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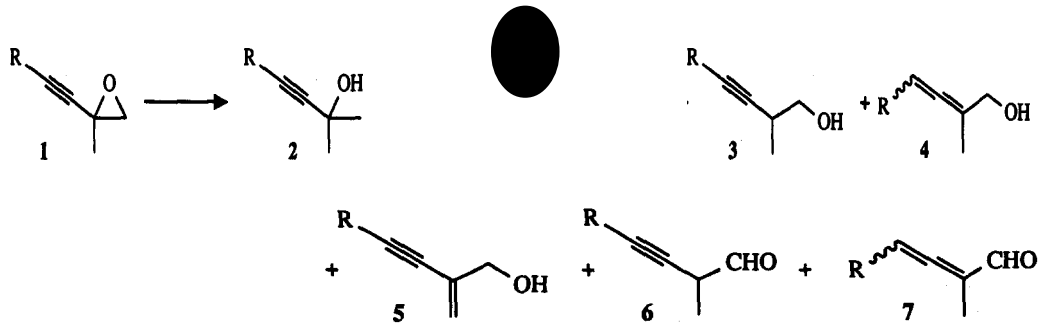
Regioselective Ring Opening of a-Substituted α-Alkynyl Oxiranes to 2-Substituted 3-Butyn-1-ols

Peter Nussbaumer*, Anton Stütz

Department of Dermatology, SANDOZ Forschungsinstitut Wien, Brunnerstraße 59, A-1235 Vienna

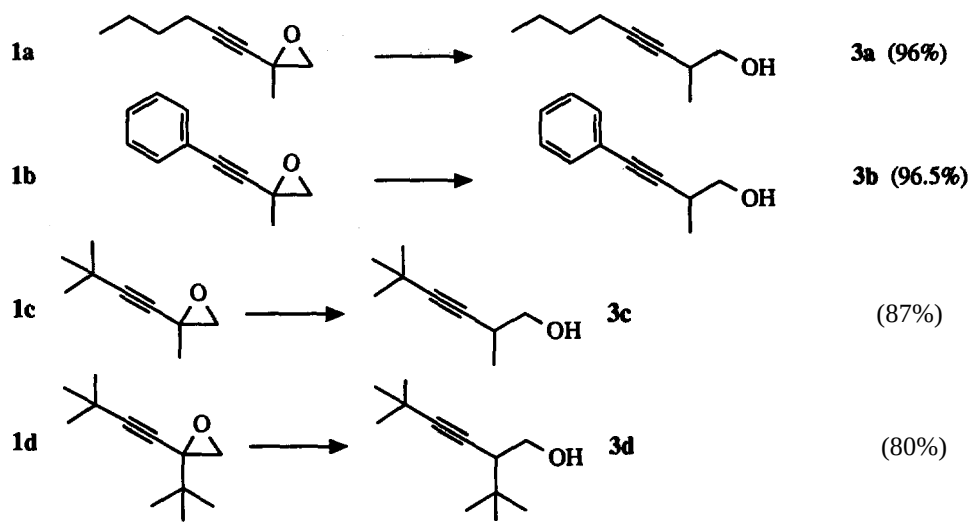
Abstract: Treatment of a-substituted a-acetylenic epoxides with DIBAH in THF provides 2-substituted 3-butyn-1-ols in high yield avoiding propargyllallene isomerixation.

Addition of titanium acetylides to monosubstituted oxiranes is the only synthesis of 2-substituted 3-butyn-1-ols 3 reported so far,[1] that generates high yields and is generally applicable. We envisaged that reduction of a-substituted a-alkynyl epoxides 1 could give ready access to homopropargylic alcohols 3. Reductive ring opening of oxirane 1 can, in principle, yield the regioisomeric alcohols 2, 3 and 4. In addition to the possibilities arising from regioselectivity and propargyl/allene isomerixation, the non reductive formation of products 5, 6 and 7 has to be considered depending on the nature of the reducing agent, which might act as (Lewis)base or (Lewis)acid, and the solvent.[2,3,4] For the reductive ring opening of a-vinylic and a-allenic oxiranes it has been reported that the regioselectivity can be influenced by varying the reducing agent and the solvent.[5,6]



Testing several combinations of reducing agents ($LiAlH_4$, $LiAlH_4/AlCl_3$, DIBAH) with different solvents in the reduction of oxirane 1a (R = n-butyl) the following results were obtained: As expected reduction of 1a with $LiAlH_4$ in ether exclusively generated propargylic alcohol 2a, whereas the use of $LiAlH_4/AlCl_3$ (1/4) in ether produced mainly the desired homopropargylic product 3a (≈ 70%) and its allene isomer 4a (≈ 20%). Treatment of 1a with DIBAH in hexane resulted in a mixture of 2a (≈ 10%), 3a (≈ 26%), 4a (≈ 45%) and 5a (≈ 15%). Finally, when DIBAH in THF was used, 1a was almost quantitatively converted to 3a (≈ 96%). In addition to the high regioselectivity observed in this reaction, the extremely low amount of allene isomer 4a produced (≈ 1%) is particularly noteworthy.

The results of the treatment of epoxides **la-d**[7] with 1.2 equivalents of **DIBAH** for one hour at **-20°** C in THF, followed by workup with aqueous ammonium chloride solution, are **summarized** in the following scheme (yields were determined by GC-analysis):



Following this **procedure,** epoxides **la and lb were** converted nearly quantitatively into **homopropargylic** alcohols **3a** and **3b, respectively. The ring opening proceeded with complete regioselectivity (propargylic** alcohols **2a** and **2b were** not detectable in the crude product mixture by comparative GC-analysis) and with extremely low isomerixation to allenic products **(4a and 4b were only** detectable by GC in about 1 and 0.6 percentage). The yield of **3c,** obtained by reduction of oxirane **lc with DIBAH/THF, was** high. However, **≈2%** of isomeric alcohol **4c** and, differing from the other reactions, about 10% of allenic aldehyde **7c** were also formed. Treatment of **1d afforded the desired** product **3d** in good yield, but gave also minor amounts of alcohols **4d (9%)** and **2d** (7%). probably due to increased steric hindrance in compound **1d.**

The usefulness of the method in preparative chemistry was demonstrated by the synthesis of analytically pure **3a** and **3c** on a gram scale with yields of 86% and 77%. Therefore, the described method is a good alternative to the ring opening of oxiranes with titanium acetylides. **In** addition, it offers the possibility of synthesizing **1,2-disubstituted 3-butyn-1-ols** starting from **α,β-disubstituted** a-acetylenic epoxides.

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7. **Epoxides la-d were synthesized** by reacting the respective lithium acetylides with the appropriate **chloromethylketones.**

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