophosphoryl chloride used.



mol % $P_2O_3Cl_4$	yield (%) (**2**)	(**3**)
100	17	11
130	27	21
180	21	25

In reactions carried out at 0 °C we have found that 9-methyltetrahydrocarbazole affords the previously unknown stable 1-formyl derivative (**4**) in an almost quantitative yield only when we used two or more equivalents of pyrophosphoryl chloride or phosphoryl chloride in the presence of an excess of DMF. We conclude that, as expected, all of the reactions of 1,2,3,4-tetrahydrocarbazole and its 9-substituted derivatives proceed by initial reaction at position-4a. and that that intermediate then reacts further. The requirement for more than one molar equivalent of formiminium reagent in reactions leading to good yields of 1-formyl-1,2,3,4-tetrahydrocarbazole suggests that the 4a-substituent is only lost at a late stage when re-aromatisation occurs, as shown in the ***Scheme*** below. We list our results of reactions of indole and substituted derivatives in ***Table 2***.

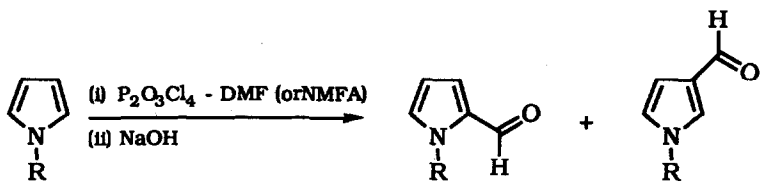


Scheme

Table 2
Preparation of Aldehydes from Indole and Substituted Indoles

Indole derivative	Reagents	Temperature (°C) / Time (h)	Product(s)	% Yield
indole	$P_2O_3Cl_4$/DMF	0 / 1; 40 / 1	3-formylindole	97
1-methylindole	$P_2O_3Cl_4$/DMF	20 / 1	1-methyl-3-formylindole	98
2-methylindole	$P_2O_3Cl_4$/DMF	40 / 1	2-methyl-3-formylindole	88
1,2-dimethylindole	$P_2O_3Cl_4$/DMF	20 / 20	1,2-dimethyl-3-formylindole	95
1,3-dimethylindole	$P_2O_3Cl_4$/DMF	20 / 40	1,3-dimethyl-2-formylindole	87
1-methyl-2-phenylindole	$P_2O_3Cl_4$/DMF	20 / 18	1-methyl-2-phenyl-3-formylindole	94
tetrahydrocarbazole	$P_2O_3Cl_4$/DMF	80 / 0.33	9-formyltetrahydrocarbazole	17
			4a,9-diformyltetrahydrocarbazole	21
tetrahydrocarbazole	$P_2O_3Cl_4$/DMF	100 / 5	9-formyltetrahydrocarbazole	70
9-methyltetrahydrocarbazole	$P_2O_3Cl_4$/DMF	0 / 3	1-formyl-9-methyl-tetrahydrocarbazole	96
9-methyltetrahydrocarbazole	$POCl_3$/DMF	0 / 3	1-formyl-9-methyl-tetrahydrocarbazole	99
9-methyltetrahydrocarbazole	$P_2O_3Cl_4$/DMF	80 / 18	1,9-dimethyl-3-formylcarbazole	21
			1-*N*,*N*-dimethylaminomethyl-3-formyl-9-methylcarbazole	25

A large body of information already exists in the literature concerning Vilsmeier reactions of pyrrole, furan, and thiophene and their derivatives.[5] Reactions of pyrrole and 1-substituted pyrroles are reported to afford the 2-formyl- derivatives except where a bulky substituent, for example t-butyl,[22] and tri-isopropylsilyl,[23] are present on the nitrogen, or where the 2- and 5- positions already carry a substituent. We have restricted our experiments to *N*-substituted pyrroles, furan and 2-methylfuran, and thiophene and 2-methoxythiophene and our results are presented in ***Table 3***.



In the reactions involving *N*-substituted pyrroles we anticipated that as the bulk of the electrophile increased so we would observe an increase in the proportion of the 3-formyl- derivative. Experiment confirmed that reasoning, but somewhat surprisingly we observed some substitution at the 3- position even in reactions of *N*-methylpyrrole. Once again it is likely that the availability of improved analytical methods, for example high field nmr spectroscopy and flash chromatography, has allowed the detection and isolation of small amounts of products that have hitherto avoided observation. Thus, we detected and isolated 1-methyl-3-formylpyrrole in

increasing amounts when using *N,N*-dimethylchloromethyleneiminium chloride, phosphoryl chloride-DMF, and pyrophosphoryl chloride-DMF. As expected, reactions of 1-benzylpyrrole gave the greatest amount of 1-benzyl-3-formylpyrrole when using pyrophosphoryl chloride-NMFA. Whereas it has been reported that the reaction of tri-isopropylsilylpyrrole with *N,N*-dimethylchloromethyleneiminium chloride leads to the exclusive formation of 3-formyl-1-triisopropylsilylpyrrole[23] our experiments using pyrophosphoryl chloride and DMF or NMFA result in the isolation of a small amount of 2-formylpyrrole. We assume that this must arise as a result desilylation by an anion before the reaction with the electrophile occurs.

Table 3

Preparation of Aldehydes from Pyrroles, Furans, and Thiophenes

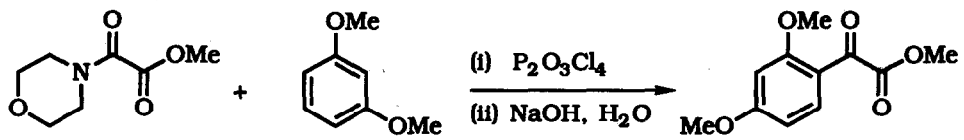
Heterocycle	Reagents	Temperature (°C) Time / (h)	Product(s)	% Yield
1-methylpyrrole	$P_2O_3Cl_4$/DMF	20 / 18	1-methyl-2-formylpyrrole	88
			1-methyl-3-formylpyrrole	5
1-methylpyrrole	$POCl_3$/DMF	20 / 18	1-methyl-2-formylpyrrole	84
			1-methyl-3-formylpyrrole	6
1-methylpyrrole	$[Me_2N{=}CHCl]^+ Cl^-$/DMF	20 / 18	1-methyl-2-formylpyrrole	88
			1-methyl-3-formylpyrrole	5
1-benzylpyrrole	$P_2O_3Cl_4$/DMF	20 / 18	1-benzyl-2-formylpyrrole	80
			1-benzyl-3-formylpyrrole	18
1-benzylpyrrole	$P_2O_3Cl_4$/NMFA	20 / 20	1-benzyl-2-formylpyrrole	75
			1-benzyl-3-formylpyrrole	22
1-benzylpyrrole	$POCl_3$/DMF	20 / 18	1-benzyl-2-formylpyrrole	86
			1-benzyl-3-formylpyrrole	10
1-tri-isopropylsilylpyrrole	$P_2O_3Cl_4$/DMF	20 / 2	2-formylpyrrole	14
			3-formylpyrrole	66
1-tri-isopropylsilylpyrrole	$P_2O_3Cl_4$/NMFA	20 / 2	2-formylpyrrole	7
			3-formylpyrrole	61
1-tri-isopropylsilylpyrrole†	$P_2O_3Cl_4$/NMFA	0-20 / 2	2-formylpyrrole	3
			3-formylpyrrole	73
furan	$P_2O_3Cl_4$/DMF	20 / 0.5; 75 / 0.5	2-formylfuran	71
2-methylfuran	$P_2O_3Cl_4$/DMF	20 / 50	2-formyl-5-methylfuran	77
thiophene	$P_2O_3Cl_4$/DMF	70 / 1.5	2-formylthiophene	60
thiophene	$P_2O_3Cl_4$/NMFA	20 / 18	2-formylthiophene	75
2-methoxythiophene	$P_2O_3Cl_4$/DMF	0 / 0.5; 20 / 5	2-formyl-5-methoxythiophene	83
2-methoxythiophene	$P_2O_3Cl_4$/NMFA	0 / 1; 20 / 5	2-formyl-5-methoxythiophene	80

† This reaction was carried out by the slow addition of tips-pyrrole to the cold pre-formed reagent.

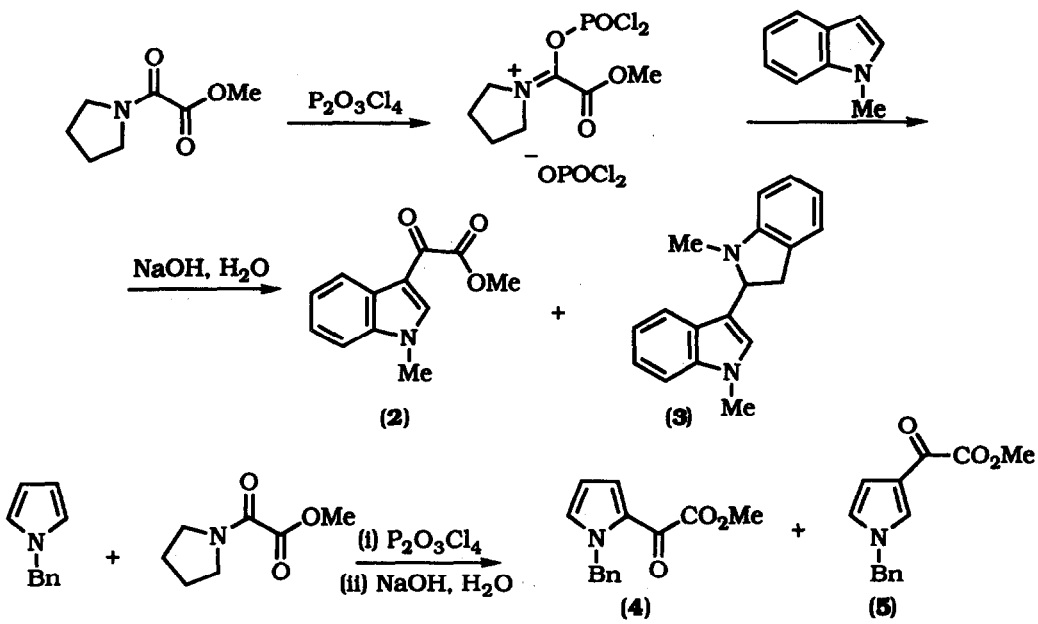
We noted above that very few reports are concerned with the formation of ketones using amides other than formamides in Vilsmeier reactions.[3,24] We required a route to arylglyoxylic esters in connection with another study.[25] Two routes have been used previously. Reactions using oxalyl chloride were among the first reports of Friedel-Crafts acylations and, with reactive substrates such as anisole or *N,N*-dimethylaniline, afford derivatives of benzil.[26] On the other hand reactions of oxalyl chloride with indole in the absence of a catalyst have been used to prepare 3-indolylglyoxylyl chloride.[27] The conversion of the intermediate acid chloride into esters

is straightforward. Similar reactions of oxalyl chloride using pyrrole derivatives have also been reported,[25,28] and appear, in most cases, not to be subject to major steric effects. Friedel-Crafts acylation reactions using alkyl oxalyl chlorides were among the first[29] reported acylations and have also been reported more recently.[30] The reaction of ethyl oxalyl chloride with tips-pyrrole gave a good yield of ethyl 3-pyrrylglyoxylate.[31] It may be anticipated from our work reported above, that the Vilsmeier variant could, because of the steric demand of the reagent, allow control over the regiochemistry where more than one product is likely. We therefore made a preliminary study of alternative syntheses of arylglyoxylates based on reactions of oxamic esters.

Reactions of *m*-dimethoxybenzene with methyl oxamates derived from methyl oxalyl chloride and either pyrrolidine or morpholine, and either phosphoryl chloride or pyrophosphoryl chloride afforded methyl 2,4-dimethoxyphenylglyoxylate. The yield obtained using phosphoryl chloride and the pyrrolidine derived amide was only 31% whereas using pyrophosphoryl chloride we obtained the expected product in 82% yield. As expected, the amide derived from morpholine gave the best yield (89%).



In reactions of 1-methylindole using the pyrrolidine derived oxamide we did observe that some of the indole was converted, by the liberated acid, into the known dimer (3),[32] which was isolated in a 20% yield. The formation of the dimer was minimised when the iminium salt intermediate was pre-formed. In this latter reaction the methyl 3-(1-methylindolyl)glyoxylate (2) was isolated in 79% yield.



Perhaps the most interesting result obtained in these preliminary reactions involved the reaction with 1-benzylpyrrole where the two products (4) and (5) in 33% and 53% respectively were isolated. This result may be compared with that obtained in a reaction of 1-benzylpyrrole with oxalyl chloride followed by methanol which gave methyl 1-benzyl-2-pyrrylglyoxylate (4) exclusively. We will report our further studies of Vilsmeier reactions using pyrophosphoryl chloride and amides derived from acids other than formic acid in a future paper.

Experimental

4-*N*,*N*-Dimethylaminobenzaldehyde

Pyrophosphoryl chloride (2.266 g, 9.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*,*N*-dimethylformamide (1.097 g, 15.0 mmol) and *N*,*N*-dimethylaniline (0.909 g, 7.5 mmol) to give a thick green syrup. The mixture was then heated at 65° C for 15 h and cooled. The resultant green solid was dissolved in water then basified with an aqueous solution of sodium hydroxide (2M) to give a yellow solid. Sublimation (Kugelrohr) (140-150° C at 0.6 mm Hg) gave 4-*N*,*N*-dimethylaminobenzaldehyde (1.109 g, 99%), m.p. 73-75° C lit.[3] m.p. 72-73° C, ν_{max} / cm^{-1} 1656 (C=O); δ_H(250 MHz; $CDCl_3$) 3.06 (6H, s), 6.67 (2H, d, J = 9.0 Hz), 7.71 (2H, d, J = 9.0 Hz), and 9.72 (1H, s) ppm; δ_C($CDCl_3$) 40.01 (2 x NCH3), 110.96 (2 x CH), 125.07 (C), 131.92 (2 x CH), 154.31 (C), and 10.22 (CHO) ppm; Found: M^+, 149.0826 calc. for $C_9H_{11}NO$ 149.0841.

Reactions with anisole

Procedure 1

Pyrophosphoryl chloride (3.273 g, 13 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*,*N*-dimethylformamide (1.097 g, 15.0 mmol) and anisole (1.081 g, 10.0 mmol). The resulting syrup was then heated at 100° C for 24 hours. The cold product was then basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane. The solution was dried ($MgSO_4$) and concentrated. Kugelrohr distillation gave a mixture of 2-anisaldehyde and 4-anisaldehyde, b.p. 40°-50° C at 0.05 mm Hg in 6:94 ratio by ^1H NMR integration. Flash chromatography on silica gel, eluting with diethyl ether-petroleum ether (b.p. 40°-60° C) (1:10) gave 2-methoxybenzaldehyde[33] and 4-methoxybenzaldehyde[11] (1.02g, 75%).

2-methoxybenzaldehyde, ν_{max} / cm^{-1} 1689 (C=O); δ_H(250 MHz; $CDCl_3$) 3.88 (3H, s), 6.94-7.01 (2H, m), 7.48-7.55 (1H, m), 7.77-7.81 (1H, m), and 10.44 (1H, s); δ_C(CDCl3) 55.59 (OCH3), 111.72 (CH), 120.60 (CH), 124.74 (C), 128.33 (CH), 136.06 (CH), 161.86 (C), and 189.75 (CHO).

4-methoxybenzaldehyde, ν_{max} / cm-1 1691 (C=O); δ_H(250 MHz; $CDCl_3$) 3.85 (3H, s), 6.98 (2H, d, J = 8.5 Hz), 7.82 (2H, d, J = 8.5 Hz), and 9.86 (1H, s) ppm; δ_C($CDCl_3$) 55.55 (OCH3), 114.33 (2 x CH), 129.92 (C), 131.96 (2 x CH), 164.64 (C), and 190.83 (CHO) ppm.

Procedure 2

Pyrophosphoryl chloride (3.273 g, 13 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*-methylformanilide (2.028 g, 15.0 mmol) and anisole (1.081 g, 10.0 mmol). The resulting syrup was then heated at 100° C for 24 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane, dried (MgSO4) and concentrated. Flash chromatography on silica gel, eluting with ether-petroleum ether (b.p. 40°-60° C) (1:10) gave 2-methoxybenzaldehyde and 4-methoxybenzaldehyde.in a ratio of 1:72 by integration of the ^1H nmr spectrum (0.99g, 73%).

Procedure 3

Phosphoryl chloride (3.0 g, 12 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*,*N*-dimethylformamide (0.877 g, 12 mmol) and anisole (1.081 g, 10.0 mmol). The resulting syrup was then heated at 100° C for 24 hours. The resulting black tar was then basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane. The solution was dried (MgSO4) and concentrated.

Kugelrohr distillation gave a mixture of 2-methoxybenzaldehyde and 4-methoxybenzaldehyde (0.517 g, 38%, bp 60° C at 0.1 mm Hg) in 6:94 ratio by ^{1}H NMR integration, spectral data were as in procedure 1.

Procedure 4

As procedure 3 except that an excess of phosphoryl chloride (9.200 g, 60 mmol) was used and gave a mixture of 2-methoxybenzaldehyde and 4-methoxybenzaldehyde (0.245 g, 18%) in 6:94 ratio by ^{1}H NMR integration, spectral data were as in procedure 1.

3,4-Dimethoxybenzaldehyde

Procedure 1

Pyrophosphoryl chloride (2.226 g, 9.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*-methylformanilide (1.21 g, 9.0 mmol) and *o*-dimethoxybenzene (1.00 g, 7.24 mmol). The resulting syrup was then heated at 115°C for 1 hour then at 100° C for 18 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane and dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate-petroleum ether (b.p. 40-60°C) (3:7) gave 3,4-dimethoxybenzaldehyde (1.00 g, 83%), m.p. 42-44°C lit.[13] 39-42°C and 42-45°C respectively; ν_{max} / cm^{-1} 1682 (C=O); δ_H(250 MHz; $CDCl_3$) 3.81 (3H, s), 3.83 (3H, s), 6.85 (1H, d, J = 8.0 Hz), 7.27 (1H, d, J = 1.9 Hz), 7.33 (1H, dd, J = 1.9 and 8.0 Hz), and 9.70 (1H, s) ppm; δ_C($CDCl_3$) 55.97 (OCH3), 56.16 (OCH3), 108.92 (CH), 110.41 (CH), 126.89 (CH), 130.11 (C), 149.60 (C), 154.49 (C), and 190.90 (CHO) ppm; Found: M$^+$, 166.0608 calc. for $C_9H_{10}O_3$ 166.0630.

Procedure 2

Pyrophosphoryl chloride (2.266 g, 9.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (1.21 g, 16.6 mmol) and *o*-dimethoxybenzene (1.00 g, 7.24 mmol). The resulting syrup was then heated at 95° C for 24 hours. The cold product was then basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate-petroleum ether (b.p. 40-60°C) (3:7) gave 3,4-dimethoxybenzaldehyde (0.63 g, 52%), m.p. 42-44°C, spectral data were as in procedure 1

2,4-Dimethoxybenzaldehyde

Pyrophosphoryl chloride (0.554 g, 2.2 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (0.161 g, 2.2 mmol) and *m*-dimethoxybenzene (0.276 g, 2.0 mmol). The resulting syrup was then heated at 100° C for 4 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane, dried (MgSO4) and concentrated. Kugelrohr distillation gave 2,4-dimethoxybenzaldehyde (0.328 g, 99%) b.p. 110° C at 0.3 mm, a white crystaline solid, m.p. 69-70°C (lit.[13] b.p. 165° C at 10 mm Hg and 110°C at 0.1 mmHg, m.p. 68-70° C); vmax / cm^{-1} 1673 (C=O); δ_H(250 MHz; $CDCl_3$) 3.86 (3H, s), 3.88 (3H, s), 6.43 (1H, d, J = 2.2 Hz), 6.52 (1H, dd, J = 8.5 and 2.2 Hz), 7.78 (1H, d, J = 8.5Hz), and 10.27 (1H, s) ppm; δ_C(CDCl3) 55.59 (OCH3), 55.62 (OCH3), 97.86 (CH), 105.90 (CH), 119.00 (C), 130.60 (CH), 163.65 (C), 166.26 (C), and 188.26 (CHO) ppm; Found: M$^+$, 166.0626 calc. for $C_9H_{10}O_3$ 166.0630.

2,5-Dimethoxybenzaldehyde

Pyrophosphoryl chloride (1.889 g, 7.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (0.731 g, 10.0 mmol) and *p*-dimethoxybenzene (0.691 g, 5.0 mmol). The resulting syrup was then heated at 100°C for 48 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Kugelrohr distillation gave 2,5-dimethoxybenzaldehyde (0.332 g, 40%), m.p. 50-51°C lit.[13] m.p. 49-52°C; b.p. 80° C at 0.1 mm Hg; ν_{max} / cm^{-1} 1677 (C=O); δ_H(250 MHz; $CDCl_3$) 3.80 (3H, s), 3.88 (3H, s), 6.94 (1H, d, J = 9.0

Hz), 7.14 (1H, dd, J = 3.3 and 9.0 Hz), 7.34 (1H, d, J = 3.3Hz), and 10.44 (1H, s) ppm; $\delta_C(CDCl_3)$ 55.80 (OCH_3), 56.14 (OCH_3), 110.35 (CH), 113.14 (CH), 123.80 (CH), 124.78 (C), 153.87 (C), 156.89 (C), and 190.16 (CHO) ppm; Found: M^+, 166.0624 calc. for $C_9H_{10}O_3$ 166.0630.

4-Methoxy-1-formylnaphthalene

Pyrophosphoryl chloride (1.92 g, 7.65 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (1.0 g, 13.69 mmol) and 1-methoxynaphthalene (1.00 g, 6.32 mmol). The resulting syrup was then heated at 100° C for 28 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with diethyl ether, dried ($MgSO_4$) and concentrated. Flash chromatography, eluting with ethyl acetate-petroleum ether (b.p. 40°-60° C) (1:5) gave 4-methoxy-1-formylnaphthalene, (1.13 g, 96%), m.p. 36°C lit.[16] m.p. 35-36°C; vmax / cm^{-1} 1678 (C=O); δ_H(250 MHz; $CDCl_3$) 3.91 (3H, s), 6.68 (1H, d, J = 8.0 Hz), 7.05 (1H, m), 7.61 (1H, m), 7.69 (1H, d, J = 8.0 Hz), 8.21 (1H, d, J = 6.8 Hz), 9.25 (1H, d, J = 6.8 Hz), and 10.07 (1H, s) ppm; δ_C(CDCl3) 55.81 (OCH3), 102.83 (CH), 122.34 (CH), 124.74 (CH), 125.55 (C), 126.22 (CH), 129.35 (CH), 131.69 (C), 139.71 (CH), 160.65 (C), and 192.20 (CHO) ppm; Found: M^+, 186.0645 calc. for $C_{12}H_{10}O_2$ 186.0681.

2-Methoxy-1-formylnaphthalene

Pyrophosphoryl chloride (1.92 g, 7.65 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (1.0 g, 13.7 mmol) and 2-methoxynaphthalene (1.00 g, 6.32 mmol). The resulting syrup was then heated at 100° C for 28 hours. The cold product was basified with an aqueous solution of sodium hydroxide (2M) and extracted with diethyl ether, dried ($MgSO_4$) and concentrated. Flash chromatography with ethyl acetate-petroleum ether (bp = 40° to 60° C) (1:5) as the eluent gave 2-methoxy-1-formylnaphthalene (1.06 g, 90%), m.p. 82-84°C lit.[17] m.p. 82-85°C; ν_{max} / cm^{-1} 1673 (C=O); δ_H(250 MHz; $CDCl_3$) 3.92 (3H, s), 7.14 (1H, d, J = 9.2 Hz), 7.36 (1H, m), 7.56 (1H, m), 7.69 (1H, d, J = 8.0 Hz), 7.93 (1H, d, J = 9.2 Hz), 9.28 (1H, d, J = 8.0 Hz), and 10.90 (1H, s) ppm; $\delta_C(CDCl_3)$ 56.43 (OCH3), 112.46 (CH), 116.47 (C), 124.66 (CH), 124.86 (CH), 128.24 (CH), 128.44 (C), 129.80 (CH), 131.49 (C), 137.54 (CH), 163.89 (C), and 191.92 (CHO) ppm; Found: M^+, 186.0661 calc. for $C_{12}H_{10}O_2$ 186.0681.

2,4-Dihydroxybenzaldehyde

Pyrophosphoryl chloride (2.0 g, 7.96 mmol) was added dropwise to *N,N*-dimethylformamide (1.2 g, 16.4 mmol) at 0°C and the resulting syrup was stirred at 20° C for 30 minutes. Resorcinol (0.8 g, 7.27 mmol) was added to the cooled (ice bath) syrup and the mixture stirred at 20° C for 5 hours. The mixture was basified with an aqueous solution of sodium acetate, extracted into diethyl ether, dried ($MgSO_4$), and the solvent evaporated to give 2,4-dihydroxybenzaldehyde (0.88 g, 88%), m.p. 135°C lit.[18] m.p. 135°C; ν_{max} / cm^{-1} 3558 (OH), 3297 (OH), and 1660 (C=O); δ_H(250 MHz; $CDCl_3$) 6.41 (1H, d, J = 2.1 Hz), 6.49 (1H, dd, J = 2.1 and 8.5 Hz), 7.35 (1H, d, J = 8.5 Hz), 9.57 (1H, broad OH), 9.66 (1H, s), and 11.42 (1H, s) ppm; $\delta_C(CDCl_3)$ 102.88 (CH), 109.27 (CH), 114.60 (C), 135.86 (CH), 164.44 (C), 165.83 (C), and 194.08 (CHO ppm); Found: M^+, 138.0314 calc. for $C_9H_{10}O_3$ 138.0316.

***N,N*-Dimethylchloromethyleneiminium chloride**[34]

Phosphorus pentachloride (10.41 g, 50 mmol) was added portionwise to *N,N*-dimethylformamide (3.66 g, 50 mmol) with cooling (ice bath). The resulting phosphoryl chloride was distilled off (ca 20 mm Hg) and the resultant solid sublimed (60-70° C, 0.01 mm Hg) to give *N,N*-dimethylchloromethyleneiminium chloride (4.16 g, 65%); δ_H(250 MHz; CD_3CN) 3.75 (6H, broad singlet), and 10.81 (1H, broad singlet) ppm.

3-Formylindole

Pyrophosphoryl chloride (1.24 g, 4.94 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (1.50 g, 20.54 mmol) and indole (0.50 g, 4.27 mmol). The resulting syrup was stirred at 0°C for 0.5 hour then at 40° C for 1 hour. Ice was added, followed by an aqueous solution of sodium

hydroxide (2M), and the mixture was heated under reflux. On cooling a precipitate of 3-formylindole was obtained (0.60 g, 97%), m.p. 196-198°C, lit.[35] m.p. 195-198°C; ν_{max} / cm^{-1} 3168 (N-H) and 1632 (C=O); δ_H(250 MHz; ([$^2H_6$]DMSO) 7.23 (2H, m), 7.48 (1H, m), 7.97 (1H, s), 8.18 (1H, m), 9.96 (1H, s), and 11.87 (1H, broad singlet, NH) ppm; δ_C([$^2H_6$]DMSO) 111.83 (CH), 118.06 (C), 120.72 (CH), 121.74 (CH), 123.08 (CH), 123.88 (C), 136.81 (C), 136.97 (CH), and 184.36 (CHO) ppm.

3-Formyl-1-methylindole

Pyrophosphoryl chloride (1.506 g, 6.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (0.439 g, 6.0 mmol) and 1-methylindole (0.656 g, 5.0 mmol). The resulting syrup was stirred at 20°C for 1 hour. The cold product was then basified with an aqueous solution of sodium hydroxide (2M) and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography with ethyl acetate-petroleum ether (b.p. 40°-60° C) (1:5) as the eluent gave 3-formyl-1-methylindole (0.780 g, 98%); m.p. 67-69° C lit.[36] m.p. 69-70° C; ν_{max} / cm^{-1} 1638 (C=O); δ_H(250 MHz; $CDCl_3$) 3.69 (3H, s), 7.25 (3H, m), 7.49 (1H, s), 8.25 (1H, m), and 9.85 (1H, s) ppm; δ_C($CDCl_3$) 33.55 (NCH3), 109.99 (CH), 117.87 (C), 121.85 (CH), 122.84 (CH), 123.95 (CH), 125.14 (C), 137.76 (C), 139.62 (CH), and 184.36 (CHO) ppm; Found: M^+, 159.0696 calc. for $C_{10}H_9NO$ 159.0684.

3-Formyl-2-methylindole

Pyrophosphoryl chloride (1.10 g, 4.38 mmol) was added dropwise to cold (ice bath) *N,N*-dimethylformamide (2.00 g, 27.39 mmol). The resulting syrup was stirred at 20°C for 0.5 hour and cooled to 0°C. 2-Methylindole (0.50 g, 3.81 mmol) was added and the resulting syrup was heated at 40°C for 1 hour. The cold product was then basified with an aqueous solution of sodium hydroxide (2M) and the resulting suspension heated to boiling point. The clear solution was cooled (0°C) and a yellow precipitate was filtered off and dried to give 3-formyl-2-methylindole (0.53 g, 88%), m.p. 199-200°C lit.[35] m.p. 200-201°C; ν_{max} / cm^{-1} 1644 (C=O); δ_H(250 MHz; $CDCl_3$) 2.70 (3H, s), 7.16 (2H, m), 7.34 (1H, m), 8.17 (1H, m), 9.85 (1H, broad singlet, NH), and 10.12 (1H, s), ppm; δ_C($CDCl_3$) 11.94 (CH3), 111.16 (CH), 114.21 (C), 120.45 (CH), 122.16 (CH), 122.79 (CH), 126.05 (C), 135.56 (C), 148.00 (C), and 184.22 (CHO) ppm; Found: M^+, 159.0661 calc. for $C_{10}H_9NO$ 159.0684.

3-Formyl-1,2-dimethylindole

Pyrophosphoryl chloride (1.80 g, 7.17 mmol) was added dropwise to stirred cold (ice bath) *N,N*-dimethylformamide (1.50 g, 20.54 mmol). The resulting syrup was stirred at 20°C for 0.5 hour and cooled to 0°C. 1,2-Dimethylindole (0.70 g, 4.82 mmol) was added and the resulting syrup was stirred at 20°C for 20 hours. The cold product was then basified with an aqueous solution of sodium hydroxide (2M), extracted with diethyl ether, dried ($MgSO_4$), and evaporated to give colourless crystals of 3-formyl-1,2-dimethylindole (0.79 g, 95%), m.p. 128-130·°C lit.[37] m.p.128-130° C; ν_{max} / cm^{-1} 1644 (C=O); δ_H(250 MHz; $CDCl_3$) 2.51 (3H, s), 3.54 (3H, s), 7.22 (3H, m), 8.23 (1H, m), 10.03 (1H, s), and 9.85 (1H, broad, N-H) ppm; δ_C($CDCl_3$) 10.36 (CH3), 29.49 (CH3), 109.17 (CH), 114.05 (C), 120.74 (CH), 122.66 (CH), 122.99 (CH), 125.55 (C), 136.78 (C), 147.84 (C), and 183.94 (CHO) ppm; Found: M^+, 173.0844 calc. for $C_{11}H_{11}NO$ 173.0841.

2-Formyl-1,3-dimethylindole

Pyrophosphoryl chloride (1.0 g, 3.98 mmol) was added dropwise to *N,N*-dimethylformamide (2.0 g, 27.4 mmol) at 0° C. 1,3-Dimethylindole (0.5 g, 3.44 mmol) was added to the resulting syrup after 0.5h. The mixture was then stirred for 40h at room temperature, cooled to 0° C and basified with aqueous sodium hydroxide (2M). The product was extracted into diethyl ether, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate-petroleum ether (1:1) gave 2-formyl-1,3-dimethylindole,

0.52 g (87%), m.p. 35-36° C, lit.[38] m.p. 35-36° C; ν_{max} /cm^{-1} 1660 (C=O); δ_H (250 MHz $CDCl_3$) 2.57 (3H, s), 3.97 (3H, s), 7.11 (1H, m), 7.28 (1H, m), 7.38 (1H, m), 7.64 (1H, m), and 10.09 (1H, s) ppm; δ_C($CDCl_3$) 8.45 (CH_3), 31.46 (CH_3), 110.1 (CH), 120.0 (CH), 121.2 (CH), 126.3 (C), 126.8 (C), 127.3 (CH), 131.1 (C), 139.2 (C), and 181.6 (CHO) ppm; Found: M^+, 173.0835 calc. for $C_{11}H_{11}NO$ 173.0841.

3-Formyl-1-methyl-2-phenylindole

Pyrophosphoryl chloride (0.88 g, 3.5 mmol) was added dropwise to a stirred solution of 1-methyl-2-phenylindole (0.6g, 2.89 mmol) in *N,N*-dimethylformamide (2.0 g, 27.4 mmol) at 0° C. The mixture was stirred at room temp-erature for 18h, cooled, basified with aqueous sodium hydroxide (2M), extracted with diethyl ether, dried ($MgSO_4$) and concentrated to give 3-formyl-1-methyl-2-phenylindole, (0.64g, 94%), gold needles mp 124-5° C (from ethyl acetate - petroleum ether (1:1), lit.[39] mp 124-126° C. ν_{max} /cm^{-1} 1638 (C=O); δ_H (250 MHz $CDCl_3$) 3.61 (3H, s), 7.34 (3H, m), 7.44 (2H, m), 7.52 (3H,m), 8.42 (1H, m), and 9.72 (1H, s) ppm; δ_C ($CDCl_3$) 30.97 (CH_3), 109.82 (CH), 115.59 (C), 122.03 (CH), 123.20 (CH), 123.96 (CH), 125.07 (C), 128.47 (C), 128.61 (CH), 129.83 (CH), 130.85 (CH), 137.28 (C), 151.43 (C), and 186.54 (CHO) ppm; Found: M^+, 235.0989 calc. for $C_{16}H_{13}NO$ 235.0997.

9-Formyl-1,2,3,4-tetrahydrocarbazole and 4a,9-diformyl-2,3,4,4a-tetrahydrocarbazole

Pyrophosphoryl chloride (1.9 g, 67.6 mmol) was added dropwise to *N,N*-dimethylformamide (4.0 g, 54.8 mmol) at 0° C and then stirred at room temperature for 0.5h. The product was cooled to 0° C and 1,2,3,4-tetrahydrocarbazole (1.0 g, 5.85 mmol) was added and the mixture was heated at 80° C for 20min, cooled, basified with an aqueous solution of sodium carbonate, extracted with diethyl ether, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with a 1:1 mixture of ethyl acetate and light petroleum (b.p. 40-60° C) gave 9-formyl-1,2,3,4-tetrahydrocarbazole (0.2 g, 17%) m.p. 60-62° C and 4a,9-diformyl-2,3,4,4a-tetrahydrocarbazole as an oil (0.28g, 21%); ν_{max} /cm^{-1} 1683 and 1723 (C=O); δ_H (250 MHz $CDCl_3$) 1.53-2.97 (6H, m), 5.68 (1H, s,br), 7.10-7.50 (3H,m), 8.00 (1H, d, J = 7.15Hz), 8.86 (1H, s) and 9.30 (1H, s) ppm; δ_C ($CDCl_3$) 18.56 (CH_2), 22.84 (CH_2), 24.77 (CH_2), 109.12 (CH), 109.60 (C), 115.13 (C), 116.56 (CH), 123.73 (CH), 124.27 (C), 125.10 (C), 125.46 (CH), 129.64 (CH), 156.85 (CHO), and 194.20 (CHO) ppm; Found: M^+, 227.0959 calc. for $C_{14}H_{13}NO_2$ 227.0946.

9-Formyl-1,2,3,4-tetrahydrocarbazole

Pyrophosphoryl chloride (1.63 g, 6.5 mmol) was added dropwise to *N,N*-dimethylformamide (4.0 g, 54.8 mmol) at 0° C and then stirred at room temperature for 0.5h. The product was cooled to 0° C and 1,2,3,4-tetrahydrocarbazole (1.0 g, 5.85 mmol) was added and the mixture was heated at 100° C for 5h, cooled, basified with an aqueous solution of sodium acetate, extracted with diethyl ether, dried ($MgSO_4$) and concentrated to afford 9-formyl-1,2,3,4-tetrahydrocarbazole (0.77 g, 70%) m.p. 60-62° C (lit.[20a] m.p. 64.5-65.5° C). ν_{max} /cm^{-1} 1702 (C=O); δ_H (250 MHz $CDCl_3$) 1.85 (4H, m), 2.58 (2H, m), 2.72 (2H, m), 7.25 (3H,m), 8.32 (1H, m), and 9.00 (1H, s, br) ppm; δ_C ($CDCl_3$) 20.63 (CH_2), 21.73 (CH_2), 22.20 (CH_2), 22.58 (CH_2), 115.91 (CH), 117.79 (CH), 118.30 (C), 124.08 (CH), 124.45 (CH), 130.42 (C), 133.16 (C), 134.58 (C), and 157.66 (CHO) ppm; Found: M^+, 199.0997 calc. for $C_{13}H_{13}NO$ 199.0997.

1-Formyl-9-methyl-1,2,3,4-tetrahydrocarbazole

Pyrophosphoryl chloride (3.67 g, 14.7 mmol) was added dropwise to *N,N*-dimethylformamide (4.0 g, 54.8 mmol) at 0° C and then stirred at room temperature for 0.5h. The product was cooled to 0° C and 9-methyl-1,2,3,4-tetrahydrocarbazole (1.0 g, 5.4 mmol) was added and the mixture was stirred at 0° C for 3h, basified with an aqueous solution of sodium acetate , extracted with diethyl ether, dried ($MgSO_4$) and concentrated to afford ***1-formyl-9-methyl-1,2,3,4-tetrahydrocarbazole*** (1.1 g, 96%) m.p. 70-72° C. ν_{max}

/cm^{-1} 1725 (C=O); δ_H (250 MHz $CDCl_3$) 1.87-2.09 (3H, m), 2.31 (1H, m), 2.72-2.85 (2H, m), 3.61 (3H, s), 3.71 (1H, m), 7.06-7.13 (1H, m), 7.18-7.30 (2H,m), 7.51 (1H, m), and 9.71 (1H, d, J = 2.74 Hz) ppm; δ_C ($CDCl_3$) 20.25 (CH_2), 20.67 (CH_2), 24.00 (CH_2), 29.48 (CH), 45.80 (CH_3), 108.85 (CH), 111.83 (C), 118.21 (CH), 118.87 (CH), 121.56 (CH), 126.65 (C), 129.50 (C), 137.32 (C), and 200.47 (CHO) ppm; Found: M^+, 213.1151 $C_{14}H_{15}NO$ requires 213.1153.

1,9-Dimethyl-3-formylcarbazole and 1-*N*,*N*-dimethylaminomethyl-3-formyl-9-methylcarbazole

Pyrophosphoryl chloride (2.44 g, 9.7 mmol) was added dropwise to a stirred mixture of *N*,*N*-dimethylformamide (4.0 g, 54.8 mmol) and 9-methyl-1,2,3,4-tetrahydrocarbazole (1.0 g, 5.4 mmol) and then heated and stirred at 80° C for 18h. The product was cooled, basified with an aqueous solution of sodium acetate , extracted with diethyl ether, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate - petroleum ether (b.p. 40-60° C) (1:3) gave 1,9-dimethyl-3-formylcarbazole (R_f 0.4) (0.25 g, 21%), m.p. 162-164° C (lit.[20b] m.p. 163-164° C). ν_{max} /cm^{-1} 1682 (C=O); δ_H (250 MHz $CDCl_3$) 2.79 (3H, s), 4.00 (3H, s), 7.24-7.35 (3H,m), 7.46-7.52 (1H, m), 7.62 (1H, d, J = 1.4 Hz), 8.05 (1H, m), 8.31 (1H, d, J = 1.4Hz) and 10.03 (1H, s) ppm; δ_C ($CDCl_3$) 20.23 (CH_3), 32.05 (CH_3), 109.10 (CH), 120.09 (CH), 120.23 (CH), 120.68 (C), 122.07 (CH), 122.80 (C), 123.41 (C), 126.48 (CH), 128.31 (C), 129.05 (CH), 141.97 (C), 143.02 (C), and 191.65 (CHO) ppm; Found: M^+, 223.1008 calc. for $C_{15}H_{13}NO$ 223.09971; and ***1-N,N-dimethylaminomethyl-3-formyl-9-methylcarbazole*** (R_f 0.13) (0.35 g, 25%), m.p. 102-104° C. ν_{max} /cm^{-1} 1683 (C=O); δ_H (250 MHz $CDCl_3$) 2.26 (6H, s CH_3 9 x 2), 3.75 (2H, s), 4.22 (3H, s), 7.26 (1H, m) , 7.41 (1H, m), 7.51 (1H, m), 7.71 (1H, d, J = 1.6Hz), 8.00 (1H, m), 8.47 (1H, d, J = 1.6Hz) and 10.00 (1H, s) ppm; δ_C ($CDCl_3$) 31.46 (CH_3), 44.73 (2 x CH_3), 62.2 (CH_2), 109.36 (CH), 120.08 (CH), 120.31 (CH), 121.93 (C), 122.86 (C), 123.62 (CH), 124.21 (C), 126.62 (CH), 127.65 (C), 130.17 (CH), 142.27 (C), 143.53 (C), and 191.60 (CHO) ppm; Found: M^+, 266.1422 $C_{17}H_{18}N_2O$ requires 266.1419.

2-Formyl-1-methylpyrrole and 3-Formyl-1-methylpyrrole

Procedure 1

Pyrophosphoryl chloride (1.506 g, 6.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*,*N*-dimethylformamide (0.439 g, 6.0 mmol) and freshly distilled 1-methylpyrrole (0.405 g, 5.0 mmol). The resulting syrup was stirred at 20° C for 18 hours. The product was then basified with an aqueous solution of sodium hydroxide (2M), extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel eluting with diethyl ether-petroleum ether (b.p. 40°-60° C) (1:5) gave 2-formyl-1-methylpyrrole[40,22] (0.481 g, 88%) and 3-formyl-1-methylpyrrole[41] (0.026 g, 5%), both as colourless oils.

2-Formyl-1-methylpyrrole, δ_H(250 MHz; $CDCl_3$) 3.94 (3H, s), 6.20 (1H, m), 6.88 (2H, m), and 9.54 (1H, s) ppm; δ_C($CDCl_3$) 36.40 (NCH_3), 109.50 (CH), 124.12 (CH), 131.97 (C), 132.07 (CH), and 179.56 (CHO) ppm.

3-Formyl-1-methylpyrrole, δ_H(250 MHz; $CDCl_3$) 3.70 (3H, s), 6.61 (2H, m), 7.23 (1H, m), and 9.71 (1H, s) ppm; δ_C($CDCl_3$) 36.68 (NCH_3), 108.46 (CH), 124.38 (CH) 126.22 (C), 129.87 (CH), and 185.78 (CHO) ppm.

Procedure 2

As procedure 1 except phosphoryl chloride (0.767 g, 5.0 mmol) was used instead of pyrophosphoryl chloride. This gave a mixture of 2-formyl-1-methylpyrrole (0.459 g, 84%) and 3-formyl-1-methylpyrrole (0.031 g, 6.0%); spectral data were as in procedure 1.

Procedure 3

N,*N*-dimethylchloromethyleneiminium chloride (0.768 g, 6 mmol) was dissolved in *N*,*N*-dimethyl-

formamide (5 g, 68 mmol) and cooled (ice bath). Freshly distilled 1-methylpyrrole (0.405 g, 5.0 mmol) was added dropwise and the resulting solution was stirred at 20° C for 18 hours. The product was then basified with an aqueous solution of sodium hydroxide (2M), extracted with dichloromethane, dried ($MgSO_4$), and concentrated. Flash chromatography on silica gel eluting with diethyl ether-petroleum ether (b.p. 40°-60° C) (1:5) gave 2-formyl-1-methylpyrrole (0.422 g, 77.4%) and 3-formyl-1-methylpyrrole (0.016 g, 3.0%); spectral data were as in procedure 1.

1-Benzyl-2-formylpyrrole and 1-benzyl-3-formylpyrrole[22,42]

Procedure 1

Pyrophosphoryl chloride (2.140 g, 8.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (1.097 g, 15.0 mmol) and 1-benzylpyrrole (1.179 g, 7.5 mmol) and the resulting syrup was stirred at 20°C for 18 hours. The cold product was then basified with an aqueous solution of sodium hydroxide (2M), extracted with dichloromethane, and dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with diethyl ether - petroleum ether (b.p. 40°-60° C) (3:7) gave 1-benzyl-2-formylpyrrole (1.112 g, 80%) and 1-benzyl-3-formylpyrrole (0.245 g, 18%), both as colourless oils.

1-Benzyl-2-formylpyrrole, ν_{max} / cm^{-1} 1658 (C=O); δ_H(250 MHz; $CDCl_3$) 5.54 (2H, s), 6.24 (1H, m), 6.94 (2H, m), 7.14-7.10 (2H, m), 7.31-7.18 (3H, m), and 9.54 (1H, s) ppm; δ_C($CDCl_3$) 51.9 (CH_2), 110.10 (CH), 124.8 (CH), 127.4 (CH), 127.7 (2 x CH), 129.7 (CH), 131.4 (2 x CH), 131.5 (C), 137.5 (C), and 179.3 (CH=O) ppm; Found: M^+, 185.0827 calc. for $C_{12}H_{11}NO$ 185.0841.

1-Benzyl-3-formylpyrrole, ν_{max} / cm^{-1} 1660 (C=O); δ_H(250 MHz; $CDCl_3$) 5.08 (2H, s), 6.65 (1H, dd, J = 2.8 and 1.8 Hz), 6.70 (1H, t, J = 2.8 Hz), 7.18-7.13 (2H, m), 7.37-7.29 (4H, m), and 9.73 (1H, s) ppm; δ_C($CDCl_3$) 54.98 (CH_2), 108.7 (CH), 123.8 (CH), 126.9 (C), 127.4 (2 x CH), 128.4 (CH), 129.0 (2 x CH), 129.2 (CH), 136.1 (C), and 185.6 (CHO) ppm; Found: M^+, 185.0830 calc. for $C_{12}H_{11}NO$ 185.0841.

Procedure 2

Pyrophosphoryl chloride (2.140 g, 8.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*-methylformanilide (2.028 g, 15.0 mmol) and 1-benzylpyrrole (1.179 g, 7.5 mmol) and the resulting syrup was stirred at 20° C for 19 hours. The cold product was then basified with NaOH (2M), extracted with dichloromethane, washed with aqueous hydrochloric acid, dried ($MgSO_4$), concentrated, and unreacted *N*-methylformanilide removed by Kugelrohr distillation (70° C at 0.1 mm Hg). Flash chromatography on silica gel, eluting with diethyl ether-petroleum ether (b.p. 40°-60° C) (1:5) gave 2-formyl-1-benzylpyrrole (1.034 g, 75%) and 3-formyl-1-benzylpyrrole (0.303 g, 22%), both as colourless oils and with spectral data as in procedure 1.

Procedure 3

As procedure 1 except of phosphoryl chloride (1.303 g, 8.5 mmol) was used instead of pyrophosphoryl chloride. This gave a mixture of 2-formyl-1-benzylpyrrole (1.194 g, 86%) and 3-formyl-1-benzylpyrrole (0.133 g, 10%), both as colourless oils and with spectral data as in procedure 1.

Reactions of 1-tri-isopropylsilylpyrrole

Procedure 1

Pyrophosphoryl chloride (1.511 g, 6.0 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N,N*-dimethylformamide (0.731 g, 10.0 mmol) and 1-tri-isopropylsilylpyrrole (1.119 g, 5.0 mmol) dissolved in acetonitrile. The resulting syrup was stirred at 20° C for 2 hours, cooled, basified with aqueous sodium hydroxide (2M) and extracted with dichloromethane. The solution was dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel (gradient elution) with 30% to 75% diethyl ether in petroleum ether (b.p. 40-60°C) gave 2-formylpyrrole[40,43] (0.065 g, 14%), 3-formylpyrrole[43] (0.313 g, 66%), and tri-isopropylsilanol (0.871g, 100%).

2-Formylpyrrole, ν_{max} / cm^{-1} 1650 (C=O), and 3280 (N-H); δ_H(250 MHz; $CDCl_3$) 6.36 (1H, m), 7.01 (1H, m), 7.16 (1H, m), 9.52 (1H, s), and 10.1 (1H, broad singlet, D_2O exchangeable) ppm; δ_C($CDCl_3$) 111.4 (CH), 121.6 (CH), 127.0 (CH), 133.5 (C), and 179.5 (CHO) ppm.

3-Formylpyrrole, ν_{max} / cm^{-1} 1650 (C=O), and 3288 (N-H); δ_H(250 MHz; $CDCl_3$) 6.67 (1H, m), 6.85 (1H, m), 7.48 (1H, m), 9.80 (1H, s), and 10.2-9.4 (1H, broad singlet, D_2O exchangeable) ppm; δ_C($CDCl_3$) 107.4 (CH), 120.9 (CH), 126.4 (CH), 127.9 (C), and 186.2 (CHO) ppm.

Triisopropylsilanol, ν_{max} / cm^{-1} 3452 (O-H); δ_H(250 MHz; $CDCl_3$) 1.05 (21H, unresolved multiplet), 1.42 (1H, D_2O exchangeable) ppm; δ_C($CDCl_3$) 12.32 (CH), 17.72 (3 x CH_3) ppm.

Procedure 2

As procedure 1 except *N*-methylformanilide (1.352 g, 10.0 mmol) was used instead of *N,N*-dimethylformamide. This gave 3-formylpyrrole (0.290 g, 61%), 2-formylpyrrole (0.033 g, 7.0%), and triisopropylsilanol (0.871 g, 100%). The spectral data obtained were as in procedure 1.

Procedure 3

Pyrophosphoryl chloride (3.64g, 14.5 mmol) was added dropwise to *N*-methylformanilide (1.96g, 14.52 mmol) at 0° C. The resulting syrup was stirred at room temperature for 0.5h and cooled to 0° C before 1-tri-isopropylsilylpyrrole (2.7g, 12.1 mmol) dissolved in acetonitrile (10ml) was added dropwise over 0.5h. The mixture was allowed to warm to room temperature and stirred for 2h and cooled again to 0° C, basified with aqueous sodium hydroxide (2M), extracted into diethyl ether, dried ($MgSO_4$), and concentrated. Flash chromatography on silica gel (gradient elution) with 30% to 75% diethyl ether in petroleum ether (b.p. 40-60°C) gave 2-formylpyrrole (0.038 g, 3%), 3-formylpyrrole (0.85 g, 73%). The spectral data obtained were as in procedure 1.

2-Formylfuran

Pyrophosphoryl chloride (4.0g, 15.93 mmol) was added dropwise to *N,N*-dimethylformamide (3.0g, 41 mmol) at 0° C. The resulting syrup was stirred at room temperature for 0.5h and cooled to 0° C before furan (1.0 g, 14.7 mmol) was added dropwise and stirred at 0° C for 0.75h and then heated at 75° C for 0.5h. The cold reaction mixture was basified with aqueous sodium hydroxide (2M) and extracted with diethyl ether, dried ($MgSO_4$) and concentrated to afford 2-formylfuran[44] (1.0g, 71%); ν_{max}/cm^{-1} 1674 (C=O); δ_H (250 MHz, $CDCl_3$) 6.62 (1H, d x d, J = 1.73 and 3.6 Hz), 7.27 (1H, d x d, J = 0.75 and 3.6 Hz), 7.70 (1H, m), and 9.67 (1H, s) ppm; δ_C 112.61 (CH), 121.08 (CH), 148.11 (CH), 152.99 (C), and 177.91 (CHO) ppm; Found M^+ 96.0208 calc. for $C_5H_4O_2$ 96.0211.

2-Formyl-5-methylfuran

Pyrophosphoryl chloride (3.36g, 13.4 mmol) was added dropwise to *N,N*-dimethylformamide (2.0g, 27.4 mmol) at 0° C. The resulting syrup was stirred at room temperature for 0.5h and cooled to 0° C before 2-methylfuran (1.0g, 12.2 mmol) was added dropwise and stirred at 0° C for 1h and at room temperature for 50h. The cold reaction mixture (0° C) was basified with aqueous sodium hydroxide (2M) and extracted with diethyl ether, dried ($MgSO_4$) and concentrated to afford 2-formyl-5-methylfuran[44] (1.03g, 77%); ν_{max}/cm^{-1} 1674 (C=O); δ_H (250 MHz, $CDCl_3$) 2.42 (3H,s), 6.25 (1H, d x d, J = 0.84 and 3.5 Hz), 7.18 (1H, d, J = 3.5 Hz), and 9.49 (1H, s) ppm; δ_C 14.0 (CH_3), 109.61 (CH), 124.16 (CH), 151.86 (C), 156.0 (C), and 177.02 (CHO) ppm; Found M^+ 110.0361 calc. for $C_6H_6O_2$ 110.0367.

2-Formylthiophene

Procedure 1

Pyrophosphoryl chloride (3.3 g, 13.14 mmol) was added dropwise to a stirred mixture of cold (ice bath)

N,N-dimethylformamide (1.50 g, 20.54 mmol) and the resulting syrup was stirred at 20°C for 0.5 hour. Thiophene (0.7 g, 8.3 mmol) was added and the mixture heated at 70°C for 1.5 hours. An aqueous solution of sodium acetate was added to the cooled solution and the product extracted with diethyl ether, dried ($MgSO_4$) and concentrated to give 2-formylthiophene[45] (0.56 g, 60%), ν_{max} / cm^{-1} 1663 (C=O); δ_H(250 MHz; $CDCl_3$) 7.22 (1H, m), 7.78 (2H, m), and 9.94 (1H, s) ppm; $\delta_C(CDCl_3)$ 128.36 (CH), 133.34 (C), 135.19 (CH), 136.41 (CH), and 183.07 (CHO) ppm; Found: M^+, 111.9975 calc. for C_5H_4OS 111.9983.

Procedure 2

Pyrophosphoryl chloride (2.2 g, 8.76 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*-methylformanilide (1.18 g, 8.74 mmol) and the resulting syrup was stirred at 20°C for 0.5 hour. Thiophene (0.7 g, 8.3 mmol) was added and the mixture stirred at 20°C for 18 hours. An aqueous solution of sodium hydroxide (2M) was added to the cooled solution and the product extracted with diethyl ether. The ether layer was washed with dilute hydrochloric acid, dried ($MgSO_4$), and concentrated to give 2-formylthiophene (0.70 g, 75%), with spectral data as in procedure 1.

2-Formyl-5-methoxythiophene

Procedure 1

Pyrophosphoryl chloride (1.84 g, 7.33 mmol) was added dropwise to cold (ice bath) *N,N*-dimethylformamide (1.0 g,13.69 mmol) and the resulting syrup was stirred at room temperature for 0.5 hour and then cooled to 0° C. 2-Methoxythiophene (0.8 g, 7.0 mmol) was added and the mixture was stirred at 0° C for 1h followed by 5h at room temperature. The mixture was cooled to 0° C and basified with aqueous sodium hydroxide (2M) and the product extracted with diethyl ether, dried ($MgSO_4$) and concentrated to give 2-formyl-5-methoxythiophene[46] (0.83 g, 83%), ν_{max} / cm^{-1} 1657 (C=O); δ_H(250 MHz; $CDCl_3$) 3.99 (3H, s), 6.35 (1H, d, J = 4.3Hz), 7.51 (1H, d, J = 4.3Hz), and 9.66 (1H, s) ppm; $\delta_C(CDCl_3)$ 60.60 (OMe), 106.38 (CH), 130.09 (C), 137.97 (CH), 175.92 (C), and 182.37 (CHO) ppm; Found: M^+, 142.0075 calc. for $C_6H_6O_2S$ 142.0088.

Procedure 2

Pyrophosphoryl chloride (2.2 g, 8.76 mmol) was added dropwise to a stirred mixture of cold (ice bath) *N*-methylformanilide (0.91 g, 6.75 mmol) and the resulting syrup was stirred at 20°C for 0.5 hour and then cooled to 0° C. 2-Methoxythiophene (0.7 g, 6.14 mmol) was added and the mixture was stirred at 0° C for 1h followed by 5h at room temperature. The mixture was cooled to 0° C and basified with aqueous sodium hydroxide (2M) and the product extracted with diethyl ether. The mixture was then washed with aqueous hydrochloric acid (2M), dried ($MgSO_4$) and concentrated to give 2-formyl-5-methoxythiophene (0.7 g, 80.5%), with spectral data as the product obtained by procedure 1.

Methyl pyrrolidinylglyoxylate

Methyl oxalyl chloride (5.63 g, 46 mmol) dissolved in ether (30 ml) was added dropwise to a stirred solution of pyrrolidine (3.91 g, 55 mmol) and triethylamine (5.57 g, 55 mmol) dissolved in ether (70 ml) with cooling from an ice bath. After 2 h at 20° C the triethylamine hydrochloride was filtered off and the solution concentrated. Distillation (Kugelrohr) gave ***methyl pyrrolidinylglyoxylate*** (6.83 g, 79%), bp = 90° C at 0.1 mm Hg; ν_{max} / cm^{-1} 1740 (ester C=O) and 1652 (amide C=O); δ_H(250 MHz; $CDCl_3$) 1.85-2.03 (4H, m), 3.54 (2H, t, J = 6.9Hz), 3.65 (2H, t, J = 6.9Hz), and 3.67 (3H, s) ppm; $\delta_C(CDCl_3)$ 23.88 (CH_2), 26.04 (CH_2), 46.26 (CH_2), 47.54 (CH_2), 52.66 (OMe), 158.87 (C=O), and 162.75 (C=O) ppm; Found: M^+, 157.0745 $C_7H_{11}NO_3$ requires 157.0739.

Methyl morpholinylglyoxylate

Methyl oxalyl chloride (2.450 g, 20 mmol) dissolved in ether (10 ml) was added dropwise to a stirred solution of morpholine (2.178 g, 25 mmol) and triethylamine (2.530 g, 25 mmol) dissolved in ether (40 ml)

with cooling from an ice bath. After 2 h at 20° C the triethylamine hydrochloride was filtered off and the solution concentrated. Distillation (Kugelrohr) gave ***methyl morpholinylglyoxylate*** (3.85 g, 89%), bp = 100° C at 0.1 mm Hg; ν_{max} / cm^{-1} 1740 (ester C=O) and 1632 (amide C=O); δ_H(250 MHz; $CDCl_3$) 3.45-3.50 (2H, m), 3.63-3.75 (6H, m), and 3.88 (3H, s) ppm; δ_C($CDCl_3$) 41.84 (CH_2), 46.45 (CH_2), 52.76 (OMe), 66.39 (CH_2), 66.67 (CH_2) 159.92 (C=O), and 162.88 (C=O) ppm; Found: M^+, 173.0691 $C_7H_{11}NO_4$ requires 173.0688.

Methyl 2,4-dimethoxyphenylglyoxylate

Procedure 1

Phosphoryl chloride (0.537 g, 3.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) methyl pyrrolidinylglyoxylate (0.550 g, 3.5 mmol) and *m*-dimethoxybenzene (0.415 g, 3.0 mmol). The resulting syrup was then heated at 60° C for 16h. The cold product was basified with NaOH (2M) and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with 30% ethyl acetate in petroleum ether (bp = 40° to 60° C) gave ***methyl 2,4-dimethoxyphenylglyoxylate*** m.p. 48.5-49.5° C (0.207 g, 31%); ν_{max} / cm^{-1} 1746 (ester C=O) and 1656 (ketone C=O); δ_H(250 MHz; $CDCl_3$) 3.85 (3H, s), 3.88 (3H, s), 3.90 (3H, s), 6.43 (1H, d, *J* = 2.2Hz), 6.60 (1H, d x d *J* = 2.2 and 8.8Hz), and 7.89 (1H, d *J* = 8.8Hz) ppm; δ_C($CDCl_3$) 52.15 (OMe), 55.64 (OMe), 56.10 (OMe), 98.07 (CH), 106.70 (CH), 115.92 (C), 132.71 (CH), 162 25 (C), 166.69 (C=O), and 184.96 (C=O) ppm; Found: M^+, 224.0685 $C_{11}H_{12}O_5$ requires 224.0685.

Procedure 2

As procedure 1 except pyrophosphoryl chloride (0.881 g, 3.5 mmol) was used instead of phosphoryl chloride with a reaction time of 11 h. This gave methyl 2,4-dimethoxyphenylglyoxylate (0.553 g, 82%).

Procedure 3

Pyrophosphoryl chloride (0.630 g, 2.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) methyl morpholinylglyoxylate (0.433 g, 2.5 mmol) and *m*-dimethoxybenzene (0.276 g, 2.0 mmol). The resulting syrup was then heated at 60° C for 24h. The cold product was then basified with NaOH (2M), extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Distillation (Kugelrohr) (bp = 140 - 150° C at 0.05 mm Hg) gave methyl 2,4-dimethoxyphenylglyoxylate (0.4 g, 89%).

Methyl 3-(1-methylindolyl)glyoxylate

Procedure 1

Pyrophosphoryl chloride (0.881g, 3.5 mmol) was added dropwise to a stirred mixture of cold (ice bath) methyl pyrrolidinylglyoxylate (0.55 g, 3.5 mmol) and 1-methylindole (0.394 g, 3.0 mmol). The resulting syrup was stirred at 20° C for 1.5h. The cold product was neutralised with a saturated aqueous solution of sodium hydrogencarbonate and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate in petroleum ether (bp = 40° to 60° C) (1:5) gave ***methyl 3-(1-methylindolyl)glyoxylate*** (2), (0.449 g, 69%), m.p. 96-97° C; ν_{max} / cm^{-1} 1730 (ester C=O) and 1643 (ketone C=O); δ_H(250 MHz; $CDCl_3$) 3.85 (3H, s), 3.94 (3H, s), 7.35 (3H, m), 8.31 (1H, s), and 8.44 (1H, m) ppm; δ_C($CDCl_3$) 33.79 (NMe), 52.69 (OMe), 109.90 (CH), 112.86 (C), 122.82 (CH), 123.58 (CH), 124.19 (CH), 127.07 (C), 140.41 (CH), 163.37 (C=O), and 176.85 (C=O) ppm; Found: M^+, 217.0754 $C_{12}H_{11}O3$ requires 217.0739. A second fraction was shown to be 2,3'-indolyl-1,1'-dimethylindoline, (0.118g, 30%), m.p. 137-138° C lit.[29] m.p. 136° C; δ_H (250 MHz; $CDCl_3$) 2.64 (3H, s), 3.27 [2H, m (ABX system), *J* = 8.9 and 11.0 Hz], 3.75 (3H, s), 4.61 (1H, dd, *J* = 8.9 and 11.0 Hz), 6.52 (1H, d, *J* = 7.8 Hz), 6.62 (1H, m), 6.96 (1H, s), 6.95-7.30 (5H, m), and 7.68 (1H, d, J = 8.0 Hz); δ_C (62.9

MHz; $CDCl_3$) 32.69 (NCH_3), 34.08 (NCH_3), 37.82 (CH_2), 64.72 (CH), 107.20 (CH), 109.35 (CH), 115.05 (C), 117.81 (CH), 118.95 (CH), 120.13 (CH), 121.75 (CH), 124.01 (CH), 126.80 (C), 127.30 (CH), 127.52 (CH), 129.24 (C), 137.50 (C), and 153.30 (C); Found: M^+, 262.1484 calc. for $C_{21}H_{20}N_2O_2$ 262.1470.

Procedure 2

Pyrophosphoryl chloride (0.881g, 3.5 mmol) was added dropwise to cold methyl pyrrolidinylglyoxylate (0.550g, 3.5 mmol) and the mixture was stirred and heated at 50° C for 5min to give a thick syrup which was cooled to 0° C before 1-methylindole (0.394g, 3.0 mmol) was added. Stirring was continued for a further 11h at 0° C and the mixture was then neutralised with a saturated aqueous solution of sodium hydrogencarbonate and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate in petroleum ether (bp = 40° to 60° C) (1:5) gave methyl 3-(1methylindolyl)glyoxylate (2), (0.514 g, 79%) and 2,3'-indolyl-1,1'-dimethylindoline, (0.079g, 20%); spectral data were as in procedure 1.

Methyl 2-(1-benzylpyrrolyl)glyoxylate and methyl 3-(1-benzylpyrrolyl)glyoxylate

Pyrophosphoryl chloride (1.506g, 6.0 mmol) was added to cold (ice bath) methyl pyrrolidinylglyoxylate (0.943g, 6.0 mmol) and stirred and heated at 20° c for 0.5h. The product was dissolved in acetonitrile (10 ml), cooled to 0° C and 1-benzylpyrrole (0.788g, 5.0 mmol) was added dropwise. The resulting solution was stirred at 0° C for 1h, basified with NaOH (2M) and extracted with dichloromethane, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel, eluting with 15% ethyl acetate in petroleum ether (bp = 40° to 60° C) gave ***methyl 2-(1-benzylpyrrolyl)glyoxylate*** (4) an oil (0.401 g, 33%); ν_{max} / cm^{-1} 1737 (ester C=O) and 1644 (ketone C=O); δ_H(250 MHz; $CDCl_3$) 3.85 (3H, s), 5.54 (2H, s), 6.24 (1H, m), 7.05 (1H, m), 7.10 (2H, m), 7.2-7.3 (3H, m), and 7.35 (1H, m) ppm; δ_C($CDCl_3$) 52.62 (OMe), 52.79 (CH_2), 110.31 (CH), 125.70 (CH), 127.11 (C), 127.27 (CH), 127.72 (CH), 128.67 (CH), 133.78 (CH), 137.16 (C), 163.53 (C=O), and 173.65 (C=O) ppm; Found: M^+, 243.0909 $C_{14}H_{13}NO_3$ requires 243.0895; and ***methyl 3-(1-benzylpyrrolyl)glyoxylate*** (5) an oil (0.645 g, 53%); ν_{max} / cm^{-1} 1732 (ester C=O) and 1655 (ketone C=O); δ_H(250 MHz; $CDCl_3$) 3.86 (3H, s), 5.05 (2H, s), 6.65 (1H, m), 6.79 (1H, m), 7.14 (2H, m), 7.29-7.35 (3H, m), and 7.75 (1H, m) ppm; δ_C($CDCl_3$) 52.60 (OMe), 53.97 (CH_2), 111.05 (CH), 121.55 (C), 123.54 (CH), 127.34 (CH), 128.32 (CH), 128.98 (CH), 130.85 (CH), 135.98 (C), 163.34 (C=O), and 178.02 (C=O) ppm; Found: M^+, 243.0914 $C_{14}H_{13}NO_3$ requires 243.0895.

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