HOMOALLYLIC ALCOHOLS FROM ALDEHYDE ACETALS BY TRANSALLYLATION

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Abstract

Homoallylic alcohols, which are widely used in organic synthesis, were prepared with moderate to good yields by a facile transallylation of aldehyde acetics with 2-methyl-4-penten-2-ol and trimethylsilyl triflate.

Keywords: Acetals, Allylation, Allyl transfer, Homoallylic alcohols, Transallylation

Introduction

Homoallylic alcohols are widely used in organic synthesis (1). They have been prepared by a variety of methods, in particular by allylation of carbonyl compounds, mostly aldehydes (1). However, many low molecular weight aldehydes or dialdehydes are unstable, and are available only in water solutions or as acetals.

To the best of our knowledge, there have been four publications describing a direct synthesis of homoallylic alcohols from acetals (2-4). Homoallylic alcohols were prepared by allylation of carbonyl compounds and some non-aromatic aldehyde acetals in water with allyldibutyltin chloride (2a), and in cyclohexane/aq.LiClO₄ with allyl halide and Zn/Bu₂SnCl₂ (2b). A treatment with either trifluoroacetic acid or silica gel followed by tetraallyltin has been used for one-pot transformation of acetals into homoallylic alcohols (3). A synthesis of homoallylic alcohols by indium mediated allylation of benzaldehyde and cinnamaldehyde dimethylacetals with allylic bromides in aqueous THF has been described recently (4). Aliphatic acetals appeared to be unreactive (4). Under similar conditions, gem-diacetates produced homoallylic acetates (5). Other Lewis acid promoted reactions of acetal allylation afforded homoallylic ethers (6).

We report here a mild, simple and inexpensive general synthesis of homoallylic alcohols 3 from aldehyde acetals 1 by catalytic transallylation with homoallylic alcohol 2 (Scheme 1).

Experimental

Flash chromatography was performed on silica gel (J. T. Baker, 40μm, p = 0.5 g/CM). Rf values pertain to TLC done on (8x2 cm) plates with UV-indicator (254 nm), manufactured by Analtech Inc. Solvents of HPLC grade were used. ¹H-NMR and ¹³C-NMR spectra were acquired on a Varian Mercury 300 NMR-Spectrometer.

Phenylacetaldehyde dimethyl acetal 1a and benzylacyetaldehyde diethyl acetal 1b, obtained from Aldrich Chemical Co., were used without purification. Phthalimidoacetaldehyde diethyl acetal 1c was prepared according to a modified literature procedure (7).

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\begin{align*}
\text{Me}_3\text{SiOTf} & \quad \text{CH}_2\text{Cl}_2, \text{-35°C} \\
\text{Me}_3\text{SiOTf} & \quad \text{CH}_2\text{Cl}_2, \text{-35°C} \\
\end{align*}
\]

Scheme 1

(a) R = Ph, R' = Me; (b) R = PhCH₂O, R' = Et; (c), R = PhthN; R' = Et
Phthalimidoacetaldehyde diethyl acetal [1c].
Potassium phthalimide (39.9 g, 215 mmol), BrCH₂CH(OEt)₂ (30 mL, 200 mmol), and anhydrous KI (4.7 g, 28 mmol) in anhydrous dimethylacetamide, DMA, (100 mL) were stirred under dry N₂ for 24 hours at 120 °C. The cooled mixture was treated with H₂O (500 mL) in one portion. After 24 hours at room temperature, a brown precipitate was suction filtered, was washed with H₂O (200 mL), and was recrystallized from MeOH, affording compound 1c (40.5 g, 77%); mp 71-73°C [lit. (7): mp 72-73 °C].

2-Methyl-4-penten-2-ol [2].
A stirred mixture of acetone (22 mL, 300 mmol), allyl bromide (26 mL, 300 mmol), saturated aqueous NH₄Cl (100 mL), and THF (50 mL) was treated with zinc dust (5x5.2 g, 400 mmol), added during 30 min. The mixture was stirred for 24 hours at room temperature, was filtered, and was extracted with Et₂O (3x200 mL). The organic phase was dried (MgSO₄), was concentrated in vacuo, and was distilled to give a fraction of compound 2 (11.4 g, 38 %) at 111-115 °C [lit. (8a): bp 119 °C]. Rf 0.43 (4:1 PhMe - i-Pr₂O). ¹H NMR (300 MHz, CDCl₃) δ: 1.21 (s, 6H, CH₃), 2.22 (brd, J = 6.7 Hz, CH₂), 2.4 (br. s, OH), 5.1 (m, 2H, C=CH₂), 5.88 (m, 1 H, CH=CH). ¹³C-NMR (75 MHz, CDCl₃) δ: 29.3, 48.5, 70.5, 118.4, 134.5. Spectral data are identical to those reported earlier (8b,c).

A typical procedure for the allyl transfer from 2 to an acetal 1 is shown below for 3c.

1-Phthalimido-4-pentene-2-ol [3c].
A solution of 1c (1.14 g, 4.3 mmol) in CH₂Cl₂ (20 mL) was added dropwise during 30 min. to a cold (-35 °C) stirred solution of 2-methyl-4-penten-2-ol, 2, (0.65 g, 6.5 mmol, 50% excess) and Me₃SiO(SO₂CF₃) (0.39 mL, 2.2 mmol) in CH₂Cl₂ (10 mL). The mixture was stirred at -10 °C for 2 hours and was quenched cold (-10 °C) by dropwise addition of saturated aqueous NaHCO₃ (50 mL). The layers were separated. The aqueous layer was extracted with CH₂Cl₂ (50 mL). The combined organic layers were washed with brine (3x100 mL), were dried (MgSO₄) and were evaporated in vacuo to give a white residue, which was column chromatographed (silica gel; 4:1 PhMe - i-Pr₂O) to give 0.71 g (71%) of compound 3c; mp 66-67 °C; Rf 0.59 (i-Pr₂O). ¹H NMR (300 MHz, CDCl₃) δ: 2.3 (m, 2H, CH₂=C=O), 2.55 (brd, J = 6 Hz, CH₂, OH), 3.78 (m, 2H, NCH₂) 4.0 (m, 1H, CHO), 5.18 (m, 2H, C=CH₂), 5.88 (m, 1H, CH=CH), 7.75 (m, 2H, arom.), 7.85 (m, 2H, arom.). ¹³C-NMR (75 MHz, CDCl₃) δ: 39.6, 43.7, 69.5, 118.7, 123.5, 131.9,
133.5, 134.1, 168.9. Analysis C\textsubscript{13}H\textsubscript{13}NO\textsubscript{3} (231.25 g/mol). Calculated (%): C 67.52%, H 5.67%, N 6.06%. Found (%): C 67.33%, H 5.75%, N 6.01%.

1-Phenyl-4-penten-2-ol [3a] was obtained from 1.03 g (6.2 mmol) of la and 0.93 g (9.3 mmol; 50% excess) of 2, and isolated by column chromatography (PhMe) as colorless viscous oil in a yield of 0.61 g (61%). R\textsubscript{f} = 0.31 (PhMe)\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ: 1.81 (brs, 1H, OH), 2.24 (m, 1H, CH\textsubscript{2}C=C), 2.35 (m, 1H, CH\textsubscript{2}C=C), 2.74 (dd, 1H, J = 7.8, 13.6 Hz, PhCH\textsubscript{2}), 2.84 (dd, 1H, J = 5.0, 13.5 Hz, PhCH\textsubscript{2}), 3.86 (m, 1H, CHO), 5.14 (m, 2H, C=CH\textsubscript{2}), 5.85 (m, 1H, CH=C), 7.25 (m, 5H, Ph). \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}) δ: 41.4, 43.5, 71.8, 118.2, 126.5, 128.6, 129.5, 134.7, 138.4. Spectral data are identical to those reported earlier (9).

1-Benzylxoy-4-penten-2-ol [3b] was prepared from 1.16 g (5.2 mmol) Ib and 0.78 g (7.8 mmol; 50% excess) of 2, and isolated by column chromatography (4:1 PhMe-i-Pr\textsubscript{2}O) as colorless oil in a yield of 0.40 g (40%). R\textsubscript{f} = 0.33 (4:1 PhMe-i-Pr\textsubscript{2}O). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ: 2.22 (brd, 1H, J = 7 Hz, CH\textsubscript{2}C=C), 2.25 (brd, J = 7 Hz, 1H, CH=C=C), 2.7 (brs, 1H, OH), 3.34 (dd, 1H, J = 9.6, 7.4 Hz; BnOCH\textsubscript{2}), 3.47 (dd, 1H, J = 9.6, 3.5 Hz, BnOCH\textsubscript{2}), 3.84 (m, 1H, CHO), 4.51 (s, 2H, PhCH\textsubscript{2}O), 5.1 (m, 2H, C=CH\textsubscript{2}), 5.80 (m, 1H, CH=C), 7.3 (m, 5H, Ph). \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}) δ: 38.2, 69.9, 73.5, 74.1, 117.7, 127.8, 127.9, 128.5, 134.4, 138.0. Spectral data are identical to those reported earlier (10).

Results and Discussion

Recently, a new method for the alkylation of aldehydes has been described, in which the allyl moiety was transferred from a sterically crowded homoallylic alcohol to an aldehyde to produce a new homoallylic alcohol 3 in a reaction of Lewis acid (Scheme 2) (11). Similar reactions have been studied by other researchers (12-14). The mechanism for the allyl transfer to aldehyde included a 2-oxonia [3.3]-sigmatropic rearrangement (11,12) (named also as "oxa Cope" rearrangement (14-16)) between cations A and B (Scheme 2). The tetrahydropyranyl cation C was also considered as a possible intermediate (11a, 13,17-19). An increased stability of the cation B directed the reaction towards the formation of a ketone (acetone, when R = R’ = Me) and the allyl-transfer product 3 (11a) rather than the cyclization product(s) 4.

Another reaction of homoallylic alcohols, supposedly proceeding via similar initial steps and the same intermediates A, B and/or C, is the cyclization with aldehydes or their acetals leading to tetrahydropyrans 4 (13-20) (Schemes 2, 3). In the course of studies on this cyclization (13,17), we observed a formation of small amounts of new homoallylic alcohols 3 and the products of their further reaction 5 (e.g. 3c and 5c Scheme 3) (see also Reference 14).

In many syntheses, acetals are excellent synths for aldehydes due to their stability and extended shelf life. Acetals have been widely used instead of aldehydes for the cyclization with homoallylic alcohols into the tetrahydropyrans 4 (13-20), but have not been used so far as starting materials for the allyl transfer reaction leading to the homoallylic alcohols 3. We carried out the reaction of acetals la-1c with 2-methyl-4-penten-2-ol 2 in presence of Me\textsubscript{3}SiOTf as Lewis acid (see Experimental). The plausible mechanism of the allyl transfer reaction and of the competing cyclization reaction is presented in Scheme 4. An additional methyl group in 2 contributes to a stabilization of cation B (R = R’ = Me), thus directing the reaction towards 3. The
Scheme 4.

non-nucleophilic character of triflate anion diminishes its nucleophilic addition to the intermediate cation(s), which would lead to tetrahydropyrans of type 4.

We did not yet isolate the expected side product 4 and the byproduct Me₂C(OEt)₂. In the allyltransfer reaction of 2 with aldehydes, dihydropyrans were detected (11a) instead of tetrahydropyrans 4.

The approach described above allows a one-step synthesis of synthetically useful homoallylic alcohols from readily available, stable precursors using inexpensive reagents.

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References

(b) C. J. Li. Chem. Rev., 1993, 93, 2023-2035.
(b) W.-C. Zhang, and C. J. Li. Tetrahedron, 2000, 56, 2403-2411.