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Highly diastereoselective dihydroxylation of *cis*-substituted sulfonyl vinyl oxiranes[1]

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Abstract

An expedient route to rare carbohydrate-like fragments that relies on the highly stereoselective osmium-catalyzed dihydroxylation of 2-sulfonyl-2-hydroxyalkyl-3-vinyloxiranes is outlined. © 2000 Elsevier Science Ltd. All rights reserved.

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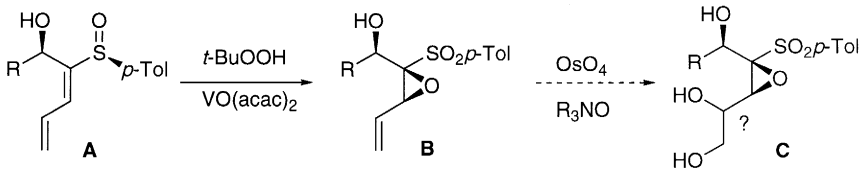
The osmium-catalyzed dihydroxylation of alkenes bearing an allylic oxygen takes place with high *anti* stereoselectivity in most cases.[2] Interestingly, to our knowledge, there are just three reports on the dihydroxylation of alkenyl *trans*-oxiranes that occurred with low stereoselectivity.[3] While the use of reagent-controlled catalytic asymmetric dihydroxylation procedures[4] provided good to excellent diastereocontrol in those cases,[3,5] we felt that *cis*-substituted oxiranes could display a useful level of diastereoselectivity even in the absence of chiral ligands. Enantiopure sulfonyl vinyl oxiranes **B**, readily available by metal-catalyzed oxidation at sulfur followed by hydroxyl-directed epoxidation at the most electron deficient double bond,[6] appeared as good test substrates for this study since the dihydroxylation to give adducts **C** would also produce rare carbohydrate-like fragments in an expedient fashion (four steps from commercially available menthyl sulfinate) (Scheme 1). The recent disclosure of the work by Cossy et al. on the dihydroxylation of *cis*-substituted isopropenyl cyclopropanes, oxiranes and aziridines,[7] prompted us to report our preliminary results on this subject.[8]



Scheme 1.

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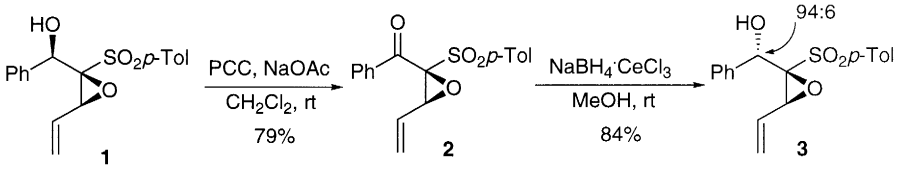
To enhance the synthetic usefulness of our proposed approach to carbohydrate-like fragments we sought an efficient procedure for preparing diastereomeric oxiranes, such as **3** (Scheme 2) from **1**. After many fruitless attempts under Mitsunobu conditions we turned our attention to an oxidation–reduction protocol. After considerable experimentation, we found that the reduction of ketone **2** with $NaBH_4 \cdot CeCl_3$[9] gave an excellent yield of the desired product **3**, readily separated from a small amount of **1**.[10] It should be pointed out that the stereoselectivity of this reduction is opposite to the literature data,[9] probably due to the presence of the sulfonyl moiety in our substrate **2**.

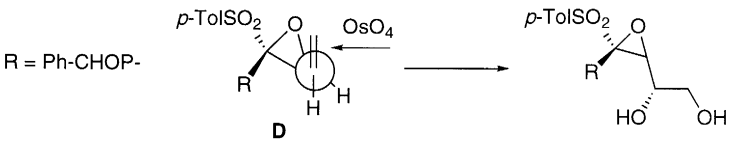


Scheme 2.

Table 1 gathers our preliminary results on the osmium-catalyzed dihydroxylation of our sulfonyl vinyl oxiranes.[11,12] To evaluate the stereodirecting capabilities of the benzylic and/or sulfinyl chiral centers, in the absence of the oxirane, the dihydroxylation of diene **4** was studied and a good yield of a 60:40 mixture of sulfinyl triacetates **5** was obtained along with some sulfone **6**, also as a 60:40 mixture; standard oxidation of **5** gave **6** in good yield. Under similar conditions, hydroxy vinyl oxirane **3** led to a fair yield of a 65:35 mixture of triacetate **7** and ketone **8**, derived from overoxidation at the benzylic position, both obtained as single isomers. In contrast, benzyl ether **9** gave the corresponding protected triol **10** with diminished diastereoselectivity (85:15). Entries 4 and 5 show that diastereomeric hydroxy vinyl oxirane **1** is also a good substrate for this protocol giving triacetate **12** as a single isomer along with a small amount of ketone **8**, provided that osmylation is not allowed to proceed for a long time.

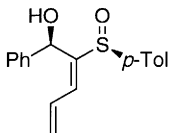
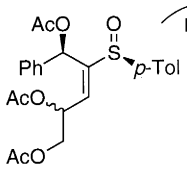
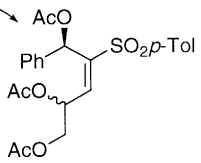
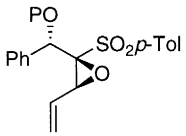
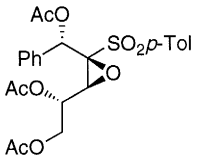
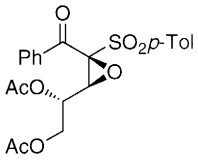
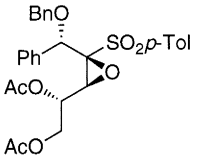
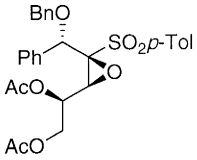
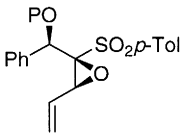
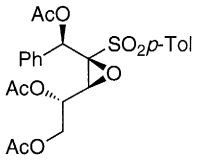
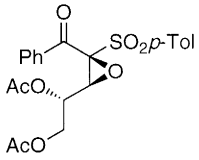
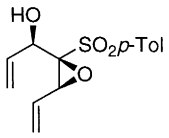
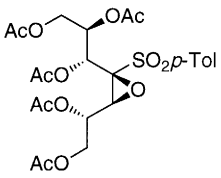
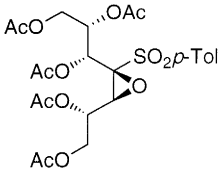
While the observed overoxidation is likely related with the reaction time and the benzylic nature of these substrates, we sought an alternative protecting group that would prevent overoxidation without compromising the facial selectivity of the process. In this regard the osmylation of acetoxy vinyl oxirane **13** was explored to give, after removal of the acetate and peracetylation, a single isomer of triacetate **12** (entry 6). Finally, we addressed the 'simultaneous' dihydroxylation of **14** at both vinyl residues that gave just two of the four possible isomers of the rare protected heptitols **15** and **16** in a highly stereoselective manner (entry 7).

The isolation of ketone **8** from both diastereomers **3** and **1** indicates that the stereochemical outcome of the process is independent of the configuration of the hydroxyalkyl substituent *cis* to the vinyl moiety. The very high selectivity found for these substrates is in sharp contrast to the recent findings of Cossy et al. for a *cis*-2-alkyl-3-vinyloxirane that, unlike the related isopropenyl oxiranes, gave a 50:50 mixture of diastereomers upon catalytic dihydroxylation.[7] These results may be accounted for largely as described by these authors in terms of electrophilic addition to the less hindered face of the *gauche* conformation **D** (Scheme 3).[13] In our case, the presence of the bulky sulfonyl moiety is likely to exert a determining influence on the conformational distribution of the key secondary alcohol center of R, and that in turn controls the conformation of the vinyl residue.



Scheme 3.

Table 1
Osmium-catalyzed dihydroxylation of sulfonyl vinyl oxiranes

Entry	Substrate	Time	Yield[a]	Products	
1	 **4**	75 min	69%	 **5** (60:40) (47%)	 **6** (60:40) (22%)
2	 **3**, P = H	18 h	52%	 **7** (65)	 **8** (35)
3	**9**, P = Bn	6 h	57%	 **10** (85)	 **11** (15)
4	 **1**, P = H	21 h	-	 **12** (60)	 **8** (40)
5	**1**, P = H	5 h	55%	**12** (86)	**8** (14)
6[b]	**13**, P = Ac	2 h	56%	**12**	-
7	 **14**	22 h	59%	 **15** (91)	 **16** (9)

[a] Unoptimized combined yields of pure products after chromatography on silica gel.
[b] The crude dihydroxylation mixture contained a 65:35 mixture of products, presumably derived from acetate migration; deacetylation (NaOMe, MeOH) gave a single isomer of a triol that afforded exclusively triacetate **12** upon peracetylation.

In conclusion, the osmium-catalyzed dihydroxylation of readily available enantiopure 2-sulfonyl-2-hydroxyalkyl-3-vinyloxiranes takes place with excellent selectivity to produce unusual carbohydrate fragments. We are currently studying the scope and limitations of this process as well as additional applications of the methodology.

Acknowledgements

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12. To facilitate evaluation of the data, the crude osmylation mixtures (5% OsO_4, 3 equiv. Me_3NO, 9:1 acetone:water, rt) were filtered through silica gel (gradient elution, 5–80% MeOH:EtOAc) and acetylated (Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt). The diastereomeric ratios were determined by integration of well resolved signals in the ^1H NMR of the crude mixtures. All products described here have been fully characterized. These stereochemical assignments are tentative and rely on examination of molecular models and on careful correlations of the ^1H and ^{13}C NMR data of our products, particularly **12**, with related oxiranes obtained by allylation of an epoxy aldehyde (Ref. 6) and with literature precedence (Nikitenko, A. N.; Arshava, B. M.; Taran, I. G.; Mikerin, I. E.; Shvets, V. I.; Raifeld, Y. E.; Lang Jr., S. A.; Lee, V. J. *Tetrahedron* **1998**, *54*, 11 731–11 740. We are currently seeking confirmation to these assignments in the context of developing applications of the methodology. Data of **12**: R_f=0.16 (30% EtOAc–hexane). $[\alpha]_D^{20}$=+19.7 (*c* 0.38, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 2.05 (s, 3H, CH_3 Ac), 2.07 (s, 3H, CH_3 Ac), 2.08 (s, 3H, CH_3 Ac), 2.41 (s, 3H, CH_3 *p*-Tol), 3.82 (dd, 1H, *J*=12.4, 5.2 Hz, H-β′), 4.09 (d, 1H, *J*=8.9 Hz, H-3), 4.12 (dd, 1H, *J*=12.4, 3.2 Hz, H-β′), 5.02 (ddd, 1H, *J*=8.7, 5.2, 3.2 Hz, H-α′), 6.40 (s, 1H, H-α), 7.20–7.27 (m, 5H, ArH), 7.35–7.38 (m, 2H, ArH), 7.57 (d, 2H, *J*=8.3 Hz, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.6, 20.6, 20.8, 21.7, 59.5, 62.6, 67.7, 69.7, 76.7, 127.1 (2C), 128.4 (2C), 128.8, 129.5 (2C), 129.8, 133.8, 134.0, 145.4, 169.0, 169.5, 170.2. IR (film): 3040, 3000, 2920, 1730, 1580, 1480, 1430, 1350, 1310, 1200, 1130, 1070, 1030, 800, 740, 710, 680, 650 cm^{-1}. EM (electrospray): 513 $[M+Na]^+$ (100%).
13. Conformation **D** follows Vedejs' model for dihydroxylation of allylic ethers, which is the commonly accepted model for most acyclic cases. See: Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094–1096.