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,[a] Akie Gondo,[a] Motoo Shiro,[b] and Ken Kanematsu*[a]

[a]Institute of Synthetic Organic Chemistry, Faculty of Pharmaceutical Sciences,
Kyushu University 62, Maidashi, Higashi-ku, Fukuoka 812, Japan
[b]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.[1] 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.[2] 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 ($TiCl_4$, Et_2AlCl, $AlCl_3$, $BF_3 \cdot OEt_2$) 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

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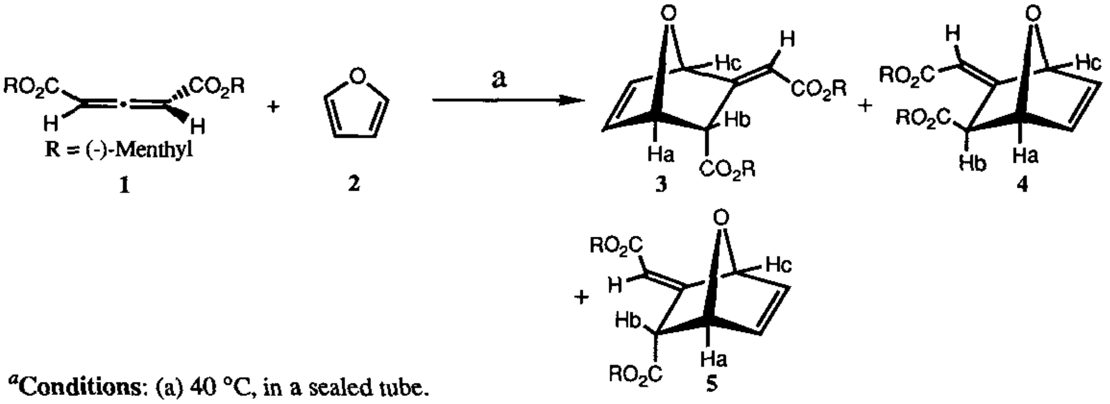
[†]This paper is dedicated to Professor Yoshifumi Maki on this occasion of his retirement from Gifu Pharmaceutical University in March 1994.

promoted by employing 2 equiv. or excess of $TiCl_4$ or Et_2AlCl, and gave higher diastereofacial selectivity compared with the uncatalyzed reaction. Generally, in case of using $AlCl_3$ or $BF_3{\cdot}OEt_2$, 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 $AlCl_3$ proceeded to afford the *endo*-adducts in high yields.[2] 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[a]



[a]**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 [b] [3] : [4] : [5]	*endo*:*exo* [b] [3] : [4]	*endo* ds [b] [3] : [5]
none		40 [a]	7.5	38 : 34 : 29	53 : 47	57 : 43
$TiCl_4$	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
	3	-40	2.2	75 : 24 : 1	76 : 24	98 : 2
Et_2AlCl	1	-40	8	60 : 27 : 13	69 : 31	82 : 18
	2	-78	10	64 : 35 : 1	65 : 35	99 : 1
		-40	1.5	62 : 35 : 3	64 : 36	96 : 4
	3	-40	1	59 : 38 : 3	62 : 38	96 : 4
	10	-40	1	60 : 40 : 0	60 : 40	100 : 0
$AlCl_3$	1	-40	10	58 : 21 : 21	73 : 27	73 : 27
	2	-40	9	56 : 19 : 25	74 : 26	69 : 31
$BF_3{\cdot}OEt_2$	1	-40	9	54 : 19 : 27	74 : 26	66 : 34
	2	-40	12.5	53 : 18 : 29	74 : 26	64 : 36

[a] Reaction conditions: at 40 °C in a sealed tube.

[b] 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), $TiCl_4$ (2 equiv.), CH_2Cl_2, -40 °C): mp 118

°C, $[\alpha]_D^{21}$ -75.0° (c = 1.01, $CHCl_3$), ms (FD) m/z (relative intensity) 472 (M^+, 100).[3] The relative configulations of adducts (**3**), (**4**), and (**5**) were elucidated on the basis of ^1H 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 protones (*J*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 ^1H nmr spectroscopy are summarized in Table II.

Table II. ^1H Nmr Spectral Data of Adducts (**3**), (**4**), and (**5**)

adduct	^1H nmr (270 MHz, $CDCl_3$) δ
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 configulation 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*)-menthoxycarbonyl-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 $TiCl_4$ (3 equiv.) at -40 °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.

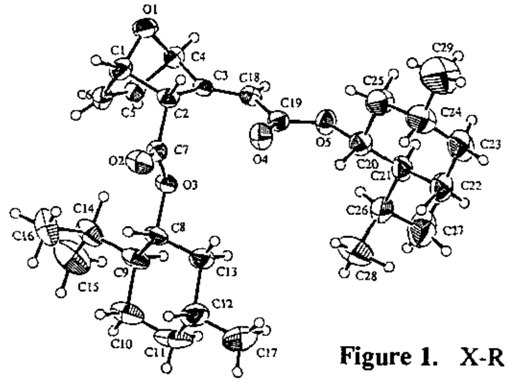


Figure 1. X-Ray Crystal Structure of Adduct (3)

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

formula	$C_{29}H_{44}O_5$	diffractometer	Rigaku AFC-5R
formula weight	472.66	radiation	CuKα (λ=1.54178 Å) graphite monochromated
crystal system	orthorhombic		
space group	$P2_12_12_1$ / c	2θ *max* / deg	120.1
a / Å	10.552 (2)	scan type	ω-2θ
b / Å	26.077 (2)	crystal dimensions / mm	0.350 x 0.150 x 0.150
c / Å	10.428 (2)	total No. of reflections measured	2476
V/ Å^3	2869.6 (6)	No. observations(I>3.00σ(I))	1688
Z value	4	R	0.036
D *calcd* / g cm^{-3}	1.320	Rw	0.039
μ(CuKα) / 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° (c = 1.01, $CHCl_3$); ^{13}C nmr (67.9 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 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.

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