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# Stereochemistry of the Intramolecular Substitution of Phenylselenonyl Group by Nitrogen Atom in Amide. Inversion of Configuration[1)]

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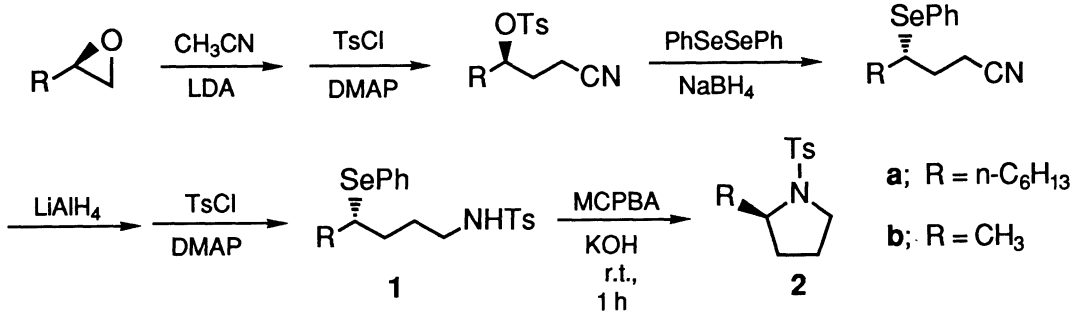
The stereochemistry of the intramolecular substitution of phenylselenonyl group by a nitrogen atom in tosylamino group was proved to be inversion by the oxidative cyclization of (*S*)-1-alkyl-4-(tosylamino)butyl phenyl selenides to (*R*)-*N*-tosyl-2-alkylpyrrolidines.

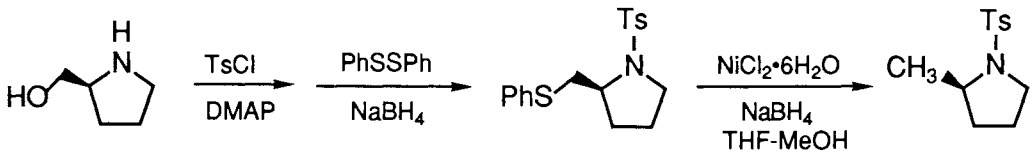
Phenylselenonyl group attached to an $sp^3$ carbon atom has been recognized as an excellent leaving group and many substitution reactions have been reported using various kinds of nucleophiles.[2)] The mechanism of the substitution, however, has not yet been reported.[3)] To clarify the stereochemistry, we applied a recently reported cyclization reaction through the substitution of phenylselenonyl group by nitrogen atom[4)] to the substrates having asymmetric carbon bearing selenium functional group. Thus, we found that the oxidation of (*S*)-1-alkyl-4-(tosylamino)butyl phenyl selenides (**1**) by excess *meta*-chloroperbenzoic acid (MCPBA) affords (*R*)-*N*-tosyl-2-alkylpyrrolidines (**2**) without loss of optical purity. These results indicate that the intramolecular substitution of the phenylselenonyl group by the nitrogen atom proceeds with inversion of configuration.




Scheme 1.

(*S*)-1-Hexyl-4-(tosylamino)butyl phenyl selenide (**1a**)[5)] (92% e.e.) was prepared from (*R*)-1,2-epoxyoctane (92% e.e.) by the procedure shown in Scheme 1. The absolute configuration of the chiral carbon was not changed in all steps except for the third step which inversed the configuration through a well known $S_N2$ displacement of the tosyloxy group by a phenylseleno group. In a typical procedure for cyclization, MCPBA (2.5 mmol) and 2-propanol (4 $cm^3$) were added to a solution of **1a** (0.5 mmol) and potassium hydroxide (5.5 mmol) in 2-propanol (16 $cm^3$) and the resulting solution was stirred at ambient temperature for 1 h. After the usual work up, column chromatography [silica gel, hexane - ethyl acetate (3:1) as eluant] afforded *N*-tosyl-2-hexylpyrrolidine (**2a**) (0.14 g, 0.44 mmol; 87%) [$[\alpha]_D^{28}$ -87.1 ± 0.4° (*c* 0.596, $CHCl_3$)]. The enantiomeric

excess of **2a** was found to be 92% by liquid chromatographic analysis using chiral column, indicating that the optical purity of the chiral carbon was not lost during the substitution reaction. Similarly, **1b** (86% e.e.) afforded **2b** (86% e.e.) [$[\alpha]_D^{19}$ -51.0 ± 0.1° (*c* 0.556, $CHCl_3$)] in 85% yield by MCPBA oxidation. To determine the absolute configuration of **2b**, the authentic sample of (*R*)-*N*-tosyl-2-methylpyrrolidine was prepared from commercially available (*S*)-2-(hydroxymethy)pyrrolidine through the displacement of the oxygen function by phenylthio group followed by desulfurization (Scheme 2) [$[\alpha]_D^{18}$ -57.6 ± 0.5° (*c* 1.066, $CHCl_3$)]. The chiral carbon has been intact in all steps. From the comparison of the retention times in liquid chromatographic analyses using chiral column[6] as well as that of the sign of optical rotation, the absolute configuration of **2b** was confirmed to be *R*.[7] Thus, we can conclude that the intramolecular substitution of phenylselenonyl group by the nitrogen atom proceeds with inversion of configuration.




Scheme 2.

This reaction should be valuable for the preparation of various chiral nitrogen heterocycles with anticipated absolute configuration. Our progress along this line will be reported in due course.

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References

1) Presented at the 63rd National Meeting of the Chemical Society of Japan, Higashi-ohsaka, March 1992.
2) See for example; M. Shimizu and I. Kuwajima, *J. Org. Chem.*, **45**, 4063(1980); M. Shimizu, R. Ando, and I. Kuwajima, *J. Org. Chem.*, **46**, 5246(1981); S. Uemura, S. Fukuzawa, and A. Toshimitsu, *J. Chem. Soc., Chem. Commun.*, **1983**, 1501; H. J. Reich, *Proc. Fourth Int. Conference Org. Chem. Selenium and Tellurium*, **1983**, 258; I. Kuwajima, R. Ando, and T. Sugawara, *Tetrahedron Lett.*, **24**, 4429(1983); A. Krief, W. Dumont, and J. N. Dennis, *J. Chem. Soc., Chem. Commun.*, **1985**, 571; M. Tiecco, D. Chianelli, L. Testaferri, M. Tingoli, and D. Bartoli, *Tetrahedron*, **42**, 4889(1986); S. Uemura, K. Ohe, and N. Sugita, *J. Chem. Soc., Chem. Commun.*, **1988**, 111; A. Krief, W. Dumont, and J. L. Laboureur, *Tetrahedron Lett.*, **29**, 3265(1988).
3) Quite recently, stereochemistry of the substitution of phenylselenonyl moiety by methoxy group (from methanol used as solvent) was reported to be *ca.* 95% inversion: Y. Nishikawa, T. Sugita, and S. Uemura, 63rd National Meeting of the Chemical Society of Japan, Higashi-ohsaka, March 1992, Abstr., No.1E1 33.
4) A. Toshimitsu, C. Hirosawa, S. Tanimoto, and S. Uemura, *Tetrahedron Lett.*, **33**, 4017(1992).
5) All new compounds gave satisfactory spectral as well as combustion analytical data. Enantiomeric excess was determined by liquid chromatographic analyses using chiral column (Daicel Chiralcel OD for **1a** and **1b**, and Chiralpak AD for **2a** and **2b**).
6) The retention time of (*R*)-**2b** was 14.1 min and that of the enantioisomer [(*S*)-**2b**] was 16.1 min [hexane - 2-propanol (10:1), 0.8 $cm^3$/min] using Daicel chiralpak AD.
7) By analogy with this result, the absolute configuration of **2a** was deduced to be *R*.

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