Pergamon

Tetrahedron Letters, Vol. 36, No. 2, pp. 307-310, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02237-2

Alkylative Elimination of α,β-Epoxy Tosylhydrazones

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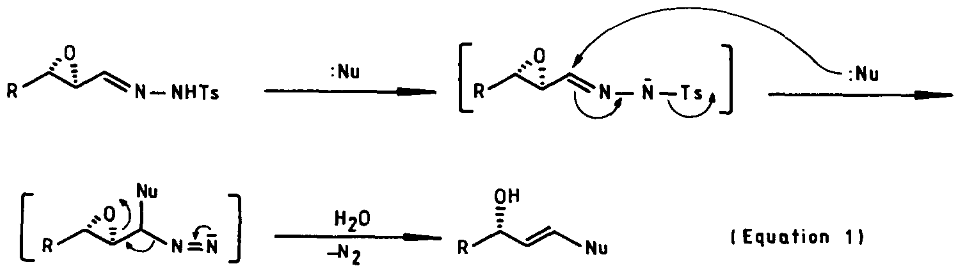
Abstract: *Optically pure allyl alcohols have been prepared from tosylhydrazones derived from chiral epoxy aldehydes by alkylative elimination utilizing alkyl magnesium reagents.*

The discovery of arylsulfonylhydrazines by Curtius and Lorenzen in 1898 and subsequently their carbonyl adducts (Hydrazones),[1] this class of compounds have been found to be very useful as exemplified by the Shapiro reaction.[2] Though this reaction has initially been restricted to simple alkene synthesis[3] has come into prominance as a vinyl anion equivalent and could be intercepted with electrophiles due to a modification involving TMEDA as solvent.[4] Furthermore, aldehyde tosylhydrazones have been shown to react with alkyllithium or cuprate reagents[5] to form anionic addition products. To further exploit the usefulness of tosylhydrazones in organic synthesis, herein, we disclose our latest findings on the alkylative elimination[6] of chiral α,β-epoxytosylhydrazones obtained from corresponding chiral epoxy aldehydes which in turn are readily accessible by Sharpless asymmetric epoxidation of allyl alcohols[7] (Equation 1). The E-allyl alcohol thus obtained forms part structure of several biological important natural products such as leukotrienes[8,9] and glycosphingolipids.[10]

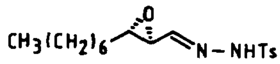
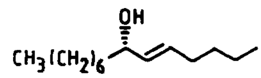
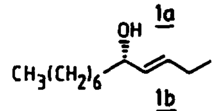
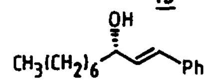
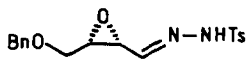
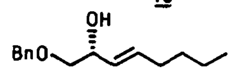
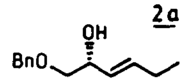
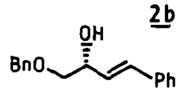
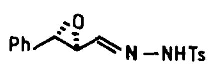
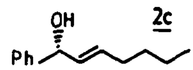
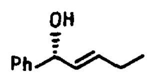
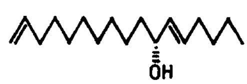
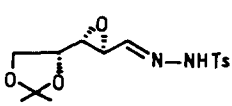
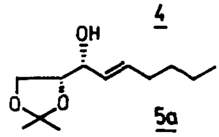
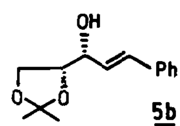


(Equation 1)

Accordingly, epoxyhydrazone (entry 1) when treated with three equivalents of BuMgBr in ether at ambient temperature furnished the alkylated chiral allyl alcohol **1a** in 68% yield. Encouraged by this finding, other carbon nucleophiles viz., PhMgBr and EtMgBr were added to ethereal solution of **1** to observe an identical

IICT Communication No.3450

Table - 1

Entry	Epoxyhydrazone[a]	Grignard Reagent	Product	Yield* (%)
1		BuMgBr	 1a	68
		EtMgBr	 1b	66
		PhMgBr	 1c	58
2		BuMgBr	 2a	65
		EtMgBr	 2b	64
		PhMgBr	 2c	70
3		BuMgBr	 3a	65
		EtMgBr	 3b	62
4		BuMgBr	 4	71
5		BuMgBr	 5a	62
		PhMgBr	 5b	60

a - Epoxyhydrazones were prepared from corresponding alcohols[11] by Collins' oxidation (CrO_3, Pyr, 0°, 3h) followed by derivatization with tosylhydrazine (MeOH, 23°C, 2h)

* - Yields calculated after column chromatography of the products.

transformation. The generality of this transformation is further strengthened by preparation of a cross section of epoxy tosyl hydrazones and exposure to carbon nucleophiles as demonstrated in Table 1. Thus, the simple epoxy tosyl hydrazone **1**, benzyloxyepoxy substrate **2**, epoxyhydrazone of cinnamyl aldehyde **3**, a terminal olefin **4**, acetonide functionality **5**, all survived the reaction conditions and gave consistantly good yield of the allyl alcohol product **1-5a,b** or **c** depending on the carbon nucleophile used. A noteworthy feature of the reaction is the exclusive formation of E-olefin as was confirmed by ^{1}H - NMR of the corresponding acetate (Ac_2O, Pyridine) and decoupling experiments.[12]

Due to ease of availability of chiral 2,3-epoxy alcohols and in turn aldehydes, it is pertinent to mention here that the new alkylative elimination reaction described herein should offer important solutions in the synthesis of natural products having (E)-allyl alcohol fragment.

General procedure:

Preformed alkyl/phenyl magnesium halide (3 mmoles) in 5 ml ether is added dropwise to a ice cold epoxytosylhydrazone (1 mmole) in 5 ml ether under nitrogen. After 30 minutes of stirring at ambient temperature, reaction mixture was quenched with saturated NH_4Cl solution (10 ml) and extracted with ether (2x25 ml). The combined ethereal layer was washed with water and brine. After drying over Na_2SO_4, the solvent is evaporated in vacuo and the residue chromatographed on SiO_2 to afford the E-allyl alcohol in the yields summarized in Table I.

Acknowledgement:

One of the authors (MT) is thankful to CSIR, New Delhi for financial assistance.

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11. Epoxy alcohol corresponding to compound **1** was prepared by alkylation of propargyl alcohol with C-7 bromide followed by LAH reduction and Sharpless asymmetric epoxidation. Compounds **2** and **3** were prepared according to reference 7. Compounds **4** and **5** were prepared from Wittig reaction of 10-undecenal or 2,3-O-isopropylidene-D-glyceraldehyde respectively with (carbo-ethoxy)methylene triphenylphosphorane followed by DIBAL-H reduction and Sharpless asymmetric epoxidation.
12. Representative PMR of **1c** ($CDCl_3$:200 MHz): δ 0.85 (dist t,3H), 1.2-1.8 (m,12H), 4.2-4.31 (m,1H), 6.20 (dd,1H,J=15.,8.5 Hz), 6.55 (d,1H,J=15 Hz), 7.10-7.40 (m,5H,aromatic).

(Received in UK 11 *October* 1994; *revised* 7 *November* 1994; *accepted* 11 *November* 1994)