Studies on Wallach's Imidazole Synthesis

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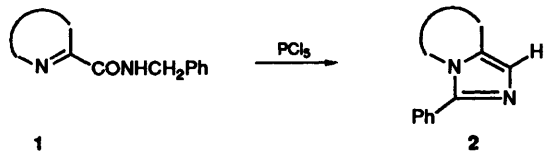
The reaction of the *N*-benzylamides of *N*-heterocyclic carboxylic acids **3** and **6–9** with phosphorus pentachloride affords heterocondensed imidazoles **4** and **10–14** by a scheme reminiscent of Wallach's imidazole synthesis starting from *N,N'*-dialkyloxamides. Kinetic and labelling experiments are described which support a mechanism involving nitrile ylide species and allow a better understanding of the Wallach reaction. The limiting parameter for the formation of heteroanellated imidazoles is the electron availability of the heterocyclic ring.

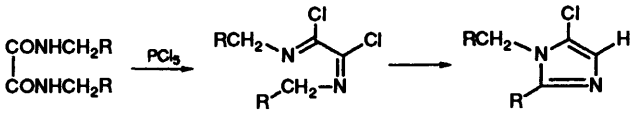
We report on the scope and limitations of the synthesis of heterocondensed imidazoles **2** from *N*-benzylamides of heterocyclic carboxylic acids **1** with phosphorus pentachloride (Scheme 1).



1 **2**

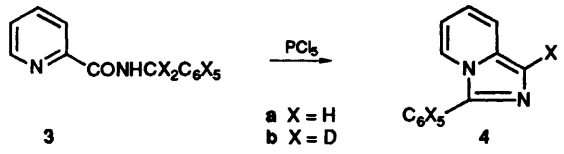
Scheme 1

The reaction can be considered as an extension of Wallach's imidazole synthesis [1] starting from dialkyloxamides (Scheme 2).



Scheme 2

In our variation one of the CN double bonds of the intermediate dichloroethanediylidenebis-*N,N'*-alkylamine is incorporated into an *N*-heteroaromatic ring. One precedent has been reported in the literature: [2] the formation of the 3-phenylimidazo[1,5-*a*]pyridine **4a** (26% yield) in the reaction of the *N*-benzylpicolinamide **3a** with a mixture of phosphorus pentachloride, phosphorus oxychloride and pyridine (Scheme 3). Total retention of deuterium in position 1 of **4b** was observed



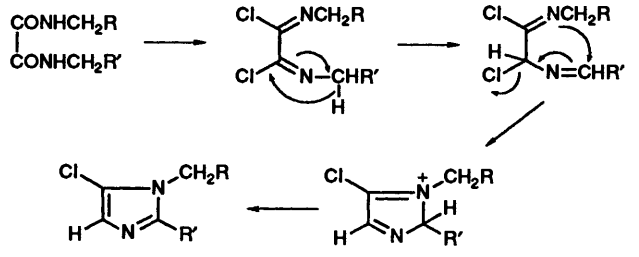
3 **a** X = H, **b** X = D **4**

Scheme 3

for the labelled substrate **3b**. However, the mechanism suggested for the formation of **4** from **3**, involving nitrile ylide species **5a** and **5b** as intermediates, does not account for this result (Scheme 4). As hydrogen chloride is produced in the formation of the intermediate in Scheme 2, and deuterium chloride in the formation of the nitrile ylide, H–D equilibration should occur; it is known that the hydrogen shift in prototropic equilibria of

Table 1

Substrate	*t*/h	Conversion (%)	Product (% yield)
6a	1	100	**10a** (70)
6b	50	30	**10b** (10)
7	0.7	100	**11** (40), **12** (15)
8	2	75	**13** (40)
9	5	50	**14** (20)



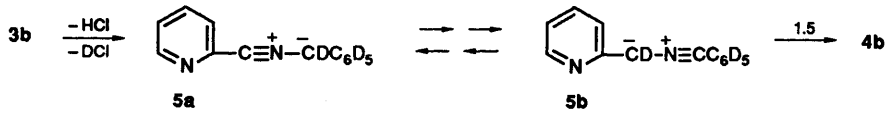
Scheme 5

nitrile ylides is not intramolecular (Scheme 5).[3] On the contrary, deuterium retention would be an argument for an intramolecular (but unlikely) hydride migration, alternatively suggested as the key step for the Wallach reaction.[4] The lack of clarity prompted us to investigate the mechanisms of the Wallach reaction and the reaction of **3** with phosphorus pentachloride; this appeared to be a prerequisite for the planned extension to the benzylamides of other *N*-heteroaromatic carboxylic acids.

Results and Discussion

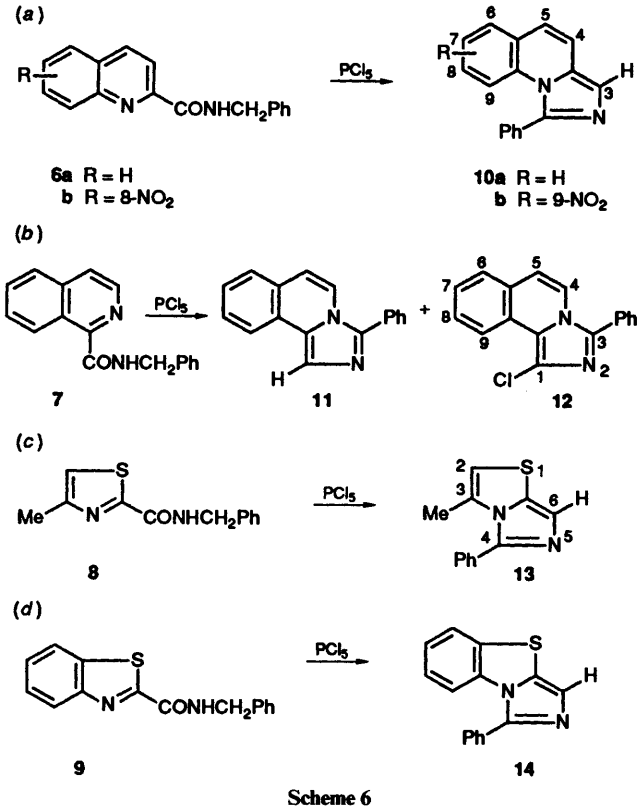
We improved the yield (up to 60%) of the conversion of **3a** into **4a** by allowing the hydrochloride of **3a** (instead of the free base) to react with an equimolar amount of phosphorus pentachloride in refluxing chloroform for 20 min. The imidazopyridine **4a** was purified as a picrate. The *N*-methylpicolinamide was found to be unreactive under these conditions.

Scheme 6 and Table 1 show our extension of this reaction to the benzylamides of other *N*-heteroaromatic carboxylic acids. The benzylamides were prepared from the corresponding esters with benzylamine in the presence of traces of sodium metal. The



5a **5b**

Scheme 4



Scheme 6

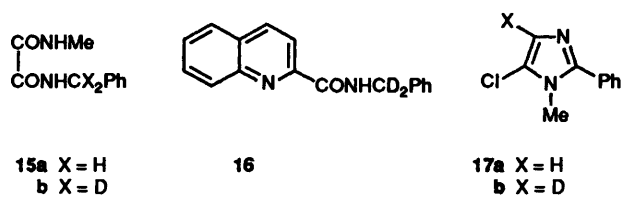
benzylamides of the 6-methyl-4-pyrimidine-, 5-phenyl-3-isoxazole- and 1-phenyl-5-methyl-3-pyrazole-carboxylic acids were shown to be totally unreactive. In contrast, the benzylamide of the 1-methylbenzimidazole-2-carboxylic acid, obtained by condensation of the *N*-methyl-*o*-phenylenediamine with alkyl benzylaminooxalate, reacted exothermally with phosphorus pentachloride giving a blue tar. The structures of the hitherto unknown products **10**–**14** were established by analytical and spectroscopic data (see Experimental section). The structural assignment of the chloro derivative **12** was confirmed by the conversion **11** ⟶ **12** with phosphorus pentachloride, in addition to spectroscopic evidence. The chlorination of the imidazole nucleus by phosphorus pentachloride is well documented.[5]

In our venture to clarify the mechanism of both the original Wallach reaction and the present extension, we prepared two new labelled substrates, **15b** and **16**, as well as the known **3b**, which was obtained by a different synthesis (see Experimental section).

The ^{1}H NMR spectrum of the 5-chloro-1-methyl-2-phenylimidazole **17a**, obtained from **15a** according to the usual procedure, showed a sharp singlet at δ 7.03 (1 H, 4-H). The same signal was likewise present in the product obtained from the labelled substrate **15b**; in this case the integral corresponded to 0.57 H (see Experimental section). This result excludes the intramolecular hydride migration during the Wallach reaction and makes the deuterium retention claimed[2] for **3b** ⟶ **4b** questionable.

We repeated the reaction of **3b** under the conditions described[2] and purified the product **4b** first by chromatography, then through its crystalline picrate. The singlet of 1-H at δ_H 7.58 in the NMR spectrum, recorded at 300 MHz, corresponded to about 0.4 H (see Experimental section).

These labelling experiments suggested the mechanistic similarity of the Wallach cyclisation of oxamides and that of the modification affording heteroimidazoles.



15a X = H
b X = D

16

17a X = H
b X = D

The third labelled substrate **16** was prepared in order to ascertain whether the removal of a benzylic hydrogen was involved in the rate-determining step. An equimolar mixture of **16** and the unlabelled substrate **6a** was submitted to the reaction with phosphorus pentachloride under strictly controlled conditions (chloroform, 55 °C). Samples were taken at different times, quenched with water, and the unchanged starting materials recovered by column chromatography and analysed by MS. It was found that the deuteriated substrate **16** is less reactive than **6a**, the difference between k_H and k_D being 1.02×10^{-3} s^{-1}. The rate constant k_H of **6a** was determined in a parallel experiment, in which the reaction progress was evaluated by ^{1}H NMR spectroscopy (see Experimental section): 1.25×10^{-3} s^{-1} was found for the first order reaction. The kinetic isotope effect, $k_H/k_D = 5.4$, demonstrates that the removal of a benzylic hydrogen is the rate-determining step of the whole process. Furthermore, the reaction of **16** with phosphorus pentachloride gave a product pointing to a 47% H–D exchange in position 3 of the imidazoquinoline ring.

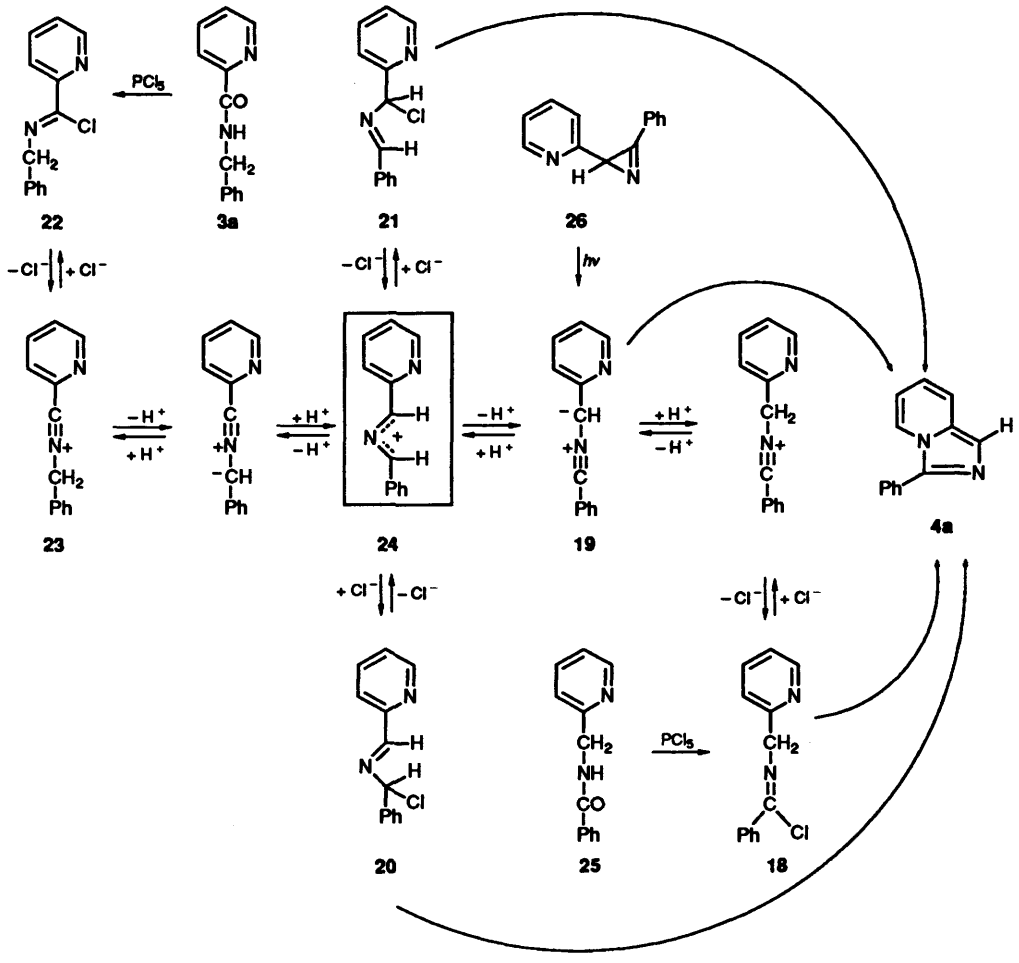
The ^{1}H NMR experiments demonstrated that the formation of the intermediate is a very fast process in comparison with the imidazole ring closure, the former being complete a few seconds after the addition of phosphorus pentachloride. The observation that benzylamides exceed alkylamides by far in reactivity is in agreement with the removal of a proton from the carbon atom bonded to the imidic nitrogen atom in the rate-determining step. We suggest that this proton loss would occur at the level of the nitrilium ion **23** resulting from the ionization of the chlorine atom of the intermediate **22** (Scheme 7); this process seems in fact easier than the hydrogen abstraction in such an acidic medium. This chloride ion loss, however, is the first step of a complex reaction sequence which, according to Huisgen,[3] establishes an equilibrium with an intermediate **18** isomeric to the one initially produced, *i.e.* **22**.

The mechanistic scheme for the formation of **4a** from **3a** fits well with the experimental observations, since prototropic equilibria are present which are responsible for the H–D exchange. Of the many species involved, only a few could, in theory, directly cyclize to **4a**, namely the intermediate **18**, the corresponding nitrile ylide **19** and the *N*-chloroalkylimines **20** and **21**.

In accordance with the proposed reaction scheme, we have confirmed the literature report[6] that *N*-(2-pyridylmethyl)-benzamide **25** gives **4a** under the usual conditions for **3a** ⟶ **4a**; **18** is now the first intermediate produced. However, we could never find benzamide **25** amongst the reaction products starting from **3a**.

We also demonstrated that the photolysis of the new 3-phenyl-2-(2-pyridyl)-2*H*-azirine **26**, prepared by a known synthetic scheme[7] (see Experimental section), furnished **4a** in 50% isolated yield. The latter result is in agreement with some reports on the cycloaddition of nitrile ylides to pyridine, quinoline and isoquinoline affording heterocondensed imidazolines.[8] Furthermore, the known formation of 2,5-diphenyloxazole by photolysis of 3-benzoyl-2-phenyl-2*H*-azirine[9] demonstrates that the linear structure generally assigned to nitrile ylides[10] is not detrimental to the intramolecular cyclization.

At present, we have no experimental evidence that the chloromethylimines **20** and **21** can cyclize to give **4a**, as **18** and **19** did. It is, however, worth noting that all four species, **18**–**21**,



Scheme 7

originate from a common precursor, the aza-allyl cation **24**, which must be considered as the key intermediate of the whole process.

The mechanistic picture does not account for the total lack of reactivity of the benzylamides of pyrimidine-, isoxazole- and pyrazole-carboxylic acids. Since the acidity of the benzylic hydrogen atoms cannot be too different in the benzylamide series, we suggest that this different behaviour might be related to the different mobility of the chlorine atom in the intermediate. The ionization of the halogen atom could be influenced by the electronic availability of the adjacent heterocyclic ring; the less electron demanding the ring the easier the halogen ionization. Pyrazole, isoxazole and pyrimidine exhibit higher electronic demand than pyridine, quinoline and nitroquinoline, isoquinoline, thiazole and benzothiazole and the corresponding substrates are unreactive. Failure to detect benzamidomethyl heterocycles which should result from equilibration of the imidoyl chlorides in the case of unreactive substrates may be evidence that this ionization does not occur.

It could well be that the ionization process discussed would become the rate-determining step in the case of the less basic, but still reactive, substrates **6b** and **9**. The failure to detect benzamidomethyl heterocycles (such as **25**) in the case of unreactive substrates may be evidence that the chloride ionization does not occur.

Experimental

M.p.s were recorded on a Buchi apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker WP 80 SY or Varian XL 300 spectrometer, with deuteriochloroform as solvent and tetramethylsilane as internal standard. Chemical shifts are given as δ and refer to the centre of the signal; J values are given in Hz. Mass spectra were performed on a VG 70-70 Eq-Hf spectrometer (DIS-EI). Irradiation was carried out with a HPK-125 W Philips, high-pressure mercury vapour lamp in a preparative photochemical reactor equipped with a Pyrex double-walled immersion well for water cooling of lamp.

Benzylamides.—General procedure. The ethyl ester (1 mmol) and benzylamine (1.2 mmol) were heated at 100 °C (1.5–4 h) in the presence of traces of sodium metal. The mixture was treated with water and exhaustively extracted with chloroform. The combined organic phases were dried (K_2CO_3) and the solvent was removed at reduced pressure; the residue was purified by chromatography, crystallization, or distillation.

N-Benzylpyridine-2-carboxamide **3a**. 3 h, 60%; m.p. 85 °C (from isopropyl ether), lit.,[11] 72–73 °C.

N-Benzylquinoline-2-carboxamide **6a**. 4 h, 84%; m.p. 121 °C (from isopropyl ether) (Found: C, 77.6; H, 5.3; N, 10.4%; M, 262. $C_{17}H_{14}N_2O$ requires C, 77.84; H, 5.38; N, 10.68%; M, 262); δ_H 4.75 (2 H, d, J 6, CH_2), 7.35 (5 H, m, C_6H_5), 7.67 (2 H, 2 dd, J 8, 6-H and 7-H), 7.94 (2 H, 2 d, J 8, 5-H and 8-H), 8.32 (2 H, 2 d, J 9, 3-H and 4-H) and 8.58 (1 H, br s, exch. D_2O, NH).

N-[α,α-$^2H_2$]Benzylquinoline-2-carboxamide **16**. [α,α-$^2H_2$]-Benzylamine, prepared by reduction of benzonitrile with lithium aluminium [$^2H_4$]hydride in tetrahydrofuran, was used; δ_H 7.35 (5 H, m, C_6H_5), 7.67 (2 H, 2 dd, J 8, 6-H and 7-H), 7.94 (2 H, 2 d, J 8, 5-H and 8-H), 8.32 (2 H, 2 d, J 9, 3-H and 4-H) and 8.58 (1 H, br s, exch. D_2O, NH).

N-Benzyl-8-nitroquinoline-2-carboxamide **6b**. 1.5 h, 84%; m.p. 136 °C (from Pr^iOH) (Found: C, 66.3; H, 4.2; N, 13.7%; M, 307. $C_{17}H_{13}N_3O_3$ requires C, 66.45; H, 4.23; N, 13.68%; *M*, 307); δ_H 4.8 (2 H, d, CH_2), 7.3 (5 H, m, C_6H_5), 7.75 (1 H, dd, 6-H), 8.1 (2 H, dd, 5-H and 7-H), 8.5 (2 H, s, 3-H and 4-H) and 8.6 (1 H, br s, NH).

N-Benzylisoquinoline-1-carboxamide **7**: 3.5 h, 73%; m.p. 85 °C (from isopropyl ether) (Found: C, 77.4; H, 5.4; N, 10.4%; M, 262. $C_{17}H_{14}N_2O$ requires C, 77.84; H, 5.38; N, 10.68%; *M*, 262); δ_H 4.71 (2 H, d, CH_2), 7.3 (5 H, m, C_6H_5), 7.74 (4 H, m, 4- to 7-H), 8.42 (1 H, d, 3-H), 8.6 (1 H, br s, exch. D_2O, NH) and 9.7 (1 H, m, 8-H).

N-Benzyl-4-methylthiazole-2-carboxamide **8**. 1.5 h, 72%; m.p. 72 °C [from water–Pr^iOH (1:1)] (Found: C, 61.9; H, 5.1; N, 12.2%; M, 232. $C_{12}H_{12}N_2OS$ requires C, 62.04; H, 5.21; N, 12.06%; *M*, 232); δ_H 2.51 (3 H, s, CH_3), 4.67 (2 H, d, CH_2), 7.12 (1 H, s, 5-H), 7.38 (5 H, s, C_6H_5), 7.5 (1 H, br s, exch. D_2O, NH).

N-Benzylbenzothiazole-2-carboxamide **9**: 3 h, 53%; m.p. 150 °C (from Et_2O) (Found: C, 67.1; H, 4.5; N, 10.3%; M, 268. $C_{15}H_{12}N_2OS$ requires C, 67.14; H, 4.51; N, 10.44%; *M*, 268).

N-Benzyl-6-methylpyrimidine-4-carboxamide. 5 h, distillation *in vacuo* (b.p. 200 °C/18 mmHg) afforded 70% yellow oil (Found: C, 68.9; H, 5.9; N, 7.2%; M, 227. C_8H_7NO requires C, 68.69; H, 5.78; N, 7.03%; *M*, 227); δ_H 2.7 (3 H, s, CH_3), 4.71 (2 H, d, CH_2), 7.37 (5 H, m, C_6H_5), 8.07 (1 H, s, 2-H), 8.40 (1 H, br s, exch. D_2O, NH) and 9.11 (1 H, s, 5-H).

N-Benzyl-5-phenylisoxazole-3-carboxamide. 2.5 h, 75%; m.p. 152 °C (from Pr^iOH) (Found: C, 73.5; H, 5.2; N, 10.0%; M, 278. $C_{17}H_{14}N_2O_2$ requires C, 73.31; H, 5.07; N, 10.13%; *M*, 278); δ_H 4.67 (2 H, d, CH_2), 6.99 (1 H, s, isoxazole H), 7.4 (9 H, m, 3, 4 and 5-H of C_6H_5, 2-H and 6-H of benzyl and NH) and 7.74 (2 H, m, 2-H and 6-H of C_6H_5).

N-Benzyl-5-methyl-1-phenylpyrazole-3-carboxamide. 4 h; chromatography on a silica gel column with ethyl acetate–toluene (7:3) and crystallization from isopropyl ether gave the title compound: m.p. 78 °C (73%) (Found: C, 74.3; H, 5.9; N, 14.4%; M, 291. $C_{18}H_{17}N_3O$ requires C, 74.19; H, 5.89; N, 14.42%; *M*, 291); δ_H 2.29 (3 H, d, CH_3), 4.62 (2 H, d, CH_2), 6.75 (1 H, q, *J* 1, pyrazole H) and 7.25 (11 H, m, 2 C_6H_5 and NH).

N-Benzyl-1-methylbenzimidazole-2-carboxamide. *N*-Methylphenylendiamine (4.0 g) and methyl *N*-benzyloxamate[4] (7.0 g) were added to a solution of sodium butanoate (3.3 g) in butanol (30 cm^3). After refluxing for 4 h the solvent was removed under reduced pressure. The residue was treated with water, washed with 10% hydrochloric acid and exhaustively extracted with chloroform. The combined organic layers were dried (K_2CO_3), evaporated and the residue crystallized from isopropyl alcohol; m.p. 130 °C (2.4 g, 28%) (Found: C, 72.8; H, 5.6; N, 15.5%; M, 265. $C_{16}H_{15}N_3O$ requires C, 72.43; H, 5.69; N, 15.83%; *M*, 265); δ_H 4.31 (3 H, s, CH_3), 4.69 (2 H, d, CH_2), 7.38 (8 H, m, ArH), 7.71 (1 H, m, 7-H) and 8.12 (1 H, br s, exch. D_2O, NH).

Cyclization.—*3-Phenylimidazo*[1,5-a]*pyridine* **4a**. A solution of **3a** (10 g) in chloroform (60 cm^3) was saturated with dry hydrogen chloride. The hydrochloride (11.6 g), collected by filtration and suspended in phosphorus oxychloride (50 cm^3), was treated with phosphorus pentachloride (9.6 g) and heated at 100 °C for 20 min. Removal of the solvent under reduced pressure left a residue which was diluted with water, neutralized with 30% ammonium hydroxide and extracted with chloroform. The residue of the organic phase was treated with picric acid (10.7 g) in ethanol. The picrate was filtered off and decomposed with 30% ammonium hydroxide and diethyl ether. The organic layer was washed with water, dried (K_2CO_3) and evaporated (5.5 g); m.p. 108 °C (from cyclohexane), lit.,[12] 107–109 °C.

1-Phenylimidazo[1,5-a]*quinoline* **10a**. A solution of **6a** (2.0 g) in chloroform (30 cm^3) was saturated with dry hydrogen chloride. The hydrochloride (1.9 g) was filtered off, suspended in phosphorus oxychloride (15 cm^3), treated with phosphorus pentachloride (1.2 g) and heated at 100 °C for 85 min. Work-up as above with 30% ammonium hydroxide and chloroform gave a residue which was chromatographed on a silica gel column with toluene–ethyl acetate (9:1). The first fractions gave **10a** (1.1 g, 70%), m.p. 96 °C (from Pr^i_2O) (Found: C, 83.3; H, 5.1; N, 11.3%; M, 244. $C_{17}H_{12}N_2$ requires C, 83.58; H, 4.95; N, 11.47%; *M*, 244); δ_H 7.02 (1 H, d, *J* 9, 4-H), 7.16 (1 H, m, 7-H), 7.31 (1 H, dd, 8-H), 7.34 (1 H, d, *J* 9, 5-H), 7.52 (5 H, m, 6-H and 9-H, 3-H, 4-H and 5-H of C_6H_5) and 7.63 [3 H, m (with s emerging at δ 7.62), 3-H, 2-H and 6-H of C_6H_5].

9-Nitro-1-phenylimidazo[1,5-a]*quinoline* **10b**. A solution of **6b** (1.1 g) in chloroform (30 cm^3) was saturated with dry hydrogen chloride. The hydrochloride (1.0 g), collected by filtration and suspended in chloroform (20 cm^3), was treated with phosphorus pentachloride (0.7 g) and refluxed for 50 h. The mixture was worked up with 30% ammonium hydroxide and chloroform as above. Chromatography on a silica gel column with chloroform gave **10b** (0.10 g, 10%); m.p. 157–159 °C; δ_H 7.01 (1 H, d, 4-H), 7.41 (6 H, m, C_6H_5 and 5-H), 7.64 (1 H, s, 3-H), 7.69 (1 H, d, 6-H), 6.78 (1 H, t, 7-H) and 7.89 (1 H, t, 8-H); *m/z* 289 (M).

3-Phenylimidazo[5,1-a]*isoquinoline* **11**. A solution of **7** (2.3 g) in chloroform (30 cm^3) was saturated with dry hydrogen chloride. The hydrochloride (2.1 g), collected by filtration and suspended in phosphorus pentachloride (20 cm^3), was treated with phosphorus pentachloride (1.4 g) and heated at 100 °C for 40 min. Removal of the solvent at reduced pressure left a residue which was worked up with ammonium hydroxide and chloroform as above. Chromatography on a silica gel column with chloroform gave 1-chloro-3-phenylimidazo[5,1-*a*]isoquinoline **12** (0.27 g, 11%) with m.p. 163 °C (from benzene) (Found: C, 73.0; H, 3.9; N, 10.2%; M, 278. $C_{17}H_{11}N_2Cl$ requires C, 73.25; H, 3.98; N, 10.05%; *M*, 278); δ_H 6.82 (1 H, d, *J* 7.6, 6-H), 7.55 (7-, 8-, 9-H and 3-, 4- and 5-H of C_6H_5), 7.76 (2 H, d, *J* 7.08, 2-H and 6-H of C_6H_5), 7.96 (1 H, d, *J* 7.6, 5-H) and 8.72 (1 H, d, *J* 8.6, 10-H).

The last fractions eluted gave **11** (0.9 g, 40%); m.p. 172 °C (from benzene) (Found: C, 83.8; H, 5.0; N, 11.0%; M, 244. $C_{17}H_{12}N_2$ requires C, 83.58; H, 4.95; N, 11.47%; *M*, 244); δ_H 6.77 (1 H, d, 5-H), 7.49 (6 H, 7, 8, 9-ArH and 3-, 4-, 5-PhH), 7.94 (1 H, s, 1-ArH), 8.02 (1 H, d, 6-ArH) and 8.05 (1 H, d, 10-ArH).

1-Chloro-3-phenylimidazo[5,1-a]*isoquinoline* **12**. Refluxing a solution of **11** (0.20 g) and phosphorus pentachloride (0.18 g) in phosphorus oxychloride (4 cm^3) for 1 h gave **12** after work-up and crystallization from benzene (0.16 g, 70%). Analytical and spectral data were identical with those reported above for the reaction of **7** with phosphorus pentachloride.

3-Methylimidazo[5,1-b]*thiazole* **13**. A suspension of **8** (0.9 g) and phosphorus pentachloride (0.8 g) in phosphorus oxychloride (15 cm^3) was heated at 100 °C for 2 h. Work-up gave a residue which was chromatographed on a silica gel column with chloroform. The last fractions eluted afforded **13** (0.33 g, 40%); m.p. 103 °C (Found: C, 67.1; H, 4.7; N, 12.9%; M, 214. $C_{12}H_{10}N_2S$ requires C, 67.27; H, 4.70; N, 13.07%; *M*, 214); δ_H 2.03 (3 H, d, CH_3), 6.37 (1 H, q, 2-H), 7.1 (1 H, s, 7-H) and 7.43 (5 H, m, C_6H_5).

1-Phenylimidazo[5,1-b]*benzothiazole* **14**. A suspension of **9** (2.4 g) and phosphorus pentachloride (1.8 g) in phosphorus oxychloride (5 cm^3) was heated at 100 °C for 4 h; work-up as described for **13**. The last fractions eluted gave an oil which was distilled (b.p. 200 °C/0.1 mmHg) (0.45 g, 20%), m.p. 68 °C (Found: C, 71.6; H, 4.05; N, 11.2%; M, 250. $C_{15}H_{10}N_2S$ requires C, 71.97; H, 4.03; N, 11.19%; *M*, 250); δ_H 7.5 [10 H, m (with s emerging at δ 7.24 corresponding to imidazole H)].

N-[α,α^2H_2]*Benzyl-N'-methyloxamide* **15b**. A solution of *N*-[α,α^2H_2]benzyl-*N'*-ethyloxamate[4] (5.0 g) in ethanol (20 cm^3)

Table 2

	m/z (relative abundance)	
t/s	106	108
0	100	97.4
60	97.5	100
180	87.1	100
300	75.6	100
600	60.0	100

Table 3

t/s	*a*	*b*	c/c^0
60	15.5	1.1	0.93
120	14.5	2.0	0.88
180	8.5	2.12	0.80
240	9.5	3.0	0.76
600	5.0	5.25	0.49

was added to 35% aq. methylamine (170 cm^3); colourless solid, m.p. 184 °C (3.8 g, 82%); δ 2.91 (3 H, d, CH_3), 7.33 (5 H, s, C_6H_5) and 7.85 (2 H, 2 br s, exch. D_2O, 2 NH). The signal at δ 4.50 assigned to PhCH_2 of **15a** is totally absent.

5-Chloro-1-methyl-2-phenylimidazole **17a** *and* [4-^{2}H]-*5-chloro-1-methyl-2-phenylimidazole* **17b**. A suspension of **15b** (2.5 g) and phosphorus pentachloride (5.4 g) in chlorobenzene (25 cm^3) was heated at 100 °C for 3 h. Work-up as described above for **13** gave a mixture 1 : 1.33 of **17a** and **17b** (1.5 g, 66%) which was crystallized from hexane; δ_H 3.65 (3 H, s, CH_3), 7.03 (0.57 H, s, imidazole H) and 7.05 (5 H, m, C_6H_5).

Mechanistic Contributions.—3-Phenyl-2-(2-pyridyl)-2H-azirine **26**. Triethylamine (1 cm^3) and tosyl chloride (1.3 g) were added to 1-phenyl-2-(2-pyridyl)ethanal oxime[12] (0.7 g) in dichloromethane (10 cm^3) and the suspension was stirred for 1 day. The reaction mixture was worked up with water and dichloromethane. The residue was chromatographed on a silica gel column with diethyl ether–light petroleum (1 : 1), the last fractions were crystallized from isopropyl ether to give the title compound with m.p. 65 °C (0.40 g, 31%) (Found: C, 80.05; H, 5.3; N, 14.3%; M, 194. $C_{13}H_{10}N_2$ requires C, 80.38; H, 5.19; N, 14.42%; *M*, 194); δ_H 3.45 (1 H, s, azirine H), 7.06 (3 H, m, 3-, 4-, 5-pyridine H), 7.55 (3 H, m, 3-, 4-, 5-phenyl H), 7.83 (2 H, m, 2-, 6-phenyl H) and 8.48 (1 H, m, 6-pyridine H).

Photocyclization of azirine **26**. A solution of **26** (0.4 g) in acetone (5 cm^3) was placed in the photochemical reactor and N_2 bubbled through the solution for 5 min before irradiation. After irradiation for 2 h, the solution was evaporated and **4a** was purified as a picrate (0.2 g, 50%). Analytical and spectral data were identical with those reported for the reaction of **3a** with phosphorus pentachloride.

Kinetic Experiments.—Isotope effect. Evaluation of $k_H - k_D$ *for substrates* **6a** *and* **16**. An intimate mixture of **6a** (0.7 g) and **16** (0.7 g) was added in a single portion to a stirred suspension of phosphorus pentachloride (0.6 g) in dry chloroform at 25 °C. The stirred mixture was quickly placed in a thermostatted bath at 55 °C. Samples (5 cm^3) were taken after 1, 3, 5 and 10 min and immediately quenched with ice-cold water (5 cm^3). Each mixture was washed with 5% ammonium hydroxide and the separated dried organic layer was chromatographed on a silica gel column with chloroform. The starting material was recovered and submitted to MS analysis. The relative concentrations of **6a** and **16** at different reaction times were given by the ratio of the intensities of the peaks *m/z* 106 and 108, corresponding to $C_6H_5CH_2NH$ and $C_6H_5CD_2NH$ fragments, which are the base peaks. Their relative abundance is given at different reaction times in Table 2.

An identical experiment was performed on **6a** in order to evaluate the rate constant of the reaction with phosphorus pentachloride: samples were taken at 1, 2, 3, 4 and 10 min and immediately quenched in ice-cold water. Work-up gave the crude reaction product, consisting of different amounts of **6a** and **10a**, which was submitted to ^{1}H NMR spectroscopy. The progress of the reaction was evaluated from the integrals of the signal at δ 4.75 (d, PhCH_2 of **6a**) related to the unchanged starting material, and of the multiplet of the aromatic protons, taken as a whole (Table 3). The equation

$$c/c^0 = a/a + b$$

was employed where

c = concentration of **6a** at different reaction times
c^0 = concentration of **6a** at $t = 0$
a = integral value of 1 H of unchanged **6a** ($\frac{1}{2}$ of the integral value of the PhCH_2 of **6a**)
b = integral value of 1 H of **10a** [namely $\frac{1}{12}$ (total integral of aromatic H − a × 11)]
11 = number of aromatic H in **6a**
12 = number of aromatic H in **10a**

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