assess the steric requirement of the departing leaving group. A reversal of the trajectories will describe the optimum path of a leaving group if appropriate entries in Table I are compared. For example, entry 16 represents formation of *cis*-pent-2-ene from 2-halopentane, and entry 28 represents the steric requirements of the halogen as it departs. The summary of this relationship involves the interchange of substituents R_1/R_3 and R_2/R_4. Again these comparisons are qualitative; however, they do represent a beginning for the establishment of a quantitative description of steric effects in the E2 reaction.

Conclusion

Computer-generated minimum-energy base trajectories for E2 reactions have been presented. A comparison of the repulsive forces yields several useful qualitative observations. The attack trajectories are consistent with what one would expect from examination of molecular models. The increase in repulsive force with increased chain length and steric bulk of alkyl substituents allows a distinction to be made between two types of steric interaction: the chain-length effect and the group-bulk effect.

The trajectories also have implications for the relative stabilities of α and β alkyl substitution. With small and intermediate sized bases the β position offers less interference to the approaching base. Large bases encounter less difficulty with an α substituent. This is probably due to a shift in importance of the groups being removed from the reaction center in the perspective and being removed via carbon insulation, since the interactions are dependent only on distance.

Most importantly, the calculations give some insight into the relative steric repulsion a base encounters when it approaches the isomeric conformations for a dehydrohalogenation. For intermediate and large bases the results are in accord with what would be expected from simple observation 1-ene < cis < trans. With small bases, however, the transition state leading to the Hofmann alkene offers a significantly increased relative steric repulsion due to a chain effect from particular rotational conformations. Removal of these rotamers restores the expected order of stability. This behavior is indicative of an entropy–enthalpy trade-off that operates to minimize the free energy of the transition state.

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Registry No. EtBr, 74-96-4; ethene, 74-85-1; propene, 115-07-1; 1-butene, 106-98-9; 3-methyl-1-butene, 563-45-1; 1-pentene, 109-67-1; 3,3-dimethyl-1-butene, 558-37-2; 1-hexene, 592-41-6; *cis*-2-butene, 590-18-1; *cis*-2-pentene, 627-20-3; *cis*-4-methyl-2-pentene, 691-38-3; *cis*-2-hexene, 7688-21-3; *cis*-4,4-dimethyl-2-pentene, 762-63-0; *trans*-2-butene, 624-64-6; *trans*-2-pentene, 646-04-8; *trans*-4-methyl-2-pentene, 674-76-0; *trans*-2-hexene, 4050-45-7; *trans*-4,4-dimethyl-2-pentene, 690-08-4; *cis*-3-hexene, 7642-09-3; *trans*-3-hexene, 13269-52-8.

Elimination and Substitution in the Reactions of Vicinal Dihalides and Oxyhalides with Trimethylstannylsodium. Effects of Solvent and of Ion Aggregation on Course and Stereochemistry

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The course and stereochemistry of the reactions of vicinal dihalides and vicinal oxyhalides with trimethylstannylsodium have been studied in THF and in other solvents. Cation solvating agent effects have also been examined. The vicinal dihalides react uniformly via anti stereochemistry to produce the corresponding alkenes in nearly quantitative yields. 2-Bromo-3-methoxybutane yields both elimination and substitution (2-methoxy-3-(trimethylstannyl)butane) products. The stereochemistry is predominantly syn when THF is the solvent, and elimination predominates. When TG is the solvent, substitution occurs as the predominant reaction; the stereochemistries of both substitution and elimination are nonspecific. The mechanistic implications of these observations are considered.

Studies on the scope and mechanisms of vicinal dehalogenations and related elimination reactions have been reported sporadically since the observation of the iodide-induced debromination of coumarin dibromide by Perkin.[1] Among the agents which have been shown to bring about these reactions are metals such as sodium in liquid ammonia[2,3] or tetrahydrofuran,[4] magnesium,[5,6] zinc,[4,6a] cadmium,[5] lithium,[6a] and sodium naphthalenide,[7,8] electrolysis,[9,10] subvalent metal ions such as Fe(II),[5] Sn(II),[5,11] Cr(II),[5,6,12,13] Pt(II),[5] Co(II),[14] $Fe(CO)_2CpNa$, and Ti(II),[16] free

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Table I. Yields of Alkenes Formed in Reactions of Vicinal Dihalides with Trimethylstannylsodium in Tetraglyme[a]

compound	X	Y	isomer	% alkene
$CH_3C(X)HC(Y)HCH_3$	Br	Br	meso[b]	96
	Cl	Cl	meso[b]	90
	Br	F	erythro	98
	Br	F	threo	98
	Br	Cl	erythro[b]	98
	Br	Cl	threo[b]	85
$(CH_3)_2CHC(X)HC(Y)HCH_3$	Br	Br	erythro[b]	90
	Br	Br	threo[b]	91
$(CH_3)_2C(X)C(Y)(CH_3)_2$	Br	Br		95
	Br	Cl		87
	Cl	Cl		87
	Br	Br	trans	90
	Br	Cl	trans	89
	Cl	Cl	trans	87

[a] 2 mol of Me_3SnNa/mol of dihalide; T ca. 20 °C. [b] At 0 °C.

radical sources such as organotin hydrides[17a] and hexaorganoditins,[17b] and a wide range of nucleophiles, including halide ions[18,19b,20,21,22a] and others.[19a,22c-e,23-26] The stereochemistry is usually nonselective or partially anti selective. The only examples of stereospecificity reported appear to involve electrolytic[9a] and iodide-induced[18,20] debromination of 2,3-dibromobutanes and the iodide-induced debromination of 1,2-deuterio-1,2-dibromoethane. Vicinal oxyhalo derivatives undergo elimination with facility only upon reaction with free metals[4,6b] or Cr(II),[13b,c] unless activation by a suitable group such as carbonyl is available.

Trimethylstannylsodium and 1,2-dichlorethane in liquid ammonia have been reported to yield a "hydrocarbon gas" presumed to be ethylene,[28] and 1,2-dibromoethane reacts with trimethylstannyllithium in tetrahydrofuran (THF) to yield ethylene also.[29] Jensen and Davis[30] have shown that triphenylstannylsodium reacts with 2-halobutanes with predominant inversion, presumably by an S_N2 reaction at carbon; we have shown that aryl bromides react with trimethylstannylsodium by halogen–metal exchange (S_N2 on halogen);[31] certain other halides such as bromocyclohexane in THF react by an electron-transfer process involving alkyl free radicals as intermediates.[32,33] It was therefore of interest to examine the reactions of vicinal dihalides and related compounds with organotin anionoids with respect to their possible synthetic utility and the mechanism(s) involved.

Table II. Stereochemistry of Eliminations from 2-X-3-Y-butanes: Effects of X, Y, Solvent, and Counterion in Me_3SnM[a]

X	Y	isomer	solvent	counterion	2-butene % cis	2-butene % trans
Br	Br	meso	TG	Na	1	99
Br	Br	*dl*	TG	Na	97	3
Br	Br	meso	TG	Li	0	100
Br	Br	*dl*	TG	Li	100	0
Br	Cl	erythro	TG[b]	Na	2	98
Br	Cl	threo	TG[b]	Na	96	4
Br	Cl	threo	TG	Na	100	0
Br	F	erythro	TG[c]	Na	2	98
Br	F	threo	TG[c]	Na	99	1
Cl	Cl	meso	TG	Na	2	98
Cl	Cl	*dl*	TG	Na	91	9
Cl	Cl	meso	TG	Li	2	98
Cl	Cl	*dl*	TG	Li	99	1
Br	Br	meso	THF	Li	2	98
Br	Br	*dl*	THF	Li	98	2
Cl	Cl	meso	THF	Li	2	98
Cl	Cl	*dl*	THF	Li	93	7

[a] At 0 °C; TG = tetraglyme [$MeO(CH_2CH_2O)_4Me$]; THF = tetrahydrofuran; M = Na or Li. [b] At 25 °C. [c] At 18 °C.

Table III. Alkene Formation from Compounds Related to Vicinal Dihalides upon Reaction with Trimethylstannylsodium in TG

compound[a]	% alkene	% cis	% trans
1,2-ditosyloxyethane	46		
erythro-2,3-dihydroxy-4-methylpentane	*d*		
trans-1-bromo-2-hydroxycyclohexane[b]	92		
erythro-2-bromo-3-formyloxybutane[e]	90	9	91
threo-2-bromo-3-formyloxybutane[f]	89	87	14
erythro-2-bromo-3-formyloxybutane[c,e]	96	4	96
threo-2-bromo-3-formyloxybutane[c,f]	98	96	4

[a] Reaction T = 18 ± 2 °C. [b] 3 mol of Me_3SnNa per mol of substrate used. [c] In THF. [d] None detected. [e] 88% erythro; 12% threo. [f] 97% threo; 3% erythro.

Results

Initial experiments showed that vicinal dibromides, for example, reacted with trimethylstannylsodium, according to eq 1. However, the trimethyltin bromide formed re-

$$>C(Br)C(Br)< + Me_3SnNa \rightarrow >C{=}C< + Me_3SnBr + NaBr \quad (1)$$

$$Me_3SnBr + Me_3SnNa \rightarrow (Me_3Sn)_2 + NaBr \quad (2)$$

acted with the Me_3SnNa in competition with the di-

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Table IV. Substitution Products from Reactions of Trimethylstannylsodium with $R^1C(R^2)(OMe)C(R^3)(Br)R^4$ in TG at 0 °C

entry no.	R^1	R^2	R^3	R^4	substitution product, %[a]
1	H	H	H	H	(31)[b]
2	Me	Me	H	H	23 (19)
3	Me	H	Me	H	34
4	Me	Me	Me	H	42 (40)
5	Me	Me	Me	Me	0

[a] Isolated yields in parentheses; others by GLC. [b] 42% of ethylene collected by a gas buret.

bromide, according to eq 2. Therefore, 2 mol of trimethylstannylsodium were used in most experiments to assure complete consumption of the dibromide. The yield of alkene was determined directly by GLC, and the isomeric composition was determined by bromination of the butenes in an acetic acid solution of pyridinium tribromide which reacts quantitatively with anti specificity. The composition of the mixture of diastereoisomeric dibromides was then determined by GLC. Reactions with the bromides occurred upon mixing as indicated by the loss of the yellow-green color of the trimethylstannyl anion and the appearance of a precipitate of sodium salt; heat was also evolved. The dichlorides were considerably less reactive, and reaction mixtures were allowed to stand overnight before analysis.

Results are gathered in Table I for dibromides, dichlorides, bromochlorides, and bromofluorides. In all cases, the yields were very high: no significant side reactions were detected.

The effects of variations in some reaction parameters are displayed in Table II, using 2,3-dihalobutanes as substrates. Alkene yields were uniformly above 90% and are not shown, but the distributions of the isomeric 2-butenes are shown. The elimination is seen to be virtually anti stereospecific, whether the halide was the dibromide, dichloride, bromochloride, or bromofluoride; whether the solvent was tetrahydrofuran (THF) or tetraglyme (TG); and whether the counterion was sodium or lithium. In the one instance shown, a lower temperature appeared to increase selectivity. Lower selectivity was observed in a few cases in the *dl* or threo isomer but was still over 90% anti.

The effects of further changes in the nature of the vicinal groups are shown in the data of Table III. 1,2-Ditosyloxyethane yielded 46% of ethylene as measured by a gas buret. The residual solution showed the presence of vinyl groups, indicating the probable presence of vinyl tosylate as the product of dehydrotosylation. *trans*-1-Bromo-2-hydroxycyclohexane yielded 92% of cyclohexene when 3 mol of trimethylstannylsodium was used. These reactions were not examined further. As expected, the single diol examined provided no detectable elimination. Highly stereoselective anti elimination occurred with the diastereoisomeric 2-bromo-3-formyloxybutanes in extremely rapid and exothermic reactions. These characteristics are unusual for nucleophile-induced eliminations which normally occur with ease only when one of the leaving groups is a halogen atom and the other a good nucleofuge such as halogen or tosylate.

A series of vicinal methoxy bromides was next examined in order to ascertain whether a poor nucleofuge such as the methoxide ion would permit the elimination to occur. Five methoxy bromides as shown in Table IV were examined. 1-Bromo-2-methoxyethane suffered both elimination and substitution according to eq 3, as shown in entry 1.

$$Me_3SnNa + \underset{\displaystyle Br\quad OMe}{\overset{\displaystyle |\quad\quad |}{CH_2{-}CH_2}} \longrightarrow CH_2{=}CH_2 + \underset{\displaystyle MeO\quad SnMe_3}{\overset{\displaystyle |\quad\quad |}{CH_2{-}CH_2}} \qquad (3)$$

Comparison of entries 2, 4, and 5 shows that the yield of the substitution product goes down from 31% for the ethane derivative to 23%, then up to 42%, and then down to 0% as the bromine-bearing carbon becomes secondary and tertiary. The absence of any monotonic trend, such as might be expected for S_N2 substitution, suggested the possibility of changes in the mechanism with structural changes. Therefore, we chose to examine the 2-halo-3-alkoxybutane system in some detail, because we could ascertain at the same time the course and stereochemistry of the reactions by using the individual diastereoisomers as substrates and examining isomeric compositions of the products.

Gross solvent effects were studied first, and results are presented in Table V. In THF, at least 97% of the reaction is elimination from isomeric 2-bromo-3-methoxybutane; only 2–3% of the substitution is observed. The stereochemistry is predominantly syn. In TG, on the other hand, the reaction occurs to the extent of 71–73% by substitution and 16–24% by elimination. In addition, the stereochemistry of elimination shows a small preference for anti, which happens to be the same for each isomer. The substitution is completely nonspecific, because both the erythro and threo methoxybromides yield the same proportions of erythro and threo methoxytins, 62 and 38%, respectively. In a one-to-one mixture of THF and tetramethylethylenediamine (TMEDA), elimination is again the strongly predominant reaction pathway, and the ratio of syn to anti elimination products is about 20 in each case.

Substantial changes in the course and stereochemistry of the reaction can be brought about by the addition of relatively small amounts of cation-coordinating ligands when THF is used as the solvent. Results are collected in Table VI. The results are for reactions in which the ligand/sodium ion concentration ratios were 1 and 2 for each methoxy bromide isomer and each ligand. It can be seen that TG, 18-crown-6, hexamethylphosphoramide (HMPA), and the cryptate "Kryptofix 2.2.2" lead to increasing degrees of substitution in the order named. Except for TG, the stereochemistry of substiution is nonspecific: erythro and threo substrates give the same proportions of the diasteroisomeric substitution products. The elimination is anti selective in all of these cases when the

Table V. Effects of Solvent Changes on the Course and Stereochemistry of the Reaction of Me_3SnNa with 2-Bromo-3-methoxybutane[a]

		elimination			substitution		
solvent	isomer[b]	yield	% cis	% trans	yield	% threo	% erythro
THF	t	97	11	89	2		
	e	95	87	13	3		
TG	t	16	58	42	73	63	37
	e	24	42	58	71	61	39
THF/TMEDA (1/1)	t	96	5	95	3		
	e	95	96	4	4		

[a] $T = 16 \pm 2$ °C; $[Me_3SnNa]_0$ = ca. 0.5 M. [b] t = threo; e = erythro.

Table VI. Effect of Cation-Coordinating Ligands on the Course and Stereochemistry of the Reaction of Me_3SnNa with 2-Bromo-3-methoxybutane in THF[a]

ligand	isomer[d]	[L]/[Sn^-]	2-butene		substitution	
			% yield	% cis[b]	% yield	% threo[c]
TG	t	1	56	48	48	59
		2	52	57	48	60
	e	1	58	36	43	63
		2	57	35	44	70
18-C-6[f]	t	1	36	54	55	62
		2	22	67	67	65
	e	1	42	27	59	67
		2	35	24	63	65
HMPA	t	1	38	41	60	59
		2	29	59	70	59
	e	1	39	36	58	59
		2	29	29	69	59
CRYP[e]	t	1	6	72	73	63
	e	1	7	17	78	80
TMEDA	t	1	94	12	4	
		2	95	12	3	
	e	1	90	89	7	
		2	90	90	6	

[a] $T = 16 \pm 2$ °C; initial [Me_3SnNa] = 0.4–0.6 M. [b] % trans = 100 − % cis. [c] % erythro = 100 − % threo. [d] e = erythro; t = threo. [e] CRYP = $N[CH_2CH_2O)_2CH_2CH_2]_3N$. [f] 18-C-6 = 18-crown-6.

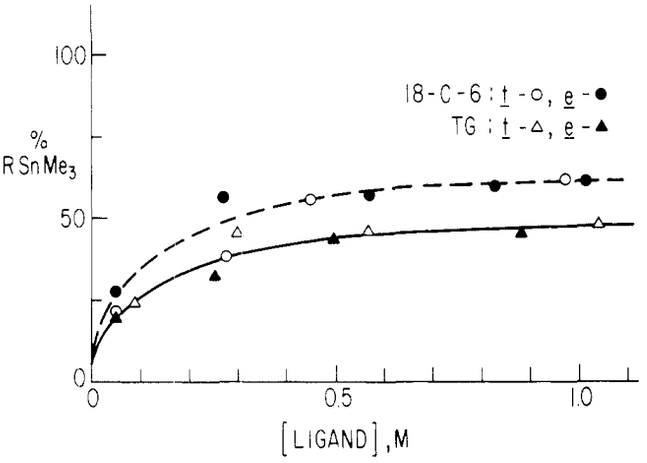


Figure 1. Effects of concentrations of 18-crown-6 ether and tetraglyme on yields of 2-methoxy-3-(trimethylstannyl)butane in tetrahydrofuran at 17 °C [initial concentrations: Me_3SnNa ca. 0.55 M; MeCHBrCH(OMe) 0.2 M].

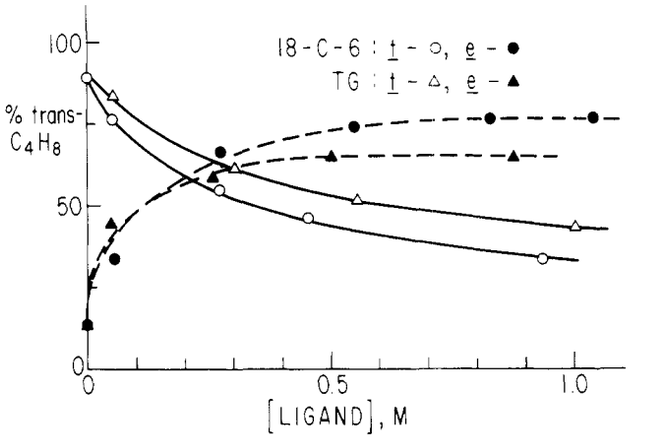


Figure 2. Effects of concentrations of 18-crown-6 ether and tetraglyme on yields of 2-butenes (conditions as for Figure 1).

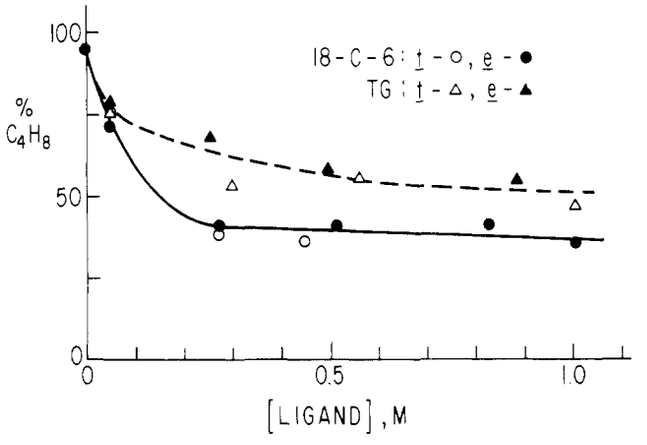


Figure 3. Effects of concentrations of 18-crown-6 ether and tetraglyme on the yield of *trans*-2-butene; yield of *cis*-2-butenes = 100 − yield of trans (conditions as for Figure 1).

ratio of ligand to sodium ion is 2. As expected from the results in Table V, the effect of TMEDA was virtually negligible, syn elimination being the major course of the reaction.

The effects of addition of incremental amounts of 18-crown-6 and TG on the yields of substitution product are plotted in Figure 1. In each case the yield increases with ligand concentration and levels off at about 1 M. In Figure 2 are shown the changes in the yields of 2-butenes in the same experiments, and the proportions of *trans*-2-butenes are displayed in Figure 3. The downward trend for the threo isomer and the upward trend for the erythro isomer both reflect decreases in the proportions of syn elimination.

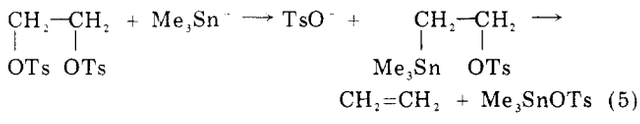
Discussion

The high yields and anti stereospecificity shown by the data in Tables I and II suggest that vicinal dehalogenation induced by trimethylstannylalkalies is useful as a synthetic reaction. An E2 mechanism as in eq 4 is indicated but

$$Me_3Sn^- + >C(X)C(Y)< \longrightarrow Me_3SnX + >C{=}C< \qquad (4)$$

remains to be supported by other probes. The stereospecificity carries over when Y is formyloxy, as shown in Table III, and would be expected also for other nucleofugal groups derived from acids of comparable pK_a's.

Formation of both ethylene and vinyl tosylate from 1,2-tosyloxyethane reveals competition between dehydrotosylation and detosylation, which probably occurs in two steps as in eq 5. The second step should be fast because it involves very good electrofugal and nucleofugal groups. A concerted process as in eq 4 is conceivable, but there is

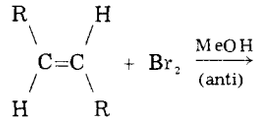


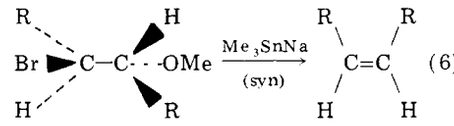
$$CH_2(OTs)CH_2(OTs) + Me_3Sn^- \longrightarrow TsO^- + CH_2(SnMe_3)CH_2(OTs) \longrightarrow CH_2{=}CH_2 + Me_3SnOTs \quad (5)$$

no precedent for nucleophilic displacement on tosylate by organotin anion. *trans*-1-Bromo-2-hydroxycyclohexane undergoes a "one-pot" dehydroxybromination in high yield. The requirement of 3 mol of organotin anion indicates a multistep process which merits further study.

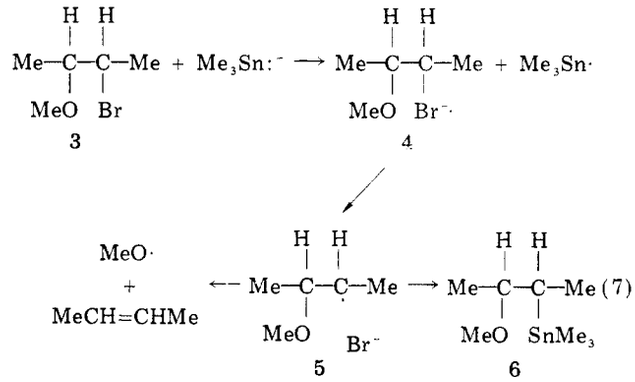
When a poor nucleofuge is present such as in vicinal methoxy bromides, elimination is no longer the exclusive reaction in TG, except for 2-bromo-3-methoxy-2,3-dimethylbutane (Table IV). This change is in part due to the solvent, for 2-bromo-3-methoxybutanes do undergo predominant elimination in THF but syn stereochemistry dominates (Table V). This is also the result when the solvent is 1/1 THF/tetramethylethylenediamine. In TG, however, nonspecific substitution dominates, and the elimination which does occur shows a slight preference for the anti course. Effects of the strong cation solvating agents TG, 18-crown-6 (18-C-6), hexamethylphosphortriamide (HMPA), and the cryptate "Kryptofix-2.2.2" when present in THF in concentrations comparable to that of the sodium ion are qualitatively similar to those due to changing the solvent to TG (Table VI). Results of the more detailed examination of the effects of 18-C-6 and TG on the yields and stereochemistry of the products plotted in Figures 1–3 show that the results from both *threo*- and *erythro*-2-bromo-3-methoxybutane are the same within the experimental error. However, 18-C-6 has a larger effect than does TG, as reflected in the values at which data for the two ligands level off. This suggests that the course of the reaction in a constant solvent is dependent to some degree on the specific nature of the ligands interacting with the cation. A further indication that this is so is shown by the greater effects on product distribution and stereochemistry of elimination caused by Kryptofix than by the other ligands (Table VI).

The role of base association in eliminations in which a proton is the electrofuge has been studied recently by Bartsch[34] and Sicher[35] and co-workers. When contact ion pairs or aggregates are involved, syn elimination occurs, presumably by way of a transition state with a geometry resembling **1**. The analogue for the demethoxybromination is **2**. This requires that the concentration of the contact ion pairs, coupled with the free energy of activation through transition state **2**, leads to the high preference for syn elimination. This has synthetic potential as a method for the "inversion" of alkenes as shown in eq 6.





The changes in the course and stereochemistry of the reaction in the presence of the cation-coordinating ligands suggest that the resultant freer trimethylstannyl anions dominate the reaction, and the mechanism changes substantially from a concerted process to one involving stereolabile intermediates. In view of the observations that simple secondary bromides react with trimethylstannylalkalies by an electron transfer process,[32,33] a similar mechanism must be considered for the methoxy bromides. This would involve initial electron transfer from the tin to the antibonding carbon–bromine orbital followed by, or concerted with, loss of bromide anion as in eq 7. The



resulting carbon radical **5** would be planar or rapidly inverting. It would lose its stereochemical identity before losing the methoxy radical or combining the trimethylstannyl radical to form alkene and substitution product **6**, respectively. This is an unlikely pathway for alkene formation, because the loss of the methoxy radical would be endothermic by about 30 kcal/mol. It would be feasible thermodynamically if an S_H2 displacement by the trimethylstannyl radical by attack on the oxygen of the methoxy group occurred. The possibility that the free-radical intermediate might be involved in the reaction was tested as follows. A solution of *erythro*-2-bromo-3-methoxybutane, containing an excess of hexamethyldistannane, was photolyzed for 70 h. No 2-butane was found in the reaction mixture, but it contained a 70% yield of 2-methoxybutane (**7**) formed presumably according to eq 8–10,[36] in which S–H is the solvent TG.

$$Me_3Sn\text{–}SnMe_3 \rightarrow 2Me_3Sn\cdot \quad (8)$$

$$Me_3Sn\cdot + MeCH(OMe)CH(Br)Me \rightarrow Me_3SnBr + MeCH(OMe)\dot{C}HMe \quad (9)$$

$$MeCH(OMe)\dot{C}HMe + S\text{–}H \rightarrow S\cdot + \underset{\mathbf{7}}{MeCH(OMe)CH_2Me} \quad (10)$$

A second mechanism, involving a stereolabile intermediate, is an analogue of the E1cB mechanism. This would

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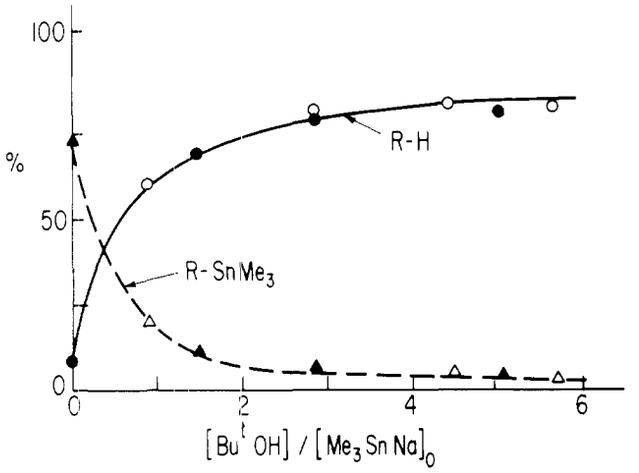
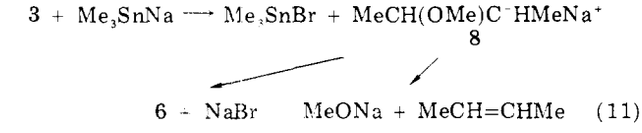


Figure 4. Effects of concentrations of *tert*-butyl alcohol on the yields of substitution products in the reaction of Me_3SnNa with MeCHBrCH(OMe)Me in tetrahydrofuran at 22 °C: Me_3SnNa ca. 0.6 M; MeCHBrCH(OMe)Me ca. 0.2 M. Open symbols indicate erythro; filled symbols indicate threo.

be initiated by nucleophilic attack by the trimethylstannyl anion on the bromine, as represented in eq 11. The intermediate carbanion 8 would undergo inversion rapidly relative to loss of methoxide ion and to reaction with trimethylbromostannane, resulting in nonspecific overall reactions. A series of experiments designed to test this mechanism by trapping any carbanion formed with *tert*-butyl alcohol was carried out with the results depicted in Figure 4. As the concentration of the alcohol was increased, the yield of the substitution product **6** decreased drastically, and the yield of the reduction product, 2-methoxybutane, increased concomitantly. It may also be significant that the results for both the erythro and threo isomers were the same within the experimental error. These observations provide strong evidence for a mechanism involving an anionic intermediate with a sufficiently long lifetime to undergo stereochemical equilibration before reacting to form the substitution product.



Conclusion

The results presented above indicate that stereospecific protection–deprotection of double bonds can be achieved by stereospecific anti addition of halogen and stereospecific anti dehalogenation by trimethylstannylsodium. Cis–trans inversion or its reverse can be achieved by stereospecific anti addition of the elements of methyl hypobromite followed by syn demethoxybromination by trimethylstannylsodium in THF. If a good cation solvating system is used as the medium for this latter reaction, the predominant product is formed by replacement of the bromine by the trimethylstannyl group by a mechanism involving a carbanion intermediate. These results again point up the importance of ionic aggregation in determining the course and stereochemistry of reactions in dipolar aprotic media.

Experimental Section

Infrared spectra were taken on Beckman IR-8 or IR-10 instruments with the 1601-cm^{-1} band of polystyrene used for calibration. NMR spectra were recorded on a Varian A-60A instrument or, when higher resolution was required, on a Varian HA-100 interfaced with a Digilab FTS/NMR3 pulse and data system. Chemical shifts are recorded downfield from Me_4Si, and H–Sn coupling constants are for the ^{119}Sn isotope. Tetraglyme (Ansul Corp.) was distilled from molten sodium, THF from sodium benzophenone ketyl, and ethylendiamine and tetramethylethylenediamine from calcium hydride in a nitrogen atmosphere. Trimethyltin chloride was a gift from M & T Chemicals. Organic halides which were commercially available were checked for purity before use. Others were prepared as described below.

2,3-Dibromobutanes. The pure diastereoisomers were prepared by bromination of 2-butenes with pyridinium tribromide[37] in acetic acid.[38] Meso: bp 36 °C (13 torr) [lit.[39] bp 73 °C (50 torr)]; NMR (CCl_4) δ 4.2 (m, 2, CH_3CHBr), 1.8 (d, 6, CH_3); IR (neat) 959 (s), 1004 (s), 1034 (m), 1154 cm^{-1} (s). *dl*: bp 38 °C (13 torr) [lit.[39] bp 77 °C (50 torr)]; NMR (CCl_4) δ (1.77, d, 6, CH_3), 4.48 (m, 2, CH_3CHBr).

2,3-Dibromo-4-methylpentanes. These were prepared in yields of about 80% by the same procedure as that indicated for the butanes. Erythro: bp 75 °C (17 torr) [lit.[38] bp 54 °C (0.25 torr)]; NMR (CCl_4) δ 0.93 (d, 3, $(CH_3)_2CH$), 1.07 (d, 3, $(CH_3)_2CH$), 1.94 (d, 3, CH_3CHBr), 2.4 (m, 1, $(CH_3)_2CH$), 4.02 (m, 2, $CH_3CHCrCHBr$); IR (neat) 2970 (s), 1455 (vs), 1160 (s), 1020 (m), 930 (w), 815 cm^{-1} (w). Threo: bp 86 °C (17 torr) [lit.[38] 54 °C 0.25 torr)]; NMR (CCl_4) δ 1.06 (d, 3, $(CH_3)_2CH$), 1.16 (d, 3, $(CH_3)_2$), 1.82 (d, 3, CH_3CHBr), 2.18 (m, 1, $(CH_3)_2CH$), 3.8 (q, 1, CH_3CHBr), 4.33 (m, 1, $(CH_2)_2CHBr$); IR (neat) 2980 (s), 1460 (vs), 1215 (s), 1140 (m), 900 (m), 700 cm^{-1} (s).

2,3-Dibromo-2,3-dimethylbutane, prepared as above in 77% yield, showed: NMR (CCl_4) δ 2.02 (s, 12, $(CH_3)_2CBr$); IR (neat) 1034 (s), 1160 (vs), 724 (vs), 875 cm^{-1} (m).

2-Bromo-3-methoxy-3-methylbutane: bp 50 °C (20 torr); NMR (CCl_4) δ 4.08 (q, 1, $CH_3CH(Br)$), 3.2 (s, 3, OCH_3), 1.64 (d, 3, $CH_3CH(Br)$), 1.23 (s, 3, $(CH_3)_2C(OCH_3)$), and 1.3 (s, 3, $(CH_3)_2C(OCH_3)$); IR (neat) 2930 (s, CH), 1090 (s, CO), 719 (ss), 627 (ss), 925 (m), 840 (m), 970 (m), and 1330 cm^{-1} (m).

2-Bromo-3-methoxy-2,3-dimethylbutane: bp 52 °C (17 torr); NMR (CCl_4) δ 3.26 (s, 3, OCH_3), 1.78 (s, 6, $(CH_3)_2CBr$), and 1.35 (s, 6, $(CH_3)_3C(OCH_3)$); IR (neat) 2955 (s, CH), 1123 (s, CO), 1360 (s), 1460 (s), 810 (m), and 880 cm^{-1} (ss).

Trimethylstannylsodium was prepared by stirring hexamethylditin with excess sodium metal in tetraglyme or THF in an atmosphere of nitrogen for 4–5 h. Yields were determined by reaction of an aliquot with bromobenzene and determination of the amount of phenyltrimethyltin formed by GLC. Yields were typically 90–95% of 0.3 to 0.4 M solutions.

Reaction of Vicinal 2-Halo-3-methoxybutanes with Trimethylstannylsodium. To 315.2 mg (1.887 mmol) of *erythro*-2-bromo-3-methoxybutane was added 10.0 mL of ca. 0.4 M trimethylstannylsodium and 104.5 mg (.915 mmol) of C_8 in TG at 18 °C under nitrogen. GLC analysis of the reaction mixture (12 ft × 0.125 in. stainless steel column, 10% UCW98 on 80–100 Chromosorb W, temperature program 40–250 °C at 5 °C/min) gave, in order of elution: 2-butene, Me_4Sn, octane, *threo*-2-bromo-3-(trimethylstannyl)butane, and hexamethylditin. This procedure was used in general for the determination of the product distributions.

In the trapping experiments, the appropriate amount of *tert*-butyl alcohol was added to the methoxy bromide before the trimethylstannylsodium was added.

In the experiments with the cation-coordinating agents, the methoxy bromide was added to a solution of trimethylstannylsodium containing the agent and the internal standard.

Isolation of *erythro*- and *threo*-2-(Trimethylstannyl)-3-methoxybutane from the Reaction of *erythro*-2-Bromo-3-methoxybutane with Trimethylstannylsodium in TG. To 2.86 g (17.2 mmol) of *erythro*-2-bromo-3-methoxybutane was added 22.4 mmol of trimethylstannylsodium in 38 mL of TG. After 1 h, the reaction mixture was quenched with 40 mL of water, extracted with 50 mL of diethyl ether, and washed repeatedly with water to remove all of the TG. The ether layer was dried

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(38) C. H. Pian, Ph.D. Thesis at the State University of New York at Albany, 1969.
(39) S. Winstein and J. J. Lucas, *J. Am. Chem. Soc.*, **61**, 1576 (1939).

over $MgSO_4$ and concentrated. Iodine in CCl_4 was added until the color persisted to remove hexamethyldistannane. Extraction with 20 mL of carbon tetrachloride and washing repeatedly with water removed trimethyltin iodide. The CCl_4 was dried over $MgSO_4$, concentrated, and subjected to GLC, using a 6 ft × 0.25 in. column, 20% SE30 on 60–30 Chromosorb W, isothermal at 90 °C. Approximately 0.5 g of the elutant tentatively assigned as a mixture of *erythro*- and *threo*-2-(trimethylstannyl)-3-methoxybutane was isolated. A mixture of the pure diastereomers of *erythro*- and *threo*-2-(trimethylstannyl)-3-methoxybutane was obtained under the following GLC conditions: 12 ft × 0.125 in. stainless steel column, 10% UCW98 on 80–100 Chromosorb W, temperature program 40–200 °C at 5 °C/min; 100 MHz proton Fourier transform (PFT); NMR (CCl_4) δ 0.02 (s, 9, ^2J(SnCH) = 50.5 Hz, *threo*-($\mathbf{CH_3}$)$_3$Sn), 0.05 (s, 9, ^2J(SnCH) = 50.5 Hz, *erythro*-($\mathbf{CH_3}$)$_3$Sn), 1.08–1.33 (A_2B_2, 6 × 2$\mathbf{CH_3}$), 1.33–1.82 (m, 1, $CH_3\mathbf{CH}$(Sn)), 3.31 (s, 3, O$\mathbf{CH_3}$), and 3.11–3.59 (m, 1, $CH_3\mathbf{CH}$(OCH$_3$)); IR (neat) 2990 (s), 1190 (s, CO), 550 (s, C**Sn**), and 760 cm^{-1} (s). Anal. Calcd for $C_8H_{20}SnO$: C, 38.30; H, 8.03. Found: C, 38.48; H, 7.96.

Determination of the Stereochemistry of 2-Butenes. After GLC determination of the yields of 2-butenes and other products, the reaction flask was connnected to another equipped with a cold finger condenser cooled to −78 °C and containing 3 mmol of pyridinium tribromide in 30 mL of glacial acetic acid and cooled at 10 °C. A volume of water equal to that of the initial solvent was added to the reaction flask, and a stream of nitrogen was passed through slowly to facilitate transfer of 2-butenes to the second flask. After 1.5 h, 20 mL of water and 30 mL of CCl_4 were added to the acetic acid, the mixture was shaken in a separatory funnel, and the organic layer was washed with water, bicarbonate solution, and then sodium hydroxide solution, dried with $MgSO_4$, and analyzed by GLC to determine the yields of *dl*- and *meso*-2,3-dibromobutanes. Because the bromine addition is quantitatively anti, these yields reflected the yields of cis and trans 2-butenes. No fractionation of the butenes occurred in the transfer from reaction product mixture to the pyridinium tribromide solution, as shown by the control experiment. GLC separation to the base line of the 2,3-dibromobutanes was achieved on the 12 ft × 0.25 in. column of 20% UCW 98 on 60–80 mesh Chromosorb W.

Determination of the Stereochemistry of the 2-(Trimethylstannyl)-3-methoxybutanes. A sample of the methoxytins containing 91% of one diastereomer and 9% of the other was collected by GLC. To 1.61 g in 20 mL of methanol and 5 mL of water at 0 °C was added 3 mL of perchloric acid. The resultant butenes were collected by reaction with pyridinium tribromide as described above, worked up in the same manner, and analyzed by GLC. The analysis showed 95% of *dl*- and 6% of *meso*-2,3-dibromobutane. Because both the demethoxybromination[132] and the debromination go by anti stereochemistry the major component in the original mixture was the threo isomer, and the minor one was the erythro.

Photolysis of *erythro*-2-Bromo-3-methoxybutane with Hexamethylditin. Into two Pyrex tubes were placed 7 mL of tetraglyme solutions 0.26 M in the methoxybromide, 0.16 M in hexamethylditin, and 0.13 M in *n*-octane as internal standard. The tubes were flushed with nitrogen, stoppered, and irradiated in a Rayonet Photochemical Reactor with 300-nm lamps. The contents were then analyzed by GLC, using the UCW 98 column. After 22 h, there was 66% of the 2-methoxybutane and less than 1% of the 2-butene, and after 69 h the values were 70% and less than 1%. The 2-methoxybutane was collected and shown to be identical by IR and NMR spectra with an authentic sample.

2,3-Dichloro-2,3-dimethylbutane was obtained in 26% yield by the reaction of iodobenzene dichloride[40] with 2,3-dimethylbutene[41] and showed NMR ($CDCl_3$) δ 1.72 (s, 12, ($\mathbf{CH_3}$)$_2$CHCl).

2-Bromo-3-chloro-2,3-dimethylbutane was prepared by the procedure of Hageman and Havinga[42] from 2,3-dimethyl-2-butene, *N*-bromosuccinimide, and hydrogen chloride in 5% yield: NMR ($CDCl_3$) δ .83 (s, 6, ($\mathbf{CH_3}$)$_2$CCl(Br)), 1.98 (s, 6, ($\mathbf{CH_3}$)$_2$CBr(Cl)); IR (neat) 2990 (s), 1455 (s), 1375 (s), 1086 (s), 806 cm^{-1} (m).

2-Bromo-3-chlorobutanes. These were prepared from the corresponding bromohydrins[43,44] in high yields. Threo: bp 48.5 °C (12 torr); NMR (CCl_4) δ 4.26 (m, 2, $CH_3\mathbf{CH}$Br), 1.72 (d, 3, $\mathbf{CH_3}$CHBr), 1.6 (d, 3, $\mathbf{CH_3}$CHCl); IR (neat) 1380 (s), 1101 (s), 1300 (m), 946 (s). Erythro: bp 37 °C (15 torr); NMR (CCl_4) δ 1.84 (dd, 6, $\mathbf{CH_3}$CHXCHX′$\mathbf{CH_3}$), 4.05 (m, 2, $CH_3\mathbf{CH}$); IR (neat) 2980 (s), 1445 (s), 1380 (s), 1170 (s), 1050 (m), 960 (s), 840 cm^{-1} (m).

2-Bromo-3-fluorobutanes. These were prepared from the 2-butenes by reaction with *N*-bromosuccinimide in hydrogen fluoride.[45] Threo: bp 112.5 °C (760 torr); NMR (CCl_4) δ 4.28 (m, 2, $CH_3CF\mathbf{CH}$), 1.64 (dd, 6, $\mathbf{CH_3}$CH(Br)), and 1.22 (d, 3, $\mathbf{CH_3}$CH(F)); IR (neat) 2990 (s), 1330 (m), 1010 (s), 795 (m), and 1210 cm^{-1} (s). Erythro: bp 97 °C (760 torr); NMR (CCl_4) δ 4.06 (m, 2, $CH_3\mathbf{CH}$(F)), 1.7 (q, 6, $\mathbf{CH_3}$HBr), and 1.3 (d, 3, $\mathbf{CH_3}$CH(F)); IR (neat) 2990 (s), 1340 (m), 1000 (s), 825 (m), and 1200 cm^{-1} (m).

2-Bromo-3-formylbutanes were prepared by the method of Micev,[46] which involved the reaction between the appropriate 2-butene and *N*-bromosuccinimide with dimethylformamide used as solvent. Threo: bp 54 °C (13 torr); NMR ($CDCl_3$) δ 4.17 (m, 2 H $CH_3\mathbf{CH}$(Br)), 1.87 (d, 6 H, 2$\mathbf{CH_3}$), and 8.06 (s, 1 H, C(O)**H**); IR (neat) 2990 (s, CH), 1723 (s, C=O), and 1171 cm^{-1} (s, CO). Erythro: bp 58 °C (13 torr); NMR ($CDCl_3$) δ 4.47 (m, 2, $CH_3\mathbf{CH}$C(Br)), 1.79 (C, 6 H, 2$\mathbf{CH_3}$), and 8.12 (s, 1, C(O)**H**); IR (neat) 2990 (s, CH), 1728 (s, C=O), and 1180 cm^{-1} (s, CO).

***erythro*-2,3-Dihydroxy-4-methylpentane** was prepared from *trans*-4-methyl-2-pentene:[47] bp 104 °C (20 torr); NMR ($CDCl_3$) δ 0.99 (2 d, 6, ($\mathbf{CH_3}$)$_2$CH), 1.66 (d, 3, $\mathbf{CH_3}$CH(OH)), 1.73 (m, 1, (CH$_3$)$_2\mathbf{CH}$), 3.25 (q, 1, (CH$_3$)$_2$C**H**CH(OH)), 3.5 (s, 2, R**OH**), and 3.85 (m, 1, (CH$_3$)$\mathbf{CH}$(OH)); IR (neat) 3200–3600 (s, OH), 2990 (vs, CH)), 1100–1040 (vs, CO), 900 (s), and 800 cm^{-1} (m).

1,2-Ditosyloxyethane was prepared according to the procedure of Corey and Mitra[48] by tosylation of ethylene glycol in the presence of pyridine: mp 114–115 °C; NMR ($CDCl_3$) δ 7.44 (A_2B_2(q), 8, Ar**H**), 4.16 (t, 4, (X)$\mathbf{CH_2}$CH$_2$(X)), and 2.42 (s, 6, Ar$\mathbf{CH_3}$).

Vicinal methoxy bromides were prepared by the method of Winstein and Lucas[49] in generally good yields. 1-Bromo-2-methoxyethane: bp 109 °C (760 torr); NMR (CCl_4) δ 3.59 (m, 4, 2$\mathbf{CH_2}$), 3.37 (s, 3, O$\mathbf{CH_3}$); IR (neat) 2900 (s, CH), 1110 (s, CO), 1280 (s), 1460 (s), and 990 cm^{-1} (s).

1-Bromo-2-methoxy-2-methylpropane: bp 46 °C (20 torr); NMR (CCL_4) δ 3.36 (s, 2, $\mathbf{CH_2}$(Br)), 3.21 (s, 3, O$\mathbf{CH_3}$), and 1.27 (s, 6, (CH$_3$)$_2$C(OCH$_3$)); IR (neat) 2990 (s, CH), 1088–1110 (s, CO), 680 (s), and 755 cm^{-1} (m).

***erythro*-2-Bromo-3-methoxybutane**: bp 41 °C (21 torr) [lit.[36] bp 56 °C (40 torr)]; NMR (CCl_4) δ 4.05 (m, 1, $CH_3\mathbf{CH}$(Br)), 3.38 (s, 3, O$\mathbf{CH_3}$), 3.3 (m, 1, $CH_2\mathbf{CH}$(OCH$_3$)), 1.64 (d, 3, $\mathbf{CH_3}$CH(Br)), and 1.2 (d, 3, $\mathbf{CH_3}$CH(OCH$_3$)); IR (neat) 2990 (s, CH), 1215 (s), 1101 (s, CO), and 7.05 cm^{-1} (m) (lit.[50] 1099 (s, CO)).

***threo*-2-Bromo-3-methoxybutane**: 55 °C (40 torr) [lit.[40] bp 138 °C (650 torr)]; NMR (CCl_4) δ 4.1 (m, 1, $CH_3\mathbf{CH}$(Br)), 3.4 (m, 1, $CH_3\mathbf{CH}$(OCH$_3$)), 3.35 (s, 3, $\mathbf{CH_3}$), 1.6 (d, 3, $\mathbf{CH_3}$CH(Br)), and 1.2 (d, 3, $\mathbf{CH_3}$CH(OCH$_3$)); IR (neat) 2990 (s, CH), 1191 (s), 1092 (s, CO), and 700 (m) (lit.[13] 1093 (s, CO)).

Acknowledgment. We are grateful to the National Science Foundation for support of this research.

Registry No. *meso*-2,3-Dibromobutane, 5780-13-2; *meso*-2,3-dichlorobutane, 4028-56-2; *erythro*-2-bromo-3-fluorobutane, 57302-16-6; *threo*-2-bromo-3-fluorobutane, 57302-15-5; *erythro*-2-bromo-3-chlorobutane, 19773-36-5; *threo*-2-bromo-3-chlorobutane, 19773-37-6; *erythro*-2,3-dibromo-4-methylpentane, 7694-00-0; *threo*-2,3-di-

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Chemistry of Diorganocuprates Containing Functionalized Ligands. 2. Methodology for Conjugate Addition of Synthetic Equivalents of Enolates and Acyl Anions

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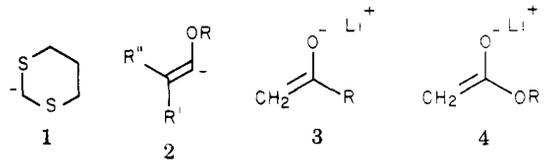
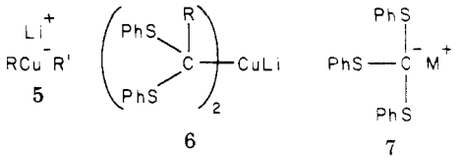
Methodology is described by which several classes of masked synthons, the synthetic equivalents of acyl anions and enolates, can be rendered reactive as ligands in the corresponding diorganocuprate complexes. Vinyl ethers and vinylsilanes were studied, and a comparison of their reactivities, stabilities and unmasking characteristics is given. The two classes of reagents prove nicely complementary in terms of their spectrum of reactivity, selectivity, and ease in unmasking.

Diorganocuprate reagents have assumed a prominent place in the arsenal of organometallic reagents which are available to the synthetic organic chemist. Two excellent reviews have documented the utility of these reagents for a variety of carbon–carbon bond-forming reactions.[2] Furthermore, significant strides have been made toward the understanding of the mechanism, the scope of reactivity, and the stereochemistry of the interaction of these reagents with a variety of organic substrates.[3] One area which has received somewhat less attention until relatively recently is the extension of the scope of the preparation and use of these reagents to functionalized ligands. Most of the studies have involved unfunctionalized hydrocarbon or olefinic groups in part due to the ease of preparation and handling of the prerequisite lithium reagents. Several examples of functionalized systems have been reported, including the work of Eaton,[4] the Syntex group (among several),[5] Marino,[6] Grieco,[6] and ourselves.[7] Among the more useful types of carbanion ligands whose cuprate complexes have not been reported when this work was begun were those of protected acyl anions such as **1** and **2** and enolates of esters and ketones such as **3** and **4**. These masked synthetic equivalents would be valuable additions to the available synthetic methodology if reactive



1 **2** **3** **4**

complexes could be prepared. Direct formation of either reactive homogeneous diorganocuprate complexes or mixed-ligand complexes (**5**) does not appear feasible par-



5 **6** **7**

R = alkyl, H, vinyl; R′ = *t*-BuO, RC≡C, PhS

ticularly in the case of the latter two types of ligands. A rough correlation of copper–ligand bond strength vs. reactivity suggests that **3** and **4** would function as nontransferable ligands in the manner of –SR, –OR, and –C≡CR. Ligands such as **3** and **4** would tend to behave as metal enolates and not undergo conjugate addition and other reactions characteristic of standard cuprate reagents, if indeed such complexes could be formed at all.

Consequently, we embarked upon a program to explore the potential of masked equivalents of these species (**1**–**4**) which could function as transferable ligands in mixed or homogeneous cuprate reagents.[8] Only a single example of an acyl anion equivalent functioning as a reactive ligand had been reported at that time. Mukaiyama had established the use of diphenyl dithioacetals (**6**) as ligands for conjugate addition to certain simple unsaturated ketones,[9]

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