Quaternary Ammonium Salts. Part IV. Hydrolysis of the Nitrile Group before Decomposition of the Quaternary Ammonium Group. Preparation and Decomposition of Some Quaternary Ammonium Salts.*

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[Reprint Order No. 4782.]

Ethanolic sodium ethoxide hydrolysed the nitrile group of *p*-cyanophenyltrimethylammonium iodide before it decomposed the ammonium group; the amide formed then gave *p*-ethoxy- and *p*-dimethylamino-benzamide. *o*- and *p*-Dimethylaminobenzoic acid gave the quaternary salts with methyl iodide only in methyl alcohol. Decomposition of 4-dimethylaminobenzophenone-4′-trimethylammonium iodide with alcoholic sodium methoxide or ethoxide gave 4-dimethylamino-4′-methoxy- or -ethoxy-benzophenone, Michler's ketone, and 4-dimethylamino-4′-hydroxybenzophenone.

WHEN *p*-cyanophenyltrimethylammonium iodide was boiled with ethanolic sodium ethoxide for 15 min., the nitrile was hydrolysed to the amide group before degradation of the quaternary ammonium group occurred. The nitrile group behaved therefore like the formyl, nitro-, methoxy- and ethoxycarbonyl groups (Parts II and III *). On prolonged boiling (2 hr.) both the nitrile and the amide yielded *p*-dimethylaminobenzamide, *p*-ethoxybenzamide, and a trace of *p*-dimethylaminobenzoic acid. The formation of *p*-ethoxybenzamide may be attributed to the electron-attracting properties of the carbamoyl group. It was noteworthy that whereas the nitrile group in the *p*-cyano-ammonium salt was readily hydrolysed, *p*-dimethylaminobenzonitrile was only hydrolysed after 6—8 hr.' refluxing (cf. *p*-dimethylaminobenzaldehyde which does not readily undergo the Cannizzaro reaction, in contrast to the quaternary salt, Part II).

When *o*-dimethylaminobenzoic acid and methyl iodide were heated on the water-bath for 3 hr. or left for 2 days at room temperature, methyl *o*-dimethylaminobenzoate hydriodide was obtained, but the *p*-dimethylamino-acid was recovered unchanged even after

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* Parts I—III, *J.*, 1949, 3337; 1951, 1890; 1953, 189.

much longer treatment. The two electrons of the tertiary nitrogen atom were not apparently available for the addition of methyl iodide (see Watson, " Modern Theories of Organic Chemistry," Oxford Univ. Press, 1941, p. 252) under the experimental conditions cited. The formation of methyl *o*-dimethylaminobenzoate hydriodide may be attributed to the betaine structure $^+NHMe_2{\cdot}C_6H_4{\cdot}CO_2^-$ (Ley and Ulrich, *Ber.*, 1909, **42**, 3440; Ley and Engelhardt, *Z. physikal. Chem.*, 1910, **74**, 1; Hünecke, *Ber.*, 1927, **60**, 1451; Devoto, *Chem. Zentr.*, 1934, II, 3753), the methyl radical adding itself to the negatively charged CO_2^- group. Ley and Ulrich gave, however, a structure which in the light of electronic theory would represent chelation between the carboxyl-hydrogen and the nitrogen atom through the unshared electrons. The failure to obtain the corresponding salt or the quaternary ammonium compound in case of the *p*-isomer may (with reservation) find explanation in the quinonoid structure $^+NMe_2{:}C_6H_4{:}C(OH){\cdot}O^-$ suggested by Kumler (*J. Amer. Chem. Soc.*, 1946, **68**, 1184) for this acid and related compounds. As already pointed out by Edsall and Wyman (*ibid.*, 1935, **57**, 1964) *o*- and *p*-dimethylaminobenzoic acid exhibit markedly different properties (melting points, solubilities, solvents, etc.). However, when either acid was refluxed with an excess of methyl iodide in solution in methyl alcohol, the corresponding quaternary salt was obtained. On prolonged boiling, the methyl ester of the *p*-compound was formed (contrast the hydrolysis of the ester group before degradation of the quaternary group; Part III). It is therefore reasonable to assume that the two acids may exist (at least at the time of the reaction) in the uncharged form when in solution in methyl alcohol, the unshared electrons thus becoming available for the addition of methyl iodide. Kuhn and Brydówna (*Ber.*, 1937, **70**, 1333), by passing diazomethane through an aqueous solution of *o*-dimethylaminobenzoic acid, obtained 18% of *o*-benzobetaine and 70% of methyl *o*-dimethylaminobenzoate, but 97% of the methyl ester was formed in ether. Edsall and Wyman (*loc. cit.*) noted that *o*-dimethylaminobenzoic acid in solvents such as water, alcohol–water, and benzene existed predominantly in the zwitterion form. *m*-Dimethylaminobenzoic, *p*-dimethylaminocinnamic, and β-*p*-dimethylaminophenylpropionic acid readily added methyl iodide on the water-bath or at room temperature (2 days).

On decomposition of 2-methoxycarbonyl-1-phenylethylene-*p*-trimethylammonium iodide with methanolic sodium methoxide the ester group was cleaved before the quaternary group was affected. Decomposition of 4-dimethylaminobenzophenone-4′-trimethylammonium iodide gave 3 fractions which were separated as reported in Part I.

EXPERIMENTAL

Quaternary Iodides.—These were obtained in most cases in almost theoretical yield at room temperature (2 days) or on the water-bath (6 hr.) from the base (1 g.) and an excess of methyl iodide (25 g.) alone or in presence of methyl alcohol (25 c.c.). The iodides from *o*- and *p*-dimethylaminobenzoic acid were formed only in presence of the solvent. *p*-Carboxyphenyltrimethylammonium iodide, m. p. 238°, showing no depression on admixture with an authentic sample (Zaki and Tadros, *J.*, 1941, 562), was obtained after 6 hr.' refluxing, but on prolonged boiling (32 hr.) the carboxyl group was esterified (the same result being obtained on prolonged boiling of a mixture of *p*-carboxyphenyltrimethylammonium iodide and methyl iodide in methanol), and *p*-methoxycarbonylphenyltrimethylammonium iodide, m. p. and mixed m. p. 170° (Part III), was formed.

Methyl *o*-dimethylaminobenzoate hydriodide, m. p. and mixed m. p. 163° (Willstätter and Kahn, *Ber.*, 1904, **37**, 401), was obtained when *o*-dimethylaminobenzoic acid and an excess of methyl iodide were refluxed for 3 hr. or left for 2 days at room temperature.

The iodides were recrystallised from alcohol or alcohol–ether from which they separated as colourless or pale yellow crystals. The picrates were prepared from the iodides.

Decomposition of Quaternary Salts.—When 4-dimethylaminobenzophenone-4′-trimethylammonium iodide (4·1 g., 1 mol.) and methanolic or ethanolic sodium methoxide or ethoxide (sodium, 0·35 g., 1·5 atoms; alcohol, 25 c.c.) had been refluxed for 3 hr., three products were separated as follows: Alcohol was distilled off and the residue was treated with hydrochloric acid (1 : 1); to the clear solution 5% aqueous sodium hydroxide was added drop by drop until a precipitate (20—25%) of 4-dimethylamino-4′-methoxy- (m. p. 132°) or -ethoxy-benzophenone (m. p. 103°) separated (no depression on admixture with authentic samples, Part I). The filtrate (which was still acid) was made alkaline; the resulting precipitate was recrystallised from alcohol and proved by m. p. and mixed m. p. to be Michler's ketone (60—65%). Acidification of the alkaline filtrate by acetic acid precipitated a small amount of 4-dimethylamino-4′-hydroxybenzophenone, m. p. and mixed m. p. 199—200° (Part I).

p-Carbamoylphenyltrimethylammonium iodide (1·51 g., 1 mol.) and ethanolic sodium ethoxide (sodium 0·23 g., 2 atoms; in ethyl alcohol, 25 c.c.), treated as above, gave 3 fractions : *p*-ethoxybenzamide (35—40%), m. p. and mixed m. p. 202° (Gattermann, *Annalen*, 1888, **244**, 29); *p*-dimethylaminobenzamide (40—45%), m. p. and mixed m. p. 206° (Bayer and Co., G.P. 77,329; Friedländer, Vol. IV, p. 173); and *p*-dimethylaminobenzoic acid, m. p. and mixed m. p. 234° showing no depression on admixture with an authentic sample (Zaki and Tadros, *loc. cit.*).

Hydrolysis of the Nitrile Group before Decomposition of the Quaternary Ammonium Group.—*p*-Cyanophenyltrimethylammonium iodide (1·44 g., 1 mol.) and ethanolic sodium ethoxide (sodium, 0·23 g., 2 atoms; in alcohol, 25 c.c.) were refluxed for 15 min. and alcohol was distilled off; the picrate obtained from the residue was *p*-carbamoylphenyltrimethylammonium picrate,

		Found (%)					Required (%)			
Salt	M. p.	C	H	N	Hal	Formula	C	H	N	Hal
Substituted phenyltrimethylammonium salts, $R\cdot C_6H_4\cdot NMe_3\}X$.										
R = *p*-CN.										
Iodide	181°	41·6	4·8	9·4	43·8	$C_{10}H_{13}N_2I$	41·7	4·5	9·7	44·1
Picrate	152	48·9	3·9	17·5	—	$C_{16}H_{15}O_7N_5$	49·4	3·9	18·0	—
R = *p*-CO·NH$_2$.										
Iodide	203—204	39·3	5·0	8·8	41·2	$C_{10}H_{15}ON_2I$	39·2	4·9	9·2	41·5
Picrate	237	47·5	4·3	17·6	—	$C_{16}H_{17}O_8N_5$	47·2	4·2	17·2	—
R = *p*-CO$_2$H.										
Iodide [a]	160—161	—	—	4·3	40·8	$C_{10}H_{14}O_2NI$	—	—	4·6	41·4
R = *m*-CO$_2$H.										
Chloride [b] ...	207	—	—	—	15·9	$C_{10}H_{14}O_2NCl$	—	—	—	16·4
Iodide [c]	204	38·9	4·4	4·8	40·8	$C_{10}H_{14}O_2NI$	39·1	4·6	4·6	41·4
R = *o*-CO$_2$Me.										
Picrate [d]	128—130	48·2	4·2	13·7	—	$C_{17}H_{18}O_9N_4$	48·3	4·3	13·3	—
R = *m*-CO$_2$Me.										
Picrate [d]	166	48·1	4·2	12·8	—	$C_{17}H_{18}O_9N_4$	48·3	4·3	13·3	—
2-*Carboxy*-1-*phenylethane*-p-*trimethylammonium Salts.*										
Iodide	206—208	42·8	5·6	4·2	38·3	$C_{12}H_{18}O_2NI$	43·0	5·4	4·2	37·9
Picrate	208—210	49·4	4·9	12·6	—	$C_{18}H_{20}O_9N_4$	49·5	4·6	12·8	—
2-*Carboxy*-1-*phenylethylene*-p-*trimethylammonium Salts.*										
Iodide [e]	210	43·2	4·8	4·1	38·0	$C_{12}H_{16}O_2NI$	43·2	4·8	4·2	38·1
Picrate	228—230	49·9	4·1	12·7	—	$C_{18}H_{18}O_9N_4$	49·8	4·1	12·9	—
2-*Methoxycarbonyl*-1-*phenylethylene*-p-*trimethylammonium Salts.*										
Picrate [f]	187—189	51·7	4·3	12·9	—	$C_{19}H_{20}O_9N_4$	50·9	4·5	12·5	—
4-*Dimethylaminobenzophenone*-4′-*trimethylammonium Salts.*										
Iodide [g]	182	53·2	5·8	7·0	31·4	$C_{18}H_{23}ON_2I$	52·7	5·6	6·8	31·0
Picrate [h]	197—198	56·1	4·9	13·2	—	$C_{24}H_{25}O_8N_5$	56·4	4·9	13·7	—

[a] Willstätter and Kahn (*loc. cit.*) gave m. p. 138° and 1 mol. of water of crystallisation. The m. p. was depressed on admixture with methyl *o*-dimethylaminobenzoate hydriodide. [b] Obtained by treatment of *m*-methoxycarbonylphenyltrimethylammonium picrate with concentrated hydrochloric acid, filtration from picric acid, washing with benzene–ether until free from picric acid, and then evaporation on the water-bath. The residue crystallised from alcohol–ether. Cumming (*Proc. Roy. Soc.*, 1907, *A*, **78**, 109), gave m. p. 192°. [c] Also obtained from the chloride by addition of aqueous potassium iodide. Cumming gave m. p. 180°. [d] Obtained from the iodides with m. p. 153° and 220—221° respectively (Willstätter and Kahn, *loc. cit.*). [e] Pfeiffer and Haeflin (*Ber.*, 1922, **55**, 1769) obtained this by heating the acid with methyl iodide for 30 hr. in a sealed tube and by addition of hydriodic acid to the betaine. During the addition of methyl iodide to *p*-dimethylaminocinnamic acid (m. p. 216°; Pandya and Sharma, *J. Indian Chem. Soc.*, 1946, **23**, 137) a part of the acid was recovered but had m. p. 235°. It crystallised from alcohol as yellow crystals (Found : C, 68·8; H, 6·5; N, 7·5. Calc. for $C_{11}H_{13}O_2N$: C, 69·1; H, 6·8; N, 7·3%); the following m. p.s have been recorded : 216° (Weil, *Chem. Zentr.*, 1908, II, 1924; Dutt, *ibid.*, 1925, II, 1852; Pandya and Sharma, *loc. cit.*); 220° (Pfeiffer and Haeflin, *loc. cit.*); 225° (Shoppee, *J.*, 1930, 968). [f] Obtained from the iodide, m. p. 186° (Pfeiffer and Haeflin, *loc. cit.*). [g] Refluxing was for 2 hr. only. Addition to both *p*-dimethylamino-groups took place on refluxing of Michler's ketone with methyl iodide in methanol for 20 hr. and not for 2 hr. as previously stated (Tadros and Latif, *loc. cit.*). [h] Reddish-brown; other picrates were yellow.

m. p. and mixed m. p. 237°. Refluxing the mixture for 2 hr. gave *p*-ethoxybenzamide and *p*-dimethylamino-benzamide and -benzoic acid.

Hydrolysis of the Ester Group before Decomposition of the Quaternary Ammonium Group.—Methanolic sodium methoxide (sodium, 0·17 g., 1·25 atoms; methanol, 20 c.c.) containing 2-methoxycarbonyl-1-phenylethylene-*p*-trimethylammonium iodide (1·75 g., 1 mol.) was left at 25—30°. A sample was daily left to evaporate at room temperature and the residue converted into the picrate. The picrate obtained after 4 days had m. p. 228—230° alone or when mixed with 2-carboxy-1-phenylethylene-*p*-trimethylammonium picrate.

p-*Dimethylaminobenzamide.*—This was also obtained on refluxing, for 6—8 hr., of *p*-dimethylaminobenzonitrile (3 g., 1 mol.) and ethanolic sodium ethoxide (sodium, 0·7 g., 1·5 atoms; ethyl alcohol, 30 c.c.). It separated from water and had m. p. and mixed m. p. 206°.

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[*Received, November 10th,* 1953.]