LIV.—*The Action of Alkyl Nitrates on Piperidine.*

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IN a previous paper (Addy and Macbeth, T., 1916, **109**, 754), attention was directed to the action of alkyl nitrites on bases of the pyridine type, and it was seen that the mixing of such compounds led to the formation of the nitrate of the base. As the nitrites were without action on secondary bases, such as piperidine, it seemed of interest to examine the effect of alkyl nitrates in such cases. The results obtained are now recorded.

A mixture of freshly distilled piperidine and *iso*amyl nitrate in a sealed tube will have separated after a few days into two layers. If special care is taken to dry the starting materials thoroughly, no such separation will take place, but after the lapse of three or four days the entire liquid mixture will have become filled with a mass of thin, lustrous plates. The crystals obtained in this way are very deliquescent and are readily soluble in water. They are soluble also in alcohol, but are insoluble in ether or benzene. Traces of water in the solvents are readily taken up by the crystals and they are thus converted into a liquid, from which it is difficult to obtain a solid product again. On this account the substance cannot be recrystallised from alcohol, and the most practical method of purification consists in repeatedly washing the crystals with ether (distilled over sodium) and subsequently drying them in a vacuum oven. The crystals purified in this way melt at 173–174°, and are found to be piperidine nitrate.

Assuming that a mixture of *iso*amyl nitrate and piperidine yields the nitrate of the base, it is possible that the reaction may follow either of two main courses, giving as a second product (a) β -methyl- Δ^2 -butylene (amylenes) or alternatively (b) amylpiperidine.

It may be stated that all the evidence is in favour of the second alternative, as no traces of unsaturated substances have been detected in any of the reactions. Substituted piperidines, on the other hand, have been isolated. This is in agreement with the results of previous work on the action of alkyl nitrates on ammonia. Thus, Juncadella (*Annalen*, 1859, **110**, 255; *Compt. rend.*, 1859, **48**, 342; *J. pr. Chem.*, 1859, [i], **77**) has shown that methyl and ethyl nitrates, when heated with ammonia for several days in a sealed tube at 100°, give good yields of methylamine and ethylamine

respectively. Lea (*Chem. News*, 1861, 4, 71, 88), and Wallach (*Ber.*, 1881, 14, 422) obtained similar results in the case of ammonia and other nitrates. The formation of substituted piperidines would thus appear to be part of a general reaction of alkyl nitrates on ammonia and partly substituted ammonias.

The nitrates employed in the present work included the ethyl, propyl, isopropyl, *n*-butyl, *tert*.-butyl, and *iso*amyl compounds. As some of the experiments were done on a comparatively small scale, the boiling points of the substituted bases were determined by the method described by Siwoloboff (*Ber.*, 1886, 19, 795), when only small quantities of liquid were available.

*iso*Amyl Nitrate and Piperidine.—This was the first case examined and from the mixture of these compounds very pure piperidine nitrate, melting at 173–174°, was obtained. On treatment with sodium hydroxide it liberated a base which gave a hydrochloride melting at 236° (piperidine hydrochloride melts at 237°). The residue gave the tests for sodium nitrate, and it would thus appear that the solid produced by the action of *iso*amyl nitrate on piperidine is the nitrate of the base. This view is supported by the results of analyses (Found: Nitritic N [nitrometer method] = 9.66; total N = 18.9. $C_5H_{11}N.HNO_3$ requires N = 18.91; nitritic N = 9.45 per cent.).

The results therefore agree with the values required for piperidine nitrate, but Cahours (*Quart. Journ. Chem. Soc.*, 1854, 6, 175) has described this compound as consisting of needle-shaped crystals prepared by the neutralisation of piperidine with dilute nitric acid, and subsequent concentration. It is evident that the substance described by us could not, on account of its deliquescence, be prepared by this method. All our attempts to prepare piperidine nitrate by neutralisation resulted in the formation of a deliquescent solid agreeing in properties with the substance obtained in the reaction of the base with *iso*amyl nitrate. The neutralisation method, however, does not yield nearly so pure a product.

After removal of the crystals of piperidine nitrate from the reaction mixture of *iso*amyl nitrate and the base, the liquid remaining was fractionally distilled. No distillate was obtained below 100°, and this points clearly to the fact that the reaction takes a course that does not involve the formation of amylene, as this boils at 33° and if present would have been detected in the distillation. A fraction was obtained distilling above 180°, but as considerable charring took place an alternative method of treatment was adopted. The liquid, after the removal of piperidine nitrate, was extracted several times with concentrated hydrochloric acid, and any bases present were thus separated from the excess of *iso*amyl nitrate.

On evaporation, a solid hydrochloride was obtained, which on analysis was found to consist largely of *iso*amylpiperidine hydrochloride (Found: Cl = 19.6. Calc., Cl = 19.1 per cent.). On treatment with sodium hydroxide, the hydrochloride liberates a base, which distils at 187—190°. The base gives a picrate on the addition of a solution of picric acid in ethyl acetate, and the recrystallised picrate melts at 134°. (*iso*Amylpiperidine, b. p. 186°, 188°; *iso*amylpiperidine picrate, m. p. 133°.) As these constants are in agreement with values recorded for *iso*amylpiperidine, it is evident that the base is the substituted piperidine required by the equation already given.

Ethyl Nitrate and Piperidine.—Two parts of piperidine were mixed with rather more than one part of ethyl nitrate and set aside in a closed tube. With thoroughly dry piperidine, the entire liquid was filled with crystals after three or four days at the ordinary temperature. The crystals, after having been separated from the liquid, were purified by the treatment already outlined, and identified as piperidine nitrate by analysis (Found: Nitritic N = 9.34 per cent.).

The liquid remaining after the removal of the piperidine nitrate was fractionally distilled and a final fraction was collected at 124—128°. On treatment with a concentrated solution of picric acid in ethyl acetate this fraction gave a yellow, crystalline picrate melting at 165—167°. Ethylpiperidine boils at 128°, and ethylpiperidine picrate melts at 163° or 167°, according to two different observations. The final fraction in the above distillation is, therefore, evidently ethylpiperidine.

Propyl Nitrate and Piperidine.—In this case also the separation of piperidine nitrate occurred in the usual way in the course of a few days. The filtrate was examined, but as considerable charring took place on distillation, the alternative process, extraction by hydrochloric acid, was adopted. The hydrochloride so obtained gave a free base which distilled at 148—149°. This yielded a picrate, melting at 108°, on treatment with a concentrated, aqueous solution of picric acid. Propylpiperidine boils at 149—150°, and propylpiperidine picrate melts at 108°.

Butyl Nitrate and Piperidine.—The reaction in this case proceeded normally, and the liquid separated from the piperidine nitrate was treated with acid as described in the preceding case. As no reference to butylpiperidine could be traced in the literature, the percentage of chlorine in the hydrochloride, and the amount of platinum in the platinichloride, m. p. 218°, of the base, were estimated (Found: Cl = 20.8. $C_5H_{10}N \cdot C_4H_9, HCl$ requires Cl = 20.1 per cent. Found: Pt = 27.3. $[C_5H_{10}N \cdot C_4H_9]_2, H_2PtCl_6$ requires Pt = 28.1

per cent.). The values obtained show that the base consists largely of butylpiperidine. On treatment of the hydrochloride with an alkali the base was liberated as an oil boiling at 170—172°.

In addition to the cases referred to above, similar results were obtained with *isopropyl* nitrate and *tert.*-butyl nitrate. In all the cases recorded the reaction was allowed to take place at the ordinary temperature, but the change can be accelerated by heating.

Ethyl Nitrate and Diethylamine.—It was thought desirable to extend the work and study the reaction in the case of bases other than piperidine; ethyl nitrate and diethylamine were examined accordingly. The reaction followed the usual course, and after three days the formation of crystals had occurred. The mixture was kept for a few more days to allow the reaction to proceed fully. The liquid was then drawn off from the crystals and examined. Treatment with hydrochloric acid extracted a base, which when liberated by sodium hydroxide distilled at 88° (triethylamine, b. p. 88—89°). The base was converted into the ferrocyanide, in which the percentage of ferric oxide was estimated (*Compt. rend.*, 1902, **134**, 901). Difficulty was experienced in preventing decomposition of the salt, but considering its nature the result was in fair agreement with the theoretical value (Found: $\text{Fe}_2\text{O}_3 = 36.5$. Calc., $\text{Fe}_2\text{O}_3 = 38.2$ per cent.). The crystals which separated from the mixture of the nitrate and the base were found to be diethylamine nitrate. This compound is not so deliquescent as piperidine nitrate, but its solubility in the various solvents is of a similar nature. It is soluble in alcohol and in water, insoluble in ether and in benzene. It was purified by solution in alcohol and precipitation by ether. The purified product melted at 100° (diethylamine nitrate, m. p. 99—100°). On treatment with sodium hydroxide a base was liberated which distilled at 53—55° (diethylamine, b. p. 55°). It is therefore evident that the reaction follows the general course, taking place according to the equation:

From the results outlined above, and the previous work on the action of alkyl nitrates on ammonia, it would appear that the reaction is a general one for the preparation of more highly substituted, aliphatic bases from ammonia or partly substituted ammonias. Solutions of diphenylamine gave no result, but this may probably be attributed to its weakly basic nature. The absence of any reaction in the case of pyridine, quinoline, and bases of this type is doubtless due to the fact that since a tertiary nitrogen atom is present in them there is no possibility of an interchange of the

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kind indicated in the typical equations of the reaction formulated above.

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