Thiourea as a Probe for Nucleophilic Solvent Assistance

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In this work we describe a useful probe for a solvolysis mechanism using the neutral nucleophile thiourea for which confusing salt effects are absent and solvent effects are small. Significant rate accelerations, linear with thiourea concentration, are observed for substrates known to react by direct nucleophilic displacement (a k_s mechanism). Reaction rates for substrates reacting without nucleophilic solvent assistance (i.e., reaction by a k_c or k_Δ mechanism) show slight rate retardation if there is no external ion return (e.g., as evidenced by a common ion rate depression); apparently thiourea reduces solvent ionizing power. In the case of k_c substrates undergoing solvolysis with external ion return, thiourea addition reduces the amount of return to give a linear rate acceleration superficially similar to that observed for k_s substrates. When used in conjunction with other mechanistic information, the kinetic effects of thiourea addition are also useful in elucidating the reaction mechanism of borderline substrates. For example, *tert*-butyl chloride solvolysis is slightly accelerated by thiourea addition and thus is indicated to receive nucleophilic participation. A product study shows that thiourea produces isobutylene, but not in the amounts expected from a rate–product correlation. Thus, nucleophilic assistance for this substrate most likely derives from nucleophilic attack both at carbon and at hydrogen.

Several probes have been developed for detecting the involvement of nucleophilic solvent assistance in substitution at saturated carbon.[1] The ones commonly used are based on the assumption that a substrate's rate behavior is dependent on a solvent's ionizing power and nucleophilicity. The Raber–Harris method, based on correlation of solvolysis rates in aqueous ethanols and trifluoroethanols with 1-adamantyl substrates,[2-4] is an example of this type that has been applied in the assignment of solvolytic mechanism. Another popular method involves measurement of the effects on rates and products of added anionic nucleophiles such as azide ion.[5] These approaches and similar ones[1] are adequate in many situations, but none is without its shortcomings. For example, methods like that of Raber and Harris utilize solvent variation, which can be quite complex. Consequently, it is not surprising that this method will fail in cases where solvent effects are not predicted by the 1-adamantyl model used. We have recently shown that the Raber–Harris probe predicts incorrectly for mustard derivatives.[6,7] Similarly, addition of nucleophilic salts produces complex changes in ionic strength and electrophilicity of the medium, thus giving rate variation independent of nucleophilic assistance.[1,4,8,9]

In evaluating the effects of poly(ethylene glycol), PEG, on the rates of some solvolytic reactions we observed that amine-terminated PEGs showed significant reactivity toward benzyl bromide but not toward (alkylthio)ethyl chlorides.[10] The effect with benzyl bromide was similar to that described by McLennan[8] and Queen,[9] who noted that addition of the neutral nucleophile thiourea gives rate enhancement with some alkyl substrates. They found that results with thiourea are relatively uncomplicated, and they have used this neutral nucleophile approach to provide unusually lucid interpretations of the solvolysis of 2-octyl mesylate and *p*-methoxybenzyl chloride. McLennan[11] has also discussed thiourea-promoted elimination. We have previously employed thiourea to assist in the characterization of solvolysis mechanisms where conflicting data were obtained.[6,10] In the present article we further examine this use of thiourea as a probe of the susceptibility of alkyl substrates to nucleophilic attack by determining the kinetic effects of thiourea addition on a range of substrates.

Results and Discussion

Nucleophilically Unassisted Solvolyses. As S_N1 substrates we have chosen to examine 1-adamantyl bromide, 2-adamantyl tosylate, and 2-(methylthio)ethyl chloride. These substrates are "simple" in that there is no kinetically important competition between return processes (ion-pair or external-ion) and nucleophilic trapping of intermediates. The two adamantyl substrates have been extensively studied and repeatedly demonstrated to react without significant neighboring-group or nucleophilic-solvent assistance (i.e., reaction by a k_c mechanism).[1,12] Common ion rate depression is not observed in either case, so external ion return from free carbocation is not important.[1] Paradisi and Bunnett have used oxygen-scrambling techniques to detect internal return in solvolysis of 2-adamantyl substrates,[13] but the insensitivity of this substrate to added nucleophiles shows that the return is "hidden" in that nucleophilic attack must only occur subsequent to rate-determining dissociation of the ion pair. The 2-(methylthio)ethyl chloride substrate reacts by a pure

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Table I. Effect of Thiourea on the Rates of Various Alkyl Substrates

substrate[a]	solvent[a]	T, °C	thiourea molarity	10^4K, s^{-1}	k_{rel}
MeOTs	50E	74.2	0	4.20 ± 0.01	1.0
			0.20	50.0 ± 0.1	11.9
			0.50	97.1 ± 3.9	23.1
EtOTs	60E	45.2	0	0.061[b]	1.0
			0.20	0.46 ± 0.01	7.54
			0.50	1.01 ± 0.01	16.6
t-BuCl	60E	25.0	0	1.84 ± 0.01	1.0
			0.50	1.93 ± 0.01	1.05
			1.00	2.28 ± 0.02	1.24
1-AdBr	50A	49.9	0	2.57[c]	1.0
			0.1	2.40[d]	0.93
			0.2	2.37[d]	0.92
2-AdOTs	50E	74.2	0	3.25 ± 0.16	1.0
			0.20	2.84 ± 0.14	0.874
			0.50	2.26 ± 0.07	0.695
endo-2-NbOTs	50E	50.0	0	1.41 ± 0.02	1.0
			0.10	1.51 ± 0.07	1.07
			0.20	1.58 ± 0.01	1.12
BzBr	100E	25.0	0	0.014[b]	1.0
			0.05	4.33 ± 0.01	309.0
			0.10	7.60 ± 0.04	543.0
			0.20	13.7 ± 0.01	979.0
BzBr	60E	25.0	0	0.194 ± 0.002	1.0
			0.10	30.6 ± 0.2	158.0
			0.20	59.3 ± 1.2	306.0
$MeSCH_2$-CH_2Cl	70A	24.9	0	3.72 ± 0.18	1.0
			0.07	2.05 ± 0.02	0.551
			0.10	2.02 ± 0.01	0.543
			0.14	2.00[e]	0.538

[a] Me = methyl, Et = ethyl, Oct = octyl, *t*-Bu = *tert*-butyl, Ad = adamantyl, Nb = norbornyl, Bz = benzyl, 50E = 50% aqueous EtOH (v/v), 70A = 70% aqueous Me_2CO (v/v), 30D = 30% aqueous dioxane (v/v), etc. [b] Rate extrapolated from data at higher temperatures. [c] Rate data from ref 4. [d] Rate data extrapolated from other temperatures to allow comparison with data from ref 4. [e] One run at this molarity.

neighboring-sulfur assisted pathway (a k_Δ mechanism), without complicating elimination or nucleophilic solvent assistance,[6,14] and thus also qualifies as a "simple" S_N1 substrate.

Let us initially consider the kinetic results for solvolysis of the tertiary model substrate, 1-adamantyl bromide, in the presence of added thiourea, Table I. As can be seen, thiourea has a rate-retarding effect. To the contrary, salts are known to cause rate accelerations by specific solvation and by affecting the ionic strength of the medium.[1,8] It is reasonable to assume that thiourea causes the 1-adamantyl bromide rate reduction by producing a slight decrease in solvent ionizing power.[1]

In most of the reactions studied in this work we found an approximately linear kinetic response to thiourea concentration. Consequently we have arbitrarily fitted the observed rates (Table I) to eq 1, to obtain k_N values that

$$k_{obsd} = k_{solv} + k_N[N] \quad (1)$$

provide a convenient measure of the effect of thiourea on reaction rate, Table II. The rate-retarding effect of added thiourea on 1-adamantyl bromide solvolysis is thus represented by a k_N value of −0.390, Table II.

If our assumption regarding the mechanism by which thiourea retards the rate of 1-adamantyl bromide is correct, we can predict that other pure S_N1 substrates should behave similarly. To confirm this we examined 2-adamantyl tosylate, a k_c substrate,[1,12] and 2-(methylthio)ethyl chloride, a k_Δ substrate.[6,14] Previous studies show that neither of these substrates are affected by solvent nucleophilicity. Our studies with added thiourea complement the previous work in showing that both substrates are slightly retarded by the added neutral nucleophile, yielding k_N values of −0.609 for 2-adamantyl tosylate and −3.42 for the thioethyl chloride, Table II. Interestingly, the rate-retarding effect on the thioethyl chloride is substantially larger than that for the adamantyl substrates, and the thioethyl chloride response is the least linear of the substrates studied. To place these differences in context, however, it should be noted that even the thioethyl chloride response is much smaller than those measured for most of the other substrates in this study.

Table II. Application of Equation 1

substrate	mechanistic type	k_{solv}^{calcd} [a]	k_N^{calcd}	r[b]	n[c]
MeOTs	k_s	1.81	43.6	0.994	3
EtOTs	k_s	1.18	31.1	1.000	3
2-OctOMs[d]	k_s	1.08	18.3	0.996	7
BzBr (100E)	k_s	37.0	4810.0	0.997	4
BzBr (60E)	k_s	2.5	1530.0	1.000	3
t-BuCl	weak k_s	0.977	0.240	0.948	3
endo-2-NbOTs	weak k_s	1.00	0.600	0.995	3
2-AdOTs	k_c	0.998	−0.609	−1.000	3
1-AdBr	k_c	0.991	−0.390	−0.929	3
$MeSCH_2CH_2Cl$	k_Δ	0.923	−3.42	−0.885	4
p-MeOBzCl[e]	k_c-return	0.989	8.87	1.000	5
benzhydryl chloride[e]	k_c-return	1.000	3.17	0.999	5

[a] Taken from the y intercept of the plot of k_{obs} vs. [N]. The experimental value is 1.0 in each case. [b] Correlation coefficient. [c] Number of data points. [d] Data from ref 8. [e] Data from ref 9.

From examination of the above three substrates reacting without nucleophilic solvent assistance, we can conclude that, in aqueous ethanol or acetone, thiourea has a slight rate-retarding effect on substrates reacting by a simple S_N1 mechanism. It is our judgement that this rate retardation results primarily from reduction in ionizing power of the medium. However, it is possible that thiourea could have an effect on reactant solvation which would affect rate. If the rate reduction is from simple medium effects, we should be able to use a modification of eq 1 or a combination of eq 1 with an extended Grunwald–Winstein equation[1b] to obtain a quantitative treatment accounting for any change in the ionizing power of the medium. However, the objectives of the present study were to qualitatively classify different mechanistic classes not to quantitatively account for small differences within the classes.

Nucleophilically Assisted Processes. In this section we examine the kinetic effects of added thiourea on the model k_s solvolyses of methyl tosylate, ethyl tosylate, 2-octyl mesylate, and benzyl bromide. A large number of studies have demonstrated that leaving group departure from these compounds is accompanied by major nucleophilic solvent assistance.[1] As shown in Table II all of these k_s compounds show large, linear kinetic responses to added thiourea. Here k_N values range from a low of 18.3 for 2-octyl to a high of 4810 for benzyl, as compared to the negative values observed for the k_c and k_Δ substrates above. Figure 1 compares the alkyl k_s substrates and 2-adamantyl, revealing the qualitative difference between these mechanistic types. Similar plots of other substrates have appeared in our other recent works.[6,10]

The relationship between pseudo-first-order rate constants and products for a bimolecular process in which

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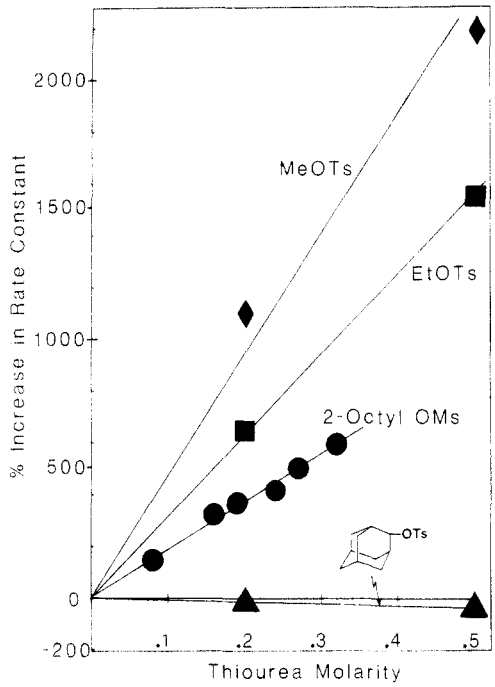

Figure 1. Plot of the percent change in rate constant, $[(k/k_0)^{-1}] \times 100$, vs. thiourea molarity for some primary and secondary alkyl sulfonate esters.

medium effects are ignored and product-determining and rate-determining steps are identical is described by eq 2,[5]

$$1 - k_0/k = \%\mathrm{RN} \qquad (2)$$

where k_0 is the rate in the absence of added nucleophile, k is the rate with added nucleophile, and RN represents the substitution product derived from attack by the added nucleophile. If thiourea is giving a rate acceleration because of nucleophilic assistance, then the rate acceleration should be reflected by a corresponding change in products as described by this equation. To confirm that this equation is applicable in these solvolytic processes, we have applied it to the solvolysis of 2-octyl mesylate for which product data is available,[8] Table III. The good correlation between the calculated and experimental product yields (Table III) is strong support for the applicability of eq 2.

The relative magnitude of the rate accelerations observed for the k_s substrates is worth comment. Proceeding from methyl to ethyl to 2-octyl is attended by a decrease in acceleration. Trends of this sort, which signal a drop in the effectiveness of nucleophilic assistance, are commonly seen for the methyl–primary alkyl–secondary alkyl series,[1,15,16] and presumably are of steric origin. The very large response of benzyl bromide is also in accord with previous observations. For example, 0.1 M sodium azide gives rate accelerations of 1260 for benzyl chloride (in 70% acetone at 20 °C) and 6.41 for 2-propyl tosylate (in 75% dioxane at 50 °C).[17] Similarly, ethoxide acceleration in ethanol (k_2/k_1) for benzyl chloride, methyl benzenesulfonate, ethyl benzenesulfonate, and isopropyl benzenesulfonate is 1950, 1460, 1310, and 69, respectively.[18] However, it should be noted that benzyl's response to nucleophilicity is not always greater than that exhibited by simple alkyl substrates; for example, the k_{EtOH}/k_{HOAc} ratios for tosylates are benzyl 22, isopropyl 5, and ethyl 126.[19]

Table III. Rate and Product Correlations for Various Substrates

substrate	[thiourea]	k_{rel}[a]	%RN[b] exptl	%RN[b] calcd
2-octyl mesylate[c]	0.0	1.0	0	0
	0.0808	2.50	59	60
	0.163	4.25	75.4	76
	0.194	4.71	78.7	79
	0.236	5.17	81.1	81
	0.270	5.86	83.4	83
	0.318	6.95	85.6	86
tert-butyl chloride[d]	0.0	1.0	0	0
	0.5	1.05	1.4	5
	1.0	1.24	4.8	19
benzhydryl chloride[e]	0.0	1.0	0	0
	0.072	1.22	19	18
	0.1035	1.31	25	24
	0.1435	1.46	34	32
	0.2061	1.66	43	40
p-methoxybenzyl chloride[e]	0.0	1.0	0	0
	0.0704	1.61	44	38
	0.1008	1.86	53	46
	0.1394	2.24	64	55
	0.2024	2.78	72	64

[a] Rates are from Table I and ref 8 and 9. [b] Calculated rates are determined by using eq 2. Experimental yields from ref 8 and 9 were determined indirectly. [c] Reference 8. [d] The experimental %RN is corrected for isobutylene formed in the absence of thiourea (3.1%). [e] Reference 9.

Borderline Substrates. Some substrates do not clearly fall into either the k_c–k_Δ or k_s categories and are therefore labeled borderline substrates.[1] It is of interest to examine the effect of added thiourea on kinetics of some substrates of this type. We have chosen to examine two of these compounds, *tert*-butyl chloride and *endo*-2-norbornyl tosylate. The solvolytic mechanisms of these compounds are controversial[1,2] and the weak nucleophilic solvent assistance claimed for them[20-23] is subject to debate.[24-26] The mechanism of *tert*-butyl chloride solvolysis is especially important since Grunwald and Winstein adopted this substrate as the k_c model with which other substrates were compared.[27]

For our treatment it is important to know that *tert*-butyl chloride solvolyses involve ion pairs in some solvents,[28] but common ion rate depression is not significant for either *tert*-butyl chloride or *endo*-2-norbornyl tosylate.[1,22] Also, no scrambling of oxygen is observed in ^{18}O-labeled *tert*-butyl *p*-nitrobenzoate solvolysis experiments.[29] In the present context, these facts imply that these reactions are

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not complicated by competition between return and nucleophilic attack on carbocations.

Addition of thiourea gives a linear rate acceleration for both substrates, Table II. Clearly, these compounds do not react by a simple k_c process since a negative k_N is not observed. Rather, reaction by a k_s mechanism with very weak nucleophilic solvent assistance is indicated. Our thiourea result provides new evidence on this topic. Because of its importance, we will treat the *tert*-butyl chloride system in detail here. Since the measured acceleration of the *tert*-butyl chloride rate by thiourea is small, we sought additional support before drawing mechanistic conclusions.

We have examined the reaction products for reaction of *tert*-butyl chloride with added thiourea, Table III. We were unable to isolate or detect by ^{1}H NMR the thiouronium salt expected from thiourea attack at carbon; we assume the salt would not be detected by GC[30] although we must consider the possibilities that the product is unstable and may decompose to form isobutylene. The products detected upon reaction in aqueous ethanol were *tert*-butyl alcohol, ethyl *tert*-butyl ether, and isobutylene.

As shown in Table III, the amount of isobutylene, which is initially a very small proportion of the products, does modestly increase with the rate acceleration produced by thiourea addition. Assuming that isobutylene is the only nucleophilically derived product, and subtracting the isobutylene formed in the absence of thiourea, we can then apply eq 2 (Table III). According to this calculation, the amount of isobutylene determined is not in accord with the amount for the assumed bimolecular mechanism. Consequently we must conclude that (1) the reaction does not proceed by a simple S_N2-type process; (2) other nucleophilically derived products (specifically the thiouronium salt) are being formed; (3) isobutylene is being lost prior to analysis; or (4) eq 2 should be modified to include the medium effects of added thiourea. Since the *tert*-butyl chloride reaction is clearly different from the S_N1 models as regards the kinetic response to thiourea addition, we are of the opinion that *tert*-butyl chloride does receive nucleophilic assistance and that the failure of eq 2 is the result of its simplicity and our inability to isolate or detect the thiouronium salt.

We note here that nucleophilic assistance, as measured by thiourea addition or by most other methods, may result from attack at hydrogen as well as attack at carbon. Thus added nucleophiles can give kinetic assistance without being required to approach the sterically hindered reactive carbon of a tertiary derivative such as *tert*-butyl chloride. Consistent with our results, Kevill and Thornton and their co-workers[20] found that comparison of the solvolysis rates and products for *tert*-butyl chloride with its d_9-labeled form shows that there is a significant secondary deuterium isotope effect and that the deuterated form produces significantly less isobutylene. Thus the sensitivity of *tert*-butyl chloride to variations in solvent nucleophilicity or basicity is undeniable. In view of these considerations and our product studies, it is very likely that *tert*-butyl chloride may be undergoing nucleophilic attack, perhaps on a tight ion pair, at both carbon and hydrogen. Regardless of the site of attack, it seems clear to us that *tert*-butyl chloride is not a good model for nucleophilically unassisted solvolysis. Because they are free of the major problems which render *tert*-butyl unacceptable, the highly predictable bridgehead systems[31] are preferred as model k_c substrates.

Complex Substrates. As a final consideration we will discuss the response to thiourea of *p*-methoxybenzyl and benzhydryl chlorides. Queen has examined this question previously;[9] the goal of the present reconsideration is to determine if our studies above with simple substrates will provide any insight to these complex mechanisms. The benzyl and benzhydryl substrates are more complex because of the occurrence in these cases of external ion return (as shown by common ion rate depression).[9,32] Also, *p*-methoxybenzyl chloride solvolysis has been said to involve ion pairs and nucleophilic solvent assistance.[17] Since benzhydryl chloride is apparently the simpler of these two we will consider its reaction first.

Benzhydryl chloride solvolysis was one of the reactions used by Hughes and Ingold in their classic studies introducing the S_N1 and S_N2 mechanisms.[17,32] The evidence for the S_N1 mechanism in this case is strong. For example, benzhydryl chloride, bromide, and iodide give the same products in aqueous ethanol with added sodium azide, thus indicating product formation, after the rate-determining step, from a free carbocation.[17,32] Observation of a common ion rate depression is also consistent with an S_N1 mechanism involving product formation and return from a free carbocation. A recent study of ours with α-deuterium isotope effects in benzhydryl solvolyses is most consistent with nucleophilic involvement of solvent in solvating the cationic intermediate.[33]

As shown in Table II, thiourea addition gives an appreciable rate acceleration for benzhydryl solvolysis. Thus, at first glance it would appear that this compound is an S_N2 substrate. However, as we will see below, this is not the case. Queen determined the kinetic effects of several nonelectrolytes (acetone, benzene, ethanol, 2,6-lutidine, and pyridine) in addition to thiourea and urea on reaction of both *p*-methoxybenzyl and benzhydryl chloride.[9] For benzhydryl chloride all the nucleophiles except urea and thiourea gave a rate retardation. The goal of Queen's study had been to test the Sneen ion pair mechanism[34] with nonionic nucleophiles; however, the effects of the added nucleophiles on the medium proved to be too complex for this purpose. McLennan had previously used urea and thiourea for this same purpose with 2-octyl mesylate solvolysis, where medium effects were minor; a simple S_N2 mechanism was found[8] and we showed that eq 2 is applicable, Table III. Also McLennan found that urea did not act nucleophilically and could be used to model changes in solvent ionizing power upon thiourea addition; very slight rate accelerations were observed for 2-octyl mesylate upon urea addition (e.g., at 0.302 M urea k/k_0 = 1.10) but the reaction products were unchanged.[8] As noted above, Queen considered the solvent effects of the various nonelectrolyte additives to be too complex to permit solution of eq 2 for benzhydryl solvolysis in the presence of thiourea. Rather his approach was to use the additive effects on benzhydryl reaction to estimate the solvent effects that could then be used to analyze the results for *p*-methoxybenzyl reaction.

It is interesting, however, to examine Queen's results for thiourea addition to benzhydryl solvolysis more closely. In Table III we have gathered the resulting rate and product data. As can be seen from Table II, the rate effect of added thiourea is linear with concentration, just as one would expect for an S_N2 process. But unlike the *tert*-butyl

(30) It is possible and indeed likely that the salt from nucleophilic attack at carbon decomposes to the alkene, especially under GC conditions, leading to an inflated isobutylene yield. However, we have sought to isolate the salt without success. Also, we have been unable to obtain NMR evidence of it. Its low calculated yield (ca. 10% if half of the product of nucleophilic attack is at carbon) may be a factor.

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case discussed above, elimination is not possible and the salt from thiourea attack at carbon is a product. In this case the amounts of the salt formed are very close to those calculated by eq 2, Table III. Normally such a rate–product correlation would be interpreted in terms of an S_N2 mechanism.[5,8] However, this equation should also closely describe the S_N1 mechanism if, as is true in the benzhydryl case, return is important (k_{-1}/k_2 or α = 39 here),[17] since again we are seeing competitive, rate-determining destruction of a species by two nucleophiles (water and thiourea in this case).

In discussing the 2-adamantyl, 1-adamantyl, and 2-(methylthio)ethyl cases above, we concluded that thiourea addition should cause a rate retardation for S_N1 substrates because of a reduction in solvent ionizing power. However, we now see that we must qualify this conclusion for "complex" S_N1 substrates in which return processes are affected by added nucleophiles. In these instances thiourea can also give a rate acceleration (and even a reasonable rate–product correlation) that looks deceptively like that observed for an S_N2 process. As noted above, Queen's other additives gave a rate retardation with benzhydryl solvolysis. Presumably these additives are too weakly nucleophilic to compete for the carbocation intermediate and give a rate acceleration by reducing the amount of return. Apparently thiourea is such a powerful nucleophile that the small changes in solvent ionizing power are overwhelmed for benzhydryl. Alternatively, but less likely, the effects on the four processes concerned (k_{-1}, k_1, k_2, k_N) balance out.

As noted above, Queen used the effects of thiourea on benzhydryl solvolysis to predict the effects of thiourea addition on the "rate of ionization" of *p*-methoxybenzyl chloride. We would concur in this approach if the term "rate of ionization" is understood to include nucleophilic attack by thiourea on the carbocation intermediate to reduce return. Queen uses this assumption to fit the data for *p*-methoxybenzyl to an expression derived for a reaction scheme including nucleophilic attack of thiourea on neutral substrate (or ion pair) as well as free carbocation. We will not review this study here, but we do note that the rate–product correlation in this case, is poor, eq 2 and Table III. This result indicates that a more complex situation does obtain and thus is consistent with Queen's conclusion.

Experimental Section

Chemicals. Reagent grade substrates, obtained commercially (Eastman and Aldrich), were used as received from freshly opened bottles. Ethyl and *endo*-2-norbornyl tosylates were prepared by the standard pyridine method[35] and purified by repeated recrystallization at −70 °C from low boiling petroleum ether. These materials had properties consistent with samples previously prepared in our laboratories.[2,22] All tosylates and brosylates were stored at −10 °C. Solvents were purified in the normal way to remove water,[2,22] distilled, and stored in a desiccator until used or mixed with cosolvents.

Kinetics. Rates were determined by an automated conductimetric procedure previously described.[36] Each kinetic sample contained about 10 mL of solvent ca. 10^{-3} M in substrate and ca. 3×10^{-3} M in 2,6-lutidine. Samples of substrate with and without thiourea were run in solvent from the same batch and rates were determined side-by-side to assure the best comparison. Unless specified in Table II, at least duplicates were determined. Thiourea molarities stated are for 25 °C.

Product Studies. In the case of *tert*-butyl chloride the products with and without thiourea were determined by gas chromatography using a packed OV-101 column and *n*-propanol as internal standard. The *tert*-butyl alcohol and ethyl *tert*-butyl ether peaks overlapped; therefore, their yields were not separately calculated. In 60% aqueous ethanol solution 0.0, 0.5, and 1.0 M in thiourea, the yields of isobutylene are, respectively, 3.1, 4.5, and 7.9%. A plot of logarithm of the *tert*-butyl chloride rates vs. isobutylene yields gave a straight line (r = 0.997). The rate–product correlation equation, eq 2, was also applied (see Discussion section). Isolation studies were attempted to see if the isothiouronium salt from carbon attack occurred. However, only the salt with HCl was found. ^{1}H NMR studies also failed to indicate presence of the *tert*-butyl thiouronium salt.

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Registry No. 1-AdBr, 768-90-1; 2-AdOTs, 25139-43-9; $MeSCH_2CH_2Cl$, 542-81-4; MeOTs, 80-48-8; EtOTs, 80-40-0; 2-OctOMs, 924-80-1; BzBr, 100-39-0; *t*-BuCl, 507-20-0; *endo*-2-NbOTs, 840-90-4; thiourea, 62-56-6.

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Transannular Addition of α-Lithio Sulfoxides to Inactivated Double Bonds. Regio- and Stereochemical Aspects

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Cyclic eight–ten-membered (*E*)-homoallylic sulfoxides undergo regiospecific BuLi-promoted transannular cyclization, yielding saturated bicyclic products. The reaction appears to be a nucleophilic addition of a "carbanion" (an α-lithium sulfoxide) to a nonactivated double bond and occurs readily provided a compatible proton source is available, proton donation being normally performed by the unmetalated sulfoxide itself. The nature of the products and the epimers distributions indicate the reaction is kinetically controlled. The regio- and stereochemical courses are suggested to be largely dependent on the conformational properties of the monocyclic precursors. The differential reactivity of *E* vs. *Z* substrates is also rationalized in conformational terms and in relation to Menger's theory of intramolecular reactivity.[43]

Polar addition to multiple bonds, like its microscopic reverse, elimination, is believed to occur by way of a spectrum of transition states gradually merging into one another and differing in the extent and timing of the bond

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