

Tetrahedron Letters 42 (2001) 7903-7905

TETRAHEDRON LETTERS

$\sigma-\pi$ Chelation-controlled chemoselective ring openings of epoxides

Naoki Asao, Taisuke Kasahara and Yoshinori Yamamoto*

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-8578, Japan Received 16 July 2001; revised 29 August 2001; accepted 5 September 2001

Abstract—The chemoselective ring opening of alkynyl epoxides in the co-existence of the corresponding alkyl epoxides is achieved in the Me₃Al mediated reaction with alkynyllithium reagents. The observed interesting chemoselectivity is most probably a reflection of bidentate complexation of the Lewis acid to an n-electron of an oxygen atom of the epoxide and π -electrons of the C–C triple bond. © 2001 Elsevier Science Ltd. All rights reserved.

Lewis acid-mediated chelation control is one of the most fundamental and efficient methodologies for effecting the selective carbon-carbon bond formation in modern organic synthesis.¹ It is well accepted that the chelationcontrolled reactions proceed through the coordination of a lone pair of heteroatoms, such as an oxygen of an aldehyde or a nitrogen atom of an imine, to a Lewis acid, which is recognized as a σ - σ type chelation. Recently, we reported that chemo- and regioselective reactions of certain alkynyl and alkenyl aldehydes were accomplished through a σ - π chelation between a lone pair of the carbonyl compounds and π -electrons of the C–C multiple bond.^{2,3} Now, we report that the chemoselective ring opening of alkynyl epoxides in the co-existence of the corresponding alkyl epoxides is achieved in a Me₃Almediated reaction with alkynyl lithium reagents; this interesting chemoselectivity is most probably a reflection of bidentate complexation to an n-electron pair of the oxygen atom of the epoxide and π -electrons of the C–C triple bond (Eq. (1)).

The reactions of a 1:1 mixture of alkynyl epoxides 1 (1 equiv.) and their saturated analogues 2 (1 equiv.) with alkynyllithiums (1.2 equiv.) were examined in the pres-

ence of Lewis acids (1.2 equiv.) in toluene (Eq. (2)) and the results are summarized in Table 1. The reaction of phenyl-substituted epoxides 1a and 2a with lithium phenylacetylide in the presence of BF₃·OEt₂ proceeded smoothly and 4a was obtained predominantly over 3a (3a:4a = 23:77) (entry 1). However, the reverse chemoselectivity was observed when we used Me₃Al as a Lewis acid: **3a** was obtained in 77% yield along with recovered 1a (9% yield), and 4a was obtained only in 2% yield together with recovered 2a (84% yield) (entry 2).⁴ The selective alkynylation reaction of 1a was also observed when the reaction was carried out using Et₃Al instead of Me₂Al, though the selectivity slightly decreased (entry 3). Other alkynyllithium reagents, such as hexyl- and trimethylsilyl-substituted lithium acetylide, also reacted chemoselectively with 1a in the presence of 2a (entries 4 and 5). Not only substrate 1a but also decyl- and trimethylsilyl-substituted alkynyl epoxides, 1b and 1c, underwent chemoselective ring opening reactions in the presence of Me₃Al (entries 6 and 7). In all the above reactions, the material balance of substrates was high; large amounts of 2 (49-90%) were recovered in entries 2-7, and small amounts (9-37%) of 1 were recovered in



Keywords: Lewis acids; chemoselectivity; coordination modes; alkynes; epoxides.

* Corresponding author. Tel.: +81-22-217-6581; fax: +81-22-217-6784; e-mail: yoshi@yamamoto1.chem.tohoku.ac.jp



Table 1. Lewis acid-mediated competitive ring opening reactions of 1 and 2 with alkynyllithium^a

Entry	Substrate			Alkynyl lithium	Lewis acid	Yield ^b		Yield ^b		Ratio 3:4
	\mathbb{R}^1	1	2			3	%	4	%	_
1	Ph	1a	2a	Ph	BF ₃ ·OEt ₂	3a	18	4a	59	23:77
2	Ph	1 a	2a	Ph	Me ₃ Al	3a	77	4a	2	97:3
3	Ph	1a	2a	Ph	Et ₂ Al	3a	69	4a	6	92:8
4	Ph	1a	2a	$C_{6}H_{13}$	Me ₃ Al	3b	78	4b	8	91:9
5	Ph	1a	2a	Me ₂ Si	Me ₂ Al	3c	54	4c	5	92:8
6	$C_{10}H_{23}$	1b	2b	Ph	Me ₃ Al	3d	72	4d	6	92:8
7	Me ₃ Si	1c	2c	Ph	Me ₃ Al	3c	75	4e	11	87:13

^a The reaction was performed in the following molar ratio at -78° C to rt; **1**:**2**: alkynyl lithium:Lewis acid=1:1:1.2:1.2. ^b Isolated yield.

the case where the yields of 3 were not as high (for example, entry 5).

Recently, we studied systematically the substituent effect on the BF₃·OEt₂-mediated electrophilic reactions of carbonyl compounds; for example, the allylation reaction of aldehydes using allyltributylstannane, the Diels–Alder reaction of aldehydes with cyclopentadiene, and the reduction of aldehydes using Bu₃SnH. We found that aldehydes **5** bearing an electron-donating group reacted with nucleophiles *in the presence of* $BF_3 \cdot OEt_2$ much faster than aldehydes **6** having an electron-withdrawing group (Eq. (3)).⁵ The above unex-

$$EDG H + EWG H \frac{O}{H} \frac{(1 \text{ eq})}{BF_3 \text{ o} \text{ OEt}_2}$$

$$5 6$$

$$OH + OH$$

$$EDG Nu + WG Nu$$

$$7 8$$
major minor
$$(3)$$

pected results are understandable if the coordination ability of more electrophilic carbonyl compounds 6 to Lewis acids is weaker than that of less electrophilic analogues 5. This concept can explain clearly why the selective reaction of 2a was observed in the competitive reaction of 1a and 2a with phenylethynyllithium in the presence of a *monodentate* BF₃·OEt₂ (entry 1). Compound 1a having an electron-withdrawing alkynyl group is less reactive to the nucleophile in the presence of BF₃·OEt₂ than 2a having an electron-donating alkyl group. On the other hand, the selective reaction of 1 in the *bidentate* Me_3Al -mediated reaction is ascribed most probably to the preferred bidentate chelation shown in 9 derived from 1 rather than the monodentate coordination shown in 10 from 2 (Fig. 1).⁶⁻⁹



Figure 1.

the above chemoselectivity might be However, explained by a selective nucleophilic substitution of epoxides by an aluminum ate complex formed from Me₃Al and alkynyllithium reagents, which might attack 1 rather than 2 selectively since the aluminum ate complex would attack directly the more electrophilic epoxide due to its nucleophilic character. In order to clarify this issue, we examined the reactions using 1d and 1e (Eq. (4)). The Me₃Al-mediated reaction of 1d with lithium phenylacetylide proceeded smoothly to give the corresponding alcohol 3e in 67% yield. In contrast, alcohol **3f** was obtained only in 19% yield in the reaction of **1e** under the same reaction conditions. If the nucleophilic character of the aluminum ate complex is responsible to the chemoselectivity, 3f should have been obtained in higher yield than 3e. Therefore, the observed higher reactivity of 1d in comparison with **1e** is due to the preferred formation of a σ - π chelation in the case of 1d rather than the formation of an aluminum ate complex.



It is now clear that the Lewis acid-mediated σ - π chelation between n- and π -electrons is operative not only in the alkyne–aldehyde system^{2,3} but also in the alkyne–epoxide analogue. Further studies on this new type of chelation control are ongoing in our laboratory.

References

- For reviews, see: (a) Lewis Acids in Organic Synthesis; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, 2000; Vols. 1–2; (b) Lewis Acid Reagents; Yamamoto, H., Ed.; Oxford University Press: New York, 1999; (c) Mahrwald, R. Chem. Rev. 1999, 99, 1095–1120; (d) Santelli, M.; Pons, J. M. Lewis Acids and Selectivity in Organic Synthesis; CRC Press: Boca Raton, 1996; (e) Shambayati, S.; Schreiber, S. L. In Comprehensive Organic Synthesis; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, pp. 283–324; (f) Yamaguchi, M. In Comprehensive Organic Synthesis; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, pp. 325–353.
- Asao, N.; Asano, T.; Ohishi, T.; Yamamoto, Y. J. Am. Chem. Soc. 2000, 122, 4817–4818.
- 3. Asao, N.; Shimada, T.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 9533–9536.
- 4. While the use of exactly 1 equiv. of Me₃Al and lithium phenylacetylide under similar reaction conditions gave the desired product **3a** with similar chemoselectively (**3a**:**4a** = 97:3), the total yield of the products was lower (66%).
- 5. Asao, N.; Asano, T.; Yamamoto, Y. Angew. Chem., Int. Ed. Engl. 2001, 40, 3206–3208.

- Trialkylaluminums and chlorodialkylaluminums are known to act as bidentate Lewis acids, see: (a) Maruoka, K.; Ooi, T. *Chem. Eur. J.* **1999**, *5*, 829–833; (b) Ooi, T.; Kagoshima, N.; Ichikawa, H.; Maruoka, K. J. Am. Chem. Soc. **1999**, *121*, 3328–3333; (c) Evans, D. A.; Allison, B. D.; Yang, M. G. *Tetrahedron Lett.* **1999**, *40*, 4457–4460; (d) Evans, D. A.; Chapman, K. T.; Bisaha, J. J. Am. Chem. Soc. **1988**, *110*, 1238–1256.
- Several examples of aluminum pentacoordinate complexes have been isolated and characterized, see: (a) Heitsch, C. W.; Nordman, C. E.; Parry, P. W. Inorg. Chem. 1963, 2, 508; (b) Palenick, G. Acta Crystallogr. 1964, 17, 1573– 1580; (c) Beattie, I. R.; Ozin, G. A. J. Chem. Soc. A 1968, 2373–2377; (d) von Vliet, M. R. P.; Buysingh, P.; von Koten, G.; Vrieze, K.; Kojic-Prodic, B.; Spek, A. L. Organometallics 1985, 4, 1701–1707; (e) Bennett, F. R.; Elms, F. M.; Gardiner, M. G.; Koutsantonis, G. A.; Raston, C. L.; Roberts, N. K. Organometallics 1992, 11, 1457–1459; (f) Muller, G.; Lachmann, J.; Rufinska, A. Organometallics 1992, 11, 2970–2972; (g) Fryzuk, M. D.; Giesbrecht, G. R.; Olovsson, G.; Rettig, S. J. Organometallics 1996, 15, 4832–4841.
- The hypercoodinated aluminum Lewis acids have been used for asymmetric reactions; see: (a) Heller, D. P.; Goldberg, D. R.; Wulff, W. D. J. Am. Chem. Soc. 1997, 119, 10551–10552; (b) Murakata, M.; Jono, T.; Mizuno, Y.; Hoshino, O. J. Am. Chem. Soc. 1997, 119, 11713– 11714; (c) Arai, T.; Sasai, H.; Yamaguchi, K.; Shibasaki, M. J. Am. Chem. Soc. 1998, 120, 441–442.
- 9. No reaction took place when a mixture of **1a** and **2a** was treated with lithium phenylacetylide *in the absence of* Lewis acids, and the starting materials were recovered.