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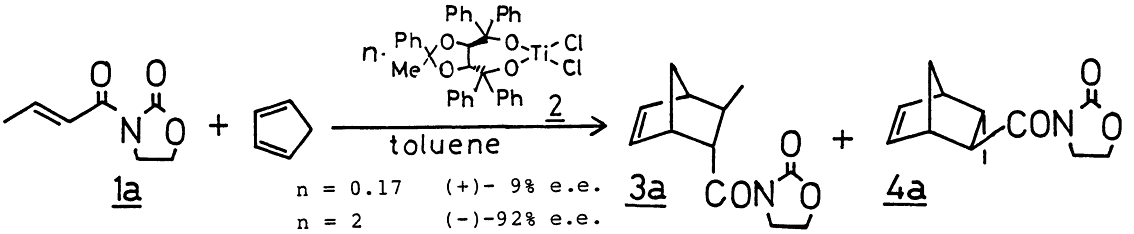
The Asymmetric Diels-Alder Reaction by the Use of a Catalytic Amount of a Chiral Titanium Reagent

Koichi NARASAKA, Masayuki INOUE, and Tohru YAMADA
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

The Diels-Alder reaction between prochiral dienophiles and cyclopentadiene proceeds in an enantioselective manner by the use of a catalytic amount of a chiral alkoxy titanium(IV) in the presence of Molecular Sieves 4A.

Recently we reported the highly enantioselective Diels-Alder reaction between prochiral dienes and dienophiles 1 prepared from α,β-unsaturated acids and 1,3-oxazolidin-2-one by employing the chiral alkoxy titanium(IV) 2.1) However, 2 molar amounts of the chiral Lewis acid 2 to 1 is indispensable for sufficiently high enantioselection. That is, when a catalytic amount (17 mol%) of the titanium reagent 2 is used in the reaction of 1a with cyclopentadiene, the endo-cycloadduct 3a is obtained in high yield (88%), very low optical purity (9% e.e.) with the enantioselectivity opposite (2R,3S) to the original procedure.



The improvement of this procedure has been investigated for the more enantioselection Diels-Alder reaction while employing a truly catalytic amount of the chiral Lewis acid,2) and it was noted that the presence of Molecular Sieves (M.S.) 4A in the reaction mixture enhances the enantioselectivity in the chiral titanium reagent-catalyzed reaction.3)

The chiral catalyst was simply prepared by mixing 10 mol% of dichlorodiisopropoxy titanium(IV) and 10.5 mol% of the chiral 1,4-diol 5, and the reaction of 1a with excess cyclopentadiene was carried out in the presence of powdered M.S. 4A4) (125 mg to 1 mmol of 1a) in toluene at 0 °C for 24 h. The endo-adduct 3a was obtained in high optical purity (91% e.e.) with the same absolute configuration (2S,3R) as that observed in the original procedure.1)

As can be seen in Table 1, various dienophiles 1a-d react with cyclopentadiene to afford the corresponding endo-adducts 3a-d in the presence of only 10 mol% of the catalyst in good to high enantioselectivity (64-91% e.e.). In

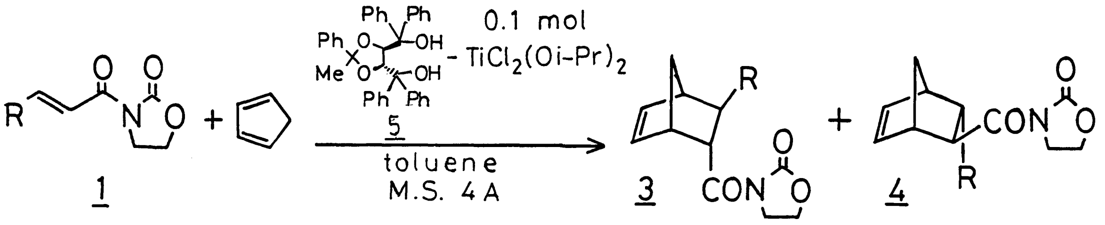


Table 1. Asymmetric Diels-Alder reaction of 1 with cyclopentadiene

Dienophiles R		React.temp °C	endo:exo (3 : 4)	Total yield %	Opt.pur.of 3 5) % e.e.	Abs.config.
Me	1a	0	92 : 8	87	91	2S,3R
H	1b	-40	96 : 4	93	64	2S
n-Pr	1c	0	91 : 9	79	72	
Ph	1d	r.t.	88 : 12	72	64	

comparison with the previous procedure,1) almost the same level of enantioselectivity is attained in the Diels-Alder reaction of 1a, and furthermore the enantioselectivity of the cycloadduct of 1b with cyclopentadiene is improved significantly.

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References

1) K. Narasaka, M. Inoue, and N. Okada, Chem. Lett., 1986, 1109.

2) The asymmetric Diels-Alder reactions catalyzed by chiral Lewis acids; see the references cited in the preliminary paper.1) Seebach et al. used alkyl titanium reagents having chiral 1,4-diols similar to 5 for the asymmetric alkylation reaction, and found that changing the remote substituents on the acetal center had an effect; D. Seebach, A. K. Beck, M. Schiess, L. Widler, and A. Wonnacott, Pure Appl. Chem., 55, 1807 (1983). They also applied the chiral titanium reagent to the asymmetric Diels-Alder reaction (private communication); D. Seebach, S. Roggo, R. Imwikelried, A. K. Beck, and A. Wonnacott, Helv. Chim. Acta, in preparation.

3) Recently, Sharpless reported improvement of the asymmetric epoxidation to a catalytic process by the use of Molecular Sieves; R. M. Hanson and K. B. Sharpless, J. Org. Chem., 51, 1922 (1986).

4) Powdered M.S. 3A and 5A were also found to enhance the enantioselectivity as M.S. 4A, but the use of M.S. 13X didn't exhibit a remarkable effect on the enantioselection.

5) Optical purity was determined by the same methods reported in the previous paper.1)

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