treated with a borane-THF (BH_3–THF) complex (500 μL of a 1 M solution), and stirred at room temperature under N_2. After 12 h an additional 300 μL of BH_3–THF solution was added, and after an additional 24 h of stirring at room temperature the reaction was quenched with saturated NH_4Cl solution (6 mL). The water layer was extracted with CH_2Cl_2 (4 × 10 mL), and the organics were combined, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude alcohol was then dissolved in CH_2Cl_2 (10 mL), and triethylamine (500 μL, 3.6 mmol), acetic anhydride (50 μL, 0.55 mmol), and a catalytic amount of (dimethylamino)pyridine were added at room temperature under N_2. After 8 h a NH_4Cl solution (5 mL) was added and the reaction mixture transferred to a separatory funnel. The water layer was extracted with CH_2Cl_2 (3 × 10 mL), and the organics were combined, washed with brine, and dried over $MgSO_4$. Concentration in vacuo followed by chromatography on silica gel, eluting with 1:2.5 ethyl acetate/hexane, gave peracetylated L-glucose **31** (20 mg, 42% from **27**): mp 110–112 °C; $[\alpha]^{23}{}_{D}$ −4.8° (*c* 0.23, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) 5.72 (d, *J* = 8.08 Hz, 1 H), 5.35–5.05 (m, 2 H), 4.30 (dd, *J* = 14.48, 12.53 Hz, 1 H), 4.12 (dd, *J* = 2.23, 12.53 Hz, 1 H), 3.92–3.80 (m, 1 H), 2.12 (s, 3 H), 2.09 (s, 3 H), 2.04, (s, 6 H), 2.02 (s, 3 H); IR ($CHCl_3$) 3020, 1758, 1370, 1220, 1080, 1040 cm^{-1}; MS (chemical ionization, ammonia), *m/e* (relative intensity) 408 (M^+ + 18, 1.1), 242 (12.7), 157 (13.9), 114 (17), 97 (19.1). A sample of β-D(+)-glucose pentaacetate was obtained from Aldrich. It was identical with compound **31** by ^1H NMR, but opposite in optical rotation, $[\alpha]^{23}{}_{D}$ +4.2° (*c* 0.25, $CHCl_3$).

L(−)-**Glucose (32).** To β-L(−)-glucose pentaacetate (**31**) (20 mg, 0.051 mmol) in methanol (5 mL) at room temperature was added a catalytic amount of NaOMe (1 mg). The reaction was allowed to stir at room temperature for 6 h at which time acidic ion-exchange resin (Dowex H CR-S) was added until pH 6–7. The solution was filtered and then the volatiles were removed in vacuo to give the unprotected L-glucose **32** (8 mg, 86%): mp 128–142 °C; $[\alpha]^{23}{}_{D}$ −52° (*c* 0.8, H_2O); ^1H NMR (D_2O, 250 MHz) δ 5.20–4.40 (m, 1 H), 4.10–3.90 (m, 1 H), 3.80–3.00 (m, 5 H). A sample of D(+)-glucose was obtained from Aldrich. Its ^1H NMR was identical with compound **32** but opposite in optical rotation $[\alpha]^{23}{}_{D}$ 52.4° (*c* 1.0, H_2O).

Acknowledgment. This research was supported by PHS Grant HL 25848. An American Chemical Society Graduate Fellowship, sponsored by Pfizer, Inc., to M. B. is gratefully acknowledged. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Grant CHE 7916210. We also thank Dr. B. Segmuller for the crystallographic determination of compound **14**.

Registry No. 6a, 88198-68-9; **7a**, 104194-94-7; **7b**, 104194-95-8; **7c**, 104263-87-8; **7d**, 90130-49-7; **9a**, 87860-23-9; **9b**, 87860-24-0; **9c**, 87860-25-1; **9d**, 87860-26-2; **10a**, 87860-19-3; **10b**, 87860-20-6; **10c**, 87860-21-7; **10d**, 87860-22-8; **14**, 87804-49-7; **15**, 104194-96-9; **16**, 104130-15-6; **17**, 87804-50-0; **18**, 87804-52-2; **19** (R = COOH), 87804-51-1; **19** (R = CH_2OH), 104130-16-7; **19** (R = CH_2OAc), 87804-53-3; **22a**, 104130-17-8; **22b**, 104130-19-0; **23a**, 104130-18-9; **23b**, 104130-23-6; **23c**, 104130-20-3; **23d**, 104130-21-4; **23e**, 104130-22-5; **24a**, 104194-97-0; **24b**, 104195-01-9; **24c**, 104194-98-1; **24d**, 104194-99-2; **24e**, 104195-00-8; **25**, 104263-88-9; **26**, 104263-89-0; **26** (X = OH, β-H), 104130-24-7; **26** (diol), 104130-25-8; α-**27**, 104195-02-0; β-**27**, 104195-03-1; **28**, 104195-04-2; **29**, 104195-05-3; **30**, 104195-06-4; **31**, 66966-07-2; **31** (R = CH_2OH; P = Ac), 104195-07-5; **32**, 39281-65-7.

Supplementary Material Available: Data for the X-ray determination of the structure of compound **14** including protocols, positional and thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

Anatomy of an S_N1 Reaction. Crystal Structure–Reactivity Correlations for 1-Arylethanol Derivatives

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Received February 28, 1986

Abstract: Crystal structures of 11 1-arylethanol derivatives show well-defined trends in bond length, angle, and conformation with changing patterns of substitution. The trends mirror changes in the reactivity of these compounds in the S_N1 reaction and show the benzylic system adjusting to accommodate developing positive charge during the early stages of C–O bond breaking. Bond length–reactivity correlations are more complicated than observed in systems previously studied, because the length of the C–OX bond depends on the dihedral angle with the aromatic ring. This dependence is systematic, and can be allowed for, but shows that bond lengths may be conformation-dependent. Thus, a compound cannot necessarily be characterized by a unique bond length R–X, as it can be by a unique rate constant for the cleavage of the R–X bond under standard conditions.

Penetrating mechanistic insights can be derived from the systematic study of crystal structures of suitable systems,[1] not least from trends in bond lengths.[2] We have demonstrated linear correlations between the lengths of C–O bonds in a range of systems R–OX and the rates at which the same bonds are broken heterolytically in solution—the longer the bond, the faster it breaks.[2-4]

In the systems we have studied so far, the group R has been held constant while the group X was varied, but there is convincing qualitative evidence[2] that the length of the R–OX bond depends also on the nature of R and specifically on its ability to stabilize a positive charge. This can be simply expressed in terms of a contribution to the ground-state structure from the valence tautomer $R^{+\,-}OX$, which depends on the stability of both cation and oxyanion.[4]

We report an investigation of the crystal structures of 11 derivatives of 1-phenylethanol (**1**), where C–O bond cleavage ($\mathbf{1} \rightleftharpoons \mathbf{1}^{\pm}$) corresponds to an S_N1 reaction at a benzylic center

The system is chosen to allow systematic variation of the stability of both ionic fragments ($\mathbf{1}^{\pm}$) by varying substituents X and Y. We can then analyze the dependence of the C–OX bond length

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[‡] Institut für Anorganische Chemie.

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(2) Allen, F. H.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6197.

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(4) Jones, P. G.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6207.

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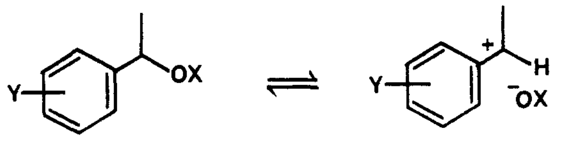
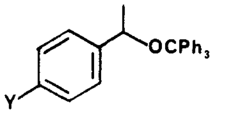


1 $1^{\pm}$

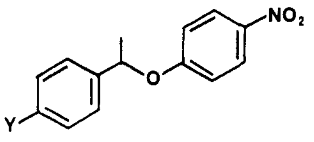
on such conventional measures of substituent effects as the pK_a of HOX and Hammett's σ_Y. In fact the results also reveal marked trends in other geometrical parameters, which are clearly related to the C–O cleavage process.

Results

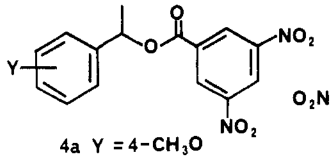
Details of compounds **1**, of the crystal structure determinations, and full structural data have been published or will appear shortly.[5] The choice of compounds, as always in an investigation of this sort, is limited by their availability as single crystals of good quality and stability. We set out to compare structures for four differently substituted (Y = *p*-MeO, H, Cl, and NO_2) 1-arylethyl alkyl ethers (**1**, X = R), aryl ethers (**1**, X = 4-nitrophenyl), esters (**1**, X = constant carboxylic acyl), and arenesulfonates (**1**, X = SO_2Ar). In practice we obtained accurate structures for 8 of a possible 16 compounds. Of several series of alkyl and silyl ethers investigated, the triphenylmethyl derivatives **2** proved clearly the most successful, and we report structures for three compounds (**2**, Y = H, Cl, and NO_2), as well as for two *p*-nitrophenyl ethers (**3**, Y = MeO and H). We have a full set of four ester structures, three of them 3,5-dinitrobenzoates (**4**, Y = 4-MeO and H and 3-F). The fourth, 1-(4-nitrophenyl)ethyl chloroacetate (**5**) is derived from an acid of almost exactly the same pK_a (2.82 compared with 2.86) as 3,5-dinitrobenzoic acid.[6] But sulfonate esters **6** were not sufficiently stable without electron-withdrawing substituents Y. We collected data for the *p*-toluenesulfonate (**6**, Y = NO_2, Ar = *p*-tolyl), but this turned out to be disordered.[5g] However, the 2-naphthalenesulfonate gave a good structure. We also prepared a number of phosphate triesters, of which only the diphenyl phosphate **7** gave useful crystals.



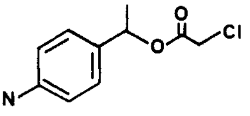
2a Y = H
2b Y = Cl
2c Y = NO_2



3a Y = CH_3O
3b Y = H



4a Y = 4-CH_3O
4b Y = H
4c Y = 3-F



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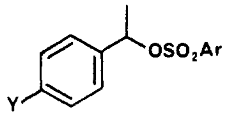
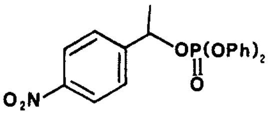


6 Y = NO_2



7

Selected data describing the geometry at the benzylic center of all 11 compounds of **1** are shown in Table I. Sources of error in structure determinations have been assessed previously.[7] We consider that we are on firm ground when analyzing *trends* in geometrical parameters for a homogeneous set of compounds, with similar thermal parameters, using results obtained in the same laboratory under standard conditions.

One apparent anomaly arises in the results for the 4-nitrophenyl ether (**3**, Y = H) of 1-phenylethanol, which has two independent molecules in the asymmetric unit. The key C–O bond length (*a*), is clearly different in the two molecules, 1.450 (4) vs. 1.420 (5) Å, through almost all other bond lengths are identical within experimental error. This discrepancy is disturbing, because our use of bond lengths as an index of reactivity depends on accurate and reproducible measurements of interatomic distances and attributes significance to small differences between related structures. In this case the C–O bond length in molecule 2 is unexpectedly short.[2]

A detailed comparison of the two molecules suggests a possible explanation. The largest difference is in the angle between the two planes defined by the nitrophenoxy ring and the nitro group. These are almost coplanar in molecule 1 (mean dihedral angle 2.2°), but the nitro group in molecule 2 is rotated out of the plane by 13.6° ± 1°, as a result of an interaction of one nitro group oxygen with the C–Me of a second molecule 2.[5d] Apparently this rotation is sufficient to reduce the "effective electronegativity" of the ether oxygen, presumably by reducing π,π-overlap between the nitro group and the ring.[8] Consistent with this explanation, the aromatic C–O bond is significantly shorter in molecule 1.[5d] It is difficult to believe that this effect, though in the correct direction, is large enough to explain the observed discrepancy. However, since molecule 2 appears to be exceptional, and the nitro group in our other nitrophenyl ether (**3**, Y = OMe) lies in the plane of the aromatic ring, we use, not without reservations, the data for molecule 1 in the comparison of structural parameters in Table I.

Discussion

The full set of C–OX bond lengths (*a* in Table I) ranges from 1.420 (5) to 1.481 (3) Å and shows a sensitivity to substitution comparable with other systems we have studied which undergo ready ionic cleavage of the C–O bond under suitable conditions.[4] The C–OX bond is significantly longer for unsubstituted 1-phenylethyl derivatives than for derivatives R_2CHOX of secondary aliphatic alcohols,[2] and this difference appears to be greater for better leaving groups HOX. For $PhCHMeOCPh_3$ the C–O bond length is 1.444 Å, compared with a mean value of 1.432 (2) Å for aliphatic ethers $R_2CH–OR'$,[2] whereas for the corresponding esters the figures are 1.481 and 1.460 (2) Å. In fact the C–OX bond lengths measured for 1-phenylethyl systems are similar to values obtained for the corresponding *tertiary* alkyl derivatives,[2] recalling Ingold's "rough rule"[9] that an α-phenyl substituent is about as effective as two alkyl substituents for determining reactivity in the S_N1 reaction.

As expected, increasing electron withdrawal in X leads to an increase in the length of the C–OX bond, and this bond lengthening is clearly reduced by electron-withdrawing substituents Y. However, there is no significant increase in the C–OX bond length when the 4-methoxy group is introduced, either for the *p*-nitrophenyl ether (**3**) or for the ester (**4**). 4-MeO is potentially a strong π-donor, commonly inducing large rate accelerations in heterolytic reactions of benzylic systems, but it clearly has no related effect in the ground states of these compounds. So very simple correlations between bond length and reactivity, of the sort we have observed previously,[4] cannot hold for these compounds. Possible reasons are discussed below. We first treat the effects of substituents X and Y separately.

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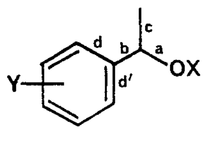
[6] Jencks, W. P.; Regenstein, J. *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; CRC: Cleveland, OH, 1976; Vol. I, p 305.

[7] Briggs, A. J.; Glenn, R.; Jones, P. G.; Kirby, A. J.; Ramaswamy, P. *J. Am. Chem. Soc.* **1984**, *106*, 6200.

[8] A search of the Cambridge Structural Database for indications of similar behavior in other 4-nitrophenoxy systems found that the small number of structures available are mostly of different types. No useful conclusions could be drawn.

[9] Ingold, C. K. *Structure and Mechanism in Organic Chemistry*; Cornell University: Ithaca, NY 1953; p 325.

Table I. Geometry at the Benzylic Center of 1



1

	bond lengths, Å			bond angles, deg			torsion angles, deg		
compd	*a*	*b*	*c*	*bc*	*ab*	*ac*	*cbd*	*abd'*	θ(90 − *abd'*)
2, Y = H	1.444 (4)	1.514 (4)	1.516 (5)	110.1 (3)	113.0 (3)	106.5 (3)	86.9 (4)	29.8 (4)	60.2
2, Y = Cl	1.442 (3)	1.510 (3)	1.518 (4)	109.5 (3)	112.5 (3)	106.3 (2)	83.1 (4)	34.9 (4)	55.1
2, Y = NO_2	1.433 (3)	1.515 (3)	1.525 (3)	108.6 (2)	108.0 (2)	111.8 (2)	74.4 (3)	20.6 (3)	69.4
3, Y = MeO	1.448 (4)	1.511 (4)	1.511 (4)	113.5 (3)	110.1 (3)	104.8 (3)	74.5 (4)	42.5 (4)	47.5
3, Y = H	1.450 (4)	1.512 (6)	1.507 (5)	111.4 (4)	111.0 (3)	105.9 (3)	71.6 (4)	46.2 (4)	43.8
	1.420 (5)	1.511 (6)	1.517 (7)	112.2 (4)	110.7 (3)	107.7 (4)	76.9 (5)	43.5 (5)	46.5
4, Y = 4-MeO	1.479 (5)	1.494 (6)	1.513 (6)	115.8 (4)	106.1 (4)	106.1 (4)	48.8 (6)	68.6 (6)	21.4
4, Y = H	1.481 (3)	1.498 (3)	1.506 (5)	114.9 (3)	106.7 (2)	108.0 (3)	56.1 (4)	63.6 (3)	26.4
4, Y = 3-F	1.459 (4)	1.500 (5)	1.511 (6)	113.1 (4)	106.2 (3)	110.1 (3)	86.2 (4)	28.7 (5)	61.3
5	1.452 (4)	1.504 (4)	1.506 (5)	112.6 (3)	107.8 (3)	108.8 (3)	78.6 (4)	18.0 (4)	72.0
6, Y = NO_2, Ar = 2-naphthalenyl	1.476 (3)	1.506 (4)	1.494 (5)	114.9 (3)	110.4 (3)	104.7 (3)	61.9 (4)	56.2 (4)	33.8
7	1.466 (3)	1.505 (4)	1.504 (4)	112.6 (2)	109.6 (3)	106.7 (2)	79.2 (3)	39.5 (3)	50.5

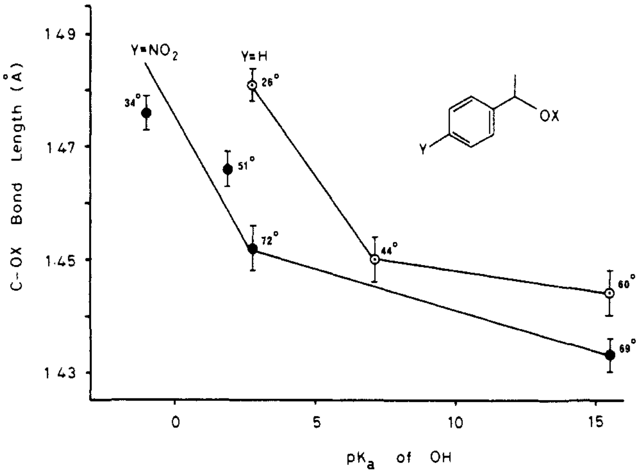
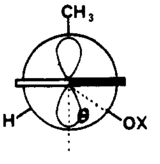


Figure 1. Plot of C–OX bond length vs. the pK_a of HOX (⊙) for 1-phenylethyl derivatives (X = triphenylmethyl, 4-nitrophenyl, and 3,5-dinitrobenzoyl) and (●) for 1-(4-nitrophenyl)ethyl derivatives (R = triphenylmethyl, chloroacetyl (**5**), diphenylphosphoryl (**7**), and 2-naphthalenesulfonyl (**6**)). Each point is marked also with the mean value of the dihedral angle θ (see text) for the compound concerned.

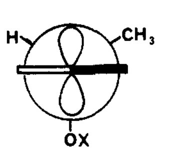
Variation in X. The dependence of the C–OX bond length on the leaving group, OX, can be examined in two series of compounds taken from Table I: the (three) unsubstituted (Y = H) and the (four) para-nitro derivatives (**1**, Y = NO_2). The usual[3,4] bond length–pK_a plots are shown in Figure 1. Unusually, they clearly are not linear. Since we have found reasonable to excellent linear correlations between bond length (C–OX, P–OX, and N–OX) and the pK_a of HOX in every one of the 14 series of compounds we have examined so far,[2,4,10,11] we regard this behavior as exceptional and requiring explanation.

The new factor in the 1-arylether system **1** is its conformational freedom. It happens that all 14 systems we have examined previously either are conformationally homogeneous, for some structural or stereoelectronic reason,[4,10,11] or represent data averaged over a very large number of structures[2] and thus conformations also. In the series of compounds **2**–**7**, on the other hand, the conformation about the C–aryl bond (*b* in **1**) is not fixed and in fact varies *systematically* with the pattern of substitution.

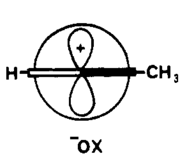
The conformation favored in most cases is that (**1a**) with the C–Me bond perpendicular to the plane of the ring: in 8 of our 12 structures (Table I) the relevant dihedral angle (*cbd*) is 90° ± 16°.



1a



1b



$1^{\pm}$

The lowest energy conformation for a symmetrical Ar–CHX_2 system has the ring eclipsing the C–H bond and thus bisecting XCX.[12] In our unsymmetrical system a conformation closer to **1a** is expected on steric grounds (a methyl group being more sterically demanding than OX) and will be favored also by any contribution from $\sigma_{C-Me}\pi^*$ overlap, which will be most important when the ring is most, and X is least, electron-deficient. In this conformation the alternative stabilizing $\pi-\sigma^*_{C-OX}$ interaction is small because of the large dihedral angle (θ = 60°) between the orbitals concerned. However, it is just this two-electron interaction which is involved in C–OX cleavage, so that the leaving group is expected to depart in the direction corresponding to θ = 0°. The conformation of the (relatively late[13]) transition state for C–OX cleavage must therefore be close to **1b**.

The transformation of **1a** to **$1^{\pm}$** must therefore involve a conformation change (**1a** → **1b**), as well as C–O bond breaking. The two processes could in principle be independent or coupled. In solution the simplest coupled process—conformation adjusting during the course of a single "productive" vibration—is precluded by the much shorter time scale of a vibration compared with a rotation. But our data provide clear indications of coupling in the ground states.

Three compounds (**4**, Y = 4-OMe and H; **6**, Y = NO_2) do not adopt conformation **1a**. All have good leaving groups and thus relatively long C–OX bonds and show a clear trend toward conformation **1b**, with the dihedral angle falling almost to 20°. Steric effects cannot have been changed significantly by the small lengthening of the C–OX bond (and certainly not in the direction of increasing steric demand by oxygen), so this trend presumably

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(11) Edwards, M. R.; Jones, P. G.; Kirby, A. J., unpublished work.

(12) Berg, U.; Liljefors, T.; Roussel, C.; Sandstrom, J. *Acc. Chem. Res.* **1985**, *18*, 80.

(13) Richard, J. P.; Rothenburg, M. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1361. These authors' analysis of substituent effects on the reactivity of 1-phenylethyl systems leads to a best description of the transition state involving a large amount of bond breaking, and thus charge separation, but with π delocalization lagging behind. Our results with 4-methoxy-substituted compounds indicate the same "relatively small expression of the resonance effect in the initial stages of bond cleavage".

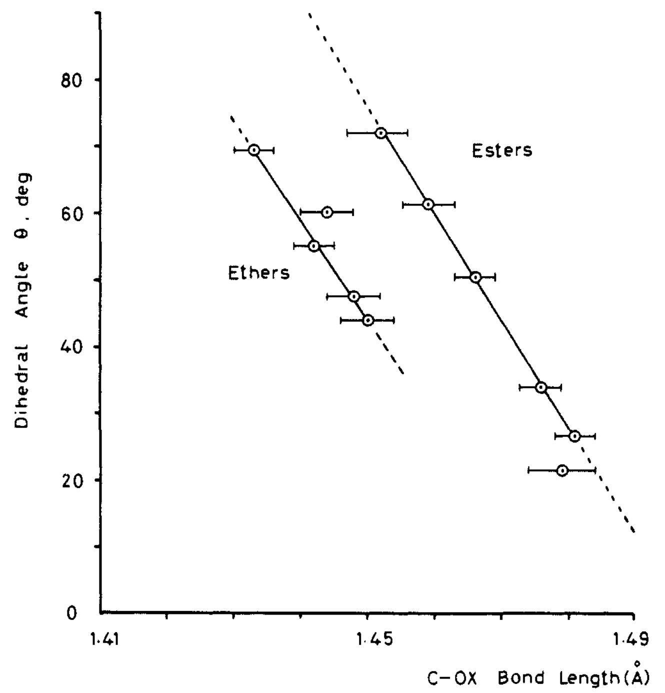

Figure 2. Correlation between the dihedral angle (**1a**) and bond length C–OX for all 11 compounds studied in this work. See text.

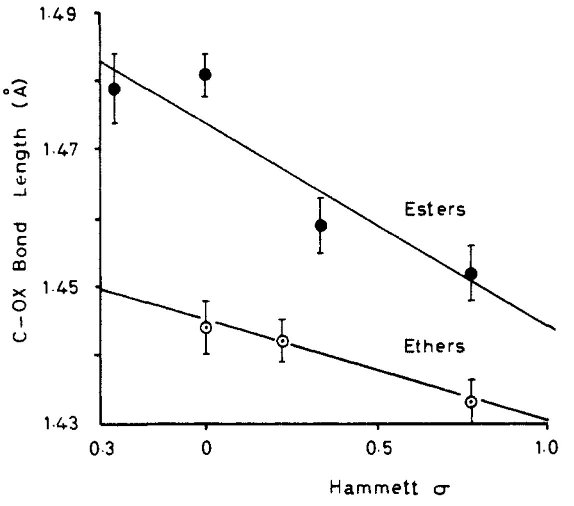

Figure 3. Plot of C–OX bond length vs. Hammett σ value for the aromatic substituent Y (⊙) for triphenylmethyl ethers **2** (Y = H, Cl, and NO_2) and esters **4** (Y = 4-MeO and H and 3-F) and **5**.

represents the increasing importance of the π–σ^*_{C-OX} interaction as the energy of the antibonding orbital is lowered by increasing electron withdrawal in X. The effect is clearly systematic, rather than the result of random crystal-packing forces, as shown by the remarkable correlation between conformation and bond length shown in Figure 2.

In Figure 2 the angle θ (**1a**), controlling π–σ^*_{C-OX} overlap, is plotted against the length of the C–OX bond, for all 11 compounds. The data fall neatly into two sets, each defining an almost perfect straight line with a single point deviating by about a standard deviation. The set defining the upper line comprises all the (carboxylate, phosphate, and naphthalenesulfonate) esters, while the points in the second set all refer to ethers (**2** and **3**). So the division is a natural one into compounds with relatively good and poor leaving groups.[14] The two lines are separated by over 30° dihedral angle, or 0.02 Å, indicating that for a given conformation the C–O bond is this much longer (or, for a given bond length, θ is this much smaller) for the better leaving groups OX. They are also almost parallel, showing that the coupling of bond length and conformation is quantitatively similar for both kinds of C–OX bonds.

This effect is sufficient to explain the nonlinearity of the plots shown in Figure 1. The correlations illustrated by Figure 2 allow us to estimate C–OX bond lengths for good leaving groups OX at high values of θ, and the differences from observed values are large enough to suggest that these leaving group plots would be linear if the conformations about the Ar–C bond *b* were fixed. (We are currently looking at a series of compounds of this sort, with restricted conformational freedom at C_α.)

Variation in Y. In two series, the triphenylmethyl ethers **2** and esters **4** and **5**, we have enough compounds to examine the dependence of the C–OX bond length on the substituent constant for the aromatic substituent Y. (As described above, chloroacetate and 3,5-dinitrobenzoate are anions of acids of almost identical leaving group capabilities.) The plots are shown in Figure 3. The lines drawn have slopes (corresponding to ρ values) of –0.015 and –0.030 (correlation coefficients 0.993 and 0.931), for the ethers and esters, respectively. (The small absolute magnitudes of the slopes reflect primarily the choice of angstrom units for bond lengths.)

In principle these plots represent new bond length–reactivity correlations. Hammett plots for the solvolysis of 1-arylethanol derivatives (vs. σ^+) have ρ values in the range –(5–7), so *insofar as both bond length and reactivity are linear functions of σ*, we can estimate the slopes of bond length–reactivity plots.[4] The calculation gives slopes of 260 kcal mol^{-1} Å^{-1} for the series of esters (**1**, X = COR) and 500–600 kcal mol^{-1} Å^{-1} for the ethers (**1**, X = CPh_3). Neither value is of high accuracy, but both lie within the range found previously for the dependence of the C–OX (P–OX) bond length *on leaving group*, for various acetals and phosphate esters.[4] Values at the top of the range, near 600 kcal mol^{-1} Å^{-1}, characterize bonds which are stable to spontaneous heterolysis under normal conditions, while values below 300 kcal mol^{-1} Å^{-1} are found for systems which undergo ready C–OX cleavage.

However, the bond length–reactivity correlation breaks down for compounds **1** with 4-methoxy substituents, which have no significant effect on the C–OX bond length in the two series (esters and 4-nitrophenyl ethers) for which data are available. But 4-MeO groups are well-known to induce large rate accelerations in heterolytic reactions of benzylic systems, as a result of π-donation to the developing cationic center. Evidently there can be no important π–σ^*_{C-OX} interaction in the ground state in **3** and **4** (Y = MeO), and presumably the π-donor and σ-acceptor effects of the substituent cancel out.

This might be because the π–σ^* interaction is intrinsically weak or because it is inefficient in these systems. The strongest interaction of this sort is π–σ^*_{C-F}, and strong, conformation-dependent effects of para substituents have been observed on the ^{19}F chemical shifts of benzyl fluorides.[15] The effect of MeO (actually a *downfield* shift of the F signal relative to benzyl fluoride itself[16]), in common with other substituent effects on the ^{19}F chemical shift, disappears almost completely when the C–F bond is fixed in the plane of the aromatic ring[17] (corresponding to θ = 90° in **1a**).

Similarly, 4-MeO is characterized by an effective substituent constant close to zero for the ionization of substituted phenylacetic acids, where π donation to the reaction center is prevented entirely by the tetrahedral carbon.[18] In the case of **3** and **4** (Y = OMe), the conformation about bond *b* (Table I) is in fact not ideal for

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[14] The esters are derived from acids with pK_a's covering a narrow range, from –1.0 to 2.8, the ethers from triphenylmethanol (pK_a = 15–16) and 4-nitrophenol (pK_a = 7–14). The phenol thus lies halfway between the acids and the alcohol in terms of leaving-group capability, but its two ethers evidently do not show intermediate behavior in the structure–structure correlation shown in Figure 2.

[15] Craik, D. J.; Brownlee, R. T. C. *Prog. Phys. Org. Chem.* **1983**, *14*, 1. Adcock, W.; Abeywickreman, A. N. *Aust. J. Chem.* **1980**, *33*, 181.

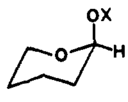
[16] Bromilow, J.; Brownlee, R. T. C.; Page, A. V. *Tetrahedron Lett.* **1976**, 3055.

[17] Adcock, W.; Abeywickreman, A. N. *Tetrahedron Lett.* **1979**, 1809.

[18] Hoefnagel, A. J.; Wepster, B. M. *J. Am. Chem. Soc.* **1977**, *95*, 5357.

π–σ^*_{C-OX} overlap, the dihedral angles between the orbitals concerned (in **1a**) being 47.5° and 21.4°, respectively. It seems clear, therefore, that we must take the conformation at the benzylic center into account if we are to treat the C–OX bond lengths of compounds **1** systematically.

Dependence on Conformation. We know from our results with other systems that the length of a C–OX bond depends on the pK_a of HOX, and Figure 3 provides some evidence for the expected dependence of σ_Y in 1-arylethyl derivatives. Our initial objective was to derive a multiple structure–reactivity correlation, relating the C–OX bond length to the two reactivity parameters. Multiple structure–reactivity correlations have been observed from time to time in kinetic studies,[19-21] and we have recently derived the first multiple crystal–structure reactivity correlation for three series of acetals **8**–**10**.[10]



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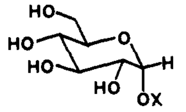

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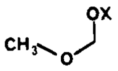

10

These acetals, however, are conformationally homogeneous, whereas our 1-arylethanol derivatives are not, and it is clear from the discussion so far that a successful correlation must include also an appropriate function of θ, the interorbital angle controlling π–σ^*_{C-OX} overlap. The appropriate function is $\cos^2\theta$,[22] and we have performed multiple linear regressions[23] of the bond length C–OX for all our compounds **1** on three variables, $\cos^2\theta$, σ_Y and the pK_a of HOX. (Other variables tested were θ itself and cos θ for the dihedral angle. σ_Y was also dissected, using Swain and Lupton's $\mathcal{F}$ and $\mathcal{R}$ constants,[21] into separate dependent variables $\mathcal{F}$ and $\mathcal{R}\cos^2\theta$. The resulting correlations were clearly poorer.)

The best fit (F ratio 21.88 for 10 degrees of freedom) was to an equation of the form

$$BL_{C\text{-}OX} = 1.448\ (8) + a\mathrm{p}K_{HOX} + b\cos^2\theta + c\sigma_Y$$

with $a = -1.33 \pm 0.42 \times 10^{-3}$, $b = 3.8 \pm 1.1 \times 10^{-2}$, and $c = 4 \pm 6 \times 10^{-3}$. This expression gives calculated values of the C–OX bond length within experimental error for 7 compounds and within two standard deviations for all 11. However, numerical analysis shows that the term in σ_Y makes a negligible contribution (less than one experimental standard deviation) to the variation in bond length, and a slightly improved correlation (F ratio 34.94 for 10 degrees of freedom) is obtained by omitting it:

$$BL_{C\text{-}OX} = 1.453\ (5) - 1.48 \times 10^{-3}\mathrm{p}K_{HOX} + 3.30 \times 10^{-2}\cos^2\theta$$

Thus (as implied also in the correlations of Figure 2), we can account for the variation in the C–OX bond length in terms of two parameters: the leaving-group capability of XO$^-$, as measured by the pK_a of HOX, and the efficiency of π–σ^*_{C-OX} overlap, as measured by $\cos^2\theta$. Ring substituents Y do affect the bond length, as shown by the "Hammett plots" of Figure 3, for a series with constant OX, but primarily through the dihedral angle θ. (For the series of esters, for example, with constant OX, θ increases monotonically with increasing σ_Y). Apparently the efficiency of the π–σ^* interaction in the ground state is more sensitive to geometry than to the modifying effects of substituents on the ring. We hope to isolate the dependence on substituent by studying a series of compounds with θ fixed, ideally at 0°.

Changes in Bond Angles. Systematic trends with varying substitution are observed exclusively within the 1-arylethyl fragment. No pattern is apparent, for example, in scatter plots of bond length vs. the dihedral angle about the C–OX bond. When individual C–C–O angles *ab* and *ac* (Table I) are plotted against the C–OX bond length, a remarkable periodicity is revealed (Figure 4). Evidently increases in one C–C–O angle are compensated by decreases in the other. Of more obvious relevance to C–O stretching is the monotonic decrease in the *mean* value of the two angles with increasing C–OX bond length: this falls from 109.9° to 107.4° over the range 1.433–1.481 Å, and the correlation is reasonably linear (r = 0.934 for nine data points: those for the two 4-methoxy compounds show marked negative deviations of about 0.02 Å or 1.4° (see Figure 4) and have been omitted from the calculation).

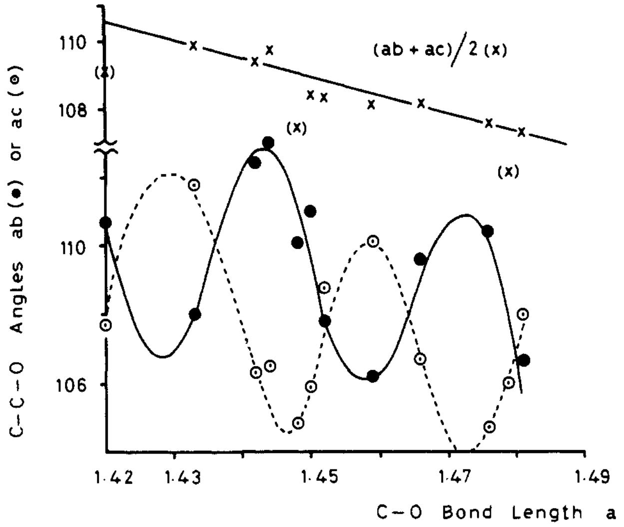

Figure 4. Plot of C–C–O bond angles vs. C–OX bond length for all 12 structures of **1**. Smooth curves are drawn simply to connect the points. The upper line illustrates the decrease in the mean C–C–O bond angle with increasing C–O bond length. See text.

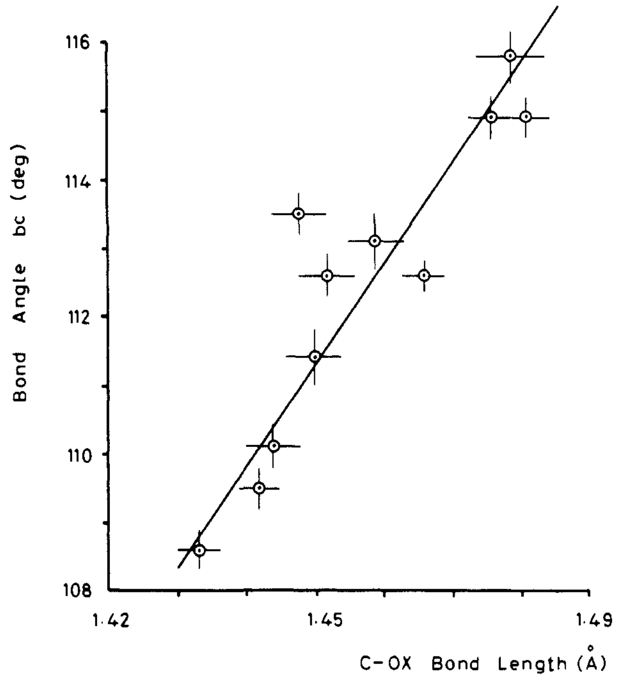

Figure 5. Correlation between bond angle CH$_3$–C–Ar (*bc* in Table I) and bond length C–OX for all 11 compounds listed in the table. The compound showing the largest deviation from the line drawn is the *p*-nitrophenyl ether **3** (Y = MeO).

The most striking effect on bond angle concerns the Ar–C–Me angle *bc* (Table I). This is in principle tetrahedral in **1** but trigonal in the carbocation **1$^+$**, so it must be near 120° in the transition state for C–O cleavage. In fact this angle opens up from a

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(19) Kirby, A. J.; Khan, S. A. *J. Chem. Soc. B* **1970**, 1172.

(20) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948.

(21) Dubois, J.-E.; Ruasse, M.-F.; Argile, A. *J. Am. Chem. Soc.* **1984**, *106*, 4840.

(22) Ingraham, L. L. In *Steric Effects in Organic Chemistry*; Newman, M. S., Wiley: New York, 1956; p 481.

(23) We are grateful to Dr. R. Taylor, of this department, for performing these calculations.

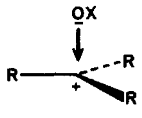
(24) Swain, C. G.; Lupton, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 4328. Swain, C. G.; Unger, S. H.; Rosenquist, S. R.; Swain, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 492.

minimum value of 108.6° in the ether **2** (Y = NO_2), which is expected to be least reactive to C–OX cleavage, to a maximum of 115.8° in **4** (Y = OMe), which is expected to be the most. The angle is plotted against the C–OX bond length for all 11 compounds in Figure 4, which shows the strong correlation between the two parameters. In terms of this angle, the geometry change over our series of compounds amounts to over 63% of that expected for the transformation of **1** to $\mathbf{1}^{\pm}$.

Exploring the Reaction Coordinate for C–O Cleavage. Only a handful of examples are known where deviations from standard bond length and angles can be correlated with kinetic behavior. As Bürgi and Dunitz have pointed out,[25] it is often difficult to decide whether observed correlations relate to minimum-energy paths or represent a response to the changing crystal environment of the structural fragment of interest. We have avoided charged or hydrogen-bond donor groups in our choice of compounds (**1**) and observe well-defined, monotonic trends consistent with the changes in geometry expected for C–OX cleavage, in the face of fluctuating changes in polarity of groups X and Y. We are therefore confident that the changes we observe represent behavior intrinsic to the 1-arylethyl system.

These changes are much more extensive than those observed in our work with acetals (**8**),[4] where only bond lengths varied significantly over most of the range of leaving groups used. So the reaction coordinate for C–OX cleavage is correspondingly more complex, and we make no attempt to derive a quantitative relationship[4] with the slopes of our bond length–reactivity plots (Figures 1 and 3). On the other hand, the extent of the changes and the strong correlations between them allow us to describe the initial stages of C–OX cleavage in considerable detail. Note that here too we are not dealing with only the very early stages of this process. Not only from the changes in angle *bc* and dihedral angle θ, discussed above, but also in terms of the free energies of activation for C–OX cleavage,[26] we estimate that our set of compounds **1** spans *at least 60%* of the reaction coordinate for the cleavage of an alkyl 1-phenylethyl ether.

We use the C–OX bond length as an index of progress along the reaction coordinate (though we have no way of extrapolating from our correlations to a meaningful estimate of the C···OX distance in the transition state), because this parameter is common to all systems where we use the "variable oxygen probe". As the C–OX bond lengthens, as a result of increased electron withdrawal by X *or* increased electron donation by Y, the geometry of the 1-arylethyl fragment adjusts to accommodate the positive charge developing at the α-carbon. The aromatic ring rotates to reduce θ (**1a**) and thus improve π overlap with the LUMO (σ^*_{C-OX}). The Ar–C–Me angle opens out from below the tetrahedral angle to almost 116°, as the geometry at the α-carbon changes toward trigonal planar. There is a significant, though somewhat irregular, shortening of both Ar–C and Me–C bonds. And the mean C–C–O value falls slightly, from 109.9° to 107.4°. (In the transition state, this angle, more usefully considered in terms of the trajectory for the addition of an oxyanion nucleophile to a carbocation, will presumably lie between the 90° expected for addition to a symmetrical species (**11**) and the near tetrahedral angle, predicted for addition to a delocalized benzylic cation (**12**)).



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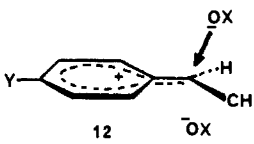

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Of course the trends we observe in the solid state refer to a series of molecules each at an energy minimum, whereas when a C–OX bond stretches, and eventually breaks, as a result of thermal vibration, the system is displaced further and further from equilibrium. Nevertheless, both static and dynamic processes lead in the direction of ionic cleavage. And since the time scale of a vibration is too short to allow significant reorganization of solvent molecules, the developing charges must in both cases be accommodated internally. So it is reasonable to expect the behavior we observe in the crystal to mirror the behavior of the same structural fragment during the course of C–OX cleavage in solution.

Our results allow us to add quantitative detail to the following qualitative description of C–OX bond cleavage ($\mathbf{1} \rightarrow \mathbf{1}^{\pm}$) in solution. Both the equilibrium C–O distance and the amplitude of the C–O stretching vibration depend on the conformation about the C–Ar bond: this bond lengthens, and the amplitude of the vibrations increases, as the dihedral angle with the aromatic ring approaches 90°. C–O stretching is also strongly coupled with bending vibrations of the C–Ar and C–Me bonds, with the C–C–C angles at the benzylic center increasing in parallel with the C–O interatomic distance. If we accept the usual estimate of about 0.1 Å for the amplitude of a thermal vibration, this implies that even unreactive compounds **1** approach trigonal geometry at the maximum extension of the C–OX bond, at least when the ring conformation favors π–σ^*_{C-OX} overlap. More reactive compounds *start* closer to the transition state, in geometry as well as free energy. The probability of a vibration leading to C–O cleavage is increased both because the bond is already longer in the ground state and also because the amplitude of the vibrations is greater. Now at the maximum extension of the bond the geometry must be close to that of the ion pair $\mathbf{1}^{\pm}$, and the energy of the system depends only weakly on the interatomic distance, by now presumably in the region of 1.6 Å.

This is as far as we can extrapolate from the results summarized in the figures. Subsequent events depend increasingly on external factors. The bond may finally break as a result of a vibration of extra amplitude to generate the ion pair $\mathbf{1}^{\pm}$, which can go on to products by diffusing apart, if its lifetime is long enough, or as a result of the intervention of a preassociated nucleophile. These questions have recently been discussed in detail by Richard and Jencks.[13,27]

Bond Length and Reactivity. An important objective of work in this area is to identify relationships between bond length and reactivity which are generally applicable. So far, we have found no exceptions to two rules related to the length of the bond being broken:

1. The longer the bond, in a given system, the faster it breaks. This has the advantage of simplicity, but the data presented in this paper suggest that occasional exceptions are to be expected in systems where the conformation can vary. The C–OX bonds in the two methoxy compounds **3** and **4** (Y = MeO) discussed above are no longer than those in the corresponding unsubstituted compounds, even though these are substantially less reactive. And although we observe a well-defined trend for conformation to change to favor bond elongation for intrinsically more reactive compounds (Figure 2), this trend could in rare cases be reversed by crystal packing forces.

A clear exception to the simplest rule (the longer the bond, the faster it breaks) has been identified by Tidwell,[28] who pointed out that cyclohexyl tosylate (a secondary aliphatic sulfonate) is solvolyzed (in trifluoroacetic acid) 200 times more slowly than the tertiary benzylic ester **13**, even though the C–O bond is longer

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[25] Bürgi, H.-B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153.

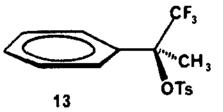
[26] We assume that the free energy of activation for C–OX cleavage is a linear function of the pK_a of HOX, as is known to be the case for the reverse reaction,[24] and that there is no significant barrier to the cleavage of the conjugate acid of an alkyl 1-phenylethyl ether. The pK_a of HOX then ranges from 16 for Ph_3COH to a limit of about −4 for ROH_2^+, which marks the potential energy of the transition state. We have crystal structures for leaving groups with pK_{HOX} ranging from about 16 to below 3 (the esters **4**).

[27] Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373.

[28] Kanagasabanathy, V. M.; Sawyer, J. F.; Tidwell, T. T. *J. Org. Chem.* **1985**, *50*, 503.

[29] For the four equatorial substituted cyclohexyl arenesulfonates for which accurate structures are available (R < 5%: Johnson, P. L.; Cheer, C. J., *Tetrahedron* **1972**, *28*, 283; and Jones, P. G.; Edwards, M. R.; Kirby, A. J., unpublished work), the mean C–O bond length is 1.476 (3) Å. Accurate data (R < 7%) are also available for two axial tosylates (James, V. J.; Grainger, C. T. *Cryst. Struct. Commun.* **1972**, *1*, 111. Johnson, P. L.; Schaefer, J. P.; James, V. J.; McConnell, J. R. *Tetrahedron* **1972**, *28*, 2901. James, V. J. *Cryst. Struct. Commun.* **1973**, *2*, 205). These have mean C–O bond lengths of 1.490 (11) Å.

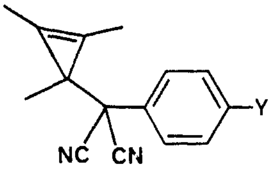
(about 1.48 Å,[24] compared with 1.457 Å for **13**). In this case,



13

13 crystallizes, primarily for steric reasons, in a conformation which allows no significant π–σ^*_{C-O} overlap, with the C–OTs bond almost in the plane (dihedral angle 17°) of the aromatic ring.[27] In our secondary benzylic system (**1**) a geometrical restriction on π–σ^* overlap of this size would reduce the C–O bond length by up to 0.046 Å (Figure 2), suggesting that the "simplest rule" quoted above remains useful in systems where the conformation is fixed, or where enough data are available to quantify, and so allow for the effects of varying conformation. However, in practical terms, it is important to recognize that the length of a bond may be conformation-dependent, so a compound cannot necessarily be characterized by a unique bond length, as it generally can be by a unique rate constant for the cleavage of that bond under standard conditions.

Similar considerations apply to the remarkable C–C bond heterolyses studied by Arnett and Molter.[30] These authors find that compounds **14** are cleaved to trimethylcyclopropenium cation and the arylmalononitrile anion in acetonitrile at 25 °C.



14

For the *p*-methoxy and *p*-nitro compounds **14** (Y = MeO and NO_2), $\Delta H°$ differs by some 8 kcal mol^{-1}. The rate of heterolysis is similarly several hundred times faster for the *p*-nitro compound, but the length of the C–C bond being broken is not significantly longer (1.588 (4), compared with 1.581 (3) Å for **14**, Y = MeO), prompting the observation[30] "clearly the stability of the heterolysis product is not reflected in the bond length of the neutral reactants". But here too a major difference in the conformation in the crystal, in this case about the bond being broken, complicates interpretation.

Finally, in one situation exemplified by the symmetrical hexaalkylethanes described by Rüchardt and Beckhaus.[31] which also have very long C–C bonds (in some cases longer than 1.6 Å), there seems no doubt that "the length of a bond is no criterion for its strength".[31] In such systems bond elongation results from steric repulsion and culminates eventually in bond *homolysis*. There is no direct link between these steric interactions and the electronic factors responsible for stabilizing the radicals produced, the substitution of aromatic for alkyl groups, for example, having opposite effects. So it is no surprise that there is no simple correlation between bond length and strength in such cases.

2. The more reactive the system, the more sensitive is the length of the bond to structural variation. In three series of acetals **8–10** (above), we have recently demonstrated[10] a linear correlation between the slopes of the bond length–reactivity plots—how easy it is to stretch a C–O bond by varying the leaving group OX—and the rate at which it is broken in solution. The variation in bond length with changing OX is very large for the tetrahydropyranyl acetals **8** and practically disappears for the glucosides **10**, which are 10^6–10^7 times less reactive.[10]

The data allow us to estimate also the slope of the bond length–reactivity plot for the variation of the acetal *type* in the series **8–10** (X = $COCH_3$: that is, varying the R and R′ in acetal esters $ROCHR'OCOCH_3$) as 190 kcal mol^{-1} Å^{-1}. This is the lowest slope—corresponding to the highest sensitivity—we have found so far, in the system we know to be the most reactive toward C–OX cleavage: the observation thus complements our similar data for variation in the leaving group in several systems.[4]

Rule 2 at any rate can be expected to be of very general validity, since insofar as it is an extension of rule 1 it says that no more than longer, which means weaker, bonds in a given system are more easily extended. It also applies, for example, to the poly(alkylethanes) of Rüchardt and Beckhaus discussed above:[31] the C–C bond length in $R_2R'C$–$CR'R_2$ (R′ = H or alkyl) is a linear function of the calculated strain energy and is most sensitive to the variation in R for bonds between two quaternary centers. This rule should also be independent of conformational variation, since conformation, like other geometrical factors, is expected to change systematically in the direction which favors bond elongation in more reactive systems.

Conclusions

We have formulated two working rules (1 and 2 above) which correlate bond length and heterolytic reactivity in very general terms. Our data concern mostly C–OX bonds, but the generalizations may be expected to apply broadly to polar covalent bonds, as shown by a recent detailed survey of a wide range of bond lengths in organic compounds.[32] Systems where bond lengths are affected by steric strain are likely exceptions, and conformational variation may introduce complications: the length of a bond may be conformation-dependent, so a compound cannot necessarily be characterized by a unique bond length.

Fortunately it appears possible to take into account the variation in conformation. The results described in this paper, together with many others which have accumulated in recent years, indicate that, in the absence of strong, specific intermolecular interactions, organic molecules generally crystallize in their ground-state conformation.[28] So, although rotational isomerism is much more sensitive than bond length or angle to the random effects of crystal packing forces, results for homogeneous series of compounds can allow us to identify trends in conformation also. The study of crystal structure correlations is the key to a treasure house of information about stereoelectronic effects on structure and reactivity.

Acknowledgment. We are grateful to the Science and Engineering Research Council of Great Britain for support and a referee for penetrating and constructive comments.

Registry No. 2a, 39834-50-9; **2b**, 104292-47-9; **2c**, 104292-48-0; **3a**, 104292-49-1; **3b**, 73259-67-3; **4a**, 88563-47-7; **4b**, 8222-60-4; **4c**, 104292-50-4; **5**, 104292-51-5; **6**, 104292-52-6; **7**, 104292-53-7.

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(30) See, for example: Arnett, E. M.; Molter, K. E. *Acc. Chem. Res.* **1985**, *18*, 339.

(31) Rüchardt, C.; Beckhaus, H.-D. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 329.

(32) Allen, F. H.; Kennard, O.; Taylor, R.; Watson, D. H.; Orpen, A. G., personal communication.

(33) Kruse, L. I.; DeBrosse, C. W.; Kruse, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 5435.

(34) Rüchardt and Beckhaus[31] have shown that molecular mechanics calculations predict the conformations observed in the crystal with remarkable accuracy, even for substituted ethanes.