

Indium(I) Iodide-Mediated Regioselective Ring Opening of Epoxides with Diphenyldiselenide: The Preparation of β -Hydroxy Selenides

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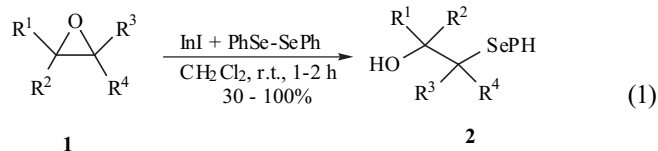
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Abstract: Epoxides were efficiently transformed into β -hydroxy selenides by the action of diphenyldiselenide and indium(I) iodide under mild conditions. The ring opening reaction is regioselective with nucleophile incorporation at the less hindered carbon atom for alkyl-substituted epoxides, and at the benzylic carbon atom for aryl derivatives.

Key Words: epoxide, ring opening reaction, indium (I), β -hydroxy selenide, regioselectivity.

1. INTRODUCTION

β -Hydroxy selenides are very useful intermediates in organic synthesis. They are transformed into allylic alcohols [1-3], olefins, [4-6] epoxides [7], halohydrins [8], and oxygenated five and six-membered heterocyclic rings. [9-13] The most common method for their preparation is the reaction between the phenyl selenide anion and epoxides. The boron complex (C₆H₅Se)₃B [14]; the reagent generated, *in situ*, from NaBH₄ and diphenyldiselenide in ethanol [2, 15]; the benzeneselenolate nucleophile generated from diphenyldiselenide and Bu₃P in alkaline medium [16]; the ytterbium(III) selenolate complex [17]; and tributylstannyl benzeneselenolate in the presence of BF₃.OEt₂ [18] were, alternatively, used as sources of the anion. Other protocols for their preparation involved the addition of organometallic or hydride reagents to α -phenylselenocarbonyl compounds [4], and the reaction of α -lithioselenides with carbonyl compounds [7]. Ring opening reactions involving some of these reagents lack rigorous regioselectivity, [2, 14, 15, 16, 17] or produce low yields [18]. Thus, the development of a new reagent, capable of promoting the ring opening reaction under mild conditions and starting from the stable reagent diphenyldiselenide is required.

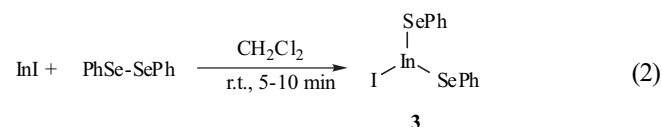


During the last few years, we turned our interest on applications of indium compounds in organic synthesis. Particularly, compounds containing the metal at its lowest oxidation state, which remain scarcely investigated. As a consequence of this work, we describe here an efficient regioselective method for ring opening of epoxides with

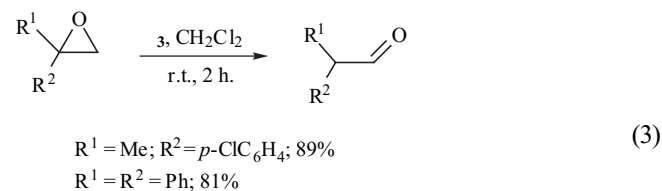
diphenyldiselenide mediated by indium monoiodide. The products are the versatile β -hydroxy selenide reagents (eq. 1).

2. RESULTS AND DISCUSSION

The most characteristic reaction of indium(I) compounds is their oxidative insertion into a suitable substrate to generate the corresponding indium(III) derivative. Thus, the complex bis(phenylseleno)-iodo-indium(III), In(SePh)₂, (**3**) is readily prepared by reacting equimolar amounts of InI and (C₆H₅Se)₂ in dichloromethane (eq. 2) [19,20].



A freshly prepared CH₂Cl₂ solution of compound (**3**) reacts with propylene oxide, (**1a**) (Table 1 – entry a) at room temperature to quickly (1h.) produce a quantitative yield of the corresponding β -hydroxy selenide, (**2a**). The mild reaction conditions, its speed and the excellent yield obtained encouraged us to examine the scope and generality of the present method. These results are given at Table 1, which reveals the regioselective attack of the benzeneselenolate anion at the less hindered carbon atom (entries a-c, h, i) for alkyl-substituted epoxides. On the contrary, with aryl-substituted epoxides, the attack occurs at the benzylic carbon atom (entries d-f, j, k). The absolute regioselectivity of this protocol is one of its highlights.



The drawback of this protocol is the failure of 1-alkyl-1-aryl and 1,1-diaryl substituted epoxides to undergo the ring opening reaction. Reactions with these substrates produced the corresponding aldehydes resulting from rearrangement of

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Table 1. Indium(I) Iodide-Mediated Regioselective Ring Opening of Epoxides. The Preparation of β -Hydroxy Selenides

Entry	Substrate, 1	Product, 2	Yield (%)	time (h)
a			100	1
b			100	1
c			95	1
d			81	1
e			100	1
f			57 61a, b	2 2
g			100 (cis:trans = 0:100)	1
h			67 (cis:trans= 4:5) ^c	1
i			30	2
j			94 (syn:anti= 4:9) ^c	1
k			60 (syn:anti= 100:0) ^c	1

^areaction with two molar equivalents of (3), ^bplus 26% of 2-(*p*-methoxyphenyl) ethanal, ^c unassigned stereochemistry

the epoxides catalyzed by indium(III) (eq. 3), as described by Ranu and co-workers [21]. This reaction, which is determined by the stability of the benzylic cation resulting from the epoxide ring opening, explains the production of

the aldehyde by-product, 2-(*p*-methoxyphenyl)ethanal, from (1f).

Some insight on the stereoselectivity of the present method was obtained from reactions involving selected

epoxides. Cyclohexene-oxide (entry g) produced stereospecifically the *trans*-diequatorial β -hydroxyselenide, in quantitative yield as revealed by ^1H and ^{13}C NMR spectroscopy. Stereospecificity was lost for 1-methylcyclohexene-oxide (entry h) and (*trans*)-1- β -naphthyl-2-*n*-propyloxirane (entry j); in these cases, unassigned mixtures of 5:4 and 9:4 of the two diastereomers were, respectively, produced.

Finally, we have determined that the epoxyketone (*trans*)-1-benzoyl-2-phenyloxirane (entry k) produced stereospecifically one of the diastereomers of α -hydroxy- α -[1-(phenylseleno)benzyl]acetophenone. The correct stereochemistry of (**2k**) still remains unassigned. The production of a single stereoisomer is believed to be governed by chelation of the indium complex (**3**) by both oxygen atoms of the epoxyketone. The scope and the correct mechanism of reactions involving related glycidic ketones and esters will be explored and reported later.

3. EXPERIMENTAL

General Procedure for the Synthesis of β -hydroxy selenides, (**2a-k**). Representative procedure for 1-(phenylseleno-2-propanol, (**2a**): InI (121 mg, 0.5 mmol) and (PhSe) $_2$ (154mg, 0.5mmol) were stirred in 3 mL of CH_2Cl_2 (dried over phosphorus pentoxide) in a Schlenk tube. After dissolving all InI (10-15 minutes), 2-methyloxirane (29 mg, 0.5 mmol) was added and the reaction was monitored by TLC. After 1 hour of continuous stirring, all the 2-methyl-oxirane was consumed. The reaction was quenched with 5 mL of H_2O and extracted with CH_2Cl_2 (2x 5 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated to dryness. The residue was purified by column chromatography on silica gel (hexane:ethyl acetate) to produce 108 mg (0.5 mmol, 100%) of 1-phenylselenio-propan-2-ol, (**2a**) as a colorless oil. This procedure was followed for the preparation of β -hydroxy selenides **2a-k**. Physical, spectral and analytical data are given below:

1-(Phenylseleno)-2-propanol, (**2a**): ^1H NMR (CDCl_3): δ = 1.16 (d, J = 6,2 Hz, 3H), 2.64 (s, 1H), 2.79 (dd, J = 12,8, 8 Hz, 1H), 2.98 (dd, J = 12.8, 4.2 Hz, 1H), 3.78 (m, 1H), 7.14 (m, 3H), 7.42 (m, 2H); ^{13}C NMR (CDCl_3): δ = 22.31, 38.12, 66.05, 127.05, 129.02, 132.78, 135.20; IR (NaCl): 3360, 1071, 737, 690 cm^{-1} ; MS (70 eV, EI): m/z (%) for ^{80}Se : 216 (M,100), 199 (16.6).

1-(Phenylseleno)-2-hexanol, (**2b**): ^1H NMR (CDCl_3): δ = 0.78 (t, J = 7,2 Hz, 3H), 1.20-1.35 (m, 6H), 2.73 (s, 1H), 2.79 (dd, J = 13.0, 8.2 Hz, 1H), 3.00 (dd, J = 13.0, 3.8 Hz 1H), 3.57 (m, 1H), 7.23 (m, 3H), 7.51 (m, 2H); ^{13}C NMR (CDCl_3): δ = 13.81, 22.44, 27.72, 36.10, 36.78, 69.70, 126.89, 128.92, 132.62, 135.04; IR (NaCl): 3360, 1071, 737, 690 cm^{-1} ; MS (70 eV, EI,): m/z (%) for ^{80}Se : 258 (M, 52), 172 (100).

3-(Phenylseleno)-1,2-propanediol, (**2c**): ^1H NMR (CDCl_3): δ = 2.98 (m, 2H), 3.26 (s, 2H), 3.67 (m, 1H), 3.73 (m, 2H), 7.23 (m, 3H), 7.51 (m, 2H); ^{13}C NMR (CDCl_3): δ = 31.54, 65.41, 70.69, 127.21, 129.15, 129.24, 132.76; IR (NaCl): 3339, 1099, 1029, 726, 685 cm^{-1} ; MS (70 eV, EI): m/z (%) for ^{80}Se : 232 (M, 63), 157 (100).

2-(Phenyl)-2-(phenylseleno)ethanol, (**2d**): ^1H NMR (CDCl_3): δ = 2.60 (s, 1H), 3.92 (m, 2H), 4.35 (t, J = 7Hz, 1H), 7.15- 7.46 (m, 10H); ^{13}C NMR (CDCl_3): δ = 50.49, 64.88, 127.34, 127.88, 127.95, 128.22, 128.29, 128.48, 135.18,139.23; IR (NaCl): 3432, 1022, 740, 694 cm^{-1} .

2-(4-Chlorophenyl)-2-(phenylseleno)ethanol, (**2e**): ^1H NMR (CDCl_3): δ = 2.39 (s, 1H), 3.99 (m, 2H), 4.21 (t, J = 7 Hz, 1H), 6.98-7.34 (m, 9H); ^{13}C NMR (CDCl_3): δ = 46.76, 64.57, 127.68, 128.23, 128.57, 128.99, 129.21, 132,96, 135.43, 137.93; IR (NaCl): 3380, 1058, 830, 689, 739 cm^{-1} ; MS (70 eV, EI): Decomposition.

2-(4-Methoxyphenyl)-2-(phenylseleno)ethanol, (**2f**): ^1H NMR (CDCl_3): δ = 2.08 (s, 1H), 3.67 (s, 3H), 3.83 (m, 2H), 4.28 (t, J = 7 Hz, 1H), 6.72 (d, 2H), 7.06 (d, 2H), 7.17 (m, 3H), 7.37 (m, 2H); ^{13}C NMR (CDCl_3): δ = 50.30, 55.22, 65.13, 114.07, 127.68, 128.01, 128.49, 128.98, 129.10, 131.19, 158.92; IR (NaCl): 3418, 1249, 1030, 832, 741, 691 cm^{-1} ; MS (70 eV, EI): m/z (%): Decomposition to 4-methoxy-benzaldehyde and diphenyldiselenide.

(*trans*)-2-(Phenylseleno)cyclohexanol, (**2g**): ^1H NMR (CDCl_3): δ = 1.10-1.27 (m, 4H), 1.49 (m, 1H), 1.61 (m, 1H), 2.04 (m, 2H), 2.82 (td, J = 9.5, 4.0 Hz, 1H), 3.07 (s, 1H), 3.25 (td, J = 9.5, 4.0 Hz, 1H), 7.18 (m, 3H), 7.49 (m, 2H); ^{13}C NMR (CDCl_3): δ = 24.18, 26.54, 33.08, 33.77, 52.96, 72.03, 126.63, 127.76, 128.71, 135.73; IR (NaCl): 3429, 1067, 738, 693 cm^{-1} ; MS (70 eV, EI): m/z (%) for ^{80}Se : 256 (M, 43), 158 (100).

(*cis* + *trans*)-1-(Methyl)-2-(phenylseleno)cyclohexanol, (**2h**): ^1H NMR (CDCl_3): δ = 1.00 - 2.00 (several multiplets, 11 H), 2.50 and 2.65 (two broad singlets, 1 H), [3.14 (dd, J = 12.0, 4.2 Hz) and 3.34 (dd, J = 11.0, 4.2 Hz), 1 H], 7.54 (m, 2H), 7.31 (m, 3H); ^{13}C NMR (CDCl_3): δ = 17.79, 22.38, 23.39, 23.93, 24.38, 27.95, 28.68, 33.36, 38.54, 39.46, 56.17, 60.18, 72.68, 73.03, 125.99, 127.43, 128.86, 128.92, 129.09, 129.95, 134.27, 138.42; MS (70 eV, EI): m/z (%) for ^{80}Se : 270 (M, 15.2), 113 (96), 95 (100).

4-(*tert*-Butyl)-1-(phenylselenomethyl)cyclohexanol, (**2i**): ^1H NMR (CDCl_3): δ = 0.75 (s, 9H), 1.45 - 1.84 (m, 9H), 2.27 (s, 1H), 3.18 (s, 2H), 7.17 (m, 3 H), 7.50 (m, 2H); ^{13}C NMR (CDCl_3): δ = 23.81, 27.52, 32.14, 38.30, 39.64, 47.32, 71.49, 127.04, 129.06, 132.94, 138.02; MS (70 eV, EI): m/z (%) for ^{80}Se : 326 (M, 16), 172 (100).

(*syn* + *anti*) 1-(2-Naphthyl)-1-(phenylseleno)-2-pentanol, (**2j**): ^1H NMR (CDCl_3): δ = 0.73 (t, J = 7.6 Hz, 3H), 1.32 (m, 4H), [2.35 (d, J = 4Hz), 2.63 (d, J = 4Hz) 1 H], 3.97 (m, 1H), [4.21 (d, J = 8.4Hz), 4.33 (d, J = 5.4 Hz) 1 H], 7.02-7.66 (m, 12H); ^{13}C NMR (CDCl_3): δ = 13.93, 19.15, 36.77, 56.31, 59.32, 72.81, 73.17, 125.77, 126.00, 127.04, 127.47, 127.75, 127.83, 128.07, 128.51, 128.77, 128.90, 129.17, 132.40, 132.56, 133.05, 134.91, 135.49, 136.37, 138.01; IR (NaCl): 3457, 1068, 744, 693 cm^{-1} ; MS (70 eV, EI): Decomposition to 1-(2-naphthyl)-pentanone-2 and diphenyldiselenide.

α -Hydroxy- α -[1-(phenylseleno)benzyl]acetophenone, (**2k**): ^1H NMR (CDCl_3): δ = 3.75 (s, 1H), 4.52 (d, 1H), 5.28 (br. s, 1H), 6.96-7.82 (m, 15H); ^{13}C NMR (CDCl_3): δ = 51.74, 74.97, 127.76, 128.02, 128.20, 128.30, 128.83, 129.09, 129.33, 129.53, 133.88, 133.97, 135.35, 136.34,

198.33; MS (70 eV, EI): Decomposition to 1,3-diphenylpropan-1,2-diona.

2-(*p*-Chlorophenyl)propanal: ^1H NMR (CDCl_3): 1.33 (d, $J=7.1$ Hz, 3H), 3.52 (qd, $J=7.1, 1.3$ Hz, 1H), 7.04 (d, 2H), 7.22 (d, 2H), 9.55 (d, $J=1.3$ Hz, 1 H).

2,2-(Diphenyl)ethanal: ^1H NMR (CDCl_3): 4.77 (d, $J=1.8$ Hz, 1H), 7.22 (m, 10 H), 9.83 (d, $J=1.8$ Hz, 1 H); ^{13}C NMR (CDCl_3): $\delta=64.00, 127.53, 128.20, 128.74, 128.91, 129.08, 129.98, 132.34, 136.26, 198.50$.

2-(*p*-Methoxyphenyl)ethanal: ^1H NMR (CDCl_3): 3.55 (d, $J=2.2$ Hz, 2H), 3.72 (s, 3H), 6.74 (d, 2H), 7.05 (d, 2H), 9.64 (t, $J=2.2$ Hz, 1 H).

4. CONCLUSION

In conclusion, we have developed a convenient protocol for ring opening of epoxides to the corresponding β -hydroxy-selenides with diphenyldiselenide, under very mild conditions. The reaction is rigorously regioselective with incorporation of the selenolate nucleophile at the less hindered carbon for alkyl-substituted epoxides, and at the benzylic carbon atom for aryl derivatives. In most cases, the yields were satisfactory and readily comparable to the yields obtained from the related tris(phenylseleno)-borane and the phenylselenoborane generated from sodium borohydride and diphenyldiselenide in ethanol. In fact, the regioselectivity obtained with the present protocol is superior than that obtained using $(\text{PhSe})_3\text{B}$, which produces mixtures of regioisomers. Furthermore, this procedure demonstrates a new application of indium (I) species as starting material for generating reactive indium(III) compounds capable of promoting organic transformations.

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6. REFERENCES

- [1] Hori, T.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1689.
- [2] Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697.
- [3] Dumont, W.; Bayet, P.; Krief, A. *Angew. Chem. Int. Ed. Eng.* **1974**, *13*, 804.
- [4] Léonard-Coppens, A. M.; Krief, A. *Tetrahedron Lett.* **1976**, *17*, 3227.
- [5] Rémion, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1976**, *17*, 1385.
- [6] Reich, H. J.; Chow, F. *J. Chem. Soc. Chem. Commun.* **1975**, 790.
- [7] Dumont, W.; Krief, A. *Angew. Chem. Int. Ed. Eng.* **1975**, *14*, 350.
- [8] Sevrin, M.; Dumont, W.; Hevesi, L.; Krief, A. *Tetrahedron Lett.* **1976**, *17*, 2647.
- [9] Gruttadauria, M.; Aprile, C.; RIELA, S.; Noto, R. *Tetrahedron Lett.* **2001**, *42*, 2213.
- [10] Gruttadauria, M.; Lo Meo, P.; Noto, R. *Tetrahedron.* **2001**, *57*, 1819.
- [11] Gruttadauria, M.; Lo Meo, P.; Noto, R. *Tetrahedron.* **1999**, *55*, 14097.
- [12] Gruttadauria, M.; Lo Meo, P.; Noto, R. *Tetrahedron.* **1999**, *55*, 4769.
- [13] Gruttadauria, M.; Noto, R. *Tetrahedron Lett.* **1999**, *40*, 8477.
- [14] Cravador, A.; Krief, A. *Tetrahedron Lett.* **1981**, *22*, 2491.
- [15] Engman, L.; Gupta, V. *J. Org. Chem.* **1997**, *62*, 157.
- [16] Sakakibara, M.; Katsumata, K.; Watanabe, Y.; Toru, T.; Ueno, Y. *Synthesis* **1992**, 377.
- [17] Dowslan, J.; McKerlie, F.; Procter, D. J. *Tetrahedron Lett.* **2000**, *41*, 4923.
- [18] Nishiyama, Y.; Ohashi, H.; Itoh, K.; Sonoda, N. *Chem. Lett.* **1998**, *27*, 159.
- [19] Peppe, C.; Tuck, D. G. *Can. J. Chem.* **1984**, *62*, 2798.
- [20] Barros, O. S. D.; Lang, E. S.; de Oliveira, C. A.; Peppe, G.; Zeni, G. *Tetrahedron Lett.* **2002**, *43*, 7921.
- [21] Ranu, B. C.; Jana, U. *J. Org. Chem.* **1998**, *63*, 8212.