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# Preparation of Optically Active (*R*)- and (*S*)-Allene-1,3-dicarboxylates and Their Asymmetric Cycloaddition Reactions with Cyclopentadiene

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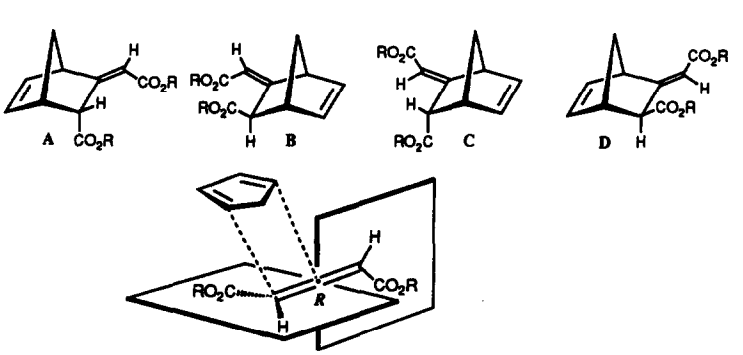
***Key words:*** optically active allene-1,3-dicarboxylate, asymmetric Diels-Alder reaction

***Abstract:*** Optically active (*R*)- and (*S*)-allene-1,3-dicarboxylates were prepared, and their asymmetric Diels-Alder reactions with cyclopentadiene in the presence of Lewis acid proceeded to afford the *endo*-adducts in high yields. The absolute configuration of the adduct was completely confirmed by X-ray analysis.

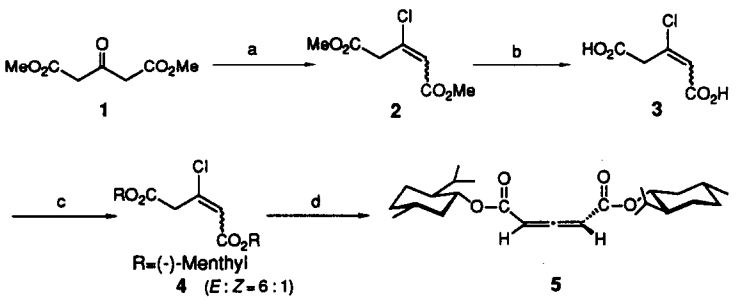
Although the activating influence that a carboxylate moiety exerts upon the 1,3-disubstituted allene framework makes these compounds excellent candidates as dienophiles in Diels-Alder reactions,[1,2] no systematic study of the cycloaddition reactions of compounds of this type has been reported. It would be predicted that Diels-Alder reaction of the optically active allene-1,3-dicarboxylate proceeds with high stereoselectivity derived from axial asymmetry of allene moiety. From this point of view, it is expected that adduct A would be preferentially obtained through the combination of the sterically favored approach owing to axial asymmetry of allene moiety and the effective secondary orbital interaction (Figure 1). While adduct B would be formed without secondary orbital interaction of carboxylate moiety, adduct C must be formed against the steric hindrance. In addition, adduct D would be scarcely formed because of two disadvantageous factors.

**Figure 1**



Optically active di-(-)-menthyl allene-1,3-dicarboxylate **5** was prepared by the modification of Smith's procedure of allene-1,3-dicarboxylate (Scheme I).[3] 3-Chloroglutaconic acid **3** was obtained from dimethyl 1,3-acetonedicarboxylate **1** by treatment with phosphorus pentachloride (1.05 equiv) followed by hydrolysis with 20% hydrochloric acid. Esterification of the diacid **3** with (-)-menthol (conc. sulfuric acid, benzene, reflux) proceeded to give chlorodimenthylester **4** in high yield. The proportion of the stereoisomers **4** was determined ($E : Z = 6 : 1$) by $^1$H-NMR spectrum inspection. Dehydrochlorination of **4** by triethylamine (1.19 equiv) in anhydrous tetrahydrofuran at 0 °C gave a mixture of diastereomers, which was recrystallized from pentane to afford pure crystals **5**; m.p. 83 °C, $[\alpha]_D^{20}$ -251.1° (c = 1.00, $CHCl_3$).

**Scheme I**[a]




[a]Reagents: (a) $PCl_5$; (b) 20% HCl, reflux; (c) (-)-menthol, conc. $H_2SO_4$, benzene, reflux; (d) $Et_3N$, THF, 0 °C, then recrystallized from pentane.

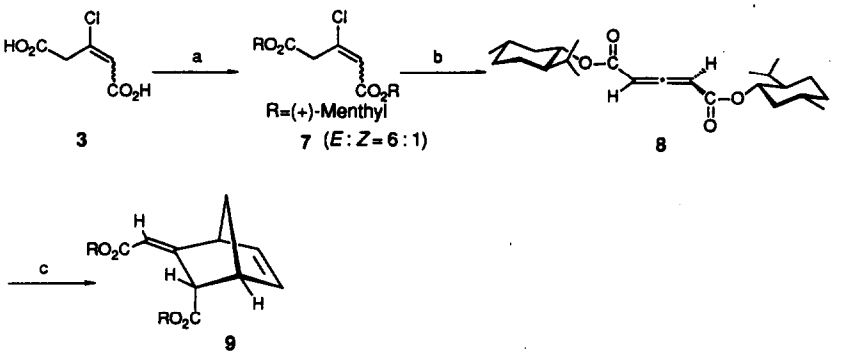
The Diels-Alder reaction of **5** with cyclopentadiene in the presence of aluminum chloride proceeded to afford the 1:1 adduct **6** in 96% yield (Scheme II).[4] A typical experimental procedure is as follows. To a suspension of aluminum chloride (592 mg, 4.44 mmol, 1.20 equiv) in 12 mL of anhydrous dichloromethane at -78 °C under nitrogen was added a solution of **5** (1.49 g, 3.69 mmol) in anhydrous dichloromethane. After 30 min, cyclopentadiene (3 mL, excess) was added. The reaction mixture was stirred at -78 °C for 5 h to give **6** (1.66 g, 96 %). The relative configuration of **6** was established by the $^1$H-NMR spectroscopy.[5] Furthermore, the absolute configuration of **5** was determined by Agosta's procedure.[6] Thus, the absolute configuration of the axial asymmetry of **5** was shown to be *R*.

**Scheme II**[a]


[a]Reagents: cyclopentadiene, $AlCl_3$, $CH_2Cl_2$, -78 °C, 5 h.

On the other hand, optically active di-(+)-menthyl allene-1,3-dicarboxylate **8** (m.p. 83 °C, $[\alpha]_D^{22}$ +262.7° (c = 0.99, $CHCl_3$)) was prepared in a similar manner as the preparation of **5** (Scheme III). Similar treatment of **8** with cyclopentadiene in the presence of aluminum chloride proceeded to afford the 1:1 adduct **9** in 89% yield. Spectral data of **9** were identical with those of **6** except for antipodal optical rotation.[5]

**Scheme III**[a]




[a]Reagents: (a) (+)-menthol, conc. $H_2SO_4$, benzene, reflux; (b) $Et_3N$, THF, 0 °C, then recrystallized from pentane; (c) cyclopentadiene, $AlCl_3$, $CH_2Cl_2$, -78 °C, 3 h.

In addition, the absolute configuration of **9** was completely confirmed by X-ray analysis (Figure 2).[7]

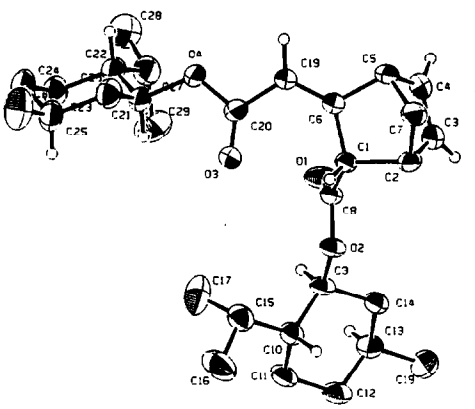



**Figure 2** X-ray crystal structure of adduct **9**

As described above, we have succeeded in preparation of optically active (*R*)- and (*S*)-allene-1,3-dicarboxylates **5** and **8** using (-)- and (+)-menthol, respectively. Moreover, the Diels-Alder reaction of **5** and **8** with cyclopentadiene in the presence of Lewis acid proceeded to afford adducts **6** and **9** in high yields, respectively. Further, the adducts **6** and **9** were supposed to be useful for synthesis of optically active natural products and its antipode. For example, *cis*-trikentrin B is a minor component of the trikentrins, and the absolute structure of natural *cis*-trikentrin B is not determined.[8] Therefore, the synthesis of optically active *cis*-trikentrin B using the obtained optically active adduct as a synthetic key intermediate is now in progress.

## References and Notes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5. Data for the synthetic **6**: $^1$H NMR (270 MHz, $CDCl_3$) δ 6.11–6.18 (m, 2H), 5.98 (d, $J$ = 2.0 Hz, 1H), 4.25-4.88 (m, 2H), 3.87 (dd, $J$ = 3.5, 2.0 Hz, 1H), 3.41 (m, 1H), 3.33 (m, 1H), 1.35-2.28 (m, 20H), 0.41-1.53 (m, 18H); IR ($CHCl_3$) cm$^{-1}$ 1710 (s), 1690 (s); EI-MS *m/z* 470 ($M^+$); *Anal.* Calcd for $C_{30}H_{46}O_4$: C, 76.55; H, 9.85. Found: C, 76.80; H, 9.77; m.p. 97 °C; $[\alpha]_D^{23}$ -48.2° (c = 1.03, $CHCl_3$). Data for the synthetic **9**: $^1$H NMR (270 MHz, $CDCl_3$) δ 6.11–6.18 (m, 2H), 5.97 (d, $J$ = 2.0 Hz, 1H), 4.25-4.88 (m, 2H), 3.87 (dd, $J$ = 3.6, 2.0 Hz, 1H), 3.41 (m, 1H), 3.33 (m, 1H), 1.35-2.28 (m, 20H), 0.41-1.53 (m, 18H); IR ($CHCl_3$) cm$^{-1}$ 1710 (s), 1690 (s); EI-MS *m/z* 470 ($M^+$); *Anal.* Calcd for $C_{30}H_{46}O_4$: C, 76.55; H, 9.85. Found: C, 76.48; H, 9.85; m.p. 104.5 °C; $[\alpha]_D^{22}$ +47.1° (c = 1.08, $CHCl_3$).
6. (+)-Norcamphor dinitrophenylhydrazone derived from adduct **6** was compared with the data of the references as follows; W. C. Agosta, *J. Am. Chem. Soc.*, **86**, 2638 (1964); (+)-norcamphor dinitrophenylhydrazone derived from adduct **6**; $[\alpha]_D^{25}$ +32.7° (c = 0.46, $CHCl_3$), m.p. 132 °C (lit. $[\alpha]_D^{28}$ +30° ($CHCl_3$), m.p. 129-130 °C). While (-)-norcamphor dinitrophenylhydrazone was derived from adduct **9**, its optical rotation was opposite to that of (+)-norcamphor derivative from adduct **6**; $[\alpha]_D^{23}$ -28.0° (c = 1.03, $CHCl_3$), m.p. 131 °C.
7. Crystal data for adduct **9**; formula $C_{30}H_{46}O_4$, formula weight 470.69, crystal system tetragonal, space group $P4_3$, a(Å) 11.665(4), c(Å) 21.778(8), V(Å$^3$) 2963(2), Z value 4, D calc(g cm$^{-3}$) 1.055, μ(CuKα)(cm$^{-1}$) 5.03, R; Rw 0.046; 0.058. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
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