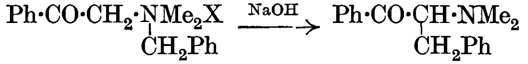
CCLXX.—*Degradation of Quaternary Ammonium Salts. Part II.*

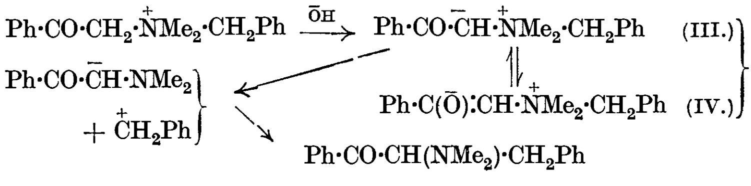
By Thomas Stevens Stevens.

This paper contains the results of a study of the generality of the reaction (I—>II) described in Part I (J., 1928, 3193). It has been found that the replacement of the benzyl radical by *m*-bromobenzyl, *p*-methoxybenzyl, α-phenylethyl, benzhydryl, or 9-fluorenyl, of the phenacyl group by *p*-bromophenacyl, or of the dimethylammonium system by piperidinium, does not prevent the migration. Indeed, the benzhydryl and fluorenyl radicals wander so readily that the quaternary salts cannot be isolated. Further examples of the reaction are recorded in Part III (following paper).

(I.)  (II.)

$$\text{Ph·CO·CH}_2\text{·}\underset{\text{CH}_2\text{Ph}}{\text{N}}\text{Me}_2\text{X} \xrightarrow{\text{NaOH}} \text{Ph·CO·}\underset{\text{CH}_2\text{Ph}}{\text{C}}\text{H·NMe}_2$$

Mechanism of the Rearrangement.—The process was shown to be an *intramolecular* one by acting on a mixture of *phenacyl-*m*-bromobenzyldimethylammonium* and p-*bromophenacylbenzyldimethylammonium bromides* with sodium ethoxide solution. Under similar conditions, the rates of transformation of the two substances separately are of the same order of magnitude, and the mixture yielded only the rearrangement products corresponding to the individual salts; neither ω-dimethylamino-ω-benzylacetophenone nor ω-dimethylamino-ω-*m*-bromobenzyl-*p*-bromoacetophenone could be detected. Further, the reaction takes place in alkaline solutions (sodium or potassium hydroxide, sodium ethoxide, ammonia), but not in a neutral medium. The most plausible mechanism of the transformation appeared to be the conversion of the salt, by alkali, into the keto-enolic betaine (III$\rightleftharpoons$IV), followed by the detachment of the benzyl radical as a kation, and its reattachment at the original methylene carbon atom. The process would thus be analogous to the conversion of betaine into methyl dimethylaminoacetate (Willstätter, *Ber.*, 1902, **35**, 603), or of the anhydride of *N*-trimethyl-*o*-aminophenol into dimethyl-*o*-anisidine (Griess, *Ber.*, 1880, **13**, 248). The marked acidity and ready alkylation of α-amino-ketones have already been recognised (Rabe and Schneider, *Ber.*, 1908, **41**, 872; Wedekind and Bruch, *Annalen*, 1929, **471**, 86).



$$\text{Ph·CO·CH}_2\text{·}\overset{+}{\text{N}}\text{Me}_2\text{·CH}_2\text{Ph} \xrightarrow{\bar{\text{O}}\text{H}} \text{Ph·CO·}\overset{-}{\text{C}}\text{H·}\overset{+}{\text{N}}\text{Me}_2\text{·CH}_2\text{Ph} \quad \text{(III.)}$$

$$\rightleftharpoons \text{Ph·C(}\bar{\text{O}}\text{):CH·}\overset{+}{\text{N}}\text{Me}_2\text{·CH}_2\text{Ph} \quad \text{(IV.)}$$

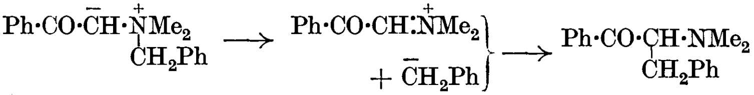
$$\longrightarrow \text{Ph·CO·}\overset{-}{\text{C}}\text{H·NMe}_2 + \overset{+}{\text{C}}\text{H}_2\text{Ph} \longrightarrow \text{Ph·CO·CH(NMe}_2\text{)·CH}_2\text{Ph}$$

The very facile migration of the benzhydryl and fluorenyl radicals (groups of high kationic stability) lent support to this explanation, and it was thought that the view could be most readily confirmed by determining the relative migratory tendencies of substituted benzyl groups. Velocity measurements showed that the reaction is unimolecular in absolute-alcoholic sodium ethoxide solution (salt-formation at the active methylene group is probably complete in sodium ethoxide solution) and the results are quite irreconcilable with the suggested mechanism :

Substituent	H.	*m*-Br.	*p*-Br.	*p*-OMe.	*p*-NO_2.
Relative velocity	1·00	1·60	2·52	0·77	*ca.* 30

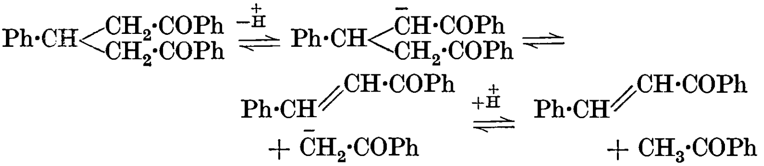
These values are of a preliminary character, as the determination of the relative quantities of the two possible products formed in the rearrangement of salts of the type $\mathrm{Ph{\cdot}CO{\cdot}CH_2{\cdot}NMeX(CH_2Ar){\cdot}CH_2Ar'}$ was expected to yield more accurate and more rigorously valid data. These expectations were not realised (see following paper), and a more accurate and comprehensive series of velocity determinations will be undertaken.

The values just mentioned suggest that the benzyl radicals are detached as *anions* and lead to the following scheme, in which the ω-carbon atom of the phenacylidene group is considered to "capture" the benzyl anion before it can escape into the bulk of the reaction mixture :



$$\mathrm{Ph{\cdot}CO{\cdot}\overset{-}{C}H{\cdot}\underset{CH_2Ph}{\overset{+}{N}}Me_2} \longrightarrow \left.\begin{matrix}\mathrm{Ph{\cdot}CO{\cdot}CH{:}\overset{+}{N}Me_2}\\ +\ \mathrm{\overset{-}{C}H_2Ph}\end{matrix}\right\} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}\underset{CH_2Ph}{C}H{\cdot}NMe_2}$$

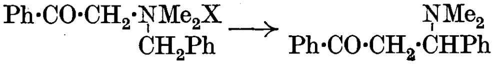
The first stage is formally analogous to the reversed Michael and allied reactions, *e.g.*,



$$\mathrm{Ph{\cdot}CH}\!\begin{matrix}\mathrm{CH_2{\cdot}COPh}\\ \mathrm{CH_2{\cdot}COPh}\end{matrix} \overset{-\overset{+}{H}}{\rightleftharpoons} \mathrm{Ph{\cdot}CH}\!\begin{matrix}\mathrm{\overset{-}{C}H{\cdot}COPh}\\ \mathrm{CH_2{\cdot}COPh}\end{matrix} \rightleftharpoons \begin{matrix}\mathrm{Ph{\cdot}CH{=}CH{\cdot}COPh}\\ +\ \mathrm{\overset{-}{C}H_2{\cdot}COPh}\end{matrix} \overset{+\overset{+}{H}}{\rightleftharpoons} \begin{matrix}\mathrm{Ph{\cdot}CH{=}CH{\cdot}COPh}\\ +\ \mathrm{CH_3{\cdot}COPh}\end{matrix}$$

(compare Vorländer, *Ber.*, 1900, **33**, 3185), and the second to the very energetic action of the Grignard reagent on salts of the pseudo-bases, $\mathrm{>C{:}NR_2X + RMgX \longrightarrow >CR{\cdot}NR_2 + MgX_2}$ (Freund, *Ber.*, 1904, **37**, 4666). (No implication is intended as to the *constitution* of the Grignard reagents : their *reactions* are, however, analogous to those of substances believed to contain anionic hydrocarbon radicals.) The ready migration of the benzhydryl and fluorenyl radicals (which tolerate anionic as well as kationic charges) is in accordance with this view also. It may be noted that, according to the above scheme, the ammonium nitrogen atom is not essential, and the reactions should be capable of wide extension.

Constitution of the Rearrangement Products.—In each case the assigned structure has been confirmed by degradation to, or synthesis from, the related chalkone or hydrochalkone. This defines the carbon skeletons of the products, but does not exclude the possibility of the reaction having taken the course



$$\mathrm{Ph{\cdot}CO{\cdot}CH_2{\cdot}\underset{\displaystyle CH_2Ph}{N}Me_2X} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}CH_2{\cdot}\overset{\displaystyle NMe_2}{C}HPh}$$

and several experiments were carried out in order to devise a practicable and rigorous method of establishing the constitutions of the new bases.

Synthesis of the type

$$\mathrm{Ph{\cdot}CO{\cdot}CH_2{\cdot}CH_2Ph} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}C({:}NOH){\cdot}CH_2Ph} \longrightarrow$$
$$\mathrm{Ph{\cdot}CO{\cdot}CH(NH_2){\cdot}CH_2Ph} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}CH(NMe_2){\cdot}CH_2Ph}$$

was projected, but preliminary experiments on the methylation of ω-aminoacetophenone by the Eschweiler reaction (alkaline reagents being presumably inadmissible owing to pyrazine formation) yielded no trace of the expected product. Again, the process $\mathrm{MgPhBr} + \mathrm{CN{\cdot}CH(NMe_2){\cdot}CH_2Ph} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}CH(NMe_2){\cdot}CH_2Ph}$ was investigated, but the only isolable product of the reaction was αβ-diphenylethyldimethylamine, $\mathrm{CHPh(NMe_2){\cdot}CH_2Ph}$. The interaction of the Grignard reagent with α-aminonitriles is under investigation, and this replacement of cyanogen by a hydrocarbon radical seems to be of somewhat general occurrence (compare the recent observations of Cocker, Lapworth, and Walton on the detachment of the cyano-group from α-substituted nitriles, this vol., p. 453).

It was considered that compounds of the type

$$\mathrm{CH_2Ph{\cdot}CH(NMe_2){\cdot}CH_2Ph}$$

might be obtained from the rearrangement products by reduction, and that their synthesis would not present great difficulties, but preliminary experiments on the reduction of phenacyldimethylamine were disappointing: hydriodic acid and red phosphorus caused decomposition, and reduction by Clemmensen's method gave only ethylbenzene.

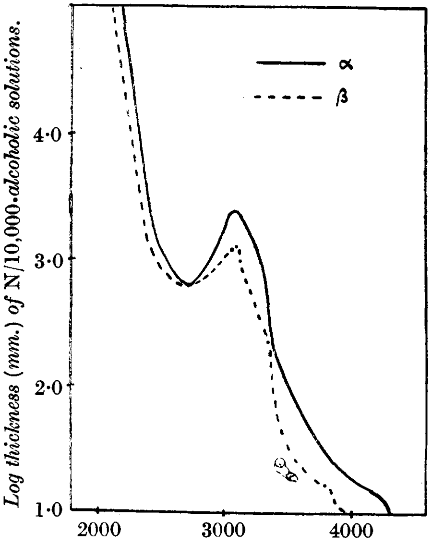
The oxidation of ω-dimethylamino-ω-*p*-bromobenzylacetophenone, $\mathrm{Ph{\cdot}CO{\cdot}CH(NMe_2){\cdot}CH_2{\cdot}C_6H_4Br}$ (following paper), was carried out under a variety of conditions, for the isolation of *p*-bromophenylacetic acid would have provided the required proof of constitution. The substance was remarkably stable towards acid oxidising agents, but was readily attacked in alkaline solution, and in each case the only brominated product was *p*-bromobenzoic acid.

ω-*Piperidino*-ω-*benzylacetophenone* was synthesised from piperidine and ω-bromo-ω-benzylacetophenone, of known constitution (Part I, p. 3194), but ω-*dimethylamino*-ω-*benzhydrylacetophenone* could not be obtained in a similar manner from ω-bromo-ω-benzhydrylacetophenone. By analogy with the last-mentioned compound, the bromination product of ω-9-fluorenylacetophenone was probably ω-*bromo*-ω-9-*fluorenylacetophenone*, $Ph\cdot CO\cdot CHBr\cdot CH<C_{12}H_8$, and it was rapidly converted in the cold by dimethylamine (or by ammonia) into ω-9-*fluorenylideneacetophenone*,

$$Ph\cdot CO\cdot CH{:}C<C_{12}H_8$$

—a striking example of the mobility of the 9-hydrogen atoms in fluorene.

FIG. 1.



Bromination of ω-α-phenylethylacetophenone gave a homogeneous product, probably

$$Ph\cdot CO\cdot CHBr\cdot CHMePh,$$

which, with dimethylamine, yielded the β-stereoisomeride (*vide infra*) of ω-dimethylamino-ω-α-phenylethylacetophenone (V). An attempt to prepare the latter compound from magnesium methyl bromide and ω-dimethylamino-ω-benzylideneacetophenone,

$$Ph\cdot CO\cdot C(NMe_2){:}CHPh$$

(from dimethylamine and α-bromochalkone, compare Dufraisse and Moureu, *Bull. Soc. chim.*, 1927, **41**, 464), was unsuccessful, the main product being a neutral, saturated ketone.

$$Ph\cdot CO\cdot CH(NMe_2)\cdot CHPhMe \quad (V.)$$

The Stereoisomeric ω-*Dimethylamino*-ω-α-*phenylethylacetophenones* (V).—The substance (V) contains two dissimilar asymmetric carbon atoms, and can therefore exist in two racemic forms. By rearrangement of *phenacyl*-α-*phenylethyldimethylammonium bromide*, the two isomerides were produced in nearly equal quantities, and were separated by fractional crystallisation of the picrates. The solid substances showed a remarkable difference in colour: one isomeride formed almost colourless needles, while the other, which appeared to be dimorphous, was usually obtained in deep yellow plates, but occasionally in light yellow nodules. This difference, unusual in such closely related stereoisomerides, is not so marked in solution as in the solid state, and the absorption spectra (for which the author is indebted to Dr. S. Mitchell and Mr. D. Greig) are very similar (Fig. 1). It may be noted that most of the rearrangement products described in this and the following paper form almost colourless needles, closely resembling the corresponding modification of the α-phenylethyl compound.

The yellow form is converted, apparently completely, into the less coloured form by hot sodium ethoxide solution. Presumably the groups round the carbon atom next to the carbonyl group undergo inversion, by enolisation, as in the epimerisation of the lactones of the sugar acids and similar compounds.

EXPERIMENTAL.

In methylations by the Eschweiler method, the hydrochloride of the initial base was heated at 130° for 3 hours with a moderate excess of 40% "formalin." The product, separated from non-basic material, was then isolated as described for the individual cases.

Several of the quaternary salts were prepared in *cold* benzene, since secondary changes appeared to take place on heating. Rearrangement was brought about by heating on the water-bath for 30 minutes with an excess of 2*N*-sodium hydroxide solution; the yields were nearly quantitative.

Low values for carbon were consistently found with some of the compounds of the benzhydryl and fluorenyl series. Better results, indicated by an asterisk, were obtained by combustion in moist oxygen. The picric acid in several of the picrates of tertiary bases was estimated by titration with potassium hydroxide in absolute alcohol, phenolphthalein being used as indicator.

m-*Bromobenzyldimethylamine*.—*m*-Bromobenzyl bromide (prepared according to Shoesmith, J., 1926, 219; bromination with liquid bromine led to an impure product) gave the tertiary base in good yield, either by the hexamine method (Sommelet and Guioth, *Compt. rend.*, 1922, **174**, 687) or by the action of dimethylamine as described for the *p*-isomeride (following paper). In the former case some *m*-bromobenzaldehyde (oxime, m. p. 72°), and in the latter some quaternary salt, was produced. m-*Bromobenzyldimethylamine picrate* was most easily isolated in the first place from ether; it crystallised from benzene or acetone–ether in spherical aggregates of minute orange prisms, m. p. 139—141° (Found: $C_6H_3O_7N_3$, 51·2. $C_9H_{14}NBr,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 51·7%).

Phenacyl-m-*bromobenzyldimethylammonium bromide*, formed fairly rapidly from bromobenzyldimethylamine and bromoacetophenone in cold benzene solution, crystallised from alcohol–ether in stout needles, m. p. 140—143° (Found: ionisable Br, 18·9. $C_{17}H_{19}ONBr{\cdot}Br$ requires Br, 19·3%).

ω-*Dimethylamino*-ω-m-*bromobenzylacetophenone* formed colourless needles from methyl alcohol, m. p. 72—73° (Found: Br, 24·1. $C_{17}H_{18}ONBr$ requires Br, 24·1%). It very slowly resinified when kept. The picrate crystallised from methyl alcohol in bright yellow plates, m. p. 141—143°. The methosulphate, prepared in hot benzene solution, was rapidly decomposed on boiling with alkali, giving *phenyl* m-*bromostyryl ketone*. The same substance (m. p. and mixed m. p. 84—85°) was formed by condensation of *m*-bromobenzaldehyde and acetophenone in warm methyl alcohol containing a little concentrated potassium hydroxide solution. It crystallised from methyl alcohol in colourless, rectangular laminæ, and gave with sulphuric acid a deep yellow coloration, changing to cherry-red on addition of nitric acid (Found: Br, 27·9. $C_{15}H_{11}OBr$ requires Br, 27·9%).

p-*Methoxybenzyldimethylamine.*—*p*-Methoxybenzylamine was prepared by reduction of anisaldoxime substantially as described by Goldschmidt and Polonowska (*Ber.*, 1887, **20**, 2407). The substitution of methyl for ethyl alcohol in this and similar preparations is advantageous, as it prevents the separation of sodium acetate. The methoxybenzylamine hydrochloride melted at 237—239° and the acetyl derivative at 96° (Goldschmidt and Polonowska give 231° and 96° respectively). *p*-Methoxybenzyldimethylamine was obtained in but moderate yield by the Eschweiler methylation of the primary base; much anisaldehyde (identified as phenylhydrazone) was also formed. The *picrate*, precipitated from the ethereal solution of the crude base by ethereal picric acid, crystallised from acetone–ether in deep yellow prisms, m. p. 103—105° (Found: $C_6H_3O_7N_3$, 57·5. $C_{10}H_{15}ON,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 58·1%). As hot alkaline picrate solutions oxidise the base, it was liberated by addition of aqueous alkali to a solution of the picrate in lukewarm acetone, and immediately extracted with benzene or ether.

Phenacyl-p-*methoxybenzyldimethylammonium bromide*, prepared from the components in cold ether, separated as an oil which slowly solidified, and crystallised from alcohol–ether in rosettes of stout needles, m. p. 133—136° (Found: Br, 21·6. $C_{18}H_{22}O_2NBr$ requires Br, 22·0%). The *picrate*, deep yellow prisms from methyl alcohol, melted at 112—113° (Found: $C_6H_2O_7N_3'$, 44·8. $C_{18}H_{22}O_2N{\cdot}C_6H_2O_7N_3$ requires $C_6H_2O_7N_3'$, 44·5%).

ω-*Dimethylamino*-ω-p-*methoxybenzylacetophenone* formed pale yellow needles from methyl alcohol, m. p. 52—54° (Found : C, 75·9 ; H, 7·0. $C_{18}H_{21}O_2N$ requires C, 76·3 ; H, 7·4%), and resinified very slowly on keeping. The picrate crystallised from methyl alcohol in thick, dark yellow laminæ, m. p. 143—145°. By heating with sodium hydroxide solution, the methosulphate, prepared in the usual manner, yielded phenyl *p*-methoxystyryl ketone, identical (mixed m. p.) with a specimen prepared from anisaldehyde and acetophenone.

α-Phenylethyldimethylamine.—The reaction mixture from the methylation of α-phenylethylamine hydrochloride by the Eschweiler method was basified, extracted with ether, and the extract mixed with ethereal picric acid solution. The resulting *picrate*, obtained in good yield, crystallised from alcohol, or from acetone–light petroleum, in yellow leaflets, m. p. 134—137° (Found : C, 50·6; H, 5·0. $C_{16}H_{18}O_7N_4$ requires C, 50·8 ; H, 4·8%). The free base is an oil with a penetrating, unpleasant, basic smell.

Phenacyl-α-phenylethyldimethylammonium bromide, prepared by the interaction of bromoacetophenone and the tertiary base for a week in cold benzene solution, formed warty masses from alcohol–ether, m. p. 155—157° (decomp.) (Found : Br, 22·8. $C_{18}H_{22}ONBr$ requires Br, 23·0%).

ω-Dimethylamino-ω-α-phenylethylacetophenones.—The crude rearrangement product melted at about 90° and contained the α- and the β-isomeride approximately in the ratio 4 : 5. To effect a separation, the mixture was dissolved in acetic acid (50 parts of 25%), and precipitated in six fractions by addition of picric acid. The first fraction consisted principally of the α-picrate, and the third and fourth of the β-compound. A complete separation was achieved by recrystallising the fractions either from aqueous acetic acid, which yielded preferentially the α-form, or from acetone–light petroleum, from which the β-form separated most readily. Although the separation was expeditious, it was somewhat erratic, and required careful control by mixed melting-point determinations.

The α-picrate formed yellowish pointed leaflets, m. p. 186—187°, and yielded on decomposition the *α-base*, almost colourless needles from methyl alcohol, m. p. 111—112° (Found : C, 80·7; H, 7·8. $C_{18}H_{21}ON$ requires C, 80·85; H, 7·8%). The β-picrate appeared to be dimorphous, since on two occasions pale yellow prisms were obtained in addition to the usual deep yellow nodules. The two forms melted, separately or mixed, at 174—176° (slight darkening), and when decomposed, gave the same *base*, which crystallised from methyl alcohol or light petroleum in bright yellow plates, m. p. 111—113° (Found : C, 80·5; H, 7·6%). The intense colour of this base was not removed by careful recrystallisation (charcoal), or even by steam-distillation, but on slow crystallisation from alcohol at room temperature, the base was obtained as primrose-yellow nodules, m. p. 111—113°. These were no doubt a polymorphic modification of the same substance, for, when heated at 100°, they rapidly reverted to the yellow form without loss in weight. The interconversion of the two stereoisomerides was investigated by heating them separately for 2 hours on the water-bath with strong alcoholic sodium ethoxide solution. The α-form was recovered unchanged, and no trace of the β-form could be detected by microscopic examination of the later crops, whereas the β-isomeride was completely converted into α- (mixed m. p.), and no unchanged material could be found.

Synthesis. ω-α-Phenylethylacetophenone, obtained in moderate yield by the action of hydriodic acid on acetophenone as described by Graebe (*Ber.*, 1874, 7, 1625), was brominated with the theoretical quantity of bromine in carbon tetrachloride solution. The mixture was washed with dilute sodium carbonate solution and evaporated to dryness, and the residue recrystallised from methyl alcohol. An apparently homogeneous bromination product resulted, in more than 80% of the theoretical quantity, and no other substance was isolated corresponding to the second possible stereoisomeride. ω-*Bromo*-ω-α-*phenylethylacetophenone* formed fine white needles, m. p. 76° (Found: Br, 26·9. $C_{16}H_{15}OBr$ requires Br, 26·4%). This was treated with dimethylamine (2 mols.) in alcoholic solution for 12 hours in the cold, and then for 2 hours on the water-bath. The diluted liquid was extracted with benzene, and the base extracted thence by hydrochloric acid and precipitated by ammonia. It was identical with the β-form of ω-dimethylamino-ω-α-phenylethylacetophenone (m. p. and mixed m. p. of base and picrate), and none of the α-form could be detected.

Benzhydryldimethylamine.—The Eschweiler reaction gave indifferent results with benzhydrylamine hydrochloride (Goldschmidt, *Ber.*, 1886, **19**, 3233): much benzophenone was produced (identified as oxime). The *base* crystallised readily on liberation from its salts, and formed colourless needles from methyl alcohol, m. p. 68—69°, which had a pronounced basic smell, and volatilised fairly readily in steam (Found: C, 84·7; H, 8·2. $C_{15}H_{17}N$ requires C, 85·25; H, 8·1%). It was not decomposed by boiling for a short time with concentrated hydrochloric acid. The picrate crystallised from methyl alcohol in yellow needles, m. p. 196—198°. The *hydrobromide* formed minute prisms from alcohol–ether, m. p. 215° (Found: Br, 25·7; loss at 120°, 5·8. $C_{15}H_{17}N,HBr,H_2O$ requires Br, 25·8; loss, 5·8%).

ω-*Dimethylamino*-ω-*benzhydrylacetophenone.*—When a benzene solution of benzhydryldimethylamine and bromoacetophenone was heated on the water-bath for 3 hours or allowed to stand for 2 weeks, crystals of benzhydryldimethylamine hydrobromide separated. These were collected, washed with warm benzene, and the filtrate and washings were extracted with dilute hydrochloric acid. The base was set free by ammonia, and any benzhydryldimethylamine removed by distillation in steam. *ω-Dimethylamino-ω-benzhydrylacetophenone* crystallised from methyl alcohol in pale yellow needles, m. p. 167°, which decomposed with effervescence at 200° (Found: C,* 84·0; H, 7·4. $C_{23}H_{23}ON$ requires C, 83·85; H, 7·0%). The methosulphate, prepared in hot benzene, gave on decomposition with alkali ω-benzhydrylideneacetophenone, which did not depress the m. p. of a specimen prepared according to Kohler and Johnstin (*Amer. Chem. J.*, 1905, **33**, 35). The synthesis of the base was attempted by acting on ω-bromo-ω-benzhydrylacetophenone (Kohler, *ibid.*, 1904, **31**, 642) with dimethylamine in alcoholic solution, but no action appeared to take place below 100°, and above that temperature decomposition set in, and no definite product could be isolated.

9-*Fluorenyldimethylamine.*—Fluorenone oxime was reduced according to the method of Schmidt and Stützel (*Ber.*, 1908, **41**, 1247); the first portions of zinc dust had to be added very cautiously, as the reaction proceeded with semi-explosive violence. The crude 9-fluorenylamine hydrochlorides were methylated by Eschweiler's method, which gave a good yield of the desired product, together with a little fluorenyl alcohol. There was no indication of the presence of a second modification, as described in the case of the primary amine. The liberated tertiary base was extracted with ether, and the gummy salt precipitated from the dried solution by hydrogen chloride was recrystallised from alcohol–ether. The free base readily solidified on liberation from its salts, and its properties, as well as those of the picrate, agreed with the description by Ingold and Jessop (J., 1929, 2361) (Found, for the free base: C, 85·6; H, 7·0. Calc. for $C_{15}H_{15}N$: C, 86·1; H, 7·2%). Short boiling with strong hydrochloric acid did not bring about hydrolysis. The *hydrobromide* crystallised from alcohol–ether in minute irregular prisms, m. p. 204—206° (Found: Br, 27·3. $C_{15}H_{15}N,HBr$ requires Br, 27·6%).

ω-Dimethylamino-ω-fluorenylacetophenone was prepared in cold benzene as described for the benzhydryl analogue. The reaction required only 4—5 days, and this less soluble product was apt to separate from the reaction mixture along with the fluorenyldimethylamine hydrobromide. Crystallised from methyl alcohol, in which it was sparingly soluble and thereby easily separated from fluorenyldimethylamine, it formed pale yellow needles, m. p. 145—

148° (efferv.) (Found : C,* 84·1; H, 6·2. $C_{23}H_{21}ON$ requires C, 84·4; H, 6·4%). If the preparation was carried out in hot benzene, in the same manner as that of the benzhydryl compound, the principal product was ω-fluorenylideneacetophenone (*vide infra*). The methosulphate, prepared as usual, was converted by reduction with zinc dust and sulphuric acid into ω-fluorenylacetophenone, identical (m. p. and mixed m. p.) with a sample prepared according to Wislicenus and Mocker (*Ber.*, 1913, **46**, 2792).

With a view to the synthesis of dimethylaminofluorenylacetophenone, fluorenylacetophenone was treated with the theoretical quantity of bromine in warm chloroform, and the product recrystallised from methyl alcohol. The *bromo*-ketone formed clusters of prisms, m. p. 111—113°, which decomposed with effervescence at 160° (Found : Br, 22·2. $C_{21}H_{15}OBr$ requires Br, 22·0%); when its cold ethereal solution was shaken with aqueous dimethylamine, it became yellow and soon deposited deep-yellow laminæ of *fluorenylideneacetophenone*, m. p. 137—140° (Found : C,* 88·6; H, 5·3. $C_{21}H_{14}O$ requires C, 89·3; H, 5·0%). Hydrogen bromide was removed equally readily when the bromo-ketone was similarly treated with ammonia.

p-*Bromophenacylbenzyldimethylammonium bromide* was prepared from *p*-bromophenacyl bromide (" Chemical Syntheses," Vol. IX, 20) and benzyldimethylamine in cold benzene. It crystallised from alcohol–ether in stout prisms, m. p. 188—191° (Found : ionisable Br, 19·2. $C_{17}H_{19}ONBr,Br$ requires Br, 19·3%). The bromide did not dissolve readily in cold water, and the nitrate was remarkably sparingly soluble—a distinct precipitate was produced on addition of *N*/10-nitric acid to an aqueous solution of the bromide.

p-*Bromo-ω-dimethylamino-ω-benzylacetophenone* formed long, pale yellow prisms, m. p. 106—107°, from methyl alcohol (Found : Br, 23·9. $C_{17}H_{18}ONBr$ requires Br, 24·1%). The hydrochloride crystallised in minute scales, m. p. 235—238° (decomp.), very sparingly soluble in dilute hydrochloric acid. The methosulphate, prepared in the usual manner, crystallised readily in rather difficultly soluble needles, which were easily " salted out " by addition of alkali to their aqueous solution. Decomposition by sodium hydroxide solution gave *p*-bromophenyl styryl ketone, colourless leaflets, m. p. 104—105°, not depressed by admixture with a specimen prepared from *p*-bromoacetophenone and benzaldehyde (Dilthey, *J. pr. Chem.*, 1921, **101**, 202). The properties of the substance agreed with those ascribed to it by Dilthey; Kohler, Heritage, and Burnley (*Amer. Chem. J.*, 1910, **44**, 60) obtained, by another method, a presumably identical compound which they described as forming yellow plates, m. p. 100—101°.

Phenacylbenzylpiperidinium bromide, prepared from 1-benzylpiperidine (Schotten, *Ber.*, 1882, **15**, 423; Haase and Wolffenstein, *ibid.*, 1904, **37**, 3232) and bromoacetophenone in cold benzene (4—5 days), crystallised from alcohol–ether in minute prisms, m. p. 135—138° (slight effervescence) (Found: Br, 20·3, 20·4. $C_{20}H_{24}ONBr,H_2O$ requires Br, 20·4%). An attempt to dehydrate the salt at 100° led to decomposition.

ω-*Piperidino*-ω-*benzylacetophenone* formed fine, colourless needles from methyl alcohol, m. p. 80—81° (Found: C, 81·8; H, 7·9. $C_{20}H_{23}ON$ requires C, 81·9; H, 7·9%), which were quite stable. The picrate, deep yellow crystals from methyl alcohol, softened at 180° and melted at 185—187° (decomp.). These properties may be compared with those of the isomeric β-piperidinobenzylacetophenone (Georgi and Schwyzer, *J. pr. Chem.*, 1912, **86**, 273). To synthesise the base, ω-bromo-ω-benzylacetophenone (Part I, p. 3197) was treated with piperidine in methyl alcohol for 12 hours in the cold and 1 hour on the water-bath. After dilution, the mixture was extracted with benzene, the base removed from the benzene by hydrochloric acid, and recovered by basification. It was identical (mixed m. p.) with that just described.

Velocity Measurements.—These were carried out at 36·9° in *N*/10-sodium ethoxide solution. Samples were withdrawn, and the reaction checked by adding them to a known excess of standard acid. The mixture was then titrated back with standard alkali, phenolphthalein being used as indicator, and the alcohol concentration adjusted to 30—40%. Under these conditions the errors resulting from the acidity (" active methylene group ") of the quaternary salts and from the basic properties of the rearrangement products were reduced. Over the range 20—80% conversion, the coefficients agreed within ± 5% of the mean, often within ± 3%. The results are nevertheless not thoroughly trustworthy, because there was some indistinctness in the end-points, because the coefficients obtained (though probably not their *ratio* for a given pair of salts) varied somewhat with the (small) water content of the alcohol used, and because small but appreciable quantities of neutral products were formed in several cases.

The velocity of rearrangement of phenacyl-*p*-nitrobenzyldimethylammonium bromide (following paper) could not be determined by the method described, for the solutions became too dark for titration; a very approximate value was obtained by direct isolation of the product, however. The reaction was checked by adding the samples to ice and ammonium chloride, and the tertiary base immediately extracted by benzene, while the aqueous layer was acidified and unchanged quaternary salt precipitated with potassium iodide.

The benzene solution was extracted with hydrochloric acid and the base recovered. Each experiment thus gave a maximum and a minimum value for the velocity coefficient :

t (mins.).	Tertiary base.	$0{\cdot}434k$.	Quaternary iodide.	$0{\cdot}434k$.
1	23%	0·111	49%	0·329
2	40	0·114	22	0·310
20	60	—	Nil	—

Much material was lost by side reactions (see following paper). Under the same conditions for phenacylbenzyldimethylammonium bromide, $0{\cdot}434k$ was 0·00475.

In order to test the intramolecular nature of the reaction, *p*-bromophenacylbenzyldimethylammonium (A) and phenacyl-*m*-bromobenzyldimethylammonium (B) bromides (2 g. of each), in sufficient *N*/10-sodium ethoxide solution to effect rearrangement of 54·1% of the material, were kept at 36·9° for 24 hours (ample time to complete the reaction). 1·912 G. (42·9%, instead of 45·9% reckoned on the total mixed initial material) were recovered as mixed quaternary iodides; and the tertiary bases were extracted with benzene, transferred to dilute sulphuric acid, and treated with hydrochloric acid, giving 0·704 g. (19·7%) of sparingly soluble hydrochloride, m. p. 235—238° (decomp.). On decomposition, this gave ω-dimethylamino-ω-benzyl-*p*-bromoacetophenone (A), m. p. 104—105° with slight previous softening; the m. p. of the hydrochloride was unaltered on recrystallisation, and careful examination of the mother-liquors yielded only a little (0·03 g.) of the isomeric dimethylamino-*m*-bromobenzylacetophenone (B). The original liquors from which the hydrochloride had separated were basified, and gave 0·819 g. (25·5%) of base, m. p. 60—65°. This was converted into the picrate, which consisted substantially of that of the base (B) (m. p. 139—142°). From the last mother-liquors, a little (0·03 g.) of the base (A) was isolated as hydrochloride, and no other compound could be detected. The deficiency in quaternary iodides (45·9—42·9 = 3·0%) was no doubt due to loss in manipulation, but the defect in tertiary bases (54·1—19·7—25·5 = 8·9%) almost certainly represented the formation of neutral by-products. If the reaction had proceeded strictly *intermolecularly*, with " impartial " recombination of the free radicals, the dibrominated and the bromine-free base would each have been produced to an extent corresponding to some 13% of the initial materials.

The ratio of the velocity coefficients for the (separate) rearrangement of the quaternary salts (A) and (B) is 1 : 2·39. Allowing for the speedier consumption of the more rapidly changing salt (B), the 54·1% of expected tertiary bases should have been composed of 19·5% (A) and 34·6% (B). That the actual figures were more nearly equal is no doubt due to the salt (A) being enabled, by its greater acidity (bromine atom nearer to active methylene group), to secure the larger share of the alkali present in the solution.

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