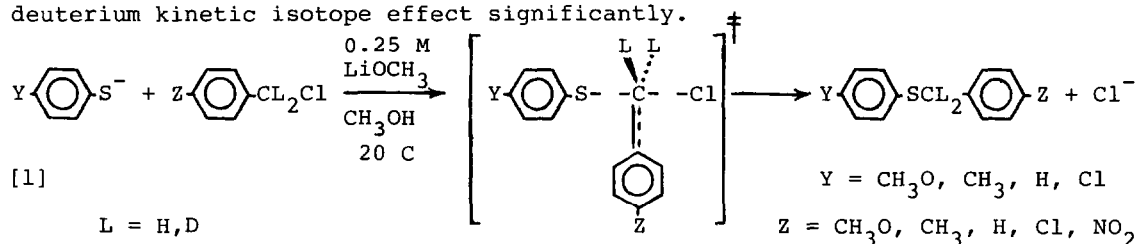


THE EFFECT OF CONJUGATION ON THE MAGNITUDE OF SECONDARY ALPHA DEUTERIUM  
 KINETIC ISOTOPE EFFECTS

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The unexpectedly small secondary alpha deuterium KIE in the 4-methoxybenzyl chloride-thiophenoxide ion reaction is attributed to the increased conjugation between the aryl group and the alpha carbon in the S<sub>N</sub>2 transition state.

Recently, the magnitudes of secondary alpha deuterium kinetic isotope effects (KIEs) have been used to shed light on the structure of S<sub>N</sub>2 transition states, i.e., to indicate the tightness of the transition state (1-3) and also to determine how substituents alter the transition state structure of closely related S<sub>N</sub>2 reactions (2, 4-6). The results from a recent study of the S<sub>N</sub>2 reactions between a series of 4-substituted thiophenoxide ions and 4-substituted benzyl chlorides in 0.25 M. lithium methoxide in methanol at 20°C<sup>1</sup>, equation 1, have shown that another factor can alter the magnitude of the secondary alpha deuterium kinetic isotope effect significantly.



The chlorine KIEs measured by Grimsrud (8), the secondary alpha deuterium KIEs and the Hammett ρ values determined by reacting four different 4-substituted thiophenoxide ions with each 4-substituted benzyl chloride, i.e., the ρ value associated with changing the substituent on the nucleophile, equation 1, are given in Table 1. The chlorine KIEs are essentially constant for this series of S<sub>N</sub>2 reactions indicating that the C<sub>α</sub>-Cl bond rupture is equally advanced (the C<sub>α</sub>-Cl transition state bond length is virtually identical) in all of these reactions.

Westaway and Ali (4) have shown that the magnitude of secondary alpha deuterium KIEs is related to the nucleophile-leaving group (S---Cl) distance in S<sub>N</sub>2 transition states and since the C<sub>α</sub>--Cl transition state bond lengths are the same in all the reactions, the magnitude of these isotope effects allows the S--C<sub>α</sub> distance in the transition state to be deduced. When the temperature dependence of the alpha deuterium KIE for the 4-methylbenzyl chloride reaction is considered, the isotope effects for the 4-methoxy and

1. The reactions involving 4-methoxybenzyl chloride were carried out at 0°C with a five fold excess of thiophenoxide ion. This was done in order to eliminate the solvolysis reaction that accompanied the S<sub>N</sub>2 reaction at 20°C.

4-methylbenzyl chlorides are identical. All of the other KIEs increase when a more electron donating substituent is added to the benzene ring on the alpha carbon. Thus, the secondary alpha deuterium KIEs indicate that with the exception of the 4-methoxybenzyl chloride-thiophenoxide ion transition state, the S--C $\alpha$  transition state bond lengthens as a more electron donating substituent is added to the substrate.

TABLE 1 Chlorine and secondary alpha deuterium KIEs and Hammett  $\rho$  values for the S $_N$ 2 reactions of 4-substituted benzyl chlorides and 4-substituted thiophenoxide ions in 0.250 M lithium methoxide in methanol at 20°C.

Z	k <sup>35</sup> /k <sup>37</sup> <sup>a</sup>	(k <sub>H</sub> /k <sub>D</sub> ) $\alpha$ <sup>c</sup>	$\rho$
CH <sub>3</sub> O	1.01012	1.096 <sup>d</sup> 1.126 <sup>e</sup> $\pm$ 0.023 <sup>f</sup>	-0.283 <sup>e</sup> $\pm$ 0.026 <sup>b</sup>
CH <sub>3</sub>	1.00963	1.096 $\pm$ 0.0015 1.125 <sup>e</sup> $\pm$ 0.009	-0.434 $\pm$ 0.026
H	1.00976	1.056 $\pm$ 0.019	-0.500 $\pm$ 0.015
Cl	1.01013	1.046 $\pm$ 0.017	-0.720 $\pm$ 0.018
NO <sub>2</sub>	1.00950	1.039 $\pm$ 0.008	-0.961 $\pm$ 0.002
			-1.035 <sup>e</sup> $\pm$ 0.002
average 1.00983 $\pm$ 0.00029 <sup>b</sup>			

<sup>a</sup> measured by Grimsrud(8) under identical conditions, <sup>b</sup> standard deviation, <sup>c</sup> determined from the rate constants for the undeuterated and deuterated substrates, <sup>d</sup> estimated at 20°C from the temperature dependence of the 4-methylbenzyl chloride KIE, <sup>e</sup> measured at 0°C, <sup>f</sup> the error is

$$1/k_D \left[ (\Delta k_H)^2 + (k_H/k_D)^2 \cdot (\Delta k_D)^2 \right]^{1/2} \text{ where the } \Delta k_H \text{ and } \Delta k_D \text{ are the standard deviation on the } k_H \text{ and } k_D \text{ respectively.}$$

The different behaviour for the 4-methoxybenzyl chloride reaction, i.e., where adding a more electron donating substituent did not affect the length of the S--C $\alpha$  bond, seemed highly unlikely in the light of the substituent effect on the S--C $\alpha$  bond in the other substrates. As a result, the Hammett  $\rho$  values obtained when four different 4-substituted thiophenoxide ions were reacted with each benzyl chloride, were measured in order to confirm that the S--C $\alpha$  transition state bonds were equal in the 4-methyl and 4-methoxybenzyl chloride reactions. The smaller, less negative,  $\rho$  value found for the 4-methoxybenzyl chloride reaction<sup>2</sup>, Table 1, indicates that the change in charge on the sulfur atom on going from the initial to the transition state is significantly less in the 4-methoxybenzyl chloride reaction than it is in the 4-methylbenzyl chloride reaction. Because the change in charge on the sulfur atom is inversely related to the amount of S--C $\alpha$  bond formation in the transition state(4,5), there is less S--C $\alpha$  bond formation in the 4-methoxybenzyl chloride-thiophenoxide ion transition state. In fact, the  $\rho$  values indicate that the S--C $\alpha$  transition state bonds lengthen in the complete series as a more electron donating substituent is added to the benzene ring on the alpha carbon.

Because the nucleophile-alpha carbon (S--C $\alpha$ ) transition state bond lengthens as a more electron donating substituent is added to the benzene ring 2. The temperature dependence of the  $\rho$  value is small. The  $\rho$  value at 20°C was estimated from the temperature dependence of the  $\rho$  value for the 4-nitrobenzyl chloride reaction, to be -0.26.

at the alpha carbon, the magnitude of the secondary alpha deuterium KIE is much smaller than expected for the looser transition state of the 4-methoxybenzyl chloride-thiophenoxide ion reaction, i.e., a larger alpha deuterium KIE is expected for the looser transition state(1-6), figure 1.

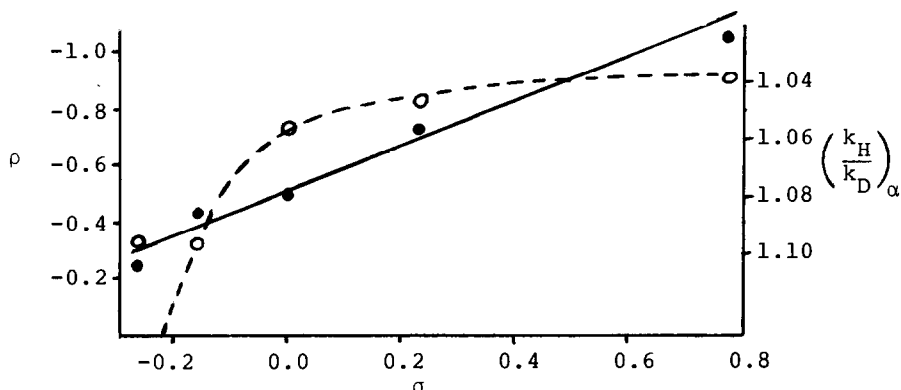


Figure 1. Hammett  $\rho$  values obtained by changing the nucleophile (solid circles) and alpha deuterium KIEs (open circles) versus the  $\sigma$  value for the 4-substituent on the benzyl chloride.

We believe that the unexpectedly small alpha deuterium KIE is the result of the increased conjugation that exists between the benzene ring and the alpha carbon in the 4-methoxybenzyl chloride-thiophenoxide ion transition state, i.e., the  $\text{CH}_3\text{O}$  substituent has a larger electron donating resonance effect than the  $\text{CH}_3$  group and the excess electron density in the benzene ring will result in greater conjugation with the alpha carbon. In fact, it is believed that the  $\text{C}_\alpha\text{---Ar}$  conjugation varies inversely with the  $\text{S---C}_\alpha$  bond length in these transition states(5). The importance of resonance between the benzene ring and the alpha carbon in determining the structure of these transition states was confirmed when the  $\rho^r$  value which represents the resonance interaction with the alpha carbon in the modified Yukawa-Tsuno equation(9), was found to be 1.78 times the  $\rho$  value representing the polar effect of the substituent, i.e.,  $\rho^r/\rho = 1.78/0.94 = 1.78(5)$  for the reactions between thiophenoxide ion and five, 4-substituted benzyl chlorides, equation 1.

The strong influence of conjugation on the magnitude of these isotope effects can be shown using the equation for the secondary alpha deuterium KIEs  $k_H/k_D = \exp\left[\frac{1}{2}\left(\sum \Delta u_i^{3n-6} - \sum \Delta u_i^{3n-7} \right)\right]$  where  $1/2\Delta u_i = 1/2(\Delta u_{iH} - \Delta u_{iD})$  is the zero-point energy difference between the  $\text{C}_\alpha\text{-H}$  and  $\text{C}_\alpha\text{-D}$  vibrations in the ground state and  $\Delta u_i$  is the corresponding difference in the transition state(10). Previous work has shown that the  $\text{C}_\alpha\text{-H}$  bending force constants depend on the hybridization and the total bond order to  $\text{C}_\alpha$  (11). Thus, increased conjugation (bond order) in the aryl group-alpha carbon bond will increase the bending force constants of the  $\text{C}_\alpha\text{-H(D)}$  bonds for a particular  $\text{S---C}_\alpha$  and  $\text{C}_\alpha\text{-Cl}$  transition state bond length (order). This increases the magnitude of the  $\sum \Delta u_i^{3n-7}$  term and reduces the magnitude of the KIE to the observed value.

Brubaker's calculations of the KIEs in the  $S_N2$  reaction between benzyl chloride and an alkoxide ion(11) also indicate that increased conjugation reduces the magnitude of alpha deuterium KIEs significantly. Increasing the conjugation to the alpha carbon in a loose transition state where the sum of the  $C_\alpha-Cl$  and  $C_\alpha-O$  transition state bond orders ( $n_{C-Cl}$  and  $n_{C-O}$ , respectively) equals 0.2, reduces the KIE from 1.50 to 1.10. The same increase in conjugation in a tight transition state ( $n_{C-Cl} + n_{C-O} = 0.8$ ) only reduces the KIE from 0.89 to 0.77. Thus the maximum effect is observed in loose  $S_N2$  transition states.

Although increased conjugation obviously reduces the magnitude of the change in the KIEs when a more electron donating substituent is present and the transition state is looser, the greatest effect should be observed in the reaction with the loosest transition state. Thus, it is only in the reaction where the substituent is changed from methyl to methoxy that the magnitude of the KIE is decreased enough by the increase in conjugation to overcome the increase in the KIE which should be observed because the  $S-C_\alpha$  bond is longer in the 4-methoxybenzyl chloride-thiophenoxide ion transition state.

In conclusion, the unexpectedly small alpha deuterium KIE observed in the 4-methoxybenzyl chloride-thiophenoxide ion  $S_N2$  reaction is attributed to an increase in conjugation between the aryl group and the alpha carbon. It is important to realize that an increase in conjugation can reduce the magnitude of secondary alpha deuterium KIEs because this effect can mask changes in transition state structure. Obviously, care must be taken in using the magnitudes of these KIEs to determine transition state structure in reactions where conjugation with the alpha carbon is possible. These effects will be of more concern in loose transition states than in tight transition states.

#### References:

1. I. Mihel, J.O. Knipe, J.K. Coward and R.L. Schowen, *J. Amer. Chem. Soc.*, 101, 4349 (1979).
2. C.H. Gray, J.K. Coward, K.B. Schowen and R.L. Schowen, *J. Amer. Chem. Soc.*, 101, 4351, (1979).
3. J.M. Harris, S.G. Shafer, J.R. Moffatt and A.R. Becker, *J. Amer. Chem. Soc.*, 101, 3295 (1979).
4. K.C. Westaway and S.F. Ali, *Can. J. Chem.*, 57, 1354 (1979).
5. K.C. Westaway and Z. Waszczylo, submitted, *Can. J. Chem.*
6. V.P. Vitullo, J. Grabowski and S. Sriharan, *J. Amer. Chem. Soc.*, 102, 6463 (1980).
7. B.L. Knier and W.P. Jencks, *J. Amer. Chem. Soc.*, 102, 6789 (1980).
8. E.P. Grimsrud, Ph.D. Thesis, University of Wisconsin, Madison, WI, 1971.
9. P.R. Young and W.P. Jencks, *J. Amer. Chem. Soc.*, 101, 3288 (1979).
10. A.Halevi, *Prog. Phys. Org. Chem.*, Vol. 1, Interscience, J. Wiley and Sons, New York, 1963, p. 131.
11. G.W. Burton, L.B. Sims, J.C. Wilson and A. Fry, *J. Amer. Chem. Soc.*, 99 3371 (1977).
12. D.M. Brubaker, Ph.D. Thesis, University of Arkansas, Fayetteville, AR, 1978.