Novel Base-induced Isomerization of Unsaturated Alcohols to Aldehydes

H. M. R. Hoffmann,* Andreas Köver, and Detlef Pauluth

Department of Organic Chemistry, University of Hannover, Schneiderberg 1 B, D-3000 Hannover, Federal Republic of Germany

A number of allylic and other unsaturated alcohols have been converted into aldehydes by treatment with *N*-lithioethylenediamine in ethylenediamine (LEDA–EDA) and also with lithium 3-aminopropanamide in 3-aminopropanamine (LAPA–APA).

In the course of attempts to induce migration of the disubstituted double bond of (**1**) into the tetrasubstituted position of (**2**) we used *N*-lithioethylenediamine–ethylenediamine (LEDA–EDA) as a base[1] and after acidic work up observed the clean formation of an aldehyde, *i.e.* (**3**) rather than (**2**). The conversion of (**1**) into (**3**) amounts to a base-promoted intramolecular oxidation–reduction of an allylic alcohol into an aldehyde and suggested the study of other unsaturated alcohols under these conditions (Table 1). All the alcohols studied were primary. Even undec-10-en-1-ol (**12**) which has a remote double bond, gave some undecanal (**13**), although in this case it was necessary to use lithium 3-aminopropanamide in 3-aminopropanamine[2] (LAPA-APA) instead of LEDA–EDA. Addition of potassium t-butoxide which appears to be useful for isomerizing alkynes,[2a] had no discernible effect on our reactions.

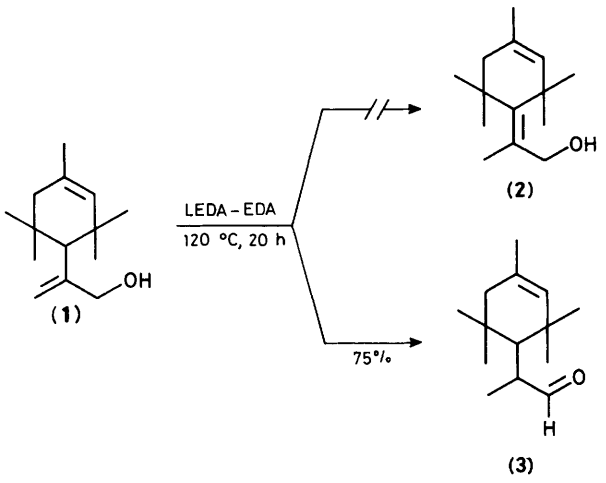
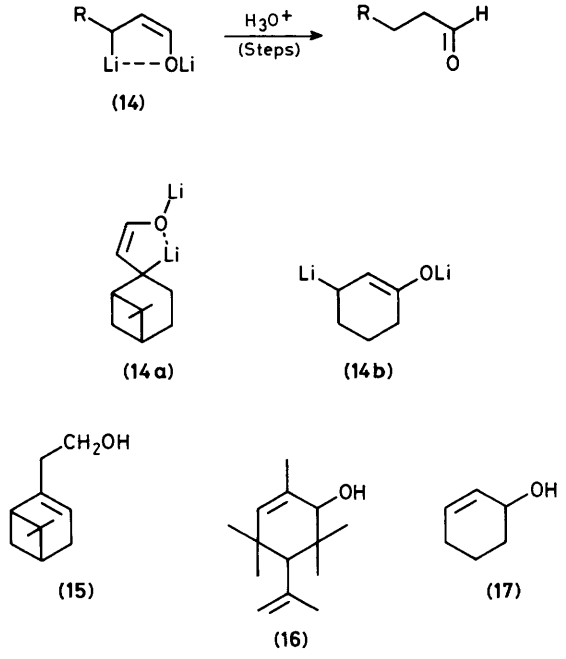


Table 1. *N*-Lithioethylenediamine promoted redox reactions of unsaturated alcohols.

Educt	Product	Reaction Conditions	Yield (%)
(1)	(3)	120 °C, 20 h	75
(4)	(5)	115 °C, 2 h	80[a]
(6)	(7)	130 °C, 17 h	74[b]
(8)	(9)	95 °C, 22 h	45[c]
10	(11)	120 °C, 21 h	25[d]
(12)	(13)	117 °C, 42 h	3[c,d]

[a] One stereoisomer, presumably *trans*-(**5**), predominates (ref. 3). The preparation of (**1**) and (**4**) is described in ref. 4. [b] *ca.* 95% *cis*-(**7**) is formed when LAPA (12 equiv.) is used; *cis*-(**7**) : *trans*-(**7**) = 88 : 12 for 2 equiv. of LAPA. *cis*-(**7**) was identified by ^{13}C n.m.r.; *cf.* ref. 5. [c] LAPA–APA used as a base. [d] Product was isolated by column chromatography (silica gel, eluant diethyl ether–light petroleum).



There has been considerable mechanistic speculation on the nature of the organolithium intermediates in reactions of unsaturated hydrocarbons with LEDA–EDA.[1b] A plausible precursor of the product aldehydes is the dianion (**14**),[6] which is also a homoenolate and which on protonation will yield the observed aldehyde. It is relevant in this context that the alcohols (**15**), (**16**), and (**17**) did not rearrange into the corresponding carbonyl compounds under these conditions.

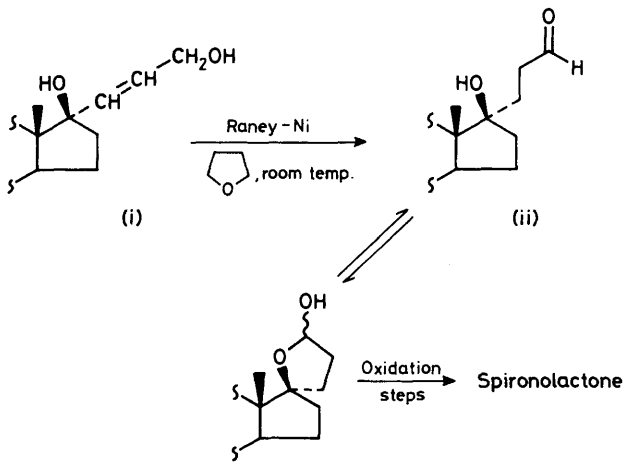
The failure of nopol (**15**) to isomerize can be attributed to the fact that the homoenolate (**14a**) has its second lithium attached to a tertiary carbon, an unfavourable situation. Compounds (**16**) and (**17**) are secondary alcohols and internal chelation of the second lithium in an intermediate homoenolate [*cf.* (**14b**)] is impossible, because of the *trans* double bond. It is also interesting that careful acidic work up of the reaction mixture from myrtenol (**6**) gave *cis*-myrtanal (**7**) as almost exclusive product. *cis*-(**7**) is more hindered than *trans*-(**7**) and is therefore the thermodynamically less stable isomer. However, *cis*-(**7**) would be expected to be formed on approach of the proton donor to the more accessible face of the enol or enolate intermediate, *i.e.* from the side opposite to the *gem*-dimethyl bridge. The one-pot isomerization of inexpensive myrtenol (**6**) constitutes a simple procedure† for obtaining *cis*-myrtanal (**7**). The higher yield of (**7**) (74%) when compared with (**9**) (45%) is probably due to relief of bicyclic strain on formation of (**7**).

† Typical experimental procedure for the isomerization with LAPA–APA: lithium (600 mg, 90 mmol) is stirred in anhydrous 3-aminopropanamine (30 ml) at 90 °C under nitrogen. After 90 min myrtenol (**6**) (1 g, 75 mmol) in 3-aminopropanamine (3 ml) is syringed into the basic suspension and heated at 130 °C for 17 h. The mixture is allowed to cool down to room temperature and worked up by being dropped slowly into a vigorously stirred mixture of 10% sulphuric acid (300 ml)–pentane (70 ml) cooled to 0 °C. After extraction with pentane (3 × 100 ml) the combined organic phase is dried ($MgSO_4$). Removal of the solvent gives *cis*-myrtanal (**7**) (740 mg, 74%), identified by ^{13}C n.m.r. spectroscopy (ref. 5). In another experiment we started from (−)-myrtenol ($[\alpha]_D^{20}$ − 48 ± 1, neat; Fluka AG) and obtained myrtanal (*cis* : *trans* = 93 : 7; $[\alpha]_D^{19}$ − 59.6, $CHCl_3$).

The base-induced redox reaction appears to work best when a reasonable molecular weight of the unsaturated alcohol facilitates the isolation of product and when other potential reactions like aromatization[1a,b] and the aldol reaction are blocked or impeded by steric hindrance. In view of the variety of routes to allylic alcohols the isomerization described here can be expected to find further applications.

We thank Dr. G. Sauer, Schering AG, Berlin, for drawing our attention to ref. 7, *i.e.* the conversion of (i) into (ii), the Deutsche Forschungsgemeinschaft, and the Land of Lower Saxony (Lotto fund) for support of this work.

Received, 29th January 1985; Com. 136



References

1 Reviews: (a) L. F. Fieser and M. F. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967, Vol. 1, p. 567; Vol. 2, 239; Vol. 4, 488; (b) L. Reggel, C. Zahn, I. Wender, and R. Raymond, U.S. Bureau of Mines, Bulletin 615, U.S. Dept. of the Interior, 1964; (c) *cf.* also J. Verghese, *Perfum. Flavor*, 1981, **6**, 23; A. S. Narula and S. Dev, *Tetrahedron*, 1971, **27**, 1119; E. Ayanoglu, A. Chan, and C. Djerassi, *ibid.*, 1979, **35**, 1591; R. J. Giguere, G. von Ilsemann, and H. M. R. Hoffmann, *J. Org. Chem.*, 1982, **47**, 4948.

2 For the use of potassium 3-aminopropanamide see (a) S. R. Abrams, *Can. J. Chem.*, 1984, **62**, 1333; S. R. Abrams, *J. Org. Chem.*, 1984, **49**, 3587; (b) C. A. Brown, *J. Chem. Soc., Chem. Commun.*, 1975, 222; C. A. Brown, *Synthesis*, 1978, 754.

3 W. Hasel, unpublished work.

4 H. M. R. Hoffmann and D. Pauluth, *Liebigs Ann. Chem.*, 1985, 396; D. Pauluth and H. M. R. Hoffmann, *ibid.*, 1985, 403; *ibid.*, p. 756.

5 J. M. Coxon, G. J. Hydes, and P. J. Steel, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1351.

6 For approaches to doubly deprotonated methanol see N. Meyer and D. Seebach, *Chem. Ber.*, 1980, **113**, 1290.

7 The conversion (i) → (ii) *en route* to spironolactone has been accomplished with Raney-nickel [3g of Raney-nickel for 3g of 4-hydroxy-2-butenol (i)]: K. Junghans, European Patent Appl. 84101780.9, 21.02.1984, Schering AG, Berlin and Bergkamen, Federal Republic of Germany.