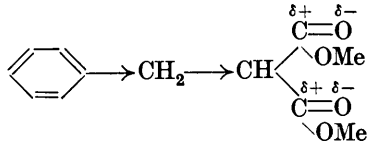
CCLXXXII.—*The Nature of the Alternating Effect in Carbon Chains. Part XXI. The Directive Influence of the Groups* $-CH_2{\cdot}CH(CO_2Me)_2$, $-CH{:}C(CO_2Me)_2$, $-C(CO_2Me){:}CH_2$, *and* $-CH{:}CH{\cdot}CH{:}C(CO_2Me)_2$ *in Aromatic Substitution.*

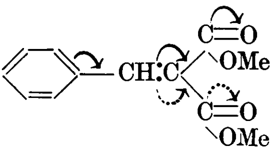
By John William Baker and Alfred Eccles.

It has already been shown (Baker and Wilson, this vol., p. 842) that mechanisms depending on complete co-valency changes between the side-chain and the benzene nucleus probably play, at the most, a subsidiary part in the propagation of meta-orienting influences. Thus, electron attraction due to the integral positive charge on the nitro-group is more readily propagated to the nucleus in the ω-nitroethyl than in the corresponding ω-nitrovinyl side-chain. In the present communication, an attempt is made to confirm the previous conclusion by a study of the nitration of the analogous compounds, methyl benzylmalonate (I) and methyl benzylidenemalonate (II), in which the *gem*-dicarbomethoxyl grouping replaces the nitro-group of the previous cases. On the view that the meta-orienting influence of the carboxyl group is due to the presence of a permanent fractional dipole in the resting state of the group (Baker and Ingold, this vol., p. 832), it is to be expected that the effects produced would be much smaller in magnitude than those due to the integral dipole charge on the nitro-group.

Again, however, on any mechanism of meta-substitution which depends on the alternation of single and double bonds, a larger proportion of meta-nitration should occur in the unsaturated compound (II), in which there is an unbroken conjugated system extending from the polar group throughout the nucleus, than in the corresponding saturated compound (I). Actually, in confirmation of previous results, we find the reverse to be the case, since, on nitration, methyl benzylmalonate yields 8% of meta-derivative, whilst methyl benzylidenemalonate yields only 3%.* Thus, here

(I.)





(II.)

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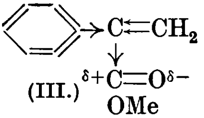
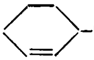
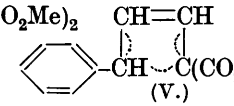
* This value is somewhat higher than that expected (1—2%). It is possible that addition of nitric acid to the double bond precedes nitration and slightly increases the proportion of meta-isomeride produced.

also the electron attraction due to the fractional positive charge on the carboxyl groups is neutralised in passing through the field of the double bond.

As in the case of the nitro-compounds previously studied, the possibility of the double linking itself acting as a dominating electron-source towards the nucleus was negatived by a study of the nitration of methyl atropate (III), in which the double bond is no longer in the path of transmission from the (single) carbomethoxyl group. We find that, on nitration, this ester yields about 5% of meta-isomeride, although, owing to the small amount of material available, the figure must be considered as approximate only.


(III.)


$-CH{:}CH{\cdot}CH{:}C(CO_2Me)_2$
(IV.)


(V.)

One other case was investigated, *viz.*, that of methyl cinnamylidenemalonate (IV). The point of interest here is that there might be the possibility of valency tautomerism in the side-chain leading to the cyclic form (V), in which electron-strain might conceivably be transmitted to the nucleus through two carbon atoms only, *via* the α : δ partial valency, and the proportion of *m*-isomeride produced might then be more or less comparable with that obtained on nitration of methyl benzylmalonate. Actually, however, we find no evidence of this type of transmission, since the proportion of *m*-isomeride produced is less than 1%. The electron attraction of the carbomethoxyl group is thus completely neutralised by the fields of the unsaturated chain in (IV).

EXPERIMENTAL.

A. *Preparation of Materials.*

Methyl Benzylidenemalonate.—This was obtained by the condensation of benzaldehyde and methyl malonate, as described by Claisen and Crismer for the ethyl ester (*Annalen*, 1883, **218**, 132; compare Liebermann, *Ber.*, 1894, **27**, 289). The product had b. p. 174—177°/15 mm., m. p. 41° (Found: C, 65·6; H, 5·5. Calc.: C, 65·4; H, 5·5%).

The methyl *o*-, *m*-, and *p*-nitrobenzylidenemalonates were obtained by the condensation of the appropriate nitrobenzaldehyde with methyl malonate in the presence of piperidine as a condensing agent (compare Knoevenagel, *Ber.*, 1898, **31**, 2593).

Methyl p-*Nitrobenzylidenemalonate.*—A mixture of *p*-nitrobenzaldehyde (7·6 g.), methyl malonate (6·6 g.), and two drops of piperidine was heated to 60° for 6 hours. On cooling, the mixture solidified, and the *nitro-ester* was recrystallised from hot alcohol; needles, m. p. 136—137° (Found: C, 54·4; H, 4·2. $C_{12}H_{11}O_6N$ requires C, 54·3; H, 4·2%). The yield is quantitative.

Methyl m-*nitrobenzylidenemalonate*, prepared similarly but in smaller yield from *m*-nitrobenzaldehyde, has m. p. 99—100° (Found: C, 54·2; H, 4·2%).

Methyl o-*nitrobenzylidenemalonate*, m. p. 65—66° (Found: C, 54·3; H, 4·3%).

Methyl benzylmalonate was prepared by esterification of the pure acid with methyl alcohol and hydrogen chloride.

Methyl o-*Nitrobenzylmalonate.*—*o*-Nitrobenzylmalonic acid (Reissert, *Ber.*, 1896, **29**, 644) was esterified through its silver salt. The *methyl* o-*nitrobenzylmalonate* was obtained as a pale yellow, viscous oil, which did not solidify on cooling to −10°, and could not be purified by distillation (Found: C, 53·8; H, 5·1. $C_{12}H_{13}O_6N$ requires C, 53·9; H, 4·9%). On oxidation with boiling 2% permanganate, it gave an acid product contaminated with gummy material in 73·3% yield (calculated as *o*-nitrobenzoic acid). By crystallisation from ether, this was shown to contain *o*-azoxybenzoic acid. Reissert (*loc. cit.*) records the formation of the latter compound by the oxidation with permanganate of 1-hydroxyindole-2-carboxylic acid formed from *o*-nitrobenzylmalonic acid by the action of potash.

Methyl m-*Nitrobenzylmalonate.*—To a solution of 4·6 g. of sodium in 50 g. of methyl alcohol, 26·4 g. of methyl malonate were added, quickly followed by a saturated solution of 17·15 g. of *m*-nitrobenzyl chloride in methyl alcohol; the mixture was heated on the steam-bath for ½ hour and filtered from sodium chloride and the *methyl di-*m-*nitrobenzylmalonate* formed as a by-product. The salt was extracted with cold water, and the dried residue crystallised from benzene; m. p. 162—162·5° (Found: C, 56·9; H, 4·6. $C_{19}H_{18}O_8N_2$ requires C, 56·7; H, 4·5%). The alcoholic mother-liquor was concentrated, poured into water, and extracted with ether. After drying the extract and evaporating the ether, the excess of methyl malonate was separated by distillation under reduced pressure. The residue, which cannot be distilled without decomposition, was dissolved in alcohol, and the solution saturated with ammonia. After standing for several days, m-*nitrobenzylmalonamide* separated as a flocculent precipitate. After several crystallisations from water, it had m. p. 203° (Found, by microcombustion: C, 51·0; H, 4·4. $C_{10}H_{11}O_4N_3$ requires C, 50·6; H, 4·6%). The amide was hydrolysed by heating at 100° with a slight excess of 10% caustic soda. On acidification of the cooled solution, m-*nitrobenzylmalonic acid* separated, and after crystallisation from water it had m. p. 164° (decomp.) (Found, by microcombustion: C, 50·5; H, 4·0. $C_{10}H_9O_6N$ requires C, 50·2; H, 3·8%). A further small quantity of the acid may be obtained by extracting the mother-liquors with ether. The yield of recrystallised acid was 2 g. Conversion of the crude methyl *m*-nitrobenzylmalonate into the amide is necessary, as treatment of the ester itself with alcoholic potash yields a very tarry product. The *m*-nitrobenzylmalonic acid was esterified through its silver salt, and *methyl* m-*nitrobenzylmalonate* obtained as a pale yellow, viscous oil, which did not solidify on cooling to −10° (Found: C, 54·2; H, 5·1%). On oxidation with boiling 2% potassium permanganate, it gave *m*-nitrobenzoic acid, m. p. 139°, in 90% yield.

Methyl p-*nitrobenzylmalonate*, m. p. 82·5—83·5° (Found: C, 53·85; H, 5·0%) was isolated from the reaction products by crystallisation from methyl alcohol (compare Section C). On oxidation, it gave *p*-nitrobenzoic acid, m. p. 237—239°, in 99% yield.

Methyl Cinnamylidenemalonate.—This was obtained by esterification of the acid (compare Liebermann, *Ber.*, 1895, **28**, 1439) by the method of Thiele and Meisenheimer (*Annalen*, 1899, **306**, 253) and had m. p. 67° (Found: C, 68·1; H, 5·9. Calc.: C, 68·3; H, 5·7%).

The isomeric nitro-derivatives were prepared by condensation of the appropriate nitro-cinnamaldehyde with methyl malonate in the presence of piperidine.

Methyl m-*Nitrocinnamylidenemalonate.*—A mixture of 8·85 g. of *m*-nitrocinnamaldehyde (Kinkelin, *Ber.*, 1885, **18**, 484), 6·6 g. of methyl malonate, and two drops of piperidine was heated to 60—70° for 5 hours. The cooled mixture, when treated with a few c.c. of ether and scratched, partly solidified. The separated crystals were washed with ether, recrystallised from alcohol, and obtained as felted needles, m. p. 125—126° (Found: C, 57·9; H, 4·6. $C_{14}H_{13}O_6N$ requires C, 57·7; H, 4·5%). The yield was small (about 15%). On oxidation with potassium permanganate, it gave *m*-nitrobenzoic acid, m. p. 129—132° (mixed m. p. 136—139°) in 76% yield.

Methyl o-*nitrocinnamylidenemalonate*, obtained in a similar manner from *o*-nitrocinnamaldehyde, and crystallised from methyl alcohol, had m. p. 114° (Found, by micro-combustion: C, 57·7; H, 4·6%). On oxidation it gave *o*-nitrobenzoic acid, m. p. 133—137° (mixed m. p. 139—141°), in 80% yield.

Methyl p-*nitrocinnamylidenemalonate* has m. p. 146—147° after crystallisation from methyl alcohol (Found: C, 57·8; H, 4·7%). On oxidation it gave *p*-nitrobenzoic acid, m. p. 229—231°, in 77% yield.

Methyl Atropate.—Tropic acid was converted into atropic acid by the method of Hesse (*J. pr. Chem.*, 1901, **64**, 287), who, however, gave no details. The tropic acid (10 g.) was refluxed with 60 c.c. of a 50% aqueous solution of potassium hydroxide for 40 minutes, the solution extracted with ether, acidified with hydrochloric acid, and again extracted with ether. The crude atropic acid obtained from this dried ethereal extract was purified by crystallisation (twice) from dilute alcohol. The acid (4·5 g.) was dissolved in a large volume (1200—1500 c.c.) of very dilute ammonia solution, boiled to expel the excess of ammonia, and a slight excess of a hot solution of silver nitrate added. On cooling, the silver salt crystallised out, and was filtered and washed in succession with water, alcohol, and ether. Treatment of the dry silver salt with an excess of methyl iodide yields the *methyl atropate* in an almost pure state as a colourless, mobile liquid, b. p. 95—98°/6 mm. (Found : C, 73·6; H, 6·2. $C_{10}H_{10}O_2$ requires C, 74·1; H, 6·2), which polymerises on keeping.

B. *Conditions of Nitration.*

In all cases, the ester was slowly added at the rate of 1—2 g. per hour to about 10 times its quantity of nitric acid (*d* 1·49) at -15—$-10°$. Isolation of the product was effected by pouring on crushed ice, exactly neutralising the solution, first with 10% sodium hydroxide solution and finally with sodium carbonate solution, filtering off any solid product, and extracting the mother-liquors with ether. Special precautions were necessary in the case of methyl cinnamylidenemalonate (see Section C).

C. *Details relating to Individual Cases and Determination of the Proportions of the Isomerides formed.*

Since the methods employed in the separation of the isomerides are those which have been described in detail in earlier papers in this series, details of procedure are omitted in the following pages.

Nitration of Methyl Benzylmalonate.—In this case, it was found that the yield of mixed acids obtained by oxidation of the nitration mixture was only about 80—85% of that calculated from the percentage oxidation yields of the pure isomerides (compare Section A) and their estimated relative proportions. This may be due to the *o*-nitrobenzylmalonate being converted into an indole derivative under the influence of alkali (Reissert, *loc. cit.*; compare p. 2127). The proportion of *m*-nitro-ester in the nitration mixture, as calculated from the quantity of *m*-nitrobenzoic acid isolated, is probably too low, since the total oxidation yield is less than the calculated yield, but it is still considerably greater than that present in the nitration of the benzylidenemalonate. The authors are of the opinion that the percentage of *m*-nitrobenzoic acid isolated from the mixed acids obtained on oxidation represents fairly closely the proportion of meta-derivative formed by nitration. The presence of the azoxybenzoic acid did not interfere with the separation of the mixed acids, except that sometimes it was found necessary to crystallise the *p*-acid from water.

(Expt. 31.) The yield of mononitro-compounds was 93% (Found: C, 53·4; H, 4·9. Calc. for $C_{12}H_{13}O_6N$: C, 53·9; H, 4·9%), a further 2% of the material being accounted for as acid products produced by oxidation. On oxidation, the mixed nitrocompounds yielded acids in 70% yield, which on separation by the usual method gave nitrobenzoic acids thus: para-, m. p. 234° (either alone or mixed), 70·4%; meta-, m. p. 128—135° (mixed m. p. 141°), 7·5%; ortho- (by difference), 22·1%.

A second portion of the same nitration product was crystallised from methyl alcohol, whereby 58·8% of practically pure methyl *p*-nitrobenzylmalonate, m. p. 82°, was isolated. On oxidation of the residue, some accidental loss occurred and only a 64% yield of mixed nitrobenzoic acids was obtained; these comprised: para-, m. p. 220—223°, 30%; meta-, m. p. 124—127° (mixed m. p. 138°), 16·5%. Hence the composition of the whole nitration mixture was: para-, 71·3%; meta-, 6·8%; ortho- (by difference), 21·9%.

(Expt. 33.) The yield of mono-nitration products was 93% (Found: C, 54·2; H, 4·9%), from which 56% of pure methyl *p*-nitrobenzylmalonate was isolated by crystallisation. The residues gave a mixture of acids (*M*, by titration, 165) in 72% yield, which on separation was found to contain: para-, m. p. 233—235°, 19·2%; meta-, m. p. 123—128° (mixed m. p. 133—137°), 20·9%; ortho- (by difference), 59·9%; whence the composition of the nitration mixture was: para-, 64%; meta-, 9%; ortho- (by difference), 27%.

(Expt. 34.) The yield of mono-nitration product was 95% (Found: C, 53·3; H, 4·9%), which on oxidation gave a mixture of nitrobenzoic acids (*M*, by titration, 169) in 77% yield; this on separation was found to contain: para-, m. p. 210—215° (mixed m. p. 227—229°), 68·6%; meta-, m. p. 122—125° (mixed m. p. 135—137°), 8·4%; ortho- (by difference), 23%.

(Expt. 35.) Nitration yields, 95% (Found: C, 53·9; H, 5·1%). On oxidation the nitration mixture gave acids in 71% yield, which on separation gave: para-, m. p. 236° (alone or mixed), 68%; meta-, m. p. 126—128° (mixed m. p. 138—140°), 7·0%; ortho- (by difference), 25%.

Nitration of Methyl Benzylidenemalonate.—(Expt. 21.) The yield of mononitro-product was 96% (Found: C, 53·9; H, 4·2. Calc.: C, 54·3; H, 4·2%). The whole product was oxidised with 2%

potassium permanganate and gave nitrobenzoic acids in 93% yield (*M*, by titration, 164), the bulk of the *p*-nitrobenzoic acid being allowed to crystallise out in the pure state. Separation by the usual methods gave: para-, m. p. 235° (alone or mixed), 67%; impure meta-, m. p. 104—110°, 5·8%. The meta-acid was recrystallised from a small quantity of ethyl acetate–ligroin, and a quantity corresponding to 2·4%, m. p. 122—126° (mixed m. p. 133—138°) was obtained. Hence the composition of the nitration mixture is: para-, 67%; meta-, 2·4%; ortho- (by difference), 30·6%.

A second portion of the nitration product was crystallised from absolute alcohol before oxidation, and 61% of pure methyl *p*-nitrobenzylidenemalonate, m. p. 134° (either alone or mixed with a synthetic specimen), separated out. The residue from the mother-liquor on oxidation gave nitrobenzoic acids in 96% yield (*M*, by titration, 168·5), which on separation gave a further 5·2% of *p*- and 5·3% of *m*-nitrobenzoic acid, m. p. 113—120° (both calculated on whole nitration product); the latter on recrystallisation from ethyl acetate–ligroin gave 3%, m. p. 134—136° (mixed m. p. 137—139°). Hence the composition of the nitration product was: para-, 66·6%; meta-, 3%; ortho- (by difference), 30·8%.

(Expt. 22.) The yield of mononitration product was 96% (Found: C, 54·0; H, 4·2%), which on oxidation gave nitrobenzoic acids in 84% yield (*M*, by titration, 166); these on separation gave: para-, m. p. 238°, 67·8%; meta- (after crystallisation), m. p. 134—136°, 3·3%; ortho- (by difference), 28·9%. A second portion of the nitration product was crystallised from alcohol, and 65·4% of nearly pure methyl *p*-nitrobenzylidenemalonate separated, m. p. 133—134° (mixed m. p. with a synthetic specimen, 135—136°). The residue on oxidation gave nitrobenzoic acids in 82% yield, which on separation yielded a further 2% of para-, m. p. 220—223°, and 3% of meta- (after crystallisation), m. p. 133—135° (mixed m. p. 137—139°) (both calculated on the whole nitration product). Hence the composition of the nitration product is: para-, 67·4%; meta-, 3·0%; ortho- (by difference), 29·6%.

Nitration of Methyl Atropate.—(Expt. 41.) The yield of mononitro-products was theoretical (Found: C, 57·4; H, 4·5. Calc. for $C_{10}H_9O_4N$: C, 57·9; H, 4·4%), and crystallisation from absolute methyl alcohol gave 16·3% of pure *methyl* p-*nitroatropate*, m. p. 110° (unchanged by further crystallisation). The residue from the mother-liquor on oxidation gave nitrobenzoic acids in 85% yield (*M*, 173; benzoic acid, by sublimation, 3%), which on separation were found to contain 44% of *p*-nitrobenzoic acid, m. p. 220° (mixed m. p. 221—225°), and 9% of *m*-nitrobenzoic acid. The latter, however, was slightly sticky, and was therefore converted into its methyl ester through the acid chloride, and the residue washed with a drop of methyl alcohol on porous porcelain; the residual ester had m. p. 75—78° (mixed m. p. 78°, with a synthetic specimen of methyl *m*-nitrobenzoate). Hence the composition of the nitration product is: para-, 16·3% + (44% of 83·7%) = 53%; meta-, approx. 9% of 83·7% = approx. 7%; ortho- (by difference), 40%.

(Expt. 42.) The yield of mononitro-product was 99% (Found: C, 57·4; H, 4·7%), which was completely oxidised to the mixed nitrobenzoic acids. These, on separation, gave para-, m. p. 220—222° (alone or mixed with a genuine specimen), 57%; meta-, m. p. 110—115° (mixed m. p. 133—135°), 4·7%; ortho- (by difference), 39·3%.

Nitration of Methyl Cinnamylidenemalonate.—In a preliminary experiment, the nitration product, on being poured on ice, gave a yellow, flocculent solid, which became sticky on filtering, and on drying overnight in a vacuum desiccator over phosphoric oxide decomposed to a semi-solid gum. The whole product was therefore oxidised with potassium permanganate, but gave only a 69% yield of mixed nitrobenzoic acids. On separation, this was shown to contain less than 2% of the meta-derivative. Under the following conditions, however, it was found possible to isolate the solid nitration product.

(Expt. 12.) The nitration was carried out with nitric acid (*d* 1·46), and the product was poured on ice, *partially* neutralised with a 10% solution of sodium hydroxide, and the separated solid rapidly filtered through a Buchner funnel surrounded with ice. After being washed with ice-cold water, the solid was quickly transferred to a vacuum desiccator over phosphoric oxide, and when dry was found to be quite stable. The aqueous mother-liquor and washings were extracted with ether, the ether extract washed five times with 2*N*-sodium carbonate solution, dried over calcium chloride, and the ether evaporated at the ordinary temperature. The yield of mono-nitration product was 103% (slight dinitration) (Found: C, 56·6; H, 4·5. Calc. for $C_{14}H_{13}O_6N$: C, 57·7; H, 4·5%). After two recrystallisations from methyl alcohol, 33·3% of practically pure methyl *p*-nitrocinnamylidenemalonate, m. p. 139—143°, separated, which after crystallisation from ethyl acetate–ligroin had m. p. 146°, either alone or mixed with a synthetic specimen. The residue from the combined mother-liquors was oxidised with a boiling 2% solution of potassium permanganate, and gave nitrobenzoic acids in 78% yield (*M*, by titration, 165). On separation, this fraction gave 9·5% of *p*-nitrobenzoic acid, whilst the meta-isomeride present was less than 1·5%, since only a negligible quantity of the meta-barium salt crystallised out, the amount present, therefore, only being represented by the solubility correction. The composition of the nitration product was thus: para-, 33·3% + (9·5% of 66·6%) = 40% ; meta-, <1%; ortho- (by difference), 59%.

Summary.

	Proportion of isomerides present,			Mean % of	
Substance nitrated.	*o*-.	*m*-.	*p*-.	*m*-.	*p*-.
$CH_2Ph\cdot CH(CO_2Me)_2$	22·1	7·5	70·4	8	68
	21·9	6·8	71·3		
	27·0	9·0	64·0		
	23·0	8·4	68·6		
	25·0	7·0	68·0		
$CHPh{:}C(CO_2Me)_2$	30·6	2·4	67	3	67
	30·8	3·0	66·2		
	28·9	3·3	67·8		
	29·6	3·0	67·4		
$CPh(CO_2Me){:}CH_2$	40	approx. 7	53	5	55
	39·3	4·7	57		
$CHPh{:}CH\cdot CH{:}C(CO_2Me)_2$	59	<1	40	<1	40

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