

RETROCYCLOADDITIONS OF ANIONS FROM TETRAHYDROFURANS
AND HEXAHYDROOXEPIN

by

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TO MOM AND DAD

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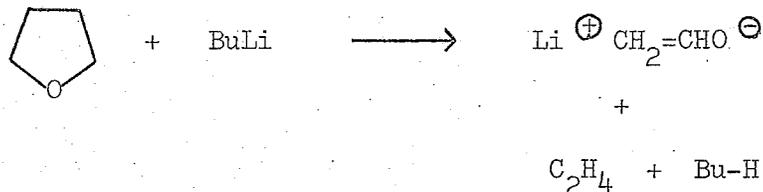
ABSTRACT

Various tetrahydrofurans and related ethers are reacted with n-butyllithium in an effort to help delineate the scope of the synthesis of lithium enolates of aldehydes by this approach. Desired enolates may be readily prepared in high yield if the corresponding symmetrical THF derivative is available. Unsymmetrical THFs and α -substituted ethers react with n-butyllithium to yield a mixture of α - and β -cleavage products or only β -elimination products and thus are of little value in the synthesis of enolates of aldehydes. Hexahydrooxepin reacts with n-butyllithium to give only the β -elimination product. Tetrahydropyran appears to react very slowly in an as yet undefined manner.

The methyl groups in 3,3-dimethylenolate are nonequivalent as shown by nmr. The barrier to rotation is at least 21 kcal/mole.

INTRODUCTION

In 1969, Potter synthesized lithium enolates of aldehydes in high yield by reacting substituted tetrahydrofurans with n-butyllithium. This thesis is primarily concerned with an investigation of the reactions of n-butyllithium with several substituted tetrahydrofurans and some related ethers to help delineate the scope of this lithium enolate synthesis (1).



(1)

Cleavage of Tetrahydrofurans by Organometallic Compounds

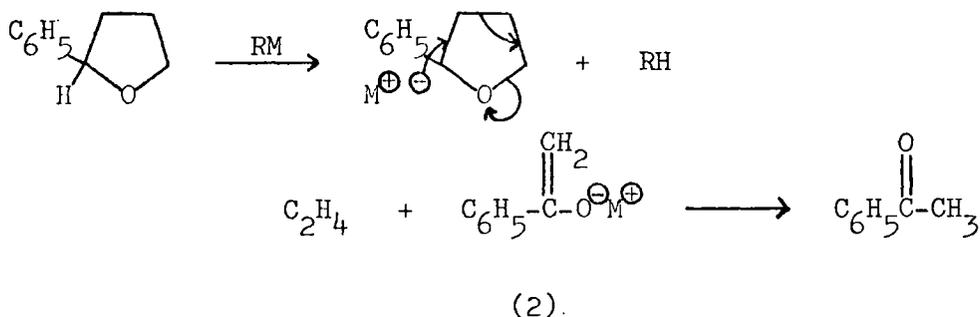
It has long been known that organometallic compounds decompose in ethers. This was first demonstrated by Schorigin in 1910, when he reported the reaction of ethylsodium with diethyl ether to produce sodium ethoxide, ethylene, and ethane. However, it has been only recently that the cleavage of THF by organometallic reagents has been investigated.

In 1950, Wittig and Ruckert found that they could cleave THF with triphenylmethylsodium when the THF was complexed with triphenylboron. Upon hydrolysis, 5,5,5-triphenylpentanol was obtained. It was

felt that the reaction was proceeding through a displacement of THF oxygen by triphenylmethylsodium.

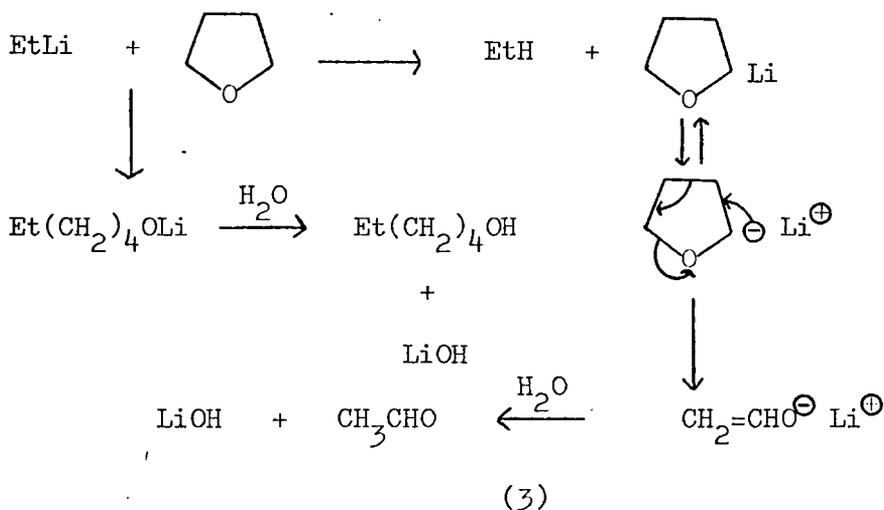
Normant (1954) used a Grignard reagent to cleave THF at temperatures exceeding 200° . The resulting compounds were of the type $R(\text{CH}_2)_4\text{OH}$. It was felt that this reaction was also occurring through a displacement of THF oxygen by the organometallic reagent.

During an investigation of α - versus β -elimination in the cleavage of ethers by organoalkali metal compounds, Letsinger and Pollart (1956) reacted 2-phenyltetrahydrofuran with propyllithium. Instead of obtaining 4-phenyl-3-butenol, the expected β -elimination product, they obtained propane, acetophenone, and ethylene. They proposed a mechanistic sequence (2) involving initial attack of the organometallic reagent on the α -position.

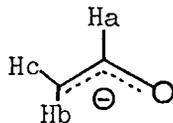


Gilman and Gaj (1957) investigated the stability of several organolithium reagents in THF. They found that methyl-, n-butyl-, and phenyllithium were less stable in THF than in ethyl ether (Gilman, Haubein, and Hartzfeld 1954; Haubein 1943). However, the order of stability was determined to be the same in both THF and ethyl ether, namely, methyl- > phenyl- > n-butyllithium.

The reaction of ethyllithium and THF was examined by Rembaum, Siao, and Indictor (1962). The products of this reaction after hydrolysis were hexanol, acetaldehyde, ethane, ethylene, and lithium hydroxide. Two reaction pathways (3), which have been mentioned earlier (Letsinger and Pollart 1956, Normant 1954), were employed to explain these results.

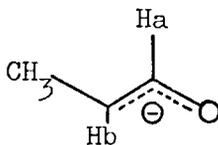


Potter (1969) studied the reaction of n-butyllithium with several tetrahydrofurans, and noted that these reactions could serve as high-yield methods for synthesizing lithium enolates of aldehydes. Tetrahydrofuran itself gave ethylene and lithium enolate, and 3,4-methyltetrahydrofuran yielded propylene and the enolate of propionaldehyde. Nmr was used to follow the course of these reactions by observing the increase in peaks at about τ 3.1 due to the enolate anion and the decrease in the methylene peaks at τ 1.1 due to n-butyllithium. Figures 1 and 2 show the chemical shifts in τ units and the coupling constants in Hertz (Hz) for lithium enolate and lithium 3-methylenolate.



<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	3.12	Jab	12.8
Hb	~ 6.4	Jac	4.8
Hc	6.85	Jbc	2.0

Figure 1. Nmr parameters for lithium enolate at 35°.



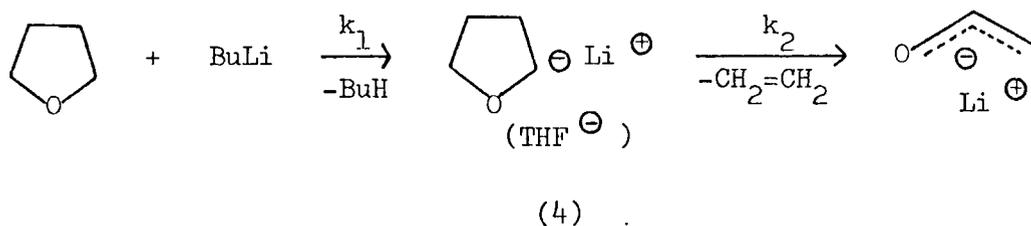
<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	3.37	Jab	11.0
Hb	~ 6.3		

Figure 2. Nmr parameters for lithium 3-methylenolate at 35°.

Mechanisms of THF Cleavage Reactions

A straightforward mechanism for α -cleavage has been mentioned previously (Letsinger and Pollart 1956). It involves the abstraction of an α -proton followed by a retrocycloaddition reaction to produce enolate and ethylene. However, no evidence supporting this mechanism was obtained; it was suggested only to explain the hydrolysis products.

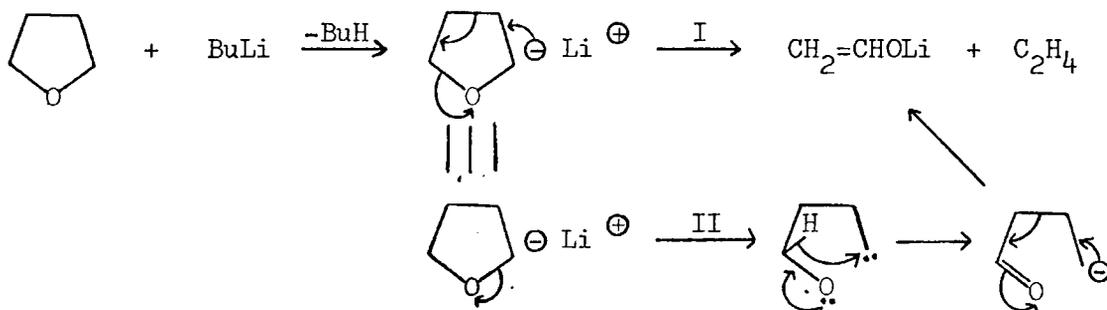
Potter (1969) presented further evidence regarding the α -cleavage mechanism. It was proposed that the reaction was proceeding according to reaction sequence (4).



The first step is pseudo first-order in n-butyllithium since THF was present in a 15-fold excess. The rate constants (obtained at 35°) were $k_1 = 1 \times 10^{-3} \text{ sec}^{-1}$ and $k_2 = 6 \times 10^{-3} \text{ sec}^{-1}$.

Evidence for the THF anion as an intermediate in the cleavage reaction was obtained by adding D_2O to the reaction sample after 4 min, since it was observed from the kinetic curves that the intermediate attained its maximum concentration after 4 min. The mass spectrum of the deuterated sample was compared to a sample to which H_2O had been added. A concentration of 8% for the THF anion was calculated.

Two possible mechanisms (I and II) were proposed. Mechanisms involving free radicals were regarded as unlikely when no radicals could be detected by EPR during the reaction.

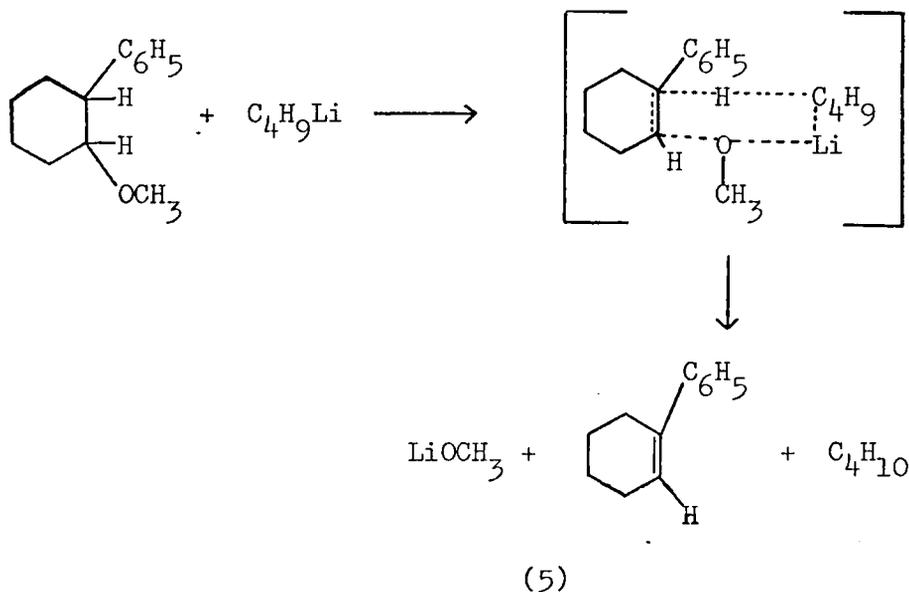


Mechanism II was excluded by considering the products obtained when 2-phenyltetrahydrofuran and 2-methyltetrahydrofuran were reacted with n-butyllithium. From the former ether, mechanism II would have been expected to give styrene and acetaldehyde; acetophenone and ethylene were the products obtained. In the case of 2-methyltetrahydrofuran, one of the two secondary α -protons would be expected to be abstracted faster than the tertiary α -proton to form the anion. Mechanism II would be expected to yield ethylene and the enolate of acetone, but propylene and lithium enolate were the resulting products. In both cases, the products are those expected from mechanism I.

These retrocycloaddition reactions probably follow the Woodward and Hoffmann rules (1965) for $4 + 2$ electrocyclic reactions, which are thermally allowed cis-cis.

In a study of the stereochemistry of elimination reactions brought about by n-butyllithium, Letsinger and Bobko (1953) investigated the reaction of n-butyllithium with the cis and trans isomers of methyl 2-phenylcyclohexyl ether. It was found that the trans isomer was converted into 1-phenylcyclohexene more rapidly than the cis isomer. To explain the product, it was postulated that a β -proton had been abstracted, followed by an elimination reaction. Since in this case

cis-elimination proceeds faster than trans-elimination, reaction sequence (5) was proposed which includes a cyclic transition state resembling those postulated for pyrolytic eliminations, where cis-elimination also takes place more readily than trans-elimination. Gould, Schaaf, and Ruigh (1951) in an investigation of the cleavage of cholesteryl ethers with sodium alkyls proposed a similar mechanism.



Potter (1969) observed that when substituted THFs were reacted with n-butyllithium, not only was α -cleavage taking place, but β -cleavage (abstraction of a β -proton followed by elimination) was occurring in some instances. Some examples of α - and β -cleavage are shown in Figure 3. A possible mechanism for β -cleavage was proposed whereby elimination can occur through a six-membered ring transition state (11).

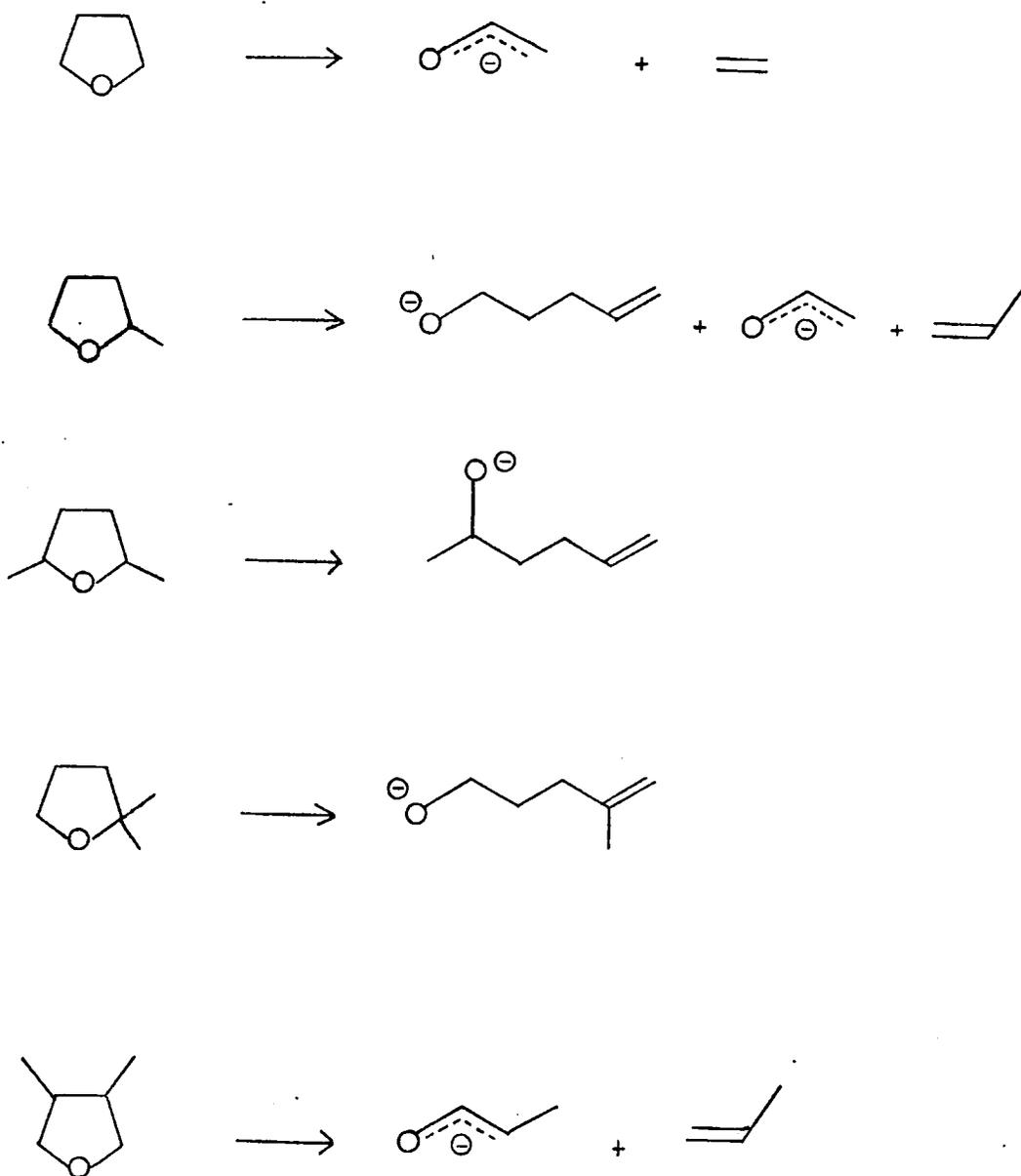
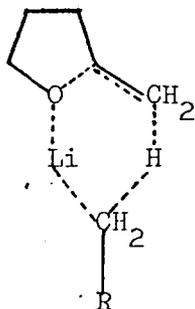


Figure 3. Examples of α - and β -cleavage of substituted tetrahydrofurans.



(11)

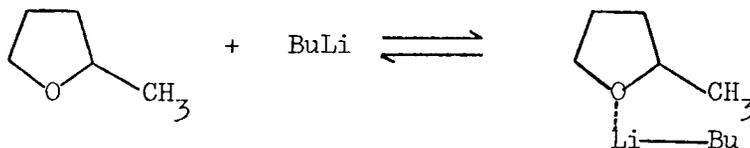
In the cases of β -cleavage where methyl groups are attached to the α -position of THF [(7), (8), and (9)], both cis- and trans- β -elimination processes are geometrically possible without too much strain. In the case of THF, models show that there is too much strain for the β -protons to attain the proper geometry for β -cleavage. No β -cleavage of THF has been detected.

Solvation Effects of Substituted Tetrahydrofurans

An investigation of the effect of solvent structure on the solvation of alkali ions was conducted by Chan and Smid (1968). THFs substituted in the α -position were found to be much poorer solvents for alkali solvation than THF or THFs substituted in the β -position. Thus, steric hindrance from substituents in the α -position affects the solvation of the alkali ion. Substituents in the β -position are located closer to the periphery of the solvating shell and have little effect on the solvation.

As more methyl groups are placed on the α -position, β -cleavage was found to progress more slowly which would be expected in accordance with the solvation studies. This seems to indicate that an

ether-butyllithium complex (12) is formed in the first step of the cleavage reaction.



(12)

When α -cleavage reactions are considered, no α -cleavage is detected for 2,2-dimethyltetrahydrofuran even though it has two secondary α -protons available for abstraction. The steric hindrance afforded by the two methyl groups might prevent the butyllithium of the ether-butyllithium complex from abstracting an α -proton. However, formation of a six-membered ring transition state for β -cleavage is quite conceivable. Both α - and β -cleavages are observed with 2-methyltetrahydrofuran. The ether molecules are near enough to permit both types of cleavage.

EXPERIMENTAL

Infrared (IR) spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer Model 137 B. Mass spectra were determined with a Hitachi-Perkin-Elmer RMU-6E Double Focusing Mass Spectrometer. Nuclear magnetic resonance (nmr) spectra were recorded at 60 MHz on a Varian HA-60 spectrometer and at 100 MHz on a Varian HA-100 spectrometer. Molecular sieves (4-A) activated by heating at 210° for 8 hr were used to dry the tetrahydrofurans. Melting points are uncorrected.

Reaction of THF with n-Butyllithium (Potter 1969)

Tetrahydrofuran (Mallinckrodt Chemical Works, 1.0 ml, 0.012 mole, dried by distillation over sodium and then stored over molecular sieves) was added to an nmr tube and cooled in a Dry Ice-isopropanol bath; n-butyllithium (Foote Mineral Company, 0.5 ml, 0.008 mole) was added and the nmr tube sealed. The reactants were mixed thoroughly while allowing the nmr tube to warm to room temperature. The reaction mixture turned a very pale yellow after several min. After 120 min at 33° the reaction was essentially complete as shown by nmr ($t_{1/2} = 8.4 \times 10^2$ sec, $k = 8.2 \times 10^{-4}$ sec⁻¹).

Reaction of 3-Methyltetrahydrofuran with n-Butyllithium

To an nmr tube, 3-methyltetrahydrofuran (Aldrich Chemical Company, 0.60 ml) was added, cooled in a Dry Ice-isopropanol bath, and

n-butyllithium (0.5 ml) was then added and the nmr tube sealed. The reactants were mixed thoroughly as the nmr tube was allowed to very slowly warm to room temperature. The solution turned a pale yellow after several min. After 220 min at 33° the reaction was essentially complete as shown by nmr ($t_{1/2} = 28.8 \times 10^2$ sec, $k = 2.4 \times 10^{-4}$ sec⁻¹). The solution was a deeper yellow.

2,2,3,3-Tetramethylbutan-1,4-diol

Analytical grade THF was refluxed over sodium, distilled, and collected over molecular sieves. Dry THF (100 ml) was added to a 200-ml, 2-necked, round-bottom flask. A condenser equipped with a calcium chloride drying tube at one end was placed in one neck of the flask. The flask was then cooled in an ice-water bath and 1.0 g of lithium aluminum hydride (Ventron Metal Hydrides) was added slowly in very small quantities. Tetramethylsuccinic anhydride (0.4864 g, 0.0031 mole) in 3 ml of dry THF was slowly added dropwise to the stirred solution. The reaction mixture was refluxed for 16 hr and the unreacted LAH was then destroyed by slowly adding dropwise 1 ml of H₂O, 1 ml of 15% NaOH, and finally 3 ml more of H₂O. The solution was stirred for 1 hr more to insure the complete destruction of the LAH. The liquid was decanted off and the white solids rinsed with ether. Evaporation left the crude diol as a yellowish-white solid.

Recrystallization from ligroin (bp 60-90°) gave 0.2133 g (47.1%) of diol, mp 210-212° (sealed capillary; reported by Ansell, Hickinbottom, and Holton (1955), 224°). An IR spectrum (KBr) showed a very strong -OH

at 3.1μ and gem-dimethyl absorption at 7.22μ and 7.32μ . The nmr spectrum showed the expected singlets for the methylene and methyl groups at $\tau 6.70$ and $\tau 9.08$, respectively, and a broad peak at $\tau 4.72$ for the hydroxyl protons.

3,3,4,4-Tetramethyltetrahydrofuran

Analytical grade dimethyl sulfoxide (DMSO, Mallinckrodt Chemical Works) was distilled under vacuum according to the procedure of Gillis and Beck (1963) in order to remove some decomposition products.

A 10-ml, round-bottom flask was equipped with a 6-in ($\frac{1}{2}$ in diam) glass tube. The other end of the tube was attached to a condenser fitted with a CaCl_2 drying tube. A mixture of the 2,2,3,3-tetramethylbutan-1,4-diol (0.2218 g) and DMSO (1.3 ml) was added to the flask which was then heated for 16 hr at 160° . The white crystalline mass on the upper walls of the tube was transferred to a microhickman flask and was resublimed at 100° to give 0.0820 g (42.1%) of 3,3,4,4-tetramethyltetrahydrofuran, mp $106-107^\circ$. The mass spectrum showed peaks at 28, 32, 41, 43, 56 (base), 72, 83, and 128 (parent), and the nmr spectrum consisted of singlets at $\tau 6.41$ and $\tau 9.08$ in a 1:3 ratio.

Reaction of 3,3,4,4-Tetramethyltetrahydrofuran with n-Butyllithium

A solution of 3,3,4,4-tetramethyltetrahydrofuran (100 mg, 0.78 mmole) and 0.05 ml of pentane was added to a thick-walled nmr tube. The nmr tube was heated in an oil bath to drive off the pentane. The reaction mixture was then cooled in a Dry Ice-isopropanol bath, 0.05 ml (0.08 mmole) of n-butyllithium was added, and the cap of the nmr tube

was sealed with Apiezon wax. After 60 min at 80°, the butyllithium peaks in the nmr spectrum at τ 11.0 were gone ($t_{1/2} = 10.5 \times 10^2$ sec, $k = 6.6 \times 10^{-4}$ sec⁻¹). The solution was pale yellow. The nmr tube was unsealed and the reaction product 3,3-dimethylenolate was hydrolyzed with 1 drop of H₂O. The enolate peak at τ 3.44 disappeared and a broad singlet peak at τ 0.33 appeared due to isobutyraldehyde.

Reaction of Hexahydrooxepin with n-Butyllithium

Hexahydrooxepin (Chemical Samples Company, 0.67 ml) was added to a nmr tube, cooled in a Dry Ice-isopropanol bath, and then 0.5 ml of n-butyllithium was added. The reaction was followed by nmr and was essentially complete after 19 hr. The solution was brownish-yellow at the end of the reaction ($t_{1/2} = 18.0 \times 10^3$ sec, $k = 3.9 \times 10^{-5}$ sec⁻¹).

Reaction of Tetrahydropyran (THP) with n-Butyllithium

Dry THP (Aldrich Chemical Company, 0.67 ml) was added to a nmr tube, cooled in a Dry Ice-isopropanol bath, and then 0.5 ml of n-butyllithium was added. The reactants were mixed thoroughly while the nmr tube slowly warmed to room temperature. The reaction was run at 33° and was followed by nmr. After 4 hr a yellow precipitate formed, but no cleavage of the THP could be detected. The nmr tube was heated at 80° in an oil bath for 3 days, but still no reaction products were seen in the nmr spectrum even though the n-butyllithium absorption at τ 11.0 was gone.

The sealed nmr tube was broken open and the ether layer was decanted from the precipitate. To one-half of the very fine crystals H₂O

(10 drops) was added to dissolve them completely. The remaining half of the solid was dissolved with 10 drops of D_2O . A mass spectrum was run on each of these samples.

Tetrahydropyran (3.5 ml) was mixed with 2.5 ml of n-butyl-lithium in a sample bottle and was allowed to form a very fine crystalline precipitate. The entire sample was then transferred to a 15-ml, round-bottom flask and 2.5 ml of methyl iodide was added. A reflux condenser with a $CaCl_2$ drying tube at one end was attached to the flask. The flask was heated in an oil bath and the reaction mixture was refluxed for $2\frac{1}{2}$ hr. The nmr spectrum showed only THP and CH_3I .

Rotation Barrier in Lithium 3,3-Dimethylenolate

The sealed nmr tube, in which 3,3,4,4-tetramethyltetrahydrofuran and n-butyllithium were reacted, was reopened. A micropipet which was attached to a nitrogen source was inserted into the tube to prevent any moisture from hydrolyzing the 3,3-dimethylenolate. The reaction tube was heated in an oil bath to drive off isobutylene, another product of this reaction, and some of the hexane which is used as the solvent for n-butyllithium. The tube was resealed, heated to 100° using the high-temperature apparatus of the HA-100, and the nmr spectrum showed no change.

DISCUSSION OF RESULTS

Several substituted tetrahydrofurans and related ethers were reacted with n-butyllithium to help delineate the scope of the synthesis of lithium enolates of aldehydes by this approach (Pötter 1969). These reactions were carried out using a 15-fold excess of the ether, thereby making the reaction pseudo first-order in butyllithium. Table 1 summarizes the rate constants and half-lives for these reactions.

Reaction of 3-Methyltetrahydrofuran with n-Butyllithium

The reaction between 3-methyltetrahydrofuran and n-butyllithium was found to produce lithium enolate, lithium 3-methylenolate, ethylene, propylene, and butane (13). The reaction goes quantitatively as shown by the complete disappearance of the triplet at τ_{11} due to n-butyllithium and the appearance of corresponding amounts of both enolates,

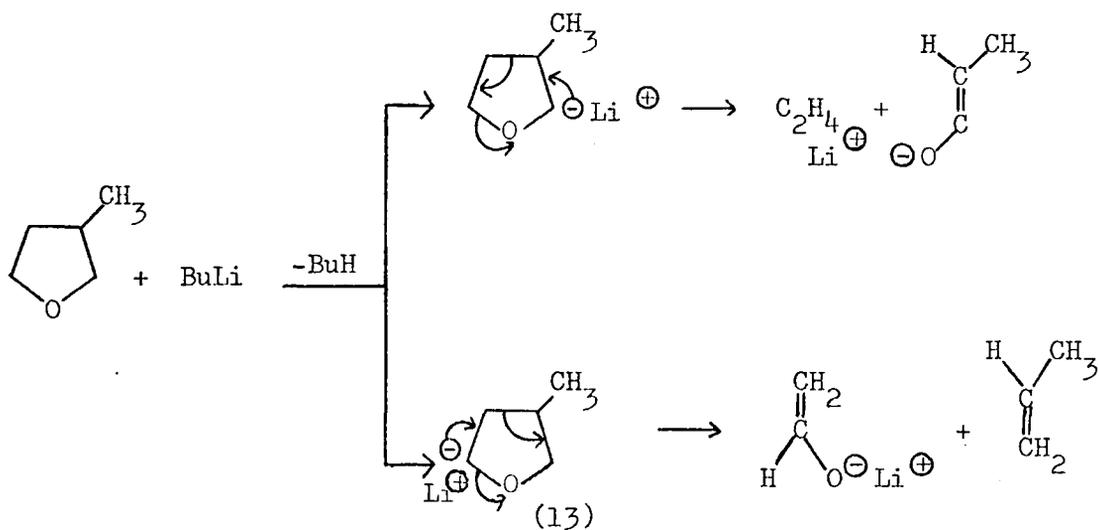


Table 1. Kinetic studies on ethers at 33°.

Ether	$t_{1/2}$ (sec)	k (sec ⁻¹)
THF	8.4×10^2	8.2×10^{-4}
3-methyl-THF	28.8×10^2	2.4×10^{-4}
3,3,4,4-tetramethyl-THF ^a	10.5×10^2	6.6×10^{-4}
Hexahydrooxepin	18.0×10^3	3.9×10^{-5}

a. Values given are for 80°.

propylene, and ethylene. The nmr spectrum (locked on the methylene peak of the hexane) shown in Figure 4 consists of a singlet at τ 4.66 due to ethylene, a downfield quartet at τ 3.04 due to enolate, a doublet at τ 3.22 due to 3-methylenolate, doublets at τ 4.98 and τ 5.12 and a multiplet at τ 4.24 due to propylene. Two other quartets which are associated with enolate absorb in the same regions (τ 6.4 and τ 6.85, Potter 1969), as 3-methyl-THF. The other doublet which is expected for 3-methylenolate also absorbs in the same region as the THF derivative (τ 6.3, Potter 1969). Figures 6 and 7 show the chemical shifts in τ units and the coupling constants in Hertz (Hz) for enolate and 3-methylenolate, respectively.

The unsymmetrical 3-methyl-THF affords two different lithium enolates upon cleavage. Lithium enolate appears to be the favored product by a ratio of 1.3 to 1.0 of enolate to 3-methylenolate. Thus, abstraction of an α -proton in the 5-position seems to be favored over abstraction in the 2-position. This may be a simple steric effect, or possibly an electronic one: the methyl group in the 3-position tends to donate more electron density through an inductive effect to the 2-position, rendering those protons less acidic than those in the 5-position.

Reaction of 3,3,4,4-Tetramethyl-THF with n-Butyllithium

The 3,3,4,4-tetramethyl-THF had not been prepared previously, but the corresponding diol, 2,2,3,3-tetramethylbutan-1,4-diol, had been synthesized from ethyl tetramethylsuccinate (Ansell et al. 1955) as

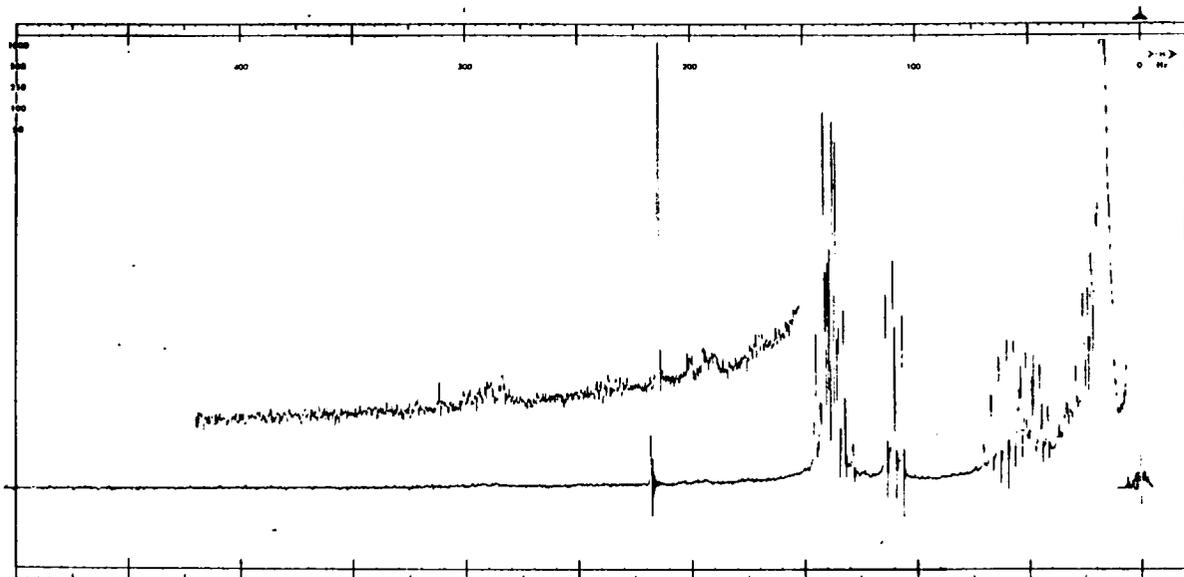


Figure 4. Nmr spectrum of lithium enolate, lithium 3-methylenolate, ethylene, and propylene.

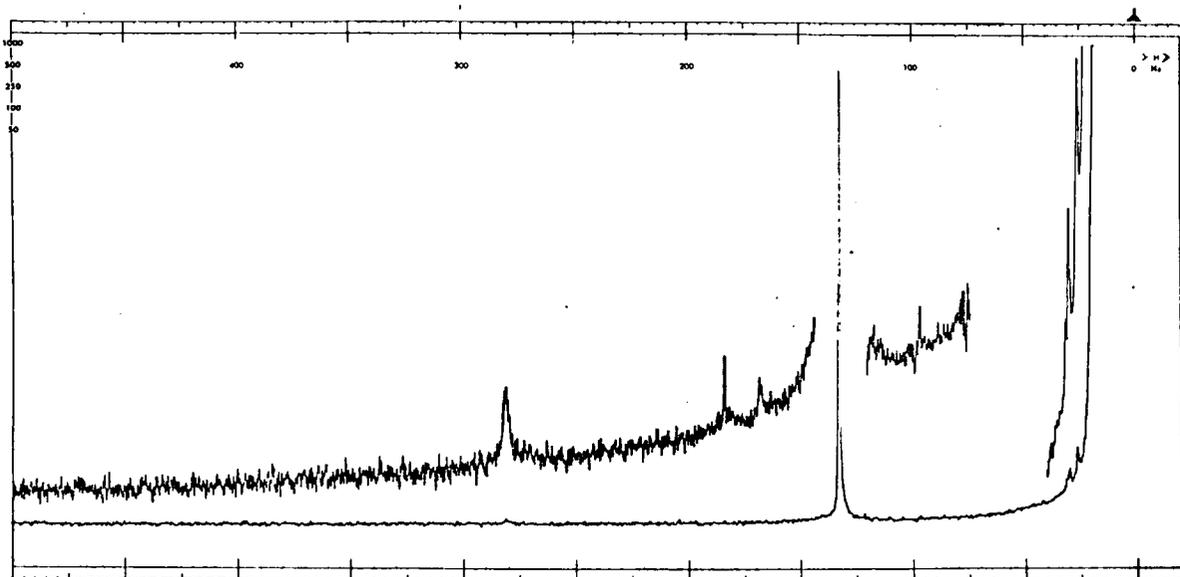
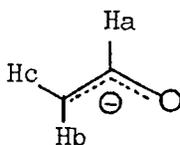
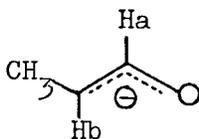


Figure 5. Nmr spectrum of lithium 3,3-dimethylenolate and isobutylene.



<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	3.04	Jab	14.0
Hb	~ 6.4	Jac	6.0
Hc	~ 6.85		

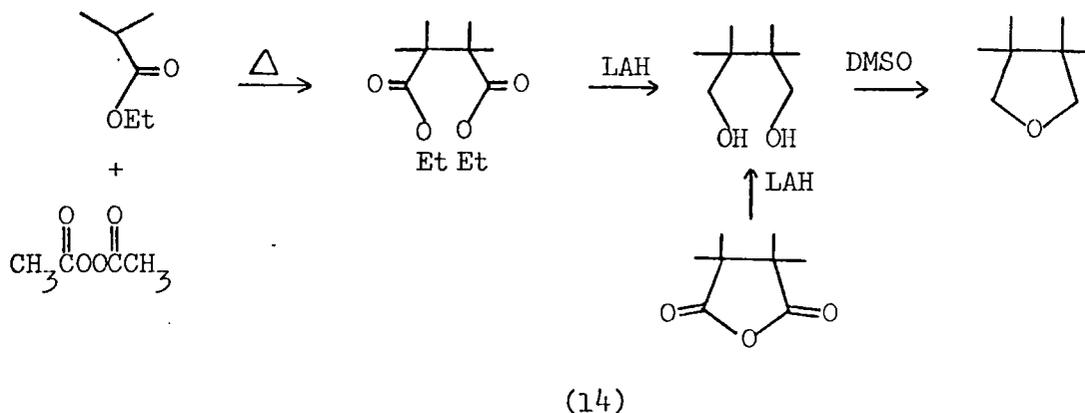
Figure 6. Nmr parameters for lithium enolate at 33° .



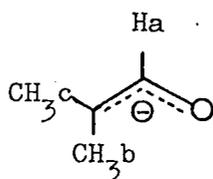
<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	3.22	Jab	12.0
Hb	~ 6.3		

Figure 7. Nmr parameters for lithium 3-methylenolate at 33° .

shown below (14). In the current work, this diol was prepared in 47% yield by lithium aluminum hydride reduction of tetramethylsuccinic anhydride (Potter 1969) and was smoothly converted (42% yield) to the THF derivative by heating in dimethylsulfoxide (Gillis and Beck 1963).

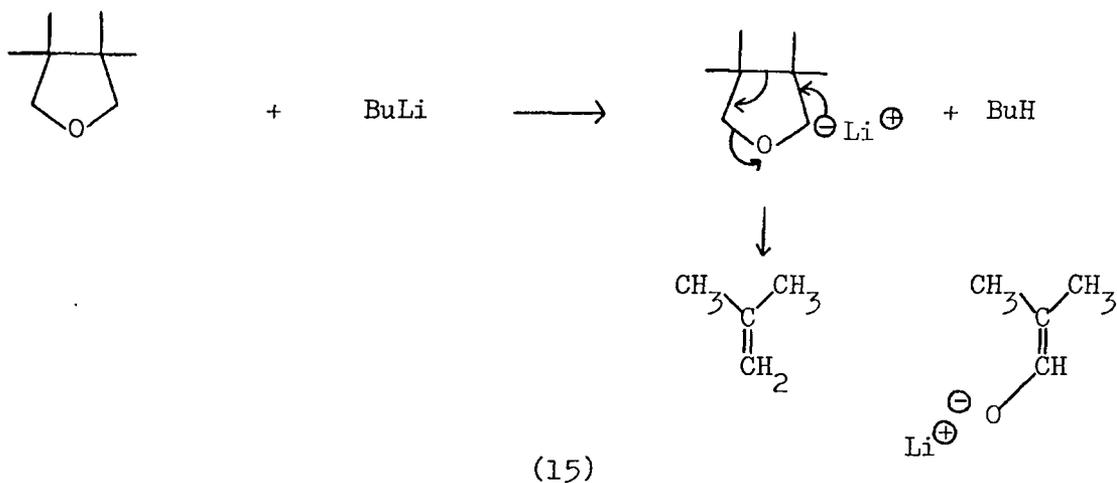


The reaction between 3,3,4,4-tetramethyl-THF and n-butyllithium produced the expected α -cleavage products, isobutylene and lithium 3,3-dimethylenolate (15). The reaction was unobservably slow at 33°, presumably for steric reasons, so it was run at 80°. The nmr spectrum (locked on the methylene peak of hexane) presented in Figure 5 consists of a multiplet at τ 5.37 due to isobutylene and a multiplet at τ 3.44 due to the enolate. The methyl groups on the enolate were seen as singlets at τ 8.44 and τ 8.51. The particular τ values were assigned to the methyl groups by analogy with the corresponding protons in lithium enolate. The nmr parameters for this anion are given in Figure 8. Hydrolysis gave isobutyraldehyde, as shown by the disappearance of the 3,3-dimethylenolate multiplet at τ 3.44 and the appearance of a singlet at τ 0.33 due to the aldehyde proton.



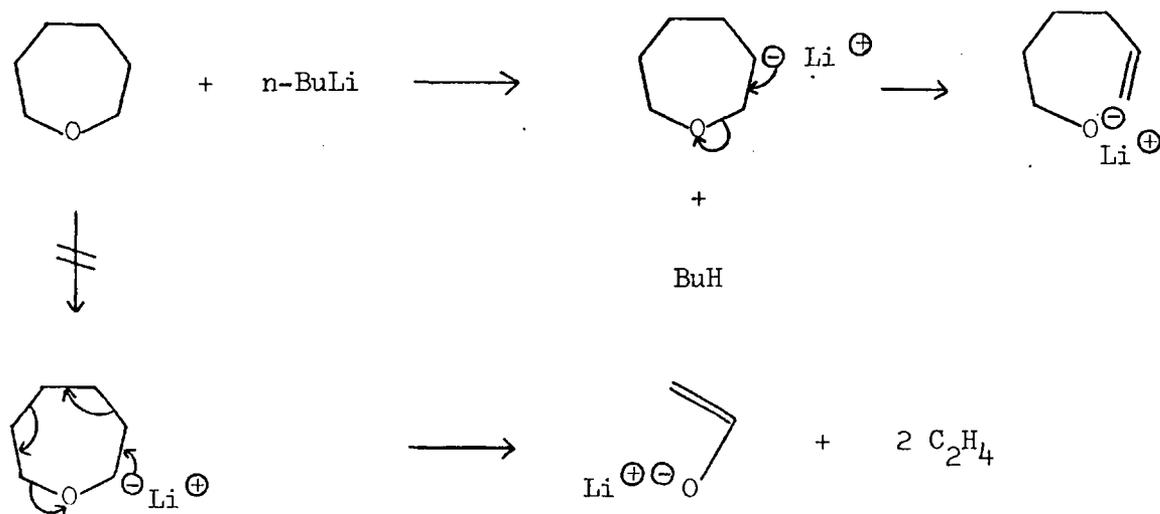
<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	3.44		
CH ₃ b	8.44	Jbc	7.0
CH ₃ c	8.51		

Figure 8. Nmr parameters for lithium 3,3-dimethylenolate at 33°.



Reaction of Hexahydrooxepin with n-Butyllithium

By analogy with the observed α -cleavages of THF, it was anticipated that hexahydrooxepin might α -cleave to give lithium enolate and 2 molecules of ethylene as shown below (16). However, no evidence for either of these products was obtained. The reaction of hexahydrooxepin with n-butyllithium instead produces the lithium salt of 5-hexen-1-ol.



The nmr spectrum (locked on the methylene peak of hexane) presented in Figure 9 consists of a broad multiplet at τ 5.48 due to the methylene group on the alkoxide ion, and a broad multiplet at τ 4.18 and doublets at τ 4.98 and τ 5.12, all due to the three vinyl protons. The nmr parameters are given in Figure 10. Thus, hexahydrooxepin reacts with n-butyllithium by β -cleavage involving abstraction of a β ring proton, a process unobserved with any THF derivatives. Models of hexahydrooxepin show that the β -protons can, without considerable strain, attain the proper geometry for the formation of a six-membered ring transition state through which the elimination process is thought to proceed (Potter 1969, Letsinger and Bobko 1953).

During the kinetic investigation of the reaction of n-butyllithium with hexahydrooxepin, a broad multiplet at τ 4.57 was observed early in the reaction. This peak is probably due to a complex of the ether with butyllithium. As the reaction progresses, the peak decreases due to the further β reaction of the butyllithium with the ether to give the β -cleavage product. This is the first observation of α -methylenes being separated from characteristic α -methylene peaks of cyclic ethers.

Reaction of Tetrahydropyran with n-Butyllithium

Cleavage products of the reaction of tetrahydropyran with n-butyllithium could not be detected. Instead a yellow precipitate began to form several hours after the reaction was started. The nmr spectrum was run on this reaction mixture, but only THP could be detected. The precipitate could possibly have been LiOH, which would form by reaction

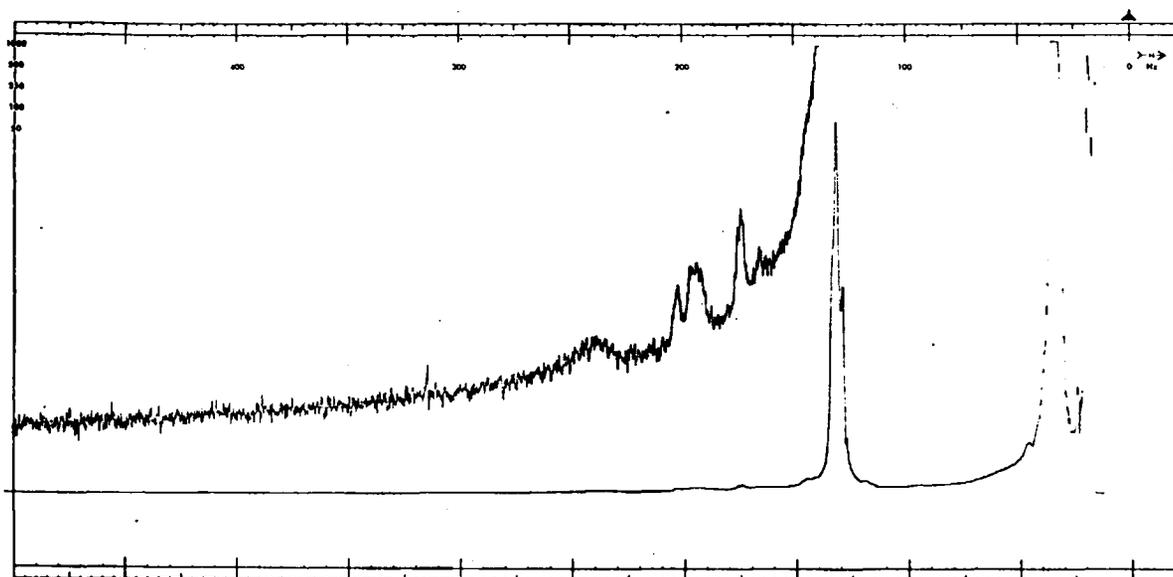
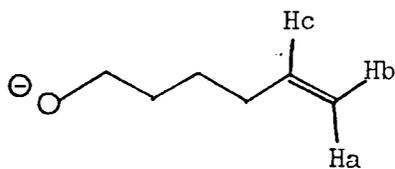


Figure 9. Nmr spectrum of lithium salt of 5-hexen-1-ol.



<u>Chemical Shifts (τ)</u>		<u>Coupling Constants (Hz)</u>	
Ha	4.98	Jac	16.0
Hb	5.12	Jbc	10.0
Hc	4.18		

Figure 10. Nmr parameters for lithium salt of 5-hexen-1-ol at 33°.

with water that may have been in the THP, so the THP was distilled and collected over molecular sieves. The reaction was then run again using a sealed nmr tube to prevent moisture from entering the tube. A precipitate was once more obtained. Heating the reaction mixture for 3 days at 80° did not facilitate any reaction. The precipitate was divided into two portions. To one sample H_2O was added and to the other sample D_2O was added to determine whether or not the precipitate was some sort of lithium salt. Mass spectra of these samples proved fruitless. Only water could be detected.

Another endeavor was undertaken to determine the nature of the solid by attempting to methylate it. Methyl iodide was added to the precipitate and the mixture was refluxed for $2\frac{1}{2}$ hr. The nmr spectrum demonstrated only THP and CH_3I . Consequently, the composition of this precipitate remains to be determined.

Speculation can, however, be made concerning THP. Tetrahydropyran exhibits no ring strain and has never been polymerized (Dainton and Ivin 1958); n-butyllithium is probably too weak to abstract a proton and effect a cleavage reaction. The precipitate may still be only LiOH which could form from moisture which is present in the air space above the reaction mixture in the sealed tube. If the reagents were added to the nmr tube under a nitrogen atmosphere, this might shed some light on the problem.

Rotation Barrier in Lithium
3,3-Dimethylenolate

Potter (1969) investigated the rotation barrier in lithium enolate. The terminal protons in the anion are nonequivalent at room temperature, so the anion was heated in a sealed nmr tube to try to cause rotation about the carbon-carbon bond fast enough so that the terminal protons become equivalent. The lithium enolate was heated to 125° with no observable change in the nmr spectrum. The rotation barrier was calculated to be quite high, $\Delta G^\ddagger > 20$ kcal/mole.

An attempt was made to study the barrier to rotation in 3,3-dimethylenolate. The enolate has 2 terminal methyl groups which are nonequivalent at room temperature. They can be readily seen in the nmr spectrum at $\tau 8.44$ and $\tau 8.51$. A sample was heated to 100° in a sealed nmr tube. There was no observable change in the appearance of the methyl peaks in the spectrum. Above 100°, a spectrum could not be obtained since the sample, which still contained some hexane from the n-butyllithium, boiled to the upper part of the tube and out of range of the nmr probe. The rotation barrier was calculated to be at least 21 kcal/mole.

CONCLUSION

In this study, it was found that enolates of aldehydes with 2 β -alkyl substituents may be readily prepared in high yield if the corresponding symmetrical THF derivative is available. Ethers substituted in the α -position react to give a mixture of α - and β -cleavage products or only β -elimination products, so they are of little utility in enolate syntheses (Potter 1969). The products from the cleavage of 3-methyl-THF indicate that unsymmetrical THFs with only β -substituents will also be of little value in enolate syntheses, since mixtures of enolates (with the undesired enolate predominating) will result. Figure 11 shows THF cleavages which are useful in the preparation of enolates of aldehydes.

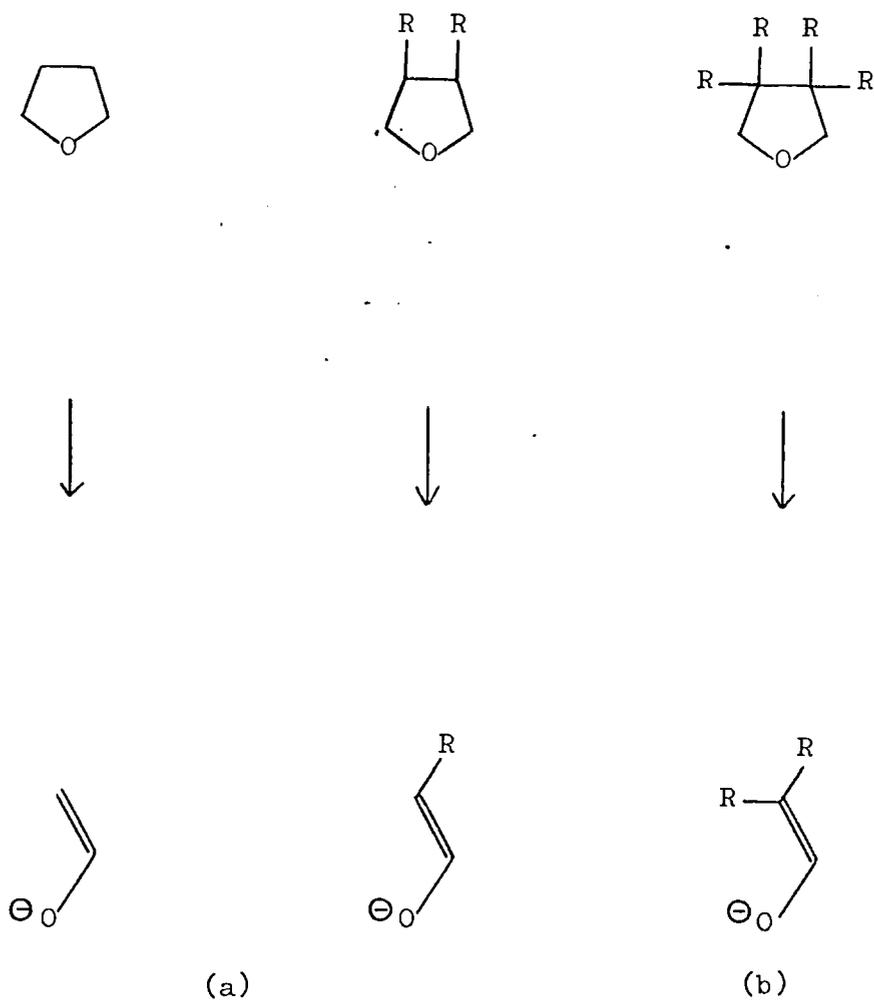


Figure 11. THF cleavages useful in the synthesis of enolates of aldehydes.

(a) Potter 1969

(b) This study

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