Highly Diastereoselective Intermolecular *β*-Addition of Alkyl Radicals to Chiral 2-(Arylsulfinyl)-2-cycloalkenones

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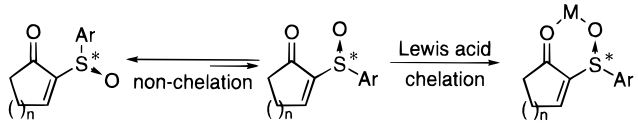
The diastereoselectivity of intermolecular *β*-addition of alkyl radicals to 2-(arylsulfinyl)-2-cycloalkenones depends largely upon the structure of the arylsulfinyl group. The reaction of 2-cyclopentenones or 2-cyclohexenones having a sterically bulky arylsulfinyl group such as (3,5-di-*tert*-butyl-4-methoxyphenyl)sulfinyl, (2,4,6-triisopropylphenyl)sulfinyl or (2,4,6-trimethylphenyl)-sulfinyl group gives 3-alkyl-2-(arylsulfinyl)-1-cyclopentanones or 3-alkyl-2-(arylsulfinyl)-1-cyclohexanones in excellent yields and with high diastereoselectivity. Both the X-ray crystallographic analysis and the NOE experiment in the ^{1}H NMR spectrum of (*S*)-2-[(2,4,6-triisopropylphenyl)-sulfinyl]- and (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenone reveal an effective shielding of one of the olefin faces at the *β*-position by *o*-isopropyl and *o*-methyl groups. The addition of bidentate Lewis acids reverses the stereoselection through chelating the intermediates to give the addition products with high diastereoselectivity.

Introduction

Recently, radical-mediated asymmetric reactions have been extensively studied.[1] The radical addition to prochiral alkenes bearing a chiral center[2] or a chiral auxiliary[3] is an important radical-mediated asymmetric process. Generally, high diastereoselectivities are observed when the addition occurs at the position α to the chiral auxiliary as in an oxazolidine,[3a] a C2-chiral pyrrolidine amide,[3b] or an (−)-8-phenylmenthyl ester.[3c] On the other hand, generally the diastereoselectivity in additions at the *β*-position to a carbonyl is not high,[3b] although Curran and co-workers have shown a successful diastereoselective *β*-addition to the alkene having a sterically bulky amide auxiliary prepared from Kemp's triacid.[4a] Recently, Sibi and co-workers also reported an excellent asymmetric radical *β*-addition that involves fixation of conformation of the oxazolidinone amide with Lewis acid.[4b]

We envisaged the diastereofacial control of the alkene face *β* to the carbonyl by a chiral sulfoxide auxiliary and have reported highly diastereoselective radical *β*-addition to 2-(arylsulfinyl)-2-cyclopentenones.[5] The sulfoxide has a trigonal pyramidal structure that is quite different from that of chiral amide and ester auxiliaries. Thus, the substituent on the sulfinyl group was expected to shield one face of the alkene at the *β*-position and thereby to control the *β*-stereoselectivity of the radical attack. A carbonyl α to the sulfinyl group can fix the conformation as well as enhance the reactivity toward alkyl radicals, where the sulfur−oxygen and carbonyl bond would be arranged in an antiperiplanar orientation.[6] The conformation could also be fixed by chelation with a bidentate metal between the carbonyl oxygen and sulfoxide oxygen (Scheme 1). Since the sulfinyl group is chemically versatile and removable under mild conditions,[7] it is attractive as a chiral auxiliary in radical reactions. There are numerous studies on the diastereofacial control at the carbon α to the chiral sulfinyl group,[8] but there are few reports on the *β*-stereoselectivity to chiral vinyl sulfoxides, except our reports,[5] and the intramolecular cyclization.[9] We now describe the influence of sulfoxide substituents and Lewis acids on the stereoselectivity in the radical *β*-addition to 2-(arylsulfinyl)-2-cyclopentenones and -cyclohexenones.

Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1997.

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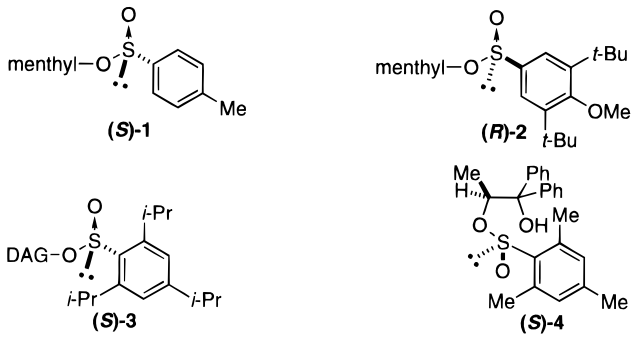
Scheme 2



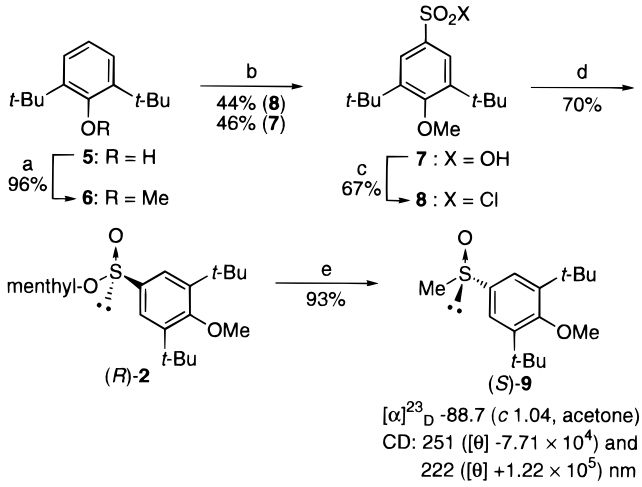
Results and Discussion

Chiral 2-(arylsulfinyl)-2-cyclopentenones **16a**−**d** and 2-(arylsulfinyl)-2-cyclohexenones **16e**,**f** were prepared from chiral sulfinates **1**−**4** by the reaction with the corresponding cyclopentenyllithium and cyclohexenyllithium (Scheme 2). (*S*)-2-(*p*-Tolylsulfinyl)-2-cyclopentenone (**16a**) was prepared from (*S*)-menthyl *p*-toluenesulfinate (*S*)-(**1**).[10] (*S*)-2,2-Diphenyl-1,2-dihydroxypropyl 2-*O*-(2,4,6-trimethylphenyl)sulfinate (*S*)-(**4**) was prepared from the cyclic sulfite according to Kagan's method.[11]

3,5-Di-*tert*-butyl-4-methoxybenzenesulfinate (**2**) was prepared from 2,6-di-*tert*-butylphenol (**5**) in three steps and resolved to the optically pure diastereoisomer of menthyl sulfinate **2**. The anisole **6**,[12] prepared from **5**, was treated with 2 equiv of chlorosulfonic acid to afford 3,5-di-*tert*-butyl-4-methoxybenzenesufonyl chloride (**8**) in 44% yield along with 3,5-di-*tert*-butyl-4-methoxybenzenesulfonic acid (**7**) (46% yield),[13] that was subsequently converted to **8** with thionyl chloride. The sulfonyl chloride **8** was then treated with *l*-menthol in the presence of trimethyl phosphite and triethylamine under reflux to give the menthyl sulfinate **2** in 70% yield.[14] The optically pure menthyl sulfinate (*R*)-**2** was obtained by multiple recrystallizations from acetone. (Scheme 3)

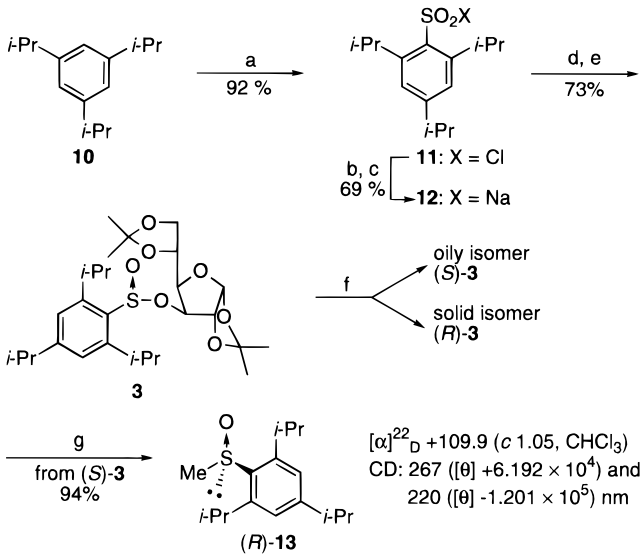
Resolution of menthyl 2,4,6-triisopropylbenzenesulfinate was difficult by either recrystallization or column chromatography.[14] We found that the optically pure sulfinate could be prepared via the diacetone D-glucose (DAG) ester[15] of 2,4,6-triisopropylbenzenesulfinic acid. Diacetone D-glucose 2,4,6-triisopropylbenzenesulfinate ester (**3**) was prepared as shown in Scheme 4. Treatment of 2,4,6-triisopropylbenzene (**10**) with 4.2 equiv of chlorosulfonic acid afforded 2,4,6-triisopropylbenzenesulfonyl chloride (**11**) in 92% yield.[16] The sulfonyl chloride **11** was reduced with zinc in water to the sulfinic acid, which was treated with an aqueous solution of NaOH and Na_2CO_3 to give the sodium sulfinate **12** in 69% yield.[17] The sodium sulfinate **12** was treated with 7.5 equiv of thionyl chloride to give the corresponding sulfinyl chloride that was used without further purification. The DAG sulfinate **3** was prepared by the reaction of the sulfinyl chloride with DAG in the presence of pyridine at 0 °C. Fortunately, both diastereoisomers of the DAG 2,4,6-triisopropylbenzenesulfinate **3** were separable by silica gel flash column chromatography to give the (*S*)-sulfinate (*S*)-**3** as an oil and the (*R*)-sulfinate (*R*)-**3** as a solid (Scheme 4).

Scheme 3[a]



[a] (a) $Ba(OH)_2 \cdot 8H_2O$, $(CH_3)_2SO_4$, DMF, rt; (b) $ClSO_3H$, $CHCl_3$, −10 °C; (c) $SOCl_2$, DMF, 0 °C−rt; (d) *l*-menthol, $(MeO)_3P$, Et_3N, CH_2Cl_2, reflux; (e) MeMgI, Et_2O/THF, O °C-rt.

Scheme 4[a]



[a] (a) $ClSO_3H$, $CHCl_3$, 0 °C; (b) Zn, H_2O, 90 °C; (c) 50% NaOH, Na_2CO_3; (d) $SOCl_2$, rt; (e) DAG, pyridine, Et_2O, 0 °C−rt; (f) flash column chromatography; (g) MeMgI, Et_2O/THF, 0 °C−rt.

Absolute configurations of the sulfinates (*R*)-**2**, (*S*)-**3**, and (*R*)-**3** were determined by CD spectral analyses of 3,5-di-*tert*-butyl-4-methoxyphenyl methyl sulfoxide (**9**) and methyl 2,4,6-triisopropylphenyl sulfoxide (**13**) according to the literature, in which (*S*)-aryl methyl sulfoxide is confirmed to show a negative first Cotton effect in the CD spectrum as well as a negative rotation of $[\alpha]_D$.[18] A single diastereoisomer of the sulfinate **2** was converted to the aryl methyl sulfoxide **9** by treatment with a methyl Grignard reagent at 0 °C.[19] The optical

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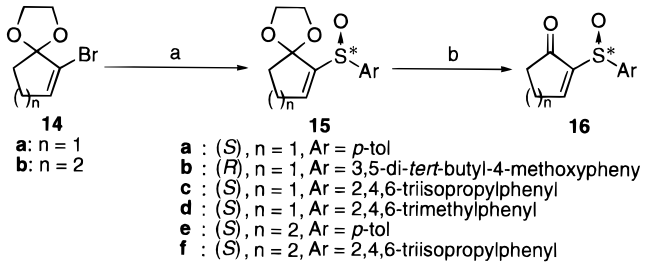
Scheme 5[a]



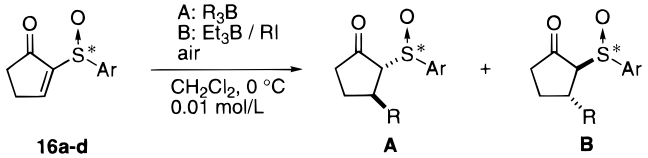
[a] (a) BuLi, chiral sulfinate, THF, −100 °C; (b) H_2SO_4-SiO_2, CH_2Cl_2, rt.

purity of the aryl methyl sulfoxide **9** was confirmed by the analysis of the ^{1}H NMR spectrum using (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol. The sulfoxide **9** showed a negative rotation ($[\alpha]^{22}_D = -88.7$ (*c* 1.04, acetone)) and a negative first Cotton effect in the CD spectrum (251 nm ($[\theta]$ -7.71×10^4) and 222 nm ($[\theta]$ $+1.22 \times 10^5$) in 2,2,4-trimethylpentane), which allowed assignment of the stereochemistry of the aryl methyl sulfoxide **9** as the (*S*)-isomer. Thus the configuration of the starting sulfinate **2** was (*R*) because of the inversion of configuration in the Grignard reaction.[20] On the other hand, the aryl methyl sulfoxide **13**, which was prepared from the oily diastereoisomer of the sulfinate **3**, showed a positive rotation ($[\alpha]^{22}_D = +105.8$ (*c* 0.82, $CHCl_3$)) and a positive first Cotton effect (267 nm ($[\theta]$ $+6.19 \times 10^4$) and 220 nm ($[\theta]$ -1.20×10^5), 2,2,4-trimethylpentane). From these results, the oily diastereoisomer of sulfinate **3** was determined to be the (*S*)-isomer and the solid diastereoisomer to be the (*R*)-isomer.

Chiral 2-(arylsulfinyl)-2-cycloalkenones **16a**−**f** were prepared by a modified procedure reported in the literature.[21] The vinyllithium formed on treatment of the bromoacetal **14**[22] with *n*-BuLi in THF was reacted with chiral arylsulfinates (*S*)-**1**, (*R*)-**2**, (*S*)-**3**, and (*S*)-**4** at −100 °C to give optically pure sulfoxides **15a**−**f** in good yields. Deprotection of the acetal with $CuSO_4$,[21] $MgSO_4$,[23] or $FeCl_3$[24] did not give 2-(arylsulfinyl)-2-cycloalkenones effectively, but the reaction was achieved efficiently with acidic silica gel.[25] Thus, the chiral sulfoxides **15a**−**f** were treated with silica gel containing a small amount of sulfuric acid to give 2-(arylsulfinyl)-2-cycloalkenones **16a**−**f** in excellent yields (Scheme 5).

We studied the radical β-addition to 2-(arylsulfinyl)-2-cyclopentenones. Addition of alkyl radicals to 2-(arylsulfinyl)-2-cyclopentenones **16a**−**d** was carried out by the following two methods. To a degassed 0.01 mol/L solution of the 2-(arylsulfinyl)-2-cyclopentenone **16** in CH_2Cl_2 was added trialkylborane[26] (10 equiv) and the mixture was stirred at 0 °C, as air was continuously passed through the solution via a needle by a microfeeder (method A).[27]

Table 1. Radical β-Addition to 2-(Arylsulfinyl)-2-cyclopentenones



entry	enone	method	R	product	yield %	ratio[a] A:B
1	**16a**	A	Et	**17**	98	57:43
2	**16a**	B	*i*-Pr	**18**	97	59:41
3	**16a**	B	*t*-Bu	**19**	96	67:33
4	**16b**	B	*t*-Bu	**20**	91	38:62
5	**16c**	A	Et	**21**	98	>98:<2
6	**16c**	B	*i*-Pr	**22**	99	>98:<2
7	**16c**	B	*c*-Hex	**23**	87	>98:<2
8	**16c**	B	*t*-Bu	**24**	97	>98:<2
9	**16d**	A	Et	**25**	94	94:6
10	**16d**	B	*i*-Pr	**26**	99	>98:<2
11	**16d**	B	*c*-Hex	**27**	89[b]	>98:<2
12	**16d**	B	*t*-Bu	**28**	99	>98:<2

[a] Determined by ^{1}H NMR analysis. [b] The ethyl adduct was also obtained in 9% yield.

Alternatively, a mixture of **16**, an alkyl iodide (10 equiv), and triethylborane (10 equiv) as a radical initiator[28] in CH_2Cl_2 was stirred at 0 °C, as air was continuously passed through the solution as descrived above (method B). In the latter reaction, 10 equiv of an alkyl iodide is used, since the competitive addition of an ethyl radical generated from triethylborane could not be avoided in a reaction with less than 10 equiv of the alkyl iodide. The results are summarized in Table 1.

The reaction of (*S*)-2-(*p*-tolylsulfinyl)-2-cyclopentenone (**16a**) with a *tert*-butyl radical, isopropyl radical, or ethyl radical gave the products in good yields but with low diastereoselectivity (Table 1, entries 1−3). (*R*)-2-[(3,5-Di-*tert*-butyl-4-methoxyphenyl)sulfinyl]-2-cyclopentenone (**16b**) having *tert*-butyl groups at the meta positions also did not give high diastereoselectivity even in the reaction with a *tert*-butyl radical (entry 4). On the other hand, (*S*)-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**16c**) having two isopropyl groups at the ortho positions gave a single diastereoisomer of (3*R*)-alkylated product in the reaction with *tert*-butyl radical (entry 8). No formation of any other stereoisomers was observed. This surprisingly high diastereoselection was also observed in the reaction with less bulky alkyl radicals such as an isopropyl or cyclohexyl radical and even with an ethyl radical (entries 5−7). The reaction of (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenone (**16d**) gave excellent diastereoselectivity, yielding a single diastereoisomer with a *tert*-butyl, isopropyl, or cyclohexyl radical (entries 10−12), and a 94:6 diastereoisomeric ratio with an ethyl radical (entry 9).

Since the transition states in the nucleophilic alkyl radical addition to electron-deficient olefins are assumed to be reactant-like, the ground-state alkene conformation should influence the stereoselection.[29] To clarify the high β-stereoselection caused by the chiral sulfinyl group having bulky ortho-substituents, the structural analysis of the 2-(arylsulfinyl)-2-cyclopentenone (**16c**) was carried

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(26) Triethylborane was purchased from Kanto Chemical Co. The other trialkylborane was prepared by the procedure reported in the literture: Brown, H. C. *J. Am. Chem. Soc.* **1945**, *67*, 374.
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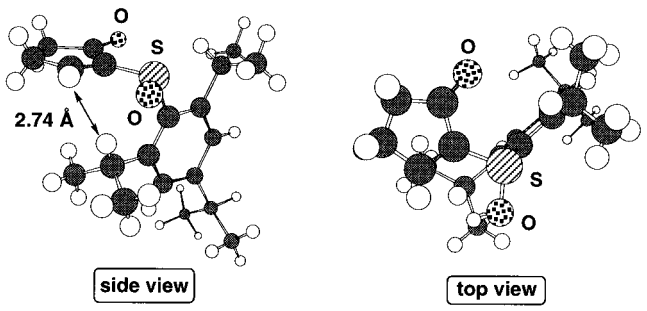
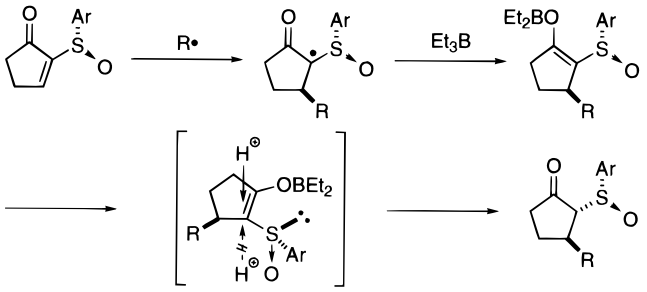


Figure 1. Chem 3D representation of the X-ray structure of **16c**.

Scheme 6



out. The X-ray crystallographic structure **16c** is shown in Figure 1.

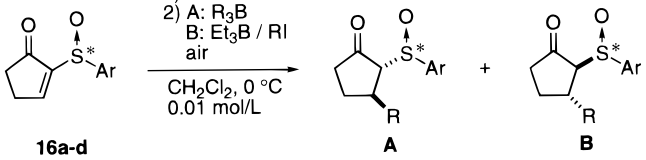
It clearly shows the antiperiplanar arrangement of the C═O and S−O bonds, in which the isopropyl group is placed in a good position to shield one face, thereby allowing radicals to attack from the other alkene face. The distance between the β-proton and the isopropyl methine proton was 2.74 Å. The NMR study supported this structure in solution by a significant nuclear Overhauser effect (9%) between the β-proton and isopropyl methine proton in the ^{1}H NMR spectrum. A comparable nuclear Overhauser effect (8%) was also observed between the corresponding protons in (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenone (**16d**). These ortho-substituents effectively shield the olefin face, and (2,4,6-triisopropyl- and (2,4,6-trimethylphenyl)sulfinyl groups induced extremely high stereoselection.

Only the trans compounds were formed in all reactions. The final products were formed via hydrolysis of the boron enolates.[28] In the boron enolates, the bulky aryl substituent on the sulfinyl group would be arranged in a position opposite to the added alkyl group by avoiding the steric interaction, and hydrolysis of the boron enolates occurs from the side opposite to the aryl group to give the trans compounds (Scheme 6).

The radical β-addition reactions were also examined in the presence of Lewis acid. The reaction was carried out in a manner similar to the reaction without Lewis acid: a mixture of the 2-(arylsulfinyl)-2-cyclopentenone **16** and Lewis acid was stirred for 1 h at 0 °C before the addition of alkyl iodide and triethylborane. The results are shown in Table 2.

Radical β-addition to (*S*)-2-(*p*-tolylsulfinyl)-2-cyclopentenone (**16a**) with *tert*-butyl iodide and triethylborane in the presence of Lewis acid gave the addition products in good to excellent yields. Addition of a *tert*-butyl radical to **16a** in the presence of 1.1 equiv of $ZnBr_2$ showed a small change in the diastereomeric ratio of the addition products (entry 2) in comparison with the reaction without Lewis acid, whereas radical additions in the

Table 2. Lewis Acid-Mediated Radical β-Addition to 2-(Arylsulfinyl)-2-cylcopentenones[a]



entry	enone	R	Lewis acid	yield %	ratio[b] A:B
1	**16a**	*t*-Bu	none	93	67:33
2	**16a**	*t*-Bu	$ZnBr_2$	98	40:60
3	**16a**	*t*-Bu	$ZnBr_2$[c]	97	62:38
4	**16a**	*t*-Bu	$EtAlCl_2$	96	18:82
5	**16a**	*t*-Bu	$EtAlCl_2$[c]	93	12:88
6	**16a**	*t*-Bu	$TiCl_2(O$*i*$-Pr)_2$	60	28:72
7	**16a**	*t*-Bu	$BF_3{\cdot}Et_2O$	99	65:35
8	**16b**	*t*-Bu	none	91	38:62
9	**16b**	*t*-Bu	$EtAlCl_2$	94	90:10
10[d]	**16b**	*t*-Bu	$Ti(O$*i*$-Pr)_4$	70	56:44
11[d]	**16b**	*t*-Bu	$TiCl(O$*i*$-Pr)_3$	79	81:19
12[d]	**16b**	*t*-Bu	$TiCl_2(O$*i*$-Pr)_2$	85	91:9
13	**16b**	*t*-Bu	$TiCl_2(O$*i*$-Pr)_2$	94	98:2
14	**16c**	Et	none	95	>98:<2
15	**16c**	Et	$ZnBr_2$	52	>98:<2
16	**16c**	Et	$MgCl_2$	30	>98:<2
17	**16c**	Et	$ZrCl_4$	82	>98:<2
18	**16c**	Et	Et_2AlCl	92	45:55
19	**16c**	Et	$EtAlCl_2$	95	21:79
20	**16c**	Et	$TiCl_2(O$*i*$-Pr)_2$	60	42:58
21	**16d**	*t*-Bu	none	99	>98:<2
22	**16d**	*t*-Bu	$ZnBr_2$	95	76:24
23	**16d**	*t*-Bu	Et_2AlCl	88	28:72
24	**16d**	*t*-Bu	$EtAlCl_2$	99	<2:>98
25	**16d**	*t*-Bu	$TiCl_2(Oi\text{-}Pr)_2$	19	<2:>98

[a] Entries 8 and 13−20, method A; entries 1−7, 9−12, and 21−25, method B. [b] Determined by ^{1}H NMR analysis. [c] 2.0 equiv of Lewis acid was used. [d] 0.1 mol/L.

presence of $EtAlCl_2$ or $TiCl_2(O$*i*$-Pr)_2$[30] led to the reversed diastereoselectivity, giving the (3*S*)-isomer as the major product (entries 4 and 6). When 2 equiv of $EtAlCl_2$ was used, the 3*R*:3*S* ratio was improved (entry 5). The change in the product distribution in these reactions is apparently due to the conformation fixed by chelation with Lewis acid between the carbonyl and sulfinyl oxygens in the starting 2-(arylsulfinyl)-2-cyclopentenone. Thus, it is not surprising that the monodentate $BF_3{\cdot}OEt_2$ did not change the diastereoselectivity (entry 7). The addition of the *tert*-butyl radical to (*R*)-2-[(3,5-di-*tert*-butyl-4-methoxyphenyl)sulfinyl]-2-cyclopentenone (**16b**) in the presence of $TiCl_2(O$*i*$-Pr)_2$ showed excellent reversed diastereoselectivity (3*R*:3*S* = 98:2, entry 13). Dichloromethane gave higher diastereoselectivity than other solvents tested such as acetonitrile (89:11), toluene (85:15), and tetrahydrofuran (76:24). The diastereoselectivity was improved in the reaction under high dilution conditions (entries 12 vs 13), suggesting that the high stereoselection is derived from the rigid 1:1 coordination of the 2-(arylsulfinyl)-2-cyclopentenone with Lewis acid. In the reaction of (*S*)-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**16c**) with an ethyl radical, Et_2AlCl, $EtAlCl_2$, or $TiCl_2(O$*i*$-Pr)_2$ did not result in completely reversed diastereoselectivity (entries 18−20). On the other hand, the addition of $ZnBr_2$, $MgCl_2$, or $ZrCl_4$ did not change the diastereoselectivity (entries 15−17). The bulky isopropyl groups on the phenyl ring seemed to

(30) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949.

inhibit the complete chelation with Lewis acid. This assumption was verified by the reaction of (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenone (**16d**). The reaction of **16d** showed a slight increase in the formation of the (3*S*)-isomer in the reaction with $ZnBr_2$ (entry 22) and a further increase with Et_2AlCl (entry 23). In the presence of $EtAlCl_2$ or $TiCl_2(O\textit{i}\text{-}Pr)_2$, the face selection was completely reversed, giving only the (3*S*)-alkylated product (entries 24 and 25). It is noteworthy that a (3*S*)-*tert*-butylated product was produced with complete diastereoselectivity in the presence of $EtAlCl_2$ or $TiCl_2(O\textit{i}\text{-}Pr)_2$, along with the exclusive formation of a (3*R*)-*tert*-butylated product in the radical addition to **16d** without Lewis acid, as shown in Table 2 (entry 21). This is the first example of the formation of both diastereoisomers of the radical β-addition products from the same chiral substrate.[31]

The stereochemistry of the addition products **17**−**28** was determined as follows: Oxidation of a mixture of (3*R*)- and (3*S*)-diastereoisomers with *m*-CPBA gave a single diastereoisomer of the sulfones **29**−**40**. The configuration was assigned to be trans. The trans configuration of the sulfones was chemically confirmed by the ready syn-elimination[6] of the sulfenic acid to 3-alkyl-2-cyclopentenone by heating at reflux in CCl_4. In addition, significant NOEs in the ^1H NMR spectra of *tert*-butyl adducts **19**, **20**, **24**, and **28** were observed between the proton α to the sulfonyl group and the methyl protons of the *tert*-butyl group. The addition products **17**−**28** were subjected to desulfurization with aluminum amalgam[7] to give 3-alkyl-1-cyclopentanones **41a**−**d**. The absolute configuration of **41a**−**d** was determined by comparison of the optical rotations with the known values for 3-alkyl-1-cyclopentanones.[32a−d] 3-Alkyl-1-cyclopentanones **41a**−**d** were then converted to the aminals in the NMR tube on treatment with (1*R*,2*R*)-1,2-diphenylethylenediamine.[33a] The optical purity was determined by ^{13}C NMR analyses of the aminals. The ^{13}C NMR spectra of each (*R*)- or (*S*)-isomer of the aminals showed chemical shifts in consistency with the general trend[33b] of the chemical shifts differentiating (*R*)-alkylcyclopentanone from the (*S*)-isomer (Scheme 7).

The radical β-addition to the 2-(arylsulfinyl)-2-cyclohexenones **16e,f** was next examined. The reaction of (*S*)-2-(*p*-tolylsulfinyl)-2-cyclohexenone (**16e**) with isopropyl iodide in the presence of triethylborane gave a mixture of four diastereomeric addition products. Removal of the sulfinyl group from the addition product with aluminum amalgam afforded 3-isopropyl-1-cyclohexanone (**43**),[32e]

Scheme 7

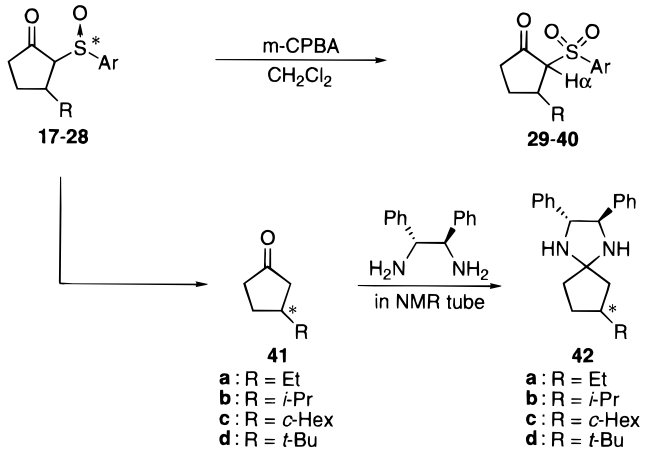
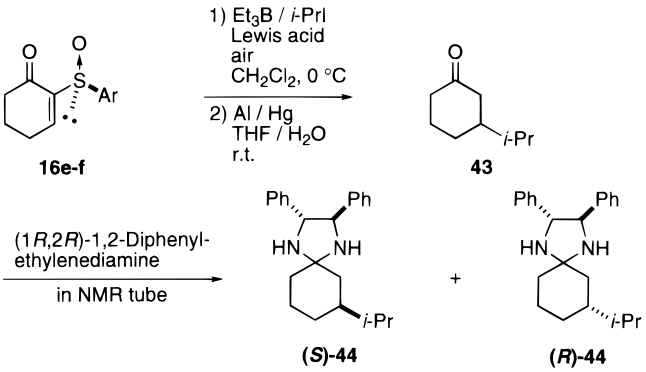


Table 3. Radical β-Addition to 2-(Arylsulfinyl)-2-cyclohexenones



entry	enone	Lewis acid	total yield of **43** (%)	ratio[a] *S*:*R*
1	**16e**	none	83	73:27
2	**16e**	$EtAlCl_2$	89	52:48
3	**16f**	none	93	>98:<2
4	**16f**	$EtAlCl_2$	83	85:15

[a] Determined by 13C NMR analysis.

which was then converted to the aminal **44** on treatment with (1*R*,2*R*)-1,2-diphenylethylenediamine. The ^{13}C NMR analysis of **44** showed *S*/*R* stereoselectivity in a ratio of 73:27 (entry 1, Table 3). The radical addition of isopropyl radical to (*S*)-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclohexenone **(16f)** again showed excellent stereoselectivity. After reductive removal of the sulfinyl group, this reaction was confirmed by the NMR analysis of the aminal **44** to give a single enantiomer (entry 3). Addition of an isopropyl radical in the presence of $EtAlCl_2$, however, did not reverse the stereoselectivity in both reactions of **16e** and **16f**, giving the corresponding aminal with lowered diastereoselectivity in ratios of 52:48 and 85:15, respectively (entries 2 and 4). These results are best ascribed to the incomplete coordination of $EtAlCl_2$ with the 2-(arylsulfinyl)-2-cyclohexenones **16e**,**f** in comparison with the 2-(arylsulfinyl)-2-cyclopentenones **16a**−**d**.

In summary, the alkyl radical addition to 2-cyclopentenones and -cylohexenones having chiral bulky arylsulfinyl groups showed excellent diastereoselectivities. The radical addition in the presence of Lewis acid reversed the stereoselectivity. Both diastereoisomers could be prepared with complete diastereoselectivities in the radical β-addition reactions to (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenone in the presence and absence of Lewis acid. Since the sulfinyl group can be

(31) There are several reports on the stereoselective formation of both diastereoisomers depending on the conditions with or without Lewis acids in the radical 1,2-asymmetric inductions, see: (a) Sibi, M. P.; Ji, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 5 (2), 190. (b) Sibi, M. P.; Ji, J. *J. Org. Chem.* **1996**, *61*, 6090. (c) Gerster, M.; Audergon, L.; Moufid, N.; Renaud, P. *Tetrahedron Lett.* **1996**, *37* (35), 6335. (d) Nagano, H.; Kuno, Y.; Omori, Y.; Iguchi, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 389. (e) Guindon, Y.; Guérin, B.; Chabot, C.; Mackintosh, N.; Ogilvie, W. W. *Synlett* **1995**, 449. (f) Renaud, P.; Bourquard, T.; Gerster, M.; Moufid, N. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1601. (g) Yamamoto, Y.; Onuki, S.; Yumoto, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 421.

(32) (a) For 3-ethyl-2-cyclopentanone, see ref 7. (b) For 3-isopropyl-2-cyclopentanone, see ref 7 and references therein. (c) For 3-cyclohexyl-2-cyclopentanone, see: Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821 and references therein. (d) For 3-*tert*-butyl-2-cyclopentanone, see: Tichy, M.; Malon, P.; Fric, I.; Blaha, K. *Collect. Czech. Chem. Commun.* **1977**, *42*, 3591. (e) For 3-isopropyl-2-cyclohexanone, see, ref 7.

(33) (a) Alexakis, A.; Frutos, J. C.; Mangeney, P. *Tetrahedron: Asymmetry* **1993**, *4* (12), 2431. (b) Lemière, G. L.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C.; Hiemstra, H.; Wynberg, H.; Jones, J. B.; Toone, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 1363.

readily removed, these reactions provide a preparative method for chiral 3-alkyl-1-cyclopentanones and -cyclohexanones.

Experimental Section

Preparation of the Chiral Sulfinates. (*R*)-(+)-Menthyl 3,5-Di-*tert*-butyl-4-methoxybenzenesulfinate ((*R*)-2). To a solution of 2,6-di-*tert*-butylanisole (**6**)[12] (31.3 g, 0.142 mol) in $CHCl_3$ (60 mL) was added dropwise chlorosulfonic acid (18.9 mL, 0.284 mol) over a period of 30 min at −10 °C. After stirring for 10 min, the mixture was poured onto crushed ice (200 mL) and extracted with $CHCl_3$. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to leave a solid, which was purified by recrystallization from hexane, giving the sulfonyl chloride **8** (19.9 g, 44%) as a colorless solid: $R_f = 0.58$ (hexane/ethyl acetate = 9/1); mp 90.2−90.7 °C; ^{1}H NMR δ 1.46 (s, 18H), 3.76 (s, 3H), 7.90 (s, 2H); ^{13}C NMR δ 31.6, 36.4, 64.9, 125.7, 138.5, 146.3, 165.6; IR (KBr) 2850, 1440, 1370, 1215, 1165, 1110, 995 cm^{-1}; MS (EI) *m*/*e* 318 (M^+, 23), 303 (100). Anal. Calcd for $C_{15}H_{23}ClO_3S$: C, 56.50; H, 7.27. Found: C, 56.44; H, 7.33.

The aqueous solution obtained in the above experiment was acidified with concentrated HCl and extracted with $CHCl_3$ and successively with aqueous $NaHCO_3$, and the resultant solution was cooled to precipitate the sodium sulfonate, which was also converted to the sulfonyl chloride **8.** To a solution of the sodium sulfonate (21.3 g, 0.066 mmol) in DMF (100 mL) was added dropwise thionyl chloride (14.4 mL, 0.198 mol) at 0 °C over a period of 90 min. Then the mixture was allowed to warm to room temperature and stirred for 1 h. The mixture was poured onto crushed ice (200 mL) and extracted with Et_2O. The combined organic extracts were washed with saturated $NaHCO_3$ (50 mL), water (50 mL), and brine (50 mL). The organic solution was dried over $MgSO_4$ and concentrated to leave a solid, which was purified by recrystallization from hexane to give the sulfonyl chloride **8** (17.7 g, 84%).

To a solution of the sulfonyl chloride **8** (3.20 g, 10.0 mmol) and (−)-(*l*)-menthol (1.05 g, 6.69 mmol) in CH_2Cl_2 (32 mL) were added trimethyl phosphite (1.58 mL, 13.4 mmol) and triethylamine (1.40 mL, 10.0 mmol) at room temperature. After heating under reflux for 8 h, the mixture was cooled to room temperature. The mixture was poured into 1 mol/L HCl (30 mL) and extracted with Et_2O. The combined organic extracts were washed with saturated $NaHCO_3$ (10 mL), water (2 × 10 mL), and brine (10 mL). The solution was dried over $MgSO_4$ and concentrated to give the crude sulfinate, which was purified by column chromatography (silica gel, hexane/ethyl acetate = 98/2) to give the sulfinate **2** (1.95 g, 70%) as a mixture of diastereoisomers. Optically pure the sulfinate (*R*)-**2** was obtained by recrystallization from acetone: $R_f = 0.51$ (hexane/ethyl acetate = 9/1); mp 138−139 °C; $[\alpha]^{20}_D = +50.4$ (*c* 0.40, acetone); ^{1}H NMR δ 0.70−1.80 (m, 7H), 0.83−0.95 (m, 9H), 1.44 (s, 18H), 2.04−2.30 (m, 2H), 3.71 (s, 3H), 4.19 (dt, *J* = 4.5, 10.7 Hz, 1H), 7.58 (s, 2H); ^{13}C NMR δ 15.5, 20.8, 21.9, 22.9, 25.4, 31.7, 33.9, 36.1, 43.5, 48.1, 64.5, 82.2, 123.0, 139.4, 144.9, 162.7; IR (KBr) 2925, 1445, 1390, 1215, 1110 cm^{-1}; MS (EI) *m*/*e* 422 (M^+, 0.3), 407 (2), 284 (100), 269 (77). Anal. Calcd for $C_{25}H_{42}O_3S$: C, 71.04; H, 10.02. Found: C, 71.03; H, 10.22.

Diacetone D-Glucose 2,4,6-Triisopropylbenzenesulfinate Ester (3). The sulfonyl chloride **11**[16] (25.0 g, 82.5 mmol) was added portionwise to a vigorously stirred suspension of zinc powder (12.5 g, 191 mmol) in hot water (120 mL, 70−75 °C). The suspension was allowed to warm to 90 °C and stirred for 1 h. To the cooled suspension was added 12 mol/L NaOH (8 mL) and then solid Na_2CO_3 (ca. 10 g) was added to make the mixture strongly basic. The suspension was filtered through Celite 500 and precipitates were washed with hot water (50 mL). The filtrate was concentrated on the hot plate to half volume. Then the solution was cooled to 0 °C to give colorless crystals which were filtered, washed with water (30 mL), and dried in an oven at 50 °C under reduced pressure. The dried solid was dissolved in EtOH, and the insoluble solid was removed by filtration. The filtrate was evaporated and dried at 50 °C under reduced pressure to give the sodium salt **12** (16.6 g, 69%).

To thionyl chloride (32.5 mL, 445 mmol) was added portionwise the sodium salt **12** (17.2 g, 59.4 mmol) over a period of 1 h and the mixture was vigorously stirred at room temperature for 2.5 h. Excess amount of thionyl chloride was stripped off under reduced pressure. To the residual oil was added Et_2O (50 mL) and then added dropwise a solution of diacetone D-glucose (14.1 g, 54.0 mmol) and pyridine (6.70 mL, 89.1 mmol) in Et_2O (50 mL) at 0 °C over a period of 20 min. After stirring overnight at room temperature, the mixture was poured into 1 mol/L HCl (50 mL) and extracted with Et_2O. The combined organic extracts were washed with saturated $NaHCO_3$ (20 mL), water (20 mL), and brine (20 mL). The solution was dried over $MgSO_4$ and concentrated to give the crude sulfinate. It was purified by column chromatography (silica gel, hexane/ethyl acetate = 92/8) to give a diastereomeric mixture of the sulfinate **4** (20.5 g, 73%) in a ratio of S_R:S_S = 38:62, which was determined by ^{1}H NMR. Each diastereoisomer was isolated by flash column chromatography. Further, the (*R*)-diastereoisomer was purified by recrystallization from hexane/Et_2O.

(*R*)-(+)-Diacetone D-Glucose 2,4,6-Triisopropylbenzenesulfinate Ester ((*R*)-3): $R_f = 0.64$ (hexane/ethyl acetate = 8/2); HPLC $t_R = 9.90$ min (eluent, hexane/ethyl acetate = 85/15); mp 142.3−143.0 °C; $[\alpha]^{18}_D = +11.0$ (*c* 1.04, acetone); ^{1}H NMR δ 1.17, 1.34, 1.39, 1.51 (4s, 12H), 1.24, 1.28 (2d, *J* = 6.9, 6.9 Hz, 18H), 2.77−3.00 (m, 1H), 3.91−4.07 (m, 5H), 4.19 (dd, *J* = 2.7, 7.9 Hz, 1H), 4.84 (d, *J* = 2.7 Hz, 1H), 4.88 (d, *J* = 3.6 Hz, 1H), 5.89 (d, *J* = 3.6 Hz, 1H), 7.08 (s, 2H); ^{13}C NMR δ 23.7, 24.2, 24.5, 25.1, 26.3, 26.9, 28.2, 34.4, 67.2, 72.0, 80.8, 82.6, 84.0, 105.3, 109.2, 112.5, 122.7, 137.9, 148.7, 153.2; IR (KBr) 2950, 1595, 1455, 1370, 1250, 1210, 1130, 1070, 1020 cm^{-1}; MS (EI) *m*/*e* 510 (M^+, 0.1), 495 (6), 250 (100), 233 (95). Anal. Calcd for $C_{27}H_{42}O_7S$: C, 63.50; H, 8.29. Found: C,63.40; H, 8.39.

(*S*)-(−)-Diacetone D-Glucose 2,4,6-Triisopropylbenzenesulfinate Ester ((*S*)-3): $R_f = 0.59$ (hexane/ethyl acetate = 8/2); HPLC $t_R = 11.18$ min (eluent, hexane/ethyl acetate = 85/15); $[\alpha]^{18}_D = -36.2$ (*c* 0.636, acetone); ^{1}H NMR δ 1.25, 1.36, 1.44, 1.52 (4s, 12H), 1.23−1.31 (m, 18H), 2.76−3.01 (m, 1H), 3.92−4.12 (m, 4H), 4.21 (dd, *J* = 2.8, 8.0 Hz, 1H), 4.34 (ddd, *J* = 8.0, 5.5, 5.5 Hz, 1H), 4.61 (d, *J* = 3.7 Hz, 1H), 4.85 (d, *J* = 2.8 Hz, 1H), 5.81 (d, *J* = 3.7 Hz, 1H), 7.10 (s, 2H); ^{13}C NMR δ 23.7, 24.1, 24.6, 25.3, 26.2, 26.8, 26.9, 28.2, 34.4, 67.1, 72,0, 80.3, 80.9, 83.2, 105.0, 109.4, 112.4, 122.9, 137.6, 148.9, 153.3; IR (neat) 2950, 1595, 1455, 1370, 1210, 1120, 1070, 1020 cm^{-1}; MS (EI) *m*/*e* 510 (M^+, 4), 495 (67), 187 (45), 163 (53), 151 (76), 129 (95), 100 (66), 85 (100). Anal. Calcd for $C_{27}H_{42}O_7S$: C, 63.50; H, 8.29. Found: C, 63.29; H, 8.50.

(*S*)-(−)-3,5-Di-*tert*-butyl-4-methoxyphenyl Methyl Sulfoxide ((*S*)-9). To a solution of the sulfinate (*R*)-**2** (1.09 g, 2.58 mmol) in a mixed solvent of Et_2O (4 mL) and THF (1.6 mL) was added dropwise a solution of MeMgI (6.44 mmol) in Et_2O (5 mL) at 0 °C over a period of 3 min. The reaction mixture was allowed to warm to room temparature and stirred for 10 min. The mixture was then quenched with saturated NH_4Cl (5 mL) at 0 °C and concentrated under reduced pressure. The aqueous mixture was extracted with AcOEt. The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, and concentrated to give the crude sulfoxide, which was purified by column chromatography (silica gel, hexane/ethyl acetate = 5/5) to give the sulfoxide (*S*)-**9** (678 mg, 93%) as a colorless solid: $R_f = 0.29$ (hexane/ethyl acetate = 5/5); mp 111−112 °C; $[\alpha]^{19}_D = -94.5$ (*c* 0.346, acetone); CD (2,2,4-trimethylpentane) 251 ($[\theta]$ -7.71×10^4) and 222 ($[\theta]$ $+1.22 \times 10^5$) nm; ^{1}H NMR δ 1.45 (s, 18H), 2.72 (s, 3H), 3.72 (s, 3H), 7.51 (s, 2H); ^{13}C NMR δ 31.8, 36.2, 43.7, 64.4, 121.9, 138.6, 145.4, 161.9; IR (KBr) 2950, 1450, 1210, 1110, 1040, 1010 cm^{-1}; MS (EI) *m*/*e* 282 (M^+, 57), 267 (100), 252 (8), 237 (14). Anal. Calcd for $C_{16}H_{26}O_2S$: C, 68.04; H, 9.28. Found: C, 67.81; H, 9.51.

(*R*)-(+)-Methyl 2,4,6-Triisopropylphenyl Sulfoxide ((*R*)-13). The reaction was carried out as described above using the sulfinate (*S*)-**3** (1.27 g, 2.49 mmol) to give the sulfoxide (*R*)-**13** (620 mg, 94%) as a colorless solid: $R_f = 0.20$ (hexane/

ethyl acetate = 8/2); mp 119.5−120.0 °C; $[\alpha]^{22}_D = +105.8$ (*c* 0.820, $CHCl_3$) ((*S*)-isomer $[\alpha]^{22}_D = -105.2$ (*c* 1.05, $CHCl_3$)); CD (2,2,4-trimethylpentane) 267 ($[\theta]$ $+6.19 \times 10^4$) and 220 ($[\theta]$ -1.20×10^5) nm; ^{1}H NMR δ 1.24, 1.25, 1.32 (3d, J = 6.7, 7.0, 6.8 Hz, 18H), 2.76−2.98 (m, 1H), 2.93 (s, 3H), 3.84−4.12 (m, 2H), 7.06 (s, 2H); ^{13}C NMR δ 23.7, 24.0, 24.6, 27.9, 34.2, 40.6, 123.0, 135.1, 149.5, 152.2; IR (KBr) 2970, 1600, 1460, 1050 cm^{-1}; MS (EI) *m*/*e* 266 (M$^+$, 19), 249 (100), 234 (15). Anal. Calcd for $C_{16}H_{26}OS$: C, 72.13; H, 9.84. Found: C, 72.21; H, 9.98.

Preparation of the Chiral 2-(Arylsulfinyl)-2-cycloalkenones. (*S*)-(+)-6-[(2,4,6-Triisopropylphenyl)sulfinyl]-1,4-dioxaspiro[4.4]nona-6-ene (15c). The sulfoxide **15c** was prepared by a modified procedure described in the literature.[21] To a solution of *n*-BuLi (6.57 mL, 1.51 mol/L, 9.92 mmol) in THF (20 mL) was added dropwise a solution of 6-bromo-1,4-dioxaspiro[4.4]non-6-ene (**14a**)[22] (2.04 g, 9.95 mmol) in THF (10 mL) over a period of 5 min at −100 °C. The mixture was stirred at −100 °C for 20 min and then added rapidly to a solution of the sulfinate (*S*)-**3** (3.90 g, 7.64 mmol) in THF (7.6 mL) at −100 °C. After stirring at the same temperature for 30 min, the reaction mixture was quenched with a saturated solution of NaH_2PO_4 (30 mL). THF was evaporated under reduced pressure and the resultant mixture was extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and concentrated to give a crude oil, which was purified by column chromatography (silica gel, hexane/ethyl acetate = 8/2) to give the sulfoxide **15c** (2.63 g, 91%): $[\alpha]^{17}_D = +131.1$ (*c* 0.860, $CHCl_3$); ^{1}H NMR δ 1.15−1.35 (m, 18H), 2.16−2.30 (m, 2H), 2.38−2.58 (m, 2H), 2.77−3.01 (m, 1H), 3.38−3.52 (m, 1H), 3.68−4.10 (m, 5H), 6.13 (t, J = 2.7 Hz, 1H), 7.05 (s, 2H); ^{13}C NMR δ 23.8, 24.1, 24.5, 28.0, 28.8, 34.4, 38.2, 65.1, 118.5, 122.6, 133.9, 140.1, 147.8, 152.8; IR (neat) 2950, 1590, 1455, 1310, 1160, 1130, 1040, 1025 cm^{-1}; MS (EI) *m*/*e* 376 (M$^+$,48), 359 (48), 284 (40), 189 (100). Anal. Calcd for $C_{22}H_{32}O_3S$: C, 70.17; H, 8.57. Found: C, 70.02; H, 8.72.

(*S*)-(+)-2-[(2,4,6-Triisopropylphenyl)sulfinyl]-2-cyclopentenone (16c). A 15% sulfuric acid solution (12 drops) was added to a suspension of SiO_2 (3.0 g) in CH_2Cl_2 (5 mL) and stirred for 5 min. Then a solution of the sulfoxide **15c** (1.07 g, 2.83 mmol) in CH_2Cl_2 (5 mL) was added and stirred for 1 h. After the mixture was stirred for 5 min with a small amount of $NaHCO_3$, the solid was filtered and washed with CH_2Cl_2 (15 mL). The filtrate was concentrated to give the sulfoxide **16c** (932 mg, 99%), which was further purified for analyses by recrystallization from hexane/Et_2O: R_f = 0.41 (hexane/ethyl acetate = 6/4); mp 139.5−140.4 °C; $[\alpha]^{17}_D = +229.2$ (*c* 0.22, $CHCl_3$); ^{1}H NMR δ 1.14, 1.23, 1.31 (3d, J = 6.7, 6.9, 6.7 Hz, 18H), 2.40−2.99 (m, 5H), 3.68−4.01 (m, 2H), 7.04 (s, 2H), 8.09 (t, J = 2.8 Hz, 1H); ^{13}C NMR δ 23.7, 24.7, 27.5, 28.2, 34.3, 38.2, 123.1, 131.9, 150.9, 151.3, 153.2, 162.9, 201.6; IR (KBr) 2975, 1705, 1590, 1460, 1430, 1290, 1240, 1160, 1050, 1030 cm^{-1}; MS (EI) *m*/*e* 332 (M$^+$, 8), 284 (50), 269 (30), 227 (22), 189 (100). Anal. Calcd for $C_{20}H_{28}O_2S$: C, 72.25; H, 8.49. Found: C, 72.13; H, 8.68.

General Procedure for the Radical Addition to 16. A solution of the 2-(arylsulfinyl)-2-cyclopentenone **16** in CH_2Cl_2 (0.01 mol/L) was degassed under reduced pressure with a sonicator. After the solution was cooled to 0 °C, trialkylborane[26] (10 equiv) (method A) or triethylborane (10 equiv)/alkyl iodide (10 equiv) (method B) was added. The reaction in the presence of Lewis acid was carried out by adding Lewis acid at 0 °C and the mixture was stirred for 1 h before addition of trialkylborane (method A) or triethylborane/alkyl iodide (method B). Then the air was passed into the solution at a rate of 90 μL/min for 1 mmol of trialkylborane with a microfeeder. The reaction mixture was poured into saturated NaH_2PO_4 and extracted with Et_2O (three times). The combined organic extracts were dried over Na_2SO_4 and concentrated to give a crude product, which was purified by column chromatography to give the addition product. Diastereomeric ratios were determined by the integration of the methine proton α to the sulfoxide in the ^{1}H NMR spectra of the crude products. These addition products could not be stored for long time without decomposition even in a refrigerator, possibly because of the syn-elimination. The spectral data of the addition product are listed below.

(3*R*)-3-*tert*-Butyl-2-[(2,4,6-triisopropylphenylsulfinyl)-1-cyclopentanone (24): R_f = 0.70 (hexane/ethyl acetate = 6/4); ^{1}H NMR δ 0.81 (s, 9H), 1.23−1.29 (m, 18H), 1.80−2.06 (m, 1H), 2.17−2.66 (m, 4H), 2.78−3.01 (m, 1H), 3.42 (d, J = 4.2 Hz, 1H), 3.39−4.03 (m, 2H), 7.07 (s, 2H); IR (neat) 2950, 1700, 1595, 1460, 1050 cm^{-1}

General procedure for oxidation of the addition products to the sulfones. To a solution of addition products in CH_2Cl_2 (0.1 mol/L) was added portionwise *m*-chloroperbenzoic acid (2 equiv) at 0 °C, and stirred for 1−5 h. The reaction mixture was poured into a mixture of saturated $NaHSO_3$ and Et_2O. The aqueous layer was extracted with Et_2O (3 times). The combined organic extracts were washed successively with saturated $NaHCO_3$, water, and brine. The solution was dried over $MgSO_4$ and concentrated, which was purified by column chromatography to give the corresponding sulfone.

3-*tert*-Butyl-2-[(2,4,6-triisopropylphenyl)sulfonyl]-1-cyclopentanone (36): yield 76%; R_f = 0.64 (hexane/ethyl acetate = 8/2); ^{1}H NMR δ 0.92 (s, 9H), 1.15−1.40 (m, 18H), 1.88−2.12 (m, 1H), 2.18−2.80 (m, 3H), 2.81−3.04 (m, 2H), 3.63 (d, J = 2.5 Hz, 1H), 3.78−4.02 (m, 2H), 7.19 (s, 2H); ^{13}C NMR δ 22.1, 23.5, 24.5, 25.3, 27.3, 29.8, 33.5, 34.2, 37.8, 46.2, 74.2, 124.1, 131.1, 151.6, 153.9, 209.2; IR (KBr) 2955, 1735, 1605, 1470, 1370, 1295, 1140 cm^{-1}; MS (EI) *m*/*e* 406 (M$^+$, 1), 349 (12), 307 (12), 267 (100). Anal. Calcd for $C_{24}H_{38}O_3S$: C, 70.89; H, 9.42. Found: C, 70.68; H, 9.38.

Determination of Enantiomeric Purity of 3-Substituted Cycloalkanones. The addition products were treated with excess amounts of freshly prepared aluminum amalgam in a mixed solvent of THF and H_2O (THF/H_2O = 9/1) at room temperature to give 3-alkyl-1-cycloalkanones, which were then converted to the cyclic aminals by mixing with (1*R*,2*R*)-1,2-diphenylethylenediamine in the NMR tubes in the presence of 4 Å molecular sieve. The ^{13}C NMR spectra showed clearly separated signals of each stereoisomers. Spectral data of 3-alkyl-1-cyclopentanones and their aminals are as follows.)-It was difficult to completely remove the solvent from the 3-alkyl-1-cycloalkanones **41a**, **41b**, **41c**, and **43** due to their volatility.)

3-*tert*-Butyl-1-cyclopentanone (41d):[32d] R_f = 0.45 (hexane/ethyl acetate = 8/2); $[\alpha]^{22}_D = -160.7$ (*c* 0.264, MeOH) (lit.[32d] $[\alpha]^{25}_D = -161.9$ (*c* 0.86, MeOH); ^{1}H NMR δ 0.91 (s, 9H), 1.09−1.34 (m, 1H), 1.49−1.75 (m, 1H), 1.77−2.47 (m, 5H)

(2*R*,3*R*,7*S*)-1,4-Diaza-2,3-diphenyl-7-*tert*-butylspiro[4.4]nonane ((7*S*)-42d): ^{13}C NMR δ 25.14, 27.35, 31.84, 40.44, 42.43, 48.71, 70.13, 86.69, 126.98, 127.26, 127.80, 127.92, 128.15, 128.36, 140.82, 141.50

(2*R*,3*R*,7*R*)-1,4-Diaza-2,3-diphenyl-7-*tert*-butylspiro[4.4]nonane ((7*R*)-42d): ^{13}C NMR δ 25.68, 27.44, 31.84, 41.52, 43.05, 49.14, 70.29, 70.50, 86.49, 126.98, 127.26, 127.80, 127.92, 128.15, 128.36, 140.47, 140.82

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Supporting Information Available: Spectroscopic characterization for **15a**,**b**,**d**−**f**, **16a**,**b**,**d**−**f**, **17**−**23**, **25**−**35**, **37**−**40**, **41a**−**c**, **42a**−**c**, **43, and 44** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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