The Reaction between Cyanide Ion and Nitrones; a Novel Imidazole Synthesis

By **Eric Cawkill**, Research Department, The Boots Company Ltd., Nottingham NG2 3AA
Nigel G. Clark,* Wye College (University of London), near Ashford, Kent TN25 5AH

By contrast with the *CN*-diphenylnitrones, cold aqueous ethanolic potassium cyanide converts *N*-methyl-*C*-phenylnitrone into 1-methyl-4,5-diphenylimidazole. The scope of this reaction has been investigated, and shown to proceed *via* intermediate cyano-imines, some of which have been synthesised by alternative routes.

DURING a programme of synthesis aimed at assessing the biological activity of nitrones and their derivatives, a large number of *CN*-diphenylnitrones (1) were prepared by condensing substituted benzaldehydes with various *N*-phenylhydroxylamines.[1] The early work employed the pure, isolated *N*-phenylhydroxylamines, but it was later found that comparable yields of nitrones were attainable by reducing the corresponding nitrobenzenes with zinc dust and aqueous ammonium chloride in the presence of the appropriate benzaldehyde. The *N*-phenylhydroxylamine produced *in situ* was immediately converted by the benzaldehyde to the desired nitrone, thereby avoiding the somewhat unsatisfactory isolation of the *N*-phenylhydroxylamine.[2] This technique was equally applicable with heterocyclic aldehydes, but proved less satisfactory with nitroalkanes. The *CN*-diarylnitrones were found to be sensitive to light, whereas the *N*-alkyl-*C*-arylnitrones did not exhibit this property. All the nitrones possessed i.r. spectra with characteristic absorption bands in the 1 200 and 1 600 cm^{-1} regions;[3] however, these are not regarded as especially useful for diagnostic purposes.

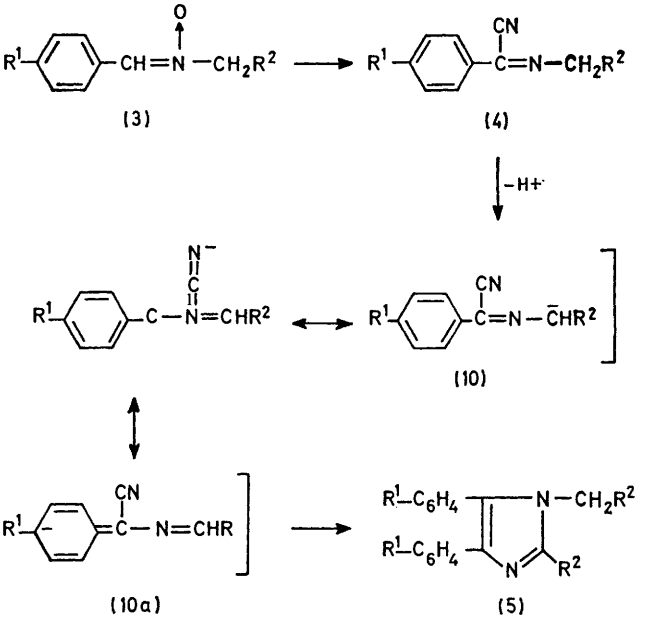
RESULTS AND DISCUSSION

The reaction between potassium cyanide and *CN*-diphenylnitrones in aqueous ethanol has been shown[4] to yield α-cyanobenzylideneanilines.

$$R^1{\cdot}C_6H_4{\cdot}CH{:}\overset{\overset{O}{\uparrow}}{N}{\cdot}C_6H_4{\cdot}R^2 \xrightarrow[-OH^-]{CN^-} R^1{\cdot}C_6H_4{\cdot}C(CN){:}N{\cdot}C_6H_4{\cdot}R^2$$
(1) (2)

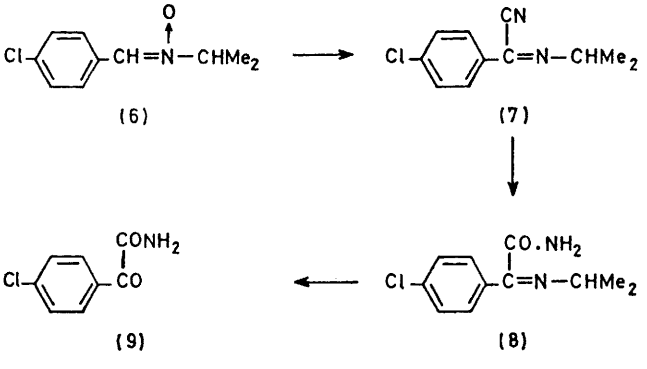
The present work confirms and extends these findings. It is worth noting that the i.r. absorption band at *ca.* 2 250 cm^{-1}, characteristic of the cyano-group, is very weak in all these compounds, in many cases being hardly distinguishable from the background absorption. This appears to be due to the influence of the adjacent phenyl group, since a more normal absorption band was exhibited by the t-butyl compound, the only *C*-alkyl compound investigated.

On allowing equimolecular proportions of potassium cyanide and *N*-(benzylidene)methylamine *N*-oxide (3) to stand overnight in aqueous ethanolic solution, a colourless crystalline solid, $C_{16}H_{14}N_2$ (m.p. 156—157 °C) was obtained (*ca.* 70% yield). It was not possible to identify any functional groups from the i.r. absorption spectrum and, in view of the preceding comments, the presence or absence of a cyano-group could not be confirmed. However, the n.m.r. spectrum (Table)



SCHEME 1

showed signals attributable to ten aromatic protons (two phenyl groups), three aliphatic protons (one methyl group), and one additional aromatic proton. These findings can be interpreted by formulating the compound as 1-methyl-4,5-diphenylimidazole (5; $R^1 = R^2 = H$) (lit.,[5] m.p. 158 °C). In a similar manner, other *N*-methyl-*C*-phenylnitrones were converted in yields of



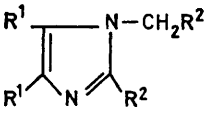
40—90% into the corresponding imidazoles; these are listed in the Table.

On following the course of the reaction by means of t.l.c., it became clear that the initial product of the reaction was formed quite rapidly and subsequently converted to the imidazole. By employing an excess of potassium cyanide and a reaction time of 15—60 min, it was possible to isolate these intermediates in yields of 40—70%. They proved to be *N*-(α-*cyanobenzylidene*)-*methylamines* (4), analogous to the compounds isolated from the *CN*-diphenylnitrones. The role of the *N*-(α-cyanobenzylidene)methylamines as true intermediates in imidazole formation was demonstrated by their conversion by potassium cyanide, and especially by potassium hydroxide, into the imidazoles in 40—90% yield. As a consequence, it has been possible, using an alternative method for synthesising the *N*-(α-cyanobenzylidene)alkylamines (see later), to prepare imidazoles without recourse to the appropriate nitrone.

Inspection of the structure of these imidazoles suggested that they were probably formed from two molecules of an *N*-(α-cyanobenzylidene)methylamine with elimination of two cyano-groups (Scheme 1). The transitory nature of cyanide ion addition to nitrone in the production of imidazoles was confirmed by the following further observations. (1) Catalytic amounts of potassium cyanide were sufficient to effect imidazole synthesis, although reaction required several days to achieve good yields. (2) Using potassium cyanide labelled with ^{14}C, it was found that none of the labelled carbon was incorporated into the imidazole structure. (3) Using *N*-(α-cyanobenzylidene)methylamine labelled with ^{14}C in the cyano-group, the resulting imidazole contained no labelled carbon.

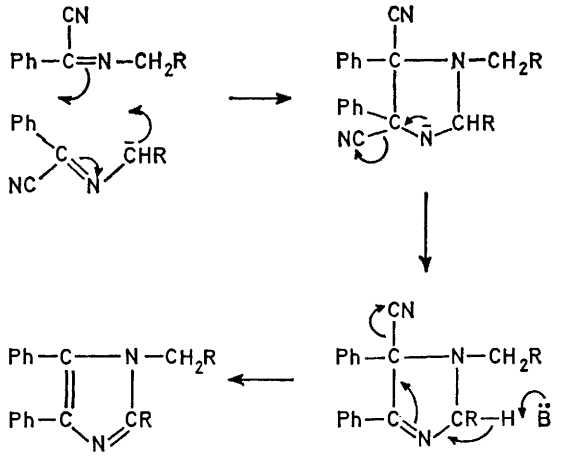
It is clear from Scheme 1 that, when the *N*-alkyl substituent in either the parent nitrone (3) or the intermediate *N*-(α-cyanobenzylidene)alkylamine (4) is ethyl or substituted ethyl (*i.e.* R = Me or CH_2X), a further *C*-substituent (R) is to be expected on the nucleus of the resulting imidazole (5). The product obtained by treating N-(*4-chlorobenzylidene*)*ethylamine* N-*oxide* with potassium cyanide was indeed found to contain the expected methyl and ethyl substituents and was consequently formulated as *4-5-bis-(4-chlorophenyl)-1-ethyl-2-methylimidazole* (5; R^1 = 4-Cl, R^2 = Me). A similar reaction with N-(*benzylidene*)*phenethylamine* N-*oxide* also yielded a product, *2-benzyl-1-phenethyl-4,5-diphenylimidazole* (5; R^1 = H, R^2 = $C_6H_5CH_2$) compatible with the proposals of Scheme 1. It is equally clear why the reaction between cyanide ion and *CN*-diphenylnitrones proceeds no further than the α-cyanobenzylideneaniline stage. In a similar manner, N-(*4-chlorobenzylidene*)*isopropylamine* N-*oxide* (6) and the related *4-chloro-α-chloro-α-cyanobenzylideneisopropylamine* (7) both contain a secondary carbon atom adjacent to the nitrogen atom, and are therefore incapable of participating in imidazole ring formation. On treating nitrone (6) with aqueous ethanolic potassium cyanide, no imidazole formation was detected (t.l.c.) and the isolated reaction product proved to be *α-(4-chlorophenyl)-α-(isopropylimino)acetamide* (8), the usual cyano-group having undergone hydration. On warming this compound with aqueous acetic acid, it was converted into (*4-chlorophenyl*)-*glyoxylamide* (9). It was not found possible to investigate

Physical and spectroscopic data for the imidazoles



R¹	R²	M.p. (B.p.) (°C)	Solvent [a]	Crystalline form [b]	Found (%) (Calc.) C	H	N	Cl	Formula	^{1}H N.m.r. (τ) [c] NCH_2R^2 protons	Imidazole R^2 proton(s)	Phenyl protons	Heterocyclic protons	Phenyl ring substituents
C_6H_5	H	156—157 [d]	A	CP	82.15 (82.0)	5.7 (6.0)	11.9 (12.0)		$C_{16}H_{14}N_2$	6.55(s)	(2.37) [e]	2.3—2.8		
4-Cl·C_6H_4	H	172—173	B	CP	63.4 (63.4)	4.4 (4.0)	9.3 (9.2)	23.9 (23.4)	$C_{16}H_{12}Cl_2N_2$	6.52(s)	2.43(s)	2.45—2.9		
3,4-(CH_2O_2)C_6H_3	H	162—163	B	CP	66.7 (67.1)	4.4 (4.35)	8.4 (8.7)		$C_{18}H_{14}N_2O_4$	6.55(s)	2.5(s)	2.85—3.35		3.95(s), 4.1(s)
3,4-Cl_2·C_6H_3	H	144—145	B	CP	52.2 (56.1)	3.0 (2.7)	7.25 (7.5)		$C_{16}H_{10}Cl_4N_2$	6.45(s)	2.38	2.2—2.95		
4-Me·C_6H_4	H	138—139	A	CN	82.8 (82.45)	7.0 (6.9)	10.6 (10.7)		$C_{18}H_{18}N_2$	6.52(s)	2.43(s)	2.5—3.05		7.56(s), 7.71(s)
3-MeO·C_6H_4	H	94—95 (197—198/ 0.1 mmHg)	A	CP	73.4 (73.5)	6.2 (6.1)	9.6 (9.5)		$C_{18}H_{18}N_2O_2$	6.48(s)	2.45(s)	2.6—3.4		6.17(s), 6.29(s)
4-Pyridyl	H	196—197	C	CP	71.15 (71.2)	5.4 (5.1)	23.8 (23.7)		$C_{14}H_{12}N_4$	6.41(s)	2.1(s)		1.2, 1.56, 2.6	
2-Thienyl	H	134—135	A	BP				S 26.1 (26.0)	$C_{12}H_{10}N_2S_2$	6.51(s)	(2.46)		2.38—2.55, 2.7—3.2	
2-C_4H_3O	H	74—76 (154—156/ 0.7 mmHg)	A	BP	67.2 (67.3)	4.9 (4.7)	13.2 (13.1)		$C_{12}H_{10}N_2O_2$	6.36(s)	(2.5)		2.42—2.65, 3.25—3.65	
2-$C_{10}H_7$	H	147—148	D	CP	86.0 (86.2)	5.6 (5.4)	7.8 (8.4)		$C_{24}H_{18}N_2$	6.58(s)	(1.82)	2.05—2.8		
4-Cl·C_6H_4	Me	202—203	B	CP	65.5 (65.6)	4.8 (4.9)	8.45 (8.5)	21.1 (21.5)	$C_{18}H_{16}Cl_2N_2$	6.17(q), 8.8(t)	7.45	2.4—2.9		
4-Cl·C_6H_4 [f]	Et	139—140	B	CP	66.7 (66.85)	5.4 (5.6)	7.7 (7.8)	20.0 (19.8)	$C_{20}H_{20}Cl_2N_2$	6.32(t), 8.5, 9.24(t)	7.232, 8.57(t)	2.5—3.0		
Ph	$PhCH_2$	141—142	B	CFN	86.9 (87.0)	6.45 (6.3)	6.55 (6.8)		$C_{30}H_{26}N_2$	6.15(t), 7.65(t)	5.9	2.35—2.9		

[a] Solvents: (A) toluene–light petroleum (b.p. 60—80 °C); (B) ethanol; (C) toluene; (D) light petroleum (b.p. 80—100 °C). [b] Crystalline form: (CP) colourless prisms; (CN) colourless needles; (BP) buff prisms; (CFN) colourless felted needles. [c] In $CDCl_3$ at 60 MHz; integrated relative intensities of the signals were in accord with the assignments; all signals were multiplets unless indicated otherwise; s = singlet, t = triplet, q = quartet. [d] Lit., m.p. 158 °C (ref. 5). [e] Values in parentheses indicate signals not allocated unequivocally due to proximity of phenyl (or heterocyclic) proton signals. [f] N.m.r. spectrum in $(CD_3)_2SO$.



SCHEME 2

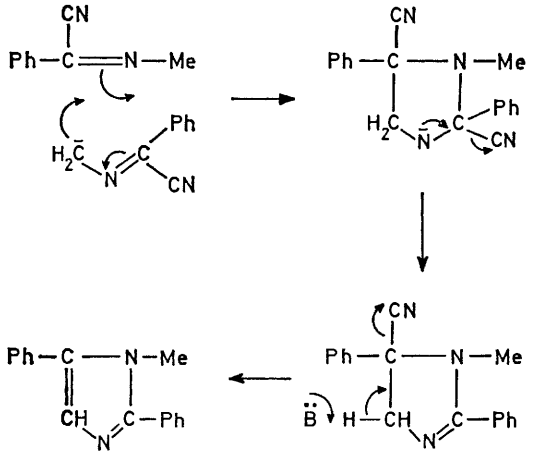
the *N*-t-butyl analogue as *N*-(4-chlorobenzylidene)-t-butylamine *N*-oxide did not react with aqueous ethanolic potassium cyanide, and attempts to prepare *N*-(4-chloro-α-cyanobenzylidene)-t-butylamine by the alternative method (see below) were unsuccessful.

The alternative method of preparing α-cyanobenzylidenealkylamines (4) started with *N*-alkylbenzamides, which were converted by cold thionyl chloride into benzimidoyl chlorides in 80—95% yield.[6] (4-Chloro-*N*-t-butylbenzamide, however, proved to be the exception, as it gave only 4-chlorobenzonitrile by von Braun degradation.[6]) On stirring the benzimidoyl chlorides in light petroleum solution with aqueous potassium cyanide,[7a] they were converted in 20—60% yield into the desired α-cyanobenzylidenealkylamines. Not surprisingly, however, much of the benzimidoyl chloride was hydrolysed back to the *N*-alkylbenzamide. In order to avoid this, aqueous potassium cyanide was replaced either by the solid salt, or by anhydrous solutions in dimethylformamide (dielectric constant, $\varepsilon = 26.6$) or tetrahydrofuran ($\varepsilon = 7.6$), but in all cases a negligible reaction occurred. However, on using the potassium cyanide dissolved in formamide ($\varepsilon = 109$), the α-cyanobenzylidenealkylamines were isolated in yields of 70—90%. By contrast with earlier reports,[7] these compounds exhibited normal stability, remaining unchanged on the bench for many months.

Mechanistically it seems reasonable to postulate the participation of the carbanion (10), on the grounds that the reaction is generally base-catalysed and that the α-C atom of the *N*-alkyl group becomes part of the heterocyclic ring. Formation of this carbanion will be assisted by delocalisation through the cyano and phenyl groups. It is interesting that no imidazole formation was detected when the phenyl group carried a 4-methoxy-substituent, the powerful $+E$ effect of the latter prohibiting any useful mesomeric contribution from the phenyl group (10a). When the methoxy-group was in the *meta* position, where it cannot prevent the mesomeric contribution from the phenyl group, imidazole formation proceeded normally.

Initial cyclisation (Scheme 2) may be ascribed to a Woodward–Hoffmann intermolecular [4 + 2] cycloaddition reaction involving one carbanion and one uncharged species, followed by elimination of cyanide ion and hydrogen cyanide. The driving force for this sequence derives from the high resonance stabilisation (22 kcal mol^{-1}) on completion of the aromatic imidazole ring.

A similar cyclisation sequence (Scheme 3), in which the carbanion presents itself for cyclisation ' the other way round ', could lead to the isomeric 1-methyl-2,5-diphenylimidazole. However, this compound [7b] has a m.p. 197.5—198.5° and was not detected (t.l.c.) in any of the cyclisation experiments carried out with *N*-(benzylidene)methylamine *N*-oxide or (α-cyanobenzylidene)-methylamine.



SCHEME 3

EXPERIMENTAL

Physical and analytical data for all the new nitrones, benzylideneanilines, and imidoyl chlorides prepared are deposited as Supplementary Publication No. SUP 22616 (14 pp.).*

Preparation of Nitrones.—Method A, using pure N-(aryl or alkyl)hydroxylamines. See Tables 1, 2, and 3 of SUP 22616. A typical procedure was as follows. A vigorously stirred mixture of 3,4-dichloronitrobenzene (260 g), ammonium chloride (170 g), ethanol (250 ml), and water (250 ml) was maintained below 60 °C whilst zinc dust (200 g) was added in small portions during 30 min. The reaction was stirred for 15 min after addition was complete, filtered while still warm, and the filter cake was washed with hot ethanol (4 × 100 ml.). The combined filtrate and washings were cooled to 0 °C, and the resulting solid was collected, dried, and taken up in ether. On evaporating the ether, there remained a pale yellow crystalline solid (114 g), m.p. 65—70 °C. Recrystallised from benzene–light petroleum (b.p. 60—80 °C), the pure *N*-(3,4-dichlorophenyl)hydroxylamine had m.p. 77.5—78 °C [lit.,[8] m.p. 75 °C (decomp.); lit.,[9] 135—137 °C] (Found: Cl, 39.9. Calc. for $C_6H_5Cl_2NO$: Cl, 39.9%).

A solution of *N*-(3,4-dichlorophenyl)hydroxylamine (17.8 g) and piperonal (15.0 g) in ethanol (35 ml) was allowed to

* For details see Notice to Authors No. 7, *J.C.S. Perkin I*, 1979, Index issue.

stand at room temperature in a dark cupboard. The following day, the solid product was collected, sucked free from solvent, and twice recrystallised from toluene; yield 9.9 g, m.p. 172—173 °C. The pure N-(3,4-*methylenedioxybenzylidene*)-3,4-*dichloroaniline* N-*oxide* formed light-sensitive yellow prisms with the same m.p. (Found: Cl, 22.8. $C_{14}H_9Cl_2NO_3$ requires Cl, 22.9%).

Method B, using N-(*aryl or alkyl*)*hydroxylamines prepared* in situ. (See Tables 1, 2, and 3 of SUP 22616). A typical procedure was as follows. A vigorously stirred mixture of veratraldehyde (40.5 g), 4-chloronitrobenzene (42.7 g), ammonium chloride (16.7 g), ethanol (150 ml), and water (150 ml) was maintained below 35 °C while zinc dust (42 g) was added in small portions during 30 min. After gentle stirring overnight at room temperature, the mixture was extracted with methylene chloride, and the extract was dried, evaporated, and the residual solid recrystallised from toluene–light petroleum (b.p. 80—100 °C); yield 53.2 g, m.p. 111—113 °C. The pure N-(3,4-*dimethoxybenzylidene*)-4-*chloroaniline* N-*oxide* was obtained as colourless prisms, m.p. 113—114 °C (Found: Cl, 12.3. $C_{15}H_{14}ClNO_3$ requires Cl, 12.2%).

Method C, using anti-*benzaldoxime*.[10] Methanolic sodium methoxide solution (167 ml, 4.35M) was stirred into a solution of *anti*-benzaldoxime hydrochloride [11] (56.9 g) in anhydrous methanol (500 ml), followed by 4-chlorobenzyl chloride (46.5 ml) added in one portion. The reaction mixture was stirred for 4 h, refluxed for 1 h, and then stirred into ice–water. The resulting sticky solid was collected, washed with water, sucked free from adhering aqueous liquors, and crystallised from toluene–light petroleum (b.p. 80—100 °C); yield, 6.3 g, m.p. 122—124 °C. Further recrystallisation gave the pure N-(*benzylidene*)-4-*chlorobenzylamine* N-*oxide* as colourless needles with the same m.p. (Found: Cl, 14.2. $C_{14}H_{12}ClNO$ requires Cl, 14.45%).

In a similar manner, methanolic sodium methoxide solution (375 ml, 4.35M), *anti*-benzaldoxime hydrochloride (128 g), anhydrous methanol (1 l), and phenethyl bromide (112 ml) gave an oily crude product, which was isolated with ether and distilled. Pure N-(*benzylidene*)*phenethylamine* N-*oxide* was obtained as a colourless oil, b.p. 110—112 °C at 0.01 mmHg (20.2 g) (Found: C, 80.6; H, 6.7; N, 6.45. $C_{15}H_{15}NO$ requires C, 80.4; H, 6.7; N, 6.25%).

Reaction of Potassium Cyanide with CN-*Diphenylnitrones*. —(See Table 4 of SUP 22616). A typical procedure was as follows. A stirred solution of *N*-(4-methylbenzylidene)-4-methylaniline *N*-oxide (17.0 g) in methanol (200 ml) was maintained at 0—5 °C while a solution of potassium cyanide (5.0 g) in water (10 ml) was added during 15 min; a yellow solid began to separate after a few minutes. After stirring the reactants with cooling for a further 2 h, the solid was collected, washed with water, dried, and recrystallised from toluene–light petroleum (b.p. 80—100 °C). The *N*-(α-*cyano*-4-*methylbenzylidene*)-4-*methylaniline* (10.5 g) had m.p. 126—127 °C. The pure material formed bright yellow needles with the same m.p. (Found: C, 82.3; H, 6.2; N, 11.9. $C_{16}H_{14}N_2$ requires C, 82.1; H, 6.0; N, 12.0%).

Reaction of Potassium Cyanide with N-*Alkyl*-C-*arylnitrones* (*see Table 5 of SUP* 22616).—*Method A* (*long reaction time*). A typical procedure was as follows: a solution of *N*-(4-chlorobenzylidene)methylamine *N*-oxide (5.1 g) in a mixture of ethanol (40 ml) and water (10 ml) was shaken with potassium cyanide (2.1 g) until it had dissolved, and the clear solution allowed to stand overnight at room temperature. The resulting crystalline solid was collected, washed with water, and dried at 100 °C; yield 3.3 g, m.p. 172—173 °C. The pure 4,5-*bis*-4-*chlorophenyl*-1-*methylimidazole*, on recrystallisation from ethanol, formed colourless prisms with the same m.p. (Found: C, 63.4; H, 4.4; N, 9.3; Cl, 23.9. $C_{16}H_{12}Cl_2N_2$ requires C, 63.4; H, 4.0; N, 9.2; Cl, 23.4%).

Method B (*short reaction time with an excess of cyanide*). (See Table 7 of SUP 22616). A typical procedure was as follows. A solution of *N*-(4-chlorobenzylidene)methylamine *N*-oxide (15.0 g) in ethanol (200 ml) was cooled to 0 °C, treated all at once with a solution of potassium cyanide (28.5 g, five-fold molar excess) in water (50 ml), maintained below 5 °C for 15 min, and then quenched in ice–water. The resulting solid was collected, washed with ice–water, and dried *in vacuo* (P_2O_5); yield, 11.2 g., m.p. 50—52 °C. The pure N-(4-*chloro*-α-*cyanobenzylidene*)*methylamine*, recrystallised from aqueous methanol, formed colourless plates, m.p. 52—53 °C (Found: C, 60.6; H, 4.2; N, 15.4; Cl, 20.0. $C_9H_7ClN_2$ requires C, 60.5; H, 3.9; N, 15.7; Cl, 19.9%.

4-*Chloro*-N-*propylbenzamide*.—4-Chlorobenzoyl chloride (30 g) was slowly added to a stirred mixture of propylamine (14.7 ml) and aqueous sodium hydroxide solution (41 ml, 5N) cooled in ice–water. After stirring for an additional 30 min, the resulting solid was collected, washed with water, and recrystallised from aqueous methanol; yield 24.0 g, m.p. 98—99 °C. The pure material (m.p. 99—100 °C) separated from the same solvent in colourless plates (Found: Cl, 17.9. $C_{10}H_{12}ClNO$ requires Cl, 18.0%).

N-*Methyl*-2-*naphthamide*.—A mixture of 2-naphthoic acid (53 g), thionyl chloride (50 ml), and pyridine (3 drops) was heated cautiously under reflux for 30 min on a steam-bath, and the excess of thionyl chloride then removed by distillation. The residual warm oil was added slowly to a stirred, cooled mixture of aqueous methylamine solution (40 ml, 33% w/v) and aqueous sodium hydroxide solution (200 ml, 2.5N), and stirring continued until the odour of acid chloride had disappeared. The resulting solid was collected, washed with water, and crystallised from aqueous ethanol; yield 37.5 g, m.p. 109—110 °C. The pure material formed colourless plates, m.p. 110—111 °C (Found: C, 78.0; H, 5.9; N, 7.4. $C_{12}H_{11}NO$ requires C, 77.8; H, 5.9; N, 7.6%).

Preparation of Imidoyl Chlorides.—(See Table 8 of SUP 22616). A typical procedure was as follows. A mixture of 4-chloro-*N*-isopropylbenzamide (43.0 g) and thionyl chloride (80 ml) was allowed to stand overnight at room temperature ($CaCl_2$ protection); the initially-suspended material dissolved in a mildly exothermic reaction. The excess of thionyl chloride was removed below 70 °C, and the residual oil purified by fractional distillation *in vacuo*. 4-*Chloro*-N-*isopropylbenzimidoyl chloride* was obtained as a colourless oil, b.p. 70—72 °C at 0.05 mmHg (45.8 g) (Found: Cl, 33.3. $C_{10}H_{11}Cl_2N$ requires Cl, 32.9%).

Action of Thionyl Chloride on 4-*Chloro*-N-*t-butylbenzamide*.—A mixture of the benzamide [12] (17.5 g) and thionyl chloride (50 ml) was allowed to stand overnight at room temperature. On removing the excess of thionyl chloride from the resulting clear solution, keeping the temperature below 70 °C, there remained a solid, which was purified by sublimation at *ca.* 100 °C and 0.05 mmHg; yield 10.2 g, m.p. 92—93 °C. Recrystallisation from ethanol gave colourless prisms, m.p. 93—94 °C, either alone or admixed with authentic 4-chlorobenzonitrile (lit.,[13] m.p. 94—96 °C) (Found: Cl, 25.7. Calc. for C_7HClN: Cl, 25.8%).

Preparation of Cyanoimines.—A typical procedure was as follows. A solution of potassium cyanide (22.5 g, 50% molar excess) in formamide (50 ml) was covered with a layer of light petroleum (b.p. 60—80 °C) (200 ml), and the mixture stirred gently while benzimidoyl chloride (35.0 g) was added during 30 min; room temperature was maintained during the early stages of the reaction by ice–water cooling. After stirring overnight, the upper layer was separated, the formamide layer washed with further light petroleum, and the combined petroleum extracts evaporated. The residual colourless crystals (26.9 g) were found to be pure (t.l.c.), m.p. 38—39 °C; *N*-(α-cyanobenzylidene)methylamine is reported [7a] to have m.p. 37 °C.

Preparation of Imidazoles from Cyanoimines.—(See Table 5 of SUP 22616). A typical procedure was as follows. A solution of α-cyanobenzylidenemethylamine (5.0 g) in aqueous methanol (50 ml, of 50% v/v) was treated with solid potassium hydroxide (1 pellet), the latter dissolved by gently shaking, and the resulting homogeneous solution allowed to stand for 2 h. During this time a crystalline solid separated which was collected, washed with a little water, and dried *in vacuo* (P_2O_5); yield, 3.1 g, m.p. 155—157 °C either alone or admixed with 1-methyl-4,5-diphenylimidazole (m.p. 156—157 °C) obtained *via* the nitrone. A further quantity (0.2 g) of the imidazole was isolated by evaporating the reaction liquors to small volume.

Reaction of Potassium Cyanide with N-(4-*Chlorobenzylidene*)*isopropylamine* N-*Oxide* (6).—A solution of the nitrone (6) (10 g) in ethanol (40 ml) was cooled in an ice-bath, treated all at once with an aqueous solution of potassium cyanide (3.1 g in 10 ml) and the clear solution kept at room temperature for 3 d. On pouring into cold water, a solid precipitated, which was collected, washed with water, and dried *in vacuo* (P_2O_5); yield 8.4 g, m.p. 112—128 °C. Extraction with boiling light petroleum (b.p. 80—100 °C) (50 ml) gave an insoluble residue (4.9 g), m.p. 130—133 °C, which yielded pure α-4-*chlorophenyl*-α-*isopropylimino*-*acetamide* (8) (0.9 g) after three recrystallisations from toluene–light petroleum (b.p. 80—100 °C); colourless prisms, m.p. 137—138 °C (Found: C, 58.6; H, 5.9; N, 12.7; Cl, 15.7. $C_{11}H_{13}ClN_2O$ requires C, 58.8; H, 5.8; N, 12.5; Cl, 15.8%); τ($CDCl_3$) 2.25(d) and 2.67(d) (aromatic H), 2.9 and 3.3(br, NH), 6.15 (CH), and 8.8(d, Me).

Repetition of the above experiment gave a crude yield, after extraction with light petroleum, of 3.1 g, m.p. 130—132 °C. Recrystallisation from aqueous acetic acid converted this material into a pale yellow solid (2.3 g), m.p. 125—126 °C. Further crystallisation from the same solvent gave pure 4-*chlorophenylglyoxylamide* (9) as colourless prisms with the same m.p. (Found: C, 52.6; H, 3.6; N, 7.8; Cl, 19.0. $C_8H_6ClNO_2$ requires C, 52.3; H, 3.3; N, 7.6; Cl, 19.3%); τ($CDCl_3$) 1.3(vbr, NH_2?), 1.72(d) and 2.47(d) (aromatic H).

We gratefully acknowledge the assistance of our colleague, Mr. M. W. Baker, for performing the radio-tracer experiments.

[9/193 *Received*, 7*th February*, 1979]

REFERENCES

[1] I. Bruning, R. Grashey, H. Hauck, R. Huisgen, and H. Seidl, *Org. Synth.*, 1966, **46**, 127.
[2] J. Wiemann and C. Glacet, *Bull. Soc. chim. France*, 1950, **17**, 176.
[3] P. A. S. Smith and J. E. Robertson, *J. Amer. Chem. Soc.*, 1962, **84**, 1197.
[4] V. Bellavita, *Gazzetta*, 1935, **65**, 889, 897; 1940, **70**, 584.
[5] A. M. Simonov and A. D. Garnovskii, *Zhur. obshchei Khim.*, 1961, **31**, 114 (*Chem. Abs.*, 1961, **55**, 22,298f).
[6] W. R. Vaughan and R. D. Carlson, *J. Amer. Chem. Soc.*, 1962, **84**, 769.
[7] (*a*) O. Mumm, H. Volquartz, and H. Hesse, *Ber.*, 1914, **47**, 751; (*b*) R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, and E. Brunn, *Tetrahedron Letters*, 1967, 1809.
[8] G. M. Kraay, Dissertation, Amsterdam, 1926 (*Chem. Abs.*, 1926, **20**, 21,525).
[9] C. V. Deliwala and S. Rajagopalan, *Proc. Indian Acad. Sci.*, 1950, **31A**, 183 (*Chem. Abs.*, 1951, **45**, 6179b).
[10] E. Buehler, *J. Org. Chem.*, 1967, **32**, 261.
[11] E. F. Schoenewaldt, R. B. Kinnel, and P. Davis, *J. Org. Chem.*, 1968, **33**, 4270.
[12] R. N. Lacey, *J. Chem. Soc.*, 1960, 1633.
[13] Heilbron and Bunbury, ' Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1946.