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[a0021]

One-Pot Synthesis of *syn*-Epoxyalcohols from a,b-Unsaturated Ketones

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Abstract: a,b-Unsaturated ketones were transformed into *syn*-epoxyalcohols by sequential use of diisobutylaluminium hydride and *tert*-butylhydroperoxide.

Keywords: Reduction of conjugated ketones, diisobutylaluminium hydride (DIBAH), *syn*-epoxidation, *tert*-butylhydroperoxide

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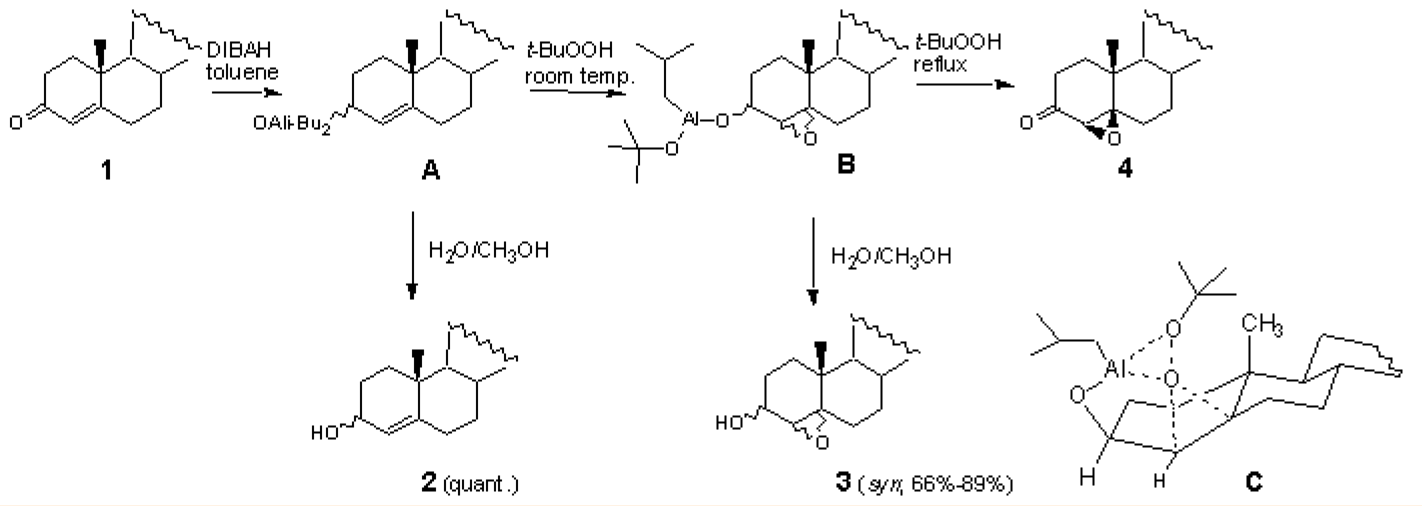
Introduction

syn-2,3-Epoxyalcohols are versatile intermediates in organic synthesis, and they are usually prepared by $Ti(OPr^i)_4$ [1] and $VO(acac)_2$ [2] catalysed *t*-BuOOH epoxydations, peroxyacid epoxidations of allylic alcohols, or more recently, by using Ti and Cr doped zeolite catalysts [3]. After initial success of oxidation of allylic aluminates by oxygen into *syn*-2,3-epoxy- alcohols [4], now we report the use of *t*-BuOOH as an oxygen donor in the epoxidation of allylic diisobutylaluminates (*Scheme*, **A**), thus establishing a simple one-pot procedure for a,b-unsaturated ketone-to-*syn*-2,3-epoxyalcohol transformation.

Scheme



Results and Discussion

Ketones given in *Table* were reduced with 1.5 M DIBAH in toluene (1.1 equiv.), the corresponding aluminates **A** were then treated at r.t. with 3 M isooctane solution of *t*-BuOOH (2 equiv.) for 2-2.5 h and the reaction mixture was quenched with methanol/water mixture. The epoxidation reaction is stereospecific and the yield of corresponding *syn*-epoxyalcohols **3** generally exceeds 75% [5]. The ratio of such formed epoxides parallels the ratio of epimeric allylic alcohols **2** obtained from the corresponding ketones [4]. The observed stereospecificity was confirmed by treatment of cholest-4-en-3b-ol (**2a**) with DIBAH followed by *t*-BuOOH under the same reaction conditions as above yielding exclusively the corresponding a,b-epoxyalcohol **3a** in 84% yield (Run 2). The stereospecificity of epoxidation reaction could be explained by directional effect of b-bounded Al as in **C** [6] (analogously to Ti-catalysed epoxidations).

By prolonging the reaction time over 2.5 h the formation of epoxyketones **4** was detected. An effort to incorporate the third step into already established two-step one-pot process depicted in *Scheme*, was not completely successful. The yield of epoxyketones did not exceed 55% with respect to monoketones, and was lower with diketones (32%-42%).

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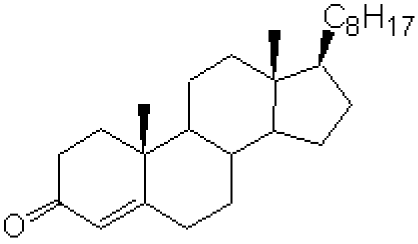
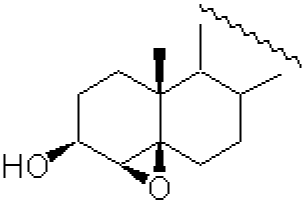
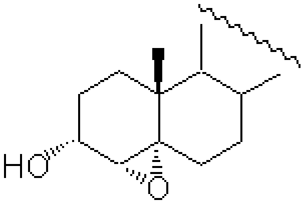
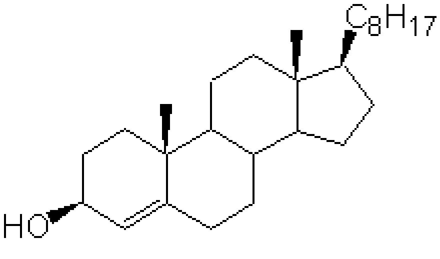
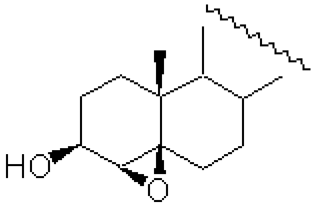
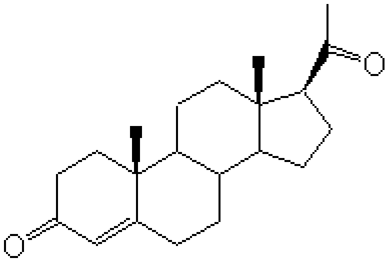
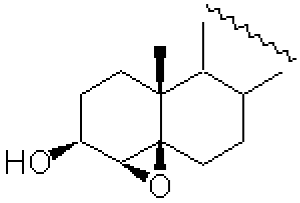
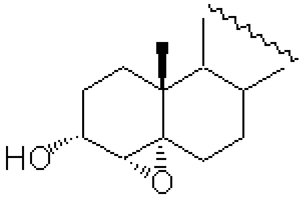
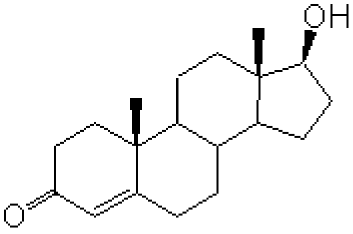
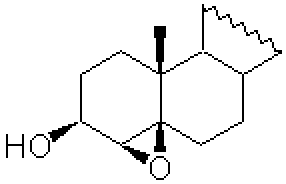
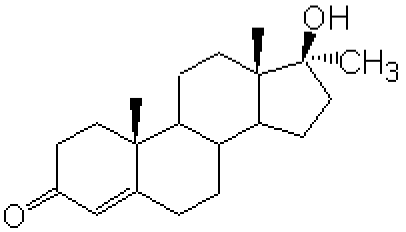
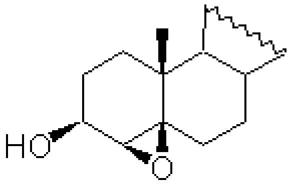
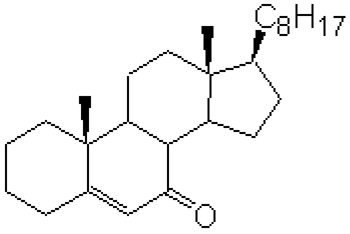
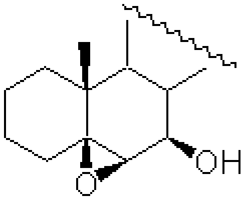
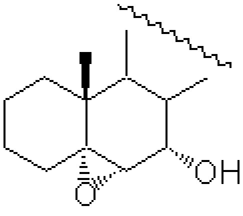
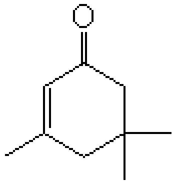
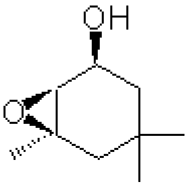
Table

Table. One-Pot Reduction �> Epoxidation Reaction of a,b-Unsaturated Ketones with DIBAH and *t*-BuOOH

Run	Substrate	Epoxyalcohol
1�	 **1a**	 **3a:** 68%  **3a':** 17% + allylic alcohols **2** (3β: 8.5%; 3α: 2.5%)

2�	 **2a**	 **3a:** 84% + **2a:** 11%
3�	 **1b**	 **3b:** 61% (20b)  **3b':** 16% (20b) + allylic alcohol **2** (3b, 20b:10%)
4�	 **1c**	 **3c:** 77% + allylic alcohol **2** (3b:10%)
5	 **1d**	 **3d:** 66% + allylic alcohol **2** (3β: 26%)
6	 **1e**	 **3e:** 73%  **3e':** 16%
4	 **1f**	 **3f:** 78%.

The following are sample procedures.

2,3-Epoxyalcohols from enones

Cholest-4-en-3-one **1** (1.0 g, 2.6 mmol) was dissolved in dry toluene (25 cm^3) under argon and DIBAH (1.5 M in toluene; 1.9 cm^3, 2.86 mmol) was added dropwise at room temperature. After 15 min *t*-BuOOH (3 M in isooctane; 1.70 cm^3, 5.2 mmol) was added and stirred at room temperature for 2.5 h. The aluminate **B** was then destroyed using H_2O/MeOH (1.7:1) mixture at 0 ^{o}C, formed precipitate was filtered off and filtrate evaporated. The resulting mixture was separated by SiO_2 chromatography (eluent: toluene) affording **3a** (752 mg, 68%), mp 94-96 ^{o}C, **3a�** (188 mg, 17%), mp 82-85 ^{o}C, and 11% (3.5 : 1 - 3b: 3a)-mixture of allylic alcohols **2** (^{1}H NMR estimation).

Epoxyketones were prepared from enones under the same reaction conditions except that *t*-BuOOH oxidation was performed at reflux for 24 h. Cholest-4-en-3-one **1** (500 mg) was transformed into 4b,5b-cholestan-3-one **4** (255 mg, 54%), mp 114-115 ^{o}C together with 14% mixture of epimeric allylic alcohols **2** and 32% mixture of epoxy alcohols **3a** and **3a�**.

References and Notes

[1] A. Pfenninger, *Synthesis* **1986**, 89.
[2] T. Itoh, K. Jitsukawa, K. Kaneda, S. Teranishi, *J. Am. Chem. Soc.* **1979**, *101*, 159.
[3] (a) W. Adam, A. Corma, T.I. Reddy, M. Renz, *J. Org. Chem.* **1997**, *62*, 3631. (b) R. Kumar, G.C.G. Pais, B. Pandey, P. Kumar, *J. Chem. Soc. Chem. Commun.* **1995**, 1315. (c) R. Joseph, M. Sasidharan, R. Kumar, A. Sudalai, T. Ravindranathan, *J. Chem. Soc. Chem. Commun.* **1995**, 1341.
[4] B. �olaja, *J. Serb. Chem. Soc.* **1993**, *58*, 155.
[5] Similar results were obtained using 80% *t*-BuOOH / t-BuOOBu^t solution.
[6] K. Takai, K. Oshima, H. Nozaki, *Tetrahedron Lett.* **1980**, *21*, 1657.

Comments

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