Conformational and Chemical Consequences of Vicinal Polar Bonds

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Summary A relationship exists between conformational energy differences in 1,2-disubstituted ethanes and the polar nature of the substituents; a parallel may be drawn with the observed stereochemistry of addition to olefins.

In a recent study,[1] Wolfe *et al.* consider the consequences of interactions between vicinal electron pairs or polar bonds upon the stability of molecular conformations, and upon the course of chemical reactions in which polar bonds are generated in a vicinal relationship to each other. They suggest a rule[1] which purports to predict conformational and configurational behaviour in such situations. If this rule is applied to the majority of 1,2-disubstituted ethanes[2] the wrong prediction is made about the relative stability of *gauche* and *trans* conformers. It does seem to apply, however, for highly electronegative substituents such as OR or F. A detailed criticism of the rule regarding vicinal electron pairs has been given by Pople *et al.*[3]

Table 1

Gas-phase energy differences, ΔE^{v}_{t-g}, *for* 1,2-*disubstituted ethanes,* XCH_2CH_2Y, (I) *and* 5-*substituted* 2-*isopropyl*-1,3-*dioxans,* (II)

	Substituent		ΔE^{v}_{t-g} (kcal mol^{-1}			Substituent	$\Delta E^{v}/2$ (kcal mol^{-1})
(I)[a]	X	Y			(II)[b]	X	
(a)	F	F	$-0{\cdot}6$,[c] 0	$(-0{\cdot}48)$[d]	(a)	F	0·3 (0·04)
(b)	F	Cl	0·5, 0·2	(0·44)	(b)	Cl	1·1 (0·89)
(c)	F	Br	0·30, 1·00	(0·66)	(c)	Br	1·25 (1·11)
(d)	Cl	Cl	1·20	(1·28)	(d)	OMe	0·63 (0·49)
(e)	Cl	Br	1·43	(1·51)			
(f)	Br	Br	1·77, 1·66	(1·74)			
(g)	I	I	2·6	(2·41)			
(h)	Me	F	$-0{\cdot}47$				
(i)	Me	Cl	$-0{\cdot}05$				
(j)	Me	Br	$-0{\cdot}28$, 0·0				

[a] Values from ref. 2. [b] Values from ref. 6. [c] Value from R. J. Abraham and R. H. Kemp, *J. Chem. Soc.* (*B*), 1971, 1240. [d] Values in parentheses calculated using the equation in the text.

Abraham and Parry[2] analyse the energy difference between various *gauche–trans* conformer pairs using the methods of classical mechanics; this approach breaks down in situations where the rule of Wolfe *et al.* holds, and is successful where this rule fails.

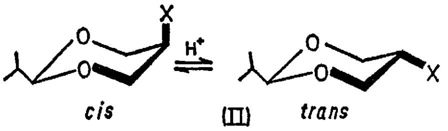
Table 1 lists the energy differences between such isomers in the gas phase. If the energy difference between *gauche* and *trans* forms of 1,2-disubstituted ethanes is considered solely in terms of the polar nature of the substituents, a significant trend emerges. For halogen substituents there is a linear relationship between the energy measured in the gas phase, ΔE^{v}_{t-g}, and the sum of their Huggins electronegativities (ΣE):

$$\Delta E^{v}_{t-g} = 8{\cdot}39 - 1{\cdot}128\Sigma E \qquad (1)$$

Values calculated for this difference are shown in Table 1 As the sum of the electronegativities increases, the *trans* conformer becomes relatively less stable and for 1,2-difluoroethane the *gauche* form predominates. The point at which *gauche* conformers become more stable occurs at an electronegativity sum of approximately 7·4 units on the Huggins scale, and 1,2-dioxygenated compounds ($\Sigma E = 7{\cdot}0$) are very near this. Solvents play an important part in deciding the point of change over, although our observations suggest that in any one solvent the correlation line is parallel to the gas-phase relationship; it appears in practice, that in any solvent 1,2-dioxygenated derivatives prefer to exist as *gauche* conformers.[4]

If one of the substituents is CH_3, the data do not fall on the main line; nevertheless, as the other group is changed for a more electronegative substituent a parallel trend is observed and the *gauche* conformer becomes increasingly favoured (Ih—j, Table 1).

These considerations have application to the conformational and configurational properties of cyclic systems in certain cases. Eliel[5] has observed that in 5-substituted 2-isopropyl-1,3-dioxans (II) there is a marked decrease in the preference for the *trans* compound, with the 5-substituent (X) equatorial, as the electronegativity of X increases:



(II)

Recently Abraham *et al*[6] have estimated the energy differences between these isomers in the vapour phase; if allowance is made for the fact that each isomer has two vicinal X–O interactions then the results lie upon the correlation line defined by equation (1) (IIa—d, Table 1). In all cases the *trans* isomer is more stable than the *cis* (contrary to the rule of Wolfe *et al.*), but as the group X changes from Br to F the energy difference decreases from 1·25 to 0·3 kcal mol^{-1}. Solvent effects result in a relative stabilisation of those isomers with *gauche* interactions, and in $CHCl_3$ solution compounds with X = F, OH, or NO_2 prefer to exist as the *cis* isomer while those in which X = Cl or Br are more stable in the *trans* form;[5] the trend does, however, parallel the vapour phase results.

It would appear that for 1,2-disubstituted situations in general, the rule of Wolfe *et al.*[1] only applies for very electronegative substituents, and for oxygen functions it is only reliable when the molecules are in solution. A better way of defining the situation would be: "When polar bonds are placed or generated on adjacent carbon atoms, the relative orientation of the bonds which is the most energetically favoured is the same as that observed in the corresponding 1,2-disubstituted ethane under the same physical conditions".

Table 2

Stereochemistry of the electrophilic addition of XY *to simple olefins*[a]

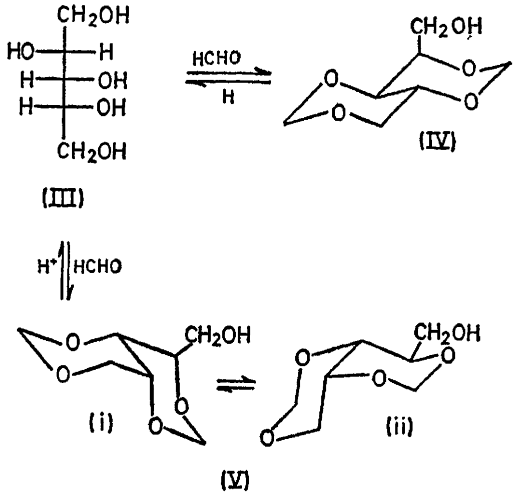
trans-Addition (predominant)[b]	*cis*-Addition (predominant)
I_2	$FOCF_3$
Br_2	$NO_2^+NO_3^-$
Cl_2	
HCl	
HBr	
HI	
ArSCl	

[a] From data in refs. 8 and 9.

[b] See text and ref. 8 for a discussion of the stereospecificity of the addition of Br_2 and Cl_2.

There are many important chemical consequences of these observations and we will present elsewhere a theoretical examination and a full account of the chemical significance. One example concerns the course of the condensation of D-arabinitol (III) with formaldehyde under acid conditions; this reaction could yield either the 2,4:3,5-diacetal with a *trans*-fused ring system (IV) or the 1,3:2,4-diacetal with the *cis*-fused rings (V). Steric considerations would clearly suggest that the *trans*-fused system (IV) should be the more stable, but experimentally it is found that (under conditions of equilibration) only the *cis*-fused isomer (V) is obtained as the thermodynamically favoured product.[7] This observation may be rationalised if it is realised that the rigid isomer (IV) has three *trans* oxygen–oxygen interactions while (V) can adopt a conformation (i) in which only *gauche* oxygen–oxygen interactions occur; in solution, the *gauche* arrangement is always preferred for vicinal oxygen substituents.

An important reaction in which polar substituents are generated in a vicinal relationship to each other is the addition of a molecule XY to an olefin. The accepted mechanism is a two-step process; initial attack by X^+ produces an intermediate carbonium ion which is captured by Y^- to yield the neutral adduct. The reaction is often markedly stereospecific, and Table 2 summarises the preferred nature of addition (*cis* or *trans*) for various addenda XY. The observation that the *trans* product is observed for the addition of, *e.g.* Br_2, has led to the suggestion that the intermediate carbonium ion formed by the attack of X^+ has a bridged structure.



Addition of Cl_2 to olefins is markedly less stereospecific than that of Br_2 however, and significant amounts of *cis* products are sometimes observed.[8] If the molecule XY has highly electronegative components, *e.g.*, N_2O_5 ($NO_2^+\,NO_3^-$) or CF_3OF ($F^+OCF_3^-$), the addition occurs specifically *cis*.[8,9] There is a remarkable parallel between these results and the trends observed for the influence of the substituents X and Y upon the relative stability of *cisoid* (*gauche*) and *trans* conformational isomers; as the sum of the electronegativities of X and Y increases there is an increasing tendency to form *cis* rather than *trans* adducts.

It may well be that the bridged carbonium ion intermediate is an unnecessary hypothesis, and that the electronic interactions which lead to the observed stereospecificity are "built in" to the potential energy profile as soon as the nucleophile Y^- approaches for the second step, even if an unsymmetrical carbonium ion ($R^1XCH\text{–}C^+HR^2$) is formed.

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[1] (a) S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc.* (*B*), 1971, 136; (b) S. Wolfe, *Accounts Chem. Res.*, 1972, **5**, 102.

[2] R. J. Abraham and K. Parry, *J. Chem. Soc.* (*B*), 1970, 539.

[3] L. Radom, W. J. Hehre, and J. A. Pople, *J. Amer. Chem. Soc.*, 1972, **94**, 2371.

[4] T. M. Connor and K. A. McLauchlan, *J. Phys. Chem.*, 1965, **69**, 1888; J. E. Mark and P. J. Flory, *J. Amer. Chem. Soc.*, 1966, **88**, 3702; R. G. Snyder and G. Zeibi, *Spectrochim. Acta*, 1967, **23A**, 391; K. G. R. Pachler and P. L. Wessels, *J. Mol. Structure*, 1970, **6**, 471.

[5] E. L. Eliel and M. K. Kaloustian, *Chem. Comm.*, 1970, 290; L. D. Hall and R. N. Johnson, *Org. Magnetic Resonance*, 1972, **4**, 369.

[6] R. J. Abraham, H. D. Banks, E. L. Eliel, O. Hofer, and M. K. Kaloustian, *J. Amer. Chem. Soc.*, 1972, **94**, 1913.

[7] J. F. Stoddart, 'Stereochemistry of Carbohydrates,' Wiley, London, 1971, p. 213.

[8] P. B. D. de la Mare and R. Bolton, 'Electrophilic Additions to Unsaturated Systems,' Elsevier, London, 1966.

[9] D. H. R. Barton, L. J. Danks, A. K. Ganguly, R. H. Hesse, G. Tarzia, and M. M. Pechet, *Chem. Comm.*, 1969, 227.

[10] L. Phillips and V. Wray, *J. Chem. Soc.* (*B*), 1971, 1618.