Reactions of *N*-(1-Cyanoalkyl)alkylideneamine *N*-Oxides with Dipolarophiles and Nucleophiles. Part I. A Novel Synthesis of 2,4(5)-Dialkyl-5(4)-phenylthioimidazoles [1]

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Reactions of *N*-(1-cyanoalkyl)alkylideneamine *N*-oxides with thiols at room temperature yielded 2,4,5-trisubstituted imidazoles (I). The reaction was accelerated by addition of a small amount of piperidine, and inhibited when carried out above the melting temperature of the nitrone in a solvent. The mechanism is discussed.

ACYCLIC aliphatic nitrones are, in general, much less stable than aromatic nitrones; few have been isolated in a pure state and there has been little work on their reactivities. Nitrones are known to react as 1,3-dipolar compounds with various dipolarophiles to give cycloaddition compounds,[2] and with nucleophilic reagents, such as Grignard reagents [3] and hydrogen cyanide,[4] to give hydroxylamine derivatives as noncyclic addition products. These reactions are all with carbon nucleophiles; no reactions with other nucleophiles have been reported.

reports that the reactions of βγ-unsaturated nitriles with the nucleophiles hydrazine and hydroxylamine yield pyrazoles [7] and isoxazoles,[8] respectively. In fact the reactions of the title nitrones with thiols gave a series of new imidazole derivatives, 2,4(5)-dialkyl-5(4)-phenylthioimidazoles, in high yield.

N-(1-Cyanobutyl)isobutylideneamine *N*-oxide (A; $R^1 = Pr^n$, $R^2 = Pr^i$) [4a] was mixed with excess of benzenethiol. After 1—2 weeks at room temperature a crystalline product had formed. When the reaction was carried out at a higher temperature, not exceeding

TABLE 1

2,4,5-Trisubstituted imidazoles (I)

	Yield (%)	M.p. (°C)	Found (%) C	H	N	Formula	Required (%) C	H	N	U.v.* $\lambda_{max.}$/nm (log ε)
(Ia)	91	155·0—155·5	69·55	7·7	10·95	$C_{15}H_{20}N_2S$	69·3	7·75	10·8	203 (4·40), 238 (4·16)
(Ib)		156·5—15·75	69·2	7·65	10·75					203 (4·37), 238 (4·13)
(Ic)		126·0—126·5	69·55	7·7	10·7					203 (4·41), 238 (4·17)
(Id)		160·0—160·5	69·1	7·65	10·8					206 (4·30), 238 (4·15)
(Ie)		119·0—120·0	68·45	7·3	11·55	$C_{14}H_{18}N_2S$	68·35	7·4	11·4	206 (4·32), 238 (4·16)
(If)		125·0—127·0	68·2	7·15	11·15					206 (4·32), 238 (4·18)
(Ig)		181·5—182·5	68·35	7·35	11·6					206 (4·31), 238 (4·16)
(Ih)		164·5	67·25	6·95	12·2	$C_{13}H_{16}N_2S$	67·3	6·95	12·05	206 (4·32), 238 (4·11)
(Ii)	81	165·0—166·0	70·15	8·0	10·25	$C_{16}H_{22}N_2S$	70·05	8·1	10·2	207 (4·41), 238 (4·20)
(Ij)	75	148·0—148·5	70·7	7·95	10·0					207 (4·48), 238 (4·15)
(Ik)	86	178·5—180·0	61·05	6·55	9·5	$C_{15}H_{19}ClN_2S$	61·15	6·5	9·5	209 (4·26), 254 (4·25)
(Il)	81	167·0—167·5	66·4	7·8	9·9	$C_{16}H_{22}N_2OS$	66·25	7·65	9·65	203 (4·36), 243 (4·21), 255 (4·03) †
(Im)	95	193·5—194·0	58·95	6·25	13·6	$C_{15}H_{19}N_3O_2S$	59·05	6·3	13·8	218 (4·31), 330 (4·15)
(In)	88	184·5—185·0	73·5	7·05	9·05	$C_{19}H_{22}N_2S$	73·6	7·15	9·05	221 (4·76), 237 (4·37),† 301 (3·93)
(Io)	28	182·0—183·5	73·5	7·2	8·9					217 (4·68), 249 (4·72), 284 (4·08)
(Ip)		133·0	58·7	7·05	10·25	$C_{13}H_{18}N_2S_2$	58·7	6·8	10·55	222 (4·13), 262 (3·80) †
(Iq)	18	88·0—89·0	69·75	8·0	10·0	$C_{16}H_{22}N_2S$	70·05	8·1	10·2	215 (4·12), 253 (3·68)
(Ir)	9	121·0—121·5	62·2	9·45	12·9	$C_{11}H_{20}N_2S$	62·25	9·5	13·2	218 (4·01), 240 (3·76) †
(It)		166·5—167·0	66·2	6·5	12·9	$C_{12}H_{14}N_2S$	66·05	6·45	12·85	207 (4·32), 239 (4·12)

* (Ia—j) and (It) have a shoulder at 246—251 nm (log ε 4·10—4·15). † Shoulder.

Thiols are reactive nucleophiles, which give sulphides with acrylonitriles.[5] Sulphur [6] and sulphur compounds such as sulphur dioxide [4b] deoxygenate nitrones, yielding the corresponding azomethines.

We have studied the reactions of thiols with the title nitrones to see whether the nitrones are deoxygenated or whether addition compounds are formed. We were also interested in the behaviour of the nitrile group towards thiols in the reaction, because there are

the m.p. (62—65°) of the nitrone, or when a little piperidine was added, it was complete within 2—4 days. The products were the imidazoles (Ia—p) (Table 1). Incubation above the m.p. of the nitrone, addition of acids, or use of solvents inhibited the reaction, which was not affected by u.v. or visible light.

The product (Ia) (M^+ 260·13 by mass spectrometry; $C_{15}H_{20}N_2S$ by elemental analysis) was apparently formed by addition of benzenethiol to the nitrone with

[1] Preliminary report, M. Masui, C. Yijima and K. Suda, *Chem. Comm.*, 1968, 1400.

[2] (*a*) J. Hamer and Macaluso, *Chem. Rev.*, 1964, **64**, 473; (*b*) G. R. Delpierre and M. Lamchen, *Quart. Rev.*, 1965, **19**, 329.

[3] (*a*) A. Dornov, H. Gehrt, and F. Ische, *Annalen*, 1954, **585**, 220; (*b*) G. E. Utzinger and F. A. Regenass, *Helv. Chim. Acta*, 1954, **37**, 1892.

[4] (*a*) M. Masui and C. Yijima, *J. Chem. Soc.* (*C*), 1967, 2022; (*b*) R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *J. Chem. Soc.*, 1959, 2094.

[5] R. M. Ross, H. L. Bushey, and R. J. Rolih, *J. Amer. Chem. Soc.*, 1951, **73**, 540.

[6] (*a*) V. Bellavita and N. Cagnoli, *Gazzetta*, 1939, **69**, 602 (*Chem. Abs.*, 1940, **34**, 1978); (*b*) M. N. Shchukina and G. S. Predvoditeleva, *Doklady Akad. Nauk S.S.S.R.*, 1956, **110**, 230 (*Chem. Abs.*, 1957, **51**, 4996).

[7] (*a*) P. Schmidt and J. Pruey, *Helv. Chim. Acta*, 1958, **41**, 306; (*b*) I. Iwai and N. Nakamura, *Chem. and Pharm. Bull.* (*Japan*), 1966, **14**, 1277.

[8] E. Haruki, Y. Hirai, and E. Imoto, *Bull. Chem. Soc. Japan*, 1968, **41**, 267.

loss of one water molecule, *i.e.* it could have been a cyanoimine (C), produced *via* a hydroxylamine (B) (a simple 1,3-dipolar addition product of the nitrone with the thiol) (Scheme 1). Similar reactions of hydroxylamines with loss of water (Scheme 2) have been reported,[2,9] supporting this conclusion. However compound (Ia) was not hydrolysed by refluxing with sodium hydroxide or aqueous hydrogen chloride.

The i.r. spectra of compounds (Ia—p) showed no C≡N absorption but a strong broad band at 3200—2300 cm^{-1} (in KBr) and a single strong band near 3400 cm^{-1} (2% in $CHCl_3$). The hydrochlorides (IIa and d) show a stronger ammonium band at 2850—2550 cm^{-1} than the corresponding free amines (Ia and d) and two absorptions at 1730 and 1615 cm^{-1} which may be assigned to the $-C=\overset{+}{N}H-$ group. Methylation of compound (Id) with methyl iodide introduced one methyl group to give compound (IIId), with loss of the i.r. absorption at 3200—2300 (in KBr) or 3430 cm^{-1} (2% in $CHCl_3$). Thus the original product was not (C), but a stable compound containing an N–H and/or an =N– system. The i.r. data correspond well with those reported [10,11] for imidazoles. Apparently the nitrile group on the α-carbon atom has taken part in the reaction.

The products (I) have stronger u.v. absorption bands (see Table 1) than benzenethiol [12] [$\lambda_{max.}$ 207 (log ε 4·11) and 236 nm (4·00)], implying that they contain an auxochromic group interacting with the phenylthio-system. The imidazole ring shows two absorption bands,[13] at 210 (log ε 3·7) and 250 nm (1·8); thus a structure in which a sulphur atom interacts with both

$$R^1CH(CN)-N(O)=CHR^2 \ (A) + HSPh \longrightarrow R^1CH(CN)-N(OH)-CH(SPh)R^2 \ (B) \xrightarrow{-H_2O} R^1C(CN)=N-CH(SPh)R^2 \ (C)$$

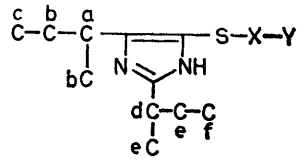
SCHEME 1

$$RCH=N(O)R + HCN \longrightarrow [RCH(CN)-N(OH)R] \xrightarrow{-H_2O} RC(CN)=NR$$

SCHEME 2

TABLE 2

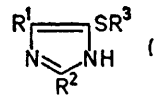
Chemical shifts (τ values) and coupling constants (Hz) for the imidazoles (I) [a] in $CDCl_3$



	a	b	c	d	e	f	X	Y	NH	J_{ab}	J_{bc}	J_{de}	J_{ef}
(Ia)	7·45	8·43	9·20	7·03	8·76		2·8—3·2		−1·11	7·5	6·9	7·1	
(Ib)	6·83	8·82		7·40	8·37	9·14	2·8—3·1		−0·27	7·0		7·4	6·9
(Ic)	7·41	8·40	9·18	7·40	8·39	9·14	2·8—3·1		−0·86	7·2	6·8	7·4	6·9
(Id)	6·82	8·78		6·97	8·72		2·8—3·1		0·39	7·0		7·0	
(Ie)	7·44	8·44	9·19	7·41	8·82		2·8—3·1		0·60	7·5	6·9	7·6	
(If)	6·83	8·83		7·39	8·83		2·8—3·2		−1·12	6·9		7·6	
(Ig)	7·35	8·86		6·98	8·73		2·8—3·1		0·89	7·5		7·2	
(Ih)	6·83	8·84		7·75			2·8—3·1		0·30	7·0			
(Ii)	7·42	8·43	9·17	7·01	8·73		3·07	7·73	0·74	7·5	6·8	7·0	
(Ij)	7·46	8·44	9·19	7·03	8·75		2·9—3·5	7·68	1·40	7·3	6·8	7·0	
(Ik)	7·43	8·44	9·18	6·99	8·74		2·83, 3·09		−0·34	7·5	6·9	7·1	
(Il)	7·40	8·44	9·16	7·00	8·74		2·97, 3·26	6·28	0·51	7·5	7·0	7·2	
(Im) *							1·97, 2·94		3·9				
(In)	7·47	8·52	9·24	7·06	8·81		1·6—3·2		−0·12	7·5	7·0	6·9	
(Io)	7·38	8·41	9·14	6·96	8·72		2·2—3·0		2·0	7·4	6·8	7·0	
(Ip)	7·30		9·11	7·10	8·74		2·7—3·2		0·63	7·4	7·0	7·1	
(Iq)	7·62		9·15	7·01	8·75		6·18			7·6	6·9	7·2	
(Ir) †	7·41	8·40	9·06	6·99	8·69		7·35		−2·1	7·2	6·8	6·9	
(It)	7·39	8·89		7·71			2·8—3·0		0·98	7·5			

* Only slightly soluble in $CDCl_3$. † In CCl_4.

[a] X = C_6H_4 for (Ia—p) and (It), X = CH_2 for (Iq and r); Y = substituent.



(I)

	R^1	R^2	R^3		R^1	R^2	R^3
a;	Pr^n	Pr^i	Ph	k;	Pr^n	Pr^i	*p*-ClC_6H_4
b;	Pr^i	Pr^n	Ph	l;	Pr^n	Pr^i	*p*-MeO·C_6H_4
c;	Pr^n	Pr^n	Ph	m;	Pr^n	Pr^n	*p*-$O_2N·C_6H_4$
d;	Pr^i	Pr^i	Ph	n;	Pr^n	Pr^i	1-$C_{10}H_7$
e;	Pr^n	Et	Ph	o;	Pr^n	Pr^i	2-$C_{10}H_7$
f;	Pr^i	Et	Ph	p;	Pr^n	Pr^i	2-Thienyl
g;	Et	Pr^i	Ph	q;	Pr^n	Pr^i	CH_2Ph
h;	Pr^i	Me	Ph	r;	Pr^n	Pr^i	Et
i;	Pr^n	Pr^i	*p*-MeC_6H_4	s;	Pr^n	Pr^i	Bu
j;	Pr^n	Pr^i	*o*-MeC_6H_4	t;	Et	Me	Ph

[9] V. Bellavita, *Gazzetta*, 1940, **70**, 584 (*Chem. Abs.*, 1941, **35**, 2127).

[10] W. Otting, *Chem. Ber.*, 1956, **89**, 2887.

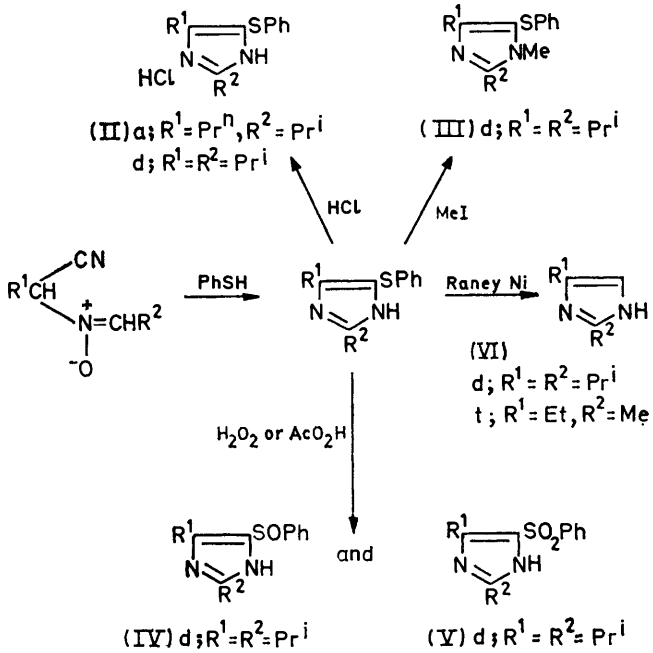
[11] H. Zimmermann, *Z. Electrochem.*, 1961, **65**, 821.

[12] H. P. Kock, *J. Chem. Soc.*, 1949, 387.

[13] E. A. Braude, *Ann. Reports.*, 1945, **42**, 105.

chromophores is not in conflict with the u.v. spectrum. The n.m.r. data (Table 2) * also support structure (I). The signals for (Ia) at τ 7·45 (t, 2H) and 7·03 (septet, 1H) are as expected for CH–C= systems; spin decoupling showed that the latter signal was only coupled to that at τ 8·76. All the compounds showed a signal due to exchangeable N–H.

Oxidation of compound (Id) with hydrogen peroxide or peracetic acid gave the corresponding sulphoxide (IVd) and sulphone (Vd). Treatment of (Id) with Raney nickel gave 2,4(5)-di-isopropylimidazole (VId), identified by analysis and spectra. Compound (VIt), obtained similarly, was converted into its oxalate, which was identical (mixed m.p. and i.r. spectra) with an authentic sample.[14]



SCHEME 3

Thus all the products appear to be 2,4,5-trisubstituted imidazoles, and the reactions described are summarized in Scheme 3.

When the reaction was carried out in a solvent, such as ethanol, dioxan, or benzene, the yield of imidazole was very low. The yield decreased with decrease in the dielectric constant of the solvent, suggesting that the reaction is ionic.

In general, alkanethiols have larger pK_a values [15] and should be more nucleophilic than aromatic ones. However, in the case of ethane-, butane-, and toluene-α-thiol the imidazole was only obtained, in low yield, when piperidine was used as a catalyst (Iq—s).

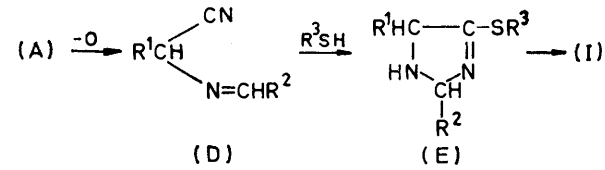
* Some of the n.m.r. data for (Ia) reported previously [1] were incorrect; τ 8·66 and 6·75—7·20 should be 8·76 and 2·8—3·2, respectively.

[14] A. Windaus and W. Langenbeck, *Ber.*, 1922, **55**, 3706.

[15] (*a*) M. M. Kreevoy, E. T. Harper, R. E. Duvall, H. S. Wilgus, and L. T. Ditsch, *J. Amer. Chem. Soc.*, 1960, **82**, 4899; (*b*) B. Dmuchovsky, F. B. Zienty, and W. A. Verdenburgh, *J. Org. Chem.*, 1966, **31**, 865.

From the foregoing results three reaction routes seem possible.

Route 1: the nitrone is deoxygenated by the thiol to form an azomethine intermediate (Scheme 4).

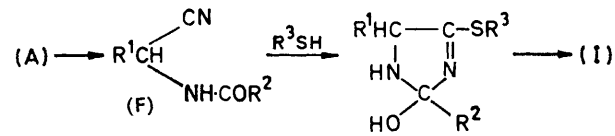


SCHEME 4

Route 2: the nitrone rearranges to give the corresponding amide intermediate (Scheme 5).

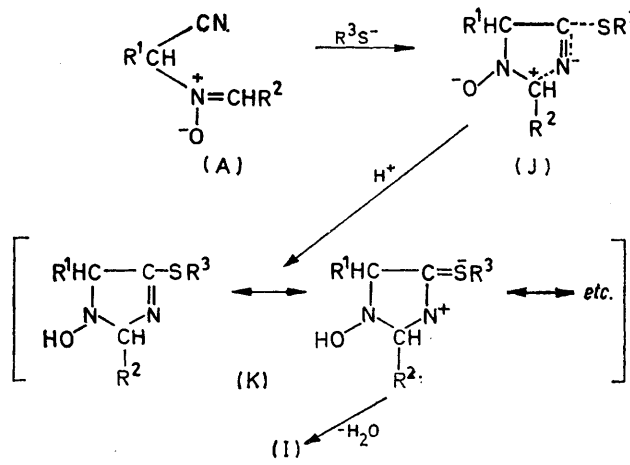
Route 3: the nitrone undergoes a specific reaction (Scheme 6).

A mechanism similar to route 1 has been proposed for the formation of the imidazolidinethione (H)



SCHEME 5

from aminoacetonitrile, hydrogen sulphide, and acetone (Scheme 7); the azomethine intermediate (G) was isolated.[16] It is unlikely, however, that structure (E)



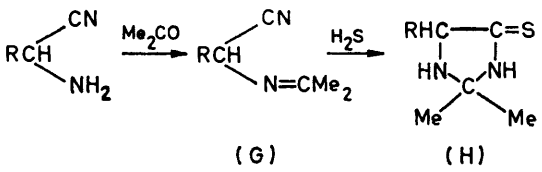
SCHEME 6

undergoes dehydrogenation under the reaction conditions, and *N*-propylidene-α-cyanopropylamine (D; $R^1 = R^2 = Et$), synthesized independently, did not give compound (I) with benzenethiol under the conditions used. 2-Acetamidobutyronitrile [17] (F; $R^1 =$ Et, $R^2 =$ Me), synthesized independently also did not give compound (I) on treatment with benzenethiol under similar conditions. Hence, routes 1 and 2 are excluded.

[16] A. H. Cook, I. Heilbron, and A. P. Mahadevan, *J. Chem. Soc.*, 1949, 1061.

[17] W. L. Hawkins and B. S. Biggs, *J. Amer. Chem. Soc.*, 1949, **71**, 253.

When the nitrone (A) was mixed with a slight excess of benzenethiol the i.r. spectrum (liquid film) immediately developed a strong, broad band at about



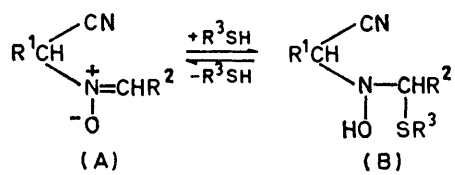
SCHEME 7

3400 cm^{-1}. The nitrile band of the mixture, like that of the nitrone (A) is weak,[4a] and the water formed in the reaction gradually obscured the i.r. spectrum as the reaction proceeded, so that it was impossible to follow the change in strength of the nitrile band with time. However, after about 6 days, double-bond absorption was noticed at about 1670 cm^{-1}; this gradually disappeared as the imidazole was produced.

In reactions with alkanethiols, the i.r. spectrum of the mixtures slowly developed the same strong, broad band. This band appeared immediately in the presence of a small amount of piperidine. The absorptions at 3060 and 1590 cm^{-1} due to the CH=N of the nitrone disappeared when this strong band appeared. On removal of the thiol from the reaction mixture at an early stage under reduced pressure, the original nitrone was recovered almost quantitatively.

In the light of these observations, the absorption at 3400 cm^{-1} seems to be due to a hydroxy-group, which results from either protonation of the nitrone by the thiol or the rapid formation of structure (B). However, the pK_a values for nitrones are in the range 2—4 in ethanol–water (1 : 9) [18] and under these conditions the pK_a of benzenethiol [18] is much higher (*ca.* 7). An acid so weak is unlikely to protonate significantly a base as weak as a nitrone.

If the i.r. absorption at about 3400 cm^{-1} is considered to be due to a hydroxy-group, the foregoing results could be explained in terms of the reversible system shown in Scheme 8, in which the conversion is easy



SCHEME 8

and rapid.* As the ultimate reaction product is (I), the hydroxylamine (B) is probably not an intermediate on the main reaction path. On evaporation of thiol from the reaction mixture, or on formation of the imidazole derivatives, (B) should easily convert into (A).

Thus, if the reaction takes place with the nitrone (A), route **3** is thought to be possible (Scheme 6).

In route **3**, the nitrile group is strongly polarized by nucleophilic attack of the thiolate anion, resulting in enhancement of its nucleophilic reactivity, and subsequently the intermediate (K) must be produced by an intramolecular Ritter-type reaction. This intermediate (K) would be stabilized by the 3*d* orbital contribution of the sulphur atom. A similar contribution has been reported in the case of thiolesters.[19] Furthermore, such a contribution by the sulphur atom would make the subsequent dehydration easy, since the C–H system between the two nitrogen atoms should be much more acidic. The formation of intermediate (K) would be expected to proceed more readily with aromatic thiols for these can contribute resonance stabilization.

The catalytic action of piperidine may be due to its ability to promote the formation of thiolate anion, and to accelerate the dissociation of the removal of the N–CH–N proton in (K). In the dehydration of *N*-aryl-*N*-(α-cyanobenzyl)hydroxylamines, a similar marked basic catalysis is observed.[20]

Consequently, it seems likely that imidazole derivatives are produced through route **3**.

Under the conditions used, the thiolate ion attacking the nitrile would presumably be very nucleophilic, since it cannot be solvated. Use of solvents would also reduce the concentration of reactants, and hence result in decrease in the reaction rate. Furthermore, aprotic nonpolar solvents suppress the dissociation of thiol to thiolate ion [21] and protic solvents would solvate both carbonium ion and thiolate ion. These effects would explain the reaction inhibition observed.

In dimethyl sulphoxide the thiol was oxidised very rapidly.

EXPERIMENTAL

U.v. spectra were recorded for solutions in ethanol with a Shimazu QV-50 instrument. I.r. spectra were recorded with a JASCO BG-402G instrument and n.m.r. spectra with a Hitachi H-60 instrument for solutions in deuteriochloroform with tetramethylsilane as internal reference.

p-Methoxybenzenethiol, *p*-chlorobenzenethiol,[22] naphthalene-α-thiol,[23] and thiophen-2-thiol [24] were prepared and purified as described in the literature; other thiols were commercial products.

2,4(5)-*Dialkyl*-5(4)-*phenylthioimidazoles* (Ia—p).—The *N*-(1-cyanoalkyl)alkylideneamine *N*-oxide (10 mmol), the thiol (11 mmol), and piperidine (0·2 mmol) in a stoppered vessel were warmed to a temperature below the m.p. of the nitrone. The product crystallized within 2—4 days. Disulphide and excess of thiol were separated by refluxing with n-hexane. The product (I) was recrystallized from ethyl acetate or aqueous ethanol. Usually the yield

* We thank the referees for suggestions concerning the interpretation.

[18] M. Masui and C. Yijima, *J. Chem. Soc.* (*B*), 1966, 56.
[19] A. W. Baker and G. H. Harris, *J. Amer. Chem. Soc.*, 1960, **82**, 1923.
[20] M. Masui, M. Yamauchi, C. Yijima, K. Suda, and K. Yoshida, *Chem. Comm.*, 1971, 312.
[21] (*a*) G. Schwarzenbach, *Helv. Chim. Acta*, 1932, **15**, 1468; (*b*) J. Burkus, *J. Org. Chem.*, 1961, **27**, 474.
[22] C. M. Suter and H. L. Hansen, *J. Amer. Chem. Soc.*, 1932, **54**, 4100.
[23] E. Knüsli, *Gazzetta*, 1949, **79**, 621 (*Chem. Abs.*, 1950, **44**, 4438).
[24] W. H. Houff and R. D. Schuetz, *J. Amer. Chem. Soc.*, 1953, **75**, 6316.

was 80—90%. With crystalline thiol derivatives, excess of nitrone was used to melt the mixture below the m.p. of the nitrone. Compounds (I) are soluble in ethanol, ethyl acetate, acetone, diethyl ether, chloroform, and acetic acid, but scarcely soluble in cold benzene and insoluble in n-hexane, light petroleum, and water.

Preparation of the Imidazole (Ia); *Solution Reactions.*—Dried solvent (20 ml) (ethanol or dioxan), *N*-(1-cyanobutyl)isobutylideneamine *N*-oxide (850 mg), benzenethiol (640 mg), and piperidine (15 mg) were mixed in a stoppered vessel. The solvent was evaporated off under reduced pressure, and the residue was dissolved in ether and extracted with 3N-hydrochloric acid. The aqueous layer was neutralized with 3N-sodium hydroxide and extracted with ether. The ether was evaporated off to leave crude imidazole (Ia), which was recrystallized from ethanol–water. The yield of (Ia) from ethanol solution was 26% after 50 days and from dioxan solution was only 12·5% after 80 days.

Various amounts of dry benzene, the nitrone (250 mg), and benzenethiol (260 mg) were mixed in a stoppered vessel. After 2 months benzene and unchanged thiol were removed under reduced pressure, leaving an oil. This treatment gave the following yields of imidazole:

Benzene (mg)	21	53	212	424
Yield of imidazole (%)	50	44	28	23

5(4)-*Alkylthio*-2-*isopropyl*-4(5)-*propylimidazoles* (Iq—s).—*N*-(1-Cyanobutyl)isobutylideneamine *N*-oxide (10 mmol), alkanethiol (15 mmol) and piperidine (0·3 mmol) were mixed in a stoppered vessel. After 1—2 weeks, ether was added and the mixture was extracted with 3N-hydrochloric acid. The aqueous solution was neutralized with 3N-sodium hydroxide and extracted with ether. The extract was dried ($CaCl_2$) and evaporated; the residue gave the imidazole. If the residue was still impure, it was applied to a neutral alumina column and eluted with benzene–ethyl acetate (4 : 1 v/v). The three following imidazoles were obtained by this procedure, and their oxalates were recrystallized from acetone–light petroleum: 5(4)-*Benzylthio*-2-*isopropyl*-4(5)-*propylimidazole* (Iq), needles (from acetone–water); *oxalate*, m.p. 146—147·5° (Found: C, 59·35; H, 6·65; N, 7·7. $C_{18}H_{24}N_2O_4S$ requires C, 58·9; H, 6·55; N, 7·75%); 5(4)-*ethylthio*-2-*isopropyl*-4(5)-*propylimidazole* (Ir), needles (from ethanol–water); *oxalate*, m.p. 177·5—178·5° (Found: C, 51·65; H, 7·35; N, 9·2. $C_{13}H_{22}N_2O_4S$ requires C, 51·8; H, 7·35; N, 9·25%); 5(4)-*butylthio*-2-*isopropyl*-4(5)-*propylimidazole* (Is), oil (11%), b.p. 131—140° (bath) at 0·08 mmHg; *oxalate*, m.p. 178·5—180·0° (Found: C, 54·5; H, 7·9; N, 8·45. $C_{15}H_{26}N_2O_4S$ requires C, 54·55; H, 7·95; N, 8·5%).

2-*Isopropyl*-5(4)-*phenylthio*-4(5)-*propylimidazole Hydrochloride* (IIa).—The imidazole (Ia) was refluxed with a large excess of 10% hydrochloric acid; when it had all dissolved the solution was evaporated to dryness under reduced pressure. The residue gave the *hydrochloride* (*ca.* 80%), m.p. 130·5—132·0° (from ethanol–ether) (Found: C, 60·45; H, 7·15; N, 9·65. $C_{15}H_{21}ClN_2S$ requires C, 60·75; H, 7·15; N, 9·45%). Similarly the *hydrochloride* (IId) was obtained from (Id); m.p. 152—154° (Found: C, 60·65; H, 7·45; N, 9·35. $C_{15}H_{21}ClN_2S$ requires C, 60·75; H, 7·15; N, 9·45%).

2,4(5)-*Di-isopropyl*-1-*methyl*-5(4)-*phenylthioimidazole* (IIId).—The imidazole (Id) (5 g) in methanol (70 ml) was mixed with methyl iodide (8 g); potassium carbonate (3 g) was added and the mixture was refluxed for 7 h on a water-bath. Methanol was removed under reduced pressure and the residue was extracted several times with ether. Evaporation of the extracts yielded a syrup and the starting material (1·0 g). The residue was extracted with n-hexane and applied to a silica gel column. The column was eluted with n-hexane and the eluate was decolourized with active charcoal. The hexane was evaporated off to leave the crystalline *product* (59%), m.p. 67—69° (from light petroleum) (Found: C, 70·2; H, 7·95; N, 10·2. $C_{16}H_{22}N_2S$ requires C, 70·15; H, 8·1; N, 10·2%), $\nu_{max.}$ 2865 cm^{-1} (*N*-alkyl C–H stretch),[25] τ 6·64 (3H, s), soluble in ethanol, ether, benzene, and acetic acid, slightly soluble in light petroleum and insoluble in water.

5(4)-(p-*Aminophenylthio*)-2,4(5)-*dipropylimidazole Hydrochloride*.—The imidazole (Im) (1 g) was dissolved in ethanol (100 ml), and stirred with granular metallic tin (2 g), hydrochloric acid (35%; 20 ml), and tin chloride (2 g) for 24 h. Then aqueous 10% sodium hydroxide (80 ml) was added and the precipitate was filtered off. The filtrate was evaporated to dryness and the residue was extracted with ether. The extract was treated with calcium chloride for 1 day and then evaporated to a syrup. The syrup was dissolved in ether and dry hydrogen chloride gas was passed through the solution to obtain the crystalline *product* (44%), m.p. 216° (from ethanol–ether) (Found: C, 57·7; H, 7·1; N, 13·3. $C_{15}H_{22}ClN_3S$ requires C, 57·8; H, 7·1; N, 13·5%).

2,4(5)-*Di-isopropyl*-5(4)-*phenylsulphinylimidazole* (IVd).—The imidazole (Id) (2 g) was dissolved in acetic acid (20 ml); 30% hydrogen peroxide (20 ml) was added and the mixture was left at room temperature for 1 week. It was then evaporated under reduced pressure and the residue was dissolved in ethanol (5 ml). Addition of water yielded a crystalline *solid* (53%), m.p. 183—185° (from acetone) (Found: C, 65·55; H, 7·3; N, 9·95. $C_{15}H_{20}N_2OS$ requires C, 65·25; H, 7·3; N, 10·15%), $\nu_{max.}$ (KBr) 1021 cm^{-1}.

2,4(5)-*Di-isopropyl*-5(4)-*phenylsulphonylimidazole* (Vd).—The imidazole (Id) (5 g) was dissolved in acetic acid (90 g) containing peracetic acid (9%) and left for 10 days at *ca.* 5°. Then aqueous sodium hydroxide (N; 10 ml) was added and the mixture was evaporated under reduced pressure. The resulting crystalline solid was dissolved in acetone to separate it from insoluble salt. The solution was concentrated, and water was added until it became cloudy. Then the mixture was cooled in ice–water to give the *product* (63%), m.p. 152—153° (Found: C, 61·25; H, 6·85; N, 9·5. $C_{15}H_{20}N_2O_2S$ requires C, 61·7; H, 6·9; N, 9·6%), $\nu_{max.}$ (KBr) 1301 and 1142 cm^{-1}.

2,4(5)-*Di-isopropylimidazole* (VId).—The imidazole (Id) (2 g) was dissolved in dry ethanol (150 ml) and mixed with Raney nickel (5 g). The mixture was refluxed for 6 h. The nickel was then removed and the ethanol was evaporated off under reduced pressure. The residue was applied to a silica gel column, which was eluted with chloroform and then ether, and the crystalline *product* (68%) was obtained from the latter eluate m.p. 140—142° (sealed tube) (from ether–light petroleum) (Found: C, 70·95; H, 10·5; N, 18·4. $C_9H_{16}N_2$ requires C, 71·0; H, 10·6; N, 18·4%), $\lambda_{max.}$ (99% EtOH) 212·5 nm (log ε 3·89), τ 6·89 (1H, septet), 8·76 (6H, d), 7·02 (1H, septet), 8·71 (6H, d), 3·39 (1H, s), and −0·26 (1H, s).

4(5)-*Ethyl*-2-*methylimidazole* (VIt).—(*a*) 4-Ethyl imidazole-2-thiol (2 g) was desulphurized with Raney nickel in ethanol

[25] R. D. Hill and G. D. Meakins, *J. Chem. Soc.*, 1958, 760.

to give 4-ethylimidazole (1·5 g), b.p. 135—140° (bath) at 3 mmHg, which was converted into compound (VIt) by a reported method.[14] The oxalate was obtained from the ethereal solution and recrystallized from methanol–light petroleum; yield 8 mg, m.p. 139—140°.

(*b*) The imidazole (It) (0·8 g) was dissolved in dry ethanol (50 ml) and mixed with Raney nickel (2·5 g). The nickel was then removed and the ethanol was evaporated off under reduced pressure. The product (VIt) was distilled *in vacuo*; yield 430 mg, b.p. 128—134° (bath) at 1 mmHg; oxalate, m.p. 140—141° (from methanol–light petroleum) (Found: C, 48·0; H, 6·05; N, 13·95. Calc. for $C_8H_{12}N_2O_4$: C, 48·0; H, 6·05; N, 14·0%); picrate, m.p. 93—94° (from water) (Found: C, 42·3; H, 3·8; N, 20·7. Calc. for $C_{12}H_{13}N_5O_7$: C, 42·5; H, 3·85; N, 20·65%).

[26] H. T. Clarke and H. J. Bean, *Org. Synth.*, 1943, Coll. Vol. II, p. 29.

N-*Propylidene-α-cyanopropylamine* (D; $R^1 = R^2 = Et$). —Excess of propionaldehyde was added to 2-aminobutyronitrile [26] in a stoppered vessel and the mixture was set aside for a day at room temperature. The organic layer was separated from the water produced and distilled in a stream of nitrogen under reduced pressure; b.p. 84—85° at 5 mmHg. A colourless viscous liquid was obtained which was unstable and gradually decomposed in air with colouration; $\nu_{max.}$ 1628 (C=N) and 2270 cm^{-1} (C≡N).

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