697. *Quaternary Ammonium Salts. Part I. A New Method for the Preparation of* p-*Substituted Alkoxy-*, cyclo*Alkoxy-, Arylalkoxy-, Aryloxy-, and Alkylthio-benzophenones.*

By WADIE TADROS and ALBERT LATIF.

Decomposition of *benzophenone*-4 : 4′-*bis*(*trimethylammonium chloride*) by sodium alkoxide, *cyclo*alkoxide, arylalkoxide, aryloxide, or thioalkoxide gave usually, as main products, the benzophenones substituted by (*a*) two dimethylamino-, (*b*) two RO (or RS) groups, and (*c*) one dimethylamino- and one RO (or RS) group. This offered a means for the preparation of 4 : 4′-*di*cyclo*hexyloxybenzophenone*. 4-*Hydroxy*-4′-tert.-*butoxybenzophenone* was obtained instead of the di-*tert*.-butoxy-compound. Decomposition of *diphenylmethane*- or *benzhydrol*-4 : 4′-*bis*(*trimethylammonium chloride*) with sodium methoxide or ethoxide gave bisdimethylamino-hydrocarbon and -alcohol respectively.

ATTEMPTS to prepare 4 : 4′-di-*tert*.-butoxy- and -*cyclo*hexyloxy-benzophenone from 4 : 4′-dihydroxybenzophenone (Jones, *J*., 1936, 1854) or 4 : 4′-dibromobenzophenone by Ullmann's method (Dilthey, *J. pr. Chem*., 1933, **136**, 49) failed. In view of the finding (Zaki and Tadros, *J*., 1941, 350) that the decomposition of *p*-formylphenyltrimethylammonium chloride and alcoholic sodium ethoxide gave a mixture of *p*-ethoxy- and *p*-dimethylamino-benzaldehyde, the preparation of the above compounds was explored on similar lines.

Benzophenone-4 : 4′-*bis*(*trimethylammonium chloride*) was decomposed with alcoholic sodium *cyclo*hexyloxide and *tert*.-butoxide whereby 4 : 4′-*di*cyclo*hexoxy*- and 4-*hydroxy*-4′-tert.-*butoxybenzophenone* were obtained, together with other fractions (see Experimental section). The reaction was extended to the preparation of other 4 : 4′-disubstituted benzophenones. Mixed benzophenones (see Table II) are thus readily obtained.

The decomposition of *diphenylmethane*- or *benzhydrol*-4 : 4′-*bis*(*trimethylammonium chloride*) with alcoholic sodium methoxide or ethoxide gave rise only to Michler's base or hydrol, respectively. The formation of the alkoxy-compounds in the decomposition of the benzophenone salt was apparently caused by the presence of the electron-attracting carbonyl group. Michler's base and hydrol were also obtained by thermal decomposition of the corresponding dichlorides, whereas the thermal decomposition of benzophenone-4 : 4′-bis(trimethylammonium chloride) gave some Michler's ketone together with unidentified products.

Oxidation of the quaternary diphenylmethane or benzhydrol chlorides with potassium permanganate or nitric acid gave the ketone salt.

EXPERIMENTAL.

(M. p.s are uncorrected. Microanalyses were by Drs. Weiler and Strauss of Oxford.)

Diphenylmethane-4 : 4′-*bis*(*trimethylammonium Methosulphate*).—A mixture of Michler's base (25 g., 1 mol.) and methyl sulphate (50 g., 4 mols.) was cautiously heated on the water-bath, the vigorous exothermic reaction being controlled by cooling. When the reaction subsided, the mixture was heated on the water-bath for 3 hours. The almost colourless semi-solid material obtained on cooling was treated with a little absolute alcohol and left overnight in the ice-chest. The crystalline *salt* was filtered off and crystallised from absolute alcohol and dry ether. It was soluble in water and alcohol but insoluble in acetone, ether, and benzene; it softens at 140° and melts at 170° (decomp.) (Found : C, 49·6; H, 6·7; N, 5·8; S, 12·5. $C_{21}H_{34}O_8N_2S_2$ requires C, 49·8; H, 6·7; N, 5·6; S, 12·6%).

Benzophenone-4 : 4′-bis(trimethylammonium methosulphate) was similarly prepared but was not isolated.

The methosulphates were converted into the dipicrates, from which the *dichlorides*, *dibromides*, *di-iodides* (also obtained by refluxing, for 2—3 hours, Michler's base or ketone with an excess of methyl iodide in methyl alcohol and then distilling off the solvent and excess of methyl iodide), and *diperchlorates* were obtained in the usual manner (cf. Zaki and Tadros, *loc. cit*.).

Benzhydrol-4 : 4′-*bis*(*trimethylammonium picrate*) was obtained from the *di-iodide*. The *dichloride* and other *salts* were then obtained from the dipicrate.

The properties and analyses of the quaternary salts are given in Table I.

Dipicrates of the Condensation Products of Benzophenone-4 : 4′-*bis*(*trimethylammonium Chloride*) *with Hydroxylamine, Semicarbazide, and Phenylhydrazine*.—A mixture of the dichloride (2 g.), hydroxylamine hydrochloride (0·5 g. in the least amount of water), anhydrous sodium carbonate (0·5 g.), and absolute alcohol (10 c.c.) was refluxed for 3 hours and then was filtered, and the alcohol distilled off. The *oxime dipicrate*, prepared from the aqueous solution of the residue, separated in yellow crystals m. p. 234° (decomp.) (Found : C, 48·2; H, 3·9; N, 16·3. $C_{31}H_{31}O_{15}N_9$ requires C, 48·3; H, 4·0; N, 16·4%).

The *dipicrates* of the semicarbazone and the phenylhydrazone, similarly prepared (dichloride, 1 g.; semicarbazide or phenylhydrazine hydrochloride, 0·5 g.; fused sodium acetate, 0·5 g.; absolute alcohol, 10 c.c.), separated from water in orange crystals. The former sintered at 164° and melted at 194° (Found : C, 47·6; H, 4·1; N, 18·3. $C_{32}H_{33}O_{15}N_{11}$ requires C, 47·4; H, 4·1; N, 18·9%). The latter had m. p. 188—190° (Found: C, 52·8; H, 4·2; N, 16·1. $C_{37}H_{36}O_{14}N_{10}$ requires C, 52·6; H, 4·3; N, 16·6%).

TABLE I.

Salt.	M. p.	Crystn. solvent.	Found, %.			Formula.	Required, %.		
			C.	H.	N.		C.	H.	N.
Benzophenone-4 : 4′-*bis*(*trimethylammonium*).									
Dipicrate	206—208°	Dil. EtOH	49·3	3·9	14·6	$C_{31}H_{30}O_{15}N_8$	49·3	4·0	14·7
Dichloride	179—180 *	EtOH–Et₂O	61·6	5·0	7·1	$C_{19}H_{26}ON_2Cl_2$	61·8	5·1	7·5
				(Cl, 18·9)				(Cl, 19·2)	
Dibromide	167 *	,,	49·5	5·9	6·1	$C_{19}H_{26}ON_2Br_2$	49·7	6·0	6·2
				(Br, 34·4)				(Br, 34·8)	
Di-iodide †	150—152 *	,,	41·0	4·6	4·8	$C_{19}H_{26}ON_2I_2$	41·4	4·7	5·1
				(I, 45·2)				(I, 45·8)	
Diperchlorate ...	281 *	Dil. EtOH	45·7	5·3	5·4	$C_{19}H_{26}O_9N_2Cl_2$	45·9	5·3	5·6
				(Cl, 13·9)				(Cl, 14·3)	
Benzhydrol-4 : 4′-*bis*(*trimethylammonium*).									
Dipicrate	191	Dil. EtOH	49·6	4·3	14·8	$C_{31}H_{32}O_{15}N_8$	49·2	4·2	14·8
Dichloride	182—183 *	EtOH–Et₂O	61·1	8·1	8·1	$C_{19}H_{28}ON_2Cl_2$	61·5	7·5	7·5
				(Cl, 18·8)				(Cl, 19·1)	
Dibromide	193—194 *	,,	49·1	5·9	6·2	$C_{19}H_{28}ON_2Br_2$	49·7	6·0	6·2
				(Br, 34·2)				(Br, 34·8)	
Di-iodide	194 *	,,	41·3	5·3	4·8	$C_{19}H_{28}ON_2I_2$	41·3	5·1	5·1
				(I, 45·1)				(I, 45·7)	
Diperchlorate ...	250—251 *	Dil. EtOH	45·2	5·6	5·4	$C_{19}H_{28}O_9N_2Cl_2$	45·7	5·6	5·6
				(Cl, 15·3)				(Cl, 15·4)	
Diphenylmethane-4 : 4′-*bis*(*trimethylammonium*).									
Dipicrate	174—176	Dil. EtOH	50·1	4·1	15·0	$C_{31}H_{32}O_{14}N_8$	50·3	4·3	15·1
Dichloride	170 *	EtOH–Et₂O	64·0	7·8	8·0	$C_{19}H_{28}N_2Cl_2$	64·2	7·9	7·9
				(Cl, 19·8)				(Cl, 20·0)	
Dibromide	206 *	,,	51·2	6·3	6·1	$C_{19}H_{28}N_2Br_2$	51·4	6·3	6·3
				(Br, 35·3)				(Br, 36·0)	
Di-iodide	246 *	,,	42·1	5·8	5·1	$C_{19}H_{28}N_2I_2$	42·5	5·9	5·3
				(I, 46·6)				(I, 47·0)	
Diperchlorate ...	278—280 *	Dil. EtOH	46·9	5·8	5·6	$C_{19}H_{28}O_8N_2Cl_2$	47·2	5·8	5·8
				(Cl, 14·7)				(Cl, 14·7)	

* M. p. with decomp.

† Nathansohn and Müller (*Ber.*, 1889, **22**, 8175) prepared this iodide by addition of methyl iodide to Michler's ketone and gave m. p. 105° (presumably a misprint).

All the salts are freely soluble in water and alcohol, but completely insoluble in ether, benzene, or acetone. The quaternary ammonium dichlorides, dibromides and di-iodides are hygroscopic and retain solvent of crystallisation (particularly alcohol) which could only be removed after heating for a considerable time in vacuum over phosphoric oxide or calcium chloride.

Oxidation of Diphenylmethane- and Benzylhydrol-4 : 4′-*bis*(*trimethylammonium Chlorides*).—(*a*) *Oxidation with potassium permanganate in acid.* A 1% solution of potassium permanganate was added drop by drop to a stirred solution of the diphenylmethane- or benzhydrol-4 : 4′-bis(trimethylammonium chloride) (1·0 g.) in 75 c.c. of 7·5% aqueous sulphuric acid at 70° until a pink colour persisted for a few minutes. The colour disappeared on further heating of the mixture on a water-bath. The manganese dioxide was filtered off, aqueous sodium hydroxide was added drop by drop to the filtrate, care being taken not to make the solution alkaline, and the solution was filtered again from the manganese dioxide. Picric acid solution was added to the filtrate. The precipitated picrate, crystallised from dilute alcohol, had m. p. 206—208° alone or when mixed with an authentic specimen of the benzophenone-4 : 4′-bis-(trimethylammonium picrate).

(*b*) *Oxidation with concentrated nitric acid.* A solution of the diphenylmethane or benzhydrol dichloride (1·0 g.) in concentrated nitric acid (20 c.c.; *d* 1·42) was heated on the water-bath for 4 hours. The mixture was then evaporated nearly to dryness on the water-bath, and the residue was treated twice with 10 c.c. of concentrated hydrochloric acid and evaporated almost to dryness after each treatment. The dipicrate prepared from the residue proved to be benzophenone-4 : 4′-bis(trimethylammonium picrate).

Diphenylmethane-4 : 4′-bis(trimethylammonium methosulphate) was similarly oxidised; the vigorous reaction was controlled by cooling and refluxing on the sand-bath was undertaken only when evolution of the nitrogen oxides subsided. The same product was obtained.

Oxidation with 50% aqueous nitric acid under the above conditions was unsuccessful.

Decomposition of Diphenylmethane-, Benzhydrol-, and Benzophenone-4 : 4′-*bis*(*trimethylammonium Chloride*).—(a) *Thermal decomposition.* (i) Diphenylmethane-4 : 4′-bis(trimethylammonium chloride) (2 g.) was heated in an oil-bath until molten and the temperature was then kept at about 180° for ½ hour. The oily residue, which solidified on cooling, consisted of Michler's base and separated from alcohol in pale greenish crystals, m. p. 90—91° alone or when mixed with an authentic specimen.

(ii) Benzhydrol-4 : 4′-bis(trimethylammonium chloride) (2 g.) was similarly treated at 200°. The product consisted of the hydrol, m. p. 99° alone or when mixed with an authentic specimen.

TABLE II.

Products (A) 4 : 4′-*di*-R-*benzophenone*, (p-$C_6H_4R)_2CO$, *and* (B) 4-*dimethylamino*-4′-R-*benzophenone*, p-NMe_2•C_6H_4•CO•C_6H_4R-p, *obtained, usually along with* 4 : 4′-*dimethylamino- and* 4-*dimethylamino*-4′-*hydroxybenzophenone, from benzophenone*-4 : 4′-*bis*(*trimethylammonium chloride*), CO(C_6H_4•NMe_3·Cl-$p)_2$, *by decomposition with* NaR *in the corresponding alcohol.*

	Product A.							Product B.								
R.	M. p.	Crystn. solvent.[11]	Found, %. C.	Found, %. H.	Formula.	Reqd., %. C.	Reqd., %. H.	M. p.[12]	Crystn. solvent.	Found, %. C.	Found, %. H.	Found, %. N.	Formula.	Reqd., %. C.	Reqd., %. H.	Reqd., %. N.
OMe[1]	146°	EtOH	74·5	5·9	$C_{15}H_{14}O_3$	74·4	5·8	130° [13]	Dil. EtOH	75·3	6·6	5·2	$C_{16}H_{17}O_2N$	75·3	6·7	5·5
OEt[2]	131	,,	75·7	6·7	$C_{17}H_{18}O_3$	75·6	6·8	108 (103—104)[10]	,,	75·9	6·9	5·3	$C_{17}H_{19}O_2N$	75·8	7·1	5·2
OPr^n [3]	127	,,	76·5	7·4	$C_{19}H_{22}O_3$	76·7	7·6	104 (100) [10]	,,	76·3	7·4	4·9	$C_{18}H_{21}O_2N$	76·3	7·4	4·9
OPr^i [4]	72—73	MeOH	76·5	7·4	$C_{19}H_{22}O_3$	76·4	7·3	116 (112) [10]	Dil. MeOH	76·1	7·4	5·2	$C_{18}H_{21}O_2N$	76·3	7·4	4·9
OBu^n [5]	118	EtOH	77·3	7·9	$C_{21}H_{26}O_3$	77·5	7·8	113—114 (96)	EtOH	76·3	7·4	4·8	$C_{19}H_{23}O_2N$	76·8	7·7	4·7
OBu^t	—	—	—	—	—	—		122—123 (101) [10]	,,	76·3	7·3	5·1	$C_{19}H_{23}O_2N$	76·8	7·7	4·7
*cyclo*Hexyloxy	139	EtOH	78·9	7·6	$C_{25}H_{30}O_3$	79·2	7·9	118 (97)	MeOH	77·6	7·4	4·9	$C_{21}H_{25}O_2N$	78·0	7·7	4·3
Benzyloxy[6] ...	188	C_6H_6	82·1	5·6	$C_{27}H_{22}O_3$	82·2	5·6	115—116	EtOH-C_6H_6	79·8	6·3	4·9	$C_{22}H_{21}O_2N$	79·8	6·4	4·3
OPh[7]	147	C_6H_6–EtOH	81·9	4·9	$C_{25}H_{18}O_3$	82·0	4·9	—	—	—	—	—	—	—	—	—
SMe[8]	126	EtOH	65·7 (S, 23·1)	5·2	$C_{15}H_{14}OS_2$	65·7 (S, 23·3)	5·1	114—115 [10]	Dil. EtOH	71·0 (S, 11·9)	6·2	5·6	$C_{16}H_{17}ONS$	70·9 (S, 11·8)	6·3	5·2
SEt[9]	117—118 [10]	Dil. EtOH	67·9 (S, 20·9)	6·1	$C_{17}H_{18}OS_2$	67·6 (S, 21·2)	5·9	104—105 [10]	,,	72·0 (S, 10·9)	7·0	4·9	$C_{17}H_{19}ONS$	71·6 (S, 11·2)	6·7	4·9

[1-5] Jones, *loc. cit.* [6, 9] Tadros, this vol., p. 442. [7] Dilthey, *loc. cit.* [8] Schönberg, *Annalen*, 1923—24, **436**, 205. [10] Pale yellow crystals. [11] Addition of few drops of glacial acetic acid aids crystallisation. [12] Figures in parentheses are temperatures of sintering. [13] D.R.-P. 295,495 (Friedländer, **13**, p. 339); Pfeiffer and Loewe, *loc. cit.*

(iii) The benzophenone dichloride (10 g.) was similarly treated at 200°. The oily residue, which solidified on cooling, consisted of some Michler's ketone together with other products which require further investigation. The same was observed when the decomposition was carried out in a current of carbon dioxide.

(b) *Decomposition with sodium alkoxide, arylalkoxide,* cyclo*alkoxide, aryloxide, and thioalkoxide.* (i) When a mixture of diphenylmethane- or benzhydrol-4 : 4′-bis(trimethylammonium chloride) (5 g.) and methyl-alcoholic sodium methoxide (2 g. of sodium in 20 c.c. of methyl alcohol) was refluxed for 3 hours and then diluted with water and acidified with hydrochloric acid, a clear solution was obtained, which was neutralised with sodium hydroxide solution drop by drop until a precipitate was formed. This separated from alcohol in colourless crystals and was proved by its m. p. and mixed m. p. to be Michler's base or hydrol respectively. The same result was obtained on decomposition with alcoholic sodium ethoxide or alcoholic sodium phenoxide.

(ii) When benzophenone-4 : 4′-bis(trimethylammonium chloride) was similarly treated, four product were obtained which were separated as follows. The mixture was treated with concentrated hydrochloric acid and the insoluble fraction filtered off. This fraction (A) (about 50—55%) separated from alcohol in colourless crystals, m. p. 144°, and was proved by its m. p. and mixed p.m. and by analysis to be 4 : 4′-dimethoxybenzophenone. The acid filtrate was then treated with 10% aqueous sodium hydroxide drop by drop until a precipitate (B) of 4-dimethylamino-4′-methoxybenzophenone (about 20—25%) was formed. This separated from dilute alcohol in colourless crystals, m. p. 132° (Pfeiffer and Loewe, *J. pr. Chem.*, 1937, **147**, 293, give m. p. 133°). The filtrate from fraction B (which was still acid) was made definitely alkaline. The resulting precipitate (fraction C) (about 5—10%) separated from alcohol in greenish crystals, proved by their m. p. and mixed m. p. to be Michler's ketone. Acidification of the alkaline filtrate with acetic acid (drop by drop) gave a little precipitate (fraction D), separating from dilute alcohol in pale greenish crystals, m. p. 198—200°. It proved to be 4-dimethylamino-4′-hydroxybenzophenone (Pfeiffer and Loewe, *loc. cit.*; Shah, Deshapande, and Chaubal, *J.*, 1932 642) (Found: C, 74·6; H, 6·1; N, 5·7. Calc. for $C_{15}H_{15}O_2N$: C, 74·7; H, 6·2; N, 5·8%).

(iii) As shown in Table II, the decomposition of benzophenone-4 : 4′-bis(trimethylammonium chloride), by the above procedure, with alcoholic sodium ethoxide, *n*-propoxide, *iso*propoxide, *n*-butoxide, benzyloxide, *cyclo*hexyloxide, and phenoxide gave Michler's ketone (fraction C), 4-dimethylamino-4′-hydroxybenzophenone (fraction D), and the compounds corresponding to the fractions A and B, except that with the phenoxide the compound corresponding to fraction B could not be isolated.

Decomposition with sodium thiomethoxide and thioethoxide (Klason, *Ber.*, 1887, **20**, **3407**) gave compounds corresponding to fractions A, B, and C.

4-*Hydroxy*-4′-tert.-*butoxybenzophenone*, obtained on the decomposition of the benzophenone dichloride with alcoholic sodium *tert.*-butoxide, separated from light petroleum (b. p. 40—60°) in almost colourless crystals sintering at 65° and melting at 85° (Found: C, 75·5; H, 6·7. $C_{17}H_{18}O_3$ requires C, 75·4; H, 6·5%).

FOUAD I UNIVERSITY, ABBASSIA, CAIRO, EGYPT.

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