Pergamon

Tetrahedron Letters 41 (2000) 2621–2624

TETRAHEDRON
LETTERS

Synthesis of cyclic sulfides by intramolecular ring opening of epoxides by thiolates generated by nickel complex catalyzed electroreduction of thioacetates

Shigeko Ozaki,* Eiki Matsui, Hideaki Yoshinaga and Satomi Kitagawa
Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita Osaka-fu 565-0871, Japan

Received 13 December 1999; revised 17 January 2000; accepted 4 February 2000

Abstract

The nickel(II) complex catalyzed electroreduction of thioacetates attached to epoxides provided five- to seven-membered cyclic sulfides in good to high yields by regioselective ring opening of epoxides followed by thioheterocyclization. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: cyclization; sulfur nucleophile; intramolecular epoxide opening; electroreduction; nickel complex.

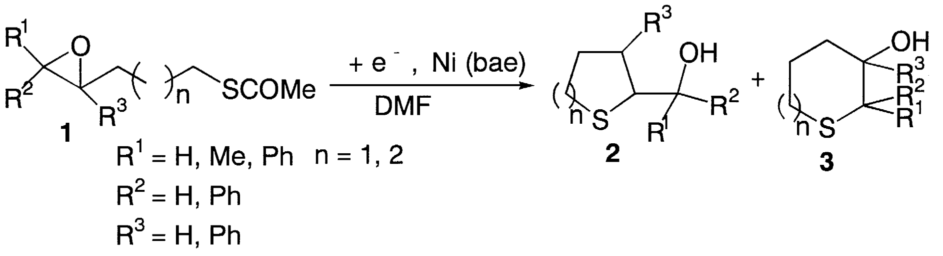
The chemistry of saturated cyclic sulfides has been developing intensively. They serve as useful intermediates for the synthesis of chemicals, and polyfunctional biologically active compounds.[1] A number of methods have been used for the synthesis of these systems.[2] Of the useful methods, the regiospecific opening of epoxy functions by a nucleophile followed with the expected cyclization could be taken as a reliable stereocontrolled synthesis of substituted five- and six-membered heterocycles. However, this approach has been centered on Brønsted or Lewis acid-catalyzed ring opening with oxygen nucleophiles.[3] Few examples of sulfur nucleophile participating an intramolecular displacement have been reported so far.[3d,4] This might be partly attributed to the reason that the choice of an appropriate procedure which could undergo efficient deprotection of the thiol group without being accompanied by ring opening of the epoxy group is usually not easy.

In connection with our study on the thioheterocyclization by the ring closure of electroreductively generated thiols to the suitably placed multiple bond,[5] we obtained the electrochemical result indicating that a thioacetate group linked to an epoxy group could be selectively subject to the catalytic electroreduction.[6] We now report the synthesis of cyclic sulfides by the thioheterocyclization initiated by intramolecular ring opening of the epoxides having a thioacetate group making use of the nickel complex catalyzed electroreduction (Scheme 1).

---

* Corresponding author.

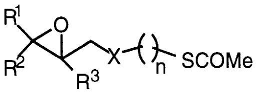
PII: S0040-4039(00)00231-8



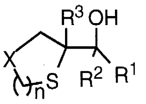
Scheme 1.

The nickel complex, Ni(bae) catalyzed electroreduction of the thioacetates bearing an epoxy group[7] was conducted by the almost same procedure used in the previous report.[5] The results are summarized in Table 1.

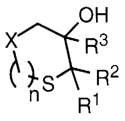
Table 1
Intramolecular ring opening reactions of epoxides initiated by nickel complex catalyzed electroreduction of thioacetate group[a]



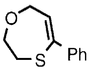
1



2



3

	Substrate							Product				
Entry		n	X	R^1	R^2	R^3	(d. r.)^b		Yield/ %^{c}	(d. r.)^b		
1	1a	1	C	Ph	H	H	(80 : 20)	2a	84	(80 : 20)	3a^d	5
2	1a'	1	C	Ph	H	H	(100 : 0)	2a	85	(100 : 0)	3a	0
3	1b	2	C	H	Ph	H	(60 : 40)	2b	57	(65 : 35)	3b^d	15
4	1c	2	C	Me	Ph	H	(65 : 35)	2c	88	(65 : 35)	3c	0
5	1d	2	C	Ph	Ph	H		2d	86		3d	0
6	1e	2	C	H	H	Ph		2e	0		3e	47
7	1f	2	O	H	Ph	H	(100 : 0)	2f	52	(100 : 0)	3f	0
											 4 f	30
8	1g	2	O	Bu	Bu	H		2g	73		3g	0

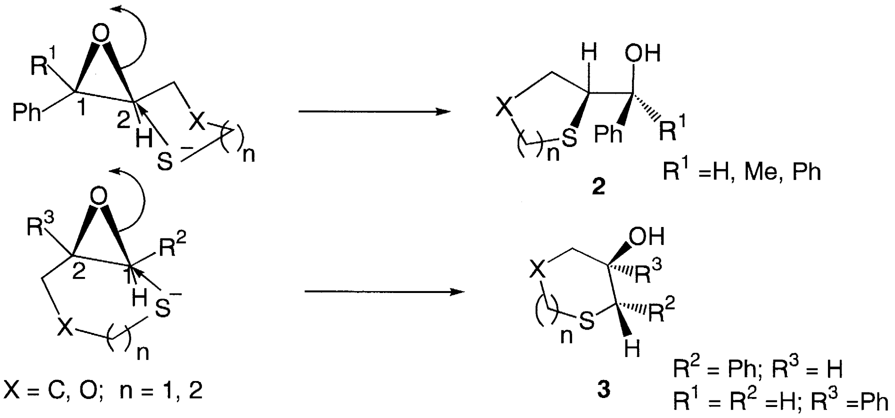
a. Electrolysis was conducted in DMF (10 ml) using a thioacetate (0.5 mmol) and Ni(bae) (0.3 mmol) in a divided cell at constant current (3 mA).

b. Diastereomeric ratio.

c. Isolated yield.

d. The stereochemistry was assigned as *trans* by ^{1}H-NMR.

Upon the catalytic electroreduction of **1a**, a thiolan **2a** was provided in a high yield along with a small amount of a thian **3a**. The ring opening/cyclization of the homologues **1b**–**d** and **1g** to the corresponding thianes **2** also turned out to proceed smoothly. The selective formations of **2a**–**d** and **2g** indicate that 5- or 6-*exo*-ring closure of the thiolate took place selectively (Scheme 2). The yields of the products derived from *endo*-cyclization **3a**, **3b** and **4f** seem to reflect the ratios of a diastereoisomer which have a hydrogen as R1 in the corresponding substrate. Consequently, the substrates which have a substituent R1 other than a hydrogen are shown to be strongly favorable for the *exo*-ring opening.



Scheme 2.

The stereochemistry of **3a** and a thiepane **3b** was found to be *trans* by NOE analysis. All products **2**, **3** and **4f** exhibited ^{13}C and ^{1}H NMR which were consistent with assigned structures. Spectral data for selected products and the postulated structure of **4f′** are shown in Fig. 1.

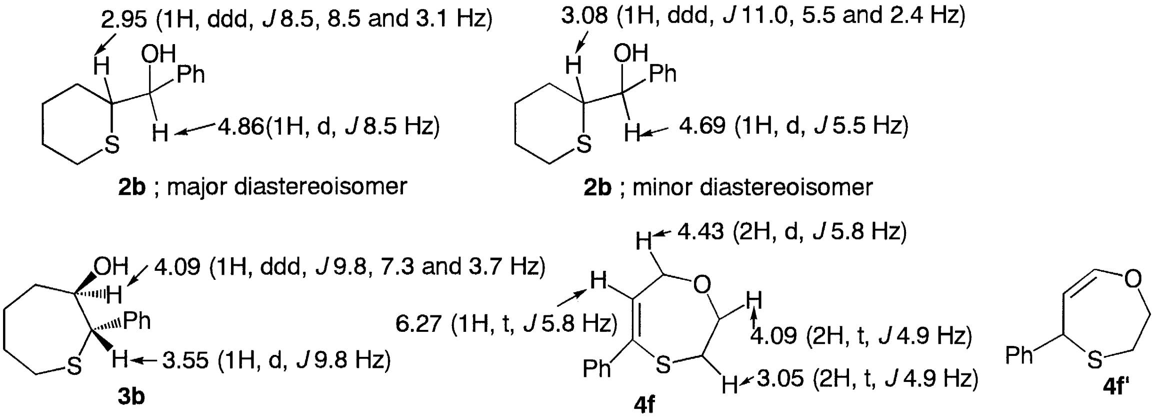


Fig. 1.

The diastereomeric ratios (d/r) of products **2a**, **2b** and **2c** indicate that the stereochemistries of C-1 and C-2 of the substrates were retained. In case of the electrolysis of **1f**, an 1,4-oxathiane **2f** was formed in 52% yield along with 30% of 5-phenyl-2,3-dihydro-7*H*-1,4-oxathiepin **4f** (entry 7, Fig. 1). The expected alcohol, *trans* 6-hydroxy-5-phenyl-1,4-oxathiepane was not obtained. The formation of **4f** was tentatively considered to be brought about by isomerization of an originally formed probably less stable isomer 5-phenyl-2,3-dihydro-1,4-oxathiepin **4f′** (Fig. 1), since *syn*-dehydration of the postulated original *trans*-alcohol to give **4f** would proceed in the rate considerably slower than that for formation of **4f′**. The study on the mechanism for formation of **4f** is now underway.

In summary, the regioselective synthesis of the five-, six-, and seven-membered cyclic sulfides was achieved by intramolecular ring opening reactions of epoxides by the thiolate which had been generated by the selective catalytic electroreduction of the thioacetate group in the substrate **1**. The present approach is very mild and convenient, and is expected to find useful applications in synthesis of *S*-heterocycles.

References

1. (a) Mukerjee, A. K.; Singh, A. K. *Synthesis* **1975**, 547–589; (b) Shibasaki, M.; Ikegami, S. *Tetrahedron Lett.* **1977**, *18*, 4037–4040; (c) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 3472–3480; (d) Bach, T.; Kather, K.; Kramer, O. *J. Org. Chem.* **1998**, *63*, 1910–1918.
2. The articles published prior to 1987 have been reviewed in: (a) Vedejs, E.; Krafft; G. A. *Tetrahedron* **1982**, *38*, 2857–2881; (b) Karaulova, E. N. *Russian Chemical Reviews* **1987**, *56*, 546–563.
3. (a) Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330–5334; (b) *ibidem*. *111*, 5335–5340; (c) Itoh, A.; Hirose, Y.; Kashiwagi, H.; Masaki, Y. *Heterocycles* **1994**, *38*, 2165–2169; (d)Bach, T.; Kather, K.; Kramer, O. *J. Org. Chem.* **1998**, *63*, 1910–1918.
4. Fuzier, M.; Merrer, Y. L.; Depezay, J.-C. *Tetrahedron Lett.* **1995**, *36*, 6443–6446.
5. Ozaki, S.; Mastui, E.; Saiki, T.; Yoshinaga, H.; Ohmori, H. *Tetrahedron Lett.* **1998**, *39*, 8121–8124.
6. The cyclic voltammeric behavior of Ni(II)(bae) in the presence of **1a** and epoxycyclohexane suggested that this complex would transfer an electron to **1a** but not to the latter. (a) Stolzenberg, A. M.; Stershic, M. T. *J. Am. Chem. Soc.* **1988**, *110*, 5397–5403; (b) Ozaki, S.; Mastushita, H.; Ohmori, H. *J. Chem. Soc*., *Perkin Trans. 1* **1993**, 649–651.
7. Ozaki, S.; Urano, Y.; Ohmori, H. *Electrochim. Acta* **1997**, *42*, 2153–2158 and Ref. 5.