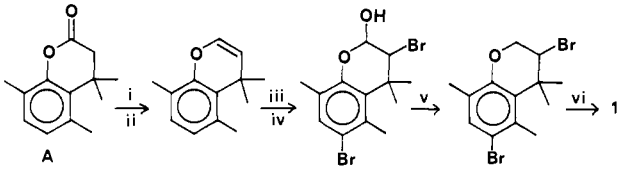

(1)

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.

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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.

(9) W. P. Jencks, *Acc. Chem. Res.*, **13**, 161 (1980).

A Very Large Stereoelectronic Effect on Acetal Cleavage

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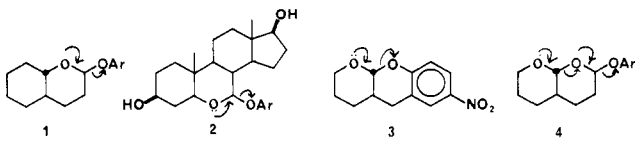
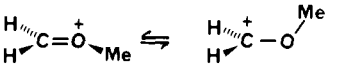
We have shown that stereoelectronic control of acetal cleavage is apparent only in conformationally rather rigid systems. We report the hydrolysis of a simple bicyclic acetal (**7**, below) which shows a stereoelectronic effect much larger than any previously observed.

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]



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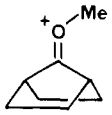

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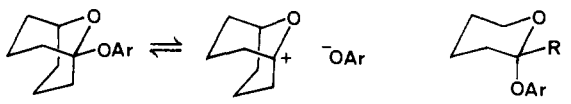
Compounds like **3** and **4** presumably react through high-energy conformations, which allow enough overlap between an oxygen lone pair and the developing cationic center to reduce the stereoelectronic barrier to the observed value of 7 kcal mol^{-1}. The magnitude of the observed barrier is thus expected 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)

8

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

(1) S. Chandrasekhar and A. J. Kirby, *J. Chem. Soc., Chem. Commun.*, 171 (1978).
(2) A. J. Kirby and R. J. Martin, unpublished work.
(3) A. J. Kirby and R. J. Martin, *J. Chem. Soc., Chem. Commun.*, 803 (1978).
(4) A. J. Kirby and R. J. Martin, *J. Chem. Soc., Chem. Commun.*, 1079 (1979).
(5) D. Farcaşiu and J. A. Horsley, *J. Am. Chem. Soc.*, **102**, 4907 (1980).
(6) R. Lustgarten, M. Brookhart, and S. Winstein, *Tetrahedron Lett.*, 141 (1971).
(7) By arylation of the known hemiacetal **7** (Ar = H)[8] with 1-fluoro-2,4-dinitrobenzene/*n*-BuLi in THF. The acetal **7** (Ar = 2,4-dinitrophenyl) (mp 148–149 °C) has been fully characterized by the usual methods and by a single-crystal X-ray structure determination.[9]
(8) C. B. Quinn and J. R. Wiseman, *J. Am. Chem. Soc.*, **95**, 1342 (1973).
(9) P. G. Jones, G. M. Sheldrick, A. J. Kirby, C. M. Evans, R. Glenn, and J. Stegemann, *Z. Kristallogr.*, in press.
(10) (a) A. J. Kirby, "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen", Springer-Verlag, Heidelberg, in press. (b) W. A. Szarek and D. Horton, Eds., "The Anomeric Effect: Origin and Consequences", ACS Symposium Series, No. 87, American Chemical Society, Washington, D.C., 1979.
(11) M. Petrzilka, D. Felix, and A. Eschenmoser, *Helv. Chim. Acta*, **56**, 2950 (1973).
(12) P. G. Jones and A. J. Kirby, *J. Chem. Soc., Chem. Commun.*, 288 (1979).
(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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is hydrolyzed at temperatures near 100 °C, and extrapolation allows an estimate of the rate constant for the spontaneous hydrolysis of **7** at 39 °C (50% aqueous dioxan) as 2.6×10^{-10} s^{-1}.[16] Thus **7** is cleaved over 10^{12} times more slowly[18] than the related axial acetal (**8**, R = Me, Ar = 2,4-dinitrophenyl), and essentially all of this large factor is a stereoelectronic effect on reactivity.

Acknowledgment. We thank the Science and Engineering Research Council of Great Britain for support.

Registry No. 7, 82390-99-6; **8** (R = CH_3; Ar = C_6H_5), 82391-00-2; **8** (R = CH_3; Ar = *m*-BrC_6H_4), 82391-01-3; **8** (R = CH_3; Ar = *m*-$NO_2C_6H_4$), 82391-02-4.

Supplementary Material Available: Kinetic data for the hydrolysis of **7** as a function of temperature and of three 2-(aryloxy)-2-methyltetrahydropyrans (**8**, Ar = Ph and 3-bromo- and 3-nitrophenyl) at 39 °C (1 page). Ordering information is given on any current masthead page.

(14) Unpublished work with A. J. Briggs.
(15) G.-A. Craze and A. J. Kirby, *J. Chem. Soc., Perkin Trans 2*, 354 (1978).
(16) Measurements at 83-117 °C in 50% dioxan/50% Tris buffer. The rate of hydrolysis is independent of pH over the range 7.77-8.99, as expected for the spontaneous cleavage of an acetal but not for the alternative nucleophilic aromatic substitution mechanism[17] of hydrolysis.
(17) G.-A. Craze and A. J. Kirby, *J. Chem. Soc., Perkin Trans. 2*, 357 (1978).
(18) W. P. Meyer and J. C. Martin, *J. Am. Chem. Soc.*, **98**, 1231 (1976). These authors have estimated an energy difference of 14 kcal mol^{-1} between transition states leading to parallel and perpendicular α-alkoxy carbinyl cations, corresponding to a rate difference of 10^{10}.
(19) Strain in the cation (**7**) is not expected to be an important factor.[20] The solvolysis of 1-chlorobicyclo[3.3.1]nonane in 60% aqueous EtOH is 60 times slower than that of *tert*-butyl chloride,[21] but this probably reflects steric inhibition of solvent assistance[22] to the ionization of the bicyclic halide.
(20) G. J. Gleicher and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **89**, 582 (1967).
(21) W. G. Dauben and C. D. Poulter, *J. Org Chem.*, **33**, 1237 (1968).
(22) T. W. Bentley and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **103**, 5466 (1981).

Crystal and Molecular Structure of a Free-Base *N*-Methylporphyrin: *N*-Methyl-5,10,15,20-tetrakis(*p*-bromophenyl)porphyrin

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Many of the properties of *N*-alkylporphyrins differ significantly from those of corresponding non-N-alkylated porphyrins, presumably due to distortion of the aromatic ring system from planarity. The opportunity to significantly alter the properties of a porphyrin was in fact the impetus leading to the first report concerning *N*-alkylporphyrins, authored by McEwen in 1936.[1] Subsequently, it has been found that *N*-alkylporphyrins form complexes with metal ions much more rapidly than corresponding non-*N*-alkylated porphyrins[2,3] and that they are more basic.[1,4-6]

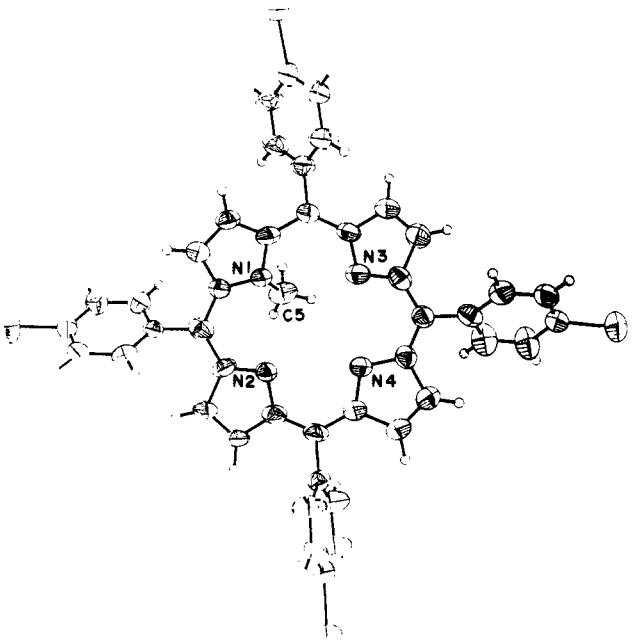

Figure 1. View of the *N*-CH_3HTPPBr$_4$ molecule. Hydrogen atoms have been rescaled for clarity, and the thermal ellipsoids have been drawn at the 50% probability level.

The *N*-alkylporphyrins exhibit visible absorption spectra that are quite similar in both energy and intensity to corresponding non-*N*-alkylated porphyrins,[4,6-8] indicating retention of a high degree of aromaticity. The proton NMR spectra of *N*-methylporphyrins show a large degree of shielding of the protons of the *N*-methyl group, in contrast to the deshielding typical of protons bound to the nitrogen atoms of porphyrins, indicating that the protons of the *N*-methyl group are significantly displaced from the plane of the aromatic system. Recent reports of the thorough characterization of *N*-alkylporphyrins as products of the decomposition of the prosthetic groups of cytochrome *P*-450 in vivo[9] add interest to a structural determination of nonmetalated species of this type.

The structures of a number of transition-metal complexes of *N*-alkylporphyrins,[10-14] together with one structure of a protonated nonmetallo *N*-substituted porphyrin,[15] have been reported, but no structures of neutral free-base *N*-alkylporphyrins have previously been described. Herein we describe the structure of such a species, *N*-methyl-5,10,15,20-tetra(*p*-bromophenyl)porphyrin, *N*-CH_3HTPPBr$_4$, which was synthesized by standard methods[6,16] and recrystallized several times from dichloromethane/acetonitrile mixtures. Using a Nicolet R3 diffractometer, we measured the intensities of 3860 unique observed reflections ($I > 2.5\sigma(I)$) by θ-2θ scans, employing Cu Kα radiation (graphite monochromator). All non-hydrogen atoms were refined with anisotropic thermal parameters, and hydrogen atoms bound to carbon were included in calculated positions. The single hydrogen atom on nitrogen in this neutral free base was strongly indicated to be on N4 by the position of the highest peak in the vicinity of the porphyrin

(1) McEwen, W. K. *J. Am. Chem. Soc.* **1936**, *58*, 1124-1129.
(2) Shah, B.; Shears, B.; Hambright, P. *Inorg. Chem.* **1971**, *10*, 1828-1830.
(3) Bain-Ackerman, M. J.; Lavallee, D. K. *Inorg. Chem.* **1979**, *18*, 3358-3364.
(4) Jackson, A. H. In "The Porphyrins"; Dolphin, D. Ed.; Academic Press: New York; Vol. 1, pp. 341-364.
(5) Neuberger, A.; Scott, J. J. *Proc. R. Soc. London, Ser. A.* **1952**, *213*, 307-310.
(6) Lavallee, D. K.; Gebala, A. E. *Inorg. Chem.* **1974**, *13*, 2004-2008.
(7) Lavallee, D. K. *Bioinorg. Chem.* **1976**, *6*, 219-227.
(8) Lavallee D. K.; Bain, M. J. *Bioinorg. Chem.* **1978**, *9*, 311-321.
(9) (a) Kunze, K. L.; Ortiz de Montellano, P. R. *J. Am. Chem. Soc.* **1981**, *103*, 4225-4230. (b) Tephly, T. R.; Coffman, B. L.; Ingall, G.; Abou Zeit-Har, M. S.; Goff, H. M.; Tabba, H. D.; Smith, K. M. *Arch. Bio. Chem. Biophys.* **1981**, *212*, 120-126.
(10) Goldberg, D. E.; Thomas, K. M. *J. Am. Chem. Soc.* **1976**, *98*, 913-919.
(11) Anderson, O. P.; Lavallee, D. K. *J. Am. Chem. Soc.* **1976**, *98*, 1404-1409.
(12) Anderson, O. P.; Lavallee, D. K. *Inorg. Chem.* **1977**, *16*, 1634-1640.
(13) Lavallee, D. K.; Kopelove, A. B.; Anderson, O. P. *J. Am. Chem. Soc.* **1978**, *100*, 3025-3033.
(14) Anderson, O. P.; Kopelove, A. B.; Lavallee, D. K. *Inorg. Chem.* **1980**, *19*, 2101-2107.
(15) McLaughlin, G. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 136-140.
(16) Adler, A. D.; Longo, F. R.; Finarelli, J. E.; Goldmacher, J.; Assou, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.

0002-7863/82/1504-4707$01.25/0