concentrated to an oil (9 g) which was chromatographed on alumina. The cobalt test for sulfonium salts was negative on both this oil and the aqueous layer.[29] Tlc of the oil showed bimesityl and mesityl sulfide to be absent. The column chromatography gave an initial fraction (5.5 g), shown to be primarily mesitylene by glc. A second fraction gave a white, crystalline, solid **14a**, mp 160–161° (acetone) [0.064 g, 1.7 mmol, 16%; mol wt by osometry in toluene, 390 (calcd, 388)].

Anal. Calcd for $C_{27}H_{32}S$: C, 83,51; H, 8.25; S, 8.25. Found: C, 83.50; H, 8.42; S, 7.98.

The remaining materials obtained from the chromatograph were not identified.

Oxidation of 14a. Compound **14a** (165 mg, 0.425 mmol) was dissolved in 15 ml of acetic acid–chloroform (2:1) and 30% hydrogen peroxide (180 mg, 1.6 mmol) in acetic acid solution (2.8 ml) added in 0.1–0.2-ml portions at room temperature. The reaction mixture was diluted with water and extracted with chloroform. The combined chloroform layers were washed with aqueous sodium carbonate and sodium bicarbonate, dried ($MgSO_4$), and concentrated to give an oil, which crystallized upon standing. Recrystallization gave 112 mg (0.28 mmol, 65%), mp 149–150° (aqueous EtOH). This product (67 mg) was further purified by preparative tlc (silica gel, methylene chloride) to give, after recrystallization, 27 mg of **14b**, mp 167–168° (MeOH).

Anal. Calcd for $C_{27}H_{32}OS$: C, 80.15; H, 7.97. Found: C, 80.21; H, 7.98.

Reaction of Triphenylsulfonium Bromide with Lithium Oxide. A slurry of triphenylsulfonium bromide (119 mg, 0.348 mmol) and lithium oxide (292 mg, 9.7 mmol) in ether was stirred continuously. After 2 days at room temperature, tlc (silica–chloroform) indicated the possible presence of phenyl sulfide. After 9 days, the mixture was hydrolyzed with dilute sulfuric acid and ether extracted. The dried ($MgSO_4$) ether extracts were concentrated to give an oil (51 mg) which was almost totally aliphatic (nmr), although a small aromatic peak (<2%) indicative of phenyl sulfide was present. Glc (5% SP-100 on 80/100 ABS, 6 ft × 2 mm, fid) gave a peak with the same retention time as phenyl sulfide. Chloroform extraction of the water layer, which was shown by the cobalt and bismuth spot tests[27] to contain a sulfonium salt, after the addition of sodium bromide (5 g) gave crude triphenylsulfonium bromide (171 mg).

Registry No.—**1**, 1774-35-2; **2**, 2417-95-0; **10**, 50546-27-5; **12**, 672-78-6; **13**, 3972-22-3; **14a**, 50273-63-7; **14b**, 50458-30-5; tri-*p*-tolylsulfonium bromide, 50273-64-8; methoxydi-*p*-tolylsulfonium fluorosulfonate, 50273-65-9; mesityllithium, 5806-59-7; triphenylsulfonium bromide, 50273-67-1; lithium oxide, 12057-24-8.

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The Mechanism of Hydride Reduction of 1-Alkyn-3-ols

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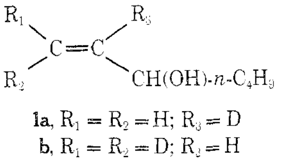
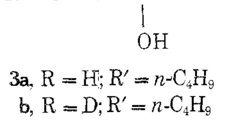
Hydride reduction of 1-alkyn-3-ols (**3**) is shown to proceed *via* site-specific hydride transfer to C-2. A mechanism is proposed which rationalizes the observed reciprocal relationship between solvent basicity and the extent of cis reduction for these systems.

In connection with another problem in this laboratory, it was necessary to synthesize the isotopically labeled allylic alcohols **1a** and **1b**. One convenient route to allylcarbinolic substrates of this type which has been of considerable synthetic use in the past is the lithium aluminum hydride reduction of propargylic alcohols.[2] Mechanistic observations reported on this and related reductions however, suggest that the detailed course of this reaction might be quite structure dependent, thus detracting from its general utility for isotopic labeling.



1a, $R_1 = R_2 = H$; $R_3 = D$
b, $R_1 = R_2 = D$; $R_3 = H$
c, $R_1 = R_3 = H$; $R_2 = D$
d, $R_2 = R_3 = H$; $R_1 = D$

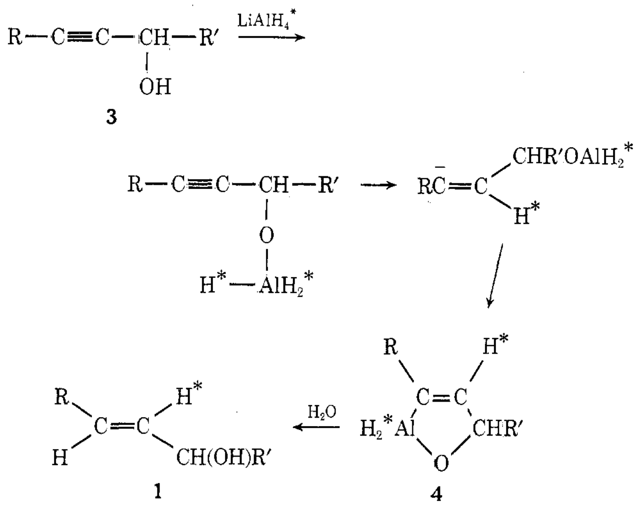


$$R-C\equiv C-\underset{OH}{\underset{|}{CH}}-R'$$

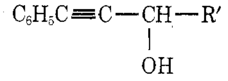
3a, $R = H$; $R' = n\text{-}C_4H_9$
b, $R = D$; $R' = n\text{-}C_4H_9$
c, $R = H$; $R' = CH_3$
d, $R = D$; $R' = CH_3$

Early work[3-5] in this area indicated that the reduction proceeded *via* specific hydride transfer from the aluminum bound to oxygen to the adjacent carbon of the acetylenic linkage, leading after hydrolysis to the olefin resulting from exclusive trans reduction (Scheme I). Corey and coworkers have since demonstrated that for certain substrates (principally 2-alkyn-1-ols) the hydride transfer was not site specific.[6] More recently it was observed that the $LiAlH_4$ reduction of phenyl-substituted propargyl alcohols of type **2** proceeded *via* specific hydride attack[7,8] as

Scheme I



had been proposed earlier,[3-5] but this anomalous specificity was attributed to the powerful directive influence of the phenyl group at C-3.[7]



$C_6H_5C{\equiv}C{-}\underset{OH}{CH}{-}R'$

2

In light of these indications that the detailed mechanism of the reduction by lithium aluminum hydride of acetylenic alcohols may be quite structure sensitive and faced with the requirement for compounds **1a** and **1b**, a systematic investigation of the mechanism of $LiAlH_4$ reduction of propargylic alcohols of general structure **3** (R = H) was undertaken.

Results and Discussion

Reduction of the acetylenic alcohol **3a** with $LiAlD_4$ in tetrahydrofuran (THF) at room temperature for 3 hr followed by hydrolysis gave a monodeuterated product in 85% yield whose structure was established as **1a** by proton nmr. Correspondingly, $LiAlH_4$ reduction of the deuterated alkynol **3b** followed by D_2O quench yielded the doubly labeled alcohol **1b** (96% d_2). This specificity of hydride attack was observed to be general for alcohols of structure **3**, since similar labeling patterns were observed for the reductions of compounds **3c** and **3d**. In addition, the position of hydride attack was not affected by the addition of trivalent aluminum species ($AlCl_3$) to the reaction medium, contrary to previous observations.[6,9,10] (The rate of reduction was observed to diminish in these cases.[11])

Reduction of alcohol **3a** with $LiAlH_4$ in THF at room temperature for 3 hr followed by D_2O quench yielded exclusively the product of trans reduction, **1c**. However, when the reduction was performed in ether, a second product was obtained which was identified by proton nmr as **1d**, the product resulting from cis reduction of the propargylic alcohol. This result had been obtained previously for the $LiAlH_4$ reduction of 1-*tert*-butyl-3-phenylpropargyl alcohol (**2**, R = t-C_4H_9) in ether.[7] Investigation of the effect of solvents on the stereochemistry of the reduction of **3a** with $LiAlH_4$ followed by D_2O quench was undertaken and Table I summarizes the data obtained.

These results indicate a strong inverse correlation between the Lewis basicity of the solvent and the extent of cis reduction such that in the extreme case, isopropyl ether, cis reduction can predominate by a ratio of 3:1.

Table I
Per Cent Trans and Cis Reduction of 1-Heptyn-3-ol (3a) as a Function of the Solvent

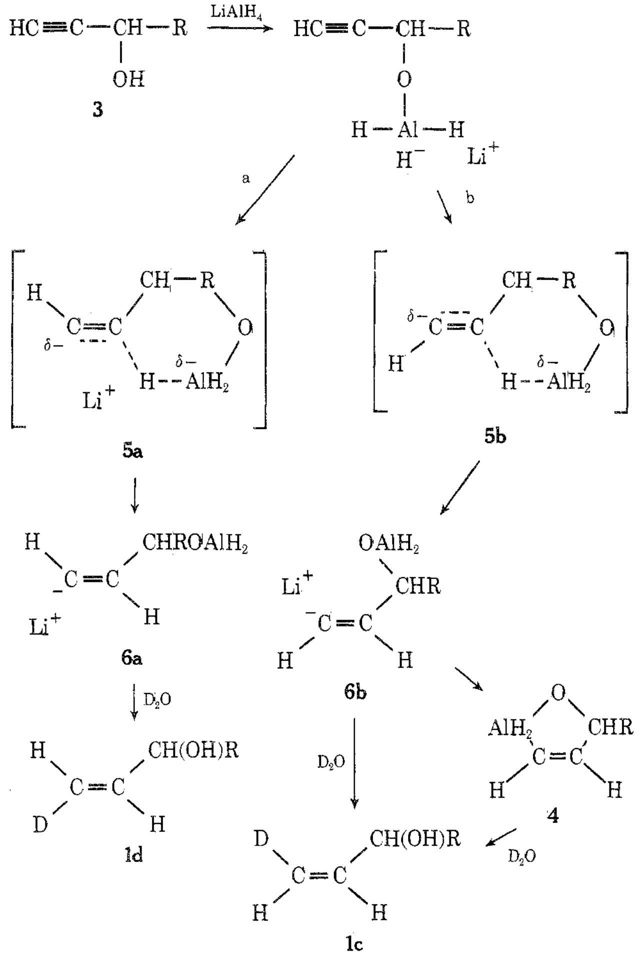
Solvent	% trans reduction[a]	% cis reduction[a]
Dioxane	100	0
Tetrahydrofuran	100	0
Tetrahydrofuran + $AlCl_3$	100	0
2,5-Dimethyltetrahydrofuran	55	45
2,2,5,5-Tetramethyltetrahydrofuran	33	67
Ethyl ether	60	40
Ethyl ether + $AlCl_3$	60	40
n-Propyl ether	50	50
Isopropyl ether	25	75

[a] Values determined using 100-MHz nmr spectrometer.

On the basis of the results obtained in this investigation, the following conclusions can be drawn concerning the mechanism of reduction of propargylic alcohols of general structure **3**. It has been established previously that the function of the aluminum bound to the alcohol oxygen in propargylic systems is to deliver the hydride intramolecularly to the triple bond.[7] This is consistent with the observation that the rate of reduction of **3a** in THF at room temperature is not dependent on the concentration of $LiAlH_4$ above a stoichiometric amount. It is apparent from this study that for propargylic alcohols of general structure **3** (R = H) this hydride transfer occurs exclusively to C-2 in contrast to the results obtained for 2-alkyn-1-ols[6] and in the absence of the powerful directive influence of a phenyl group as proposed by Borden.[7] In addition, the reciprocal relationship between solvent basicity and the extent of cis reduction has been demonstrated. The cis reduction observed in these systems negates the possibility of intramolecular stabilization of the resulting vinylic carbanion by the aluminum bound to oxygen as outlined in Scheme I, since this would impose unlikely geometrical constraints (trans double bond in a five-membered ring) on the resulting oxoaluminum species (assuming that hydrolysis of the C–Al bond occurs with retention of configuration[12]). The stabilization of the vinyl carbanion formed during the cis reduction may therefore best be accomplished by other Lewis acids in the reaction medium. Experiments by Borden[7] on the phenyl-substituted propargylic alcohol **2** (R = *tert*-butyl) suggested that even for trans reduction intramolecular stabilization of the carbanion does not occur initially. Since the extent of cis reduction varies inversely with the ability of the solvent to solvate Lewis acids in the reaction medium, it appears reasonable to assume that these Lewis acids play an important role in the determination of the stereochemistry of the vinyl carbanion. In support of this view recent experiments have indicated that vinyl carbanions exhibit a high degree of stereochemical stability,[13,14] which has been attributed to either sufficiently long lifetimes of the anion in its trigonal configuration or the formation of stereochemically distinct intimate ion pairs with available counterions.[14]

With this information in hand the mechanism outlined in Scheme II is presented, which incorporates all of the available data and provides a rational explanation of the observed results. Logically the first step involves formation of the oxygen–aluminum bond followed by intramolecular hydride transfer to C-2 with concomitant formation of one of two stereochemically stable vinyl carbanions (**6a** or **6b**). In the weaker Lewis base solvents (*e.g.*, ether, 2,5-dimethyltetrahydrofuran) the available counterions (depicted here as Li^+) are less solvated and hence readily available to stabilize existing anionic charges in the transition state (**5a**). This presumably would be best accomplished *via* pathway a. Conversely, in strong Lewis bases (*e.g.*, dioxane, tetrahydrofuran) the highly solvated counterions would not be as available for stabilization of the

Scheme II



developing anionic centers and the configuration yielding greatest separation of these sites (**5b**) would be more energetically favorable (pathway b). Hydrolysis of the resulting ion pair **6a** or **6b** with retention of configuration[12] would result in the product of cis (**1d**) or trans (**1c**) reduction, respectively. On the basis of these results a cyclic organoaluminum species (4) cannot be ruled out completely and may be involved prior to hydrolysis to the trans-reduction product (**1c**). Finally, the assumption that protonolysis of the carbon-metal bond in the final step proceeds with retention of configuration appears to be quite common in the literature,[3,4,7,12] but definitive experiments on substrates of this particular structure are not yet available. Final experimental proof for this assumption is therefore still lacking.

Two interesting observations have been made which further support the mechanism outlined above (Scheme II). When the reduction of alcohol **3a** was performed in isopropyl ether containing a small amount of the crown ether, dicyclohexyl-18-crown-6, the extent of trans reduction was observed to increase dramatically (approximately 70% trans reduction *vs.* 25% in the absence of the crown ether, Table I).[15] Hence, as the proposed mechanism would predict, the addition of the crown ether, which complexes the lithium counterion[16] rendering it unavailable for stabilization of the developing anionic centers in the transition state, forces the reaction along pathway b. Conversely, from Scheme II it might be expected that lowering the temperature of the reaction would favor pathway a, and this was observed to be the case. Reduction of **3a** at −25° for 6 days in ethyl ether increased the extent of cis reduction by approximately 15%.

Experimental Section

General. The THF used was distilled frum Na and benzophenone under N_2 atmosphere. All other solvents were dried by distillation from $LiAlH_4$. Reductions were run under an atmosphere of purified nitrogen. The alkynols employed were purchased from Farchan Research Laboratories, Willoughby, Ohio. The $LiAlH_4$ was obtained from Alfa Inorganics, Beverly, Mass., and the $LiAlD_4$ from Carl Roth OHG, Karlsruhe, Germany. All products were purified by preparative glpc on an Aerograph gas chromatograph using a 10 ft × 0.25 in. 15% Carbowax M on Chromosorb W column operated at 120°. Isotopic purities were determined using an AEI-MS 9 mass spectrometer. Nmr spectra were recorded on a Varian HA-100 spectrometer.

1-Heptyn-3-ol-*1-d* (2b). Sodium metal (70 mg) was dissolved in 2.5 ml of D_2O and 1-heptyn-3-ol (360 mg) was added. The solution was stirred overnight at room temperature. This procedure was repeated twice, after which the product was purified by microdistillation (97% d_1).

General Procedure for Lithium Aluminum Hydride (or Deuteride) Reduction of the 1-Alkyn-3-ols 2a–d. One millimole of the appropriate alcohol and 1.3 mmol of $LiAlH_4$ (or $LiAlD_4$) was stirred in 3 ml of solvent for 3 hr. Hydrolysis was effected by careful dropwise addition of H_2O (or D_2O). The nmr spectrum ($CDCl_3$) of **1a** had signals at δ 0.95 (m, 3), 1.2–1.4 (m, 6), 3.5 (s, 1), 4.13 (q, 1), 5.05 (m, 2); **1b** at δ 0.95 (m, 3), 1.2–1.4 (m, 6), 3.7 (s, 1), 4.13 (q, 1), 6.0 (m, 1). The per cents of cis and trans reduction that appear in Table I were calculated using the C-1 vinyl signal at δ 6.0 (J_{cis} = 10.5 and J_{trans} = 17.0 Hz).

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Registry No.—**1a,** 50600-35-6; **1b,** 50600-36-7; **1c,** 50600-37-8; **1d,** 50600-38-9; **3a,** 7383-19-9.

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