

electrode, the titrant being a standard aqueous solution of silver nitrate. Proton NMR spectra were recorded on a JEOL EM360L spectrometer. Melting points and boiling points are uncorrected.

Kinetics Procedure. Besides the reactants mentioned in Tables I-III, most reaction solutions also contained a hydrocarbon to act as internal standard for product determination purposes; the internal standard was mostly cyclohexene, but sometimes methylcyclohexane.

For each run, the appropriate reaction solution was prepared at or about room temperature; 5-mL aliquots were dispensed into ampules of ca. 10 mL capacity, which were then cooled by means of dry ice, flushed with N_2 , and sealed with a torch.²⁸ The ampules for a run, usually 15 in number, were placed all at once in a thermostat at 70.0 ± 0.1 °C. At recorded times, ampules were removed, plunged into ice/water, and after 1 min placed (unopened) in storage in contact with dry ice or in a freezing cabinet at -20 °C. Usually 11 ampules were so removed during about 2.5 half-lives. The other four ampules were allowed to react for 10 half-lives. For analysis of its contents, an ampule was allowed to warm to perhaps 0 °C and carefully broken open, and its contents were transferred quantitatively to a separatory funnel containing 10 mL of CH_2Cl_2 and 5 mL of 12% aqueous HNO_3 , rinsing of the ampule and its cap being performed with the nitric acid solution. The contents of the funnel were shaken, the dichloromethane layer was drawn off, and the aqueous layer was extracted with a second 10-mL portion of dichloromethane. The aqueous layer was transferred quantitatively to a 150-mL beaker, 2% aqueous nitric acid was added until the volume was about 50 mL, and then 50 mL of acetone was added. (The purpose of the acetone is to decrease the solubility of $AgCl$ and thereby give a sharper titration end point.) The chloride ion in the solution

was determined by potentiometric titration with silver nitrate.²⁹ The ampules so analyzed included two of the four that had been allowed to react for 10 half-lives, as "infinity" samples.

Plots of $\ln(V_\infty - V_t)$, where V is the volume of $AgNO_3$ solution, versus time were uniformly linear; the negatives of their slopes were taken as pseudo-first-order rate constants.

Product Determination. For the most part, 2-methylpropene and *tert*-butyl methyl ether were identified by the identity of their GC retention times on two or more columns with those of authentic samples. In one case, the "infinity" solution from a reaction with 0.7 M $MeONa$ in 36.8 mol % $Me_2SO/MeOH$ was examined by proton NMR; the observed peaks and chemical shifts matched those of an authentic sample of 2-methylpropene.

Products present in "infinity" ampules were determined quantitatively by GC. Inasmuch as 2-methylpropene has a low boiling point, the ampules were opened while chilled (at ca. -78 °C for runs in $MeOH$, at ca. -15 °C for runs in Me_2SO -containing solvents) and capped with a rubber septum, and the contained solution was injected into the gas chromatograph by means of a precooled syringe. The determination was calibrated by injection of mixtures containing the alkene and the ether in known concentrations, precautions being taken to prevent escape of the volatile alkene during injection or during pauses. Analyses were found to be reproducible, and analyses of mixtures of known composition verified that they were accurate. The "infinity" ampule product compositions are those reported in Tables I-III.

Registry No. *t*-BuCl, 507-20-0; $MeONa$, 124-41-4.

(29) That no significant decomposition of Me_2SO , to form substances reactive with silver ion, occurred during reactions involving $MeONa$ is shown by the small magnitude of the Δ values listed in Table II. Observations reported by Alexander et al.³⁰ are of similar import.

(30) Alexander, R.; Ko, E. C. F.; Parker, A. J.; Broxton, T. J. *J. Am. Chem. Soc.* 1968, 90, 5049.

(28) Reference 13, p 215.

Kinetics, Products, and Mechanism of Reaction of *tert*-Butyl Chloride with Sodium Ethanethiolate in Methanol and Dimethyl Sulfoxide/Methanol Solvents. Insight into the Occasional Superiority of Thiolate over Alkoxide Ions in Effecting E2 Eliminations^{1,2}

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In three solvents, with $EtSNa$ in great excess over *t*-BuCl, the pseudo-first-order rate constant is linearly related to $[EtSNa]$. The slopes, which can be taken as second-order rate constants, increase by 50% from methanol to 36.8 mol % $Me_2SO/MeOH$, and by 3.2-fold from that solvent to 64.2 mol % $Me_2SO/MeOH$. The product is overwhelmingly 2-methylpropene; some *tert*-butyl methyl ether is formed, but no *tert*-butyl ethyl sulfide. Comparison with data for reactions of sodium methoxide (with *tert*-butyl chloride) in the same three solvents shows that the thiolate reagent is more effective at inducing elimination in the two solvents richer in methanol, but that sodium methoxide surpasses it in the solvent rich in dimethyl sulfoxide. These results are compatible with the theory of the variable E2 transition state; there is no need to invoke the "E2C" mechanism to interpret them.

It was a third of a century ago that de la Mare and Vernon³ shocked the world by their observation that benzenethiolate ion is more effective than ethoxide ion in producing 2-methylpropene from *tert*-butyl chloride (*t*-BuCl) in ethanol solution. It seemed contrary to reason that a weaker base should be more effective than a stronger one in a reaction that involves hydron⁴ abstraction.

The E2C Hypothesis. Meanwhile Winstein, Darwish, and Holness⁵ found halide ions to function surprisingly well as reagents to convert 4-*tert*-butylcyclohexyl *p*-toluenesulfonates to 4-*tert*-butylcyclohexene in acetone solution. They believed the unexpected elimination-inducing reactivity of halide ions to stem from their considerable nucleophilicity in acetone and proposed a mechanism of merged substitution and elimination, with a transition state much like that for S_N2 reactions but with concurrent

(1) Research supported in part by the National Science Foundation.

(2) Based in part on the Dissertation of C. A. Migdal, University of California, Santa Cruz, CA, June 1985.

(3) de la Mare, P. B. D.; Vernon, C. A. *J. Chem. Soc.* 1956, 41.

(4) "Hydrons" comprise protons, deuterons, and tritons.

(5) Winstein, S.; Darwish, D.; Holness, N. *J. Am. Chem. Soc.* 1956, 78, 2915.

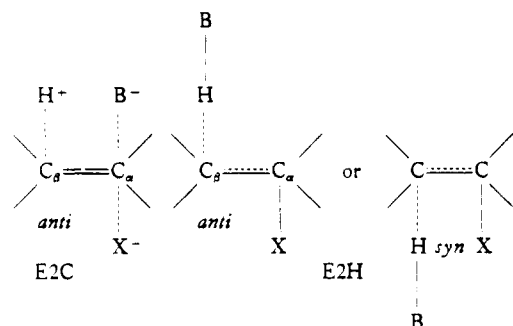


Figure 1. Representations of the visualized E2C and E2H transition states, as given by Parker^{9a} in 1971.

interaction of the nucleophile (base) with a β -hydrogen atom. In fashion characteristic of a strong scientist, Winstein subjected this hypothesis to a severe test, which it failed, and therefore he withdrew it.^{6,7} Winstein and Parker⁸ proposed instead the "E2C" mechanism, in which the nucleophile (base) attacks simultaneously the α -carbon, which bears the nucleofugal group, and the β -hydrogen. The E2C transition state concept has been sketched as Figure 1. After Winstein's death, Parker continued to be a strong advocate of the E2C hypothesis.⁹

Probing of the E2C hypothesis has revealed some behavior that is not consistent with it, at least as originally proposed. If the transition state were structurally similar to that for the S_N2 mechanism, the reaction should be similarly sensitive to steric hindrance about the α -carbon, which carries the nucleofugal group. But eliminations induced by thiolate ions are remarkably insensitive to such steric hindrance.¹⁰⁻¹² In that regard, data of Bailey and Saunders,¹³ discussed by Bunnett, Sridharan, and Cavin,¹⁴ are additionally cogent.

In view of such problems, McLennan¹⁵ suggested that eliminations induced by thiolate ions may go via a "stretched" E2C transition state (our term) with geometric characteristics rather different from those of the S_N2 transition state, that is, having the nucleophile (base) much closer to H _{β} than to C _{α} , but nevertheless somewhat bonded to C _{α} . Pross,¹⁶ in the course of treating several sorts of transition states in terms of configuration mixing theory, accommodates the E2C mechanism; his model would be compatible with the "stretched" E2C transition state of McLennan.

Solvation Effects on E2 Reactivity. No doubt the willingness of some chemists tentatively to accept the E2C hypothesis was based on the seeming absence of any other rational explanation of why weakly basic RS⁻ should surpass strongly basic RO⁻ as E2 reagents. There is, however, a rational interpretation, in terms of the theory of the variable E2 transition state.^{17,18} It considers evi-

Table I. Reactions of *tert*-Butyl Chloride with Sodium Ethanethiolate in Methanol: Kinetic and Product Data^a

[NaSEt], M	$k_{\psi}/10^{-4}$, s ⁻¹	alkene, ^b %	ether, ^c %	Δ , ^d %	$k_{\psi}^E/10^{-4}$, s ⁻¹
nil ^e	2.15 ± 0.19	26.2	73.8	0.7	0.56
0.20	3.68 ± 0.07	55.8	44.2	1.2	2.05
0.30	4.26 ± 0.05	62.4	37.6	7.5	2.66
0.40	4.88 ± 0.05	68.6	31.4	4.9	3.35
0.50	5.69 ± 0.08	71.1	28.9	4.5	4.05
0.60	6.04 ± 0.14	73.5	26.5	16.0	4.44
0.60	6.04 ± 0.06				
0.70	6.70 ± 0.15	74.0	26.0	12.5	4.96
0.80	7.28 ± 0.10	78.0	22.0	3.0	5.68

^a All reactions at 70 °C, with [*t*-BuCl] ca. 0.02 M and EtSH 0.18–0.38 M. ^b 2-Methylpropene. ^c *tert*-Butyl methyl ether. ^d Discrepancy between moles of Cl⁻ (by titration) and sum of moles of alkene and moles of ether (by GC). ^e No EtSH present.

Table II. Reactions of *tert*-Butyl Chloride with Sodium Ethanethiolate in 36.8 mol % Dimethyl Sulfoxide/Methanol: Kinetic and Product Data^a

[NaSEt], M	$k_{\psi}/10^{-4}$, s ⁻¹	alkene, ^b %	ether, ^c %	Δ , ^d %	$k_{\psi}^E/10^{-4}$, s ⁻¹
nil ^e	0.81 ± 0.14	50.0	50.0	0.2	0.40
0.20	2.70 ± 0.08	92.3	7.7	2.8	2.49
0.40	4.58 ± 0.11	97.3	2.7	0.0	4.46
0.60	6.59 ± 0.09	99 ^f	1 ^f		6.52
0.80	8.58 ± 0.21	99 ^f	1 ^f		8.49

^a All reactions at 70 °C, with [*t*-BuCl] ca. 0.02 M and EtSH (except as noted^e) 0.06–0.40 M. ^b 2-Methylpropene. ^c *tert*-Butyl methyl ether. ^d Discrepancy between moles of Cl⁻ (by titration) and sum of moles of alkene and moles of ether (by GC). ^e Two runs, one with 0.022 M 2,6-lutidine, the other with 0.020 M 2,6-lutidine, gave identical product proportions; the rate constant listed is the mean value; no EtSH present. ^f Because of nearly identical retention times for cyclohexene (internal standard) and EtSH, quantitative determination of alkene and ether products was not possible; the figures given are based on peak areas; our belief is that if anything is 1% of ether is an overestimate.

dence that thiolate ion reagents surpass alkoxide ions when E2 reactions go via a transition state of *paenecarbonium* (nearly E1) character, with considerable detachment of the nucleofuge and development of positive charge on C _{α} , little bonding of the base to H _{β} , and little development of C=C character. In such a transition state, an oxyanion base does not get much advantage from the greater strength of H–O as compared to H–S bonds, but does suffer in a good hydrogen-bonding solvent from its heavy solvation, part of which must be shed (at energetic cost) in order for it to commence bonding with H _{β} . A thiolate ion has, on the other hand, solvation that is less tightly held and suffers less of an energetic penalty when partial desolvation must occur.

This desolvation explanation was criticized¹⁵ on grounds that the superiority of thiolate ions is evidenced even in dipolar "aprotic" solvents. That criticism was shown¹⁴ not strictly to be justified, for the available evidence pertained largely to arenethiolate ions versus phenoxide ions. It was nevertheless clear that good data concerning true alkanethiolate and alkoxide ion reagents would be welcome. It was with the intent of obtaining such data that the work described in this and the companion paper¹⁹ was undertaken.

Results

Kinetics and products from reactions of *tert*-butyl chloride with excess ethanethiolate ion were determined

(6) Winstein, S. *Chimica Teorica, VIII Corso Estivo di Chimica, Milano 7–19 Oct., 1963*; Accad. Nazionale dei Lincei: Roma, 1965; p 339.

(7) Biale, G.; Parker, A. J.; Smith, S. G.; Stevens, I. D. R.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 115.

(8) Parker, A. J.; Ruane, M.; Biale, G.; Winstein, S. *Tetrahedron Lett.* **1968**, 2113.

(9) (a) Parker, A. J. *Chem. Technol.* **1971**, *1*, 297. (b) *Proc. R. Aust. Chem. Inst.* **1976**, 105. (These are reviews.)

(10) Eck, D. L.; Bunnett, J. F. *J. Am. Chem. Soc.* **1969**, *91*, 3099; **1973**, *95*, 1897.

(11) Bunnett, J. F.; Eck, D. L. *J. Am. Chem. Soc.* **1973**, *95*, 1900, 4473.

(12) Paradisi, C.; Bunnett, J. F.; Eck, D. L. *J. Org. Chem.* **1980**, *45*, 2506.

(13) Bailey, D. S.; Saunders, W. H., Jr. *J. Org. Chem.* **1973**, *38*, 3363.

(14) Bunnett, J. F.; Sridharan, S.; Cavin, W. P. *J. Org. Chem.* **1979**, *44*, 1463.

(15) McLennan, D. J. *Tetrahedron* **1975**, *31*, 2999.

(16) Pross, A. *Adv. Phys. Org. Chem.* **1985**, *21*, 99.

(17) Bunnett, J. F. *Angew. Chem.* **1962**, *74*, 731; *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 225.

(18) Bunnett, J. F. *Surv. Prog. Chem.* **1969**, *5*, 53.

(19) Bunnett, J. F.; Migdal, C. A. *J. Org. Chem.*, preceding paper in this issue.

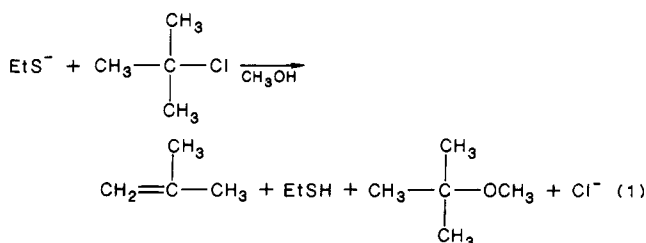
Table III. Reactions of *tert*-Butyl Chloride with Sodium Ethanethiolate in 64.2 mol % Dimethyl Sulfoxide/Methanol: Kinetic Data^a

[EtSNa], M	[EtSH], M	$k_{\psi}/10^{-4}, \text{s}^{-1}$
nil	nil	0.24 ± 0.04^b
0.20	nil	5.7 ± 0.1
0.20	0.10	6.3 ± 0.2
0.30	nil	8.8 ± 0.3
0.30	0.15	9.5 ± 0.4
0.40	nil	11.4 ± 0.6
0.40	0.21	12.8 ± 0.6
0.50	nil	14.0 ± 0.4
0.50	0.17	15.9 ± 0.8

^a All reactions at 70 °C, with [*t*-BuCl] ca. 0.02 M. The product is exclusively 2-methylpropene, except in the absence of EtSNa. For all runs with EtSNa, $k_{\psi}^E = k_{\psi}$. ^b Average of three runs, conducted with 2,6-lutidine (0.02–0.10 M) and 2,6-lutidinium bisulfate (0.05 M) present; the value of k_{ψ}^E is $0.18 \times 10^{-4} \text{ s}^{-1}$.

in three solvents: methanol, 36.2 mol % dimethyl oxide/methanol, and 64.2 mol % dimethyl sulfoxide/methanol, at 70 °C. For all kinetic runs, linear pseudo-first-order kinetic plots were obtained. Products were determined by GC. Our principal data are presented in Tables I–III.

In all three solvents, reactions of *tert*-butyl chloride with ethanethiolate ion afforded mainly 2-methylpropene as a product. The only other detectable product was *tert*-butyl methyl ether. *tert*-Butyl ethyl sulfide was sought as a product but never found. What happened can thus be represented as in eq 1.



Not surprisingly, the amount of the ether product diminished as the mole fraction of methanol in the solvent waned, and the dimethyl sulfoxide mole fraction waxed. In 64.2 mol % Me₂SO/MeOH, the product was exclusively the alkene at all concentrations of EtSNa. In 36.8 mol % Me₂SO/MeOH, even at 0.2 M EtSNa the product is 92% alkene, and it predominates even more at higher [EtSNa] (Table II).

In all three solvents, the pseudo-first-order rate constant, k_{ψ} , increased strongly as the concentration of sodium ethanethiolate rose. Plots of k_{ψ} versus [EtSNa] (not shown) were in all cases linear. The intercepts in all cases are the same as the rate constants for solvolysis of *t*-BuCl in the respective solvents, within experimental error. The slopes can be taken as second-order E2 rate constants for reactions of *t*-BuCl with EtSNa. They are $6.4 \pm 0.2 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in methanol, $9.7 \pm 0.2 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in 36.8 mol % Me₂SO/MeOH, and $31.2 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in 64.2 mol % Me₂SO/MeOH (all at 70.0 °C).

For purposes of comparison with parallel data concerning reactions with sodium methoxide, from the companion paper,¹⁹ we reckoned k_{ψ}^E at each [EtSNa] in each solvent; k_{ψ}^E is the part of k_{ψ} that pertains to elimination, without reference to what reaction mechanism is involved. Values of k_{ψ}^E are presented in Tables I–III.

For most experiments, reaction mixtures contained ethanethiol in a concentration about half that of sodium ethanethiolate. The ethanethiol was put there to repress the acid–base reaction of ethanethiolate ion with metha-

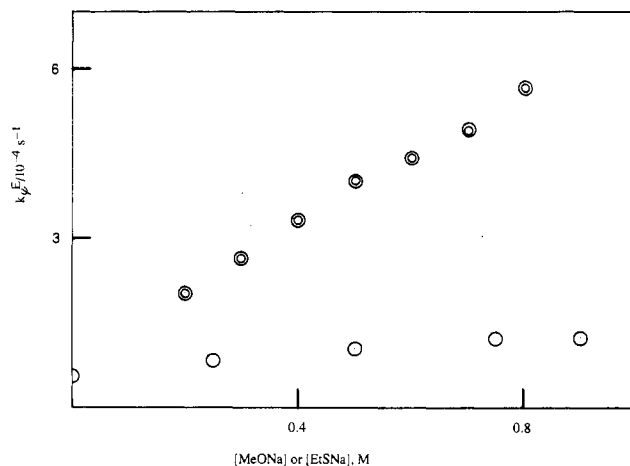


Figure 2. Dissected pseudo-first-order rate constant for elimination, k_{ψ}^E , as a function of [MeONa] or [EtSNa], for reactions in methanol. Open circles: MeONa data. Bull's-eyes: EtSNa data.

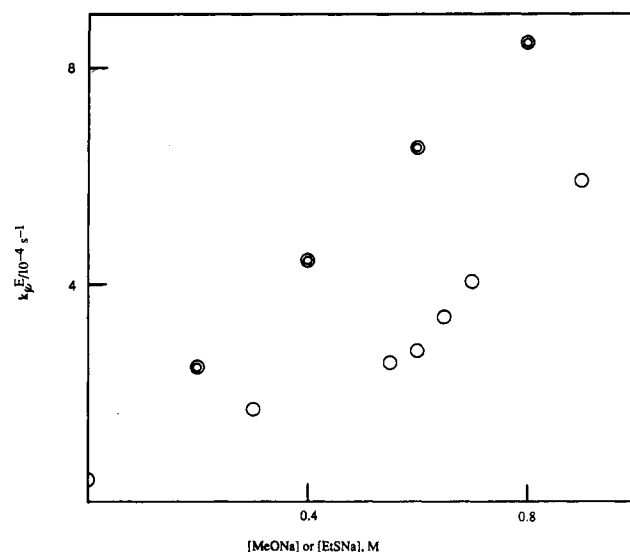


Figure 3. Dissected pseudo-first-order rate constant for elimination, k_{ψ}^E , as a function of [MeONa] or [EtSNa], for reactions in 36.8 mol % Me₂SO/MeOH. Open circles: MeONa data. Bull's-eyes: EtSNa data.

anol,²⁰ $\text{EtS}^- + \text{MeOH} \rightleftharpoons \text{EtSH} + \text{MeO}^-$, and thereby avoid any complication due to reaction by methoxide ion. In order to assess whether the ethanethiol itself might have some kinetic effect, we conducted some experiments in 64.2 mol % Me₂SO/MeOH with EtSNa but without EtSH, as reported in Table III. At each of our levels of sodium ethanethiolate concentration, the observed k_{ψ} with ethanethiol was a little higher than in its absence. The acceleration, if real, was not much more than the sum of the standard deviations of the two rate constants.

Discussion

For the purpose of comparing the olefin-forming elimination reactivity of methoxide and ethanethiolate ions, we plot for each of the three solvents investigated the overall pseudo-first-order rate constants for elimination, k_{ψ}^E , against base concentration. The three plots appear in Figures 2–4.

In these figures, the k_{ψ}^E values for MeONa and EtSNa are plotted to facilitate comparison, solvent by solvent. Plainly, EtSNa excels MeONa as an olefin-forming elim-

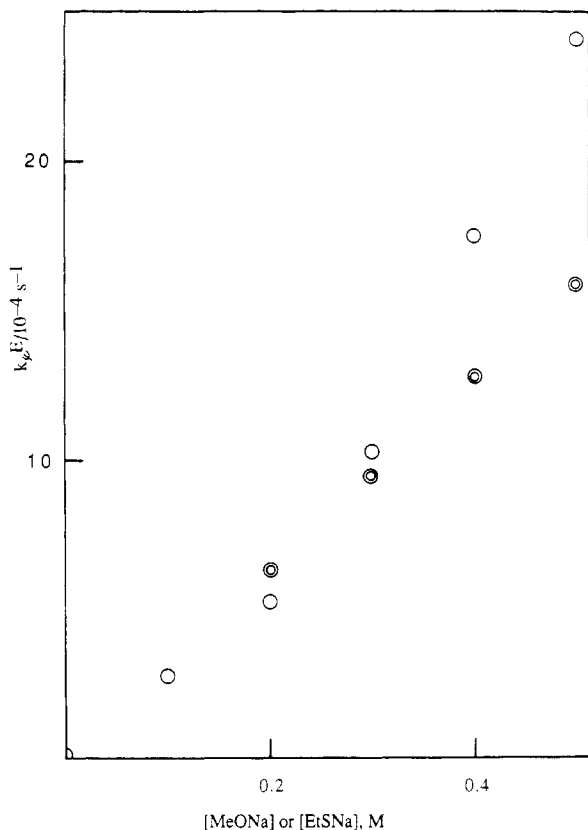


Figure 4. Dissected pseudo-first-order rate constant for elimination, k_p^E , as a function of [MeONa] or [EtSNa], for reactions in 64.2 mol % $\text{Me}_2\text{SO}/\text{MeOH}$. Open circles: MeONa data. Bull's-eyes: EtSNa data.

ination reagent, in reaction with *t*-BuCl, in the two solvents rich in methanol. In 64.2 mol % $\text{Me}_2\text{SO}/\text{MeOH}$ (Figure 4), sodium methoxide is, however, more effective than sodium ethanethiolate at all base concentrations above 0.2 M.

In 36.8 mol % $\text{Me}_2\text{SO}/\text{MeOH}$ (Figure 3), it is noteworthy that the plot of k_p^E versus [MeONa] suddenly becomes steeper beyond 0.6 M MeONa. As said elsewhere,¹⁹ we think this represents an activity coefficient effect. A similar change of slope occurs in 64.2 mol % $\text{Me}_2\text{SO}/\text{MeOH}$ at about 0.3 M MeONa (Figure 4).

One might prefer instead to compare the two reagents in terms of E2 rate constants. The E2 rate constants for EtSNa are easily evaluated and are given above. For sodium methoxide, the second-order E2 rate constants are not quite so easy to assign, for two reasons. One is uncertainty as to how one should interpret the juxtaposition of a near absence of kinetic effect of MeONa on the reactivity of *t*-BuCl in methanol with a substantial effect on product composition.¹⁹ The other question is what to choose as the E2 rate constant when the plot of k_p^E versus [MeONa] increases in slope as [MeONa] augments. We have presented estimates as to what the E2 rate constants for reaction with MeONa are, in the companion paper.¹⁹ Without taking space to detail the comparisons, let us say that the relative reactivities of the two bases in terms of E2 rate constants are qualitatively the same as presented graphically in Figures 2–4. Ethanethiolate is superior to methoxide ion in two solvents rich in methanol, while methoxide ion surpasses the thiolate reagent in 64.2 mol % $\text{Me}_2\text{SO}/\text{MeOH}$.

On the Occasional Superiority of Thiolate Ion Bases. Our chief interest is to understand why weakly basic thiolate ions sometimes surpass strongly basic alk-

oxide ions as reagents to effect bimolecular β -elimination. We now examine whether and how the present results, and some earlier ones, support the two mechanistic hypotheses that have predominated in recent discussions. These are on the one hand the E2C hypothesis and on the other hand the fundamental E2 hypothesis, first outlined by Ingold²¹ and subsequently¹⁷ elaborated to accommodate variation of transition-state character as the constitution of the substrate and reaction conditions are changed.

Supporting the view that both alkoxide and thiolate reagents react by the fundamental E2 mechanism is, first, the variation of $\text{EtS}^-/\text{MeO}^-$ reactivity ratio as the solvent is changed, as reported in the present paper and discussed in the introduction, above. Other facts that are in harmony with the fundamental E2 interpretation are the patterns of variation of the $\text{EtS}^-/\text{MeO}^-$ reactivity ratio with the identity of the nucleofugal group²² and with the identity of para substituents¹⁴ in eliminations from substrates of the type $p\text{-RC}_6\text{H}_4\text{CH}_2\text{CMe}_2\text{X}$. It appears that thiolate ions surpass alkoxide ions when the E2 transition state has *paenecarbonium* character, with little bonding of base to $\beta\text{-H}$, little formation of the $\text{C}=\text{C}$ double bond, and much detachment of the nucleofugal group from C_α .

The transition state is shifted toward the *paenecarbonium* extreme, where alkoxide ions excel, by change to a "worse" leaving group or by installation of a substituent that stabilizes negative charge on C_β .

The change of solvent explored in the present research doubtless affected not only the condition of solvation of the bases but also the character of the transition states. Specifically, as a solvent is enriched in dimethyl sulfoxide in place of methanol, solvation of the detaching chlorine in the transition state is reduced. That should increase the energy required to separate the chlorine (partially) from C_α and therefore cause the transition state to alter in the direction of less *paenecarbonium*, more *paenecarbonium* character. That shift alone would, on the theory of the variable E2 transition state, be expected to increase the relative reactivity of methoxide as compared to ethanethiolate ion. How much of the change of relative reactivity with change of solvent that we have observed should be attributed to changing solvation of the nucleofuge and how much to changing solvation of the base, we cannot say.

The E2C mechanism differs from the fundamental E2 in that it postulates also some covalent bonding of the base (nucleophile) with C_α in the transition state. That some such bonding should occur is theoretically admissible.¹⁶ Inveighing against covalent interaction of the base with C_α , at least in fashion similar to an $\text{S}_\text{N}2$ transition state as proposed in 1968,²³ is evidence that thiolate ions as elimination reagents are not much if at all hindered by large substituents near C_α ,^{10–12} whereas $\text{S}_\text{N}2$ reactions at neopentyl sites are severely hindered. A relaxation of the requirement for the base (nucleophile) to approach C_α closely would, however, enable the E2C mechanism to accommodate the insensitivity to steric hindrance of C_α , as suggested by McLennan.¹⁵

In proposing the E2C mechanism in 1968, Winstein and Parker had in mind especially eliminations induced by halide ions in solvents such as acetone. Inclusion of eliminations induced by thiolate ions in solvents like methanol in their proposed E2C family appears to have been incidental. We do not believe that the E2C mechanism, even in its "stretched" modification, provides a good basis for

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(22) Bunnett, J. F.; Baciocchi, E. *J. Org. Chem.* 1967, 32, 11.

(23) Lloyd, D. J.; Parker, A. *J. Tetrahedron Lett.* 1968, 5183.

interpreting the leaving-group, substituent, and solvent effects on the RS^-/RO^- reactivity ratio mentioned above. On the other hand, we cannot utterly exclude it on experimental grounds. Perhaps it will be possible to make a firm decision on the basis of theory. Some many prefer to rely on faith.

Experimental Section

Materials. Most materials were prepared or purified as described in the companion paper.¹⁹ Ethanethiol (Aldrich Chemical Co.) was distilled, and a middle cut (bp 34.5 °C) was taken; its purity was confirmed by GC. *tert*-Butyl ethyl sulfide was prepared, after McAllan et al.,²⁴ by reaction of the sodium salt of 2-methyl-2-propanethiol with ethyl iodide: ¹H NMR (CCl₄) δ 1.15 (t, 3 H), 1.25 (s, 9 H), 2.40 (q, 2 H).

Instruments and methods were as described in the companion paper.¹⁹

(24) McAllan, D. T.; Cullum, T. V.; Dean, R. A.; Fidler, F. A. *J. Am. Chem. Soc.* 1951, 73, 3627.

Kinetics Procedure. The procedure was as described elsewhere.¹⁹ A special feature is that, after ampules had been opened and extractions performed, the aqueous solution for titration with silver nitrate received an addition of 1 mL of aqueous hydrogen peroxide, for the purpose of oxidizing any traces of thiol that may have been present, before titration was performed.

Memorial. This paper was composed in a mood of sadness, for A. J. "Jim" Parker will not be able to read it. He died in 1982, while a strong and vigorous man in what should have been midcareer. Although Jim and I differed in our views on elimination mechanisms, we had much in common scientifically and were personal friends. On our 25th wedding anniversary, my wife and I were guests at a party at his home. The people of Australia and we in the world community of chemists were fortunate to have had Jim Parker among us. (J.F.B.)

Registry No. *t*-BuCl, 507-20-0; EtS⁻-Na, 811-51-8; MeONa, 124-41-4.

Mechanism of the Mitsunobu Esterification Reaction. 1. The Involvement of Phosphoranes and Oxyphosphonium Salts

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In contrast to previous studies, a ³¹P NMR examination of the Mitsunobu reaction using an unreactive alcohol, ROH, and a carboxylic acid, R'COOH, reveals the presence of *two* intermediates—an alkoxytriphenylphosphonium salt, Ph₃POR⁺ R'COO⁻, in equilibrium with a dialkoxytriphenylphosphorane, Ph₃P(OR)₂. The position of the equilibrium depends on the pK_a of the acid and the polarity of the solvent. The alkoxyphosphonium salt is favored in polar solvents or with acids of low pK_a. Where there is a choice between a primary and a secondary alcohol, only the phosphorane and oxyphosphonium salt corresponding to the primary alcohol are observed. The implications of these findings for the regioselectivity and stereoselectivity of the Mitsunobu reaction are discussed.

Introduction

Recent publications by Walker and co-workers^{1a} and by Hughes et al.^{1b} on the mechanism of the Mitsunobu reaction² prompt us to report the results of our work³ in this area. This study complements the work of Walker and of Hughes, and together with the following paper, provides a clearer understanding of the mechanism of this important synthetic reaction.

Previous work from this laboratory⁴⁻⁷ and others⁸ has shown that treatment of alcohols or phenols with triphenylphosphine (TPP) and diethyl or diisopropyl azodicarboxylate (DEAD or DIAD, respectively) leads to the

formation of dioxytriphenylphosphoranes. Such phosphoranes are clearly intermediates in Mitsunobu reactions involving formation of ethers as, for example, in the formation of sucrose 2',3'-epoxide and 3',6'-anhydrosucrose from sucrose,⁹ but may not of course be involved in the more common Mitsunobu esterification reaction where a carboxylic acid is present. Indeed, Walker suggests^{1a} that a dioxytriphenylphosphorane is only an intermediate in the Mitsunobu reaction in the special case where the acid is added last. In contrast to both Walker's and our own findings, Hughes was unable to observe any phosphoranes, even in the absence of an acid. However, Hughes used an alcohol that is prone to elimination and β-fragmentation.

The experiments to be described below illustrate that the pK_a of the acid and the polarity of the solvent can have a profound effect on the reaction pathway and demonstrate that the true mechanism of the Mitsunobu reaction is more complex than previous studies suggest.

Results and Discussion

For our studies, we employed two alcohols that do not readily undergo elimination or S_N2 attack, the primary

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