2,3-dichloropropanoate, 3674-09-7; methyl 2,3-dibromopropanoate, 1729-67-5; methyl 2,3-dichlorobutanoate, 54460-97-8; methyl 2,3-dibromobutanoate, 5469-24-9; methyl 2,3-dichloro-2-methylpropanoate, 918-78-5; methyl 2,3-dibromo-2-methylpropanoate, 3673-79-8; butyl 2,3-dichloropropanoate, 72726-18-2; butyl 2,3-dibromopropanoate, 21179-48-6; butyl 2,3-dichloro-2-methylpropanoate, 72726-19-3; butyl 2,3-dibromo-2-methylpropanoate, 72726-20-6; 2,3-dichloroacrylamide, 19433-84-2; 2,3-dibromoacrylamide, 15102-42-8; 2,3-dichloro-2-methylpropanamide, 7017-20-1; 2,3-dibromo-2-methylpropanamide, 72726-21-7.

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# Steric Effects. 4.[1] Multiparameter Correlation Models. Geometrical and Proximity Site Effects for Carboxylic Acid Esterification and Related Reactions

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A recent article[3] concerning the validity and importance of Hancock-type steric parameters[4] ($E_s^c$) prompts us to report our own results and observations in this area. This is a subject currently under controversy,[5a,b] and we feel that a careful analysis of the factors involved is necessary in order to reach conclusions that will stand the test of time. After a summary and analysis of the arguments of this article, we set forth our own approach to the problem of steric hindrance and its use in comparing the reactivities of methyl carboxylates and alkyl acetates.

In the article in question the authors, from Hancock's school, have attempted to revive interest in the use of Hancock's $E_s^c$ parameter. They base their argument, in part, on an analysis of the rate data for the alkaline hydrolysis of methyl carboxylates and alkyl acetates. It is worth noting that the alkaline hydrolysis of methyl carboxylates ($RCO_2Me$) was originally used by Hancock to justify the development of the $E_s^c$ scale.[4] This recent work considers that the data are adequately represented in terms of Taft's $E_s$ parameters, thus sweeping aside one of the original arguments.

The situation is somewhat different in the case of alkyl acetates ($CH_3CO_2R$). Here the R group is in the nonacyl portion of the molecule, and its steric effect is not adequately reflected by the $E_s$ parameter which was defined with respect to the acyl portion of an ester.

Correlations in terms of $E_s(R)$ and $E_s^c(R)$ were found to be unsatisfactory, with the latter more successful than the former. However, a correlation in terms of $E_s^c(RCH_2)$ was found to be excellent ($r = 0.9925$, $\psi = 0.141$); surprisingly enough a correlation in terms of $E_s(RCH_2)$ is not considered. Correlations in terms of $E_s^c(RCH_2)$ are taken as evidence for the validity and importance of this kind of parameter. Such an interpretation has to be treated with caution. It must be remembered that $E_s^c$ is defined with respect to Taft's $E_s$ as $E_s^c = E_s + 0.306(n_H - 3)$. When the groups used in a correlation are all of the form $RCH_2$, then $E_s^c$ and $E_s$ differ by a constant term (i.e., $E_s^c = E_s - 0.306$). This means, of course, that modifying $E_s$ to give $E_s^c$ produces no change in the validity of the correlation and provides no positive evidence in favor of $E_s^c$.

These remarks apply equally well to acid- and base-catalyzed hydrolysis. We agree with these authors when they question the necessity of developing sets of steric parameters from a variety of defining basis sets. This remark might well apply to Hancock-type parameters.

In our own work we have developed a scale of steric parameters[5a] ($E_s'$) based on the Taft–Ingold hypothesis and a single reference reaction, i.e., the acid-catalyzed esterification of carboxylic acids in methanol at 40 °C, rather than average data for a variety of similar reactions. This revised Taft steric scale combines literature data with new rate-constant measurements to cover a range of greater than eight powers of ten in rate constant. Table I gives the appropriate $E_s'$ values for a set of 13 alkyl groups which have been found by molecular-mechanics calculations to exist in predominantly eclipsed conformations in the presence of a carbonyl function.[7] Our strategy here is to correlate the *overall* steric effect of a group $R_1R_2R_3C$ as a function of a linear combination of the steric effects of the subgroups $R_1$, $R_2$, and $R_3$, taking into account the orientation of these subgroups with respect to the carbonyl. This may be carried out in a variety of ways, depending on the model chosen.

As a first approach we correlate $E_s'(R_1R_2R_3C)$ as a linear combination of $E_s'(R_iCH_2)$, the *equidistant site model*, where the atoms of $R_i$ on both sides of eq 1 are the same

$$E_s'(R_1R_2R_3C) = \sum_i a_i E_s'(R_iCH_2) + a_0 \qquad (1)$$

distance from the carbonyl group. But for $CHEt_2$ [which presents a large deviation (0.67)] this correlation is surprisingly good, considering the simplicity and weakness of the equidistance approximation.

Another approach is to consider a correlation in terms of $E_s'(R_i)$, the *subgroup additivity model*, as in eq 2. The

$$E_s'(R_1R_2R_3C) = \sum_i a_i E_s'(R_i) + a_0 \qquad (2)$$

correlation is seen to be mediocre. The reason for this may be that the model is unsuitable or that some essential element is missing from eq 2. The key lies in the idea of six-number first proposed by Newman[8] in a qualitative way and later used quantitatively by Hancock.[9] This idea is based on the topology of groups since certain sites (i.e., position six) are singled out as having an effect different from that of the others. Equation 2 may be expanded to incorporate the six-number, eq 3. This *hybrid* equation,

$$E_s'(R_1R_2R_3C) = \sum_i (a_i E_s'(R_i) + b_i \Delta x_i) + a_0 \qquad (3)$$

made up from the contribution of subgroups and six-number (*subgroup additivity plus topology model*), gives an excellent correlation. The $a_i$ terms weight the individual contributions of the subgroups $R_i$ whose orientations with respect to the carbonyl group have been determined by molecular mechanics, the $b_i$ terms represent the supple-

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(1) Part 3: Dubois, J. E.; MacPhee, J. A.; Panaye, A. *Tetrahedron*, in press.

(2) (a) MacPhee J. A., Chargé de Recherche, Centre National de la Recherche Scientifique, France. (b) Panaye A., Maitre-Assistant à l'Université Paris VII.

(3) Idoux, J. P.; Schreck, J. O. *J. Org. Chem.* **1978**, *43*, 4002.

(4) Hancock, C. K.; Meyers, E. A.; Yager, B. J. *J. Am. Chem. Soc.* **1961**, *83*, 4211.

(5) (a) MacPhee, J. A.; Panaye, A.; Dubois, J. E. *Tetrahedron* **1978**, *34*, 3553. (b) Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 1552.

(6) Taft, R. W., Jr. In "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.; Wiley: New York, 1956; Chapter 3.

(7) Dubois, J. E.; MacPhee, J. A.; Panaye, A. *Tetrahedron Lett.* **1978**, 4099.

(8) Newman, M. S. *J. Am. Chem. Soc.* **1950**, *72*, 4783.

(9) Hancock, C. K.; Yager, B. J.; Falls, C. P.; Schreck, J. O. *J. Am. Chem. Soc.* **1963**, *85*, 1297.

0022-3263/80/1945-1164$01.00/0

Table I. Steric Parameters of Alkyl Groups Having Eclipsed Conformations

| | | ordering of subgroups[b] | | | $E_s'(i)$ of subgroups $R_iCH_2$ | | | $E_s'(i)$ of subgroups $R_i$ | | | six-number of subgroup $R_i$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| group | $E_s'$[a] | $R_1$ | $R_2$ | $R_3$ | $E_s'(1)$ | $E_s'(2)$ | $E_s'(3)$ | $E_s'(1)$ | $E_s'(2)$ | $E_s'(3)$ | $\Delta x_1$ | $\Delta x_2$ | $\Delta x_3$ |
| $CH_3$ | 0.0 | H | H | H | 0.00 | 0.00 | 0.00 | 1.12 | 1.12 | 1.12 | 0 | 0 | 0 |
| $MeCH_2$ | -0.08 | H | H | Me | 0.00 | 0.00 | -0.08 | 1.12 | 1.12 | 0.00 | 0 | 0 | 0 |
| $EtCH_2$ | -0.31 | H | H | Et | 0.00 | 0.00 | -0.31 | 1.12 | 1.12 | -0.08 | 0 | 0 | 0 |
| *i*-$PrCH_2$ | -0.93 | H | H | *i*-Pr | 0.00 | 0.00 | -0.93 | 1.12 | 1.12 | -0.48 | 0 | 0 | 6 |
| *t*-$BuCH_2$ | -1.63 | H | H | *t*-Bu | 0.00 | 0.00 | -1.63 | 1.12 | 1.12 | -1.43 | 0 | 0 | 9 |
| $Me_2CH$ | -0.48 | H | Me | Me | 0.00 | -0.08 | -0.08 | 1.12 | 0.00 | 0.00 | 0 | 0 | 0 |
| EtMeCH | -1.00 | H | Et | Me | 0.00 | -0.31 | -0.08 | 1.12 | -0.08 | 0.00 | 0 | 3 | 0 |
| $Et_2CH$ | -2.00 | H | Et | Et | 0.00 | -0.31 | -0.31 | 1.12 | -0.08 | -0.08 | 0 | 3 | 3 |
| *i*-PrEtCH | -3.23 | H | *i*-Pr | Et | 0.00 | -0.93 | -0.31 | 1.12 | -0.48 | -0.08 | 0 | 6 | 3 |
| $Me_3C$ | -1.43 | Me | Me | Me | -0.08 | -0.08 | -0.08 | 0.00 | 0.00 | 0.00 | 0 | 0 | 0 |
| $EtMe_2C$ | -2.28 | Me | Et | Me | -0.08 | -0.31 | -0.08 | 0.00 | -0.08 | 0.00 | 0 | 3 | 0 |
| *i*-$PrMe_2C$ | -3.54 | Me | *i*-Pr | Me | -0.08 | -0.93 | -0.08 | 0.00 | -0.48 | 0.00 | 0 | 6 | 0 |
| $Et_3C$ | -5.29 | Et | Et | Et | -0.31 | -0.31 | -0.31 | -0.08 | -0.08 | -0.08 | 3 | 3 | 3 |

[a] Overall steric parameter of the group. [b] The subgroups $R_1$, $R_2$, and $R_3$ are ordered as follows:

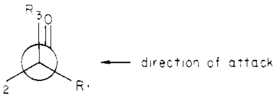

Table II. Correlation of Overall Steric Effects by Additive Contributions of Subgroups, Eclipsed Set

| eq no.[a] | parameters | $a_0$ | $a_1$ | $b_1$ | $a_2$ | $b_2$ | $a_3$ | $b_3$ | $r$ | $\psi$[b] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $E_s'(RCH_2)$ | -0.134 | 12.59 | | 2.89 | | 0.96 | | 0.988 | 0.187 |
| 2 | $E_s'(R)$ | -2.96 | 1.24 | | 1.10 | | 0.786 | | 0.800 | 0.723 |
| 3 | $E_s'(R)$, $\Delta x$ | -1.39 | 0.91 | -0.75 | 0.46 | -0.31 | -0.10 | -0.21 | 0.996 | 0.139 |
| 4 | $E_s^{c\prime}(R)$ | -2.25 | 6.88 | | 2.37 | | 0.707 | | 0.991 | 0.159 |
| 5 | $E_s'(R)$, $\Delta n$ | -1.40 | 6.74 | -2.23 | 2.15 | -0.612 | 0.653 | -0.278 | 0.995 | 0.149 |
| 6 | $E_s^{c\prime}(R)$, $\Delta n$ | -2.32 | 7.10 | -2.27 | 2.34 | -0.578 | 0.779 | -0.221 | 0.995 | 0.143 |

[a] Correlation eq 5 and 6 compare $E_s'(R_1R_2R_3C)$ and $E_s^{c\prime}(R_1R_2R_3C)$ in the same way, i.e., in terms of the same six parameters, $E_s'(R_i)$ and $\Delta n_i$. It is seen that the derived parameter $E_s^{c\prime}$ offers no advantage over the simpler $E_s'$, in this context. [b] $\psi$ from Exner's test, cf.: Exner, O. *Collect Czech. Chem. Commun.* **1966**, *31*, 3222.

mentary weight given to the six-number contribution from each subgroup $R_i$ and $x$ is the six-number. In this correlation (3) the only important divergence, $\Delta = 0.35$, is that ascertained for CHMeEt. The explanation for this variation no doubt lies in the conformational filiations. The CHMeEt group is but slightly hindered; other conformations besides that in which Me eclipses carbonyl are equally probable. If, by applying correlation 3, one calculates the $E_s'$ of the CHMeEt group for the conformation in which Et eclipses carbonyl, one finds a value of -0.99, corresponding to the experimental value -1.00. It is therefore probable that the conformational mixture is greater for CHMeEt than for the other groups. In effect, if eq 1 and 3 take the variation of $E_s'(R_1R_2R_3C)$ into account with similar degrees of success, it is mainly because the former includes the six-number contribution *implicity* while the latter takes it into account *explicitly*.

The poor quality of correlations of the form of eq 2 has already been noted.[10] The explanation, however, differs from that given above because the search for the best correlation was conducted in a different way. It was pointed out that the correlation is remarkably improved when Taft's $E_s$ values were replaced by Hancock's $E_s^c$ values in eq 2; this was taken as evidence for the superiority of Hancock-type parameters over Taft-type parameters as a measure of the steric effect. Our revised Taft $E_s'$ values lend themselves well to this kind of analysis since they extend over a wide range (Table I) and have been calculated with respect to a single reference reaction. It is possible to apply the Hancock correction term to the $E_s'$ values to obtain $E_s^{c\prime}$ values, i.e., $E_s^{c\prime} = E_s' + 0.306(n_H - 3)$, where $n_H$ is the number of $\alpha$-hydrogens of the alkyl group. We then have eq 4, where it is seen that the resulting correlation is excellent.

$$E_s^{c\prime}(R_1R_2R_3C) = \sum a_i E_s^{c\prime}(R_i) + a_0 \qquad (4)$$

It is tempting to compare the correlations based on eq 2 and 4 particularly since the results are so different. Statistically speaking, however, it is incorrect to compare the two correlations since eq 4 contains three more parameters than eq 2 "hidden" within the $E_s^{c\prime}$ values, i.e., the $0.306(n_H - 3)$ terms. The correct way to compare $E_s'$ and $E_s^{c\prime}$ is to consider two correlations with the same number of parameters. In this case we naturally choose six parameters, three $E_s'(R_i)$ and three $\Delta n_i$ terms as in eq 5 and 6, where $\Delta n_i = n_{H,i} - 3$. These

$$E_s'(R_1R_2R_3C) = \sum(a_i E_s'(R_i) + b_i \Delta n_i) + a_0 \qquad (5)$$

$$E_s^{c\prime}(R_1R_2R_3C) = \sum(a_i E_s^{c\prime}(R_i) + b_i \Delta n) + a_0 \qquad (6)$$

two correlations may now be properly compared. It is immediately evident that they are both excellent and statistically equivalent, indicating that, from this point of view, there is no reason to suppose that the derived $E_s^{c\prime}$ scale is superior to the simple $E_s'$ scale, contrary to previous suppositions. The performance of eq 1 and 3 is such that there is no need to modify the $E_s'$ values to obtain a satisfactory correlation so long as the six-number effect is included, implicitly or explicitly as the case may be. In our opinion the $\Delta n$ term in eq 5 and 6 is not associated with hyperconjugation. Indeed, the $\Delta n$ of a subgroup $R_i$ reflects the degree of substitution of that group and is not in any general sense related to the degree of substitution of the overall group $R_1R_2R_3C$.

It is possible to apply the idea behind eq 3 to the data for the alkaline hydrolysis of alkyl acetates discussed above. In this case we use as parameters the $E_s'$ of the

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(10) Fujita, T.; Takayama, C.; Nakajima, M. *J. Org. Chem.*, **1973**, *38*, 1623.

group R and the change in six-number ($\Delta x$) of the group between an acyl and a nonacyl environment (eq 7). The

$$\log k = 1.02E_s' + 0.916(\Delta x) + 0.867 \qquad r = 0.994 \qquad \psi = 0.135 \tag{7}$$

hydrolysis of symmetrically substituted alkyl carboxylates[3] ($RCO_2R$) is likewise amenable to such a treatment. For symmetry reasons only two parameters are necessary: an $E_s'$ term which represents the combined steric effects of R in its acyl and nonacyl environment and $\Delta x$. This yields eq 8. Thus it appears that the steric effects of alkyl groups

$$\log k = 2.44E_s' + 1.29\Delta x + 0.804 \qquad r = 0.994 \qquad \psi = 0.136 \tag{8}$$

in the nonacyl portion of an ester are adequately taken into account by $E_s'$ and $\Delta x$ steric parameters.

## Overview

The revised Taft steric parameter[5a] $E_s'$ is based on the Taft-Ingold hypothesis and is calculable directly from the rate constants for acid-catalyzed esterification of carboxylic acids in methanol at 40 °C. Hancock-type parameters are *derived* from these by means of the correction term $0.306(n_H - 3)$. It is shown that the use of such derived parameters does not improve the different correlations where steric effects either are taken care of by straightforward Taft-type parameters or are used in a manner where conformational orientations and terminal site effects ($\Delta x$) are carefully considered.

Though this analysis shows no need for the Hancock data treatment, it does not exclude the existence of hyperconjugation effects in certain cases. Their role, however, becomes more difficult to identify and estimate in the esterification reactions, particularly so if one points to the behavior of the methyl group in our totally steric interpretation. One would expect this $E_s'$ value to drop out of the general correlation. In fact, such is not the case, and this observation may be considered as a strong argument against the need for correction, implying a hyperconjugative interpretation.

The different models considered favor the hypothesis of a complex behavior of pure steric parameters. This is further backed by the coherence of these conclusions with Charton's point of view.[11] There is, in fact, an excellent correlation between $E_s'$ and the van der Waals radius, $r_{v,\min}$, of Charton for symmetrical groups: for the groups H, Me, *t*-Bu, $Cl_3C$, and $Br_3C$ the correlation is excellent, $r = 0.99993$ and $\psi = 0.015$, for an $E_s'$ variation of greater than three units. For these simple symmetrical groups, where the subgroups are indistinguishable and proximity site effects (six-number) are absent, the interpretation of $E_s'$ in terms of $r_{v,\min}$ confirms the very general treatment based on pure steric factors (eq 7 and 3).

It is noteworthy that for all simple groups, symmetrical and nonsymmetrical, a physical interpretation of $E_s'$ in terms of site, bond, and angle interaction functions can be developed by means of a molecular mechanics (MM) treatment,[12] whereas all our data handling has been inspired by the chemist's usual data compression, i.e., visualization of subgroups, conformations, and specific site effects. Both treatments have complementary merits for usual environments, but for complex ones with extremely large $E_s'$ values where no valid MM parameters are available, the steric hindrance "subgroup additivity plus topology model" seems to yield more than reasonable success for interpretation and prediction purposes.

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(11) Charton, M.; *J. Am. Chem. Soc.* **1969**, *91*, 615.

(12) DeTar, D. F.; Tenpas, C. J. *J. Am. Chem. Soc.* **1976**, *98*, 7903.

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# Structural Effects on the Reactivity of Ethers in Donor-Acceptor Reactions

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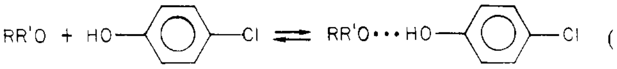
As indicated by West and co-workers[2] and by Arnett,[3] it seems fairly well established that donor-acceptor interactions (either through hydrogen bonding or charge transfer) of ethers are quite sensitive to both steric and electronic effects. In order to help unravel the contributions from these effects we present here new data for two simple reactions: (1) the hydrogen-bonding complexing of several cyclic and acyclic ethers with *p*-chlorophenol in dilute solution in cyclohexane (the equilibrium constants, *K*, for process 1 have been measured at 20 °C by UV absorption spectrometry; the experimental results are given in Table I); (2) the gas-phase protonation of some selected ethers. Their basicities relative to ammonia, i.e., the free energies of reaction 2, have been determined by ion cyclotron resonance spectroscopy (ICR).[4] These free energies, ΔG°, and the corresponding equilibrium constants, $K_p$, are summarized in Table II.



(1)

$$NH_4^+ + RR'O \rightleftarrows RR'OH^+ + NH_3 \tag{2}$$

## Discussion

Rather than attempting to undertake a full quantitative structure-reactivity study, we shall focus attention on some conspicuous features of these sets of results.

(1) The values of *K* for cyclic ethers are systematically higher than those for the acyclic compounds of same carbon content. More precisely, for compounds having the same carbon content and the same degree of branching, the ratio $K_{\text{cyclic}}/K_{\text{acyclic}}$ takes values of 2-3 (Table III).

(2) Consider now a series of acyclic ethers, ROR', in which the substituent R is kept constant while the R' moiety undergoes successive α-methyl substitutions. On a quantitative basis, the effects of these substitutions on the constant *K* are quite small, frequently of the order of magnitude of experimental error. Typical results follow: $K_{\text{EtO-}n\text{-Pr}}/K_{\text{MeO-}n\text{-Pr}} = 1.11 \pm 0.07$, $K_{i\text{-PrO-}n\text{-Pr}}/K_{\text{EtO-}n\text{-Pr}} = 0.95 \pm 0.06$, $K_{t\text{-BuO-}n\text{-Pr}}/K_{i\text{-PrO-}n\text{-Pr}} = 0.92 \pm 0.06$. On the other hand, $(t\text{-Bu})_2O$, relative to other members of the RO-*t*-Bu family, is an important exception: while $K_{\text{EtO-}t\text{-Bu}}/K_{\text{MeO-}t\text{-Bu}} = 1.03 \pm 0.06$ and $K_{i\text{-PrO-}t\text{-Bu}}/K_{\text{EtO-}t\text{-Bu}} = 1.04 \pm 0.06$, one finds $K_{(t\text{-Bu})_2O}/K_{i\text{-PrO-}t\text{-Bu}} = 0.39 \pm 0.03$. In the cyclic series, the effect is a sizable, but seemingly not additive, increase

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(1) Département des Sciences, Université Cadi Iyad, Marrakech, Morocco.

(2) R. West, D. L. Powell, M. K. T. Lee, and L. S. Whatley, *J. Am. Chem. Soc.*, **81**, 6141 (1959).

(3) E. M. Arnett, *Prog. Phys. Org. Chem.*, 1, 223 (1963).

(4) J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, Jr., J. L. Beauchamp, and R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5417 (1977).

(5) The gas-phase basicity of oxetane has not been determined so far because of side reactions following protonation.

(6) This work.

(7) P. Gately, J-L. M. Abboud, K. L. Marsi, and R. W. Taft, Abstracts of the Euchem Conference on Ring Closure Reactions and Related Topics., Castel Gandolfo, Italy, Aug-Sept 1978.

0022-3263/80/1945-1166$01.00/0