LETTER TO THE EDITOR

The Reaction of Bases with Chloroform

SIR,—Klemperer and Warren[1] observed a reaction between certain alkaloids, including strychnine and brucine, with chloroform and concluded that the latter had reacted with the bases to form the corresponding quaternary dichloromethochlorides. Caws and Foster[2] found that the bases actually reacted with impurities in the chloroform and showed that small amounts of methylene chloride and bromochloromethane present in B.P. chloroform were responsible. Williams[3] has recently shown that other bases including pyrrolidine and piperidine also react with the methylene halides in chloroform and he gave a stereochemical explanation of the preferential reaction with the dihalogen compounds. There is still some doubt, however, whether chloroform free from methylene halides would react with these bases.

It appears rather unlikely that a reaction between strychnine and chloroform in which a white precipitate is visible after refluxing for an hour or two would have escaped notice until quite recently and it is possible that the reacting methylene compounds were not present in chloroform as manufactured years ago. A sample of chloroform produced some years ago proved difficult to find but eventually a number of ampoules were obtained with dates of manufacture between 1927 and 1941. These had been stored away from light and the only purification carried out was a simple distillation to remove a dyestuff which was present. This would not be sufficient to fractionate any impurities such as methylene halides. Two of these samples (dated 1936 and 1941) were refluxed with strychnine for nine hours and no reaction occurred, the solution remaining clear and bright and the strychnine recovered after removal of the solvent gave the same figure for titratable base in aqueous solution as did the untreated material. These results were confirmed by Dr. G. E. Foster in a personal communication.

Two samples of chloroform (dated 1936 and 1939) were examined by gas chromatography after a preliminary fractionation and there was no evidence of the presence of methylene chloride or of bromochloromethane. Samples of recently manufactured B.P. chloroform had been found to contain both these impurities.

A sample of chloroform prepared in the laboratory by the action of bleaching powder on acetone did not react with strychnine after refluxing for nine hours.

TABLE I

REACTION BETWEEN STRYCHNINE AND CHLOROFORM

0·3 g. strychnine refluxed with 35 ml. chloroform for 9 hours

Origin of chloroform	Appearance of solution after reflux	Free base after reaction per cent	Base reacted per cent
Manufactured A 1936	clear	98·5	nil
Manufactured A 1941	clear	98·0	nil
Manufactured A 1958	cloudy with precpt.	87·3 (6 hours reflux)	11·2
Manufactured B 1958	cloudy with precpt.	82·5	16·0
Prepared in laboratory bleaching powder method..	clear	98·5	nil
Prepared in laboratory bleaching powder method with potassium bromide present	clear	99·0	nil
	Assay of untreated strychnine	98·5	

A further sample prepared from bleaching powder to which had been added 1 per cent of potassium bromide also failed to react with strychnine. These results are shown in Table I.

When strychnine was refluxed with B.P. chloroform of recent origin which had been treated at the boiling point with bromine in a silica flask while irradiated with ultra-violet light for four hours 30 per cent of the strychnine reacted while only 17 per cent reacted with untreated chloroform under the same conditions. This can be explained by the conversion of methylene chloride to the more reactive bromo-compound[4].

It is concluded that strychnine does not react with chloroform made by the bleaching powder process even when bromine is present in appreciable quantities in the latter. Chloroform made by chlorination of methane or by the reduction of carbon tetrachloride would be expected to contain methylene chloride and if bromine is present possibly the bromochloride also. Since chloroform bleaching powder does not appear to contain these impurities it is likely to be the best material for use in the analysis of organic bases.

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REFERENCES

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2. Caws and Foster, *J. Pharm. Pharmacol.*, 1956, **8**, 790; 1957, **9**, 824.
3. Williams, *ibid.*, 1959, **11**, 400.
4. Huntress, *Organic Chlorine Compounds*, 1948, John Wiley, p. 526.