Studies on Chiral Organosulfur Compounds. VI.[1] The Use of a Chiral Diene Bearing an Optically Active Sulfinylmethyl Group in the Lewis Acid-Catalyzed Intramolecular Asymmetric Hetero Diels–Alder Reaction

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An asymmetric Diels–Alder reaction with a diene bearing a chiral sulfinyl group is described. The Lewis acid-catalyzed intramolecular asymmetric hetero Diels–Alder reaction of a chiral α′-sulfinyl-α,β-unsaturated ketone derived from 3-methylcitronellal produced optically active 4a,5,6,7,8,8a-hexahydro-1*H*-2-benzopyran derivatives. On the basis of the stereochemical results obtained, a plausible mechanism for the asymmetric induction is presented.

Key words asymmetric hetero Diels–Alder reaction; chiral sulfinyl; Lewis acid; benzopyran

The Diels–Alder reaction[2] constitutes one of the most widely used synthetic methods for the preparation of six-membered cyclic systems *via* pericyclic reactions proceeding in a highly regio-, diastereo-, and enantioselective manner.[3] Asymmetric Diels–Alder reactions have been widely used for the stereoselective construction of optically active six-membered compounds of interest in natural product and medicinal chemistry.[4] Many novel methodologies have been developed for asymmetric Diels–Alder reactions using various kinds of chiral auxiliaries,[5] among which chiral organosulfur groups have recently received much attention.[6] However, the known asymmetric Diels–Alder reactions with organosulfur compounds have been limited to intermolecular ones using chiral vinylic sulfoxides[7,8] and sulfoximines[8] as chiral dienophiles. We have recently reported some intramolecular asymmetric hetero Diels–Alder reactions[9] of a chiral α-sulfinyl-α,β-unsaturated ketone, which is the first example of the use of a chiral sulfinyl functionality as a chiral diene.[10] Subsequently, other examples of asymmetric Diels–Alder reactions using 1,3-dienes bearing chiral sulfinyl groups were reported.[11] We report here another example of the intramolecular asymmetric Diels–Alder reaction with a chiral diene bearing an optically active sulfinylmethyl function.[12]

Previously we reported the first successful example of Lewis acid-catalyzed intramolecular asymmetric ene reactions of chiral α-cyano and methoxycarbonylvinylic sulfoxides **1a**, **b**, in which vinylic sulfinyl groups served as chiral efficient enophiles.[13] Our further studies on this line revealed that the α-acetyl vinylic sulfoxide **3** underwent the intramolecular hetero Diels–Alder and ene reactions, upon treatment with Lewis acids, to give the cyclic enol ether **4** along with the ene reaction product **5**.[10]

In the present work, a model compound for the intramolecular hetero Diels–Alder reaction, bearing a chiral α′-sulfinyl-α,β-unsaturated ketone moiety as a chiral diene, was prepared starting from 3-methylcitronellal (**6**),[14] which was derived from citral. The Horner–Emmons condensation of ethyl diethoxyphosphonylacetate with **6** at 0 °C for 1 h using sodium hydride as a base gave ethyl 5,5,9-trimethyl-2(*E*)-8-decadienoate (**7**) in 87% yield. The α-sulfinyl carbanion, prepared by treating optically pure (*R*)-methyl *p*-tolyl sulfoxide (**8**)[15] with lithium diisopropylamide, was condensed with the ester group of (*E*)-**7** in tetrahydrofuran (THF) at 0 °C to give

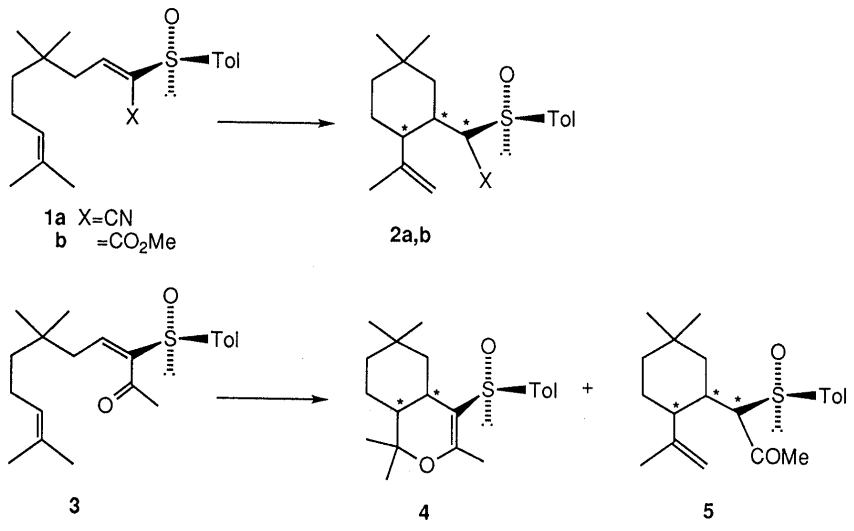

Chart 1

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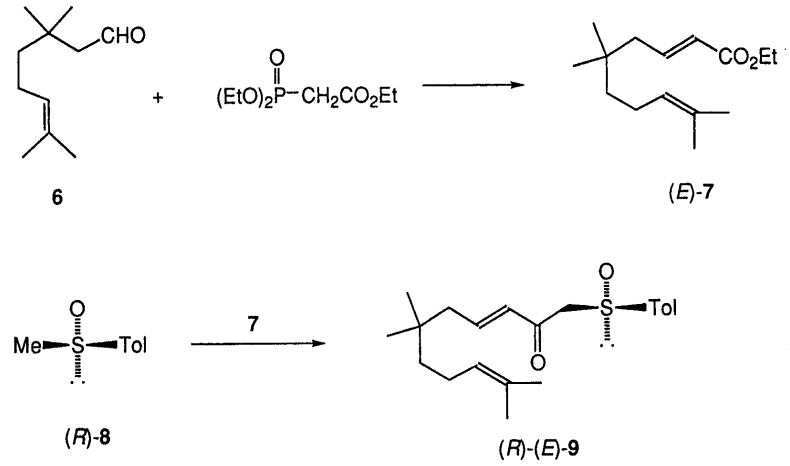


Chart 2

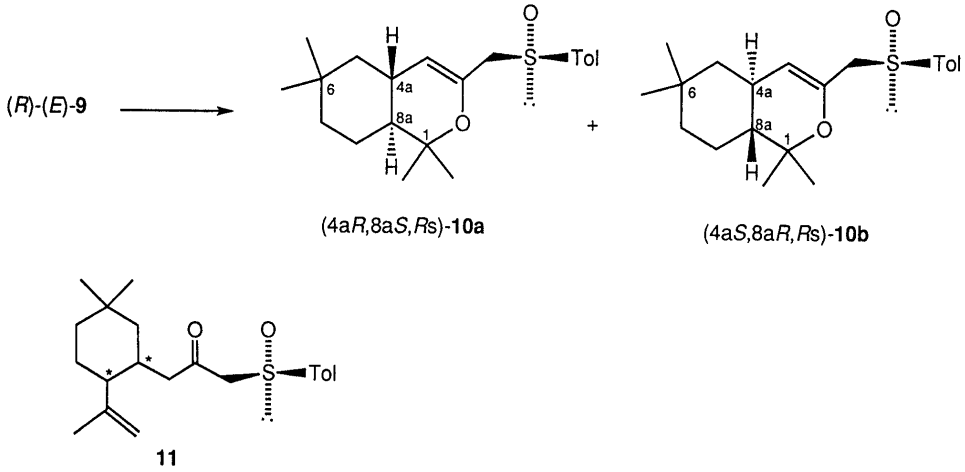


Chart 3

Table 1. Studies on the Lewis Acid-Catalyzed Intramolecular Asymmetric Hetero Diels–Alder Reactions of (*R*)-**9**

Lewis acid	Solvent	Reaction conditions[a]		Yield of **10** (%)	de (%) of **10**[b]
		Temp. (°C)	Time (h)		
$ZnCl_2$	CH_2Cl_2	0	2	94	40.0
$ZnCl_2$	Toluene	0	2	63	48.6
$ZnBr_2$	CH_2Cl_2	0	3	47	40.2
$ZnBr_2$	Toluene	0	3	75	38.3
Zn I_2	CH_2Cl_2	0	2	82	44.2
Zn I_2	Toluene	0	2	82	38.6
Et_2AlCl	CH_2Cl_2	−78	1	84	42.5
Et_2AlCl	Toluene	−78	1	100	28.5
Et_2AlCl	Hexane	r.t.	18	48	34.7
$EtAlCl_2$	CH_2Cl_2	−78	2	72	38.5
$EtAlCl_2$	Toluene	−78	1	82	35.8
$AlCl_3$	CH_2Cl_2	−78	2	77	29.0
AlC_3	Toluene	−78	2	54	38.0
Me_3Al	CH_2Cl_2	−78	1	61	18.5[c]
$FeCl_3$	CH_2Cl_2	0	2	42	44.8
$FeCl_3$	Toluene	0	1	68	36.6
$TiCl_4$	CH_2Cl_2	−78	1	85	31.7
$SnCl_4$	CH_2Cl_2	−78	1	82	45.4
$SnCl_4$	Toluene	−78	1	81	60.6
$BF_3 \cdot OEt_2$	CH_2Cl_2	0	2	74	15.2[c]
$BF_3 \cdot OEt_2$	Toluene	0	2	70	3.0[c]

a) The reactions of (*R*)-**9** were carried out in the presence of a Lewis acid (1.5 eq). *b*) The diastereomeric excess (de) of **10a** over **10b** was determined by HPLC analysis. *c*) Compound (4a*S*,8a*R*,*Rs*)-**10b** was obtained as the main product.

(*R*)-(+)-(*E*)-1-(*p*-toluenesulfinyl)-6,6,10-trimethyl-3,9-undecadien-2-one (**9**) in 81% yield. The chirality of the sulfinyl function in (*R*)-**8** was retained in this condensation.

The Lewis acid-catalyzed reactions of (*R*)-(*E*)-**9** were carried out in dichloromethane, toluene, or hexane at −78—0 °C to give optically active hetero Diels–Alder reaction products, (4a*R*,8a*S*,*R*s)- and (4a*S*,8a*R*,*R*s)-4a,5,6,7,8,8a,-hexahydro-1,1,6,6-tetramethyl-2-*p*-toluenesulfinylmethyl-1*H*-2-benzopyran (**10a**) and (**10b**), with no ene reaction product **11**. The results obtained by using various Lewis acids are summarized in Table 1. The ratios of the diastereomers **10a** to **10b** obtained under various reaction conditions were determined by high-performance liquid chromatographic (HPLC) analysis and are listed in Table 1.

Upon treatment with zinc(II) halide (chloride, bromide, or iodide) in dichloromethane or toluene at 0 °C for 2—3 h, (*R*)-**9** underwent exclusively an intramolecular hetero Diels–Alder reaction to give **10a, b** with a moderate diastereomeric excess (de) of **10a** over **10b** (38—48%). A slightly increasing de of the product **10a, b** was observed in the reaction of (*R*)-**9** catalyzed with $ZnCl_2$ in toluene at 0 °C. However, rather a high yield (94 or 82—84%) of **10a, b** was obtained by catalysis with $ZnCl_2$ in dichloromethane or with ZnI_2 in dichloromethane or toluene, respectively.

The use of aluminum compounds (Et_2AlCl, $EtAlCl_2$, $AlCl_3$, Me_3Al) as Lewis acids in dichloromethane or toluene at −78 °C led to smooth conversion of (*R*)-**9** into hetero Diels–Alder products **10a, b** with rather lower de in good yield (quantitatively with the use of Et_2AlCl at −78 °C in toluene). However, the opposite distereoselectivity of **10a, b** was observed on the use of trimethylaluminum (18.5% de of **10b** over **10a**).

Further studies on this asymmetric reaction were carried out using other Lewis acids (*e.g.* $FeCl_3$, $TiCl_4$, $SnCl_4$, $BF_3 \cdot OEt_2$). The highest de (60.6%) of the products **10a, b** was obtained with $SnCl_4$ under the reaction conditions of −78 °C in toluene for 1 h. Slight preference for **10b** over **10a** was seen with $BF_3 \cdot OEt_2$ as a catalyst.

No hetero Diels–Alder reaction occurred under thermal reaction conditions (in toluene under reflux for 48 h) without any catalyst.

The stereochemistry of the products (**10a, b**) was confirmed as *trans* by the observation of nuclear Overhauser effects (NOE) between the C_{4a} hydrogen atom and the methyl groups at the C_1 and C_6 positions in the NMR spectral analysis of the sulfide (4a*R*,8a*S*)- and (4a*S*,8a*R*)-**12** obtained by the $TiCl_3$ reduction of the sulfinyl function in (4a*R*,8a*S*,*R*s)-**10a** and (4a*S*,8a*R*,*R*s)-**10b**, respectively.

The absolute configuration of the two newly created asymmetric carbons in the hetero Diels–Alder products **10a, b** was determined by chemical correlation to the chiral sulfinyl compound **15** of known absolute configuration[10] as follows. The reductive desulfinylation of the chiral sulfoxide **10a** with sodium was carried out in isopropanol–THF[16] at room temperature for 2 h to give (4a*R*,8a*S*)-(+)-4a,5,6,7,8,8a-hexahydro-1,1,3,6,6-pentamethyl-1*H*-2-benzopyran (**13**) in 90% yield. The same reaction of the chiral sulfoxide **10b** with sodium gave (4a*S*,8a*R*)-(−)-**13**. The bromination of the cyclic enol ether (4a*R*,8a*S*)- or (4a*S*,8a*R*)-**13** with *N*-bromosuccinimide in THF–H_2O (4:1) at room temperature for 3 h gave an α-bromo cyclic enol ether (4a*S*,8a*S*)- or (4a*R*,8a*R*)-**14**, respectively. After treatment of the vinylic bromide (4a*S*,8a*S*)- or (4a*R*,8a*R*)-**14** with butyllithium at −78 °C in THF, the sulfinylation reaction of the carbanion generated with methyl (*S*)-*p*-toluenesulfinate at −78 °C for 2 h produced the known chiral sulfinyl compounds, (4a*S*,8a*S*,*S*s)-**15a**[10] and (4a*R*,8a*R*,*S*s)-**15b**,[10] respectively. The reduction of the sulfinyl groups in (4a*S*,8a*S*,*S*s)-**15a**

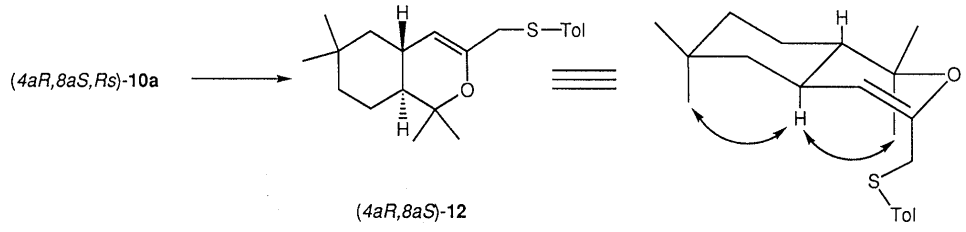


Chart 4

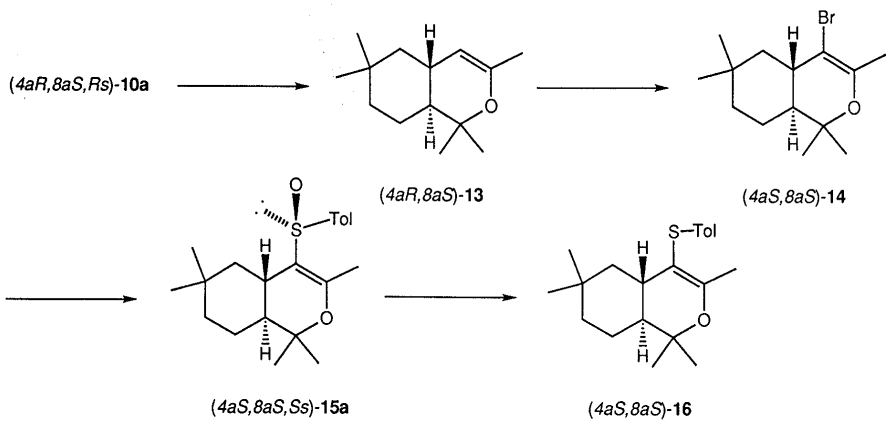
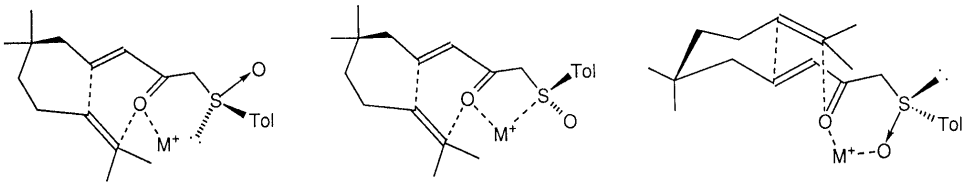


Chart 5



17a 17b 17c

Chart 6

and (4a*R*,8a*R*,*S*s)-**15b** with $TiCl_3$ in THF at room temperature furnished the known chiral sulfenyl compound, (4a*S*,8a*S*)-(−)-**16**[10] and (4a*R*,8a*R*)-(+)-**16**,[10] respectively, in 90% yield in both cases. Thus, the absolute configuration of the two newly created asymmetric carbons in **10a** and **10b** formed by this hetero Diels–Alder reaction was determined as (4a*R*,8a*S*) and (4a*S*,8a*R*), respectively.

The mechanism of the asymmetric induction in this hetero Diels–Alder reaction was rationalized on the basis of the following stereochemical considerations. The intramolecular cycloaddition of the olefin to the α,β-unsaturated ketone in (*R*)-**9** would occur preferentially from the side with the less hindered lone pair of the chiral sulfinyl group in the preferred conformation **17a** generated by dipole–dipole repulsion between the carbonyl group of the ketone and the sulfinyl sulfur–oxygen bond, yielding (4a*R*,8a*S*,*R*s)-**10a** as a main product. The stereochemical results could also be rationalized in terms of cycloaddition from the same side as the oxygen atom of the sulfinyl group in the alternative possible intermediate **17b** formed by the chelation of the carbonyl oxygen and the lone pair of the sulfinyl group to the metal function. On the use of $BF_3 \cdot Et_2O$ or Me_3Al as a catalyst, (4a*S*,8a*R*,*R*s)-**10b** was formed, with slight de, presumably through the predominant intramolecular cycloaddition of (*R*)-**9** from the side with the less hindered lone pair of the chiral sulfinyl group in the six-membered transition state **17c** formed by the chelation of the carbonyl oxygen and the sulfinyl oxygen to the Lewis acid metals used.

The reaction path in this hetero Diels–Alder reaction depended on the Lewis acids used. The role of Lewis acids in this reaction is unclear. Presumably the acidity of the Lewis acids used would determine the reaction path. It should be noted that rather strong Lewis acids such as $AlCl_3$ and $TiCl_4$ provided lower de of **10a** over **10b**, whereas rather weak Lewis acids such as $SnCl_4$ and $ZnCl_2$ resulted in higher de. The slightly stronger affinity of the sulfinyl oxygen atom to Me_3Al and BF_3 would favor the intermediate **17c** over **17a**, **b**, generating the slight diastereoselectivity for **10b** over **10a**.

Thus, the chiral α′-sulfinyl-α,β-unsaturated ketone was demonstrated to serve as a chiral diene in the Lewis acid-catalyzed reaction to provide the asymmetric hetero Diels–Alder adducts with moderate stereoselectivity. This method provided an alternative route to optically active cyclic enol ethers, based on the effect of the chirality of the optically active sulfinyl group.

Experimental

Infrared (IR) spectra were obtained in the indicated state with a JASCO DR-81 Fourier-transform IR spectrometer. NMR spectra were determined in the indicated solvent with JEOL EX-270 (^{1}H-NMR; 270 MHz, ^{13}C-NMR; 67.5 MHz) and JNM PMX-60SI (60 MHz) high-resolution NMR spectrometers; chemical shifts are given in ppm from tetramethylsilane as an internal standard. Splitting patterns are designated as s, singlet; d, doublet; dd, doublets of doublet; t, triplet; q, quartet; m, multiplet. Mass spectra (MS) were taken on a JEOL JMS-DX 303/JMA-DA 5000 system. Optical rotations were measured at 25 °C with a JASCO DIP-370 polarimeter. HPLC data were obtained with a Tosoh UV-8010 CCPM (column: Tosoh TSK-Gel ODS-80TM). Flash column chromatography was performed with Merck Silica gel 60 (230—400 mesh). Thin layer or thick layer plates (preparative TLC) were made of Merck Silica gel 60PF-254 activated by drying at 140 °C for 3.5 h.

Ethyl (*E*)-5,5,9-Trimethyl-2,8-decadienoate (7) A dry 100 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing sodium hydride (0.37 g, 7.79 mmol, 50% oil dispersion), was flushed with nitrogen and maintained under a positive pressure of nitrogen. THF (10 ml) was added to the flask and the mixture was cooled to 0 °C. A solution of ethyl diethoxyphosphonyl acetate (1.75 g, 7.79 mmol) in THF (10 ml) was added and the mixture was stirred at 0 °C for 30 min. A solution of 3-methylcitronellal (**6**)[14] (1.00 g, 6.49 mmol) in THF (10 ml) was further added and the reaction mixture was stirred at 0 °C for 30 min. It was diluted with ether and the solution was washed successively with saturated aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1:30) to give (*E*)-**7** (1.25 g, 81% yield).

(*E*)-**7**: IR ν_{max}^{film} cm^{-1}: 1700 (ester), 1640 (C=C). ^{1}H-NMR (60 MHz) (CCl_4) δ: 0.92 (6H, s, $(CH_3)_2C$), 1.00—2.05 (6H, m, $CH_2C(CH_2)_2$), 1.25 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.58, 1.65 (6H, s, s, $(CH_3)_2$=C), 4.10 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 4.96 (1H, t, *J*=6 Hz, CH=C), 5.68 (1H, d, *J*=16 Hz, CH=C$\underline{H}$CO), 6.67 (1H, dd, *J*=8, 16 Hz, C$\underline{H}$=CHCO). MS *m/z*: 238 (M^+). Exact mass determination: 238.1931 (Calcd for $C_{15}H_{26}O_2$: 238.1933).

(*R*)-(+)-(*E*)-1-(*p*-Toluenesulfinyl)-6,6,10-trimethyl-3,9-undecadien-2-one (9) A dry 50 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with nitrogen, and maintained under a positive pressure of nitrogen. A solution of diisopropylamine (0.68 ml, 4.87 mmol) in THF (10 ml) was added to the flask and a 1.17 M ether solution of methyllithium (4.16 ml, 4.87 mmol) was further added at 0 °C. The mixture was stirred for 15 min. A solution of optically pure (*R*)-(+)-methyl *p*-tolyl sulfoxide (**8**)[15] (500 mg, 3.24 mmol, $[\alpha]_D$ +158.3° (*c*=1.03, acetone)) in THF (10 ml) was added. The whole was stirred for 1 h, then a solution of (*E*)-**7** (855 mg, 3.89 mmol) in THF (10 ml) was added and stirring was continued at 0 °C for 30 min. The reaction mixture was diluted with dichloromethane. The solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether) to give (*R*)-(*E*)-**9** (448 mg, 85% yield).

(*R*)-(+)-(*E*)-**9**: $[\alpha]_D$ +132.5° (*c*=1.61, $CHCl_3$) IR ν_{max}^{film} cm^{-1}: 1660 (C=O), 1680, 1620 (C=C), 1600 (aromatic), 1050 (S=O). ^{1}H-NMR (60 MHz) (CCl_4) δ: 0.98, (6H, s, $(CH_3)_2C$), 1.00—2.33 (6H, m, $CH_2C(CH_2)_2$), 1.60, 1.66 (6H, ss, $(CH_3)_2$=C), 2.45 (3H, s, $C_6H_4C\underline{H}_3$), 3.85—4.00 (2H, m, SCH_2), 4.95 (1H, t, *J*=6 Hz, CH=C), 5.95 (1H, d, *J*=16 Hz, CH=C$\underline{H}$CO), 6.67 (1H, dd, *J*=8, 16 Hz, C$\underline{H}$=CHCO), 7.20—7.66 (4H, m, C_6H_4). MS *m/z*: 346 (M^+). Exact mass determination: 346.1987 (Calcd for $C_{21}H_{30}O_2S$: 346.1967).

Lewis Acid-Catalyzed Intramolecular Asymmetric Hetero Diels–Alder Reaction of (*R*)-(*E*)-9 A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with nitrogen and maintained under a positive pressure of nitrogen. A solution of a Lewis acid (0.22 mmol) in dichloromethane (2 ml) was added to the flask. A solution of (*R*)-(*E*)-**9** (50 mg, 0.14 mmol, $[\alpha]_D$ +132.5° (*c*=1.61, $CHCl_3$)) in dichloromethane (2 ml) was further added. The reaction mixture was stirred under the conditions listed in Table 1, then diluted with dichloromethane and the solution was washed with saturated aqueous

$NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane, 1 : 2) to give (4a*R*,8a*S*,*Rs*)- and (4a*S*,8a*R*,*Rs*)-4a,5,6,7,8,8a-hexahydro-1,1,6,6-tetramethyl-2-(*p*-toluenesulfinylmethyl)-1*H*-2-benzopyran (**10a**, **10b**). The yields and the diastereomeric excess of the products are summarized in Table 1.

(4a*R*,8a*S*,*Rs*)-**10a**: $[\alpha]_D$ +137.1° (c=2.50, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1640 (C=C), 1600 (aromatic), 1050 (S=O). ^{1}H-NMR (270 MHz) ($CDCl_3$) δ: 0.90, (6H, s, $(CH_3)_2C$), 1.12 (3H, s, CH_3CO), 1.26 (3H, s, CH_3CO), 1.30—2.05 (8H, m, $CHCH_2C(CH_2)CH$), 2.41 (3H, s, $C_6H_4CH_3$), 3.21—3.50 (2H, m, CH_2SO), 4.40 (1H, s, CH=C), 7.26—7.54 (4H, m, C_6H_4). ^{13}C-NMR ($CDCl_3$) δ: 21.4, 22.4, 25.3, 26.1, 27.1, 30.3, 33.1, 39.7, 41.2, 47.2, 64.0, 106.6, 124.6, 129.8. MS *m/z*: 346 (M^+). Exact mass determination: 346.2048 (Calcd for $C_{21}H_{30}O_2S$: 346.1967).

(4a*S*,8a*R*,*Rs*)-**10b**: $[\alpha]_D$ +122.0° (c=2.50, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1640 (C=C), 1600 (aromatic), 1050 (S=O). ^{1}H-NMR (270 MHz) ($CDCl_3$) δ: 0.90, (6H, s, $(CH_3)_2C$), 1.03 (3H, s, CH_3CO), 1.19 (3H, s, CH_3CO), 1.30—2.05 (8H, m, $CHCH_2C(CH_2)CH$), 2.41 (3H, s, $C_6H_4CH_3$), 3.21—3.81 (2H, m, CH_2SO), 4.33 (1H, s, CH=C), 7.27—7.54 (4H, m, C_6H_4). ^{13}C-NMR ($CDCl_3$) δ: 19.7, 21.4, 23.4, 24.9, 27.3, 30.1, 33.0, 39.8, 45.4, 48.1, 64.2, 107.3, 124.4, 129.6. MS *m/z*: 346 (M^+). Exact mass determination: 346.1957 (Calcd for $C_{21}H_{30}O_2S$: 346.1967).

(4a*R*,8a*S*)-(+)-4a,5,6,7,8,8a-Hexahydro-1,1,6,6-tetramethyl-2-(*p*-toluenesulfenylmethyl)-1*H*-2-benzopyran (12) A 1.1 M aqueous solution of $TiCl_3$ (0.95 ml, 1.04 mmol) was added to a solution of (4a*R*,8a*R*,*Ss*)-**10a** (120 mg, 0.35 mmol) in THF (3 ml) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. The reaction solution was quenched with saturated aqueous $NaHCO_3$ and the mixture was diluted with dichloromethane. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 10) to give (4a*R*,8a*S*)-(+)-**12** (98 mg, 86% yield). The reaction of (4a*S*,8a*R*,*Ss*)-**10b** (100 mg, 0.29 mmol) with $TiCl_3$ (0.79 ml, 0.87 mmol), was carried out in the same way to afford (4a*S*,8a*R*)-(−)-**12** (82 mg, 86% yield, $[\alpha]_D$ −38.0° (c=1.53, $CHCl_3$)).

(4a*R*,8a*S*)-(+)-**12**: $[\alpha]_D$ +38.4° (c=1.60, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1670 (C=C), 1600 (aromatic). ^{1}H-NMR (270 MHz) ($CDCl_3$) δ: 0.90, (6H, s, $(CH_3)_2C$), 0.90—1.93 (8H, m, $CHCH_2C(CH_2)_2CH$), 1.21, 1.24 (6H, s, s, $(CH_3)_2CO$), 2.40 (3H, s, $C_6H_4CH_3$), 2.30 (2H, d, J=3 Hz, CH_2S), 3.37 (1H, d, J=3 Hz, CH=C), 7.05—7.34 (4H, m, C_6H_4). ^{13}C-NMR ($CDCl_3$) δ: 19.6, 21.0, 23.5, 25.1, 27.4, 30.0, 30.9, 33.1, 38.7, 39.9, 45.7, 48.4, 77.7, 96.1, 102.7, 129.4, 130.9, 136.2, 147.4. MS *m/z*: 330 (M^+). Exact mass determination: 330.1968 (Calcd for $C_{21}H_{30}OS$: 330.2017).

(4a*R*,8a*S*)-(+)-4a,5,6,7,8,8a-Hexahydro-1,1,3,6,6-pentamethyl-1*H*-2-benzopyran (13) A solution of (4a*R*,8a*S*,*Rs*)-**10a** (100 mg, 0.29 mmol) in THF–isopropanol (1 : 1) (4 ml) was added to a mixture of sodium (1.00 g, 43.48 mmol) in THF (2 ml) and the reaction mixture was stirred at room temperature for 2 h. A small amount of methanol was added to decompose excess sodium and the mixture was concentrated *in vacuo*. The residue was dissolved in ether and the ethereal solution was washed with saturated aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 30) to give (4a*R*,8a*S*)-(+)-**13** (53 mg, 90% yield). The reductive desulfinylation of (4a*S*,8a*R*,*Rs*)-**10b** (90 mg, 0.26 mmol) with sodium was carried out in the same way to give (4a*S*,8a*R*)-(−)-**13** (49 mg, 90% yield, $[\alpha]_D$ −56.0° (c=3.50, $CHCl_3$)).

(4a*R*,8a*S*)-(+)-**13**: $[\alpha]_D$ +56.4° (c=3.60, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1680 (C=C). ^{1}H-NMR (CCl_4) δ: 0.95, (6H, s, $(CH_3)_2C$), 0.95—2.15 (8H, m, $CHCH_2C(CH_2)_2CH$), 1.04, 1.08 (6H, s, s, $(CH_3)_2CO$), 1.60 (3H, s, CH_3C=C), 4.01 (1H, s, CH=C). MS *m/z*: 208 (M^+). Exact mass determination: 208.1825 (Calcd for $C_{14}H_{24}O$: 208.1827).

(4a*S*,8a*S*)-(−)-4-Bromo-4a,5,6,7,8,8a-hexahydro-1,1,3,6,6-pentamethyl-1*H*-2-benzopyran (14) *N*-Bromosuccinimide (94 mg, 0.48 mmol) was added to a solution of (4a*R*,8a*S*)-(+)-**13** (90 mg, 0.43 mmol, $[\alpha]_D$ +56.4° (c=3.60, $CHCl_3$)) in aqueous THF (THF–H_2O, 10 : 1) (4 ml) and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was diluted with dichloromethane. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 10) to give (4a*S*,8a*S*)-(−)-**14** (43 mg, 35% yield). The reaction of (4a*S*,8a*R*)-(−)-**13** (80 mg, 0.38 mmol, $[\alpha]_D$ −56.0° (c=3.50, $CHCl_3$)) with *N*-bromosuccinimide (84 mg, 0.43 mmol) was carried out in the same way to afford (4a*R*,8a*R*)-(+)-**14** (37 mg, 34% yield, $[\alpha]_D$ +36.0° (c=1.65, $CHCl_3$)).

(4a*S*,8a*S*)-(−)-**14**: $[\alpha]_D$ −36.4° (c=1.70, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1660 (C=C). ^{1}H-NMR (CCl_4) δ: 0.99, 1.00 (6H, s, s, $(CH_3)_2C$), 1.00—2.33 (8H, m, $CHCH_2C(CH_2)_2CH$), 1.10, 1.30 (6H, s, s, $(CH_3)_2CO$), 1.95 (3H, s, CH_3C=C). MS *m/z*: 286(M^+). Exact mass determination : 286.0941 (Calcd for $C_{14}H_{23}OBr$: 286.0950).

Sulfinylation of (4a*S*,8a*S*)-14 A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with nitrogen and maintained under a positive pressure of nitrogen. A solution of (4a*S*,8a*S*)-(−)-**14** (38 mg, 0.13 mmol, $[\alpha]_D$ −36.4° (c=1.70, $CHCl_3$)) in THF (2 ml) was added to the flask. A 1.5 M hexane solution of butyllithium (0.13 ml, 0.20 mmol) was further added at −78 °C and the mixture was stirred at −78 °C for 1 h. A solution of methyl (*S*)-(−)-*p*-toluenesulfinate (34 mg, 0.20 mmol, 87% ee) in THF (1 ml) was next added and the reaction solution was stirred at −78 °C for 1 h. It was then diluted with dichloromethane and the solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane, 1 : 2) to give (4a*S*,8a*S*,*Ss*)-4a,5,6,7,8,8a-hexahydro-1,1,3,6,6-pentamethyl-4-(*p*-toluenesulfinyl)-1*H*-2-benzopyran (**15a**) (17 mg, 37% yield, $[\alpha]_D$ −106.2° (c=0.87, $CHCl_3$)). The reaction of (4a*R*,8a*R*)-(+)-**14** (35 mg, 0.12 mmol, $[\alpha]_D$ +36.0° (c=1.65, $CHCl_3$)) with methyl (*S*)-(−)-*p*-toluenesulfinate (31 mg, 0.18 mmol, 87% ee) was carried out in the same way to give (4a*R*,8a*R*,*Ss*)-**15b** (16 mg, 38% yield, $[\alpha]_D$ −83.1° (c=0.67, $CHCl_3$)).

The spectral data of the diastereomer isolated above were superimposable on those of the products obtained by us previously.[10]

(4a*S*,8a*S*)-(+)-4a,5,6,7,8,8a-Hexahydro-1,1,3,6,6-pentamethyl-4-(*p*-toluenesulfenyl)-1*H*-2-benzopyran (16) A 1.1 M aqueous solution of $TiCl_3$ (0.13 ml, 0.14 mmol) was added to a solution of (4a*S*,8a*S*,*Ss*)-**15a** (22 mg, 0.06 mmol, $[\alpha]_D$ −106.2° (c=0.87, $CHCl_3$)) in THF (1 ml) and the reaction solution was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous NaCl and the mixture was diluted with dichloromethane. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 10) to give (4a*S*,8a*S*)-(−)-**16** (19 mg, 90% yield, $[\alpha]_D$ −30.6° (c=1.03, $CHCl_3$)). The reduction of (4a*R*,8a*R*,*Ss*)-**15b** (20 mg, 0.06 mmol, $[\alpha]_D$ −83.1° (c=0.67, $CHCl_3$)) was carried out in the same manner to give (4a*R*,8a*R*)-(+)-**16** (17 mg, 90% yield, $[\alpha]_D$ +27.5° (c=1.06, $CHCl_3$)). The spectral data of **16** obtained above were superimposable on those of the product obtained by us previously.[10]

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