soning, ‡ (addition) has both a less delocalized positive charge and a greater requirement for hydrogen bonding of the above type since there is a larger buildup of positive charge on the oxygen of the attacking water. From the previous discussion, these two related effects must result in its greater salting-out.

Even if ‡ (substitution) were fully product-like (amide + $CH_3O^+H_2$), ‡ (addition) would be expected to be relatively salted-out since it contains two additional electronegative groups ($-NH_2$ and $-OCH_3$) in the vicinity of the positive charge. These would inductively destabilize the cation and force a greater requirement for solvent stabilization of the $^+O-H\cdots OH_2$ type.

Significantly, entropies of activation, not only for the imidates but also in general for bimolecular acid-catalyzed reactions, are in accord with the above discussions. In particular it was shown previously (Table V) that $\Delta S^\ddagger$ values for SN2-type reactions were significantly less negative than $\Delta S^\ddagger$ values for reactions involving a tetrahedral intermediate. This again can be explained in terms of a lower solvation requirement in the transition states for the substitution reactions, i.e., less restrictions of solvent molecules.

These same effects are mirrored, although to a much smaller extent, in a comparison of the two imidates of this study. The O-ethyl compound shows a slightly shallower acidity dependence (Figure 1), and also a slightly more positive entropy of activation. This suggests that the extra methyl group results in a smaller hydration requirement for the transition state. This can be attributed either to a steric hindrance to solvation or to an increased stabilization of the delocalized positive charge.

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Role of Water in the Hydrolysis of BH_4^- [1]

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Abstract: The rate law for the hydrolysis of BH_4^- in Me_2SO as a solvent has the form of that for a general-acid catalyzed reaction. Rate coefficients for H^+, H_2O, and 2,6-dinitrophenol are 0.74 ± 0.15, $1.5 \pm 0.2 \times 10^{-2}$, and $0.19 \pm 0.4\ M^{-1}\ sec^{-1}$, respectively. That for water is six powers of ten *larger* than the comparable quantity in H_2O, but that for H^+ is six powers of ten *smaller*. It is postulated that proton transfer from hydronium ion to BH_4^- in water uses a water molecule as a proton relay. The H^+ rate coefficient in Me_2SO is much smaller because Me_2SO cannot function as a relay, and because of the instability of the structure $Me_2SO\cdots H\cdots HBH_3^+$.

Previous work on the hydrolysis of BH_4^- by aqueous acid (eq 1) has shown that the loss of the first hydrogen determines the overall rate, that the reaction

$$H^+ + BH_4^- + 3H_2O \longrightarrow 4H_2 + B(OH)_3 \qquad (1)$$

is first order in BH_4^- and first order in H^+, and that, in acidic solution, the product of the rate-determining step is H_2BH_3.[2] Solvent isotope effects have suggested that, in aqueous solution, a water molecule is intimately involved in the rate-determining step for the reaction with H^+, probably acting as a relay for the proton.[3] The purpose of this study was to test that suggestion by examining the reaction in nearly dry dimethyl sulfoxide (Me_2SO).

Dilute solutions in Me_2SO are well suited to such a study because H_2O is very nearly an ideal solute in Me_2SO up to at least 1.2 *M*,[4] and H^+ is only slightly hydrated in the concentration range of the present study.[5] A proton-transfer reaction, using water as a relay in aqueous solution, should be many powers of 10 slower in nearly anhydrous Me_2SO than in water as a solvent, because Me_2SO is not able to serve such a function. By contrast, ordinary A-SE2 reactions, which do not involve water in the rate-determining step, show rates only one to two powers of ten slower in Me_2SO than in water as a solvent and, in nearly anhydrous solution, their H^+ rate coefficients *decrease* slightly with increasing water concentration.[6,7] It should, therefore, be

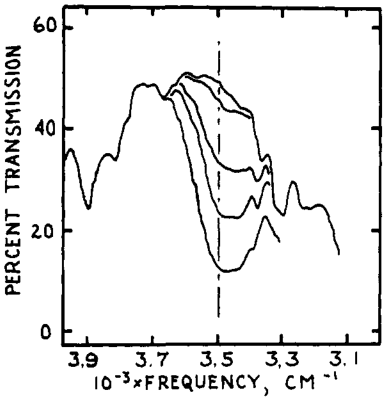

Figure 1. Spectra of Me_2SO containing small amounts of water in the region of the O-H stretching vibration. The base line is given by a solution from which H_2O has been displaced with D_2O. The water concentrations in the solutions generating the other spectra were 0.014, 0.048, 0.099, and 0.184 *M*.

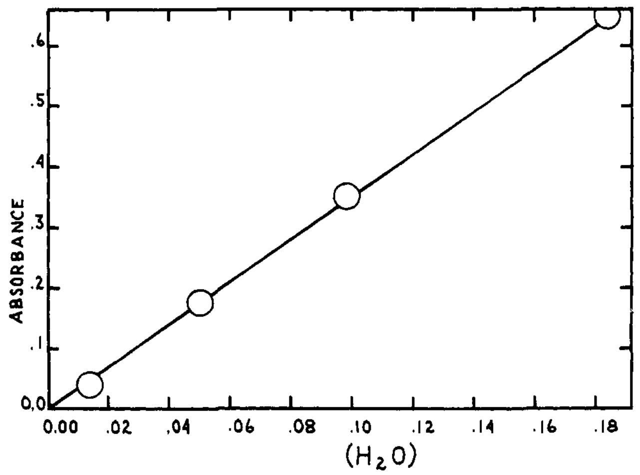

Figure 2. A test of the Beer-Lambert law for H_2O in Me_2SO at 3500 cm^{-1}. The data points are taken from the spectra shown in Figure 1.

possible to make a very clear distinction between these two possibilities.

Experimental Section

Materials. $NaBH_4$ was obtained from Alfa Inorganics and was purified according to the method described by Hutchins.[2] Trifluoromethanesulfonic acid was obtained from the 3M Company. It was distilled before use (bp 162°; previously reported[10] 162°). 2,6-Dinitrophenol was purchased from Aldrich Chemical Co. and purified by repeated recrystallization from water. It has mp 61.5–62.5° (values between 61 and 63° have been previously reported).[9] Tetramethylammonium 2,6-dinitrophenate was prepared by carefully neutralizing the phenol with tetramethylammonium hydroxide, in aqueous solution, using a pH meter to locate the end point. The water was removed by evaporation, and the salt was purified by recrystallization from ethyl acetate containing a trace of methanol. Its identity and purity were verified by means of its visible spectrum: λ_{max}, 470 nm; ϵ_{max}, 1.1×10^4 (previously reported 475 nm and 1.2×10^4).[8]

Me_2SO (Aldrich Chemical Co.) was stirred for a number of hours with CaH_2 and then distilled under vacuum, discarding the first and last 5%. The temperature at which the distillations were conducted was 40 ± 5°. Such Me_2SO was shown, by the analytical methods described below, to have a water content between 0.005 and 0.015 *M*, depending on the water content of the starting material and the length of contact with CaH_2. Deuterium oxide, 99.7 atom % deuterium, was obtained from the Aldrich Chemical Co. and was used without further purification or analysis.

Water Analyses. Three methods were used to determine water in the "anhydrous" Me_2SO described above. Karl Fischer titration[11] was used to determine the water content of one of our standard preparations.

Solutions of known water concentration were made up from this, and their ir spectra in the region of 3500 cm^{-1} were obtained with a Perkin-Elmer 521 infrared spectrophotometer. A cell with Irtran-2[12] windows and a pathlength of 200 μm was used. Transmittance (100%) was set with only air in the sample and the reference beam. A base line, uninfluenced by OH absorption, was obtained for this region of the spectrum from a sample of Me_2SO which had been redried after the residual water had been exchanged with a large excess of D_2O. The exchange was effected by adding 2 ml of D_2O to 100 ml of the Me_2SO, then removing the D_2O by distillation. Figure 1 shows the spectra. Figure 2 shows a plot of absorbance at 3500 cm^{-1}, *A*, as a function of (H_2O). It is linear, as required by the Beer-Lambert law,[13] and gives an extinction coefficient, ϵ, of 1.75×10^2. The regression line in Figure 2 was used to determine the water content of Me_2SO samples and reaction mixtures. This method was useful with water concentrations down to 0.005 *M*. If transmittance readings are assumed to be uncertain by about 0.3%, which conforms to our experience, then the concentrations of water given by this method around 0.008 *M* are uncertain by about 15% and those around 0.1 *M* by about 2%. The ideality of solutions of water in Me_2SO[4] makes serious deviations from the Beer-Lambert law unlikely in this system.

When the (H_2O) was equal to or greater than about 0.02 *M*, it could also be determined by NMR spectroscopy. The height of the water signal, I_{H_2O}, was compared with that of the ^{13}C satellite of the Me_2SO signal, I_0, the intensity of which, relative to the main Me_2SO peak, is known from the known relative abundance of ^{13}C. The (H_2O) is given by eq 2, in which 0.158 is obtained by multiplying 0.2325, the theoretical intensity ratio, by 0.68, which is a correction factor presumably due to the difference in the widths of the two peaks. The correction factor was determined, with an average deviation from the mean of 3%, by obtaining the signal height of four samples whose water content was otherwise known.

$$(H_2O) = 0.158 I_{H_2O}/I_0 \qquad (2)$$

Kinetic Method. Rates were measured manometrically, using a modified version of the compensated manometer originally described by Moelwyn-Hughes and Johnson.[14,15] The temperature was maintained at 25.0 by a continuously cooled, intermittently heated, water thermostat of conventional design. Reaction was initiated by adding a small substrate sample to an otherwise complete reaction mixture.

Unfortunately the rate of equilibration of H_2 across the gas-liquid interface could not be made infinitely fast compared with the hydrolysis rates of interest. Therefore the equilibration rate was studied separately by allowing the hydrolysis to proceed through at least 10 half-lives without stirring to produce a supersaturated solution, then turning on the stirrers. Reasonably linear plots of log $(P_\infty - P_t)$ against *t* were obtained. Eleven experiments of this sort were carried out, interspersed among the other rate measurements. The concentrations of acid and water spanned the ranges used in the kinetic experiments. First-order rate constants, k_E, were obtained from eq 3.[16] The average value of k_E was 1.9×10^{-3} sec^{-1} with an average deviation from the mean of 0.4×10^{-3} sec^{-1}. No systematic variation of k_E with (H^+) or (H_2O) could be detected. The rather large scatter in k_E is attributed to the difficulty of reproducing the stirring rate and the interfacial area.

$$k_E = \frac{2.303}{t - t_0} \log \frac{P_\infty - P_0}{P_\infty - P_t} \qquad (3)$$

To determine the hydrolysis rate, stirring was begun as soon as possible after the reaction mixture was complete. The pseudo-first-order rate constants for the chemical reactions were obtained using eq 4.[17] For each value of p_t/p_∞ and *t*, there is a unique, nontrivial, value of k_C which will satisfy eq 4. However, we were not able to solve for k_C explicitly. It was found for each P_t by systematic trial and error routines using a CDC 6600 digital computer to do the numerical computation. Table I shows the constancy of the calculated values of k_C in a typical experiment.

$$\frac{P_t}{P_\infty} = 1 + \frac{1}{k_C + k_E}(k_E e^{-k_C t} - k_C e^{-k_E t}) \qquad (4)$$

Table I. Hydrolysis of BH_4^- by 2.0×10^{-2} *M* H_2O and 9.85×10^{-4} *M* 2,6-Dinitrophenol in Me_2SO[a]

$10^{-2}t$, sec	P_t/P_∞	10^4k_C, sec^{-1}
5.0	0.0505	3.0
7.0	0.1380	4.8
9.0	0.2176	5.5
11.0	0.2911	5.7
13.0	0.3541	5.7
15.0	0.4132	5.7
17.0	0.4667	5.5
19.0	0.5132	5.3
21.0	0.5592	5.3
25.0	0.6373	5.3
28.0	0.6858	5.3
31.0	0.7313	5.3
36.0	0.7908	5.2
40.0	0.8309	5.2
45.0	0.8709	5.3
51.0	0.9074	5.3
57.0	0.9329	5.3

[a] The reaction mixture also contained 1.14×10^{-3} *M* 2,6-dinitrophenate.

In all experiments, it was assumed that the first P_t was measured 5 min after mixing. This is 2 or 3 min longer than actually required to put the apparatus together and begin stirring, but it gave more constant values of k_C than a more realistic time. It probably takes account of the fact that eq 4 assumes that interfacial equilibration and the chemical hydrolysis begin simultaneously, which was impossible for us to arrange. It is also possible that our stock solutions contained small amounts of partially hydrolyzed material, which caused the initial hydrolysis rate to be faster than anticipated. Also, in some reactions there was only a threefold excess of acid (which is consumed in the reaction) over BH_4^-. A pseudo-first-order rate law will only describe such reactions as they approach completion. For these reasons, the k_C values used were taken from 50 to 90% completion. In this range, the k_C values were reasonably constant for any one experiment and nearly independent of the elapsed time assumed between the initiation of the reaction and the first measurement of P_t. For the slower reactions, k_C was, also, very similar to the first-order rate constant which could be obtained by treating the data graphically, as for a first-order reaction, using eq 3. The average deviation from the mean value, when k_C values were determined repetitively, was about 10% for the slower reactions and about 20% for values of k_C approaching k_E. These uncertainties were probably due, in about equal proportions, to the difficulty of measuring k_C and the uncertainty in the water content of the reaction mixtures.

Table II. Hydrolysis of BH_4^- by CF_3SO_2OH in Moist Me_2SO

$10^4(H^+)$, *M*	$10^2(H_2O)$, *M*	10^4k_C, sec^{-1}	10^4k_C[a], sec^{-1}
1.90	1.4[f]	4.35[b]	3.96
1.90	1.8[h]	5.30	4.69
1.90	2.6[g]	7.30	6.15
1.90	2,9[g]	7.70	6.70
1,90	4.8[g]	10.3[b]	10.3
1.90	5.4[g]	14.2	11.3
1.90	6.1[g]	12.7	12.6
1.90	7.3[g]	13.5	14.8
1.90	8.3[h]	15.8[c]	16.5
2.16	0.9[i]	2.83	3.28
4.40	1.4[f]	6.65[d]	6.48
4,83	0.9[i]	4.17	5.72
7.16	0.5[i]	4.50	6.70
9.00	0.75[i]	8.00	9.04
9.40[e]	1.4[f]	12.1[e]	11.5

[a] Calculated using eq 5 and the parameters given in Table IV. [b] Average of two determinations with discrepancy of 3%. [c] Average of five determinations with an average deviation from the mean of 13%. [d] Average of two determinations with discrepancy of 2%. [e] Average of five determinations with an average deviation from the mean of 21%. [f] Determined by the Karl Fischer method. [g] Determined by the NMR method. [h] Determined by both NMR and ir methods. [i] Determined by the ir method.

Table III. Hydrolysis of BH_4^- by 2,6-Dinitrophenol Solutions in Moist Me_2SO

10^4 (H Phen),[a] *M*	10^4 ($Phen^-$),[a] *M*	$10^5(H^+)$, *M*	10^2 (H_2O),[c] *M*	10^4k_C, sec^{-1}	10^4k_C,[b] sec^{-1}
2.70	3.70	0.92	1.2	3.33	2.34
2.81	4.02	0.88	0.6	2.33	1.47
2.87	3.96	0.91	7.3	13.2	11.4
4.24	5.74	0.93	1.4	3.83	2.92
4.66	6.14	0.96	1.5	3.83	3.14
6.96	8.44	1.04	0.5	3.17	2.10
7.06	8.54	1.04	1.0	3.67	2.86
7.06	8.54	1.04	4.6	6.17	8.18
7.26	8.65	1.06	3.2	6.17	6.15
7.32	8.53	1.08	2.8	6.33	5.57
7.36	8.38	1.11	4.5	8.50	8.09
9.85	11.4	1.09	2.0	5.33	4.86
10.2	11.6	1.11	1.2	4.50	3.74
33.2	34.7	1.21	1.5	9.50	8.45
50.6	52.0	1.23	5.6	16.3	17.7

[a] Phen is 2,6-dinitrophenate. [b] Calculated using eq 5 and the parameters given in Table IV, omitting the (H_3O^+) term. [c] Determined by the ir method.

Results

To verify that the reaction does not stop at some intermediate, still preserving hydridic hydrogen, the ^{11}B NMR spectrum of a product solution was obtained under conditions in which a comparable concentration of BH_4^- gave full-scale deflection for the central line of the five-line spectrum. In this experiment, (BH_4^-) was 0.06 *M* and the initial (H_2O) was 0.22 *M*. No sharp line spectrum at all could be detected in the product solution. The only detectable signal was a broad, undifferentiated one, identical with that generated by boric acid, which may be a finely divided solid in this medium, although none was visible. It was concluded that the reaction is adequately represented by eq 1 in Me_2SO as a solvent, as it is in water.

To determine the order of the reaction with respect to the acids and water, and the rate coefficients, two series of experiments were carried out. In one, various combinations of trifluoromethanesulfonic acid and water were used. The acid concentration ranged from 2.5×10^{-4} to 1×10^{-3} *M*. This acid can be presumed to be completely dissociated in this concentration range as it is one of the strongest acids known,[18] and Me_2SO is a good solvent for the ionization and dissociation of strong acids[5] so that the nominal acid concentration is actually (H^+). In the second series, the acid was 2,6-dinitrophenol, which has a p*K* of 4.9 in this solvent.[9] Its concentration varied from 3×10^{-4} to 5×10^{-3} *M*. These solutions were buffered with tetramethylammonium 2,6-dinitrophenate. The 2,6-dinitrophenate concentrations given also include contributions from the spontaneous dissociation of the phenol, which is substantial at low concentration. For both sets of experiments, (H_2O) ranged from 5×10^{-3} to 10^{-1} *M*, and initial (BH_4^-) was 8-9 $\times 10^{-5}$ *M*. The results for the first series are given in Table II and those for the second series in Table III. These tables give the concentrations of the acidic and buffering species thought to be present in the reaction mixtures, rather than formal concentrations. In cases where an initial concentration could be expected to change by more than 10% because of the reaction, the concentration given is that prevailing at 70% reaction, in the center of the range of results used to determine k_C. All told, 41 values of k_C were obtained, ranging from 2×10^{-4} to 2×10^{-3} sec^{-1}.

These values of k_C were fitted to eq 5, using a least-squares criterion to evaluate the parameters, which are

Table IV. Parameters of Equation 5

Rate coefficient	Value	Value[a,b]
k_H, M^{-1} sec^{-1}	$7.4 \pm 1.5 \times 10^{-1}$	$9.4 \pm 0.8 \times 10^{-1}$
k_{H_2O}, M^{-1} sec^{-1}	$1.5 \pm 0.2 \times 10^{-1}$	$1.7 \pm 0.1 \times 10^{-2}$
k_{HA}, M^{-1} sec^{-1}	$1.9 \pm 0.4 \times 10^{-1}$	$1.5 \pm 0.3 \times 10^{-1}$
k_{H_3O}, M^{-2} sec^{-1}	$2 \pm 1 \times 10$	

[a] Arbitrarily setting k_{H_3O} to zero. [b] The uncertainties all become smaller, because the data set is required to fix one fewer parameter.

given in Table IV. HA is 2,6-dinitrophenol. Equation 5 reproduces the k_C values with an average discrepancy of 15%, about the replicability of the experimental values.

$$k_C = k_H(H^+) + k_{H_2O}(H_2O) + k_{HA}(HA) + k_{H_3O}(H^+)(H_2O) \quad (5)$$

All the rate coefficients seem to be determined with adequate accuracy except k_{H_3O}, which cannot be made to contribute more than a minor fraction of k_C in the range of concentrations accessible to us. It is unambiguously determined, however, that k_{H_3O} is well under 10^2 M^{-2} sec^{-1}. If the last term in eq 5 is arbitrarily excluded, the other parameters change only a little, and the average discrepancy between calculated and observed k_C values is less than 1% larger.

The reaction was expected to be first order with respect to BH_4^-, and the constancy of k_C within each experiment supports this view. In addition an experiment was carried out in which the initial (BH_4^-) was lowered by over a factor of 2. It gave a k_C of 5.2×10^{-4} sec^{-1}, while eq 5 predicted a value of 6.2×10^{-4} sec^{-1}. This is quite consistent with our experimental uncertainty and the usual goodness of fit of eq 5, further supporting the original hypothesis.

Discussion

The value of k_H is smaller than the comparable quantity in aqueous solution by six powers of ten. This is completely consistent with the conclusions reached on the basis of isotope effects.[3] The water appears intimately involved in the rate-determining step. It was previously postulated that a water molecule serves to relay a proton from a more remote site to the substrate. Structurally Me_2SO can replace water as a base, but it cannot serve as the relay. The relay may operate in a concerted fashion, or it may be, to varying degrees, disconcerted.[19] The alternative process, in which $(CH_3)_2SOH^+$ comes right up to BH_4^-, is over 8 kcal mol^{-1} higher in free energy. It seems reasonable that H^+ in Me_2SO is tightly bound to two Me_2SO molecules[20] since Me_2SO is a good hydrogen-bond acceptor.[21] Much of this 8 kcal mol^{-1} is probably expended in replacing one of the Me_2SO molecules with a BH_4^- ion so that the proton can be transferred. While BH_4^- probably can act as a hydrogen-bond acceptor,[22] it is probably much poorer in this capacity than Me_2SO.

Still another piece of evidence favoring the relay mechanism in aqueous solution is the observation that boric acid is an effective catalyst for BH_4^- hydrolysis.[23] Boric acid is apparently a pseudo-acid in aqueous solution and, consequently, a very ineffective proton source when the relay mechanism does not operate.[24]

In contrast to k_H, k_{H_2O} is *larger* than the similar rate coefficient in aqueous solution by a factor of about 10^6. "k_{H_2O}", in aqueous solution, is a first-order rate constant with a value around 10^{-6} sec^{-1}.[2] To get a quantity comparable to our present k_{H_2O}, the aqueous solution value has been divided by the concentration of water in liquid water, to give around 2×10^{-8}. While this suffers from all the problems associated with treating water as a solute when it is the solvent, it serves to show the contrast between the solvent effect on k_{H_2O} and that on k_H. Water apparently does not use the relay mechanism even in liquid water or, if it does, does not find it energetically difficult to get along without. The difference between H^+ and H_2O as acids reflects the large differences between them in acidity and the strength of their bonds to solvent. The solvent effect on k_{H_2O} also must reflect the general exaltation of the reactivity of anions in Me_2SO as a solvent.[25] For k_H, this is presumed to be masked by the change in mechanism.

If one makes a Brønsted plot out of the three available rate constants, it has a slope of about 0.1.[26] The acids are of very disparate types, and the quantitative significance of the value is hard to assess, but it is in marked contrast with the value, close to unity, observed in water as a solvent.[23] We hope to investigate general-acid catalysis of this reaction further.

The availability of the relay process may be one of the reasons that hydrolysis of BH_4^- by aqueous acid is so fast. Proton transfer to carbon, which seems not to be able to use the relay mechanism,[6] often reaches limiting rates several powers of ten below k_H for BH_4^- hydrolysis in water.[27,28] Structurally the availability of the relay mechanism, which is also used by many proton transfers between oxygen and nitrogen,[29] may be limited to substrates which have some capacity to accept a hydrogen bond and/or do not undergo extensive structural reorganization when they accept the proton. If this is so, it might also account for the very high rates of protonation of CCl_3^-,[30] sulfone anions,[31] and $C_6H_5C{\equiv}C^-$.[32] Variants on all of these ideas have been previously suggested.[30-32]

These observations also have useful practical consequences, as $NaBH_4$ is widely used as a reducing agent. In water, its acid-catalyzed reactions are inaccessable, as the hydrolysis is too fast. We have recently succeeded in reducing vat dyes (highly conjugated carbonyl compounds) with BH_4^- in acidic Me_2SO,[33] and we hope to carry out other reductions which do not proceed in conventional media.

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References and Notes

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A General Synthetic Method for Non-K-Region Arene Oxides

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Abstract: A general method has been developed for the synthesis of non-K-region arene oxides of polycyclic aromatic hydrocarbons. The procedure involves construction of a halohydrin ester at the desired position of a saturated ring in the hydrocarbon, bromination of the unsubstituted benzylic position with *N*-bromosuccinimide, and direct treatment of the resulting dibromo ester with dry sodium methoxide. Cyclization to form the oxirane ring and dehydrohalogenation to introduce the double bond occur in a single step. Syntheses of naphthalene 1,2-oxide, phenanthrene 1,2- and 3,4-oxides, and benzo[*a*]pyrene 7,8- and 9,10-oxides were achieved in high yield.

Since the initial demonstration of an arene oxide as an obligatory intermediate in the metabolism of naphthalene by mammals,[1] substantial interest has developed in the chemistry, biochemistry, and pharmacology of arene oxides.[2] Subsequent reports have implicated arene oxides in the metabolism of several other polycyclic aromatic hydrocarbons. Arene oxides are capable of transforming cells in culture and are potent frameshift mutagens in bacterial test systems. In addition, substantial evidence has accumulated which implicates metabolically formed arene oxides as the causative agents which account for the toxicity of several aromatic hydrocarbons. The broad spectrum of biological activity displayed by arene oxides has prompted the exploration of convenient synthetic routes into this class of compounds.

For polycyclic aromatic hydrocarbons, both K-region and non-K-region arene oxides are possible. Enhanced stability of K-region versus non-K-region arene oxides with regard to isomerization to phenols in the neutral and basic pH regions[3] has permitted more flexibility in the choice of synthetic routes to K-region arene oxides. Thus, closure of the corresponding dialdehydes with tris(dimethylamino)phosphine,[4] dehydration of *trans*-dihydrodiols with the dimethylacetal of dimethylformamide,[5] and cyclization of *trans*-halohydrin acetates[6] have all proved useful in the synthesis of K-region arene oxides. Unavailability of requisite starting materials and overly vigorous reaction conditions have precluded the use of these routes for the preparation of non-K-region arene oxides.

Vogel and coworkers[7] have devised a dehydrohalogenation route to non-K-region arene oxides in which HBr is eliminated from bromotetrahydro epoxides to generate the necessary double bonds in the final step. Conversion of 1,2-epoxy-4,5-dibromocyclohexane to benzene oxide with dry sodium methoxide and of 1,2-epoxy-4-bromotetralin to naphthalene 1,2-oxide with diazabicyclononene are typical examples.[8] Although elegantly conceived, this approach suffers from a serious drawback in that the tetrahydro epoxides of polycyclic hydrocarbons are relatively unstable to the conditions of bromination with NBS (*N*-bromosuccinimide) and suffer extensive polymerization and isomerization to ketones. The low yields and difficulties in purification at this step[8c,9] prompted a search for efficient and convenient alternatives.

The optimum situation for synthesis of labile non-K-region arene oxides requires the preparation of a stable, easily purified immediate precursor which can be converted into the desired arene oxide in high yield under mild conditions. Bromination of tetrahydro epoxides results in a mixture of stereoisomers which are difficult to separate from impurities by crystallization. In marked contrast, bromination of *trans*-bromohydrin trifluoroacetates with NBS has been found to proceed in excellent yield and with high stereoselectivity.[10] Bromohydrin esters were employed rather than the free benzylic alcohols in order to avoid oxidation to ketones. Labile trifluoroacetates were selected as blocking groups for the benzylic alcohol since they could be removed in the presence of the reactive bromine introduced at the other benzylic position. Elimination of 2 mol of HBr with dry sodium methoxide in tetrahydrofuran cyclized the bromohydrin to an oxirane and introduced the final double bond to produce the desired arene oxides in excellent yield and high purity. While the halohydrin ester route as initially described[10] has proved most effective in the synthesis of labile arene oxides, there are inherent disadvantages in that an ester blocking group must be introduced and later removed and in that certain dibromo esters are not readily hydrolyzed without loss of the benzylic bromine. Subsequent studies of the halohydrin ester route have shown that the above disadvantages can be avoided. Dihydroaromatic hydrocarbons can be converted to bromohydrin acetates in a single step with *N*-bromoacetamide in acetic acid, brominated at the benzylic position with NBS, and converted directly to the desired arene oxide without an intervening hydrolysis step. Since separate steps are not required for the introduction and later removal of a blocking group, the halohydrin ester route becomes a classic example of latent functionality[11] in the synthesis of arene oxides. The procedure is exemplified by the synthesis of naphthalene, phenanthrene, and benzo[*a*]pyrene oxides. The basic scheme is