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The Ωs Constant for Polar Substituents. Reinvestigation on the Separation of the Steric and the Polar Effects[+]

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The steric substituent constants Ωs for 16 heteroalkyl groups were calculated and compared with Taft's Es constants. The Es vs. Ωs plot showed two parallel but separated lines each for alkyl and heteroalkyl groups. This fact was rationalized as the conformational effect.

Previously we proposed a new steric substituent constant Ωs defined as the solid angle of the substituent measured from the reactions center.[1)] Actually the solid angle was calculated by molecular mechanics[2)] assuning that the substituent has a contour defined by the van der Waals radii of constituting atoms, and the population-weighted mean was used as Ωs when the substituent has more than one conformers. In this report, we evaluated the Ωs constants for a variety of hetero-atom containing substituents in order to compare with the steric constants Es for these groups, which had already been determined from the rates of hydrolysis of the carboxylate esters bearing these groups.[3)]

In the process of definition and estimation of conventional steric substituent constants (Es and its modifications),[3,4)] careful consideration to exclude the electronic inductive and resonance effects had been taken. Thus, the independence of Es from the electronic effect was justified by the fact that the reaction used to define the steric constant has a nearly zero reaction constant in the Taft plot, i. e. $\rho = 0$.

The calculated Ωs constants for various polar substituents are given in Table 1. In calculating the surface of the substituent, Bondi's van der Waals radii were employed.[5)] The Ωs constants were then plotted against Es in order to examine the correlation between these steric con-

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[+] Dedicated to Professor Emeritus Osamu Simamura of The University of Tokyo on the occasion of his 80th birthday.

stants (Fig. 1). The Es vs. Ωs plots for α-hetero-atom substituted methyl groups consist a straight regression line [Es = (-25.79+2.55)Ωs +(5.86+0.23)] with a good correlation (r=0.961). The line is nearly parallel to the regression line for the assembly of alkyl groups, but separated clearly from the alkyl line[Es = (-20.27+0.92)Ωs +(5.10+0.06)]. The parallelism implies that the Es constant evaluates appropriately the steric effect by the substituent.$^{6)}$ However, the position of the α-heteroalkyl line lower than the alkyl line (in Fig. 1) suggests the participation of uncharacterized effect which retards the reaction of α-hetero-substituted alkanecarboxylates. As the deviation (separation in the vertical direction) of the plotted points of α-heteroalkyl groups from the alkyl line could not be correlated well with any electronic substituent constants, the separation must not be originated from any through-bond electronic effect, such as inductive or resonance effect.

Table 1. Ωs for Heteroalkyl Groups

Substituent	Ωs(R-CH_3)	Es$^{a)}$
FCH_2	0.228	-0.240
$ClCH_2$	0.239	-0.240
$BrCH_2$	0.242	-0.270
ICH_2	0.245	-0.370
$HOCH_2$	0.232	0.030
CH_3OCH_2	0.240	-0.190
$NCCH_2$	0.274	-1.140
CH_3COCH_2	0.267	-0.750
F_2CH	0.248	-0.670
Cl_2CH	0.275	-1.540
Br_2CH	0.280	-1.860
F_3C	0.268	-1.160
Cl_3C	0.318	-0.206
Br_3C	0.323	-2.430
$ClCH_2CH_2$	0.257	-0.900
$CH_3OCH_2CH_2$	0.267	-0.770

a) Ref. 3.

The effect could be interpreted as the conformational effect. The α-alkyl-substituted acetyl derivative (X=alkyl) generally takes an alkyl-carbonyl eclipsed conformation (1) preferably; while α-haloacetyl derivative tends to prefer the hydrogen-carbonyl eclipsed conformation (2) in most cases.$^{7)}$ This trend of conformation is in accord with our preliminary calculation of their conformational energies by PM3 (Table 2).$^{8)}$

As shown by Dubois and coworkers,$^{9)}$ the anti-clinal substituents [X in (2), stretching in the direction perpendicular to the carbonyl plane] on the α-carbon atom affect the rates of carboxylate reactions far more predominantly than the syn-periplanar substituent [X in (1), located cis to the carbonyl group]. Thus, the steric effect by α-halogen substituent should be overestimated in comparison to the effect by α-alkyl substitu-

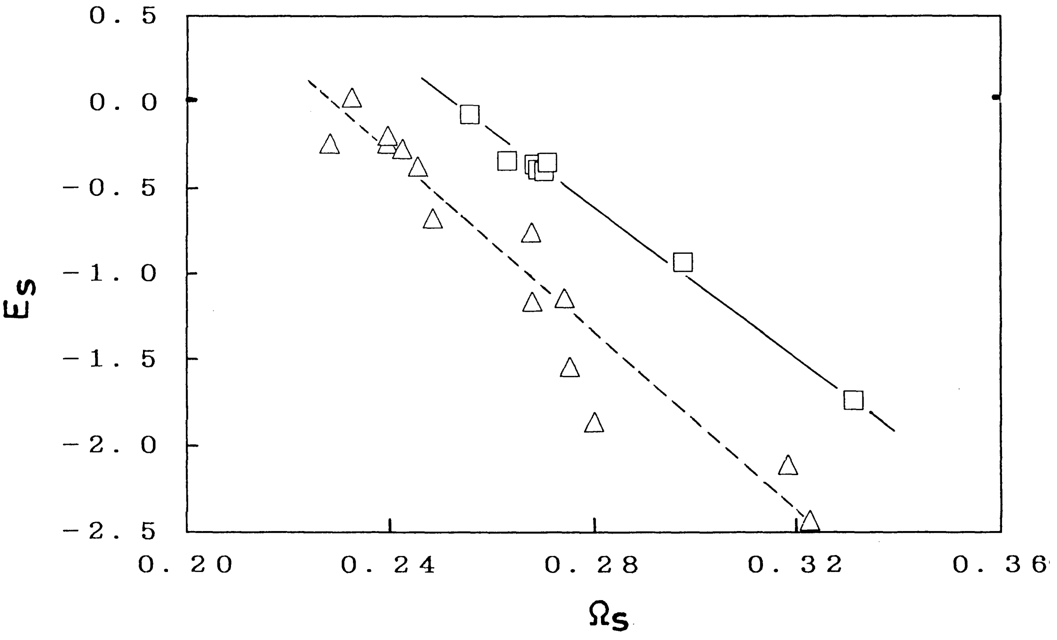
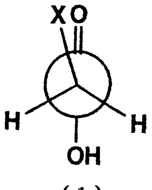
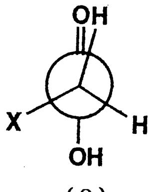
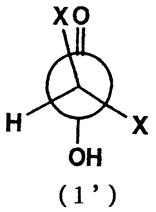
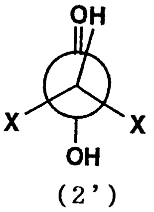


Fig. 1. The Es vs. Ωs plots for prim-alkyl and α-heteroaklyl groups, shown by the squares and the triangles, respectively.

Table 2. Relative Energies (kcal/mol) for the Conformers of XCH_2COOH and $X_2CHCOOH$ by PM3 MO Calculations$^{a)}$

	XCH_2COOH		$X_2CHCOOH$	
Conformer	 (1)	 (2)	 (1')	 (2')
X = CH_3	0.0 (0.0)	0.145 (0.538)	0.0 (0.0)	0.151 (0.520)
X = Cl	0.0	-0.044	0.0	-0.167

a) Steric energies from MM2 are given in parentheses.

ent, when the reaction of carboxylate is chosen as the reference. This is a sort of conformational effect which cannot be measured by the electronic substituent constants. The retarding effect by the α-clinal substituent can further be exaggerated by the repulsive electrostatic interaction between the electronegative hetero-atom substituent and the approaching nucleophile in the reference reaction of Es.

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6) This cannot be very clear evidence for the complete separation of the steric effect from the electronic effect in Es, however. Multi-variable correlation assuming that Es is dependent on both purely steric Ωs and electronic σ^* constants with an assembly including 7 aklyl and 16 hetero-alkyl groups gave the regression equation $Es = -14.71\Omega s - 0.316\sigma^* + 3.434$ with considerable reliability ($r=0.932$). The simple Es vs. Ωs correlation with the same assembly is only fair [$Es = -19.53\Omega s + 4.41$; $r=0.823$].

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