Heteroatom Chemistry
Volume 13, Number 5, 2002

Heteroatoms and Substituent Effects: The Importance of Heteroatom Hyperconjugation

James F. King, Manqing Li, Allan Z. Cheng, and Vinod Dave

Department of Chemistry, The University of Western Ontario, London, Ontario, Canada N6A 5B7

Received 22 June 2001; revised 30 March 2002

ABSTRACT: *We have found that the specific rate of α-sulfonyl carbanion formation in a β-substituted sulfone shows a sizable dependence on the* $H{-}C_{\alpha}{-}C_{\beta}{-}X$ *torsion angle. Defining* $k_N = (k_{exch})_X/(k_{exch})_{model}$ *(where the model has* $X = H$ *or an alkyl group) we observed for a collection of β-alkoxy sulfones* ($X = OR$) *acceptable agreement with the expression* $\log k_N = a + b\cos^2\theta$ *(where* $a = 1.70$ *and* $b = 2.62$*). Extension to other β-substituents* ($X = RS$, R_2N, *and* R_3N^+) *yields the same pattern, with the last showing very large dependence of* k_N *on the torsion angle* ($b = 6.3$). *These observations are ascribed to the presence (in addition to the inductive and field effects) of negative hyperconjugation responsible for accelerations of 1000-fold and more, deriving from donation of the incipient negative charge on carbon into the* σ^*_{C-X} *orbital in the transition state. These observations reflect, and at the same time underline, the importance of the low-lying antibonding orbitals present in heteroatomic molecules.* Heteroatom Chem 13:397–405, 2002; DOI 10.1002/hc.10067

INTRODUCTION

How does a change in one part of the structure of a molecule affect a reaction elsewhere in the molecule? This is one of the most basic questions of chemical reactivity, especially in organic chemistry in which the molecules are commonly large and stable enough that a wide range of substituent groups may be present leading to a wide variation in the course or ease of reaction. The question may be asked within two contexts: (a) the simple general query as to how a particular change in another structure will influence a proposed reaction, and (b) a more specific question forming part of a mechanistic study of quantitative effects in a carefully controlled system; in the latter instance an alteration is made at a point in the molecule sufficiently removed from the reaction center that it will alter the ease but not the pathway of the reaction under investigation. Both of the above questions are commonplace enough to experimental chemists, and it has been the view of physical organic chemists over much of the recent century that a precisely formulated substituent effect question is one of the most fruitful sources of information about reaction mechanisms available to the inquiring practitioner.

In the picture presented in current textbooks and monographs [1], substituent effects fall into two broad classes: (a) steric and (b) electronic. Steric effects comprise nonbonding interactions along with effects arising from distortion from minimal energy forms of bond angles, bond lengths, and torsion angles; these are serviceably dealt with by molecular mechanics calculations. Electronic effects, as commonly presented, consist of (i) conjugation (alias resonance or mesomerism) and (ii) the polar effect, itself regarded as made up of the inductive effect (in which the effect is propagated via bond polarization) and the field effect (the interaction of charges through space as described by Coulomb's law). Other factors sometimes invoked are polarizability and hyperconjugation, though these are called upon by

---

Correspondence to: James F. King; e-mail; scijfk@uwo.ca.
Contract grant sponsor: NSERC, Canada.

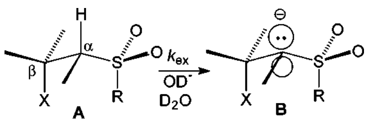
most writers on an ad hoc rather than systematic fashion. It is our contention that it would be fruitful for practising organic chemists to regard hyperconjugation as one of the major electronic effects, comparable to, or even more important than the inductive or field effects. We have reached this conclusion by studying a particular reaction—the base promoted formation of α-sulfonyl carbanions in an aqueous medium—with an eye to discerning if the effects predicted by theory for the intervention of hyperconjugation are in evidence or not. In our view the results are in full accord with the need to invoke negative hyperconjugation.

The initial impetus to examine this reaction arose from a paper by Thomas and Stirling [2] reporting the influence of substituents on the hydrogen isotope exchange reaction shown in Eq. (1):

$$\mathrm{PhSO_2CHTCH_2X} \xrightarrow{\mathrm{EtO^-}} \mathrm{PhSO_2\bar{C}HCH_2X} \xrightarrow{\mathrm{EtOH}} \mathrm{PhSO_2CH_2CH_2X} \qquad (1)$$

They found a good correlation with the Taft substituent constant (σ^*) in accord with the expression $\log(k_X/k_H) = 4.89\sigma^*$. The remarkable dependence of the rate on the substituent implied by this equation is readily illustrated by the result that $PhSO_2CH_2CH_2OPh$ reacts 5.3×10^4 times faster than $PhSO_2CH_2CH_2CH_3$. It was our view that any attempt to account for this substituent effect by considering only the conventional inductive and field effects would not suffice and that another effect, namely negative hyperconjugation [3] (alias the generalized anomeric effect [4]), was sufficiently likely that the matter should be put to the appropriate test.

The nature of the appropriate test becomes evident on examining the α-sulfonyl carbanion forming process. It had been shown by experimental and theoretical investigations [5] that removal of a proton from a sulfone to form the carbanion is a process with a very strong preference for having the C—SO$_2$—R array as shown in Eq. (2):



(2)

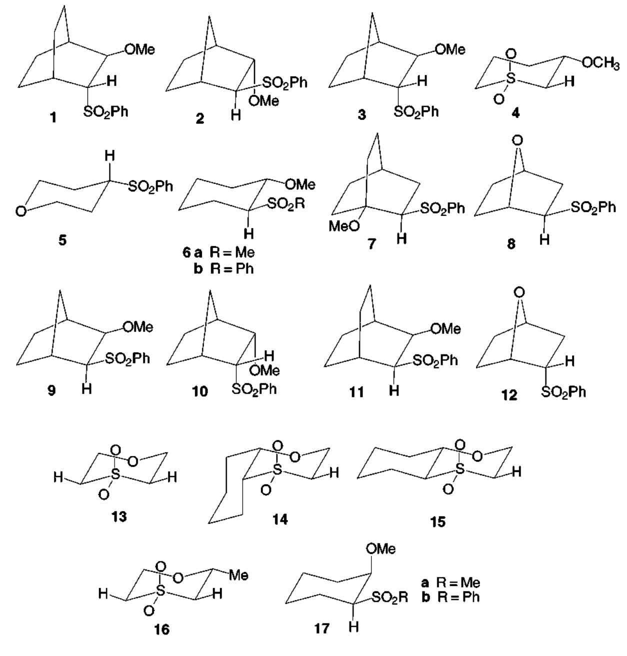
It was suggested by Wolfe et al. [6] that the preference for the carbanion conformation shown in **B** could be ascribed, at least in part, to a particular stabilization arising from the donation of the electron pair of the carbanion into $\sigma^*_{C\text{–}S}$, the antibonding C—S orbital. It is evident that a β-substituent X, if (a) placed in a position as shown in **A** and **B** and (b) having a sufficiently low energy antibonding orbital $\sigma^*_{C\text{–}X}$ would be perfectly set up to stabilize the free electron pair in **B** by negative hyperconjugation, i.e., by donation into the $\sigma^*_{C\text{–}X}$ orbital in exactly the same manner as that postulated for the stabilization by donation into the $\sigma^*_{C\text{–}S}$ orbital. By the same token attack of **A** by base should lead to an incipient carbanion stabilized in precisely the same way as **B**. Whenever this stabilization is possible, the result will be a substantial acceleration of carbanion formation by negative hyperconjugation. The $n \rightarrow \sigma^*$ interaction proposed for the effect of the substituent X on the stability of **B** (and by extension to the transition state leading to **B**) is π-type overlap. Such overlap has clear geometrical requirements, being maximal when the main axes of the interacting orbitals are at 0 or 180° angles with respect to each other and minimal when at 90°; a $\cos^2\theta$ (or, equivalently, $\cos 2\theta$) relation describes this interaction in simple form. The obvious test of this hypothesis was to prepare a set of sulfones with a β-substituent making different torsion angles with respect to the hydrogen to be removed by base, and to find if the rate constants for these reactions correlated with the torsion angles.

β-*ALKOXY SUBSTITUENTS*

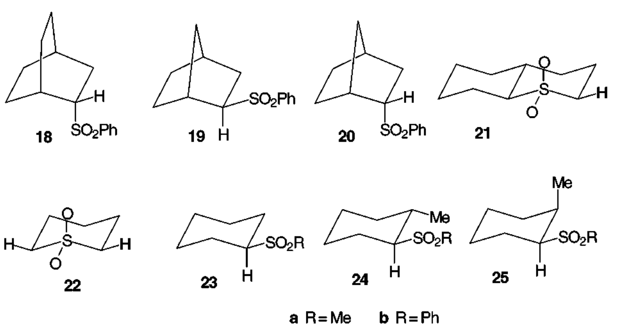
Materials, Rate Constants, and Angle Dependent k_N Values

Our first substituent was the alkoxy group [7,8]. The full array of β-alkoxy sulfones along with the appropriate unsubstituted analogues lacking the alkoxy group ("model" compounds) are shown as structures **1–25**.

ALKOXY SULFONES



MODEL COMPOUNDS

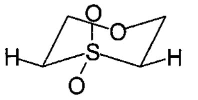
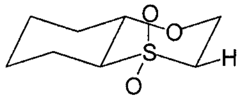
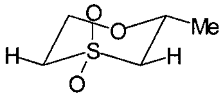
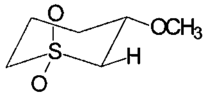


The method is perhaps most easily illustrated by the examples in Table 1 [7]. It is evident on comparing the rate constants for substrates **13, 15**, and **16** that a torsion angle of close to 180° leads to a reaction nearly 100 times faster than that of an analogous species **4** with a torsion angle of roughly 60°. This observation was sufficiently encouraging and we proceeded with the daunting task of synthesizing the rest of the sulfones in this array (**1–25**) and determining their H–D exchange rate constants. To avoid confusion from effects deriving from the presence of different ring structures in the set of β-alkoxysulfones (**1–17**), we chose to determine k_N, as defined in Eq. (3), where $(k_{exch})_{OR}$ is the second-order rate constant for H–D exchange for the β-alkoxysulfone and $(k_{exch})_{model}$ is the rate constant under the same conditions for a model compound in which the alkoxy group is replaced by either a hydrogen atom or a carbon substituent (CH_3— or —CH_2—, as appropriate).

$$k_N = (k_{exch})_{OR}/(k_{exch})_{model} \qquad (3)$$

In this way we hoped to be able to see the effect of replacing the β-hydrogen (or carbon) by the alkoxy group with all other factors cancelling out. A plot of log k_N vs the torsion angle θ for 19 different H–D exchange reactions of β-alkoxysulfones is shown in Fig. 1. In this plot the experimental points believed to be least perturbed by extraneous factors (solid circles or solid diamonds) are grouped around θ values of roughly 10°, 60°, and 175° and suffice in themselves to establish the point that k_N depends on θ. Of the remaining points five (**8–12**) are believed to reflect two effects: (a) a steric acceleration deriving from a strong nonbonding eclipsing interaction between

TABLE 1 First Studies of the Variation with Different H—C—C—O Torsion Angles of the Rates of Carbanion Formation from *β*-Alkoxysulfones

Sulfone[a]		θ (°)[b]	k_{exch} (M^{-1} s^{-1})[c]	log k_N[d]
13		172.9	4.30×10^{-2e}	4.55
15		173.5	3.2×10^{-2}	4.43
16		173.7 (C-5 H_e) 174.0 (C-3 H_e)	2.3×10^{-2} 1.6×10^{-2}	4.28 4.12
4		59.3	4.5×10^{-4}	2.57

[a] The ^{1}H NMR spectra of **15** and **21** before and during exchange showed that the equatorial H's (shown) underwent exchange more than 100 times faster than the axial hydrogen atoms on the same carbon, as expected from the earlier work summarized in the text. It should also be noted that in **13** (and in the alternative model **22**) only half of the hydrogens ultimately to be exchanged are in the equatorial conformation at any time and that their rate constants must be multiplied by 2 for comparison with the rate constants measured for **15, 16**, and **4**.

[b] H—C—C—O torsion angle as estimated by PCModel.

[c] Rate constants for the exchange of the equatorial hydrogen(s) shown in D_2O at 20°C as determined by ^{1}H NMR. The equatorial hydrogen signals were clearly distinguishable and assignable in the spectra of **4, 15, 16**, and **21**.

[d] $k_N = (k_{exch})_{OR}/(k_{exch})_{model}$; in the present instances $(k_{exch})_{OR}$ is the rate constant given in column 3 and $(k_{exch})_{model}$ is the rate constant (1.2×10^{-6} M^{-1} s^{-1}) for the exchange of the analogous equatorial hydrogen atom in *trans*-1-thiadecalin 1,1-dioxide (**21**) under the same conditions.

[e] Experimental rate constant multiplied by the statistical factor 2; see first footnote.

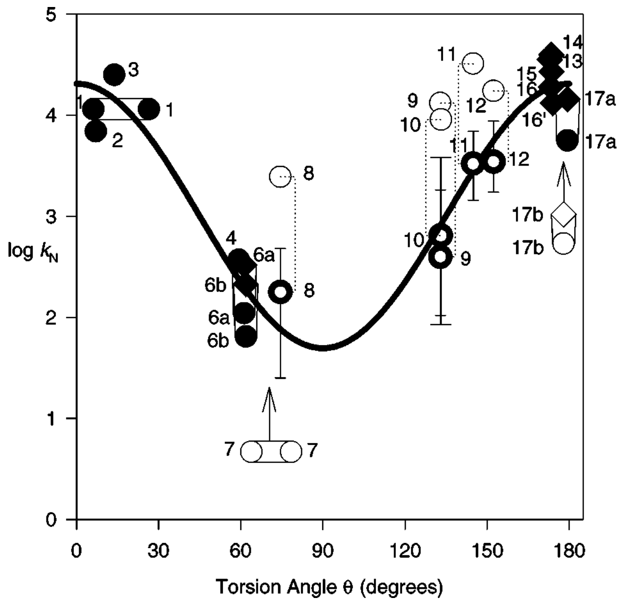


FIGURE 1 Plot of log k_N vs the torsion angle (θ) for the β-alkoxysulfones. Circles (filled or open) refer to k_N values based on a hydrogen model (e.g., **18–20, 23**), and the diamonds to those from a carbon model (**21, 24, 25**). Filled circles and filled black diamonds show the effect of the alkoxy substituent without requiring any correction for steric or other effects. The heavily outlined circles (bull's-eyes) are values corrected for steric and γ effects. Note that points for **1** and **7** are each yoked horizontally, reflecting discrepancies between the estimated (PCModel) and X-ray crystallographic torsion angles. Compounds **6a, 6b, 17a**, and **17b** are shown with vertically yoked points (circles and diamonds, from hydrogen and carbon models, respectively). The curve corresponds to log $k_N = 1.70 + 2.62\cos^2\theta$, obtained from a nonlinear least squares fit. Further details are given in Ref. [8].

the RO— and PhSO$_2$— groups (in **9–12**) and (b) the additional accelerating influence of the alkoxy group in the γ (as well as the β) orientation (in **8** and **12**). A roughly quantitative estimate of these effects made it possible to correct these log k_N values giving the points shown as heavily outlined circles (bull's eyes) in Fig. 1; further details on these and other points are given in Ref. [8].

Ths solid line shown in Fig. 1 corresponds to Eq. (4) where $a = 1.70 \pm 0.17$ and $b = 2.62 \pm 0.20$ was obtained from a weighted nonlinear least squares treatment of the solid circles and solid diamonds.

$$\log k_N = a + b\cos^2\theta \qquad (4)$$

Because of the errors in the bull's eyes introduced by the correction process, inclusion of these points in the least squares analysis has no effect on the parameters given.

Torsion Angle Dependence and Hyperconjugation

We take the results summarized in Fig. 1 as evidence for a torsion-angle dependent variation of the electronic effect of the β-alkoxy substituent in α-sulfonyl carbanion formation, and we interpret the observed variation of log k_N with θ as due to the variation of the magnitude of the negative hyperconjugation of the incipient carbanion with the alkoxy group with variation in θ. Specifically at $\theta \approx 180^\circ$ the hyperconjugative influence is maximal and at 60° (and 120°) the effect is much reduced, presumably diminishing to zero at 90° in the event that unperturbed examples with that torsion angle could be studied. Interestingly, the influence of the substituent is also very strong when $\theta \approx 0^\circ$, as one might expect from the simplest picture of π-overlap of the incipient carbanion with the $\sigma^*_{\text{C–OR}}$ orbital. The substituent effect of a β-alkoxy group at 90° is reasonably assigned to the sum of the inductive and field effects (only), with the effects at 0° and 180° representing the sum of all three effects; at 0° and 180° hyperconjugation is clearly the major effect, distinctly greater than the sum of the other two.

Inductive and Field Effects

The angle-independence term, a in Eq. (4), merits discussion in terms of the relative roles of the inductive and field effects. The inductive effect is defined in terms of a successive polarization of the sigma bonds and depends on the number of intervening bonds but not their orientation, i.e., the inductive effect is completely independent of θ. The field effect, however, derives from the interaction of charged bodies in space according to Coulomb's law, which describes the energy of the interaction as proportional to the reciprocal of the distance between the charges, hence leading to variation of the field effect with both the number and the orientation of the intervening bonds. We have examined the present example of a partial negative charge interacting with the dipole of a C—O bond in the light of the Kirkwood–Westheimer [9] treatment for the interaction of charges with dipolar substituents. Our calculations [10a] indicated that one might expect a small variation corresponding to a sigmoid curve with (a) a minimal value at low values of θ, (b) a fairly sharp increase in the range of 60–120°, and (c) an asymptotic approach to a maximal value at $\theta = 180^\circ$. The magnitude of the maximal effect depends on the choice of the "effective dielectric constant," but it seems likely that an effect on k_N as high as a factor of 10 might be possible. Such a variation of field effect is clearly quite different from that indicated by

Fig. 1, i.e., neither the field nor the inductive effects can account for the observed $\cos^2\theta$ dependence. The intervention of a small field effect, however, is consistent with the results shown in Fig. 1. With such a picture the major influence is the torsion angle dependent negative hyperconjugation with minor effects from both the angle independent inductive effect and a weak sigmoidal field effect (increasing as θ varies from 0 to 180° for uncharged substituents) following the Kirkwood–Westheimer model.

It is important to recognize that the terms hyperconjugation and polar effects, like all substituent effects as commonly defined, reflect the difference in the influence of the substituent from that of the substituent in the model, i.e., the hydrogen atom or carbon grouping. In other words the hyperconjugative effect of an alkoxy group with $\theta = 180°$ leading to an enhancement in k_N of 400 times, represents not the effect of the OR group alone, but rather the extent by which the hyperconjugative effect of the β-alkoxy group exceeds that of the hydrogen or carbon substituent in the same position [11].

Angle Dependence of σ^*, a New Parameter σ^*_θ

One way of treating the observation of a torsion angle dependent substituent effect is to propose a torsion angle dependent version of the Taft substituent constant, σ^*, which we may symbolize as σ^*_θ, and which may be derived as follows. Noting that the rate of the H–D exchange in $PhSO_2CH_2CH_2OMe$ vs that of $PhSO_2CH_2CH_3$ in our most generally used system (D_2O–dioxane-d_8, 25°C) was the same (1.2×10^3) as that found by Thomas and Stirling [2] in their experiments (in EtOH, 25°C) which had led to the expression $\log k_X/k_H = 4.89\sigma^*$, we feel justified in concluding that $\log k_N \approx 4.9\sigma^*_\theta$ is a reasonably close approximation. Combining this with Eq. (4) ($\log k_N = 1.70 + 2.62\cos^2\theta$), we write Eq. (5), where $(\sigma^*_\theta)_{OR}$ is the Taft substituent constant for the alkoxy group for the specific torsion angle, θ.

$$(\sigma^*_\theta)_{OR} \approx 0.35 + 0.53\cos^2\theta \qquad (5)$$

This yields the following $(\sigma^*_\theta)_{OR}$ values: $(\sigma^*_0)_{OR} = (\sigma^*_{180})_{OR} = 0.88$, $(\sigma^*_{60})_{OR} = 0.48$, and $(\sigma^*_{90})_{OR} = 0.35$.

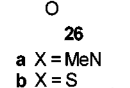
One may note that the maximal value of $(\sigma^*_\theta)_{OR}$ (0.88) is distinctly larger than the range of values (0.51–0.76) usually given for the methoxy group [12]. This is readily accounted for in terms of the array of conformations that can be expected for a conformationally mobile substrate (such as $PhSO_2CH_2CH_2OMe$); some of the conformations are unreactive, one (probably not more) maximally reactive (with the conformation as in **A**), and some less reactive, with the overall reaction reflecting the weighted average as prescribed by Winstein–Holness kinetics. This picture may well account, at least in part, for the considerable variation in the reported σ^* values (cf. the range for OMe above) with variation in σ^* arising simply because of differing conformational equilibria in the reacting systems.

The present idea may be usefully applied to the long-standing question of the mechanisms of elimination reactions in some β-substituted cyclohexyl aryl sulfones studied extensively in the 1950s and 1960s by Pearson, Bordwell, Hine, and Goering and coworkers, and terminated somewhat inconclusively in the 1970s. As we have shown elsewhere [8], the concept of the variation of substituent effect with torsion angle establishes the *E*1cB mechanism without recourse to further hypotheses.

OTHER SUBSTITUENTS—GENERALITY

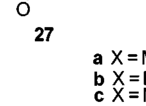
The above experiments led us to the conclusion that negative hyperconjugation is important with at least one substituent (the alkoxy group) in at least one reaction (α-H–D exchange in sulfones). This raised the obvious question of other substituents and other reactions. The finding of Thomas and Stirling [2] that the isotopic exchange process in Eq. (1) showed a good correlation with the Taft σ^* values for a wide array of substituents, indicates that the alkoxy substituent is not behaving exceptionally in this reaction. This in turn would suggest that other substituents in this correlation might also be expected to have hyperconjugative components in their substituent effects and to display them in appropriate H–D exchange reactions.

We have therefore synthesized the nine β-substituted sulfones shown by structures **26–28**; these correspond to approximate θ values of, respectively, 180°, 60°, and 0°; compounds **20** and **21** serve as the models. Our results [10b,10c,13, A. Z. Cheng, V. Dave, unpublished work] are summarized by Fig. 2, and clearly establish the generality of the dependence of the variation of $\log k_N$ on the torsion angle (θ). The message is clear: negative hyperconjugation can be expected under the appropriate circumstances with any substituent, especially heteroatomic substituents in which the electronic properties are quite different from those of the model substituent (hydrogen or carbon).

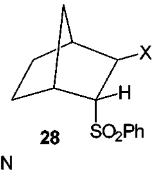


26

a X = MeN
b X = S
c X = Me_2N^+ (I^-)



27



28

a X = Me_2N
b X = MeS
c X = Me_3N^+ (I^-)

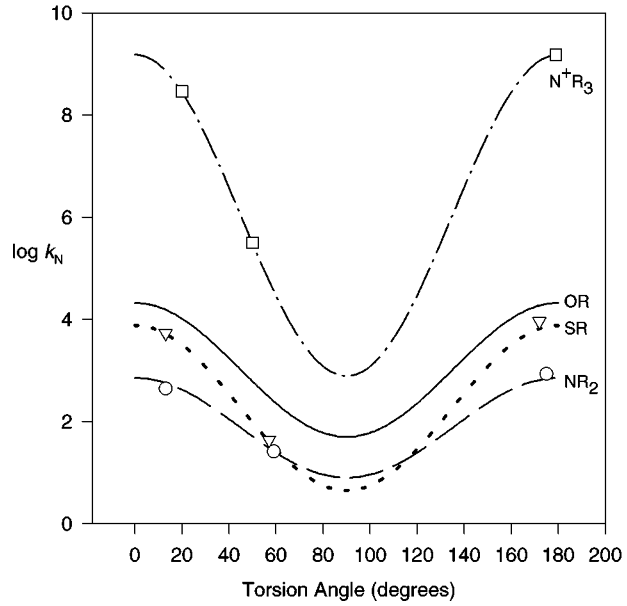


FIGURE 2 Plot of log k_N vs torsion angle for β-substituted sulfones **26–28**. Experimental points and *a* and *b* parameters for Eq. (4) (derived from nonlinear least squares fits) are shown as follows: X = trialkylammonio, squares, dot–dash line from $a = 2.89 \pm 0.0002$, $b = 6.29 \pm 0.0002$; X = alkylthio, inverted triangles, dotted line from $a = 0.65 \pm 0.12$, $b = 3.23 \pm 0.15$; X = tertiary amino, circles, dashed line from $a = 0.90 \pm 0.19$, $b = 1.95 \pm 0.24$. The solid line is that for X = alkoxy transferred from Fig. 1 for comparison.

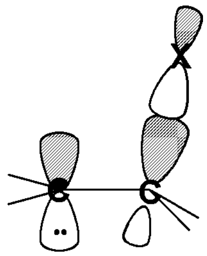
Examination of the parameters recorded in the caption to Fig. 2 reveals two features of note. First, we look at the parameters for *a*, the angle independence term in Eq. (4), which vary from 0.65 for the thioalkoxy (RS) group to 2.89 for the trialkylammonio (R_3N^+) function. As was described in the previous section, division of *a* (the angle independence parameter) by 4.9 yields $(\sigma^*_{90})_X$, the angle dependent σ^* value for the torsion angle of 90°, i.e. the Taft substituent constant in which there is no hyperconjugation and the electronic effect reflects only the field and inductive effects. The values of $(\sigma^*_{90})_X$ so obtained are RS 0.13, R_2N 0.18, RO 0.35 (as above), and R_3N^+ 0.59. The order of listing is, of course, simply that of increasing $(\sigma^*_{90})_X$ values; this order, however, also corresponds to the order of increasing electronegativities of these groups, a pattern fully consistent with our assignment of the angle independence terms to the field and inductive effects. It should be explicitly noted that standard σ^* (and σ_I) values do not show such a simple correlation with electronegativity, e.g., the value for the least electronegative group, the alkylthio (RS) group (e.g. MeS σ^* 0.29–0.69) lies between those for the amino function (e.g. Me_2N σ^* 0.13–0.42) and the alkoxy group (e.g. MeO σ^* 0.51–0.76) [12].

We note as our second point the variation of *b*, the angle dependence parameter, from 1.95 for R_2N, through 2.62 for RO, and 3.23 for RS, to 6.29 for R_3N^+. We interpret this parameter as a quantitative index of the extent of hyperconjugation in this reaction, i.e., showing that hyperconjugation has the smallest effect with R_2N, somewhat larger with RO, larger still with RS, and finally substantially greater yet with R_3N^+ groups.

At the qualitative level of simple orbital interaction diagrams [14] the observed pattern is fully consonant with simple MO theory. It is necessary to recall [14] that the energy change on interaction of two orbitals (i.e., the extent of lowering of the resulting lower energy orbital or of the increase of the higher energy orbital) is given approximately by Eq. (6), where the h^2_{AB} term is the interaction matrix element, and ϵ_A and ϵ_B are the energies of the interacting orbitals; it should also be recalled that ϵ_A for an atomic orbital decreases as the electronegativity (or formal positive charge) of the atom increases.

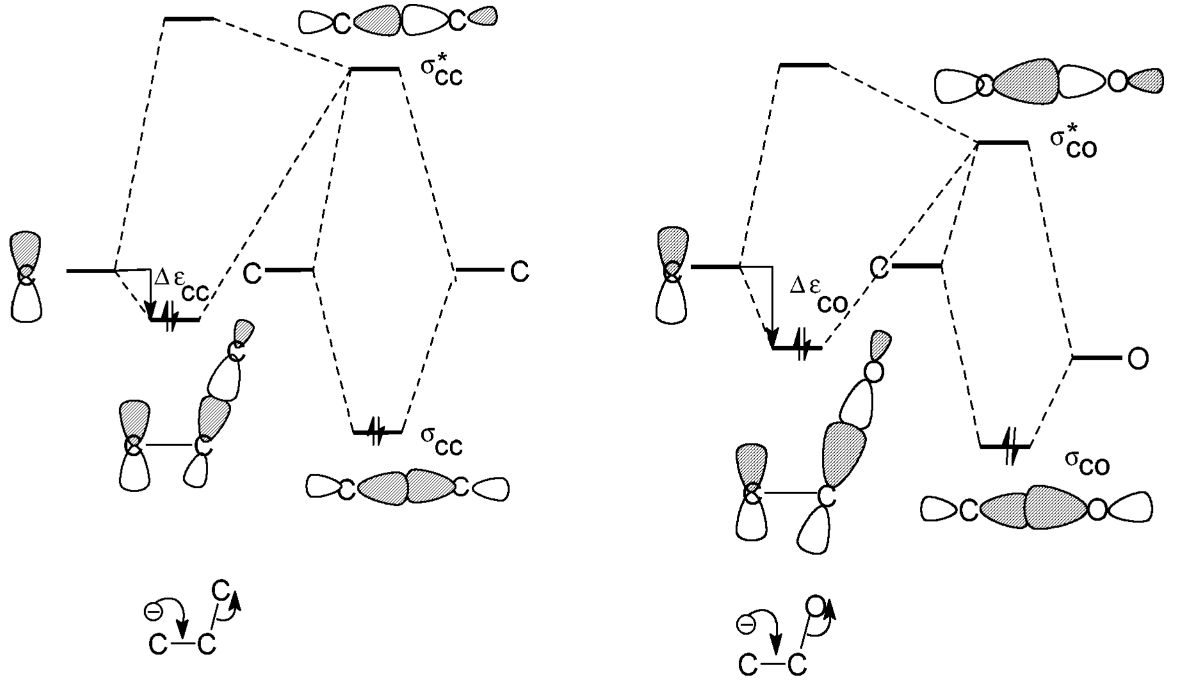
$$\Delta\epsilon \approx \frac{h^2_{AB}}{\epsilon_A - \epsilon_B} \qquad (6)$$

If we examine the negative hyperconjugative stabilization of a β-substituted carbanion ($\bar{C}$—C—X) in terms of a simple MO picture, we first illustrate the interaction as a π-type overlap of a filled p-orbital with an unoccupied σ^* orbital as in **29** [15].



29

The corresponding orbital interaction diagrams for both X = C and X = O are given in Fig. 3 wherein we see that the net result of the two sets of orbital interactions is $\Delta\epsilon_{CO} > \Delta\epsilon_{CC}$, i.e., the negative hyperconjugative interaction is predicted to be greater for X = O than for X = C. This pattern arises primarily because the energy of σ^*_{CC} is higher than that of σ^*_{CO} and hence the denominator of Eq. (6) in the CC case ($\epsilon_{\sigma^*CC} - \epsilon_C$) is larger than that in the CO interaction ($\epsilon_{\sigma^*CO} - \epsilon_C$). The higher energy of σ^*_{CC} vs. σ^*_{CO} arises in turn from essentially the same cause, i.e., the denominator for the CO sigma system is larger than that for the CC sigma array [16] and the σ^*_{CO} energy level is



(a) carbon

(b) oxygen

FIGURE 3 Orbital interaction diagrams comparing negative hyperconjugation in $\bar{C}$—C—X with (a) X = carbon and (b) X = oxygen. The left side of each diagram shows the interaction of the filled p-orbital of the carbanion with each σ^* orbital. The resulting energy lowering is given by $\Delta\epsilon_{CC}$ for X = C and $\Delta\epsilon_{CO}$ for X = O; $\Delta\epsilon_{CO} > \Delta\epsilon_{CC}$, the difference being due to the lower energy of σ^*_{CO} vs σ^*_{CC}, the origin of which in turn is shown on the right side of each diagram.

lower than that for σ^*_{CC}. Another feature contributing to the larger value of $\Delta\epsilon_{CO}$ with respect to $\Delta\epsilon_{CC}$ is the improved π-overlap arising because of the larger coefficient of σ^*_{CO} on the carbon atom relative to that on (either) carbon in σ^*_{CC}. An attempt has been made in Fig. 3 to indicate qualitatively the magnitude of these coefficients by varying the sizes of the orbitals.

For the amino group (R_2N) we can readily interpolate to predict that $\Delta\epsilon_{CO} > \Delta\epsilon_{CN} > \Delta\epsilon_{CC}$, while for the trialkylammonio group (R_3N^+) the much lower energy of the nitrogen atomic orbital due to the positive charge leads to a low value of $\sigma^*_{CN^+}$ and from this to a large value of $\Delta\epsilon_{CN^+}$ (larger than $\Delta\epsilon_{CO}$). With the thioalkyl group (RS) the origin of the fairly high negative hyperconjugation (as indicated by the value of 3.2 for the angle dependence parameter) is to be found not in high electronegativity, but rather in the comparatively poor σ-overlap of the 2p-orbital on carbon with the 3-orbital on sulfur. This produces a much smaller value of h^2_{AB} in Eq. (6) which leads to a low energy value for σ^*_{CS}; thus both the h^2_{AB} and $\epsilon_A - \epsilon_B$ terms are smaller for thioalkyl vs. the alkoxy group and it is not surprising that the angle dependence parameter b is higher for RS than for RO.

RELATED WORK

The concept of hyperconjugation has been extant for more than 60 years and it is appropriate to specify what is new in this investigation and how it relates to other studies. The theoretical concept of negative hyperconjugation, especially in connection with the generalized anomeric effect, was dealt with in a number of papers [3] in the 1970s and 1980s. The present work provides simple, readily understood experimental support for the predictions made in these studies. The paper by Schleyer and Kos [3c] is particularly relevant. The authors estimated that a total stabilization energy of 23.5 kcal mol^{-1} results from replacement of X = H by X = OH in $XCH_2CH_2^-$. Of this 13.2 kcal mol^{-1}, (or 56%) was ascribed to hyperconjugation; a similar estimate for X = NH_2 indicated 55% hyperconjugation contribution. From our experiments we may estimate the hyperconjugation percentage from the a and b parameters in Eq. (4), specifically, the ratio $100b/(a + b)$. From this we estimate that the percentage of hyperconjugation in the substituent effect is 61% for OH and 68% for NH_2. Given the completely different sources for these estimates we regard the substantial agreement between our results and those of Schleyer and Kos as reassuring.

The concept of negative hyperconjugation has been invoked in the chemistry of carbanions previously by Ahlberg and Thibblin [17] to account for the effects of oxygen substituents in 1,3-proton transfer in indenes and in clarifying aspects of the *E*2-*E*1cB borderline. In studying the mechanism of nucleophilic substitution at electrophilic olefins, Rappoport [18] has noted that the reaction commonly proceeds with retention. Rappoport and Apeloig [3d] account for this behavior in terms of the intermediate carbanion and its stabilization by negative hyperconjugation.

During much of the time when we were busy making β-alkoxy sulfones Lambert and his coworkers [19] were investigating the corresponding angle dependence of "ordinary" or "positive" hyperconjugation. In this investigation Lambert and coworkers synthesized a set of β-trimethylsilyl alcohol derivatives and found that the solvolysis rate constants varied spectacularly with the torsion angle, exactly as expected from hyperconjugative stabilization of the incipient carbocation by the σ_{CSi} electrons.

The mutual consistency of these various theoretical and experimental studies is such that, in our view, it would be perverse to draw any other conclusion than that hyperconjugation can lead to large chemical effects, especially with heteroatoms.

REFERENCES

[1] (a) Hine, J. Physical Organic Chemistry, 2nd ed.; McGraw-Hill: New York, 1962; p. 83; (b) Lowry, T. H.; Richardson, K. S. Mechanism and Theory in Organic Chemistry, 3rd ed.; Harper and Row: New York, 1987, p. 152; (c) Topsom, R. D. Prog Phys Org Chem 1976, 12, 1–20; (d) Reynolds, W. F. Prog Phys Org Chem 1983, 14, 165–203; (e) Taft, R. W.; Topsom, R. D. Prog Phys Org Chem 1987, 16, 1–83.

[2] Thomas, P. J.; Stirling, C. J. M. J Chem Soc, Perkin Trans 2 1977, 1909–1913.

[3] (a) David, S.; Eisenstein, O.; Hehre, W. J.; Salem, L.; Hoffmann, R. J Am Chem Soc 1973, 95, 3806–3807; (b) Bingham, R. C. J Am Chem Soc 1975, 97, 6743–6746; (c) Schleyer, P. v. R.; Kos, A. J. Tetrahedron 1983, 39, 1141–1150; (d) Apeloig, Y.; Rappoport, Z. J Am Chem Soc 1979, 101, 5095–5098; (e) Apeloig, Y.; Karni, M.; Rappoport, Z. J Am Chem Soc 1983, 105, 2784–2793.

[4] (a) Lemieux, R. U. Pure Appl Chem 1971, 25, 527–548; (b) Eliel, E. L. Angew Chem, Int Ed Engl 1972, 11, 739–750; see also (c) Kirby, A. J. The Anomeric Effect and Related Stereoelectronic Effects at Oxygen; Springer: New York, 1983; (d) Thatcher, G. R. J. (Ed.). ACS Symposium Series, Vol. 539: The Anomeric Effect and Associated Stereoelectronic Effects; American Chemical Society: Washington, DC, 1993; (e) Eliel, E. L.; Wilen, S. H. Stereochemistry of Organic Compounds; Wiley: New York, 1994, pp. 611, 753.

[5] (a) Boche, G. Angew Chem, Int Ed Engl 1989, 28, 277–297; (b) Boche, G.; Lohrenz, J. C. W.; Cioslowski, J.; Koch, W.; Patai, S.; Rappoport, Z. (Eds.). Supplement S: The Chemistry of Sulfur-Containing Functional Groups; Wiley: New York, 1993, Ch. 7, pp. 339–362.

[6] Wolfe, S.; Stolow, A.; LaJohn, L. A. Tetrahedron Lett 1983, 24, 4071–4074.

[7] King, J. F.; Rathore, R. J Am Chem Soc 1990, 112, 2001–2002.

[8] King, J. F.; Rathore, R.; Guo, Z.; Li, M.; Payne, N. C. J Am Chem Soc 2000, 122, 10308–10324.

[9] Kirkwood, J. G.; Westheimer, F. H. J Chem Phys 1938, 6, 506–512; Westheimer, F. H.; Kirkwood, J. G. J Chem Phys 1938, 6, 513–517.

[10] Li, M. Ph.D. thesis, The University of Western Ontario, London, Ontario, 1999; (a) pp. 71–79, (b) pp. 125–130, (c) pp. 121–128.

[11] One may note at this point that the hyperconjugation involving interaction of the carbanion with the $\sigma^*_{\mathrm{C-OR}}$ is not the only possible orbital–orbital interaction in this system. Apeloig and Rappoport [3d] describe a two-orbital-four-electron destabilizing interaction of the carbanion with the filled bonding $\sigma_{\mathrm{C-OR}}$ orbital; the four electron interaction was regarded as less important than the hyperconjugation.

[12] Exner, O. In Correlation Analysis in Chemistry: Recent Advances; Chapman, N. B.; Shorter, J. (Eds.); Plenum Press: New York, 1978, Ch. 10, pp. 439–540.

[13] The amino and alkylthio substituted sulfones underwent simple H–D exchange, but two of the trialkylammonio compounds (**27c** and **28c**) gave Hofmann elimination products; evidence is given elsewhere [10b] that the reaction is $(E1\mathrm{cB})_{\mathrm{I}}$ and hence the measured rate constant is that of the carbanion formation. Attempts to extend this study to the alkylsulfonyl group are incomplete [10c], (A. Z. Cheng, V. Dave, unpublished work); the log k_{N} values for the "180° sulfone" (**15** with O replaced by SO_2) and the "60° sulfone" (**27** with $X = MeSO_2$) were, respectively, 8.16 and 4.75, i.e., quite close to those for corresponding trialkylammonio compounds. Attempts to determine k_{N} for the "0° sulfone" (obtained by oxidation of **27b**) have proved frustrating owing to low solubility, concurrent elimination, and NMR signal overlap (A. Z. Cheng, V. Dave, unpublished work).

[14] The monograph by Arvi Rauk, Orbital Interaction Theory of Organic Chemistry, Wiley-Interscience: New York, now in its second edition (2001), was found to be most helpful in explaining the MO basis of negative hyperconjugation, especially pp. 44, 73, 74, 83, and 84.

[15] It may be helpful to point to the curious feature that σ^* symbolizes two quite different things in this paper, one the Taft substituent constant, the other the antibonding sigma orbital; the reader should have no difficulty determining which is meant in any particular context.

[16] In fact, for the CC system the energy difference is zero and a different equation is required to evaluate $\Delta\epsilon$, but the point is still valid.
[17] (a) Ahlberg, P. Chem Scr 1973, 3, 183–189; (b) Thibblin, A.; Ahlberg, P. J Am Chem Soc 1977, 99, 7926–7930; (c) Thibblin, A. J Am Chem Soc 1988, 110, 4582–4586 and papers cited.
[18] Rappoport, Z. Acc Chem Res 1981, 14, 7–15.
[19] (a) Lambert, J. B.; Liu, X. J Organomet Chem 1996, 521, 203–210; (b) Lambert, J. B.; Zhao, Y.; Emblidge, R. W.; Salvador, L. A.; Liu, X.; So, J.-H.; Chelius, E. C. Acc Chem Res 1999, 32, 183–190.