984. *Amine Oxidation. Part IV.*[1] *Reactions of Tertiary Amines with* N-*Bromosuccinimide: the Formation of Aldehydes and Secondary Amines.*

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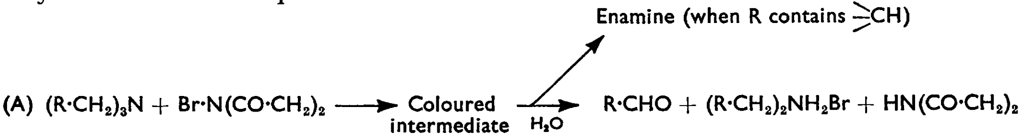
In appropriate experimental conditions, good yields of aldehydes and secondary amines can be obtained from tertiary amines and *N*-bromosuccinimide. The course of reaction can be followed by the appearance and disappearance of a coloured intermediate. An amine (triethylenediamine) in which inversion at nitrogen is prohibited gave a crystalline adduct.

In the previous paper[1] it was reported that *N*-bromosuccinimide effected the dehydrogenation of triethylamine because a blue dialkylaminovinyl-quinone was formed in the presence of a dichlorodimethoxy-*p*-benzoquinone. This led to the present more detailed investigation of the tertiary amine–bromo-imide reaction, the results of which for many amines may be summarised in equation A:



$$\text{(A)}\quad (\text{R·CH}_2)_3\text{N} + \text{Br·N(CO·CH}_2)_2 \longrightarrow \text{Coloured intermediate} \xrightarrow[\text{H}_2\text{O}]{} \text{R·CHO} + (\text{R·CH}_2)_2\text{NH}_2\text{Br} + \text{HN(CO·CH}_2)_2$$

$$\text{Coloured intermediate} \longrightarrow \text{Enamine (when R contains} \gt\text{CH)}$$

Nothing definite is known at present about the structures of the coloured intermediates or of their possible relation to conjugate acids, $\text{R·CH:N}^+(\text{CH}_2\text{R})_2$, from which the hydrolysis products or the enamines (where possible) could also be formed.

*Tri-*n*-propylamine.*—No attempt was made to isolate the (very reactive) enamine which, on the basis of the colour test,[1] can be formed by reaction of the amine with *N*-bromosuccinimide. Attention was focused instead on isolating the more stable products (propionaldehyde and di-*n*-propylamine) to be expected from hydrolysis of the enamine or a related intermediate. For this reason the reactions were carried out in dioxan containing 10% of water. On mixing solutions of the reactants a strong yellow colour appeared

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[1] Buckley, Dunstan, and Henbest, preceding paper.

which more slowly faded to give a colourless solution. During the fading the colour given in a starch–iodide test for " positive halogen " also diminished, becoming very faint as the solution became colourless. Propionaldehyde was obtained as its 2 : 4-dinitrophenylhydrazone in 63% yield and di-*n*-propylamine in over 80% yield (estimated by titration and by the isolation of the toluene-*p*-sulphonyl derivative).

Tribenzylamine.—Most of the reactions between this amine and *N*-bromosuccinimide were carried out in benzene with a view to attempt the isolation of the expected coloured intermediate (decomposition into an enamine being impossible in this case). Admixture of solutions of the reactants in benzene in an open flask produced a deep orange colour, which faded while dibenzylamine hydrobromide and succinimide were precipitated: under these conditions atmospheric moisture was responsible for the fading. From the final colourless mixture, benzaldehyde (85—90% as its 2 : 4-dinitrophenylhydrazone) and dibenzylamine (85%) were isolated. The aldehyde and the secondary amine were each obtained in 90% yields from a similar reaction in aqueous dioxan.

By conducting the reaction in benzene with the exclusion of water, the intermediate complex was obtained as a deep orange oil giving a positive starch–iodide test. The infrared spectrum of this product was similar to that of a mixture of the starting materials, although there were some changes in positions and intensities of the bands. Hydrolysis of the coloured oil gave benzaldehyde and dibenzylamine.

Benzyldimethylamine.—This was the only unsymmetrical amine studied: benzaldehyde (65%) was isolated after a reaction in benzene in an open flask. This yield shows that the choice of alkyl group oxidised is not random. The yield of benzaldehyde is similar to that obtained on oxidation of this amine with benzoyl peroxide.[1]

Triethylenediamine.—In an attempt to obtain a more stable intermediate, the reaction between triethylenediamine, $N[CH_2{\cdot}CH_2]_3{\cdot}N$, and *N*-bromosuccinimide was examined. When benzene was used as solvent, a colourless crystalline compound (~80%) separated rapidly which gave analyses for an adduct, $C_6H_{12}N_2,2(CH_2{\cdot}CO)_2NBr$. This, like the orange intermediate obtained from tribenzylamine, gave a positive starch–iodide test and gave an infrared spectrum similar to the combined spectra of its components. Whether the colourless product from the diamine and the orange oil from tribenzylamine represent (despite the difference in colour) analogous stages in the respective reactions, or whether the colourless product represents a stage in the general reaction preceding the formation of the usual coloured intermediate (its special geometry preventing the further change), cannot be decided with certainty at present.

By comparing our results with previous work,[2,3] it may be concluded that the most effective conversion of a tertiary amine into an aldehyde and a secondary amine can be achieved (*a*) when one mole of each reactant is used (cf. equation A), (*b*) when both reactants are in solution, thus helping to moderate the reaction, and (*c*) when water is present for the hydrolysis stage; the last factor is of greatest importance for aliphatic tertiary amines where the coloured intermediates can decompose to an enamine and thence give rise to other products.

In a previous brief study[3] of the triethylamine reaction, it was shown that the precipitate formed on addition of the solid bromo-imide (one mol.) to a solution of the amine (two mols.) in carbon tetrachloride at 0° was a mixture of triethylamine hydrobromide and succinimide. The reaction under these conditions can be written as:

$$2Et_3N + Br{\cdot}N(CO{\cdot}CH_2)_2 \longrightarrow Et_2N{\cdot}CH{:}CH_2 + Et_3NHBr + HN(CO{\cdot}CH_2)_2$$

the second molecule of triethylamine effectively taking up the molecule of hydrogen bromide from the enamine precursor. On this basis the quoted yields of hydrobromide and succinimide are 48% and 74% respectively. If some addition of bromo-imide to the enamine occurs, these yields become higher.

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[2] Cosgrove and Waters, *J.*, 1949, 907.
[3] Braude and Waight, *J.*, 1952, 1116.

In another investigation,[2] the solid bromo-imide was added to solutions of amines in a non-polar solvent, and water was afterwards added, giving low yields of aldehydes and secondary amines. The isolation of some glyoxal (as its bis-2 : 4-dinitro-osazone) from the triethylamine reaction is of interest, for it could clearly arise by further reaction of the bromo-imide with the enamine ($Et_2N{\cdot}CH{:}CH_2$) produced by decomposition of the coloured type of intermediate (cf. equation A), followed by unexceptional hydrolysis and oxidation during the isolation. The initial product, $(CH_2{\cdot}CO)_2N{\cdot}CH(NEt_2){\cdot}CH_2Br$, to be expected from the bromo-imide–enamine reaction would be analogous to those isolated [$(CH_2{\cdot}CO)_2N{\cdot}CH(OR){\cdot}CH_2Br$] on addition of the bromo-imide to vinyl ethers.[4]

EXPERIMENTAL

Purified materials were used. It is particularly important to remove acetal impurities from dioxan.

*Tri-*n*-propylamine.*—The amine (0·286 g., 0·002 mole) in dioxan (9 c.c.) and water (1 c.c.) was added to *N*-bromosuccinimide (0·356 g., 0·002 mole) in the same solvent mixture (10 c.c.) at 20°. A strong yellow colour developed immediately and soon began to fade. After 2 min. the solution was almost colourless and the starch–iodide test was only faintly positive and an excess of methanolic 2 : 4-dinitrophenylhydrazine sulphate reagent was then added. The derivative was isolated with benzene and chromatographed on bentonite–kieselguhr.[5] Elution with chloroform gave a small amount of a yellow compound, m. p. 132—136° (after many crystallisations from ethanol). Elution with chloroform–ethanol (19 : 1) gave propionaldehyde 2 : 4-dinitrophenylhydrazone (56, 65, 68%), m. p. and mixed m. p. 153—156° (from ethanol) (Found: C, 45·6; H, 4·0; N, 23·7. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·25; N, 23·5%).

For the estimation of amines another reaction mixture was partially evaporated under reduced pressure, treated with an excess of aqueous sodium carbonate solution, and distilled into an excess of 0·1N-hydrochloric acid which was finally back-titrated with standard alkali to pH 5: the total amine recovery was 98—99%. Di-*n*-propylamine hydrochloride was isolated from another experiment by evaporating the acid solution (containing the amine distillate) to dryness: crystallisation from acetone gave the hydrochloride, m. p. 268—269° (sealed tube) (Found: C, 52·2; H, 11·6; N, 10·7; Cl, 25·6. Calc. for $C_6H_{16}NCl$: C, 52·4; H, 11·6; N, 10·2; Cl, 25·8%). A similar procedure was used to estimate unchanged tertiary amine, except that toluene-*p*-sulphonyl chloride was added to the alkaline solution before the distillation into acid. Unchanged tri-*n*-propylamine (11%; average of two experiments) was obtained: obviously this could be decreased by using slightly more bromo-imide. The yield of di-*n*-propylamine was therefore 87%, and this was confirmed by ether-extraction of the residual mixture from the last distillation, crude *NN*-di-*n*-propyltoluene-*p*-sulphonamide being obtained in this yield. The pure *sulphonamide* had m. p. 31—31·5° (from ether–light petroleum) (Found: C, 61·1; H, 8·1; N, 5·7. $C_{13}H_{21}O_2NS$ requires C, 61·2; H, 8·25; N, 5·5%).

Tribenzylamine.—(a) *Reactions in benzene.* The amine (0·574 g., 0·002 mole) in benzene (5 c.c.) was added to a solution of *N*-bromosuccinimide (0·357 g., 0·002 mole) in the minimum amount of benzene. An intense orange colour developed rapidly, but within a few minutes this began to fade and a mixture of dibenzylamine hydrobromide and some succinimide began to be precipitated. When the reaction was complete (negative starch–iodide test), the mixture was filtered (see below) into a methanolic solution of 2 : 4-dinitrophenylhydrazine sulphate. The 2 : 4-dinitrophenylhydrazone was collected; a further small amount was isolated by addition of water and benzene to the mother-liquor and chromatography of the benzene-soluble material on a column of bentonite–kieselguhr. The yields of benzaldehyde derivative were 85—90%; after crystallisation from dioxan–ethyl acetate the m. p. and mixed m. p. was 243—244° (Found: C, 54·5; H, 3·6; N, 19·9. Calc. for $C_{13}H_{10}O_4N_4$: C, 54·55; H, 3·5; N, 19·6%). The precipitate from the reaction mixture consisted predominantly of dibenzylamine hydrobromide: crystallisation from ethanol–ether gave the pure hydrobromide, subliming at 254° (Found: C, 60·5; H, 5·75; N, 4·7; Br, 28·8. Calc. for $C_{14}H_{16}NBr$: C, 60·4; H, 5·75; N, 5·05; Br, 28·8%).

If the filtrate from the reaction mixture was evaporated to a small bulk and benzene–light

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[4] Paul and Tchelitcheff, *Compt. rend.*, 1953, **236**, 1968.

[5] Elvidge and Whalley, *Chem. and Ind.*, 1955, 589.

petroleum (1 : 1) was added, succinimide (+ some residual hydrobromide) was precipitated. The combined hydrobromide and succinimide precipitates were treated with ether and 0·2N-sodium hydroxide. The product from the ether extract was chromatographed on alumina. Elution with benzene–light petroleum (1 : 2) gave unchanged tribenzylamine (<2% from different experiments). Elution with ether gave dibenzylamine (85% yield), detected in the eluate (*a*) by universal indicator paper, and (*b*) by immediate production of a blue colour on treatment with a benzene solution of chloranil and acetaldehyde.[6] For general preparative purposes the partially evaporated reaction mixture can be treated with light petroleum to complete the separation of secondary amine hydrobromide (+ succinimide) which, after being washed with light petroleum, can be treated with alkali and the secondary amine then isolated with ether.

Addition of methanol (0·02 mole) to the amine solution before admixture with the bromo-imide caused the yields of benzaldehyde and dibenzylamine to fall to 51 and 63% respectively, and the yield of recovered tribenzylamine to change to 34%.

The reaction in benzene (see above) was also performed under dry nitrogen, and when the intense orange colour had developed the solution was evaporated under reduced pressure. During this operation an orange oil separated as a lower layer. On exposure to moist air this quickly began to change to a white solid (hydrobromide + succinimide), but by rapid manipulation it was possible to place some of the oil between rock-salt plates for determination of the infrared spectrum.

(b) *Reactions in dioxan.* These were carried out as described for benzene, except that a smaller quantity of solvent could be used to dissolve the bromo-imide: the same colour changes were observed during the reaction. With a 1 : 1 molar ratio of amine and bromo-imide, benzaldehyde 2 : 4-dinitrophenylhydrazone, dibenzylamine, and tribenzylamine were obtained in 90, 90, and 2% yield respectively, the reaction time being 5 hr. (solution then colourless).

In another experiment an amine : bromo-imide ratio of 1 : 2 was used. The solution then remained yellow for much longer and precipitation of hydrobromide was retarded. After 24 hr. benzaldehyde 2 : 4-dinitrobenzylhydrazone (74%) was isolated.

Reaction with Dimethylbenzylamine.—The amine (0·27 g., 0·002 mole) in benzene (10 c.c.) was added to a solution of the bromo-imide (0·356 g., 0·002 mole) in benzene (40 c.c.) at 20° in an open flask. A yellow colour developed rapidly which then faded slowly, but in this case very little hydrobromide crystallised. When the reaction was complete (negative starch–iodide test on colourless solution), benzaldehyde 2 : 4-dinitrophenylhydrazone (64, 66%) was isolated as before.

Reaction with Triethylenediamine.—A solution of *N*-bromosuccinimide (0·356 g., 0·002 mole) in benzene (15 c.c.) was added to the amine (0·112 g., 0·001 mole) in benzene (5 c.c.) at 20° in an open flask. Within a minute a colourless product began to be precipitated from the colourless solution. After 1·5 hr. the crystalline *adduct* (83%) was collected; it had m. p. 109—111° (decomp.) (Found: C, 36·9, 36·9; H, 4·35, 4·5; N, 11·9; Br, 34·3. $C_{14}H_{20}O_4N_4Br_2$ requires C, 35·9; H, 4·25; N, 12·0; Br, 34·2%). This compound did not crystallise without decomposition, even at low temperatures; it also decomposed slowly on storage at 0° *in vacuo* in the dark.

The filtrate from the preparation of the adduct gave a weak positive starch–iodide test, apparently owing to the slight solubility of the compound as the adduct itself gave a very strong positive test. The adduct gave no precipitate of silver bromide on addition to silver nitrate in dilute nitric acid. As far as such tests were concerned the properties of the adduct were qualitatively indistinguishable from those of *N*-bromosuccinimide. The same adduct (same tests given) was obtained (lower yield) when equimolar quantities of amine and bromo-imide were used in the preparation. The infrared spectrum of the adduct in Nujol showed peaks at 1732 (w), 1680 (s), 1310 (m), 1245 (w), 1195 (ms), 1060 (w), and 790 (m) cm.$^{-1}$. *N*-Bromosuccinimide under the same conditions gave peaks at 1762 (w), 1700 (s), 1330 (m), 1255 (w), 1188, 1172 (ms), and 818 (w) cm.$^{-1}$. The peak at 1060 cm.$^{-1}$ given by the adduct appears to be associated with the amine which also gives a band at this position.

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[6] Buckley, Henbest, and Slade, *J.*, 1957, 4891.