Tetrahedron Letters,Vol.30,No.51,pp 7231-7232,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

ASYMMETRIC INTRAMOLECULAR DIELS-ALDER REACTION CATALYZED BY CHIRAL ACYLOXYBORANE COMPLEX.

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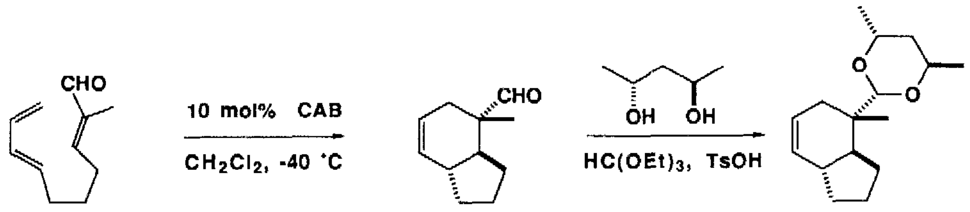
Abstract: *Intramolecular Diels-Alder reaction of 2-methyl-(E,E)-2,7,9-decatrienal catalyzed by chiral acyloxyborane complex proceeds with high stereo and enantioselectivities.*

Recently, we have disclosed the use of chiral acyloxyborane complex as an efficient catalyst in asymmetric intermolecular Diels-Alder reactions.[1] In which the reactions proceeded with a catalytic amount of chiral Lewis acid and afforded the adducts with high enantioselectivity. Herein we describe the extension of this catalyst system to the intramolecular Diels-Alder process which succeeded in affording an adduct with high optical purity.[2]

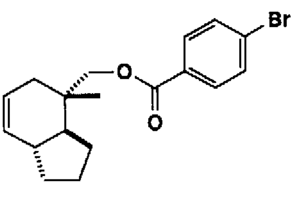
Addition of 2-methyl-(E,E)-2,7,9-decatrienal **1**[3] to a solution of CAB catalyst (0.1 equiv to the substrate) in CH_2Cl_2 at -40 °C, prepared from mono(2,6-dimethoxybenzoyl)tartaric acid[4] and borane as previously described, provided an isomeric mixture of adducts in 84 % yield. Glc analysis of the products revealed 99 : 1 endo/exo ratio.[5] The optical purity of the product was determined by conversion to chiral acetals. Thus treatment of the adducts with (2R, 4R)-2,4-pentanediol and TsOH in dry benzene afforded acetals 3 in quantitative yield. Isomers ratio of the chiral acetals derived from major adduct was determined to be 96 : 4 on glc analysis which corresponded to 92 %ee.



1 **2** **3**

The absolute configuration and stereochemistry at ring junction of the adduct were determined based on the X-ray analysis after leading to ester **4**.[6] The X-ray structure was depicted in Fig 1.[7] According to this analysis, S-configuration was assigned to the formylated carbon and the trans ring junction was confirmed.

The analogous triene without α-methyl substituent at α,β-unsaturated aldehyde moiety was also subjected to this reaction (-20 °C) affording the adduct in 74 % yield but lower enantioselectivity (46 %ee for endo adduct; endo/exo = 99/1).[8] Thus α-substituent is essential for the high asymmetric induction. These features were fully consistent with those for intermolecular version of the reaction.



4

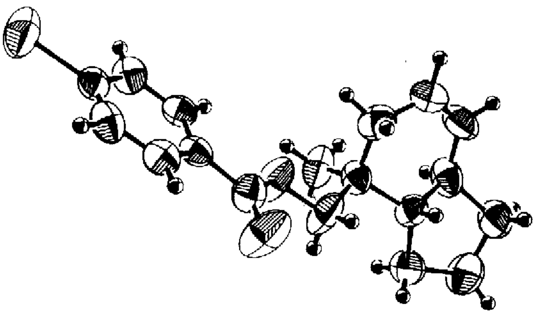


Figure 1. Crystal Structure of Compound **4**.

In conclusion, our chiral acyloxyborane catalyst enables to control inter- and intramolecular Diels-Alder reaction in terms of enantioselection together with the stereodifferentiation, thus provides a strong methodology for the constructions of chiral cyclic structures mediated by the catalytic amount of chiral source.

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

References and Notes

1) (a) Furuta, K.; Simizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1481. (b) Furuta, K.; Miwa, Y.; Iwanaga, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 6254.
2) For references on asymmetric Diels-Alder reactions using chiral Lewis acid catalysts, see: (a) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493; (b) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340; and references cited therein.
3) Prepared from 7-cyano-1,3-heptadiene through DIBAH reduction followed by Wittig reaction. For the synthesis of starting cyanide, see: Roush, W. R.; Gillis, H. R.; Ko, A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269.
4) Natural tartaric acid was used as a starting chiral source.
5) Spectral data of adduct **2**: ^{1}H NMR ($CDCl_3$) δ 9.46 (s, 1H), 5.82 (br d, 1H), 5.57 (m, 1H), 2.42 (br d, 1H), 2.1-1.4 (m, 7H), 1.18 (m, 2H), 0.98 (s, 3H); IR (film) 2920, 2850, 2700, 1720, 1660, 1450, 1400, 1380 cm^{-1}; $[\alpha]_D^{24}$ -14.4° (c 1.065, $CHCl_3$).
6) Prepared by reduction of **2** with sodium borohydride followed by esterification with *p*-bromobenzoyl chloride.
7) A single crystal of **4** was grown from a methanol solution at room temperature. Crystal data: $C_{18}H_{21}O_2Br$, formula weight 349.27; monoclinic, space group $P2_1$; a=14.90(0) Å, b=18.42(0) Å, c=6.04(0) Å, β=95.42(0) °, V=1651.15(0) Å^3, Z=4, d_{calcd}=1.40 g/cm^3. The 1734 observed data (I>3σI) were collected by using graphite-monochromated Cu Kα radiation at room temperature on a Rigaku AFC5R diffractometer. Refinement with 378 variables converged at R=0.038 and Rw=0.049 with goodness of fit=1.56. These data have been deposited with the Cambridge Crystallographic Data Center.
8) The stereochemistry and optical purity of the adduct were determined after conversion to corresponding alcohol, see a paper listed in reference 3.

(Received in Japan 21 September 1989)