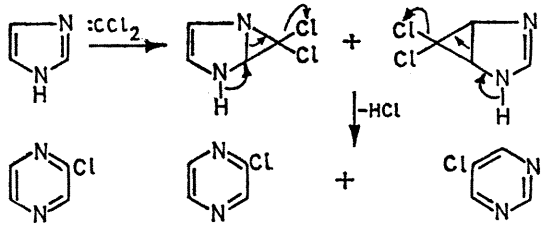
The Reaction of Imidazole with Dichlorocarbene in the Vapour Phase: a New Route to the Pyrimidine Ring System

By R. E. BUSBY, M. IQBAL, J. PARRICK, and C. J. G. SHAW*

(*Department of Chemistry, Brunel University, Woodlands Avenue, London*, W.3)

Summary Reaction of imidazole with dichlorocarbene at 550° gives a mixture of 5-chloropyrimidine and chloropyrazine (10 : 1).

RECENTLY we reported the preparation of 2- and 3-chloropyridine in high yield (86%) by the reaction of pyrrole with dichlorocarbene generated from $CHCl_3$ in the vapour phase.[1] Using essentially the same conditions, we have now studied the reaction between imidazole and dichlorocarbene. The best yields were obtained by introducing a solution of imidazole in $CHCl_3$ (5 M) into a stream of N_2, pre-heating the reactants at 350°, and then passing them through a vertically mounted Pyrex glass tube maintained at 550°. Unchanged imidazole (30%) was recovered and re-cycled, and a 33% yield† of ring-expanded products obtained. These were separated by preparative g.l.c. [7 ft. × $\frac{3}{8}$ in. glass column, 20% w/w Carbowax 20 M on Diatomite CAW (60—72 mesh), 100°] into 5-chloropyrimidine (30%) and chloropyrazine (3%).‡



Addition of dichlorocarbene to the C=C or C=N double bonds of imidazole followed by ring expansion would give 5-chloropyrimidine and chloropyrazine, respectively. It appears that the C=C double bond is more susceptible to attack by dichlorocarbene than the C=N double bond. This trend is in keeping with the work of Jones and Rees,[2] who treated 2,4,5-trimethylimidazole with dichlorocarbene, generated either under neutral conditions from the thermal decarboxylation of sodium trichloroacetate, or under basic conditions from $CHCl_3$ and EtONa. In each case only a single ring-expanded product, 5-chloro-2,4,6-trimethylpyrimidine (best yield: 12·4%), was obtained. This must arise from attack of dichlorocarbene on the 4,5-C=C double bond. No product arising from addition to the 2,3-C=N double bond could be detected.

We are investigating this type of selective reactivity of carbenes in other systems (benzimidazole, methylimidazoles, *etc.*), and preliminary results confirm our findings with imidazole.

5-Chloropyrimidine was reduced at atm. press. using a $Pd/BaSO_4$ catalyst in the presence of MgO.[3] The dehalogenated compound was separated (85%) and shown to be pyrimidine. It is thus possible to convert imidazole into pyrimidine in 28% overall yield by this method.

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† Based on imidazole changed.

‡ Structures confirmed by elemental analysis, i.r., u.v., n.m.r., and mass spectra.

[1] F. S. Baker, R. E. Busby, M. Iqbal, J. Parrick, and C. J. G. Shaw, *Chem. and Ind.*, 1969, 1344.

[2] R. L. Jones and C. W. Rees, *J. Chem. Soc.* (*C*), 1969, in the press. We thank Professor Rees for permission to quote his results prior to publication.

[3] B. Lythgoe and L. S. Raynor, *J. Chem. Soc.*, 1951, 2323.