The Action of Cyanamide on 1,3,4-Oxadiazolium and Pyrylium Salts

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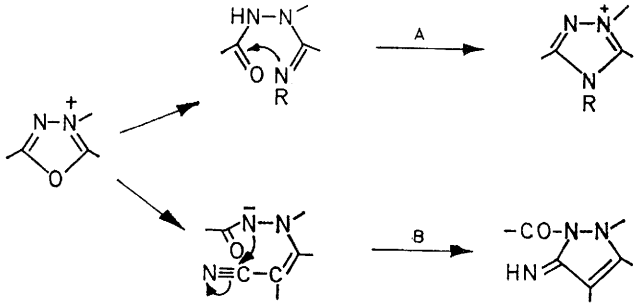
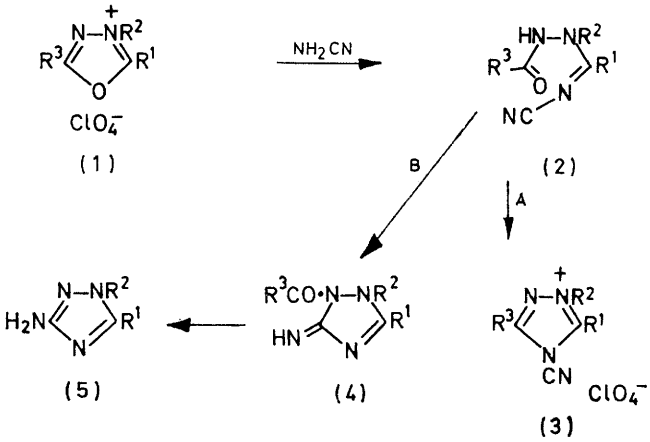
1,3,4-Oxadiazolium salts react with cyanamide in the presence of triethylamine to give good yields of 1-substituted 3-amino-1,2,4-triazoles. Four 2,4,6-triarylpyrylium perchlorates have been converted into 2-amino-3-aroyl-4,6-diarylpyridines in an analogous manner.

1,3,4-Oxadiazolium salts have been shown to undergo a variety of ring transformations when treated with nucleophilic reagents (Scheme 1). These reactions are of two types: in the first, one atom of the nucleophile is incorporated in the new ring and the cyclisation involves electrophilic attack by an amide carbonyl group. This type is observed in the conversion of oxadiazolium salts into *s*-triazolium [1] and 1,3,4-thiadiazolium salts [2] by reaction with primary amines and sodium sulphide, respectively (see path A). In the second group of reactions (path B) two atoms of the reagent serve to build the new ring and the cyclisation proceeds by nucleophilic attack of a nitrogen atom. The formation of pyrazoles from oxadiazolium salts and various reactive methylene compounds such as ethyl cyanoacetate [3] and the dimerisation of methyleneoxadiazolines to yield hydrazinopyrazoles [4] are of this type. The present report concerns the action of cyanamide on oxadiazolium salts, a reaction that was expected to give an adduct (2) which could in principle cyclise in either of the two ways just described to yield a cyanotriazolium salt (3) or an aminotriazole (5) (see Scheme 2).



SCHEME 1

Formation of triazolium salts was not observed when oxadiazolium salts were heated with cyanamide in acetic acid solution; an attempted reaction of the triphenyl compound (1a) resulted in a 58% recovery of starting material together with 37% of *NN'*-dibenzoylphenylhydrazine, its hydrolysis product. In the presence of ethanolic triethylamine, however, the known [5] 3-amino-1,5-diphenyl-*s*-triazole (5a) was produced. The same triazole was obtained from the methyldiphenyloxadiazolium salt (1b), showing that this reaction, like those mentioned previously,[1-3] involves initial attack at C-2 of the oxadiazolium ring as indicated in the Scheme. The acyl group is removed in the form of an ethyl ester; in one experiment involving a 3-phenyl-substituted oxadiazolium salt ethyl benzoate was



SCHEME 2

	R^1	R^2	R^3
a;	Ph	Ph	Ph
b;	Ph	Ph	Me
c;	Me	Ph	Ph
d;	Me	Me	Ph
e;	Me	*p*-$O_2N{\cdot}C_6H_4$	Me

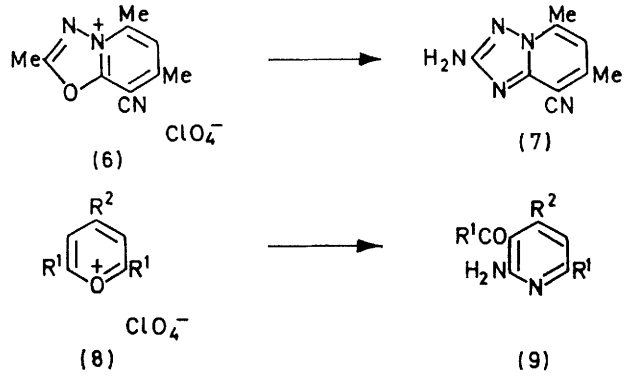
obtained as a by-product. Attempts to isolate the acyclic intermediate (2) or an aminoacyltriazoline (4) failed: the reaction of cyanamide with triphenyloxadiazolium perchlorate in acetonitrile resulted in a complex mixture from which no pure compound could be isolated.

3-Amino-*s*-triazoles have been obtained previously by acylation of aminoguanidines; [5] the present method uses readily available oxadiazolium salts [6] and we have briefly examined its scope. The triazoles (5c—e) were prepared from the perchlorates (1c—e), respectively; and the oxadiazolopyridinium salt (6) [6] gave the amino-*s*-triazolo[1,5-*a*]pyridine (7).

The smooth reaction of cyanamide with oxadiazolium salts suggested a study of the behaviour of the iso-π-electronic pyrylium salts towards the reagent. Ring transformations of pyrylium salts have been extensively explored [7] but their reaction with cyanamide does not appear to have been reported.

[1] G. V. Boyd and A. J. H. Summers, *J. Chem. Soc.* (*C*), 1971, 409.
[2] G. V. Boyd and A. J. H. Summers, *J. Chem. Soc.* (*C*), 1971, 2311.
[3] G. V. Boyd and S. R. Dando, *J. Chem. Soc.* (*C*), 1971, 225.
[4] G. V. Boyd and S. R. Dando, *J. Chem. Soc.* (*C*), 1971, 2314.
[5] G. Cuneo, *Gazzetta*, 1899, **29**, 89.
[6] G. V. Boyd and S. R. Dando, *J. Chem. Soc.* (*C*), 1970, 1397.
[7] K. Dimroth and K. H. Wolf in 'Newer Methods of Preparative Organic Chemistry,' ed. W. Foerst, Academic Press, New York, 1964, p. 357.

The 2,4,6-triarylpyrylium perchlorates (8a—d) readily yielded the 2-amino-3-aroylpyridines (9a—d), respectively, when treated with cyanamide in the presence of triethylamine. The structures of the products were assigned on the basis of analyses and of i.r. spectra,

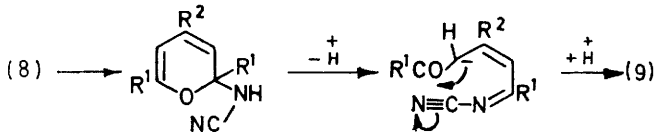


(6) (7)

(8) (9)

a; R^1 = Ph, R^2 = Ph
b; R^1 = Ph, R^2 = *p*-MeO·C_6H_4
c; R^1 = Ph, R^2 = *p*-ClC_6H_4
d; R^1 = *p*-MeC_6H_4, R^2 = Ph

which exhibit primary amine and ketone bands but lack nitrile absorptions. Attempts to extend the reaction to alkyl-substituted pyrylium salts (2,4,6-trimethyl-, 2-methyl-4,6-diphenyl-, and 2,4-diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyrylium perchlorates) and to 2,6-diphenylpyrylium perchlorate failed; intractable coloured mixtures resulted.



SCHEME 3

Although no intermediates could be isolated in this aminopyridine synthesis a mechanism can be suggested (Scheme 3) which is analogous to the type B oxadiazolium reaction except that the acyl group, being a *C*-acyl group, is retained in the product. This type of transformation, in which a reagent functions first as a nucleophile and then as an electrophile, is unusual in pyrylium chemistry; the closest analogy is the conversion of 2,4,6-triphenylpyrylium fluoroborate into ethyl 3-benzoyl-2-hydroxy-4,6-diphenylbenzoate and into 2-amino-3-benzoyl-4,6-diphenylbenzonitrile by diethyl malonate and malononitrile, respectively.[8]

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra refer to Nujol mulls. The preparation of 1,3,4-oxadiazolium salts has been described.[6]

Reaction of **1**,3,4-*Oxadiazolium Perchlorates with Cyanamide.*—Triphenyloxadiazolium perchlorate (1a) (4·0 g, 0·01 mol) was added to a solution of cyanamide (1·0 g, 2·4 mol. equiv.) and triethylamine (3·0 g, 3 mol. equiv.) in ethanol (20 ml). After 1 h the solution was poured into water and the precipitated 3-amino-1,5-diphenyl-1,2,4-triazole (5a) (2·0 g, 85%) was recrystallised from ethanol; m.p. 155° (lit.,[5] 156°), $\nu_{max.}$ 3475, 3300, 3200, 3160, 1627, and 1597 cm^{-1}. The same triazole was obtained in 80% yield from a similar reaction of 5-methyl-2,3-diphenyloxadiazolium perchlorate (1b) after refluxing overnight.

The solution obtained from 2-methyl-3,5-diphenyloxadiazolium perchlorate (1c) (3·37 g, 0·01 mol), cyanamide (1·0 g), triethylamine (3·0 g), and ethanol (20 ml) was heated under reflux overnight. The solution was evaporated and the residue triturated with ethanol to give 3-amino-5-methyl-1-phenyl-1,2,4-triazole (5c) (1·0 g, 57%), m.p. 183—185° (from ethanol) (lit.,[5] 186°), $\nu_{max.}$ 3320, 3185, 1650, and 1598 cm^{-1}. The filtrate was extracted with ether and the extract was washed with dilute hydrochloric acid and dried ($MgSO_4$). Removal of the ether and distillation of the residue gave ethyl benzoate, b.p. 205—210°, identified by its i.r. spectrum.

2,3-Dimethyl-5-phenyloxadiazolium perchlorate (1d) (2·75 g, 0·01 mol) similarly gave 3-*amino*-1,5-*dimethyl*-1,2,4-*triazole* (5d) (0·6 g, 54%), m.p. 210—212° (from ethanol), $\nu_{max.}$ 3330, 3180, and 1650 cm^{-1} (Found: C, 42·5; H, 7·3; N, 50·2. $C_4H_8N_4$ requires C, 42·85; H, 7·2; N, 49·95%).

The solution obtained by adding triethylamine (3·0 g) to a mixture of 2,5-dimethyl-3-*p*-nitrophenyloxadiazolium perchlorate (1e) (3·2 g, 0·01 mol), cyanamide (1·0 g), and ethanol (20 ml) deposited 3-*amino*-5-*methyl*-1-p-*nitrophenyl*-1,2,4-*triazole* (5e) (1·3 g, 60%) after 30 s as yellow needles, m.p. 214—216° (from ethanol), $\nu_{max.}$ 3340, 3310, 3180, 1644, 1610, 1600, and 1340 cm^{-1} (Found: C, 49·2; H, 4·3; N, 32·4. $C_9H_9N_5O_2$ requires C, 49·3; H, 4·15; N, 31·95%).

A mixture of 8-cyano-2,5,7-trimethyl-1,3,4-oxadiazolo-[3,2-*a*]pyridinium perchlorate (6) (2·88 g, 0·01 mol), cyanamide (1·0 g), triethylamine (3·0 g), and ethanol (20 ml) was heated under reflux overnight. The precipitated 2-*amino*-8-*cyano*-5,7-*dimethyl*-s-*triazolo*[1,5-a]*pyridine* (7) (1·7 g, 90%) crystallised from acetonitrile as prisms, m.p. 308—311°, $\nu_{max.}$ 3410, 3300, 3200, 2235, 1640, and 1630 cm^{-1} (Found: C, 57·9; H, 5·0; N, 37·7. $C_9H_9N_5$ requires C, 57·75; H, 4·85; N, 37·4%).

Reaction of Pyrylium Perchlorates with Cyanamide.—Triethylamine (1·5 g, 3 mol. equiv.) was added to a mixture of 2,4,6-triphenylpyrylium perchlorate (8a)[9] (2·05 g, 0·005 mol), cyanamide (0·5 g, 2·4 mol. equiv.), and ethanol (10 ml). 2-*Amino*-3-*benzoyl*-4,6-*diphenylpyridine* (9a) separated (0·5 g, 29%). It was collected next day, washed with ether, and recrystallised from ethanol to give yellow needles, m.p. 193·5—195·5°, $\nu_{max.}$ 3440, 3280, 3175, 1647, 1620, 1598, and 1571 cm^{-1} (Found: C, 82·2; H, 5·3; N, 8·0. $C_{24}H_{18}N_2O$ requires C, 82·25; H, 5·2; N, 8·0%).

A similar reaction employing 4-*p*-methoxyphenyl-2,6-diphenylpyrylium perchlorate (8b)[10] (2·2 g, 0·005 mol) gave a red solution which, on evaporation, yielded 2-*amino*-3-*benzoyl*-4-p-*methoxyphenyl*-6-*phenylpyridine* (9b) (0·6 g, 31·5%), yellow needles (from ethanol), m.p. 151—152·5°, $\nu_{max.}$ 3460, 3290, 3170, 1636, 1610, 1580, and 1565 cm^{-1} (Found: C, 78·6; H, 5·3; N, 7·3. $C_{25}H_{20}N_2O_2$ requires C, 78·9; H, 5·3; N, 7·35%).

[8] K. Dimroth and G. Neubauer, *Chem. Ber.*, 1959, **92**, 2046.
[9] W. Dilthey, *J. prakt. Chem.*, 1916, **94**, 53.
[10] W. Dilthey, G. Frode, and H. Koenen, *J. prakt. Chem.*, 1926, **114**, 153.

A mixture of 4-*p*-chlorophenyl-2,6-diphenylpyrylium perchlorate (8c) [11] (4·43 g, 0·01 mol), cyanamide (1·0 g), triethylamine (3·0 g), and acetonitrile (20 ml) was refluxed overnight. The solution was evaporated; the residual oil solidified in contact with warm aqueous ethanol to give yellow 2-*amino*-3-*benzoyl*-4-p-*chlorophenyl*-6-*phenylpyridine* (9c) (2·9 g, 75%), m.p. 175—177° (from ethanol), $\nu_{max.}$ 3465, 3310, 3200, 1640, 1620, 1597, 1572, and 1562 cm^{-1} (Found: C, 74·7; H, 4·3; N, 7·3. $C_{24}H_{17}ClN_2O$ requires C, 74·9; H, 4·45; N, 7·3%).

A similar reaction of 4-phenyl-2,6-di-*p*-tolylpyrylium perchlorate (8d) [12] (2·2 g, 0·005 mol) in boiling acetonitrile overnight gave yellow 2-*amino*-4-*phenyl*-3-p-*toluoyl*-6-p-*tolylpyridine* (9d) (1·3 g, 68·5%), m.p. 190—192° (from ethanol), $\nu_{max.}$ 3460, 3300, 3180, 1643, 1620, 1610, and 1570 cm^{-1} (Found: C, 82·3; H, 5·9; N, 7·4. $C_{26}H_{22}N_2O$ requires C, 82·5; H, 5·85; N, 7·4%).

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[11] K. Dimroth, C. Reichardt, T. Siepmann, and F. Bohlmann, *Annalen*, 1963, **661**, 1.

[12] H. E. Johnston and R. J. W. LeFèvre, *J. Chem. Soc.*, 1932, 2900.