Bull. Chem. Soc. Jpn., 72, 1057—1062 (1999)

Stereochemical Behaviors of Cyclohexyl α-Sulfonyl Carbanions

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(Received October 26, 1998)

Diastereoisomeric 4-(*t*-butyl)-1-(phenylsulfonyl)cyclohexanes **3** and 4-(*t*-butyl)-2-phenylsulfonyl-1-cyclohexanols **10** were subjected to H–D exchange, methylation, and allylation. The anions generated from **3** and **10** rapidly isomerized to those having a sulfonyl group in an equatorial position to form both equatorial and axial carbanions, in which a slight difference was found toward the subsequent electrophilic attack. The reaction of the dianion of **10** was little affected by an adjacent oxyanion and its countercation. The steric requirement of a bulky aggregate containing a sulfonyl group and a THF-solvated metal counterion may play an important role in the stereochemical behavior of α-sulfonyl carbanions.

Since sulfones are the ease of formation of carbanions α to the sulfonyl group to enable efficient C–C bond formation via alkylations, acylations, and aldol-like processes, the synthetic importance of α-sulfonyl carbanions, combined with their interesting stereochemical characteristics, has made them targets for intensive studies.[1—4]

Although the question as to whether the structure of α-sulfonyl carbanion is planar or pyramidal had been the subject of continuing interest,[5,6] X-ray structure analyses of crystal lithiosulfones have proved that the configuration of the carbanionic center is actually dependent on the structure of the sulfone concerned.[7,8]

An ab initio calculation suggested the stabilization of α-sulfonyl carbanions in terms of an n,σ^* interaction between the lone pair and the antiplanar C–S bond.[9,10] Recent X-ray and NMR studies have concluded that the THF-solvated metal counterion (usually Li^+) is associated with the sulfonyl O-atoms, but not bound to the C-atom.[7,8,11]

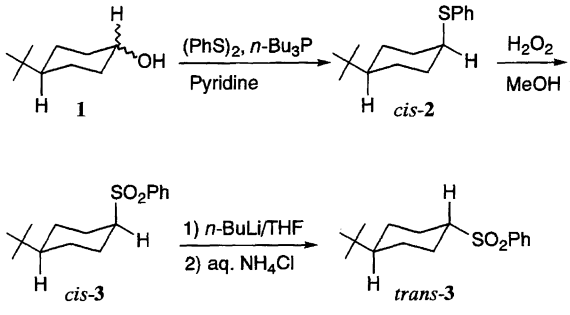
Although there have been a number of studies on the reactions of α-sulfinyl carbanions, the stereochemical behaviors in the reactions of α-sulfonyl carbanions have not been widely investigated.[5,6,12] The stereochemistry in the protonation of 2-phenylcyclohexyl- or 4-(*t*-butyl)cyclohexyl α-sulfonyl carbanions has been discussed,[13,14] while there has been no report of stereochemical studies on alkylations of cyclohexyl α-sulfonyl carbanions.

The α-sulfonyl carbanion in a dianion derived from β-hydroxysulfone[15,16] is important in synthetic aspects because enantiomerically pure (1*R*,2*R*)-2-(phenylthio)cyclohexanol is readily obtained by the lipase-mediated resolution of 2-(phenylthio)cyclohexanol,[17] and (1*S*,2*R*)-2-(phenylthio)cyclohexanol is prepared by a Baker's yeast reduction of 2-(phenylthio)cyclohexanone.[18] It is also interesting to clarify whether an oxyanion or its metal countercation has the ability to stabilize the neighboring α-sulfonyl carbanion.

We here report on the stereochemical behaviors of the configurationally and conformationally defined α-sulfonyl carbanions on a cyclohexane ring. In this system it is easy to clarify the configurational changes of the first-formed carbanion and at the same time the attacking mode of electrophiles.

Results and Discussion

To study the conformationally biased system *cis*- and *trans*-4-(*t*-butyl)-1-(phenylsulfonyl)cyclohexanes, *cis*-**3** and *trans*-**3** were prepared in a similar manner as that decribed in the literature.[14,19] The treatment of 4-(*t*-butyl)cyclohexanols **1** (*cis*/*trans* = 17/83) with tributylphosphine and diphenyl disulfide led to the formation of sulfide *cis*-**2**, which was then converted into *cis*-**3** by oxidation. The diastereoisomeric *trans*-**3** was obtained by protonation of a carbanion generated from *cis*-**3** (Eq. 1). The structures of two isomers were confirmed by a comparison of the coupling constants ($J_{H(1)H(2)}$) in their ^{1}H NMR spectra [*trans*-**3**; $J_{ax\text{-}H(1)ax\text{-}H(2)} = 12.4$ Hz, $J_{ax\text{-}H(1)eq\text{-}H(2)} = 3.5$ Hz: *cis*-**3**; $J_{eq\text{-}H(1)ax\text{-}H(2)}$, $J_{eq\text{-}H(1)ax\text{-}H(2)} <$ 2.0 Hz].

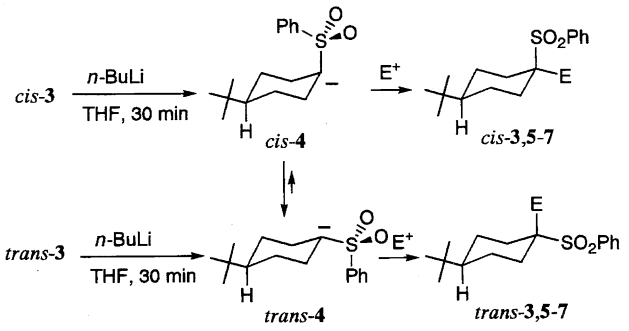


(1)

Protonation (or deuteration) of an anion generated from *cis*-**3** or *trans*-**3** in THF using *n*-BuLi at −80 °C gave a mixture of *cis*-**3** and *trans*-**3** (*cis*-**5** and *trans*-**5**); the yield of a *trans*-product was always higher than that of a *cis*-product. A similar treatment of that anion with iodomethane or 3-bromo-1-propene led to similar result; that is, the predominant formation of a *trans*-product *trans*-**6**,**7** along with a minor product *cis*-**6**,**7** and a protonated one *trans*-**3** recovered by a

quenching process (Eq. 2).

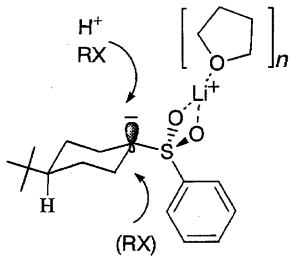
In the NMR spectra of *trans*-**6** or *trans*-**7** NOE was observed between an ax-H(3) and a methyl or an allyl group, while in those of *cis*-**6** and *cis*-**7** the chemical shift (δ_H) of an ax-H(3) was found in a low field, for example, $\delta_{ax\text{-}H(3)}$=1.62 (*cis*-**5**) and $\delta_{ax\text{-}H(3)}$=1.11 (*trans*-**5**). The NMR spectra of **6** and **7** revealed that a *t*-butyl group always occupies an equatorial position. These results are shown in Table 1. The use of lithium diisopropylamide (LDA) as a base or diethyl ether as a solvent resulted in the formation of products in similar *cis*/*trans* ratios.



3, E = H
5, E = D
6, E = Me
7, E = $CH_2CH{=}CH_2$

(2)

The present findings suggest that the first-formed carbanion *cis*-**4** might undergo isomerization to *trans*-**4**, and then equilibrium is established. The rapid conversion was confirmed by the predominant formation of *trans*-**3** by quenching immediately after the addition of *n*-BuLi to *cis*-**3**. Interestingly, a similar isomerization is found in a cyclopropyl α-sulfonyl carbanion.[20] In an acyclic α-sulfinyl carbanion, a polar sulfinyl group causes a variety of stereochemical behaviors.[21] On the other hand, the attacking mode of an electrophile to the present α-sulfonyl carbanion seems to be influenced simply by the steric requirement of the carbanion, around which a Li cation between two oxygen atoms is solvated by THF molecules to form a bulky aggregate,[13] as shown in Fig. 1.



trans-**4**

Fig. 1.

A proton-donating reagent comes from the lithiated side of the carbanion because its polarization causes it to initially interact with the countercation. Therefore, the *cis*/*trans* ratio of **3** is assumed to be nearly equal to that of the intermediary anions **4**. Although a nonpolar haloalkane could react on the other side to some extent, the *cis*/*trans* ratio of **6** was found to be comparable to that of **3**, probably because the attack of an electrophile from the other side was subject to the steric hindrance of a phenyl group.

The structure of α-sulfonyl carbanion is tentatively shown to be pyramidal, because that structure is general in the nonconjugated α-sulfonyl carbanion.[7,8] The same argument may be valid by assuming a planar carbanion, provided that the countercation coordinates the anion. However, the difference in the steric requirements of planar *trans*-**4** and *cis*-**4** must be smaller than that in the pyramidal ones. Interestingly, protonation of the 1-nitro-2-phenylcyclohexyl carbanion having sp^2 yielded mainly a *cis*-product.[22]

In order to clarify the structure of the intemediary carbanion, the anion **4** was prepared in a NMR tube (containing THF-d_8) from *cis*-**3** (0.20 mmol) and *n*-Bu^{6}Li, which had been prepared from ^{6}Li (0.72 mmol) and 1-bromobutane (0.30 mmol) according to a similar procedure as that described in the reaction of diphenylacetylene and *n*-Bu^{6}Li.[23] Unfortunately, the complete assignment of the ^{1}H and ^{13}C NMR spectra was unsuccessful, because no ^{1}H atom was bound to a carbanion, and impurities were formed during the reaction. However, splittings of ^{13}C signals based on the ^{6}Li–^{13}C interaction were not observed in the spectrum; that is, a Li cation might be remote from a cyclohexane ring.

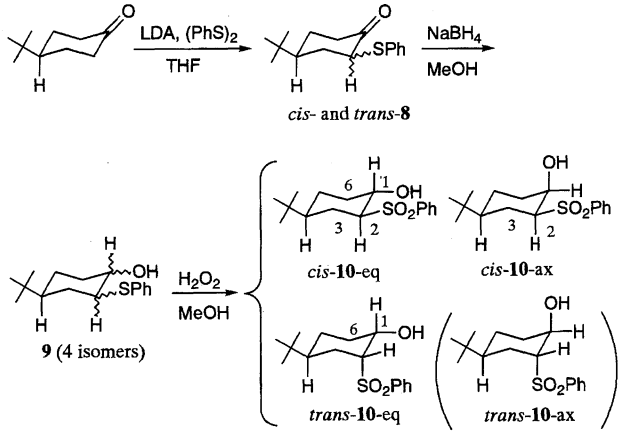
Table 1. Reaction of a Carbanion **4** Generated from *cis*-**3** or *trans*-**3** in THF Using *n*-BuLi at −80 °C

Entry		Electrophile (E)	Reaction time[a]/h	Product	Yield[b] %	Ratio of *cis*/*trans*[c]
1	*cis*-**3**	aq NH_4Cl	0.5	**3**	91	12/88
2	*cis*-**3**[d]	aq NH_4Cl	0.5	**3**	89	13/87
3	*cis*-**3**	D_2O	6	**5**	62	13/87
4	*cis*-**3**	MeI	6	**6**	79	18/82
5	*cis*-**3**[d]	MeI	6	**6**	74	20/80
6	*cis*-**3**	$CH_2{=}CHCH_2Br$	6	**7**	87	36/64
7	*trans*-**3**	aq NH_4Cl	0.5	**3**	90	10/90
8	*trans*-**3**	MeI	6	**6**	81	16/84

a) Reaction time after addition of an electrophile. b) Isolated yield. c) Determined by HPLC analysis of the reaction mixture. d) Diethyl ether was used as a solvent.

Neither acylation nor an aldol-type reaction occurred through **4**, presumably owing to the steric shielding by axial H-atoms.

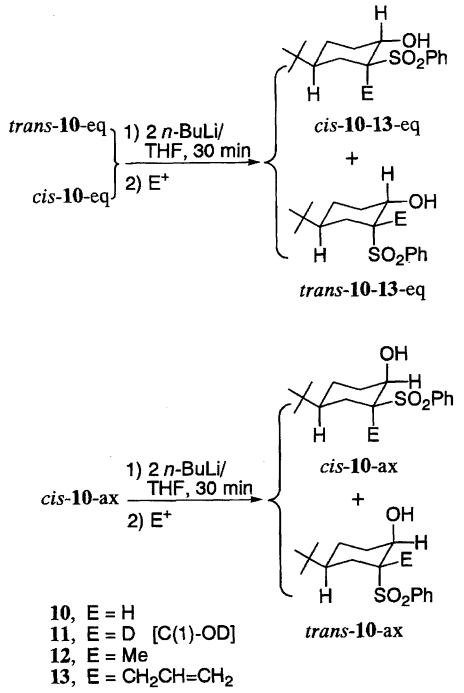
In order to elucidate the influence of a countercation, sulfonylcyclohexanes containing a hydroxy adjacent to a sulfonyl group were prepared. Sulfenylation of 4-(*t*-butyl)cyclohexanone, followed by reduction, afforded four diastereomeric isomers of sulfenylcyclohexanols **9**. After the separation of a mixture of four isomers **9** by column chromatography, oxidations of the mixture gave 4-(*t*-butyl)-2-phenylsulfonyl-1-cyclohexanols *cis*-**10**-eq, *cis*-**10**-ax, *trans*-**10**-eq, and *trans*-**10**-ax in ca. 2 : 2 : 9 : 0.1 ratio, respectively (Eq. 3). The compound *cis*-**10**-eq means *cis*-4-*t*-Bu-2-PhSO$_2$-cyclohexane containing eq-OH.



(3)

The structures of four isomers were deduced by a combination of H–C COSY measurements and the detections of large coupling constants $J_{ax\text{-}Hax\text{-}H}$ between neighboring ax-H in their NMR spectra [*cis*-**10**-eq; $J_{ax\text{-}H(1)ax\text{-}H(2)}$ = 10.3, $J_{ax\text{-}H(1)ax\text{-}H(6)}$ = 10.5, $J_{ax\text{-}H(2)ax\text{-}H(3)}$ = 13.0 Hz: *cis*-**10**-ax; $J_{ax\text{-}H(2)ax\text{-}H(3)}$ = 13.1 Hz: *trans*-**10**-eq; $J_{ax\text{-}H(1)ax\text{-}H(6)}$ = 11.0 Hz: *trans*-**10**-ax; $J_{H(1)H(2)}$, $J_{H(1)H(6)}$, $J_{H(2)H(3)}$ < 5.0 Hz].

The dianions formed from *trans*-**10**-eq, *cis*-**10**-eq, and *cis*-**10**-ax were treated with electrophiles in a similar manner as that described above (Eq. 4). These results are given in Table 2.



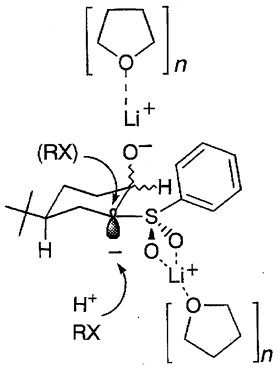
(4)

The structures of **12** and **13** were determined by means of NMR as follows: The NOE was observed between an ax-H-(4) and a methyl or an allyl group in *cis*-**12** and *cis*-**13**, while

Table 2. Reaction of a Carbanion Generated from **10** Using *n*-BuLi

Entry		Electrophile (E)	Solvent	Reaction temp/°C	Reaction time[a]/h	Product	Yield[b] %	Ratio[c] of *cis*/*trans*
1	*trans*-**10**-eq	aq NH_4Cl	THF	−80	0.5	**10**-eq	94	51/49
2	*trans*-**10**-eq	aq NH_4Cl	Et_2O	−80	0.5	**10**-eq	91	46/54
3	*trans*-**10**-eq	aq NH_4Cl	THF–HMPA[d]	−80	0.5	**10**-eq	96	58/42
4	*trans*-**10**-eq	aq NH_4Cl	THF	0	0.5	**10**-eq	91	92/8
5	*trans*-**10**-eq	aq NH_4Cl	Et_2O	0	0.5	**10**-eq	90	82/18
6	*trans*-**10**-eq	D_2O	THF	0	6	**11**-eq	69	93/7
						(**10**-eq	24	94/6)[e]
7	*trans*-**10**-eq	MeI	THF	−80	6	**12**-eq	37	76/24
						(**10**-eq	57	96/4)[e]
8	*trans*-**10**-eq	MeI	Et_2O	−80	6	**12**-eq	32	72/28
						(**10**-eq	57	91/9)[e]
9	*trans*-**10**-eq	CH_2=$CHCH_2Br$	THF	0	6	**13**-eq	31	55/45
						(**10**-eq	62	96/4)[e]
10	*cis*-**10**-eq	aq NH_4Cl	THF	−80	0.5	**10**-eq	88	100/0
11	*cis*-**10**-eq	aq NH_4Cl	THF	0	0.5	**10**-eq	90	95/5
12	*cis*-**10**-eq	D_2O	THF	0	6	**11**-eq	47	93/7
13	*cis*-**10**-ax	aq NH_4Cl	THF	−80	0.5	**10**-ax	97	100/0
14	*cis*-**10**-ax	aq NH_4Cl	THF	0	0.5	**10**-ax	91	91/9

a) Reaction time after addition of an electrophile. b) Isolated yield. c) Determined by HPLC analysis of the reaction mixture. d) HMPA (2 mol amt.) was used as an additive. e) Recovery after being quenched with aq NH_4Cl.



cis-**14**

Fig. 2.

an axial sulfonyl group in *trans*-**12** and *trans*-**13** caused a downfield shift of an ax-H(4).

Both protonation and alkylation of the dianion **14** generated from *trans*-**10**-eq resulted in the dominant formation of *cis*-**10**-eq, *cis*-**12**-eq, and *cis*-**13**-eq, especially at 0 °C (Entries 1—6). The *cis*/*trans* ratio of **10**-eq found in the protonation of **14** at 0 °C was the same as that obtained using *cis*-**10**-eq at that temperature (Entries 3,8); a similar result was also found in **10**-eq recovered after methylation of **14** at −80 °C for a longer time (Entry 5). These findings mean that **14** underwent a configurational inversion of the carbanion, though a little slowly, to form the dianion containing a sulfonyl group dominantly in an equatorial position, and electrophiles might come to the axial carbanion in a similar mode as that found in *trans*-**4** (Fig. 2). The conversion of *trans*-**10**-eq to *cis*-**10**-eq through a deprotonation/protonation process suggests that an equatorial oxyanion or its Li countercation was slightly effective in stabilizing of the first-formed carbanion generated from *trans*-**10**-eq, while an axial sulfonyl group gradually migrated to a thermodynamically-stable equatorial one. During this migration, chelation between an equatorial oxyanion and a sulfonyl group may exist to some extent.[16]

Unfortunately, the yield in the reaction via the present cyclohexyl α-sulfonyl carbanion decreased with increasing the bulkiness of an electrophile and the carbanion scarecely reacted with 1-bromohexane. One reason for the low reactivity is that the 1,3-diaxial interaction might hinder the reaction at the axial carbanion.

It may be concluded that in the stereochemical behavior of α-sufonyl carbanions the bulkiness of an aggregation containing a sulfonyl group and a solvated Li cation play an important role. On the other hand, the control of their reactions by means of an electronic effect of a neighboring group seems to be difficult, because the solvated metal cation is located between sulfonyl O-atoms, but not bound to the C-atom.

Experimental

NMR spectra were recorded with a JEOL JNM-A-400 (400 MHz) or a Bruker AC-300 (300 MHz) using tetramethylsilane as an internal standard and $CDCl_3$ as a solvent. IR spectra were taken on a Shimadzu FT-IR-8600 instrument. HPLC analyses were carried out with a Shimadzu LC-6A machine equipped with a nacalai tesque C_{18}-AR or a nacalai tesque PYE column. Column chromatography was performed with Wakogel 200 silica gel, and TLC with Merck silica gel 60 F_{254}. THF is freshly distilled from calcium hydride before use. Other solvents were dried over molecular sieves and reagents used as received.

Preparation of *cis*-4-(*t*-Butyl)-1-(phenylsulfonyl)cyclohexane (*cis*-3). To a stirred solution of 4-(*t*-butyl)cyclohexanol (*cis*/*trans* = 17/83) (4.68 g, 30.0 mmol) and diphenyl disulfide (9.83 g, 45.0 mmol) in pyridine (30 mL) was added tributylphosphine (9.1 g, 45.0 mmol)[19] at room temperature, and the resulting solution was stirred for 10 h. After removal of pyridine by distillation, chromatography [silica gel; eluent hexane] of the residue gave crude 4-(*t*-butyl)-1-(phenylthio)cyclohexane[24] (5.9 g, 24 mmol), which was then dissolved in methanol (100 mL) containing $Na_2WO_4 \cdot 2H_2O$ (0.3 g, 0.1 mmol). To the solution was added dropwise 30% aqueous H_2O_2 (5.89 g, 52 mmol) with stirring at 0 °C; the resultant mixture was allowed to warm to room temperature over a period of 1 h, after which it was stirred at this temperature for 15 h. The reaction mixture was then diluted with water (200 mL) and extracted with ethyl acetate (3×100 mL). The extracts were washed with brine, dried ($MgSO_4$) and evaporated to dryness. The crude product was purified by column chromatography [silica gel; eluent hexane–ethyl acetate (5 : 1)] to afford *cis*-**3**[14] (5.79 g, 69%).

trans-4-(*t*-Butyl)-1-(phenylsulfonyl)cyclohexane (*trans*-**3**)[14] was prepared by protonation of an anion generated from *cis*-**3** as described below.

Preparation of 4-(*t*-Butyl)-2-phenylthio-1-cyclohexanols (9). A solution of LDA was prepared from diisopropylamine (3.34 g, 33.0 mmol) and butyllithium (1.67 mol dm^{-3} in hexane; 19.8 mL, 33.0 mmol) in dry THF (10 mL) at −80 °C in the customary manner and was added dropwise to a stirred solution of 4-(*t*-butyl)cyclohexanone (4.63 g, 30 mmol) in dry THF (20 mL) at −80 °C under Ar. The resulting solution was stirred for 30 min and then allowed to warm to 0 °C over a period of 30 min. After being stirred at room temperature for an additional 1h, a solution of diphenyl disulfide (7.86 g, 36.0 mmol) in dry THF (15 mL) was added, and the resulting solution was stirred for an additional 15 h before being quenched with saturated aqueous NH_4Cl (30 mL). The aqueous phase was separated and extracted with ethyl actetate (3×100 mL). The combined organic phase and extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Column chromatography [silica gel; eluent hexane–ethyl acetate (10 : 1)] of the residue gave a diastereoisomeric mixture of 4-(*t*-butyl)-2-phenylthio-1-cyclohexanones *cis*-**8** & *trans*-**8** (5.34 g, 68 %) as a viscous liquid.

To a solution of a mixture of *cis*- and *trans*-**8** (5.34 g, 20.0 mmol) in methanol (100 mL) was added $NaBH_4$ (0.34 g, 10.2 mmol) with stirring at 0 °C; the resulting mixture was stirred at room temperature for 8 h, and then diluted with saturated aqueous NaCl (150 mL) and extracted with ethyl acetate (3×150 mL); the extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography [silica gel; eluent hexane–ethyl acetate (20 : 1)] gave three isomers of **9**.

***t*-4-(*t*-Butyl)-*t*-2-phenylthio-1-cyclohexanol:** Yield 0.66 g (12%), viscous liquid; IR (neat) ν_{max} = 3439 (OH) and 1439 cm^{-1} (PhS); ^1H NMR ($CDCl_3$) δ = 0.82 (9 H, s, 3 Me), 0.96—1.06 (1 H, m), 1.10—1.20 (2 H, m), 1.37 (1 H, ddt, J = 3.7, 10.9, 13.0 Hz, ax-H(6)). 1.74—1.79 (1 H, m), 2.10—2.19 (2 H, m), 2.78—2.86 (1 H, m), 2.97 (1 H, s, OH), 3.25—3.32 (1 H, td, J = 10.7, 4.6 Hz, ax-H(2)), and 7.24—7.49 (5 H, m, PhH). Found: C, 72.63; H, 9.10%. Calcd for $C_{16}H_{24}OS$: C, 72.67; H, 9.15%.

***c*-4-(*t*-Butyl)-*c*-2-phenylthio-1-cyclohexanol:** Yield 0.56 g

(11%), viscous liquid; IR (neat) ν_{max} = 3425 (OH) and 1439 cm^{-1} (PhS); ^1H NMR ($CDCl_3$) δ = 0.88 (9 H, s, 3 Me), 1.11—1.18 (1 H, m), 1.31—1.53 (4 H, m), 1.81—1.84 (1 H, m), 2.04—2.08 (1 H, m), 2.50 (1 H, s, OH), 3.25 (1 H, ddd, J = 2.3, 3.8, 12.9 Hz, ax-H(2)), 3.71—3.72 (1 H, m), and 7.22—7.45 (5 H, m, PhH). Found: C, 72.57; H, 9.16%. Calcd for $C_{16}H_{24}OS$: C, 72.67; H, 9.15%.

***t*-4-(*t*-Butyl)-*c*-2-phenylthio-1-cyclohexanol:** Yield 2.03 g (38%), viscous liquid; IR (neat) ν_{max} = 3265 (OH) and 1464 cm^{-1} (PhS); ^1H NMR ($CDCl_3$) δ = 0.86 (9 H, s, 3 Me), 1.01—1.11 (1 H, m), 1.39—1.56 (3 H, m), 1.75—1.81 (1 H, m), 1.84—1.92 (1 H, m), 2.11—2.15 (1 H, m), 2.27 (1 H, s, OH), 3.66—3.70 (1 H, m), 3.75 (1 H, ddd, J = 4.4, 11.7, 4.4 Hz, ax-H(1)), and 7.20—7.50 (5 H, m, PhH). Found: C, 72.50; H, 9.30%. Calcd for $C_{16}H_{24}OS$: C, 72.67; H, 9.15%.

Typical Procedure for Preparation of 4-(*t*-Butyl)-2-phenylsulfonyl-1-cyclohexanols (10). To a stirred solution of *t*-4-(*t*-butyl)-*t*-2-phenylthio-1-cyclohexanol (0.79 g, 3.0 mmol) and $Na_2WO_4 \cdot 2H_2O$ (0.1 g) in methanol (100 mL) was added dropwise 30% aqueous H_2O_2 (0.71 g, 6.2 mmol) at 0 °C; the resulting solution was allowed to warm to room temperature, after which it was stirred at this temperature for 10 h, and then at 50 °C for 1 h. After being cooled the reaction mixture was diluted with water (150 mL) and extracted with ethyl acetate (3×100 mL). The extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated to dryness. Column chromatography [silica gel; eluent hexane–ethyl acetate (6 : 1)] afforded *cis*-**10**-eq (0.73 g, 82%) as a colorless solid.

***t*-4-(*t*-Butyl)-*t*-2-(phenylsulfonyl)-1-cyclohexanol (*cis*-10-eq):** Mp 95 °C; IR (Nujol) ν_{max} = 3439 (OH), 1285 and 1142 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.79 (9 H, s, 3 Me), 0.91—1.10 (3 H, m), 1.32—1.42 (1 H, m), 1.72—1.75 (1 H, m), 1.93—1.97 (1 H, m), 2.17 (1 H, dddd, J = 13.1, 3.4, 3.7, 5.1 Hz, eq-H(6)), 3.01 (1 H, ddd, J = 10.3, 13.0, 3.3 Hz, ax-H(2)), 3.86 (1 H, ddd, J = 10.3, 10.5, 5.1 Hz, ax-H(1)), 4.24 (1 H, s, OH), and 7.59—7.93 (5 H, m, PhH). Found: C, 64.63; H, 8.10%. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16%.

***c*-4-(*t*-Butyl)-*c*-2-phenylsulfonyl-1-cyclohexanol (*cis*-10-ax):** The compound was prepared from *c*-4-(*t*-butyl)-*c*-2-phenylthio-1-cyclohexanol and isolated as a colorless solid (79%); mp 64 °C; IR (Nujol) ν_{max} = 3514 (OH), 1296 and 1136 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.89 (9 H, s, 3 Me), 1.03—1.11 (1 H, m), 1.19—1.28 (1 H, m), 1.49—1.60 (2 H, m), 1.76—1.85 (1 H, m), 1.99 (1 H, dq, J = 14.2, 3.4 Hz, eq-H(6)), 2.06 (1 H, dt, J = 12.4, 3.2 Hz, eq-H(3)), 2.93 (1 H, ddd, J = 1.7, 3.3, 13.1 Hz, ax-H(2)), 3.40 (1 H, s, OH), 4.13 (1 H, m, eq-H(1)), and 7.58—7.94 (5 H, m PhH). Found: C, 64.98; H, 8.32%. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16%.

***t*-4-(*t*-Butyl)-*c*-2-phenylsulfonyl-1-cyclohexanol (*trans*-10-eq):** The compound was obtained from *t*-4-(*t*-butyl)-*c*-2-phenylthio-1-cyclohexanol as a colorless solid (77%); mp 88 °C; IR (Nujol) ν_{max} = 3470 (OH), 1304 and 1138 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.84 (9 H, s, 3 Me), 1.05—1.15 (1 H, m), 1.29—1.37 (1 H, ddd, J = 5.2, 12.3, 14.5 Hz, ax-H(3)), 1.83—2.00 (3 H, m), 2.09—2.22 (2 H, m), 3.05 (1 H, s, OH), 3.59 (1 H, J = 4.6, 4.2, 3.9 Hz, eq-H(2)), 3.96 (1 H, ddd, J = 4.6, 11.0, 4.6 Hz, ax-H(1)), and 7.55—7.95 (5 H, m, PhH). Found: C, 64.60; H, 8.22%. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16%.

Typical Procedure for Protonation or Deuteration of an Anion of 3. To a stirred solution of *cis*-**3** (0.28 g, 1.00 mmol) in dry THF (20 mL) was added dropwise butyllithium (1.67 mol dm^{-3} in hexane; 0.60 mL, 1.00 mmol) at −80 °C under Ar. The resultant solution was stirred at that temperature for an additional 30 min and then quenched with saturated aqueous NH_4Cl (20 mL). [For deuteration D_2O (0.09 mL, 5.00 mmol) was added in the place of aqueous NH_4Cl and stirring was further continued at −80 °C for 6 h before being diluted with saturated aqueous NH_4Cl (20 mL).] The aqueous layer was separated and extracted with ethyl acetate (2×20 mL). The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated. Column chromatography [silica gel; eluent hexane–ethyl acetate (9 : 1)] of the residue gave *cis*-**3** (0.03 g, 11%) and *trans*-**3** (0.22 g, 80%), respectively. HPLC analysis before isolation by chromatography indicated the same *cis*-**3**/*trans*-**3** ratio. The *cis*/*trans* ratio in deuterated 4-(*t*-butyl)-1-(phenylsulfonyl)cyclohexanes-1-*d* **5** was same to that in **3**.

Typical Procedure for Alkylation of 3. To a stirred solution of *cis*-**3** (0.28 g, 1.00 mmol) in dry THF (20 mL) was added dropwise butyllithium (1.67 mol dm^{-3} in hexane; 0.60 mL, 1.00 mmol) at −80 °C under Ar; stirring was continued for 30 min after which iodomethane (0.31 mL, 5.00 mmol) was added slowly to the mixture. The resultant solution was further stirred at −80 °C for 6 h and then quenched with saturated aqueous NH_4Cl (20 mL). The aqueous layer was separated and extracted with ethyl acetate (2×20 mL). The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated. Column chromatography [silica gel; eluent hexane–ethyl acetate (5 : 1)] of the residue gave *trans*-**6** (0.19 g, 65%), *cis*-**6** (0.04 g, 14%), and *trans*-**3** (0.03 g, 12%), respectively. HPLC analysis before isolation by chromatography indicated the same ratio of *trans*-**6** and *cis*-**6**.

***t*-4-(*t*-Butyl)-1-methyl-*r*-1-(phenylsulfonyl)cyclohexane (*trans*-6):** Colorless liquid; IR (neat) ν_{max} = 1393 and 1140 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.83 (9 H, s, 3 Me), 0.94—0.99 (1 H, m), 1.11 (2 H, qd, J = 13.2, 3.4 Hz, ax-H(3)), 1.30 (3 H, s, Me), 1.72—1.76 (4 H, m), 1.88 (2 H, td, J = 12.9, 3.7 Hz, ax-H(2)), and 7.53—7.88 (5 H, m, PhH). Found: C, 69.18; H, 8.92%. Calcd for $C_{17}H_{26}O_2S$: C, 69.34; H, 8.90%.

***c*-4-(*t*-Butyl)-1-methyl-*r*-1-(phenylsulfonyl)cyclohexane (*cis*-6):** Colorless liquid; IR (neat) ν_{max} = 1288 and 1145 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.89 (9 H, s, 3 Me), 0.91—1.02 (1 H, m), 1.12 (3 H, s, Me), 1.59—1.64 (2 H, m), 1.72—1.92 (4 H, m), 2.35—2.39 (2 H, m), and 7.53—7.89 (5 H, m, PhH). Found: C, 69.24; H, 9.01%. Calcd for $C_{17}H_{26}O_2S$: C, 69.34; H, 8.90%.

In a similar manner to that described above, treatment of *cis*-**3** with 3-bromo-1-propene afforded *trans*-**7**, *cis*-**7**, and *trans*-**3** in 56%, 31%, and 9% yields, respectively.

***t*-4-(*t*-Butyl)-1-allyl-*r*-1-(phenylsulfonyl)cyclohexane (*trans*-7):** Colorless liquid; IR (neat) ν_{max} = 1288 and 1140 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.88 (9 H, s, 3 Me), 0.94 (1 H, tt, J = 12.2, 3.4 Hz, ax-H(4)), 1.50—1.65 (4 H, m), 1.93 (2 H, qd, J = 12.9, 3.7 Hz, ax-H(3)), 2.17—2.21 (4 H, m), 5.00 (1 H, qd, J = 1.5, 17.0 Hz, =CHH), 5.11—5.14 (1 H, m, =CHH), 5.70 (1 H, tdd, J = 7.3, 10.0, 17.1 Hz, –CH=), and 7.54—7.91 (5 H, m, PhH). Found: C, 70.99; H, 8.84%. Calcd for $C_{19}H_{28}O_2S$: C, 71.20; H, 8.81%.

***c*-4-(*t*-Butyl)-1-allyl-*r*-1-(phenylsulfonyl)cyclohexane (*cis*-7):** Colorless liquid; IR (neat) ν_{max} = 1279 and 1150 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.83 (9 H, s, 3 Me), 0.91 (1 H, tt, J = 12.3, 3.3 Hz, ax-H(4)), 1.13 (2 H, dq, J = 3.5, 12.9 Hz, ax-H(3)), 1.67—1.89 (6 H, m), 2.50 (2 H, d, J = 7.2 Hz, –CH$_2$–CH=), 5.06—5.14 (2 H, m, =CH$_2$), 6.07 (1 H, tdd, J = 7.2, 10.0, 17.1 Hz, –CH=), and 7.54—7.88 (5 H, m, PhH). Found: C, 71.11; H, 8.90%. Calcd for $C_{19}H_{28}O_2S$: C, 71.20; H, 8.81%.

Protonation or Deuteration of a Dianion of 10. To a stirred solution of *trans*-**10**-eq (0.30 g, 1.00 mmol) in dry THF (20 mL) was added dropwise butyllithium (1.67 mol dm^{-3} in hexane; 1.20 mL, 2.00 mmol) at −80 °C under Ar and stirring was continued for 30 min. The resultant solution was quenched with saturated aqueous NH_4Cl (20 mL) and then treated in a similar fashion to that

described in the reaction of **3**. Column chromatography [silica gel; eluent hexane–ethyl acetate (4 : 1)] of the residue gave *trans*-**10**-eq (0.13 g, 43%) and *cis*-**10**-eq (0.13 g, 42%), respectively.

The similar treatment of a dianion formed from *cis*-**10**-eq or *cis*-**10**-ax gave a mixture of *cis*-**10**-eq and *cis*-10-ax as shown in Table 2.

***c*-4-(*t*-Butyl)-*t*-2-phenylsulfonyl-1-cyclohexanol (*trans*-10-ax):** The product was obtained by protonation of a dianion generated from *cis*-**10**-ax at 0 °C; colorless solid; mp 58 °C; IR (Nujol) ν_{max} = 3514 (OH), 1300 and 1136 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.82 (9 H, s, 3 Me), 1.37 (1 H, dq, J = 3.8, 12.2 Hz, ax-H(5)), 1.58—1.74 (3 H, m), 1.76—1.86 (2 H, m), 2.07—2.16 (1 H, m), 2.38 (1 H, s, OH), 3.28—3.31 (1 H, m, eq-H(1)), 4.46 (1 H, q, J = 3.4 Hz, eq-H(2)), and 7.56—7.92 (5 H, m, PhH). Found: C, 64.68; H, 8.12%. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16%.

Methylation of *trans*-10-eq. To a stirred solution of *trans*-**10**-eq (0.30 g, 1.00 mmol) in dry THF (20 mL) was added dropwise butyllithium (1.67 mol dm^{-3} in hexane; 1.20 mL, 2.00 mmol) at −80 °C under Ar; stirring was continued for 30 min, after which iodomethane (0.31 mL, 5.00 mmol) was added slowly to the mixture and the resultant solution was further stirred at −80 °C for 6 h. After being quenched with saturated aqueous NH_4Cl (20 mL), the aqueous layer was separated and extracted with ethyl acetate (2×20 mL). The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated. Column chromatography [silica gel; eluent hexane–ethyl acetate (4 : 1)] of the residue gave *trans*-**12**-eq (0.027 g, 9%), *cis*-**12**-eq (0.086 g, 28%), and *cis*-**10**-eq (0.17 g, 57%), respectively. HPLC analysis before isolation of the products indicated that the *cis*-**12**-eq/*trans*-**12**-eq ratio was 76/24.

***t*-(4-t-Butyl)-*t*-2-methyl-*c*-2-phenylsulfonyl-1-cyclohexanol (*trans*-12-eq):** Colorless solid; mp 93 °C; IR (Nujol) ν_{max} = 3514 (OH), 1296 and 1136 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.87 (9 H, s, 3 Me), 1.03 (1 H, dd, J = 13.1, 14.8 Hz, ax-H(3)), 1.12 (1 H, dq, J = 4.0, 12.9 Hz, ax-H(5)), 1.34 (3 H, s, Me), 1.93—2.01 (3 H, m), 2.03—2.14 (2 H, m), 3.28 (1 H, s, OH), 3.59 (1 H, dd, J = 4.3, 12.3 Hz, ax-H(1)), and 7.54—7.91 (5 H, m, PhH). Found: C, 65.70; H, 8.34%. Calcd for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44%.

***t*-(4-*t*-Butyl)-*c*-2-methyl-*t*-2-phenylsulfonyl-1-cyclohexanol (*cis*-12-eq):** Colorless solid; mp 101 °C; IR (Nujol) ν_{max} = 3514 (OH), 1296 and 1136 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.78 (9 H, s, 3 Me), 0.85—0.96 (1 H, m), 1.11 (1 H, tt, J = 2.9, 12.4 Hz, ax-H(4)), 1.48 (1 H, t, J = 12.6 Hz, ax-H(3)), 1.38—1.49 (1 H, m), 1.42 (3 H, s, Me), 1.65—1.72 (2 H, m), 1.92—1.98 (1 H, m), 3.71 (1 H, s, OH), 4.07 (1 H, dd, J = 5.1, 11.2 Hz, ax-H(1)), and 7.58—7.93 (5 H, m, PhH). Found: C, 65.68; H, 8.32%. Calcd for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44%.

Allylation of *trans*-10-eq. Treatment of *trans*-**10**-eq with 3-bromo-1-propene in a similar fashion to that described above gave *trans*-**13**-eq, *cis*-**13**-eq, and *cis*-**10**-eq in 14%, 17%, and 62% yields, respectively. Complete separation of *trans*-**13**-eq and *cis*-**13**-eq by column chromatograsphy was unsuccessful.

***t*-2-Allyl-*t*-(4-*t*-butyl)-*c*-2-phenylsulfonyl-1-cyclohexanol (*trans*-13-eq):** Viscous liquid; IR (Nujol) ν_{max} = 3514 (OH), 1296 and 1136 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.86 (9 H, s, 3 Me), 0.99—1.10 (2 H, m), 1.65—1.70 (3 H, m), 2.04—2.14 (2 H, m), 2.48—2.84 (2 H, m), 3.65 (1 H, s, OH), 3.88 (1 H, dd, J = 5.2, 11.1 Hz, ax-H(1)), 5.06—5.19 (2 H, m, =CH_2), 5.86 (1 H, tdd, J = 5.4, 9.8, 17.1 Hz, –CH=), and 7.54—7.92 (5 H, m, PhH). Found: C, 67.58; H, 8.12%. Calcd for $C_{19}H_{28}O_3S$: C, 67.82; H, 8.39%.

***c*-2-Allyl-*t*-(4-*t*-butyl)-*c*-2-allyl-*t*-2-phenylsulfonyl-1-cyclohexanol (*cis*-13-eq):** Viscous liquid; IR (Nujol) ν_{max} = 3520 (OH), 1298 and 1138 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ = 0.77 (9 H, s, 3 Me), 1.14—1.29 (3 H, m), 1.83—1.98 (4 H, m), 1.85 (1 H, m), 2.94 (1 H, dd, J = 4.5, 12.3 Hz, eq-H(3)), 3.23 (1 H, s, OH), 3.73 (1 H, dd, J = 4.5, 12.3 Hz, ax-H(1)), 5.06—5.19 (2 H, m, =CH_2), 5.72 (1 H, tdd, J = 7.3, 9.9, 17.0 Hz, –CH=), and 7.54—7.92 (5 H, m, PhH). Found: C, 67.70; H, 8.30%. Calcd for $C_{19}H_{28}O_3S$: C, 67.82; H, 8.39%.

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