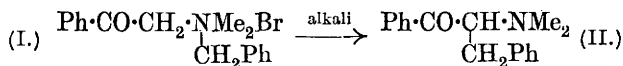**262.** *Degradation of Quaternary Ammonium Salts. Part VI. Effect of Substitution on Velocity of Intramolecular Rearrangement.*

By JOHN LAING DUNN and THOMAS STEVENS STEVENS.

THE effect of substitution in the phenacyl radical on the velocity of migration of the benzyl group in the rearrangement (I) $\longrightarrow$ (II)

has now been examined (compare Thomson and Stevens, this vol., p. 55).

$$(\text{I.}) \quad \underset{\underset{\displaystyle \dot{C}H_2Ph}{|}}{Ph \cdot CO \cdot CH_2 \cdot NMe_2 Br} \xrightarrow{\text{alkali}} \underset{\underset{\displaystyle \dot{C}H_2Ph}{|}}{Ph \cdot CO \cdot \dot{C}H \cdot NMe_2} \quad (\text{II.})$$

The reactions were carried out in dry methyl-alcoholic solutions $0 \cdot 05N$ with respect to the salts and $0 \cdot 1N$ with respect to sodium methoxide, at $37 \cdot 7°$, as previously described (*loc. cit.*). In general, the quaternary bromides were used, but in the cases of the *o*- and *m*-bromo-compounds, the iodides, and in that of the *p*-nitro-, the chloride was employed, the previous investigation having shown this procedure to be admissible. The velocity coefficients are recorded in Table I; the number in parentheses may have no other significance than that of the maximum value (compare experimental part). The precision of the method has already been discussed (*loc. cit.*); in the present study the inequality $p\text{-Me}>(\text{H})$ is considered established, but not the smaller differences. On account of the comparatively small effect of substitution on the reaction velocity, and of certain practical complications referred to in the experimental part, the scope of the investigation was not extended.

The results may be summarised, independently of any theory of the reaction mechanism, by the statement that the presence of so-called "negative" substituents in the benzene nucleus of the phenacyl group retards the reaction, whereas their presence in the benzyl radical causes marked acceleration (Thomson and Stevens, *loc. cit.*). It was suggested (Stevens, J., 1930, 2108; Thomson and Stevens, *loc. cit.*) that the alkaline medium first converts the salts nearly completely into neutral ions of the type $Ph \cdot CO \cdot \bar{C}H \cdot \overset{+}{N}Me_2 \cdot CH_2Ph$, and that the velocity of the rearrangement is then determined by that of the detachment of the migrating radical from the nitrogen atom. If now the instability of the anionic carbon atom in the neutral ion is regarded as supplying the driving force of the reaction, the velocity of rearrangement would increase with diminishing acidity of the phenacyl methylene group in the original salt, and substitution in the phenacyl radical would be expected to influence the velocity of rearrangement mainly by its effect on this acidity. Preliminary experiments carried out by Mr. T. Thomson, to determine the acid dissociation constants of such salts, did not give encouraging results, and as the similarly substituted benzoic acids are the most legitimate analogues for which data are available, their dissociation constants K_a are recorded along with the velocity coefficients in Table I. The two sets of values show a fair degree of parallelism in the inverse sense, except

TABLE I.

Substituent.	$k \cdot 10^4$.	$K_a \cdot 10^5$.	Substituent.	$k \cdot 10^4$.	$K_a \cdot 10^5$.
p-OMe	31·9	3·2	m-Br	34·2	13·7
p-Me	46·1	4·3	m-NO$_2$	‡ 22·5	34·8
(H)	*41·9	6·6	o-Br	‡ 8	145
p-Cl	33·9	9·3	o-NO$_2$	(<8)	630
p-Br	*33·6	†			
p-I	32·8	†			

* Thomson and Stevens, *loc. cit.*

† The dissociation constants of these acids have not been measured in aqueous solution, but in 50% methyl alcohol they are practically the same as that of p-chlorobenzoic acid (Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 31).

‡ Derived by slightly modified methods (compare experimental part).

in the case of the p-methoxy-compounds, but the experimental data are not sufficiently extensive to justify great stress being laid on the fact.

EXPERIMENTAL.

Technique of Measurements.—The measurements were carried out as described by Thomson and Stevens (*loc. cit.*).

p-Iodo-ω-dimethylamino-ω-benzylacetophenone gave a hydrochloride rather sparingly soluble in water, making it necessary to precipitate the free base with ammonia from the *hot* aqueous solution.

As the o-bromo-analogue was an oil, the normal procedure could not be adopted. Attempts to isolate it quantitatively as picrate proving unsuccessful, the bromine content of the total basic material formed after 8 hours was estimated, and some 90% of the original material thus accounted for, a figure which agrees well with the usual side-reaction losses. Runs of 2, 4, and 6 hours in which only the quaternary salt was recovered as picrate were made and from these and the above a figure for k was deduced which is probably comparable in accuracy with the other values in Table I.

The o- and p-nitro-salts were destroyed by alkali, but under no conditions could any tertiary base be recovered. On treatment in aqueous solution both substances gave tarry material, but in sodium methoxide solution the o-nitro-salt gave water-soluble products only. The half-life period of the o-nitro-compound was about 900 and that of the p-nitro- about 150 minutes; the maximum value for the o-compound given in Table I is based on these figures.

The m-nitro-salt on degradation gave a series of values of $k \cdot 10^4$ which showed a progressive diminution from 21 to 15. This can be accounted for by the destruction of the normal degradation product by the alkali, for when 0·3 g. of that base was subjected for 4 hours

to conditions similar to those used in the degradation, less than
0·1 g. could be recovered.

t	90	180	270	360	450
Recovered quaternary salt	70·5	52·8	40·3	31·4	24·3
Tertiary base	17·5	24·8	30·0	33·4	38·5
$k \cdot 10^4$	21·0	19·7	17·8	16·4	15·4

The figure given in Table I is the value arrived at by extrapolating
these values to zero time.

Table II shows the values of $k \cdot 10^4$ for the remaining salts,
together with the mean deviations from the average. Column b
contains the percentages of by-product formed when 60% of the
initial material has disappeared, very little being formed subse-
quently. In general, five determinations were made.

TABLE II.

Substituent.	b %.	$k \cdot 10^4$.	Substituent.	b %.	$k \cdot 10^4$.
o-Br	12	8	p-I	10	$32·8 \pm 0·6$
m-Br	7	$34·2 \pm 1·3$	p-Me	8	$46·1 \pm 0·8$
p-Cl	11	$33·9 \pm 1·5$	p-OMe	11	$31·9 \pm 1·2$

Preparation and Characterisation of Materials.—The p-methyl-,
-methoxy-, -chloro-, and -iodo-acetophenones prepared by the
Friedel–Crafts reaction were converted into the ω-bromo-derivatives
by bromination in glacial acetic acid (Judefind and Reid, *J. Amer.
Chem. Soc.*, 1920, **42**, 1044). The substituted phenacyl bromides
so obtained had the properties attributed to them in the literature.
The quaternary salts were formed in cold benzene or ether from the
bromo-ketones and benzyldimethylamine.

p-*Methylphenacylbenzyldimethylammonium bromide* (ether; yield,
almost quantitative) crystallised from alcohol–ether in small pris-
matic needles, m. p. 185—186° (Found : Br, 23·1. $C_{18}H_{22}ONBr$
requires Br, 23·0%); *picrate*, yellow needles, m. p. 149—150°, from
methyl alcohol (Found : $C_6H_2O_7N_3'$, 45·9. $C_{18}H_{22}ON \cdot C_6H_2O_7N_3$
requires $C_6H_2O_7N_3'$, 46·0%). ω-*Dimethylamino-ω-benzyl-p-methyl-
acetophenone*, obtained by the degradation of the quaternary
ammonium salt, gave minute prismatic needles, m. p. 62°, from
methyl alcohol; it rapidly decomposed even in a sealed tube
(Found : N, 5·4. $C_{18}H_{21}ON$ requires N, 5·2%).

p-*Methoxyphenacylbenzyldimethylammonium bromide* (benzene;
good yield) crystallised from alcohol–ether in colourless prismatic
needles, m. p. 202—203° (Found : Br, 21·7. $C_{18}H_{22}O_2NBr$ requires
Br, 22·0%), and its *picrate* from methyl alcohol in yellow needles,
m. p. 144—145° (Found : $C_6H_2O_7N_3'$, 44·7. $C_{18}H_{22}O_2N \cdot C_6H_2O_7N_3$
requires $C_6H_2O_7N_3'$, 44·6%). ω-*Dimethylamino-p-methoxy-ω-benzyl-
acetophenone* crystallised from methyl alcohol in clusters of colour-

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less needles, m. p. 57—58° (Found : N, 4·7. $C_{18}H_{21}O_2N$ requires N, 4·9%).

p-*Iodophenacylbenzyldimethylammonium bromide* (benzene) crystallised from absolute alcohol in small plates, m. p. 179—180° (Found : Br, 16·9. $C_{17}H_{19}ONBrI,H_2O$ requires Br, 16·7%). Decomposition set in at 105—110°. The *picrate* crystallised from methyl alcohol in yellow prismatic needles, m. p. 151—152° (Found : $C_6H_2O_7N_3'$, 37·4. $C_{17}H_{19}ONI \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 37·6%), and p-*iodo-ω-dimethylamino-ω-benzylacetophenone* in clusters of yellow needles, m. p. 119—120° (Found : I, 33·6. $C_{17}H_{18}ONI$ requires I, 33·5%).

p-*Chlorophenacylbenzyldimethylammonium bromide* (benzene ; good yield) crystallised from alcohol–ether in small microcrystalline masses, m. p. 175—176° (Found : Br, 20·8 ; loss at 100°, 4·5. $C_{17}H_{19}ONClBr,H_2O$ requires Br, 20·7 ; loss, 4·7%) ; *picrate*, yellow prismatic needles, m. p. 155—156°, from methyl alcohol (Found : $C_6H_2O_7N_3'$, 44·1. $C_{17}H_{19}ONCl \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 44·3%). p-*Chloro-ω-dimethylamino-ω-benzylacetophenone*, yellow prisms, m. p. 91—92°, from methyl alcohol (Found : Cl, 12·5. $C_{17}H_{18}ONCl$ requires Cl, 12·3%).

o-Nitroacetophenone was prepared by the hydrolysis of *o*-nitrobenzoylacetoacetic ester (Needham and Perkin, J., 1904, **85**, 152 ; Kermack and Smith, J., 1929, 814) and brominated in glacial acetic acid (Gevekoht, *Annalen*, 1883, **221**, 327). *o*-*Nitrophenacylbenzyldimethylammonium bromide* (benzene) crystallised from absolute alcohol in small, slightly yellow rhombs, m. p. 168—169° (decomp.) (Found : Br, 21·1. $C_{17}H_{19}O_3N_2Br$ requires Br, 21·1%), and its *picrate* from acetone–methyl alcohol (1 : 1) in stout yellow needles, m. p. 167—168° (Found : $C_6H_2O_7N_3'$, 43·5. $C_{17}H_{19}O_3N_2 \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 43·6%).

m-*Nitrophenacylbenzyldimethylammonium bromide*, prepared from ω-bromo-*m*-nitroacetophenone (Hunnius, *Ber.*, 1877, **10**, 2008) and benzyldimethylamine in cold benzene, crystallised from alcohol–ether in yellow cubes, m. p. 153—154° (Found : Br, 20·1. $C_{17}H_{19}O_3N_2Br,H_2O$ requires Br, 20·1%. Heating at 100° leads to decomposition). The *picrate* crystallised from methyl alcohol in slender brown needles, m. p. 134—135° (Found : $C_6H_2O_7N_3'$, 43·9), and m-*nitro-ω-dimethylamino-ω-benzylacetophenone* in yellow prismatic needles, m. p. 77—78° (Found : N, 9·5. $C_{17}H_{18}O_3N_2$ requires N, 9·4%).

p-*Nitrophenacylbenzyldimethylammonium chloride*, obtained as a slowly crystallising oil from ω-chloro-*p*-nitroacetophenone (Bradley and Schwarzenbach, J., 1928, 2907) and benzyldimethylamine in cold benzene, separated from absolute alcohol in small, slightly

yellow needles, m. p. 176° (Found : Cl, 10·7. $C_{17}H_{19}O_3N_2Cl$ requires Cl, 10·6%); *picrate*, stout, almost brown cubes, m. p. 164—165°, from methyl alcohol (Found : $C_6H_2O_7N_3'$, 43·7%).

ω-*Chloro*-m-*bromoacetophenone*, prepared in good yield from diazomethane and *m*-bromobenzoyl chloride (compare Bradley and Schwarzenbach, *loc. cit.*), crystallised from ligroin (b. p. 40—60°) in small plates, m. p. 47—48° [0·1034 g. required 23·4 c.c. 0·0382*N*-AgNO₃ (Robertson). C_8H_6OClBr requires 23·3 c.c.]. The quaternary chloride separated very slowly from cold benzene as an oil and was converted by treatment with potassium iodide into m-*bromophenacylbenzyldimethylammonium iodide*, which crystallised from absolute alcohol in fine needles, m. p. 180—181° (Found : I, 27·5. $C_{17}H_{19}ONBrI$ requires I, 27·9%); *picrate*, yellow needles, m. p. 149—150°, from methyl alcohol (Found : $C_6H_2O_7N_3'$, 41·2. $C_{17}H_{19}ONBr \cdot C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 40·9%). m-*Bromo-ω-dimethylamino-ω-benzylacetophenone*, yellow needles, m. p. 99—100°, from methyl alcohol (Found : Br, 24·3. $C_{17}H_{18}ONBr$ requires Br, 24·1%).

ω-*Chloro*-o-*bromoacetophenone* was prepared by the action of diazomethane on *o*-bromobenzoyl chloride. Owing to the small difference in b. p. between it (164°/10 mm.) and *o*-bromobenzoyl chloride (158°/49 mm.), and to the small quantities used, it could not be obtained sufficiently pure for analysis and was accordingly converted directly in benzene solution into the quaternary chloride, a non-crystallising oil which was converted into o-*bromophenacylbenzyldimethylammonium iodide* : this crystallised from absolute alcohol in small white cubes, m. p. 134—135° (Found : I, 27·6%), its *picrate* in yellow needles, m. p. 125—126° (Found : $C_6H_2O_7N_3'$, 41·1%), and o-*bromo-ω-dimethylamino-ω-benzylacetophenone picrate* from methyl alcohol in clusters of yellow needles, m. p. 126—127° (Found : Br, 14·9. $C_{17}H_{18}ONBr,C_6H_3O_7N_3$ requires Br, 14·6%).