7. Degradation of Quaternary Ammonium Salts. Part IV. Relative Migratory Velocities of Substituted Benzyl Radicals.
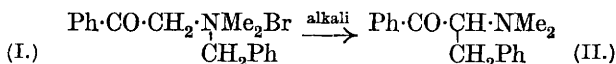
By Thomas Thomson and Thomas Stevens Stevens.

THE effect of substitution, by Cl, Br, I, NO_2, Me, or OMe, in the o-, m-, or p-position in the benzyl group, on the velocity of the rearrangement (I) $\longrightarrow$ (II) has now been examined (compare J., 1928, 3193; 1930, 2107, 2119).

$$Ph \cdot CO \cdot CH_2 \cdot \underset{\underset{CH_2Ph}{|}}{N}Me_2Br \xrightarrow{\text{alkali}} Ph \cdot CO \cdot \underset{\underset{CH_2Ph}{|}}{C}H \cdot NMe_2$$

(I.)   (II.)

As a necessary preliminary, the rearrangement of the unsubstituted compound (I) was investigated in some detail. It was found that the reaction did not proceed quantitatively, but gave rise to some 12—15% of by-product, isolated as a neutral gum from which no definite compound could be extracted. In view of this complication, the course of the rearrangement was followed by direct isolation both of (II) as such and of (I) as picrate. The quantity k, defined by the equation

$$x = k \int_0^t y \, . \, dt$$

where x and y are the concentrations of (II) and (I) respectively at time t, was arbitrarily taken as a measure of the progress of the reaction. This is equivalent to the assumptions that the main reaction is of the first order with respect to (I) and of zero order with respect to the alkali, and that the side reaction is simultaneous with the rate-determining stage of the main process. In the absence of evidence as to the nature of the side reaction, however, the procedure is to be regarded as empirical, and justified as a method of comparison by the facts that the values of k found during the reaction did, indeed, show satisfactory constancy, and that the ratios of the migratory velocities of a series of substituted benzyl radicals were the same whether the radicals were associated with phenacyl or with p-bromophenacyl in the quaternary salts.

The reaction was carried out in methyl-, ethyl-, n-propyl-, and *iso*propyl-alcoholic solutions of the corresponding sodium alkoxides, with the following general results (compare Table I). (1) The use of two mols. of alkoxide in place of one caused an appreciable, but not a proportional, increase in velocity; a third molecule had little further effect. (2) The velocity varied with the medium in the order $\text{MeOH} \ll \text{EtOH} < \text{Pr}^{\alpha}\text{OH} \ll \text{Pr}^{\beta}\text{OH}$. (3) The by-product was formed principally in the early stages of the reaction, and its quantity, which could be determined only roughly, was largely independent of the conditions, in particular, of the dilution. (4) The temperature coefficient of the reaction has the high value $Q_{10°} = 5.70$ for the temperature interval 16.4—$37.7°$. (5) The quaternary *iodide* corresponding to (I) is rearranged at the same rate as the bromide.

The inequalities [(2) above] might be attributed either to " medium effects," or, as the observed order would indeed suggest, to the difference in reagent (sodium alkoxide) (compare Kon and Linstead, J., 1929, 1271). The second alternative is, however, improbable, for the reaction velocity showed comparatively little dependence on, still less proportionality to, the alkoxide concentration, even for the less effective reagent sodium methoxide. Moreover, although salt formation, presumably at the " reactive " methylene group, actually takes place, the process is rapid and extensive, since the quaternary salt neutralised 0.5—0.75 equiv. of sodium ethoxide on titration with thymolphthalein as indicator. That the reaction is indeed sensitive to change of medium was shown by replacing 60% of the methyl or ethyl alcohol as solvent by toluene, whereupon the velocity was increased 2.7- and 2.3-fold respectively : on the other hand, the disparity in effectiveness between the two reagents was but little diminished. An effective study of this point was hindered by the paucity of media in which sodium alkoxides dissolve unchanged.

TABLE I.

Concentration (N).		Coefficients $k \cdot 10^4$ in			
Salt.	Alkoxide.	MeOH.	EtOH.	Pr^{a}OH.	Pr$^\beta$OH.
0·10	0·10	33·0	99	111	242
0·05	0·05	32·0	106	112	254
0·05	0·10	41·9	107	126	288
0·05	0·15	44·9	—	—	—·—
0·025	0·05	41·9	—	—	—

Measurements were also made in aqueous sodium hydroxide solution. Here the (much smaller) initial velocities were nearly proportional to the alkali concentrations, as well as to those of the quaternary salt; and as the reaction proceeded, the values of k fell off, but not in such a way as to suggest an essentially " bimolecular " process.

Effect of Substitution.—The measurements summarised in Table II were carried out in methyl-alcoholic solutions $0·05N$ with respect to the salts and $0·1N$ with respect to sodium methoxide. Two of the salts were studied as iodides instead of bromides, since the latter could not be crystallised, and in two cases the p-bromophenacyl radical was used in place of phenacyl, for the same reason. The validity of the first expedient has been tested by the experiments, already mentioned, on phenacylbenzyldimethylammonium iodide; the checks on the second are recorded in the table itself. Owing to the wide range of velocities, several measurements were made at $16·4°$, and the others at $37·7°$. p-Bromophenacylbenzyldimethylammonium bromide was studied at both temperatures, and showed the temperature coefficient $Q_{10}. = 5·61$, compared with 5·70 for the unsubstituted compound; the two values for m-nitrobenzyl (Table II) may also be cited.

TABLE II.

Substituent in benzyl group.

	Cl.	Br.	I.	NO$_2$.	OMe.	Me.
o-	*35·6*	*47·7*	*81*	*1040*	†*1·91*	**15·3*
m-	2·44	2·09 } †2·10 }	1·92	†*3·80* } *3·81* }	0·93	**0·97*
p-	2·77 } †2·58 }	2·86 } †2·68 }	3·25	73	0·76	†1·06

* Measured as phenacyldimethylammonium iodide.

† Measured as p-bromophenacyldimethylammonium bromide.

The figure recorded in Table II is in each case the ratio of the speed of migration of the substituted benzyl radical to unsubstituted benzyl under the same conditions; the italicised values refer to measurements at $16·4°$, the others to $37·7°$. The errors of manipulation probably do not exceed $\pm 2\%$, but the existence of the side reaction introduces an uncertainty which is difficult to assess, and

may be considerably greater than this. The amount of by-product formed is very similar for those salts which do not contain either a nitro-substituted benzyl or a p-bromophenacyl radical. The presence of these radicals usually increases the extent of the side reaction, but when the same substituted benzyl radical is investigated in combination both with phenacyl and with p-bromophenacyl, the two values for the relative migratory velocity are in reasonably good agreement.

Attention is drawn to the following points. (1) The order $OMe < Me < Hals. < NO_2$ holds for all three positions (the inequality m-$OMe < m$-Me is not established). (2) In the o-series the halogens fall in the order $Cl < Br < I$ (compare Ingold, *Ann. Reports*, 1927, **24**, 156). This order, at least as regards Cl and I, appears to be retained in the p-, but reversed in the m-position. (3) The compounds of the o-series show the same arrangement among themselves qualitatively, and to some extent quantitatively, as the p-compounds, but with greatly increased velocity of rearrangement (except in the case of OMe). (4) For each substituent the m- and p-values are of the same order of magnitude, except that (5) p-nitrobenzyl migrates far more rapidly than m-nitrobenzyl.
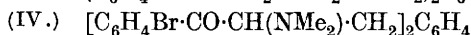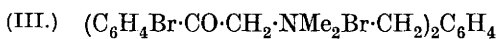
The series (1) is of common occurrence, and could be accommodated on most theories relating to reactivities of organic molecules in general, and on several hypotheses as to the mechanism of the present rearrangement. It constitutes, however, an exception to the generalisation of von Braun, Kühn, and Weismantel (*Annalen*, 1926, **449**, 252), that, although the behaviour of radicals attached to carbon is less simple, those attached to nitrogen show a specific tenacity nearly independent of the nature of the molecule in which they are contained. In the present investigation, the normal " tenacity series " is roughly reversed.

If it be justifiable to correlate exaggerated " alternate " effects in conjugated systems with the structural possibility of the stabilisation of the end-product (or an essential intermediate) by a tautomeric rearrangement, then the observation (5) is evidence in favour of such a mechanism as (*A*) below, as against that proposed by Bennett and Chapman (*Ann. Reports*, 1930, **27**, 123), which may be crudely represented by (*B*)
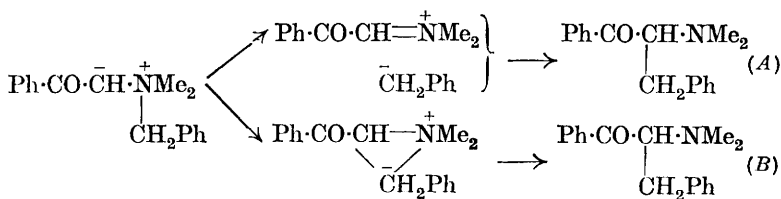
The materials were prepared by methods analogous to those described in Parts II and III. The various sets of isomerides show unusual behaviour as to melting points, in that the p-compound is more frequently the lowest- than the highest-melting of the three. No general regularities have, however, been recognised.

A sample of s.-p-*xylylenebis*-p-*bromophenacyltetramethyldiammonium dibromide* (III) happened to be available, and it was found that treatment with alkali caused a double migration, resulting in (IV). The m-xylylene analogue was also prepared, and behaved in a similar manner.

(III.) $(C_6H_4Br \cdot CO \cdot CH_2 \cdot NMe_2Br \cdot CH_2)_2C_6H_4$

(IV.) $[C_6H_4Br \cdot CO \cdot CH(NMe_2) \cdot CH_2]_2C_6H_4$

EXPERIMENTAL.

Technique of Measurements.—The volumetric process described in Part II depends on the assumption that the reaction proceeds substantially quantitatively, without the formation of by-products, and a fresh method had therefore to be devised, allowing the estimation *both* of rearrangement product *and* of unaltered quaternary salt. After numerous unsuccessful attempts to achieve this object by titration, the following gravimetric procedure was adopted.

The reaction was carried out in a flask (frequently 15 c.c.) filled to the neck by the solution under investigation (to prevent atmospheric oxidation of the rearrangement product; it is not, however, necessary to use boiled-out reagents), and the process effectively checked by pouring into water (40 c.c.) containing ammonium chloride equivalent to the alkali originally used. The product (II) was extracted with ether (3 × 20 c.c.), and the united extracts were washed once with water. The aqueous layer and washings were acidified with acetic acid, warmed to 30—40°, freed from ether by a current of air, and treated gradually with 0·2N-sodium picrate solution (2 c.c. excess; larger quantities of sodium picrate or of ammonium chloride may cause separation of ammonium picrate). The precipitate of quaternary picrate crystallised readily on scratching; after remaining over-night it was collected and dried at 100°. The tertiary base was extracted from the ethereal solution by hydrochloric acid (3 × 10 c.c. of 0·1N); and the acid solution heated on the water-bath to expel ether, cooled in ice, and treated with ammonia; the precipitated base then crystallised readily on agitation. After some hours it was collected and brought to constant weight in a current of dry air.

On the basis of control experiments with known quantities of material, the manipulatory losses were estimated at 5 mg. for the tertiary base, and for the picrate, 1 mg. + (1 mg. per 5 c.c. of

alcohol used). These corrections raise the reaction coefficients by some 4%.

The tertiary base is little affected by caustic alkali in the absence of air, or by air in the absence of caustic alkali. The quaternary compound is not extracted from its aqueous solutions by ether, nor is it affected by $0.1N$-ammonia in several days at room temperature.

The alcohols used were lime-dried and distilled over sodium. With ethyl and *iso*propyl alcohols, results some 15% lower were obtained in different specimens; the recorded figures all relate to the same sample. No such behaviour was observed with methyl alcohol.

The measurements on the substituted salts were carried out in the same manner, and it was considered sufficiently accurate to use the same corrections for manipulatory losses. In one or two cases in which the quaternary picrate showed a tendency to separate out in an oily condition, the sodium picrate was added dropwise to the hot solution of the quaternary salt.

Results.—The data for phenacylbenzyldimethylammonium brom-ide $(0.50N)$ in sodium methoxide $(0.1N)$ at $16.4°$ are given in full as a specimen. The definite integral in the expression for k (p. 55) is evaluated by Simpson's rules; x and y are expressed in mols.% on the initial material, and t in minutes.

t	2880	5760	8640	11,520	14,400
x	24·5	41·8	54·0	63·6	69·4
y	68·1	48·8	35·4	26·7	19·6
$k \times 10^4$	1·02	1·03	1·03	1·04	1·02

Phenacylbenzyldimethylammonium bromide at $37.7°$.

Medium.	Conc. of salt, N.	b, %.	$k \cdot 10^4$.
$0.10N$-NaOMe	0·10	9	33.0 ± 0.6
$0.05N$-NaOMe	0·05	12	32.0 ± 0.5
$0.10N$-NaOMe	0·05	13	41.9 ± 0.4
$0.15N$-NaOMe	0·05	12	44.9 ± 1.0
$0.05N$-NaOMe	0·025	14	41.9 ± 1.1
*$0.10N$-NaOMe	0·05	14	41.5 ± 0.1
$0.10N$-NaOEt	0·10	8	99 ± 2
$0.05N$-NaOEt	0·05	9	106 ± 2
$0.10N$-NaOEt	0·05	9	107 ± 2
$0.10N$-NaOPr^a	0·10	9	111 ± 1
$0.05N$-NaOPr^a	0·05	13	112 ± 1
$0.10N$-NaOPr^a	0·05	12	126 ± 1
$0.10N$-NaOPr$^\beta$	0·10	7	242 ± 4
$0.05N$-NaOPr$^\beta$	0·05	8	254 ± 8
$0.10N$-NaOPr$^\beta$	0·05	8	288 ± 2
†$0.05N$-NaOMe	0·05	12	87 ± 2
†$0.05N$-NaOEt	0·05	11	240 ± 4
$0.10N$-NaOH	0·10	11	$2.53 - 2.33$
$0.05N$-NaOH	0·05	12	$1.40 - 1.18$
$0.10N$-NaOH	0·05	9	$2.77 - 2.60$

* Phenacylbenzyldimethylammonium iodide.

† Medium : alcohol–toluene, 2 : 3 by wt.

The values in the column headed b are the percentages of by-product formed (estimated by difference) when 60% of the initial material has disappeared; very little is produced subsequently. To indicate the degree of consistency of the results, the mean deviations from the average are annexed to the k values. On an average, five determinations were made in each case.

The measurements in aqueous sodium hydroxide were carried out with greater quantities of material, and the manipulatory errors were smaller. In each case the coefficients fell off steadily as the reaction proceeded.

Substituted quaternary salts at 37·7°.

Substituent.	b, %.	$k . 10^4$.	Substituent.	b, %.	$k . 10^4$.
m-Cl	13	102 ± 1·5	p-I	12	136 ± 2
{ p-Cl	9	116·5 ± 1·5	†m-NO₂	24	128 ± 2
{ †p-Cl	22	86·8 ± 0·5	m-OMe	15	38·9 ± 0·3
{ m-Br	12	87·7 ± 1·1	p-OMe	13	31·8 ± 0·7
{ †m-Br	17	70·5 ± 0·3	*m-Me	15	40·2 ± 1·0
{ p-Br	10	120 ± 2	†p-Me	21	35·6 ± 0·8
{ †p-Br	22	90·1 ± 0·8	†(H)	14	33·6 ± 0·3
m-I	14	80·3 ± 0·5			

Substituted quaternary salts at 16·4°.

Substituent.	b, %.	$k . 10^4$.	Substituent.	b, %.	$k . 10^4$.
o-Cl	10	36·7 ± 0·5	p-NO₂	25	75·3 ± 0·5
o-Br	12	49·1 ± 0·7	†o-OMe	14	1·63 ± 0·01
o-I	13	83·0 ± 1·3	*o-Me	13	15·8 ± 0·5
o-NO₂	16	1070 ± 20	†(H)	14	0·854 ± 0·012
m-NO₂	20	3·92 ± 0·08			

* Measured as phenacyldimethylammonium iodide.

† Measured as p-bromophenacyldimethylammonium bromide.

Preparation and Characterisation of Materials.—Phenacylbenzyldimethylammonium picrate formed deep yellow needles or stout laminæ from methyl alcohol, m. p. 132—134° (Found : $C_6H_2O_7N_3'$, 47·3. $C_{17}H_{20}ON \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 47·3%). The *iodide* crystallised from water in colourless, sparingly soluble prisms, m. p. 174—176° (Found : I, 33·4. $C_{17}H_{20}ONI$ requires I, 33·3%). The crystalline ferrocyanide and the amorphous mercuri-iodide and the bismuthi-iodide are highly insoluble, but of inconstant composition.

o-*Chlorobenzyldimethylamine.—o*-Chlorobenzyl bromide was conveniently prepared by brominating *o*-chlorotoluene with undiluted bromine; the reaction, which set in spontaneously, was completed by heating under reflux, and the product isolated by distillation in a vacuum. Conversion into the tertiary base by the hexamine method (Sommelet and Guioth, *Compt. rend.*, 1922, **174**, 687) gave a moderate yield, together with a considerable quantity of *o*-chlorobenzaldehyde (oxime, m. p. 76°). *o*-Chlorobenzyldimethylamine picrate was isolated in the first place from ether and recrystallised from aqueous methyl alcohol, m. p. 145—146° (von Braun, Kühn,

and Weismantel, *loc. cit.*, give m. p. 146°). *Phenacyl-o-chlorobenzyl-dimethylammonium bromide*, formed fairly rapidly from chloro-benzyldimethylamine and bromoacetophenone in cold benzene solution, separated as an oil which gradually solidified. It crystal-lised from alcohol–ether in minute prismatic needles, m. p. 149—150° (Found : Br, 20·4, 20·3. $C_{17}H_{19}ONClBr,H_2O$ requires Br, 20·7%). An attempt to dehydrate the salt at 105—110° led to decomposition. The *picrate*, fine, glistening, yellow needles from methyl alcohol, melted at 154—156° (Found : $C_6H_2O_7N_3'$, 44·6. $C_{17}H_{19}ONCl \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 44·1%).

ω-*Dimethylamino-ω-o-chlorobenzylacetophenone*, obtained by the degradation of the quaternary salt, formed long, prismatic needles from methyl alcohol, m. p. 69—71° (Found : Cl, 12·5. $C_{17}H_{18}ONCl$ requires Cl, 12·3%).

m-*Chlorobenzyldimethylamine.*—m-Chlorobenzyl bromide was pre pared by brominating *m*-chlorotoluene with undiluted bromine at 130°, the bromine being added, dropwise, under the surface of the liquid. The resultant liquid was kept in an evacuated desiccator over potassium hydroxide until free from hydrobromic acid, dried with anhydrous sodium sulphate, and distilled in a vacuum, the *m*-chlorobenzyl bromide being isolated as an oil, b. p. 108—111°/10 mm. Conversion into the tertiary base by the hexamine method gave a fair yield. m-*Chlorobenzyldimethylamine picrate* was isolated in the first instance from aqueous methyl alcohol, and crystallised from benzene in aggregates of minute yellow prisms, m. p. 128—130° (Found : $C_6H_3O_7N_3$, 58·0. $C_9H_{12}NCl,C_6H_3O_7N_3$ requires $C_6H_3O_3N_7$, 57·5%). *Phenacyl-m-chlorobenzyldimethylammonium bromide*, pre-pared from the components in cold benzene, separated as an oil which slowly solidified, and crystallised from alcohol–ether in warty masses of minute prisms, m. p. 132—134° (Found : Br, 21·9%). The *picrate*, fine yellow needles from methyl alcohol, melted at 141—143° (decomp.) (Found : $C_6H_2O_7N_3'$, 43·7%). ω-*Dimethyl-amino-ω-m-chlorobenzylacetophenone* formed minute, short prisms from methyl alcohol, m. p. 52—53° (Found : Cl, 12·4%).

p-*Chlorobenzyldimethylamine.*—p-Chlorobenzyl bromide was pre-pared as for the ortho-compound, except that the solid reaction product was not distilled, but was recrystallised from methyl alcohol, and obtained in colourless needles, m. p. 62—63°. Conversion into the tertiary base by the hexamine method gave a very good yield. p-*Chlorobenzyldimethylamine picrate* was isolated in the first place from ether; it crystallised from acetone–ether in stout, yellow prisms, m. p. 125—126° (Found : $C_6H_3O_7N_3$, 57·7%). *Phenacyl-p-chlorobenzyldimethylammonium bromide*, prepared from the com-ponents in cold benzene, separated as a colourless crystalline solid,

and crystallised from alcohol–ether in short prisms, m. p. 186—187° (decomp.) (Found : Br, 21·7%). The *picrate,* yellow prismatic needles from methyl alcohol, melted at 125—126° (Found : $C_6H_2O_7N_3'$, 44·0%). ω-*Dimethylamino*-ω-p-*chlorobenzylacetophenone* formed fine needles from methyl alcohol, m. p. 59—61° (Found : Cl, 12·0%).

o-*Bromobenzyldimethylamine.*—o-Bromobenzyl bromide was prepared as for the o-chloro-compound, and gave the tertiary base in good yield by the hexamine method. o-*Bromobenzyldimethylamine picrate,* obtained in the first instance from ether, crystallised from aqueous methyl alcohol in small, bright yellow prisms, m. p. 149—150° (Found : $C_6H_3O_7N_3$, 51·5. $C_9H_{12}NBr,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 51·7%).

Phenacyl-o-*bromobenzyldimethylammonium bromide,* prepared from the components in cold benzene, separated as a crystalline solid, and crystallised from alcohol–ether in minute prismatic needles, m. p. 153—154° (Found : ionisable Br, 18·2, 18·6; loss at 100°, 4·3. $C_{17}H_{19}ONBr·Br',H_2O$ requires Br', 18·6; loss, 4·2%). The *picrate,* fine, glistening yellow needles, from methyl alcohol, melted at 151—153° (Found : $C_6H_2O_7N_3'$, 41·0. $C_{17}H_{19}ONBr·C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 40·6%).

ω-*Dimethylamino*-ω-o-*bromobenzylacetophenone* formed fine needles from methyl alcohol, m. p. 79—81° (Found : Br, 23·8. $C_{17}H_{18}ONBr$ requires Br, 24·1%).

Phenacyl-*m*-bromobenzyldimethylammonium bromide was prepared as described in Part II (*loc. cit.*). The *picrate* formed yellow prismatic needles from methyl alcohol, m. p. 132—134° (Found : $C_6H_2O_7N_3'$, 41·0%).

Phenacyl-*p*-bromobenzyldimethylammonium bromide was prepared as described in Part III (J., 1930, 2122). The *picrate* formed fine, yellow, prismatic needles from methyl alcohol, m. p. 130—131° (Found : $C_6H_2O_7N_3'$, 40·8%).

The Isomeric Iodobenzyldimethylamines.—The preparation of the isomeric iodobenzyl bromides was attempted as described by Olivier (*Rec. trav. chim.,* 1923, **42**, 519), *i.e.,* by the bromination of the corresponding iodotoluenes, the ortho-compound at 200—205°, the meta- at 200°, and the para- at 150—155°, but the yields were unsatisfactory. Good yields were obtained, however, by carrying out the bromination in the light of a carbon arc lamp (silica flask), in carbon tetrachloride solution at the boiling point. For example, o-iodotoluene (20 g.), carbon tetrachloride (80 c.c.), and water (40 c.c.) were refluxed during the dropwise addition of bromine (5·5 c.c. in 20 c.c. of carbon tetrachloride) and until decolorisation took place. The carbon tetrachloride layer was dried, the solvent distilled off,

and the residue crystallised from methyl alcohol. The yields of bromides obtained were 74% for the ortho-compound, 78% for the meta-, and 74% for the para-. The bromides were converted into the tertiary bases by the hexamine method. o-*Iodobenzyldimethylamine picrate* was obtained in the first instance from ether, and crystallised from aqueous methyl alcohol in aggregates of minute yellow prisms, m. p. 134—136° (Found: $C_6H_3O_7N_3$, 46·2. $C_9H_{12}NI,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 46·7%). m-*Iodobenzyldimethylamine picrate* was obtained in the first place from ether, and crystallised from benzene in spherical aggregates of minute yellow prisms, m. p. 128—130° (Found: $C_6H_3O_7N_3$, 46·6%). p-Iodobenzyldimethylamine was identified as the picrate, m. p. 146—148° (von Braun, Kühn, and Weismantel, *loc. cit.*, give m. p. 148°).

Phenacyl-o-*iodobenzyldimethylammonium bromide*, prepared from the components in cold benzene, separated as an oil which solidified rapidly, and crystallised from alcohol–ether in minute, prismatic needles, m. p. 174—176° (Found: Br, 17·2. $C_{17}H_{19}ONBrI$ requires Br, 17·4%). The *picrate*, fine, yellow needles from methyl alcohol, melted at 149—151° (Found: $C_6H_2O_7N_3'$, 37·3. $C_{17}H_{19}ONI \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 37·5%). ω-*Dimethylamino-ω-o-iodobenzylacetophenone* formed rectangular prisms from methyl alcohol, m. p. 97—98° (Found: I, 33·8. $C_{17}H_{18}ONI$ requires I, 33·5%).

Phenacyl-m-*iodobenzyldimethylammonium bromide*, prepared from the components in cold benzene, separated as an oil which gradually solidified, and crystallised from alcohol–ether in rosettes of stout prismatic needles, m. p. 176—177° (slight decomp.) (Found: Br, 17·6%). The *picrate*, rosettes of stout, yellow prisms from acetone, melted at 123—125° (Found: $C_6H_2O_7N_3'$, 38·0%). ω-*Dimethylamino-ω-m-iodobenzylacetophenone* formed rosettes of fine, very faintly yellow needles, m. p. 82—83° (Found: I, 33·4%).

Phenacyl-p-*iodobenzyldimethylammonium bromide*, prepared from the components in cold benzene, separated as an oil which solidified quite rapidly, and crystallised from alcohol–ether in minute, cubical crystals, m. p. 183—185° (Found: ionisable Br, 16·4, 16·8; loss at 105°, 3·7. $C_{17}H_{19}ONIBr,H_2O$ requires Br, 16·7; loss, 3·8%). The *picrate* formed minute, yellow prisms from methyl alcohol, m. p. 139—141° (Found: $C_6H_2O_7N_3'$, 37·2%). ω-*Dimethylamino-ω-p-iodobenzylacetophenone* formed stout, prismatic needles from methyl alcohol, m. p. 67—68° (Found: I, 33·3%).

o-*Nitrobenzyldimethylamine.*—o-Nitrobenzyl bromide was conveniently prepared by brominating o-nitrotoluene in carbon tetrachloride solution in the light from an arc lamp, as described above for the preparation of the iodobenzyl bromides. Conversion to the tertiary base was accomplished by the action of dimethylamine

(compare Part III, p. 2122). The *picrate* formed clusters of short, yellow prisms from acetone–ligroin, m. p. 138—141° (Found : $C_6H_3O_7N_3$, 55·7. $C_9H_{12}O_2N_2,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 56·0%). *Phenacyl-o-nitrobenzyldimethylammonium bromide,* prepared from the components in cold benzene, separated as an oil which gradually solidified, and crystallised from alcohol–ether in minute prisms, m. p. 142—144° (Found : Br, 20·8. $C_{17}H_{19}O_3N_2Br$ requires Br, 21·1%). The *picrate,* minute, yellow, prismatic needles from methyl alcohol, melted at 155—158° (Found : $C_6H_2O_7N_3'$, 43·0. $C_{17}H_{19}O_3N_2 \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 43·3%). *ω-Dimethyl-amino-ω-o-nitrobenzylacetophenone* formed clusters of light yellow stout prisms from methyl alcohol, m. p. 75—77° (Found : N, 9·7. $C_{17}H_{18}O_3N_2$ requires N, 9·4%).

m-*Nitrobenzyldimethylamine.*—m-Nitrobenzyl bromide was prepared by converting m-nitrobenzaldehyde into the alcohol (Becker, *Ber.,* 1882, **15**, 2090), and treating the latter in benzene solution with hydrogen bromide. The bromide was converted into the tertiary base by the hexamine method. The *picrate* formed yellow rectangular prisms from acetone, m. p. 209—211° (decomp.) (Found : $C_6H_3O_7N_3$, 56·5%). *Phenacyl-*m-*nitrobenzyldimethylammonium bromide,* prepared from m-nitrobenzyldimethylamine and ω-bromoacetophenone in cold benzene, crystallised from alcohol–ether in minute prismatic needles, m. p. 174—175° (Found : Br, 20·7%). The *picrate* formed minute, yellow, prismatic needles from methyl alcohol, m. p. 154—156° (Found : $C_6H_2O_7N_3'$, 43·6%). *ω-Dimethyl-amino-ω-*m-*nitrobenzylacetophenone* formed long, fine, straw-coloured needles from methyl alcohol, m. p. 70—72° (Found : N, 9·3%).

Phenacyl-*p*-nitrobenzyldimethylammonium bromide was prepared as described in Part III (p. 2123). The *picrate* formed fine, yellow needles from methyl alcohol, m. p. 110—113° (Found : $C_6H_2O_7N_3'$, 43·7%).

o-*Methoxybenzyldimethylamine.*—Salicylaldehyde was methylated as described by Sidgwick and Bayliss (J., 1930, 2028). *o*-Methoxybenzaldoxime was reduced as described for the *p*-isomeride (Part III, p. 2112). The *o*-methoxybenzylamine hydrochloride formed fine glistening plates, m. p. 149—150° (Goldschmidt and Ernst, *Ber.,* 1890, **23**, 2742, give m. p. 150°). *o*-Methoxybenzyldimethylamine was obtained by the Eschweiler methylation of the primary base, and identified as hydrochloride, m. p. 149° (compare Stedman, J., 1927, 1904). With ω-bromoacetophenone in benzene, the tertiary base gave a yellow, viscous oil which could not be induced to crystallise. However, p-*bromophenacyl-o-methoxybenzyldimethylammonium bromide* was prepared from *o*-methoxybenzyldimethylamine and ωp-dibromoacetophenone in cold benzene, and separated as an oily

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solid, crystallising from alcohol–ether in minute, prismatic needles, m. p. 173—176° (Found: ionisable Br, 17·9. $C_{18}H_{21}O_2NBr·Br'$ requires Br', 18·1%). The *picrate* formed minute, yellow prisms from acetone–ligroin, m. p. 116—119° (Found: $C_6H_2O_7N_3'$, 38·9. $C_{18}H_{21}O_2NBr·C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 38·6%). p-*Bromo-ω-dimethylamino-ω-o-methoxybenzylacetophenone* formed minute prisms from methyl alcohol, m. p. 82—83° (Found: Br, 21·8. $C_{18}H_{20}O_2NBr$ requires Br, 22·1%).

m-Methoxybenzyldimethylamine was prepared from m-hydroxy-benzaldehyde in an analogous manner to the foregoing ortho-compound, and was identified as hydrochloride (compare Stedman, *loc. cit.*). *Phenacyl-m-methoxybenzyldimethylammonium bromide*, prepared from the components in cold benzene, separated as an oil which slowly solidified, and crystallised from alcohol–ether in short, stout prisms, m. p. 150—152° (Found: Br, 21·6; $C_{18}H_{22}O_2NBr$ requires Br, 22·0%). The *picrate*, stout, yellow prisms from methyl alcohol, melted at 111—112° (Found: $C_6H_2O_7N_3'$, 44·2. $C_{18}H_{22}O_2N·C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 44·5%).

ω-*Dimethylamino-ω-m-methoxybenzylacetophenone*, glistening plates from methyl alcohol, melted at 61—63° (Found: N, 5·04. $C_{18}H_{21}O_2N$ requires N, 4·95%).

o-*Methylbenzyldimethylamine.*—o-Xylyl bromide was conveniently prepared by bromination of o-xylene as described by Atkinson and Thorpe (J., 1907, **91**, 1695). Conversion into the tertiary base was accomplished by the hexamine method. o-*Methylbenzyldimethylamine picrate* formed aggregates of minute yellow prisms from benzene, m. p. 148—150° (Found: $C_6H_3O_7N_3$, 60·2. $C_{10}H_{15}N,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 60·6%). Phenacyl-o-methyl-benzyldimethylammonium bromide, prepared from the components in cold benzene, separated as a dark oil which could not be induced to crystallise. Conversion into the *iodide* resulted in a gummy product which, after many attempts, was obtained crystalline from aqueous acetone in the form of minute prisms, m. p. 160—162° (decomp.) (Found: I, 32·3. $C_{18}H_{22}ONI$ requires I, 32·2%). The *picrate* formed deep yellow, short prisms from methyl alcohol, m. p. 131—133° (Found: $C_6H_2O_7N_3'$, 46·5. $C_{18}H_{22}ON·C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 46·0%).

ω-*Dimethylamino-ω-o-methylbenzylacetophenone* formed minute prisms from methyl alcohol, m. p. 62—63° (Found: N, 5·45. $C_{18}H_{21}ON$ requires N, 5·24%).

m-*Methylbenzyldimethylamine.*—m-Xylyl bromide, prepared as for the o-isomeride, was converted into the tertiary base by the hexamine method. m-*Methylbenzyldimethylamine picrate* formed aggregates

of minute yellow prisms from benzene, m. p. 136—138° (Found :
$C_6H_3O_7N_3$, 60·3%). Phenacyl-*m*-methylbenzyldimethylammonium
bromide, prepared from the components in cold benzene, separated
as a dark oil which could not be induced to crystallise. It was
converted into a viscous *iodide*, which, after many attempts in a
variety of solvents, was crystallised from aqueous methyl alcohol
in clusters of minute prisms, m. p. 134—135° (decomp.) (Found :
I, 32·0%). ω-*Dimethylamino*-ω-m-*methylbenzylacetophenone* formed
rosettes of faintly yellow, short prisms from methyl alcohol, m. p.
74—76° (Found : N, 5·32%).

Tetramethyl-m-*xylylenediamine*.—*m*-Xylylene dibromide, obtained
along with *m*-xylyl bromide in the bromination of *m*-xylene, was
treated with dimethylamine (4—6 mols.) in alcoholic solution. After
remaining for 12 hours, the mixture was heated for 2 hours on the
water-bath, concentrated, diluted with water, and extracted with
benzene. On treatment with picric acid the benzene extract yielded
tetramethyl-m-*xylylenediamine picrate*, which crystallised from
acetone–ligroin in masses of minute, yellow prisms, m. p. 190—193°
(decomp.) (Found : $C_6H_3O_7N_3$, 71·0. $C_{12}H_{20}N_2,2C_6H_3O_7N_3$
requires $C_6H_3O_7N_3$, 70·5%).

s.-m-*Xylylenebis*-p-*bromophenacyltetramethyldiammonium dibrom-
ide*, prepared from the foregoing diamine and *p*-bromophenacyl
bromide in cold benzene, formed minute prisms from alcohol–ether,
m. p. 205—206° (Found : ionisable Br, 21·2. $C_{28}H_{32}O_2N_2Br_4$
requires 2Br, 21·4%).

4 : 4′ - *Dibromo* - ω : ω′ - *bisdimethylamino*-ω : ω′ - m-*xylylenebisaceto-
phenone*.—The foregoing bromide was heated on the water-bath for
15 minutes with excess sodium hydroxide solution, and the product
recrystallised from methyl alcohol, giving fine, pale yellow needles,
m. p. 143—144° (Found : Br, 27·1. $C_{28}H_{30}O_2N_2Br_2$ requires Br,
27·3%).

p-*Methylbenzyldimethylamine*.—Bromination of *p*-xylene by the
method of Atkinson and Thorpe (*loc. cit.*) led to a mixture of *p*-xylyl
bromide and *p*-xylylene dibromide, which could only be separated
from each other with difficulty on the small scale. Crude *p*-xylyl
bromide was treated with dimethylamine (2—3 mols.) in alcoholic
solution, and the reaction mixture worked up in the usual way. On
treatment with picric acid, the benzene layer yielded the picrate of
tetramethyl-*p*-xylylenediamine, and the aqueous layer gave glisten-
ing, yellow plates of di-*p*-methylbenzyldimethylammonium picrate.
The latter was converted into the quaternary chloride, and heated
with dimethylamine (3 mols.) at 200° for 3 hours. The reaction
mixture was basified, extracted with ether, and the *p*-methylbenzyl-

dimethylamine isolated by distillation, b. p. 196—199°. Neither the phenacylobromide nor the corresponding iodide could be obtained in crystalline condition.

p-*Bromophenacyl*-p-*methylbenzyldimethylammonium bromide*, prepared from the components in cold benzene, formed rosettes of minute prismatic needles, m. p. 174—176° (decomp.) (Found : ionisable Br, 18·7. $C_{18}H_{21}ONBr \cdot Br'$ requires Br′, 18·7%). The *picrate* formed clusters of fine yellow needles from methyl alcohol, m. p. 128—130° (decomp.) (Found : $C_6H_2O_7N_3'$, 40·1. $C_{18}H_{21}ONBr \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 39·7%). p-*Bromo-ω-dimethylamino-ω*-p-*methylbenzylacetophenone* formed fine needles from methyl alcohol, m. p. 91—93° (Found : Br, 23·4. $C_{18}H_{20}ONBr$ requires Br, 23·1%).

s.-p-*Xylylenebis*-p-*bromophenacyltetramethyldiammonium dibromide*, prepared from tetramethyl-p-xylylenediamine and p-bromophenacyl bromide in cold benzene, formed minute prismatic needles from alcohol–ether, m. p. 220—222° (decomp.) (Found : ionisable Br, 21·7%).

4 : 4′ - *Dibromo* - ω : ω′ - *bisdimethylamino* - ω : ω′ - p - *xylylenebisacetophenone*.—The foregoing bromide was heated on the water-bath with excess sodium hydroxide solution for 10 minutes, and the product recrystallised from methyl alcohol, giving minute, faintly yellow prisms, m. p. 138—140° (Found : Br, 27·0%).

p-Bromophenacylbenzyldimethylammonium bromide was prepared as described in Part II (J., 1930, 2116). The *picrate* formed glistening, yellow prisms from methyl alcohol, m. p. 159—160° (Found : $C_6H_2O_7N_3'$, 40·4. $C_{17}H_{19}ONBr \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 40·6%).

p-*Bromophenacyl*-p-*chlorobenzyldimethylammonium bromide*, prepared from p-bromophenacyl bromide and p-chlorobenzyldimethylamine in cold benzene, formed rosettes of minute, needle-shaped prisms, m. p. 174—175° (Found: ionisable Br, 18·2. $C_{17}H_{18}ONClBr \cdot Br'$ requires Br′, 17·9%). The *picrate* formed yellow, lustrous, prismatic needles from methyl alcohol, m. p. 146—147° (decomp.) (Found : $C_6H_2O_7N_3'$, 38·4. $C_{17}H_{18}ONClBr \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 38·3%).

p-*Bromo-ω-dimethylamino-ω*-p-*chlorobenzylacetophenone* formed fine, very faintly yellow, prismatic needles from methyl alcohol, m. p. 75—76° (0·1210 gave 0·1086 AgCl + AgBr. $C_{17}H_{17}ONClBr$ requires 0·1094).

p-*Bromophenacyl*-p-*bromobenzyldimethylammonium bromide*, prepared from p-bromophenacyl bromide and p-bromobenzyldimethylamine in cold benzene, formed minute prismatic needles from alcohol–ether, m. p. 187—188° (decomp.) (Found : ionisable Br,

16·6. $C_{17}H_{18}ONBr_3$ requires 1Br, 16·3%). The *picrate* formed short, stout, yellow prisms from acetone, m. p. 157—158° (decomp. gradually above 128°) (Found : $C_6H_2O_7N_3'$, 35·2. $C_{17}H_{18}ONBr_2 \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 35·6%). p-*Bromo-ω-dimethylamino-ω-p-bromobenzylacetophenone* formed rosettes of fine, pale yellow needles from methyl alcohol, m. p. 77—78° (Found : Br, 38·6. $C_{17}H_{17}ONBr_2$ requires Br, 38·9%).

p-*Bromophenacyl*-m-*bromobenzyldimethylammonium bromide*, prepared from p-bromophenacyl bromide and m-bromobenzyldimethyl-amine in cold benzene, formed stout prisms from alcohol, m. p. 193° (decomp.) (Found : ionisable Br, 16·4. $C_{17}H_{18}ONBr_3$ requires ionisable Br, 16·3%). The *picrate* formed short, yellow prisms from methyl alcohol, m. p. 136—137° (Found : $C_6H_2O_7N_3'$, 35·3. $C_{17}H_{18}ONBr_2 \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 35·6%). p-*Bromo-ω-dimethylamino-ω-m-bromobenzylacetophenone* formed rosettes of stout, straw-coloured prisms from methyl alcohol, m. p. 68—70° (Found : Br, 38·7. $C_{17}H_{17}ONBr_2$ requires Br, 38·9%).

p-*Bromophenacyl*-m-*nitrobenzyldimethylammonium bromide*, prepared from p-bromophenacyl bromide and m-nitrobenzyldimethyl-amine in cold benzene, formed minute, prismatic needles from alcohol, m. p. 200—201° (decomp.) (Found : ionisable Br, 17·7. $C_{17}H_{18}O_3N_2Br_2$ requires ionisable Br, 17·5%). The *picrate* formed small, thick, yellow prisms from methyl alcohol, m. p. 158—159° (Found : $C_6H_2O_7N_3'$, 37·9. $C_{17}H_{18}O_3N_2Br \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 37·6%). p-*Bromo-ω-dimethylamino-ω-m-nitrobenzylaceto-phenone* formed small, faintly straw-coloured prisms from methyl alcohol, m. p. 72—73° (Found : Br, 21·0. $C_{17}H_{17}O_3N_2Br$ requires Br, 21·2%).