Tetrahedron: Asymmetry Vol. 2, No. 10, pp. 993-996, 1991
Printed in Great Britain

0957-4166/91 $3.00+.00
Pergamon Press plc

Lanthanide(III) Catalyzed Aldol Reactions of Glyceraldehyde Acetonide with Ketene Silyl Acetals: Catalytic Asymmetric Route to Monosaccharides

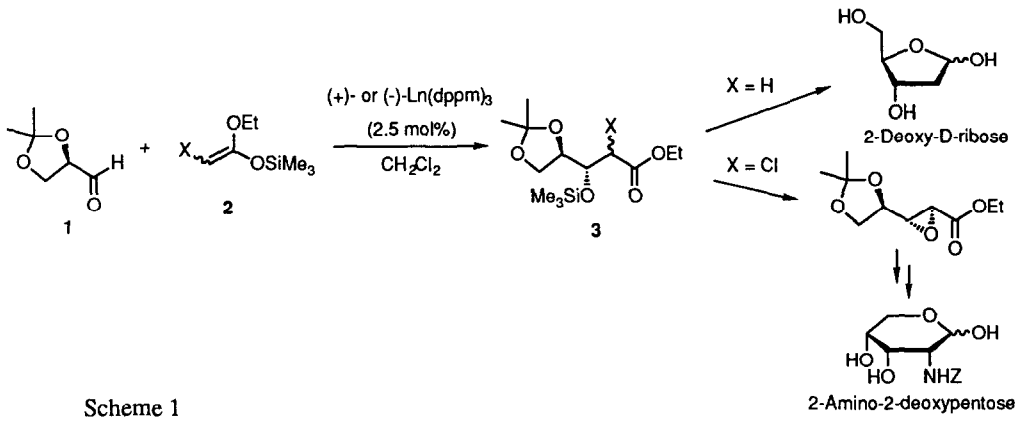
Koichi Mikami,* Masahiro Terada, and Takeshi Nakai*

Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan

(*Received* 29 *August* 1991)

Abstract: The Pr-, Eu- and Ho(dppm)$_3$ catalyzed aldol reactions of glyceraldehyde acetonide with ketene silyl acetals are described, where remarkably high *anti*-diastereofacial selection is achieved. Thus, the asymmetrc synthesis of 2-deoxy-D-ribonolactone and formal synthesis of 2-amino-2-deoxy-D-pentose by the lanthanide(III) catalyzed aldol reaction with ketene silyl acetals of acetate and α-chloroacetate, respectively are described.

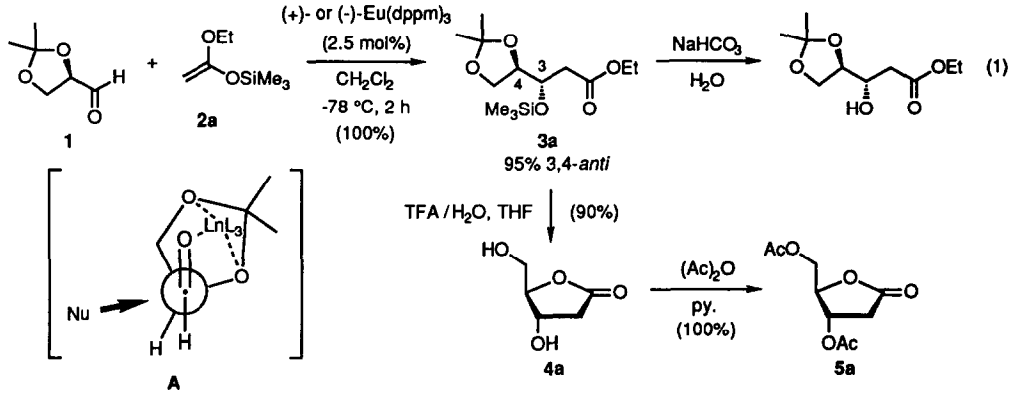
The development of efficient catalysis for carbon-carbon bond formation, particularly in asymmetric cases, is the subject of intense current study.[1] While much attention has recently been focused on the enantioselective catalysis for aldol reactions involving prochiral aldehydes,[2] the development of diastereoselective catalysis of the reaction of chiral aldehydes is synthetically important as well. Carbohydrates constitute a highly significant class of (un)natural targets for asymmetric synthesis. In the past decade, the asymmetric syntheses of monosaccharides have been made mainly by diastereoselective addition reactions of 2,3-*O*-isopropylidene-D- or -L-glyceraldehyde with allylic metal species or enolate components.[3] Recently, we have reported that an europium(III) complex exhibits unique catalysis for the aldol reaction with ketene silyl acetals (KSA), which proceeds under chelation control.[4] Herein, we report an efficient method for the formal asymmetric synthesis of 2-amino-2-deoxy-D-pentose and 2-deoxy-D-ribose based on the lanthanide(III) catalyzed aldol reactions of D-glyceraldehyde acetonide (**1**) (Scheme 1).



Scheme 1

First, we found that acetate-derived KSA **2a** reacts readily with **1** even at -78 °C within 2 h in the presence of a catalytic amount of (+)- or (-)-Eu(dppm)$_3$[5] (2.5 mol%) in dichloromethane to give the

corresponding *O*-silylated aldol adducts **3a** in quantitative yield (eq. 1). The diastereofacial selectivity was determined after desilylation with aqueous sodium bicarbonate by ^{13}C NMR analysis following a literature procedure.[6] Thus, the 3,4-*anti* adduct **3a** was obtained in higher (95%) diastereoselectivity than those obtained with lithium acetate[6a] or KSA/ZnI_2 (5 mol%).[6b] Aldol **3a** was converted to 2-deoxyribonolactone (**4a**) by deprotection with aqueous trifluoroacetic acid in 90% yield after chromatographic purification.[6,7] The optical purity of **4a** was determined to be almost 100% ee by optical rotation after conversion to the known diacetate **5a** in quantitative yield with acetic anhydride in pyridine ($[\alpha]_D^{20}$ -5.3 (c 1.20, EtOH) lit[6] $[\alpha]_D^{25}$ -5.2 (c 0.93, EtOH)). The observed *anti*-diastereofacial selectivity is reasonably explained by the tridentate chelation (**A**)[8] by virtue of the high coordination number (common coordination numbers: 6 ~ 9[9]) of lanthanides.[10] Indeed, glyceraldehyde acetonide **1** is found to coordinate with Eu(dppm)$_3$ in preference to α-benzyloxy propanal as judged by ^1H NMR analysis.



Our attention was then focused on the 2,3-diastereoselectivity of the aldol reaction with α-monoalkyl-substituted KSA (**2b**) (eq. 2, Table 1). The stereochemical assignment of the aldol adduct **3b** was made by ^{13}C NMR analysis after reduction to the known diol **4b**.[6] In the aldol reaction of **2b** with **1**, however, the simple 2,3-diastereoselectivity was found to depend on the nature of Ln(dppm)$_3$ rather than the geometry of KSA.[11] This is presumably because of the steric bulkiness of the tridentate chelate (**A**), which is determined by the ionic radii of Ln(III).[12] The stereoselectivity at C-2 is further influenced by the chirality of (+)- or (-)-Ln(dppm)$_3$ used, in terms of the double asymmetric induction[13] by the combination of chiral aldehyde **1** and lanthanide complex.[14]

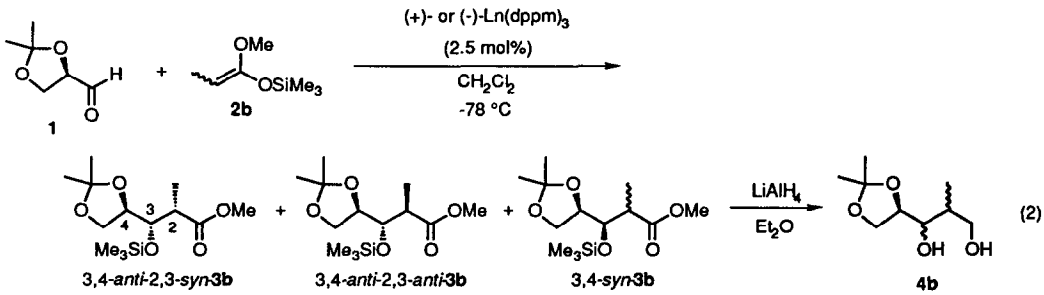
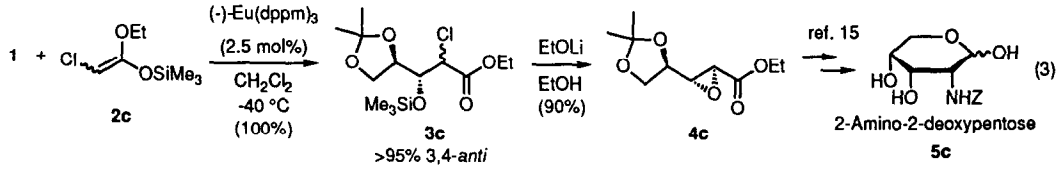


Table 1. (+)- or (-)-Ln(dppm)$_3$ catalyzed aldol reaction of **1** with **2b**.[a]

Entry	Ln(dppm)$_3$	**2b**	% yield	3,4-*anti* / *syn*	2,3-*syn* / *anti*[b]
1	(+)-Pr(dppm)$_3$	90% *Z*	82	> 99 : < 1	92 : 8[c]
2	(-)-Pr(dppm)$_3$	90% *Z*	78	95 : 5	89 : 11[c]
3	(+)-Pr(dppm)$_3$	85% *E*	50	> 95 : < 5	75 : 25[d]
4	(-)-Pr(dppm)$_3$	85% *E*	62	> 95 : < 5	70 : 30[d]
5	(+)-Eu(dppm)$_3$	90% *Z*	85	93 : 7	85 : 15[c]
6	(+)-Eu(dppm)$_3$	85% *E*	82	95 : 5	65 : 35[c]
7	(-)-Eu(dppm)$_3$	85% *E*	60	> 95 : < 5	54 : 46[d]
8	(+)-Ho(dppm)$_3$	85% *E*	80	> 95 : < 5	34 : 66[d]

[a] All reactions were run at -78 °C for several hours in 1.0 mmol of **1**, 1.5 mmol of **2b** and 0.025 mmol of Ln(dppm)$_3$. [b] Refer to the 3,4-*anti* diastereomer. [c] 3,4- and 2,3-diastereomeric ratio was determined by capillary GC analysis. [d] 3,4- and 2,3- diastereomeric ratio was determined by ^{13}C NMR analysis after reduction to the diols (**4b**).

Finally, we decided to synthesize the 2-substituted ribose via the 2,3-epoxide intermediate **4c**[15] by using α-chloroacetate-derived KSA (**2c**) as the enolate component to define the desired stereochemistry at C-2 after epoxidation of the aldol adduct **3c** (eq. 3). Thus, α-chloro KSA **2c** was easily prepared by treatment with trimethylsilyl triflate and triethylamine in dichloromethane. The aldol reaction of **1** with **2c** was conducted as above to give the aldol product **3c** in quantitative yield as the epimeric mixture at C-2.[16] Then **3c** was treated with lithium ethoxide (1.1 equiv.) in ethanol at 0 °C for 2 h to give the 2,3-*trans*-epoxide stereoselectively in 90% isolated yield. ^{13}C and ^{1}H NMR of **4c** indicates that **4c** was a single *trans*-diastereomer, which has been reported to be convertible into 2-amino-2-deoxypentose (**5c**).[15]



In conclusion, lanthanide(III) complex catalyzed aldol reactions of glyceraldehyde acetonide with KSA are shown to give the aldol adducts with remarkably high 3,4-*anti*-diastereofacial control. The remaining stereocontrol at C-2 is achieved by base-catalyzed isomerization to the thermodynamically more stable 2,3-*anti*-diasteromer through epoxide formation. Thus, 2-deoxy-D-ribonolactone and, in principle, 2-amino-2-deoxy-D-pentose and 2-deoxy-D-ribose are conveniently synthesized by the lanthanide(III) catalyzed aldol reaction with KSA.

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

References and Notes

(1) Reviews: (a) J. D. Morrison, *Asymmetric Synthesis*; Academic Press: New York, 1984; Vol. 3B. (b) R. Noyori, M. Kitamura, in *Modern Synthetic Methods 1989*; R. Scheffold, ed.; Springer-Verlag: Berlin, 1989; Vol. 5. (c) B. Bosnich, *Asymmetric Catalysis*; Martinus Nijhohoff Publishers: Dordrecht, 1986. (d) K. Narasaka, *Synthesis*, **1991**, 1. (e) K. Mikami, M. Terada, S. Narisawa, T. Nakai, *Synlett*, in press.

(2) (a) K. Furuta, T. Maruyama, H. Yamamoto, *J. Am. Chem. Soc.*, **1991**, *113*, 1041. (b) S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina, T. Mukaiyama, *ibid.* **1991**, *113*, 4247.

(3) J. Jurczak, S. Pikul, T. Bauer, *Tetrahedron*, **1986**, *42*, 447; G. J. McGarvey, M. Kimura, T. Oh, *J. Carbohydr. Chem.*, **1984**, *3*, 125.

(4) K. Mikami, M. Terada, T. Nakai, *J. Org. Chem.* in press.

(5) Tris[di(perfluoro-2-propoxypropionyl)methanato]europium(III): H. Kawa, F. Yamaguchi, N. Ishikawa, *Chem. Lett.*, **1982**, 2063.

(6) (a) C. H. Heathcock, S. D. Young, J. P. Hagen, M. C. Pirrung, C. T. White, D. VanDerveer, *J. Org. Chem.*, **1980**, *45*, 3846. (b) Y. Kita, O. Tamura, F. Itho, H. Yasuda, H. Kishino, Y. Y. Ke, Y. Tamura, *ibid*, **1988**, *53*, 554.

(7) For the synthesis of D-ribonolactone and its reduction to D-ribose, see: T. Mukaiyama, I. Shiina, S. Kobayashi, *Chem. Lett.*, **1990**, 2201, and references cited therein.

(8) (a) J. Mulzer, A. Angermann, *Tetrahedron. Lett.*, **1983**, *24*, 2843. (b) S. Pikul, J. Jurczak, *ibid*, **1985**, *26*, 4145.

(9) J. E. Huheey, *Inorganic Chemistry: Principles of Structure and Reactivity*, Harper & Row: New York, 1972, Chap. 14.

(10) In the addition reaction to glycelaldehyde acetonide, the β-chelation conformation has often been used to explain the *anti* diastereofacial selectivity (ref. 3). However, the β-chelation selectivity in $Eu(dppm)_3$ catalyzed reaction of β-benzyloxy aldehyde with **2a** was quite low.

(11) Diastereoselection irrespective of the enolate geometry is well explicable in terms of the antiperiplanar transition state model. For a general discussion on the transition state geometry of the aldol addition, see; S. E. Denmark, B. R. Henke, *J. Am. Chem. Soc.*, **1991**, *113*, 2177.

(12) Ionic radii (C.N. = 6) of Pr^{+3}, Eu^{+3}, and Ho^{+3} ions are 101, 95.5, and 89.4 pm, respectively (ref 9).

(13) (a) S. Masamune, W. Choy, J. S. Peterson, L. R. Sita, *Angew. Chem. Int. Ed. Engl.*, **1980**, *24*, 1. (b) C. H. Heathcock, *Asymmetric Synthesis*; J. D. Morrison, ed.; Academic Press: New York, 1984; Vol. 3B.

(14) In fact, a moderate level of asymmetric induction (~20% ee) was observed in the aldol reaction of α-benzyloxy acetaldehyde with **2b.**

(15) (a) M. Murakami, T. Mukaiyama, *Chem. Lett.*, **1982**, 1271. (b) H. Akita, H. Matsukura, T. Oishi, *Tetrahedron Lett.*, **1986**, *27*, 5397.

(16) In fact, treatment of the aldol **3c** with tetrabutylammonium fluoride in THF in the presence of MS 4A resulted in the formation of the diastereomeric mixture of the 2,3-epoxide (2,3-trans/cis = 2 : 1).