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A Versatile Synthesis of α-Allenic Alcohols*

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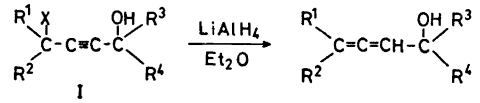
The reaction of 4-alkoxy-2-butynols with $LiAlH_4$ afford α-allenic alcohols in good yields. Various types of alkoxy groups (*e.g.* methoxy, propoxy, *t*-butoxy, allyloxy, and diethylaminoethoxy) function well as leaving groups in this reaction. The number of easily obtainable α-allenic alcohols is extended by a procedure based upon this principle.

The reaction between $LiAlH_4$ and acetylenic derivatives of type I (*cf.* Scheme 1) affords α-allenic alcohols in good to excellent yields *via* an S_N2' reaction, X serving as a leaving group. To date, the following derivatives of type I have been explored: X = Cl[1,2], 2-tetrahydropyranyloxy (THP-oxy),[3] and R_3N^+.[4] The THP-derivatives have been most frequently used owing to the general applicability of their use and their convenient synthesis.[5,6]



I

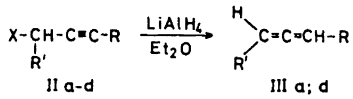
Scheme 1.

In this paper we report that equally good results are obtained with ordinary alkoxy groups as leaving groups. This makes the method more versatile and useful.

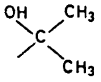
The acetylenic derivatives IIb – IId afforded the allenic alcohols IIIb and IIId upon treatment with $LiAlH_4$ in ether. The yields in these reactions (*cf.* Table 1) are comparable to that obtained by the original method[3] (IIa – IIIa). The acetylenic alcohols (IIb – IId) were obtained by reacting the Grignard derivatives of the corresponding acetylenic ethers (*e.g.* VII) with an appropriate ketone. The ethers required were prepared according to two principal routes, using acidic or basic conditions.

* Allenes and Acetylenes III. Part II: Olsson, L-I., Claesson, A. and Bogentoft, C. *Acta Chem. Scand.* **27** (1973) 1629.

Table 1.



II a-d III a; d

Compound	X	R′	R	Yield %[a]
a	THP -oxy	H		72[7]
b	n-C_3H_7O	H		65
c	t-C_4H_9O	H		67
d	$(C_2H_5)_2N-(CH_2)_2O$	n-C_3H_7		70

[a] After distillation.

Catalysis by strong acids is used in the synthesis of THP-derivatives applied in the method by Cowie *et al.*[3] On the other hand, no acidic conditions are necessary at any stage in the preparation of IIb and IId. The ethers used here (*e.g.* VII) were prepared according to the Williamson method.

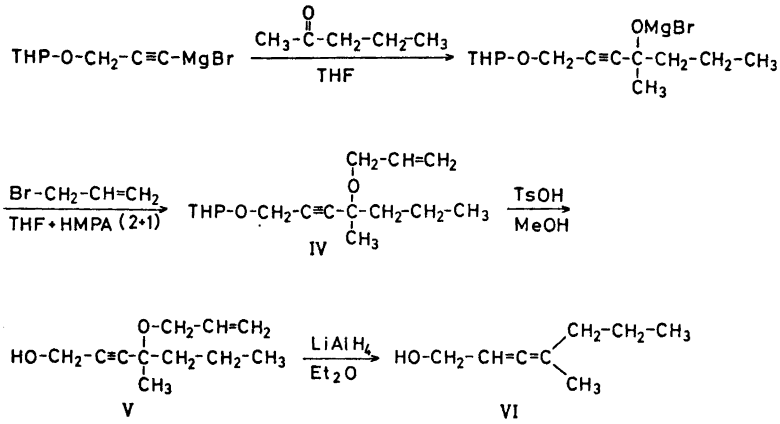
Especially, *t*-butyl ethers offer some advantages over the corresponding THP-derivatives: (i) lower boiling points, (ii) *t*-butyl ethers can easily be obtained through the acid catalyzed addition of isobutene to primary and secondary propargylic alcohols,[8] (iii) the absence of an asymmetric center may be advantageous in special cases.

The method by Cowie *et al.*[3] requires a suitable acetylenic alcohol as starting material but the commercial availability of such compounds is limited. Thus it is usually necessary first to synthesize the desired acetylenic alcohol which makes the over-all route to the allenic alcohols tedious. In Scheme 2 we present a procedure which avoids this drawback of the THP-method and extends the number of easily obtainable α-allenic alcohols. A similar procedure, where a CH_3O functions as leaving group, was used for the synthesis of 6,6-dimethoxy-4-methyl-2,3-hexadienol (IX) from 4,6,6-trimethoxy-4-methyl-2-hexynol (VIII).

Reaction of magnesium halide alcoholates with halides in pure HMPA has been reported.[9] We used a mixture of THF and HMPA with good result in the present case (*cf.* Scheme 2).

EXPERIMENTAL. GENERAL

IR and NMR spectra were routinely recorded and in agreement with the expected structures. IR-spectra were run on a Perkin-Elmer 157 G spectrophotometer using liquid films on NaCl discs. NMR-spectra were obtained in $CDCl_3$ with a Varian A 60



Scheme 2.

spectrometer and with tetramethylsilane as internal standard. Mass spectra were run on an AEI MS-30 mass spectrometer connected to a Pye 104 gas chromatograph. The ionizing energy was maintained at 70 eV, the accelerating energy at 4 kV, and the temperature of the ion source at 200°C.

Elemental analyses were performed in the laboratories of Dr. A. Bernhardt, Mülheim, West Germany. All reactions where Grignard reagents and $LiAlH_4$ were used, were performed under nitrogen.

1-(3-Propoxy-1-propynyl)cyclohexanol (IIb). To the Grignard reagent from magnesium (2.6 g, 0.107 mol) and ethyl bromide (11.7 g, 0.107 mol) in 100 ml of THF were added propyl propargyl ether (0.09 mol) with stirring during 15 min. After stirring for another 15 min, cyclohexanone (8.0 g, 0.082 mol) in 30 ml of THF was added during 20 min. Stirring was continued for 1 h and the reaction mixture poured on ice and the product taken up in light petroleum-ether (1:1), which was washed several times with saturated NH_4Cl, dried over Na_2SO_4-K_2CO_3 and distilled. B.p. 85°/0.15 mmHg. Yield: 68 %. (Found: C 73,2; H 9.9. Calc. for $C_{12}H_{20}O_2$: C 73.4; H 10.3).

1-(3-t-Butoxy-1-propynyl)cyclohexanol (IIc) was prepared similarly from *t*-butyl propargyl ether.[8] Yield: 69 %. B.p. 90°/0.15 mmHg. NMR ($CDCl_3$) δ (ppm) = 4.05 (s, 2 H), 2.70 (s, 1 H), 1.9 – 1.2 (m, 10 H), 1.18 (s, 9 H).

1-Propadienylcyclohexanol (IIIa).[7] IIc (3.3 g, 0.0157 mol) in 10 ml of ether was slowly added to an ice-cold, stirred mixture of $LiAlH_4$ (0.7 g, 0.0185 mol) in 40 ml of ether. The mixture was refluxed for 45 min and then cautiously poured on ice and taken up in ether, which was washed with saturated NH_4Cl and dried over Na_2SO_4-K_2CO_3. Distillation yielded 1.45 g (67 %) of IIIa. B.p. 93°/16 mmHg. IIIa was similarly prepared from IIb in 65 % yield.

3-(2-Diethylaminoethoxy)hexyne (VII). To a stirred suspension of 3.0 g (0.123 mol) of NaH in 100 ml of DMF was added dropwise 9.6 g (0.082 mol) of diethylaminoethanol at 0° during 15 min. The solution was stirred for another 2 h at 50° and then cooled to −40°. A solution of 15.6 g (0.082 mol) of tosyl chloride in 100 ml of benzene was added dropwise and stirring was continued for 2 h at −40°. An ice-cold solution of the sodium salt of 1-hexyn-3-ol, prepared from the alcohol (9.6 g, 0.098 mol) and NaH (2.6 g, 0.11 mol) in 100 ml of DMF, was then added and stirring continued overnight. The solution was then poured on ice and the product taken up in light petroleum, washed twice with 25 % Na_2SO_4, twice with water, dried over Na_2SO_4 and distilled. B. p. 105°/15 mmHg. Yield: 45 %. IR: 3310 cm^{-1} (≡C–H), 2100 cm^{-1} (–C≡C–). NMR: δ (ppm) 4.10 – 3.17 (m, 3 H), 2.77 – 2.28 (m, 7 H), 1.77 – 0.75 (m, 13 H).

5-(2-Diethylaminoethoxy)-2-methyl-3-octyn-2-ol (IId). To the Grignard reagent prepared in ether from magnesium (1.56 g, 0.064 mol) and ethyl bromide (6.5, 0.06 mol)

was added 75 ml of THF. A solution of VII (10 g, 0.051 mol) in 50 ml of THF was then added dropwise to the stirred solution at 15 – 20° during 0.5 h. The solution was stirred for another 15 min at room temperature and 2.7 g (0.0456 mol) of acetone in 25 ml of THF was added during 0.5 h. The mixture was kept at 50° for 5 h. After cooling, the reaction mixture was poured on ice. The alcohol was taken up in ether, washed twice with 25 % Na_2SO_4, twice with water, dried over Na_2SO_4 and distilled. B. p. 110°/1 mmHg. Yield: 50 %. IR: 2230 cm^{-1} (–C≡C–). NMR: δ (ppm) 4.40 (s, 1 H), 4.10 – 3.20 (m, 3 H), 2.76 – 2.30 (m, 6 H), 1.71 – 0.75 (m, 13 H), 1.46 (s, 6 H).

2-Methyl-3,4-octadien-2-ol (IIId). Prepared as described for 1-propadienylcyclohexanol (IIIa) from 6.0 g (0.024 mol) of IId. B.p. 82 – 86°/18 mmHg. Yield: 70 %. IR: 1960 cm^{-1} (C=C=C). (Found: C 76.9; H 11.4. Calc. for $C_9H_{16}O$: C 77.1; H 11.5).

4-Allyloxy-4-methyl-1-(tetrahydro-2-pyranyloxy)-2-heptyne (IV). To the Grignard reagent prepared in ether from magnesium (5.0 g, 0.206 mol) and ethyl bromide (22.4 g, 0.206 mol) was added 100 ml of THF. The solution was stirred at 15 – 20° and 3-(tetrahydro-2-pyranyloxy)propyne (22.6 g, 0.162 mol) in 100 ml of THF added during 20 min. The solution was stirred for another 15 min at room temperature and 12.6 g (0.147 mol) of 2-pentanone in 25 ml of THF was added during 1 h. Stirring was continued for 2 h at room temperature. To the solution was then added 21.4 g (0.177 mol) of allyl bromide in 25 ml of THF and 100 ml of HMPA. The mixture was refluxed (80°) for 5 h and poured on ice. The product was taken up in light petroleum, washed several times with 25 % $(NH_4)_2SO_4$, twice with water, dried over Na_2SO_4 and distilled. B.p. 126 – 132°/ 1 mmHg. Yield: 91 %. (Found: C 72.0; H 9.7. Calc. for $C_{16}H_{26}O_3$: C 72.1; H 9.8).

4-Allyloxy-4-methyl-2-heptynol (V). A solution of 3 g (0.0113 mol) of IV, 15 ml of methanol, and 50 mg of *p*-toluenesulfonic acid was stirred at room temperature for 10 h. The solution was diluted with light petroleum and ether (1:1), the organic phase was washed several times with water, dried over K_2CO_3 and distilled. B.p. 120°/4 mmHg. Yield: 90 %. (Found: C 72.2; H 9.9. Calc. for $C_{11}H_{18}O_2$: C 72.5; H 9.9).

4-Methyl-2,3-heptadienol (VI) was prepared as described for IIIa from 2.1 g (0.0115 mol) of V. B.p. 165 – 170°/760 mmHg. Yield: 60 %. (Found: C 75.9; H 11.0. Calc. for $C_8H_{14}O$: C 76.1; H 11.2).

4,6,6-Trimethoxy-4-methyl-2-hexynol (VIII) was prepared as described for V from 3-(tetrahydro-2-pyranyloxy)propyne (35.0 g, 0.25 mol) and acetoacetaldehyde dimethyl acetal (29.7 g, 0.225 mol) and dimethyl sulphate (46.2 g, 0.366 mol). Distillation (b.p. 116°/0.15 mmHg) yielded 74 % of the THP – protected intermediate, which was methanolyzed as above (*cf.* V). The over-all yield from the ketone was 69 %. B.p. 100°/0.4 mmHg. (Found: C 59.4; H 9.0. Calc. for $C_{10}H_{18}O_4$: C 59.4; H 9.0).

6,6-Dimethoxy-4-methyl-2,3-hexadienol (IX) was prepared from VIII (2.3 g, 0.013 mol) as described for IIIa. Yield: 70 % IR: 1960 cm^{-1} (C=C=C). NMR: δ (ppm) = 5.30 – 4.25 (m, 1 H), 4.40 (t, 1 H, J = 5.5 Hz), 3.94 (d, 2 H), 3.23 and 3.22 (two s, 6 H), 3.0 (s, 1 H), 2.20 (d, 2 H, J = 5.5 Hz, further split into doublets. J = 2.5 Hz), 1.70 (d, 3 H, J = 2.5 Hz). Mol.wt. 172 (MS).

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