A Simple and Direct Synthesis of α-Hydroxy Unsaturated Aldehydes from α-Cyano- α-Hydroxymethyl Epoxides

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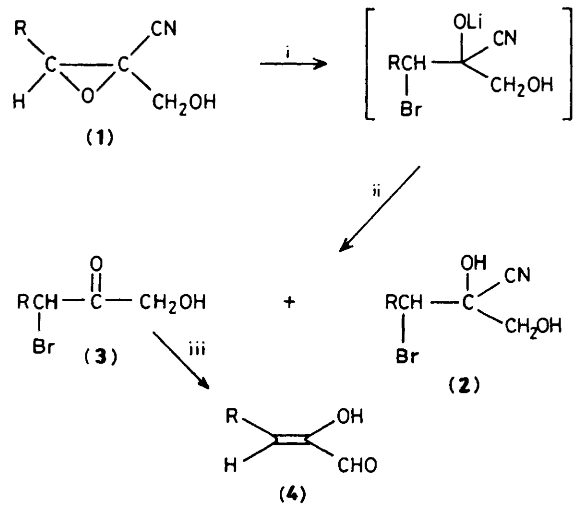
The ring opening of α-cyano-α-hydroxymethyl epoxides by a solution of the complex Li_2NiBr_4 in tetrahydrofuran leads to α-bromo-α′-hydroxy ketones which in treatment with pyridine give good yields of α-hydroxy unsaturated aldehydes.

α-Dicarbonyl compounds are important synthetic intermediates; there is also substantial interest in their antiviral properties.[1—3] α-Hydroxy unsaturated aldehydes are tautomeric forms of α-dicarbonyl compounds. However, despite two recent interesting reports describing multistage syntheses of α-hydroxy unsaturated aldehydes from 2,2-dimethyl-1,3-dioxole[3] or from dioxolanones,[4] the preparation of derivatives of this series remains difficult, and such compounds are poorly represented in the literature.

α-Cyano-α-carboxyethyl epoxides are readily accessible starting materials[5] which are reduced by sodium borohydride within 5 min into the corresponding α-cyano-α-hydroxymethyl epoxides (**1**).[6] We describe here a one-pot synthesis of the α-hydroxy unsaturated aldehydes (**4**) starting from the epoxides (**1**).

As dilithium tetrabromonickel(II) in tetrahydrofuran (THF) is known to be a mild reagent for the ring opening of epoxides,[7,8] we treated the epoxides (**1**) with this complex and obtained the α-bromo-α′-hydroxy ketone derivatives (**3**) contaminated by about 20% of the cyanohydrin (**2**). The mixture of (**2**) and (**3**) was characterized by ^1H n.m.r. spectroscopy and directly treated with pyridine to give moderate yields of the α-hydroxy unsaturated aldehydes (**4**) (Scheme 1; Table 1).



Scheme 1. *Reagents and conditions:* i, epoxide (**1**) (5.7 mmol), Li_2NiBr_4 (2.85 mmol), THF (27 ml), room temp., 6 h under N_2; ii, H_2O; iii, pyridine (5.7 mmol), reflux, 2 h.

Table 1. Preparation of the unsaturated aldehydes (**4**).†

R	Ph[a]	*p*-ClC_6H_4	*p*-MeC_6H_4	*p*-$O_2NC_6H_4$	Et[d]
M.p., *t*/°C	119	162	176	173—175	—
(**3**)/(**2**)[b]	85/15	90/10	80/20	65/35	—
% Yield[c]	70	68	50	57	44

[a] Lit.[3,4,9,10] m.p. 119 °C. The ^1H n.m.r. and i.r. spectra of compound (**4**; R = Ph) are representative: δ_H ($CDCl_3$) 9.22 (1H, d, $^4J_{OH}$ 1.4 Hz, CHO), 7.87—7.27 (5H, m, Ph), 6.71 (1H, t, $^4J_{OH}$ = $^4J_{CH}$ = 1.4 Hz, OH), and 6.14 (1H, d, $^4J_{OH}$ 1.4 Hz, PhC*H*); the coupling constants could only be measured for a very pure sublimed sample and were assigned using spin decoupling; i.r. (CCl_4, cm^{-1}) 3446, 1672, 1648 cm^{-1}. [b] Ratio determinated by n.m.r. spectroscopy before elimination of HBr from (**3**). [c] Yield of the pure isolated aldehyde (**4**). [d] Compound (**4**; R = Et) was not stable and was characterized as its acetate (*Z*)-EtCH=C(OAc)CHO.

Their n.m.r. and i.r. spectra show that these compounds exist in the enol form. The reaction leads to only one isomer, probably the *Z*-isomer (**4**). This *cis*-relationship between C*H* and C*H*O is consistent with the ^1H n.m.r. spectra (no coupling observed between these two protons) and also with the ^{13}C n.m.r. spectra: $\delta_{C=O}$ 190.8, ^1J 185, ^3J 6 Hz.‡

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† The α-hydroxyaldehydes (**4**) gave satisfactory elemental analyses.

‡ ^3J for the *E*-isomer would be expected to be larger (*ca.* 12—14 Hz): V. Vogeli and W. Von Philipsborn, *Org. Magn. Reson.*, 1975, **7**, 617.