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REGIO- AND STEREOSELECTIVE RING OPENING OF EPOXY ALCOHOLS WITH ORGANOALUMINIUM COMPOUNDS LEADING TO 1,2-DIOLS

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Abstract: Introduction of alkyl, alkynyl group, or hydride occurs regioselectively at the 3 position of the epoxy alcohols with inversion of the configuration upon treatment with organoaluminium reagents to produce *vic*-diols.

Recent development of asymmetric epoxidation of allylic alcohols[1] attracts much attention to the ring opening of epoxy alcohols.[2] Regioselective epoxide opening by such nucleophiles as dialkylcuprate[3] and $NaAlH_2(OCH_2CH_2OCH_3)_2$[2a,4] producing 1,3-diols has been well studied and found applications in the synthesis of natural products. Few examples[5] are known, however, for the regioselective production of 1,2-diols. Here we wish to report that the treatment of some 2,3-epoxy-1-alkanols with trialkylaluminium compounds provides 1,2-diols regioselectively.

A solution of epoxy alcohol Ia (0.26 g, 2.0 mmol) in hexane (3.0 ml) was added dropwise to a solution of trimethylaluminium (1.0 *M*, 6.0 ml, 6.0 mmol) in hexane at 0°C under argon atmosphere. After stirring for 30 min at 0°C, the resulting mixture was diluted with CH_2Cl_2 (20 ml), treated with NaF (2.5 g, 60 mmol) and water (1.1 ml, 60 mmol). Vigorous stirring of the resulting suspension was continued at 25°C for 0.5 h. The semi-solid was filtered and the remaining solid was washed with ether (3x15 ml). The combined filtrate and washings were dried and concentrated. Purification of the residue by silica gel column chromatography gave 1,2-diol IIa (0.27 g, 94% yield) as a colourless oil.[6] The product was identical with the compound prepared by the hydroboration of (*E*)-3-methyl-2-hepten-1-ol. Thus the methyl group was introduced regioselectively at the 3 position with inversion of the configuration.

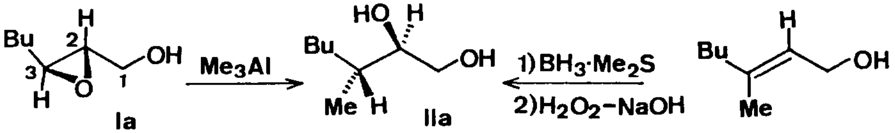
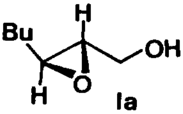
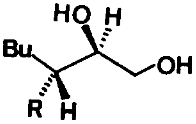
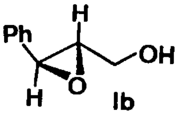
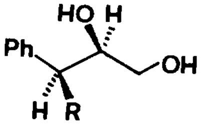
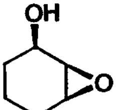
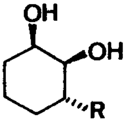
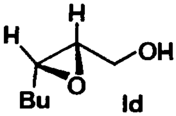
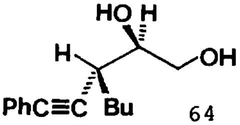
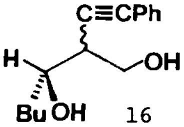
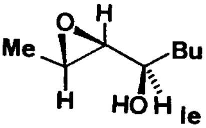
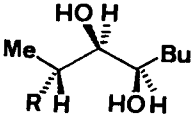
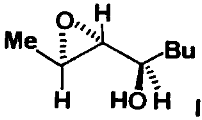
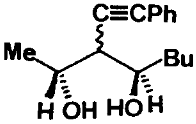


Table 1. Ring opening of epoxy alcohols with organoaluminium compounds^{a}

Run	Epoxy Alcohol	Reagent	Conditions		Product		Yield^{b}
			(°C)	(h)			(%)
1	 Ia	Me_3Al	0	0.5		IIa:R = Me	94
2		$PhC{\equiv}CAlEt_2$	0	2		R = PhC≡C-	95
3		$Me_3SiC{\equiv}CAlEt_2$	0	2		R = $Me_3SiC{\equiv}C$-	72
4		$^{i}Bu_2AlH$	0	1		R = H	72^{c}
5	 Ib	Me_3Al	0	1		IIb:R = Me	80^{d}
6		$PhC{\equiv}CAlEt_2$	25	1.5		R = PhC≡C-	80
7		$^{i}Bu_2AlH$	25	2		R = H R = ^{i}Bu	79 2
8		$^{i}Bu_3Al$	25	2		R = H R = ^{i}Bu	64 18
9	 Ic	$PhC{\equiv}CAlEt_2$	25	2		IIc:R = PhC≡C-	65^{e}
10		$^{i}Bu_2AlH$	25	1		R = H	47
11	 Id	$PhC{\equiv}CAlEt_2$	25	1	 64  16		
12	 Ie	Me_3Al	25	2		R = Me	86
13		$PhC{\equiv}CAlEt_2$	25	2		IIe:R = PhC≡C-	60^{f}
14		$Me_3SiC{\equiv}CAlEt_2$	25	2		R = $Me_3SiC{\equiv}C$-	77
15	 If	$PhC{\equiv}CAlEt_2$	25	4			20^{g}

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[a] One mol of epoxy alcohol and three mol of organoaluminium reagent were employed. [b] Isolated yields. [c] Heptan-1,3-diol (14%) was also obtained along with 1,2-diol. [d] See ref. 7. [e] See ref. 8. [f] See ref. 9. [g] The rest contained a couple of products whose structures could not be determined. No trace of 1,2-diol was observed.

As shown in Table 1, alkynyl group and hydride are introduced selectively in preference to the ubiquitous alkyl group. Nonpolar solvents such as hexane or dichloromethane gave the best results. In ether or THF the reaction did not take place.

The observed reactions are characterized by following features. (1) The ring opening proceeds with inversion of its stereochemistry at carbon 3 with the substrates Ia, Ic, Id, and Ie. In contrast, treatment of epoxy alcohol Ib derived from cinnamyl alcohol with Me_3Al gives 1,2-diol with retention of the configuration. (2) Epoxy alcohols generated from (*E*)-allylic alcohols (Ia, Ib) and threo epoxy alcohol (Ie) provide 1,2-diols smoothly in good yields and with high stereoselectivity, whereas epoxides derived from (*Z*)-allylic alcohols (Ic, Id) and erythro epoxide (If) react sluggishly[10] with organoaluminium reagents to give 1,2-diols in relatively low yields and with less regioselectivity.[11] In the extreme, no trace of 1,2-diol was obtained in the case of the reaction of If and $PhC{\equiv}CAlEt_2$ (run 15).[12,14]

References and Notes

1. T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 102, 5974 (1980); V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, *ibid.*, 103, 6237 (1980).
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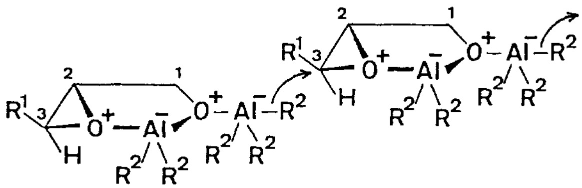
3. M. R. Johnson, T. Nakata, and Y. Kishi, *Tetrahedron Lett.*, 1979, 4343; R. D. Wood and B. Ganem, *ibid.*, 23, 707 (1982).
4. P. Ma, V. S. Martin, S. Masamune, K. B. Sharpless, and S. M. Viti, *J. Org. Chem.*, 47, 1380 (1982).
5. The reaction of Ic with $Et_2AlC{\equiv}COEt$ has been reported to give 1,2-diol selectively. S. Danishefsky, M-Y. Tsai, and T. Kitahara, *J. Org. Chem.*, 42, 394 (1977). More recently, regioselective ring opening of benzyl ether derived from 2,3-epoxy alcohol with Me_3Al in the presence of a catalytic amount of BuLi has been reported. A. Pfaltz and A. Mattenberger, *Angew. Chem. Suppl.*, 1982, 161.
6. The diols were transformed into diacetates which were characterized spectrometrically. Diacetate of IIa: bp 80°C (bath temp, 1 Torr); IR (neat) 1745 1225, 1050 cm^{-1}; NMR (CCl_4) δ0.91 (d, J = 6.6 Hz, 3H), 1.0-2.0 (m, 10H), 2.0 (s, 6H), 3.88 (dd, J = 7.5 and 12 Hz, 1H), 4.23 (dd, J = 3.0 and 12 Hz, 1H), 4.80 (ddd, J = 3.0, 6.3, and 7.5 Hz, 1H). Found: *m/e* 231.1649. Calcd for $C_{12}H_{23}O_4$: M+1, 231.1595.
7. Diacetate of IIb: bp 100°C (bath temp, 1 Torr); IR (neat) 1745, 1500, 1240, 1220, 1050, 760, 700 cm^{-1}; NMR (CCl_4) δ1.3 (d, J = 7.0 Hz, 3H), 2.03 (s, 3H), 2.13 (s, 3H), 3.10 (dq, J = 2.0 and 7.5 Hz, 1H), 3.83 (dd, J = 6.7 and 14 Hz, 1H), 4.30 (dd, J = 3.5 and 14 Hz, 1H), 5.37 (ddd, J = 3.5, 6.7, and 9.5 Hz, 1H), 7.6 (m, 5H). Hydroboration-oxidation of (*Z*)-3-phenyl-2-buten-1-ol gave erythro diol which was identical with IIb.

8. The product IIc was identical with the compound prepared by the reaction of 3-phenylethynylcyclohexene with N-methylmorpholine-N-oxide in the presence of OsO_4 (V. VanRheenen, R. C. Kelly, and D. Y. Vha, *Tetrahedron Lett.*, 1976, 1973). Diacetate of IIc: bp 172°C (bath temp, 0.05 Torr); IR (neat) 1745, 1600, 1495, 1250, 1045, 760 cm^{-1}; NMR (CCl_4) δ1.5-1.9 (m, 6H), 2.0 (s, 6H), 3.0 (m, 1H), 4.95 (dd, $J = 2.7$ and 8.3 Hz, 1H), 5.2 (m, 1H), 7.3 (m, 5H). Found: C, 71.87; H, 6.71%. Calcd for $C_{18}H_{20}O_4$: C, 71.99; H, 6.71%.
9. Diacetate of IIe: bp 140°C (bath temp, 0.15 Torr); IR (neat) 1750, 1600, 1500, 1225, 1020, 760 cm^{-1}; NMR (CCl_4) δ0.75-1.0 (m, 3H), 1.2 (d, $J = 6.5$ Hz, 3H), 1.0-1.7 (m, 9H), 2.06 (s, 3H), 2.10 (s, 3H), 2.87 (dq, $J = 9.0$ and 7.0 Hz, 1H), 4.93 (dd, $J = 3.0$ and 9.0 Hz, 1H), 5.33 (dt, $J = 3.0$ and 6.0 Hz, 1H). Hydroboration-oxidation of (*Z*)-7-methyl-9-phenyl-6-nonen-5-ol gave the diol which was identical with the sample derived from hydrogenation of IIe.
10. Trimethylaluminium is quite reluctant to react with Ic and Id. These epoxides were recovered unchanged after 5 h at 25°C.
11. For these substrates, the coordination of epoxy-oxygen to aluminium is possibly interfered by the steric repulsion between alkyl group on carbon 3 and alkyl groups attached on aluminium.
12. The stereochemical outcome of the reaction can be understood as follows. The hydroxy group is converted into aluminium alkoxide with the first trialkylaluminium molecule. The epoxy-oxygen coordinates to the aluminium and this coordination plays the important role in the product- and rate-determining ring opening step. The epoxide carbon (C_3)-oxygen bond is thus loosened at C_3 and the bond is cleaved by the attack of the alkyl anion liberated from the second molecule of trialkylaluminium possibly coordinated on another substrate molecule. This S_N2 type reaction via tight ion pair is well precedented.[13] Meanwhile, the reason for the reaction being proceed with retention of the configuration in the case of Ib is not clear. An intimate ion pair containing the carbonium ion stabilized by the phenyl group in the solvent cage may explain the observed stereochemistry.



13. A. Itoh, S. Ozawa, K. Oshima, S. Sasaki, H. Yamamoto, T. Hiyama, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 53, 2357 (1980); T. Hiyama, Y. Morizawa, H. Yamamoto, and H. Nozaki, *ibid.*, 54, 2151 (1981).
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