CCCXXXII.—*Examples of Feeble Activation of Certain Extended Conjugated Systems by Doubly Bound Oxygen.*

By ROBERT ROBINSON and AHMAD ZAKI.

ALTHOUGH it has recently been shown (Moore and Tucker, *J. Amer. Chem. Soc.*, 1927, **49**, 258) that one of the products of the sulphonation of cinnamic acid is the *m*-derivative, there is a mass of evidence demonstrating the *op*-orienting influence of ethenoid and benzenoid groups. It is therefore surprising to find this contested by Baker and Wilson (this vol., p. 843), especially on the basis of the facts summarised in the scheme below dealing with the results of nitration experiments.

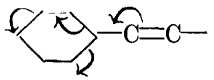
$Ph\cdot CH{:}CH\cdot NO_2$ (meta, 2%)	$Ph\cdot CH_2\cdot CH_2\cdot NO_2$ (meta, 13%)
$Ph\cdot C(NO_2){:}CH\cdot C_6H_4\cdot NO_2$ (meta, 21%)	$Ph\cdot CH_2\cdot NO_2$ (meta, 50%)

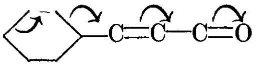
The first three cases are quoted by Baker and Wilson, and instead of phenylnitromethane they mention its dimethyl derivative, $Ph\cdot CMe_2\cdot NO_2$ (meta, 29%). This comparison is not just, because the electron displacement due to the methyl groups must, in accordance with the theory of Allan, Oxford, Robinson, and Smith (J., 1926, 401) (adopted by Baker and Wilson), have an *op*-orienting effect. Again the nitroxyl group in the *p*-nitrobenzylidenephenylnitromethane should have a weak *m*-directive influence. The disparity, 21—29, in itself indicates the *op*-influence of the unsaturated group, whilst the disparity 21—50 demonstrates it. The argument may be stated as follows. The substitution of nitroxyl for hydrogen in toluene and in the corresponding position in nitrostilbene produces a much smaller change in the direction of *m*-orientation in the latter case. Therefore the *op*-directive power of $\cdot CH{:}CH\cdot C_6H_4\cdot NO_2$ is greater than that of $\cdot CH_3$. Thus the actual evidence put forward by Baker and Wilson leads to a conclusion diametrically opposed to that which they draw.

The view advanced by Baker and Wilson is that the effect of the positive change of the nitro-group in ω-nitrostyrene may conceivably be neutralised in the adjustable electric field of the unsaturated centre. Unless the whole unsaturated group has a real net negative charge, this does not appeal as sound electrostatics; and if it has a negative charge, as the result of interaction with the surroundings, then *ipso facto* it would be *op*-directive. The *op*-directive effect of unsaturated groups may be deduced, not only from such widespread phenomena as the *op*-substitution of diphenyl and derivatives, but also indirectly from the increased reactivity of conjugated unsaturated substances in certain directions and especially towards kationoid reagents (compare, for example, K. Meyer and Schoeller, *Ber.*, 1919, **52**, 1468, on the preparation of an azo-derivative of dimethylbutadiene). An interesting example of *op*-direction by an unsaturated group was encountered a few years ago by Miss Margaret D. Scott Murray (University of St. Andrews), who nitrated ethyl benzylidenecyanoacetate in sulphuric acid solution at — 5° to — 10° by means of potassium nitrate (5 mols.). The *o*- and *p*-nitro-derivatives were alone isolated, although not in good yield, and identified by comparison with authentic specimens.

Our view of the cause of the *op*-substitution of cinnamic acid and similar substances is that it is due to the butadienoid-type conjugation of the centre with the nucleus as shown in the expression (I).

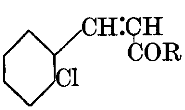
(I.)



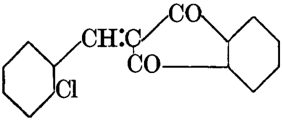


(II.)

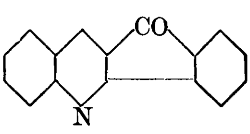
The crotonoid, conjugated polarisation shown in (II) will doubtless exist in certain phases of the molecule, but should not lead to *m*-substitution, because in these phases the reaction velocity is greatly diminished as the result of the positive field over the nucleus, the reagent being kationoid. If the conjugated polarisation were permanent and pronounced, the condition (I) might never be realised, but there is reason to believe that the degree of activation and coherence of all such systems is small. An excellent example is that of *m*-nitrotoluene, in the further nitration of which the methyl group is able to take complete control (Vorländer has shown that the same conditions obtain in quaternary salts derived from *m*-toluidine). Here the methyl group initiates a process favouring reaction, whilst the effect of the nitroxyl is to diminish the reaction velocity, and although the charges associated with the nitroxyl are generally supposed to be much greater than those appearing as the result of the small electron displacement caused by the methyl group, yet it is obvious that phases must occur in which the latter can be effective. The positive field due to the nitroxyl is thus considered to undergo variations; whilst it is considerable over the nucleus, nothing happens, but when, probably as the result of the approach of other charges, the shadow lifts, the molecule becomes, momentarily, equivalent to one of toluene, and substitution in the *o*- and *p*-positions with respect to the methyl group occurs rapidly. An analogous conception applies to systems like those of phenylnitromethane (with two obvious modifications), ω-nitrostyrene and cinnamic acid. The weak coherence of the unsaturated units (C═C, C═O, N═O, C≡N, etc.) in the crotonoid and semi-crotonoid systems is obviously better demonstrated by the occasional failure to exhibit their characteristic properties than by the absence of an anticipated inhibitory effect as in the examples discussed above. We suspect that activation of a mixed system comprising the characteristic group (CO, NO_2, etc.), an aromatic unsaturated group including an even number of carbon atoms, and an ethenoid group is always feeble and have investigated this in three directions. The behaviour of the chlorine atom of *o*- and *p*-nitrochlorobenzene, which is replaceable by anions, is simulated by that of *o*-chlorobenzaldehyde and *o*-chlorobenzoic acid. We have tested the degree of reactivity



(III.)



(IV.)

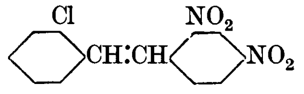


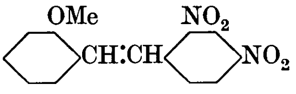
(V.)

of the chlorine atom in the system (III) by attempting a condensation with ammonia which might give a quinoline derivative.

This is a stringent test, in view of the facility with which the quinoline ring may be constructed, but it gave entirely negative results under varied conditions with *o*-chlorobenzylideneacetophenone and ethyl *o*-chlorobenzylidenecyanoacetate. In the case of *o*-chlorobenzylidenediketohydrindene (IV), a greater reactivity would be expected owing to the existence of the two carbonyl groups and it was indeed found possible to convert the substance into the ketoindenoquinoline (V), although in very small yield.

(VI.)

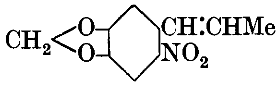


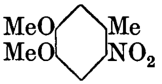


(VII.)

Similar inactivity has been noted in the stilbene derivatives (VI) and (VII); the former does not react with *p*-toluidine as 2 : 4-dinitrochlorobenzene does, and the latter, unlike 2 : 4-dinitroanisole, is resistant to hydrolytic agents. The inactivity of 1 : 5-dinitronaphthalene, of 2 : 2′-dinitrodiphenyl, and of 2 : 2′-dichloro-6 : 6′-dinitro-4 : 4′-ditolyl towards methyl-alcoholic ammonia at 150° (Burton and Kenner, J., 1922, **121**, 495) also exemplifies the phenomenon of limited conjugation. Finally, 6-nitro*iso*safrole (VIII) has been prepared and we find that the methyl group in it is relatively inert, because an anhydrocotarninenitro*iso*safrole could not be obtained, although 6-nitrohomoveratrole (IX) is readily converted into anhydrocotarninenitrohomoveratrole (Robinson and Robinson, J., 1914, **105**, 1456).

(VIII.)





(IX.)

In this case, the dissociating semi-crotonoid system, which the molecule formally contains, does not function.

EXPERIMENTAL.

Phenyl 2-chlorostyryl ketone did not yield a quinoline derivative and was recovered unchanged after heating with alcoholic urea and copper powder at 200°, or after boiling with aniline and copper powder. Ethyl 2-chloro-α-cyanocinnamate behaved similarly.

2-o-*Chlorobenzylidene*-1 : 3-*diketohydrindene* (IV).—*o*-Chlorobenzaldehyde and diketohydrindene in molecular proportion were heated together at 120°; the product, obtained in excellent yield, crystallised from alcohol in yellow, prismatic needles, m. p. 130—131° (Found: C, 71·3; H, 3·4. $C_{16}H_9O_2Cl$ requires C, 71·5; H, 3·3%). This diketone (2·9 g.), mixed with urea (1 g.), 95% alcohol (5 c.c.), copper powder (0·25 g.), and a trace of cupric chloride, was heated in a sealed tube at 240—250° for 14 hours. On working up the products from three such experiments, 100 mg. of a weak, yellow base, crystallising from alcohol, were obtained. The substance had m. p. 172—173°, and mixed with ketoindenoquinoline (m. p. 176°; Noelting and Blum, *Ber.*, 1901, **34**, 2470) it melted at 174—175°. The substance could not be obtained at all in experiments made under less drastic conditions and the degree of lability of the halogen in the chlorobenzylideneindandione is evidently negligible.

2'-Chloro-2 : 4-dinitrostilbene (VI).—A mixture of 2 : 4-dinitrotoluene (52 g.), *o*-chlorobenzaldehyde (40 g.), and piperidine (5 c.c.) was heated on the steam-bath until it set to a solid mass. The product was broken up and boiled with alcohol, the mixture cooled, and the solid isolated. The substance crystallised from alcohol in slender, lemon-yellow needles or from ethyl acetate in bright yellow, prismatic needles, m. p. 174°, that reflect light of many colours (Found: N, 9·4. $C_{14}H_9O_4N_2Cl$ requires N, 9·2%). This stilbene derivative is sparingly soluble in most organic solvents and is most easily crystallised in quantity from acetic acid or by the addition of alcohol to a solution in nitrobenzene. The reactivity of the chlorine atom could not be demonstrated, the substance being recovered unchanged after prolonged boiling with alcoholic *p*-toluidine or after heating with alcoholic ammonia at 100° for several hours. Its hot solution in piperidine is brownish-yellow and becomes green on cooling; if alcohol is added to the hot solution, a copious separation of unchanged material occurs.

2 : 4-Dinitro-2'-methoxystilbene (VII).—The preparation was like that just described and the product crystallised from acetone in reddish-orange, stout, prismatic needles, m. p. 176° (Found: N, 9·5. $C_{15}H_{12}O_5N_2$ requires N, 9·3%). This substance is more sparingly soluble in most solvents than the chlorodinitrostilbene; its solutions are yellow and deposit orange needles on cooling. All attempts to replace the methoxy-group by NH_2, NHR, or NR_2, and also to hydrolyse the substance by boiling aqueous and aqueous-alcoholic alkalis, were fruitless.

*6-Nitro*iso*safrole* (VIII).—Bromodihydrosafrole, b. p. 160°/16 mm., is a heavy, almost colourless oil which was obtained by the action of hydrobromic acid (saturated at 0°) on an equal weight of safrole. On heating with aniline, it yields *iso*safrole unmixed with safrole. Since *iso*safrole could not be directly nitrated, the safrole hydrobromide was nitrated and nitro*iso*safrole obtained from the product. Bromodihydrosafrole (20 g.) dissolved in acetic acid (120 c.c.) was nitrated by the gradual addition, with cooling, of a mixture of nitric acid (30 c.c.; *d* 1·42) and acetic acid (30 c.c.). The product was isolated by means of ether after 20 minutes and boiled for

5 minutes with alcohol (100 c.c.) containing potassium hydroxide (10 g.). The solid then precipitated by water crystallised from aqueous methyl alcohol in lemon-yellow needles, m. p. 88° (Found: C, 58·2; H, 4·4; N, 7·0. $C_{10}H_9O_4N$ requires C, 58·0; H, 4·3; N, 6·8%). The substance is readily soluble in most organic solvents, giving yellow solutions, and in sulphuric acid, from the bright red solution in which it is not recovered unchanged. It yields 6-nitropiperonal, recognised by the preparation of its phenylhydrazone, on oxidation with sodium dichromate and hot dilute sulphuric acid. Experiments on the condensation of this substance with ethyl oxalate in presence of alcoholic potassium ethoxide gave ambiguous results; no definite product was isolated. On the other hand, condensation with cotarnine in ethyl-alcoholic solution containing sodium ethoxide did not occur at all.

6-*Amino*iso*safrole.*—Nitro*iso*safrole (6 g.) mixed with tin (15 g.) and concentrated hydrochloric acid (35 c.c.) was heated on the steam-bath until reduction was complete. The amine was extracted by ether and isolated as its very sparingly soluble hydrochloride. The regenerated base crystallised from light petroleum in colourless needles, m. p. 68—69° (Found: C, 67·5; H, 6·2. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2%). It is readily soluble in organic solvents, and may be diazotised and thereafter coupled with β-naphthol to give a crimson azo-derivative. The *hydrochloride* separates from hot water in colourless needles. *Acetamido*iso*safrole* crystallises from alcohol in slender, colourless needles, m. p. 206°, and yields an oily dibromide which is converted into 5 : 6-methylenedioxy-2-methylindole by treatment with alcoholic potassium hydroxide (compare Foulds and Robinson, J., 1914, **105**, 1967).

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