(before phase-shift correction) in the Fourier transform[18] (due to Fourier truncation and/or residual background), the result obtained for the FeMo(co) (which shows a peak at 1.33 Å, before correction, in the Fourier transform; cf. Figure 1c) may be in error by as much as 50%. If we subtract a "background peak" estimated from $[Fe_4S_4(SPh)_4]^{2-}$, the number of Fe–O bonds reduces to 1.2. Despite these cautions, the data in Table I support the use of the EXAFS of **1** and **2** as good models for the Fe–S(Cl), Fe–Fe(Mo), and Fe–O(N) interactions in the FeMo(co).

In summary, the iron atoms in the FeMo(co) have an average of 3.4 ± 1.6 S(Cl) atoms at 2.25 (2) Å, 2.3 ± 0.9 Fe atoms at 2.66 (3) Å, 0.4 ± 0.1 Mo atoms at 2.76 (3) Å, and 1.2 ± 1.0 O(N) atoms at 1.81 (7) Å as nearest neighbors. The large standard deviation in the number of sulfur and iron atoms may be due to the presence of *different iron sites* with varying number and/or types of sulfur and iron neighbors. Our findings are consistent with (although certainly not limited to) models 4[11] and 5[12] described above. Note that model 4 calls for 3–4 S (or Cl), 2 Fe, 0.3–0.5 Mo, and 1–2 O (or N) neighbors per iron atom, whereas model 5 predicts 4 S, 2.6 Fe, and 0.4 Mo neighbors per iron atom. Finally, it should be cautioned that the structure of the NMF-extracted FeMo(co) from Av1 may be different from the novel cluster in the native enzyme, due to the coordinating power of NMF.

Acknowledgment. We thank Drs. L. S. Powers and B. Chance for generous assistance with the experimental apparatus at SSRL (see supplementary material). This research was supported in part by an NSF grant (8008733 PCM), a USDA/SEA Competitive Research Grant Office grant (5901-0410-8-0175-0), an NIH grant (GM 28636), and by two fellowships (NSF-SPI-7914823 and NIH-GM07294).

Registry No. FeMo(co), 72994-52-6.

Supplementary Material Available: Detailed Experimental Section with five references and five figures, A–E (8 pages). Ordering information is given on any current masthead page.

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(18) Antonio, M. R.; Teo, B. K.; Averill, B. A., to be submitted for publication.

Nucleophilic Addition of Phenolate Oxygen to an Unactivated C=C Double Bond

Christopher M. Evans and Anthony J. Kirby*

University Chemical Laboratory
Cambridge CB2 1EW, England
Received April 9, 1982

Under normal conditions ethylene and simple alkyl ethylenes react exclusively with electrophiles: nucleophilic additions are observed only when strongly electron-withdrawing substituents are present. Certain reactions catalyzed by enzymes[1] suggest that this prohibition is not absolute, and we are exploring possible intramolecular additions of oxygen and nitrogen nucleophiles to unactivated C=C double bonds under mild conditions. We have shown[2] that in a suitable system activated by ground-state strain amine nitrogen will add very rapidly to the transannular double bond of an electron-rich stilbene. We now report that phenolate oxygen will add readily to a neighboring monoalkyl ethylene when the groups are brought together in a system exhibiting high effective molarity (EM).[4]

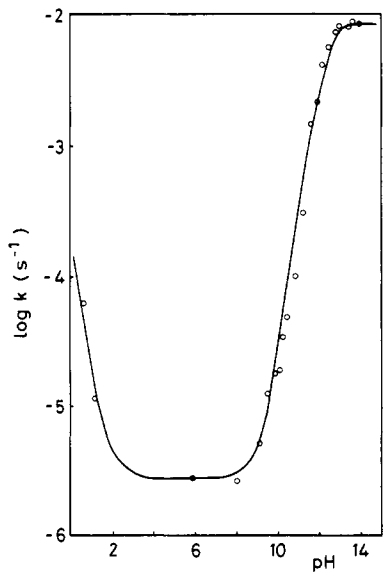
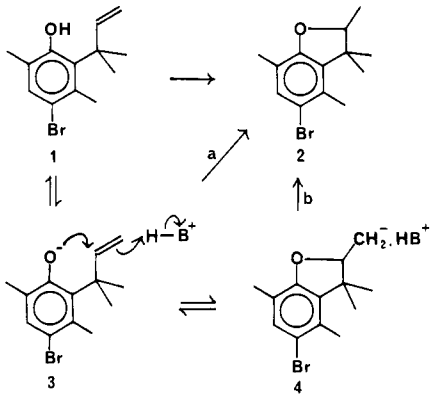


Figure 1. pH profile for the cyclization of **1** → **2** at 39 °C and ionic strength 0.2 M (KCl) in 50% aqueous acetonitrile. The points are experimental; the curve is calculated, by using $k_{H^+} = 2.2 \times 10^{-4}$, $k_0 = 1.8 \times 10^{-6}$ and 8.4×10^{-3} s^{-1}, and pK_a 12.5.

Ganter[5] and Grob[6] and their co-workers have reported relevant cyclizations of several polycyclic olefin–alcohols under basic as well as the more generally favorable acidic conditions. We preferred an olefin–phenol system, which could be converted completely to the phenolate anion and could thus be studied in the absence of complications from the initial ionization step. The key requirement was thus a phenol–olefin that would undergo intramolecular cyclization with a very high EM, and we have prepared several such compounds based on the "trialkyl lock" system of Milstien and Cohen.[7]

The most reactive of these is the phenol–olefin **1** (prepared from



the lactone A[7] by the route shown in eq 1, with the following reagents: (i) Dibal-H; (ii) $(COOH)_2$ in PhMe; (iii) Br_2/CCl_4; (iv) H_2O/THF; (v) $Et_3SiH/BF_3{\cdot}OEt_2$; (vi) Zn/95% EtOH. Both **1** and its cyclization product **2** have been fully characterized spectroscopically). **1** cyclizes to **2** very slowly at neutral or acidic pH, but reaction is rapid above pH 10, and the half-life of the anion is 82 s at 39 °C. The pH–rate profile (Figure 1) shows pH-independent regions from pH 2.5 to 8.5 and above 13, and

(1) Of particular interest are those amino acid ammonia lyases which are reversible and can thus catalyze the addition of ammonia to double bonds without assistance from electron-withdrawing substituents,[2] and oleate hydratase (EC 4.2.1.53), which catalyses the stereospecific hydration of oleic acid to 10-hydroxy stearate.[3]
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(8) M. Caswell and G. L. Schmir, *J. Am. Chem. Soc.*, **102**, 4815 (1980).

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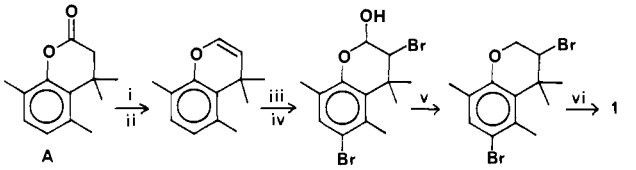

(1)

follows the dissociation curve of the phenol above pH 9. Cyclization is catalyzed by cationic (NH^+) but not neutral (trifluoroethanol) or negatively charged (HCO_3^-) general acids.

The parameters we have measured so far suggest that the mechanism of addition is primarily nucleophilic attack on the monoalkyl olefin by the phenolate oxygen, and it is significant that this mode of cyclization is substantially more efficient than the acid-catalyzed reaction (figure). The primary carbanion (**4**) is not likely to have a significant lifetime in aqueous solution so general acid catalysis (path a) is expected to be enforced.[9] The data (k_{H_2O}/k_{D_2O} 1.70, $\Delta H^{\ddagger}$ = 18.8 kcal mol^{-1}, $\Delta S^{\ddagger}$ = −7.7 eu, and Bronsted β = 0.94 ± 0.06 for general base catalysis of the cyclization of the phenol, corresponding to α near zero for the general acid-catalyzed reaction (**3**) of the anion) are consistent with proton transfer being only weakly coupled with C–O bond formation and thus with substantial carbanion character in the transition state. The reaction is thus qualitatively similar to the transannular addition of amine nitrogen observed previously.[2] It also defines the mechanism of the reverse reaction, the base-catalyzed elimination of a poor leaving group (PhO^-) from an ether without acidic protons.

Acknowledgment. We are grateful to the Science and Engineering Research Council of Great Britain for support.

Registry No. **1**, 82391-03-5; **2**, 82391-04-6; A, 40662-15-5; B, 82391-05-7; C, 82391-06-8; E, 82391-07-9; F, 82391-08-0; G, 82391-09-1.

Supplementary Material Available: Experimental details for the synthesis and characterization of compounds **1** and **2** (4 pages). Ordering information is given on any current masthead page.

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A Very Large Stereoelectronic Effect on Acetal Cleavage

Christopher M. Evans, Robert Glenn, and Anthony J. Kirby*

University Chemical Laboratory
Cambridge CB2 1EW, England
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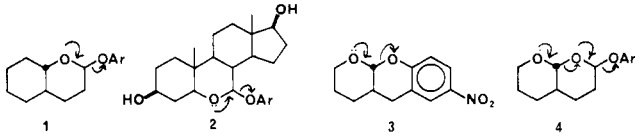
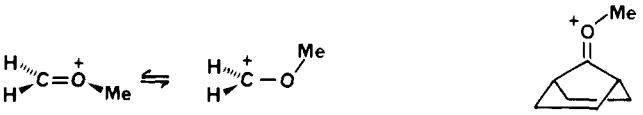
We have shown that stereoelectronic control of acetal cleavage is apparent only in conformationally rather rigid systems. We report the hydrolysis of a simple bicyclic acetal (**7**, below) which shows a stereoelectronic effect much larger than any previously observed.

The spontaneous hydrolysis of equatorial 1-oxadecalin acetals (**1**), which have no lone pairs *antiperiplanar* to the OAr leaving



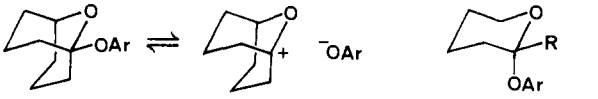
group, is actually a few times faster than that of the axial anomers,[1] presumably because cleavage with stereoelectronic control is possible via twist-boat conformations. The same is true even in the 6-oxasteroid series (**2**),[2] but when the conformation is locked by a trans ring junction *at the acetal center* significant stereoelectronic effects can be observed. Thus both **3**[3] and **4**[4] are hydrolyzed some 2–4 orders of magnitude more slowly than the corresponding cis-fused compounds, and the stereoelectronic barrier is estimated to be about 7 kcal mol^{-1} in each case.

The stereoelectronic barrier to acetal cleavage is potentially much larger than this. It is given, to a close approximation, by the difference in energy between the planar and perpendicular conformations of the oxocarbenium ion intermediate. This difference has been calculated[5] for the methoxy-methyl cation (**5**) as 20.8 kcal mol^{-1}, and the barrier to rotation in cation **6** is >18.4 kcal mol^{-1}.[6]



Compounds like **3** and **4** presumably react through high-energy conformations, which allow enough overlap between an oxygen lone pair and the developing cationic center to reduce the stereoelectronic barrier to the observed value of 7 kcal mol^{-1}. The magnitude of the observed barrier is thus expected to depend primarily on the rigidity of the system, with larger barriers associated with more rigid acetals.

We have now prepared[7] 1-(2,4-dinitrophenoxy)-9-oxabicyclo[3.3.1]nonane (**7**), an acetal with the leaving group fixed in the



7 (Ar = 2,4-dinitrophenyl)

equatorial position by the geometry of the system. The lone pairs on the ring oxygen are *synclinal* to the C–OAr bond, so that n–σ^* overlap is minimal. As a result both anomeric[10] and kinetic anomeric[10,11] effects are suppressed. In the ground state the C–OAr bond is unusually long (1.448 Å)[9] for an acetal, but this lengthening is not accompanied by the pronounced shortening of the endocyclic C–O bond (here 1.411 Å, the same as in equatorial **1**, Ar = Ph) observed for axial tetrahydropyran acetals.[12] And the effect on reactivity is enormous.

For comparison, an appropriate model axial tetrahydropyran acetal would be **8** (R = Me, Ar = 2,4-dinitrophenyl). This is far too reactive to prepare, but we can estimate a rate constant for its spontaneous hydrolysis of about 600 s^{-1} (50% aqueous dioxan, 39 °C).[13] Under these conditions **7** is stable indefinitely, but it

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(13) Estimate based on a measured rate constant of 9 × 10^{-3} s^{-1} for the spontaneous hydrolysis of **8** (R = Me, Ar = 3-nitrophenyl) in 50% aqueous dioxan at 39 °C[14] and the good linear free-energy relationship[15] correlating the rates of hydrolysis of a series of related acetals (**8**, R = H) in water. Preliminary data[14] for **8** (R = Me, Ar = Ph and 3-bromophenyl) show that the sensitivity to the leaving group is similar for the reactions of acetals (**8**, R = Me) in 50% dioxan.

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