SECONDARY ISOTOPE EFFECTS ON PI-COMPLEX FORMATION

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An attempt has recently been made by one of us[1] to bring secondary isotope effects into the empirical framework of ordinary substituent effects. The formal justification for discussing such eminently vibrational phenomena in the "electronic" parlance of physical organic chemistry rests on the validity of averaging electronic properties of molecules or transition states over the occupied levels (in practice, invariably over the "zeroth" level) of the vibrational modes describing motion of the hydrogen atoms. These averages are necessarily different for protio- and deuterio-molecules, by virtue of their different average configurations and mean-square vibrational amplitudes, and it is to these differences that secondary isotope effects were related[2]. We will here take the validity of this justification for granted, and will therefore simply consider a CD_3 group, for example, to be a slightly but genuinely different substituent from an ordinary methyl group, the differences being ascribed to the factors usually considered when comparing different alkyl groups: induction, hyperconjugation, steric effects, *etc.*

This paper is concerned with the effect of deuteration in the aromatic nucleus and in a methyl group substituted on the aromatic ring:

(*a*) Deuteration in the ring leads, quite generally to an apparent increase in electron accession to the ring[1]. It is probable, but not relevant to the present discussion, that this behaviour is due both to the shorter average CD bond length and to the smaller amplitude of the out-of-plane motions of the deuterium atoms.

(*b*) The effect of methyl deuteration is less consistent. On the one hand, CD_3 does genuinely behave in its effect on numerous equilibria and rates as if it were effectively more electron-releasing than CH_3. This is sometimes referred to as the "inductive effect of deuterium". When, however, the deuterated methyl group is at a site from which hyperconjugation can be invoked, its apparent electron-releasing power often turns out to be considerably less than that of CH_3†. One of the early examples which led to the recognition that hyperconjugation is a factor in secondary isotope effects was the observation that deuteration in either of the methyl groups of methyl *p*-tolylcarbinyl chloride (I) decreases its acetolysis rate[3].

There are, however, a number of perplexing exceptions. For example, the stability of diphenyl *p*-tolylcarbonium ion (II) is *not* appreciably decreased

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† Here too, we will not consider further whether isotopic differences in mean bond lengths and angles or in mean-square amplitudes are dominant in determining this complex behaviour, or to what extent the effect of three deuterium atoms on one carbon atom must be regarded as co-operative rather than additive. These questions are discussed in detail elsewhere[1].

by p-methyl deuteration[4]; nor is the nitration of toluene retarded signifi-
cantly by deuteration or tritiation in the methyl group[5, 6].

Hyperconjugation has for some time been a controversial concept[7, 8].
Some of the firmest support for its being a factor in chemical reactivity
comes from solvolytic secondary isotope effects, in which the stereochemistry

(I)

(II)
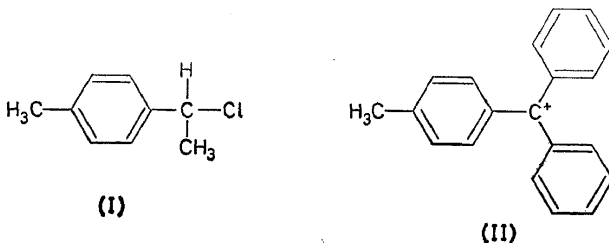
of the isotope effects is precisely that predicted by the hyperconjugaton
hypothesis[9, 10]. However, a consideration of all the various "hypercon-
jugative" secondary isotope effects: their relative magnitude and occasional
absence, the effect of solvent and leaving groups *etc.*, strongly suggests that
conventional ideas about "hyperconjugative electron release" need to under-
go some revision[1].

Two factors determine the effectiveness of hyperconjugation of a methyl
group with an unsaturated system, and these are oppositely affected by
deuteration:

(a) The $H_3 \equiv C$ overlap is increased by deuteration, with the consequence
that the electrons of the C—D bonds are less mobile, and less able to interact
with the adjacent conjugated system. This factor leads to destabilization
by deuterium not only of carbonium ions but also of radicals and other
conjugated systems.

(b) CD_3 is effectively more electropositive than CH_3, so that it more
effectively helps stabilize a *positively charged* electron-deficient system. This
is again equivalent to the "inductive" effect of deuterium, now however
being transmitted through the conjugated system.

The empirical evidence suggests, as do approximate theoretical calcula-
tions[11], that in a fully developed carbonium ion the two effects largely cancel.
Conversely, when charge development is only partial, as in the transition
state for solvolysis of a halide, the effect of overlap should predominate,
and the usual "hyperconjugative" isotope effect ($k_H > k_D$) is observed.

Secondary isotope effects on pi-complex equilibria offer an excellent
opportunity for testing these ideas. Aromatic hydrocarbons form pi-
complexes with a wide variety of electron acceptors. These range from
metallic cations, in which the interaction would classically be described
as "charge-induced dipole", through dipolar molecules like HCl (classically:
"dipole-induced dipole") to aromatic molecules like trinitrobenzene and
chloranil ("induced dipole-induced dipole").

ALKYLBENZENE-CHLORANIL COMPLEXES[12, 13]

Electron-deficient aromatic systems like chloranil, picric acid or trinitro-
benzene form well defined 1:1 complexes with aromatic hydrocarbons, in

which the rings lie parallel to one another, and there is strong overlap between the two *pi*-electron systems. Alkyl groups in the donor stabilize these complexes according to the Baker–Nathan order:

$$H < CH_3 > C_2H_5 > iso\text{-}C_3H_7 > t\text{-}C_4H_9$$

which ordinarily suggests hyperconjugation. One might well expect hyperconjugation to be important in this system, but the results could be equally well accommodated by postulating that steric interference to approach of the acceptor by the increasingly bulky alkyl group, opposes and eventually overcomes their increasing inductive effect.

The importance of hyperconjugation was demonstrated in this system, as it had been in solvolysis[9, 10], by the effect of deuterating the methyl group[13]. Toluene-α-d$_3$ and *m*-xylene-α-d$_3$ are subject to a similar reduction in stability of the chloranil complex:

$$\text{Toluene-d}_3: K_H/K_D = 1\cdot07_{\overline{1}}; \Delta\Delta F^\circ/3 = 13\cdot_{\overline{3}} \text{ cal}$$

$$\text{\textit{m}-Xylene-d}_3: K_H/K_D = 1\cdot08_{2}; \Delta\Delta F^\circ/3 = 15\cdot_{\overline{2}} \text{ cal}$$

The steric requirements of CH_3 and CD_3 are negligible in this system, and—if they were not—any difference would tend to *stabilize* the deuterated complex, as would the greater electropositivity of CD_3. There thus seems to be no simple alternative to calling in hyperconjugation as a significant factor in the formation of complexes of this sort.

According to the re-interpretation of "hyperconjugative" secondary isotope effects outlined above, this system is a favourable one for an effect in the observed direction, $(K_H > K_D)$. There is very strong overlap between the two *pi*-electron systems, but not much transfer of charge in the ground state. It is reasonable that the isotope effect on $H_3\equiv C$ overlap should predominate over that on electropositivity.

THE RATE OF PI-COMPLEX FORMATION IN NITRATION[14]

At the other end of the spectrum from the chloranil complexes just discussed, lie those with positively charged ions. We would expect a small positive ion to distort the electron cloud of the donor considerably, although the overlap of its vacant orbital with the *pi*-electron system is, on simple geometrical grounds, relatively small.

While no secondary isotope effect has been reported on *pi*-complex *equilibria* of this class, there is very strong indirect evidence of such an effect on the *rate* of formation of a complex between the nitronium ion (NO_2^+) and aromatic hydrocarbons in the path of nitration with nitronium salts[14].

Only by postulating the slow formation of a *pi*-complex, followed by a rapid, product-determining, competition among the available nuclear positions, were Olah, Kuhn and Flood[14] able to reconcile the marked intermolecular unselectivity $(k_{\text{Toluene}}/k_{\text{Benzene}} = 1\cdot7)$ with the intramolecular specificity $(ortho\text{:}meta\text{:}para = 23\text{:}1\text{:}11)$. Their scheme, to which it is difficult to take serious exception, can be written:

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$$(1)$$

Here k_1 is rate-determining, k_2 is larger than k_{-1} but still sufficiently activated to be product-determining, and k_{-2} is negligible relative to a very large and essentially irreversible k_3.

The isotope effects, determined by stepwise competition among deuterated and undeuterated benzenes and toluenes, are:

$$k_{C_6H_6}/k_{C_6D_6} = \cdot 87_0; \ \Delta\Delta F\ddagger = -83\cdot \text{ cal}$$

$$k_{C_7H_8}/k_{C_7D_8} = \cdot 82_6; \ \Delta\Delta F\ddagger = -113\cdot \text{ cal}$$

Unaccountably, the authors lose sight of their own mechanism when discussing the isotope effects, which they simply compare with isotope effects under more usual nitrating conditions, when k_2 is rate-determining. According to their mechanism, the isotope effect observed in a competition experiment is necessarily one on k_1, the rate of pi-complex formation. It follows that nuclear deuteration increases the rate of complex formation with benzene, and thus presumably must be enhancing its donor properties. In the absence of experiments with $CD_3C_6H_5$ or $CH_3C_6D_5$, we can only assess the relative effects of methyl and nuclear deuteration of toluene indirectly. If the effect of the latter is taken to be the same *per* deuterium atom as in benzene, we can assign respective values of $\Delta\Delta F_N\ddagger = -14\cdot_6$ and $\Delta\Delta F_M\ddagger = -13\cdot_8$ cal to each nuclear and methyl deuterium atom.

We thus see that methyl deuteration too increases the ease of formation of the pi-complex with NO_2^+, even though it destabilizes the complex with chloranil, in agreement with expectations.

HCl-ALKYLBENZENE COMPLEX[15, 16]

The inferences drawn from the isotope effect on nitration rate necessarily rest on presumptive evidence; if it could be shown that the same type of behaviour obtained in a system at equilibrium, our conclusions would be

lent considerably more weight. We therefore went on to look for secondary isotope effects on pi-complex equilibria between HCl and alkylbenzenes, a system which had been thoroughly investigated by Brown and Brady[15]:

$$HAr + HCl \underset{}{\overset{K_{Ar}}{\rightleftharpoons}} HAr \cdots HCl \qquad (2)$$

Although this is a complex of the "dipole-induced dipole" rather than "charge-induced dipole" type, one would expect it to behave much like the latter. The acceptor is the proton at the positive end of the HCl dipole, which would presumably cause local distortion of the electron cloud in which it is imbedded, but the partially vacant $1s$ orbital of which would overlap only slightly the very much larger pi-system of the donor†. The system is not encumbered by steric effects; alkyl substituents enhance donor properties in the normal inductive order:

$$H < CH_3 < C_2H_5 < \text{iso-}C_3H_7 < \text{t-}C_4H_9$$

The experimental procedure of Brown and Brady[15] had to be modified at the cost of a slight loss of absolute accuracy, in order to enable us to measure precisely the small anticipated isotope effects directly[16]. Our figures for benzene and toluene are shown along with those of the earlier investigators in *Table 1*. Making due allowance for the different solvents and a minor change in the way the association constant is defined, we find reasonable concordance in the absolute magnitude of the association constants and good agreement in their relative values.

Table 1. Association constants of HCl-hydrocarbon complexes at $-80°$

Hydrocarbon	$10^3 \times K_{Ar}$ (mm Hg^{-1}) (Methyl cyclohexane sol.) Ref. 16	$10^3 \times K_{diss.}{}^{-1}$ (mm Hg^{-1}) (n-heptane sol.) Ref. 15[a]
Benzene	$1·9_8$	$1·4_8$
Toluene	$2·7_8$	$2·1_5$
K_{Tol}/K_{Bz}	$1·4$	$1·5$

[a] The definition of K_{Ar} is not identical with that of the reciprocal of Brown and Brady's $K_{diss.}$ but is similar to i·.

Our differential method was based on measuring gasometrically the difference in the amount of undissolved HCl in equilibrium with identical solutions of the isotopic variants in methyl cyclohexane at the same HCl pressure.

The results, which are still provisional, are shown in *Table 2*. Six nuclear deuterium atoms are seen to increase the donor properties of benzene by some 5 per cent corresponding to a standard free energy increment per nuclear deuterium atom: $\Delta\Delta F_N° = -3·1$ cal.

† "Extent of overlap" is measured by the overlap integral between the appropriate orbitals of the donor and acceptor. It is small when they are grossly disparate in size, as they are here.

The data on the toluenes are fitted statistically to the equation:

$$\Delta\Delta F^\circ = \Delta n_N (\Delta\Delta F_N{}^\circ) + \Delta n_M (\Delta\Delta F_M{}^\circ) \tag{3}$$

where Δn_N and Δn_M are the differences in number of nuclear and methyl deuterium atoms respectively and $\Delta\Delta F_N{}^\circ$ and $\Delta\Delta F_M{}^\circ$ are the corresponding

Table 2. Secondary isotope effects on association of HCl-hydrocarbon complexes at -80° (Ref. 16)

Run no.	Isotopic pair (heavy-light)	$K_{Ar}{}^{light}/K_{Ar}{}^{heavy}$	
		Found†	Calc. with equation (3)
(a) Benzenes			
(1)	d_6–d_0	0·95$_7$	—
(2)	d_6–d_0	0·94$_8$	—
(b) Toluenes			
(1)	d_3–d_0	0·98$_8$	0·98$_0$
(2)	d_3–d_0	0·97$_3$	0·98$_0$
(3)	d_8–d_0	0·92$_0$	0·92$_8$
(4)	d_8–d_0	0·93$_5$	0·92$_8$

† The value quoted for each run is the average of three values determined at different HCl pressures.

isotope effects per deuterium atom on the free energy of complex formation. The "least squares" values obtained are:

$$\Delta\Delta F_N{}^\circ = -4\cdot\bar{3} \text{ cal}; \ \Delta\Delta F_M{}^\circ = -2\cdot\bar{5} \text{ cal}$$

Values of $\Delta\Delta F^\circ$ calculated with these figures are entered in the final column of Table 2. It can be seen that both nuclear and methyl deuteration increases complex stability. The effects are much smaller than on the nitration rates but are unquestionably real. The effect of nuclear and methyl deuteration of toluene is additive within experimental error ($\pm \sim 1$ per cent in k_H/k_D), and, pending further results with other isotopic pairs, the former seems to be somewhat larger than the latter. It is more doubtful whether the one calorie difference in $\Delta\Delta F_N{}^\circ/n$ between benzene and toluene is significant, since it rests on the K_{Tol}/K_{Bz} ratio which has not yet been determined differentially, and so is known with considerably less accuracy than the isotopic ratios.

CONCLUSIONS

We have thus qualitatively reproduced, in a system at equlibrium, Olah, Kuhn and Flood's[14] kinetic isotope effects, as required by our interpretation of them. All the results discussed in this paper are consistent with our interpretation of Olah et al.'s isotope effects in nitration, and with our re-formulation of the rôle of the hyperconjugation in electron-deficient systems, which resolves the apparent contradiction between the direction of secondary isotope effects on the formation of superficially similar pi-complexes with acceptors of different types. These would be very difficult to rationalize in the conventional interpretation of "hyperconjugative electron release",

or—if it is kept in mind that both the chloranil and HCl complexes were studied in the non-polar solvents cyclohexane and methylcyclohexane— by an invocation of "steric hindrance to solvation"[17].

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