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COMPOSITION OF THE E_s' PARAMETER - CONTRIBUTION OF CONFORMATION AND SIX-NUMBER TO THE OVERALL STERIC EFFECT

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The development of a homogeneous and relatively complete scale of steric parameters[1] makes possible a close examination of the factors which make up the overall steric effects of groups in general and alkyl groups in particular. In this note we report some interesting findings concerning the "composition" of the steric effects of alkyl groups.

Minimum Energy Conformations

In an effort to rationalise, in conformational terms, the behaviour of the steric effects of alkyl groups with increasing substitution, we have undertaken a determination of the privileged conformations of carboxylic acids and restrict our attention to acids with carbon atoms extending to the γ position but not beyond.

To do this we have used a molecular mechanics method and the Allinger force field[2] which yield results in agreement with experiment when available.[3] Unfortunately, this force field is not parametrized for carboxylic acids. We have therefore chosen as a model for the acids, RCOOH, the corresponding methyl ketones, RCOMe. The replacement of OH by Me has, moreover, given satisfactory results in the study of certain alcohols.[4]

Complete details of this study will be given in a full paper. The results of interest in this context are the minimum energy conformations within series of related carboxylic acids, which may be summarized as follows :

- for primary groups RCH_2-, the alkyl substituent R eclipses the carbonyl. The stability difference between the eclipsed and bisected conformations decreases with the increasing steric hindrance of R.
- for secondary groups, the smaller members are eclipsed but from six carbons on are bisected. The group i-PrEtCH- constitutes the changeover point between the eclipsed and bisected populations.
- for the tertiary groups tested, up to seven carbons inclusive, only the group t-$BuMe_2C$- is not eclipsed. This is consistent with the x-ray crystal structure of n-Pr_3CCO_2H which is found to exist in the solid state in an eclipsed conformation.[5]

The molecular mechanics method yields valuable information concerning privileged conformations. This information must be used in keeping with the approximations involved in the method. Instead of making use of the actual conformational energies which differ but slightly from one compound to the next we have chosen to use the privileged conformations themselves to define a structural model of the reference reaction corresponding to the steric parameter E_S'. The correctness of this approach is shown by the consistency between the conformational information and the analysis of the behaviour of the steric effects of alkyls groups as a function of substitution which follows.

Correlation in Terms of Sub-Groups

The reaction system used to define the E_S' parameter (esterification) involves attack on the carbonyl of the carboxylic acid from the less hindered side of a low energy conformation. Table I lists 13 groups which have been found above to have low lying *eclipsed conformations*. Our model deals with the steric requirements of this conformationally homogeneous set. These groups all belong to a structural region in which there is a monotonic increase in the contribution of successive methyl groups to the overall steric effect.[6]

The corresponding E_S' values span a range of more than five powers of ten. Figure 1 represents a three-dimensional conformational model, where $|E_S'(R_1)| \leqslant |E_S'(R_2)|$. The sub-group R_3 is, however, not necessarily the most hindered. This is the case for primary, but not secondary and tertiary groups.

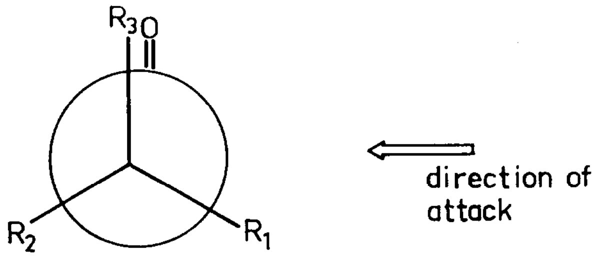

Figure 1. Eclipsed conformation used in correlations (Table I). For secondary and tertiary groups $|E_S'(R_1)| \leqslant |E_S'(R_2)| \geqslant |E_S'(R_3)|$. For primary groups RCH_2-, the group R corresponds to R_3.

Within the framework of this three-dimensional model we have attempted to determine the contributions of sub-groups (R) to the overall steric effect E_S' of groups $R_1R_2R_3C-$ making use of equations involving linear combinations of the E_S' values of these sub-groups. In the first model to be tested we have considered the effect of the group $R_1R_2R_3C-$ as the result of the superposition of the three groups R_iCH_2-. This model expressed by Equation 1, leads to a satisfactory correlation (Table II).

$$E_S'(R_1R_2R_3C-) = \sum_i a_iE_S'(R_iCH_2-) + a_0 \qquad (1)$$

The values of the coefficients a_i are related to the spatial orientation of the sub-groups

TABLE I : Steric Parameters of Alkyl Groups Having Eclipsed Conformations

Group	Overall Steric Parameters of Groups E'_S	Ordering of Sub-Groups[a]			E'_S parameter of sub-Groups R_iCH_2-			E'_S Parameter of Sub-Groups R_i			six-number parameter of Sub-Group R_i		
		R_1	R_2	R_3	$E'_S(1)$	$E'_S(2)$	$E'_S(3)$	$E'_S(1)$	$E'_2(2)$	$E'_S(3)$	$\Delta 6_1$	$\Delta 6_2$	$\Delta 6_3$
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	3
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] The sub-groups R_1, R_2 and R_3 correspond to the minimum energy conformations determined above (Fig.1).

TABLE II : Correlation of Overall Steric Effects by Additive Contributions of Sub-Groups. Eclipsed Set (Table I).

Corr.	a_o	a_1	b_1	a_2	b_2	a_3	b_3	r	ψ
1	-0.134	12.59	-	2.89	-	0.96	-	0.9878	0.187
2	-0.053	0.51	-0.095	-	-	-	-	0.9968	0.160
3	-1.39	0.91	-0.75	0.46	-0.31	-0.10	-0.21	0.9955	0.139

(Fig.1). In this approach the atoms of the sub-groups R_iCH_2- are in the same topological situation as the atoms of the overall group $R_1R_2R_3C$-.

The steric importance of the number of atoms in position 6 relative to the carbonyl oxygen taken as 1-i.e. the six-number - has been pointed out *qualitatively* by Newman.[7] The *quantitative* importance of the "change in six-number" as a significant parameter in the correlation of the rates of alkaline hydrolysis of alkyl acetates has been shown by Hancock.[8] In this study it is particularly interesting to determine the importance of the six-number effect by correlation since the molecular mechanics method does not provide us with a means of separating such an effect from others which may be operating. A correlation of the E'_S values of primary groups RCH_2 - where R = Me, Et, i-Pr and t-Bu as a function of E'_S of R and the six-number, Equation 2, furnishes an indication of the reality of the six-number effect. This result for primary groups is

$$E'_S(RCH_2-) = aE'_S(R) + b\Delta 6 + a_0 \qquad (2)$$

confirmed by the excellent correlation obtained from Eq.3 for the complete set of groups in Table I.

$$E'_S(R_1R_2R_3C-) = \sum_i (a_iE'_S(R_i) + b_i\ \Delta 6_i) + a_0 \qquad (3)$$

While the correlations based on Eq.1 and 3 are excellent, Eq.3 provides a more detailed analysis of the contributions of sub-groups and priviliged topological sites (the six-number) to the overall steric effect. Eq.1 contains the six-number contribution *implicitly* within the E'_S values of the groups R_iCH_2-. In Eq.3, which make use of a different model, these contributions are absent from the $E'_S(R_i)$ terms and are included *explicitly* as Δ6 terms, with a concomitant increase in precision.

Such models do not take into consideration the existence of interactions between the subgroups themselves. One minor point is the possibility of interactions between the methyls, responsible for the six-number effect, of different sub-groups. Only three groups are candidates for such an effect, Et_2CH-, i-PrEtCH- and Et_3C- with 1,2 and 3 such interactions respectively. Taking these interactions into account does yield an improved correlation with respect to correlation 3 ($r=0.997$, $\psi=0.124$). Such minor details will be fully discussed in a forthcoming article.

Correlations 1 and 3 then furnish a rather plausible account of the composition of the revised Taft steric parameter, E'_S, namely : a. a conformational effect determined by the relative positions of the sub-groups with respect to the carbonyl group ; b. non-identical contributions from the three groups R_1, R_2 and R_3 ; and c. a six-number effect, proportional to the number of atoms in position 6 relative to the carbonyl oxygen.

For our set of conformationally similar (i.e. eclipsed) groups we have obtained a straightforward interpretation of the Taft E'_S scale in terms of known steric effects. Even the well-known "telescopic effect"[9] of the steric constants of the groups Me, Et, i-Pr, and t-Bu is explained by a simple conformational effect. The three-dimensional model proposed in this note leads to very satisfying results concerning the contribution of sub-groups and the six-number to steric effects because it involves a conformationally homogeneous set of groups. The choice of this set was made possible by the molecular mechanics method. It is the complementary nature of the two approaches which allows a detailed picture of the nature of steric effects.

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