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Asymmetric Synthesis Using C_2-Symmetric Diols: Use of (5*R*,6*R*)-2,3-Diacetoxy-5,6-diphenyl-1,4-dioxane as a Chiral Synthetic Equivalent of 1,2-Ethanediol 1,2-Dicarbocation

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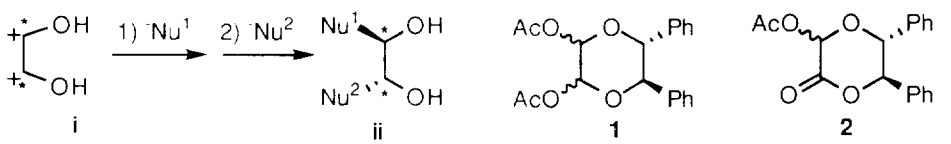
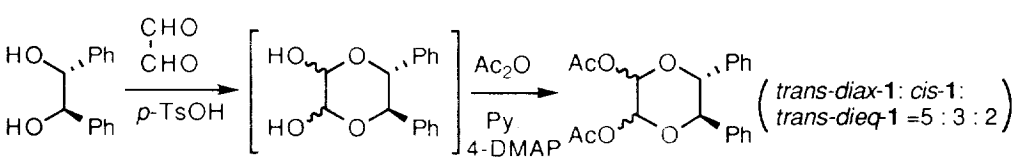
Abstract: A new route to chiral diol systems has been developed based on the double nucleophilic addition to the (5*R*,6*R*)-2,3-diacetoxy-5,6-diphenyl-1,4-dioxanes using chiral hydrobenzoin as an auxiliary.

The development of the stereoselective synthesis of chiral 1,2-disubstituted 1,2-diols is a very important subject in the organic synthetic area and many methodologies have been devised so far.[1,2] Our continuing efforts for developing a new approach to the chiral 1,2-diol systems based on the concept using a synthetic equivalent of the chiral 1,2-ethanediol 1,2-dicarbocation **i**, we recently reported the acetoxydiphenyldioxanone **2** as a synthetic equivalent of **i**.[3] In that case, nucleophilic addition was separately carried out two times and a way to produce dissymmetric diols has been achieved. We present here another candidate for cation **i**, diacetoxydiphenyldioxane **1**, which allows the extremely highly stereoselective introduction of two nucleophiles in a one-pot reaction.



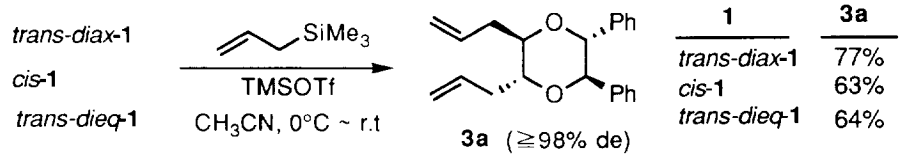
Scheme 1

Compound **1** was prepared as shown in Scheme 2. Chiral hydrobenzoin and glyoxal in the presence of a catalytic amount of *p*-TsOH in dioxane were reacted under azeotropic conditions to give dioxanediol,[4] which was acetylated without purification to afford (5*R*,6*R*)-2,3-diacetoxy-5,6-diphenyl-1,4-dioxane **1** as a mixture of three diastereomers containing *trans-diax*-**1**, *cis*-**1**, and *trans-dieq*-**1** (see Scheme 4) in a ratio of 5 to 3 to 2 at the C-2 and C-3 positions. These compounds were easily separated from each other by SiO_2 column chromatography and their stereochemistries of those were determined by ^1H NMR analysis.[5]



Scheme 2

Initially, the nucleophilic addition of allyltrimethylsilane to **1** was separately studied using the three species. The reaction of *trans-diax*-**1** and allyltrimethylsilane in the presence of 1 eq. of $Me_3SiOSO_2CF_3$ (TMSOTf) in CH_3CN was carried out to give the diallyl product **3a** with an extremely high stereoselectivity (≧98% de) in good yield in a one-pot operation. The same product was obtained from *cis*-**1** and *trans-dieq*-**1**



1	3a
trans-diax-**1**	77%
cis-**1**	63%
trans-dieq-**1**	64%

Scheme 3

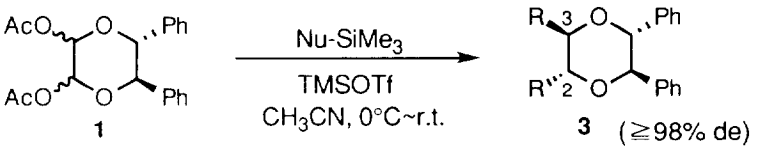
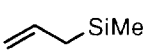
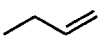
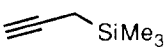
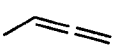
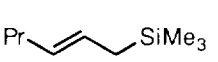
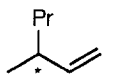
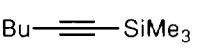
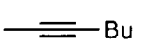
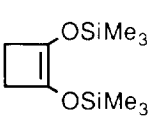
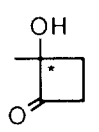
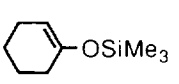
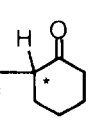
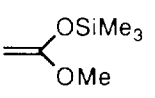
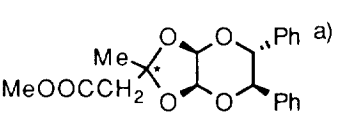


Table 1. Nucleophilic Addition to **1**

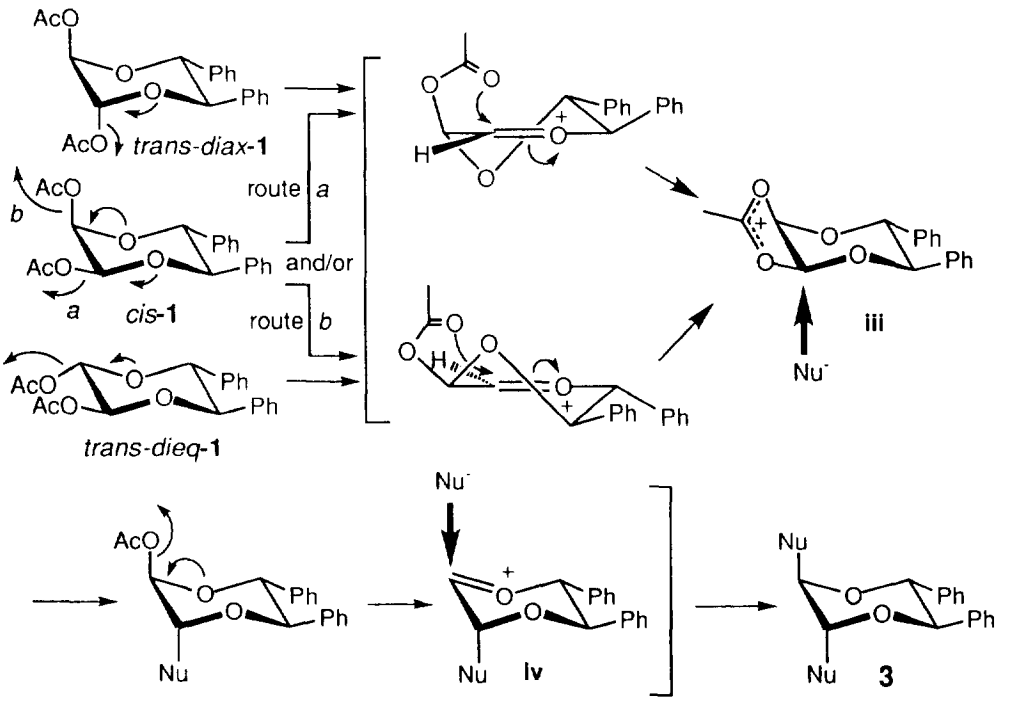
Entry	Nu-$SiMe_3$	Product	Yield(%)
1		**3a** R= 	75
2		**3b** R= 	57
3		**3c** R=  a)	48
4		**3d** R= 	30
5		**3e** R=  a)	74 b)
6		**3f** R=  a)	61
7		 a) **4**	35

a) Diastereomixtures at the asterisked carbon and the stereochemistries of the carbons were not determined. b) Obtained by HCl aq. treatment before work-up.

under the same reaction conditions (Scheme 3). The mixture of three diastereomers **1** was then reacted with several kinds of nucleophiles (Table 1) and in every case, the reaction proceeded in an extremely highly stereoselective manner with respect to the stereochemistries of the C-2 and C-3 carbons to give compounds **3**, though the use of silyl enol ether and silyl ketene acetals afforded two products, **3** and the acetal compound **4** formed by the reaction on the acetoxy carbon of the dioxenium ion intermediate (**iii** in Scheme 4), depending on the reagent (entries 5-7).[6]

The stereochemistry of diallyl compound **3a** was determined by comparison with an authentic sample prepared earlier by us.[3] The stereochemistries of the products for the other entries were tentatively assigned by assuming the same type of stereoselection and considering the reaction mechanism (Scheme 4).[7]

As shown above, every stereoisomer of **1** afforded the same product, in every entry, which has the 2*R*,3*R*-configuration. These results point out that every reaction proceeded *via* the same reaction intermediate. That is, every stereoisomer of **1** would afford the same 1,3-dioxolane-2-ylium ion intermediate **iii** through elimination of one acetoxy group followed by the next acetoxy group participation[7] and the first nucleophilic addition proceeds from the α-axial side for a stereoelectronic effect. The second nucleophile was introduced from the *re*-face of the oxonium ion intermediate **iv** in an extremely high stereoselective manner for steric repulsion of the next substituent in addition to the stereoelectronic effect (Scheme 4).



Scheme 4

Since several cleavage methods for the benzyl ether derivatives are available[8] and we also have proven that hydrogenolysis conditions [$Pd(OH)_2$-C, H_2, AcOEt] and Birch reduction condition (Ca/ liq. NH_3, EtOH) are available for such a reaction in a preceding paper,[3] the methodology described here opens a way to

symmetrical chiral 1,2-disubstituted 1,2-diol systems though some products having such functions as diallenyl or dipropargyl group still need transformation of such functions before cleaving the benzyl ether bond.

Acknowledgement: This research was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan.

References and Notes

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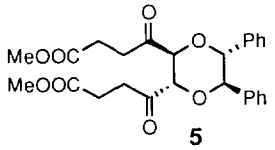
2. For recent reviews, see: Lohray, B. B. *Tetrahedron: Asymmetry* **1992**, *3*, 1317; Johnson, R. A.; Sharpless, K. B.Catalytic Asymmetric Dihydroxylation. In *Catalytic Asymmetrc Synthesis*; Ojima, I., Ed; VCH: Weinheim, Germany, 1993; pp 227-272. For recent examples, see: Lohray, B. B.; Nandanan, E.; Bhushan, V. *Tetrahedron Lett.* **1994**, *35*, 6559; Corey, E. J.; Noe, M. C.; Grogan, M. J. *Tetrahedron Lett.* **1994**, *35*, 6427; Kolb, H. C.; Andersson, P. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1994**, *116*, 1278; Hanessian, S.; Meffre, P.; Girard, M.; Beaudoin, S.; Sancéau, J-Y.; Bennani, Y. *J. Org. Chem.* **1993**, *58*, 1991 and references cited therein.
3. Fujioka, H.; Matsunaga, N.; Kitagawa, H.; Nagatomi, Y.; Kondo, M.; Kita, Y., the preceding paper.
4. Synthetic procedure of 1,4-dioxane-2,3-diol was used except for the reaction solvent. See: Venuti, M. C. *Synthesis* **1982**, 61.
5. ^{1}H NMR spectra of *trans-diax*-**1** and *trans-dieq*-**1** showed good symmetrization, respectively. Those stereochemistries were assigned from the presence of NOE between the C-2 and C-4 protons of *trans-dieq*-**1**, whreas no NOE between the C-2 and C-4 protons of *trans-diax*-**1** was observed.
^{1}H NMR (270MHz, $CDCl_3$): (*trans-diax*-**1**) δ 2.232 (6H, s, CH_3-CO-), 4.967 (2H, s, -O-CH-Ph), 6.127 (2H, s, AcO-CH-O-); (*trans-dieq*-**1**) δ 2.174 (6H, s, CH_3-CO-), 4.815 (2H, s, -O-CH-Ph), 6.028 (2H, s, AcO-CH-O-) ; (*cis*-**1**) δ 2.135 (3H, s, CH_3-CO-), 2.276 (3H, s, CH_3-CO-), 4.813 (1H, d, *J*=9.4 Hz, -O-CH-Ph), 4.938 (1H, d, *J*=9.4 Hz, -O-CH-Ph), 6.257 (1H, d, *J*=1.8 Hz, AcO-CH-O-), 6.274 (1H, d, *J*=1.8 Hz, AcO-CH-O-).
6. Difference in the reaction site depending on the reagents (enole ethers and silyl ketene acetals) in the reactions of the dioxcenium ion intermediates has been reported, see: Yokoyama, Y. S.; Elmoghayar, M. R. H.; Kuwajima, I. *Tetrahedron Lett.* **1982**, *23*, 2673.
7. The single strereochemistry of the C-2 and C-3 carbons in compound **3e** was ascertained since the bis-keto ester **5** was obtained by an oxidative cleavage reaction [$Pb(OAc)_4$, MeOH] of **3e**.



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8. Greene, T. W.; Wuts, P. G. M "Protective Groups in Organic Synthesis, Second Edition", John Wiley and Sons, New York, 1991.

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