

The Substituent Effect of a β -Carbon-Oxygen Bond in Radical Reactions

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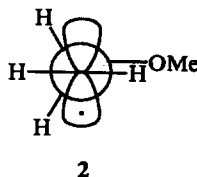
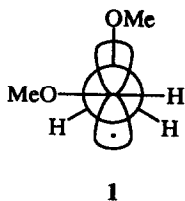
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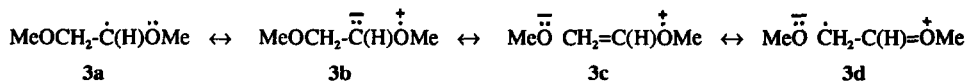
Abstract: Rates of chlorine-atom abstraction by $\text{Me}_2\text{N}\rightarrow\dot{\text{B}}\text{HBu}$ and $\text{Et}_3\text{Si}\cdot$ from RCH_2Cl [$\text{R} = \text{Pr}$, MeOCH_2 , $(\text{MeO})_2\text{CH}$, Me_2Si] have been determined using ESR spectroscopy. The relatively rapid abstraction of chlorine from $\text{MeOCH}_2\text{CH}_2\text{Cl}$ by the very nucleophilic $\text{Me}_2\text{N}\rightarrow\dot{\text{B}}\text{HBu}$ is attributed to a kinetic anomeric effect.

The importance of polar effects on the reactions of electrically-neutral free radicals has been recognised for very many years.¹ Such effects can be understood in terms of the frontier molecular orbital interactions² between a radical and its co-reactant, or by including canonical structures which reflect charge transfer between the reactant residues in a valence-bond description of the transition state.^{1a,b} Polar factors have often been invoked to account for α -substituent effects³ on radical reactions, however the possible part played by polar factors in determining β -substituent effects³ has often been overlooked in favour of enthalpic factors (*i.e.* the effect of the substituent on the thermochemistry of the overall reaction). Indeed, the polar and enthalpic effects of a given substituent can affect the activation energy of a reaction in the same or in opposite senses, depending on the direction of charge transfer in the particular transition state.⁴

In 1982, Barton, Hartwig and Motherwell⁶ proposed that alkyl radicals were stabilised by β -alkoxy substituents and that this *purely enthalpic* effect resulted in the more ready formation of β -alkoxyalkyl radicals compared with unsubstituted radicals of otherwise similar structure. However, these conclusions were based on the overall rates of chain reactions, which do not necessarily parallel the rate of an individual propagation step.

The radical $\text{MeOCH}_2\dot{\text{C}}(\text{H})\text{OMe}$ adopts the conformation **1**,⁷⁻⁹ in which the β -C-O bond eclipses the axis of the semi-occupied orbital on C_α , and the conformational preference shown by this type of radical has been attributed to the desire to optimise the stabilising interaction between the unpaired electron on C_α , a lone pair on the α -oxygen atom, and the β -C-O σ^* orbital.^{8,10,11} In valence-bond terms, conformation **1** allows maximum contribution from structures **3c** and **3d**, in which the negative charge on C_α in **3b** has been transferred to the β -oxygen atom.⁸ This is an example of the generalised anomeric effect¹² and may be described equivalently in the language of perturbational

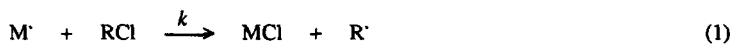




molecular orbital theory.^{10,11} In contrast, the radical $\text{MeOCH}_2\dot{\text{C}}\text{H}_2$, which lacks the α -methoxy group, is believed to adopt the conformation 2,⁷ in which hyperconjugative interaction between the unpaired electron and a β -C-H σ -bonding electron pair is preferred over any interaction with the β -C-O bond.^{13,14}

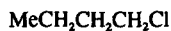
Beckwith and Brumby⁹ have concluded that the β -MeO substituent has only a minor influence on the rate of hydrogen-atom abstraction by $\text{Bu}'\text{O}'$ from $\text{MeOCH}_2\text{CH}_2\text{OMe}$ to give $\text{MeOCH}_2\dot{\text{C}}(\text{H})\text{OMe}$, although it does confer on the latter radical a preference for the conformation 1. However, Dupuis *et al.*¹¹ have reported that a β -C-O bond influences not only the ground-state conformation of carbon-centred radicals, but also increases the rate of their formation by chlorine-atom abstraction using tributylstannyl radicals, provided that the C-O bond is correctly orientated with respect to the C-Cl bond undergoing cleavage in the transition state.¹¹ Thus, the existence of a *kinetic* β -oxygen substituent effect remains a subject of controversy and, as noted above, the magnitude of any such effect is not necessarily related to the influence of a β -oxygen atom on the overall reaction enthalpy.

Against this background, we have determined the relative rates of halogen abstraction from a number of alkyl chlorides (eqn. 1), using ESR spectroscopy to monitor the elementary atom-transfer process in isolation.¹⁶ The



abstracting metalloidal radicals M' investigated were $\text{Me}_3\text{N} \rightarrow \dot{\text{B}}\text{HBu}$ (TBB') and $\text{Et}_3\text{Si}'$ (TES'), produced by reaction of photochemically-generated t-butoxyl radicals with MH (eqns. 2 and 3). Cyclopropane solutions containing di-t-butyl peroxide (DTBP), MH, and two chlorides R^1Cl and R^2Cl were irradiated with UV light at 153-253 K while the sample was positioned in the microwave cavity of an ESR spectrometer.¹⁶ The steady-state value of $[\text{R}^1']/[\text{R}^2']$ during continuous photolysis was determined by double-integration and/or computer simulation of appropriate lines in the ESR spectra and is related to the relative rate constants for chlorine-atom abstraction by eqn. 4, provided that R^1 and R^2 are removed by self- and cross-reactions which have equal (diffusion-controlled) rate constants.¹⁷ The chlorides 4-7 were chosen for our initial studies and the relative rate data obtained are presented in the Table.¹⁸

$$k_1/k_2 = [\text{R}^1][\text{R}^2\text{Cl}]/[\text{R}^2][\text{R}^1\text{Cl}] \quad (4)$$



4



5



6



7

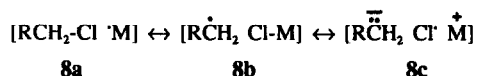
Our previous work¹⁹ has shown that TBB' abstracts chlorine much more rapidly from 1-chlorobutane 4 than does TES'. Despite being the *more reactive* radical, TBB' is *more selective* than TES' in competitive abstraction of chlorine from 4 and 5 or from 4 and 6, a trend which provides evidence for the importance of polar factors in determining the rates of halogen abstraction. As is evident from the tabulated data, the relative rates of chlorine-atom abstraction are governed mainly by differences in activation energies. The transition state for chlorine-atom transfer to a nucleophilic metalloidal radical M' can be described as a resonance hybrid of the structures 8a-c and the

TABLE: Rate constants (k_{rel}) at 200 K and Arrhenius parameters (A_{rel} and E_{rel}) for chlorine-atom abstraction from RCH_2Cl relative to abstraction from 1-chlorobutane **4** in cyclopropane.

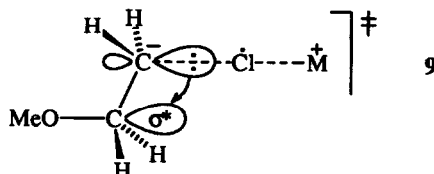
RCH_2Cl	Abstracting radical M^\cdot					
	TBB $^\cdot$			TES $^\cdot$		
	k_{rel}	A_{rel}^a	E_{rel}^b	k_{rel}	A_{rel}^a	E_{rel}^b
$\text{MeCH}_2\text{CH}_2\text{CH}_2\text{Cl}$ 4	(1)	(1)	(0)	(1)	(1)	(0)
$\text{MeOCH}_2\text{CH}_2\text{Cl}$ 5	5.5	0.82	3.16	1.4	1.38	0.05
$(\text{MeO})_2\text{CHCH}_2\text{Cl}$ 6	17.2	0.52	5.82	2.2	1.44	0.68
$\text{Me}_3\text{SiCH}_2\text{Cl}$ 7	46.3	0.78	6.79	38.2	0.66	6.75

a $A_{\text{rel}} = A(\text{RCH}_2\text{Cl})/A(\text{BuCl})$. b $E_{\text{rel}} = E_{\text{a}}(\text{BuCl}) - E_{\text{a}}(\text{RCH}_2\text{Cl})$ in kJ mol^{-1} .

contribution from **8c** will increase as the ionisation energy of M^\cdot decreases and as the electron affinity of $\text{R}\dot{\text{C}}\text{H}_2$ increases.



Charge transfer will be especially important in the transition state for abstraction of chlorine by the very nucleophilic²⁰ TBB $^\cdot$. The calculated²¹ vertical ionisation energy of $\text{H}_3\text{N} \rightarrow \dot{\text{B}}\text{HMe}$ is only 5.47 eV, appreciably less than the ionisation energy of $\text{Me}_3\text{Si}^\cdot$ (6.81 eV),²² which is expected to be similar to that of TES $^\cdot$. While the β -MeO groups in **5** and **6** exert only a small activating effect on chlorine-atom abstraction by TES $^\cdot$, they do substantially increase the rate of abstraction by TBB $^\cdot$. When $\text{M}^\cdot = \text{TBB}^\cdot$, structure **8c** evidently contributes more to the transition state for abstraction from **5** or **6** than to that for abstraction from **4**. We propose that negative charge on C_α in the transition state for abstraction from **5** is delocalised into the β -C-O σ^* orbital, an anomeric stabilisation not possible for abstraction from **4**.²³ The preferred orientation of the β -C-O bond with respect to the C-Cl bond undergoing cleavage and the developing radical centre in the transition state should be as shown in **9** (*cf.* the reason for the adoption of conformation **1**, discussed above). Once the chlorine has departed, interaction of the unpaired electron in $\text{MeOCH}_2\dot{\text{C}}\text{H}_2$ with the β -C-O σ or σ^* orbitals is insufficient to maintain the eclipsing C-O bond and the preferred geometry of this radical is as shown in **2**.



Both TBB $^\cdot$ and TES $^\cdot$ abstract chlorine much more rapidly from chloromethyl(trimethyl)silane **7** than from 1-chlorobutane. The strength of the C-Cl bond in **7** has not been determined, but $DH^\circ(\text{Me}_3\text{SiCH}_2\text{-H})$ is 415 kJ mol^{-1}

[compared with 417 kJ mol^{-1} for $DH^*(\text{Me}_3\text{CCH}_2\text{-H})$], indicating that the radical-stabilising power of an α -silyl substituent is very small.²⁴ As discussed by Wilt *et al.*,⁵ it is the ability of an α -silyl substituent to stabilise negative charge on an adjacent carbon atom in the transition state that is probably dominant in conferring high reactivity on **7** in chlorine-atom transfer to the nucleophilic $\text{Bu}_3\text{Sn}^{\cdot}$. We attribute the high reactivity of **7** towards TBB $^{\cdot}$ and TES $^{\cdot}$ to this polar effect of the α -silyl substituent in the transition state and, in this respect, an α -Me $_3$ Si group is more effective than a β -MeO group.

The value of k_{rel} for **5** is 5.3 in oxirane-Bu t OH (2:1 v/v) at 200 K, very close to the value in cyclopropane, suggesting that the reactants and the transition state are stabilised to similar extents in the more polar solvent.

We conclude that although the enthalpic effect of a β -C-O bond on chlorine abstraction from C_α is probably negligible, nevertheless a β -oxygen substituent can exert a stabilising effect on the polar transition state for abstraction of chlorine by the very nucleophilic TBB $^{\cdot}$, probably *via* the same type of anomeric effect which leads to the conformation **1** being favoured for the radical $\text{MeOCH}_2\dot{\text{C}}(\text{H})\text{OMe}$.

REFERENCES AND NOTES

- (a) Walling, C. *Free Radicals in Solution*, Wiley, New York, 1957. (b) Russell, G.A. in *Free Radicals*, vol. I, ed. Kochi, J.K., Wiley-Interscience, New York, 1973, pp.293-311. (c) Minisci, F.; Citterio, A. *Adv. Free Radical Chem.*, **1980**, *6*, 65.
- Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*, Wiley-Interscience, 1976, ch.5.
- An α -substituent is one attached directly to the original or the new radical centre; a β -substituent is one attached to an atom adjacent to these centres.
- The distinction between the enthalpic and the kinetic polar effect of an α -silyl substituent is very clearly made by Wilt *et al.*⁵ in their discussion of the reduction of (halogenoalkyl)silanes by organotin hydrides.
- Wilt, J.W.; Belmonte, F.G.; Zieske, P.A. *J. Am. Chem. Soc.*, **1983**, *105*, 5665.
- Barton, D.H.R.; Hartwig, W.; Motherwell, W.B. *J. Chem. Soc., Chem. Commun.*, **1982**, 447.
- For simplicity, the radical centre is shown as planar in **1** and **2**. In both, the equilibrium geometry at C_α is likely to be slightly non-planar with a low barrier to inversion.
- Dobbs, A.J.; Gilbert, B.C.; Norman, R.O.C. *J. Chem. Soc., Perkin Trans. 2*, **1972**, 786. Gilbert, B.C.; Trenwith, M.; Dobbs, A.J. *J. Chem. Soc., Perkin Trans. 2*, **1974**, 1772.
- Beckwith, A.L.J.; Brumby, S. *J. Chem. Soc., Perkin Trans. 2*, **1987**, 1801.
- Korth, H.-G.; Sustmann, R.; Dupuis, J.; Giese, B. *J. Chem. Soc., Perkin Trans. 2*, **1986**, 1453.
- Dupuis, J.; Giese, B.; Rülegge, D.; Fischer, H.; Korth, H.-G.; Sustmann, R. *Angew. Chem. Internat. Edn. Engl.*, **1984**, *23*, 896.
- Kirby, A.J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer-Verlag, Berlin, 1983, pp.75-77.
- Chen, K.S.; Kochi, J.K. *J. Am. Chem. Soc.*, **1974**, *96*, 1383.
- The preferred conformation calculated¹⁵ for the closely-related 2-hydroxyethyl radical differs appreciably from that shown in **2**. Although this does not affect our arguments, we confirm the report¹⁵ that the ESR spectrum of $\text{MeOCH}_2\dot{\text{C}}\text{H}_2$ shows no significant line-broadening down to 150 K, consistent with equivalent or very rapidly-exchanging β -protons.
- Guerra, M. *J. Am. Chem. Soc.*, **1992**, *114*, 2077. Sosa, C.; Schlegel, H.B. *J. Am. Chem. Soc.*, **1987**, *109*, 7007.
- Diart, V.; Roberts, B.P. *J. Chem. Soc., Perkin Trans. 2*, **1992**, 1761.
- Davies, A.G.; Griller, D.; Roberts, B.P. *J. Chem. Soc. B*, **1971**, 1823.
- Hyperfine splittings (in G) at 200 K in cyclopropane. $\text{MeOCH}_2\dot{\text{C}}\text{H}_2$: 21.95 ($2H_\alpha$), 32.59 ($2H_\beta$), $g = 2.0026$. No splitting from the methoxy-protons was resolvable; the reported¹³ splitting of 0.41 G at 137 K from three equivalent protons is clearly an error (see Figure 2 in ref. 13). $(\text{MeO})_2\text{CH}\dot{\text{C}}\text{H}_2$: 22.68 ($2H_\alpha$), 25.67 ($1H_\beta$), $g = 2.0026$; no splitting from the methoxy-protons was resolved, but at lower temperature (160 K) a quartet splitting of 0.18 G from one methyl group was detected. $\text{Me}_3\text{Si}\dot{\text{C}}\text{H}_2$: 20.92 ($2H_\alpha$), 0.42 ($9H_\beta$), [15.48 (^29Si) and 5.53 (^{13}C)] at 160 K], $g = 2.0024$.
- Kaushal, P.; Mok, P.L.H.; Roberts, B.P. *J. Chem. Soc., Perkin Trans. 2*, **1990**, 1663.
- Paul, V.; Roberts, B.P.; Willis, C.R. *J. Chem. Soc., Perkin Trans. 2*, **1989**, 1953.
- The difference between the UMP3(full)/6-31G**//UHF/6-31G** energy for $\text{H}_2\text{N}\rightarrow\text{BHMe}$ (-121.498211 hartree)²⁰ and the spin-restricted energy at this level for the corresponding cation (-121.297110 hartree) of the same geometry as the radical.
- Danovich, D.; Apeloig, Y.; Shaik, S. *J. Chem. Soc., Perkin Trans. 2*, **1993**, 321.
- The inductive effect of the β -oxygen atoms may also assist in stabilising the negative charge on the α -carbon atom.
- Walsh, R. *Acc. Chem. Res.*, **1981**, *14*, 246.

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