A Directed Synthesis of Alkyl, Aryl, and Heteroaryl-*ONN*-azoxycyanides

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A variety of R-*ONN*-azoxycyanides can be prepared in high yield from the nitroso-derivatives with cyanamide and (diacetoxyiodo)benzene.

Until now only two methods for the regiospecific synthesis of R-*ONN*-azoxycyanides (**1**) (R = aryl) have been reported, namely the dehydration of the corresponding amides (**2**) using thionyl chloride in dimethylformamide,[1] and the oxidation of the parent arenediazocyanides (aryldiazenecarbonitriles) (**3**) (R = aryl) with 85% hydrogen peroxide in trifluoroacetic acid.[2]†

We now report a regiospecific synthesis of the azoxycyanides (**1**) (R = alkyl, aryl, and heteroaryl) from the appropriate nitroso-compounds and cyanamide–(diacetoxyiodo)benzene [equation (1)], a reagent able to give cyanonitrene adducts of sulphides, sulphoxides, phosphines, and olefins.[3]

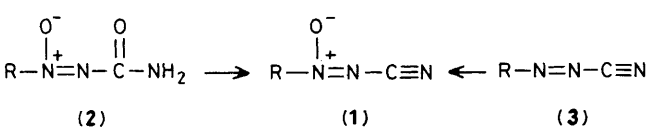
A mixture of the nitroso-derivative (3 mmol) and cyanamide (3.6 mmol) in methylene chloride (5 ml) was treated at 30 °C with (diacetoxyiodo)benzene (3.6 mmol) in portions over 15 min. Stirring was continued for a further 15 min and then the reaction mixture was washed with water. The organic phase, dried on magnesium sulphate, was evaporated and the residue chromatographed on a short silica gel column using chloroform–light petroleum (30 : 70) as eluant. Evaporation of the solvent afforded the pure azoxy-compounds (see Table 1).

The new compounds (**1a**) and (**1e**) gave satisfactory elemental analyses. Their n.m.r. and i.r. spectra were in agreement with the proposed structures. The other derivatives were identical (i.r. spectra, mixed m.p.) to the corresponding products previously described.[2]‡

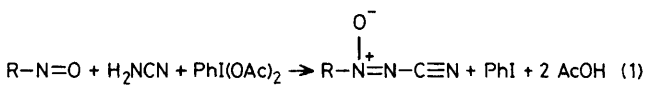
The mechanism of the reaction probably involves the intermediacy of cyanonitrene. The apparent inability of the reaction to discriminate nitroso groups bound to electron-withdrawing or electron-releasing moieties suggests that a transition state with little charge separation is involved.

These results offer new possibilities for obtaining analogues of calvatic acid (**1**, R = *p*-carboxyphenyl), an interesting antibiotic with the azoxycyanide structure.[1,4]

Preliminary experiments were made to determine whether the use of (diacetoxyiodo)benzene with appropriate nitrene precursors could be extended to obtain other azoxy-derivatives containing electron-withdrawing functions. Working under conditions similar to those described above (reaction time: 4 h) with nitrosobenzene and (diacetoxyiodo)benzene in the presence of benzensulphonamide and ethyl carbamate, the azoxysulphone [PhN(O)=N–SO_2Ph, m.p. 122 °C, lit.[5] 123 °C] and the azoxyester [PhN(O)=N–CO_2Et, m.p. 37 °C, lit.[6] 37 °C] were obtained, respectively, but in poor yields (*ca.* 30%).



(2) (1) (3)



† In the course of our studies on analogues of calvatic acid, we prepared, in poor yields, three aryl-*ONN*-azoxycyanides from the parent nitroso-derivatives and cyanogen azide [N_3(CN)], but this reaction was not optimized or further developed owing to the danger which is inherent in the use of cyanogen azide.[2]

‡ The structures of (**1b**) and (**1e**) were also confirmed by ^{15}N n.m.r. spectroscopy. The spectra were recorded in *ca.* 1 mol [$^2H_6$]acetone solutions with the addition of Cr(MeCOCHCOMe)$_3$ (*ca.* 0.05 mol). δ in p.p.m. relative to neat nitromethane: (**1b**), −122.9 (–C≡N), −109.3 (=N(+)–O), −22.0(=N–) (**1e**), −120.6(–C≡N), −104.7(N=N(+)–O(−)). −85.7 (N–pyridyl), −21.5 (=N–).

Table 1. Formation of the azoxycyanides (**1**).

Product	R	Description	M.p./°C (Solvent of recrystallization)	Yield, %
(**1a**)[a]	t-Butyl	White transparent plates	30 (Light petroleum, 40—60°C)	85
(**1b**)	Phenyl	Pale yellow prisms	66 (Lit.[2] 66) (Light petroleum, 40—60°C)	95
(**1c**)	*p*-Chlorophenyl	Pale yellow flakes	122 (Lit.[2] 122) (Light petroleum, 100—140°C)	95
(**1d**)[b]	*p*-(Dimethylamino)phenyl	Red needles	203 (Lit.[2] 203) (Chloroform)	95
(**1e**)	2-Pyridyl	Pale yellow plates	74—75 (Diethyl ether)	85

[a] Volatile. [b] As this product was sparingly soluble in methylene chloride, the reaction mixture was not washed with water, but directly evaporated under vacuum. The residue was chromatographed on a silica gel column using chloroform–light petroleum (50 : 50) as eluant.

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