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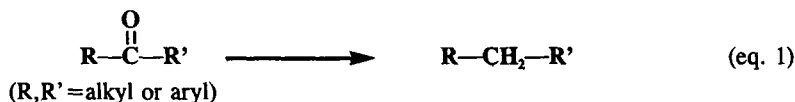
Chemoselective Reductive Deoxygenation of α,β-Unsaturated Ketones and Allyl Alcohols

Adusumilli Srikrishna,* Ranganathan Viswajanani, Jitendra A. Sattigeri
and Channabasaveshwar V. Yelamaggad

Department of Organic Chemistry, Indian Institute of Science
Bangalore - 560 012, India.

Abstract: *A simple and convenient procedure for a highly chemoselective reductive deoxygenation of α,β-unsaturated ketones and allyl alcohols to olefins by sodium cyanoborohydride and boron trifluoride etherate in dry THF is described.*
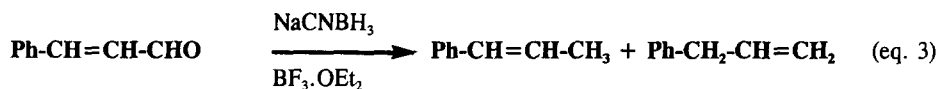
The reduction of the carbonyl group of aldehydes and ketones to methylene has enjoyed wide application in organic synthesis. Whereas there are several methods available for the direct conversion of simple and aryl ketones to the corresponding hydrocarbons (eq. 1),[1] to our knowledge, there is no general chemoselective method reported for the direct reduction of α,β-unsaturated carbonyl compounds to the corresponding olefins (eq. 2), *e.g.* Wolff-Kishner reduction is not suitable for the selective deoxygenation of enones to olefins if a saturated ketone is also present in the molecule. The conventional ionic hydrogenation reaction[2] using trialkylsilanes in the presence of an acid, a very convenient method for the deoxygenation of aryl ketones, transforms the unsaturated ketones first to the saturated ketones and finally to the corresponding alcohols,[3,4] perhaps *via* 1,4-hydrosilylation. Recently, Wustrow and co-workers[5] have reported the lithium perchlorate-triethylsilane mediated ionic hydrogenation of secondary allyl alcohols and acetates to olefins. Recently we have discovered[6] that a combination of sodium cyanoborohydride and boron trifluoride etherate efficiently deoxygenates aryl ketones to corresponding hydrocarbons (eq. 1). In continuation of our studies, we have now discovered that sodium cyanoborohydride and boron trifluoride

$$\underset{\text{(R,R'=alkyl or aryl)}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-R'} \longrightarrow R-CH_2-R' \qquad \text{(eq. 1)}$$

(eq. 2)

etherate, in contrast to other ionic hydrogenation conditions, deoxygenates α,β-unsaturated ketones as well as allyl alcohols to olefins efficiently with a very high degree of chemoselectivity.

a) $NaCNBH_3/BF_3.OEt_2/THF$
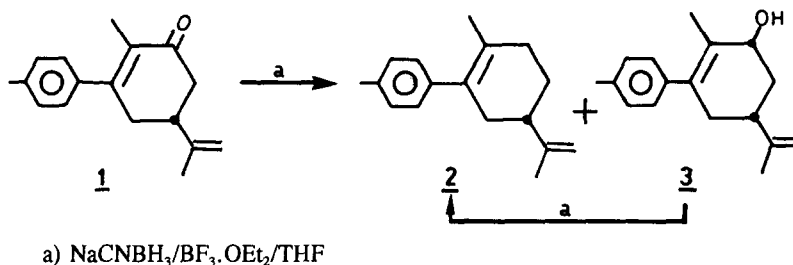
To begin with, we have investigated the reduction of β-arylcarvone **1**.[7] Reaction of the enone **1** with sodium cyanoborohydride and boron trifluoride etherate in dry THF at room temperature for 12 hrs furnished, in 95% yield, a $\approx 1:1$ mixture of the deoxygenated product **2** and the allyl alcohol **3**. When the reaction was carried out at reflux temperature for 30 min the deoxygenated product **2** was obtained in 75% yield with only a trace amount of the allyl alcohol **3**. The structure of the deoxygenated product **2** was established from its spectral data.[#] The formation of the allyl alcohol clearly implicates it as an intermediate in the carbonyl deoxygenation. This was further established when the allyl alcohol **3** was deoxygenated to **2** by $NaCNBH_3$ and $BF_3.OEt_2$ in refluxing THF. To establish the generality of this methodology, various unsaturated ketones and allyl alcohols were deoxygenated to olefins[8] using $NaCNBH_3$ and $BF_3.OEt_2$ in dry THF, and the results are summarised in the table. The salient features are as follows: The reaction exhibited excellent chemoselectivity. Only α,β-unsaturated ketones and allyl alcohols were deoxygenated, whereas α,β-unsaturated esters (entry 5), isolated olefins, styrenic olefins, esters (entry 8) and alcohols (non-allylic) were not effected. Saturated ketones were not deoxygenated to hydrocarbons but reduced to the corresponding secondary alcohols (entries 4 and 9). Since the present transformation is analogous to ionic hydrogenation reactions, quite expectedly, acetals will be reductively cleaved, e.g. THP ether furnished the corresponding alcohol (entry 10). The absence of either the saturated ketones or the corresponding secondary alcohols indicates that formation of the allyl alcohol is the first step in the deoxygenation reaction, hence it is possible to adopt this methodology for the regiospecific 1,2-reduction of enones. The deoxygenation of the primary allyl alcohols (entries 13 and 14) is noteworthy, since deoxygenation employing the procedure developed by Wustrow et al. was documented[5] to be not suitable for primary allyl alcohols. In addition it also suggests the suitability of the present method for the deoxygenation of conjugated aldehydes. This was established by the deoxygenation of the cinnamaldehyde to a 4:1 mixture of 1-phenylpropene and 3-phenylpropene[1] (eq. 3) using the present procedure at room temperature.

$$\text{Ph-CH=CH-CHO} \xrightarrow[\text{BF}_3.\text{OEt}_2]{\text{NaCNBH}_3} \text{Ph-CH=CH-CH}_3 + \text{Ph-CH}_2\text{-CH=CH}_2 \quad \text{(eq. 3)}$$

Table: Reductive deoxygenation of enones and allyl alcohols

entry	enone/ allyl alcohol	Products[a]	time/ temp.	yield[b] %
1)	**1**	**2** + **3** (1:1)	12 h/rt	95
2)	**1**	**2**	0.5 h/65°C	75[c]
3)	**3**	**2**	1 h/65°C	70
4)	Cyclododecanone	Cyclododecanol	11 h/65°C	100[d]
5)	Ph-CH=CH-COOMe	-----	4 h/65°C	--[e]
6)		3:2	0.5 h/rt	85
7)		2:1	3 h/rt	82
8)		20:1	12 h/rt	78
9)		3:1	12 h/rt	85
10)		5:4	13 h/rt	78
11)			3 h/rt	50[f]
12)		4:5	12 h/rt	50[f]
13)		1:1	8 h/65°C	50[f,g]
14)		4:1	4 h/65°C	87

a. Ratios were determined by GC and/or NMR integrations. **b.** Yields (unoptimised) refers to isolated and chromatographically pure compounds. **c.** Trace amounts of the alcohol **3** and olefin isomerised products were also present. **d.** The alcohol was formed in < 15 min at room temperature, and no deoxygenation was observed even after refluxing the reaction mixture for 11 h. **e.** No reduction was observed and only starting material was recovered. **f.** Low yields are probably due to the volatality of the products. **g.** Trace amount of dehydration product was also present.

Typical Experimental Procedure: Sodium cyanoborohydride (3 mmol) was added to a magnetically stirred solution of the enone or allyl alcohol (1 mmol) and boron trifluoride etherate (3-4 mmol) in 3 ml of dry THF and the reaction was either stirred at room temperature or refluxed (see table). After the completion of the reaction (monitored by TLC), saturated aqueous $NaHCO_3$ solution was added to the reaction mixture and extracted with ether (3 x 5 ml). The ether extract was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column furnished the products.

In conclusion, we have discovered a new ionic hydrogenation combination, which is suitable for a highly chemoselective deoxygenation of α,β-unsaturated ketones, and allyl alcohols to the corresponding olefins.

All the products exhibited spectral data consistent with their structures. Selected spectral data for **2**: $[\alpha]_D^{26}$ -105° (c 2.0, $CHCl_3$). UV: λ_{max} (CH_3OH) 238 nm (ϵ, 8830). IR (neat): ν_{max} 1650, 1510, 890, 820 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 7.15 and 7.07 (4 H, AB q, J 7.9, aromatic), 2.36 (3 H, s, Ar-CH_3), 1.5-2.5 (7 H, m), 1.77 (3 H, s) and 1.6 (3 H, s) (2 x olefinic CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 141.3, 135.6, 131.9, 128.9 (2 C), 128.6, 128.5 (2 C), 108.8, 42.2, 37.6, 32.4, 28.2, 21.3, 21.0 and 20.6 ppm.

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