

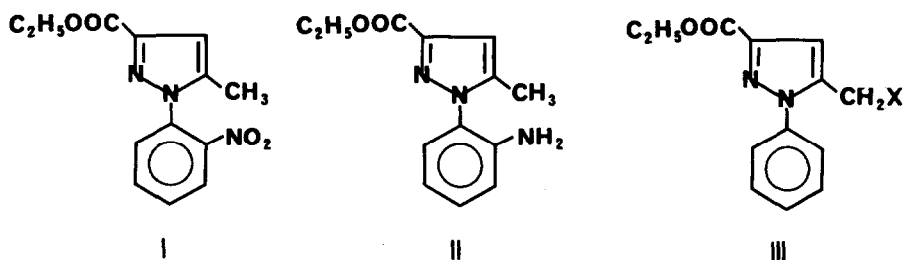
AN UNUSUAL DIAZONIUM SALT REACTION

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As part of a study of the synthetic potential of the Pschorr cyclisation in heterocyclic chemistry, the pyrazole derivative (II) was examined in an attempt to prepare the hitherto unreported pyrazolo[1,2-b]indole ring system. Ring-closure onto a methyl group had been observed once previously^{1,2}, when N-methylphthalimidine was isolated from thermal decomposition of diazonium salts derived from *o*-amino-N,N-dimethylbenzamide.



Condensation of *o*-nitrophenylhydrazine³ with ethyl acetoxyacetate gave a mixture of two isomers (c.f.³), from which the required nitro compound (I) was readily separated by fractional crystallisation. Catalytic hydrogenation afforded the amine (II) in almost quantitative yield.

As thermal decomposition^{1,2} of diazonium salts derived from (II) failed to yield recognisable products, attention was directed to the alternative copper-catalysed reaction.

The amine (II) was diazotised in 5% hydrochloric acid and the diazonium salt decomposed with copper powder⁴. Extraction of the crude product with chloroform, followed by chromatography on silica-gel, gave 5-chloromethyl-3-ethoxycarbonyl-1-phenylpyrazole (III, X=Cl), m.p. 64-65°, in 69% yield. Structural assignment followed from analytical data⁵ and the n.m.r. spectrum which showed signals at 7.5 δ (5H, s, aromatic), 7.0 δ (1H, s, H(C-4) in pyrazole ring), 4.5 δ (2H, s, CH₂), 4.4 δ (2H, q, COOCH₂CH₃) and 1.35 δ (3H, t, COOCH₂CH₃). No evidence for the expected ring-closed product could be found.

Similarly, when 5% hydrobromic acid was used as solvent for the reaction, the

corresponding bromomethyl derivative (III, X=Br), m.p. 80-81°, was obtained in 76% yield.

This unusual diazonium salt reaction represents a new route to halomethyl pyrazoles; the compounds described above undergo the normal reactions of alkyl halides, e.g., the amine (III, X=N(CH₃)₂), thiocyanate (III, X=SCN) and the nitrile (III, X=CN) were prepared by standard methods.

The mechanism of the reaction is presumed to initially involve elimination of the diazonium group as nitrogen with the formation of a phenyl radical coordinated with copper (probably as either a Cu^I or Cu^{II} species)^{6,7}. Hydrogen abstraction from the methyl group^{1,2,6} then occurs, followed by transfer of halogen already present as a ligand in the organo-copper intermediate, to form the halomethyl derivative.

Although ligand radical transfer of halogen to a site in the molecule other than the position vacated by the diazonium group is unprecedented, a similar reaction involving alcohol formation has been observed in a Pschorr reaction carried out in dilute sulphuric acid⁸. Identical treatment of the amine (II) failed to give any recognisable product. Moreover, copper-catalysed decomposition of the diazonium sulphate of (II) gave, not the expected alcohol (III, X=OH), but the dimer (III, X= 3-ethoxycarbonyl-1-phenyl-5-pyrazolyl-methyl), m.p. 203-204°, in 55% yield. Structural assignment was consistent with analytical data and the n.m.r. spectrum which showed signals at 7.15-7.55 δ (10H, m, aromatic), 6.63 δ (2H, s, H(C-4) of pyrazole rings), 4.4 δ (4H, q, COOCH₂CH₃), 2.9 δ (4H, s, CH₂) and 1.38 δ (6H, t, COOCH₂CH₃). Thus, in this case, it would appear that dimerisation, rather than ligand radical transfer, is the preferred reaction.

Further investigation of the mechanism of these diazonium salt reactions is continuing.

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