SYNTHESIS OF THIOALDEHYDES HAVING OPTICALLY ACTIVE ALKOXY MOIETY AND THEIR ASYMMETRIC HETERO DIELS-ALDER REACTION

Tamiko Takahashi, Noriyuki Kurose and Toru Koizumi*

Faculty of Pharmaceutical Sciences, Toyama Medical & Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan

Motoo Shiro*

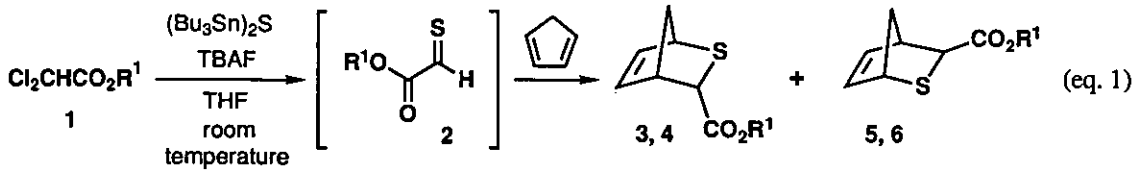
Rigaku Corporation, 3-9-12 Matsubara, Akishima, Tokyo, 196, Japan

Abstract -- Optically active α-alkoxycarbonylthioaldehydes (**2a-g**) were prepared using 8-arylmenthols as chiral auxiliaries. Their asymmetric hetero Diels-Alder reactions with cyclopentadiene gave the *endo* cycloadducts (**3** and **4**) and *exo* cycloadducts (**5** and **6**) with moderate diastereomeric excesses. However, the major *endo* cycloadducts (**3b-g**) were isolated in optically pure form. This is the first chiral synthesis of 2-thiabicyclo[2.2.1]hept-5-ene ring system. The absolute configuration of the cyclic carbonate (**12**), which was prepared from the major *endo* cycloadduct (**3c**) *via* the epimerization, or the minor *exo* compound (**6c**), was determined as 1*R* by X-ray analysis. The cycloadduct (**3c**) was transformed to a potential intermediate (**14**) for the synthesis of carbocyclic homonucleosides.

Thioaldehydes are very attractive heterodienophiles because of their high reactivity. Recently, efficient synthetic methods of these unstable compounds have been developed.[1] In the presence of a diene, the thioaldehydes have been trapped as hetero Diels-Alder adducts. However, little attention has so far been focused on the application of such hetero Diels-Alder reactions to synthetic organic chemistry.[1,2] To the best of our knowledge, there have been no reports on an asymmetric cycloaddition reaction of the thioaldehydes having a chiral auxiliary.[3] We thus

proceeded to the synthesis of the thioaldehydes having optically active alkoxy moiety and their utilization to an asymmetric reaction.

Optically active thioaldehydes (**2**) were prepared from the corresponding α-dichloroacetates (**1**) and S^{2-} which was formed by a fluorodestannylation reaction of bis(tributyltin) sulfide with tetrabutylammonium fluoride (TBAF) (eq. 1).[4] The thioaldehydes were generated and trapped *in situ* with cyclopentadiene to give the cycloadducts (**3-6**).



(eq. 1)

In the preliminary experiments, we examined the ability of asymmetric induction of some commercially available alcohols, such as (1*S*)-*endo*-(-)-borneol, (*S*)-(-)-α-phenethyl alcohol, (-)-menthol and (-)-8-phenylmenthol. As the result of the asymmetric hetero Diels-Alder reaction of these thioaldehydes (**2**), the diastereomeric excesses (de's) of the *endo* cycloadducts increased from 14% to 23% by replacing (-)-menthyl group (R^2 = H) with (-)-8-phenylmenthyl group (R^2 = Ph) (Table I). π-π Stacking effect[5] between the aromatic moiety of the auxiliary and the thiocarbonyl group was suggested as the reason for the diastereofacial selection in this cycloaddition reaction (Figure 1). We predicted that the absolute configuration of the major *endo* cycloadducts would be 1*S*. To obtain higher diastereoselectivity, we designed various chiral α-menthyloxycarbonylthioaldehydes having a *p*-substituted 8-aryl group by their steric and/or electronic effects.

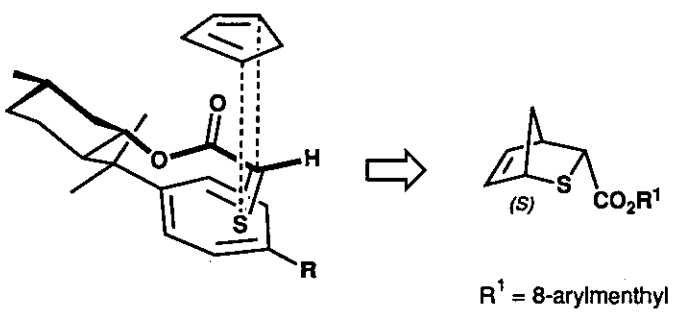
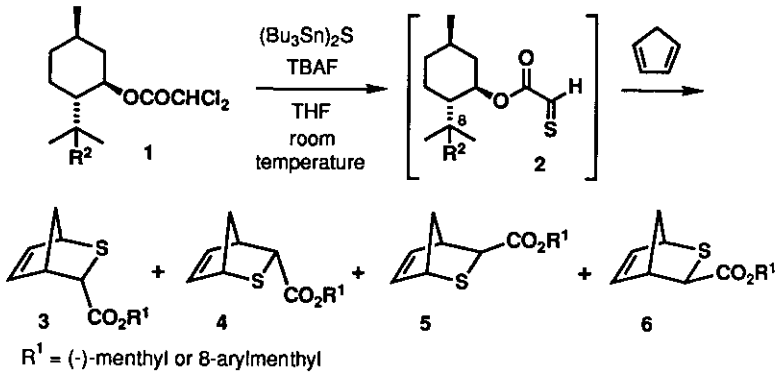


Figure 1

Optically active 8-arylmenthols (**9c-g**) were prepared according to a modified method of Ort[6] as shown in Scheme 1. The alcohols (**9a-g**) were converted to the corresponding α-dichloroacetates (**1a-g**) by heating with

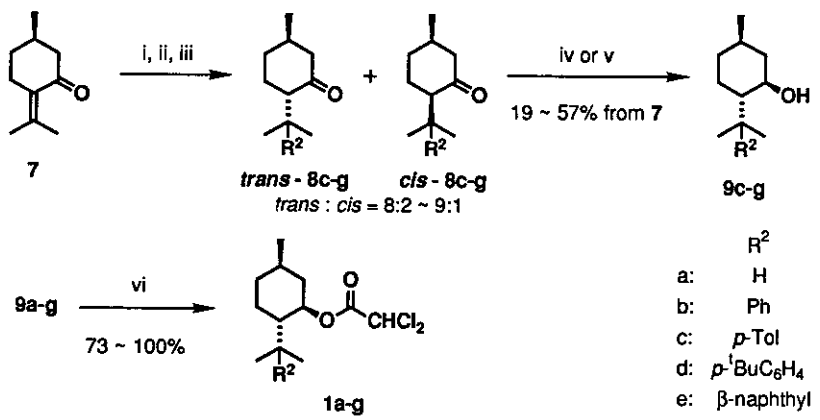


R^1 = (-)-menthyl or 8-arylmenthyl

TABLE I. Asymmetric Hetero Diels-Alder Reaction of Chiral α-Alkoxycarbonylthioaldehyde (**2**)

thioaldehyde	R^2	**3+4+5+6** yield (%)[a]	*endo* de (%)[b]	*exo* de (%)[b]	**(3+4) : (5+6)**[b]
2a	H	78	14	5	69 : 31
2b	Ph	73	23	45	61 : 39
2c	*p*-Tol	85	16	34	63 : 27
2d	*p*-^{t}BuC$_6$H$_4$	61	43	46	64 : 36
2e	β-naphthyl	69	17	30	66 : 34
2f	*p*-MeOC$_6$H$_4$	65	12	25	62 : 38
2g	*p*-FC$_6$H$_4$	74	20	58	62 : 38

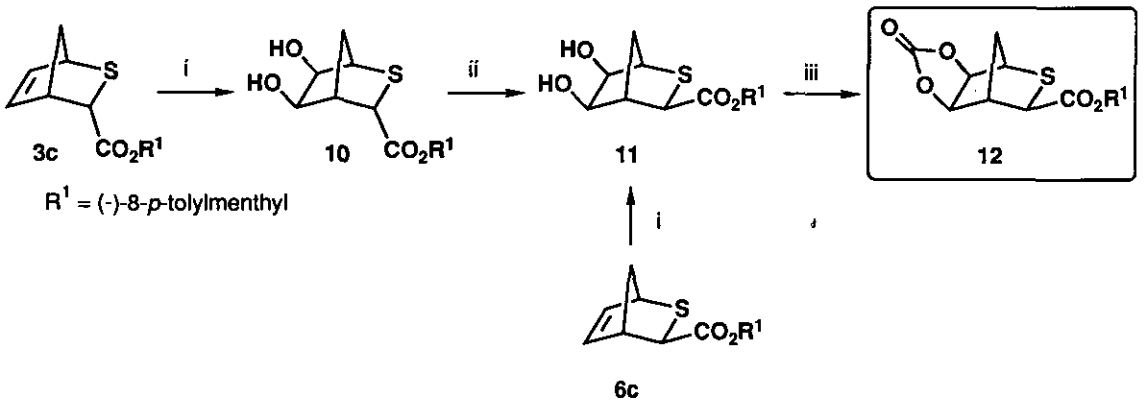
[a] Isolated yield. [b] Determined by ^{1}H-nmr of the crude product.



i) R^2MgBr, CuBr•Me_2S, TMSCl, HMPA, THF, -78 °C; ii) cat. KF, MeOH; iii) KOH, EtOH, reflux; iv) Na, ^{i}PrOH, toluene, reflux; separation; v) $LiAlH_4$, Et_2O; separation; vi) $Cl_2CHCOCl$, 100 °C

Scheme 1

dichloroacetyl chloride[7] in quantitative yield. These esters (**1**) were transformed to the thioaldehydes (**2**) which were used in the subsequent asymmetric hetero Diels-Alder reaction. The results are shown in Table I. The diastereoselectivity of the *endo* cycloaddition was the highest (43% de) in the case of **2d** ($R^2 = p$-^{t}BuC$_6$H$_4$) and that of the *exo* cycloaddition was enhanced in the cases of **2d** and **2g** ($R^2 = p$-FC$_6$H$_4$). These results could be explained by means of the steric effect of *p-tert*-butyl group and the electronic effect of fluorine atom, respectively. To determine the absolute configuration of the major *endo* cycloadducts (**3**), **3c** was transferred to cyclic carbonate (**12**) (Scheme 2). Oxidation of the adduct (**3c**) with osmium tetroxide gave the diol (**10**).



i) OsO_4, DMF-H_2O; ii) ^{t}BuOK, THF, 0 °C; iii) diphosgene or triphosgene, pyridine, CH_2Cl_2, 0 °C

Scheme 2

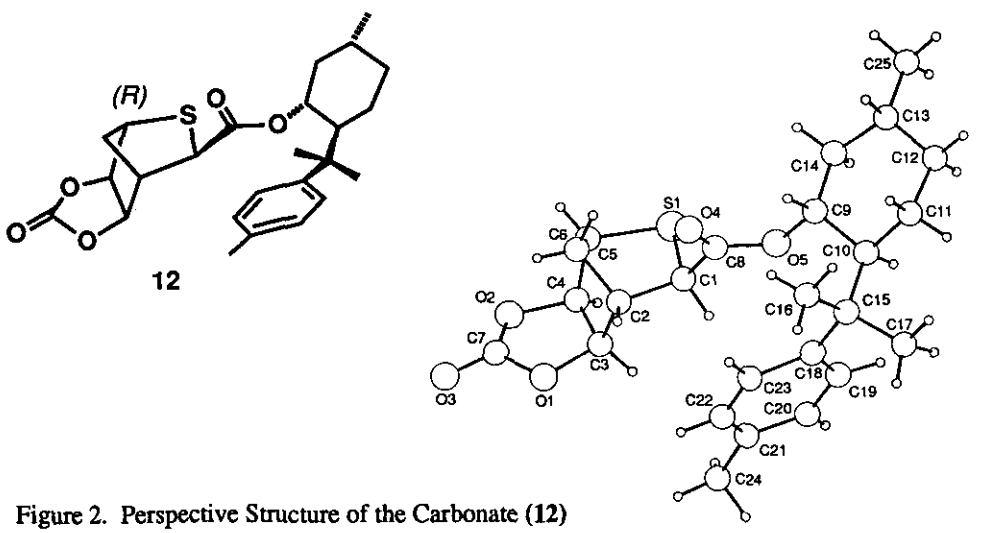
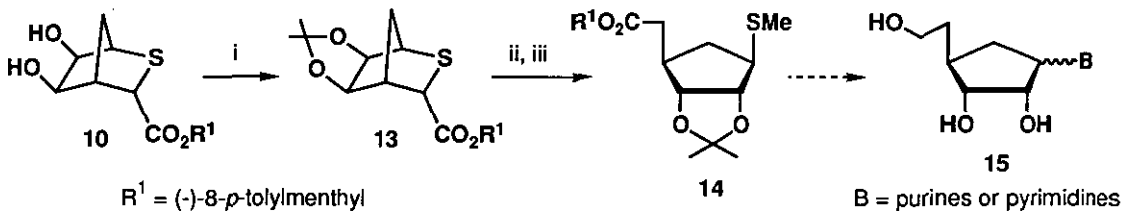


Figure 2. Perspective Structure of the Carbonate (**12**)

Epimerization of the ester moiety of the diol (**10**) followed by treatment with diphosgene gave crystals of the cyclic *exo* carbonate (**12**). Recrystallization of the carbonate from ethyl acetate-isopropyl ether gave the pure diastereomer (**12**) {mp 236-238 °C, $[\alpha]_D$ = +2.5° ($CHCl_3$)}. The compound (**12**) was identical with the cyclic carbonate made from the minor *exo* cycloadduct (**6c**). The absolute configuration of the cyclic carbonate (**12**) was determined as 1*R* by X-ray crystallographic analysis as shown in Figure 2. The configuration was opposite to that we predicted from π-π stacking effect between the aromatic moiety of the auxiliary and the thiocarbonyl group. The steric course of the cycloaddition remains unresolved.

Next, we attempted a utilization of the major *endo* cycloadduct (**3c**) to an enantioselective synthesis of carbocyclic homonucleosides by C-S bond scission (Scheme 3). The diol (**10**), which was obtained from the adduct (**3c**), was transformed to the acetonide (**13**) with 2,2-dimethoxypropane. *S*-Methylation followed by reduction with zinc gave the methyl sulfide (**14**). This compound (**14**) will be a potential intermediate for the chiral synthesis of carbocyclic homonucleoside derivatives (**15**).[8]



i) 2,2-dimethoxypropane, *p*-TsOH, acetone, reflux; ii) Me_3OBF_4, DME; iii) Zn, AcOH, CH_2Cl_2, reflux

Scheme 3

Thus, we developed the asymmetric hetero Diels-Alder reaction of the thioaldehydes having optically active alkoxy moiety (**2a-g**). Although the diastereoselectivity has been moderate to date, we isolated the major *endo* cycloadducts (**3b-g**) in optically pure form. This is the first chiral synthesis of 2-thiabicyclo[2.2.1]hept-5-ene ring system. Moreover, the adduct (**3c**) was utilized to the attempt for the enantioselective synthesis of carbocyclic homonucleoside derivatives (**15**). It is expected that the diastereoselectivity can be improved considerably by choosing better chiral inductors.

EXPERIMENTAL

Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. Microanalyses were performed by Microanalysis Center of Toyama Medical & Pharmaceutical University. Spectroscopic measurements were carried out with the following instruments: optical rotations, JASCO DIP-140 digital

polarimeter; ir, Perkin-Elmer 1600 Series FTIR; ^{1}H-nmr, JEOL JNM-GX 270 (270 MHz) for solutions in $CDCl_3$ with Me_4Si as internal standard; mass (ms) and high resolution mass spectra (hrms), JEOL JMS D-200. Column chromatography, flash column chromatography, and preparative tlc (plc) were performed on Kieselgel 60 (Merck, Art. 7734, Art. 9385 and Art. 7748, respectively).

General Procedure for the Preparation of 8-Arylmenthols (9) A 1 M-solution of Grignard reagent in THF was prepared from magnesium tunings (20 mmol) and the corresponding *p*-substituted bromobenzene (22 mmol) in THF (20 ml).[6a] $CuBr{\bullet}Me_2S$[6b] (1 mmol), Grignard reagent (20 mmol), and HMPA (20 mmol) were placed in a two necked flask under argon. To this was added a solution of (*R*)-(+)-pulegone (**7**) (10 mmol) and TMSCl (20 mmol) in THF (10 ml) below -70 °C within 5 min. After being stirred at -40~-70 °C for 2 h, the reaction temperature was raised to ambient temperature. Dry hexane (50 ml) was added to the reaction mixture and the mixture was stirred for 0.5 h. After dilution with hexane (50 ml), the organic layer was washed with water and brine, and the solvent was evaporated. The residue was treated with MeOH (30 ml) and KF (ca. 20 mg) at room temperature for 15 min. The mixture was diluted with water (100 ml) and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and concentrated. A solution of KOH (30-50 mmol) in 90% EtOH (30-50 ml) was added to the residue and the solution was refluxed for 3 h. The solution was concentrated to a volume of *ca.* 10 ml and water (20 ml) was added to the residue. The aqueous solution was saturated with NaCl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was subjected to flash column chromatography (hexane : Et_2O = 5:1~25:1) to give a mixture of *trans*- and *cis*-**8**. A solution of menthones (**8c**, **8d**, **8f** and **8g**) (3.5-9 mmol) in ^{i}PrOH (21-53 mmol) was added dropwise to a refluxed suspension of Na (28-48 mmol) in toluene (30-35 ml). The reaction mixture was refluxed for an additional 8 h and cooled to 0 °C. The mixture was diluted with Et_2O (50 ml) and ice-water (50 ml). The organic layer was separated and the aqueous layer was saturated with NaCl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash column chromatography (hexane : Et_2O = 10:1~15:1). Menthone (**8e**) was reduced with $LiAlH_4$ in Et_2O. Yields are overall yield from (*R*)-(+)-pulegone (**7**).

(1*R*,2*S*,5*R*)-(-)-2-(1-Methyl-1-*p*-tolylethyl)-5-methylcyclohexanol (9c): Yield 19%. Oil. $[\alpha]_D^{26}$ -22.6° (*c* 1.69, EtOH). Ir ν_{max} (neat) cm^{-1}: 3567, 3447. ^{1}H-Nmr δ: 0.8-1.9 (9H, m), 0.87 (3H, d, *J* = 6.4 Hz), 1.27, 1.39 and 2.30 (each 3H, s), 3.52 (1H, ddd, *J* = 4, 10, 10 Hz), 7.13 (2H, d, *J* = 8.1 Hz), 7.29 (2H, d, *J* = 8.3 Hz). Ms *m/z*: 246 (M^+). *Anal.* Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.97; H, 10.73.

(1*R*,2*S*,5*R*)-(-)-2-(1-Methyl-1-*p*-*tert*-butylphenylethyl)-5-methylcyclohexanol (9d): Yield 32%. Oil. $[\alpha]_D^{24}$ -19.2° (*c* 1.11, EtOH). Ir ν_{max} (neat) cm^{-1}: 3566, 3420. ^{1}H-Nmr δ: 0.8-1.9 (9H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.27 and 1.39 (each 3H, s), 1.29 (9H, s), 3.53 (1H, ddd, *J* = 4.5, 11.0, 11.0 Hz), 7.33 (4H, s). Ms *m/z*: 288 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{20}H_{32}O$ (M^+), 288.2482 (288.2454).

(1*R*,2*S*,5*R*)-(-)-2-(1-Methyl-1-β-naphthylethyl)-5-methylcyclohexanol (9e): Yield 32%. Oil. $[\alpha]_D^{26}$ -3.5° (*c* 0.56, EtOH). Ir ν_{max} (neat) cm^{-1}: 3567, 3422. ^{1}H-Nmr δ: 0.8-2.0 (9H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.38 and 1.54 (each 3H, s), 3.59 (1H, br t, *J* = 11 Hz), 7.4-7.9 (7H, m). Ms *m/z*: 282 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{20}H_{26}O$ (M^+), 282.1971 (282.1982).

(1*R*,2*S*,5*R*)-(-)-2-(1-Methyl-1-*p*-methoxyphenylethyl)-5-methylcyclohexanol (9f): Yield 31%. Oil. $[\alpha]_D^{25}$ -19.5° (*c* 1.33, EtOH). Ir ν_{max} (neat) cm^{-1}: 3567, 3447. ^{1}H-Nmr δ: 0.8-1.9 (9H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.26, 1.39 and 3.78 (each 3H, s), 3.51 (1H, ddd, *J* = 4.5, 10.2, 10.2 Hz), 6.86 (2H, d, *J* = 8.8 Hz), 7.31 (2H, d, *J* = 9.0 Hz). Ms *m/z*: 263 (M^++1). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{26}O_2$ (M^+), 262.1934 (262.1933).

(1*R*,2*S*,5*R*)-(-)-2-(1-Methyl-l-*p*-fluorophenylethyl)-5-methylcyclohexanol (9g): Yield 57%. Oil. $[\alpha]_D^{25}$ -29.5° (*c* 1.20, EtOH). Ir ν_{max} (neat) cm^{-1}: 3568, 3414. ^{1}H-Nmr δ: 0.8-1.9 (9H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.28 and 1.41 (each 3H, s), 3.50 (1H, ddd, *J* = 4.1, 10.1, 10.1 Hz), 6.99 (2H, dd, *J* = 8.7, 8.7 Hz), 7.34 (2H, dd, *J* = 5.2, 8.9 Hz). Ms *m/z*: 250 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{16}H_{23}OF$ (M^+), 250.1753 (250.1733).

General Procedure for the Formation of the Dichloroacetic Acid Esters A mixture of the chiral alcohols (1.91-2.80 mmol) and dichloroacetyl chloride (2.10-3.00 mmol) was heated at 100 °C for 1-1.5 h. Saturated aqueous $NaHCO_3$ (10 ml) was added to the reaction mixture at 0 °C and the mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by distillation, recrystallization or flash column chromatography (haxane : Et_2O = 15:1~20:1).

(1*R*,2*S*,5*R*)-(-)-Menthyl Dichloroacetate (1a): Yield 87%. Oil. bp 117 °C (5 mmHg), lit.,[6] bp 173-174 °C (37 mmHg). $[\alpha]_D^{26}$ -64.2° (*c* 1.29, $CHCl_3$), lit.,[6] $[\alpha]_D^{20}$ -62.8°.

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl Dichloroacetate (1b): Yield 100%. Oil. $[\alpha]_D^{24}$ +33.2° (*c* 0.77, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1758. ^{1}H-Nmr δ: 0.8-2.2 (8H, m), 0.90 (3H, d, *J* = 6.3 Hz), 1.23 and 1.31 (each 3H, s), 4.74 (1H, s), 4.83 (1H, ddd, *J* = 4.5, 10.8, 10.8 Hz), 7.1-7.2 (1H,

m), 7.25-7.35 (4H, m). Ms *m/z*: 344 (M^+, ^{37}Cl), 342 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{18}H_{24}O_2Cl_2$ (M^+), 342.1152 (342.1111).

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-*p*-tolylethyl)-5-methylcyclohexyl Dichloroacetate (1c): Yield 91%. Oil. $[\alpha]_D^{26}$ +30.3° (*c* 0.96, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1759. ^{1}H-Nmr δ: 0.8-2.2 (8H, m), 0.89 (3H, d, *J* = 6.4 Hz), 1.22, 1.30 and 2.32 (each 3H, s), 4.83 (1H, s), 4.87 (1H, ddd, *J* = 4.6, 10.7, 10.7 Hz), 7.10 (2H, d, *J* = 8.3 Hz), 7.16 (2H, d, *J* = 8.6 Hz). Ms *m/z*: 360 (M^+, ^{37}Cl x 2), 358 (M^+, ^{37}Cl), 356 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{19}H_{26}O_2{}^{37}Cl_2$ (M^+, ^{37}Cl x 2), 360.1214 (360.1250), $C_{19}H_{26}O_2Cl_2$ (M^+), 356.1265 (356.1308).

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-*p*-*tert*-butylphenylethyl)-5-methylcyclohexyl Dichloroacetate (1d): Yield 86%. Needles. mp 107-110 °C (EtOH). $[\alpha]_D^{26}$ +49.7° (*c* 1.12, $CHCl_3$). Ir ν_{max} (KBr) cm^{-1}: 1758. ^{1}H-Nmr δ: 0.8-2.2 (8H, m), 0.90 (3H, d, *J* = 6.6 Hz), 1.20 and 1.29 (each 3H, s), 1.33 (9H, s), 4.47 (1H, s), 4.87 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 7.19 and 7.33 (each 2H, d, *J* = 8.5 Hz). Ms *m/z*: 402 (M^+, ^{37}Cl x 2), 400 (M^+, ^{37}Cl), 398 (M^+). *Anal.* Calcd for $C_{22}H_{32}O_2Cl_2$: C, 66.16; H, 8.08. Found: C, 66.09; H, 8.06.

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-β-naphthylethyl)-5-methylcyclohexyl Dichloroacetate (1e): Yield 75%. Columns. mp 95-98 °C (EtOH). $[\alpha]_D^{25}$ +15.1° (*c* 1.00, $CHCl_3$). Ir ν_{max} (KBr) cm^{-1}: 1753. ^{1}H-Nmr δ: 0.8-2.3 (8H, m), 0.90 (3H, d, *J* = 6.6 Hz), 1.32 and 1.44 (each 3H, s), 4.54 (1H, s), 4.95 (1H, ddd, *J* = 4.6, 10.7, 10.7 Hz), 7.4-7.9 (7H, m). Ms *m/z*: 396 (M^+, ^{37}Cl x 2), 394 (M^+, ^{37}Cl), 392 (M^+). *Anal.* Calcd for $C_{22}H_{26}O_2Cl_2$: C, 67.17; H, 6.66. Found: C, 67.38; H, 6.60.

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-*p*-methoxyphenylethyl)-5-methylcyclohexyl Dichloroacetate (1f): Yield 90%. Oil. $[\alpha]_D^{25}$ +28.7° (*c* 1.07, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1758. ^{1}H-Nmr δ: 0.8-2.1 (8H, m), 0.89 (3H, d, *J* = 6.6 Hz), 1.21, 1.30 and 3.80 (each 3H, s), 4.87 (1H, ddd, *J* = 4.6, 10.7, 10.7 Hz), 4.95 (1H, s), 6.84 and 7.18 (each 2H, d, *J* = 8.8 Hz). Ms *m/z*: 375 (M^++1, ^{37}Cl), 373 (M^++1). Hrms [Found (Calcd)] *m/z*: $C_{19}H_{26}O_3{}^{37}Cl_2$ (M^+, ^{37}Cl x 2), 376.1216 (376.1201), $C_{19}H_{26}O_3Cl_2$ (M^+), 372.1279 (372.1259).

(1*R*,2*S*,5*R*)-(+)-2-(1-Methyl-1-*p*-fluorophenylethyl)-5-methylcyclohexyl Dichloroacetate (1g): Yield 89%. Oil. $[\alpha]_D^{25}$ +16.3° (*c* 1.08, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1758. ^{1}H-Nmr δ: 0.8-2.1 (8H, m), 0.90 (3H, d, *J* = 6.6 Hz), 1.22 and 1.31 (each 3H, s), 4.87 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.04 (1H, s), 6.98 (2H, dd, *J* = 8.8, 8.8 Hz), 7.23 (2H, dd, *J* = 5.4, 8.8 Hz), 7.20-7.29 (2H, m). Ms *m/z*: 362 (M^+, ^{37}Cl), 360 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{18}H_{23}O_2{}^{37}Cl_2F$ (M^+, ^{37}Cl x 2), 364.1023 (364.1001), $C_{18}H_{23}O_2{}^{37}ClClF$ (M^+, ^{37}Cl), 362.1023 (362.1028), $C_{18}H_{23}O_2Cl_2F$ (M^+), 360.1079 (360.1059).

A Typical Procedure for the Asymmetric Hetero Diels-Alder Reaction of Chiral α-Alkoxycarbonylthioaldehydes (2) A THF (10 ml) solution of $Bu_4NF•3H_2O$ (1.19 g, 3.76 mmol) was added dropwise to a solution of $(Bu_3Sn)_2S$ (1.05 g, 1.71 mmol), the dichloroacetate (**1c**) (670 mg, 1.88 mmol), and cyclopentadiene (1.41 ml) in THF (60 ml) over a period of 2 h at room temperature under argon. After stirring for 3 h, the reaction mixture was worked up with water (20 ml) and concentrated. The aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Extraction with hexane and evaporation followed by open (hexane : Et_2O = 5:1) and flash column chromatographies (hexane : Et_2O = 15:1) gave the Diels-Alder adducts. Reactions with **1a**, **1b**, **1d-h** were also performed similarly. Yields and de's of the cycloadducts are given in Table I.

3a + 4a: Yield 54%. Oil: For a mixture of **3a** and **4a** (35:65): Ir ν_{max} (neat) cm^{-1}: 1730. ^{1}H-Nmr δ: 0.71 (1H, d, *J* = 6.8 Hz), 0.76 (2H, d, *J* = 6.8 Hz), 0.8-2.0 (17H, m), 3.75 and 4.08 (each 1H, br s), 4.41 (0.65H, d, *J* = 4.2 Hz), 4.42 (0.35H, d, *J* = 4.2 Hz), 4.63 (0.35H, ddd, *J* = 4.3, 10.9, 10.9 Hz), 4.65 (0.65H, ddd, *J* = 4.2, 10.9, 10.9 Hz), 5.86 (1H, dd, *J* = 2.9, 5.4 Hz), 6.47 (0.35H, dd, *J* = 2.9, 5.4 Hz), 6.49 (0.65H, dd, *J* = 2.9, 5.4 Hz). Ms *m/z*: 294 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{17}H_{26}O_2S$ (M^+), 294.1669 (294.1653).

5a + 6a: Yield 24%. Oil: For a mixture of **5a** and **6a** (47:53): Ir ν_{max} (neat) cm^{-1}: 1729. ^{1}H-Nmr δ: 0.77 (1.6H, d, *J* = 7.1 Hz), 0.78 (1.4H, d, *J* = 6.8 Hz), 0.8-2.1 (17H, m), 3.27 (0.53H, s), 3.29 (0.47H, s), 3.52 and 4.10 (each 1H, br s), 4.72 (0.53H, ddd, *J* = 4.3, 10.9, 10.9 Hz), 4.74 (0.47H, ddd, *J* = 4.2, 11.0, 11.0 Hz), 5.94 (0.47H, dd, *J* = 3.1, 5.5 Hz), 5.95 (0.53H, dd, *J* = 2.8, 5.7 Hz), 6.37 (0.53H, dd, *J* = 2.4, 5.1 Hz), 6.38 (0.47H, dd, *J* = 2.6, 5.3 Hz). Ms *m/z*: 294 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{17}H_{26}O_2S$ (M^+), 294.1658 (294.1653).

3b: Yield 33%. Oil. $[\alpha]_D^{24}$ +82.3° (*c* 0.49, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1728. ^{1}H-Nmr δ: 0.8-2.2 (10H, m), 0.87 (3H, d, *J* = 6.6 Hz), 1.20 and 1.30 (each 3H, s), 3.16 and 3.98 (each 1H, br s), 3.63 (1H, d, *J* = 3.9 Hz), 4.77 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.59 (1H, dd, *J* = 3.1, 5.5 Hz), 6.39 (1H, dd, *J* = 2.9, 5.4 Hz), 7.1-7.4 (5H, m). Ms *m/z*: 370 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{23}H_{30}O_2S$ (M^+), 370.1967 (370.1965).

4b + 5b + 6b: Yield 40%.

4b: Oil. Ir ν_{max} (neat) cm^{-1}: 1728. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.83 (3H, d, *J* = 6.6 Hz), 1.21 and 1.33 (each 3H, s), 3.50 (2H, br s), 3.94 (1H, br s), 4.78 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.94 (1H, br d, *J* = 4.2 Hz),

6.38 (1H, dd, J = 2.9, 5.4 Hz), 7.1-7.3 (5H, m). Ms m/z: 370 (M^+). Hrms [Found (Calcd)] m/z: $C_{23}H_{30}O_2S$ (M^+), 370.1984 (370.1965).

5b: Oil. Ir ν_{max} (neat) cm^{-1}: 1727. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, J = 6.4 Hz), 1.24 and 1.35 (each 3H, s), 2.78 (1H, s), 3.04 and 4.04 (each 1H, br s), 4.86 (1H, ddd, J = 4.4, 10.7, 10.7 Hz), 5.79 (1H, dd, J = 3.4, 5.1 Hz), 6.32 (1H, dd, J = 2.7, 5.4 Hz), 7.1-7.4 (5H, m). Ms m/z: 370 (M^+). Hrms [Found (Calcd)] m/z: $C_{23}H_{30}O_2S$ (M^+), 370.1953 (370.1965).

6b: Oil. Ir ν_{max} (neat) cm^{-1}: 1726. ^{1}H-Nmr δ: 0.8-2.2 (10H, m), 0.87 (3H, d, J = 6.4 Hz), 1.21 and 1.34 (each 3H, s), 2.12 (1H, s), 3.27 and 3.97 (each 1H, br s), 4.89 (1H, ddd, J = 4.4, 10.7, 10.7 Hz), 5.82 (1H, dd, J = 3.4, 5.1 Hz), 6.29 (1H, dd, J = 2.8, 5.2 Hz), 7.1-7.4 (5H, m). Ms m/z: 370 (M^+). Hrms [Found (Calcd)] m/z: $C_{23}H_{30}O_2S$ (M^+), 370.1970 (370.1965).

3c: Yield 31%. Oil. $[\alpha]_D^{25}$ +79.3° (c 1.20, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1726. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.86 (3H, d, J = 6.4 Hz), 1.19, 1.28 and 2.30 (each 3H, s), 3.17 and 3.98 (each 1H, br s), 3.68 (1H, d, J = 4.2 Hz), 4.75 (1H, ddd, J = 4.4, 10.7, 10.7 Hz), 5.60 and 6.39 (each 1H, dd, J = 2.9, 5.4 Hz), 7.12 and 7.20 (each 2H, d, J = 8.3 Hz). Ms m/z: 384 (M^+). Hrms [Found (Calcd)] m/z: $C_{24}H_{32}O_2S$ (M^+), 384.2098 (384.2121).

4c + 5c + 6c: Yield 54%.

4c: Oil. Ir ν_{max} (neat) cm^{-1}: 1732. ^{1}H-Nmr δ: 0.8-2.2 (10H, m), 0.88 (3H, d, J = 6.6 Hz), 1.21, 1.32 and 2.30 (each 3H, s), 3.51 and 3.96 (each 1H, br s), 3.54 (1H, d, J = 3.7 Hz), 4.80 (1H, ddd, J = 4.6, 10.7, 10.7 Hz), 5.94 (1H, dd, J = 2.9, 5.4 Hz), 6.39 (1H, dd, J = 2.7, 5.4 Hz), 7.11 and 7.19 (each 2H, d, J = 8.1 Hz). Ms m/z: 384 (M^+). Hrms [Found (Calcd)] m/z: $C_{24}H_{32}O_2S$ (M^+), 384.2117 (384.2121).

5c: Oil. Ir ν_{max} (neat) cm^{-1}: 1725. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, J = 6.6 Hz), 1.23, 1.33 and 2.29 (each 3H, s), 2.82 (1H, s), 3.04 and 4.04 (each 1H, br s), 4.85 (1H, ddd, J = 4.4, 10.6, 10.6 Hz), 5.80 (1H, dd, J = 3.4, 5.4 Hz), 6.32 (1H, dd, J = 2.9, 5.4 Hz), 7.08 (2H, d, J = 8.1 Hz), 7.18 (2H, d, J = 8.3 Hz). Ms m/z: 384 (M^+). Hrms [Found (Calcd)] m/z: $C_{24}H_{32}O_2S$ (M^+), 384.2102 (384.2121).

6c: Oil. Ir ν_{max} (neat) cm^{-1}: 1727. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, J = 6.6 Hz), 1.20, 1.32 and 2.28 (each 3H, s), 2.13 (1H, s), 3.27 and 3.98 (each 1H, br s), 4.88 (1H, ddd, J = 4.6, 10.7, 10.7 Hz), 5.81 (1H, dd, J = 3.2, 5.4 Hz), 6.30 (1H, dd, J = 2.7, 5.4 Hz), 7.08 (2H, d, J = 8.1 Hz), 7.19 (2H, d, J = 8.3Hz). Ms m/z: 384 (M^+). Hrms [Found (Calcd)] m/z: $C_{24}H_{32}O_2S$ (M^+), 384.2104 (384.2121).

3d: Yield 34%. Oil. $[\alpha]_D^{26}$ +64.2° (*c* 1.07, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1729. ^{1}H-Nmr δ: 0.8-2.2 (10H, m), 0.87 (3H, d, *J* = 6.6 Hz), 1.17 and 1.28 (each 3H, s), 1.30 (9H, s), 3.05 and 3.96 (each 1H, br s), 3.50 (1H, d, *J* = 3.9 Hz), 4.78 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.55 (1H, dd, *J* = 3.1, 5.3 Hz), 6.37 (1H, dd, *J* = 2.9, 5.4 Hz), 7.22 (2H, d, *J* = 8.5 Hz), 7.33 (2H, d, *J* = 8.6 Hz). Ms *m/z*: 426 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{38}O_2S$ (M^+), 426.2558 (426.2591).

4d: Yield 10%. Needles. mp 122-125 °C (hexane). $[\alpha]_D^{26}$ -51.7° (*c* 0.80, $CHCl_3$). Ir ν_{max} (KBr) cm^{-1}: 1718. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.84 (3H, d, *J* = 6.4 Hz), 1.19 and 1.32 (each 3H, s), 1.30 (9H, s), 3.36 (1H, d, *J* = 3.7 Hz), 3.44 and 3.92 (each 1H, br s), 4.78 (1H, ddd, *J* = 4.4, 10.8, 10.8 Hz), 5.96 (1H, dd, *J* = 3.1, 5.2 Hz), 6.37 (1H, dd, *J* = 2.9, 5.4 Hz), 7.23 (2H, d, *J* = 8.5 Hz), 7.31 (2H, d, *J* = 8.6 Hz). Ms *m/z*: 426 (M^+). *Anal.* Calcd for $C_{27}H_{38}O_2S$: C,76.01; H, 8.98. Found: C, 75.83; H, 9.06.

5d: Yield 9%. Oil. $[\alpha]_D^{26}$ +14.1° (*c* 1.65, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1725. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.88 (3H, d, *J* = 6.4 Hz), 1.21 and 1.32 (each 3H, s), 1.26 (9H, s), 2.55 (1H, s), 3.09 and 4.06 (each 1H, br s), 4.86 (1H, ddd, *J* = 4.2, 10.7, 10.7 Hz), 5.76 (1H, dd, *J* = 3.2, 5.4 Hz), 6.29 (1H, dd, *J* = 2.9, 5.4 Hz), 7.19 and 7.27 (each 2H, d, *J* = 8.5 Hz). Ms *m/z*: 426 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{38}O_2S$ (M^+), 426.2588 (426.2591).

6d: Yield 8%. Oil. $[\alpha]_D^{26}$ +45.1° (*c* 1.30, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1725. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, *J* = 6.4 Hz), 1.20 and 1.31 (each 3H, s), 1.28 (9H, s), 2.30 (1H, s), 3.35 and 3.96 (each 1H, br s), 4.87 (1H, ddd, *J* = 4.4, 10.6, 10.6 Hz), 5.84 (1H, dd, *J* = 3.3, 5.3 Hz), 6.29 (1H, dd, *J* = 2.8, 5.5 Hz), 7.20 and 7.27 (each 2H, d, *J* = 8.6 Hz). Ms *m/z*: 426 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{38}O_2S$ (M^+), 426.2579 (426.2591).

3e: Yield 23%. Columns. mp 134-135 °C ($CHCl_3$-hexane). $[\alpha]_D^{25}$ +41.5° (*c* 0.72, $CHCl_3$). Ir ν_{max} (KBr) cm^{-1}: 1723. ^{1}H-Nmr δ: 0.8-2.3 (10H, m), 0.87 (3H, d, *J* = 6.3 Hz), 1.30 and 1.42 (each 3H, s), 2.74 and 3.82 (each 1H, br s), 3.32 (1H, d, *J* = 3.9 Hz), 4.80 (1H, ddd, *J* = 4.2, 10.7, 10.7 Hz), 5.49 and 6.30 (each 1H, dd, *J* = 2.9, 5.4 Hz), 7.3-7.9 (7H, m). Ms *m/z*: 421 (M^++1). *Anal.* Calcd for $C_{27}H_{32}O_2S$: C,77.10; H, 7.67. Found: C, 76.70; H, 7.60.

4e: Yield 18%. Oil. Ir ν_{max} (neat) cm^{-1}: 1727. ^{1}H-Nmr δ: 0.8-2.3 (10H, m), 0.84 (3H, d, *J* = 6.6 Hz), 1.30 and 1.45 (each 3H, s), 2.81 (1H, d, *J* = 3.7 Hz), 3.00 and 3.80 (each 1H, br s), 4.82 (1H, ddd, *J* = 4.6, 10.6, 10.6 Hz), 5.87 (1H, dd, *J* = 3.2, 5.4 Hz), 6.30 (1H, dd, *J* = 2.9, 5.4 Hz), 7.3-7.9 (7H, m). Ms *m/z*: 420 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{32}O_2S$ (M^+), 420.2161 (420.2121).

5e: Yield 18%. Oil. Ir ν_{max} (neat) cm^{-1}: 1728. ^{1}H-Nmr δ: 0.8-2.3 (10H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.33 and 1.46 (each 3H, s), 2.52 and 3.92 (each 1H, br s), 2.65 (1H, s), 4.94 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.17 (1H, dd, *J* = 3.4, 5.4 Hz), 6.14 (1H, dd, *J* = 2.8, 5.5 Hz), 7.3-7.9 (7H, m). Ms *m/z*: 420 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{32}O_2S$ (M^+), 420.2167 (420.2121).

6e: Yield 10%. Oil. Ir ν_{max} (neat) cm^{-1}: 1726. ^{1}H-Nmr δ: 0.8-2.3 (11H, m), 0.89 (3H, d, *J* = 6.6Hz), 1.26 and 1.47 (each 3H, s), 2.68 and 3.80 (each 1H, br s), 4.74 (1H, dd, *J* = 3.3, 5.3 Hz), 4.96 (1H, ddd, *J* = 4.6, 10.8, 10.8 Hz), 6.00 (1H, dd, *J* = 2.7, 5.4 Hz), 7.3-7.9 (7H, m). Ms *m/z*: 420 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{32}O_2S$ (M^+), 420.2075 (420.2121).

3f: Yield 29%. Oil. $[\alpha]_D^{25}$ +65.7° (*c* 1.24, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1723. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, *J* = 6.6 Hz), 1.19 and 1.29 (each 3H, s), 3.28 and 4.00 (each 1H, br s), 3.74 (1H, d, *J* = 4.2 Hz), 3.78 (3H, s), 4.76 (1H, ddd, *J* = 4.4, 10.7, 10.7 Hz), 5.63 and 6.41 (each 1H, dd, *J* = 2.9, 5.4 Hz), 6.85 and 7.21 (each 2H, d, *J* = 8.8 Hz). Ms *m/z*: 400 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{24}H_{32}O_3S$ (M^+), 400.2122 (400.2072).

4f + **5f**: Yield 30%.

4f: Oil. Ir ν_{max} (neat) cm^{-1}: 1726. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.83 (3H, d, *J* = 6.6 Hz), 1.20 and 1.31 (each 3H, s), 3.55 and 3.97 (each 1H, br s), 3.68 (1H, d, *J* = 3.7 Hz), 3.78 (3H, s), 4.77 (1H, ddd, *J* = 4.5, 10.7, 10.7 Hz), 5.94 (1H, dd, *J* = 3.1, 5.2 Hz), 6.40 (1H, dd, *J* = 2.9, 5.4 Hz), 6.85 and 7.21 (each 2H, d, *J* = 8.8 Hz). Ms *m/z*: 400 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{24}H_{32}O_3S$ (M^+), 400.2104 (400.2072).

5f: Oil. Ir ν_{max} (neat) cm^{-1}: 1724. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, *J* = 6.4 Hz), 1.23 and 1.33 (each 3H, s), 2.85 (1H, s), 3.10 and 4.06 (each 1H, br s), 3.77 (3H, s), 4.85 (1H, ddd, *J* = 4.3, 10.6, 10.6 Hz), 5.82 and 6.32 (each 1H, dd, *J* = 3, 5 Hz), 6.82 and 7.20 (each 2H, d, *J* = 8.8 Hz). Ms *m/z*: 400 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{24}H_{32}O_3S$ (M^+), 400.2085 (400.2072).

6f: Yield 6%. Oil. Ir ν_{max} (neat) cm^{-1}: 1718. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.88 (3H, d, *J* = 6.6 Hz), 1.20 and 1.32 (each 3H, s), 2.29 (1H, s), 3.29 and 3.99 (each 1H, br s), 3.77 (3H, s), 4.88 (1H, ddd, *J* = 4.4, 10.5, 10.5Hz), 5.83 (1H, dd, *J* = 3.2, 5.4 Hz), 6.30 (1H, dd, *J* = 2.8, 5.4 Hz), 6.82 and 7.21 (each 2H, d, *J* = 8.8 Hz). Ms *m/z*: 400 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{24}H_{32}O_3S$ (M^+), 400.2107 (400.2072).

3g: Yield 42%. Oil. $[\alpha]_D^{25}$ +75.8° (*c* 1.49, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1734. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, *J* = 6.6 Hz), 1.19 and 1.29 (each 3H, s), 3.27 and 4.01 (each 1H, br s), 3.73 (1H, d, *J* = 3.9 Hz),

4.75 (1H, ddd, J = 4.4, 10.6, 10.6 Hz), 5.63 and 6.41 (each 1H, dd, J = 2.9, 5.4 Hz), 6.99 (2H, dd, J = 8.7, 8.7 Hz), 7.2-7.35 (2H, m). Ms *m/z*: 388 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{23}H_{29}O_2FS$ (M^+), 388.1868 (388.1871).

4g + 5g + 6g: Yield 32%.

4g: Oil. Ir ν_{max} (neat) cm^{-1}: 1728. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.84 (3H, d, J = 6.6 Hz), 1.20 and 1.32 (each 3H, s), 3.54 and 3.97 (each 1H, br s), 3.64 (1H, d, J = 3.7 Hz), 4.77 (11H, ddd, J = 4.5, 10.6, 10.6 Hz), 5.93 and 6.40 (each 1H, dd, J = 2.9, 5.1 Hz), 6.99 (2H, dd, J = 8.8, 8.8 Hz), 7.2-7.35 (2H, m). Ms *m/z*: 388 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{23}H_{29}O_2FS$ (M^+), 388.1855 (388.1871).

5g: Oil. Ir ν_{max} (neat) cm^{-1}: 1727. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.88 (3H, d, J = 6.4 Hz), 1.23 and 1.34 (each 3H, s), 2.85 (1H, s), 3.10 and 4.07 (each 1H, br s), 4.83 (1H, ddd, J = 4.3, 10.7, 10.7Hz), 5.84 (1H, dd, J = 3.4, 5.4 Hz), 6.34 (1H, dd, J = 2.7, 5.4 Hz), 6.96 (2H, dd, J = 8.7, 8.7 Hz), 7.2-7.35 (2H, m). Ms *m/z*: 388 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{23}H_{29}O_2FS$ (M^+), 388.1881(388.1871).

6g: Oil. Ir ν_{max} (neat) cm^{-1}: 1727. ^{1}H-Nmr δ: 0.8-2.1 (10H, m), 0.87 (3H, d, J = 6.6 Hz), 1.20 and 1.33 (each 3H, s), 2.20 (1H, s), 3.26 and 4.00 (each 1H, br s), 4.87 (1H, ddd, J = 4.5, 10.7, 10.7Hz), 5.85 (1H, dd, J = 3.2, 5.4 Hz), 6.30 (1H, dd, J = 2.7, 5.4 Hz), 6.96 (2H, dd, J = 8.7, 8.7 Hz), 7.2-7.35 (2H, m). Ms *m/z*: 388 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{23}H_{29}O_2FS$ (M^+), 388.1891 (388.1871).

(1*R*,1'*R*,2'*S*,5'*R*)-(+)-2'-(1'-Methyl-1'-*p*-tolylethyl)-5'-methylcyclohexyl 5-*exo*,6-*exo*-(Carbonyldioxy)-2-thiabicyclo[2.2.1]heptane-3-*exo*-carboxylate (12) Procedure A. A mixture of the major *endo* cycloadduct (**3c**) (100 mg, 0.26 mmol) and a 0.1 M solution of OsO_4 in ^{t}BuOH (0.03 ml, 2.6 μmol) in DMF-water (9:1, 5 ml) was stirred at room temperature for 2 h. Saturated aqueous $Na_2S_2O_3$ (3 drops) was added to the mixture and the solvent was evaporated. AcOEt (10 ml) and water (2 ml) were added to the residue. The organic layer was separated, dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography (hexane : AcOEt = 5:1) to give (1*R*,1'*R*,2'*S*,5'*R*)-(+)-2'-(1'-methyl-1'-*p*-tolylethyl)-5'-methylcyclohexyl 5-*exo*,6-*exo*-dihydroxy-2-thiabicyclo[2.2.1]heptane-3-*endo*-carboxylate (**10**) as a pale yellow oil (74 mg, 68%). $[\alpha]_D^{25}$ +21.4° (*c* 1.08, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 3421, 1725. ^{1}H-Nmr δ: 0.8-2.4 (11H, m), 0.88 (3H, d, J = 6.4 Hz), 1.18, 1.27 and 2.30 (each 3H, s), 3.01 (1H, br s, disappeared with D_2O), 3.05 (1H, d, J = 3.7 Hz), 3.09 (1H, s), 3.32 (1H, br s, disappeared with D_2O), 3.82 (1H, d, J = 4.9 Hz), 4.11 (1H, d, J = 5.6 Hz), 4.81 (1H, ddd, J = 4.4, 10.7, 10.7 Hz), 7.09 and 7.16 (each 2H, d, J = 8.3 Hz). Ms *m/z*: 418 (M^+), 400 (M^+-H_2O). Hrms [Found (Calcd)] *m/z*: $C_{24}H_{34}O_4S$ (M^+), 418.2171 (418.2176).

A suspension of ^{t}BuOK (32 mg, 0.29 mmol) in THF (0.5 ml) was added to a solution of the diol **(10)** (30 mg, 0.072 mmol) in THF (2.5 ml) within 5 min at 0 °C. After being stirred under nitrogen for 0.5 h, the excess reagent was decomposed by 1 N aqueous HCl (6 drops). Water (3 ml) was added to the mixture and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash column chromatography (hexane : AcOEt = 2:1) to give **11** as a pale yellow oil (24 mg, 80%). The *exo* ester **(11)** was subjected to cyclic carbonate formation. A mixture of **11** (24 mg, 0.057 mmol), pyridine (14 µl, 0.17 mmol), and diphosgene (13 µl, 0.12 mmol) in dry CH_2Cl_2 (3 ml) was stirred under argon at 0 °C for 10 min. The mixture was diluted with CH_2Cl_2 (10 ml), washed with water, saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and the solvent was evaporated. The residue was passed through a short column ($CHCl_3$) to give the cyclic carbonate **(12)** as needles (24 mg, 94%). mp 236-238 °C (^{i}PrOH-AcOEt). $[\alpha]_D^{25}$ +2.5° (*c* 0.47, $CHCl_3$). Ir ν_{max} (KBr) cm^{-1}: 1791, 1724. ^{1}H-Nmr δ: 0.8-2.2 (11H, m), 0.89 (3H, d, *J* = 6.6 Hz), 1.16, 1.28 and 2.33 (each 3H, s), 2.85 and 3.38 (each 1H, br s), 4.27 (1H, d, *J* = 6.1 Hz), 4.81 (1H, ddd, *J* = 4.6, 10.7, 10.7 Hz), 4.83 (1H, d, *J* = 6.4 Hz), 7.10 (2H, d, *J* = 8.1 Hz), 7.18 (1H, d, *J* = 8.3 Hz). Ms *m/z*: 444 (M^+). *Anal.* Calcd for $C_{25}H_{32}O_5S$: C, 67.54; H, 7.26. Found: C, 67.38; H, 7.21.

Procedure B. A mixture of the cycloadducts (**4c** : **5c** : **6c** = 39.7 : 40.4 : 19.9; 280 mg, 0.73 mmol) was converted to a mixture of the diols (235 mg, 77%) with OsO_4 as described above. The resulting mixture of diols (185 mg, 0.44 mmol) was treated with triphosgene (198 mg, 0.67 mmol) and pyridine (70 ml. 0.67 mmol) as described above. Carbonate **(12)** (32 mg, 16% yield from the mixture of the diols) was separated from the crude reaction mixture by plc ($CHCl_3$). Carbonates formed from **4c** (59 mg) and **5c** (61 mg) were isolated in 30% and 31% yield, respectively. Compound **(12)** was identical (^{1}H nmr, tlc) with the sample obtained from **3c**.

(1*R*,1'*R*,2'*S*,5'*R*)-(+)-2'-(1'-Methyl-1'-*p*-tolylethyl)-5'-methylcyclohexyl 5-*exo*,6-*exo*-(Isopropylidenedioxy)-2-thiabicyclo[2.2.1]heptane-3-*endo*-carboxylate (13) A mixture of the diol **(10)** (230 mg, 0.55 mmol), 2,2-dimethoxypropane (0.20 ml, 1.7 mmol) and *p*-toluenesulfonic acid (5 mg) in acetone (10 ml) was refluxed for 2 h and the solution was concentrated to a volume of *ca.* 2 ml. Et_2O (10 ml) and saturated aqueous $NaHCO_3$ (5 ml) were added to the residue and the organic layer was separated. The aqueous layer was extracted with Et_2O. The combined organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash column chromatography (hexane : AcOEt = 10:1) to give the acetonide **(13)** (240 mg, 95%) as a pale yellow oil. $[\alpha]_D^{25}$ +24.5° (*c* 1.41, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1734.

^{1}H-Nmr δ: 0.8-2.3 (10H, m), 0.88 (3H, d, *J* = 6.3 Hz), 1.17, 1.23, 1.27, 1.40 and 2.30 (each 3H, s), 2.35 and 3.17 (each 1H, br s), 2.96 (1H, d, *J* = 4.2 Hz), 4.02 (1H, d, *J* = 4.4 Hz), 4.42 (1H, d, *J* = 5.1 Hz), 4.82 (1H, ddd, *J* = 4.5, 10.7, 10.7 Hz), 7.10 and 7.15 (each 2H, d, *J* = 8.3 Hz). Ms *m/z*: 458 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{27}H_{38}O_4S$ (M^+), 458.2499 (458.2491).

(1*R*,4*S*,1'*R*,2'*S*,5'*R*)-(+)-2α,3α-(Isopropylidenedioxy)-1β-methylthio-4β-[2'-(1'-methyl-1'-*p*-tolylethyl)-5'-methylcyclohexyloxycarbonylmethyl]cyclopentane (14) Me_3OBF_4 (97%, 133 mg, 0.87 mmol) was added to a solution of the acetonide (**13**) (200 mg, 0.44 mmol) in DME (8 ml) at 0 °C and the mixture was stirred at room temperature for 2 h. After the solvent was evaporated, the residue was purified by column chromatography ($CHCl_3$: MeOH = 9:1) to give the methylsulfonium tetrafluoroborate (165 mg, 67%) as a pale yellow oil. Zn (84 mg, 1.3 mmol) and AcOH (0.08 ml, 1.3 mmol) were added to a solution of the oil (150 mg, 0.27 mmol) in dry CH_2Cl_2 (10 ml) at 0 °C and the mixture was refluxed for 12 h. The metal powder was filtered off and the filtrate was diluted with CH_2Cl_2 (10 ml). The organic layer was washed with brine and the solvent was evaporated. The residue was purified by plc (hexane : AcOEt = 5:1) to give the methyl sulfide (**14**) (52 mg, 41%) as a pale yellow oil. $[\alpha]_D^{25}$ +18.4° (*c* 2.03, $CHCl_3$). Ir ν_{max} (neat) cm^{-1}: 1726. ^{1}H-Nmr δ: 0.8-2.4 (13H, m), 0.86 (3H, d, *J* = 6.6 Hz), 1.19, 1.47, 2.16 and 2.30 (each 3H, s), 1.28 (6H, s), 3.01 (1H, ddd, *J* = 3.7, 7.5, 7.5 Hz), 4.23 and 4.43 (each 1H, dd, *J* = 3.9, 6.4 Hz), 4.80 (1H, ddd, *J* = 4.3, 10.7, 10.7 Hz), 7.08 and 7.16 (2H, d, *J* = 8.3 Hz). Ms *m/z*: 474 (M^+). Hrms [Found (Calcd)] *m/z*: $C_{28}H_{42}O_4S$ (M^+), 474.2806 (474.2804).

X-Ray Structure Determination of Compound (12) $C_{25}H_{32}O_5S$, M, 444.58, orthorhombic, space group $P2_12_12_1$, a = 11.925 (8) Å, b = 30.85 (2) Å, c = 6.336 (4) Å, V = 2331 (2) $Å^3$, Z = 4, D_c = 1.267 g cm^{-3}, μ (Cu Kα) = 14.61 cm^{-1}, Cu Kα (λ = 1.54178 Å). Single crystals (prismatic) were prepared by recrystallization from ^{i}PrOH-Et_2O. Intensity data were collected on a Rigaku AFC-5R diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares method to R = 0.068 for 518 reflections with $I > 3.00\sigma(I)$. All calculations were performed using the TEXAN crystallographic software package of Molecular Structure Corporation.[10]

ACKNOWLEDGEMENT

This work was supported in part by a grant from Hayashi Memorial Foundation for Female Natural Scientists (to T.T.).

REFERENCES AND NOTES

1. D. L. Boger and S. M. Weinreb, "Hetero Diels-Alder Methodology in Organic Synthesis," Academic Press, Inc., San Diego, 1985, p. 120.
2. D. Adam, A. A. Freer, N. W. Issacs, G. W. Kirby, A. Littlejohn, and M. S. Rahman, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1261.
3. Vedejs and his co-workers have reported the diastereoselective Diels-Alder reaction of racemic α-alkoxythioaldehydes: E. Vedejs, J. S. Stults, and R. G. Wilde, *J. Am. Chem. Soc.*, 1988, **110**, 5452.
4. M. Segi, M. Kato, and T. Nakajima, *Tetrahedron Lett.*, 1991, **32**, 7427.
5. W. Oppolzer, C. Robbiani, and K. Bättig, *Helv. Chim. Acta*, 1980, **63**, 2015.
6. (a) O. Ort, *Org. Synth.*, 1987, **65**, 203; (b) Y. Horinouchi, S. Matsuzawa, E. Nakamura, and I. Kuwajima, *Tetrahedron Lett.*, 1986, **27**, 4025; (c) J. K. Whitesell, *Chem. Rev.*, 1992, **92**, 953, and references cited therein.
7. J. B. Cohen, *J. Chem. Soc.*, 1911, **99**, 1058.
8. M. F. Jones and S. M. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2927.
9. W. Oppolzer, C. Chapuis, and G. Bernardinelli, *Tetrahedron Lett.*, 1984, **25**, 5885.
10. TEXAN-TEXRAY Structure Analysis Package, Molecular Structure Corporation, 1985.

Received, 3rd February, 1993