

**STRUCTURE OF THE *ENDO* 1:1 ADDUCT BY ASYMMETRIC  
CYCLOADDITION REACTIONS OF OPTICALLY ACTIVE  
(*R*)-ALLENE-1,3-DICARBOXYLATE WITH FURAN:  
DETERMINATION OF ITS ABSOLUTE CONFIGURATION  
BY X-RAY ANALYSIS**

Izumi Ikeda,<sup>a</sup> Akie Gondo,<sup>a</sup> Motoo Shiro,<sup>b</sup> and Ken Kanematsu<sup>\*a</sup>

<sup>a</sup>Institute of Synthetic Organic Chemistry, Faculty of Pharmaceutical Sciences,  
Kyushu University 62, Maidashi, Higashi-ku, Fukuoka 812, Japan

<sup>b</sup>Rigaku Corporation, 3-9-12, Matsubara-cho, Akishima, Tokyo 196, Japan

**Abstract** - Asymmetric Diels-Alder reactions of optically active (*R*)-allene-1,3-dicarboxylate with furan in the presence of Lewis acid proceeded to afford the *endo*-adduct selectively in moderate yield. The absolute configuration of the adduct was confirmed by X-ray analysis.

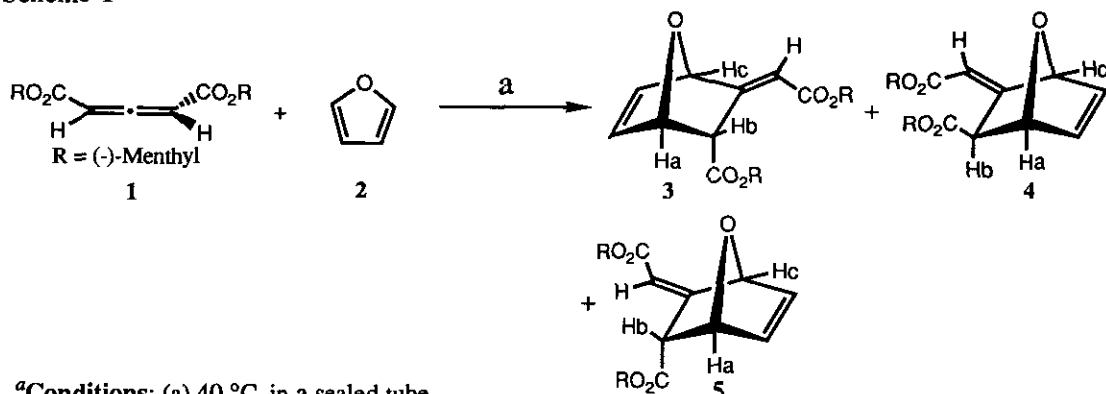
For the last decade asymmetric Diels-Alder reactions with furan are reported in some laboratories with the object of supplying the chiral 7-oxabicyclo[2.2.1]heptene derivatives.<sup>1</sup> They have not yet been effected with less satisfactory results in regard to their selectivity for the cycloadditions. Recently we reported that optically active allene-1,3-dicarboxylates are excellent chiral dienophiles for Lewis acid catalyzed asymmetric Diels-Alder reactions with cyclopentadiene.<sup>2</sup> In the course of our studies on the asymmetric Diels-Alder reaction, we now wish to describe the asymmetric Diels-Alder reaction of (*R*)-di(-)-menthyl allene-1,3-dicarboxylate (**1**) with furan (**2**).

The reaction of allene-1,3-dicarboxylate (**1**) with furan (**2**) runs at 40 °C in a sealed tube to give three 1:1 adducts (**3**), (**4**), and (**5**) (Scheme I). The results of the cycloaddition reactions of **1** with **2** in the presence and absence of Lewis acid (TiCl<sub>4</sub>, Et<sub>2</sub>AlCl, AlCl<sub>3</sub>, BF<sub>3</sub>·OEt<sub>2</sub>) at -40 °C or -78 °C are summarized in Table I. Using 1 equiv. of any Lewis acid, the reaction was not complete. However, the reaction was successfully

---

<sup>†</sup>This paper is dedicated to Professor Yoshifumi Maki on this occasion of his retirement from Gifu Pharmaceutical University in March 1994.

promoted by employing 2 equiv. or excess of  $\text{TiCl}_4$  or  $\text{Et}_2\text{AlCl}$ , and gave higher diastereofacial selectivity compared with the uncatalyzed reaction. Generally, in case of using  $\text{AlCl}_3$  or  $\text{BF}_3\cdot\text{OEt}_2$ , the diastereofacial selectivity is not as high as the *endo/exo* one. In the previous report, the Diels-Alder reactions with cyclopentadiene in the presence of  $\text{AlCl}_3$  proceeded to afford the *endo*-adducts in high yields.<sup>2</sup> Judging from these results, it is thought that the lowering of selectivity occurs by coordination of Lewis acid to the oxygen atom contained in the furan molecule.

Scheme I<sup>a</sup>

<sup>a</sup>Conditions: (a) 40 °C, in a sealed tube.

**Table I.** Product Ratios of the Diels-Alder Adducts of Allene-1, 3-dicarboxylate and Furan under Lewis Acid Catalyzed Conditions by Hplc Analysis

| Lewis acid                     | equiv. of Lewis acid     | temp. °C        | time h | ratios of isomers <sup>b</sup><br>[3] : [4] : [5] | <i>endo:exo</i> <sup>b</sup><br>[3] : [4] | <i>endo ds</i> <sup>b</sup><br>[3] : [5] |
|--------------------------------|--------------------------|-----------------|--------|---|---|--|
| none                           |                          | 40 <sup>a</sup> | 7.5    | 38 : 34 : 29                                      | 53 : 47                                   | 57 : 43                                  |
| $\text{TiCl}_4$                | 1                        | -40             | 8      | 72 : 23 : 5                                       | 75 : 25                                   | 94 : 6                                   |
|                                | 2                        | -78             | 11     | 79 : 19 : 2                                       | 81 : 19                                   | 97 : 3                                   |
|                                |                          | -40             | 2.5    | 70 : 23 : 7                                       | 75 : 25                                   | 90 : 10                                  |
|                                | $\text{Et}_2\text{AlCl}$ | 3               | -40    | 2.2   | 75 : 24 : 1                               | 76 : 24                                  |
| 1                              |                          | -40             | 8      | 60 : 27 : 13                                      | 69 : 31                                   | 82 : 18                                  |
|                                |                          | -78             | 10     | 64 : 35 : 1                                       | 65 : 35                                   | 99 : 1                                   |
| 2                              |                          | -40             | 1.5    | 62 : 35 : 3                                       | 64 : 36                                   | 96 : 4                                   |
|                                |                          | -40             | 1      | 59 : 38 : 3                                       | 62 : 38                                   | 96 : 4                                   |
| $\text{AlCl}_3$                | 10                       | -40             | 1      | 60 : 40 : 0                                       | 60 : 40                                   | 100 : 0                                  |
|                                | 1                        | -40             | 10     | 58 : 21 : 21                                      | 73 : 27                                   | 73 : 27                                  |
| $\text{BF}_3\cdot\text{OEt}_2$ | 2                        | -40             | 9      | 56 : 19 : 25                                      | 74 : 26                                   | 69 : 31                                  |
|                                | 1                        | -40             | 9      | 54 : 19 : 27                                      | 74 : 26                                   | 66 : 34                                  |
| 2                              |                          | -40             | 12.5   | 53 : 18 : 29                                      | 74 : 26                                   | 64 : 36                                  |

<sup>a</sup> Reaction conditions: at 40 °C in a sealed tube.

<sup>b</sup> Ratios of the isomers determined by hplc (TSK-GEL SILICA-60).

Each adduct of this cycloaddition reaction was separated by flash column chromatography on silica gel. The major isomer (3) could be isolated in 53 % yield (furan (excess),  $\text{TiCl}_4$  (2 equiv.),  $\text{CH}_2\text{Cl}_2$ , -40 °C): mp 118

$^{\circ}\text{C}$ ,  $[\alpha]_{\text{D}}^{21} -75.0^{\circ}$  ( $c = 1.01$ ,  $\text{CHCl}_3$ ),  $m\text{s}^+$  (FD)  $m/z$  (relative intensity) 472 ( $\text{M}^+$ , 100).<sup>3</sup> The relative configurations of adducts (3), (4), and (5) were elucidated on the basis of  $^1\text{H}$  nmr spectroscopy and other spectral data. Especially, the following characteristic spectral features were instrumental assignments. The methine proton (Hb) of the *exo* isomer (4) appeared at higher field (3.52 ppm) compared with that of each *endo* isomers (3) and (5) (4.03 ppm and 3.63 ppm, respectively) due to the shielding effect of the endocyclic double bond. The coupling constants between two adjacent methine protons ( $J_{\text{ab}}$ ) of the *endo* isomers (3) and (5) were shown to be 4.4 Hz and 4.3 Hz, respectively, whereas the coupling between Ha and Hb of the *exo* isomer (4) was not observed. On the other hand, the methine proton (Hb) of the adduct (5) appeared at higher field (3.63 ppm) compared with that of the adduct (3) (4.03 ppm), whereas the methine proton (Hc) of the adduct (5) appeared at lower field (5.98 ppm) compared with that of the adduct (3) (5.19 ppm) due to the anisotropic effect of the ester moiety of the *exo* olefine part in the adduct. These data of  $^1\text{H}$  nmr spectroscopy are summarized in Table II.

**Table II.**  $^1\text{H}$  Nmr Spectral Data of Adducts (3), (4), and (5)

| adduct | $^1\text{H}$ nmr (270 MHz, $\text{CDCl}_3$ ) $\delta$  |
|--------|--|
| 3      | 6.48 (dd, $J = 5.8, 1.8$ Hz, 1H), 6.37 (dd, $J = 5.8, 1.5$ Hz, 1H), 6.02 (d, $J = 2.0$ Hz, 1H), 5.29 (d, $J = 3.6$ Hz, 1H), 5.19 (t, $J = 1.0$ Hz, 1H), 4.64 (dt, $J = 4.3, 10.7$ Hz, 1H), 4.56 (dt, $J = 4.3, 10.9$ Hz, 1H), 4.03 (dd, $J = 4.4, 2.0$ Hz, 1H), 2.11-1.24 (m, 14 H), 1.15-0.62 (m, 22 H) |
| 4      | 6.52 (dd, $J = 5.6, 1.7$ Hz, 1H), 6.43 (dd, $J = 5.6, 1.7$ Hz, 1H), 6.05-6.02 (m, 1H), 5.24 (d, $J = 1.0$ Hz, 1H), 5.21 (d, $J = 0.7$ Hz, 1H), 4.71 (dt, $J = 4.3, 11.1$ Hz, 1H), 4.67 (dt, $J = 4.3, 10.9$ Hz, 1H), 3.52 (d, $J = 1.3$ Hz, 1H), 2.12-1.80 (m, 4H), 1.74-0.61 (m, 32H)                   |
| 5      | 6.57-6.50 (m, 2H), 6.16 (d, $J = 1.3$ Hz, 1H), 5.98 (dd, $J = 2.0, 1.0$ Hz, 1H), 5.23 (d, $J = 4.0$ Hz, 1H), 4.71 (dt, $J = 4.3, 10.9$ Hz, 1H), 4.67 (dt, $J = 4.3, 10.9$ Hz, 1H), 3.63 (dd, $J = 4.3, 2.0$ Hz, 1H), 2.10-1.19 (m, 16H), 1.19-0.63 (m, 20H)  |

The absolute configuration of major adduct (3) was confirmed as (-)-(1*R*, 2*S*, 5*R*)-menthyl (1*R*, 4*S*)-*endo*-3-(1*R*, 2*S*, 5*R*)-menthoxy carbonyl-7-oxabicyclo[2.2.1]hexa-5-ene- $\Delta^{2,\alpha}$ -acetate by X-ray analysis (Figure 1 and Table III).

In conclusion, we have carried out that the reactions of optically active (*R*)-allene-1,3-dicarboxylate with furan run using a variety of Lewis acids due to higher selectivity. The condition of using  $\text{TiCl}_4$  (3 equiv.) at  $-40^{\circ}\text{C}$  was found to be optimum as shown in Table I. Therefore, the adduct (3) was supposed to be useful as a

chiral synthon for synthesis of optically active natural products. Chemical conversion leading to shikimic acid and showdomycin using the optically active adduct (3) will be reported elsewhere.

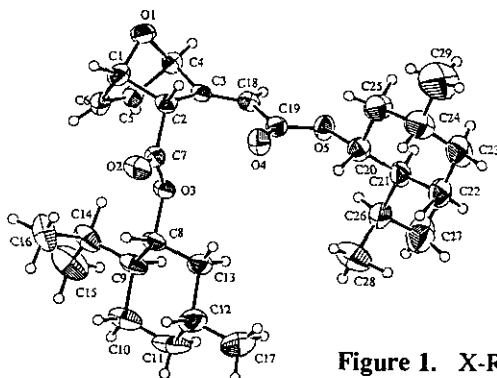


Figure 1. X-Ray Crystal Structure of Adduct (3)

Table III. Summary of Crystal Data, Intensity Collection and Least-squares Processing of Adduct (3)

|                                   |                   |  |   |
|-----------------------------------|-------------------|--|---|
| formula                           | $C_{29}H_{44}O_5$ | diffractometer                           | Rigaku AFC-5R                                 |
| formula weight                    | 472.66            | radiation                                | $CuK\alpha$ ( $\lambda=1.54178 \text{ \AA}$ ) |
| crystal system                    | orthorhombic      |  | graphite monochromated                        |
| space group                       | $P2_12_12_1 / c$  | $2\theta$ max / deg                      | 120.1   |
| a / $\text{\AA}$                  | 10.552 (2)        | scan type                                | $\omega$ - $2\theta$                          |
| b / $\text{\AA}$                  | 26.077 (2)        | crystal dimensions / mm                  | 0.350 x 0.150 x 0.150                         |
| c / $\text{\AA}$                  | 10.428 (2)        | total No. of reflections measured        | 2476  |
| V / $\text{\AA}^3$                | 2869.6 (6)        | No. observations ( $I > 3.00\sigma(I)$ ) | 1688  |
| Z value                           | 4                 | R  | 0.036   |
| D calcd / $\text{g cm}^{-3}$      | 1.320             | Rw                                       | 0.039   |
| $\mu(CuK\alpha) / \text{cm}^{-1}$ | 5.81              | goodness of fit indicator                | 1.42  |

## REFERENCES AND NOTES

1. E. Vieira and P. Vogel, *Helv. Chim. Acta*, 1983, **66**, 1865; H. Takayama, A. Iyobe, and T. Koizumi, *J. Chem. Soc., Chem. Commun.*, 1986, 771; N. Katagiri, H. Akatsuka, C. Kaneko, and A. Sera, *Tetrahedron Lett.*, 1988, **29**, 5397.
2. M. Aso, I. Ikeda, T. Kawabe, M. Shiro, and K. Kanematsu, *Tetrahedron Lett.*, 1992, **33**, 5787.
3. Data for the synthetic 3: mp 118 °C;  $[\alpha]_D^{21} -75.0^\circ$  ( $c = 1.01$ ,  $\text{CHCl}_3$ );  $^{13}\text{C}$  nmr (67.9 MHz,  $\text{CDCl}_3$ )  $\delta$  168.37 (s), 165.57 (s), 151.73 (s), 135.55 (d), 133.50 (d), 114.90 (d), 83.55 (d), 80.18 (d), 74.86 (d), 74.21 (d), 50.02 (d), 46.97 (d), 46.89 (d), 40.95 (t), 40.61 (t), 34.30 (t), 34.27 (t); 31.47 (d), 31.36 (d), 26.20 (d), 25.68 (d), 23.59 (t), 23.11 (t), 22.02 (q), 20.91 (q), 20.72 (q), 16.50 (q), 16.10 (q); ir ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$  1730 (s), 1710 (s); LR ms (FD)  $m/z$  (relative intensity) 472 ( $M^+$ , 100). *Anal.* Calcd for  $C_{29}H_{44}O_5$ : C, 73.69; H, 9.38. Found: C, 73.74; H, 9.37.

Received, 16th July, 1993