

Direct Observation of Acyl Anion Equivalents by Carbon-13 Fourier Transform Nuclear Magnetic Resonance

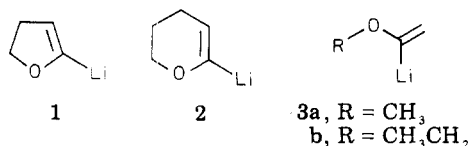
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Received April 4, 1980

The vinyl anions derived from 2,3-dihydrofuran, 2,3-dihydro-4H-pyran, and ethoxyethene have been examined by carbon-13 FT NMR. The vinyl C-H coupling constants ($^1J_{13C-1H}$) have been measured for the ethers and the anions. Observation of vinyl anions derived from vinyl ethers is readily accomplished with carbon-13 NMR. While all carbon resonances are shifted upon formation of the anion the most obvious effect is the large (56-61 ppm) downfield shift of the vinyl carbon bonded to lithium. In no case was allylic deprotonation observed under the reaction conditions.

Masked acyl anions derived from the vinyl ethers have generated considerable interest primarily due to their successful applications in organic synthesis.¹⁻⁷ Recently, 1-3 have been shown to be useful synthetic equivalents



of acyl anions. Boeckman and Bruza prepared 1 and 2 by allowing the appropriate vinyl ether to react with 1.1 equiv of *t*-BuLi/0.5 equiv of THF at -78 to 5 °C.⁶ The resulting carbanions reacted with a variety of electrophiles to afford the expected products in good to excellent yields. 3b has been prepared by Schöllkopf and Hänssle.¹ Baldwin and co-workers have deprotonated methoxyethene (to give 3a) by the addition of *tert*-butyllithium in pentane to a cold (-65 °C) solution of the vinyl ether in THF and subsequent warming to ca. 0 °C.²

We have found that 1 and 2 may be prepared conveniently at ambient temperature from the corresponding ether with *n*-butyllithium in hexane and a catalytic amount of tetramethylethylenediamine (TMEDA). In the present study, 3b was synthesized by the metalation of ethoxyethene in THF with *tert*-butyllithium.

The metalation of 2,3-dihydrofuran and 2,3-dihydro-4H-pyran to give 1 and 2 poses several interesting questions. Why do alkyllithium reagents abstract vinylic protons in preference to allylic protons in these systems? Is carbon-13 NMR a useful probe of anion formation and of ring-size effects and conformational changes of the cyclic vinyl ethers and their respective vinyl anions? Can the percent s character, as determined from $^1J_{13C-1H}$ of the α -vinyl C-H bond in the ether, be correlated with the chemical shift of the metalated vinyl carbon atom?

We here report the first direct observation of the lithiated vinyl ethers 1-3 by carbon-13 NMR. In addition, we have measured the vinyl $^1J_{13C-1H}$ coupling constants for 2,3-dihydrofuran, 2,3-dihydro-4H-pyran, and ethoxyethene and for the anions derived from these ethers.

Results and Discussion

The carbon-13 shifts for the vinyl ethers and the metalated products are presented in Table I. Typical car-

Table I. ^{13}C Chemical Shifts^a of Vinyl Ethers and Lithiated Vinyl Ethers

vinyl ethers	lithiated vinyl ethers	$\Delta\delta$
28.49, 98.41, 68.63, 145.6	30.70, 109.6, 56.04, 202.5	+2.21, -56.6
22.55, 99.22, 64.91, 144.0	24.71, 111.1, 62.8, 201.2	-2.16, +11.9, -2.11, +57.2
13.55, 84.65, 62.35, 151.4	14.45, 93.46, 56.83, 212.1	+9.0, -5.52, -60.7

^a In parts per million relative to external Me₄Si.

Table II. Vinyl $^1J_{13C-1H}$ Coupling Constants and Percent s Character^a

174.5 (34.9), 189.3 (37.8), 160.0 (32.0), 185.0 (37.0), 160.8 (32.2), 156.4 (31.3), 160.1 (36.0), 165.9 (33.1), 154.8 (31.0), 156.0 (31.2), 154.6 (30.9)

^a In parentheses.

bon-13 spectra are shown in Figure 1. In Table I are also listed the $\Delta\delta$ values ($\delta_{\text{anion}} - \delta_{\text{neutral}}$) for each vinyl ether/lithiated vinyl ether pair. Formation of the lithiated species is readily confirmed in all cases by the large downfield shift (56-61 ppm) observed upon lithiation of the vinylic carbon atom bonded to oxygen and by the off-resonance spectra which show a singlet for the metalated carbon. The resonance of the β -vinyl carbon is also shifted downfield (9-12 ppm). The downfield shifts of the α - and β -vinyl carbons on formation of the anions are not unexpected as similar results have been reported for phenyllithium⁸ and ortho-lithiated *N,N*-dimethylbenzylamines.⁹ The resonance of the saturated carbon atom α to oxygen is unique in that it is shifted upfield upon metalation. The origin of these shift differences is undoubtedly complex and in addition to anisotropy effects arising from the electron pair on the vinylic carbon of the anion^{8,9} conformational changes upon metalation (see below) may make small contributions to the shift differences.

Electrophiles react at the metalated vinyl carbon to give the expected products (see the Experimental Section).

In Table II are listed the $^1J_{13C-1H}$ coupling constants and the percent s character calculated (from $^1J_{13C-1H}/5$)¹⁰ for

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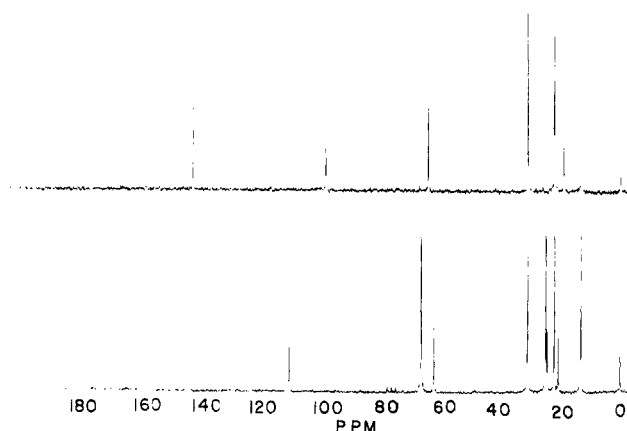
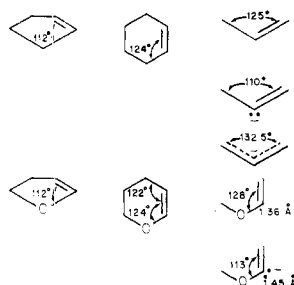


Figure 1. Carbon-13 NMR spectrum (22.625 MHz) of 2,3-dihydro-4H-pyran in hexane (top) and carbon-13 NMR spectrum of 6-lithio-2,3-dihydro-4H-pyran in THF/hexane (bottom).

Table III. Geometries of Selected Cycloalkenes and Vinyl Ethers^a



^a Geometries either estimated or taken from the literature: propene, cyclopentene, cyclohexene, 2-propenyl anion, allyl anion;¹¹ methoxyethene;¹² methoxyvinyl-lithium;¹³ and 2,3-dihydro-4H-pyran.¹⁴ The *s*-cis form of methoxyethene has been found to be the most stable with a barrier of 4.35 kcal/mol.¹⁵

each vinyl carbon orbital bonded to hydrogen in the ethers and the vinyl ether anions. The percent *s* character is greater for the vinyl carbons of the dihydrofuran than for the respective carbon orbitals of the dihydropyran. This result is consistent with the smaller O—C=C angle (112°) estimated (Table III) for the dihydrofuran as compared with that of the dihydropyran (124°). The C=C—C angle in the dihydropyran is estimated to be approximately 122°. The corresponding angle in the dihydrofuran is probably close to 112°. Calculations indicate that the C=C—O angle (128°) in methoxyethene contracts to ca. 113° upon formation of the vinyl anion.¹³ This substantial reduction in bond angle should be much less in the more constrained cyclic vinyl ethers. In view of these geometrical constraints and the lack of information on both the geometries of the cyclic vinyl anions and the percent *s*-character of the α -vinyl carbon orbitals of the anions, the trends observed in Table IV may be fortuitous. Nevertheless, it is tempting to suggest that the trend observed in the percent *s* character of the α -vinyl carbon orbitals of the three neutral vinyl ethers implies the relative kinetic acidities: dihydrofuran > dihydropyran > ethoxyethene.

We have not observed to date formation of allylic anions derived from the cyclic vinyl ethers. The absence of such

Table IV. Comparison of Shift and Geometrical Data for the α -Vinyl Carbon Atom of Vinyl Ethers

compd	$\Delta\delta(\alpha\text{-C})$	% <i>s</i> character of α -vinyl C-H of neutral vinyl ether	estimated C=C—O angle of neutral vinyl ether, deg
	+56.6	37.8	112
	+57.2	37.0	124
	+60.7	36.0	128

anions may be due to the expected relative instability of an allylic anion bonded at a terminal carbon atom to oxygen. Such a π system would be isoelectronic with the butadiene dianion. In addition, abstraction of an allylic proton would be expected to proceed at a slower rate than abstraction of the vinyl proton of the carbon atom bonded to oxygen. It has been reported that an allylic dihydropyranyllithium, prepared from 3,6-dihydro-2H-pyran and *n*-butyllithium in THF, has been trapped with trimethylsilyl chloride.¹⁶

Experimental Section

NMR Measurements. Proton NMR spectra were obtained on a JEOL C-60H 60-MHz spectrometer with shifts (δ) determined relative to internal Me₄Si. Broadband (5 W) proton-decoupled carbon-13 spectra were recorded at 22.625 MHz on a Bruker WH-90DS spectrometer equipped with a Nicolet 1180 16K computer/Diablo disk drive and a Bruker B-ST 100/700 C variable-temperature unit. Chemical shifts (δ) were measured relative to external Me₄Si. Carbon-13 spectra were obtained by securely positioning an 8-mm NMR tube containing the sample within a 10-mm NMR tube containing CDCl₃ (for lock) and Me₄Si. Generally, 800–1500 scans were collected at a pulse width of 3–5 μ s, in the quadrature detection mode, and with a sweep width of 5000 Hz (1.22 Hz/pt) or 5555 Hz (1.36 Hz/pt). A line broadening of 1.00 was employed in all cases. Off-resonance spectra were measured in the CW mode with a decoupler power of 0.5 W. Completely coupled spectra were obtained with sweep widths ranging from 400 to 5500 Hz, using 5000 to 53 000 scans.

Preparation of Lithiated Compounds. Glassware, syringes, syringe stopcock, and needles were dried in a 110 °C oven before use. THF was dried over sodium metal and distilled under argon. All reactions were carried out under argon.

A. 6-Lithio-2,3-dihydro-4H-pyran. To a stirred mixture of 4.0 g (0.048 mol) of 2,3-dihydropyran and 0.50 g 0.0043 mole of TMEDA at ambient temperature in a small reaction vessel was added 23 mL 0.058 mol) of 2.5 M *n*-butyllithium in *n*-hexane via syringe under an argon atmosphere. The metalated dihydropyran precipitated after several hours of slight heating to give an off-white solid. The mixture was centrifuged and hexane layer discarded. The solid was washed with (3 \times 10 mL), *n*-hexane giving a white solid which was then dissolved in dry THF. An aliquot was transferred via syringe under argon to an 8-mm NMR tube capped with a rubber septum. The carbon-13 spectrum was recorded at 308 K.

B. Preparation of 5-Lithio-2,3-dihydrofuran. To a freshly distilled sample of 2,3-dihydrofuran, 2.0 g (0.029 mol), was added 0.6 g (0.005 mol) of TMEDA. Then 15 mL (0.036 mol) of 2.4 M *n*-butyllithium was added rapidly via syringe until a precipitate began to form. The solution was cooled immediately with a room-temperature water bath, thus preventing dissolution of the solid. The remaining portion of *n*-butyllithium was added with intermittent cooling between additions to maximize precipitation. The hexane was removed after centrifugation and the solid washed

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with *n*-hexane (2 × 6 mL). The resultant white solid was dissolved in 1.2 mL of THF distilled from sodium and the solution transferred to a serum-capped 8-mm NMR tube.

C. Preparation of 1-Ethoxy-1-lithioethene. To an 8-mm NMR tube capped with a rubber septum was introduced 1.0 mL of freshly distilled THF. Ethoxyethene (0.25 g, 0.0035 mol) was added via syringe and the sample then cooled to -78 °C. Slow addition of 3.0 mL (0.0054 mol) of 1.8 M *tert*-butyllithium in *n*-pentane to the mixture caused formation of a yellow precipitate. After the tube was shaken intermittently, the solid dissolved at ca. -30 °C. The solution was recooled to -78 °C for 1 h and then warmed to -50 °C for 4 h. After the mixture was warmed to ambient temperature the carbon-13 spectrum showed quantitative conversion to the anion as well as a slight amount of the enolate of acetaldehyde and ethylene from the base-promoted decomposition of THF.

D. Preparation of 6-Methyl-2,3-dihydropyran. To a mixture of 3.0 g (0.036 mol) of 2,3-dihydropyran and 0.50 g (0.0043 mol) of TMEDA was added 18.0 mL (0.045 mol) of 2.5 M *n*-butyllithium in hexane. This solution was stirred overnight, the resulting suspension was centrifuged, and the hexane was removed. The solid was washed with ethyl ether and then suspended in that solvent. An excess of methyl iodide was added cautiously to the ether solution. This mixture was stirred for 3 h and the solution then filtered. The carbon-13 spectrum showed greater than 95% conversion of the anion to 6-methyl-2,3-dihydropyran. The shifts were 150.7, 95.0, 65.8, 22.3, 20.2, and 19.7 ppm.

E. Preparation of 6-Deuterio-2,3-dihydropyran. To 4.0 g (0.048 mol) of 2,3-dihydropyran in a serum-capped reaction vessel was added 23 mL (0.058 mol) of 2.5 M *n*-butyllithium in *n*-hexane. After several hours the lithiated vinyl ether precipitated. The solid was centrifuged and washed with hexane (3 × 10 mL) and then suspended in 10 mL of hexane. To this suspension was added excess D₂O and the layers were subsequently separated. The carbon-13 spectrum of the hexane layer showed a conversion of more than 95% of the anion to the 6-deuterio-2,3-dihydropyran. The shifts were 143.78 (t), 98.63, 64.69, 22.55, and 19.21 ppm. Proton NMR indicated the virtual absence of the α -vinyl ¹H resonance of the starting material.

F. Preparation of 5-Methyl-2,3-dihydrofuran and 5-(Trimethylsilyl)-2,3-dihydrofuran. Dihydrofuran (2.0 g, 0.029 mol) and TMEDA (0.6 g, 0.005 mol) were mixed and then 15.0

mL (0.032 mol) of 2.1 M *n*-butyllithium in hexane was added. The reaction mixture was cooled to room temperature after precipitation began. The solid was washed with hexane (2 × 4 mL) and then excess methyl iodide in ethyl ether or excess trimethylsilyl chloride was added cautiously. The solution containing the 5-methyl-2,3-dihydrofuran was centrifuged and the carbon-13 spectrum indicated ca 85% conversion to the methyl derivative based upon the washed anion. The 5-(trimethylsilyl)-2,3-dihydrofuran was distilled and the carbon-13 spectrum showed greater than 95% conversion based upon the washed anion. The shifts for the methyl derivative were 154.8, 93.55, 69.43, 29.94, and 12.73 ppm. The shifts for the trimethylsilyl derivative were 162.2, 109.9, 69.66, 30.39, and -2.76 ppm.

G. Preparation of 5-Deuterio-2,3-dihydrofuran. To a solution of 0.9 g (0.013 mol) of 2,3-dihydrofuran and 0.3 g (0.0025 mol) of TMEDA was added rapidly 6.0 mL (0.013 mol) of 2.1 M *n*-butyllithium until precipitation of solid began. The reaction mixture was cooled with a room-temperature water bath and then addition of *n*-butyllithium was completed. The resulting solid was washed with hexane (3 × 4 mL) and then suspended in 1.0 mL of hexane. To this solution was added 1.0 mL of D₂O. The carbon-13 and proton NMR spectra showed essentially quantitative conversion to the deuterio compound. The carbon-13 shifts were 145.40 (t), 97.11, 68.20, and 28.38 ppm.

H. Preparation of 1-Deuterio-1-ethoxyethene. To the sample of the 1-lithio-1-ethoxyethene used in the NMR study described previously was added excess D₂O. The top layer was separated. The carbon-13 spectrum of this layer indicated a 70% yield of the deuterated product. The carbon-13 shifts were 150.65 (t), 83.79, 61.62, and 13.11 ppm.

Acknowledgment. We are grateful to the Faculty Research Committee of Miami University for partial support of this research.

Registry No. 2,3-Dihydrofuran, 1191-99-7; 2,3-dihydropyran, 110-87-2; ethoxyethene, 109-92-2; 5-lithio-2,3-dihydrofuran, 75213-94-4; 6-lithio-2,3-dihydro-4H-pyran, 72081-15-3; 1-ethoxy-1-lithioethene, 40207-59-8; 6-methyl-2,3-dihydropyran, 16015-11-5; 6-deuterio-2,3-dihydropyran, 75213-95-5; 5-methyl-2,3-dihydrofuran, 1487-15-6; 5-(trimethylsilyl)-2,3-dihydrofuran, 75213-96-6; 5-deuterio-2,3-dihydrofuran, 75213-97-7; 1-deuterio-1-ethoxyethene, 75213-98-8.

Neighboring-Group Participation by Hydroxyl Oxygen in Nucleophilic Aromatic Substitution. Smiles Rearrangements of (ω -Hydroxyalkyl)methyl(*p*-nitrophenyl)sulfonium Perchlorates in Aqueous Alkali

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Received April 9, 1980

(2-Hydroxyethyl)- (1), (3-hydroxy-*n*-propyl)- (2), and (4-hydroxy-*n*-butyl)methyl(*p*-nitrophenyl)sulfonium perchlorates (3) were prepared. Products by Smiles rearrangements (intramolecular S_NAr reactions) were obtained from 1 as β -(methylthio)ethyl *p*-nitrophenyl ether (9) in 37-42% yield and from 2 as γ -(methylthio)propyl *p*-nitrophenyl ether (8) in quantitative yields, and none were obtained from 3. The rearrangement rates and yields were compared with an intermolecular S_N2 reaction of dimethyl(*p*-nitrophenyl)sulfonium perchlorate (4) (displacement of the sulfonium group by a *n*-propoxy group) to estimate participation by the ω -hydroxyl oxygen. The rate ratios between the rearrangements (first order) and the S_N2 *n*-propoxy attack (second order), effective molarities, were obtained as 6.02×10^3 M for 1 vs. 4 and 4.64×10^3 M for 2 vs. 4.

The importance of neighboring-group participation has been well recognized in carbonium ion reactions (e.g., solvolysis) and substitution reactions of carbonyl (e.g., ester hydrolysis) but not in other kinds of reactions.¹ Recent

papers including ours have provided evidence of participation by hydroxyl oxygen for the one-step substitution reactions at the saturated carbon (S_N2).²⁻⁴ Intramolecular

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