LVII.—*The Nature of the Alternating Effect in Carbon Chains. Part XXIII. Anomalous Orientation by Halogens, and its Bearing on the Problem of the Ortho–Para Ratio, in Aromatic Substitution.*

By Christopher Kelk Ingold and Charles Cyril Norrey Vass.

The theory that the *op*-directive efficiencies of the halogens in the halogenobenzenes varies directly with the tendency of the halogen atom to share additional electrons ($+ T$) and inversely as its attraction for electrons, shared and unshared ($- I$), and therefore ($+ T - I$) corresponds to the sequence I>Br>Cl>F, is in accord with much indirect evidence. For example, the relative speeds of nitration of halogenobenzenes indicate I>Br>Cl>F (Ingold and Shaw, J., 1927, 2918), the relative basicities of combined halogens demand I>Br, the data on molecular dipole moments suggest I>Br>Cl, and the substitution of ω-halogenated toluenes requires Cl>F, for the phenomenon under discussion. The same sequence is also in agreement with the available data on the nitration of *o*- and *p*-dihalogenobenzenes with the following significant * exception. Holleman (*Rec. trav. chim.*, 1915, **34**, 216) found that whereas the nitration of *p*-chlorobromobenzene proceeded normally,

Direction by Cl : *Direction by Br* = 45·2% : 54·8% . . (para)

the nitration of *o*-chlorobromobenzene gave an abnormal result :

Direction by Cl : *Direction by Br* = 55·5% : 45·5% . (ortho)

The present paper is the result of an attempt to test a possible explanation of this anomaly on the following lines. The inductive effect ($- I$), which, according to the sequence, should be greater for Cl than for Br, is regarded as originating in a contracted electron shell around the halogen atom, as compared with a hypothetical

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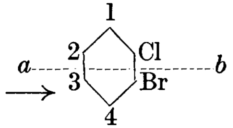
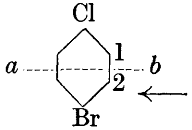
* The apparent exception represented by van Hove's recent experiments (*Bull. Acad. roy. Belg.*, 1926, **12**, 801) is not regarded as significant for our purpose in view of the special experimental conditions employed. The point will be dealt with more fully in a future paper.

non-orienting atom having the same number of electrons of each class. This should not only produce electron displacements relayed from bond to bond, but might also, by direct action through space, modify existing electrical fields in such a way that the potentially active electrons of the benzene ring would be subjected to an additional electrostatic restraint. The " direct " effect of halogens is therefore a deactivating influence ($- D$). Since its genesis is also that of the inductive effect ($- I$), its variation as between different directing atoms will be the same as that of the inductive effect. Because, however, it is propagated, not through the bonds, but through space, its distribution in the ring will be, not in the order $op > m$, but in the order $o > m > p$. The full expression for the directive action of halogens in halogenobenzenes is therefore $+ T - I - D$. The modes of distribution in the ring of T and of I were dealt with by Ingold and Shaw (*loc. cit.*).

(A)





(B)

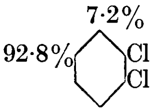
Let X and X' represent the intensities of the direct effects due to Cl and Br respectively, so that $X > X'$; and let f, f' and f'' be factors (assumed to be substantially the same for Cl and Br) expressing the distribution of the effect as between the *o*-, *m*-, and *p*-positions respectively, so that $f > f' > f''$. In *o*-chlorobromobenzene the direct effects ($- D$) at positions 1, 2, 3, and 4 (A) will be as follows :

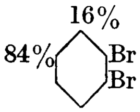
$$(1) = fX + f'X', \qquad (2) = f'X + f''X',$$
$$(3) = f''X + f'X', \qquad (4) = f'X + fX'.$$

From the inequalities mentioned it follows, first, that $(1) + (4) > (2) + (3)$ because every term in $fX + f'X + fX' + f'X'$ is greater than the corresponding term in $f'X + f''X + f'X' + f''X'$. That is, in so far as the direct effect controls the situation, substitution will occur mainly at (2) and (3). Secondly, since $(2) - (3) = (f' - f'')(X - X') =$ positive, therefore $(2) > (3)$. Hence the direct effect will deactivate position (2) more strongly, and will favour substitution at position (3). Similarly, $(1) > (4)$; so that if the molecule be divided symmetrically between the halogens by a line *ab*, the half containing Cl will be deactivated relatively to the half containing Br. In *p*-chlorobromobenzene (B) we have

$$(1) = fX + f'X' \qquad \text{and} \qquad (2) = f'X + fX',$$

so that $(1) > (2)$, and here again the rule relating to symmetrical division applies. That is to say, in the para-compound the direct effect will collaborate with the tautomeric and inductive effects in favouring substitution in position (2), and an anomalous result is not to be expected; but in the ortho-compound the direct effect opposes the other influences, and this might explain the apparent reversal of directive efficiencies observed by Holleman. It is also obvious that the above considerations accord with the small amounts of vicinal substitution observed (Reiding, *Rec. trav. chim.*, 1904, **23**, 359; Holleman, Reiding, Sirks, and Sluiter, *ibid.*, 1906, **25**, 183; 1907, **26**, 153) in the nitration of *o*-dichloro- and *o*-dibromobenzene (see also Holmes, Ingold, Ingold, and Smith, J., 1926, 1684, 3093; 1927, 1690):





and that they afford a partial explanation of such facts as the diminishing *o*-nitration towards fluorobenzene in the series of halogenobenzenes:

	PhF.	PhCl.	PhBr.	PhI.
Ortho	12·7	30·1	37·6	41·1
Para	87·4	69·9	62·1	58·7

(Holleman, Holleman, and de Bruyn, *Rec. trav. chim.*, 1900, **19**, 189, 364; 1903, **22**, 263; 1905, **24**, 140; 1913, **32**, 134), and the displacement from *o*-substitution in the direction of *p*-substitution which occurs on increasing the acidity of the medium employed in the nitration of acetanilide (direct effect of weak dipole arising from loose salt-formation). Again the conception of an influence "distributed over the molecule" by which Allan, Oxford, Robinson, and Smith (J., 1926, 406) explained the diminishing disparity in the directive powers of the groups in an ascending series of the higher alkyl ethers of guaiacol may be translated into the following: The sign of the inductive effect of alkyl groups ($+ I$), established by Lucas and his collaborators (*J. Amer. Chem. Soc.*, 1924, **46**, 2475; 1925, **47**, 1459, 1462) and subsequently confirmed by many orientation experiments, suggests that electrons in the neighbourhood of an alkyl group would suffer repulsion (diminished attraction) by electrostatic action through space; in the high alkyl ethers of guaiacol the field at the two oxygen atoms * due to the direct effect

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* Since in orientation by ·OR the tautomeric effect overwhelmingly predominates, it is unnecessary to consider the direct effects at the distant points of reaction in the benzene ring. Furthermore, there is no necessity for the supposition that the effect considered is distributed *equally* between the two oxygen atoms, or between the nuclear positions they respectively activate.

of the larger alkyl group will increase the displacements of the unshared electrons of both oxygen atoms towards the benzene ring. The effects observed are precisely those to be expected, and an intelligible * mechanism is thus provided.

Definite prediction in regard to the direct effect is possible in simple cases, (*a*) because this effect, representing a permanent molecular condition, will follow the inductive, and not the tautomeric, effect in sign and magnitude, so far as concerns its origination (compare Ingold and Shaw, *loc. cit.*); and (*b*) because, once originated, its distribution is a matter of molecular geometry. When considering cases in which the operation of the direct effect might be expected to give rise to notable anomalies, we selected a fluorine compound, because the inductive effect, and therefore presumably the direct effect, is strongest at the fluorine end of the halogen series. Furthermore, the very large disparity in the orientation by fluorine and chlorine observed by Swartz (*Rec. trav. chim.*, 1915, **34**, 131) in the nitration of *p*-fluorochlorobenzene,

Direction by F : *Direction by Cl* = 27·7% : 72·3% . . (para)

(we have confirmed this result) † gave rise to the suspicion that the normal difference between the directive powers of these elements (*i.e.*, that due to $+T-I$) is greatly augmented in this substance by the direct effect ($-D$) in accordance with the theory outlined above. It followed that the small anomaly observed by Holleman in *o*-chlorobromobenzene should become notably increased in *o*-fluorochlorobenzene. We have therefore examined the nitration of the latter and are able to show that the substitution occurs mainly in the two para-positions, as was expected, and that the relative direction by the two halogens is as follows :

Direction by F : *Direction by Cl* = 78·7% : 21·3% . (ortho)

We venture to suggest that this strikingly anomalous result definitely requires a theoretical explanation along the lines indicated; and it is consistent therewith that in the nitration of *o*-bromoiodobenzene ($-D$, much weaker) the anomaly disappears (Holleman, *Rec. trav. chim.*, 1915, **34**, 228).

EXPERIMENTAL.

3-*Fluoro*-4-*chloronitrobenzene*.—The scheme of preparation was as follows : *m*-Nitroaniline ⟶ *m*-nitrobenzenediazonium fluoride

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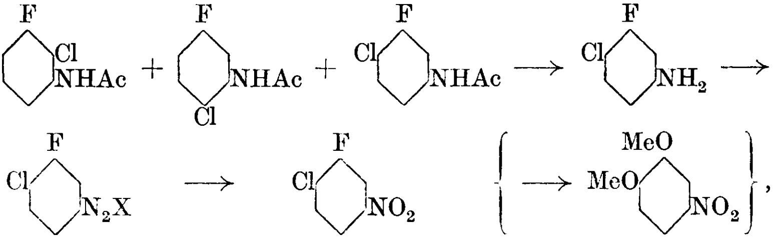
* We do not mean that it is possible precisely to specify all the details of the mechanism in this or any of the other cases discussed in this paper.

† There is an arithmetical error in Swartz's paper; the figures here shown represent a correct interpretation of his data.

$\longrightarrow$ *m*-nitrofluorobenzene $\longrightarrow$ *m*-fluoroaniline $\longrightarrow$ *m*-fluoroacetanilide $\longrightarrow$ *N*-chloro-*m*-fluoroacetanilide $\xrightarrow[\text{(re-arrangement)}]{}$



the reaction indicated in brackets serving to identify the fluorochloroacetanilide selected from the mixture obtained by re-arrangement. The process is obviously diagnostic.

Beekman has prepared *m*-fluoronitrobenzene in a somewhat complicated apparatus (*Rec. trav. chim.*, 1904, **23**, 235), and we have obtained an equivalent result by the following simple method. *m*-Nitroaniline (69 g.), suspended in a solution of sulphuric acid (60 g., *d* 1·80) in water (150 g.), was diazotised at 0° with a solution of sodium nitrite (36 g.) in water (50 g.), efficient mechanical stirring being maintained. The product, mixed with 60% hydrofluoric acid (400 c.c.), was distilled from a copper can (2·5 l.) through a copper condenser, and the *m*-nitrofluorobenzene, the last traces of which were driven over with a current of steam, was collected in a rubber beaker, separated from the bulk of the acid liquid by decantation, extracted with ether after addition of alkali, and distilled (b. p. 199—200°; yield 30%). The *m*-fluoroaniline (Wallach and Heusler, *Annalen*, 1888, **243**, 225; Swartz, *Rec. trav. chim.*, 1915, **34**, 131) had b. p. 187—189° (yield 90%), and the *m*-fluoroacetanilide (Swartz, *loc. cit.*) had m. p. 83°, and crystallised usually in rhombs, but occasionally in oblique-ended needles.

m-Fluoroacetanilide (10 g.), suspended in a solution of potassium hydrogen carbonate (30 g.) in water (200 c.c.), was mechanically stirred and treated during 1 hour at the ordinary temperature with an aqueous paste of bleaching powder (32 g.; available Cl, 28%). The stirring was continued for 24 hours, the solution was then acidified with hydrochloric acid, and stirred for a further 12 hours. The mixed fluorochloro-compounds were obtained in approximately theoretical yield by collecting and drying the precipitate, and extracting the filtrate with ether. The separation of the products necessitated a lengthy series of fractional crystallisations from ethyl acetate–ligroin, and even then was incomplete. Thus from 18 g. of *m*-fluoroacetanilide we obtained the quantities given as yields below, together with much unresolved mixture. 3-*Fluoro*-4-*chloro*-

acetanilide (yield 9·5 g.) was obtained as glistening plates, m. p. 115° (Found: Cl, 19·3. C_8H_7ONClF requires Cl, 18·9%). Its constitution follows from its conversion into 4-nitroveratrole by the reactions described below. 3-*Fluoro*-6-*chloroacetanilide*, or, less probably, 3-fluoro-2-chloroacetanilide (yield 0·2 g.), was isolated as long, slender needles, m. p. 143° (Found: C, 51·8; H, 4·2. C_8H_7ONClF requires C, 51·2; H, 3·7%). 3-*Fluoro*-4 : 6-*dichloroacetanilide*, or, less probably, 3-fluoro-2 : 6-dichloroacetanilide (yield 0·8 g.), forms prisms, m. p. 124° (Found: C, 43·6; H, 2·9. $C_8H_6ONCl_2F$ requires C, 43·2; H, 2·7%).

3-*Fluoro*-4-*chloroaniline* was obtained by hydrolysing its acetyl derivative with alcohol and sulphuric acid (Perkin's method), but by-products were also formed. The anilide was therefore boiled for 24 hours with 20% hydrochloric acid, and the amine distilled in steam after basification. Isolated by extraction with ether, it had b. p. about 226°, and separated from ligroin in long, fibrous needles, m. p. 61—62° (Found: Cl, 23·8. C_6H_5NClF requires Cl, 24·3%).

For the preparation of 3-*fluoro*-4-*chloronitrobenzene*, the base (6·0 g.) was suspended in water (100 c.c.), containing sulphuric acid (3·84 g., *d* 1·80), and diazotised at − 5° with a solution of sodium nitrite (4·0 g.) in water (100 c.c.). The bright yellow, sparingly soluble diazo-compound so formed was collected and suspended in water (1 l.), and the suspension poured, with vigorous stirring, into a freshly prepared aqueous solution (100 c.c.) of sodium nitrite (40 g.) and cuprocupric sulphite (Chevreul's salt) (15 g.). A rapid evolution of nitrogen occurred, and, 15 minutes later, when a brown deposit had covered the surface of the dark green liquid, the stirring was discontinued, and the faintly acid solution distilled in steam. The oil was extracted with ether from the distillate, and the extract washed with very dilute alkali, dried with calcium chloride, and distilled. The residue (4·0 g.), which was brown and semi-solid at the ordinary temperature, was distilled and the nitro-compound was then obtained (2·7 g.) as a pale yellow oil, b. p. 114—116°/24 mm., which crystallised in the receiver. It was finally purified by crystallisation from ligroin and obtained as very pale yellow leaflets, m. p. 63—64° (Found : Cl, 20·7. $C_6H_3O_2NClF$ requires Cl, 20·2%).

4-*Fluoro*-3-*chloronitrobenzene*.—This isomeride was obtained from *p*-fluoronitrobenzene (which was prepared in 33% yield from *p*-nitroaniline by the method described for the *m*-compound) by chlorination in the presence of anhydrous ferric chloride (Rinkes, *Chem. Weekblad*, 1914, **11**, 952). It had m. p. 41·5°.

o-*Fluorochlorobenzene* was prepared from the second of the above nitro-derivatives by elimination of the nitro-group according to

Rinkes's method (*loc. cit.*). 4-Fluoro-3-chloroaniline (m. p. 44°) was obtained without difficulty (yield 90%). The base (16 g.), suspended in concentrated hydrochloric acid (100 c.c.) at − 5°, was diazotised with a solution of sodium nitrite (10 g.) in water (15 c.c.), and the solution cautiously treated below 0° with one of stannous chloride (60 g.) in concentrated hydrochloric acid (50 c.c.), with efficient mechanical stirring. Thirty minutes after the addition was complete the hydrazine hydrochloride was collected and decomposed with cold sodium hydroxide solution. The hydrazine was extracted with ether and obtained as a brown solid (12 g.), but attempts to purify it by crystallisation failed owing to its tendency to autoxidation. It was therefore dissolved in the minimal amount of 75% acetic acid, and the solution added drop by drop to a boiling solution of crystallised cupric sulphate (50 g.) in water (150 c.c.). Nitrogen was evolved and the solution on distillation yielded *o*-fluorochlorobenzene (6·5 g.) as an almost colourless oil, b. p. 138—140°/758 mm.

Nitration of o-*Fluorochlorobenzene.*—*o*-Fluorochlorobenzene (5·0 g.) was added during 1 hour through a capillary tube to nitric acid (15 g., *d* 1·49) at 0°, and the stirring of the mixture was continued for a further 3 hours at the same temperature. The product was extracted with ether, after addition of ice (50 g.) and aqueous sodium hydrogen carbonate (slight deficit), and distilled. Allowing for the small amounts of unchanged *o*-fluorochlorobenzene (b. p. 37°/16 mm.) which were always recovered, the yields of mononitro-derivatives, b. p. 113°/16 mm., 114°/18 mm., 118—119°/26 mm., ranged from 91% to 98%. Repetition of the purification, followed by determinations of the freezing point and labile halogen (see below) showed that the losses were mainly mechanical and that the change of composition during isolation was certainly not more than 1% (Found : N, 7·9. $C_6H_3O_2NClF$ requires N, 8·0%). The nitration product is a very pale yellow solid at the ordinary temperature, and it is possible to separate pure 4-fluoro-3-chloronitrobenzene from it by crystallisation from methyl alcohol.

Action of Sodium Methoxide on the Isomeric Fluorochloronitrobenzenes and on the Nitration Product of o-*Fluorochlorobenzene.*—About 1 g. of the nitro-compound or mixture of nitro-compounds, dissolved in methyl alcohol (100 c.c.) containing 15 mols. of sodium methoxide, was heated at 80° for 60 hours, and the product poured into chloride-free water. Attempts to estimate the loss of alkalinity by titration were not entirely satisfactory owing to the masking of the end-point by the yellow colour of the solution. The solution was nearly neutralised with halogen-free nitric acid, made definitely alkaline with 2 c.c. of 2*N*-sodium carbonate, evaporated to remove the methyl alcohol, and extracted with ether. The extract was washed with water, and the fluoride and chloride were then estimated in the combined aqueous solutions.

4-Fluoro-3-chloronitrobenzene (0·8947 g.) gave calcium fluoride (0·1972 g., corr.) corresponding to 99·5% of labile fluorine; but 7·0% of the value represents the correction for the solubility of calcium fluoride in water and in the dilute acetic acid used to wash it. The chloride estimation represented 1·3% of labile chlorine, and blank experiments indicated that this figure was real and not due to chloride in the reagents or apparatus. The ethereal extract was not examined.

3-Fluoro-4-chloronitrobenzene gave fluoride and chloride corresponding to 47·3% and 100·0% of labile fluorine and chlorine respectively. A large proportion of the fluorine in this *m*-fluoronitro-compound is therefore ejected from the molecule under the conditions used. For this reason, and also because the accuracy of the fluoride estimation is impaired by the considerable solubility of calcium fluoride (above), we decided to use chloride estimations for the analysis of the nitration product. The ethereal extract on evaporation yielded a yellow solid, which, after crystallisation from methyl alcohol, was identified as 4-nitroveratrole by direct comparison and a mixed m. p. determination with a specimen prepared by Vermeulen's method (*Rec. trav. chim.*, 1906, **25**, 24).

The products of the nitration experiments gave the following percentages of labile chlorine: (1) 22·41, (2) 22·74, (3) 22·07, (4) 22·72 (mean, 22·49%). Three estimations, carried out at the same time and in the same way, of the labile chlorine in the 4-fluoro-3-chloro-isomeride gave (α) 1·13, (β) 1·04, (γ) 1·36% (mean 1·17%). It is shown below that the nitration product of *o*-fluorochlorobenzene is essentially a mixture of 3-fluoro-4-chloro- and 4-fluoro-3-chloro-compounds and contains only a small proportion of the vicinal isomerides. We therefore feel justified in applying to the two *m*-chloronitro-compounds taken together, the small correction (1·17%) determined on the principal member of the pair. Hence it follows that: Orientation by F/Orientation by Cl = 78·68%/21·32%.

Freezing Points of Mixtures of the Isomeric Fluorochloronitrobenzenes and of the Nitration Product of o-*Fluorochlorobenzene.*— In the following table *p* denotes the percentage of 4-fluoro-3-chloronitrobenzene in a mixture with 3-fluoro-4-chloronitrobenzene, and *t* represents the uncorrected freezing point:

p	0·0	10·0	21·1	28·7	34·8	40·5	45·9	51·0	56·2
t	60·0°	55·3°	49·1°	45·0°	41·1°	37·1°	33·0°	26·8°	24·8°
p	59·8	64·1	66·6	71·9	75·4	81·0	87·4	92·2	100·0
t	22·7°	24·7°	26·3°	29·2°	31·1°	34·0°	37·0°	39·1°	42·1°

These points lie on a two-branch diagram, with the eutectic point at $p = 59{\cdot}5\%$ and $t = 22{\cdot}1°$.

The next table refers to the product of the second nitration experiment; x represents the parts of 4-fluoro-3-chloronitrobenzene and y the parts of 3-fluoro-4-chloronitrobenzene added to 100 parts of the nitration product. The freezing points (t) were determined with the same thermometer and apparatus and under the same conditions as those recorded in the previous table.

x	0·0	20·2	72·5	0·0	0·0	0·0	0·0	0·0
y	0·0	0·0	0·0	16·0	24·5	32·8	49·3	63·1
t	28·3°	31·0°	34·8°	22·8°	21·4°	24·5°	28·8°	31·3°

These values lie on a two-branch curve with a eutectic point at 20·7°, and thus show that the depression of the eutectic temperature of the 4-fluoro-3-chloro- and 3-fluoro-4-chloro-compounds caused by the presence of vicinal isomerides in the nitration product is 1·4°. If the first point be placed at the correct temperature on the appropriate branch of the binary diagram, that branch fits accurately, but the second branch is displaced to an extent indicated by a displacement in apparent composition of the eutectic mixture amounting to 2·3% in the direction of the 3-fluoro-4-chloro-isomeride.

A corresponding investigation of the third nitration product gave the following data :

x	0·0	184·1	0·0	0·0	0·0	0·0
y	0·0	0·0	20·4	28·0	33·1	47·5
t	29·0°	35·7°	22·4°	22·2°	24·1°	28·6°

The eutectic point is at 20·9°, so that the depression of the binary eutectic temperature is 1·2°. If the first point is fitted to the binary diagram, the apparent displacement in composition of the eutectic mixture is 2·0% towards the 3-fluoro-4-chloro-compound.

It is evident from these results that, although the nitration products do not accurately behave as binary mixtures of 4-fluoro-3-chloro- and 3-fluoro-4-chloro-nitrobenzenes, they can hardly contain more than a few units % of either of the vicinal isomerides.

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