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Stereoselective Synthesis of Allyl and Homoallyl Alcohols by the Ring Opening Reactions of 2-(2-Phenylthiocyclobutyl)oxiranes and Oxetanes

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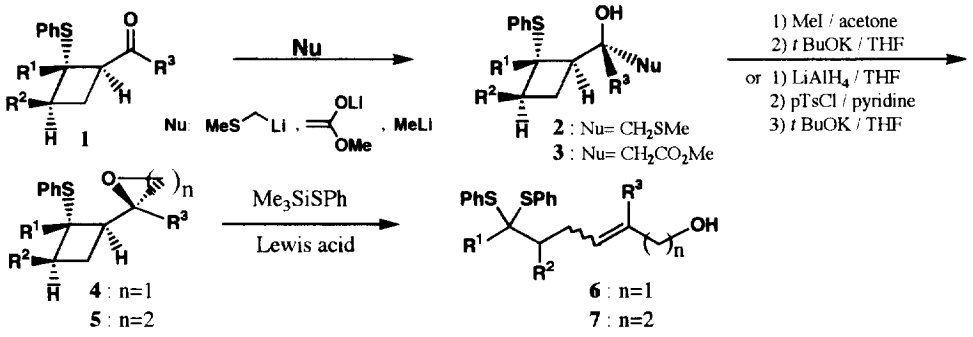
Abstract: Titanium(IV)-promoted ring opening reactions of 2-(2-phenylthiocyclobutyl)oxiranes and the corresponding oxetanes proceeded with high stereospecificity to give allyl and homoallyl alcohols in good yields. The reversal of stereoselectivity was observed in the similar reaction of the oxiranes using ethylaluminum dichloride as a catalyst.

The stereoselective synthesis of trisubstituted olefins is one of the most important problems in organic synthesis and numerous efforts have been directed to the construction of such compounds.[1] Recently, we have developed a useful method for the highly stereoselective synthesis of various β, γ-unsaturated ketones utilizing *trans*-2-phenylthiocyclobutyl ketones **1**,[2] which are easily prepared by the [2+2] cycloaddition of alkenyl sulfides with vinyl ketones.[3] The high stereoselectivity of this transformation is accomplished by a combination of the diastereoselective addition of Grignard reagents to **1** and Lewis acid-promoted stereospecific ring opening reaction of the resulting cyclobutanemethanol derivatives. These results prompted us to apply this methodology to the stereoselective syntheses of olefins with various functional groups. In this communication, we wish to report the preparation of allyl and homoallyl alcohols **6** and **7** by the Lewis acid-promoted ring opening reactions of 2-(2-phenylthiocyclobutyl)oxiranes **4** and the corresponding oxetanes **5** (Eq. 1), in which unusual Lewis acid dependence of stereoselectivity was observed.

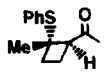
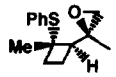
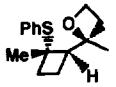
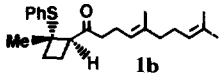
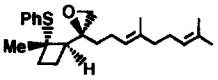
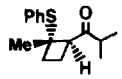
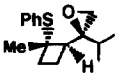
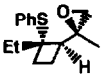
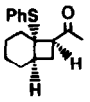
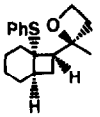
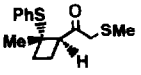
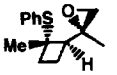


(1)

First the preparations of starting materials **4** and **5** from *trans*-2-phenylthiocyclobutyl ketones **1**[4] were examined (Table 1). Transformation of **1** to the oxiranes **4** was performed resulting good overall yields by the similar method reported by Tanis *et al*,[5] in which the addition of methylthiomethyllithium to **1** proceeded with high diastereoselectivity (>99%). The oxirane **4a'**, the epimer of **4a**, was also obtained by similar procedures using the methylthiomethyl ketone **1f** and methyllithium (run 7). The cyclobutyl ketones **1** were treated with the lithium enolate of methyl acetate[6] at -78 °C to give the β-hydroxy esters. The reduction of the esters ($LiAlH_4$ / THF / 0 °C) followed by the tosylation (*p*-TsCl / pyridine / 0 °C) and intramolecular etherification (*t*-BuOK / THF / room temperature) of the resulting diols afforded the corresponding oxetanes **5** in good yields with high diastereoselectivity (runs 2 and 6).

Next the Lewis acid-promoted ring opening reaction of the oxiranes **4** outlined in Eq. 1 was studied. It is

Table 1. Preparation of 2-(2-Phenylthiocyclobutyl)oxirane **4** and Oxetane **5**.

Run	Cyclobutyl ketone **1**	Nucleophile (1.5 equiv.)	**2** or **3**[a] (Yield / %)	Diastereoisomeric purity (%)[b]	**4** or **5**[a] (Overall yield / %)
1	 **1a**	CH_3SCH_2Li	**2a** (85)	99	 **4a** (77)
2	**1a**		**3a** (92)	99.5	 **5a** (66)
3	 **1b**	CH_3SCH_2Li	**2b** (94)	—	 **4b** (70)
4	 **1c**	CH_3SCH_2Li	**2c** (97)	99	 **4c** (62)
5	 **1d**	CH_3SCH_2Li[c]	**2d** (87)	100[d]	 **4d** (82)
6	 **1e**		**3e** (95)	100[d]	 **5e** (74)
7	 **1f**	CH_3Li	**2a'** (82)	95	 **4a'** (71)

a) The structures of these compounds were supported by IR and NMR spectra. b) Determined by HPLC analysis. c) The reaction was carried out using 2 equiv. of methylthiomethyllithium. d) The minor isomer could not be detected.

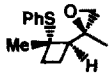
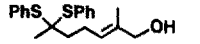
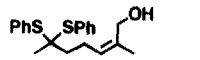
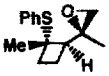
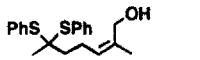
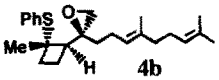
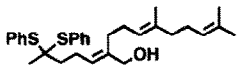
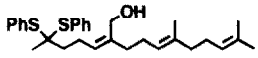
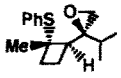
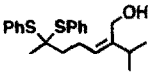
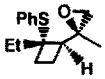
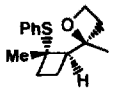
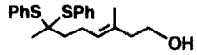
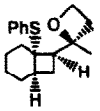
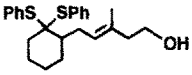
reasonable to assume that the stereochemistry of olefin formed was determined by the conformation of the oxirane moiety of **4** in the transition state. Since **4** possessing a phenylthio group would serve as a bidentate ligand for association with Lewis acid, we expected that its conformation is dependent on the number of empty sites of coordination of the catalyst. On the basis of this consideration, we examined the ring opening reaction of **4** using titanium(IV) and aluminum(III) catalysts.

The oxirane **4a** was treated with phenylthiotrimethylsilane in the presence of dichlorodiisopropoxytitanium(IV) to give the allyl alcohol (*E*)-**6a** with high stereoselectivity (run 1). In a similar manner, various (*E*)-allyl alcohols **6** were obtained as shown in Table 2. Since the reaction of the epimer **4a'** gave (*Z*)-**6a** predominantly (run 3), it is clear that the present reaction is stereospecific. The extremely high *E*-selectivity was observed in the titanium(IV)-promoted transformation of oxetanes **5** to the homoallyl alcohols **7** (runs 10 and 12).

Contrary to the above observations, (*Z*)-**6a-c** were isolated as major products after hydrolysis (KF / EtOH / room temperature) of the initially formed trimethylsilyl ethers when the reactions of **4a-c** were carried out using ethylaluminum dichloride as a catalyst (runs 2, 6, and 8). The reversal of selectivity, however, was not observed in the aluminum(III)-catalyzed reaction of the epimer **4a'** and the oxetane **5a** (runs 4 and 11).

The stereoselectivity observed in these reactions is well explained by considering the conformation of the oxirane **4** or oxetane **5** complexed with Lewis acid. The Lewis acid possessing two empty sites of coordination such as titanium(IV) species coordinates with **4** to form the conformationally rigid cyclic chelate **A**, which in turn reacts with phenylthiotrimethylsilane to produce the *E*-isomer as depicted in Fig.1. On the other hand, the aluminum(III) catalyst coordinated only by oxirane would be located so as to minimize the steric repulsion

Table 2. The Ring Opening Reactions of 2-(2-Phenylthiocyclobutyl)oxirane **4** and Oxetane **5**.[7]

Run	**4** or **5**[a]	Lewis acid (equiv.)	Time (min)	**6** or **7**[b,c] (Yield / %)		*E* : *Z*[d]
1	 **4a**	$TiCl_2(O^iPr)_2$ (1.5)	30		**6a** (77)	97 : 3
2		$EtAlCl_2$ (0.1)	30		**6a** (85)[e]	8 : 92
3	 **4a'**	$TiCl_2(O^iPr)_2$ (1.5)	20		**6a** (62)	5 : 95
4		$EtAlCl_2$ (0.1)	25		**6a** (43)	17 : 83
5	 **4b**	$TiCl_2(O^iPr)_2$ (1.5)	15		**6b** (75)	75 : 25
6		$EtAlCl_2$ (0.1)	30		**6b** (83)	6 : 94
7	 **4c**	$TiCl_2(O^iPr)_2$ (1.5)	10		**6c** (85)	96 : 4
8		$EtAlCl_2$ (0.1)	20		**6c** (72)	15 : 85
9	 **4d**	$TiCl_2(O^iPr)_2$ (1.5)	20		**6d** (81)	98 : 2
10	 **5a**	$TiCl_3(O^iPr)$ (1.5)	15		**7a** (88)[e]	99.5 : 0.5[f]
11		$EtAlCl_2$ (1.5)	90		**7a** (50)	72 : 28
12	 **5e**	$TiCl_3(O^iPr)$ (1.5)	15		**7e** (70)[e,g]	99 : 1[h]

a) The starting materials were used without separation of the stereoisomers. b) The structures of these compounds were supported by IR and NMR spectra. c) The configurations of the products were determined by NOE experiments. d) Determined by NMR spectra. e) The configurations were determined by the comparison with the authentic samples. f) Determined by HPLC analysis. g) The configuration was determined after the transformation to 2-(3-methyl-2-pentenyl)cyclohexanone.[2a] h) Determined by capillary GLC analysis after the transformation to 3-methyl-1-(2-methylenecyclohexyl)-2-pentene.[8]

between the cyclobutane ring and maintain the antiperiplanar arrangement of breaking σ-orbitals of cyclobutane and oxirane rings (conformer **B**). As a result, the corresponding Z-isomer becomes the main product in this reaction.[9] It is assumed that the other steric factor such as repulsion between the cyclobutane ring and the substituents on the oxirane or oxetane would be predominant in the aluminum(III)-catalyzed reactions of oxirane **4a'** and oxetane **5a**, hence the reversal of stereoselectivity was not observed.

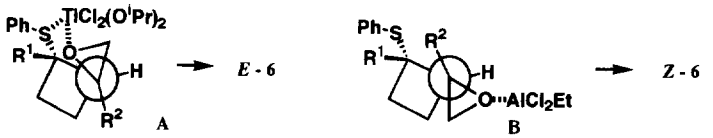
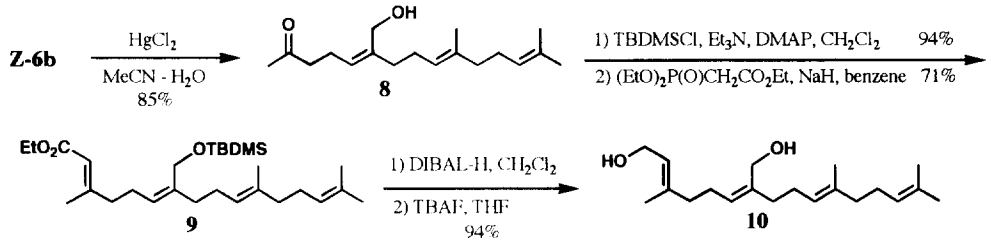


Fig. 1

The typical experimental procedure for the titanium(IV)-promoted reaction is as follows: To a CH_2Cl_2 (1.5 ml) solution of dichlorodiisopropoxytitanium(IV) (0.45 mmol) was added a CH_2Cl_2 solution of phenylthiotrimethylsilane (0.45 mmol, 1.07M) at -78 °C and the reaction mixture was stirred for 30 min. A CH_2Cl_2 (1.2 ml) solution of 2-methyl-2-(2-methyl-2-phenylthiocyclobutyl)oxirane (**4a**) (70 mg, 0.3 mmol) was then added to the reaction mixture. After stirring for 30 min at the same temperature, the reaction was quenched by addition of 1N NaOH aqueous solution. The reaction mixture was filtered through cerite and the filtrate was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and condensed in vacuo. The residue was purified by chromatography on silica gel (AcOEt-hexane) to give 2-methyl-6,6-bis(phenylthio)-2-hepten-1-ol (**6a**) (79 mg, 77%).

The synthetic utility of the present reaction is briefly demonstrated in the following scheme. The allylic alcohol *Z*-**6b**[10] was hydrolyzed to the ketone **8**. After protection of hydroxyl group, the ketone was treated with the phosphonate carbanion to produce the α,β-unsaturated ester **9**.[11] The reduction of **9** with diisobutylaluminum hydride followed by the deprotection gave the diterpene alcohol with antipeptic ulcer activities, plaunotol **10**.[12]



REFERENCES AND NOTES

1. T. Takeda, Y. Kabasawa, and T. Fujiwara, *Tetrahedron*, **51**, 2515 (1995) and references cited therein.
2. a) T. Fujiwara, T. Iwasaki, and T. Takeda, *Chem. Lett.*, **1993**, 1321. b) T. Fujiwara, T. Iwasaki, J. Miyagawa, and T. Takeda, *Chem. Lett.*, **1994**, 343.
3. T. Takeda, K. Morita, T. Fujii, and T. Fujiwara, *Chem. Lett.*, **1986**, 1311.
4. The cyclobutyl ketone **1b** was prepared by the alkylation of the lithium enolate of **1a** with geranyl bromide (2 equiv.) in 50% yield. In a similar manner, **1c** was obtained by methylation (MeI (3 equiv.)) of lithium enolate of ethyl (1R*, 2S*)-2-methyl-2-phenylthiocyclobutyl ketone in 88% yield. The cyclobutyl ketone **1f** was synthesized by the sulfenylation of the lithium enolate of **1a** with methyl *p*-toluenethiosulfonate in 66% yield.
5. S. P. Tanis, M. C. McMills, and P. M. Herrinton, *J. Org. Chem.*, **50**, 5887 (1985).
6. M. W. Rathke, *J. Am. Chem. Soc.*, **92**, 3222 (1970).
7. The titanium(IV)-promoted reaction was performed with a same procedure as described in the text, unless otherwise noted. The ethylaluminum dichloride-promoted reaction was carried out by the addition of a hexane solution of ethylaluminum dichloride (0.1 or 1.5 equiv.) to a CH_2Cl_2 solution of the cyclobutane **4** or **5** and phenylthiotrimethylsilane (1.5 equiv.) at -78 °C. The product was obtained after the treatment of the crude trimethylsilyl ether with potassium fluoride (10 equiv.) in EtOH at room temperature.
8. T. Fujiwara, A. Suda, and T. Takeda, *Chem. Lett.*, **1992**, 1631.
9. The metal cation dependence of stereoselectivity in the reactions of ester enolates with imines has been reported. M. Shimizu, Y. Kooriyama, and T. Fujisawa, *Chem. Lett.*, **1994**, 2419 and references cited therein.
10. The *Z*-isomer of **6b** could be isolated by the preparative TLC and was used for the synthesis of **10**.
11. The 2,3-double bond isomer of **9** was isolated as a by-product in 15% yield.
12. A. Ogiso, E. Kitazawa, M. Kurabayashi, A. Sato, S. Takahashi, H. Noguchi, H. Kuwano, S. Kobayashi, and H. Mishima, *Chem. Pharm. Bull.*, **26**, 3117 (1978); S. Inoue, K. Honda, N. Iwase, and K. Sato, *Bull. Chem. Soc. Jpn.*, **63**, 1629 (1990).

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