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INTRAMOLECULAR RING CLOSURE OF α,β-EPOXY SULFOXIDES WITH HYDROXYL GROUP: A NOVEL SYNTHESIS OF 2-ACYL CYCLIC ETHERS AND 3-KETO CYCLIC ETHERS[1)]

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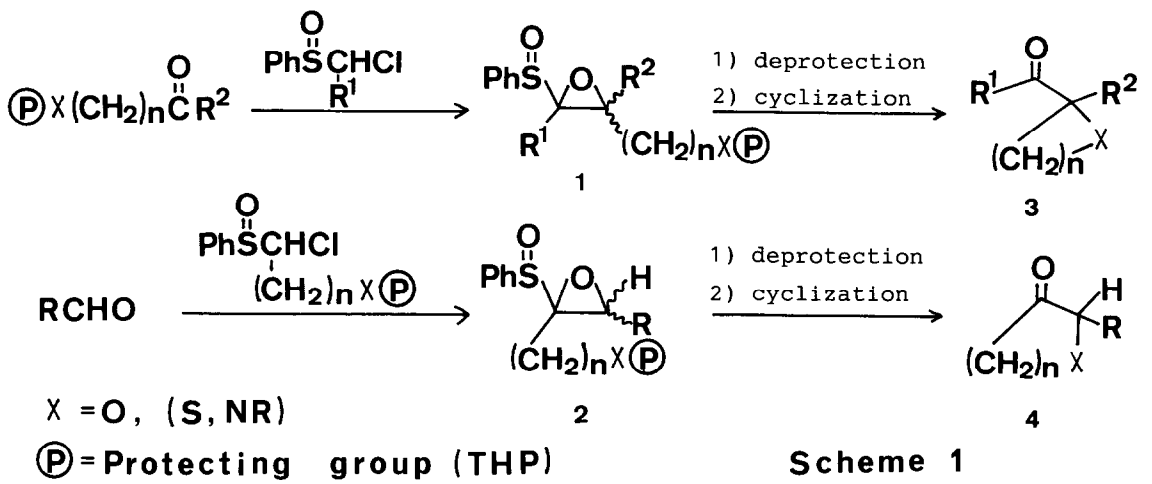
Summary Exo-trigonal-type intramolecular ring closure of the α,β-epoxy sulfoxides with hydroxyl group gave 2-acyl cyclic ethers (5, 6, and 13 membered rings) in good yields. In contrast to this, endo-trigonal-type ring closure of the α,β-epoxy sulfoxides was rather difficult.

Recently, cyclic ethers have received much attention regarding synthetic organic chemistry. They are found in many natural products having remarkable biological activity, such as polyether ionophor antibiotics.[2)] Many methods for a synthesis of cyclic ethers have already been reported;[3)] however, much more new methods have been desired concerning this area of chemistry.

We have reported a new synthetic method for the preparation of α-substituted carbonyl compounds from carbonyl compounds with carbon homologation through α,β-epoxy sulfoxides.[4)] In the continuation of our studies on the novel synthetic methods through α,β-epoxy sulfoxides, here we report a new method for the synthesis of 2-acyl cyclic ethers (3; X=O) and 3-keto cyclic ethers (4; X=O) as shown in Scheme 1.



1 2 3 4

Scheme 1

In previous papers,[4)] we reported that the β-position of α,β-epoxy sulfoxides was quite reactive toward many kinds of nucleophiles, such as selenolate, thiolates, and amines, giving α-substituted carbonyl compounds in very good yields. With these results in hand, it was anticipated that the intramolecular version of this reactions were quite promising to construct heterocyclic com-

pounds having ketone group. At first, we selected oxygen (hydroxyl group) as a nucleophile (X=oxygen in 1 and 2) because the products, cyclic ethers having ketone group, are very useful in synthetic organic chemistry as mentioned above. Intermolecular reaction of the α,β-epoxy sulfoxides with alcohols did not work well;[4d] however, intramolecular reactions were thought to be possible because usually the rate of the intramolecular reaction was much faster than that of intermolecular reaction.

α,β-Epoxy sulfoxides (1 or 2; X=O, Ⓟ=THP) were quite easily prepared from carbonyl compounds and 1-chloroalkyl phenyl sulfoxides in nearly quantitative yields as shown in Scheme 1. The α,β-epoxy sulfoxide (1b; Table 1, entry 4; 0.7 mmol in 6 ml of EtOH) was heated in refluxing ethanol in the presence of 0.2 equivalents of pyridinium p-toluenesulfonate (PPTS) to give deprotected alcohol very quickly. Then cyclization of this intermediate alcohol took place slowly with liberation of phenylsulfenic acid to give 2-acyl tetrahydropyran (3b) in 86% yield after 6 h heating. The reaction time was shortned to 2.5 h by using refluxing 1-propanol. In this reaction PPTS was found to be essential; by heating the isolated intermediate alcohol in refluxing 1-propanol without PPTS, completely no reaction occured. It is worthy of note that in this reaction no trace of the coupling product from 1b and the alcohol used as the solvent was produced. This fact means that high dilution conditions (in fear of the intermolecular reaction) are not necessary.

The representative examples of the preparation of 2-acyl cyclic ethers from the α,β-epoxy sulfoxides are listed in Table 1. The product (5) in entry 1 was thought to come from the normal product, epoxy ketone (6), and 1-propanol. Though the yield is moderate so far, the result in entry 7 implies that this method is useful for the preparation of 2-acyl cyclic ethers having large ring.

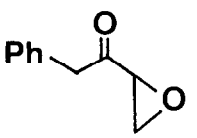


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Table 2 shows the results of the ring closure from the α,β-epoxy sulfoxides (2). The α,β-epoxy sulfoxide (2a) quickly gave the intermediate alcohol upon heating in refluxing ethanol with PPTS; however, this alcohol was quite inert under these conditions. Prolonged heating of this reaction mixture resulted in a complex mixture. This result is in consistent with the Baldwin rule,[5] which indicates that the 5-endo-trigonal ring closure[6] is disfavorable process. 2b gave the desired tetrahydropyran derivative (4b) in moderate yield; however, compared to the results in Table 1, entry 4, the reaction rate of this 6-endo-trigonal ring closure was rater slow. It is noteworthy that 2b only gave 4b, not 7 (via generally preferring 5-exo-trigonal ring closure). This result is in consistent with our finding that the β-position of α,β-epoxy sulfoxides is much more reactive than the α-position.

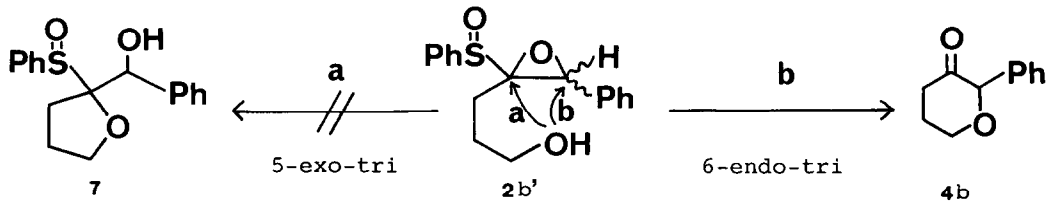
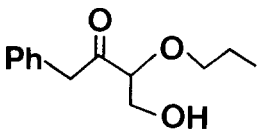
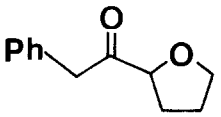
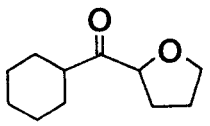
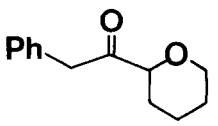
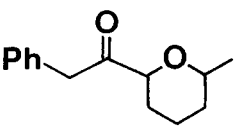
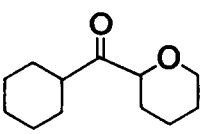
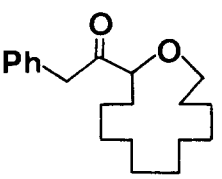


Table 1

Preparation of 2-acyl cyclic ethers from α,β-epoxy sulfoxides (1; X=O, Ⓟ=THP)

Entry	α,β-Epoxy sulfoxide (1) R^1	R^2	n		Conditions[a]	Product		Yield[b] %
1	$PhCH_2$	H	1	**1a**	n-PrOH 5 h		**5**	70
2	$PhCH_2$	H	3		EtOH (50 °C) 30 min			90
3		H	3		EtOH 1 h			83
4	$PhCH_2$	H	4	**1b**	EtOH 6 h n-PrOH 2.5 h		**3b**	86 85
5	$PhCH_2$	H[d]	4		n-PrOH 4.5 h			81[c]
6		H	4		n-PrOH 5 h			85
7	$PhCH_2$	H	11		n-PrOH 2 d			52

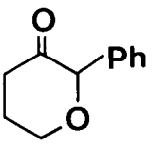
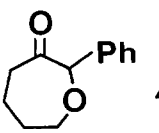
a) Unless otherwise noted the reaction was carried out in refluxing solvent.
b) Isolated yield after silica gel column chromatography. c) Single isomer.
d) $THPO(CH_3)CH(CH_2)_3CHO$ was used as the carbonyl compound.

Entry 3 shows that the ring closure giving 7-membered cyclic ether is rather difficult.

More details of this reaction and the application of this reaction for the preparation of nitrogen and sulfur containing heterocyclic compounds (3, 4; X=N or S) are under active investigation in these laboratories.

Table 2

Preparation of 3-keto cyclic ethers from α,β-epoxy sulfoxides (2; X=O, Ⓟ=THP, R=Ph)

Entry	α,β-Epoxy sulfoxide (2) n		Conditions[a]		Product		Yield[b] %
1	2	**2a**	EtOH	2 d	----[c]		--
2	3	**2b**	EtOH	17 h		**4b**	60
			n-PrOH	4 h			57
3	4	**2c**	n-PrOH	3 d		**4c**	11

a) All reactions were carried out in refluxing solvent. b) Isolated yield after silica gel column chromatography. c) A complex mixture.

References

1) α,β-Epoxy sulfoxides as useful intermediates in organic synthesis XI. Part X: T. Satoh, M. Itoh, T. Ohara, and K. Yamakawa, Bull. Chem. Soc. Jpn., in press.
2) Structure: D. E. Cane, W. D. Celmer, and J. W. Westley, J. Am. Chem. Soc., 105, 3594 (1983) and the references cited therein. Synthesis: Y. Kishi Aldrichimica Acta, 13, 23 (1980); P-T. Ho, Can. J. Chem., 60, 90 (1982); R. E. Ireland, L. Courtney, and B. J. Fitzsimmons, J. Org. Chem., 48, 5186 (1983); M. Isobe, Y. Ichikawa, and T. Goto, Tetrahedron Lett., 26, 5199; (1985); M. Isobe, Y. Ichikawa, D-lu. Bai, and T. Goto, ibid., 26, 5203 (1985).
3) D. R. Williams, Y. Harigaya, J. L. Moore, and A. D'sa, J. Am. Chem. Soc., 106, 2641 (1984); D. R. Williams, J. Grote, and Y. Harigaya, Tetrahedron Lett., 25, 5231 (1984); Y. Tamaru, S. Kawamura, and Z. Yoshida, ibid., 26, 2885 (1985); J. W. Kelly, P. L. Robinson, and S. A. Evans, Jr., J. Org. Chem., 50, 5007 (1985); P. A. Bartlett, and C. Chapuis, ibid., 51, 2799 (1986); I. Noda, K. Horita, Y. Oikawa, and O. Yonemitsu, Tetrahedron Lett., 27, 1917 (1986) and the references cited therein.
4) a) T. Satoh, Y. Kaneko, T. Izawa, K. Sakata, and K. Yamakawa, Bull. Chem. Soc. Jpn., 58, 1983 (1985); b) T. Satoh, T. Kumagawa, and K. Yamakawa, ibid., 58, 2849 (1985); c) T. Satoh, Y. Kaneko, K. Sakata, and K. Yamakawa, ibid., 59, 457 (1986); d) T. Satoh, S. Motohashi, and K. Yamakawa, ibid., 59, 946 (1986); e) T. Satoh, T. Kumagawa, and K. Yamakawa, Tetrahedron Lett., 27, 2471 (1986); f) T. Satoh, S. Motohashi, and K. Yamakawa, ibid., 27, 2889 (1986).
5) J. E. Baldwin, J. Chem. Soc., Chem. Commun., 1976, 734.
6) J. E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman, and R. C. Thomas, ibid., 1976, 736.

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