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HIGHLY DIASTEREOSELECTIVE DIELS-ALDER REACTION OF OPTICALLY ACTIVE ETHYL 2-p-TOLYLSULFINYLMETHYLENEPROPIONATE WITH CYCLOPENTADIENE1)

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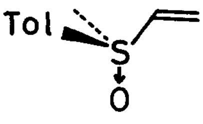
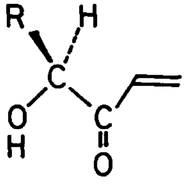
Summary   Stereochemistry of the Diels-Alder reaction of ethyl Z- and E-2-p-tolylsulfinylmethylenepropionate with cyclopentadiene has been studied. The high diastereoselectivity was observed especially in the case of exo-cycloaddition.

We have previously reported that (+)-$(R)_S$ p-tolyl vinyl sulfoxide 1 is a good chiral dipolarophile in the 1,3-dipolar cycloaddition reaction with acyclic nitrones.2) The observed high diastereoselectivity could be attributed to the characteristic structure of the vinyl sulfoxide 1, that is, it has a chiral center extremely close to the reaction site, C=C double bond. Very recently, Masamune et al.3) successfully designed a new dienophile 2 having a chiral auxiliary at the position one atom closer to the reaction center than those acrylate esters frequently used in the asymmetric Diels-Alder reactions. Here we would like to report that a new chiral dienophile, ethyl p-tolylsulfinylmethylenepropionate 3, which has a chiral auxiliary directly attached to the reaction center showed a high diastereoselectivity in the asymmetric Diels-Alder reaction with cyclopentadiene.



1



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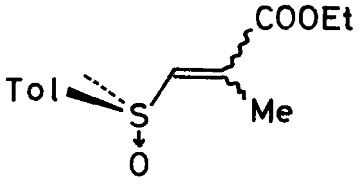

3

The Emmons-Horner reaction4) of optically active diethyl p-tolylsulfinylmethanephosphonate5) with ethyl pyruvate gave optically active E- and Z-$(R)_S$-3 in 23 and 10 % yields respectively.6) A mixture of E-$(R)_S$-3 and 10 eq of cyclopentadiene was heated at 90° for 5 hr in a sealed tube to give the endo sulfoxides 4a and 4b7) and the exo sulfoxide 5a8) in 63, 15, and 22 % yields respectively.9) The diastereoisomeric exo sulfoxide 5b could not be detected even by the careful examination of the every chromatographic fraction(Chart 1). Similarly, Z-$(R)_S$-3 afforded the endo sulfoxides 6a and 6b, and the exo sulfoxide 7a in 63, 2, and 35 % yields respectively.10) Again, the diastereomeric exo sulfoxide 7b could not be detected. From the above results, the diastereoselectivity of both reactions was calculated as follows.

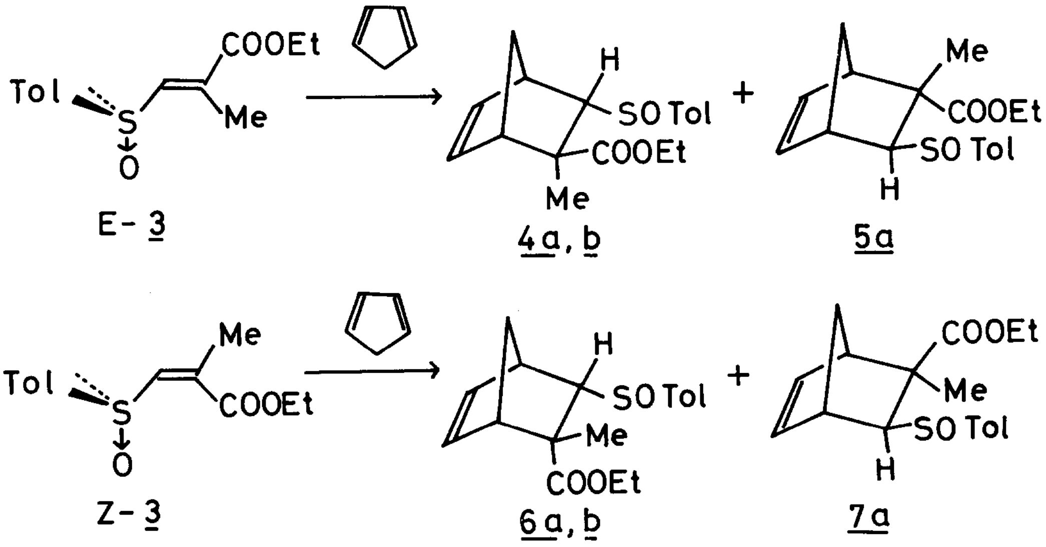

Chart 1.

endo addition of E-(R)$_{S}$-3 d.e. 62 % exo addition of E-(R)$_{S}$-3 d.e. 100 %

endo addition of Z-(R)$_{S}$-3 d.e. 94 % exo addition of Z-(R)$_{S}$-3 d.e. 100 %

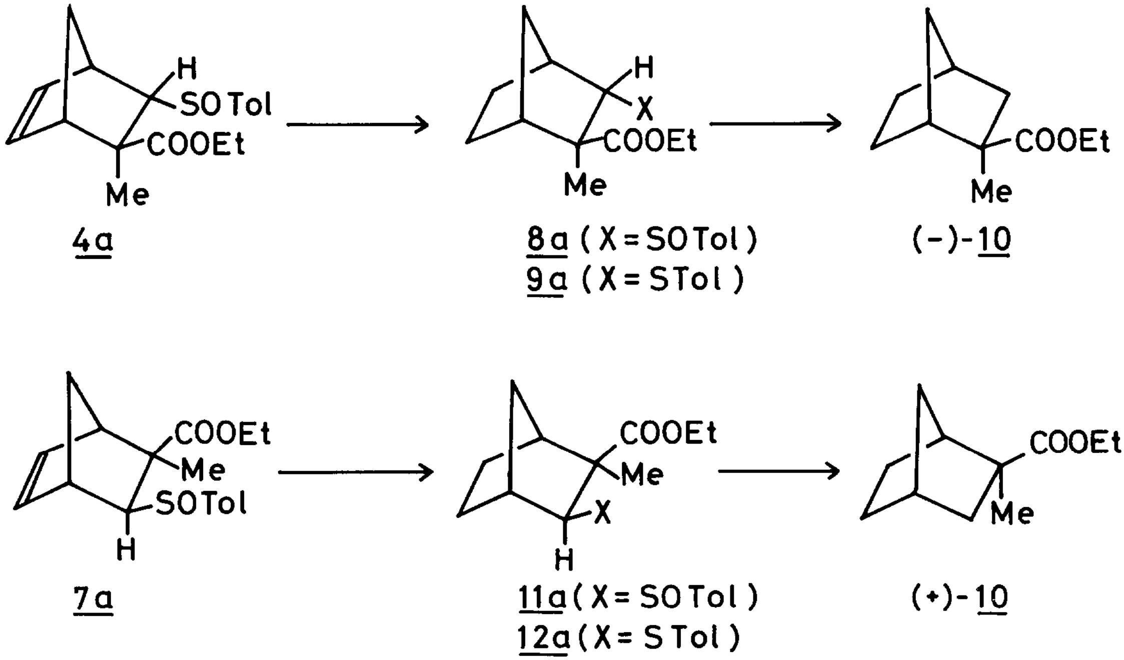

Chart 2.

To elucidate the steric course of the above Diels-Alder reaction, the absolute configurations of 4a and 7a were determined by chemical correlation as follows(Chart 2)[11]. The cycloadduct 4a was catalytically hydrogenated to give in 69 % yield the dihydro derivative 8a[12], which was then treated with $TiCl_3$ in AcOH-AcONa to give the sulfide 9a[13] in 77 % yield. The sulfide 9a was treated with Raney Ni(W4) to afford ethyl 2-endo-methyl-2-exo-norbornanecarboxylate (-)-10,[14] $[\alpha]_D^{22}$ -4.9° in 67 % yield. The cycloadduct 7a was subjected to the same sequence of reactions[15] to give ethyl 2-endo-methyl-2-exo-norbornanecarboxylate (+)-10, $[\alpha]_D^{22}$ +4.8° in 23 % overall yield. The absolute configuration of (+)-10 was confirmed by the comparison with the authentic prepared from known (+)-2-endo-methyl-2-exo-norbornane carboxylic acid.[16]

The most plausible mechanism for the above Diels-Alder reaction may be described as shown below by the case of E-$(R)_S$-3 assuming that, in the transition state, the α,β-unsaturated sulfoxide takes the s-trans conformation with respect to the S→O and C=C bonds as depicted in Chart 3.[17]

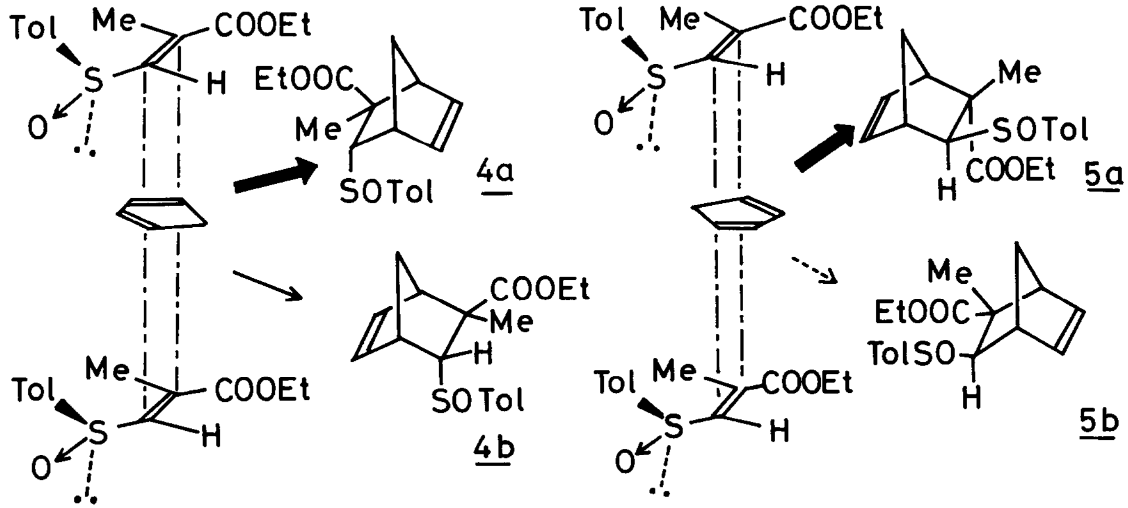

Chart 3.

The high diastereoselectivity observed could be explained in terms of the difference of steric bulkiness between the p-tolyl group and the lone-paired electrons. In the case of endo cycloaddition, the steric interaction of p-electrons at C_2 and C_3 in cyclopentadiene with the lone-paired electrons should be much smaller than that with the p-tolyl group, resulting in the predominant formation of 4a.[18]

The present investigation may provide a new entry to the asymmetric organic synthesis using chiral α,β-unsaturated sulfoxides, since those compounds in racemic form have been recently received much attention as versatile dienophile in the Diels-Alder reaction.[19]

References and Notes

1) All new compounds were fully characterized spectroscopically(IR, ^{1}H NMR, and MS spectra) and by combustion and/or high resolution mass spectral analyses.

2) T. Koizumi, H. Hirai, and E. Yoshii, J. Org. Chem., 47, 4004(1982).

3) W. Choy, L. A. Reed, III and S. Masamune, J. Org. Chem., 48, 1137(1983).

4) The Emmons-Horner reaction was conducted in dry THF using NaH as a base.

5) Optically active diethyl $(R)_S$-p-tolylsulfinylmethanephosphonate, bp(torr) 130-140(0.2); $[\alpha]_D^{22}$ +91.8°(c 0.52, $CHCl_3$), was prepared by the reaction of (-)-$(S)_S$ menthyl p-tolylsulfinate with diethyl methanephosphonate and n-BuLi. All distillations were carried out by use of Kugelrohr apparatus and the bath temperatures are indicated.

6) E-$(R)_S$-3: bp(torr) 120-130(0.2); $[\alpha]_D^{22}$ -66.9°(c 0.93, $CHCl_3$). Z-$(R)_S$-3: bp(torr) 120-130 (0.2); $[\alpha]_D^{22}$ -292.5°(c 0.39, $CHCl_3$).

7) The endo sulfinyl structure of 4a,b was established by converting both compounds into the same sulfide 9a. The same sequence of reactions was also applied to 6a and 6b and the endo sulfinyl structure was established.

   4a: bp(torr) 140-150(0.1); $[\alpha]_D^{19}$ +155.1°(c 0.28, $CHCl_3$); TLC R_f 0.34(n-hexane-AcOEt 1:1).

   4b: bp(torr) 140-150(0.2); $[\alpha]_D^{22}$ +92.3°(c 0.46, $CHCl_3$); TLC R_f 0.27(n-hexane-AcOEt 1:1).

8) 5a: mp 75°(n-hexane); $[\alpha]_D^{19}$ +129.9°(c 0.27, $CHCl_3$); TLC R_f 0.51(n-hexane-AcOEt 1:1).

9) The yields were calculated by HPLC using μ-Porasil and n-hexane-AcOEt(2:1). The isolated yields were as follows. 4a 68 %, 4b 8 %, 5a 15 %(Silica gel column chromatography, AcOEt-n-hexane as a solvent).

10) 6a: isolated yield 45 %; mp 86°(n-hexane); $[\alpha]_D^{19}$ -4.8°(c 0.65, $CHCl_3$); TLC R_f 0.14(n-hexane-AcOEt 1:1). 6b: isolated yield 1 %; bp(torr) 140-150(0.1); $[\alpha]_D^{19}$ +71.7°(c 0.30, $CHCl_3$); TLC R_f 0.10(n-hexane-AcOEt 1:1). 7a: isolated yield 25 %; mp 91°(n-hexane); $[\alpha]_D^{19}$ +43.3° (c 0.06, $CHCl_3$); TLC R_f 0.33(n-hexane-AcOEt 1:1).

11) The absolute configurations of 5a, 6a, and 6b were determined as those shown in Chart 1, based on the mechanistic consideration illustrated in Chart 3.

12) 8a: bp(torr) 135-140(0.2); $[\alpha]_D^{21}$ +250.2°(c 0.29, $CHCl_3$).

13) 9a: bp(torr) 110-120(0.07); $[\alpha]_D^{22}$ +16.4°(c 0.66, $CHCl_3$).

14) (-)-10: bp(torr) 90-100(8); $[\alpha]_D^{22}$ -4.9°(c 0.82, EtOH).

15) 11a: bp(torr) 140-150(0.2); $[\alpha]_D^{22}$ +23.1°(c 0.24, $CHCl_3$). 12a: bp(torr) 95-105(0.1); $[\alpha]_D^{22}$ -12.2°(c 0.12, $CHCl_3$). (+)-10: bp(torr) 85-95(8); $[\alpha]_D^{22}$ +4.8°(c 0.40, EtOH).

16) 2-endo-methyl-2-exo-norbornenecarboxylic acid was resolved with (-)-quinine according to the method of J. A. Berson et al, J. Amer. Chem. Soc., 83, 3986(1961).

    The optically active acid $[\alpha]_D^{22}$ +44.7°(c 0.25, EtOH, ee 66.3 %) was catalytically hydrogenated using Pd/C to give in 92 % yield dihydro compound, $[\alpha]_D^{22}$ +4.4°(c 4.1, EtOH), which was esterified with H^+-EtOH to give ethyl 2-endo-methyl-2-exo-norbornanecarboxylate, $[\alpha]_D^{22}$ +3.1°(c 4.33, EtOH) in 53 % yield. The optical rotation of (+)-10 was calculated as +4.7°, which was in good agreement with those of 10 obtained from 4a and 7a.

17) If the sulfoxide is assumed to take the other conformation in which the S→O and C=C bonds are placed coplanarly in a s-cis manner, the absolute stereochemistry of the cycloadducts becomes inconsistent with that determined by chemical correlations.

18) The exclusive formation of 5a in the exo cycloaddition may be attributed to the considerable bulkiness of the methylene group compared with the p-electrons at C_2 and C_3 position.

19) S. Danishefsky, T. Harayama, and R. K. Singh, J. Amer. Chem. Soc., 101, 7008(1979).

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