We would anticipate, by analogy to our previous work,[1,2] that secondary and tertiary organolithium reagents would show a greater preference for reaction with acidic hydrocarbons and halobenzenes in these competitive reactions because of the greater sensitivity of the reaction with chlorosilane to steric factors.[8]

These data again show the utility of trimethylchlorosilane in the trapping of specific organolithium reagents in a reaction sequence. It should also be noted that extreme caution must be exercised in assigning the structure of an organolithium reagent *via* derivative formation, since the rate of such a reaction may well be slower than the interconversions among several organolithium reagents.

Experimental Section

All experiments were carried out under dry nitrogen in a flask fitted with stirrer and reflux condenser. Boiling points and melting points are uncorrected.

9-Trimethylsilylfluorene (II).—A solution of *n*-butyllithium in hexane (96 ml, 0.15 mole) was added during 3 hr at 25–32° to 8.31 g (0.05 mole) of fluorene in 125 ml of THF. The resulting orange-brown solution was added *via* a capillary tube to 97.4 g (0.90 mole) of rapidly stirred trimethylchlorosilane. The temperature was maintained at 10–20° during the 1.25-hr addition. Analysis by vpc showed the absence of fluorene and the presence of two compounds (*ca.* 20:1 ratio) with retention times greater than fluorene. After solvent removal by distillation, the residue was dissolved in 200 ml of chloroform and filtered, giving 5.98 g (0.14 mole) of lithium chloride. The filtrate was concentrated on a rotary evaporator to afford 13.2 g of solid. Crystallization from 150 ml of ethanol gave 5.82 g (0.0244 mole) of II, mp 96–97° (lit.[9] mp 97.5°). Further concentration of the ethanol solution gave an additional 3.01 g (0.0126 mole) of II, mp 95–97°; the total yield was 74%. The H^1 nmr spectrum of II showed singlets for trimethylsilyl (τ 10.11) and methine protons (6.29), and a multiplet for aromatic protons (2.2–2.9). The integrated intensities were in accord with the proposed structure. The infrared spectrum showed the characteristic absorptions for aromatic structures (5–6, 13.5 μ) and for the trimethylsilyl group (8.0, 11.9 μ).

Anal. Calcd for $SiC_{15}H_{18}$: Si, 11.8; C, 80.6; H, 7.6. Found: Si, 12.4, 12.06; C, 80.3, 80.7; H, 7.84, 7.85.

9,9-Bis(trimethylsilyl)fluorene (III).—A solution of *n*-butyllithium in hexane (36 ml, 0.06 mole) was added during 45 min at 10–20° to 10.8 g (0.10 mole) of trimethylchlorosilane and 16.6 g (0.10 mole) of fluorene in 100 ml of THF. After stirring 16 hr at room temperature, 32.6 g (0.30 mole) of trimethylchlorosilane and 50 ml of THF were added to the mixture. An additional 155 ml (0.25 mole) of *n*-butyllithium solution was then added at 10–20° over a period of 3 hr. Analysis by vpc showed solvents, *n*-butyltrimethylsilane (I), and a single peak with a retention time greater than that of fluorene. Distillation and crystallization from ethanol afforded 25.2 g (0.084 mole) of III, mp 109–110° (lit.[9] mp 110°), 84% yield. The H^1 nmr spectrum showed a singlet for trimethylsilyl (τ 9.91) and a multiplet for the aromatic protons (1.9–2.8) in a ratio of 18:8. The infrared spectrum showed the characteristic absorptions noted for II.

Anal. Calcd for $Si_2C_{19}H_{26}$: Si, 18.1; C, 73.5; H, 8.4. Found: Si, 18.0, 18.1; C, 74.3, 74.8; H, 8.68, 8.87.

Competition of Fluorene and Trimethylchlorosilane for *n*-Butyllithium.—A solution of *n*-butyllithium in hexane (31.5 ml, 0.05 mole) was added during 45 min at 30–40° to 27.2 g (0.25 mole) of trimethylchlorosilane and 41.6 g (0.25 mole) of fluorene. Analysis by vpc showed a 1:3:1 molar ratio of I:II:III. Calibration of the vpc (thermal conductivity detectors) gave the following relationship: area I to area II to area III = 1.50 mole of I to 1.05 mole of II to 0.75 mole of III.

Competititon of Triphenylmethane and Trimethylchlorosilane for *n*-Butyllithium.—A solution of *n*-butyllithium in hexane (25.1 ml, 0.04 mole) was added during 2.5 hr at 5–25° to 21.7 g (0.20 mole) of trimethylchlorosilane and 48.9 g (0.20 mole) of triphenylmethane in 80 ml of THF. No color change was observed during the addition. Analysis by vpc revealed the presence of starting materials and I. No compounds with retention times greater than triphenylmethane could be detected.

When *n*-butyllithium was added to a solution of triphenylmethane in THF, the characteristic red color of triphenylmethyllithium was immediately evident. The red color rapidly disappeared when the organolithium solution was mixed with trimethylchlorosilane. Analysis by vpc showed that the major component present had a retention time greater than that of triphenylmethane.

Competition of Bromobenzene and Trimethylchlorosilane for *n*-Butyllithium.—A solution of *n*-butyllithium in hexane (126 ml, 0.20 mole) was added to 157.0 g (1.0 mole) of bromobenzene and 108.6 g (1.0 mole) of trimethylchlorosilane in 200 ml of THF. The temperature was maintained at 5–15° during the 2-hr addition. Fractional distillation of the mixture afforded 4.0 g (0.0306 mole) of I and 10.7 g (0.071 mole) of phenyltrimethylsilane (IV) in addition to solvent starting materials and *n*-butyl bromide. Compounds I and IV were identified by vpc retention times and by comparison of their infrared spectra with those of authentic samples.

Competition of Chlorobenzene and Trimethylchlorosilane for *n*-Butyllithium.—A solution of *n*-butyllithium in hexane (62.9 ml, 0.10 mole) was added to 56.1 g (0.50 mole) of chlorobenzene and 54.3 g (0.50 mole) of trimethylchlorosilane in 100 ml of THF. The temperature was maintained at 5–15° during the 1.5-hr addition. Analysis by vpc showed starting materials and I. Distillation afforded 11.1 g (0.085 mole) of I.

(8) See ref 7, Chapter 2.

(9) C. Eaborn and R. A. Shaw, *J. Chem. Soc.*, 1420 (1955).

Alkoxide-Initiated Eliminations on Substrates Bearing Poor Leaving Groups. I. Diglyme as Substrate in Potassium *t*-Butoxide Initiated Elimination

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Acid- and base-catalyzed elimination reactions have been very extensively studied.[1-3] However, the alkoxide- and hydroxide-initiated elimination reactions on substrates carrying poor leaving groups such as alkoxyl and hydroxyl have received little attention. In most of the examples of this type of elimination reaction reported in the literature, the hydrogen β to the leaving group is activated by a substituent which allows formation of a relatively stable carbanion.[4-6] It was therefore of interest to investigate substrates which contain poor carbanion-stabilizing groups, *i.e.*, alkoxyl. Snyder[7] in a preliminary investigation demonstrated that diglyme (the dimethyl ether of diethylene glycol) undergoes elimination in the presence of potassium *t*-butoxide at 160°. We have examined this elimination in more detail.

(1) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 420–472.

(2) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, Chapter 12.

(3) D. J. Cram, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 6, p 304.

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(6) R. L. Letsinger and E. Bobko, *J. Am. Chem. Soc.*, **75**, 2649 (1953).

(7) W. H. Snyder, unpublished research done as a graduate student at the University of Pennsylvania, Philadelphia, Pa.

The elimination reactions and analyses were carried out as described in the Experimental Section. The results of two eliminations are shown in Table I.

TABLE I

POTASSIUM *t*-BUTOXIDE INITIATED ELIMINATION ON DIGLYME

Run no.[a]	*T*, °C	*t*, min	Products, moles		
			t-BuOH	MVE[b]	MEVE[c]
1	160 ± 2	158	0.083	0.056	0.014
2	161 ± 2	203	0.076	0.057	0.011

[a] The solutions were initially 1.73 *M* in potassium *t*-butoxide and 50 ml of solution was utilized for each run. The amount of *t*-butoxide used was thus 0.086 mole. [b] Methyl vinyl ether. [c] 2-Methoxyethyl vinyl ether.

The data show that better than 96 and 88% of the *t*-butoxide was converted into *t*-butyl alcohol in runs 1 and 2, respectively. Reactions 1–3 would explain these observations.

$$(CH_3{-}O{-}CH_2{-}CH_2)_2O \xrightarrow{KO\text{-}t\text{-}Bu} CH_2{=}CH{-}OCH_3 + HO{-}CH_2{-}CH_2{-}OCH_3 \quad (1)$$

$$(CH_3{-}O{-}CH_2{-}CH_2)_2O \longrightarrow CH_2{=}CH{-}O{-}CH_2{-}CH_2{-}OCH_3 + CH_3OH \quad (2)$$

$$ROH + KO\text{-}t\text{-}Bu \longrightarrow ROK + t\text{-}BuOH \quad (3)$$

$$R = CH_3,\ CH_3{-}O{-}CH_2{-}CH_2$$

Thus there should be a 1:1 correspondence between the alkoxide and the respective vinyl ether produced according to the above scheme. However, methylation of the reaction mixture at the end of the runs with excess methyl iodide produced 0.015 and 0.019 mole of 1,2-dimethoxyethane and 0.041 and 0.025 mole of dimethyl ether in runs 1 and 2, respectively. Clearly, the amount of methoxide present was too large and the 2-methoxyethoxide too small to be accounted for by the scheme proposed. This suggested that additional methyl vinyl ether might be formed by elimination from 2-methoxyethyl vinyl ether. In order to test

$$CH_2{=}CH{-}O{-}CH_2{-}CH_2{-}OCH_3 \longrightarrow CH_2{=}CH{-}OCH_3 + CH_3C(H){=}O \quad (4)$$

this hypothesis 11.67 g (0.1039 mole) of potassium *t*-butoxide was dissolved in 46 ml of 2-methoxyethyl vinyl ether and the solution was heated for 160 min at 110° (the boiling point of the ether). The volatile products collected in a Dry Ice cooled receiver were found to contain 0.018 mole of methyl vinyl ether which would correspond to about 16% elimination based on the amount of *t*-butoxide used initially. Thus, the assumption that some of the methyl vinyl ether in the diglyme elimination comes from elimination from the 2-methoxyethyl vinyl derivative appears reasonable and at the higher temperatures employed in the former case this could be the major source of methyl vinyl ether.

Methylation of the reaction mixture from the 2-methoxyethyl run gave approximately 0.02 mole of 1,2-dimethoxyethane and 0.05 mole of methyl *t*-butyl ether. The dimethoxyethane came from 2-methoxyethoxide ion which may have been formed by elimination from the 2-methoxy derivative to acetylene. Unfortunately, the acetylene, if formed, would not have been trapped under our conditions (Dry Ice cooled receiver). The solid residue from the methylation reaction (chiefly potassium iodide) was found to contain

$$CH_2{=}CH{-}O{-}CH_2{-}CH_2{-}OCH_3 \xrightarrow{KO\text{-}t\text{-}Bu} CH{\equiv}CH + HOCH_2CH_2OCH_3 \quad (5)$$

considerable amounts of a carboxylate ion (strong absorption at 1568 and 1412 cm^{-1} run in a potassium bromide pellet).[8] Potassium acetate also shows similar absorption at the same frequencies. This observation would make the formation of acetaldehyde in the elimination from the 2-methoxyethyl derivative appear quite reasonable since a Cannizzaro reaction on acetaldehyde or its aldol condensation products would produce carboxylate ion. The hydroxide ion necessary for the Cannizzaro reaction would come from base-initiated elimination of hydroxide ion from aldol, a known reaction.[4,9]

It is significant that there was no evidence for the formation of divinyl ether either in the diglyme or the 2-methoxyethyl vinyl ether runs. In addition, we found no evidence for the formation of displacement products before the methylation reactions were carried out. The latter observation is to be expected since our conditions, *i.e.*, high temperature, low dielectric constant, strongly basic *t*-butoxide ion, should all favor the elimination process.[10]

These eliminations are very likely examples of E2 reactions which involve both substrate and nucleophile in the transition state. Preliminary carbanion formation (E1cB mechanism) seems unlikely since alkoxy groups are poor carbanion stabilizing groups. Investigation on this and other systems is being continued in an effort to learn more about the nature of these eliminations.

Experimental Section

Methyl vinyl ether, 2-methoxyethyl vinyl ether, *t*-butyl alcohol, diglyme, di-*t*-butyl peroxide, and methyl iodide were all commercially available. All liquid materials were examined for purity by gas chromatography and infrared absorption.

The diglyme and 2-methoxyethyl vinyl ether were distilled from sodium and then stored under nitrogen until used. The potassium *t*-butoxide was conveniently prepared free of *t*-butyl alcohol by dropwise addition of di-*t*-butyl peroxide to a suspension of molten potassium metal in diglyme under nitrogen at 80–95°.[11] The heat of this reaction was sufficient to maintain the temperature. The *t*-butoxide was completely soluble under the conditions we employed (1.73 *M*). The total basicity of these solutions checked closely against the amount of *t*-butyl methyl ether which was formed by methylation of measured amounts of the same solutions with methyl iodide.

The elimination reactions were carried out by heating the potassium *t*-butoxide solution in the substrate to its boiling point in a distillation apparatus under a slow stream of nitrogen. Products were trapped in a Dry Ice cooled receiver. The pot residue was treated with an excess (based on *t*-butoxide) of methyl iodide and then was allowed to stand for at least 14 hr.

Analysis of the distillates and methylation products was made by a combination of gas chromatography and infrared absorption. Quantitative gas chromatographic analysis was always made by comparison of the unknown mixtures with synthetic mixtures made up to approximately the same composition.

In the elimination reaction performed on 2-methoxyethyl vinyl ether, dry potassium *t*-butoxide (recovered from diglyme solution by removal of the solvent under vacuum in a rotary evaporation apparatus) was dissolved in this ether and the reaction was carried out as previously described.

(8) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, pp 174–176.
(9) V. Grignard and P. Abelmann, *Bull. Soc. Chim.*, [4] **7**, 638 (1910).
(10) Reference 1, p 419.
(11) N. A. Milas and D. M. Surgenor, *J. Am. Chem. Soc.*, **68**, 205 (1946).

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N-Aryl- and N-*t*-Butylisoxazolium Salts

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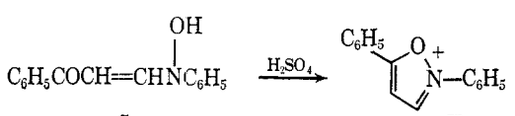
As part of an investigation[2] of the isoxazolium salt method of peptide synthesis,[3,4] we have found methods for preparing two new types of isoxazolium salts, those bearing aryl and *t*-butyl groups on the quaternary nitrogen atom.

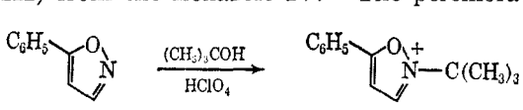
The route to N-arylisoxazolium salts, illustrated by the conversion of 3-(N-hydroxyanilino)acrylophenone (I)[5,6] to the N,5-diphenylisoxazolium cation (II), resembles the synthesis of 5-isoxazolones from β-keto esters and phenyl- or methylhydroxylamine,[7,8] in that the substituent is attached to nitrogen prior to ring formation. Cyclization of I is effected simply by dissolving the compound in concentrated sulfuric acid. The ultraviolet maximum of the solution is at



I II

328 mμ, in the range anticipated for II. On dilution of the reaction mixture with ice, the bisulfate salt of II precipitates in good yield. Alternatively, the less soluble perchlorate salt can be obtained by further dilution with enough water to redissolve the bisulfate of II and addition of sodium perchlorate solution.

N-*t*-Butylisoxazolium salts can be obtained by the usual tactic of alkylating the isoxazole ring. The *t*-butylation of isoxazoles is readily achieved with *t*-butyl alcohol and perchloric acid, as shown by the preparation of the N-*t*-butyl-5-phenylisoxazolium cation (III) from the isoxazole IV. The perchlorate of



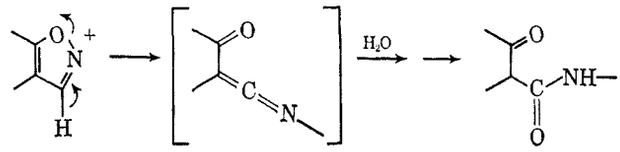
IV III

III precipitates in 90% yield from a mixture of IV and *t*-butyl alcohol with excess 70% perchloric acid.

Both preparative procedures should have broad applicability, in the former case because compounds of the type I are obtainable by condensation of various hydroxymethylene ketones with N-arylhydroxylamines (from reduction of the readily available aromatic nitro compounds). The generality of these reactions and use of the product isoxazolium salts in peptide synthesis are under investigation.

The N-*t*-butylisoxazolium cation III and related cations have been proposed by Eugster, Leichner, and Jenny as intermediates in the reaction of 3-unsubstituted isoxazoles with various carbonium ion precursors in concentrated sulfuric acid.[9] However, these authors isolated, rather than the isoxazolium salts, products that would be expected from the established[3] ring-opening mechanism for 3-unsubstituted isoxazolium salts, followed by hydration (Scheme I). These authors considered the established mecha-

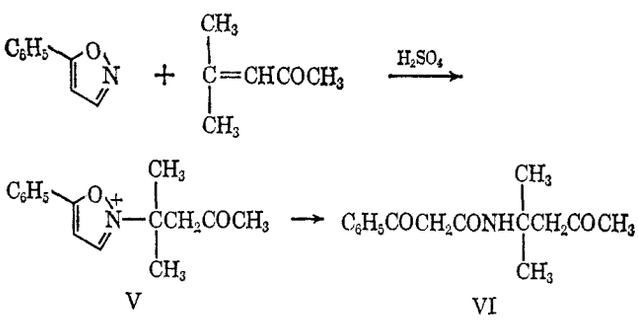
SCHEME I



nism, since it involves hydrogen abstraction by some base, unlikely in their acidic reaction media. Instead, they proposed an alternative ring-opening mechanism for 3-unsubstituted isoxazolium salts in concentrated sulfuric acid.

It seemed more likely to us that destruction of the isoxazolium salts occurred in the work-up method used by Eugster, Leichner, and Jenny, because the reported procedures include neutralization of the reaction mixtures, an operation fraught with peril for base-sensitive isoxazolium salts. To test this possibility we have repeated one such experiment, omitting the neutralization step.

Cautious neutralization with bicarbonate of a sulfuric acid solution of 5-phenylisoxazole and mesityl oxide, extraction with dichloromethane, and removal of the organic solvent was reported[9] to give an oil in 60% yield (based on IV), which afforded the keto amide VI on purification. However, when we merely diluted a similar reaction mixture with water, washed the solution with dichloromethane to remove any neutral organic impurities, and added sodium perchlorate solution, we obtained the perchlorate salt of the isoxazolium cation V. Isolation of the isoxazolium salt confirms the proposed alkylation of isoxazoles under these conditions and shows that the destruction of the isoxazolium cations took place



V VI

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