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THE HYDROGEN HALIDE-CATALYSED REARRANGEMENT OF N-METHYLANILINE TO *o*- AND *p*-TOLUIDINES

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Abstract—The reactions of N-methylanilinium chloride, iodide and bromide at 250–300° (Hofmann-Martius rearrangement) were carried out in a sealed tube or in an open vessel. The reaction products were analysed by gas chromatography. The products were found to contain *o*- and *p*-toluidines, aniline, N,N-dimethylaniline, *p*-methyl-N,N-dimethylaniline, *p*-methyl-N-methylaniline, 2,4-dimethyl- and 2,4,5-trimethylanilines. The *p*:*o* ratio of formed toluidines depends on the nature of the halogen in the N-methylanilium halides, i.e., 6–7 for the chloride, 1·1–1·5 for the iodide. These facts are not in agreement with an intramolecular migration of free methyl carbonium ion for the rearrangement, but suggest a mechanism involving an intermediary formation of methyl halide.

THE acid (or Lewis acid)-catalysed rearrangement of N-alkylaniline to *o*- and *p*-alkylanilines, or Hofmann–Martius rearrangement,[1,2] has been studied by Hickinbottom *et al.*[3] and some other investigators.[4] It is of interest that the hydrogen halide-catalysed reaction is accompanied by the formation of alkyl halide and olefins and that the alkyl halide produced is partly isomerized. Since the analysis of the reaction products was performed by means of fractional distillation, crystallization, mixed m.p. determination etc., reexamination of the products by means of modern analytical tools is desirable.

The present paper describes the hydrogen halide-catalysed reaction of N-methylaniline in a sealed tube, and the products of the reaction were analysed quantitatively by gas chromatography.

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[1] A. W. Hofmann and C. A. Martius, *Ber. Dtsch. Chem. Ges.* **4**, 742 (1871); A. W. Hofmann, *Ibid.* **5**, 704, 720 (1872); **7**, 526 (1874).

[2] J. E. Gowan and T. S. Wheeler, *Name Index of Organic Reactions* p. 126. Interscience, New York. (1960).

[3a] W. J. Hickinbottom, *J. Chem. Soc.* **117**, 103 (1920);
[b] W. J. Hickinbottom, *Ibid.* 64 (1927);
[c] W. J. Hickinbottom and A. C. Waine, *Ibid.* 1558 (1930);
[d] W. J. Hickinbottom and G. H. Preston, *Ibid.* 1566 (1930);
[e] W. J. Hickinbottom and S. E. A. Ryder, *Ibid.* 1281 (1931);
[f] W. J. Hickinbottom, *Ibid.* 2396 (1932);
[g] W. J. Hickinbottom, *Ibid.* 1700 (1934);
[h] W. J. Hickinbottom, *Ibid.* 404 (1937);
[i] W. J. Hickinbottom, *Ibid.* 1119 (1937).

[4a] J. H. Howard and C. G. Derick, *J. Amer. Chem. Soc.* **46**, 166 (1924);
[b] J. Thesing and H. Mayer, *Ber. Dtsh. Chem. Ges.* **87**, 1084 (1954);
[c] M. J. Molera, J. M. Gamboa and M. del Val Cob, *An. Real Soc. Espan Fis. Quim.* **55** B, 493 (1959);
[d] M. J. Molera, J. M. Gamboa and N. Ortin, *Ibid.* **57** B 595 (1961);
[e] H. Hard and J. R. Kosak, *J. Org. Chem.* **27**, 116 (1962).

RESULTS AND DISCUSSION

The yields of products produced in the hydrogen halide-catalysed rearrangement of N-methylaniline at 250–300° in a sealed tube are listed in Tables 1, 2 and 3. The products were found to contain *o*- and *p*-toluidines together with aniline, N-methyl- and N,N-dimethyl-*p*-toluidines, 2,4-dimethylaniline and polymethylanilines including 2,4,5-trimethylaniline.

The formation of polymethylanilines and free aniline precludes an intramolecular rearrangement such as that via π-complex.[5] The fact that the *p*:*o* ratio in the toluidines produced is different with HCl (6–8), HI (1–1·5) and HBr (ca. 1) suggests that the attacking intermediate may be alkyl halide which has been isolated in the reaction,[3e,g] and that the intermediary free alkyl carbonium ion as an attacking species is improbable. *o*- and *p*-Toluidines are not interchangeable and they cannot give N-methylaniline with hydrochloric acid catalysts under these conditions.

The reaction is faster with the hydroiodide than with the hydrochloride; hence, the necessary temperature is lower with hydroiodide (Tables 1 and 2). This phenomenon is in keeping with the lower activity of methyl chloride as compared with that of methyl iodide. This lower reactivity and hence higher selectivity may explain the higher *p*:*o* ratio of the toluidines formed in hydrogen chloride catalysis.

If the reaction of N-methylanilinium chloride is carried out at 300° in an open vessel equipped with a reflux condenser, no rearranged product is obtained but instead aniline and N,N-dimethylaniline is produced (No. 6 in Table 1), while with N-methylanilium iodide under similar conditions the rearrangement occurs. These facts may be explained by the fact that the intermediary methyl chloride being more volatile (b.p. −24·22°) is lost from the system in the open vessel, but methyl iodide which is less volatile (b.p. 42·5°) and more reactive is retained in the system.

The reaction products at early stages or under milder conditions contain N,N-dimethylaniline, N-methyl-*p*-toluidine and N,N-dimethyl-*p*-toluidine; the presence of N-methylated toluidines also supports the intermolecular methylation of the rearranged product. These results suggest the following scheme for the reaction, where X is halogen atom.

$$C_6H_5\overset{+}{N}H_2CH_3 + X^- \rightleftarrows C_6H_5NH_2 + CH_3X$$

$$C_6H_5NH_2 + CH_3X \rightarrow o\text{- and } p\text{-}CH_3C_6H_4NH_2$$

$$CH_3C_6H_4NH_2 \xrightarrow{CH_3X} (CH_3)_2C_6H_3NH_2 \xrightarrow{CH_3X} (CH_3)_3C_6H_2NH_2$$

$$C_6H_5NHCH_3 + CH_3X \rightleftarrows C_6H_5N(CH_3)_2 + HX$$

$$C_6H_5NHCH_3 + CH_3X \rightarrow CH_3C_6H_4NHCH_3 + HX \rightleftarrows CH_3C_6H_4NH_2 + CH_3X$$

$$C_6H_5N(CH_3)_2 + CH_3X \rightarrow CH_3C_6H_4N(CH_3)_2 + HX$$

On heating an equimolar mixture of anilinium chloride and methanol in a sealed tube at 300° for 3 hr, *p*-toluidine (28·4%), *o*-toluidine (4·0%), aniline (14·5%), 2,4-dimethylaniline (13·5%) and 2,4,5-trimethylaniline (1·5%) were obtained. The composition of these products is analogous to the reaction of N-methyanilinium

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[5] M. J. S. Dewar, *The Electronic Theory of Organic Chemistry*, p. 227. Oxford Univ. Press, London (1949).

TABLE 1. REACTION PRODUCTS OF N-METHYLANILINIUM CHLORIDE IN A SEALED TUBE

No.	Temp °C	Reaction time hr	Unreacted C_6H_5NHMe %	C_6H_5-NMe_2 %	*p*-MeC_6-H_4NMe_2 %	*p*-MeC_6-H_4NHMe %	2,4-Me_2-$C_6H_3NH_2$ %	2,4,5-Me_3-$C_6H_2NH_2$ %	C_6H_5-NH_2 %	*o*-MeC_6-H_4NH_2 %	*p*-MeC_6-H_4NH_2 %	$MeC_6H_4NH_2$ *p*/*o*
1	250	5	48·7	16·4	0	0	0	0	10·4	0	0	—
2	275	6	25·2	9·5	1·6	5·4	0	0	30·7	3·8	5·2	1·37
3	300	1	5·1	0·4	0·3	5·2	8·5	1·1	19·1	3·4	26·2	7·71
4	300	3	0	0	0	0	15·3	2·0	11·3	4·7	29·4	6·26
5	300	5	0	0	0	0	11·9	3·3	11·2	3.5	25·7	7·34
6	300[a]	3	21·2	2·6	0	0	0	0	35·9	0	0	—

[a] An open vessel with a reflux condenser was used.

TABLE 2. REACTION PRODUCTS OF N-METHYLANILINIUM IODIDE IN A SEALED TUBE

No.	Temp °C	Reaction time hr	Unreacted C_6H_5NHMe %	C_6H_5-NMe_2 %	p-MeC_6-H_4NMe_2 %	p-MeC_6-H_4NHMe %	2,4-Me_2-$C_6H_3NH_2$ %	2,4,5-Me_3-$C_6H_2NH_2$ %	C_6H_5-NH_2 %	o-MeC_6-H_4NH_2 %	p-MeC_6-H_4NH_2 %	$MeC_6H_4NH_2$ p/o
1	250	5	12·8	1·1	0·2	3·0	4·4	trace	21·8	12.9	16·7	1·39
2	275	6	0	0	0	0	12·6	7·1	20·8	18·5	21·5	1·16
3	300	0·5	0	0	0	0	15·2	7·6	22·9	18·9	26·1	1·38
4	300	1	0	0	0	0	12·6	5·3	25·2	16·8	22·2	1·32
5	300	3	0	0	0	0	3·4	trace	23·7	10·5	16·1	1·53
6	300	5	0	0	0	0	7·2	trace	13·8	11·6	15·4	1·33
7	300[a]	3	2·4	0·9	0·3	0	8·9	3·8	22·2	15·7	19.3	1.23

[a] An open vessel with a reflux condenser was used.

TABLE 3. REACTION PRODUCTS OF N-METHYLANILINIUM BROMIDE IN A SEALED TUBE

No.	Temp °C	Reaction time hr	Unreacted C_6H_5NHMe %	C_6H_5-NMe_2 %	p-MeC_6-H_4NMe_2 %	p-MeC_6-H_4NHMe %	2,4-Me_2-$C_6H_3NH_2$ %	2,4,5-Me_3-$C_6H_2NH_2$ %	C_6H_5-NH_2 %	o-MeC_6-H_4NH_2 %	p-MeC_6-H_4NH_2 %	$MeC_6H_4NH_2$ p/o
1	300	1	6·5	0·3	0	0	11·5	5·2	28·2	22·6	23·4	1·04
2	300	3	0	0	0	0	15·2	17·0	27·4	20·7	21·6	1·04

chloride under similar conditions (No. 4 in Table 1) and supports the mechanism involving the intermediate formation of methyl chloride from methanol and hydrogen chloride.

EXPERIMENTAL

Materials. Excess aqueous hydrogen halide was added to N-methylaniline, b.p. 89–90°/24 mm, and the residue after evaporation to dryness was recrystallized from a mixture of ether and ethanol, m.p. of the chloride, 126·5°; the iodide, 124·5°; the bromide, 99°; these m.ps are in agreement with those in the literature. The same procedure was employed for anilinium chloride, m.p. 199·5°. All other materials[6] were purified by fractional distillations or recrystallizations and the m.ps for solids or b.ps for liquids agreed with those in the literature.

The reaction of N-*methylanilinium halides in sealed tubes.* N-Methylanilinium halide (0·01 mole) in a 10 ml sealed tube was introduced into an autoclave. Toluene was added to balance inside and outside pressures, and the autoclave was heated to the given temp. About 30 min being necessary to raise the temp to 250° and ca. 45–50 min to 300° and after the reaction, ca. 1 hr was necessary to cool the reaction vessel to the room temp.

The reaction of N-*methylanilinium halide in an open vessel.* N-Methylanilinium halide (0·01 mole) was heated at 300° (oil bath) ±5° in a 50 ml flask fitted with a reflux condenser.

The reaction of anilinium chloride with methanol in a sealed tube. Anilinium chloride (0·01 mole) and methanol (0·01 mole) was introduced into a tube, the latter being sealed at −10° to avoid the evaporation of methanol. A work-up was similar to that used for the reaction in an autoclave.

Analysis of reaction products. The products after addition of warm dil. HCl aq were steam-distilled to remove neutral oily materials. After addition of NaOH aq, the solution was again steam-distilled. The distillate was extracted with ether; the extract dried with Na_2SO_4 and the solvent evaporated. The condensed extract was analysed by gas chromatography employing a Yanagimoto Model GCG-220 operated with a 255 cm column packed with polyethylene glycol #4000 on Firebrick using a flow rate of 46 ml He per min at 145°. Retention times (in min) were; N,N-dimethylaniline, 7·3; N,N-dimethyl-*p*-toluidine, 18·7; *o*-toluidine, 19·6; *p*-toluidine, 21·8; 2,4-dimethylaniline, 27·2; 2,4,5-trimethylaniline, 31·4. These products were identified by comparison with the corresponding authentic samples. All quantitative analysis were carried out using bromobenezene as an internal standard.

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[6] W. J. Hickinbottom, *Reactions of Organic Compounds.* Longmans, Green Co., London (1936).