Synthesis of 1*H*-1,2,4-Triazole 2-Oxides and Annelated Derivatives [1]

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SS-Dimethylsulphimides (1)—(4) have been prepared from *N*-arylbenzamidines, 2-aminopyridines, 2-aminopyrazine, and 2-aminopyrimidines. The sulphimides react with nitrile oxides at room temperature or below to give the 1*H*-1,2,4-triazole 2-oxides (5) and the annelated derivatives (6)—(8). The structures of the 1,2,4-triazolo-[1,5-*a*]pyridine 3-oxides (6a, d, e, and h) are established by an independent synthesis involving the oxidation by lead tetra-acetate of the amidoximes (9a—d).

The *N*-oxides are readily deoxygenated by reaction with phosphorus trichloride; in addition the *N*-oxides (6d and e) are deoxygenated by heating under reflux in toluene, oxygen being transferred to the solvent. The reversible ring-opening of 5,7-dimethyl-2-(4-tolyl)-*s*-triazolo[1,5-*a*]pyrimidine (8c) is detected by n.m.r. spectroscopy.

REACTIONS of *N*-aryl-*SS*-dimethylsulphimides with nitrile oxides lead to the formation of 1,2,4-benzoxadiazines by way of *C*-nitroso-imine intermediates.[2] In order to explore the effect on the reaction of introducing a nucleophilic centre into the *N*-substituent we prepared a series of sulphimides (1)—(4) containing imidoyl and heterocyclic groups. These sulphimides are available from the corresponding amino-compounds and dimethyl sulphide, by their reaction in the presence of an oxidising agent such as *N*-chlorosuccinimide or t-butyl hypochlorite. We have previously reported details of the preparation of imidoyl sulphimides (1),[3] and *SS*-dimethyl-*N*-2-pyridylsulphimide (2a) has also been prepared before;[4] the other sulphimides are new. These sulphimides can be stored for several weeks below room temperature and in the absence of moisture, but several are oils or hygroscopic solids which were characterised by means of their n.m.r. spectra and by the formation of picrates.

SS-Dimethyl-*N*-(*N*-phenylbenzimidoyl)sulphimide (1a) reacted slowly with benzonitrile oxide at 0 °C to give 1,3,5-triphenyl-1,2,4-triazole 2-oxide (5a) which was isolated in 29% yield by layer chromatography. The structure of the product was established by its deoxygenation to the known[5] 1,3,5-triphenyl-1,2,4-triazole, using phosphorus trichloride in boiling chloroform. The triazole *N*-oxides (5b and c) were similarly prepared in moderate yields from the sulphimides (1a and b) and 4-toluonitrile oxide.

The 2-pyridylsulphimides (2) reacted more rapidly with nitrile oxides than the benzimidoyl compounds; adducts which were assigned the 1,2,4-triazolo[1,5-*a*]-pyridine structures (6) were isolated from the sulphimides and nitrile oxides bearing aryl, acyl, and ethoxycarbonyl substituents. Using equimolar amounts of the nitrile oxides or their precursors and the sulphimides, the yields of the recrystallised *N*-oxides were in the range 40—80%; these yields were not optimized.

Reactions of *SS*-dimethyl-*N*-pyrazin-2-ylsulphimide (3) and of the pyrimidin-2-ylsulphimides (4) with nitrile oxides gave the corresponding adducts (7) and (8), respectively. The sulphimide (4b) and 4-toluonitrile oxide gave only one adduct which was assigned the structure (8b) on the basis of its n.m.r. spectrum; of the alternative adduct (8) (R^1 = H, R^2 = Me) was detected.

The structure of 2-(4-tolyl)-1,2,4-triazolo[1,5-*a*]pyridine 3-oxide (6a) was established in two ways. Deoxygenation by phosphorus trichloride gave 2-(4-tolyl)1,2,4-triazolo[1,5-*a*]pyridine, a known compound[6] which was synthesised by the reported route and was found to be identical with the deoxygenation product. The *N*-oxide (6a) was also synthesised by the alternative route outlined in Scheme 1; oxidation of the amidoxime (9b) with lead tetra-acetate gave a product which was identical with that from the sulphimide reaction. This route to triazolo[1,5-*a*]pyridine 3-oxides was explored further by the synthesis and oxidation of the amidoximes (9a, c, and d), all of which gave the expected products in good yields. Recently, a similar synthesis of the triazolo-[1,5-*a*]pyridazine (10) has been reported.[7]

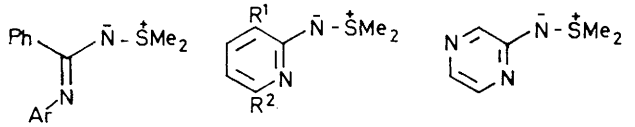
A likely common intermediate in the two syntheses of the *N*-oxide (6e) is the nitroso-imine (11). The nitrogen atom of the pyridine ring is then suitably placed to intercept the intermediate by attack on the nitroso-group, thus giving the aromatic product (6e) directly. This rationalisation is supported by the results of low-temperature oxidation of the amidoxime (9d) in the presence of the nucleophilic diene thebaine. A 1 : 1 adduct, which was assigned the structure (12), was isolated; on heating in benzene this gave thebaine and the *N*-oxide (6e) in high yield (Scheme 2).

In contrast to the reactions of *N*-arylnitroso-imines,[2] no cyclisation to give six-membered rings (oxadiazines) was observed; the products involve exclusive cyclisation on to nitrogen. The cyclisation of the *N*-arylnitroso-imines can be represented as an electrocyclic ring-closure. With the nitroso-imines bearing a suitably placed nitrogen atom, cyclisation to a five-membered ring product may supervene either because of the greater nucleophilicity of the nitrogen atom or because of the aromatic character of the products.

Properties of the N-*Oxides*.—The *N*-oxide (6a) is a crystalline solid which is not decomposed in solution below 130 °C and which shows a temperature-independent n.m.r. spectrum. The n.m.r. spectra of compound

[1] Preliminary communication, T. L. Gilchrist, C. J. Harris, C. J. Moody, and C. W. Rees, *J.C.S. Chem. Comm.*, 1974, 486.
[2] T. L. Gilchrist, C. J. Harris, F. D. King, M. E. Peek, and C. W. Rees, *J.C.S. Perkin I*, preceding paper.
[3] T. L. Gilchrist, C. J. Moody, and C. W. Rees, *J.C.S. Perkin I*, 1975, 1964.
[4] (*a*) P. K. Claus, W. Rieder, P. Hofbauer, and E. Vilsmaier, *Tetrahedron*, 1975, **31**, 505; (*b*) P. G. Gassman and C. T. Huang, *J. Amer. Chem. Soc.*, 1973, **95**, 4453.
[5] R. Engelhardt, *J. prakt. Chem.*, 1896, **54**, 143.
[6] J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 1957, 4506.
[7] J. Bratož-Stres, S. Polanc, B. Stanovnik, and M. Tišler, *Tetrahedron Letters*, 1975, 4429.

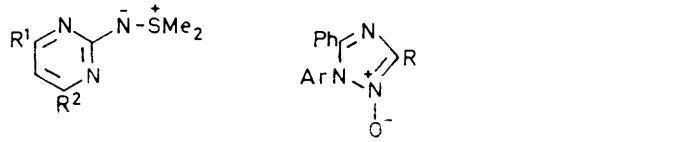
(6a) and the ethoxycarbonyl compound (6b) both contain a signal at low field (δ 8.69 and 8.71, respectively)



(1) a; Ar = Ph
b; Ar = 2-MeC$_6$H$_4$

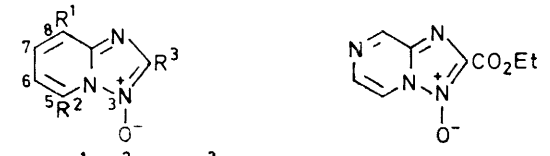
(2) a; R^1 = R^2 = H
b; R^1 = H, R^2 = Me
c; R^1 = Me, R^2 = H

(3)



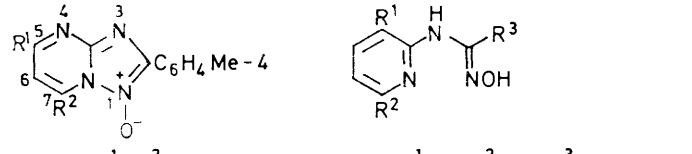
(4) a; R^1 = R^2 = H
b; R^1 = Me, R^2 = H
c; R^1 = R^2 = Me

(5) a; R = Ar = Ph
b; R = 4-MeC$_6$H$_4$, Ar = Ph
c; R = 4-MeC$_6$H$_4$, Ar = 2-MeC$_6$H$_4$



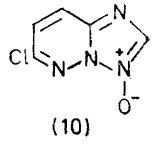
(6) a; R^1 = R^2 = H, R^3 = 4-MeC$_6$H$_4$
b; R^1 = R^2 = H, R^3 = CO$_2$Et
c; R^1 = R^2 = H, R^3 = COMe
d; R^1 = H, R^2 = Me, R^3 = Ph
e; R^1 = H, R^2 = Me, R^3 = 4-MeC$_6$H$_4$
f; R^1 = H, R^2 = Me, R^3 = CO$_2$Et
g; R^1 = H, R^2 = Me, R^3 = COPh
h; R^1 = Me, R^2 = H, R^3 = 4-MeC$_6$H$_4$
i; R^1 = Me, R^2 = H, R^3 = CO$_2$Et

(7)



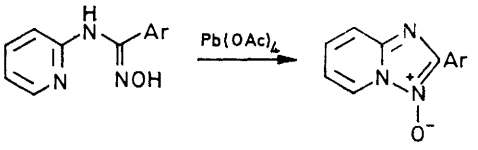
(8) a; R^1 = R^2 = H
b; R^1 = Me, R^2 = H
c; R^1 = R^2 = Me

(9) a; R^1 = H, R^2 = Me, R^3 = Ph
b; R^1 = R^2 = H, R^3 = 4-MeC$_6$H$_4$
c; R^1 = Me, R^2 = H, R^3 = 4-MeC$_6$H$_4$
d; R^1 = H, R^2 = Me, R^3 = 4-MeC$_6$H$_4$



(10)

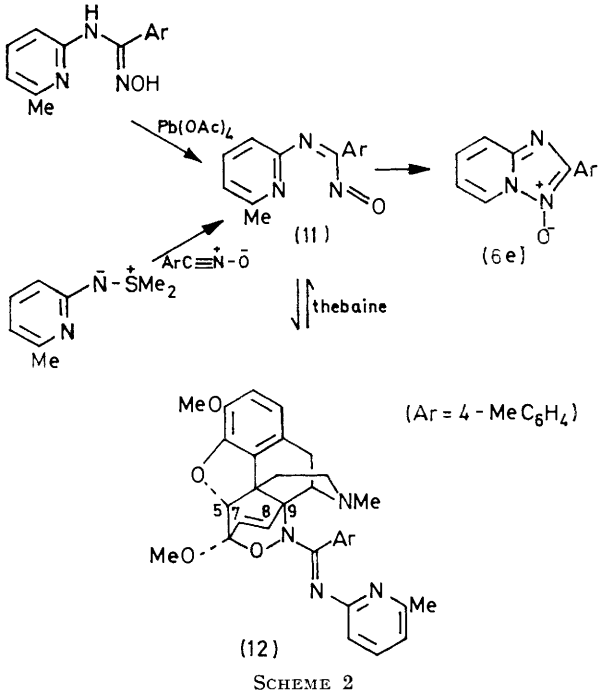
which is assigned to the hydrogen atom on C-5. The deshielding effect of the *N*-oxide function is also very marked in the 5-methyl compounds (6d—g): the n.m.r. signal for the 5-methyl group is at δ 3.24—3.30. This interaction between the 5-methyl substituent and the adjacent *N*-oxide group results in a noticeable decrease in the thermal stability of compounds (6d—g), as compared with (6a). Thus, when the *N*-oxides (6d and e) were heated under reflux in toluene, they were deoxygenated, and the corresponding *s*-triazolo[1,5-*a*]pyridines were isolated after 7—8 h. An examination of the solution by g.l.c. showed that it contained benzyl alcohol, and



SCHEME 1

this was confirmed by mass spectroscopic identification; bibenzyl was also detected by g.l.c. The *N*-oxides (6d and e) therefore act as thermal oxygen-transfer agents. If the ease of thermal deoxygenation is indeed related to the extent of interaction between the *N*-oxide function and the substituent at C-5, then it should be possible to design *N*-oxides which will act as oxygen-transfer agents under even milder conditions; we are preparing suitable model systems to test this possibility.

5,7-Dimethyl-2-(4-tolyl)-*s*-triazolo[1,5-*a*]pyrimidine 1-oxide (8c) was found to have a temperature-dependent n.m.r. spectrum. At 30 °C, the ^{1}H spectrum of (8c) in



(11)

(6e)

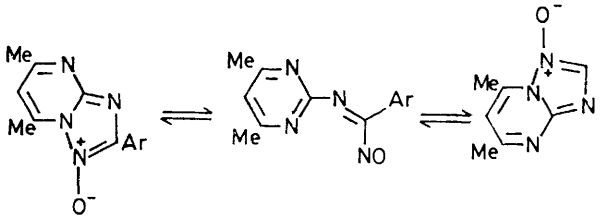
(Ar = 4-MeC$_6$H$_4$)

(12)

SCHEME 2

dichlorobenzene showed separate signals for the methyl groups at C-5 and -7, at δ 3.24 and 2.55; the signals broadened above 90 °C and collapsed to a singlet (δ 2.90) above 110 °C. When the solution was cooled, the original spectrum reappeared, although prolonged heating of the solution at 110 °C caused an irreversible change in the spectrum.

The temperature dependence of the spectrum is attributed to reversible ring-opening of (8c) to the nitroso-imine tautomer (Scheme 3); closure of the nitroso-imine



SCHEME 3

on to either pyrimidine nitrogen atom results in the regeneration of (8c). From the n.m.r. data, $\Delta G^{\ddagger}$ for the process was calculated as 85 ± 10 kJ mol^{-1}.

EXPERIMENTAL

Preparation of Sulphimides.—*SS*-Dimethyl-*N*-(*N*-phenylbenzimidoyl)sulphimide (1a) and *SS*-Dimethyl-*N*-(*N*-2-tolylbenzimidoyl)sulphimide (1b) were prepared as previously reported.[3]

SS-*Dimethyl*-N-(*2-pyridyl*)*sulphimide* (2a). 2-Aminopyridine (9.4 g, 0.10 mol) and dimethyl sulphide (6.8 g, 0.11 mol) were dissolved in dry dichloromethane (100 ml) and the solution was cooled to −20 °C. *N*-Chlorosuccinimide (13.3 g, 0.10 ml) in dichloromethane (150 ml) was added dropwise during 30 min. The mixture was stirred for 1 h at −20 °C and for 0.5 h at room temperature; it was then shaken with an excess of aqueous sodium hydroxide and water, dried, and evaporated to leave the sulphimide (13.4 g, 87%) as an oil, δ($CDCl_3$) 2.78 (6 H), 6.4—6.8 (2 H, m), 7.2—7.5 (2 H, m), and 8.0—8.1 (1 H, m). It was characterised as its *picrate*, m.p. 127—130° (from acetone) (Found: C, 40.9; H, 3.5; N, 18.2. $C_{13}H_{13}N_5O_7S$ requires C, 40.7; H, 3.4; N, 18.3%).

The following sulphimides were prepared in an analogous way: SS-*Dimethyl*-N-(*3-methyl-2-pyridyl*)*sulphimide* (2b) (76%), oil; δ($CDCl_3$) 2.20 (3 H), 2.72 (6 H), 6.3—6.7 (1 H, m), 7.1—7.4 (1 H, m), and 7.9—8.1 (1 H, m); *picrate*, m.p. 185° (decomp.) (from acetone) (Found: C, 42.2; H, 3.8; N, 17.6. $C_{14}H_{15}N_5O_7S$ requires C, 42.3; H, 3.8; N, 17.6%); SS-*dimethyl*-N-(*6-methyl-2-pyridyl*)*sulphimide* (2c) (85%), oil; δ($CDCl_3$) 2.31 (3 H), 2.63 (6 H), 6.2—6.7 (2 H, m), and 7.1—7.4 (1 H, m); *picrate*, m.p. 136° (from acetone) (Found: C, 42.4; H, 3.9; N, 17.7%).

A similar reaction performed in tetrahydrofuran gave SS-*dimethyl*-N-*pyrazinylsulphimide* (3) (54%), oil; δ($CDCl_3$) 2.75 (6 H), 7.65—7.75 (1 H, m), 7.80—7.95 (1 H, m), and 8.05—8.15 (1 H, m); *picrate*, m.p. 148—150° (from acetone) (Found: C, 37.8; H, 3.2; N, 21.9. $C_{12}H_{12}N_6O_7S$ requires C, 37.5; H, 3.1; N, 21.9%).

SS-*Dimethyl*-N-*pyrimidin-2-ylsulphimide* (4a). Freshly prepared t-butyl hypochlorite (9.26 g, 0.085 mol) in dry dichloromethane (50 ml) was added dropwise over 0.5 h to a solution of 2-aminopyrimidine (8.00 g, 0.084 mol) in dry dichloromethane (100 ml) at −60 °C. After a further 20 min, dimethyl sulphide (7.00 g, 0.113 mol) in dichloromethane (20 ml) was added. The solution was stirred for 0.5 h at −60 °C and sodium methoxide [from sodium (1.93 g, 0.084 mol) in methanol (30 ml)] was added. After a further 0.5 h at −60 °C the mixture was allowed to warm to room temperature; it was washed with water and dried; evaporation left a semi-crystalline oil. Crystallisation from ether–petroleum at −78 °C gave the sulphimide (3.92 g, 33%) as a hygroscopic solid; δ($CDCl_3$) 2.75 (6 H), 6.3—6.7 (1 H, m), and 8.2—8.4 (2 H, m). The sulphimide was stored at −10 °C and was used in subsequent experiments without further characterisation.

The following sulphimides were prepared in a similar way: SS-*dimethyl*-N-(*4-methylpyrimidin-2-yl*)*sulphimide* (4b), δ($CDCl_3$) 2.32 (3 H), 2.74 (6 H), 6.42 (1 H, d, *J* 10 Hz), and 8.20 (1 H, d, *J* 10 Hz); and SS-*dimethyl*-N-(*4,6-dimethylpyrimidin-2-yl*)*sulphimide* (4c), δ($CDCl_3$) 2.26 (6 H), 2.72 (6 H), and 6.27 (1 H).

Preparation of Triazole N-*Oxides.*—*Method A.* (a) *Amidoximes.* The appropriate amine was converted, by acylation and reaction of the amide with phosphorus pentasulphide, into the corresponding thioamide. The thioamide (0.01 mol) was added to a solution of hydroxylamine (0.01 mol) (generated from the hydrochloride *in situ*) in ethanol and the solution was then heated under reflux for 5 h, or until evolution of hydrogen sulphide ceased. The solvent was removed and the residue was extracted with dichloromethane to yield the crude amidoxime, which was recrystallised from ethanol. The following amidoximes were prepared in this way: N-(*6-methyl-2-pyridyl*)*benzamide oxime* (9a), m.p. 157—158° (from ethanol) (Found: C, 68.8; H, 5.9; N, 18.5. $C_{13}H_{13}N_3O$ requires C, 68.7; H, 5.7; N, 18.5%), prepared (49% overall) from 2-benzamido-6-methylpyridine [this *amide* had m.p. 79—80° (from ethanol) (Found: C, 73.5; H, 5.7; N, 13.4. $C_{13}H_{12}N_2O$ requires C, 73.6; H, 5.7; N, 13.2%)]; N-(*2-pyridyl*)-*4-toluamide oxime* (9b), m.p. 205—206° (Found: C, 68.2; H, 5.9; N, 18.6), prepared (50% overall) from 2-(4-toluamido)pyridine; N-(*3-methyl-2-pyridyl*)-*4-toluamide oxime* (9c), m.p. 193—195° (from ethanol) (Found: C, 69.8; H, 6.4; N, 17.4. $C_{14}H_{15}N_3O$ requires C, 69.7; H, 6.2; N, 17.4%), prepared (45% overall) from 3-methyl-2-(4-toluamido)pyridine;[8] N-(*6-methyl-2-pyridyl*)-*4-toluamide oxime* (9d), m.p. 215—216° (from ethanol) (Found: C, 69.4; H, 6.1; N, 17.3%), prepared (70% overall) from 6-methyl-2-(4-toluamido)pyridine [this *amide* had m.p. 118—120° (from benzene–hexane) (Found: C, 74.2; H, 6.2; N, 12.4%. $C_{14}H_{14}N_2O$ requires C, 74.3; H, 6.2; N, 12.4%)].

(b) *Oxidation of amidoximes.* (i) Lead tetra-acetate (443 mg, 1.0 mmol) was added to a solution of *N*-(6-methyl-2-pyridyl)benzamide oxime (9a) (227 mg, 1.0 mmol) in dry dichloromethane (20 ml) at −20 °C under nitrogen. The mixture was allowed to warm to room temperature and was stirred for a further 0.5 h; it was then washed with water and the organic layer was dried and evaporated. The crude product was crystallised to give *5-methyl-2-phenyl-1,2,4-triazolo*[1,5-a]*pyridine* 3-*oxide* (6d) (146 mg, 65%), m.p. 125° (from ethanol) (Found: C, 69.4; H, 4.9; N, 18.9. $C_{13}H_{11}N_3O$ requires C, 69.3; H, 4.9; N, 18.7%); $\nu_{max.}$ (K Br) 1 437 and 1 218 cm^{-1}; δ (100 MHz; $CDCl_3$) 3.30 (3 H), 6.57 (1 H, d, *J* 7 Hz H-6), 7.1—7.6 (5 H, m), and 8.6—8.75 (2 H, m); *m/e* 225 (M^+), 209, and 195.

(ii) By the method described in (i), *N*-(2-pyridyl)-4-toluamide oxime (9b) (76 mg, 0.33 mmol) and lead tetra-acetate (148 mg, 0.33 mmol) gave 2-(*4-tolyl*)-1,2,*4-triazolo*-[1,5-a]*pyridine* 3-*oxide* (6a) (62 mg, 81%), m.p. 163—164° (from dichloromethane–pentane) (Found: C, 69.1; H, 4.8; N, 18.9%); δ (100 MHz; $CDCl_3$) 2.41 (3 H), 7.0—7.8 (5 H, m), 8.61 (2 H, d, *J* 8.5 Hz), and 8.69 (1 H, m); *m/e* 225 (M^+), 209, and 195 (M^+ — NO, base); *m** (225 ⟶ 195) 169.

[8] R. B. Moffett, A. Robert, and L. L. Skaletzky, *J. Medicin. Chem.*, 1971, **14**, 963.

(iii) By the same procedure, *N*-(3-methyl-2-pyridyl)-4-toluamide oxime (9c) (241 mg, 1.0 mmol) and lead tetra-acetate (443 mg, 1.0 mmol) gave 8-*methyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyridine* 3-*oxide* (6 h) (179 mg, 75%), m.p. 139° (from ethanol) (Found: C, 70.0; H, 5.6; N, 17.8. $C_{14}H_{13}N_3O$ requires C, 70.3; H, 5.5; N, 17.6%); δ($CDCl_3$) 2.21 (3 H), 2.57 (3 H), 6.5—6.8 (2 H, m), 7.2—7.4 (4 H, m), and 8.1—8.3 (1 H, m).

(iv) *N*-(6-Methyl-2-pyridyl)-4-toluamide oxime (9d) (241 mg, 1.0 mmol) and lead tetra-acetate (443 mg, 1.0 mmol) similarly gave 5-*methyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyridine* 3-*oxide* (6e) (140 mg, 52%), m.p. 146—148° (from ethanol) (Found: C, 70.15; H, 5.6; N, 17.8%); $\nu_{max.}$ (KBr) 1 440 and 1 220 cm^{-1}; δ (100 MHz; $CDCl_3$) 2.41 (3 H), 3.30 (3 H), 6.57 (1 H, d, *J* 7 Hz, H-6), 7.00—7.50 (4 H, m), and 8.55 (2 H, d, *J* 8.5 Hz); *m/e* 239 (M^+), 233, and 209 (M^+ —NO); *m** (239 ⟶ 209) 182.7.

Method B. Reaction of sulphimides with nitrile oxides. (a) *With* 4-*toluonitrile oxide. General procedure.* The sulphimide (2 mmol) in dichloromethane (20 ml) was added to a solution of 4-toluonitrile oxide [prepared from 4-methylbenzohydroximoyl chloride (2 mmol) and triethylamine] in ether (15 ml) at room temperature. After 20 h the mixture was evaporated to leave a solid residue of the triazole *N*-oxide, which was purified by crystallisation.

(i) *SS*-Dimethyl-*N*-(2-pyridyl)sulphimide and 4-toluonitrile oxide gave 2-(4-tolyl)-1,2,4-triazolo[1,5-*a*]pyridine 3-oxide (6a) (77%), m.p. 161—162 °C (from dichloromethane–pentane), identical with that formed by oxidation of the amidoxime (9b).

(ii) *SS*-Dimethyl-*N*-(6-methyl-2-pyridyl)sulphimide and 4-toluonitrile oxide gave 5-methyl-2-(4-tolyl)-1,2,4-triazolo[1,5-*a*]pyridine 3-oxide (6e) (74%), m.p. 146—148° (from ethanol), identical with that formed by oxidation of the amidoxime (9d).

(iii) *SS*-Dimethyl-*N*-pyrimidin-2-ylsulphimide and 4-toluonitrile oxide gave 2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyrimidine* 1-*oxide* (8a) (56%), m.p. 204—206° (decomp.) (from dichloromethane–hexane) (Found: C, 63.45; H, 4.45; N, 24.85. $C_{12}H_{10}N_4O$ requires C, 63.7; H, 4.5; N, 24.8%); δ($CDCl_3$) 2.47 (3 H), 7.1—7.5 (3 H, m), and 8.6—9.1 (4 H, m); *m/e* 226 (M^+), 210, and 196 (M^+ — NO, base).

(iv) *SS*-Dimethyl-*N*-(4-methylpyrimidin-2-yl)sulphimide and 4-toluonitrile oxide gave 5-*methyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyrimidine* 1-*oxide* (8b) (50%), m.p. 217° (decomp.) (from ethanol) (Found: C, 64.8; H, 5.2; N, 23.6. $C_{13}H_{12}N_4O$ requires C, 65.0; H, 5.0; N, 23.3%); δ($CDCl_3$) 2.45 (3 H), 2.75 (3 H), 7.00 (1 H, d, *J* 8 Hz), 7.31 (2 H, d, *J* 9 Hz), 8.58 (2 H, d, *J* 9 Hz), and 8.70 (1 H, d, *J* 8 Hz).

(v) *SS*-Dimethyl-*N*-(4,6-dimethylpyrimidin-2-yl)sulphimide and 4-toluonitrile oxide gave 5,7-*dimethyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyrimidine* 1-*oxide* (8c) (44%), m.p. 184—185° (from ethanol) (Found: C, 65.8; H, 5.5; N, 22.0. $C_{14}H_{14}N_4O$ requires C, 66.1; H, 5.55; N, 22.0%); δ($CDCl_3$) 2.43 (3 H), 2.55 (3 H), 3.24 (3 H), 6.48 (1 H), 7.30 (2 H, d, *J* 8.5 Hz), and 8.56 (2 H, d, *J* 8.5 Hz).

(vi) *SS*-Dimethyl-*N*-(*N*-phenylbenzimidoyl)sulphimide and 4-toluonitrile oxide gave 1,5-*diphenyl*-3-(4-*tolyl*)-1H-1,2,-4-*triazole* 2-*oxide* (5b) (20%), m.p. 252—254° (from dichloromethane–pentane) (Found: *m/e* 327.1380. $C_{21}H_{17}N_3O$ requires *M*, 327.1372); δ($CDCl_3$) 2.43 (3 H), 7.1—7.7 (12 H, m), and 8.4—8.6 (2 H, m); *m/e* 327, 311, 208, and 180 (base); *m** (311 ⟶ 208) 139.1.

(vii) *SS*-Dimethyl-*N*-(*N*-2-tolylbenzimidoyl)sulphimide and 4-toluonitrile oxide gave 5-*phenyl*-1-(2-*tolyl*)-3-(4-*tolyl*)-1H-1,2,4-*triazole* 2-*oxide* (5c) (45%), m.p. 190° (from ethanol) (Found: C, 77.0; H, 5.7; N, 12.3. $C_{22}H_{19}N_3O$ requires C, 77.4; H, 5.6; N, 12.3%); δ($CDCl_3$) 2.20 (3 H), 2.45 (3 H), 7.2—7.7 (11 H, m), and 8.5—8.6 (2 H, m); *m/e* 341, 325, and and 194 (base).

(b) *With benzonitrile oxide.* (i) *SS*-Dimethyl-*N*-(*N*-phenylbenzimidoyl)sulphimide (256 mg, 1 mmol) and triethylamine (101 mg, 1 mmol) were dissolved in dry dichloromethane (20 ml). Benzohydroximoyl chloride (155 mg, 1 mmol) in dichloromethane (10 ml) was added dropwise at 0 °C. After 22 h at room temperature the mixture was evaporated; layer chromatography (silica; chloroform–acetone, 9 : 1) gave 1,3,5-*triphenyl*-1H-1,2,4-*triazole* 2-*oxide* (5a) (90 mg, 29%), m.p. 249—252° (from dichloromethane–pentane) (Found: *m/e*, 313.1215. $C_{20}H_{15}N_3O$ requires M, 313.1215); δ($CDCl_3$) 7.1—7.7 (13 H, m), and 8.8 (2 H, m); *m/e* 313, 297, 194, and 180 (base).

(ii) *SS*-Dimethyl-*N*-(6-methyl-2-pyridyl)sulphimide (0.504 g, 3 mmol) and benzonitrile oxide generated from α-chlorobenzaldoxime (0.465 g, 3 mmol) and triethylamine (300 mg) gave 5-methyl-2-phenyl-1,2,4-triazolo[1,5-*a*]pyridine 3-oxide (6d) (0.459 g, 68%), m.p. 125 ° (from ethanol), identical with that prepared by oxidation of the amidoxime (9a).

(c) *With ethyl cyanoformate* N-*oxide. General procedure.* Ethyl chloroglyoxylate oxime [9] (1.3 mmol) in dichloromethane (20 ml) was added dropwise to the sulphimide (1 mmol) and triethylamine (1.3 mmol) in dichloromethane (20 ml) at —20 °C. The mixture was allowed to attain room temperature; it was stirred for a further 0.5 h and washed with water. The organic solution was dried and evaporated; the residue was then triturated with cold ether to remove the dimer of the nitrile oxide, and the ether-insoluble material was crystallised.

(i) *SS*-Dimethyl-*N*-(2-pyridyl)sulphimide and ethyl cyanoformate *N*-oxide gave *ethyl* 1,2,4-*triazolo*[1,5-a]*pyridine*-2-*carboxylate* 3-*oxide* (6b) (63%), m.p. 143—144° (from ethanol) (Found: C, 52.5; H, 4.5; N, 20.6. $C_9H_9N_3O_3$ requires C, 52.2; H, 4.4; N, 20.3%); δ($CDCl_3$) 1.48 (3 H, t, *J* 7 Hz), 4.58 (2 H, q, *J* 7 Hz), 7.1—7.4 (1 H, m), 7.50—7.85 (2 H, m), and 8.71 (1 H, dd, *J* 7 and 1 Hz).

(ii) *SS*-Dimethyl-*N*-(3-methyl-2-pyridyl)sulphimide and ethyl cyanoformate *N*-oxide gave *ethyl* 8-*methyl*-1,2,4-*triazolo*[1,5-a]*pyridine*-2-*carboxylate* 3-*oxide* (6j) (39%), m.p. 108° (from ethanol) (Found: C, 53.9; H, 5.0; N, 19.2. $C_{10}H_{11}N_3O_3$ requires C, 54.3; H, 5.0; N, 19.0%); δ($CDCl_3$) 1.64 (3 H, t, *J* 7 Hz), 2.36 (3 H), 4.72 (2 H, q, *J* 7 Hz), 6.73 (1 H, dd, *J* 5 and 7 Hz), 7.45 (1 H, d, *J* 7 Hz), and 8.19 (1 H, d, *J* 5 Hz).

(iii) *SS*-Dimethyl-*N*-(6-methyl-2-pyridyl)sulphimide and ethyl cyanoformate *N*-oxide gave *ethyl* 5-*methyl*-1,2,4-*triazolo*[1,5-a]*pyridine*-2-*carboxylate* 3-*oxide* (6f) (55%), m.p. 115—117° (from ethanol) (Found: C, 54.0; H, 5.1; N, 18.7%); $\nu_{max.}$ (KBr) 1 718 (C=O) and 1 213 cm^{-1}; δ($CDCl_3$) 1.46 (3 H, t, *J* 7 Hz), 3.24 (3 H), 4.52 (2 H, q, *J* 7 Hz), 6.64 (1 H, d, *J* 7 Hz), and 7.20—7.55 (2 H, m); *m/e* 221 (M^+), 205, and 191 (M^+ — NO); *m** (221 ⟶ 191) 164.1.

(iv) *SS*-Dimethyl-*N*-pyrazinylsulphimide and ethyl cyanoformate *N*-oxide gave ethyl 1,2,4-*triazolo*[1,5-a]*pyrazine*-2-*carboxylate* 3-*oxide* (7) (31%), m.p. 166—168° (from ethanol) (Found: C, 45.75; H, 4.0; N, 26.4. $C_8H_8N_4O_3$ requires C, 46.15; H, 3.9; N, 26.9%); δ($CDCl_3$) 1.31 (3 H, t, *J* 7 Hz), 4.70 (2 H, q, *J* 7 Hz), and 7.50—7.80 (3 H, m); *m/e* 208 (M^+), 192, and 178 (M^+ — NO).

[9] G. S. Skinner, *J. Amer. Chem. Soc.*, 1924, **46**, 731.

(d) *With pyruvonitrile* N-*oxide*. To *SS*-dimethyl-*N*-(2-pyridyl)sulphimide (770 mg, 5 mmol) and triethylamine (500 mg) in dichloromethane (20 ml) at −20 °C was added 1-chloropyruvaldoxime [10] (620 mg, 5.1 mmol) in dichloromethane (10 ml) during 30 min. The mixture was allowed to warm to room temperature; it was then washed with water, dried, and evaporated. This gave 2-*acetyl*-1,2,4-*triazolo*-[1,5-a]*pyridine* 3-*oxide* (6c) (412 mg, 47%), m.p. 127—128° (from ethanol) (Found: C, 54.0; H, 3.9; N, 23.5. $C_8H_7N_3O_2$ requires C, 54.2; H, 4.0; N, 23.7%); δ($CDCl_3$) 2.78 (3 H), 6.45—6.85 (2 H, m), 7.35—7.72 (1 H, m), and 8.00—8.20 (1 H, m).

(e) *With benzoyl cyanide* N-*oxide*. *SS*-Dimethyl-*N*-(6-methyl-2-pyridyl)sulphimide (0.168 g, 1.0 mmol) and triethylamine (0.1 g) were stirred in dichloromethane (15 ml) at −20 °C and phenylglyoxylyl chloride oxime [11] (0.183 g, 1.0 mmol) in dichloromethane (5 ml) was added dropwise. After 0.5 h the mixture was allowed to attain room temperature. Layer chromatography gave 2-*benzoyl*-5-*methyl*-1,2,4-*triazolo*[1,5-a]*pyridine* 3-*oxide* (6g) (0.106 g, 42%), m.p. 109—111° (from ethanol) (Found: C, 66.7; H, 4.35; N, 16.6. $C_{14}H_{11}N_3O_2$ requires C, 66.4; H, 4.4; N, 16.6%); δ($CDCl_3$) 3.30 (3 H), 6.56 (1 H, d, *J* 7 Hz), 7.10—7.60 (6 H, m), and 8.18—8.35 (2 H, m); *m/e* (no M^+) 237 ($M^+ - 16$), 149, and 105 (base).

Deoxygenation of Triazole N-*Oxides with Phosphorus Trichloride. General Procedure*.—The triazole *N*-oxide (0.05 mmol), freshly distilled phosphorus trichloride (1.0 mmol), and dry chloroform (5 ml) were mixed at room temperature. The solution was set aside for 5 h and ice–water was then added. The organic phase was dried and evaporated; the residue was then crystallised.

(*a*) 2-(4-Tolyl)-1,2,4-triazolo[1,5-*a*]pyridine 3-oxide (6a) gave 2-(4-tolyl)-1,2,4-triazolo[1,5-*a*]pyridine (90%), m.p. 168—169° (lit.,[6] 173°); mixed m.p. with authentic specimen, 168—169°.

(*b*) Ethyl 1,2,4-triazolo[1,5-*a*]pyridine-2-carboxylate 3-oxide (6b) gave *ethyl* 1,2,4-*triazolo*[1,5-a]*pyridine* 2-*carboxylate* (85%), m.p. 136—138° (from ethanol) (Found: C, 56.4; H, 4.8; N, 22.25. $C_9H_9N_3O_2$ requires C, 56.5; H, 4.7; N, 22.0%).

(*c*) 2-(4-Tolyl)-1,2,4-triazolo[1,5-*a*]pyrimidine 1-oxide (8a) gave 2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyrimidine* (92%), m.p. 217—218° (from chloroform–pentane) (Found: C, 68.3; H, H, 4.8; N, 26.65. $C_{12}H_{10}N_4$ requires C, 68.6; H, 4.8; N, 26.65%).

(*d*) 1,3,5-Triphenyl-1,2,4-triazole 2-oxide (5a) (27 mg, 0.09 mmol) and phosphorus trichloride (27 mg, 0.20 mmol), heated under reflux in chloroform for 2 h, gave 1,3,5-triphenyl-1,2,4-triazole [5] (25 mg, 100%), m.p. and mixed m.p. 104—105° (from ether–hexane).

(*e*) 1,5-Diphenyl-3-(4-tolyl)-1,2,4-triazole 2-oxide (5b) (18 mg, 0.055 mmol) and phosphorus trichloride (30 mg, 0.22 mmol) in chloroform (10 ml) gave, after 2 h at reflux, 1,5-*diphenyl*-3-(4-*tolyl*)-1,2,4-*triazole* (16 mg, 80%), m.p. 146—147° (from ether–hexane) (Found: *m/e*, 311.1394. $C_{21}H_{17}N_3$ requires *M*, 311.1422).

(*f*) 5-Phenyl-1-(2-tolyl)-3-(4-tolyl)-1,2,4-triazole 2-oxide (5c) (63 mg, 0.18 mmol) and phosphorus trichloride (30 mg, 0.22 mmol) in chloroform (15 ml) gave, after 1 h at reflux, 5-*phenyl*-1-(2-*tolyl*)-3-(4-*tolyl*)-1,2,4-*triazole* (55 mg, 91%), m.p. 120—121° (from ethanol) (Found: C, 80.7; H, 6.1; N, 12.9. $C_{22}H_{19}N_3$ requires C, 81.2; H, 5.9; N, 12.9%).

Thermal Deoxygenation.—(a) 5-*Methyl*-2-*phenyl*-1,2,4-*triazolo*[1,5-a]*pyridine* 3-*oxide*. The N-*oxide* (6d) (50 mg, 0.22 mmol) was heated under reflux in dry toluene. After 2 h, formation of the deoxygenated triazole could be detected by t.l.c., and after 7 h this was the major component. The solution was evaporated to leave a solid (38 mg) which by crystallisation gave 5-methyl-2-phenyl-1,2,4-triazolo[1,5-*a*]-pyridine (30 mg, 65%), m.p. 83—85° (from benzene) (lit.,[12] 84—85°).

In a second experiment the solution was concentrated to small bulk after heating and examined by g.l.c. (Pye Unicam 104; 5% OV 225). This showed peaks with retention times identical with those of benzyl alcohol and bibenzyl. A coupled mass spectrometer (Micromass MM12) gave a spectrum with *m/e* 108 (M^+) and a breakdown pattern identical with that of benzyl alcohol for the first peak, and *m/e* 182 (M^+, bibenzyl) for the second peak.

(b) 5-*Methyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]*pyridine* 3-*oxide*. The *N*-oxide (6e) (30 mg, 0.125 mmol) was heated under reflux in dry toluene. After 7 h, deoxygenation appeared to be almost complete (t.l.c.). A specimen of the solution was examined by g.l.c.–mass spectrometry as in experiment (a); benzyl alcohol and bibenzyl were again detected. The solution was evaporated to leave a semi-solid residue which by layer chromatography gave a solid identified as 5-*methyl*-2-(4-*tolyl*)-1,2,4-*triazolo*[1,5-a]-*pyridine* (15 mg, 55%), m.p. 112—113° (from benzene–petroleum), *m/e* 209 (M^+), δ($CDCl_3$) 2.38 (6 H), 6.40—6.65 (1 H, m), 7.15—7.40 (4 H, m), and 8.40—8.60 (2 H, m). A specimen of the substance synthesised by a standard route [12] from 2-amino-6-methylpyridine and 4-methylbenzonitrile had m.p. 114—116° (from benzene–petroleum) and was identical (i.r., t.l.c.) with the product of deoxygenation.

Interception of α-(6-*Methyl*-2-*pyridylimino*)-α-*nitrosotolulene by Thebaine*.—*N*-(6-Methyl-2-pyridyl)-4-tolualdehyde-oxime (121 mg, 0.5 mmol) and thebaine (160 mg, 0.63 mmol) were dissolved in dichloromethane (30 ml). The solution was stirred under N_2 at −78 °C and lead tetra-acetate (222 mg, 0.5 mmol) was added during 20 min. The mixture was stirred for 1 h at −78 °C and was then allowed to reach room temperature. Layer chromatography (silica; acetone) gave the *thebaine adduct* (12) (189 mg, 71%), m.p. 92—95° (decomp.) (from dichloromethane–hexane) (Found: C, 72.0; H, 6.2. $C_{33}H_{34}N_4O_4$ requires C, 71.8; H, 6.5%); δ[$(CD_3)_2CO$] 4.39 (1 H, H on C-5), 4.68 (1 H, d, *J* 6.5 Hz, H on C-9), 6.03 (1 H, d, *J* 8.5 Hz, H on C-8), and 6.23 (1 H, d, *J* 8.5 Hz, H on C-7).

The adduct (12) (100 mg), heated in dry benzene under N_2 at 80 °C for 5 h, gave 5-methyl-2-(4-tolyl)-1,2,4-triazolo-[1,5-*a*]pyridine 3-oxide (6e) (36 mg, 87%), m.p. 147°, and thebaine (55 mg, 97%).

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