Tetrahedron Letters,Vol.28,No.47,pp 5903-5906,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

SILICON PUMMERER REACTION OF THIAZOLIDINE S-OXIDES; A NEW METHOD FOR STEREOSPECIFIC C-5 FUNCTIONALIZATION OF THIAZOLIDINES

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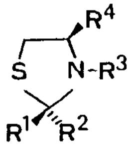
Summary: Silicon Pummerer reaction of optically active thiazolidine S-oxides using trialkylsilyl triflate led to a stereospecific formation of α-siloxysulfides, while the use of iodotrimethylsilane resulted in a facile formation of α-iodosulfides.

The Pummerer reaction of sulfoxides, which provides a useful method for the synthesis of α-substituted and/or α,β-unsaturated sulfides, has been widely applied to the synthesis of organosulfur compounds.[1)] In addition, some examples of silicon induced Pummerer rearrangement were reported using several kinds of silylating reagents such as iodotrimethylsilane,[2)] chlorotrimethylsilane,[3)] and ketene methyl t-butyldimethylsilyl acetal.[4)] However, they were limited only to simple dialkyl and alkyl aryl sulfoxides and the application to the more functionalized substrate has not been attempted yet. Recently, we have described a facile α-hydroxylation of optically active thiazolidines(**1**) by stereospecific photohydroxyperoxidataion and subsequent reduction.[5)] Here, we present another useful functionalization method of **1** by the silicon induced Pummerer reaction via their S-oxides(**2**).



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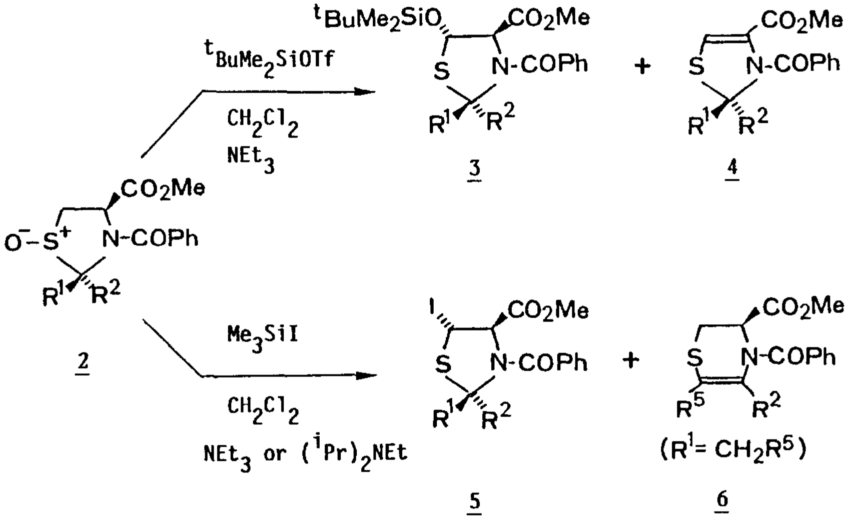
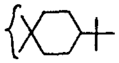
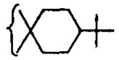
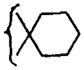


When thiazolidine S-oxides (**2a-d**) were treated with 1.2-1.3 eq. of t-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf)[6] as a silylating reagent in dichloromethane in the presence of 1.3 eq. of triethylamine at 0°C for several hours, the corresponding α-siloxysulfides(**3a-d**) were obtained in moderate to good yields as a single stereoisomer, respectively, together with considerable amounts of α,β-unsaturated sulfides (**4c** and **4d**) in the cases of mono-substituted derivatives (**2c** and **2d**). **2a-d** was also treated with iodotrimethylsilane in the presence of triethylamine to afford the corresponding α-iodosulfides (**5a-d**) along with the dihydro-1,4-derivatives (**6a** and **6b**), the ring expansion products,[7]. The use of rather hindered base such as diisopropylethylamine gave mainly the α-iodosulfides (**5c** and **5d**) in the cases of **2c** and **2d**, and no ring expansion products were obtained. The results obtained from the above-mentioned two types of silicon Pummerer reaction of thiazolidine S-oxides(**2a-2d**) were summarized in Table 1.

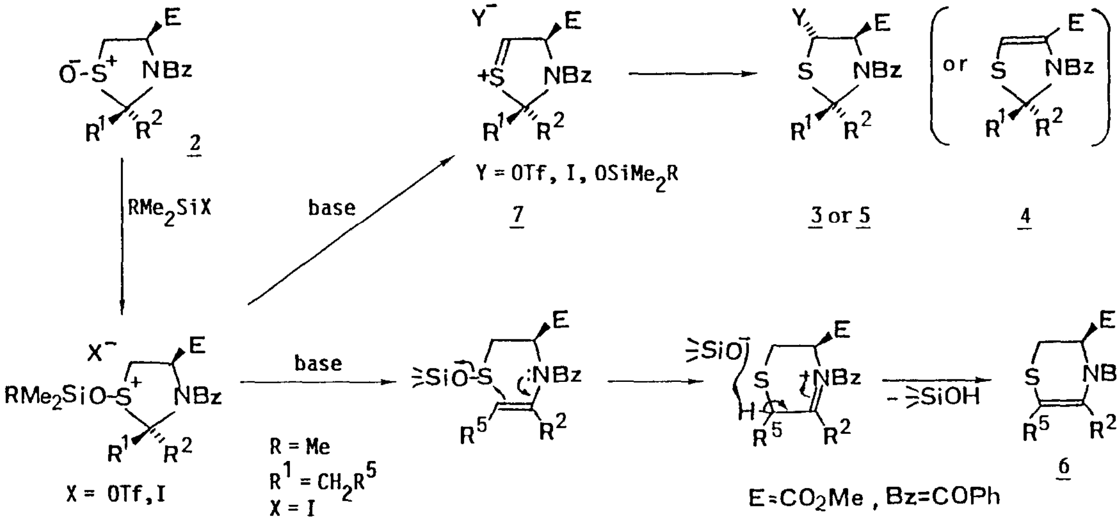
Table 1. Silicon Pummerer Reactions of Thiazolidine S-Oxide(2).

Entry	Substrate	R^1 R^2	Silylating Reagent	Base	Products and Yields[a]
1	**2a**		$^tBuMe_2SiOTf$	NEt_3	**3a**(72%) + **4a**(5%)
2	**2a**		Me_3SiI	NEt_3	**5a**(54%) + **6a**(20%) (R^5,R^2 = $-CH_2CH(^tBu)CH_2CH_2-$)
3	**2b**		$^tBuMe_2SiOTf$	NEt_3	**3b**(49%)
4	**2b**		Me_3SiI	NEt_3	**5b**(42%) + **6b**(14%) (R^5,R^2 = $-(CH_2)_4-$)
5	**2c**	^tBu, H	$^tBuMe_2SiOTf$	NEt_3	**3c**(59%) + **4c**(9%)
6	**2c**	^tBu, H	Me_3SiI	$(^iPr)_2NEt$	**5c**(52%)
7	**2d**	p-Tol,[b] H	$^tBuMe_2SiOTf$	NEt_3	**3d**(27%) + **4d**(50%)
8	**2d**	p-Tol,[b] H	Me_3SiI	$(^iPr)_2NEt$	**5d**(53%)

a) Isolated yields. b) p-Tol = p-methylphenyl.

The structures of the products(3, 4, 5, and 6) were confirmed by the ^{1}H-NMR, ^{13}C-NMR, mass spectra, and elemental analysis,[8) and the stereochemistry of the newly introduced α-siloxy group in 3 was determined by the comparison with the authentic sample prepared from the previously reported α-hydroxysulfide.

The mechanism of the silicon Pummerer reaction described here is rationalized with the formation of the sulfonium salts(7), the intermediacy of which was confirmed by the fact that the same products were obtained from the reactions using either of the possible syn and anti stereoisomeric sulfoxides, and their subsequent α-substitution by the counteranionic nucleophiles. In the reaction of TBDMSOTf the relatively low nucleophilicity of the triflate anion to the siloxy anion resulted in the formation of α-siloxysulfide(3), while the rather higher nucleophilicity of iodide ion than that of trimethylsilyloxy anion led to the novel formation of α-iodosulfide(5), which is noteworthy as the first example of an isolation of a stable α-halosulfide without further elimination in the silicon induced Pummerer rearrangement using halotrimethylsilane as a silylating reagent. The considerable stability of 5 implied the cis configuration of the iodine atom to the neighboring hydrogen atom at 4-position which might be undesirable for the trans elimination of hydrogen iodide. As for the difference of the side reactions between the two silylating reagents, the bulkiness of the alkyl groups on the silicon atom and the leaving ability of the siloxy group seem to alter the direction of the reactions.



Thus, we have found that the facile and stereospecific substitution at C-5 position of thiazolidines with either siloxy group or iodine atom was possible by silicon Pummerer reaction using an appropriate silylating reagent. In view of the potential utility of the newly introduced α-functionalities, the new methodology presented here will provide a useful and highly stereoselective β-modification method for a sulfur-containing amino acid such as cysteine. Furthermore, the stereochemical investigation using a kiral cyclic sulfoxide as a substrate will contribute to the more clear and detailed elucidation of the mechanism of the silicon Pummerer reactions.

REFERENCES

1) L. Horner and P. Kaiser, Ann., **626**, 19 (1959); L. Horner, Ann., **631**, 198 (1960); T. Durst, "Advances in Organic Chemistry," **6**, 285 (1969); T. Numata and S. Oae, Yuki Gosei Kagaku Kyokai Shi, **35**, 726 (1977); T. Numata, ibid.,**36**, 845 (1978); T. Durst, "Comprehensive Organic Chemistry," ed by D. Barton, vol. 3, Part 11, Pergamon Press, New York (1979).

2) R. D. Miller and D. R. Mackean, Tetrahedron Lett., **24**, 2619 (1983).

3) S. Lane, S. J. Quick, and R. J. K. Taylor, Tetrahedron Lett., **25**, 1039 (1984).

4) Y. Kita, H. Yasuda, O. Tamura, F. Itoh, and Y. Tamura, Tetrahedron Lett., **25**, 4681 (1984).

5) T. Takata, K. Hoshino, E. Takeuchi, Y. Tamura, and W. Ando, Tetrahedron Lett., **25**, 4767 (1984).

6) The effectiveness of this silylating reagent has been demonstrated in the analogous base-promoted rearrangement of siloxyammonium salt, i.e. silicon induced Polonovski reaction; R. Okazaki and N. Tokitoh, J. Chem. Soc., Chem. Commun., **1984**, 192.

7) Analogous ring expansion reaction of benzothiazoline S-oxide has been reported; M. Hori, T. Kataoka, H. Shimizu, and Y. Imai, Chem. Pharm. Bull.(Tokyo), **27**, 1982 (1979); M. Hori, T. Kataoka, H. Shimizu, and N. Ueda, Tetrahedron Lett., **22** 1701 (1981).

8) The following spectral data of **3a**, **4a**, **5a**, and **6a** are shown as representative.
3a; colorless oil, ^{1}H-NMR(CDCl$_3$) δ 0.13(s,3H), 0.18(s,3H), 0.87(s,9H), 0.93(s,9H), 1.05-2.10(m,9H), 3.67(s,3H), 4.88(s,1H), 5.53(s,1H), and 7.35(s,5H); ^{13}C-NMR(CDCl$_3$) δ -5.5(q), -4.4(q), 17.8(s), 25.5(q), 26.1(tx2), 27.6(q), 32.3(s), 36.6(t), 37.2(t), 46.2(d), 52.7(q), 76.8(d), 77.7(d), 81.8(s), 125.9(d), 128.6(d), 129.2(d), 139.2(s), 168.8(s), and 170.1(s); MS, m/z 505(M$^+$,13%), 448(78), 374(34), and 105(100); Exact mass, found m/z 505.2663: Calcd for $C_{27}H_{43}NO_4SSi$ 505.2680.
4a; white crystals, mp. 149-151 °C, ^{1}H-NMR(CDCl$_3$) δ 0.88(s,9H), 0.9-2.4(m,9H), 3.24(s,3H), 6.74(s,1H), and 7.2-7.7(m,5H); ^{13}C-NMR(CDCl$_3$)δ 24.5(t), 27.4(q), 32.2(s), 35.2(t), 46.4(d), 51.5(q), 90.1(s), 120.9(d), 128.0(d), 131.3(d), 137.2(s), 159.9(s), and 168.9(s); MS, m/z 373 (M$^+$,20%), 105(100), and 57(29); E. A. Found:C, 67.38; H, 7.38; N, 3.75%. Calcd for $C_{21}H_{27}NO_3S$: C, 67.52; H, 7.28; N, 3.75%.
5a; white crystals, mp. 141-2 °C, ^{1}H-NMR(CDCl$_3$) δ 0.90(s,9H), 0.9-2.2(m,9H), 3.66(s,3H), 5.06(s, 1H), and 7.2-7.7(m,5H); ^{13}C-NMR(CDCl$_3$) δ 21.2(d), 25.9(t), 26.7(t), 27.5(q), 32.2(s), 34.5(t), 37.3(t), 45.7(d), 53.1(q), 79.9(d), 84.1(s), 125.8(d), 128.7(d), 129.5(d), 138.5(s), 167.1(s), and 170.1(s); MS, m/z 374(M$^+$-127, 4%), 373(5), 273 (4), 127(7), and 105(100); E.A. Found: C, 50.54; H, 5.67; N, 2.81%. Calcd for $C_{21}H_{28}INO_3S$: C, 50.30; H, 5.63; N, 2.79%.
6a; colorless oil, ^{1}H-NMR(CDCl$_3$) δ 0.82(s,9H), 1.0-2.1(m,7H), 3.41(H$_B$,J$_{BX}$=5.7Hz,J$_{AB}$=12.4Hz,1H), 3.53(H$_A$, J$_{AX}$=3.1Hz,J$_{AB}$=12.4Hz,1H), 3.78(s,3H), 5.89(H$_X$, J$_{AX}$=3.1Hz, J$_{BX}$=5.7Hz, 1H),and 7.2-7.7(m,5H); ^{13}C-NMR(CDCl$_3$) δ 23.7(t), 27.1(q), 31.3(t), 31.5(t), 31.6(t), 32.2(s), 44.3(d), 52.6(q), 53.6(q), 120.8(s), 127.8(d), 128.4(d), 129.8(s), 131.1(d), 136.2(s), 169.1(s), and 169.4(s); MS,m/z 373(M$^+$,85%), 268(28), and 105(100); Exact mass, found m/z 373.1722: Calcd for $C_{21}H_{27}NO_3S$ 373.1712.

(Received in Japan 7 August 1987)