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Asymmetric Synthesis Using C_2 -Symmetric Diols: Use of (5R,6R)-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 (5R,6R)-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-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 (5R,6R)-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 SiO₂ column chromatography and their stereochemistries of those were determined by ¹H NMR analysis.⁵



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 Me₃SiOSO₂CF₃ (TMSOTf) in CH₃CN was carried out to give the diallyl product 3a with an extremely high stereoselectivity (\geq 98% de) in good yield in a one-pot operation. The same product was obtained from *cis-1* and *trans-dieq-1*



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 2R,3R-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 participation⁷ 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).



Since several cleavage methods for the benzyl ether derivatives are available⁸ and we also have proven that hydrogenolysis conditions [Pd(OH)₂-C, H₂, AcOEt] and Birch reduction condition (Ca/ liq. NH₃, 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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- 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.
- ¹H 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.
 ¹H NMR (270MHz, CDCl₃): (*trans-diax-1*) δ 2.232 (6H, s, CH₃-CO-), 4.967 (2H, s, -O-CH-Ph), 6.127 (2H, s, AcO-CH-O-); (*trans-dieq-1*) δ 2.174 (6H, s, CH₃-CO-), 4.815 (2H, s, -O-CH-Ph), 6.028 (2H, s, AcO-CH-O-); (*cis-1*) δ 2.135 (3H, s, CH₃-CO-), 2.276 (3H, s, CH₃-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-).
- 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.
- 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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