Vicinal Diol Cyclic Thionocarbonates: Like Cyclic Sulfates, and More

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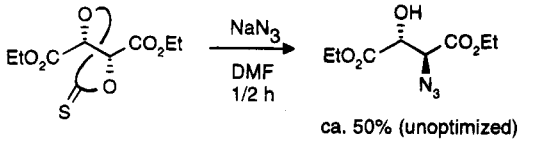
With the recent advent of the asymmetric dihydroxylation (AD) process of olefins, chemistry of vicinal diols is gaining rapid interest.[1] Selective transformations of *vic*-diols expand the synthetic utility of the AD process beyond the preparation of dihydroxy compounds. One of the most efficient ways of transforming *vic*-diols is *via* the corresponding cyclic sulfates. They are easily prepared, and, from the viewpoint of their reactivity toward nucleophiles, are said to be "like epoxides, only more reactive."[2]

In the course of our recent synthetic applications of cyclic sulfate chemistry, it was observed that some cyclic sulfates were quite unstable under even mildly acidic conditions, forcing a revision of our synthetic strategy involving these epoxide surrogates.[3] This prompted us to search for an alternative, more acid-stable, activated diol species. To this end, several cyclic diesters were considered.[4]

Much is known about the reactivity of cyclic carbonates, as they are often used as a protecting group of diols.[5] In particular, it is known that nucleophiles tend to attack—albeit sluggishly—the carbonyl carbon of cyclic carbonates, resulting in diol-deprotection (hence the protecting group), rather than the carbinol carbon, which would result in a desired nucleophilic substitution reaction.[6] We envisaged that cyclic thionocarbonates would satisfy our needs: the presence of a sulfur atom would render the carbonyl carbon less reactive, while at the same time, rendering the carbinol carbon more reactive toward nucleophiles.[7]

Thus, diethyl tartrate was converted to the cyclic thionocarbonate ($CSCl_2$, pyr, DMAP, 78%). Upon reaction with NaN_3, the thionocarbonate was smoothly converted to the hydroxy azide within 30 min (eq 1). In

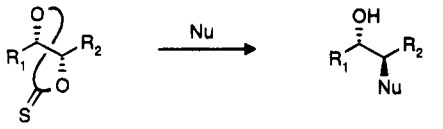


Eq. 1

ca. 50% (unoptimized)

contrast, the corresponding cyclic carbonate failed to react with NaN_3 in our hands under the identical conditions, confirming our view that cyclic thionocarbonates are indeed more reactive than the oxo-counterparts toward nucleophiles.[8] After the electrophilicity of a cyclic thionocarbonate was ascertained, several other cyclic thionocarbonates were reacted with various heteroatom nucleophiles. The results are summarized in Table 1.

Table 1. Nucleophilic Ring-opening Reactions of Cyclic Thionocarbonates



entry	cyclic thionocarbonate [(% yield),[a] R_1, R_2]	Nu	yield[b] (%)
1	**1** [(78%), $CO_2{}^i$Pr, $CO_2{}^i$Pr]	$N_3{}^{-c}$	84
2	**1**	PhS^{-d}	100
3	**1**	$PhCO_2{}^{-e}$	59
4	**2** [(97%), nC_7H_{15}, CO_2Et]	$N_3{}^{-f}$	77
5	**2**	PhS^{-g}	90
6	**2**	$PhCOS^{-h}$	82
7	**3** [(83%), Ph, CO_2Et]	$N_3{}^{-i}$	99[j]
8	**3**	PhS^{-k}	98
9	**4** [(92%), $CH_2OTBDMS$, Ph]	$PhCOS^{-l}$	68

[a] Prepared from the corresponding *vic*-diols ($CSCl_2$, pyr, DMAP, in DCM). [b] Isolated yield of the ring-opened product. [c] NaN_3 (3 equiv), PPTS (2 equiv), in DMF, 0 °C, 1 h. [d] PhSH (2 equiv), Et_3N (2 equiv), in THF, 0 °C, 1 h. [e] $PhCO_2H$ (2 equiv), Et_3N (2 equiv), in DMF, rt, 24 h. [f] As in *c*, rt, 8 h. [g] As in d, 0 °C, 3 h. [h] PhCOSH (2 equiv), Et_3N (2 equiv), in DMF, rt, 2 h. [i] As in *c*, rt, 4 h. [j] A mixture of the C-α and C-β regioisomers (1.3:1) was obtained. [k] As in *d*, 0 °C, 1 h. [l] As in h, rt, 40 h.

All the nucleophiles tried cleanly opened the cyclic thionocarbonates. With the cyclic thionocarbonates derived from *threo*-2,3-dihydroxy esters, the opening reactions took place exclusively at the α-position (entries 4–6). Not unexpectedly, however, when the β-position was activated by a phenyl ring, the azide nucleophile opened the cyclic thionocarbonate ring to produce a 1.3:1 mixture of C-α- and C-β-opened regioisomers (entry 7). With benzenethiolate as the nucleophile, however, the reaction was again regioselective at the C-α center (entry 8). The regioselectivity may be reversed by changing the substituents around the cyclic thionocarbonates. Thus, the cyclic thionocarbonate derived from *threo*-3-[(*tert*-butyldimethylsilyl)oxy]-1-phenylpropane-1,2-diol was opened exclusively at the benzylic site with thiobenzoate as the nucleophile (entry 9).

From these results, it seems that cyclic thionocarbonates are slightly less reactive toward nucleophiles than are the corresponding cyclic sulfates.[2] On the other hand, there is a clear advantage—apart from the acid-stability of the intermediates—in the cyclic thionocarbonate ring-opening reactions. With cyclic sulfates, the initial ring-opened products are β-sulfate anions, which are subsequently hydrolyzed, often using concd sulfuric acid, to yield β-hydroxy products.[2c] In contrast, cyclic thionocarbonates are opened to produce initially β-thiocarbonate anions, which smoothly undergo a decomposition to β-hydroxy products either *in situ* or during the aqueous workup stage. Therefore, no extra hydrolysis step is necessary with cyclic thionocarbonates. This realization led us to the discovery described below.

(1) For a recent comprehensive review, see: Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

(2) (a) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538. (b) Lohray, B. B. *Synthesis* **1992**, 1035. (c) Kim, B. M.; Sharpless, K. B. *Tetrahedron Lett.* **1989**, *30*, 655.

(3) Ko, S. Y.; Lerpiniere, J. *Tetrahedron Lett.* **1995**, *36*, 2101.

(4) Cyclic sulfites, believed to be more acid-stable than the sulfates, have been used, but may not be ideal because an additional (and unnecessary) stereocenter is generated during their formation. See: (a) Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun.* **1991**, 95. (b) Gao, Y.; Zepp, C. M. *Tetrahedron Lett.* **1991**, *32*, 3155.

(5) Greene, T. W.; Wuts, P. G. M. in *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991.

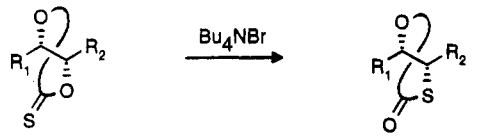
(6) For related reactions, see: (a) Katuski, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D. Walker, F. *J. Org. Chem.* **1982**, *47*, 1373. (b) Myers, A. G.; Widdowson, K. L. *Tetrahedron Lett.* **1988**, *29*, 6389.

(7) For a related example, see: Uenishi, J.; Motoyama, M.; Nishiyama, Y.; Wakabayashi, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1421.

(8) While the present work was in progress, it was reported that this same cyclic carbonate undergoes a ring-opening reaction with azide upon a prolonged treatment. See: Kang, S.-K.; Park, D.-C.; Rho, H.-S.; Yoon, S.-H.; Shin, J.-S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3513.

0022-3263/95/1960-6250$09.00/0

Table 2. Rearrangement of Cyclic Thionocarbonates



entry	cyclic thionocarbonate[a]	Bu_4NBr (equiv)	time (h)	yield (%)
1	**1**	1.0	1	100
2	**1**	0.1	1	98
3	**2**	0.1	60	83
4	**3**	0.1	32	78[b]

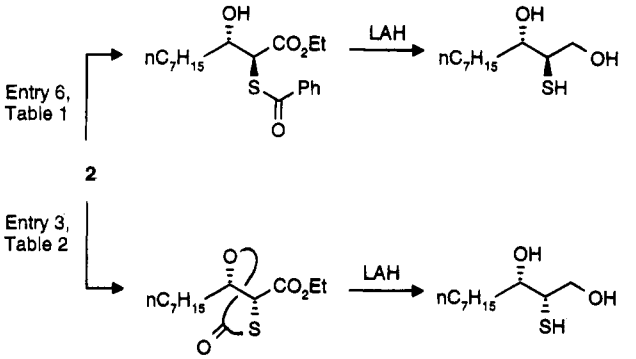
[a] For the structures of R_1 and R_2, see Table 1. [b] A mixture of the C-α and C-β regioisomers (4:1) was obtained.

Unlike sulfate anions, thiocarbonate anions are somewhat nucleophilic. Therefore, the initial ring-opened products of cyclic thionocarbonates could undergo, prior to decomposition, another nucleophilic substitution reaction, but this time with the substrates acting as nucleophile. More interestingly, it was envisaged that if halides were used as the nucleophile in the first substitution (ring-opening) reaction, the initial ring-opened thiocarbonate anions could displace the halides—the newly introduced nucleophiles—in the second, intramolecular substitution (cyclization) step. As the sulfur will be the nucleophilic terminus of the thiocarbonate anions in the second displacement step, the net result of the two-step, tandem displacement reaction will be a rearrangement from cyclic thionocarbonates to thiolcarbonates *with net retention (double-inversion) of stereochemistry*.[9,10]

Thus, **1** was reacted with 1 equiv of tetrabutylammonium bromide in THF to yield the corresponding cyclic thiolcarbonate in a quantitative yield (entry 1, Table 2). It was soon realized that only a catalytic amount of bromide was sufficient for this transformation (entry 2). Likewise, **2** was converted to the corresponding *threo*-2-mercapto-3-hydroxy cyclic carbonate (entry 3). With the thionocarbonate **3**, the rearrangement produced a 4:1 mixture of the C-2 and C-3 mercapto regioisomers (entry 4).

The rearrangement reactions summarized in Table 2 are complementary to some of the cyclic thionocarbonate ring-opening reactions of Table 1. This point is illustrated in Scheme 1. Starting from the same *threo-vic*-diol cyclic thionocarbonate **2**, the ring-opening reaction of entry 6, Table 1, produces, after $LiAlH_4$ reduction, *erythro*-2-mercapto 1,3-diol with an inversion of configuration at the C-2, while the tandem displacement (rearrangement) of entry 3, Table 2, followed by $LiAlH_4$ reduction, produces the *threo*-diastereomeric mercapto diol with retention of configuration. This complementarity is of particular significance when one considers that the AD process is not practical with (*Z*)-olefin substrates, limiting its use to the preparation of two out of four possible stereoisomeric *vic*-diols.[11] With the two complementary processes described in this paper, any one of a complete set of stereoisomeric *vic*-mercapto alcohols is now accessible from a common (*E*)-olefin, following an AD reaction. These processes should find some use in the synthesis of natural and unnatural products including thiocarbohydrates, which have gained much interest in recent years due to their interesting biological properties.[12]

Scheme 1



Future work will include, on the one hand, expanding the scope of the cyclic thionocarbonate ring-opening process, and on the other hand, extending the tandem displacement (rearrangement) process further to other cyclic carbonate systems.[13]

Acknowledgment. We thank Prof. Kang for providing us with the detailed experimental procedure for the reactions described in ref 8 and Ms. Ambarine Ghauri for her technical assistance.

Supporting Information Available: Representative experimental procedure for the preparation of cyclic thionocarbonates as well as the ring-opening and the rearrangement reactions, and spectroscopic data of the compounds described in Tables 1 and 2 (5 pages).[14]

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(9) This rearrangement was in fact known for a long time. However, the reactions were carried out on terminal cyclic thionocarbonate substrates, and the stereochemical implications were not realized. See: (a) Jones, F. N.; Andreades, S. *J. Org. Chem.* **1969**, *34*, 3011. (b) Trimnell, D.; Doane, W. M.; Russell, C. R.; Rist, C. E. *Carbohydr. Res.* **1971**, *17*. 319.

(10) A similar rearrangement has also been reported under radical conditions, but this process is not stereoselective. See: (a) Tsuda, Y.; Kanemitsu, K.; Kakimoto, K.; Kikuchi, T. *Chem. Pharm. Bull.* **1987**, *35*, 2148. (b) Kanemitsu, K.; Tsuda, Y.; Haque, M. E.; Tsubono, K.; Kikuchi, T. *Chem. Pharm. Bull.* **1987**, *35*, 3874. (c) Laak, K. V.; Scharf, H.-D. *Tetrahedron Lett.* **1989**, *30*, 4505.

(11) (a) Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568. (b) Ko, S. Y.; Malik, M.; Dickinson, A. F. *J. Org. Chem.* **1994**, *59*, 2570.

(12) (a) Horton, D.; Wander, J. D. In *The Carbohydrates, Chemistry and Biochemistry*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. 1B, Chapter 18. (b) For a recent example, see: Waldner, A.; Mesmaeker, A. D. *Synlett* **1995**, 108.

(13) *Cf.* Barton, D. H. R.; Motherwell, W. *Nouv. J. Chim.* **1978**, *2*, 301.

(14) The author has deposited atomic coordinates for cyclic thionocarbonate **1** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.