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Acid-promoted Rearrangement of α,β-Epoxy Acylates: Remarkable Effects of an Acyl Group and a Lewis Acid

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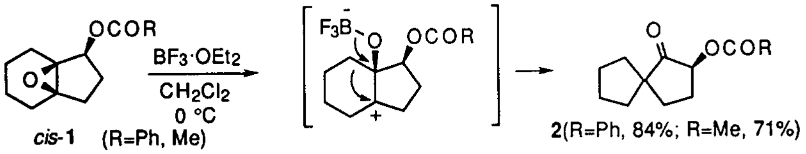
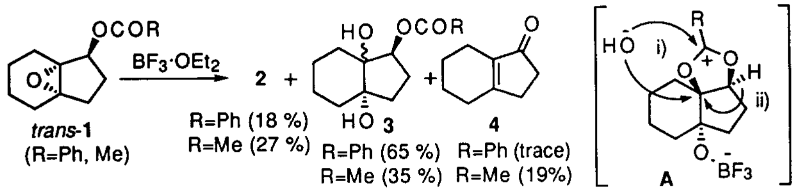
Abstract: Remarkable steric and electrostatic effects of acyl groups and exceptionally bulky Lewis acid, (MABR), which make the rearrangement reaction applicable to various types of reaction systems including acyclic ones in the acid-promoted rearrangement of α,β-epoxy acylates, were found. © 1997, Elsevier Science Ltd. All rights reserved.

Although the rearrangement reactions of α,β-epoxy alcohols and their silyl ethers have been frequently used for the transformations of carbon skeletons,[1] the use of the rearrangement reactions of α,β-epoxy acylates is rare.[2] This is due to the neighboring group participation of the acyloxy group that assists in the cleavage of the epoxide by forming a dioxenium ion, which prevents any successive rearrangement.[3] Recently, we found that Lewis acid treatment of bicyclic tetrasubstituted α,β-epoxy acylates afforded the spiro compounds by cleavage of the oxirane ring at the β-position of the acyloxy group due to its inducing effect, followed by successive rearrangement of the carbon skeleton.[4] However, the success of this reaction is governed by the stereochemistries of the substrates. Namely, the bicyclic *cis*-epoxy acylates (*cis*-**1**) afforded the rearranged products in good yields (eq. 1), whereas the bicyclic *trans*-ones (*trans*-**1**) gave unsuccessful results via intermediate **A** because of the neighboring group participation of the acyloxy group (eq. 2). Suppression of this neighboring group participation was then strongly desirable in order to make this rearrangement reaction applicable to many reaction systems. We have now found such remarkable effects (steric and electrostatic effects) of acyl groups and exceptionally bulky Lewis acid, methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR),[5] which make the rearrangement reaction applicable to not only bicyclic *trans*-epoxy acylates but also to monocyclic and acyclic systems.



(eq. 1)

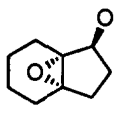
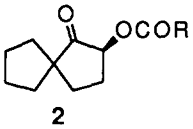
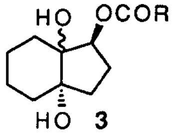
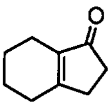
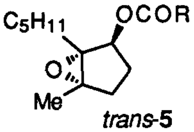
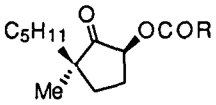
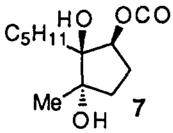
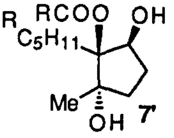
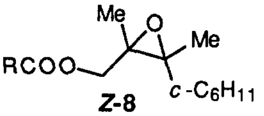
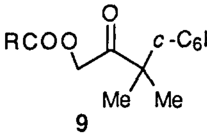
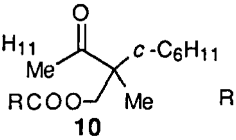
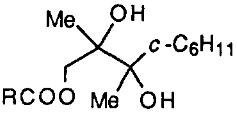


(eq. 2)

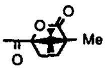
We initially examined an acyl group with less neighboring group participation using *trans*-**1** as the substrate and 1 equivalent of $BF_3 \bullet OEt_2$ as the Lewis acid in CH_2Cl_2 at 0°C (Table 1). Although only a small amount of rearranged product was obtained along with the diols and the enone in the cases of a benzoyl group (entry 1), the use of a *p*-nitrobenzoyl group dramatically increased the yield of the rearranged product (entry 2). The use of a bulky camphanoyl group also gave the desired product in good yield (entry 3) though the substrates with a trifluoroacetyl or a pivaloyl group gave poor results due to their instability. We then examined the effect of an acyl group using monocyclic *trans*-**5**. The same tendency as *trans*-**1** was observed. Thus, benzoyloxy derivative **5a** gave a 92% yield of diols (**7a** and **7'a**) with no rearranged product (entry 4)

Table 1. Lewis Acid Treatment of α,β-Epoxy Acylates.[6,7]

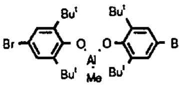
(Acyl groups of the products, **a**: R=Ph; **b**: R=*p*-NO_2Ph; **c**: COR=(-)-camphanoyl[a])

Entry	Substrate	Lewis Acid	Rearranged Product (Yield)		Other Products (Yield)	
	 *trans*-**1**		 **2**		 **3**	 **4**
1	**a**; R=Ph	$BF_3•OEt_2$	**2a** (18%)		**3a**(65%)	**4a** (trace)
2	**b**; R=*p*-NO_2Ph		**2b** (63%)		**3b** (trace)	**4b** (20%)
3	**c**; COR=(-)-camphanoyl		**2c** (65%)		**3c** (trace)	**4c** (6%)
	 *trans*-**5**		 **6**		 **7**	 **7'**
4	**a**; R=Ph	$BF_3•OEt_2$	--		**7a** (42%)	**7'a** (50%)
5	**c**; COR=(-)-camphanoyl		**6c** (56%)		**7c** (trace)	--
6	**c**; COR=(-)-camphanoyl	MABR	**6c** (83%)		--	--
	 **Z-8**		 **9**	 **10**	 **11**	
7	**a**; R=Ph	$BF_3•OEt_2$	--	--	**11a** (54%)	
8	**a**; R=Ph	MABR	**9a** (58%)	**10a** (12%)	--	
9	**b**; R=*p*-NO_2Ph		**9b** (73%)	**10b** (6%)	--	
10	**c**; COR=(-)-camphanoyl		**9c** (82%)	**10c** (11%)	--	

[a] (-)-camphanoyl=



[b] MABR=



but **5c** with a camphanoyl group afforded 56% of the rearranged product **6c** (entry 5). The use of a bulky Lewis acid, MABR,[5] in *trans*-**5** gave 83% yield of the rearranged product in combination with the bulky camphanoyl functionality (entry 6). MABR is also effective in the acyclic systems. Although acyclic α,β-epoxy benzoate (Z-**8a**) afforded the diol **11a** by the use of $BF_3 \cdot OEt_2$ (entry 7), the use of MABR predominantly afforded the rearranged products (**9** and **10**) in good yields. Thus, Z-**8** afforded **9**, formed by the migration of a methyl group, predominantly along with minor **10**, formed by the migration of an acyloxymethyl group (entries 8-10). The result is rationalized as follows. MABR coordinates with the epoxide from the less hindered site to cleave the oxirane ring at the β-position of the acyloxy group. Increasing steric repulsion between a bulky MABR ligand and substituents at the α-position of the acyloxy group prompts successive migration. Transition state of the reaction is depicted in Figure 1. The repulsion between the MABR ligand and the methyl group accelerates migration of the methyl group and **9** was predominantly produced.

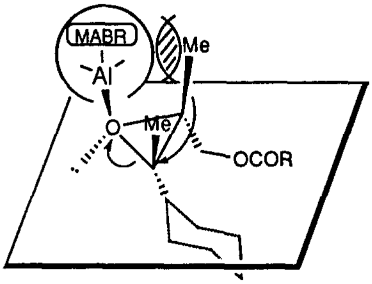
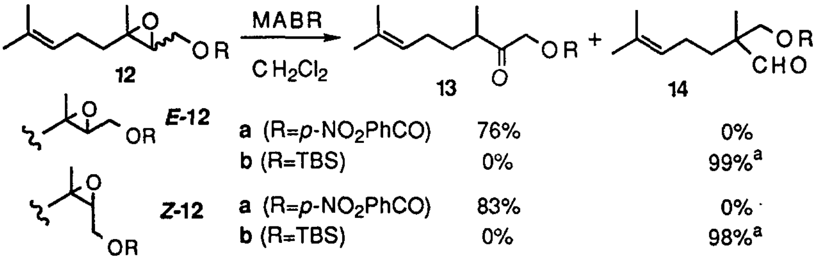


Figure 1

A characteristic feature of our rearrangement reaction using an electron-withdrawing acyloxy group is exemplified by the following experiments (Scheme 1). Thus, treatment of trisubstituted epoxy *p*-nitrobenzoates *E*-**12a** and *Z*-**12a** with MABR afforded **13a** (R=*p*-NO_2PhCO-) by hydride migration in good yields, and not **14a** (R=*p*-NO_2PhCO-). These results are in striking contrast with Yamamoto's results,[8] in which the reaction of epoxides *E*-**12b** and *Z*-**12b** having an electron-donating silyl ether (TBS: *tert*-butyldimethylsilyl) with MABR selectively afforded β-siloxy aldehydes **14b** (R=TBS) and not **13b** (R=TBS). It is noteworthy that a change in the protective group of an alcohol can control the migratory aptitude of the substituents.



		13	14
E-12	a (R=*p*-NO_2PhCO)	76%	0%
	b (R=TBS)	0%	99%[a]
Z-12	a (R=*p*-NO_2PhCO)	83%	0%
	b (R=TBS)	0%	98%[a]

Scheme 1

[a] Yamamoto's results (see ref. 8)

In conclusion, the successful rearrangement of acyclic epoxy acylates was achieved in addition to cyclic ones by controlling the electron-withdrawing nature and ability of the neigboring group participation of acyl groups by proper combination of an acyl group and a Lewis acid. The work here will promise the successful transformation of the carbon skeleton based on the rearrangement of various types of α,β-epoxy acylates.

References and Notes

1. For examples where electron-donating hydroxy derivatives initiate cleavage of the oxirane ring at the α-position of the hydroxy function and successive migration, see: Maruoka, K.; Sato, J.; Yamamoto, H. *Tetrahedron* **1992**, *48*, 3749-3762; Nagasawa, T.; Taya, K.; Kitamura, M. Suzuki, K. *J. Am. Chem. Soc.* **1996**, *118*, 8949-8950 and references cited therein. For rearrangement of epoxy alcohol derivative, see: Marson, C. M.; Walker, A. J.; Pickering, J.; Hobson A. D.; Wrigglesworth, R.; Edge, S. J. *J. Org. Chem.* **1993**, *58*, 5944-5951 and references cited therein.
2. For an example of epoxy acetates, see: Coxon, J. M.; Hartshorn, M. P.; Kirk, D. N. *Tetrahedron* **1964**, *20*, 2531-2545; **1964**, *20*, 2547-2552. In the cases, however, the yields of the rearranged products were very low and the regioselective cleavage of oxirane ring was not observed.
3. Pittman, JR., C. U.; McManus, S. P.; Larsen, J. W. *Chem. Rev.* **1972**, *72*, 357-438.
4. Fujioka, H.; Kitagaki, S.; Imai, R.; Kondo, M.; Okamoto, S.; Yoshida, Y.; Akai, S.; Kita, Y. *Tetrahedron Lett.* **1995**, *36*, 3219-3222.
5. For preparation, see: Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 316-322.
6. Racemic α,β-epoxy acylates in the cases of benzoates and *p*-nitrobenzoates and diastereomeric isomers (1:1 mixture) in the cases of (-)-camphanoates were used in the reactions. Epoxy acylates **8**, *E*-**12** and *Z*-**12** were prepared by epoxidation (MCPBA) followed by acylation of the corresponding allyl alcohols. *trans*-Epoxy acylates (*trans*-**1** and **5**) were prepared by epimerization of *cis*-epoxy alcohols, which were stereoselectively obtained by epoxidation of the corresponding allyl alcohols with ^{t}BuOOH/VO(acac)$_2$, using the Mitsunobu reaction [Mitsunobu, O. *Synthesis* **1981**, 1-28].
7. **Reaction with BF_3•OEt_2.** To a solution of epoxy acylate (0.1mmol) in CH_2Cl_2 (2.8ml) was added BF_3•OEt_2 (0.1mmol) at 0°C under N_2, and the reaction mixture was stirred at 0°C for 10 ~ 30 min. After having been diluted with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate) to give the pure rearrangement product.

   Reaction with MABR. To a solution of MABR (0.2mmol) in CH_2Cl_2 (2.2ml) was added an epoxy acylate (0.1mmol) in CH_2Cl_2 (2.2ml) at 0°C under Ar. The mixture was stirred at 0°C for 10 ~ 30 min. After having been diluted with CH_2Cl_2, 1N HCl was added to the mixture. The same procedure as stated above then gave the pure rearrangement product.

   Satisfactory spectroscopic data were obtained for all new compounds.
8. (a) Maruoka, K.; Ooi, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 6431-6432. (b) Maruoka, K.; Ooi, T.; Nagahara, S.; Yamamoto, H. *Tetrahedron* **1991**, *47*, 6983-6998.

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