Diastereomer-Differentiating Radical *β*-Addition to 4- or 5-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones

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Addition of alkyl radicals to a diastereomeric mixture of (4*R*)- and (4*S*)-4-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones gave the diastereomerically pure addition product derived from the (4*R*)-isomer, while the (4*S*)-isomer remained unreacted. The *tert*-butyl radical addition to a diastereomeric mixture of (5*R*)- and (5*S*)-5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones also gave the diastereomerically pure addition product. These results show that (4*R*) and (4*S*) or (5*R*) and (5*S*) diastereomers were kinetically separated in the radical *β*-addition. The 1,2- and 1,3-steric interactions in the radical addition to 4- or 5-methyl-2-cyclopentenones were also examined.

Radical-mediated conjugate addition to α,*β*-unsaturated carbonyl compounds is an important procedure for the carbon−carbon bond formation.[1] A number of radical asymmetric reactions, in particular, involve induction of chirality at the position α or *β* to the carbonyl. In the nucleophilic addition to chiral 2-(arylsulfinyl)-2-cycloalkenones, the *p*-tolylsulfinyl group effectively acts as a chiral auxiliary to give addition products in good diastereomeric excess.[2] On the other hand, we found that the stereoselectivity in the radical reaction depended largely upon the substituent on the sulfoxide and reported a complete diastereofacial control of cycloalkenes *β* to a carbonyl group by a chiral sulfoxide bearing an *o*-alkyl-substituted phenyl group,[3] in which a *tert*-butyl, isopropyl, or even an ethyl radical added to (*S*)-2-[(2,4,6-triisopropylphenyl)sulfinyl]- and (*S*)-2-[(2,4,6-trimethylphenyl)sulfinyl]-2-cyclopentenones to give addition products in good yields with extremely high diastereofacial selection; moreover, it was found that diastereoselectivity could be reversed by the chelation with a bidentate Lewis acid. There are several reports on the stereoselectivity in trapping the *β*- or *γ*-substituted five-membered cyclic radicals with tributyltin hydride or allyltributyltin showing moderate to high diastereoselectivity,[4] whereas there are only a few reports on the stereoselectivity of the radical addition to α,*β*-unsaturated cycloalkenones having substituents.[5] We report herein the radical *β*-addition to 4- and 5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone in order to clarify the steric influence of the substituent on the cyclopentenone as well as the sulfinyl group.

Results and Discussion

4-Methyl- and 5-methyl-2-(arylsulfinyl)-2-cyclopentenones **4a** and **4b** were prepared by the reaction of a chiral sulfinate with the corresponding cyclopentenyllithiums as shown in Scheme 1. A THF solution of 6-bromo-8-methyl-1,4-dioxaspiro[4.4]non-6-ene (**2a**),[6] which was prepared from 4-methyl-2-cyclopentenone (**1a**),[7] was treated with *n*-BuLi at −100 °C to give the vinyllithium. The vinyllithium was reacted with diacetone D-glucose 2,4,6-triisopropylbenzenesulfinate ester[3a] to afford a diastereomeric mixture of 8-methyl-6-[(2,4,6-triisopropylphenyl)sulfinyl]-1,4-dioxaspiro[4.4]non-6-ene (**3a**) in 93% yield in a ratio of 50:50. The acetal was deprotected by treatment with silica gel containing a small amount of sulfuric acid[8] to give 4-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**4a**) in 99% yield. (4*R*)- and (4*S*)-diastereomers **4a** were isolated by flash column chromatography. The absolute configuration of **4a** was established by the X-ray crystallographic analysis of the less polar diastereomer (4*S*)-**4a** (Figure 1). Similarly, 5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**4b**) was prepared from 5-methyl-2-cyclopenten-

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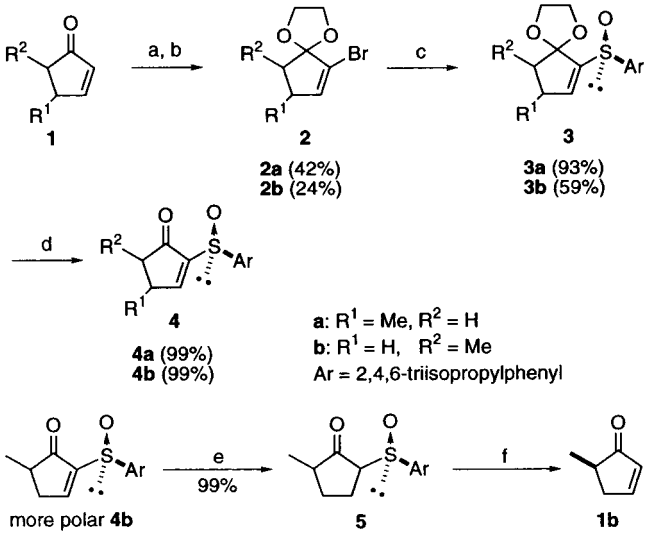
Scheme 1[a]



[a] Key: (a) Br_2, Et_3N, CH_2Cl_2, 0 °C; (b) $HOCH_2CH_2OH$, *p*-TsOH, benzene, reflux; (c) *n*-BuLi, (*S*)-diacetone D-glucose 2,4,6-triisopropylbenzenesulfinate ester, THF, −100 °C; (d) H_2SO_4−SiO_2, CH_2Cl_2, rt; (e) DIBAL, THF, −78 °C; (f) CCl_4, reflux.

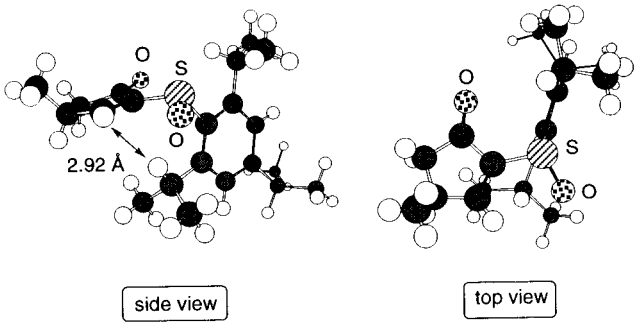
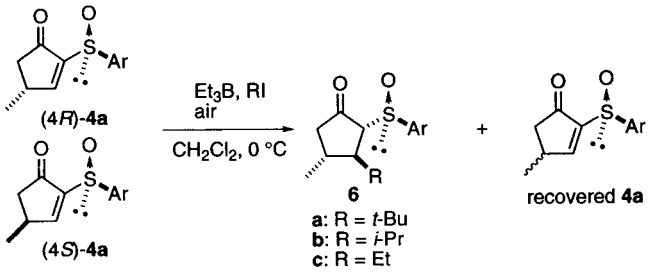


Figure 1. Chem 3D representation of the X-ray structure of (4*S*)-**4a**.

one (**1b**).[9a] The absolute configuration of **4b** was determined as shown in Scheme 1. Reduction of the more polar diastereomer **4b** with diisobutylaluminum hydride and subsequent syn-elimination of the sulfenic acid[10] by heating under reflux in CCl_4 afforded (5*R*)-5-methyl-2-cyclopentenone (**1b**), the structure of which was determined by comparison of the optical rotation with the value for the known compound.[9b]

First, we studied the radical *β*-addition to 4-methyl-2-(arylsulfinyl)-2-cyclopentenone **4a**. Results are shown in Table 1. Addition of alkyl radicals to 4-methyl-2-(arylsulfinyl)-2-cyclopentenone **4a** was carried out as follows. To a degassed 0.01 mol/L CH_2Cl_2 solution of a 69:31 diastereomeric mixture of (4*R*)- and (4*S*)-**4a** was added 5 equiv of *tert*-butyl iodide[11] and 5 equiv of triethylborane as a radical initiator[12] at 0 °C, and then air was continuously passed through the solution via a needle by a microfeeder.[13] After being stirred for 1 h, the addition product **6a** was obtained in 68% yield

Table 1. Radical *β*-Addition to 4-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (4a)



			time	**6**	recovered **4a**	
entry	4*R*:4*S*	R	(h)	yield (%)	yield (%)	4*R*:4*S*
1	69:31	*t*-Bu	1	68 (99)[a]	31	2:>98
2	69:31	*i*-Pr	1.3	67 (97)[a]	25	2:>98
3	69:31	Et	1.5	55 (80)[a]	31	18:82
4	100:0	*t*-Bu	1	99	0	
5	100:0	*i*-Pr	1	92	0	
6	100:0	Et	1	76	0	
7	0:100	*t*-Bu	24	0	100	
8	0:100	*i*-Pr	1	*b*	59	
9	0:100	Et	1	*b*	67	

[a] Yields in parentheses are based on the (4*R*)-**4a** isomer. [b] Several unidentified products were obtained.

together with the starting **4a** recovered in 31% yield (Table 1, entry 1). We did not observe the competitive addition of an ethyl radical generated from triethylborane according to the mechanism for the radical addition (Supporting Information). The addition product **6a** was found to be a single diastereomer by the analysis of the ^{1}H NMR spectrum. Furthermore, the recovered **4a** was composed of only (4*S*)-**4a**. Thus, (4*R*)-**4a** was reacted quantitatively with a *tert*-butyl radical to give the addition product **6a** (99% yield based on (4*R*)-**4a**), while (4*S*)-**4a** remained entirely unreacted. The reaction of the same diastereomeric mixture of (4*R*)- and (4*S*)-**4a** with an isopropyl radical gave the addition product **6b** as a single diastereomer in 67% yield (97% yield based on (4*R*)-**4a**) together with the starting (4*S*)-**4a** recovered in 25% yield (Table 1, entry 2). Surprisingly, the reaction with a less bulky ethyl radical gave the diastereomerically pure addition product **6c** in 55% yield (80% yield based on (4*R*)-**4a**) when **4a** was recovered in 31% yield as an 18:82 mixture of (4*R*)- and (4*S*)-**4a** (Table 1, entry 3). These results show that (4*R*)-**4a** is much more reactive toward alkyl radicals than (4*S*)-**4a**, and hence, a diastereomeric mixture of **4a** can be kinetically separated. In fact, the diastereomerically pure (4*R*)-**4a** was reacted with *tert*-butyl, isopropyl, and ethyl radicals to give (2*R*,3*R*,4*R*)-**6a**, -**6b**, and -**6c**, respectively, in good to excellent yields within 1 h (Table 1, entries 4−6). On the other hand, the reaction of the diastereomerically pure (4*S*)-**4a** with a *tert*-butyl radical did not occur at all even after 24 h, where the starting (4*S*)-**4a** was quantitatively recovered (Table 1, entry 7). In the reactions of (4*S*)-**4a** with isopropyl and ethyl radicals, the starting (4*S*)-**4a** was recovered in lower yields due to the formation of several unidentified products (Table 1, entries 8 and 9).

The stereochemistry of the addition product **6a** was determined as follows (Scheme 2). The stereochemistry of the addition product at the 2- and 3-positions was determined to be trans, since a significant nuclear

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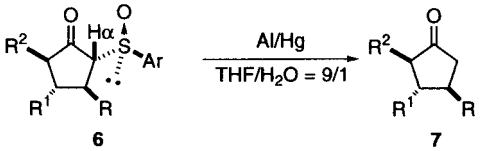
Scheme 2



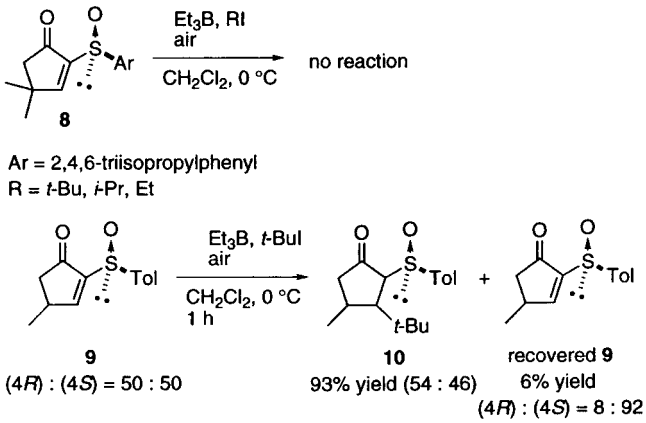
6 7

a: R^1 = Me , R^2 = H , R = *t*-Bu
b: R^1 = Me , R^2 = H , R = *i*-Pr
c: R^1 = Me , R^2 = H , R = Et
d: R^1 = H , R^2 = Me , R = *t*-Bu
Ar = 2,4,6-triisopropylphenyl

Overhauser effect (21%) was observed between the proton α to the sulfinyl group and the methyl protons of the *tert*-butyl group.[14] In addition, desulfurization of **6a** with aluminum amalgam[15] gave the *trans*-3-*tert*-butyl-4-methylcyclopentanone (**7a**), the trans configuration of which was confirmed by ^{1}H and ^{13}C NMR. Furthermore, this compound was identical to the one obtained in the *tert*-butyl radical addition to 4-methyl-2-cyclopentenone (**1a**) (vide infra). Since the structure of the starting compound (4*R*)-**4a** was confirmed by the X-ray crystallographic analysis of (4*S*)-**4a** (Figure 1), the stereochemistry of **6a** was assigned to be (2*R*,3*R*,4*R*). This stereochemical outcome shows that the alkyl radical approaches from the side opposite to the aryl moiety in an antiperiplanar orientation of the carbonyl and sulfoxide bonds (vide infra). This is in accord with the previously obtained stereochemical results in the alkyl radical addition to 2-(arylsulfinyl)-2-cyclopentenones.[3] The structure of the adducts **6b** and **6c** was deduced from the results described above as well as the desulfurization of **6b** to the known *trans*-3-isopropyl-4-methylcyclopentanone (**7b**),[16] which was identified with the product obtained in the isopropyl radical addition to 4-methyl-2-cyclopentenone (vide infra).

Generally, a transition state of a radical addition to a double bond can be approximated to a reactant.[17] Therefore, the reaction pathway of this stereospecific radical addition may be explained by the results of the X-ray crystallographic analysis and nuclear Overhauser effect measurements of the ^{1}H NMR. The X-ray analysis of (4*S*)-**4a** is shown in Figure 1. The X-ray crystallographic analysis of (4*S*)-**4a** clearly shows that the carbonyl and sulfoxide bonds take an antiperiplanar arrangement and the olefin face is effectively shielded at the β-position by one of the *o*-isopropyl groups on the phenyl. The distance between the methine proton of the isopropyl group and the β-proton was 2.92 Å. A similar conformation is presumed in solution because a nuclear Overhauser effect (12%) was observed between the methine proton of the isopropyl group and the β-proton. In the case of (4*S*)-**4a**, attacks of an alkyl radical from both the *Re* and *Si* faces are inhibited by the *o*-isopropyl group on the phenyl ring and by the 4-methyl group on the cyclopentenone ring, respectively; therefore, the radical addition does not occur from either side, especially with a *tert*-butyl radical. This assumption was supported by the following reactions. The radical reaction of 4,4-dimethyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**8**) with *tert*-butyl, isopropyl, and ethyl radicals did not give the addition products at all but resulted in the complete recovery of the starting **8** (Scheme 3). Thus, the 2,4,6-triisopropylphenyl group on sulfur plays a critical role in inducing remarkable stereoselection in the radical addition. This is understood by the reaction of 4-methyl-2-(*p*-tolylsulfinyl)-2-cyclopentenone (**9**). The radical addition of a *tert*-butyl radical to a 50:50 diastereomeric mixture of (4*S*)- and (4*R*)-4-methyl-2-(*p*-tolylsulfinyl)-2-cyclopentenones (**9**) gave, after 1 h, a 54:46 diastereomeric mixture of the addition products **10** in 93% yield together with the recovery of an 8:92 diastereomeric mixture of (4*R*)- and (4*S*)-**9** in 6% yield (Scheme 3). The addition products **10** were tentatively assigned as (2*R*,3*R*,4*R*)- and (2*S*,3*S*,4*S*)-isomers, since oxidation of **10** gave the sulfone as a single diastereomer. This stereochemical outcome is in accord with the previously observed low stereoselective results in the *tert*-butyl radical addition to 2-(*p*-tolylsulfinyl)-2-cyclopentenone.[3]

Scheme 3



The results obtained above show that a substituent adjacent to the reaction site has a significant effect on the stereoselectivity in the radical addition to 2-cyclopentenone. To confirm the 1,2- and 1,3-steric interactions in the radical addition to 2-cyclopentenone, the radical additions to 4- or 5-methyl-2-cyclopentenones were examined. Results are shown in Table 2. The 4-methyl group vicinal to the reaction site markedly affected the direction of the attack of *tert*-butyl and isopropyl radicals to the olefin to give only trans isomers. The notable 1,2-steric interaction in 4-methyl-2-cyclopentenone (**1a**) is in accord with the results previously reported on the selective formation of the trans adducts in the 1,4-conjugate addition of organocuprates to 4-methyl-2-cyclopentenone[16,18] and in the radical β-addition to 4-isopropyl-2-cyclohexenone.[5a] On the other hand, it was surprising that the *tert*-butyl radical addition to 5-methyl-2-cyclopentenone (**1b**) gave the cis addition product *cis*-**7d** as a major diastereomer (trans:cis = 32:68 in CH_2Cl_2; 24:76 in *i*-PrOH determined by GC).[19] This result is in contrast to the 1,4-conjugate addition to 5-methyl-2-cyclopentenone with Me_2CuLi, which gives a trans/cis mixture in a

(14) Only the trans compounds were formed in all reactions. The final products were formed via hydrolysis of the boron enolates; see the Supporting Information. 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; see also ref 3a.

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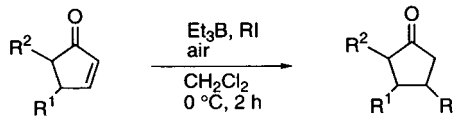
Table 2. Radical β-Addition to 4- or 5-Methyl-2-cyclopentenone



1a: R^1 = Me, R^2 = H
1b: R^1 = H, R^2 = Me

7a: R^1 = Me, R^2 = H, R = *t*-Bu
7b: R^1 = Me, R^2 = H, R = *i*-Pr
7d: R^1 = H, R^2 = Me, R = *t*-Bu

entry	substrate	R	product	yield (%)	trans/cis
1	**1a**	*t*-Bu	**7a**	92	>98:2[a]
2	**1a**	*i*-Pr	**7b**	59	>98:2[a]
3	**1b**	*t*-Bu	**7d**	75	32:68[b]
4[c]	**1b**	*t*-Bu	**7d**	64	24:76[b]

[a] Determined by ^{1}H and ^{13}C NMR. [b] Determined by ^{1}H NMR and GC. [c] The reaction was carried out in *i*-PrOH.

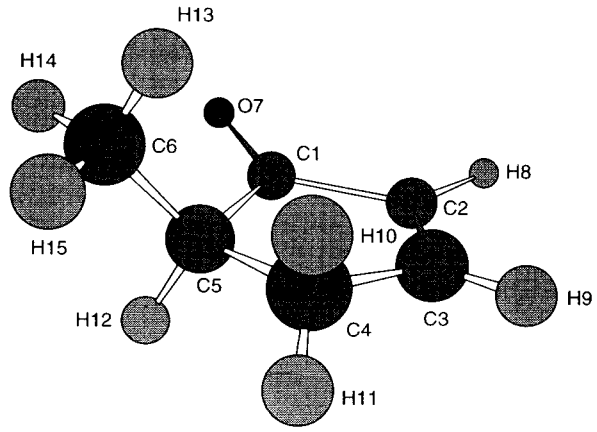
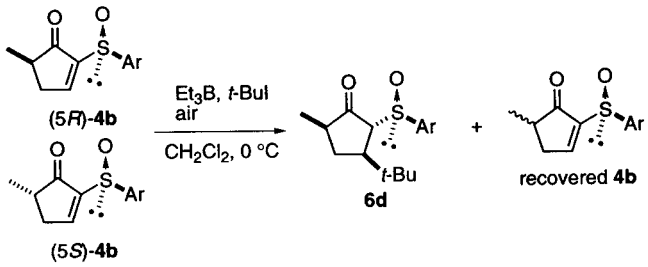


Figure 2. Optimized energy minimum structure of 5-methyl-2-cyclopentenone (**1b**).

ratio of 3.5:1.[18] To clarify the energy-minimized structure of 5-methyl-2-cyclopentenone (**1b**), we performed ab initio calculations using the Gaussian 94 program at the MP2 level of theory with the 6-31G* basis set.[20] The minimized structure is shown in Figure 2. The protons, H(10) and H(11), vicinal to the reaction site seem not to have much influence on the direction of the approach of a *tert*-butyl radical because H(10) and H(11) are placed a similar distance from C(3): C(3)−H(10), 2.151 Å; (C)−H(11), 2.165 Å. The distances of C(3)−H(12), C(3)−C(6), and C(3)−H(13) are 3.051, 3.629, and 3.648 Å, and the torsional angles of C(3)−C(4)−C(5)−H(12) and C(3)−C(4)−C(5)−C(6) are 107.0° and −129.2°, respectively. Therefore, the 5-methyl group bends to the outside, and hence, the 5-methine proton directs toward the perpendicular to the cyclopentenone face. The approach of a *tert*-butyl radical from the side opposite to the methyl would be interrupted to some extent by this proton, and the radical would approach more favorably from the methyl side to give the cis adduct.

Table 3. Radical β-Addition to 5-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (4b)



entry	5*R*:5*S*	*t*-BuI (equiv)	time (h)	**6d** yield (%)	recovered **4b** yield (%)	5*R*:5*S*
1	43:57	1.5	0.5	40 (93)[a]	42	7:93
2	43:57	3.0	0.5	*b*	46	2:98
3	43:57	5.0	0.5	*b*	34	3:97
4[c]	43:57	5.0	3	*b*	43	2:>98
5	100:0	10	1	97	0	
6	1:99	10	1	0	100	
7	1:99	10	15	*d*	12	

[a] Yields in parentheses are based on the (5*R*)-**4b** isomer. [b] The addition of **6d** and several unidentified products were formed. [c] The reaction was carried out at −78 °C. [d] Several unidentified products were formed.

This unexpected outcome prompted us to examine the radical addition of a *tert*-butyl radical to 5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (**4b**). The results are shown in Table 3. A 43:57 diastereomeric mixture of (5*R*)- and (5*S*)-5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones ((5*R*)- and (5*S*)-**4b**) was reacted with 1.5 equiv of *tert*-butyl iodide in the presence of 1.5 equiv of triethylborane to give the addition product **6d** as a single diastereomer in 40% yield (93% yield based on (5*R*)-**4b**) together with a 7:93 diastereomeric mixture of (5*R*)- and (5*S*)-**4b** (42%) (Table 3, entry 1). In the reactions of the same diastereomeric mixture of (5*R*)- and (5*S*)-**4b** with more than 3 equiv of *tert*-butyl iodide in the presence of triethylborane, the addition product and several unidentified products were formed, although somewhat better diastereomeric ratios of recovered (5*R*)- and (5*S*)-**4b** were observed (Table 3, entries 2−4). The pure (5*R*)-**4b** was reacted with 10 equiv of *tert*-butyl iodide and triethylborane for 1 h to give the addition product **6d** in 97% yield as a single diastereomer (Table 3, entry 5). In the reaction of (5*S*)-**4b** using even a large excess amount of *tert*-butyl iodide, the formation of the addition product from (5*S*)-**4b** was not observed, giving the starting (5*S*)-**4b** in 100% yield after 1 h (Table 3, entry 6) and in 12% yield after 15 h together with several unidentified products (Table 3, entry 7).

The stereochemistry of the addition product **6d** was determined as follows (Scheme 2). The significant nuclear Overhauser effect (11%) observed in the ^{1}H NMR spectrum of **6d** between the proton α to the sulfinyl group and the methyl protons of the *tert*-butyl group showed the trans configuration at the 2- and 3-positions.[14] Desulfurization of the addition product **6d** with aluminum amalgam gave the known *cis*-4-*tert*-butyl-2-methylcyclopentanone (*cis*-**7d**).[21] This compound was identical to the major product obtained in the radical addition to 5-methyl-2-cyclopentenone (**1b**) (see above). Since the structure of the starting compound (5*R*)-**4b** was con-

(19) Syn attack of tributyltin hydride to the γ-substituted five-membered radical was reported: Beckwith, A. L. J.; Chai, C. L. L. *J. Chem. Soc., Chem. Commun.* **1990**, 1087.

(20) (a) After semiempirical results were obtained using the PM3 parameter set as implemented in MOPAC 6,[20b] ab initio calculations were performed with the Gaussian 94 program system.[20c] (b) MOPAC 6: Stewart, J. J. P. *QCPE Bull.* **1989**, *9*, 10. (c) Gaussian 94 (Revision E.2): Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. A.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1995.

firmed (Scheme 1), the stereochemistry of the addition adduct **6d** was assigned to be (2*R*,3*R*,5*R*).

Preferential formation of the 3,5-cis addition product **6d** can be rationalized by the following mechanistic consideration: From the results obtained in the reaction of 5-methyl-2-cyclopentenone (**1b**), the 2,4-cis compound **7d** is preferentially formed. In the reaction of (5*R*)-**4b**, the 3,5-cis compound **6d** should be more preferentially formed because the opposite *Re* face is completely shielded by the bulky 2,4,6-triisopropylphenyl group. On the other hand, (5*S*)-**4b** would not give the addition product because the 2,4,6-triisopropylphenyl group shields the preferential *Re* face.

In summary, the radical β-addition to 4- or 5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones gave the addition products as a single diastereomer sterically controlled by both the chiral sulfinyl group and the 4- or 5-methyl group on the cyclopentenone. (4*R*)-4-Methyl- and (5*R*)-5-methyl-2-[(2,4,6-triisopropylphenyl)-sulfinyl]-2-cyclopentenone reacted with alkyl radicals much faster than the corresponding (4*S*)- and (5*S*)-isomers, respectively. A diastereomeric mixture of these compounds could be kinetically separated to give optically active 3,4-dialkyl- and 2,4-dialkylcyclopentanones after desulfurization.

Experimental Section

Preparation of the 4- or 5-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenones. 6-Bromo-9-methyl-1,4-dioxaspiro[4.4]non-6-ene (2b). To a solution of 5-methyl-2-cyclopentenone (**1b**)[9] (2.37 g, 24.7 mmol) in CH_2Cl_2 (40 mL) was added dropwise a solution of bromine (1.33 mL, 25.8 mmol) in CH_2Cl_2 (37 mL) at 0 °C over a period of 20 min, and the mixture was stirred for 30 min at 0 °C. To this mixture was added dropwise a solution of triethylamine (5.16 mL, 37.0 mmol) in CH_2Cl_2 (18 mL) over a period of 15 min. The reaction mixture was stirred for 15 min and warmed to room temperature slowly. The reaction mixture was quenched with 1 mol/L HCl solution (40 mL). The mixture was extracted with CH_2Cl_2, and the combined organic extracts were washed with 10% $NaHSO_3$ solution (20 mL) and brine (20 mL) and dried over Na_2SO_4. The organic solution was filtered through the silica gel pad (20 g) and evaporated. To a solution of this residue (3.38 g) in benzene (120 mL) were added ethylene glycol (2.69 mL, 48.2 mmol) and *p*-toluenesulfonic acid (18.4 mg, 96.7 μmol). The flask was equipped with a Dean−Stark trap, and the mixture was heated to reflux with azeotropic removal of water over a period of 12 h. The flask was cooled and filtered through a silica gel pad (20 g) and $MgSO_4$ (20 g). The organic solution was concentrated to give the crude oil, which was purified by column chromatography (silica gel, hexane/ethyl acetate = 97/3) to give the bromo acetal **2b** (1.29 g, 24% yield based on 5-methyl-2-cyclopentenone). Since the bromo acetal **2b** was quite unstable, it had to be stored in the freezer: R_f = 0.73 (hexane/ethyl acetate = 70/30); ^{1}H NMR δ 1.07 (d, *J* = 6.9 Hz, 3H), 1.81−2.10 (m, 1H), 2.28−2.60 (m, 2H), 3.83−4.39 (m, 4H), 6.14 (t, *J* = 3.0 Hz, 1H); IR (neat) 2970, 1620, 1305, 1200, 1050 cm^{-1}.

8-Methyl-6-[(2,4,6-triisopropylphenyl)sulfinyl]-1,4-dioxaspiro[4.4]non-6-ene (3a). To a solution of *n*-BuLi (5.01 mL, 1.54 mol/L, 7.71 mmol) in THF (13 mL) at −100 °C was added dropwise a solution of 6-bromo-8-methyl-1,4-dioxaspiro[4.4]non-6-ene (**2a**)[6] (1.69 g, 7.71 mmol) in THF (6.0 mL) over a period of 5 min, and the mixture was stirred at −100 °C for 30 min. To this mixture was added rapidly a cooled solution of (*S*)-diacetone D-glucose 2,4,6-triisopropylbenzenesulfinate ester[3a] (3.03 g, 5.93 mmol) in THF (10 mL), and the reaction mixture was stirred for 30 min at −100 °C and subsequently warmed to room temperature slowly. The reaction mixture was quenched with saturated NaH_2PO_4 (5 mL) and concentrated under reduced pressure. The aqueous mixture was extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated to give the crude oil, which was purified by column chromatography (silica gel, hexane/ethyl acetate = 90/10) to give a diastereomeric mixture of the sulfoxide **3a** (2.15 g, 93% yield) in a ratio of 50:50 determined by ^{1}H NMR: R_f = 0.41 (hexane/ethyl acetate = 60/40); ^{1}H NMR δ 1.03−1.39 (m, 21H), 1.70−1.87 (m, 1H), 2.33−2.53 (m, 1H), 2.68−3.02 (m, 2H), 3.28−3.56 (m, 1H), 3.63−4.08 (m, 5H), 6.05 and 6.09 (2d, *J* = 2.3, 2.5 Hz, 1H), 7.05 (s, 2H); IR (KBr) 2960, 1330, 1135, 1050 cm^{-1}; MS (EI) *m*/*z* 390 (M$^+$, 100), 373 (65), 287 (73), 235 (47). Anal. Calcd for $C_{23}H_{34}O_3S$: C, 70.73; H, 8.77. Found: C, 70.55; H, 8.94.

9-Methyl-6-[(2,4,6-triisopropylphenyl)sulfinyl]-1,4-dioxaspiro[4.4]non-6-ene (3b). The reaction was carried out as described above using the sulfinate[3a] (1.61 g, 3.15 mmol) to give the sulfoxide **3b** (726 mg, 59%) in a ratio of 48:52 determined by HPLC: R_f = 0.49 (hexane/ethyl acetate = 70/30); t_R = 9.96, 11.14 min (hexane/ethyl acetate = 60/40); ^{1}H NMR δ 1.03 and 1.04 (2d, *J* = 6.8, 6.9 Hz, 3H), 1.13−1.40 (m, 18H), 1.88−2.17 (m, 1H), 2.22−2.72 (m, 2H), 2.78−3.02 (m, 1H), 3.38−4.40 (m, 6H), 5.95−6.10 (m, 1H), 7.06 (s, 2H); IR (neat) 2970, 1600, 1465, 1175, 1050 cm^{-1}; MS (EI) *m*/*z* 390 (M$^+$, 53), 373 (100). Anal. Calcd for $C_{23}H_{34}O_3S$: C, 70.73; H, 8.77. Found: C, 70.48; H, 8.63.

4-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (4a). A 15% sulfuric acid solution (8 drops) was added to a suspension of SiO_2 (2.0 g) in CH_2Cl_2 (4 mL) and stirred for 5 min. Then to this suspension was added a solution of the sulfoxide **3a** (889 mg, 2.28 mmol) in CH_2Cl_2 (5 mL) and the mixture was 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 diastereomeric mixture of sulfoxide **4a** (784 mg, 99%), which was separated by flash column chromatography (silica gel, hexane/ethyl acetate = 80/20). **(4*S*)-Isomer**: R_f = 0.46 (hexane/ethyl acetate = 60/40); t_R = 10.14 min (hexane/ethyl acetate = 60/40); mp 180−181 °C (recrystallized from hexanes−Et_2O); $[\alpha]^{25}_D$ = +165.0 (*c* 0.566, $CHCl_3$); ^{1}H NMR δ 1.05−1.44 (m, 21H), 2.18 (dd, *J* = 2.0, 19.0 Hz, 1H), 2.75 (dd, *J* = 6.4, 19.0 Hz, 1H), 2.72−2.98 (m, 1H), 2.98−3.20 (m, 1H), 3.73−3.96 (m, 2H), 7.04 (s, 2H), 7.95 (d, *J* = 2.6 Hz, 1H); ^{13}C NMR δ 19.8, 23.7, 24.7, 28.2, 34.3, 34.7, 44.8, 123.1, 131.7, 149.9, 150.9, 153.2, 167.7, 201.5; IR (KBr) 2960, 1705, 1050 cm^{-1}; MS (EI) *m*/*z* 346 (M$^+$, 7), 328 (8), 298 (44), 283 (29), 241 (18), 189 (100). Anal. Calcd for $C_{21}H_{30}O_2S$: C, 72.79; H, 8.73. Found: C, 72.65; H, 8.87. **(4*R*)-Isomer**: R_f = 0.44 (hexane/ethyl acetate = 60/40); t_R = 13.53 min (hexane/ethyl acetate = 60/40); $[\alpha]^{25}_D$ = +289.2 (*c* 0.448, $CHCl_3$); ^{1}H NMR δ 1.08−1.41 (m, 21H), 2.09 (dd, *J* = 2.5, 18.9 Hz, 1H), 2.80 (dd, *J* = 6.4, 18.9 Hz, 1H), 2.72−2.98 (m, 1H), 3.08−3.29 (m, 1H), 3.73−3.96 (m, 2H), 7.04 (s, 2H), 7.97 (d, *J* = 2.7 Hz, 1H); ^{13}C NMR δ 19.3, 23.6, 24.8, 28.1, 34.3, 34.4, 44.8, 123.1, 131.6, 150.1, 150.8, 153.1, 167.5, 201.2; IR (KBr) 2960, 1710, 1050 cm^{-1}; MS (EI) *m*/*z* 346 (M$^+$, 7), 330 (14), 298 (26), 283 (21), 252 (35), 236 (51), 221 (37), 203 (30), 189 (100). Anal. Calcd for $C_{21}H_{30}O_2S$: C, 72.79; H, 8.73. Found: C, 72.76; H, 8.66.

5-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (4b). The reaction was carried out as described above using the sulfoxide **3b** (721 mg, 1.84 mmol) to give the sulfoxide **4b** (638 mg, 99%), which was separated by flash column chromatography (silica gel, hexane/ethyl acetate = 80/20). **(5*S*)-Isomer:** R_f = 0.32 (hexane/ethyl acetate = 70/30); t_R = 12.64 min (hexane/ethyl acetate = 60/40); $[\alpha]^{26}_D$ = +114.6 (*c* 0.554, $CHCl_3$); ^{1}H NMR δ 1.05−1.40 (m, 21H), 2.38−2.60 (m, 2H), 2.75−3.13 (m, 2H), 3.78−4.01 (m, 2H), 7.03 (s, 2H), 8.05 (t, *J* = 2.8 Hz, 1H); ^{13}C NMR δ 15.5, 23.6, 24.7, 28.2, 34.3, 36.4, 42.1, 123.1, 131.8, 150.3, 150.9, 153.2, 161.0, 204.3; IR (neat) 2970, 1705, 1050 cm^{-1}; MS (EI) *m*/*z* 346 (M$^+$, 11), 328 (32), 298 (49), 283 (32), 189 (100). Anal. Calcd for $C_{21}H_{30}O_2S$: C, 72.79; H, 8.73. Found: C, 72.58; H, 8.55. **(5*R*)-Isomer**:

(21) Varech, D.; Jacques, J. *Bull. Soc. Chim. Fr.* **1969**, *10*, 3505.

R_f = 0.26 (hexane/ethyl acetate = 70/30); t_R = 17.12 min (hexane/ethyl acetate = 60/40); $[\alpha]^{26}_D$ = +172.0 (*c* 0.470, $CHCl_3$); ^{1}H NMR δ 1.09−1.42 (m, 21H), 2.35 (ddd, *J* = 2.8, 2.8, 20.0 Hz, 1H), 2.50−2.75 (m, 1H), 2.72−2.98 (m, 1H), 3.13 (ddd, *J* = 2.8, 6.7, 20.0 Hz, 1H), 3.73−3.96 (m, 2H), 7.05 (s, 2H), 8.06 (t, *J* = 2.8 Hz, 1H); ^{13}C NMR δ 16.0, 23.6, 23.7, 24.7, 28.2, 34.2, 36.2, 42.2, 123.1, 131.7, 149.8, 150.9, 153.1, 161.8, 204.0; IR (KBr) 2960, 1710, 1040 cm^{-1}; MS (EI) *m*/*z* 346 (M^+, 11), 328 (30), 298 (33), 203 (50), 189 (100). Anal. Calcd for $C_{21}H_{30}O_2S$: C, 72.79; H, 8.73. Found: C, 72.91; H, 8.77.

General Procedure for the Radical Addition to 4- or 5-Methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentenone (4). A solution of the cyclopentenone **4** in CH_2Cl_2 (0.01 mol/L) was degassed under reduced pressure by a sonicator. Alkyl iodide and triethylborane were added at 0 °C, and then the air was passed into the solution at a rate of 90 μL/min per 1 mmol of triethylborane by a microfeeder. To the reaction mixture was added acetic acid (10 equiv) to quench excess triethylborane.[22] No epimerization of the addition product **6d** was observed at the C-5 stereocenter. After being stirred for 10 min, the mixture was poured into saturated NaH_2PO_4 and extracted with Et_2O (three times). The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give the crude product, which was purified by column chromatography to give the addition products and unreacted substrates. Addition products could not be stored for a long time without decomposition even in a freezer possibly because of the syn-elimination. To confirm the characterization, the addition products were oxidized to the sulfones. See the Supporting Information.

3-*tert*-Butyl-4-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-1-cyclopentanone (6a): R_f = 0.46 (hexane/ethyl acetate = 80/20); ^{1}H NMR δ 0.70 (s, 9H), 1.13−1.43 (m, 21H), 1.83 (dd, *J* = 2.2, 3.7 Hz, 1H), 2.18−2.49 (m, 2H), 2.51−2.75 (m, 1H), 2.72−2.98 (m, 1H), 3.30−4.50 (m, 2H), 3.55 (dd, *J* = 2.2, 2.2 Hz, 1H), 7.07 (s, 2H); IR (neat) 2960, 1740, 1080 cm^{-1}.

3-Isopropyl-4-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-1-cyclopentanone (6b): R_f = 0.39 (hexane/ethyl acetate = 80/20); ^{1}H NMR δ 0.76, 0.82 (2d, *J* = 6.8, 6.8 Hz, 6H), 1.10−1.41 (m, 21H), 1.50−1.80 (m, 1H), 1.97−2.45 (m, 3H), 2.45−2.69 (m, 1H), 2.72−2.98 (m, 1H), 3.41 (dd, *J* = 1.6, 5.0 Hz, 1H), 3.42−4.07 (m, 2H), 7.07 (s, 2H); IR (KBr) 2965, 1750, 1050 cm^{-1}.

3-Ethyl-4-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-1-cyclopentanone (6c): R_f = 0.36 (hexane/ethyl acetate = 80/20); ^{1}H NMR δ 0.80 (t, *J* = 7.5 Hz, 3H), 1.10−1.72 (m, 23H), 1.81−2.42 (m, 3H), 2.44−2.65 (m, 1H), 2.72−2.98 (m, 1H), 3.36 (dd, *J* = 1.5, 6.9 Hz, 1H), 3.42−4.07 (m, 2H), 7.07 (s, 2H); IR (neat) 2965, 1745, 1055 cm^{-1}.

3-*tert*-Butyl-5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]-2-cyclopentanone (6d): R_f = 0.65 (hexane/ethyl acetate = 70/30); ^{1}H NMR δ 0.70 (s, 9H), 1.10−1.45 (m, 21H), 1.85−2.15 (m, 2H), 2.22−2.55 (m, 2H), 2.72−2.98 (m, 1H), 3.30−4.20 (m, 2H), 3.77 (s, 1H), 7.07 (s, 2H); IR (neat) 2965, 1725, 1075 cm^{-1}.

General Procedure for Reduction of Sulfinyl Group from the Addition Product. The addition product **6** was treated with excess amounts of freshly prepared aluminum amalgam[15] in a mixed solvent of THF and H_2O (THF/H_2O = 90/10) at room temperature and the mixture was stirred overnight. Anhydrous $MgSO_4$ was added, filtered, and washed with Et_2O. The filtrate was concentrated to give the crude oil, which was purified by column chromatography (silica gel) to give the cyclopentanone **7**. It was difficult to remove the solvent completely from the cyclopentanone **7** due to their volatility.

***trans*-3-*tert*-Butyl-4-methyl-1-cyclopentanone (7a):** R_f = 0.72 (hexane/ethyl acetate = 70/30); $[\alpha]^{22}_D$ = −37.9 (*c* 0.506, $CHCl_3$); ^{1}H NMR δ 0.92 (s, 9H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.63−1.79 (m, 1H), 1.81−1.98 (m, 1H), 2.02−2.57 (m, 4H); ^{13}C NMR δ 22.9, 27.8, 32.0, 33.0, 41.1, 47.7, 53.8, 219.7; IR (neat) 2970, 1740 cm^{-1}; MS (EI) *m*/*z* 154 (M^+, 17), 97 (100).

***trans*-3-Isopropyl-4-methyl-1-cyclopentanone[16] (7b):** R_f = 0.70 (hexane/ethyl acetate = 70/30); $[\alpha]^{22}_D$ = −134.6 (*c* 0.204, $CHCl_3$); ^{1}H NMR δ 0.85 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.55−2.14 (m, 5H), 2.15−2.34 (m, 1H), 2.35−2.53 (m, 1H); ^{13}C NMR δ 16.7, 19.0, 22.1, 27.5, 33.9, 39.9, 47.7, 50.3, 218.9; IR (neat) 2960, 1745 cm^{-1}; MS (EI) *m*/*z* 140 (M^+, 65), 97 (100).

***trans*-3-Ethyl-4-methyl-1-cyclopentanone (7c):** R_f = 0.70 (hexane/ethyl acetate = 80/20); $[\alpha]^{26}_D$ = −74.2 (*c* 0.348, $CHCl_3$); ^{1}H NMR δ 0.93 (t, *J* = 7.4 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 1.10−1.48 (m, 2H), 1.51−2.10 (m, 4H), 2.31−2.58 (m, 2H); ^{13}C NMR δ 12.3, 18.6, 26.2, 37.1, 44.8, 46.2, 47.5, 218.8; IR (neat) 2960, 1745 cm^{-1}.

***cis*-4-*tert*-Butyl-2-methylcyclopentanone[21] (*cis*-7d).** The enantiomeric purity (>98% ee) was confirmed by ^{1}H NMR using Eu(hfc)$_3$: GC t_R = 50.97 min; R_f = 0.61 (hexane/ethyl acetate = 80/20); $[\alpha]^{22}_D$ = −43.4 (*c* 0.666, $CHCl_3$); ^{1}H NMR δ 0.90 (s, 9H), 1.09 (d, *J* = 7.6 Hz, 3H), 1.56−1.70 (m, 1H), 1.79−2.47 (m, 5H); ^{13}C NMR δ 16.5, 27.1, 31.8, 40.1, 42.6, 44.6, 45.6, 222.2; IR (neat) 2970, 1750 cm^{-1}; MS (EI) *m*/*z* 154 (M^+, 25), 97 (100). A cis and trans mixture of the cyclopentanone **7d** was obtained by the reaction of 5-methyl-2-cyclopentenone (**1b**) with *tert*-butyl radical (Table 2). The selected spectral data for *trans*-**7d** are listed below. *trans*-**7d**: GC: t_R = 49.67 min; R_f = 0.61 (hexane/ethyl acetate = 80/20); ^{1}H NMR δ 0.94 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 220.8.

General Procedure for the Radical Addition to 4- or 5-Methyl-2-cyclopentenone (1). After the reaction of **1** in CH_2Cl_2 or *i*-PrOH performed in a manner similar to the procedure for the radical reaction of **4**, the mixture was poured into saturated NaH_2PO_4 and extracted with Et_2O (three times). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated to give the crude product, which was purified by column chromatography to give the addition products **7**. Spectroscopic data of the addition products **7** are listed above.

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Supporting Information Available: The X-ray data of (4*S*)-**4a** are available from the Cambridge Crystallographic Data Centre. Determination of absolute configuration of the sulfoxide **4b**. Spectroscopic characterization for **5**, **8**−**10**, and sulfones. Characterization for the addition products **6a**−**d**. Copies of the ^{1}H NMR spectra of compounds **2b**, **6a**−**c**, and **7c**. The mechanism of the radical β-addition to (4*R*)-4-methyl-2-(arylsulfinyl)-2-cyclopentenone (4*R*)-**4a** (12 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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(22) When saturated NaH_2PO_4 was added to hydrolyze the boron enolate without addition of acetic acid, excess triethylborane generated vast numbers of radicals on exposure to a large amount of oxygen to give unidentified products probably derived from the unreacted compound (4*S*)-**4a** or (5*S*)-**4b**. Acetic acid is known to react with trialkylborane; see: Brown, H. C.; Murray, K. *J. Am. Chem. Soc.* **1959**, *81*, 4108.