Solvolysis Mechanisms. Sulfur Kinetic Isotope Effects in the Hydrolysis of Substituted Benzyldimethylsulfonium Tosylates[1]

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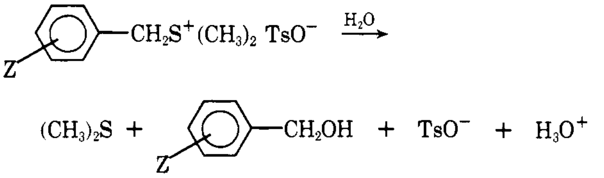
Abstract: Hydrolysis at 68.73 °C of substituted benzyldimethylsulfonium *p*-toluenesulfonates, producing the corresponding benzyl alcohol, dimethyl sulfide, and acid, gave sulfur isotope effects, k_{32}/k_{34}, and rate constants ($k \times 10^8$, s^{-1}, in parentheses) as follows: *m*-Br, 1.00967 ± 0.00041 (2.61 ± 0.16); *m*-CH_3O, 1.00898 ± 0.00026 (4.34 ± 0.08); *p*-Br, 1.00983 ± 0.00029 (4.51 ± 0.03); H, 1.00976 ± 0.00012 (5.86 ± 0.20); *m*-CH_3, 1.01008 ± 0.00014 (6.98 ± 0.10); *p*-CH_3, 1.01027 ± 0.00038 (21.4 ± 0.56); *p*-CH_3O, 1.01077 ± 0.00017 (37 500 ± 200). These data seem most consistent with similar mechanisms for all substituents and do not provide any indication of a change of mechanism with *p*-MeO in spite of the very large rate effect. Although fortuitous equality of sulfur isotope effects for different mechanisms cannot be ruled out as an explanation of the data, it is argued that an SN2-like mechanism, with varying degrees of nucleophilic participation by solvent depending on the nucleophilic capability of the ring substituent, best fits this and related data.

Structural and substituent effects on heavy-atom kinetic isotope effects offer a powerful way of probing reaction mechanisms.[2,3] An interesting and somewhat unexpected result was reported by Hill and Fry,[4] who found that hydrolysis of substituted benzyl chlorides (80% aqueous dioxane, 30 °C) gave chlorine kinetic isotope effects (KIE), k_{35}/k_{37}, essentially independent of substituents from *p*-nitro to *p*-methoxy, near 1.0078. On the other hand, for those substituents giving second-order reactions with cyanide or thiosulfate, the chlorine KIE in the second-order reactions were all near 1.0058. Given the large rate enhancement in hydrolysis of *p*-methoxybenzyl chloride (over 10^3-fold faster than *p*-methyl) and other indications of carbonium ion[5,6] or ion-pair[7] involvement, the constancy of these hydrolysis KIE was deemed worthy of further investigation.

We have therefore studied the hydrolysis of substituted benzyldimethylsulfonium ions (with the extremely weak nucleophile tosylate as counterion), eq 1. The rates of hydrolysis of such ions have been previously studied,[8] as have rates and sulfur KIE for SN2 reactions with hydroxide,[9] lyoxide KIE (k_{HO^-}/k_{DO^-}),[10] and rates for SN2 reactions with azide ion.[11] Studies of *p*-methoxy and unsubstituted benzyldimethylsulfonium ions with added azide ion and iodide ion, respectively, have been interpreted as implicating not an ion pair, but an ion–dipole pair consisting of the benzylic cation complexed with dimethyl sulfide.[12] The SN2 reactions of tribenzylsulfonium salts were shown to exhibit odd salt effects which make their kinetics appear first order.[13]



(1)

If, like Hill and Fry's chlorine KIE, the sulfur KIE were nearly independent of substituent, this would establish the generality of a rather unexpected phenomenon. If the KIE were dependent on substituent, then we could establish their trend and thus their agreement with predictions for SN1, SN2, or ion-dipole pair mechanisms.[14,15] A trend to larger sulfur isotope effects with electron-releasing groups in the SN2 reactions of these sulfonium ions with hydroxide ion has been reported.[9]

Graczyk and Taylor have determined chlorine KIE for the solvolysis of *p*-methoxybenzyl chloride (70% aqueous acetone, 20 °C) and shown that the solvolysis KIE (1.0079) *increases* to 1.0105 in the presence of 0.25 *M* azide ion,[16] in contrast to the lowering observed by Hill and Fry[4] for more electron-withdrawing groups (EWG). Hill and Fry did not see any second-order reaction or any change in KIE at 0.05 *M* nucleophile with *p*-methoxybenzyl chloride. The observation of Graczyk and Taylor seems consistent with the interpretation by Sneen and Larsen[17] of the kinetic and product data of Kohnstam, Queen, and Shillaker[6] on this same reaction in terms of a mechanism involving partially rate-determining attack of solvent on the intimate ion pair.

Our data do appear to establish the generality of Hill and Fry's observed insensitivity of KIE to substituent. Rate-determining attack of solvent on ion pair or ion–dipole pair[7,12,16,17] is an attractive explanation of constant KIE with substituent, though it seems to require an odd fortuity[18] in which partly rate-determining attack on ion pair in the case of *p*-methoxybenzyl chloride happens to give the same average isotope effect as completely rate-determining attack on ion pair in the case of more EWG.[16] Other difficulties exist with the ion pair and ion–dipole pair interpretations for these benzylic systems, which we discuss below. In view of these difficulties, we also suggest an alternate interpretation of the mechanism for these systems.

Experimental Section[1b]

Materials. Substituted benzyldimethylsulfonium tosylates were prepared from the corresponding alcohols, aldehydes, or acids. The aldehydes or acids were first reduced to the alcohols by lithium aluminum hydride,[19] and the benzyl tosylates were formed by reaction of the corresponding alcohols with sodium hydride, followed by *p*-toluenesulfonyl chloride.[20] The benzyl tosylate was separated from the reaction mixture, quickly dried, and then dissolved in excess dimethyl sulfide. After the sulfonium salt precipitated out, it was filtered, dried, and purified by cold recrystallization several times. The recrystallization procedure involved dissolving the sulfonium salt in a minimum amount of boiling ethanol, decolorizing with charcoal, filtering, and then pouring the solution into a large excess of cold ethyl acetate.[9] The recrystallized material was filtered out and then dried under vacuum for several hours.

Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Analyses were by Midwest Microlab, Ltd., Indianapolis, Ind.

The following compounds were synthesized.

Benzyldimethylsulfonium tosylate: mp 121.8–122.4 °C (lit.[9] 124–124.8 °C); saponification equivalent, 100.5% of theoretical. *Anal.* Calcd for $C_{16}H_{20}O_3S_2$: C, 59.23; H, 6.21; S, 19.76. Found: C, 59.07; H, 6.25; S, 19.71.

***p*-Methylbenzyldimethylsulfonium tosylate:** mp 106.0–106.8 °C (lit.[9] 108–109 °C). *Anal.* Calcd for $C_{17}H_{22}O_3S_2$: C, 60.32; H, 6.55; S, 18.94. Found: C, 60.59; H, 6.40; S, 19.07.

***m*-Methylbenzyldimethylsulfonium tosylate:** mp 89.9–90.7 °C. *Anal.* Calcd for $C_{17}H_{22}O_3S_2$: C, 60.32; H, 6.55; S, 18.94. Found: C, 60.33; H, 6.68; S, 18.97.

***p*-Bromobenzyldimethylsulfonium tosylate:** mp 150.0–151.0 °C. *Anal.* Calcd for $C_{16}H_{19}BrO_3S_2$: C, 47.64; H, 4.75; Br, 19.81; S, 15.90. Found: C, 47.42; H, 4.55; Br, 19.99; S, 15.94.

***m*-Bromobenzyldimethylsulfonium tosylate:** mp 113.6–114.0 °C; saponification equivalent, 100.6% of theoretical. *Anal.* Calcd for $C_{16}H_{19}BrO_3S_2$: C, 47.64; H, 4.75; Br, 19.81; S, 15.90. Found: C, 47.68; H, 4.47; Br, 19.67; S, 16.04.

Two other batches of this salt were also prepared and used; they differed in mp, saponification equivalent, and microanalysis by only minor amounts from that reported.

***p*-Methoxybenzyldimethylsulfonium tosylate:** mp 122.4–124.0 °C; saponification equivalent, 97.6% of theoretical. *Anal.* Calcd for $C_{17}H_{22}O_4S_2$: C, 57.60; H, 6.26; S, 18.09. Found: C, 57.76; H, 6.24; S, 17.93.

***m*-Methoxybenzyldimethylsulfonium tosylate:** mp 103.0–103.8 °C. *Anal.* Calcd for $C_{17}H_{22}O_4S_2$: C, 57.60; H, 6.26; S, 18.09. Found: C, 57.83; H, 6.40; S, 18.05.

Other Reagents. Distilled water redistilled from a trace of potassium permanganate was used as solvent. Carbonate-free sodium hydroxide solution was used for base reactions and titrations.

Kinetic Measurements. Solvolyses were carried out at 68.73 ± 0.02 °C in a constant temperature bath calibrated with an NBS Certified thermometer, using solutions 0.1 *M* in sulfonium salt. Rate constants were shown to be nearly the same at 0.2 *M* sulfonium salt for the *p*-methyl, unsubstituted, and *m*-bromo derivatives. Aliquots were sealed into glass ampules and placed in the constant temperature bath, then periodically an ampule was removed and titrated for liberated acid with standard sodium hydroxide solution. With the *p*-methoxy derivative, the reaction was so fast that each kinetic point was obtained by pipetting an aliquot of preheated water into an open test tube which contained a measured amount of substrate, then proceeding as above.

Rough kinetic measurements were made at 94.0 ± 0.5 °C on solutions 0.1 *M* in sulfonium salt and 0.2 *M* in sodium hydroxide, except for the *p*-methoxy derivative, which was too fast to measure. These rates were needed only to establish the necessary time for greater than 99.99% completion. The values obtained are (10^4k_2, l. mol^{-1} s^{-1}): *p*-CH_3, 4.15; *m*-CH_3, 3.76; H, 3.68; *m*-CH_3O, 3.01; *p*-Br, 3.94; *m*-Br, 6.89.

Product Identification and Measurement. Samples of dimethyl sulfide (DMS) for isotope ratio analysis were shown to be pure by comparison of the mass spectra with that of authentic material. Agreement was very close in all cases.

Samples carried to about 2% completion were generally used for isotope effect measurements. The extent of reaction was checked by titration after the DMS had been removed.

The other product was studied by high-pressure liquid chromatography. The solvolysis mixture was extracted three times with ether and the ether was evaporated with bubbling nitrogen. A chloroform solution of known volume was made of the residue, and an aliquot was injected into the liquid chromatograph. The amount of benzyl alcohol present was determined by area measurement using a calibration curve made with authentic samples. The yields found in this way are not quantitative, because benzyl alcohol is lost in evaporation, as shown by control experiments with authentic benzyl alcohol: *p*-CH_3O, 87%; *p*-CH_3, 69%; *m*-CH_3, 80%; H, 85%; *p*-Br, 105%; *m*-CH_3O, 95%; *m*-Br, 61%.

Infrared spectra of the residues from the ether extracts were identical with authentic benzyl alcohols. Liquid chromatographic retention volumes were identical with authentic samples, using a Waters Associates Model ALC 202 equipped with a uv detector (254 nm) with chloroform as eluant and a 3 mm by 60 cm Porasil-T column. No product peak other than the benzyl alcohol could be detected by liquid chromatography.

Measurement of Isotope Effects. Reactions were carried out in Pyrex ampules which had been sealed under vacuum. After the desired amount of reaction had occurred, as determined from previously measured rate constants, the contents of the ampule were frozen at the bottom by partial immersion in liquid nitrogen. The ampule was then scratched and cracked open with a hot glass rod, and a rubber stopper was fitted, one bore of which contained a ground glass joint for attachment to a vacuum manifold and another bore of which contained a flexible polyethylene tube which continued down into the ampule and had a brass weight at the end. The ampule was attached to a U-tube on the vacuum system which had been previously flushed with dry nitrogen and which was arranged such that, after melting of the ampule's contents, which allowed the weighted polyethylene tube to sink to the bottom of the ampoule, dry nitrogen could be bubbled through the solution (ca. 1.5 h for quantitative removal of DMS), then passing through the U-tube, now immersed in liquid nitrogen, and to the atmosphere.

After all the DMS had been collected in the U-tube, it was isolated and evacuated while the sample was still frozen in liquid nitrogen, and purification was carried out in the vacuum system at high vacuum maintained by a mercury diffusion pump. The DMS was first passed through a tube packed with Ascarite, to remove CO_2, and then condensed in liquid nitrogen in the U-tube. Vacuum distillation from the U-tube, immersed in a dry ice–acetone bath, into a mass spectrometer sample tube, immersed in liquid nitrogen, gave pure DMS, with water retained in the U-tube. Several times during each distillation, the U-tube was sealed off, its contents thawed and then cooled again, to ensure that no DMS was trapped in the ice.

Control experiments showed that this purification technique alters the $^{34}S/^{32}S$ ratio of a sample by a negligible amount (0.02%), whereas a previously used method[9,21] produced a 0.12% effect on the ratio. Such errors, of course, tend to cancel in the determination of the isotope effect since the samples for both partial and complete reaction are treated in the same way, but better reproducibility can be expected with the present method. The vacuum system and mass spectrometer sample tubes were fitted with threaded Teflon stopcocks to avoid any possibility of fractionation of DMS through solubility in stopcock grease.

Isotope ratios were observed with a Nuclide RMS 6-60 ratio-measuring mass spectrometer, equipped with a dual inlet and dual detectors. The inlet system was specially designed, made of stainless steel, with stainless steel high-vacuum valves, thus avoiding all stopcock grease.

Most experiments were done using partial-reaction samples at about 2% reaction. The sulfur isotope effect is given by eq 2,[22] where the

$$k_{32}/k_{34} = (^{34}S/^{32}S)_{100\%}/(^{34}S/^{32}S)_{2\%} \tag{2}$$

sulfur isotope ratios are given by the ratio of *m/e* 64/62 peaks in the mass spectrometer, and the percent subscripts refer to percent reaction, with >99.99% samples used as equivalent in ratio to 100%. The ratio changes by an extremely small amount from 0 to 3% reaction, so that eq 2 holds anywhere in this range.

Since the ratio of ratios of eq 2 is measured directly by difference with the dual inlet mass spectrometer, drifts are canceled out even though absolute ratio readings may differ from day to day. We were able to show that k_{32}/k_{34} values remained constant from day to day, from year to year, and from building to building, as the mass spectrometer was torn apart, moved into a new building, and reassembled during the course of these experiments. Therefore, we can be confident of the reproducibility of our results.

Since the *m/e* 63 peak was unavoidably focussed on the same collector with 62 (although micrometer gates permitted elimination of masses higher than 64 and lower than 62), a small correction was applied to the isotope effects calculated from eq 2. This correction factor took into account species containing ^{33}S, ^{13}C, and D, as well as fragments containing all isotopic species. The abundance for ^{33}S-containing species was calculated with the Swain equation from the $^{34}S/^{32}S$ ratios.[23] The correction to the ratio of ratios (eq 2) was given by 0.979 602 + 0.020 405 6 (ratio of ratios). The isotope effect given by eq 2, multiplied by this correction factor, gives the corrected isotope effect.

For higher percent reaction than 3%, eq 3 gives the isotope effect,

$$k_{32}/k_{34} = \log(1 - f)/\log(1 - rf) \tag{3}$$

where *f* is the percent reaction, and *r* is the reciprocal of the ratio of ratios in eq 2.[24]

Results

First-order kinetics was observed for each reaction (eq 1), and the only products detectable were those shown, except where Z = *p*-methoxy. The other substrates were not followed to high percents of reaction, since the rates were so slow, and the isotope fractionation experiments ran only to about 2%

reaction. The fast *p*-methoxy derivative was found to be first-order up to about 40% reaction, so that no problems exist with the isotope effect experiments, carried in this case to 25% reaction. After 40%, the rate slowed and became very slow by 60% reaction. We suspect this phenomenon may result from significant amounts of product *p*-methoxybenzyl alcohol separating from the reaction mixture at the concentrations used (0.1 *M*), and in some way interacting with or extracting the sulfonium ion from solution. Similar rate plots were obtained when *p*-methoxybenzyl alcohol was followed by liquid chromatography and when acid was followed by titration. Liquid chromatography also showed that, as the rate of hydrolysis slowed, a new product appeared which was less polar than the *p*-methoxybenzyl alcohol, and that after an extended period, the alcohol peak had disappeared and the new peak had enlarged. With a less polar eluant, liquid chromatography showed that this new peak was actually five peaks, which could not be resolved sufficiently for isolation; therefore, we did not further investigate these products, since we had shown that they did not affect the isotope effect measurements. These observations may be closely related to the observation of Quelet and Allard[25] that *p*-methoxybenzyl alcohol rapidly dimerizes into bis-*p*-methoxybenzyl ether at 25 °C in ether with a trace of acid.

We have also observed an odd phenomenon in measuring the isotope effects for the *p*-methoxy derivative. Some runs gave anomalously low isotope effects, seeming to correlate with anomalously low percent reaction, as determined by titration, for a given reaction time. Whether this problem is associated with the kinetic problem discussed in the previous paragraph we could not ascertain, but control experiments showed that $({}^{34}S/{}^{32}S)_{100\%}$ (eq 2) was exactly the same as that for the unsubstituted compound. There is no reason that these ratios should be exactly equal, but it is difficult to dismiss this equality as fortuitous. Therefore, we believe the anomalous results occurred in the 2% ratios. The presence of a rapidly reacting impurity producing DMS could have an effect in this direction, but cannot account for more than a minor fraction of the observed anomaly. The whole problem was bypassed by carrying the reaction to 25% completion, where we had shown that there was still no problem with the side reaction. Highly reproducible isotope effects were then obtained.

The rate constants and isotope effects are shown in Table I. The rate constant for the *p*-methoxy derivative seems quite compatible with that reported by Sneen for a lower temperature (60 °C), 1.78×10^{-4} s^{-1}.[12]

Plots vs. σ^+ give, for the rate constants, a curve without a minimum, and, for the isotope effects, a reasonable approximation to a straight line. In the isotope effect plot, *m*-methoxy seems quite low and *m*-bromo quite high relative to the best straight line, but significantly, *p*-methoxy does not appear to be anomalous at all.

Discussion

The primary conclusion is that the sulfur isotope effects are relatively insensitive to substituent, thus paralleling the insensitivity of chlorine KIE reported by Hill and Fry.[4] There is a trend toward larger KIE with electron-releasing groups (ERG), analogous to that observed in the SN2 reactions of benzyldimethylsulfonium ions with hydroxide,[9] and as expected for an SN2-like or a loose, ion pair-like or ion-dipole pair-like transition state, but the opposite of expectation for a classical SN1 transition state.[14,15] Increased sulfur KIE are considered to demonstrate increased carbon-sulfur bond breaking at the transition state.[26,27]

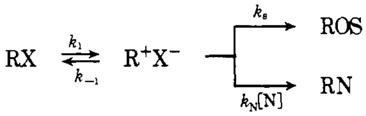
If there is a change of rate-determining step for *p*-methoxy as compared with the other substituents,[12,17] the lack of any discontinuity in the sulfur or the chlorine KIE certainly requires explanation.

Table I. Rate Constants and Sulfur Isotope Effects in the Hydrolysis of Substituted Benzyldimethylsulfonium Tosylates at 68.73 °C

Substituent	$10^8 k$, s^{-1} [a]	k_{32}/k_{34} [a]
m-Br	2.61 ± 0.16	1.009 67 ± 0.000 41
m-CH_3O	4.34 ± 0.08	1.008 98 ± 0.000 26
p-Br	4.51 ± 0.03	1.009 83 ± 0.000 29
H	5.86 ± 0.20	1.009 76 ± 0.000 12
m-CH_3	6.98 ± 0.10	1.010 08 ± 0.000 14
p-CH_3	21.4 ± 0.56	1.010 27 ± 0.000 38
p-CH_3O	37 500 ± 200	1.010 77 ± 0.000 17[b]

[a] The ± values are standard deviations. [b] Calculated from 25%-reacted samples.

Ion Pair and Ion–Dipole Mechanisms. It thus becomes crucial to know whether Sneen's ion-pair mechanism is required by the data. For substrates capable of forming reasonably stable carbonium ion species, this type of mechanism is certainly not unreasonable. The conclusion was that k_{-1}/k_s (eq 4) is 1.98 for *p*-methoxybenzyl chloride,[17] 1.19 for *p*-methoxybenzyldimethylsulfonium, and 14.3 for benzyldimethylsulfonium tosylates.[12] We believe that the sulfonium ion results are inconsistent with the selectivity principle,[28] in that the benzyl cation-dimethyl sulfide ion-dipole pair should be less stable relative to reactants and products than the *p*-methoxy substituted one, and should therefore be less selective and have a k_{-1}/k_s ratio closer to unity than the *p*-methoxy system's ratio.



(4)

There has also been a good deal of difference of interpretation of kinetic data for several of the systems believed by Sneen to be consistent only with eq 4. The *p*-methoxybenzyl chloride data has also been interpreted as involving simultaneous SN2 and SN1-like processes.[6] This type of mechanism[5] has been dismissed[29] for the 2-octyl system on the basis that the product azide is not racemic but inverted. However, rate-determining formation of ion pair (eq 4) accompanied by SN2 would be consistent with the stereochemistry.

The major question has to do with the influence of salt effects upon addition of nucleophilic ions.[30-33] Although Sneen has cogently defended his interpretation against simultaneous SN1 and SN2 mechanisms,[29] this defense is based on the assumption that no alkyl azide is produced in the SN1 mechanism, since the SN2 line is drawn with a slope equal to the slope of a plot of observed product ratio RN_3/ROS vs. $[N_3^-]$ (see eq 4). That is, the slope derived from the product data is assumed to be equal to the ratio of rate constants k_{SN2}/k_S. Thus, in the SN2 scheme k_S, the rate constant for solvolysis, is assumed to be incapable of accounting for any production of RN_3 through trapping of an intermediate after the rate-determining step, and so all RN_3 is assumed to arise from the SN2 mechanism. On the other hand, if a straight line is simply drawn through Sneen's data, there is a rather good fit, though some curvature is certainly seen. This linearity holds whether the concentration or the activity[31,32] of azide is plotted. In sum, it seems that Sneen can rule out the simultaneous SN1 and SN2 mechanisms under his assumption, but that it is much more difficult to rule them out if one assumes that some of the alkyl azide product can arise from the SN1 route by trapping of the intermediate.

There is also evidence which is difficult to explain with the mechanism of eq 4, coming from α-deuterium and ${}^{14}C$ isotope effects for solvolysis of benzyl and *p*-methylbenzyl chlorides.[34]

The observed large carbon isotope effects and very small deuterium isotope effects seem almost to require a tighter SN2-like transition state, rather than a loose, ion pair-like one.[34] It would appear, however, that the revised interpretation of the chlorine isotope effects for *p*-methoxybenzyl chloride with added azide ion,[16] suggested by these workers,[34] is questionable; in an SN2 process, azide as nucleophile would be expected[14] to give a more reactant-like transition state than the much weaker nucleophile water. Similar α-deuterium results have been reported in a slightly different solvent system.[35] On the other hand, larger α-D effects,[36,37] but still only partway to the limit expected[38] for an ion pair-like transition state, have been observed for benzyl chlorides. These isotope effects vary with solvent and appear to decrease with increasing solvent nucleophilicity.[36,37] The corresponding transition states therefore probably become tighter as solvent nucleophilicity is increased. This increased tightness would be expected for a mechanism involving nucleophilic solvent interaction in a rate-determining step leading to SN2 displacement product or to ion pair only if a significant perpendicular effect were associated with the parallel (Hammond postulate[39]) effect leading to a more reactant-like transition state for increased nucleophilicity.[14,15] There is now good evidence that such a perpendicular effect is significant along with the parallel effect in the E2 elimination mechanism.[40]

There is also other evidence, pro[41,42] and con,[43,44] on the universality of the ion-pair mechanism.

The essential conclusion is that there is not general agreement on Sneen's ion-pair interpretation, and in fact there is additional evidence against it in certain systems, including benzylic ones. Even if it is not as general as Sneen believes, it is certainly plausible that rate-determining or partly rate-determining attack on ion pairs or ion-dipole pairs is the mechanism for some systems.

Heavy-Atom Isotope Effects and Mechanistic Interpretation. Model calculations of chlorine[45-47] and carbon[47,48] KIE show that the experimental results are quite reasonable in general, but cannot really distinguish between the mechanisms under consideration.

Chlorine KIE in SN2 displacements on substituted benzyl chlorides[49] agree with predictions.[14] Carbon KIE in the same system studied by Hill and Fry[4] actually become significantly smaller with ERG, especially with *p*-methoxy,[2] in spite of the constancy of the chlorine KIE.

tert-Butyldimethylsulfonium iodide, which solvolyzes by an SN1-like mechanism, has a sulfur KIE of 1.0180 (59 °C).[21]

Taking into account possible ambiguities in the interpretation of the data for benzyl chlorides and benzyldimethylsulfonium ions, the problem of constancy of chlorine and sulfur isotope effects still stands out. There seems to be no really satisfactory explanation of constant isotope effects with a change of mechanism. Three possibilities merit consideration.

(1) Constancy of isotope effects with substituent changes is, as we have noted above, explained by the Sneen mechanism (eq 4).[7,12,17] However, it is difficult to believe in rate-determining attack of nucleophile on preformed ion pair or ion-dipole pair for strongly electron-withdrawing groups such as *p*-nitro, which should have a very large destabilizing influence. The idea of more selectivity (greater k_{-1}/k_s) for such species seems to be a major violation of the selectivity principle. The carbon and α-D isotope effects imply an SN2-like transition state for the substituents studied.[34] Also, Graczyk and Taylor find increased chlorine KIE for *p*-methoxybenzyl chloride with added azide,[16] yet Hill and Fry find decreases with other nucleophiles for other substituents.[4] One can discard "principles" if the evidence is strong enough. One can also argue that the carbon and α-D isotope effects expected for the Sneen mechanism are not established well enough to use such evidence to rule out this mechanism. It is quite difficult to explain the different effects of nucleophiles on chlorine KIE,[4,16] and a new mechanism, perhaps classical SN2,[4] must probably be brought in along with the ion-pair mechanism to explain the data along these lines. In sum, the ion pair and ion–neutral pair mechanisms cannot easily accommodate the data, and the kinetic results suggesting that attack on the paired species is only partly rate determining in the case of *p*-methoxy require a fortuity to explain the constancies of chlorine and sulfur KIE with substituents.

(2) It could instead be argued that the rate-determining transition states are SN2-like, though perhaps loose and somewhat ion pair-like.[15] This interpretation would be consistent with the carbon and α-D KIE data.[34] It might be expected that such a mechanism would lead to changes in chlorine and sulfur KIE with substituent, but the SN2-like system has the property of being mainly sensitive to substituents in the benzyl group via changes in TL character (tight-loose).[14,15] If this type of transition state has substantial restoring forces for the TL distortion, then its structure may be relatively insensitive to substituent.[14] There is still the problem of the Graczyk and Taylor and the Hill and Fry observations alluded to in the previous paragraph.[4,16] It now becomes possible to understand the Hill and Fry data as resulting from a more reactant-like transition state for the strong nucleophiles.[14,15,39] However, the Graczyk and Taylor evidence cannot be explained with an SN2-type mechanism.

(3) The evidence against ion pair and ion–neutral pair mechanisms in these benzylic systems and the evidence favoring SN2-like transition states, explicated in the two previous paragraphs, suggest that the mechanism is SN2-like for all substituents studied, except *p*-methoxy.

If one feels that the near equality of KIE with substituent changes in the solvolysis reactions is not necessarily indicative of a single mechanism, encompassing all substituents, then it is reasonable to conclude that *p*-methoxy alone may involve an ion-pair mechanism, and thus to explain Graczyk and Taylor's result.[16]

If, on the other hand, one feels that the equality is not fortuitous, and this seems to be supported by the similar observations for both chlorides and sulfonium ions, then it is reasonable to conclude that the *solvolyses* are SN2-like, even for *p*-methoxy. The effect of added azide in the reaction of *p*-methoxybenzyl chloride cannot then be the type of trapping of ion pair previously suggested,[16] and a "peculiar" mechanism for the azide reaction is required. We believe this reaction may involve formation of an ion triplet or "sandwich".[50-52] The sandwich, being a relatively high-energy intermediate, should have a high degree of carbon–chlorine bond breaking in the transition state for its formation.[14,39] An approximately central SN2-like transition state, as suggested for solvolysis, would then have considerably less carbon–chlorine bond breaking. A higher chlorine KIE would be seen in the sandwich-forming reaction than in the solvolysis, as observed.[16]

We favor the SN2-like interpretation for these (primary) benzylic systems, together with the sandwich mechanism for azide with *p*-methoxybenzyl chloride. This SN2-like interpretation seems appropriate to the sulfonium ion case also, and is consistent with the considerably smaller sulfur KIE observed for the benzylsulfonium systems (Table I, ref 9) than for *tert*-butyldimethylsulfonium ion.[21] Also, the small trend of sulfur KIE with substituents is in the direction expected for an SN2-like mechanism.[9,14,15]

Conclusions

We have shown that the Hill and Fry result[4] is independent of the charge type of the leaving group. It could, of course, depend on other variables not yet explored, such as the nature of the alkyl group or the solvent (all so far studied contained water). We believe that the constancy of KIE with substituents is more than fortuitous. The extended independence now demonstrated casts doubt upon the ion pair or ion–neutral pair mechanism for benzylic systems, even for *p*-methoxy. We therefore believe that the evidence points to S_N2-like transition states for solvolysis and a "sandwich" (ion triplet) mechanism for the azide reaction with *p*-methoxybenzyl chloride. It should be emphasized that the suggestion of an S_N2-like transition state does not imply a necessarily concerted mechanism, since it could, if loose, still lead to carbonium ion type intermediates. The magnitudes and constancy of the observed chlorine and sulfur KIE suggest that the mechanism may well be concerted, however, as might be expected for a primary system passing through a relatively tight transition state,[34] not sterically loosened by congestion at the central carbon atom.[14,15]

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References and Notes

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Stereochemistry of Solvolytic Substitution of Cyclopentyl *p*-Bromobenzenesulfonate

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Abstract: The stereochemical result of solvolytic substitution of cyclopentyl-*2-d* *p*-bromobenzenesulfonate in several solvents has been determined by ^{2}H NMR. Cyclopentanol was found to be formed in the following solvents with the parenthetically indicated percent inversions: 70% ethanol–water (99%), 80% ethanol–water (100%), 80% dioxane–water (92%), and 80% 2,2,2-trifluoroethanol–water (100%). Cyclopentyl ethyl ether was formed in 70, 80, and 100% ethanol–water with 100, 96, and 99% inversion, respectively. Cyclopentyl 2,2,2-trifluoroethyl ether was formed in both 80 and 97.5% trifluoroethanol–water with 92% inversion-8% retention (errors are ~3%). The detailed mechanistic interpretation of these and earlier results on deuterium rate effects and elimination stereochemistry requires the existence of two product-forming ion pair intermediates.

Earlier studies[2,3] on the solvolysis of cyclopentyl *p*-bromobenzenesulfonate (I) have reported secondary deuterium rate effects[2] and the stereochemistry of the olefin-forming elimination reaction.[3] The steric course of cyclopentanol formation from *cis*-cyclopentyl-*2-d* *p*-bromobenzenesulfonate (*cis*-I-*2-d*) was originally determined through ^{1}H NMR analysis[2] using tris(dipivalomethanato)praseodymium(III)[4] as a shift reagent.[2] Subsequently an additional, more rapid, more precise method using ^{2}H NMR was developed.[2b] The ^{1}H NMR method did not prove satisfactory for determining the con-

Shiner et al. / Solvolytic Substitution of Cyclopentyl p-Bromobenzenesulfonate