

SHORT COMMUNICATION

**An one-pot synthesis of *syn*-2,3-epoxyalcohols from
 α,β -unsaturated ketones**

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Facile one-pot synthesis of *syn*-2,3-epoxyalcohols from α,β -unsaturated ketones was achieved by consecutive addition of diisobutylaluminium hydride and *t*-butyl hydroperoxide.

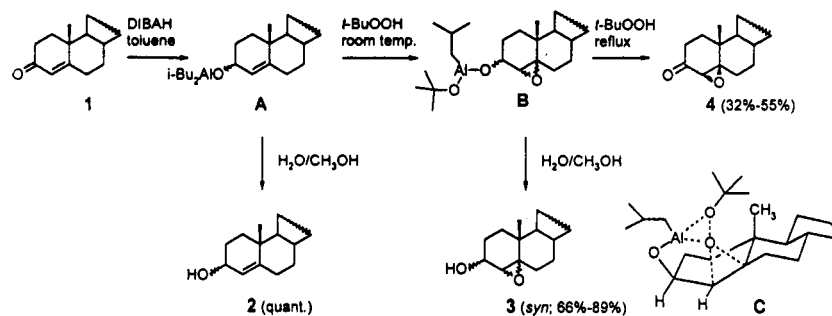
Key words: reduction, epoxidation, diisobutylaluminium hydride, *t*-butyl hydroperoxide, *syn*-epoxyalcohols, steroid.

Syn-2,3-epoxyalcohols are versatile intermediates in organic synthesis which are usually prepared by $\text{Ti}(\text{OPr}^t)_4$ ¹ or $\text{VO}(\text{acac})_2$ ² catalyzed *t*-BuOOH, by peroxyacid epoxidation of allylic alcohols, or by using Ti and Cr doped zeolite catalysts.³ Recently, it has been shown that oxygen transfer from the hydroperoxy group in allylic and homoallylic systems, whereby *syn*-2,3-epoxyalcohols are formed, can also be achieved.⁴

It is well known that diisobutylaluminium hydride (DIBAH) stereoselectively reduces α,β -unsaturated ketones to allylic aluminates (**A**, Scheme 1).⁵ Alkylalanes are readily oxidised by oxygen to the corresponding aluminates (*via* the corresponding peroxides),^{5,6} thus establishing the process of hydroalumination of terminal C=C bonds as a useful method for *anti*-Markovnikov alcohol synthesis.^{5c,5d,7} Such findings prompted us to couple the reduction of α,β -unsaturated ketones with the oxidation (O_2) of the obtained allylic aluminates, in an one-pot process affording *syn*-2,3-epoxyalcohols in 40-50% yield.^{5f,8} Now, we report the use of *t*-BuOOH as the oxygen donor in the epoxidation of allylic diisobutylaluminates **A** (Scheme 1).

The above given ketones were reduced with 1.5 M DIBAH in toluene (1.1 equiv.). The obtained aluminates **A** were then treated at room temperature with 3 M *t*-BuOOH in isooctane (2 equiv.) for 2–2.5 h and the reaction mixture was quenched with a methanol/water mixture. The epoxidation reaction is stereospecific and the yield of the corresponding *syn*-epoxyalcohols generally exceeds 75%.^{*} The propor-

* Similar results were obtained using 80% *t*-BuOOH/*t*-BuOOBu-*t* solution.



Scheme 1.

tion of the so-formed epoxyketones **3** in accordance with the ratio of the epimeric allylic alcohols **2** obtained from the corresponding ketones.^{5f} The observed stereospecificity of the epoxidation reaction was confirmed by treatment of previously prepared cholest-4-en-3 β -ol (**2a**) with DIBAH, followed by *t*-BuOOH under the same reaction conditions as above, yielding exclusively the corresponding *syn*-epoxyalcohol **3a** in 84% yield (Run 2, Table 1).

The stereospecificity of the reaction can be explained by the directional effect of the β -bound Al as in **C**⁹ (analogous to Ti-catalyzed epoxidations).

On prolongation of the reaction time over 2.5 h, the formation of epoxyketones was detected. Attempts to incorporate a third step into the already established two-step one-pot process, depicted in Scheme 1, was not completely successful. The yield of epoxyketones did not exceed 55% with respect to the mono- α,β -unsaturated ketones, and was lower with the corresponding diketones (32%–42%).

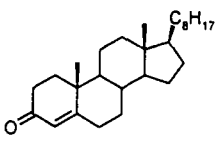
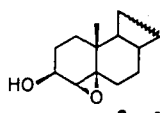
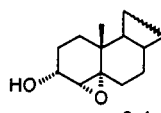
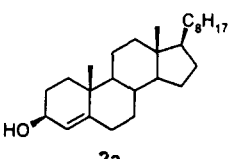
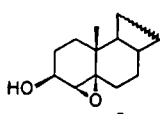
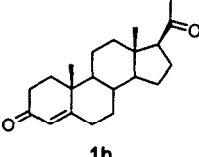
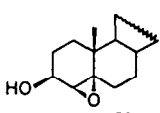
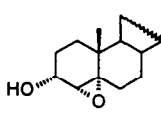
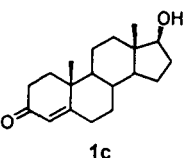
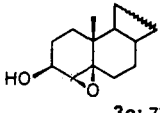
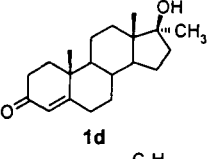
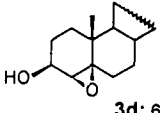
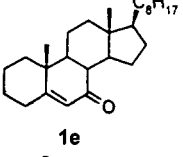
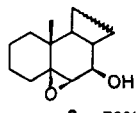
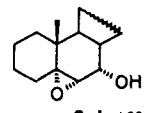
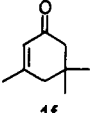
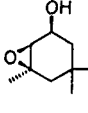
EXPERIMENTAL

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 mL) under argon and DIBAH (1.5 M in toluene; 1.9 mL, 2.86 mmol) was added dropwise at room temperature. After 15 min., *t*-BuOOH (3 M in isooctane; 1.70 mL, 5.2 mmol) was added and stirred at room temperature for 2.5 h. The aluminate **B** was then decomposed using a H₂O/MeOH (1.7:1) mixture at 0 °C. The formed precipitate was filtered off and filtrate evaporated. The resulting mixture was separated by SiO₂ chromatography (eluent: toluene) affording **3a** (752 mg, 68%), mp. 94–96 °C (Ref. 8, 94–95 °C), **3a'** (188 mg, 17%), mp 82–85 °C (Ref. 8, oil), and 11% (3.5 : 1–3 β :3 α)-mixture of allylic alcohols **2** (¹H-NMR estimation).

Epoxyketones were prepared from conjugated ketones under the same reaction conditions except that the *t*-BuOOH oxidation was performed at reflux for 24 h. Cholest-4-en-3-one **1** (500 mg) was transformed into 4 β ,5 β -epoxycholestan-3-one **4** (281 mg, 54%), mp 114–115 °C (Ref. 10, 116–117 °C) together with 14% of a mixture of epimeric allylic alcohols **2** and 32% of a mixture of epoxy alcohols **3a** and **3a'**.

Table 1. One-Pot Reduction → Epoxidation Reaction Sequence of α,β -Unsaturated Ketones with DIBAH and <i>t</i> -BuOOH		
Run	Substrate	Epoxyalcohol [∇]
1	 1a	 3a: 68%  3a': 17% + allylic alcohols 2 (3 β : 8.5%; 3 α : 2.5%)
2	 2a	 3a: 84% + 2a: 11%
3	 1b	 3b: 61% (20β)  3b': 16% (20β) + allylic alcohol 2 (3 β , 20 β : 10%)
4	 1c	 3c: 77% + allylic alcohol 2 (3β: 10%)
5	 1d	 3d: 66% + allylic alcohol 2 (3β: 26%)
6	 1e	 3e: 73%  3e': 16%
7	 1f	 3f: 78%

[∇] Yields of isolated compounds. For yields of allylic alcohols **2** see ref. 8. All products have correct spectral data.

ИЗВОД

СИНТЕЗА *sin*-2,3-ЕПОКСИАЛКОХОЛА ИЗ α,β -НЕЗАСИЋЕНИХ КЕТОНАИРИС ЂОРЂЕВИЋ^а и БОГДАН ШОЛАЈА^б^аВетеринарски факултет Универзитета у Београду и ^бХемијски факултет Универзитета у Београду,
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Приказан је једноставан поступак за синтезу *sin*-2,3-епоксиалкохола редукцијом α,β -незасићених кетона диизобутилалуминијум хидридом и епоксидацијом награвљених алумината *t*-бутил-хидропероксидом.

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