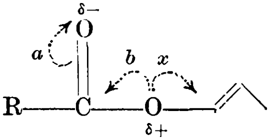
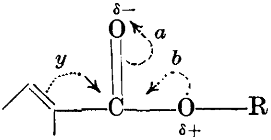
CXXI.—*The Nature of the Alternating Effect in Carbon Chains. Part XVI. The Directive Action of Some Groups of the Form* –COR *in Aromatic Substitution.*

By Kenneth Ernest Cooper and Christopher Kelk Ingold.

In Part V (J., 1926, 1310), Ingold and Ingold considered the diminution in the *op*-directive power of a phenoxyl oxygen atom arising from its attachment to a carbonyl group (R·CO·OPh) and attributed the effect to the establishment of a weak electrovalency between the carboxyl oxygen atoms, thus adapting a previous theory (Smedley, J., 1909, **95**, 231) of the structure of the carboxyl group. Expressed in terms of electron-strain transmission, the conception (I) was that the process (*b*), actuated by (*a*), competes with the process (*x*) to which the *op*-directing action of the group is due; or, in other words, that the charge $\delta +$, set up by (*a*) and (*b*) together, works against the repulsion of electrons towards the nucleus :

(I.)





(II.)

At first sight it might appear to follow that the *m*-directive power of a benzoyl carbonyl-group should be decreased by its attachment to a hydroxylic or ethereal oxygen atom (Ph·CO·OR) for a precisely similar reason (II) : the demand created by process (*a*) can be supplied, not only by (*y*) leading to *m*-substitution, but also by (*b*), which therefore works against *m*-substitution. At least it seems that there can be no escape from this conclusion for any theory which regards the "conjugation" of the carbonyl group with the nucleus as the sole cause of its *m*-directive effect.

On the other hand, if the view (this vol., p. 833) be adopted that the action of the carbonyl group in benzoyl compounds (to illustrate by this example) arises largely from permanent electron-strain (J., 1926, 2442, 2463 ; this vol., pp. 813–815) set up by the fractional dipole in the resting state of the carbonyl group, then, whilst the conclusion represented by (I) remains (for the charge $\delta +$ created by strains *a* and *b* must necessarily oppose *op*-substitution), that represented by (II) becomes inverted. For each of the bonds between carbon and oxygen represents a fractional dipole (arising from the greater electron-attraction of the stronger nucleus,—see the preceding paper), the group as a whole being represented $—\overset{\delta+}{C}\ \overset{\delta-}{O_2}—$; and the processes (*a*) and (*b*) merely transfer electricity from one oxygen atom to the other, leaving unchanged the total negative electrification on the two taken together, and leaving unchanged also the total positive electrification on the carbon atom to which both are attached. Thus the dipole in $—\overset{\delta+}{C}\ \overset{\delta-}{O_2}—$ is two-fold, the smaller separation of charges in C—O being *added* to the larger separation in C═O (compare Part XV), so far as concerns the total charge on the common carbon atom; that is to say, the attachment of ethereal or hydroxylic oxygen should *enhance* the *m*-directing effect of the carbonyl group. Thus the examination of benzoyl compounds is capable of furnishing definite information as to the type of theory which should be adopted.

The main recorded observations bearing on the point are those of Camps (*Arch. Pharm.*, 1901, **240**, 1), who obtained 55% of *m*-derivative from acetophenone by nitration in nitric acid below 0°, and of Holleman (*Rec. trav. chim.*, 1899, **18**, 267; *Z. physikal. Chem.*, 1899, **31**, 79), who, under similar conditions, obtained 80% of *m*-compound from benzoic acid. Experience of the former reaction has shown the essential correctness of the estimate, and we have closely confirmed Holleman's result for the latter. These facts clearly find their most consistent interpretation in the permanent-strain hypothesis (above), but we have supplemented the evidence thus furnished by a series of experiments designed to determine the relative actions of the groups $-CH_3$, $-NH_2$, $-OH$, $-Cl$ in association with a carbonyl group attached to the benzene nucleus.

According to the conjugative mechanism (above), a series of groups, CR_3, NR_2, OR, Cl, should stand in the same order, as regards their power of competing with phenyl in supplying electrons to the carbonyl group, as they do in regard to their power of furnishing electrons, by an identical mechanism, to a directly attached benzene ring (in $CPhR_3$, $NPhR_2$, etc.), when *op*-substitution results. This order is known and is given by $N > O > Cl > C$, the atom with the most active lone-electrons heading, and that with none terminating, the series. Hence the order of the composite groups should be *

$$\xleftarrow{\text{increasing } m\text{-directive power}}$$
$$\cdot CO\cdot CH_3 > CO\cdot Cl > CO\cdot OH > CO\cdot NH_2$$

On the other hand, according to the hypothesis of permanent electron strain, the *m*-directive action should increase with increasing total dipole moment of the group, and this will depend on the disparity in the nuclear attractions exerted on the electrons held in common by two nuclei (Parts XIV and XV). The theoretical sequence is $C\cdot F > C\cdot O > C\cdot N > C\cdot C$; and, on the probable assumption that chlorine will resemble fluorine rather than oxygen, the order of the composite groups should be

$$\xleftarrow{\text{increasing } m\text{-directive power}}$$
$$\cdot CO\cdot Cl > \cdot CO\cdot OH > \cdot CO\cdot NH_2 > \cdot CO\cdot CH_3$$

Found (% *meta*-; temp. − 10° to − 15°):

(90%) (82%) (69%) (55%)

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* In processes where the mechanism depends upon formal conjugation, such as the activation of the three-carbon system, this is actually the order of the groups (compare Ingold, Shoppee, and Thorpe, J., 1926, 1482).

The numbers in the lower line * represent our results, the last figure being due to Camps, and it will be seen that they give support to the assumptions on the basis of which this sequence is deduced. We have not investigated benzoyl fluoride, but it would probably give a rather higher value than the chloride, and if it were substituted for the chloride in the above table the gaps between the successive members would be still more even than they are at present.

EXPERIMENTAL.

Nitration of Benzoyl Chloride.—The action of nitric acid on benzoyl chloride has been studied by Karslake and Huston (*J. Amer. Chem. Soc.*, 1909, **31**, 479), who used acetic anhydride as the solvent and observed complicated actions during which acetyl as well as nitro-groups entered the nucleus. Preliminary experiments having shown that complete hydrolysis accompanies (and probably precedes) nitration when nitric acid is used both as solvent and as nitrating agent, we operated in our final series with a mixture of nitrogen pentoxide and phosphorus pentoxide in carbon tetrachloride as solvent (compare Part I, J., 1925, **127**, 517). The temperatures ranged from −10° to −15°. Due care being taken in the preparation of the nitrogen pentoxide, it is possible under these conditions entirely to avoid hydrolysis, as was shown by evaporating the nitration solution in a slow stream of phosphorus

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* It is unnecessary to discuss in detail all the disturbances which might affect the numerical data, because in every case there are reasons either of analogy or of theory for supposing that they would not affect the main result. Thus the figure for acetophenone may be slightly lower than corresponds with the true action of the acetyl group owing to the presence of a small amount of the enol form during nitration; but analogy with the nitration of the nitrobenzophenones (Staedel), where enolisation is impossible, shows that such a disturbance could not be serious; besides, nitration through the enol would lead to the *p*-derivative (Part II, J., 1925, **127**, 873), and actually scarcely any *p*-compound is formed. Some slight additional control might be obtained by the investigation of $\omega\omega'\omega''$-trialkylacetophenones, but we have little doubt that, owing to the polar disturbance of the alkyl groups (as previously illustrated for methyl and ethyl benzoates; J., 1926, 2466), these ketones would give lower, and not higher, meta-values than acetophenone itself. The possible small effects of imidolisation and hydrion addition act in opposite directions as regards the action of the carboxylamide group, and the ionisation of the benzoic acid in the nitric acid solvent would tend to lower the percentage of *m*-isomeride formed (this vol., p. 817, footnote). Even in water, however, the ionisation at a corresponding concentration would only be 0·2%, and it is clear both from an extrapolation of the figures for the benzoic esters (Holleman) and from our experiments on the nitration of benzoic acid in a non-ionising medium ($N_2O_5+CCl_4$) that the disturbance arising from electrolytic dissociation is negligible in comparison with the differences shown in the table above.

pentoxide-dried air, which removes the excess of nitrogen pentoxide and any hydrogen chloride arising from hydrolysis, and then hydrolysing the residue with pure potassium carbonate, when the liberated chloride ion was found to be equivalent to the organic acids to within the limits of experimental error. If the nitrogen pentoxide used is contaminated with its double compound with nitric acid, a certain amount of hydrolysis may occur, but as this appears to make no difference whatever to the proportions of isomerides ultimately found, it is concluded that nitration by nitrogen pentoxide is rapid and that the hydrolysis is subsequent. The separation of the isomeric nitrobenzoic acids was carried out by the methods illustrated in previous papers of this series, which were again checked by application to artificial mixtures. It should, however, be mentioned that the proportion of *p*-isomeride formed in the present instance was smaller than the corresponding solubility correction (2%), so that we can only assign this value as a maximal limit. The values for the *m*-isomeride ranged from 90—91%, except one (Expt. 11; 89%) which is known to be low as a trace of *m*-acid was lost through the " creeping " of the ethereal solution.

(Expt. 3.) Conditions: benzoyl chloride, 2·545 g.; nitrogen pentoxide, 10 g.; carbon tetrachloride, 50 g. containing phosphorus pentoxide in suspension; temperature, − 10°; time allowed for nitration, 2 hours. Results: benzoic acid, by sublimation, nil; *p*-nitrobenzoic acid, less than 2·1%; *m*-nitrobenzoic acid, 90·2%.

The mean (excluding Expt. 11) was 90·3% meta-, the mean temperature being −12·5°.

Nitration of Benzoic Acid.—These experiments need not be described in view of Holleman's previous investigation, and it suffices to state that our value for the proportion of *m*-isomeride formed by nitration at 0° by 10 parts by weight of nitric acid (d^{16° 1·505) is 80·0%, closely agreeing with Holleman's figure, 80·3%, for the same temperature. The value 81·7%, given in the introduction as 82%, is corrected to correspond with − 12·5° (the approximate mean temperature of the other nitrations) by means of Holleman's correction factor.*

As shown above (p. 839, footnote), the value 82% may be slightly lower than corresponds with the true action of the un-

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* In a preliminary experiment on the nitration of benzoyl chloride by excess of fuming nitric acid at +15°, the value 78·6% was obtained for the proportion of *m*-isomeride. This experiment was done before it was realised that hydrolysis precedes nitration under these conditions, but it is now evident that the value agrees with Holleman's figure for the *nitration of benzoic acid* corrected to that temperature (78·3%), and with our own value similarly corrected (78·0%).

ionised carboxyl group, but the other value, namely 85·7%, which we have obtained by nitrating benzoic acid with nitrogen and phosphorus pentoxides in carbon tetrachloride under the conditions used for benzoyl chloride is almost certainly too high, since part of the material will doubtless have been nitrated as benzoic anhydride, which would be expected to give a definitely higher value than the un-ionised acid.

Nitration of Benzamide.—Benzamide was nitrated with excess of fuming nitric acid in the usual way and any nitrobenzoic acids formed by hydrolysis were separated from the neutral amides by means of ether and potassium carbonate. The hydrolysis accompanying nitration was usually of the order of 10%, and the degree of mononitration 97—100%. After analysis, the amides were hydrolysed by boiling for 16 hours with 8% potassium hydroxide solution, preliminary experiments with *m*-nitrobenzamide having shown that hydrolysis is complete and quantitative under these conditions. The nitrobenzoic acids were then separated as usual, any benzoic acid arising from incomplete nitration being previously eliminated by sublimation below 100°. Since it is not known whether the hydrolysis which occurs during nitration is antecedent or subsequent to the entrance of the nitro-group, the acid by-product was also separated into its component isomerides in order to see how each of these two alternative hypotheses would affect the result: actually it makes very little difference which view is adopted. On either hypothesis, the individual values for the proportion of *m*-nitrobenzamide formed all lay between 69 and 70%. The proportions of *p*-derivative being always less than the corresponding solubility correction, we are only able to quote 3% as a maximal limit.

(Expt. 44.) Conditions: benzamide, 2·00 g.; nitric acid ($d^{16°}$ 1·505), 30 g.; temperature, − 15°; time allowed for nitration, 6 hours. Results: hydrolysis, 10%; benzoic acid, nil; *p*-nitrobenzoic acid, less than 3%; *m*-nitrobenzoic acid, 69·6%. This is the proportion of *m*-nitrobenzamide formed if the 10% of hydrolysis entirely precedes nitration. The acid by-product contained 66% of *m*-isomeride, so that if the hydrolysis is wholly subsequent to nitration, the proportion of *m*-nitrobenzamide *formed* would be 69·2%. The mean value 69·4% is regarded as the most trustworthy.

The final mean is the same figure, *viz.*, 69·4% meta-. This, and the other mean figures, are rounded in the table given in the introduction, since it is doubtful if much significance attaches to the decimals.

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