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Synthesis of Optically Active 2-Sila-1,3-propanediols Derivatives by Enzymatic Transesterification.

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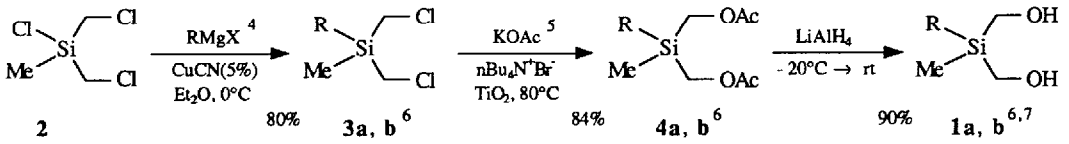
Key Words : Lipases ; Silicon-chiral optically active compounds.

Abstract : *Lipase from Candida cylindracea and lipase from Chromobacterium viscosum allowed the synthesis of silyl-chiral optically active compounds by mono-transesterification of 2-sila-1,3-propanediols.*

For another project, we need silyl-chiral optically active compounds. In this letter is described the preparation of optically active 2-sila-1,3-propanediols monoesters by enzymatic transesterification.

It was shown recently that organosilicon [1] and organotin compounds [2] can be substrates of esterases and lipases. We have focused our work on *meso*-2-sila-1,3-propanediols because many reports were devoted to the preparation of optically active 1,3-propanediols derivatives by enzyme-catalyzed esterification, transesterification or hydrolysis. In order to obviate by-products formation through reaction of H-Si bond, tetrasubstituted siladiols **1** were choosen despite the poor results reported for enzymatic reactions of similar quaternary carbon compounds [3]. The syntheses of 2-methyl-2-phenyl- and 2-methyl-2-octylpropanediol **1a** and **1b** were run from commercially available bis(chloromethyl)chloromethylsilane **2** as reported in scheme I and they were isolated with about 60% overall yields after purification by silica gel column chromatography.

Scheme I



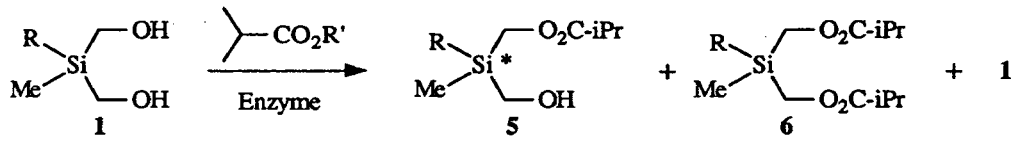
2 — 80% → **3a, b** [6] — 84% → **4a, b** [6] — 90% → **1a, b** [6,7]

a R = Ph ; **b** R = n-Octyl

Enzymatic transesterifications were performed in the usual manner using various lipases [8]. The best results, reported in scheme II, were obtained using lipase from *Candida cylindracea* (LCC) and lipase from *Chromobacterium viscosum* (LCV). When diols **1a** and **1b** [9] were treated at -20°C during respectively 5 and 8 days with LCC, using methyl isobutyrate [10] as solvent and acylating agent, the dextrorotatory monoesters **5a** and **5b** [6,7] were isolated by silica gel column chromatography next to small amounts of diesters and their enantiomeric excesses [11] were respectively 70% and 75%. When the reactions were performed at higher temperatures, the transesterification reaction rates increased as expected, but the enantiomeric excesses decreased : for example reactions of **1b** at -10°, 0 and 20°C gave the monoester **5b** with 67, 56 and 51% enantiomeric excesses respectively for similar conversion ratios (60 - 80%).

With LCV the reaction rates in the presence of methyl isobutyrate were too slow, so acetoxime isobutyrate [12] was used. Using this activated acylating agent the best results were obtained at 40°C for diol **1a** in

Scheme II : Preparation of optically active silicon compounds by enzymatic transesterification



R	R'	Enzyme	Reaction conditions	Products yield (%) 5	6	1	Monoester 5 ee (%)	$[\alpha]_D$[a]
Ph **1a**	Me	LCC	-20°C, 120 h	80	4	10	70	+5
	N=	LCV	40°C, 48 h	50	9	35	70	-5
n-Octyl **1b**	Me	LCC	-20°C, 150 h	63	2	30	75	+1
	N=	LCV	4°C, 150 h	70	25	3	76	-1

[a] in THF (c ≈ 1)

diisopropyl ether as solvent and at 4°C for the diol **1b** in tetrahydrofuran. In both cases, the levorotatory monoesters **5a** and **5b** were mainly obtained with respectively 70 and 76 enantiomeric excess [11].

Further work is currently in progress to determine the absolute configuration of the optically active silicon compounds.

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References and Notes

1. De Jeso, B.; Belair, N.; Deleuze, H.; Rascle, M.C.; Maillard, B. *Tetrahedron Lett.* **1990**, *31*, 653.
2. Therisod, M. *J. Organomet. Chem.* **1989**, *361*, C8 ; Itoh, T.; Ohta, T.; Sano, M. *Tetrahedron Lett.***1990**, *31*, 6387 ; Itoh, T.; Ohta, T. *Chem. Lett.* **1991**, 217.
3. Green, F.R. III ; Olyslager, R.J.E. *Eur. Pat. Appl.* EP 280, 232 (1988) [C.A. **1989**, *110*, 37813h].
4. Lennon, P.J.; Mack, D.P.; Thompson, Q.E. *Organometallics* **1989.**, *8*, 1121.
5. Barry, J.; Bram, G.; Decodts, G.; Loupy, A.; Pigeon, P.; Sansoulet, J. *Tetrahedron* **1983**, *39*, 2673.
6. Spectral data are in agreement with the structure. ^{1}H NMR (250 MHz, $CDCl_3$) δ selected values : **1a** : 7.68 - 7.57 (m, 2H), 7.47 - 7.34 (m, 3H), 3.90 (d, J = 14.0 Hz, 2H), 3.78 (d, J = 14.0 Hz, 2H), 2.5 (m, 2H, OH), 0.43 (s, 3H). **1b** : 3.60 (d, J = 14.0 Hz, 2H), 3.78 (d, J = 14.0 Hz, 2H), 3.53 (d, J = 14.0 Hz, 2H), 2.80 (m, 2H, OH), 1.44 - 1.17 (m, 12H), 0.87 (t, J = 6.5 Hz, 3H) ; 0.69 - 0.57 (m, 2H), 0.08 (s, 3H). **5a** : 7.67 - 7.52 (m, 2H), 7.50 - 7.33 (m, 3H), 4.20 - 4.08 (AB system, J = 14.3 Hz, 2H), 3.73 (d, J = 14.6 Hz, 1H), 3.64 (d, J = 14.6 Hz, 1H), 2.56 (qq, J = 6.9 and 7.1 Hz, 1H) ; 2.03 (m, 1H, OH), 1.14 (d, J = 6.9 Hz, 3H), 1.13 (brd, J = 7.1 Hz, 3H), 0.40 (s, 3H). **5b** : 3.93 (s, 2H), 3.52 - 3.38 (AB system, J = 14.5 Hz, 2H), 2.58 (septuplet, J = 6.9 Hz, 1H) ; 1.41 - 1.21 (m, 12H), 1.17 (d, J = 6.9 Hz, 6H), 0.89 (t, J = 6.6 Hz, 3H), 0.72 - 0.58 (m, 2H), 0.09 (s, 3H).
7. Elemental analyses (C, H) were satisfactory.
8. Apart LCC (Sigma) and LCV (Toyo Jozo Co. Ltd.) (see the text), Pig pancreatic lipase (PPL, Sigma), lipase from *Pseudomonas cepacia* (LP, Amano) and lipase from *Mucor miehie* (Lipozyme, NOVO) were tested. For example with **1a** working at 20°C, PPL gave after 2 weeks a mixture of **1a** (21%), **6a** (23%) and **5a** (57%, ee = 19%), with LP **5a** was isolated with 70% yield and 64% ee (levorotatory isomer) after 2 weeks and with lipozyme the diol was mainly transformed into **6a** after 1 day (**5a** was not detected).
9. The more crowded 1-dimethylphenylsilyl-1-propanol was not substrate of LCC, see Wang, Y.F.; Lalonde, J.J.; Momongan, M.; Bergbreiter, D.E.; Wong, C.H. *J. Am. Chem. Soc.* **1988**, *110*, 7200.
10. Reactions with methyl acetate gave lower enantiomeric excesses.
11. Enantiomeric excesses were measured by ^{1}H NMR spectroscopy using the chiral shift reagent Eu(D-hfc)$_3$, when the high field singlet of the silicon methyl protons was shifted to about 4.5 ppm.
12. Ghogare, A.; Sudesh Kumar, G. *J. Chem. Soc. Chem. Comm.* **1989**, 1533.

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