no conformational preference in the torsion angles of ω_2 and ω_4 was observed: conformers with gauche$^+$ (g$^+$), gauche$^-$ (g$^-$), and trans (t) existed to almost the same extent in the stable SAH conformers. Therefore, these torsion angles are conformationally flexible.

Energetically Stable SAH Conformation and Its Biological Implication. The conformation of the SAH molecule can be characterized by the ribose puckering and seven torsion angles. Among these, the combination of χ, ψ, and ϕ torsion angles may be highly important for the energetically favored conformers having either C(2′)-endo or C(3′)-endo ribose puckering. From the calculated energy listed in Tables VII and VIII, the stable conformation could be divided into the following sets of (χ,ψ,ϕ): (anti,(g/t),g$^-$) and (syn,(g/t),g$^+$) for C(2′)-endo ribose pucker; anti,(g/g),g$^+$), (anti,(g/t),g$^-$), and (syn,(g/t),g$^-$) for C(3′)-endo pucker. The most stable conformers belonging to the respective ribose puckering are shown in Figures 8 and 9. These five stable SAH conformers, obtained by energy calculations, coincide with the data obtained from ^{1}H NMR spectra, which provide information as to the averaged conformation. On the other hand, the conformation observed in the crystal structure is also in the region having energy minima (−30.7 kcal/mol for molecule A and −29.4 kcal/mol for molecule B). These conformers may represent slightly unfavored ones upon interaction between the neighboring molecules accompanying the crystal packing.

The functional groups of primary importance for the binding to methyltransferases are terminal carboxyl (O(1) and O(2)) and amino (N(α)) groups, sulfur atom (S), the amino nitrogen atom of adenine base (N(6)), and the 3′- and 2′-hydroxyl groups of ribose ring (O(2′) and O(3′)). Binding may require the energetically most stable conformer; therefore, we propose that the conformer shown in Figure 8a may be the most likely candidate of the SAH molecule required for binding to the methyltransferases. This hypothesis is based on the opinion that the energy value (−37.6 kcal/mol) can reasonably be regarded as significantly stable compared with the other conformers shown in Figures 8b and 9 (−34.2 to 36.1 kcal/mol). It is interesting to note that the conformer shown in Figure 8a is compactly folded and that all of its functional groups protrude to the surface, resulting in the capacity for hydrogen bondings with the functional groups at the binding site of methyltransferases.

The functional groups of SAM essential for binding to methyltransferases have been determined by synthetic procedures,[47,48] and the groups effective in methyl donor activity are identical with those that in SAH are necessary for binding to the enzymes. This observation and the potent inhibition of methyltransferases by SAH, a metabolite of SAM, imply that the spatial conformation of SAH at the active site must be identical with that of SAM, except in the configuration of the sulfonium center. As the sulfonium atom of the SAM molecule takes the S configuration,[34] methylation by methyltransferases at the sulfur atom for the conformer shown in Figure 8a would be stereochemically most preferable. There are no short contacts between the methyl group and L-homocysteine or the adenosine moiety. Further physicochemical investigations are required to support these suggestions.

Acknowledgment. We are indebted to Dr. M. Sugiura, Kobe Women's College of Pharmacy, for the measurements of 200-MHz NMR spectra.

Supplementary Material Available: Tables of observed and calculated structure factors, anisotropic thermal parameters, and the bond lengths and angles of non-hydrogen atoms (14 pages). Ordering information is given on any current masthead page.

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[47] V. Zappia, C. R. Zydek-Cwick, and F. Schlenk, *J. Biol. Chem.*, **244**, 4499 (1969).

[48] R. T. Borchardt, Y. S. Wu, J. A. Huber, and A. F. Wycpalek, *J. Med. Chem.*, **19**, 1104 (1976).

Stereoelectronic and Conformational Effects in Meisenheimer Complexes. Intrinsic Reactivities of Spiro vs. 1,1-Dimethoxy and 1-Methoxy-1-phenoxy Complexes[1]

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Abstract: Rate and equilibrium constants of formation of spiro Meisenheimer complexes derived from 1-(2-hydroxyethoxy)-2,6-dinitro-4-X-benzenes in aqueous solution are compared with those for 1,1-dimethoxy Meisenheimer complexes derived from 2,6-dinitro-4-X-anisoles. Hammett ρ values for the equilibrium constants are 8.2 for the dimethoxy and 5.9 for the spiro complexes, while the normalized ρ values for the rate constants of complex formation (cleavage) are 0.44 (−0.56) for the dimethoxy and 0.58 (−0.42) for the spiro complexes. The large difference in the equilibrium ρ values is attributed to a conformation of the dimethoxy complexes in which there is repulsion between the lone pairs on the ketal and the *o*-nitro group oxygens. A procedure for making the reactions in the two families thermodynamically comparable by correcting the rate and equilibrium constants for the pK_a difference in the nucleophile and for the intramolecularity of spiro complex formation was applied. The corrected parameters show that the spiro complexes form and decompose much faster than the dimethoxy complexes. This enhanced reactivity, $\Delta\Delta G^\ddagger$, is attributed to a stereoelectronic effect or p–π overlap between a lone pair orbital of the nonreacting oxygen and the benzene ring, which is only feasible in the transition state of the spiro complex reaction (**14**) but not in the transition state of the dimethoxy complex reaction (**15**). This interpretation is strongly supported by the fact that $\Delta\Delta G^\ddagger$ increases with increasing electron-withdrawing strength of the X substituent. The enhanced rate of formation and decomposition of the spiro complex from catechol 2,4,6-trinitrophenyl ether compared to that of the corresponding 1-methoxy-1-phenoxy complex can be explained in a similar way.

There is a striking difference between the intrinsic reactivities of 1,1-dimethoxy and of spiro Meisenheimer complexes.[2] The work to be described in this paper is aimed at obtaining a more quantitative measure of this difference, at sorting out transi-

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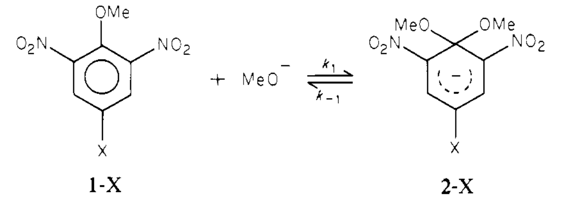
Table I. Rate and Equilibrium Constants for Spiro Meisenheimer Complexes at 25 °C in Water (Reaction 2)[a]

constant	**5**-SO_2CF_3 (1.36)[f]	**5**-NO_2[b] (1.23)[f]	**5**-CF_3 (0.74)[f]	**5**-Cl (0.23)[f]	**5**-H[c] (0)[f]
$K_{OH}k_2$, $M^{-1}\ s^{-1}$	8.51×10^6	1.71×10^6	4.20×10^4	9.76×10^2	
k_2,[d] s^{-1}	3.64×10^7	5.69×10^6	1.40×10^5	3.25×10^3	5.82×10^2
k_{-2}, s^{-1}	8.90×10^{-2}	0.10	4.30	50.5	1.37×10^2
K_2[e]	4.09×10^8	5.69×10^7	3.25×10^4	64.4	4.25

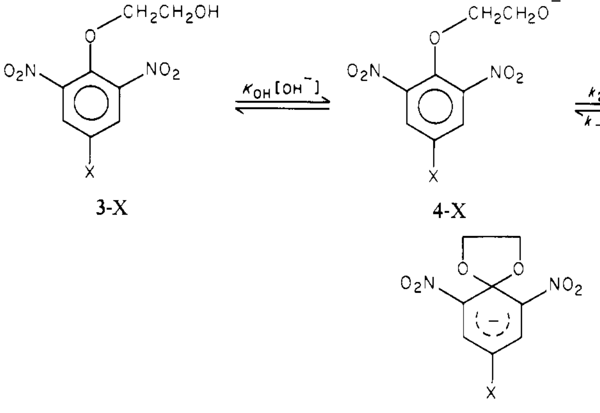
[a] μ 0.2 M (KCl). [b] Crampton and Willison[3] report $K_{OH}k_2 = 1.6 \times 10^6\ M^{-1}\ s^{-1}$ and $k_{-2} = 0.095\ s^{-1}$ at $\mu = 0.2$ M (NaCl). [c] Reference 3. [d] Calculated from $K_{OH}k_2$ assuming $K_{OH} = 0.3$; see text. [e] K_2 obtained from k_2/k_{-2}. [f] σ^-, ref 20.

tion-state and ground-state effects, and at providing a more definite interpretation than has been possible in the past.[2-4]

The reactions we will primarily focus upon are eq 1 and the second step of eq 2. The dramatic difference in reactivity is most easily recognized by comparing rates of decomposition of the complexes with their respective equilibrium constants of formation. The common observation is that the spiro complexes decompose much more rapidly than the corresponding 1,1-dimethoxy complexes ($k_{-2} \gg k_{-1}$) despite the much higher stability of the spiro complexes ($K_2 \gg K_1$; note that because of the different units of $K_2 = k_2/k_{-2}$ and $K_1 = k_1/k_{-1}$ the comparison should be made with reference to the standard state of 1 M MeO^- in the case of eq 1). For example, with X = NO_2 in water[5] $k_{-1} = 5 \times 10^{-4}\ s^{-1}$[6,7] and $k_{-2} = 0.1\ s^{-1}$[3,4] (k_{-2}/k_{-1} = 200). Similar results have been reported for 2,4-dinitronaphthyl and 2,4-dinitrophenyl systems.[2]



(1)



(2)

5-X

A direct comparison of the k_{-2}/k_{-1} ratios with the K_2/K_1 ratios is of course misleading because a major factor enhancing the stability of the spiro complexes is the intramolecularity of the reaction. As we will show, even after making the most conservative allowances for the intramolecularity the spiro complexes still remain much more reactive than the 1,1-dimethoxy complexes. We will argue that stereoelectronic effects[8] are the most likely reason for this exalted reactivity.

The experimental work to be reported includes a kinetic study of eq 2 for X = SO_2CF_3, CF_3, and Cl, which complements earlier work on **5**-NO_2[3,4] and **5**-H,[3] and some kinetic data on the k_1 step of reaction 1 for X = SO_2CF_3, NO_2, CN, and CF_3 in 5% methanol–95% water. These latter data, in combination with the k_{-1} values measured earlier,[7] complete the kinetic and thermodynamic characterization of eq 1 in aqueous[5] solution.

Results

General Features. All experiments were carried out under pseudo-first-order conditions in aqueous solution or 5% methanol–95% water (v/v) (eq 1) at 25 °C and μ = 0.2 M (KCl). The reactions involving Meisenheimer complexes were monitored spectrophotometrically in the range 400–500 nm, i.e., where the complexes have an intense absorption.[9] The rates were measured in the stopped-flow apparatus. Determination of the hydrolysis rates of **1**-SO_2CF_3, **1**-NO_2, **1**-CN, and **1**-CF_3 were also made by monitoring the formation of the 2,6-dinitro-4-X-phenoxide ion at 360 nm.

Spiro Complexes. Table I summarizes rate and equilibrium constants according to eq 2. In the following we describe how these results were obtained.

5-SO_2CF_3 and 5-NO_2. The rates of complex formation for **5**-SO_2CF_3 were measured by mixing a slightly acidic solution of **3**-SO_2CF_3 with dilute phosphate buffers at pH 7.0–7.8. These somewhat unorthodox reaction conditions were mandated by the high reactivity of **4**-SO_2CF_3: complex formation is half-complete at a pH around 6 and k_2 is so high that experiments in KOH solutions would lead to rates beyond the stopped-flow range. Catalysis by the phosphate buffer was undetectable at the concentrations used (≤0.05 M total buffer concentration).

The data, which are summarized in Table S1,[10] can be described by[3,4]

$$k_{obsd} = K_{OH}k_2[OH^-] + k_{-2} \qquad (3)$$

They provide a reliable value for $K_{OH}k_2$, but k_{-2} is too small to be accurately determined. A more precise value for k_{-2} was obtained from pH-jump experiments at pH 4.7–5.5. In these experiments the complex was first generated by placing the substrate (**3**-SO_2CF_3) into a 0.001 or 0.02 M KOH solution. This solution was then mixed with a dilute pyridine buffer in the stopped-flow apparatus. Under these conditions the equilibrium of eq 2 is virtually completely on the side of **3**-SO_2CF_3 and the observed process corresponds to the k_{-2} step. The data are summarized in Table S2.[10] They indicate a small contribution by a hydronium ion catalyzed pathway but no significant buffer catalysis, according to

$$k_{obsd} = k_{-2} + k_{-2}^{H}[H^+] \qquad (4)$$

Even though similar data for **5**-NO_2 have been reported previously,[3,4] the ionic strength and/or the identity of the compensating electrolyte (NaCl instead of KCl) were different. We therefore carried out a few experiments under the current conditions. Since **4**-NO_2 is also very reactive, we used the same procedures as with the SO_2CF_3-derivative. The results are in Table S1[10] (complex formation) and Table S2[10] (pH jumps). They afford $K_{OH}k_2$ and k_{-2} values that are virtually identical with those determined before.[3,4]

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(1) This is part 21 of the series "Intermediates in Nucleophilic Aromatic Substitution". Part 20: Bernasconi, C. F.; Muller, M. C.; Schmid, P. *J. Org. Chem.* **1979**, *44*, 3189.

(2) For a recent review see: Terrier, F. *Chem. Rev.* **1982**, *82*, 77.

(3) Crampton, M. R.; Willison, M. J. *J. Chem. Soc., Perkin Trans. 2*: **1974**, *1681*.

(4) Bernasconi, C. F.; Gandler, J. R. *J. Org. Chem.* **1977**, *42*, 3387.

(5) In the case of the 1,1-dimethoxy complexes the solvent contained a few percent methanol in order to generate methoxide ion.[6]

(6) Murto, J.; Kohvakka, E. *Suom. Kemistil. B* **1966**, *39*, 128.

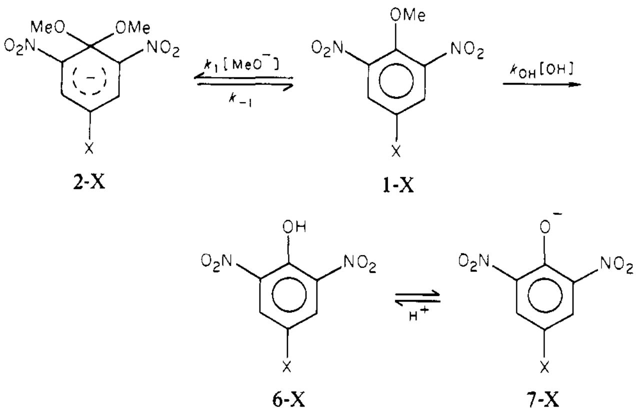
(7) Bernasconi, C. F.; Gandler, J. R. *J. Am. Chem. Soc.* **1978**, *100*, 8117.

(8) Deslongchamps, P. *Tetrahedron*, **1975**, *31*, 2463.

(9) For reviews, see: (a) Crampton, M. R. *Adv. Phys. Org. Chem.* **1969**, *7*, 211. (b) Strauss, M. J. *Chem. Rev.* **1970**, *70*, 667.

(10) See paragraph at end of paper regarding supplementary material.

Scheme I

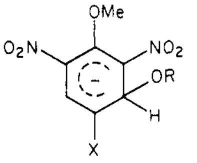


5-CF$_3$ and 5-Cl. Owing to the much lower reactivity of **4**-CF$_3$ and **4**-Cl the rates of complex formation could be conveniently determined in KOH solution. The data are in Table S1;[10] they obey eq 3 from which both $K_{OH}k_2$ and k_{-2} could be evaluated. In the case of **5**-CF$_3$, k_{-2} was independently determined by the pH-jump method (eq 4, results in Table S2[10]).

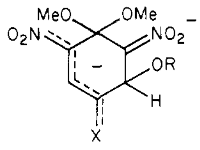
5-H. In view of the fact that for 5-NO$_2$ we obtained results which showed that the change in compensating electrolyte from NaCl to KCl has a negligible effect, we did not feel a need to reinvestigate this compound, studied before by Crampton and Willison.[3]

1,1-Dimethoxy Complexes. Rate constants for the collapse of **2**-X (k_{-1}) have been measured in purely aqueous solution by placing the isolated complex into the solution and monitoring the decomposition.[7] Rate constants for the *formation* of **2**-X (k_1) in water can only be measured in an "aqueous" solvent that contains enough methanol to generate sufficient amounts of MeO$^-$. For the most reactive substrates (X = SO$_2$CF$_3$, NO$_2$) 1–2% methanol would have been adequate,[6] but in order to be able to study **1**-CN and **1**-CF$_3$ a somewhat higher methoxide concentration seemed desirable. Thus we chose 5% methanol.

The problems in measuring k_1 under these conditions are not trivial because one has to contend with several competing reactions. The major competition is hydrolysis to the corresponding 2,6-dinitro-4-X-phenol as shown in Scheme I. Other possible competing reactions are methoxide and hydroxide ion attack at the 3-position of **1**-X to form **8**-X[2,11] and the addition of a second nucleophile to **2**-X or **8**-X to form **9**-X.[2] These complications could be avoided by keeping the base concentration low, as described in more detail below.



8-X (R = H or Me)



9-X (R = H or Me)

2-SO$_2$CF$_3$. The reaction of **1**-SO$_2$CF$_3$ was studied at [KOH]$_0$ ranging from 2.23 × 10^{-3} to 1.54 × 10^{-2} M. The effective concentrations of MeO$^-$ and OH$^-$ are given by

$$[\mathrm{MeO^-}] = f[\mathrm{KOH}]_0 \quad (5)$$

$$[\mathrm{OH^-}] = (1 - f)[\mathrm{KOH}]_0 \quad (6)$$

with $f = 0.0957$ based on Murto's work.[12] According to Scheme I one expects to see two kinetic processes, a fast one corresponding to the simultaneous formation of **2**-SO$_2$CF$_3$ and **6**-SO$_2$CF$_3$/**7**-SO$_2$CF$_3$ and a slow one corresponding to the irreversible conversion of **2**-SO$_2$CF$_3$ and of any remaining **1**-SO$_2$CF$_3$ into **6**-SO$_2$CF$_3$/**7**-SO$_2$CF$_3$. This is indeed the observed behavior. The two processes occur on widely separated time scales (>100-fold separation), implying that the fast process is completely decoupled from the slow one. Because of this and since the information we are seeking is to be obtained from the former one, we shall only focus on the fast reaction.

The results are summarized in Table S3.[10] A plot (not shown) of k_{obsd} vs. [KOH]$_0$ is linear, with a slope of 17.1 M^{-1} s^{-1} and a zero intercept. The zero intercept implies that in Scheme I k_1[MeO$^-$] + k_{OH}[OH$^-$] ≫ k_{-1} while the linearity demonstrates that OH$^-$ and/or MeO$^-$ addition to the 3-position of **1**-SO$_2$CF$_3$ is not a significant reaction at the base concentrations used.[13] Hence we have $k_{obsd} \approx k_1[\mathrm{MeO^-}] + k_{OH}[\mathrm{OH^-}]$; this is consistent with $k_{-1} = 2.56 \times 10^{-4}$ s^{-1},[7] which is much smaller than k_{obsd} for any [KOH]$_0$ used. Thus the slope is given by

$$\text{slope} = k_1 f + k_{OH}(1 - f) \quad (7)$$

In order to obtain k_1 one also needs to know k_{OH}. We assumed that k_{OH} measured in pure water would give a good approximation of k_{OH} in 5% methanol, and thus k_{OH} was determined in aqueous solution in a pH range of 10.9–11.9. The results are summarized in Table S4.[10] A plot of k_{obsd} vs. [OH$^-$] (not shown) is linear with zero intercept and affords k_{OH} = 4.95 M^{-1} s^{-1}. From eq 7 we now obtain k_1 = 132 M^{-1} s^{-1}.

2-NO$_2$. The reaction of **1**-NO$_2$ was already studied by Murto et al.[6] in 3.17 and 3.98% methanol. In order to have data for all compounds under strictly uniform conditions we reinvestigated the reaction. The procedure was the same as for **2**-SO$_2$CF$_3$. The data are summarized in Table S3[10] (5% methanol) and Table S4[10] (water). One obtains k_{OH} = 1.39 M^{-1} s^{-1} and k_1 = 17.5 M^{-1} s^{-1}. The former value compares with k_{OH} = 1.4 M^{-1} s^{-1} reported by Gibson and Crampton[11] at μ = 2 M (NaCl), the latter with Murto's[6] k_1 = 18 M^{-1} s^{-1} in 3.17 and 3.98% methanol.

2-CN. The reaction of **1**-CN shows somewhat different characteristics than the reactions of **1**-NO$_2$ and **1**-SO$_2$CF$_3$. The separation between the fast and the slow process is smaller and, at low base concentrations, amounts to less than a factor of 10, implying some coupling between the two processes. Furthermore, at high base concentration ([KOH]$_0$ > 0.05 M) a third kinetic process becomes visible in a time range intermediate between the first two. Its concentration and ionic strength dependence suggests that it is associated with the formation of a 1:2 complex such as **9**-CN. We did not investigate this reaction further and restricted our study to base concentrations where 1:2 complex formation interfered minimally.

The k_{obsd} values for the two processes of Scheme I are summarized in Table S5.[10] The coupling between the two and the fact that a plot of k_{obsd}^{fast} vs. [KOH]$_0$ has a nonnegligible intercept make it desirable to treat the data by the general equations 8 and 9.[16]

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[11] Gibson, B.; Crampton, M. R. *J. Chem. Soc., Perkin Trans. 2* **1979**, 648.

[12] Murto, J. *Ann. Acad. Sci. Fenn., Ser. A2* **1962**, 117.

[13] This is consistent with known data. In methanol K = 30 M^{-1} for methoxide ion addition to the 3-position of **1**-SO$_2$CF$_3$ while the rate constant for its decomposition is 25 s^{-1}.[14] Assuming similar rate and equilibrium constants in our solvent, these numbers indicate that this reaction would act as a rapid preequilibrium to the reactions in Scheme I and that even at the highest base concentration used, only about 4% of the substrate would be in the form of this complex. Data on the hydroxide ion addition at the 3-position are not available for **1**-SO$_2$CF$_3$ but they are for **1**-NO$_2$. Here K = 1.4 M^{-1} and k for decomposition is 8.4 s^{-1}.[11] Assuming a 7-fold[15] larger K and a 6-fold[15] smaller k for the decomposition leads to $K \approx 10$ M^{-1} and $k \approx 1.4$ s^{-1}. On the basis of these numbers 3-addition acts as a rapid and insignificant preequilibrium in the lower range of base concentrations used but should start to become nonnegligible at the high end of the range. At the highest [KOH]$_0$ perhaps as much as 14% of the substrate might be in the form of the 3-addition complex. On the other hand the fact that the plot of k_{obsd} vs. [KOH]$_0$ shows no sign of curvature either in 5% methanol or in pure water (see ref 15) suggests that the actual K is somewhat lower than these extrapolations imply.

[14] Terrier, F.; Millot, F.; Morel, J. *J. Org. Chem.* **1976**, *41*, 3892.

[15] In methanol K is 11.7 times larger and k 10.8 times smaller than for **1**-NO$_2$.[14] Since substituent effects are usually somewhat smaller in water than in methanol we have reduced these factors somewhat. A case in point is the ratio $K_1^{\mathrm{SO_2CF_3}}/K_1^{\mathrm{NO_2}}$, which in water is 14.6 (this work, see text) as compared to 61.5 in methanol.[14]

[16] Bernasconi, C. F.; "Relaxation Kinetics"; Academic Press: New York, 1976; p 27.

$$k_{\text{obsd}}{}^{\text{fast}} = \frac{1}{2}(a_{11} + a_{22}) + \left[\left(\frac{a_{11} + a_{22}}{2}\right)^2 + a_{12}a_{21} - a_{11}a_{22}\right]^{1/2} \quad (8)$$

$$k_{\text{obsd}}{}^{\text{slow}} = \frac{1}{2}(a_{11} + a_{22}) - \left[\left(\frac{a_{11} + a_{22}}{2}\right)^2 + a_{12}a_{21} - a_{11}a_{22}\right]^{1/2} \quad (9)$$

with

$$a_{11} = k_{-1} + k_1 f[\text{KOH}]_0 \quad (10)$$

$$a_{12} = k_1 f[\text{KOH}]_0 \quad (11)$$

$$a_{21} = k_{\text{OH}}(1 - f)[\text{KOH}]_0 \quad (12)$$

$$a_{22} = k_{\text{OH}}(1 - f)[\text{KOH}]_0 \quad (13)$$

Analysis of the data according to eq 14 and 15, which are easily

$$k_{\text{obsd}}{}^{\text{fast}} + k_{\text{obsd}}{}^{\text{slow}} = k_{-1} + \{k_1 f + k_{\text{OH}}(1 - f)\}[\text{KOH}]_0 \quad (14)$$

$$k_{\text{obsd}}{}^{\text{fast}}\, k_{\text{obsd}}{}^{\text{slow}} = k_{-1}k_{\text{OH}}(1 - f)[\text{KOH}]_0 \quad (15)$$

derived from eq 8–13,[16] affords $k_{\text{OH}} = 0.56$ M^{-1} s^{-1}, $k_1 = 8.37$ M^{-1} s^{-1}, and $k_{-1} = 1.13 \times 10^{-2}$ s^{-1}. This latter value is in very good agreement with $k_{-1} = 1.30 \times 10^{-2}$ s^{-1} determined directly by measuring the decomposition of an authentic sample of **2**-CN in water.[7] On the other hand k_{OH} differs by a factor of about 2 from $k_{\text{OH}} = 0.24$ M^{-1} s^{-1} determined in pure water (data in Table S4[10]). We do not know whether this represents a genuine solvent effect or whether the discrepancy is, in part, due to experimental error because our data treatment did not make any allowance for the small amounts of 1:2 complex being formed.

2-CF_3. In the reaction of **1**-CF_3 the two kinetic processes are again widely separated, but, in contrast to the situation with **1**-SO_2CF_3 and **1**-NO_2, this is because of $k_{-1} \gg k_{\text{OH}}[\text{OH}^-]$, with $k_{\text{obsd}}{}^{\text{fast}}$ given by

$$k_{\text{obsd}}{}^{\text{fast}} = k_{-1} + k_1 f[\text{KOH}]_0 \quad (16)$$

However, k_1 could not be determined from $k_{\text{obsd}}{}^{\text{fast}}$ because the $k_1 f[\text{KOH}]_0$ term in eq 16 is very small at all base concentrations used. We therefore calculated k_1 as K_1k_{-1} where K_1 is the equilibrium constant for **2**-CF_3 formation. This latter was estimated via

$$K_1 = \frac{\text{OD}}{\epsilon_{2\text{-CF}_3}[2\text{-CF}_3]_0 f[\text{KOH}]_0} \quad (17)$$

where OD is the measured absorbance of $\lambda_{\max}$ 545 nm and $\epsilon_{2\text{-CF}_3}$ 2.8×10^4 is the extinction coefficient determined by Terrier and Millot[17] in 92.6% Me_2SO–7.4% methanol (v/v). We obtained $K_1 = 3.89$ M^{-1} as an average of five measurements in a range of $[\text{KOH}]_0$ from 0.02 to 0.19 M. In combination with $k_{-1} = 0.134$ s^{-1}[7] one obtains $k_1 = 0.521$ M^{-1} s^{-1}.

Discussion

Substituent Effects. Rate and equilibrium constants are summarized in Table I for the spiro and in Table II for the 1,1-dimethoxy complexes. In order to calculate k_2 from $K_{\text{OH}}k_2$ for the spiro complexes we used Crampton's[3] estimate of 0.3 M^{-1} for the experimentally inaccessible K_{OH}. We assumed that K_{OH} depends so little on the X substituent in comparison to the substituent dependence of k_2 and K_2 (see Table I) that the same value can be used for all compounds studied.[18] At any rate a slight substituent dependence of K_{OH} would cancel out in the pK_a adjustments to the applied below.

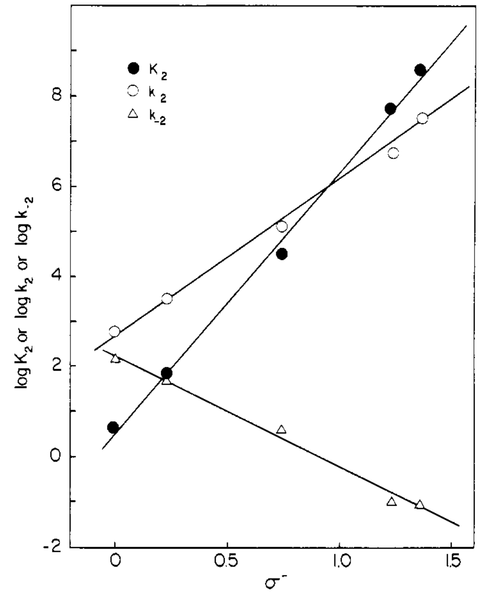

Figure 1. Hammett plots for the spiro complexes.

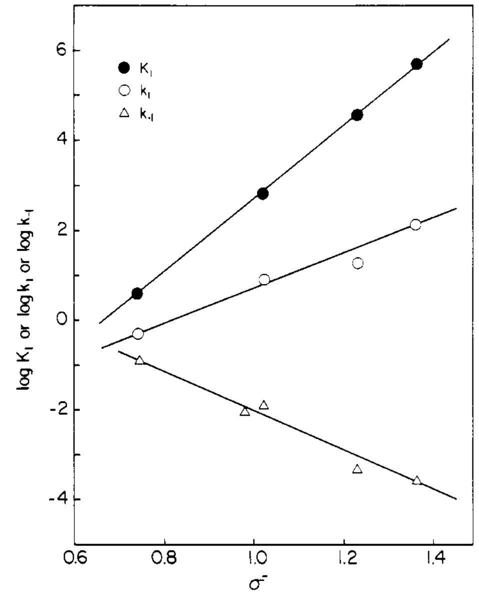

Figure 2. Hammett plots for the 1,1-dimethoxy complexes.

Hammett plots for rate and equilibrium constants are shown in Figure 1 for the spiro and in Figure 2 for the 1,1-dimethoxy complexes; they are based on the σ^- values listed in Tables I and II.

In view of the multitude of published σ^- values for some of our substituents,[20] the choice of a set of substituent constants is to some extent arbitrary. In the interest of comparability between the two families of complexes we chose a single set of σ^- values, even though two different sets would have led to slightly better correlations within a family. As can be seen from Figures 1 and 2, the correlations are quite satisfactory except for some negative deviations by the nitro group; such deviations are not uncommon.[21] We have calculated ρ values both including and excluding the nitro group. As is obvious from Table III, inclusion or exclusion of the nitro group has only a small effect on most ρ values. Table III includes ρ values for 1,1-dimethoxy complex formation in methanol.[14]

We note that $\rho_{\text{equil}} = 5.92$ for the spiro complexes is about 2.3 units smaller than $\rho_{\text{equil}} = 8.23$ for the 1,1-dimethoxy complexes. In view of the great similarity of the structures of **2**-X and **5**-X

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(17) Terrier F.; Millot, F. *C. R. Acad. Sci., Ser. C* **1969**, 808.

(18) ρ for K_{OH} may be in the order of 0.3 based on $\rho = 0.27$ for K_a of $ArCH_2CH_2COOH$[19] while $\rho(k_2) = 3.46$ and $\rho(K_2) = 5.92$. (See Table III.)

(19) Wells, P. R. *Chem. Rev.* **1963**, *63*, 171.

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(21) (a) Bordwell, F. G.; Anderson, H. M. *J. Am. Chem. Soc.* **1953**, *75*, 6019. (b) Dolman, D.; Stewart, R. *Can. J. Chem.* **1967**, *45*, 911.

Table II. Rate and Equilibrium Constants for 1,1-Dimethoxy Meisenheimer Complexes at 25 °C in Water (Reaction 1)[a]

constant	2-SO_2CF_3 (1.36)[d]	2-NO_2 (1.23)[d]	2-CN (1.02)[d]	2-SO_2CH_3 (0.98)[d]	2-CF_3 (0.74)[d]
k_1, M^{-1} s^{-1}	132[b]	17.5[b]	8.37[b]		0.52
k_{-1},[c] s^{-1}	2.56×10^{-4}	4.96×10^{-4}	1.30×10^{-2}	1.06×10^{-2}	1.34×10^{-1}
$K_1 = k_1/k_{-1}$, M^{-1}	5.16×10^5	3.53×10^4	6.44×10^2		3.89

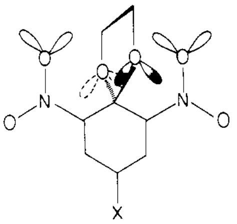
[a] $\mu = 0.2$ M (KCl). [b] From measurements in 5% MeOH-95% water (v/v), this work. [c] Reference 7. [d] σ^-, ref 20.

Table III. Hammett ρ Values[a]

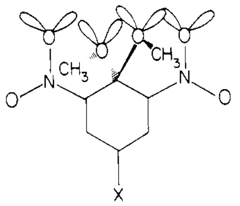
			1,1-dimethoxy complexes	
ρ	spiro complexes in H_2O	ρ	in H_2O	in MeOH[b]
$\rho(k_2)$	3.46 ± 0.09, $r = 0.999$	$\rho(k_1)$	3.60 ± 0.20, $r = 0.979$	3.91 ± 0.23, $r = 0.971$
	(3.53 ± 0.06, $r = 0.999$)		(3.86 ± 0.07, $r = 0.998$)	(4.20 ± 0.19, $r = 0.985$)
$\rho(k_{-2})$	-2.46 ± 0.16, $r = 0.994$	$\rho(k_{-1})$	-4.63 ± 0.17, $r = 0.988$	-4.77 ± 0.27, $r = 0.974$
	(-2.34 ± 0.11, $r = 0.977$)		(-4.41 ± 0.12, $r = 0.996$)	(-4.68 ± 0.30, $r = 0.969$)
$\rho_{equil}(K_2)$	5.92 ± 0.16, $r = 0.999$	$\rho_{equil}(K_1)$	8.23 ± 0.05, $r = 0.999$	8.68 ± 0.44, $r = 0.979$
	(5.87 ± 0.17, $r = 0.998$)		(8.27 ± 0.03, $r = 0.999$)	(8.88 ± 0.49, $r = 0.978$)
$\rho_n(k_2) = \rho(k_2)/\rho_{equil}(K_2)$	0.58 ± 0.03	$\rho_n(k_1) = \rho(k_1)/\rho_{equil}(K_1)$	0.44 ± 0.03	0.45 ± 0.05
$\rho_n(k_{-2}) = \rho(k_{-2})/\rho_{equil}(K_2)$	(0.60 ± 0.03)		(0.47 ± 0.02)	(0.47 ± 0.05)
	-0.42 ± 0.03	$\rho_n(k_{-1}) = \rho(k_{-1})/\rho_{equil}(K_1)$	-0.56 ± 0.03	-0.55 ± 0.05
	(-0.40 ± 0.03)		(-0.53 ± 0.02)	(-0.53 ± 0.05)

[a] Values in parentheses are calculated omitting NO_2; error limits are standard deviations; r is the correlation coefficient. [b] Data from ref 14; substituents used are CF_3, SO_2CH_3, CN, NO_2, and SO_2CF_3.

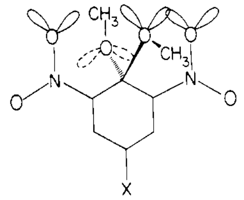
this large difference in ρ_{equil} seems surprising. This difference is most likely related to differences in conformation between the two types of complexes. Due to geometric constraints there is only one possible conformation for the spiro complexes (**10**) while for the 1,1-dimethoxy complexes one can think of at least three major conformations. One of them is analogous to **10**, i.e., with both methyl groups pointing up, another is shown in **11** with both methyl groups down, while the third has one methyl group up, the other down, as shown in **12**.



10



11



12

The conformation that is analogous to **10** is strongly disfavored on steric grounds and can be safely excluded from further considerations. Conformation **11** seems disfavored on electronic grounds. The lone-pair orbitals on the ketal oxygens are subject to unfavorable dipole–dipole interaction between themselves as well as with the oxygens of the *o*-nitro groups. The former interaction is well-known as the anomeric effect.[22] On the basis of these considerations one would expect **12** to be the preferred conformer. However, there are two observations which seem inconsistent with **12**. (1) X-ray data on **2-NO_2** shows that **11** is the preferred conformation.[23] (2) In methanol solution 1,1-dimethoxy complexes are stabilized by association with cations while spiro complexes and the complex between 1,3,5-trinitrobenzene and methoxide ion do not undergo such association.[24,25] This latter observation shows that association requires favorable interaction of the cation with the lone pairs of *two* ketal oxygens, which is feasible with **11** but not with **12**.

With reference to the X-ray data one might argue that in the crystalline state intermolecular forces are more important in determining the conformation than in solution and that these data are therefore irrelevant. However, the second observation does refer to solutions and is therefore not as easily dismissed. In fact it suggests a possible explanation as to why **11** might be favored over **12**. It is that the accumulation of all the negative charge density from the oxygen lone pairs and their spatial arrangement makes solvation particularly effective, in a similar way as it makes complexation with metal ions favorable. In order to invalidate this line of reasoning one would have to argue that there is an equilibrium between **11** and **12** that favors **12** in aqueous solution and in methanol at low salt concentration but which shifts toward **11** by complexation with the metal cation at high salt concentrations.

It is obvious that the evidence for either conformer is not compelling. However, evidence based on *rates*, discussed below, seems to strongly favor **11**, and we shall therefore assume that **11** is the favored conformer. It should be noted, though, that our explanation of why $\rho_{equil}(K_1)$ is larger than $\rho_{equil}(K_2)$ only depends on the conformation of the 1,1-dimethoxy complexes to be different from **10** and not on whether **11** or **12** is preferred. This explanation is based on the above-mentioned fact that in **11** there are unfavorable dipole–dipole interactions between the ketal oxygen and the *o*-nitro oxygens while for the spiro complexes the lone pairs are arranged in such a way as to avoid such repulsive interactions. The repulsive interaction between the ketal oxygens and the oxygens of the *o*-nitro groups in **11** can be reduced by shifting some of the negative charge from the *o*-nitro groups into the X substituent. It is this shift that apparently manifests itself by an enhanced $\rho_{equil}(K_1)$ value.[26] Note that if **12** was the preferred

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(22) See, e.g.: (a) Lemieux, R. U. *Pure Appl. Chem.* **1971**, *25*, 527. (b) Eliel, E. L. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 739. (c) Jeffrey, G. A.; Pople, J. A.; Brinkley, J. S.; Vishveshwara, S. *J. Am. Chem. Soc.* **1978**, *100*, 373. (d) Tvaroska, I.; Bleha, T. *Can. J. Chem.* **1979**, *57*, 424.

(23) Ueda, H.; Sakabe, N.; Tanaka, J. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2866.

(24) (a) Crampton, M. R.; Khan, H. A. *J. Chem. Soc., Perkin Trans. 2*: **1972**, 1173, 2286. (b) Crampton, M. R.; Khan, H. A. *Ibid.* **1973**, 1103. (c) Crampton, M. R. *Ibid.* **1975**, 825.

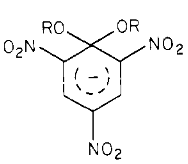
(25) Crampton, M. R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 2157.

(26) In **10** there is not only an absence of repulsive dipole–dipole interactions but probably also a stabilizing interaction between the ketal oxygen lone pairs and the positive centers on the nitrogens of the *o*-nitro groups. A similar stabilizing interaction was shown to occur between the carbonyl oxygen and an *o*-nitro group in the Meisenheimer complex between 1,3,5-trinitrobenzene and cyclopentanone anion.[27] In our case this interaction could be partly responsible for the higher stability of the spiro complexes; its effect on ρ_{equil} is less clearly predictable because the nitrogen of the nitro groups is positive both in the reactant and complex state.

conformer, there would still be one ketal oxygen that interacts unfavorably with one *o*-nitro oxygen, also leading to a shift of negative charge into the X substituent. The rather large difference between $\rho_{\text{equil}}(K_1) = 8.2$ and $\rho_{\text{equil}}(K_2) = 5.9$ might be regarded as suggestive, though not conclusive, additional evidence for **11** as opposed to **12**.

We now turn to the kinetic ρ values. In order to allow meaningful comparisons to be made between the two families the kinetic ρ values have been normalized (Table III). The simplest interpretation of the normalized ρ values in the forward direction ($\rho_n(k_1)$, $\rho_n(k_2)$) would be that they are an approximate measure of the degree of charge transfer from the nucleophile to the aromatic ring, and perhaps also of the degree of C–O bond formation in the transition state, or, in the reverse direction ($\rho_n(k_{-1})$, $\rho_n(k_{-2})$) of the amount of negative charge still left in the ring and of the degree of C–O bond cleavage. According to this interpretation it would appear then that charge transfer and C–O bond formation are about 60% complete for the spiro and about 45% complete for the 1,1-dimethoxy complexes.

The notion that $\rho_n(k_1)$ (or $\rho_n(k_{-1})$) might be a fairly good measure of the degree of C–O bond formation (or cleavage) in the transition state of the 1,1-dimethoxy complexes is supported by data on β_{lg} for the collapse of 1,1-dialkoxy complexes such as **13**.[7] β_{lg} may be regarded as another probe of the degree of



13

C–O bond cleavage in the transition state. Because a plot of log k_{-1} vs. $\text{p}K_a^{\text{ROH}}$ for the collapse of **13** with R = CH_3CH_2, CH_3, $CH_3OCH_2CH_2$, $ClCH_2CH_2$, and $HC{\equiv}CCH_2$ is curved, β_{lg} could only be approximated by evaluating the slope of the tangent through a given point.[7] For R = CH_3 $\beta_{\text{lg}} \approx -0.5$. This β_{lg} value probably underestimates the degree of C–O bond cleavage due to solvation and possibly other effects;[7] i.e., the actual amount of cleavage might be as high as, or even somewhat higher than, that suggested by $\rho_n(k_{-1}) = -0.56$. Whatever the fine points are, the picture which emerges from $\rho_n(k_{-1})$ and β_{lg} seems quite consistent in that both parameters suggest that C–O bond cleavage is somewhat more than half complete.

The situation is more ambiguous for the spiro complexes. As will be shown later, $\rho_n(k_2)$ and $\rho_n(k_{-2})$ include contributions from other effects and are probably not very reliable measures of C–O bond formation/cleavage. In fact the normalized ρ values referring to the 1,1-dimethoxy complexes may give a better approximation to the transition structure of the spiro complexes than do $\rho_n(k_2)$ and $\rho_n(k_{-2})$, and we shall make this assumption whenever a characterization of the transition state is needed.

A comparison of ρ values for the 1,1-dimethoxy complexes in water with those in methanol is of interest. The Hammett correlations in methanol show considerably more scatter than in water, possibly because some of the rate and equilibrium constants represent extrapolations of data obtained in Me_2SO–methanol mixtures[14] which may introduce some errors. Even though the correlations improve slightly if one uses a different set of σ^- values, we kept the set used in water in order to make the ρ values comparable in the two solvents. We note that $\rho(K_1) = 8.68$ in methanol is just barely larger than $\rho(K_1) = 8.23$ in water. Usually equilibrium ρ values increase significantly upon changing from water to an alcoholic solvent.[28] The smallness of the increase observed here is probably due to the strong charge delocalization, which reduces the need for stabilization by the solvent.

The kinetic ρ values (and also the normalized ρ values) are quite similar in both solvents, suggesting that the transition state does not change much upon changing the solvent.

Intrinsic Reactivities of Spiro vs. 1,1-Dimethoxy Complexes. Effective molarities (EM) are a convenient way of assessing the effect of intramolecularity on a reaction. Before we can calculate meaningful EM's for the spiro complexes we need to correct for the approximately 10-fold lower basicity of $ArOCH_2CH_2O^-$ compared to MeO^-.[30] We shall assume that the relative carbon basicities[31] of oxyanions are proportional to their relative proton basicities. This means that if $ArOCH_2CH_2O^-$ had the same basicity as MeO^-, K_2 would be 10-fold higher than observed. Thus we adjust all our K_2 values by increasing them 10-fold[32] ($K_2^{\text{ad}} = 10K_2$; see Table IVA).

In order to assess how this 10-fold increase in K_2 is to be distributed between k_2 and k_{-2} one needs to know β_{nuc} and/or β_{lg}. In the absence of such data for the spiro complexes we shall use β_{lg} determined for the collapse of **13**[7] and assume $\beta_{\text{nuc}} = 1 - \beta_{\text{lg}}$. From the curved dependence of log k_{-1} vs. $\text{p}K_a^{\text{ROH}}$ (see above) one obtains $\beta_{\text{lg}} \approx -0.8$ in the $\text{p}K_a^{\text{ROH}}$ range from 15.5 to 14.5. Thus k_2 needs to be increased by a factor of $10^{0.2}$ and k_{-2} decreased by a factor of $10^{0.8}$. It should be pointed out that any error in the assumed β_{nuc} and β_{lg} values would have an insignificant effect on the broad picture to emerge and would not change any of the general conclusions to be reached.[33]

The rate and equilibrium constants adjusted as described above are summarized in Table IVA. The ratios K_2^{ad}/K_1, k_2^{ad}/k_1, and $k_{-2}^{\text{ad}}/k_{-1}$ are also listed in the table (B); K_2^{ad}/K_1 corresponds to the equilibrium effective molarity, EM_{equil}, while k_2^{ad}/k_1 is the kinetic effective molarity, EM_{k}.

EM_{equil} is seen to be in the order of 10^4 to 10^7 M, quite comparable to the range typically observed for nucleophilic additions;[29] the increasing trend as X becomes less electron withdrawing is a consequence of $\rho_{\text{equil}}(K_1) > \rho_{\text{equil}}(K_2)$.

There are many factors, both enthalpic and entropic, that can contribute to high EM's.[29,34] Our data do not allow a detailed analysis of these factors, some of which have been discussed earlier.[3,4] Nevertheless, it is worth mentioning that with X = NO_2 the major factor appears to be of enthalpic rather than of entropic origin: ΔS^0 for $K_{\text{OH}}K_2$ (**5-NO₂**) is 1.0 ± 1.5 Gibbs/mol[4] while ΔS^0 for K_1 (**2-NO₂**) is 4 ± 5 Gibbs/mol.[6] If one assumes that ΔS^0 for K_{OH} is close to zero, the spiro complex does not seem favored, and may even be slightly disfavored, on entropy grounds. There is no easy explanation for this unusual behavior, but more extensive thermodynamic data would of course be necessary to establish the generality of these results.

Turning to the kinetic effective molarities we note that these are larger than the EM_{equil}'s for the three strongest electron-withdrawing substituents (Table IVB). This is unusual.[29] Our large $\text{EM}_{\text{k}}/\text{EM}_{\text{equil}}$ ratios indicate that there is another factor besides intramolecularity that only operates in the transition state and that makes spiro complex formation intrinsically faster than dimethoxy complex formation. The $k_{-2}^{\text{ad}}/k_{-1}$ ratios being larger than unity for these substituents is another manifestation of the same phenomenon. In order to evaluate how large this "other factor" is, one needs to separate it from the effect of intramo-

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(27) Renfrow, R. A.; Strauss, M. J.; Terrier, F. *J. Org. Chem.* **1980**, *45*, 471.

(28) Fuchs, R.; Lewis, E. S. In "Investigation of Rates and Mechanisms of Reactions", 3rd ed.; Lewis, E. S., Ed.; Wiley-Interscience: New York, 1974; p 777.

(29) For a recent review, see: Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.

(30) $\text{p}K_a$ = 15.54 for methanol: Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1960**, *82*, 795.

(31) Hine, J.; Weimar, R. D. *J. Am. Chem. Soc.* **1965**, *87*, 3387.

(32) If K_2 had been calculated based on slightly substituent-dependent K_{OH} values one would need to take this into account now in making these corrections. The resulting adjusted K_2 values would of course be the same.

(33) If one feels uncomfortable using β_{lg} from the reactions of **13** to adjust the rate constants for the *spiro* complexes one can simply turn things around and adjust the rates of the 1,1-dimethoxy complexes to the $\text{p}K_a$ of **3-X**. Since the intent is to adjust the two families of complexes *relative* to one another, such an inverted procedure would lead to the same qualitative and quantitative conclusions.

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(35) (a) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891. (b) Cohen, A. O.; Marcus, R. A. *Ibid.* **1968**, *72*, 4249. (c) Hine, J. *J. Am. Chem. Soc.* **1971**, *93*, 3701. (d) Albery, W. J. *Annu. Rev. Phys. Chem.* **1980**, *31*, 227.

Table IV. Rate and Equilibrium Constants for Spiro Complexes Adjusted to the pK_a of Methanol and Corrected for Intramolecularity

constant	SO_2CF_3	NO_2	CF_3	Cl[a]	H[a]
A. Adjusted to pK_a of MeOH					
K_2^{ad}	4.09×10^9	5.69×10^8	3.25×10^5	6.44×10^2	42.5
k_2^{ad}, s^{-1}	5.77×10^7	9.02×10^6	2.60×10^5	5.15×10^3	9.22×10^2
k_{-2}^{ad}, s^{-1}	1.41×10^{-2}	1.58×10^{-2}	6.81×10^{-1}	8.00	21.7
B. Effective Molarities					
$EM_{equil} = K_2^{ad}/K_1$, M	7.93×10^3	1.61×10^4	8.35×10^4	6.44×10^6	3.37×10^7
$EM_k = k_2^{ad}/k_1$, M	4.37×10^5	5.15×10^5	5.00×10^5	8.96×10^5	1.27×10^6
k_{-2}^{ad}/k_{-1}	55.1	31.8	5.08	1.39×10^{-1}	3.77×10^{-2}
C1. Effective Molarities due to Intramolecularity.[b] Based on $\rho_n(k_1)$ and $\rho_n(k_{-1})$					
$EM_k^{i,lp}$, M	52.0	70.9	1.46×10^2	9.91×10^2	2.05×10^3
$(k_{-2}^{ad}/k_{-1})^{i,lp}$	6.55×10^{-3}	4.41×10^{-3}	1.75×10^{-3}	1.54×10^{-4}	6.09×10^{-5}
C2. Effective Molarities due to Intramolecularity.[b] Based on $\rho_n(k_2)$ and $\rho_n(k_{-2})$					
$EM_k^{i,lp}$, M	1.83×10^2	2.75×10^2	7.15×10^2	8.90×10^3	2.32×10^4
$(k_{-2}^{ad}/k_{-1})^{i,lp}$	2.30×10^{-2}	1.71×10^{-2}	8.57×10^{-3}	1.38×10^{-3}	6.89×10^{-4}
D1. Corrected Ratios and $\Delta\Delta G^{\ddagger}$. Based on $\rho_n(k_1)$ and $\rho_n(k_{-1})$					
$k_2^{ad,corr}/k_1$[c]	8.40×10^3	7.26×10^3	3.42×10^3	9.04×10^2	6.20×10^2
$\Delta\Delta G^{\ddagger}$,[d] kcal/mol	5.34	5.25	4.81	4.02	3.80
ΔG^0,[e] kcal/mol	−7.77	−6.18	−0.80	5.44	8.02
D2. Corrected Ratios and $\Delta\Delta G^{\ddagger}$. Based on $\rho_n(k_2)$ and $\rho_n(k_{-2})$					
$k_2^{ad,corr}/k_1$[c]	2.38×10^3	1.86×10^3	5.93×10^2	1.01×10^2	54.7
$\Delta\Delta G^{\ddagger}$,[d] kcal/mol	4.59	4.45	3.77	2.73	2.36
ΔG^0,[e] kcal/mol	−7.77	−6.18	−0.80	5.44	8.02

[a] K_1, k_1, and k_{-1} used in the calculations were obtained by extrapolation of the Hammett plots. [b] Includes the contribution from lone pair repulsion in the dimethoxy complexes; see text. [c] $k_{-2}^{ad,corr}/k_{-1} = k_2^{ad,corr}/k_1$; see text. [d] $\Delta\Delta G^{\ddagger} = \Delta G_1^{\ddagger} - \Delta G_2^{\ddagger ad,corr} = RT \ln (k_2^{ad,corr}/k_1)$. [e] $\Delta G^0 = -RT \ln K_1$.

Table V. Rate and Equilibrium Constants for Aryloxide Complexes in 50% Me_2SO–50% Water[a]

1-methoxy-1-phenoxy complex[b]	catechol spiro complex[c]
$K_1 = 0.5\ M^{-1}$	$K_2 \approx 1.2 \times 10^5$
$k_1 = 425\ M^{-1}\ s^{-1}$	$k_2 \approx 1.2 \times 10^9\ s^{-1}$
$k_1 = 850\ s^{-1}$	$k_{-1} \approx 1.0 \times 10^4\ s^{-1}$

[a] Reference 47. [b] Reaction 22. [c] Reaction 23.

lecularity and other possible effects on the stability of the complexes. We shall correct for these effects by making the following two assumptions.

(1) The higher stability of the spiro complexes is a consequence of only two factors, the intramolecularity of the reaction and the absence of lone-pair repulsion between the ketal and *o*-nitro oxygens discussed earlier. This means that the formation of a hypothetical "*inter*molecular spiro complex" derived from an oxyanion of the same basicity as MeO^- would have an (adjusted, corrected) equilibrium constant $K_2^{ad,corr} = K_1$.

(2) The contribution to EM_k that arises solely from intramolecularity (i) and from the absence of lone pair repulsion (lp) is given by

$$EM_k^{i,lp} = (EM_{equil})^{\alpha} \quad (18)$$

while the contribution from the same factors to k_{-2}^{ad}/k_{-1} is given by

$$(k_{-2}^{ad}/k_{-1})^{i,lp} = (EM_{equil})^{1-\alpha} \quad (19)$$

Equations 18 and 19 are based on the idea that there is a parameter, α, which reflects both the tightness[34] of the transition state in the spiro series and the degree of lone-pair repulsion in the transition state in the dimethoxy family. It is likely that α_i, pertaining to the tightness and relevant to the contribution of the intramolecularity to EM_k, is different from α_{lp}, referring to the lone pair repulsion, and that α in eq 18 and 19 is a weighted average of α_i and α_{lp}. Since neither of these parameters is known, we shall assume that our normalized ρ values are an approximation of α and $1 - \alpha$, respectively.

We have calculated $EM_k^{i,lp}$ and $(k_{-2}^{ad}/k_{-1})^{i,lp}$ based on $\alpha = \rho_n(k_1)$ and $1 - \alpha = \rho_n(k_{-1})$ (Table IV, C1) as well as based on $\rho_n(k_2)$ and $\rho_n(k_{-2})$ (Table IV, C2). As mentioned earlier and discussed in more detail below, the former set is probably to be preferred because it is a better measure of transition-state structure even for the spiro complexes.

One now obtains the *corrected* rate constant ratios as

$$k_2^{ad,corr}/k_1 = EM_k/EM_k^{i,lp} \quad (20)$$

$$k_{-2}^{ad,corr}/k_{-1} = (k_{-2}^{ad}/k_{-1})/(k_{-2}^{ad}/k_{-1})^{i,lp} \quad (21)$$

These corrected ratios (Table IV, D1, and D2) represent the difference in intrinsic reactivity between the two families of complexes after correcting for intramolecularity, lone-pair repulsion, and pK_a of the nucleophile. Since $K_2^{ad,corr} = K_1$ we also have $k_2^{ad,corr}/k_1 = k_{-2}^{ad,corr}/k_{-1}$. These ratios are quite large and increase with increasing electron-withdrawing strength of the X substituent. Translated into differences of free energies of activation, $\Delta\Delta G^{\ddagger} = \Delta G_1^{\ddagger} - \Delta G_2^{\ddagger ad,corr}$, the numbers indicate differences in transition-state energies in the order of several kcal/mol (Table IV, D1 and D2). From a correlation of $\Delta\Delta G^{\ddagger}$ with ΔG^0 one obtains $\Delta\Delta G_0^{\ddagger} = 4.6$ kcal/mol (3.5 kcal/mol if $\rho_n(k_2)$ and $\rho_n(k_{-2})$ are used) for the differences in the intrinsic barriers in the Marcus[35] sense.

It should be noted that the exact values of $k_2^{ad,corr}/k_1$ or $\Delta\Delta G^{\ddagger}$ depend of course on the choice of ρ_n. However, as our calculations with different ρ_n values show, the *qualitative* conclusions are not sensitive to the choice of ρ_n.

What Makes the Spiro Complexes Intrinsically More Reactive? Since our adjustment and correction procedures make the spiro and dimethoxy complexes thermodynamically equivalent, the only acceptable explanations can be those invoking transition-state effects. This means that the factors that stabilize the transition state of the spiro-complex reactions over that of the dimethoxy complex reactions are either absent from the reactant and product states or, if they are present, their energetic effects on these states must be of comparable magnitude.

Recognition of these criteria immediately excludes from further consideration a number of explanations presented previously. For example, one factor which was recognized as contributing to the high k_{-2}/k_{-1} ratios is the lower basicity of the oxyanion in $ArOCH_2CH_2O^-$ compared to methoxide ion.[4] In our corrected k_{-2}/k_{-1} ratios this factor is already taken into account and can no longer be invoked. Relief of strain in the spiro ring was suggested as another factor that increases k_{-2}.[3,4] Inasmuch as this strain can be expected to decrease gradually as the C–O bond is being broken,

Table VI. Rate and Equilibrium Constants for Catechol Spiro Complex Adjusted to pK_a of Phenol and Corrected for Intramolecularity

A. adjusted to pK_a of phenol[a]	B. effective molarities	C. $(\mathrm{EM}_k{}^{\mathrm{i,lp}})$[b]	D. corrected ratios, $\Delta\Delta G^{\ddagger}$ [c]
$K_2{}^{\mathrm{ad}} = 1.55 \times 10^6$ s^{-1}	$\mathrm{EM}_{\mathrm{equil}} = K_2{}^{\mathrm{ad}}/K_1 = 3.10 \times 10^6$ M	$\mathrm{EM}^{\mathrm{i,lp}} = 9.68 \times 10^2$	$k_2{}^{\mathrm{ad,corr}}/k_1 = 9.45 \times 10^3$
$k_2{}^{\mathrm{ad}} = 3.89 \times 10^9$ s^{-1}	$\mathrm{EM}_{\mathrm{k}} = k_2{}^{\mathrm{ad}}/k_1 = 9.15 \times 10^6$ M	$(k_{-2}{}^{\mathrm{ad}}/k_{-1})^{\mathrm{i,lp}} = 3.12 \times 10^{-4}$	$\Delta\Delta G^{\ddagger} = 5.40$ kcal/mol
$k_{-2}{}^{\mathrm{ad}} = 2.51 \times 10^3$ s^{-1}	$k_{-2}{}^{\mathrm{ad}}/k_{-1} = 2.95$		$\Delta G^0 = -0.41$ kcal/mol

[a] pK_a of phenol = 11.45 (ref 47b), pK_a of 19 = 10.34 (ref 47a), leading to adjustment factor of 12.9 for K_2; $k_2{}^{\mathrm{ad}} = k_2 \times 12.9^{0.46}$, $k_{-2}{}^{\mathrm{ad}} = k_{-2} \times 12.9^{-0.54}$, where 0.46 and −0.54 are normalized β_{nuc} and β_{lg} values (ref 47b). [b] From eqs 18 and 19, respectively, with $\alpha = \beta_{\mathrm{nuc}}{}^{\mathrm{n}} = 0.46$ (see footnote *a*). [c] From eq 20 and 21, respectively. [d] See footnote *d* in Table IV.

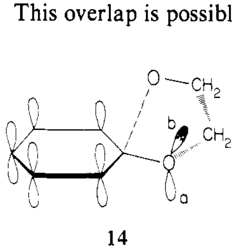
our procedure for correcting k_2 and k_{-2} for intramolecularity essentially also corrects for this strain factor.[36] The same holds true for an explanation that was based on the premise that there is more conformational freedom about the C–O bonds in the 1,1-dimethoxy complexes than in the spiro complexes. According to this view this would have the effect of lowering k_{-1} because this freedom is being partially lost on passage to the transition state.[37] Here again we are dealing with an effect that would affect the relative free energies of the transition state as well as that of the complex.[38]

One explanation that meets the imposed criteria is the notion of stereoelectronic control.[8] According to this notion the breakdown of a tetrahedral intermediate derived from esters, amides, etc.,[8] or more recently also shown to be true for acetals,[40,41] is greatly facilitated if the lone-pair orbitals(s) of the remaining oxygen(s) or nitrogen(s) is (are) antiperiplanar with respect to the departing group. Since our Meisenheimer complexes are similar to acetals one would expect this factor to play a significant role in our reactions as well. In the case of the spiro complexes an approximate antiperiplanar alignment is easily accomplished (**10**). This alignment is not feasible for the dimethoxy complexes in conformation **11**, but it is available in conformation **12** when the methoxy group pointing down is the one that leaves.

The higher intrinsic reactivity of the spiro complexes would therefore find a natural explanation if **11** is the favored conformation of the dimethoxy complexes, as suggested by other observations discussed earlier. The slower rates for the dimethoxy complexes could then either come about because **11** is the reacting species or the reaction might proceed via **12**, with **12** being in a very unfavorable equilibrium with **11**.

Stereoelectronic control has been recently invoked as a possible explanation as to why ethoxide ion departs 1.1 × 10^4 times more rapidly from the σ complex between 2,4-dinitro-1-naphthyl ethyl ether and pyrrolidine than from the analogous piperidine complex.[42]

We should note that an earlier attempt to explain the higher reactivity of spiro complexes by stereoelectronic arguments was phrased in terms of "p–π overlap" of one of the lone pairs of the nonreacting oxygens with the aromatic π system in the transition state.[4,37] This overlap is possible in **14** (orbital a) but not in **15**.



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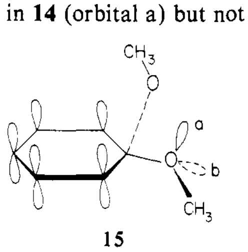

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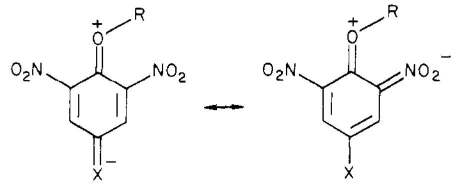
The two explanations are of course equivalent. The description in terms of p–π overlap has the advantage of visualizing why the antiperiplanar alignment only discriminates between the *transition states* but not between reactant or product states. In the fully sp^3-hybridized product state p–π overlap is expected to be minimal or nonexistent and thus cannot affect the relative energies of the complexes. In the reactant state p–π overlap *is* present; it is even stronger than in the transition state and leads to the resonance stabilization commonly expressed by **16**. However, there is no conformational advantage for **4**-X over **1**-X and the electronic effect of R on **16** is expected to be very similar in the two families. Hence, resonance stabilization should affect the reactant states about equally.



16a 16b

The notion of p–π overlap is further supported by the fact that $k_2{}^{\mathrm{ad,corr}}/k_1$ or $\Delta\Delta G^{\ddagger}$ increases with the electron-withdrawing strength of the X substituent (Table IV, D1 and D2). This is because p–π overlap leads to a transfer of charge density from the nonreacting oxygen into the benzene ring, a process that should be favored by stronger electron-withdrawing substituents, thus increasing $\Delta\Delta G^{\ddagger}$. Another implication is that, everything else being equal (same degree of C–O bond formation), the amount of charge transfer seen by the X substituent in the transition state should be larger in the spiro series. The fact that $\rho_{\mathrm{n}}(k_2) = 0.58$ is larger than $\rho_{\mathrm{n}}(k_1) = 0.44$ is probably a manifestation of this phenomenon. This would imply that $\rho_{\mathrm{n}}(k_2)$ is not a good measure of C–O bond formation and would be a further example of a growing list of reactions that have "imbalanced" transition states.[7,43]

Whether the enhanced $\rho_{\mathrm{n}}(k_2)$ is entirely due to p–π overlap or whether part of it is a consequence of a later transition state we cannot say. In using $\rho_{\mathrm{n}}(k_1)$ instead of $\rho_{\mathrm{n}}(k_2)$ to characterize the transition state for spiro complex formation we have implicitly assumed the former to be the case. It is even conceivable that the transition state is *earlier* than for dimethoxy complex formation, with p–π overlap being so strong as to overcompensate for this in the normalized ρ values. Again our data cannot tell. In view of these ambiguities a discussion of our results in terms of the Bell–Evans–Polanyi–Hammond–Leffler postulate[44] or the reactivity–selectivity principle[45] seems rather pointless, irrespective of where one stands in the current controversy surrounding this principle.[45,46]

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(36) If $\rho_{\mathrm{n}}(k_{-1})$ were an exact measure of the effect of strain in the transition state compared to the strain in the complex the correction would be perfect.

(37) Crampton, M. R.; Willison, M. J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 155.

(38) For additional comments about this interpretation see also ref 4.

(39) I.e., the oxygen which is not involved in the nucleophilic attack.

(40) (a) Kirby, A. J.; Martin, R. J. *J. Chem. Soc., Chem. Commun.* **1978**, 803. (b) Kirby, A. J.; Martin, R. J. *Ibid.* **1979**, 1079.

(41) Beaulieu, N.; Dickinson, R. A.; Deslongchamps, P. *Can. J. Chem.* **1980**, *58*, 2531.

(42) (a) Bunnett, J. F.; Sekiguchi, S.; Smith, L. A. *J. Am. Chem. Soc.* **1981**, *103*, 4865. (b) See also: Sekiguchi S.; Bunnett, J. F. *Ibid.* **1981**, *103*, 4871.

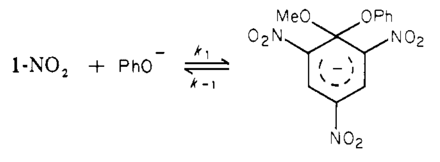
(43) For a partial list, see: Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5133.

(44) (a) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* **1938**, *34*, 11. (b) Bell, R. P. "The Proton in Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1973; p 206. (c) Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963; p 162. (d) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(45) For a recent review, see: Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69.

(46) See, for example: (a) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755. (b) McLennan, D. J. *Tetrahedron* **1978**, *34*, 2331. (c) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288. (d) Buncel, E.; Chuaqui, C.; Wilson, H. *J. Org. Chem.* **1980**, *45*, 3621. (e) Bordwell, F. G.; Hughes, D. L. *Ibid.* **1980**, *45*, 3314. (f) Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1980**, *102*, 5892.

Aryloxide Complexes. Data for the reactions shown in eq 22 and 23 obtained in 50% Me_2SO–50% water[47] allow a similar comparison to be made between the intrinsic reactivities of the spiro (**21**) and the 1-methoxy-1-phenoxy complex (**18**). The rate and equilibrium constants are summarized in Table V while the p*K*-adjusted and corrected (for intramolecularity) parameters are summarized in Table VI. The adjustment and corrections for intramolecularity were applied in a similar way as those for the **5-X** complexes, as explained in the footnotes of Table VI. It is noteworthy that $\Delta\Delta G^{\ddagger} = 5.4$ kcal/mol for the **18**/**21** pair is quite comparable in magnitude to $\Delta\Delta G^{\ddagger}$ estimated for the **2-NO$_2$**/**5-NO$_2$** pair. The effect must have the same origin, i.e., stereoelectronic control or p–π overlap. Note that this explanation requires **18** to be in a conformation analogous to **11**, or to **12** with the phenyl group pointing up, the methyl group down; there is no antiperiplanar arrangement of the pushing lone pair with respect to the leaving phenoxy group in either conformation. However it cannot be in conformation **12** with the phenyl group pointing down and the methyl group up because here there *is* optimal antiperiplanar arrangement. In view of recent results by Buncel et al.,[48] which indicate that the phenyl group points down in the addition complex between 1,3,5-trinitrobenzene and 2,4,6-trimethylphenoxide, conformation **11** seems most likely, just as for the dimethoxy complexes.



(22)

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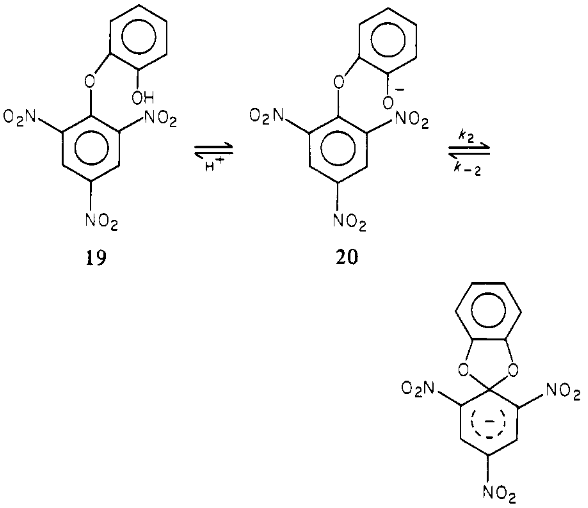

19 **20**

(23)

21

Experimental Section

Materials. All inorganic salts were analytical grade and used as commercially available. Pyridine was refluxed overnight with BaO and distilled under a nitrogen atmosphere. Anhydrous methanol (Mallinkrodt) was used directly. 2,4,6-Trinitroanisole (**1-NO$_2$**) was commercially (Eastman) available, 2,6-dinitro-4-trifluoromethylanisole (**1-CF$_3$**) was a gift from Dr. F. Terrier, 1-(2-hydroxyethoxy)-2,4,6-trinitrobenzene (**3-NO$_2$**) was available from a previous study,[4] and 2,6-dinitro-4-cyanoanisole (**1-CN**) was prepared by Fendler's[49] procedure: mp 112–4 °C (lit.[49] mp 113–113.5 °C).

2,6-Dinitro-4-((trifluoromethyl)sulfonyl)anisole (1-SO$_2$CF$_3$). This compound has been synthesized before;[50,51] while we used the same sequence of steps, our procedures differed in important details from those reported earlier and are now described.

4-Chlorophenyl Trichloromethyl Sulfide (B). To a three-necked flask containing 16 g (0.1 mol) of 4-chlorophenyl methyl sulfide (A) (K&K Labs) was added 60 mL of chloroform that had been distilled from P_2O_5. The solution was placed under a dry nitrogen atmosphere and cooled to 5 °C. The flask was irradiated with a 100-W bulb as chlorine gas (Matheson High Purity) was bubbled through the solution. After 1 h the solution was allowed to warm to room temperature. The apparatus was kept cool with a fan, chlorine was continued for another 6 h, and irradiation for another 16 h. Analysis by TLC indicated a trace of starting material; the solution was again treated with chlorine for an additional hour and the solvent evaporated, leaving a white solid. Recrystallization from acetonitrile yielded 22 g (83%): mp 60.5–61.5 °C (lit.[50] mp 59–60 °C); IR (TF) 3085, 1525, 1480, 800–700 cm^{-1}; mass spectrum, *m*/*e* 262 (parent ion).

4-Chlorophenyl Trifluoromethyl Sulfide (C). In a 100-mL round-bottom flask containing 20.68 g of B was added 16.91 g of SbF_3. The mixture was heated until it was apparent a reaction had begun. The crude product was distilled as a milky liquid (bp 160–165 °C) under dry nitrogen. The material was dissolved in 50 mL of ether and extracted as follows: 4 × 20 mL of 6 N HCl, 3 × 10 mL of saturated NaCl. The etheral solution was dried and filtered twice from anhydrous $MgSO_4$ and the solvent removed. The residue was drawn through a thin layer of diatomaceous earth, yielding 7.0 g of a colorless liquid: IR (TF) 3100, 1575, 1475, 1200–1080 cm^{-1}; mass spectrum, *m*/*e* 212 (parent ion).

4-Chlorophenyl Trifluoromethyl Sulfone (D). To a flask equipped with a reflux condenser containing 10 g of CrO_3 dissolved in 20 mL of acetic acid was added dropwise a solution of 5.29 g of C in 5.30 mL of acetic acid while the temperature was maintained at 35–40 °C. The temperature was slowly raised to 100–105 °C and maintained for 3 h, whereupon the reaction solution was quenched with 100 mL of ice water. The crude product was washed with cold water, recrystallized from MeOH–H_2O, and dried in vacuo, yielding 5.2 g (85.4%): mp 60–61 °C (lit.[50] mp 55–56 °C); IR (TF) 3100, 1577, 1470, 1375, 1250–1200, 1200–1080 cm^{-1}; mass spectrum, *m*/*e* 244 (parent ion).

1-Chloro-2-nitro-4-((trifluoromethyl)sulfonyl)benzene (E). To a 3-necked flask containing 5.55 g of KNO_3 was added 20 mL of concentrated H_2SO_4 (d = 1.84 g/mL). Five grams of D was added in small amounts over a 20-min period. The apparatus was equipped with a condenser and drying tube and then stirred at 100–110 °C for 4 h. The reaction mixture was cooled and poured over 150 mL of ice water. A yellow oil separated out; it crystallized upon removal of water and air contact. Recrystallization from methanol yielded 4.13 g (70%) of pale yellow needles, mp 54–56 °C (lit.[50] mp 55–56 °C).

2-Nitro-4-((trifluoromethyl)sulfonyl)anisole (F). To a solution of 3.94 g of E dissolved in 34 mL of absolute methanol was added 9.6 mL of 1.43 N sodium methoxide/methanol solution that had been freshly prepared. The resulting solution was refluxed for 1.5 h. The reaction flask was cooled, the contents filtered to remove NaCl, and most of the solvent evaporated. Water was added to effect complete precipitation. The crude solid was recrystallized from absolute methanol, yielding 3.55 g (92%) of the anisole, mp 81.5–82.5 °C (lit.[52] mp 81–82 °C).

1-SO$_2$CF$_3$. To a 100-mL flask containing 2.0 g of F in 1.6 mL of concentrated H_2SO_4 was added dropwise a solution prepared from 16 mL of concentrated H_2SO_4 and 16 mL of concentrated HNO_3. The stirred reaction mixture was maintained at 30–40 °C until the addition was completed, whereupon the temperature was raised slowly to 80 °C and maintained between 75 and 80 °C for 2 h. The cooled solution was poured over 150 mL of crushed ice and the crude solid collected and dried in vacuo. Recrystallization was successful from chloroform at −10 °C, or a slightly acidic solution of methanol (carefully) or hexane at room temperature. Yield: 1.3 g (56%) of pale yellow needles, mp 58–59 °C (lit.[51] mp 59 °C).

1-(2-Hydroxyethoxy)-2,6-dinitro-4-chlorobenzene (3-Cl). To a flask containing 0.65 g (2.7 mmol) of 1,4-dichloro-2,6-dinitrobenzene[53] was added enough dry Me_2SO to completely dissolve the chloride (1.5 mL), whereupon 3 mL of 1.7 M $NaO(CH_2)_2OH$ in ethylene glycol was added. A few drops of Me_2SO were added to keep the starting material in solution. The violet-colored solution was shaken for approximately 15 min, cooled in an ice bath, and acidified with concentrated HCl until the solution was yellow. Water was added, causing a yellowish-brown oil to form (mostly starting material). The liquid phase was separated from the oil and kept in an ice bath. The product crystallized as pale yellow needles. Repeated recrystallization from water yielded 25 mg: mp

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[52] Millot, F.; Terrier, F. *Nouv. J. Chim.* **1980**, *4*, 255.

[53] Gift from Professor Bunnett.

64.5–65.5 °C; ^{1}H NMR (60 MHz, Me_2SO-d_6) δ hydroxy ether 3.68 (m, H_β, H_{OH}), 4.12 (m, H_α), 8.47 (s, Ar H); complex 4.16 (s, H_α, H_β), 7.80 (s, Ar H); UV (H_2O) λ_{max} 599 nm (ϵ 1.5 × 10^4).

1-(2-Hydroxyethoxy)-2,6-dinitro-4-(trifluoromethyl)benzene (3-CF_3). 2,6-Dinitro-4-(trifluoromethyl)chlorobenzene (Pierce) (4.0 g, 0.015 mol) was dissolved in 10 mL of anhydrous ether, whereupon 42 mL of a 0.4 M (10% mol excess) of a $NaOCH_2CH_2OH/HOCH_2CH_2OH$ solution was added. The resulting mixture was stirred vigorously overnight at room temperature. The crude product was isolated as described for **3**-Cl. Repeated recrystallization from water yielded pale yellow needles: mp 99.5–100 °C; ^{1}H NMR (60 MHz, Me_2SO-d_6 + concentrated HCl) δ 4.30 (m, H_α), 3.60 (m, H_β), 8.72 (s, Ar H) (note: hydroxyl proton obscured by H_2O); ($CDCl_3$) δ 4.40 (m, H_α), 3.78 (m, H_β), 3.36 (s, H_{OH}), 8.75 (s, Ar H); UV (H_2O) λ_{max} 528 nm (ϵ 2.3 × 10^4).

1-(2-Hydroxyethoxy)-2,6-dinitro-4-((trifluoromethyl)sulfonyl)benzene (3-SO_2CF_3). In a flask containing 250 mg (0.758 mmol) of **1**-SO_2CF_3 dissolved in a minimum volume of Me_2SO was added a 5% excess of freshly prepared 2.45 M sodium glycolate solution (0.32 mL). The solution was allowed to stand overnight, whereupon it was acidified, water was added, and it was cooled to effect precipitation. The yellowish brown amorphous solid was collected and dissolved in hexane. The hot mother liquor was separated from an insoluble oil that forms and the product crystallized from hexane as white needles (49 mg): mp 88–89 °C; ^{1}H NMR (60 MHz, $CDCl_3$) hydroxy ether δ 4.34 (m, H_α), 3.86 (m, H_β), 3.35 (s, H_{OH}), 8.67 (ArH); (Me_2SO-d_6) complex 4.20 (s, H_α, H_β), 8.94 (s, ArH); UV (H_2O) λ_{max} 470 (ϵ 1.1 × 10^4).

Kinetics. The slow reactions were measured with a Gilford 2000 spectrophotometer, the fast ones with a Durrum–Gibson stopped-flow apparatus. Evaluation of the first-order plots was by standard procedures; reproducibility was usually in the range 1–3%. pH measurements, accurate within ±0.01 unit, were carried out with a Corning 110 pH meter; the pH in the stopped flow experiments was measured in mock mixing experiments.

Acknowledgment. This work was supported by Grants CHE77-27998 and CHE80-24261 from the National Science Foundation.

Registry No. **1**-SO_2CF_3, 19822-29-8; **1**-NO_2, 606-35-9; **1**-CN, 19018-96-3; **1**-SO_2CH_3, 39880-50-7; **1**-CF_3, 317-70-4; **2**-SO_2CF_3, 35298-04-5; **2**-NO_2, 12128-30-2; **2**-CN, 25549-13-7; **2**-SO_2CH_3, 40203-26-7; **2**-CF_3, 28933-97-3; **3**-SO_2CF_3, 83547-68-6; **3**-NO_2, 6478-31-5; **3**-CF_3, 83547-69-7; **3**-Cl, 83547-70-0; **5**-SO_2CF_3, 83547-66-4; **5**-NO_2, 54846-61-6; **5**-CF_3, 83547-67-5; **5**-Cl, 83560-63-8; A, 123-09-1; B, 706-29-6; C, 407-16-9; D, 383-11-9; E, 1550-27-2; F, 360-00-9; 1,4-dichloro-2,6-dinitrobenzene, 2213-82-3; 2,6-dinitro-4-(trifluoromethyl)chlorobenzene, 393-75-9.

Supplementary Material Available: Tables S1-S5, observed pseudo-first-order rate constants (6 pages). Ordering information is given on any current masthead page.

Excited-State σ Succinimidyl and Glutarimidyl Radicals: Reversible Ring Opening

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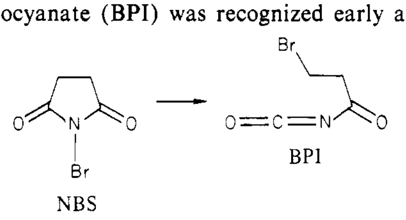
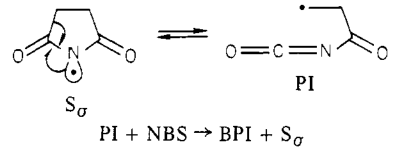
Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. *Received October 26, 1981*

Abstract: The free-radical isomerization of *N*-bromosuccinimide to β-bromopropionyl isocyanate has been examined. Of the two varieties of succinimidyl radical (S_π or S_σ), only the σ excited state undergoes the ring opening to the β-propionyl isocyanatyl radical. The conversion optimally takes place in >95% yield. The dependence on NBS concentration along with results obtained from deuterium labeling studies indicate that the ring opening of S_σ is a reversible process. This explains the failure of *N*-chlorosuccinimide to produce β-chloropropionyl isocyanate, as well as the increase in ring-opened product for *N*-bromosuccinimides upon methyl substitution at the 2- and/or 3-position of the succinimidyl ring, since the open-chain radical intermediates are more stable. In the *N*-bromoglutarimide system, methyl groups on the 2-position are required for the glutarimidyl radicals to undergo the isomerization, ultimately producing isocyanates. The radical-chain nature of these systems is confirmed.

The rearrangement of *N*-bromosuccinimide to β-bromopropionyl isocyanate (BPI) was recognized early as a radical process, but only recently have the numerous puzzling aspects of this reaction fallen into a framework consistent with the known S_π and S_σ succinimidyl chemistry.[1]





$$PI + NBS \rightarrow BPI + S_\sigma$$

The isomerization of NBS to BPI was reported (1957) independently by Johnson and Bublitz[3] and Martin and Bartlett.[4] The reaction was inititated by benzoyl peroxide, and this led to the conclusion that the isomerization could be described as a radical-chain process with PI as the radical intermediate. The radical-chain character is now confirmed (vide infra) for the ring opening and the other addition and substitution reactions attributed to succinimidyls.[1]

In an important theory paper that received little attention, Koenig and Wielesek (1975)[5] suggested that ground-state succinimidyl and some of its excited states could be described as S_π and S_{σ_N} or S_{σ_O}, respectively, and that only the excited-state S_{σ_N} and S_{σ_O} had symmetries that correlated with the open-chain radical, PI. The energy sorting of these states by the INDO calculation was recognized to be of little value other than to point to the possibility that the energy separation was small.

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