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Stereochemistry of Asymmetric 1,2-Rearrangements of Chiral Sulfenylcyclopropanes into Cyclobutane Derivatives. A Novel Entry to Chiral Cyclobutane Systems Using Chiral Sulfinyl Groups

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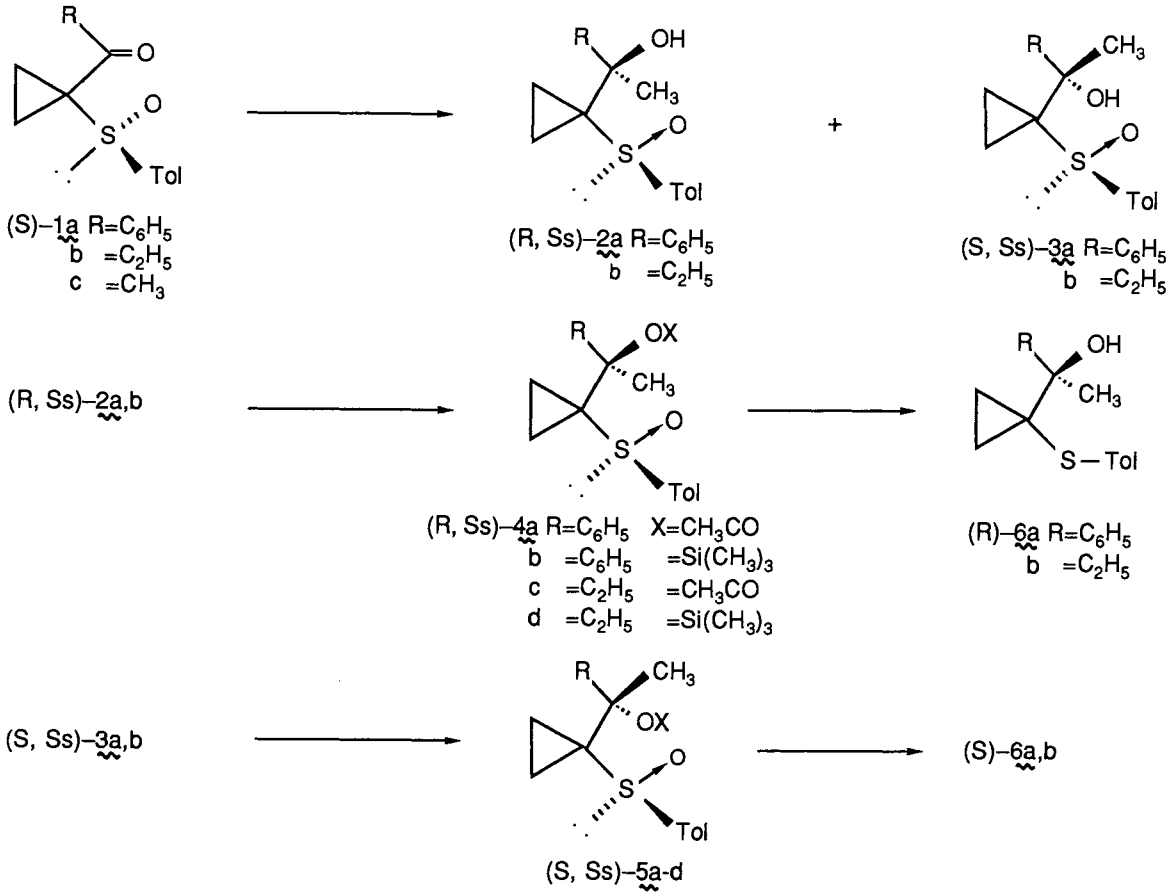
Stereochemistry of 1,2-rearrangements in optically active 1-(1-hydroxyalkyl)-1-sulfenylcyclopropane derivatives was determined. Both of the enantiomers underwent smoothly a 1,2-rearrangement of carbon-carbon bonds in cyclopropanes via the mesylates with complete stereospecificity to provide chiral cyclobutane derivatives with high enantiomeric excess.

A cyclopropane framework has played an important role in organic synthesis for providing a carbon three unit in molecules.[1] During the course of our stereochemical investigations in cyclopropane chemistry using chirality of organosulfur compounds,[2] we have demonstrated successful 1,2-asymmetric rearrangements in chiral sulfinylcyclopropanes and determined the stereochemistry of the rearrangements.[3]

We wish to communicate herein the stereochemistry of 1,2-rearrangements in chiral sulfenylcyclopropanes derived from optically active sulfinyl compounds.

Stereoselective preparation of 1-(1-hydroxyalkyl)-1-p-toluenesulfinylcyclopropanes (2a,b and 3a,b) has been achieved with extremely high stereoselectivity by the addition of Grignard reagents to chiral 1-acyl-1-p-toluenesulfinylcyclopropanes, (S)-1a-c.[3b] Reductive transformation of the optically active sulfoxides 2a,b and 3a,b into chiral 1-(1-hydroxyalkyl)-1-p-toluenesulfenylcyclopropanes 6a,b was studied. Reduction of 2a with lithium aluminum hydride was carried out in tetrahydrofuran (THF) at 0 °C for 14 h to give sulfide (R)-6a in a very poor yield (24%). Reduction of 2a with other reducing reagents resulted in low yield of (R)-6a. Reaction of 2a with sodium borohydride-cobalt(II) chloride (in ethanol at -20 °C for 8 h) or titanium(III) chloride (in THF at -20 °C for 15 h) produced (R)-



6a in 19 or 37% yield, respectively. This difficulty was circumvented by protecting the hydroxyl group as an acetate 4a or a silyl ether 4b, because the above poor yields were rationalized by occurrence of retro-aldol condensation of 2a under the conditions used. Reaction of the acetate 4a with titanium(III) chloride at -20 °C in THF for 12 h, followed by hydrolysis of the acetate with potassium hydroxide, afforded (R)-6a in 63% yield. Similarly, reduction of the silyl ether 4b with lithium aluminum hydride at room temperature,followed by desilylation with 10% aqueous hydrochloric acid,produced (R)-6a in 76% yield. The results are summarized in Table 1. Other stereoisomers, (S)-6a, and (R)- and (S)-6b were obtained in the same way via 5a,b, 4c,d, and 5c,d from the corresponding sulfoxides 3a, and 2b, and 3b with high optical purity. The optical rotation of the products are listed in Table 2.

1,2-Rearrangements of sulfenylcyclopropanes 6a,b occurred under mild conditions more smoothly than those of sulfinylcyclopropanes 2 and 3.[3] Upon treatment of (R)-(-)-6a with methanesulfonyl chloride and triethylamine in THF at 0 °C for 12 h, the sulfenylcyclopropane (R)-(-)-6a underwent a stereospecific 1,2-rearrangement via a mesylate (R)-7a to produce (R)-(-)-9a with retention of configu-

Table 1. Studies on Reduction of the Sulfoxides 2a and 4a,b

Sulfoxides	Reducing reagents (equiv.)	Solvent	Reaction temp / °C	Reaction time /h	Yields of 6a / %
2a	$LiAlH_4$ (1.5)	THF	0	14	24
2a	$NaBH_4$(5.0)-$CoCl_2$(2.0)	EtOH	-20	8	19
2a	$TiCl_3$ (3.0)	THF	-20	15	37
4a	$NaBH_4$(5.0)-$CoCl_2$(2.0)	EtOH	-20	15	24[a]
4a	$TiCl_3$ (3.0)	THF	-20	12	63[a]
4b	$LiAlH_4$ (1.5)	THF	0	24	71[b]
4b	$LiAlH_4$ (1.5)	THF	r.t.	20	76[b]

a) Treated with 10% KOH in methanol at room temperature after reduction.
b) Treated with 10% aqueous HCl after reduction.

ration with 99% stereospecificity. Reaction of the enantiomer (S)-(+)-6a under the same conditions provided (S)-(+)-9a with 94% stereospecificity. The similar stereochemical results were observed in other systems. The same procedures of (R)-(-)- and (S)-(+)-6b under the mesylation conditions led to the formation of (S)-(-)- and (R)-(+)-9b in almost complete stereospecificity with retention of configuration. The results are summarized in Table 2. The rearrangements were conducted with almost completely stereospecific retention of configuration, including errors of the order of a few per cent in the measurement of the optical rotations.

Chirality at the parts of the alcohols in 6a,b was transferred to cyclobutane systems in these rearrangements with retention of configuration. The stereochemical results are explained by double inversion of configuration in transformation of the mesylates 7a,b into cyclobutenes 9a,b via sulfonium salts 8a,b. Namely, in these reactions, the sulfonium salts 8a,b would be formed as the inter-

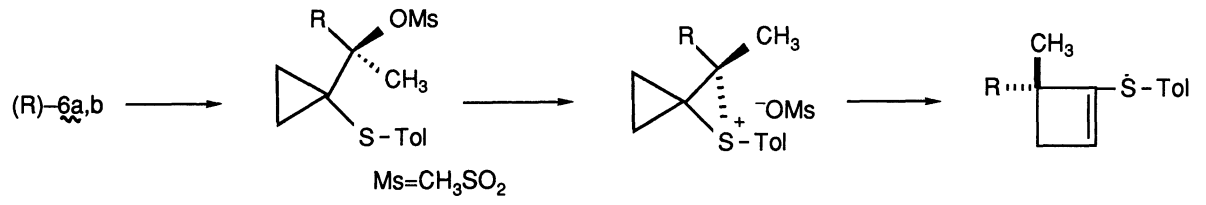


Table 2. The Stereospecificity in 1,2-Rearrangements of 6a,b to 9[a)]

Sulfenylcyclopropanes 6	$[\alpha]_D$/°(EtOH)	Reaction time/h	Cyclobutene derivatives 9 Product	$[\alpha]_D$ /°(EtOH)	Stereospecificity in 6a,b→9 /%[b)]
(R)-6a	-19.2	13	(R)-9a	-14.6	99
(S)-6a	+19.2	8	(S)-9a	+13.8	94
(R)-6b	-9.4	8	(S)-9b	-11.6	99
(S)-6b	+9.4	15	(R)-9b	+11.7	100

a) (R)- or (S)-6a,b were treated with methanesulfonyl chloride (3.0 equiv.)-triethylamine (5.0 equiv.) in THF at 0 °C to afford 9a,b in moderate yields (42-44%).

b) Based on the optical rotations of optically pure (R)-9a ($[\alpha]_D$ -14.7° (EtOH)) and (S)-9b ($[\alpha]_D$ -11.7°(EtOH)).[3)]

mediates by attack of the sulfenyl groups from the back side of the mesylate group, and a 1,2-rearrangement of one of the carbon-carbon bonds in the cyclopropanes would occur from the rear side of the sulfur atoms in the sulfonium salts 8a,b with complete stereospecificity, producing optically active cyclobutene derivatives (R)- or (S)-9a,b with high enantiomeric excess.

Thus, both of the enantiomers of cyclobutene derivatives were readily obtainable depending on the chiral alcohols used, originated from chiral sulfinyl group of the same absolute configuration. Therefore, this novel method provides a useful and facile alternative entry to chiral cyclobutane derivatives.

References

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