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α-SUBSTITUENT EFFECTS AND NON-BONDING ELECTRON INTERACTIONS AT THE S_N2 TRANSITION STATE, AN AB-INITIO STUDY.

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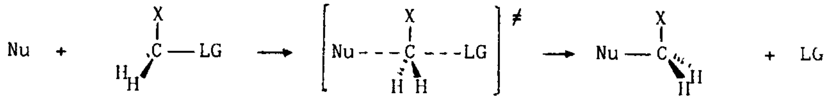
Abstract The trend in reactivity observed for methyl-, methylene-, and methoxymethyl-chlorides is rationalized in terms of turning on and off the four electron repulsion, at the transition state, between a lone pair on the substituent and a π orbital along the reaction coordinate

Despite extensive studies of the S_N2 reaction in solution,[1] in the gas phase,[2] and by application of molecular orbital (MC)[3] and valence bond (VB)[4] theories, some fundamental observations are not yet fully understood These include the trend in reactivity towards nucleophiles found in the series $CH_3OCH_2Cl > CH_3Cl > CH_2Cl_2$, which is the subject of the present study

While methyl chloride reacts readily with nucleophiles in the S_N2 mechanism, the replacement of one of its hydrogens by chlorine in methylene chloride results in a dramatic decrease in S_N2 reactivity [5] If instead of chlorine the equally electronegative oxygen replaces one of the hydrogens of methyl chloride, the resulting methoxymethyl chloride shows greatly enhanced reactivity towards nucleophiles, in both the S_N1 and S_N2 mechanisms [5] [6]

We submit that the major interaction responsible for the deactivating effect of an α chlorine substituent (X = Cl in Equation 1) is the four-electron repulsion between a p-lone pair on chlorine with the high lying, π-type orbital (HOMO-1) associated with the reaction coordinate at the S_N2 transition state (Fig 1a). The different behaviour of the methoxy substituent



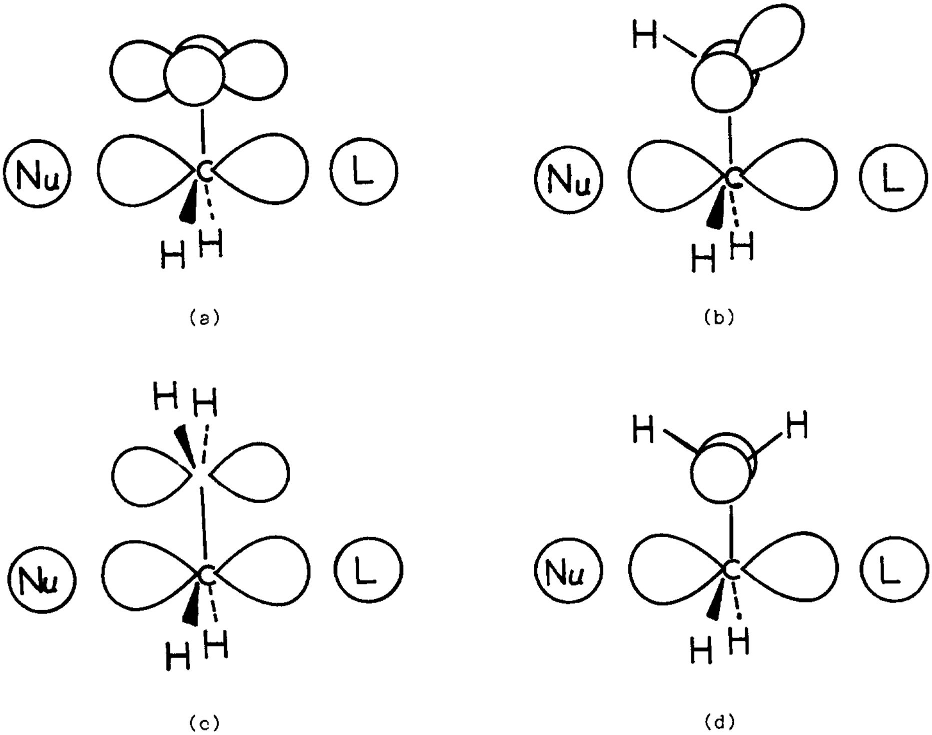
(1)

derives from its ability to adopt a geometry in which the p-lone pair orbital on oxygen is

TABLE Calculated 4-31G Activation Energies (Kcal/mol) for the S_N2 Reaction. For definitions of (a), (b), (c), and (d) see text.

Subst X (geometry)	Activation Energy (a)	(b)	Isodesmic E[1] (c)	ΔE(TS) (d)
H	48.8	57.3	0.0	
NH_2(off)	44.7	59.2	4.1	11.3
NH_2(on)	56.0	70.4	-7.2	
BH_2(off)	51.6	58.6	-2.9	-28.7
BH_2(on)	22.9	29.8	25.9	
OH(off)	41.8	-	7.0	11.7
OH(on)	53.5	-	-2.8	

[1] Positive values express a stabilizing effect of X on TS relative to H.



(a) (b)

(c) (d)

FIGURE 1 Schematic representation of MO interactions at the S_N2 TS· (a) X = halogen, (b) X OR, (c) X = planar NH_2, BH_2 in "on" geometry, (d) X = planar NH_2, BH_2 in "off" geometry.

perpendicular to the reaction coordinate orbitals, and overlap repulsion is minimized (Fig 1b). The other lone pair of electrons on oxygen does not effect similar repulsion because it has substantial s character, and hence is both lower in energy as well as less suitable for π-overlap than the p-lone pair.

To demonstrate these ideas we carried out ab-initio SCF-MO calculations[8] on a model S_N2 identity reaction (Equation 1, Nu = LG = H^-), with different α-substituents X In the model reaction hydride serves both as nucleophile and leaving group. While such a model is not expected to yield reliable activation energies, it nevertheless will produce the right trend in activation energies as X groups are changed.

We have used planar NH_2 and BH_2 as model substituents in order to test directly the effect of a p-lone pair or a vacant p-orbital on transition state (TS). These groups offer the advantage that their π interaction with the reaction coordinate orbitals can be turned on and off at will, by rotation about the C-X bond (Fig. 1c,d) The effect has been analyzed in terms of four methods: (a)comparison of activation energies taken as differences between TS energy and reactants' energy $\{\Delta E = E_{TS}-(E_{GS} + E_{H^-})\}$; (b)activation energies taken as $\Delta E = E_{TS} - E_{complex}$, where the complex is the optimized minimum energy structure when H is moved towards CH_3X; (c) the effect of X on TS and GS, relative to X = H, as measured by the isodesmic reaction[9] (Equation 2); and (d) the change in TS energy when X is rotated by 90° from on to off geometry

$$CH_5^- + CH_3X \rightleftharpoons CH_4 + CH_4X^- + \Delta E \qquad (2)$$

All structures in Equation 2 and in the Table represent fully optimized geometries at the 4-31G level,[10] the only constraint being C_{2v} symmetry of the TS[11] and planarity of NH_2 and BH_2 The results are shown in the Table.[12] Clearly, a very strong effect is observed in any one of the methods, where turning on the repulsive π interaction of planar NH_2 (or OH) strongly raises the activation barrier Conversely, in X = BH_2 turning on the π interaction produces a stabilizing, two electron interaction, manifest in the dramatic lowering of the S_N2 barrier.

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References and Notes

For leading references see (1-4)

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[6] It has been argued that electronegative substituents on the central carbon decrease the reactivity towards nucleophiles However, under strict S_N2 reaction conditions the substituted benzyl chlorides $X\text{-}C_6H_4CH_2Cl$ show *increased* rates of displacement when substituted with electron withdrawing groups (Hammett reaction constant $\rho = 0.8$).[7]

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[8] The GAUSSIAN 70 system of programs was used. W. J. Hehre, W. A Lathan, R Ditchfield, M. D Newton, and J A. Pople, QCPE 236, Indiana University

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[10] R Ditchfield, W. J. Hehre, and J. A. Pople, *J. Chem. Phys* , *54*, 724 (1971)

[11] With the exception of X = OH, where only the bonds between axial hydrogens and carbon were kept equal

[12] X = Cl could not be included in the Table due to difficulties in optimization at the 4-31G level This transition state tends to decompose to CH_4 and X^-

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