Pergamon

Tetrahedron, Vol. 52, No. 12, pp. 4303-4310, 1996

0040-4020/96 $15.00 + 0.00

S0040-4020(96)00130-5

Electrooxidative Pinacol-Type Rearrangement of β-Hydroxy Sulfides. Efficient C-S Cleavage Mediated by Chloride Ion Oxidation

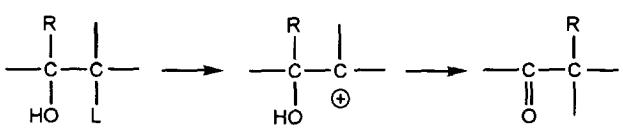
Makoto Kimura, Kazutaka Kobayashi, Yasushi Yamamoto, and Yasuhiko Sawaki*

Department of Applied Chemistry, Faculty of Engineering,
Nagoya University, Chikusa, Nagoya 464-01, Japan

Abstract: Electrooxidation of α-phenyl substituted β-hydroxy sulfides in dichloromethane in the presence of chloride ions as the electrolyte results in a novel pinacol-type rearrangement to give 2-phenyl substituted ketones like 2-phenylcycloalkanone as the ring expansion product. The rearrangement is induced by an electrogenerated chloronium ion, which effects, instead of common C-C scission, a selective C-S cleavage of β-hydroxy sulfides.

Introduction

The pinacol and related rearrangements are important for the construction of carbon skeletons.[1,2,3] For the selective rearrangement, heteroatoms such as nitrogen, sulfur and selenium have been utilized by generating cationic intermediates to direct the migrating group as exemplified by the rearrangement of α-amino alcohols (Tiffeneau-Demyanov)[4], β-hydroxy dithioacetals,[5] β-hydroxy orthothioesters[6] and β-hydroxy selenides[7](Eq. 1). These heteroatoms are cleaved by various oxidative or metallic reagents. For example, sulfur groups are eliminated by thiophilic reagents like copper (I) or mercury (II) salts[5,6] and a thallium compound.[7]

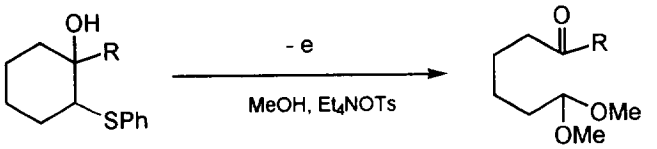


(1)

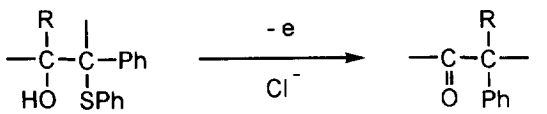
Electrooxidation of sulfides is a useful means to effect C-S cleavages in various electroorganic syntheses.[8,9] Especially, the electrooxidation of benzyl sulfides results in a facile generation of benzylic cation intermediates.[10-12] We have anticipated that β-hydroxy sulfides may be re-

arranged to give ketones by an appropriate electrooxidation. However some β-hydroxy cycloalkyl sulfides have been reported to suffer the carbon-carbon bond cleavage giving ring-opened ketonic products (Eq. 2).[13] Electrooxidation of α-methoxy or α-amino alcohols leads to analogous C-C bond cleavage.[14] Thus, for the pinacol rearrangement of β-hydroxy sulfides, it is necessary to suppress such C-C cleavage reactions by choosing appropriate reaction conditions. The acid-catalyzed migration of phenylthio group is known for numerous β-hydroxy sulfides.[15] Similar participation of neighboring phenylthio group is exploited in the regioselective pinacol rearrangement of sulfenylmethylated glycols.[16] On the other hand, relevant β-hydroxy sulfonium salts give epoxides upon treatment with strong bases.[17,18] So that, strong acidic and basic conditions should be avoided for selective pinacol-type rearrangements.

We have explored such a reaction control in the electrooxidation of α-phenyl substituted β-hydroxy sulfides **1** to get rearranged ketones **2**. It was found that the use of chloride ions as the electrolyte effects an efficient pinacol-type rearrangements of **1** (Eq 3).



(2)



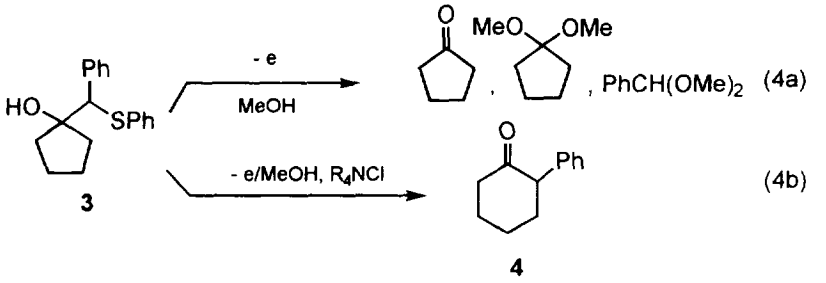
(3)

1 **2**

Typically, the electrooxidation of a β–hydroxycyclopentyl sulfide resulted in an efficient ring expansion to give 2-phenylcyclohexanone. This sort rearrangement is shown to be possible in some of acyclic sulfides. The mechanism is understood in terms of the mediation of chloronium ions,[19] inducing the efficient C-S cleavage.

Results and Discussion

Electrolytic Conditions. As a typical substrate, the adduct of lithio benzyl phenyl sulfide to cyclopentanone was used. 1-(α-Phenylthiobenzyl)cyclopentanol **3** was electrolyzed using common electrolytes such as tetraethylammonium *p*-toluenesulfonate Et_4NOTs and tetrabutylammonium perchlorate Bu_4NClO_4, but the products were only materials cleaved at the central carbon-carbon bond. For example, a constant current electrolysis of **3** in methanol containing Et_4NOTs using platinum electrodes in an undivided cell gave cyclopentanone, its dimethyl acetal and benzaldehyde dimethylacetal in 13, 42 and 52% yields, respectively, after passage of 6 F/mol of electricity (Eq. 4a).



When the electrolyte was changed to chloride ion salts such as lithium or tetraalkylammonium chloride, the desired ring-expanded ketone **4** was successfully obtained (Eq. 4b). Analogous bromide and iodide salts were far less effective. The preferred solvent turned out to be dichloromethane containing a small amount of methanol, as shown in Table 1. Use of carbon electrodes in CH_2Cl_2-10% MeOH gave the best yield of **4**; thereafter the system is referred as typical conditions. The effect of added methanol is probably due to keeping the electrode surface clean.

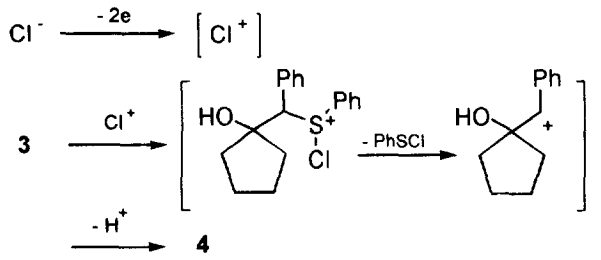
Cyclic voltammetry (CV) of β-hydroxy sulfide **3** in acetonitrile showed an anodic irreversible wave, the peak potential being 1.71 V *vs.* Ag/AgCl. Since chloride ion salts discharge at the much lower potential of *ca.* 1.3 V *vs.* Ag/AgCl, the initial electrochemical process is the oxidation of chloride ion to chloronium ion.[19] Therefore, the reaction sequence can be depicted as Scheme I. The chloronium ion has a thiophilic nature to generate a chloro-sulfonium intermediate,[20] which undergoes an efficient C-S cleavage to yield PhSCl and a benzylic cation intermediate and ultimately the rearranged ketone **4**. Methyl benzenesulfinate PhSO(OMe)[21] was always formed as the major side product.

Table 1. Electrolysis of β-Hydroxy Sulfide **3** in Various Solvent Containing Et_4NCl as the Electrolyte. [a]

Solvent	F/mol [b]	Yield of **4**, % [c]
MeOH	5.0	34
MeOH[d]	8.0	19
CH_2Cl_2-10%MeOH	7.0	46
CH_2Cl_2-10%MeOH[d]	9.0	61
MeCN-10%MeOH[d]	7.0	49

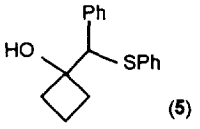
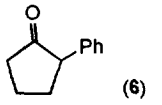
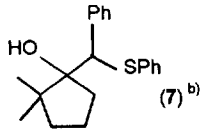
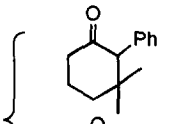
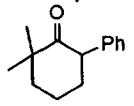
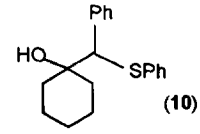
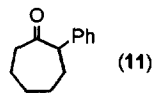
a) Reaction conditions: **3** 1 mmol, Et_4NCl 2 mmol, solvent 25 mL, constant current of 100 mA. b) Amounts of electricity required for ~95% consumption of **3**. c) Determined by GLC. d) Carbon electrodes.

Scheme 1



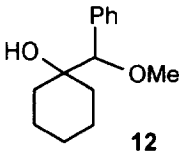
Ring Expansion. The electrooxidative ring expansion was examined for other cyclic alcohols (Table 2). The cyclobutanol analogue **5** gave a good yield of 2-phenylcyclopentanone **6**. Electrolysis of 2,2-dimethyl substituted cyclopentanol **7** under the typical conditions resulted in the formation of two isomeric ketones **8** and **9**, the combined yield being the same as that of non-substituted **3**. The predominant migrating group in **7** was the dimethyl substituted carbon, in

Table 2. Electrooxidative Ring Expansion of (α-Phenylthiobenzyl)cycloalkanols to 2-Phenylcycloalkanones.[a)]

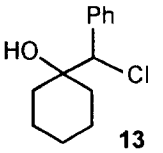
Substrate	F/mol	Product	Yield,%
 (5)	6.0	 (6)	78
3	9.0	4	61
 (7)[b)]	8.0	 (8)	52
		 (9)	7
 (10)	5.0	 (11)	16[c)]

a) Reaction conditions; see footnote a) in Table 1. b) A 9 : 1 inseparable diastereomeric mixture was used. c) Other products were un-rearranged α-methoxy (**12**) and α-chloro alcohol (**13**). See text.

accord with the mechanism of nucleophilic rearrangement as shown in Scheme I. The regioselectivity seems remarkably low as compared with the other relevant ring expansions.[5,6,22] Analogous ring expansion of **10** to 7-membered ring was of low yield (i.e., 16%); instead, α-methoxy (**12**) or α-chloro alcohol (**13**) were formed in 41 and 21% yields, respectively, as the simple C-S cleavage products of **10**. These reactivities for the present ring expansion suggest that the release of ring strain of **3**, **5** and **7** is the driving force for the successful rearrangement.



12

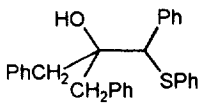
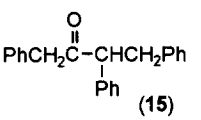
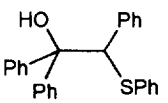
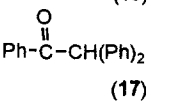
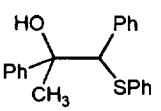
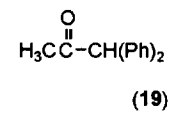


13

Acyclic Rearrangements. The electrooxidative rearrangement was attempted in acyclic systems with methyl, benzyl and phenyl groups. The electrolysis of 2-(α-phenylthiobenzyl-2-propanol as an acyclic counterpart of **3** under the typical conditions gave only 10% yield of 3-phenyl-2-butanone as the desired rearranged product; the major product was α-methoxy substituted alcohol which corresponds to **12** in the electrolysis of **10**. These results indicate that the migration of methyl group is not efficient.

When dibenzylated tertiary alcohol **14** was similarly electrolyzed, the expected ketone **15** was obtained in 61% yield (Table 3). Phenyl-group substituted alcohols **16** and **18** were electrolyzed under the typical conditions, but expected ketones **17** and **19** were formed only in unsatisfactory yields lower than 50%. Good yields of **17** and **19** were obtained under slightly modified

Table 3. Electrooxidative Rearrangement of Acyclic β-Hydroxy Sulfides.

Substrate	Conditions	F/mol	Product	Yield,%
 **(14)**	a)	6.0	 **(15)**	61
 **(16)**	b)	6.0	 **(17)**	83
 **(18)** c)	b)	6.0	 **(19)**	69

a) Typical conditions using carbon electrodes (footnote a) in Table 1). b) In a divided cell. c) A mixture of *erythro* and *threo* isomers was used.

conditions where the anodic electrolysis was carried out in a divided cell (see Table 3). In the case of **18**, only phenyl migrated ketone **19** was produced; here, the starting sulfide **18** was mixtures of *erythro* and *threo* isomers of varying contents, but the resulting product was **19** only. Thus, there is no stereoelectronic requirement in this electrooxidative rearrangement.

Conclusively, the present electrooxidation for the pinacol-type rearrangement of **1** can be achiedved under neutral conditions simply by choosing chloride ions as the electrolyte.[23,24] In this respect, the method is advantageous over that using the troublesome metallic reagents[5-7] used often in large excess.

Experimental

Apparatus for electrolysis, CV and various spectroscopy were described elsewhere.[18] Melting points were uncorrected. NMR spectra were recorded on a 200 MHz model.

Starting Materials. α-Phenyl substituted β-hydroxy sulfides were prepared by the literal method.[25]

1-(α-Phenylthiobenzyl)cyclopentanol (3), 75% yield, mp 43-44°C, NMR($CDCl_3$) δ 1.25-1.95 (m,8H), 1.99(s, 1H), 4.27 (s, 1H), 7.1-7.45 (m, 10H). Anal calcd. for $C_{18}H_{20}OS$, C 76.01, H 7.09; found C 75.74, H 7.12.

1-(α-Phenylthiobenzyl)cyclobutanol (5), 90% yield, mp 45-47°C,δ 1.4-2.4 (m, 6H), 2.43 (s, 1H), 4.35 (s, 1H), 7.15-7.5 (m, 10H). Anal calcd. for $C_{17}H_{18}OS$, C 75.71, H 6.71; found C 75.58, H 6.42.

2,2-Dimethyl-1-(α-phenylthiobenzyl)cyclopentanol (7), 42% yield, a colorless liquid obtained by column chromatography as an inseparable mixture. NMR spectra indicated two components of 9 : 1 ratio; the major one (in $CDCl_3$) δ 1.17 (s, 3H), 1.41 (s, 3H), 1.0-2.0 (m, 6H), 4.31 (s, 1H), 7.1-7.4 (m, 10H) and the minor one δ 0.29 (s, 3H) 0.98 (s, 3H), 1.0-2.0 (m, 6H), 4.29 (s, 1H), 7.1-7.4 (m, 10H).

1-(α-Phenylthiobenzyl)cyclohexanol (10), 79% yield, mp 78-79°C, δ 0.95-1.95 (m, 10H), 2.10 (s, 1H), 4.17 (s, 1H), 7.1-7.4 (m, 10H). Anal calcd. for $C_{19}H_{22}OS$, C 76.47, H 7.43; found C 76.66, H 7.48.

2-Benzyl-1,3-diphenyl-1-phenylthio-2-propanol (14), 80% yield, mp 109-111°C, δ 1.77 (s, 1H), 2.75(d, J = 13.8 Hz, 1H), centered at 3.02 (ABq, 13.8 Hz, 2H), 3.23 (d, J = 13.8Hz, 1H), 4.17 (s, 1H), 7.05-7.4 (m, 20H). Anal calcd. for $C_{28}H_{26}OS$, C 81.91, H 6.38; found C 81.75, H 6.25.

1,1,2-Triphenyl-2-phenylthioethanol (16), 85% yield, mp 119-120°C, δ 3.26(s,1H), 5.22(s, 1H), 7.0-7.65 (m, 20H). Anal calcd. for $C_{26}H_{22}OS$, C 81.64, H 5.80; found C 81.87, H 5.69.

1,2-Diphenyl-1-phenylthio-2-propanol (18), 77% yield, a white solid, mp 111-114°C. NMR analysis of this material showed a 1 : 1 mixture of **18**. Attempts to separate the *erythro* and *threo* isomers in enough pure state were failed. One isomer enriched in 90% purity showed the following NMR spectrum; δ 1.53 (s, 3H), 3.01 (s, 1H), 4.47 (s, 1H), 7.1-7.35 (m, 20H). Then, another was δ 1.78 (s, 3H), 2.82 (s, 1H), 4.48 (s, 1H), 7.1-7.35 (m, 20H).

Typical Procedure of Electrolytic Reaction. A solution of β-hydroxy sulfide **1** (1 mmol) in dichloromethane-methanol (9 : 1, 25 mL), containing tetraethylammonium chloride (2 mmol) was electrolyzed in an undivided cell equipped with carbon plate electrodes with a constant current of 100 mA. The electrolysis was continued until over 95% of starting **1** was consumed. The electrolysis mixture was diluted with 100 mL of ether, treated with 100mL of water, separated and extracted with ether, and finally the combined organic layer was dried over magnesium sul-

fate. Solvent was removed in vacuo. The resulting residue was chromatographed on silica gel using hexane and ethyl acetate (10-20 : 1) as an eluent. The structure of each product isolated was determined by MS, IR and NMR spectroscopy, of which NMR data are recorded here.

2-Phenylcyclohexanone (4), mp 55-56 °C (lit., [26] 63°C), NMR ($CDCl_3$) δ 1.7-2.6 (m, 8H), 3.59 (dd, J = 11.0, 5.0Hz, 1H) 7.1-7.6 (m, 5H).

2-Phenylcyclopentanone (6), mp 33-34°C (lit.,[27] 35-37°C), δ 1.8-2.6 (m, 6H), 3.33 (dd, J = 10.0, 8.0 Hz, 1H), 7.2-7.4 (m, 5H).

3,3-Dimethyl-2-phenylcyclohexanone (8), Rf 0.32 (hexane : ethyl acetate = 15 : 1) mp 66-68 °C (lit., [28] 67-68°C), δ 0.86 (s, 3H) 1.7-2.1 (m, 6H), 2.3-2.6 (m, 2H), 3.49 (s, 1H), 7.2-7.4 (m, 5H).

2,2-Dimethyl-5-phenylcyclohexanone (9), this minor product was obtained as slightly in pure state; Rf 0.40, a liquid, δ 1.09 (s, 3H), 1.31 (s, 3H) 1.6-2.3 (m, 6H) 3.87 (dd, J = 12.6, 5.4 Hz, 1H) 7.1-7.4 (m, 5H).

2-Phenylcycloheptanone (11), [29] a colorless liquid, δ 1.4-2.8 (m, 10H), 3.74 (dd, J = 11.0, 4.2 Hz, 1H), 7.2-7.4 (m, 5H). In this case, other products were α-methoxy alcohol **12** (δ 1.05-1.7 (m, 11H), 3.25 (s, 3H), 3.95 (s, 1H), 7.2-7.35 (m, 5H)) and α-chloro alcohol **13**, isolated as an unstable liquid (δ 1.1-1.7 (m 11H), 4.83 (s, 1H), 7.3-7.5 (m, 5H)).

1,3,4-Triphenyl-2-butanone (15), mp 73-74°C(lit.,[30] 75-76°C), δ 2.88 (dd, J = 13.7, 6.8 Hz, 1H) 3.38 (dd, J = 13.7 , 8.0 Hz, 1H), centered at 3.55 (ABq, J = 16 Hz, 2H), 4.2 (dd, J = 8.0, 6.8 Hz, 1H) 6.9-7.3 (m, 15H), being in accord with lit. [30]

Electrolysis in a Divided Cell. Electrolysis in a divided cell was carried out using a cylindrical glass vessel (ϕ 30mm, H 50 mm) equipped with a porous porcelain cup (ϕ 15 mm) as the cathodic chamber. The anodic chamber was set with a carbon rod electrode (ϕ = 8 mm), a platinum sheet electrode being inserted to the cathodic chamber. The electrolytic procedure was the same as described above except for that the amount of electrolyte Et_4NCl was doubled, *i.e.*, 4 mmol. The anolyte was worked-up similarly.

α,α-Diphenylacetophenone (17), mp 138-139 °C (lit., [31] 137-139°C), δ 6.04 (s, 1H), 7.15-8.0 (m, 15H).

1,1-Diphenylacetone (19), mp 50-53 °C (lit., [32] 46 or 60-61°C), δ 2.25 (s, 3H), 5.11 (s, 1H), 7.2-7.4 (m, 10H), which corresponds to the reported data.[33]

Acknowledgments This study was supported partly by a Grant-in Aid for Scientific Research from Ministry of Education, Science and Culture of Japan.

References and Notes

1. Rickborn, B. *Comprehensive Organic Synthesis*; Trost, B. M. Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 721.
2. Coveney, D. J. *Comprehensive Organic Synthesis*; Trost, B. H. , Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol.3, p777.
3. Wovkulich, P. M. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol 1, p861.
4. Smith, P. A. S.; Baer, D. R. *Org. React.* **1960**, *11*, 157.
5. Cohen, T.; Kuhn, D.; Falck, J. R. *J. Am. Chem. Soc.* **1975**, *97*, 4749.
6. (a) Knapp, S.; Trope, A. F. ; Ornaf, R. M. *Tetrahedron Lett.* **1980**, 4301. (b) Knapp, S.; Trope, A. F.; Theodrore, M. S. ; Hirata, N. ; Barchi, J. J. *J. Org. Chem.* **1984**, *49*, 608.

7. (a) Laboureur, J. L.; Krief, K. *Tetrahedron Lett.* **1984**, *25*, 2713. (b) See also, Krief, A. ; Laboueur, J. L.; Dumont, W.; Labar, D. *Bull. Soc. Chim. Fr.* **1990**, *127*, 681.
8. Torii, S. *Electroorganic Synthesis*; Kodansha: Tokyo, 1985; Chapter 6.
9. Svensmark, B. ; Hammerich, O. *Organic Electrochemistry*, 3rd Ed., Lund, H., Baizar, M. M., Eds.; Marcel Dekker: New York, 1991; Chapter 17.
10. Uneyama, K.; Torii, S. *Tetrahedron Lett.* **1971**, 329.
11. (a) Baciocchi, E.; Roe, C.; Scamossi, E.; Sebastiani, G. V. *J. Org. Chem.* **1991**, *56*, 5498. (b) Baciocchi, E.; Fasella, E. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1071.
12. Kimura, M.; Yamamoto, Y.; Sawaki, Y. *Denki kagaku* **1993**, *61*, 862.
13. Torii, S.; Inokuchi, T.; Araki, Y. *Synth. Commun.* **1987**, *17*, 1797.
14. Shono, T.; Hamaguchi, H.; Matsumura, Y.; Yoshida, K. *Tetrahedron Lett.* **1977**, 3625.
15. Hannaby, M.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3007.
16. Kudo, K.; Saigo, K.; Hashimoto, Y.; Saito, K.; Hasegawa, M. *Chem. Lett.* 1992, 1449.
17. Shanklin, J. R.; Johnson, C. R.; Ollinger, J.; Coats, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3429.
18. Grieco, P. A.; Wang, C.-L. *J. Chem. Soc., Chem. Commun.* **1975**, 714.
19. For example, Kimura, M.; Matsubara, S.; Yamamoto, Y.; Sawaki, Y. *Tetrahedron* **1991**, *47*, 867 and references cited therein.
20. Kimura, M.; Kuriki, N.; Inaishi, M.; Sawaki, Y. *Tetrahedron Lett.* **1984**, *25*, 4665.
21. Nokami, J.; Fujita, Y.; Okawara, R. *Tetrahedron Lett.* 1979, 3659.
22. Trost, B. M.; Mikhail, G. K. *J. Am. Chem. Soc.* **1987**, *109*, 4124.
23. This electrooxidative rearrangement is possible for β-hydroxysulfides other than benzylic sulfides **1**. For example, electrolysis of 2-methyl-1-phenyl-2-phenylthio-1-propanol with 6 F/mol of electricity in MeCN-4% MeOH containing tetraethylammonium chloride gave a rearrangement product 2-methyl-2-phenylpropanol in 18% isolated yield. Similarly, 1-[methoxy(phenylthio)methyl]cyclopentanol underwent a low yield (*ca.* 10%) of rearrangement giving 2-methoxycyclohexanone. Therefore, utilization of benzylic sulfides **1** in the present rearrangement seems to be more appropriate to effect an efficient C-S cleavage and stabilization of the resulting cationic species (see Scheme I).
24. Use of mercury (II) chloride as a common thiophilic reagent effected the rearrangement of **3**, but the reaction was sluggish; the reaction of **3** with 2 equiv of $HgCl_2$ in MeCN-H_2O (4:1, **3** 0.1 M) by refluxing for 24 h gave a mixture of desired **4** (52%), unreacted **3** and others.
25. (a) Song, S.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1974**, 1161. (b) Kingsbury, C. A. *J. Org. Chem.* **1972**, *37*, 102.
26. Price, C. C.; Karabinos, J. V. *J. Am. Chem. Soc.* **1940**, *62*, 1159.
27. Arnold, R. T.; Buckley, J. S. Jr.; Dodson, R. M. *J. Am. Chem. Soc.* **1950**, *72*, 3153.
28. Balsamo, A ; Ciotti, P.; Macchia, B.; Macchia, F. *Tetrahedron* **1973**, *29*, 199.
29. Gutsche, C. D. *J. Am. Chem. Soc.* **1949**, *71*, 3513.
30. Baretz, B. H.; Turro, N. J. *J. Am. Chem. Soc.* **1983**, *105*, 1309.
31. Cope, A. C.; Trumbull, P. A.; Trumbull, E. R. *J. Am. Chem. Soc.* **1958**, *80*, 2844.
32. Schultz, E. M.; Mickey, S. *Org. Syn. Coll. Vol. III* **1955**, 343.
33. Bagnell, L.; Jeffery, E. A.; Meisters, A.; Mole, T. *Aust. J. Chem.* **1974**. *27*, 2577.

(*Received in Japan* 20 *November* 1995; *accepted* 24 *January* 1996)