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Formation of β-Allenic Alcohols in Reactions of Acetylenes with Lithium Aluminium Hydride*

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β-Allenic alcohols can be prepared in low to good yields upon treatment of 5-alkoxy-, 5-tetrahydro-2-pyranyloxy-, and 5-trialkylamino-4-pentyn-1-ols (*1*—*10*) with $LiAlH_4$. The reactions proceed in some cases *via* detectable carbanionic intermediates (*21*).

The most convenient way to obtain β-allenic alcohols seems to be the $LiAlH_4$ reduction of alkenynols.[1-3] This reaction has also been applied to stereoselective synthesis.[4] Less used are the following methods: (*i*) the reaction of dihalocyclopropanes with alkyllithium, which was used for preparation of cyclic derivatives,[5] (*ii*) $LiAlH_4$ reduction of β-allenic aldehydes [4] and ketones,[6] (*iii*) addition of propadienyllithium derivatives to oxiranes,[7] and (*iv*) reduction of hydroxy propargylchlorides with a zinc-copper couple.[8]

α-Allenic alcohols are readily prepared by the reaction of 2-butyn-1-ol derivatives with $LiAlH_4$ (Scheme 1).[9-12] The reaction proceeds through an S_N2' mechanism, where X serves as a leaving group (Thp-oxy = tetrahydro-2-pyranyloxy).

Scheme 1.

In this paper we report on an extension of this reaction, in which β-allenic alcohols are formed from the homologous acetylenic derivatives *1*—*10* (Table 1) upon treatment with $LiAlH_4$ under suitable conditions.

RESULTS

The starting acetylenes *1*—*4*, *6*, and *7* were prepared using standard procedures, *i.e.* addition of lithiumalkynides to oxiranes in NH_3.[14] HMPA was used as co-solvent to increase nucleophilicity of the alkynides. *5* was made in analogy to similar compounds [13] and the ammonium salts *8* and *9* were prepared *via* the Mannich reaction [15] of the corresponding β-acetylenic alcohols followed by quaternization. Compound *10* originates from the addition of 3-piperidino-1-butyne to ethylene oxide.

Upon treatment of the acetylenic derivatives *1*—*7* with an excess of $LiAlH_4$ in tetrahydrofuran (THF) at 65 °C and the ammonium salts *8*—*10* at 35 °C the corresponding β-allenic alcohols *10*—*17* were formed in the indicated yields (*cf.* Table 1). No reaction occurs with compounds *1*—*7* when ether is used as a solvent. THF is used for compounds *8*—*10* because of its ability to dissolve the quaternary ammonium salts.[9] In all the reactions except that of *10* reduced allenes are formed as by-products (called "alkenols" in Table 1). In refluxing dioxane these alcohols are main products but so far they have not been further examined.

In some of the reactions one of the major products was the semi-reduced form of the starting acetylene, a fact that made possible a mechanistic interpretation of the formation

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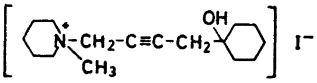
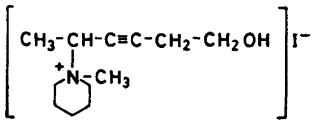
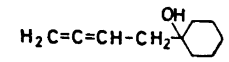
Table 1. $LiAlH_4$ reductions of acetylenic derivatives.

Starting acetylenes	B.p. °C/mmHg	Yield (%)	Reaction time (h)
Thp–O–CH_2C≡C–CH_2–CH_2OH *1*[24]	117/0.6	82	6
t-But–O–CH_2–C≡C–CH_2–CH_2OH *2*[a]	129/10	70	22
Thp–O | C_3H_7–CH–C≡C–CH_2–CH_2OH *3*[a]	114/0.3	73	22
t-But-O | C_3H_7–CH–C≡C–CH_2–CH_2OH *4*[a]	75/0.15	71	5
CH_3–O OH | | C_2H_5–CH–C≡C–CH_2–C–CH_3 | CH_3 *5*[a]	115/12	67	22
Thp–O–$C(CH_3)_2$–C≡C–CH_2–CH_2–OH *6*[a]	85/0.2	81	3
Thp–O OH | | C_2H_5–C–C≡C–CH_2–CH–CH_3 | CH_3 *7*[a]	108/0.4	90	6
$[(C_6H_5–CH_2)_2\overset{+}{N}–CH_2–C≡C–CH_2–CH_2–OH]\ I^-$ | CH_3 *8*		88[c]	2
 *9*		95[c]	2
 *10*		45[c]	2

[a] C and H analyses within ± 0.4 % of the calculated values. [b] Composition of the isolated yield. [c] Yield

Products	Yield GLC[d] (%)	B.p. °C/mmHg	Isolated yield (%)
$H_2C=C=CH-CH_2-CH_2-OH$ *11*[2](+ alkenols	96[b] 4[b])	80/45	55
11+	8		
t-But$-O-CH_2-CH=CH-CH_2-CH_2OH$ *18* (+ alkenols	84 7)		
$C_3H_7-CH=C=CH-CH_2-CH_2OH$ *12*[a] (+ alkenols	66[b] 34[b])	85/13	68
12+ *t*-But-O $C_3H_7-CH-CH=CH-CH_2-CH_2OH$ *19* (+ alkenols	10 40 5)		
$C_2H_5-CH=C=CH-CH_2-COH(CH_3)_2$ *13*+ CH_3-O $C_2H_5-CH-CH=CH-CH_2-COH(CH_3)_2$ *20* (+ alkenols	37 28 3)		
$(CH_3)_2C=C=CH-CH_2-CH_2OH$ *14*[a] (+ alkenols	92[b] 8[b])	75/20	62
$C_2H_5-C(CH_3)=C=CH-CH_2-CH(CH_3)-OH$ *15*[a] (+ alkenols	90[b] 10[b])	81/6	68
11+	97[b]	80/45	67
alkenols	3[b]		
 *16*[a] (+ alkenols	97[b] 3[b])	95/10	78
$CH_3-CH=C=CH-CH_2-CH_2OH$ *17*[4,5]	100[b]	60/11	70

of amino alcohol. Quaternization is quantitative. [d] Rel. areas of peaks. Not corrected for detector response.

of the β-allenic alcohols (*cf.* Discussion). Three of these compounds (*18–20*) were isolated by GLC and characterized (*cf.* Table 2).

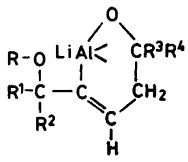
By use of GLC+MS it was easy to indicate a similar product, 5-Thp-oxy-3-octen-1-ol, from the reduction of *3* with $LiAlH_4$. In the mass spectrum of this compound there was no M^+ ion but the $M^+ - Thp\text{-}oxy$ peak was as predicted shifted two mass units compared with the corresponding peak in the spectrum of *3*.

In the reactions of *6* and *7*, where the Thp-oxy groups leave tertiary carbons, no products of this type were encountered.

5-*t*-Butoxy-3-octen-1-ol (*19*) obtained from the acetylenic derivative *4* has the *trans* configuration as indicated by GLC using the corresponding *cis*-alkenol for comparison. The latter originated from partial hydrogenation of *4* over a Lindlar catalyst. Compound *19* also shows strong absorption at 970 cm^{-1} in the IR spectrum. The finding is in accordance with the well known reduction of propargylic alcohols with $LiAlH_4$ to form *trans* allylic alcohols.[13]

DISCUSSION

After the initial alcoholate formation the reductions of *1–5* with $LiAlH_4$ proceed in two distinct steps (i) attack by $LiAlH_4$ on the triple bond to form *21* or a similar carbanion intermediate (*ii*) elimination of an alkoxy or Thp-oxy group.



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Using D_2O to hydrolyze the $LiAlH_4$ reaction mixture from the acetylene *4* confirmed the presence of an intermediate like *21*. NMR analysis of the labeled *19* thus obtained proved that the deuterium occupied exclusively the 4-position; the proton at C-5 became a triplet and spin decoupling of the C-1 protons made the allylic protons at C-2 appear as a doublet ($J = 6$ Hz).

Some of the intermediates are surprisingly stable as can be seen in the reaction of *2*, where the intermediate constitutes 84 % after 22 h. It is interesting to note that the Grignard reagent from *t*-butyl-2-bromoallyl ether also shows remarkable stability, only giving rise to small amounts of allene through elimination of bromomagnesium *t*-butoxide.[17]

It has not been possible to determine whether the quaternary ammonium compounds *8–10* give β-allenic alcohols *via* similar long-lived intermediates.

The Thp-oxy group seems to be a better leaving group than *t*-butoxide (*cf.* the reactions of 1 and 2). This is in some contrast to two analogous reactions that we have examined. We have used the *t*-butoxy and Thp-oxy groups with approximately equal success in a modification[12] of Landor's preparation of α-allenic alcohols (*cf.* Scheme 1) and also in a S_N2' type reaction which gives *trans* homoallylic alcohols from $LiAlH_4$ reduction of 4-alkoxy-2-buten-1-ols.[15]

The β-allenic alcohols are susceptible to attack by hydride on the allenic group and further reduction to a mixture of unsaturated alcohols ("alkenols" in Table 1) occurs in most cases. The reaction temperature, which will minimize this reaction and yet get an acceptable reaction rate for compounds similar to *1–7*, seems to be 55–60 °C. The quaternary ammonium compounds react at a lower temperature(~35 °C) and only small amounts of alkenols (≤3 %) are formed as by-products.

Though β-allenic alcohols in a few cases are obtained in acceptable yields and purity by reaction of acetylenic Thp-oxy derivatives with $LiAlH_4$ (Table 1) it can be concluded that quaternary ammonium compounds like *8–10* seem to be the most suitable substrates for their preparation by this method.

EXPERIMENTAL

General. IR spectra were run on a Perkin-Elmer Infracord 157 G spectrophotometer using liquid films between NaCl discs. NMR spectra were obtained in $CDCl_3$ with tetramethylsilane as internal standard, using a Perkin-Elmer R-12 B spectrometer. These spectra were routinely recorded and are in full agreement with the proposed structures. Mass spectra were obtained at 70 eV with an AEI MS-30 mass spectrometer connected to a Pye 104 gas chromatograph. Columns; 1.5 m glass columns packed with 5 % Carbowax 20 M or 3 % OV-17 on Gas-Chrom Q. Correct mass spectral data were obtained for all products in Table 1.

Table 2. Spectral data of compounds *11*–*20*.

Compound	IR[a] (cm^{-1})	NMR (δ)
11[2]	1955	5.40–4.87 (m, 1 H)
	860	4.80–4.54 (m, 2 H)
	842	3.90–3.48 (m, 2 H)
		2.73 (s, 1 H)
		2.50–1.98 (m, 2 H)
12	1958	5.34–4.89 (m, 2 H)
	875	4.86–4.54 (t, 2 H)
		2.50–1.74 (m, 4 H)
		2.00 (s, 1 H)
		1.74–1.13 (m, 2 H)
		1.08–0.73 (t, 3 H)
13	1958	5.38–4.98 (m, 2 H)
	874	2.35–1.92 (m, 4 H)
		1.82 (s, 1 H)
		1.27 (s, 6 H)
		1.19–0.88 (t, 3 H)
14	1963	5.12–4.65 (m, 1 H)
		3.77–3.49 (t, 2 H)
		2.36–1.97 (q, 2 H)
		1.73 (s, 1 H)
		1.69–1.63 (d, 6 H)
15	1961	5.27–4.80 (m, 1 H)
		4.16–3.53 (m, 1 H)
		2.25–1.95 (t, 2 H)
		2.15–1.78 (m, 2 H)
		2.04 (s, 1 H)
		1.74–1.60 (d, 3 H)
		1.32–1.11 (d, 3 H)
		1.11–0.77 (t, 3 H)
16	1951	5.49–4.90 (m, 1 H)
	877	4.81–4.53 (m, 2 H)
	837	2.36–2.05 (m, 2 H)
		1.87–1.15 (m, 11H)
17[1,3]	1960	5.33–4.80 (m, 2 H)
	870	3.87–3.47 (t, 2 H)
		3.25 (s, 1 H)
		2.50–1.94 (m, 2 H)
		1.84–1.43 (t, 3 H)
18	1360	5.84–5.57 (m, 2 H)
	968	4.00–3.78 (m, 2 H)
		3.78–3.51 (t, 2 H)
		2.60–2.18 (m, 2 H)
		2.03 (s, 1 H)
		1.30 (s, 9 H)
19	1363	5.65–5.42 (m, 2 H)
	970	4.04–3.77 (m, 1 H)
		3.77–3.48 (t, 2 H)
		2.45–2.03 (m, 2 H)
		2.14 (s, 1 H)
		1.58–1.09 (m, 4 H)
		1.17 (s, 9 H)
		1.07–0.76 (t, 3 H)
20	972	5.98–5.10 (m, 2 H)
		3.68–3.17 (m, 1 H)
		3.26 (s, 3 H)
		2.39–2.17 (d, 2 H)
		1.98 (s, 1 H)
		1.77–1.15 (m, 2 H)
		1.23 (s, 6 H)
		1.04–0.82 (t, 3 H)

[a] Only bands of diagnostic value are listed.

For GLC analyses a 2.7 m glass column containing 3 % OV-25 was used. Individual compounds were isolated on a 300 × 0.94 cm aluminium column packed with 20 % Carbowax 20 M on Chromosorb W (60–80).

All reactions with $LiAlH_4$ and Grignard reagents were performed under nitrogen.

Propargylic ethers used in the subsequent preparations were 3-(tetrahydro-2-pyranyloxy)-propyne,[18] *t*-butyl propargyl ether,[19] 3-(tetrahydro-2-pyranyloxy)-1-hexyne,[10,11] 3-*t*-butoxy-1-hexyne,[15] 3-methyl-3-(tetrahydro-2-pyranyloxy)-1-butyne,[20] and 3-methyl-3-(tetrahydro-2-pyranyloxy)-1-pentyne.[20]

Preparation of 1–4, 6, and 7. To 1.14 mol of lithium amide in 1000 ml of liquid ammonia the appropriate propargylic ether (1 mol, see below) dissolved in 100 ml of THF was added during 30 min. 2.4 mol of ethylene oxide or propylene oxide was added and then 100 ml of HMPA. The mixture was stirred overnight and the ammonia allowed to evaporate. Water was added and the products taken up in ether, which was washed with saturated NH_4Cl and several times with 0.01 M hydrochloric acid to remove all traces of HMPA, dried over Na_2SO_4–K_2CO_3 and distilled. For boiling points and yields see Table 1.

2-Methyl-6-methoxy-4-octyne-2-ol (5). Addition[20] of dihydropyran to 2-methyl-4-pentyne-2-ol[21] gave the tetrahydropyranyl protected alcohol (b.p. 96 °C/14 mmHg) in 85 % yield. This (25.0 g; 0.137 mol) in 50 ml of THF was added dropwise during 0.5 h at room temperature to ethylmagnesium bromide [prepared in ether-THF (1:4) from ethyl bromide (19.0 g; 0.174 mol) and magnesium (4.25 g; 0.174 mol)] and stirring was continued for 1 h to give the corresponding acetylenic Grignard derivative. To this reagent propionaldehyde (7.25 g; 0.25 mol) in 25 ml of THF was added dropwise during 0.5 h and the mixture was stirred at room temperature for 2 h. Dimethyl sulfate (23.6 g; 0.187 mol) was added during 0.5 h and then 50 ml of HMPA. The mixture was refluxed for 10 h. After cooling, water was added and the product was taken up in light petroleum, which was then evaporated. The residue was methanolyzed by stirring with 0.5 g of *p*-toluenesulfonic acid in 400 ml of methanol at room temperature for 1 h. 10 g of K_2CO_3 was added and the mixture diluted with 400 ml of ether. Filtering and distillation yielded *5*.

Reactions of 1–7 with $LiAlH_4$. 0.02 mol of the acetylenes 1–7 in 20 ml of THF was slowly dropped to an ice-cooled, stirred suspension of $LiAlH_4$ (0.03 mol for Thp-oxy derivatives and 0.022 for the others). The mixture was then kept at an oil bath temperature of 70 °C and the reactions were followed by GLC (*cf.* Table 1). Work-up using NaOH-water[22] yielded the products in Table 1.

3,4-Pentadien-1-ol[2] *(11) from 8.* Dibenzylamin (11.8 g; 0.06 mol), 3-butyn-1-ol (4.0 g; 0.057 mol), paraformaldehyde (3 g; 0.1 mol)

and 0.2 g of Cu(I)Br were mixed in 25 ml of dry dioxane and refluxed for 1.5 h. The mixture was poured into 100 ml of water, acidified to pH ~ 2 and extracted twice with ether. The aqueous phase was made alkaline with conc. ammonia and extracted three times with ether (3 × 100 ml). Drying over K_2CO_3 and evaporation of solvents yielded 5-dibenzylamino-3-pentyn-1-ol (14 g; 88 %). This crude amino alcohol was treated with an 100 % excess of methyl iodide in refluxing acetone for 1 h. Evaporation yielded the ammonium iodide *8* to which 75 ml of THF was added. $LiAlH_4$ (3.02 g; 0.08 mol) was added in small portions with ice-cooling and swirling. The mixture was then kept in an oil bath of 35 °C during 2 h. Work-up using the NaOH method [22] and distillation yielded the title compound.

1-(2,3-Butadienyl)cyclohexanol (16) was similarly prepared from 1-(2-propynyl)cyclohexanol [21] and piperidine.

3,4-Hexadien-1-ol [4] *(17)*. 3-Piperidino-1-butyne [23] (from the propargylic tosylate and piperidine) was added to ethylene oxide *via* its lithium derivative as described for *1–4*. HMPA was omitted. 5-Piperidino-3-hexyn-1-ol was obtained in 45 % yield. (B.p. 110 °C/0.1 mmHg). This alcohol was treated as described in the preparation of *11* to give the title compound.

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