341. *The Mechanism of the Deamination of Amino-alcohols. Part II. Amino-alcohols derived from α-Aminopropiophenone Hydrochloride.*

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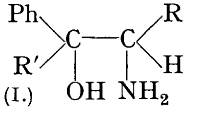
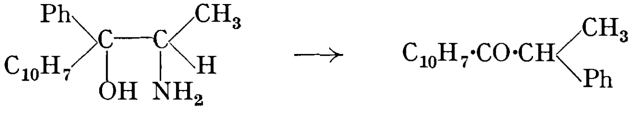
As described in Part I (Mills, preceding paper), the deamination by means of nitrous acid of amino-alcohols of the type (I) has led to the following results: (i) R = H, R′ = α-naphthyl, *p*-tolyl, or anisyl—migration of R′—type (A) (Luce, *Compt. rend.*, 1925, **180**, 145; Orékhoff and Roger, *Compt. rend.*, 1925, **180**, 70; McKenzie, Mills, and Myles, *Ber.*, 1930, **63**, 904); (ii) R = Ph, R′ = α-naphthyl, *p*-tolyl, anisyl, methyl, or ethyl—migration of Ph—type (B) (McKenzie and Richardson, J., 1923, **123**, 79; McKenzie and Roger, J., 1924, **125**, 844; 1927, 571; McKenzie and Mills, *Ber.*, 1929, **62**, 1784; McKenzie, Mills, and Myles, *loc. cit.*). It was shown that if R = CH_2Ph, there is again a migration of the phenyl group when R′ is the α-naphthyl, *p*-tolyl, or benzyl radical. During the deamination of two series of amino-alcohols (R = Ph and CH_2Ph) the phenyl group shows a greater tendency to migrate than the α-naphthyl or the *p*-tolyl group, although contrary results have been obtained from the dehydration of glycols and *sym.*-pinacones (Tiffeneau and Lévy, *Bull. Soc. chim.*, 1931, **49**, 1661).

In order to determine whether type (B) is the normal rearrangement during the deamination of such amino-alcohols, our observations have been extended to the series for which R = CH_3, where the migrations occur towards a secondary carbon atom with a methyl group attached.

The amino-alcohols were obtained by the action of Grignard reagents on α-aminopropiophenone hydrochloride. When β-*amino*-α-*phenyl*-α-1-*naphthyl*-n-*propyl alcohol*, prepared by the action of naphthylmagnesium bromide, was treated with nitrous acid, the reaction product was identified as α-*phenylethyl* α-*naphthyl ketone*. It was again evident that the phenyl group had migrated in preference to the α-naphthyl group during semi-pinacolinic deamination.


(I.)

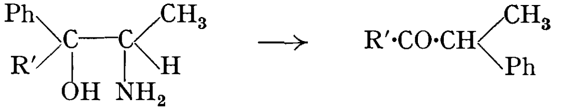


As a publication appeared by Tiffeneau (*Bull. Soc. chim.*, 1931, **49**, 1686) indicating that the phenyl group had been found to migrate in the deamination of amino-alcohols of this type (I; R = CH_3, R′ = *p*-tolyl or anisyl), we discontinued the preparation of amino-alcohols of this series by means of aromatic Grignard reagents.

The practical details of Tiffeneau's semi-pinacolinic deaminations have not yet been published, but the conclusion can now be drawn that the normal course of rearrangement during semi-pinacolinic deamination involves the migration of the phenyl group in preference to the more negative aromatic radicals, *i.e.*, type (B). As the results of these rearrangements are the reverse of those obtained from dehydration experiments it seems possible that there is either a greater difference between the mechanisms of semi-pinacolinic dehydration and semi-pinacolinic deamination than has usually been assumed, or that the presence of the amino-group is the ultimate cause of the altered tendencies of the aromatic groupings to migrate during deamination.

Migita (*Bull. Chem. Soc. Japan*, 1928, **3**, 308) presents an electronic interpretation of the mechanism of the deamination of amino-alcohols, and quotes the migration of the more negative aromatic group (R = H, R′ = α-naphthyl) as the normal reaction, whilst attributing the migration of the phenyl group (R = Ph, R′ = α-naphthyl) to steric influences. Although the importance of steric influences cannot be overlooked, the evidence collected in the present paper and in Part I now shows that the migration of the more negative aromatic radical is the abnormal reaction, and that this electronic conception cannot be applied to the deamination of amino-alcohols. Nor can support be found in the literature for Migita's assumption that a glycol is an intermediate stage of such deaminations. The reaction of semi-pinacolinic deamination was originally discovered by McKenzie and Richardson (*loc. cit.*) in an endeavour to convert β-amino-ααβ-triphenylethyl alcohol into triphenylethylene glycol by means of nitrous acid. It was found that the reaction product was phenyldeoxybenzoin and no trace of triphenylethylene glycol could ever be isolated, although the conditions of the reactions were such as to prevent the dehydration of any glycol formed. Several instances of the conversion of α-amino-alcohols into glycols have since been recorded (McKenzie and Roger, J., 1927, 571), but these glycols have been formed by a different mechanism and have not subsequently given rise to ketones.

β-Amino-α-phenyl-α-methyl- and -α-benzyl-*n*-propyl alcohols have also been prepared from α-aminopropiophenone hydrochloride and subjected to deamination by nitrous acid. In each case the phenyl group migrated in preference to the methyl or benzyl group, and α-phenylethyl methyl and benzyl ketones were identified as the products of the respective reactions :



(R′ = CH_3 or $C_6H_5{\cdot}CH_2$.)

These results correspond with the conclusions derived from the dehydration of glycols and pinacones (Tiffeneau and Lévy, *loc. cit.*), that an aromatic grouping always migrates in preference to an aliphatic grouping, and are also in uniformity with the results of previous deaminations (R = Ph, R′ = CH_3, McKenzie and Richardson; McKenzie and Mills, *locc. cit.*: R′ = C_2H_5, McKenzie and Roger, *loc. cit.*: R = R′ = $C_6H_5{\cdot}CH_2$, Mills, *loc. cit.*). Although the forces acting on migrating groups during dehydration and deamination rearrangements may vary sufficiently to cause the migration of different aromatic radicals, no such alteration of the forces effecting the migration can produce any other result than the migration of the aromatic grouping, where both an aromatic and an aliphatic grouping are in a position to migrate.

EXPERIMENTAL.

α-Aminopropiophenone hydrochloride was prepared by catalytic reduction in hydrogen (Hartung, *J. Amer. Chem. Soc.*, 1931, **53**, 2248) of *iso*nitrosopropiophenone (Hartung and Munch, *ibid.*, 1929, **51**, 2264), the m. p. of which was 113—114° (cf. Beilstein), whereas Hartung and Munch quote 106—106·5°. 15 G. of *iso*nitrosopropiophenone were dissolved in 300 c.c. of absolute alcohol containing hydrochloric acid (3 mols.) and shaken with 7 g. of palladium charcoal (8% Pd) in an atmosphere of hydrogen. After 145 mins., the required 4125 c.c. of hydrogen had been absorbed. The catalyst was filtered off, and the solution evaporated almost to dryness in a vacuum. Ether was added, and the precipitated α-aminopropiophenone hydrochloride filtered off, washed well with ether and hot benzene, and crystallised from alcohol and ether. 15 G. of pure amino-ketone hydrochloride were obtained.

β-*Amino-α-phenyl-α-*1-*naphthyl-*n-*propyl Alcohol.*—6·0 G. of the foregoing hydrochloride were added to the Grignard reagent prepared from α-naphthyl bromide (33·5 g.), and the mixture heated for 3 hours on a water-bath; it was then decomposed by ice and dilute hydrochloric acid, and after some time a white solid separated. This was filtered off, washed with ether, and dissolved in alcohol. Aqueous ammonia was added, and the precipitated white solid collected and crystallised from aqueous alcohol. 4·5 G. of pure *β-amino-α-phenyl-α-1-naphthyl-*n*-propyl alcohol* crystallised from alcohol as fine needles, m. p. 160° (Found: C, 82·0; H, 7·0. $C_{19}H_{19}ON$ requires C, 82·3; H, 6·9%); hydrochloride, m. p. 253—254° (decomp.).

Deamination. 6 G. of the amino-alcohol were dissolved in dilute acetic acid (150 c.c.) and a solution of sodium nitrite (4·4 g.) slowly added at 0°. A yellow oil separated, which was extracted with ether, and distilled in a vacuum. 4 G. of an extremely viscous yellow oil distilled at 190—192°/2—3 mm.; it eventually solidified, and crystallised from light petroleum (b. p. 50—70°) in rectangular prisms, m. p. 49·5—50·5°, undepressed when admixed with α-phenylethyl α-naphthyl ketone synthesised as under. Its oxime, m. p. 160·5—161·5°, was similarly identified with that of the synthesised material.

α-Phenylethyl α-naphthyl ketone. Sodium (1 mol.) dissolved in 20 c.c. of absolute alcohol was refluxed on a water-bath for 5 mins. with benzyl α-naphthyl ketone (5·0 g.) (Luce, *loc. cit.*). Methyl iodide (1 mol.) was then added, and the mixture refluxed for 2½ hours, then poured into water and extracted with ether. On evaporation of the ether, an oily solid was obtained which contained much unchanged ketone. The oil was extracted with light petroleum (b. p. 50—70°), and the extract evaporated, and distilled in a vacuum; 3·5 g. of *α-phenylethyl α-naphthyl ketone* were obtained, m. p. 49·5—50·5° (Found: C, 87·4; H, 6·3. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). Oxime, m. p. 160·5—161·5°.

*β-Amino-α-phenyl-α-benzyl-*n*-propyl Alcohol.*—8 G. of α-aminopropiophenone hydrochloride were added to the Grignard reagent from benzyl chloride (6 mols.) and heated for 2 hours on a water-bath. After the same procedure as above, the white solid was crystallised from benzene to which a few drops of alcohol had been added, 8·5 g. of β-amino-α-phenyl-α-benzyl-*n*-propyl alcohol hydrochloride being obtained as rectangular prisms, m. p. 235—236°. The *alcohol* was precipitated as a white solid when an aqueous solution of the hydrochloride was made alkaline with ammonia; it crystallised from aqueous alcohol in rectangular prisms, m. p. 69·5° (Found: C, 79·4; H, 8·0. $C_{16}H_{19}ON$ requires C, 79·6; H, 7·9%).

Deamination. 6 G. of the amino-alcohol were deaminated as before (100 c.c. dilute acetic acid; 4·5 g. sodium nitrite). The ethereal extract was washed with sodium carbonate solution, then with water, the ether evaporated off, and the resulting oil was distilled, b. p. 175°/12—13 mm. 4 G. of α-phenylethyl benzyl ketone were thus obtained; it formed an oxime, m. p. 83—84°. The ketone is described by Lévy and Jullien (*Bull. Soc. chim.*, 1929, **45**, 946) as an oil, b. p. 205—206°/40 mm., forming an oxime, m. p. 82—83°.

*β-Amino-α-phenyl-α-methyl-*n*-propyl Alcohol.*—9 G. of α-aminopropiophenone hydrochloride and the Grignard reagent from methyl iodide (6 mols.) were caused to react, and the product was worked up, as before, crystallisation being as in the last case. 5·5 G. of pure *β-amino-α-phenyl-α-methyl-*n*-propyl alcohol hydrochloride* were obtained in shiny plates, m. p. 244° (Found: C, 59·4; H, 7·8. $C_{10}H_{16}ONCl$ requires C, 59·5; H, 8·0%). The hydrochloride was dissolved in water, aqueous ammonia added, and the precipitated oil extracted with ether. The alcohol was obtained from the extract as an oil, which eventually crystallised in the form of needles from ligroin to which a few drops of alcohol had been added, m. p. 82—83°.

Deamination. 5 G. of the amino-alcohol hydrochloride were deaminated by sodium nitrite (3 mols.) as before; 3·1 g. of a colourless oil were obtained, b. p. 94—96°/12—13 mm., which formed a semicarbazone, m. p. 172—173°. α-Phenylethyl methyl ketone has b. p. 106—107°/17 mm., semicarbazone, m. p. 172° (Lévy, *Bull. Soc. chim.*, 1921, **29**, 825). The ketone was also synthesised by the action of sodium ethoxide and methyl iodide on benzyl methyl ketone, and the resulting semicarbazone showed no depression of m. p. when mixed with the semicarbazone of the deamination product.

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