

A New Preparative Method for *trans* Alkenols*

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Four 4-alken-1-ols (*3b-f*) have been prepared in a new stereoselective mode, which involves treatment of 5-(tetrahydro-2-pyranyloxy)-3-penten-1-ols and the corresponding 5-alkoxy derivatives (*2b-f*) with lithium aluminium hydride in refluxing dioxane. The method is an extension of a reported analogous reaction of 4-alkoxy-2-buten-1-ols, which gives rise to 3-alken-1-ols. 3-Penten-1-ol is prepared here using this latter method. Disubstituted olefinic alcohols are formed in a minimum *trans:cis* ratio of 97:3. The reaction is proposed to have a transition state with strong carbanion character.

According to our recent publication,¹ 3-alken-1-ols can be prepared in good yields using readily available acetylenes as key intermediates (cf. Scheme 1, $n = 0$). Furthermore, this reaction is stereoselective as shown by the formation of 3-hepten-1-ol in a *trans:cis* ratio of 97:3 and ~100% pure 2-methyl-*trans*-4-octen-2-ol. In the present paper we have included the preparation of *trans*-3-penten-1-ol, to further verify the

high stereoselectivity in the formation of 3-alken-1-ols. Trisubstituted olefins, however, are formed with poor stereoselectivity, the ratio of *trans:cis* being 3:2 in the typical case.

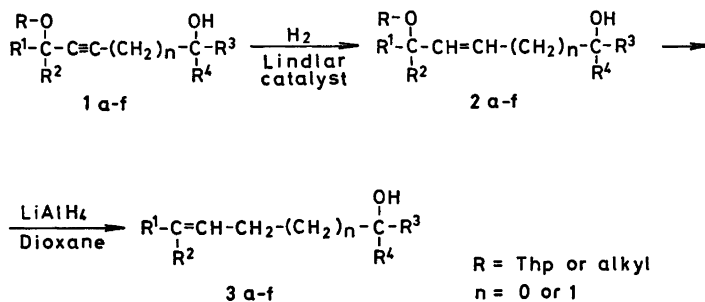
We here wish to report on an extension of this new synthetic method to the stereoselective preparation of *trans*-4-alken-1-ols starting with the acetylenic derivatives *1b-f* (cf. Scheme 1, $n = 1$, and Table 1).

RESULTS

The starting acetylenes *1a-f* were obtained using standard procedures. Their preparation has been described elsewhere.^{8,28}

The preparations of *trans*-3-penten-1-ol (*3a*) and the 4-alkenols *3b-f* from the acetylenes *1a-f* were carried out as described for 3-alkenols in our previous work¹ (cf. Scheme 1 and Table 1). Partial hydrogenation of *1a-f* in hexane gave the corresponding alkoxy- or Thp-oxy-alkenols (*2a-f*) which without prior

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Scheme 1

Table 1. Starting acetylenes and products in the LAH reductions of 1a-f according to Scheme 1.

Acetylenic substrate	Product	Reaction time (h)	Yield ^a GLC (%)	Isolated yield (%)	trans	cis
Thp-O CH ₃ -CH-C≡C-CH ₂ OH 1a ²³	CH ₃ -CH=CH-CH ₂ -CH ₂ OH 3a ²	2.5	95	-	97	3
Thp-O CH ₃ -CH-C≡C-CH ₂ -CH ₂ OH 1b ²³	CH ₃ -CH=CH-CH-(CH ₂) ₂ OH 3b ²	6	93	71	~100	<0.2
Thp-O C ₂ H ₅ -CH-C≡C-CH ₂ -CH ₂ OH 1c ²	C ₂ H ₅ -CH=CH-CH-(CH ₂) ₂ OH 3c ²	38	65	-	>98	<2
t-But-O C ₃ H ₇ -CH-C≡C-CH ₂ -OH 1d ²	C ₃ H ₇ -CH=CH-CH-(CH ₂) ₂ OH 3d ²	28	60	48	>98	<2
CH ₃ -O C ₂ H ₅ -CH-C≡C-CH ₂ -CH ₃ 1e ²	CH ₃ -O C ₂ H ₅ -CH=CH-CH ₂ -CH ₂ -CH ₃ 3e	13	95	-	100 ^b	0 ^b
CH ₃ -O C ₂ H ₅ -C≡C-CH ₂ -CH ₃ 1f ²	CH ₃ -O C ₂ H ₅ -C=CH-CH ₂ -CH ₂ -CH ₃ 3f	15	85	62	~60	~40

^a From rel. areas of peaks. Not corrected for detector response. ^b Cf. text.

purification were allowed to react with lithium aluminium hydride (LAH) in refluxing dioxane.

The *cis:trans* ratios of the so obtained alkenols *3a-e* were determined on GLC using 3 or 6 m long columns containing 20 % Carbowax 20 M or SE-30. In all cases, except that of *3e*, the corresponding *cis* alkenols were prepared independently to allow a correct assignment of the *cis:trans* ratios. *cis*-4-Hexen-1-ol,² *cis*-3-penten-1-ol,³ and *cis*-4-octen-1-ol were obtained through partial hydrogenation of the corresponding 4-alkyn-1-ols.²⁻⁴

The *cis* and *trans*-4-hexen-1-ols separated on a 6 m Carbowax 20 M column with a ratio of retention times *cis:trans* = 1.09 at 25 min. Other authors have reported clean separation on PEG-1500.⁵ In contrast, the isomers of 4-octen-1-ol could not be completely separated on a 6 m Carbowax column and there was no separation on a 3 m SE-30 column. The ratio of retention times for the *cis* and *trans* isomers was 1.06 at 25 min on Carbowax. However, the separation attained allowed an estimation accurate enough to establish the maximum content of the *cis* isomer indicated in the Table 1. No difference in the *cis:trans* ratios of 4-octen-1-ol from different starting materials (*1c* and *1d*) could be detected.

The tertiary alcohol *3e* was homogeneous on all the above columns even at retention times of about 1 h.

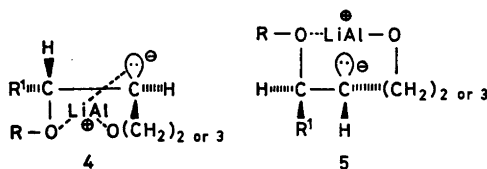
3-Penten-1-ol (*3a*) contained 3 % of the *cis* isomer, which is the same percentage, that we have reported¹ for 3-hepten-1-ol prepared in the same way. (R_t *cis*: R_t *trans* = 1.14 at 22 min on a 3 m Carbowax column).

We have made use of the different chemical shifts in NMR of *cis* and *trans* methyl groups in trisubstituted olefins⁶ in determining the isomer composition of some 4-methyl-3-alken-1-ols.¹ From the 100 MHz NMR spectrum of *3f*, it could be estimated that the *trans:cis* ratio was 3:2, in spite of some interference from methylene protons at δ 1.50.

DISCUSSION

The above formations of 3- and 4-alkenols formally constitute a type of allylic rearrangement (S_N2' reaction). However, mechanistically the question arises as to what degree the attack

by hydride on the double bond and the expulsion of alkoxide are concerted.



There are essentially two main reaction mechanisms. (i) The first is a normal concerted reaction with a more or less synchronous attack by hydride and allylic rearrangement in the transition state. (ii) The reaction may also, in the extreme case, proceed in two steps *via* carbanions, that might be pictured as *4* or *5*, both of them affording *trans* olefins upon decomposition.

When considering the most likely mechanism one should have in mind that the double bond of allylic alcohols having a carbanion stabilizing group at C-3 is easily reduced by LAH with formation of an organometallic bond at this position. The cinnamyl alcohol system is particularly well investigated.⁷

Therefore, in the present case it seems reasonable to assume that attack by hydride on the double bond is well ahead of the expulsion of the alkoxide group, leading to a transition state having strong carbanion character. The reaction might possibly proceed *via* organometallic intermediates, which then is especially conceivable, when the poorly leaving *t*-butoxy group is substituted.

We have not been able to detect a hydrolysis product derived from carbanions such as *4* and *5*, which is not surprising in view of their expected instability. In an analogous reaction we have allowed acetylenic derivatives of type *1b-f* to react with LAH in tetrahydrofuran.⁸ In contrast, this reaction proceeds *via* clearly detectable vinylic organometallic intermediates to β -allenic alcohols.

For a hypothetical organometallic intermediate there should be two possible modes of elimination, which are depicted as *4* and *5* and which are suggestive of the *anti* and *syn* modes of β -elimination⁹⁻¹² respectively, terms which, however, refer to the relative positions of groups, when they are eliminated from a stable molecule.

Drawings, such as 4 and 5, also give a clear indication why the reaction is stereoselective, though they cannot explain the reason why the formation of 4-alken-1-ols is more stereoselective than that of 3-alken-1-ols (cf. 3a and 3b).

When speculating about the mechanism it is interesting to note the resemblance of the above new *trans* alkenol synthesis to some other more or less stereoselective formations of these products, which also proceed *via* elimination of an alkoxy group from an organometallic intermediate or *via* carbanionic transition states.^{3,13-22}

One example of the reaction dealt with in this paper has actually been reported by other authors but was not applied to stereoselective synthesis. LAH reduction of 3,4-diphenyl-4-methoxy-2-cyclopenten-1-one gave 3,4-diphenyl-3-cyclopenten-1-ol in good yield.²²

As indicated in Table 1 the yields of 4-alken-1-ols in the above reactions of 5-alkoxy-3-penten-1-ols with LAH are variable and they are also poorly reproducible ($\pm 15\%$ yield). However, because of the high stereoselectivity of the reaction it can be concluded that it should in some cases be useful for preparing *trans* 4-alken-1-ols.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer 15G spectrophotometer as a film between NaCl discs. NMR spectra were taken on solutions in CDCl_3 with tetramethylsilane as an internal standard, using a Perkin-Elmer R 12 B or a Varian HA 100 D spectrometer.

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

4-Alken-1-ols (3b-f) and 3-penten-1-ol (3a). *General procedure.* The acetylenes (1a-f) (0.02 mol) were hydrogenated in hexane over Lindlar catalyst (Fluka) at atmospheric pressure until the calculated volumes of hydrogen were adsorbed (1-3h) to give the corresponding olefinic alcohols (2a-f). The catalyst was filtered off and the solvent evaporated. The residue was dissolved in 15 ml of dioxane and slowly added dropwise to a stirred suspension of LiAlH_4 (0.03 mol) in dioxane. *Note:* It is important to allow complete alcoholate formation between LiAlH_4 and the alcohol before heating is started as otherwise a violent reaction may occur. After refluxing the reaction mixture was cautiously poured on ice and ether. The alcohol was taken up in ether, which was washed once with a saturated ammonium chloride solution and dried

over potassium carbonate. Microdistillation or preparative GLC yielded the title compounds in states of purity exceeding 96% on GLC.

2-Methyl-trans-5-octen-2-ol (3e) was isolated by preparative GLC (Carbowax 20 M). IR: 965

cm^{-1} ($\text{HC}=\text{CH}$, *trans*). NMR: δ 5.60-5.40 (m, 2 H), 2.30-1.75 (m, 5 H), 1.50 (t, 2 H), 1.20 (s, 6 H), 0.97 (t, 3 H). (Found: C 75.7; H 12.6. Calc. for $\text{C}_9\text{H}_{18}\text{O}$: C 76.02; H 12.76).

6-Methyl-5-octen-2-ol (3f) was isolated by microdistillation at an oil-bath temperature of 95°C and a pressure of 11 mmHg. NMR: δ 5.35-5.05 (m, 1 H), 3.80 (sextet, 1 H), 2.80 (s, 1 H), 2.30-1.75 (m, 4 H), 1.65 (m, 3 H), 1.50 (q, 2 H), 1.20 (d, 3 H) and 0.96 (t, 3 H). The multiplet at δ 1.65 could be resolved at 100 MHz into a downfield multiplet and an upfield singlet, the latter interfering with the methylene quartet. Rel. areas \sim 2:3. (Found: C 75.9; H 12.7. Calc. for $\text{C}_9\text{H}_{18}\text{O}$: C 76.02; H 12.76).

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