LXXXV.—*Nature of the Alternating Effect in Carbon Chains. Part XII. Nitration of some Derivatives of Methyl Benzylaminoformate.*

By John William Baker.

It has recently been shown (Goss, Ingold, and Wilson, J., 1926, 2440) that the acetyl derivatives of benzylamine, methylbenzylamine, and dibenzylamine nitrate mainly in the *op*-positions, it being assumed that the dissociation of the entity $R_3\overset{+}{N}\!:\overset{x}{\underset{x}{\vdots}}\overset{-}{H}\!:\overset{y}{\underset{y}{\vdots}}O{\cdot}NO_2$ (I) at *xx* becomes important and leads to the formation of a smaller amount of the *m*-isomeride than in the cases of the corresponding unacetylated bases. It was also assumed that the nitrogen atom does not acquire a sufficiently strong or permanent charge by betaine isomerisation for any considerable *m*-substitution to arise from this cause.

In order, if possible, to obtain further information as to the relative effects of these two opposing influences (internal and external ammonium-salt formation), it was considered of interest to determine the behaviour on nitration of the corresponding methyl benzylaminoformates, $C_6H_5{\cdot}CH_2{\cdot}NR{\cdot}CO_2Me$ (II), which are constituted similarly to the acetobenzylamides in so far as concerns the possibility of betaine isomerisation, $R_2\overset{+}{N}\rbrace{=}C{<}^{\overset{-}{O}}_{OMe}$, excepting that, presumably owing to this cause, their basicity appears to be less. The present communication deals with the nitration of methyl benzyl-, dibenzyl-, and benzylmethyl-aminoformates (II; R=H, CH_2Ph, and Me, respectively). These substances are less basic than the corresponding acetyl derivatives; *e.g.*, acetomethylbenzylamide is completely soluble in cold 3% hydrochloric acid, whilst the benzylmethylaminoformate is soluble only in concentrated acid; acetodibenzylamide is easily soluble in concentrated hydrochloric acid, whereas the dibenzylaminoformate is almost insoluble. Hence it would be expected that dissociation of the salt (I) at *yy* (promoting meta-substitution) will be somewhat less, and at *xx* (promoting primarily *op*-substitution) somewhat greater, in the urethanes than in the corresponding acetobenzylamides. On the other hand, the urethanes would probably have a greater tendency towards a betaine phase, so that it is difficult to foretell how the proportions of meta-isomeride formed on nitration should compare with those obtained from the acetyl compounds; they should, however, be of the same order of magnitude, and therefore considerably less than those obtained from the corresponding unsubstituted bases.

Whilst great accuracy cannot be claimed for the figures obtained where only small quantities of the *m*-compound are produced (compare the following paragraph), the actual proportions of meta-isomeride found in the cases considered, $C_6H_5{\cdot}CH_2{\cdot}NR{\cdot}CO_2Me$, are as follows: R = Bz, 14%; R = Me, 12%; R = H, 11%; the corresponding figures for the acetyl derivatives, $C_6H_5{\cdot}CH_2{\cdot}NRAc$, being R = Bz, 25%; R = Me, 8%; R = H, 7%; whilst those of the unsubstituted bases, $C_6H_5{\cdot}CH_2{\cdot}NHR$, are, respectively, 76%, 69%, and 44%.

Unfortunately, the determination of the meta-content of the nitration mixtures by the bromate-titration method (Goss, Ingold, and Wilson, *loc. cit.*) was possible only in the case of the dibenzyl compound (see p. 571), and, moreover, the experimental error in this method is relatively great when only small amounts of the meta-isomeride are present. A method, based on that given by Holleman (*Rec. trav. chim.*, 1899, **18**, 268) and believed to be, when applicable, a definite improvement on the preceding one, was tested in this investigation with a view to its use in future cases in which only very small amounts of meta-isomeride might have to be estimated. In principle, the method depends on the extraction, at a constant temperature, of a known weight of the mixed nitrobenzoic acids, formed on oxidation of the nitration product, with a solution saturated with respect to the *o*- and *p*-isomerides and determination of the increase in acidity due to the dissolved meta-compound by titration with standard ($N/100$) baryta solution. Subsequent extraction with a solution saturated with respect to the *o*-, *p*-, and *m*-acids allows a correction to be applied for any small amount of foreign acid matter present. Full details will be found in the experimental portion of this paper, and the results show that the method gives moderately consistent values for the meta-content of the mixtures.

EXPERIMENTAL.

A. *Preparation of Derivatives of Methyl Benzylaminoformate.*

Methyl benzylaminoformate was prepared by the method of Wieman and Jongkees (*Rec. trav. chim.*, 1906, **25**, 243) and had m. p. 62—64° (Found : N, 8·5. Calc. : N, 8·5%).

Methyl Benzylmethylaminoformate.—A solution of methyl chloroformate (2·7 g.) in dry ether was added dropwise with efficient cooling to an ethereal solution of benzylmethylamine (Holmes and Ingold, J., 1925, **127**, 1813) (3·5 g.). A vigorous action took place and the hydrochloride of the base separated. This was decomposed by a slight excess of 10% caustic soda solution, a second molecule (2·7 g.) of methyl chloroformate added, and after a while the whole was acidified with hydrochloric acid and shaken with ether. The residue obtained from the ethereal solution (dried with sodium sulphate) was a colourless, viscous liquid, which was distilled twice under reduced pressure. *Methyl benzylmethylaminoformate* has b. p. 118°/5 mm. (Found : C, 66·3, 66·8; H, 7·5, 7·2; N, 7·5. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%).

Great difficulty was experienced in proving the purity of this compound, due, it was subsequently found, to the production of methane during combustion. In order to ensure its purity, benzylmethylamine was fractionated twice under reduced pressure and converted into its hydrochloride by the action of dry hydrogen chloride in dry ether, the hydrochloride was crystallised from absolute alcohol, and the regenerated base again distilled under reduced pressure. This purified specimen and freshly-distilled methyl chloroformate in equimolecular proportion were mixed, with cooling, in dry ethereal solution, the hydrochloride of the base that separated was filtered off, and the methyl benzylmethylaminoformate obtained from the ethereal solution was twice carefully distilled under reduced pressure. The specimen so obtained was a colourless, highly refractive liquid, b. p. 118°/5 mm. On analysis under ordinary conditions, it gave C, 64·6; H, 7·3%, but when mixed with cuprous chloride and slowly burnt in a very hot combustion tube it gave the values recorded above. The gas obtained in the nitrogen determination (Dumas) contained 43·1% of combustible gas, of which 39·7% was methane, whence the value for the nitrogen content given above was calculated.

Methyl dibenzylaminoformate, obtained in a similar manner from methyl chloroformate and dibenzylamine, had b. p. 199°/13 mm. (Found : C, 75·0; H, 6·7. $C_{16}H_{17}O_2N$ requires C, 75·4; H, 6·7%).

Methyl pp′-*dinitrodibenzylaminoformate* was prepared by the condensation of *pp*′-dinitrodibenzylamine with methyl chloroformate. After crystallisation from ethyl acetate–ligroin it had m. p. 140° (Found : C, 55·8; H, 4·5. $C_{16}H_{15}O_6N_3$ requires C, 55·6; H, 4·4%).

Methyl p-*nitrobenzylaminoformate* was obtained by adding 2·4 g. of methyl chloroformate to molten *p*-nitrobenzylamine (45°), the reaction mixture being diluted with dry ether when it became too solid owing to the separation of the hydrochloride of the base. Isolated as above and crystallised from absolute alcohol, the product had m. p. 109·5° (Found : C, 51·4; H, 4·9. $C_9H_{10}O_4N_2$ requires C, 51·4; H, 4·8%).

B. *Nitration of the Benzylaminoformates and Determination of the Proportion of* m-*Isomeride : General Procedure.*

The conditions of nitration were similar in all three cases studied, the aminoformate being run in (or added in small successive portions if a solid) at the rate of approximately 1 g. per hour to mechanically stirred nitric acid (*d* 1·442 : acid of greater density produces a large proportion of dinitrated compounds) at 0°. The isolation of the product varied somewhat from case to case and is described below.

As stated in the introduction, the bromate-titration method gave trustworthy results only for methyl dibenzylaminoformate. In the other cases, the proportion of *m*-isomeride was determined by the solubility method described below.

In each of four 200 c.c. stoppered bottles (*A*, *B*, *C*, and *D*) were placed 80 c.c. of a solution of *o*- and *p*-nitrobenzoic acids saturated at 24°, together with some of the pure solid acids in order to ensure saturation. *A* served as a control. Into *B*, *C*, and *D* were weighed quantities (about 1 g.) of the mixtures of nitrobenzoic acids obtained by oxidation of the nitration products, the weight in each being such that the quantity of *m*-acid was considerably less than that required to saturate the 80 c.c. of water present. The four bottles were fixed in a frame and rotated for 36—48 hours in an electrically controlled thermostat at 24·5° (±0·5°). They were kept stationary at the same temperature for a further period of 24 hours and the clear supernatant liquors were then filtered, the first few c.c. being rejected, since a certain error is otherwise introduced owing to slight adsorption on the filter-paper. All the operations, except the final titration, were carried out in the thermostat, and all the apparatus used was stored therein. An aliquot portion (10 c.c.) of each filtrate was withdrawn (in pipettes calibrated relatively to one another) and titrated with $N/100$-baryta and phenolphthalein. The residual untitrated liquors were returned to their respective flasks and to each was added sufficient pure *m*-nitrobenzoic acid to saturate it, and the operations were repeated. The differences between the volumes of baryta required for B, C, and D, respectively, and the volume required for A represent the amounts of foreign acid present which must be subtracted from the volume differences found in the first titrations in order to give correct values for the *m*-nitrobenzoic acid present. Holleman (*loc. cit.*) found that the solubility of the *o*- and *p*-acids increased in the presence of an appreciable quantity of the *m*-isomeride, and therefore a correction curve was plotted from the following figures, obtained in preliminary determinations of small, weighed amounts of *m*-isomeride added :

Meta added	14·6	19·5	23·3	39·4	54·0	61·2	87·2	115·1 mg.
Meta found	13·0	15·0	22·2	38·6	52·7	66·6	92·9	133·4 „

C. *Details of Individual Cases.*

I. *Methyl Dibenzylaminoformate.—Experiment* 11. The nitration product was poured on crushed ice and made alkaline by the addition of potassium hydroxide solution. The somewhat sticky precipitate produced was filtered off and washed free from gum with a large volume of ether (it dissolved and almost immediately crystallised). The aqueous filtrate was extracted with ether, and the combined extract and washings were worked up in the usual manner, yielding a very viscous gum which slowly solidified (total yield, 94% of the theoretical) [Found for the crystalline solid (30% of the product) : C, 55·9; H, 4·6. Found for the gum (70%) : C, 55·1 ; H, 4·4. $C_{16}H_{15}O_6N_3$ requires C, 55·6 ; H, 4·4%]. The titration of the pure *p*-nitro-isomeride gave a mean bromination number (compare Goss, Ingold, and Wilson, *loc. cit.*) $F = 2·175$, whilst for the crystalline solid and the gum were found $F = 2·373$ and 2·282, respectively, representing meta-contents of 20% and 11%, respectively. Hence the meta-content of the whole nitration product is (20% of 30%) + (11% of 70%) = 14%.

Experiment 12. The nitration product obtained from 5·0 g. of methyl dibenzylaminoformate was separated into three fractions : (α) a solid, 1·44 g., m. p. 132—135°; (β) a second solid fraction, 2·482 g., m. p. 100—103°, which crystallised from the ethereal extract; and (γ) a residual gum, 2·374 g. (total yield, 93% of the theoretical) [Found: (α) C, 55·9; H, 4·6; (β) C, 55·9; H, 4·7; (γ) C, 55·8; H, 4·6%]. Each fraction was separately titrated by the bromate method and gave bromination numbers α, 2·195; β, 2·225; γ, 2·435, corresponding to respective meta-contents of 2%, 5%, and 26%, whence the meta-content of the whole nitration product is 13%. Fraction (γ) was oxidised by potassium permanganate to the mixed nitrobenzoic acids (yield, 64%) (Found: M, by titration, 165·8. Calc.: M, 167), which were separated by the method of Baker and Ingold (J., 1926, 2469). The separated *p*-acid (57%) had m. p. 210—215°; after crystallisation from water it had m. p. 232° (mixed m. p. with pure *p*-acid, 237°). The separated *m*-acid (19%) had m. p. 122°, which was raised to 136° by crystallisation from ethyl acetate–ligroin (mixed with the pure *m*-acid, it melted at 141°). Crystallisation of the fraction α from ethyl acetate–ligroin gave pure methyl *pp'*-dinitrodibenzylaminoformate, which, alone or mixed with a synthetic specimen, melted at 140°.

II. *Methyl Benzylmethylaminoformate.—Experiment* 21. The nitration product was poured on crushed ice, an oil being precipitated, and was made alkaline with potassium hydroxide solution; the whole was then extracted with ether. The gum obtained from the dried ethereal extract failed to crystallise (yield, 92·5% of the theoretical) (Found: C, 54·4; H, 5·8. $C_{10}H_{12}O_4N_2$ requires C, 53·6; H, 5·4%). A further 3% of the material was accounted for as an acid fraction produced by oxidation during the nitration. The neutral nitration product was oxidised with boiling 2% potassium permanganate solution (yield, 77%), and the content of *m*-acid in the mixed nitrobenzoic acids produced (Found: M, by titration, 162. Calc.: M, 167) was determined by the solubility method: 0·6052 g. required 48·00 c.c. of 0·01029*N*-baryta for the *m*-acid present; this corresponds to 0·08251 g. of *m*-acid, which becomes 0·0735 g. after correction. The content of *m*-acid is therefore 12%.

III. *Methyl Benzylaminoformate.—Experiment* 33. The nitration product, worked up as in the previous case, gave a solid (yield, 81%) (Found: C, 51·1; H, 4·8. $C_9H_{10}O_4N_2$ requires C, 51·4; H, 4·8%) which, after crystallisation from ethyl alcohol, had m. p. 109·5°. This consisted of the pure *p*-nitro-compound, since it gave no m. p. depression in admixture with a synthetic specimen and on oxidation with 2% potassium permanganate solution gave pure *p*-nitrobenzoic acid, m. p. 237° (alone or mixed with a genuine specimen). Determinations of the content of *m*-acid by the bromate method gave bromination numbers of $F = 2·850$, 2·880, 2·850, 2·900. The values of F for the pure *p*- and *m*-isomerides are, however, 2·870 and 3·050, respectively. The difference is too small for this method to give trustworthy results.

Experiment 34. The nitration product (yield, 83%, a further 6% being accounted for as acid products) (Found: C, 51·2; H, 5·0%) was oxidised with 2% potassium permanganate solution (yield, 86%), and the meta-content of the resulting mixture of nitrobenzoic acids (Found: *M*, by titration, 165·6. Calc.: *M*, 167) determined by the solubility method: 0·8424 g. of the mixed acids required 59·84 c.c. of 0·01029*N*-baryta for the *m*-acid present; this corresponds to 0·1029 g. of *m*-acid, which becomes 0·091 g. after correction. The content of *m*-acid is therefore 11%.

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