A Novel Ring Cleavage of Pyrrolo[1,2-c]pyrimidines and Indolizines

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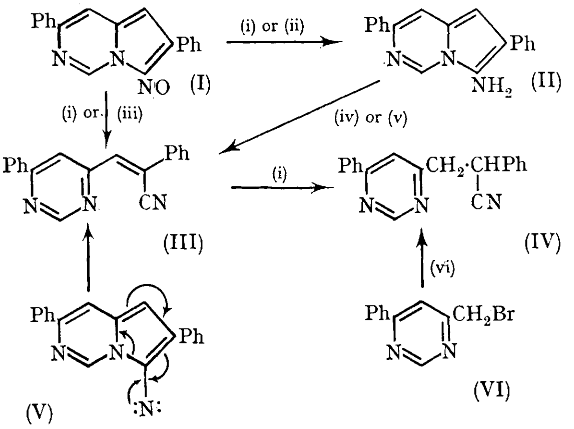
RING-OPENING REACTIONS of nitrogen bridgehead compounds have been initiated by both nucleophilic[1] and electrophilic[2] reagents. We now report a novel cleavage of the pyrrole ring in pyrrolo[1,2-*c*]pyrimidines and indolizines under mild, neutral conditions.



Reagents: (i) H_2, Pd–C; (ii) N_2H_4, Pd–C; (iii) cyclohexene, Pd–C; (iv) Pd–C; (v) $Pb(OAc)_4$; (vi) $PhCH_2$·CN, $NaNH_2$.

We have recently described the synthesis and electrophilic substitution reactions of certain pyrrolo[1,2-*c*]pyrimidines,[3] and, in an attempt to obtain the 7-amino-compounds, we have examined the reduction of the corresponding 7-nitroso-derivatives. Catalytic hydrogenation of 7-nitroso-3,6-diphenylpyrrolo[1,2-*c*] pyrimidine (I) gave the expected amine (II), but in poor yield, and two further products were also isolated. These were identified as 1-cyano-1-phenyl-2-(6-phenylpyrimidin-4-yl)ethylene (III) and 1-cyano-1-phenyl-2-(6-phenylpyrimidin-4-yl)ethane (IV).

A rapid hydrogenation of the 7-nitroso-compound (I) with hydrazine hydrate and palladium–charcoal gave solely 7-amino-3,6-diphenylpyrrolo-[1,2-*c*]pyrimidine (II) [*M* (mass spec.), 285; ν_{max} ($CHCl_3$) 3400 and 3325 (NH_2), and 1620 cm.$^{-1}$ (NH_2); τ 1·22d, *J* 1·3 c./sec. (1-H), 1·93—2·10 m and 2·29—2·60 m (10 phenyl protons), 2·65 d, *J* 1·3 c./sec. (4-H), 3·48 s (5-H), and 6·58 br s disappearing on deuteriation (NH_2)]. The sole product of a transfer hydrogenation of the 7-nitroso-compound (I) with cyclohexene and palladium–charcoal was the cyanoethylene (III) [*M* (mass spec.), 283; ν_{max} ($CHCl_3$) 2225 (C≡N), 1610 (C=C), and 910 cm.$^{-1}$ (=CH); τ 0·63 d, *J* 1·3 c./sec. (2-H), 1·65—1·92 m and 2·22—2·52 m (10 phenyl protons, 4-H and =C*H*)]. Treatment of the amine (II) with either palladium–charcoal in ethanol or with lead tetra-acetate gave the same nitrile (III). The cyanoethane (IV) [*M* (mass spec), 285; ν_{max} ($CHCl_3$) 2260 cm.$^{-1}$ (C≡N), τ 0·73 d, *J* 1·3 c./sec. (2-H), 1·87—2·03 m and 2·47—2·63 m (10 phenyl protons and 4-H), 5·43 t, *J* 7·5 c./sec. (C*H*–CH_2), 6·67d, *J* 7·5 c./sec. (CH–CH_2)] was prepared by catalytic reduction of the cyanoethylene (III) or by synthesis from 4-bromomethyl-6-phenylpyrimidine (VI) and benzyl cyanide.

The corresponding amines and nitriles have been obtained by similar reactions of 6-methyl-7-nitroso-3-phenylpyrrolo[1,2-*c*]pyrimidine and 3-nitroso-2-phenylindolizine.

We suggest that the reaction probably proceeds *via* the nitrene (V) which undergoes rapid bond isomerisations to yield the unsaturated nitrile. Similar types of cleavage of *o*-phenylenediamines with nickel peroxide[4] or 2-aminobenzotriazole with lead tetra-acetate[5] yielded *cis-cis*-muconitrile. The latter reaction has also been explained in terms of a nitrene intermediate.

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