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FOREWORD TO A COMMUNICATION SUBMITTED BY H-D. SCHARF, J. FLEISCHHAUER AND F. KORTE*

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KORTE, Klein and Schmid[1] and Korte, Schumacher, Klein and Daffertshofer[2] have re-examined the orientation of nitration in *p*-methoxyphenyl alkyl ethers, using present day resources of physical techniques for the analyses. The individual results differ somewhat from those obtained earlier[3] by the writer and his collaborators, but not by so much as to alter the order of the orientating effects or to change in any way the conclusions that can be drawn from them.

At several points in the memoirs cited, Korte and his colleagues have made claims of novelty for interpretations respecting the electronic effects of substituting CH_3 for H in the alkyloxy groups, which were advanced by the writer and his collaborators more than forty years earlier.[3] The nitration of mixed ethers of catechol and quinol was, in fact, studied with the definite object of throwing light on the manner in which a general electrical effect, through the chain, or more directly through space, can help to activate a system that operates by conjugative displacement of electrons. We chose these series because they were likely to meet our theoretical requirements and also because of the near quantitative yields of mono-nitro-derivatives that can be obtained in the catechol and quinol ethers series.

The general, or field, electrical effect was early recognised as originating in a separation of the charges and it was assumed to be propagated by electrostatic induction; hence, the term 'inductive effect'. Its importance in helping to explain the variation in the strengths of acids and bases was early and convincingly demonstrated. However, when Lucas[4] used the inductive effect in explanation of the results of his study of the hydrobromination of 2-pentene, it appeared that a detail had been overlooked. Preferable (for reasons not connected with this example) seemed the idea that the inductive effect of —CH_3 versus —H tends to promote the polarization of the ethenoid group in a favoured direction.

$\mathrm{H{-}CH_2{-}CH{\Leftarrow}CH{\leftarrow}CH_2{\leftarrow}CH_3}$

(General effect throughout)
(Lucas)

$\mathrm{H{-}CH_2{-}\overset{\frown}{CH{=}}CH{\leftarrow}CH_2{\leftarrow}CH_3}$

General effect favouring a particular direction of polarization.
(Robinson)

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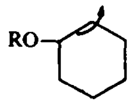
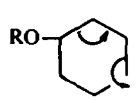
* *Tetrahedron* **26**, 2070 (1970).

In this example there is so little difference between the two ideas that progress of an attempt to show which is the nearer to the truth would certainly be slow, if possible at all. It was for this reason that a case was selected in which the inductive effect and conjugative process were clearly distinct.

The hetero-enoid conjugation was established when our theoretical basis was that of polarized partial valencies which were not the same as Thiele's, but were fractions of full bonds. The hetero-enoid conjugations were experimentally illustrated by work on the alkylation of enamines[5] and applied by analogy to the reaction of phenols, aromatic amines,[6] pyrrole and similar heterocycles. When the easy translation of the partial valency formulae into electronic valency expressions was made[7] the reactivity of aryl alkyl ethers was represented by the annexed symbols, which satisfy the demand that the numbers of associated electrons in the configuration of the C-atoms of the chain, must remain unchanged.

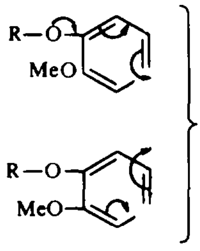


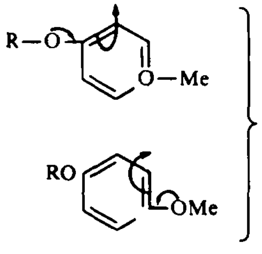
o-*activation*



p-*activation*

The reagent (HNO_3) is electron accepting, then termed "cationoid" and now, with no change of meaning, "electrophilic". We accordingly proposed to examine the effect of R as against that of Me in the systems:

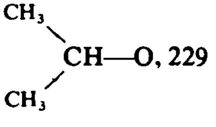
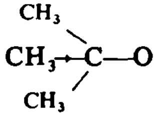


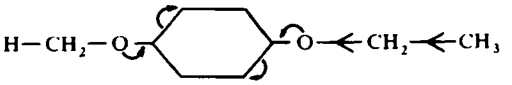


The bracketed pairs may operate simultaneously in any one molecule, but the two possible modes of conjugation are shown separately for clarity. Thus, the polarization by electron displacement (modern term—delocation) starts by the unshared electrons of O increasing their co-valency with nuclear carbon and the effect of R on O is not part of this conjugation, but by a general electrical effect facilitates (or hinders) it to a certain extent.

In the series of mixed catechol ethers the anticipated effect of the electron push of Me substituent in the RO group was observed, but on increasing the size of R a maximum was reached followed by a fall in the ratio: nitration *p*- to OR/nitration *p*- to OMe. Thus, taking the orientating value for OMe as 100, we found[8] $CH_3—CH_2—O$, 135; $CH_3—CH_2—CH_2—CH_2—O$, 128. The explanation offered was that in the catechol series a direct, or field, inductive effect across space will activate both oxygen atoms, that of OR and also that of OMe. This must reduce the disparity between their orientating powers. In the quinol series, however, any direct effect will work in the same direction as that operating through the chain. This reinforcement of the disparity was noted in all cases examined. As a result of this finding, work in the catechol series was discontinued.

Since the results in the quinol series showed a steady rise in orientating power of OR, as the length of the chain R was increased, J. C. Smith[9] examined the case of *p*-cetyloxyanisole and found for $n{-}C_{16}H_{33}O{-}$ the surprisingly high value 212 relative to MeO, 100.

Another study was undertaken in order to confirm the anticipated effect of closer proximity of methyl groups to the oxygen of OR.[10] The values $CH_3\rightarrow CH_2\rightarrow CH_2\rightarrow O$, 180 and $CH_3\rightarrow CH_2\rightarrow CH_2\rightarrow CH_2\rightarrow O$, 186 had already been estimated; Goldsworthy found for  $(CH_3)_2CH{-}O$, 229 and for  $CH_3\rightarrow C(CH_3)_2{-}O$, 328. Unfortunately, the nitro-derivatives in these cases did not crystallize well and recourse was taken to methods based on chemical degradation. In the first publication[11] a figure showing how the extra Me of the Et group (as compared with OMe) was printed and is here reproduced.



(At that time a plain ring implied a benzene ring). We did not trouble to write in the arrows showing inductive effects stemming from $CH_3{-}$ in every case as the theory was implicit and could not be misunderstood. It was described in very many lectures in various chemical schools and was emphasised in teaching over a span of 30 yrs. A relatively recent statement respecting the proximity effect may be cited.[12] The effects of R— benzyl and substituted benzyl were discussed from the same point of view, as also the results of a study of the nitration of acylphenetidines.[13] In several of these cases the effects of electron-attracting groups, especially NO_2, were shown to fit the general idea of an influence of inductive effects on the orientating power of OR.

The electron-push effect of the substituent CH_3 was early established by a number of different methods. For example, interpretation of the strengths of acids and bases, and the fact that the dipole moment of *p*-nitrotoluene is greater than that of nitrobenzene. As seen above, this direction of the inductive effect fitted in with our anticipations and, moreover, it was also required by the more general theory of orientation in aromatic substitution.

It was with surprise and some incredulity that the conclusions of some theoretical physical chemists were noted. These were to the effect that the C—H bond has a small dipole, $C\overset{\delta+\ \delta-}{-\!\!-}H$.* It was only between 1935 and 1940 that the present writer realised that this presents no difficulty. It is necessary to speak of the inductive effect of $-CH_3$, not in isolation, but as replacing —H. It must be that the hydrogen directly linked to the relevant C-atom exercises a stronger attraction on the electrons of the C—H bond than do three similar dipoles situated at one C atom remove. A similar result of position relative to an active centre was mentioned in the author's Faraday

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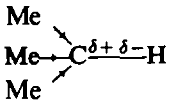
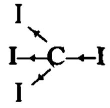
* This matter is fully discussed in an article by W. L. G. Gent (*Quarterly Reviews* II, No. 4, 383 (1948). I am grateful to Prof. C. A. Coulson for *inter alia* drawing my attention to this Review.

Lecture.[14] The ion $\bar{O}_3S$  CO_2H is a stronger acid than benzoic acid. This was attributed to the fact that S^{++} directly attached to the nucleus is more effective than the more distant 3 O^- so that SO_3^- is an electron attracting group. CH_3 is electron repelling only because it replaces H in C—H and therefore it is always necessary to say that CH_3 *replacing* C—H is relatively an electron-push group.

Much of the chemistry of the C—H bond becomes easier to understand in terms of the $\mathrm{C}\underset{\delta+\,\delta-}{\text{—}}\mathrm{H}$ hypothesis. Some striking results reported by Bickel and Hogeveen and their collaborators[15] are particularly relevant. In the reversible reaction:

$$RH + H^+ \rightleftarrows R^+ + H_2{}^{16}$$

it has been found that isobutane is especially reactive. It suffices to shake isobutane with aqueous $HSbF_6$ at the ordinary temperature. This is evidently due to the condition:

 which may be contrasted with 

producing a phase in which one I is virtually + and reacts with $O\bar{H}$ to form HOI. The relative ease with which (t)  $—\overset{|}{C}H—$ is oxidized by CrO_3, or takes up O_2 to form hydroperoxide, are other manifestations of $\overset{\delta+}{C}$——$\overset{\delta-}{H}$.

Finally, the inductive effect in carbon chains was always regarded as transmitted from C to C, in one sense, but with diminished values. We have found nothing that required subsidiary hypotheses, such as that of Baker and Nathan's 'hyperconjugation'.

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[1] F. Korte, W. Klein, and E. D. Schmid, *Tetrahedron* **58**, 93 (1966).

[2] F. Korte, H. Schumacher, W. Klein and G. Daffertshofer, *Ibid.* **24**, 5601 (1968).

[3] Refs. 8, 9, 11 and A. E. Oxford and R. Robinson, *J. Chem. Soc.* 383 (1962).

[4] A. J. Lucas and H. W. Moyse, *J. Am. Chem. Soc.* **47**, 1459 (1925).

[5] E. E. P. Hamilton and R. Robinson, *J. Chem. Soc.* **109**, 1029 (1916); R. Robinson, *Ibid.* 1037 (1916).

[6] E. E. P. Hamilton and R. Robinson, *loc. cit.* (1916); G. M. Robinson and R. Robinson, *J. Chem. Soc.* **111**, 958 (1917); Cf. Ref. 7.

[7] W.O. Kermack and R. Robinson, *J. Chem. Soc.* **121**, 427 (1922).

[8] J. Allen and R. Robinson, *Ibid.*, 376 (1926).

[9] J. C. Smith, *Ibid.*, 251 (1931).

[10] L. J. Goldsworthy, *Ibid.*, 1148 (1936).

[11] J. Allen, A. E. Oxford, R. Robinson and J. C. Smith, *Ibid.*, 407 (1926).

[12] R. Robinson, *J. Indian Chem. Soc.* **38**, 8, 149 (1961).

[13] R. C. Fawcett and R. Robinson, *J. Chem. Soc.* 2414 (1927).

[14] R. Robinson's Faraday Lecture *Ibid.*, 1288 (1949).

[15] A. F. Bickel, C. J. Gaasbeek, H. Hogeveen, J. M. Oelderik and J. C. Platteeuw, *Chem. Comm.* **13**, 634 (1967); H. Hogeveen and A. F. Bickel, *Ibid.* 635 (1967). Cf. also H. Hogeveen, J. Lukas and C. F. Roobeek, *Ibid: D*, **16**, 920 (1969) where a list of earlier papers is given.

[16] Cf. H. S. Bolch, H. Pines and J. Schmerling, *J. Am. Chem. Soc.* **68**, 153 (1946).