Synthesis of the glycidol (1*R*,2*R*)-1-iodo-2-(triphenylsilyloxy)cyclopropane: new rearrangements of 2,3-epoxy-3-(trialkyl/arylsilyl)-propan-1-ols

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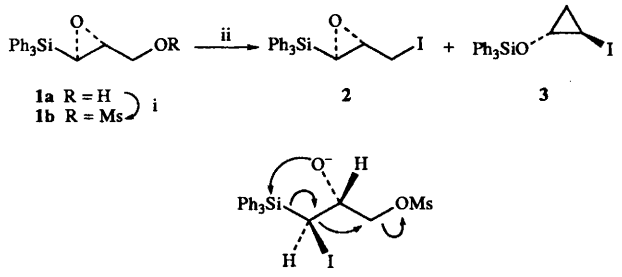
Reaction of the mesylates of selected glycidols **1b**, **5a**, **5b** and **5c** with sodium iodide in acetone has been investigated. The mesylate **1b** afforded the iodide **2** and the cyclopropane derivative **3** in a ratio which depended upon the reaction time. Whilst the mesylate **5a** provided the iodide **6a** as the sole product, the mesylates **5b** and **5c** gave mixtures of the corresponding unrearranged iodoepoxysilanes **6b** and **6c**, and the epoxides **7b** and **7c**.

To prepare the target compound, 2,3-epoxy-1-iodo-3-(triphenylsilyl)propane† **2** (Scheme 1), the mesylate **1b** (obtained in

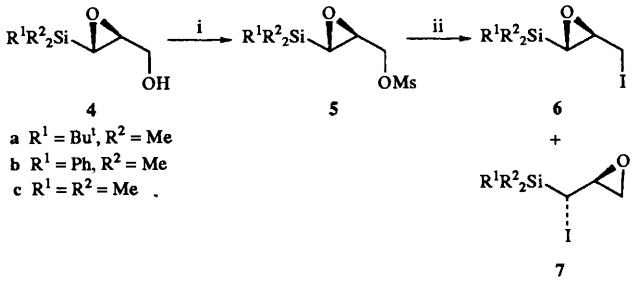


Scheme 1 *Reagents and conditions:* i, MsCl, Et_3N, CH_2Cl_2; ii, NaI, acetone, room temp.

almost quantitative yield from the glycidol **1a**[1,2]) was treated with an excess of sodium iodide in acetone (4 h, room temperature) to give two products separable by chromatography. The major product (46% yield), was the expected iodide **2** whilst the minor constituent (18% yield) was identified as the cyclopropane **3** on the basis of the following spectral evidence. Its ^1H NMR spectrum differed from those of the glycidols, exhibiting signals corresponding to aromatic protons (15 H, δ_H 7.65–7.30) and four eight-line one-proton multiplets centred at δ_H 3.81, 2.44, 1.36 and 0.91. The ^{13}C NMR spectrum indicated the presence of aromatic carbon atoms (δ_C 135–125) and of three carbon atoms with signals at δ_C 56.53, 19.34 and −14.29. The structure **3** was confirmed by decoupling experiments and by elemental analysis. Although compound **3** was optically active it was unstable in the presence of the shift reagent {tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III), [Eu(hfc)$_3$]}, and the enantiomeric excess could not be determined.

When the mesylate **1b** was allowed to react with sodium iodide for longer periods of time there was an increase in the yield of cyclopropane **3**: thus, after 20 h at room temperature, **3** was isolated in 49% yield and iodo epoxide **2** in 13% yield. This result indicates that **2** partly rearranged into **3**, a plausible mechanism for which is outlined in Scheme 1. After addition of an iodide anion at the 3-position of the epoxysilane,[3] [1,3]-migration of the triphenylsilyl group from carbon to oxygen occurs, followed by intramolecular displacement of the mesyloxy group (or the iodide). A concerted process providing *trans*-substituted cyclopropane is proposed. The *J* value of 2.14 Hz for 1-H and 2-H supports the stereochemical assignment. To our knowledge no similar rearrangement has been recorded for glycidol derivatives.[4]

Since the preparation and synthetic application of alkoxycyclopropanes are of interest,[5] we examined whether other silyl substituted glycidols underwent similar rearrangements. To this end, the alcohols **4a**,[2] **4b**[2] and **4c**[6] were converted into the mesylates **5a–5c**, respectively, the latter then being treated with sodium iodide in acetone. The results are shown in Scheme 2.



Scheme 2 *Reagents and conditions:* i, MsCl, Et_3N, CH_2Cl_2; ii, NaI, acetone, room temp.

Reaction of mesylates **5** with NaI in acetone at room temp.

Mesylate	Reaction time (h)	Product(s) (% yield, ratio)
5a	6	**6a** (89) —
5b	6	**6b** **7b** (66, 2.6:1)[a]
5c	6	**6c** **7c** (80, 1.6:1)[a]

[a] The mixture could not be separated by chromatography; the isomer ratio was determined by NMR.

The mesylate **5a** on treatment with sodium iodide in acetone for 6 h gave the iodide **6a** as the sole product (89% yield). A longer reaction time gave a slight decrease in the yield of **6a** but no side products could be detected. The mesylate **5b** afforded two products (isolated in 66% yield) that were inseparable by chromatography. However the ^1H and ^{13}C NMR spectra of this mixture indicated that it consisted of epoxysilanes **6b** and **7b** in a ratio of *ca.* 2.6:1. Similarly, treatment of the mesylate **5c** with sodium iodide in acetone yielded the epoxysilanes **6c** and **7c** (1.6:1). Formation of compounds **7** may be explained in

† Glycidol carbon numbering is retained for the iodo derivatives. The name glycidol is retained for convenience and refers to 2,3-epoxypropan-1-ol.

terms of attack by the iodide anion at the 3-position of the respective epoxysilanes **5** or **6**, followed by epoxide ring closure and loss of the mesyloxy group, or iodide, respectively.

In conclusion, it was shown that the reactivity of the glycidols investigated depends in a remarkable way upon the nature of the silyl substituent.

Experimental

Mps were determined on a Kofler hot-stage microscope and are uncorrected. ^1H and ^{13}C NMR were obtained on either a Bruker AM 500 (500 and 125 MHz) or a Varian GEM 200 (200 and 50 MHz) spectrometer with $SiMe_4$ as an internal standard. *J* values are given in Hz. Column chromatography was performed using silica gel, 60 (Merck), 230–400 mesh. Optical rotations, measured using a 1 cm^3 capacity cell (10 cm path length), are recorded as 10^{-1} deg cm^2 g^{-1}.

Preparation of (2*R*,3*R*)-2,3-epoxy-1-mesyloxy-3-(triphenylsilyl) propane 1b

Mesyl chloride (0.2 cm^3, 2.6 mmol) was added at 0–5 °C to a stirred solution of **1a**[2] (227 mg, 0.68 mmol) and triethylamine (0.4 cm^3) in methylene dichloride (3 cm^3). The mixture was kept at 0–5 °C for 30 min after which it was diluted with ether (35 cm^3), washed with water (3 × 10 cm^3), dried (Na_2SO_4) and evaporated. The residue was dissolved in hexane and the solution filtered through a pad of silica gel to give **1b** (270 mg, 96%), mp 127–128 °C (acetone–hexane); $[\alpha]_D^{21}$ +20.1 (*c* 1.61 in $CHCl_3$); δ_H(200 MHz) 2.92 (1 H, d, *J* 3.3, 3-H), 3.03 (s, 3, $MeSO_3$), 3.11 (1 H, ddd, *J* 3.3, 2-H), 3.17 (1 H, dd , *J* 6.5, and 11.7, 1-H_a), 4.59 (1 H, dd, *J* 2.7 and 11.7, 1-H_b) and 7.3–7.6 (20 H, m, ArH); δ_C(50 MHz) 37.8 ($MeSO_3$), 46.9 (C-3), 53.0 (C-2), 71.2 (C-1), 128.2 (C_m), 130.4 (C_p), 131.3 (C_{ipso}) and 135.9 (C_o) (Found: C, 64.0; H, 5.6. $C_{22}H_{22}O_4SSi$ requires C, 64.36; H, 5.40%).

Preparation of (2*S*,3*S*)-3-(*tert*-butyldimethylsilyl)-2,3-epoxy-1-mesyloxy propane 5a

This compound was obtained by an analogous method to that described above using the alcohol **4a**[2] (310 mg, 1.65 mmol), triethylamine (0.4 cm^3), methylene dichloride (4 cm^3) and mesyl chloride (0.2 cm^3, 2.6 mmol). Product **5a** (439 mg, 100%); $[\alpha]_D^{25}$ −24.5 (*c* 2.18 in $CHCl_3$); δ_H(200 MHz) −0.04 and 0.01 (6 H, s, Me_2Si), 0.95 (9 H, s, Bu^{t}Si), 2.22 (1 H, d, *J* 3.5, 3-H), 3.07 (3 H, s, $MeSO_3$), 3.12 (1 H, ddd, *J* 2.7, 3.5 and 6.8, 2-H), 4.06 (1 H, dd, *J* 6.8 and 11.7, 1-H_a) and 4.53 (1 H, dd, *J* 2.7 and 11.7, 1-H_b); δ_C(50 MHz) −8.5 (Me_2Si), 16.5 (Me_3CSi), 26.4 (Me_3CSi), 37.7 ($MeSO_3$), 47.0 (C-3), 52.2 (C-2) and 72.0 (C-1) (Found: C, 45.0; H, 8.5. $C_{10}H_{22}O_4SSi$ requires C, 45.08; H, 8.32%).

Preparation of (2*S*,3*S*)-3-dimethylphenylsilyl-2,3-epoxy-1-mesyloxypropane 5b

This compound was obtained by an analogous method to that described for **1b** using the alcohol **4b**[2] (204 mg, 0.98 mmol), triethylamine (0.25 cm^3), methylene dichloride (3 cm^3) and mesyl chloride (0.12 cm^3) to give **5b** (280 mg, 100%); $[\alpha]_D^{25}$ −14.15 (*c* 1.62 in $CHCl_3$); δ_H(200 MHz) 0.35 and 0.39 (6 H, s, Me_2Si), 2.36 (1 H, d, *J* 3.5, 3-H), 3.05 (3 H, s, $MeSO_3$), 3.12 (1 H, ddd, *J* 2.7, 3.4 and 6.7, 2-H), 4.06 (1 H, dd, *J* 6.7 and 11.8, 1-H_a) and 4.54 (1 H, dd, *J* 2.6 and 11.8, 1-H_b); δ_C −5.4 and −5.3 (Me_2Si), 37.8 ($MeSO_3$), 48.3 (C-3), 52.8 (C-2), 71.8 (C-1), 128.0 (C_m), 129.8 (C_p), 133.8 (C_o) 134.8 (C_{ipso}) (Found: C, 50.3; H, 6.5. $C_{12}H_{18}O_4SSi$ requires C, 50.32; H, 6.33%).

Preparation of (2*S*,3*S*)-2,3-epoxy-1-mesyloxy-3-(trimethylsilyl)propane 5c

This compound was obtained by an analogous method to that described for **1b** using the alcohol **4c**[6] (248 mg, 1.7 mmol), triethylamine (0.4 cm^3), methylene dichloride (3 cm^3) and mesyl chloride (0.2 cm^3). Product **5c**: (380 mg, 100%); $[\alpha]_D^{25}$ −22.8 (*c* 1.1 in $CHCl_3$); δ_H(200 MHz) 0.9 (9 H, s, Me_3Si), 2.18 (1 H, d, *J* 3.5, 3-H), 3.08 (3 H, s, $MeSO_3$), 3.13 (1 H, ddd, *J* 2.7, 3.4 and 6.7, 2-H), 4.05 (1 H, dd, *J* 6.7 and 11.7, 1-H_a) and 4.56 (1 H, dd, *J* 2.7 and 11.7, 1-H_b); δ_C(50 MHz) −3.8 (Me_3Si), 37.8 ($MeSO_3$), 48.9 (C-3), 52.7 (C-2) and 72.0 (C-1) (Found: C, 37.3; H, 7.2. $C_7H_{16}O_4SSi$ requires C, 37.47; H, 7.19%).

Reaction of the mesylate 1b with NaI

Method A. Dry NaI (570 mg, 3.8 mmol) was added to a solution of **1b** (340 mg, 0.83 mmol) in dry acetone (3 cm^3). The mixture was stirred at room temp. for 4 h, after which it was diluted with hexane (30 cm^3), washed with water (3 × 10 cm^3) and dried (Na_2SO_4). The mixture was evaporated and the residue chromatographed on silica gel (2.5 g, hexane–acetone) to give:

(i) (1*R*,2*R*)-1-iodo-2-(triphenylsilyloxy)cyclopropane **3** (66 mg, 18%); $[\alpha]_D^{20}$ −51.9 (*c* 2.2 in $CHCl_3$); δ_H(500 MHz) 0.908 (1 H, ddd, $J_{3a,1}$ 5.58, $J_{3a,3b}$ 7.55, $J_{3a,2}$ 9.30 3-H_a), 1.356 (1 H, ddd, $J_{3b,2}$ 3.66, $J_{3b,1}$ 7.05, $J_{3b,3a}$ 7.55, 3-H_b), 2.440 (1 H, ddd, $J_{2,1}$ 2.14, $J_{2,3a}$ 3.66, $J_{2,3b}$ 9.30, 1-H), 3.813 (1 H, ddd, $J_{1,2}$ 2.14, $J_{1,3b}$ 5.58, $J_{1,3a}$ 7.05, 2-H) and 7.3–7.6 (15 H, m, ArH); δ_C(125 MHz) −14.29 (C-1), 19.34 (C-3), 56.53 (C-2), 128.01 (C_m), 130.32 (C_p), 133.33 (C_{ipso}) and 135.38 (C_o) (Found: C, 57.1; H, 4.4. $C_{21}H_{19}IOSi$ requires C, 57.02; H, 4.32%).

(ii) (2*R*,3*R*)-2,3-epoxy-1-iodo-3-(triphenylsilyl)propane **2** (170 mg, 46%); $[\alpha]_D^{25}$ +5.0 (*c* 2.01 in benzene); δ_H(200 MHz) 2.87 (1 H, d, *J* 2.9, 3-H), 3.03–3.21 (2 H, m, 2- and 1-H), 3.41 (1 H, dd, *J* 4.6 and 8.8, 1-H) and 7.3–7.6 (20 H, m, ArH); δ_C(50 MHz) 6.7 (C-1), 53.8, 56.4 (C-2 and C-3), 128.1 (C_m), 130.2 (C_p), 131.6 (C_{ipso}) and 135.9 (C_o) [Found: C, 57.00; H, 4.12. $C_{21}H_{19}IOSi$ (442.36) requires C, 57.02; H, 4.32].

Method B. In an analogous experiment where mesylate **1b** (84 mg), NaI (400 mg) and acetone (3 cm^3) were used, the mixture was stirred for 20 h at room temp. to give the iodide **2** (12 mg, 13%) and the cyclopropane **3** (44 mg, 49%).

Reaction of the mesylate 5a with NaI

NaI (400 mg, 2.66 mmol) was added to a solution of **5a** (100 mg, 0.38 mmol) in acetone (3 cm^3). The mixture was stirred at room temp. for 6 h after which it was diluted with hexane (30 cm^3), washed with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (1.5 g, hexane–acetone) to give (2*S*,3*S*)-3-(*tert*-butyldimethylsilyl)-2,3-epoxy-1-iodopropane **6a** (100 mg, 89%); $[\alpha]_D^{25}$ +9.0 (*c* 1.25 in benzene); δ_H(200 MHz) −0.03 and 0.02 (6 H, s, Me_2Si), 0.97 (9 H, s, Me_3CSi), 2.18 (1 H, d, *J* 3.0, 3-H), 3.02–3.13 (2 H, m, 1- and 2-H) and 3.34 (1 H, dd, *J* 8.3 and 12.3, 1-H); δ_C(50 MHz) −8.4 and −8.3 (Me_2Si), 7.6 (C-1), 16.6 (Me_3CSi), 26.5 (Me_3CSi), 54.4 and 55.8 (C-2 and C-3) (Found: C, 36.4; H, 6.4. $C_{19}H_{19}IOSi$ requires C, 36.24; H, 6.42%).

Reaction of the mesylate 5b with NaI

NaI (470 mg, 2.66 mmol) was added to a solution of **5b** (114 mg, 0.4 mmol) in acetone (3 cm^3). The mixture was stirred at room temp. for 6 h after which it was diluted with hexane (30 cm^3), washed with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (1.5 g, hexane–acetone) to give a mixture of (2*S*,3*S*)-3-dimethylphenylsilyl-2,3-epoxy-1-iodopropane **6b** and (1*S*,2*S*)-1-dimethylphenylsilyl-2,3-epoxy-1-iodopropane **7b** (84 mg, 66%, 2.6:1). **6b**: δ_H(200 MHz) 0.35 and 0.38 (6 H, s, Me_2Si), 2.32 (1 H, d, *J* 2.8, 3-H), 3.05–3.17 (2 H, m, 2-H and 1-H_a) and 3.31 (1 H, dd, *J* 8.8 and 12.6, 1-H_b); δ_C(50 MHz) −5.2 (Me_2Si), 7.4 (C-1), 55.6, 56.3 (C-2 and C-3), 128.0 (C_m), 129.7 (C_p), 133.9 (C_o) and 135.2 (C_{ipso}). **7b**: δ_H(200 MHz) 0.55 and 0.57 (6 H, s, Me_2Si), 2.50 (1 H, m, 3-H_a), 2.81 (1 H, m, 3-H_b) and 2.90–3.01 (2 H, m, 1- and 2-H); δ_C(50 MHz) −3.1 and −3.0 (Me_2Si), 17.6 (C-1), 50.2, 53.7 (C-2

and C-3), 127.8 (C_m), 129.8 (C_p), 134.2 (C_o) and 135.2 (C_{ipso}) (Found: C, 41.73; H, 4.97. $C_{11}H_{15}IOSi$ requires C, 41.52; H, 4.75%).

Reaction of the mesylate 5c with NaI

NaI (600 mg, 2.66 mmol) was added to a solution of **5c** (197 mg, 0.88 mmol) in acetone (8 cm^3). The mixture was stirred at 0–5 °C for 6 h after which it was diluted with pentane containing 0.1% of triethylamine (30 cm^3), washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (1.5 g; pentane with 0.1% of triethylamine) to give a mixture of (2*S*,3*S*)-2,3-epoxy-1-iodo-3-(trimethylsilyl)-propane (**6c**) and (1*S*,2*S*)-2,3-epoxy-1-iodo-1-(trimethylsilyl)-propane (**7c**) (160 mg, 80%, 1.6:1). **6c**: δ_H(200 MHz) 0.08 (9 H, s, $SiCH_3$), 2.13 (1 H, d, *J* 3, 3-H), 3.2 (2 H, m, 2-H and 1-H_b) and 3.3 (1 H, m, 1-H_a); δ_C(50 MHz) 3.689 (Me_3Si), 7.796 (C-1), 56.208 and 56.277 (C-2 and C-3). **7c**: δ_H(200 MHz) 0.24 (9 H, s, Me_3Si), 2.50 (1 H, dd, *J* 3.7 and 3.0, 3-H_b), 2.72 (1 H, d, *J* 9.5, 1-H), 2.85 (1 H, dd, *J* 5.0 and 3.7, 3-H) and 3.10 (1 H, m, 2-H); δ_C(50 MHz) 1.833 (SiMe), 18.803 (C-1), 50.339 and 53.823 (C-2 and C-3). Although the sample could be stored for several hours as a solution (pentane) in a refrigerator, it rapidly decomposed on evaporation of the solvent.

References

1 For a review on glycidols, see: R. M. Hanson, *Chem. Rev.*, 1991, **91**, 437.

2 P. Raubo and J. Wicha, *Tetrahedron: Asymmetry*, 1995, **6**, 577.

3 P. F. Hudrlik and A. M. Hudrlik in *Advances in Silicon Chemistry*, ed. G. L. Larson, JAI Press, Greenwich, 1993, vol. 2, p. 1.

4 (*a*) For a review on tandem transformations initiated by the silyl group migration, see: P. Jankowski, P. Raubo and J. Wicha, *Synlett*, 1994, 985. (*b*) For a recent relevant work, see: M.-R. Fischer, A. Kirschning, T. Michel and E. Schaumann, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 217.

5 (*a*) S. Murai, I. Ryu and N. Sonoda, *J. Organomet. Chem.*, 1983, **250**, 121; (*b*) D. H. Gibson and C. H. DePuy, *Chem. Rev.*, 1974, **74**, 605; (*c*) O. G. Kulinkovich, *Russ. Chem. Rev.*, 1993, **62**, 839; (*d*) O. G. Kulinkovich, S. V. Sviridov and D. A. Vasilievski, *Synthesis*, 1991, 234; (*e*) E. J. Corey, S. A. Rao and M. C. Noe, *J. Am. Chem. Soc.*, 1994, **116**, 9345.

6 (*a*) T. Katsuki, *Tetrahedron Lett.*, 1984, **25**, 2821; (*b*) Y. Kobayashi, T. Ito, I. Yamakawa, H. Urabe and F. Sato, *Synlett*, 1991, 811; (*c*) Y. Kitano, T. Matsumoto and F. Sato, *Tetrahedron*, 1988, **44**, 4073; (*d*) P. Raubo and J. Wicha, *Synth. Commun.*, 1993, **23**, 1273.

7 A. G. Brook, *Acc. Chem. Res.*, 1974, **7**, 77.

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