Regioselective alkylation of phenol with cyclopentanol over montmorillonite K10: An efficient synthesis of 1-(2-cyclopentylphenoxy)-3-[(1,1-dimethylethyl)amino]propan-2-ol {(*S*)-penbutolol}

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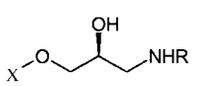
Regioselective alkylation of phenol with cyclopentanol is achieved over Montmorillonite K10 clay, producing 2-cyclopentylphenol, the key intermediate. The synthesis of optically active (*S*)-penbutolol **1**, an important antihypertensive drug, is realized in 5 steps from 2-cyclopentylphenol by employing Sharpless asymmetric dihydroxylation.

β-Adrenergic blocking agents (β-blockers) are important drugs widely used for the treatment of hypertension, *angina pectoris*, glaucoma, anxiety and obesity.[1] The discovery of propranolol, the first successful drug having antianginal and antihypertensive effects, prompted the synthesis of many thousands of compounds containing an aryloxypropanolamine nucleus including *ortho*-substitution in the aromatic ring, for example, (*S*)-penbutolol **1**. Although *S*-isomers are known to be much more effective (50–100-fold) than the *R*-isomers, these antihypertensive drugs are sold as racemic mixtures.[2] To avoid unnecessary stress, or in some cases toxicity to an organism caused by the *R*-isomers, the administration of optically pure *S*-isomers having higher affinity towards β-receptors becomes mandatory. A literature search reveals that while considerable efforts have been made in recent years for the preparation of (*S*)-propranolol,[3–6] scant attention has been paid to the synthesis of (*S*)-penbutolol[7] in enantiomerically pure form. There are three methods known for the synthesis of (*S*)-penbutolol involving resolution of racemates,[7a,b] enzymic hydrolysis of acetates[7c] or epoxidation of allylic alcohols[7d,e] as key steps. All the reported methods for the synthesis of (*S*)-penbutolol suffer from drawbacks such as the use of expensive enzymes and resolving agents, low yields, greater number of steps, low optical purity, *etc.* The major problem associated with the synthesis of penbutolol is the synthesis of the starting material, 2-cyclopentylphenol itself. The general method for the preparation of 2-cyclopentylphenol involves the Lewis acid-catalyzed Friedel–Crafts reaction of phenol with cyclopentanol in the presence of $AlCl_3$, but this method gives 4-cyclopentylphenol as the major product and the yield of the *ortho* product is found to be low. Hence, there is a need to develop a more convenient route for the synthesis of 2-cyclopentylphenol, which in turn can be utilized for the asymmetric synthesis of (*S*)-penbutolol. We report herein the synthesis of (*S*)-(−)-penbutonol starting from phenol. The two notable features of this method are: (a) 2-cyclopentylphenol is prepared in high yield and selectivity; (b) *S*-(−)-penbutolol is synthesized by regioselective opening of chiral cyclic sulfate, **6**, with *tert*-butylamine in the terminal position (Scheme 1).



R = Pr^i, X = 1-Naphthyl, (*S*)-Propranolol

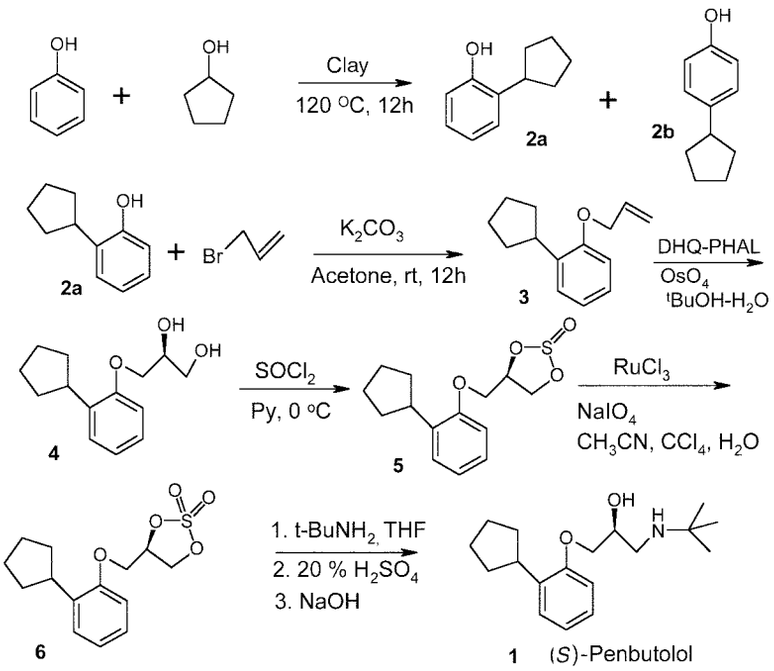
1, R = Bu^t, X = 2-Cyclopentylphenyl, (*S*)-Penbutolol

Results and discussion

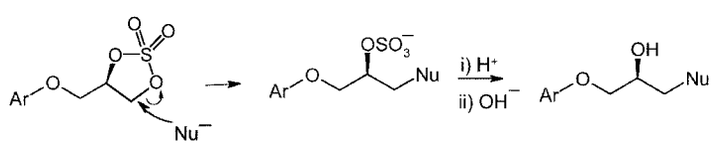
The present synthetic route employed for the synthesis of (*S*)-penbutolol is depicted in Scheme 1. 2-Cyclopentylphenol **2a**, the key starting material, was prepared by alkylation of phenol with cyclopentanol in the presence of montmorillonite K10 clay at 120 °C without any solvent.[8] Interestingly, the reaction proceeded with 62% yield and 68% *ortho*-selectivity (Table 1). This result may be contrasted with the literature method where alkylation of cyclopentanol with phenol using $AlCl_3$ as catalyst generally gives mixtures of products enriched in the *para* isomer. However, when phenol was alkylated with cyclohexanol under similar conditions using montmorillonite K10 clay as catalyst, both *ortho* and *para* isomers were formed in almost equal proportions. Mechanistically, it is possible that cyclopentanol and cyclohexanol react with the Lewis acid sites present on the surface and interlamellar space of the clay to produce their respective carbenium ions which in turn attack phenol at the *ortho* and *para* positions. The cyclopentyl cation can approach the *ortho* position of phenol embedded in the interlamellar space of the clay better conformationally as compared with the conformationally more hindered cyclohexyl cation. The same procedure was successfully applied to alkylate 4-chlorophenol with cyclopentanol to produce 4-chloro-2-cyclopentylphenol (dowicide), a germicide, in 78% yield. O-Alkylation of 2-cyclopentylphenol **2a** with allyl bromide in the presence of K_2CO_3 in acetone gave allyl 2-cyclopentylphenyl ether **3** in 91% yield. Compound **3** was subjected to Sharpless asymmetric dihydroxylation[9] using $(DHQ)_2PHAL$ as chiral ligand in *t*-BuOH–H_2O (1 : 1) as solvent to get the diol **4** in 90% yield {$[a]_D$ −12.3† (*c* 0.8, MeOH)}. The diol **4** was converted to cyclic sulfite **5** using thionyl dichloride in pyridine in 93% yield {$[a]_D$ +12.05 (*c* 0.8, MeOH)}.

The cyclic sulfite **5** on treatment with *tert*-butylamine in DMF at reflux was expected to give the desired compound (*S*)-penbutolol, **1**. In this connection, Lohray and Ahuja have reported the ring opening of cyclic sulfites with LiN_3 in DMF.[10] However, in our case, by following the same procedure, the opening of cyclic sulfite **5** with *tert*-butylamine did not proceed at all. The reaction was further tried in toluene and THF as solvent. Here again, the reaction failed. Hence, the cyclic sulfite **5** was then oxidized to cyclic sulfate **6** using sodium periodate in the presence of a catalytic amount of $RuCl_3$. The cyclic sulfate **6** was subjected to nucleophilic opening with *tert*-butylamine in dry THF. The reaction mixture was first acidified with 20%

† $[a]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}.

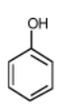
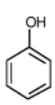
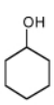
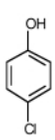


Scheme 1



Scheme 2

Table 1 Montmorillonite K10-catalyzed alkylation of phenols [a]

Entry	Substrate	Alcohol	Yields [b] (%) of the alkylated product	
			ortho	*para*
1			62	28
2			32	40
3			78 [c]	

[a] Reaction conditions: substrate 21 mmol, alcohol 26 mmol, temp. 120 °C. [b] Isolated yield after chromotographic purification. [c] Product has cyclopentyl group *ortho* to the OH group.

sulfuric acid and then basified with 20% aq. NaOH to afford the required compound penbutolol **1** in 72% yield {$[\alpha]_D$ −10.9 (*c* 0.8, MeOH)}. It is possible that the N-nucleophile (*tert*-butylamine) attacks the cyclic sulfate at the less hindered terminal carbon in an S_N2 pathway under neutral conditions without the help of any catalysts to furnish the chiral β-hydroxybutylamine in good yields (Scheme 2).

The optical purity of the final product **1** was determined by comparing the optical rotation with that reported in the literature [4b] and was found to be 95% ee.

Conclusions

2-Cyclopentylphenol was prepared by the clay-catalyzed alkylation of phenol with cyclopentanol under solvent-free conditions. In this case the *ortho*-substituted product predominates whereas in the case of alkylation with cyclohexanol *ortho*:*para* ratios are found to be almost equal. 2-Cyclopentylphenol was further transformed into a very useful β-adrenergic blocker, (*S*)-(−)-penbutolol with 95% optical purity *via* highly efficient Sharpless asymmetric dihydroxylation. This methodology can be further extended to the synthesis of various β-adrenergic blockers with great scope.

Experimental

All solvents were distilled before use. Compounds are purified by flash chromatography over silica gel. IR spectra were recorded on a Perkin-Elmer 137 E spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker 200 (200 MHz) and MSL-300 (300 MHz) instruments using TMS as internal standard. Mass spectra (MS) were recorded on an automated Finnigan MAT 1020C mass spectrometer using an ionization energy of 70 eV. Optical rotations were measured on a JASCO-181 digital polarimeter at 25 °C using sodium D light. Petroleum ether refers to that petroleum fraction with distillation range 60–80 °C. Ether refers to diethyl ether.

Preparation of 2-cyclopentylphenol

Phenol (2 g, 21 mmol), cyclopentanol (2.2 g, 26 mmol) and montmorillonite K10 (Aldrich USA) (200 mg, 10 wt% based on phenol) were placed in a 50 ml round-bottomed flask and heated at 120 °C for 12 h. Dichloromethane was added to the reaction mixture and the catalyst was filtered off. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The crude reaction mixture which contained both 2-cyclo-

pentylphenol and 4-cyclopentylphenol was chromatographed over silica gel (60–120 mesh) using petroleum ether as eluent to give pure 2-cyclopentyl phenol (2.1 g, 62%) as a colorless oil.

2-Cyclopentylphenol 2a. Viscous liquid (yield 62%), IR (neat, cm^{-1}) 3400, 2910, 1600, 1480, 1290; ^1H NMR (200 MHz; $CDCl_3$) δ 1.5–2.0 (m, 6H), 2.0–2.2 (m, 2H), 3.15–3.3 (m, 1H), 4.9 (s, 1H), 6.8 (d, *J* 8.1 Hz, 2H), 6.95 (t, *J* 8.1 Hz, 1H), 7.1 (t, *J* 8.1 Hz, 1H), 7.25 (d, *J* 8.1 Hz, 1H); ^{13}C NMR (50.3 MHz; $CDCl_3$) δ_C 25.5, 33.1, 39.05, 115.5, 121.04, 126.8, 127.8, 132.42, 153.43; MS (*m/z*, % rel. intensity) 162 (M^+, 42), 147 (31), 133 (100), 120 (65), 115 (22), 107 (97), 91 (54), 77 (16).

4-Cyclopentylphenol 2b. Viscous liquid (yield 28%), IR (neat, cm^{-1}) 3400, 2920, 1600, 1480, 1290; ^1H NMR (200 MHz; $CDCl_3$) δ 1.2–1.9 (m, 6H), 1.9–2.2 (m, 2H), 3.15 (m, 1H), 4.8 (s, 1H), 6.95 (m, 2H), 7.05 (m, 2H).

2-Cyclohexylphenol. Viscous liquid (yield 38%), IR (neat, cm^{-1}) 3300, 2910, 1610, 1495, 1270; ^1H NMR (200 MHz; $CDCl_3$) δ 1.1–1.6 (m, 6H), 1.6–2.1 (m, 4H), 2.3 (m, 1H), 4.9 (s, 1H), 6.8 (d, *J* 8.1 Hz, 1H), 6.95 (t, *J* 8.1 Hz, 1H), 7.1 (t, *J* 8.1 Hz, 1H), 7.2 (d, *J* 8.1 Hz, 1H).

4-Cyclohexylphenol. Viscous liquid (yield 41%), IR (neat, cm^{-1}) 3300, 2910, 1610, 1480, 1285; ^1H NMR (200 MHz; $CDCl_3$) δ 1.2–1.55 (m, 6H), 1.55–1.8 (m, 4H), 4.1 (m, 1H), 4.8 (s, 1H), 6.9 (m, 2H), 7.3 (m, 2H).

4-Chloro-2-cyclopentylphenol (dowicide). Viscous liquid (yield 78%), IR (neat, cm^{-1}) 3400, 2940, 2855, 1600, 1480, 1420, 1325, 1255, 1185, 1120; ^1H NMR (200 MHz; $CDCl_3$) δ 1.5–2.0 (m, 6H), 2.0–2.2 (m, 2H), 3.2 (m, 1H), 4.95 (s, 1H), 6.7 (d, *J* 8.1 Hz, 1H), 7.05 (d, *J* 8.1 Hz, 1H), 7.2 (s, 1H); ^{13}C NMR (50.3 MHz; $CDCl_3$) δ_C 25.60, 33.06, 39.33, 116.74, 125.93, 126.67, 127.34, 134.40, 152.28.

Preparation of allyl 2-cyclopentylphenyl ether 3

A mixture of 2-cyclopentylphenol (1.5 g, 9.3 mmol), allyl bromide (2.24 g, 18.5 mmol) and potassium carbonate (3.2 g, 23 mmol) in acetone (50 ml) was stirred at room temperature for 12 h (TLC). The mixture was filtered through a sintered-glass funnel and the filtrate was evaporated to dryness. The residue was purified by flash chromatography using 1% EtOAc in petroleum ether to furnish the title allyl phenyl ether as light yellow liquid (1.7 g, 91%), IR (neat, cm^{-1}) 2920, 1630, 1390, 1225; ^1H NMR (200 MHz; $CDCl_3$) δ 1.4–1.9 (m, 6H), 1.9–2.15 (m, 2H), 3.35 (m, 1H), 4.5 (br d, 2H), 5.15–5.5 (dd, *J* 8.1 Hz each, 2H), 6.1 (m, 1H), 6.7–7.05 (m, 2H), 7.05–7.3 (m, 2H); ^{13}C NMR (50.3 MHz; $CDCl_3$) δ_C 25.76, 33.17, 35.17, 39.59, 69.14, 112.03, 116.89, 120.93, 126.65, 127.0, 134.05, 135.21, 156.73; MS (% rel. intensity) 202 (M^+, 4), 161 (27), 145 (17), 133 (28), 107 (100), 91 (54), 77 (8).

Procedure for asymmetric dihydroxylation of 3 to afford diol 4

A 250 ml round-bottomed flask was charged with $K_3Fe(CN)_6$ (3.4 g, 10 mmol), K_2CO_3 (1.43 g, 10 mmol), $(DHQ)_2PHAL$ (54 mg, 0.07 mmol) and *t*-BuOH–H_2O (1 : 1; 80 ml) and the mixture was stirred for 5 min at room temperature. The flask was cooled to 0 °C and a solution of OsO_4 (0.17 ml of a 0.2 M solution in toluene, 0.03 mmol) was added followed by the allyl 2-cyclopentylphenyl ether **3** (0.7 g, 3.5 mmol). The reaction mixture was stirred for 24 h at room temperature (TLC). Ethyl acetate (20 ml) and sodium metabisulfite (1 g) were added to the mixture, which was stirred for 1 h. Two layers separated out. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic layer was washed with brine, dried over sodium sulfate, and evaporated to dryness. The crude product was purified by flash column chromatography using EtOH–petroleum ether (1 : 1) to yield the diol **4** as a colorless liquid (0.74 g, 90%); $[\alpha]_D$ −12.3 (*c* 0.8, MeOH); IR (neat, cm^{-1}) 3300–3550, 1600, 1492, 1452, 1242, 1112, 1046; ^1H NMR (200 MHz; $CDCl_3$) δ 1.4–1.9 (m, 6H), 1.9–2.15 (m, 2H), 2.3 (br s, 1H), 2.7 (br s, 1H), 3.2–3.35 (m, 1H), 3.7–3.9 (m, 2H, CH_2), 4.05 (d, *J* 5.4 Hz, 2H, OCH_2), 4.1–4.25 (m, 1H, CH), 6.85 (d, *J* 8.1 Hz, 1H), 7.0 (t, *J* 8.2 Hz, 1H), 7.15 (t, *J* 8.1 Hz, 1H), 7.25 (d, *J* 8.1 Hz, 1H); ^{13}C NMR (50.3 MHz; $CDCl_3$) δ_C 25.85, 33.35, 39.35, 64.29, 69.58, 71.18, 112.08, 121.49, 126.96, 127.17, 135.16, 156.58; MS (% rel. intensity) 236 (M^+, 11), 162 (60), 133 (100), 120 (43.1), 107 (47), 91 (21), 77 (4).

Procedure for the preparation of cyclic sulfite 5

The diol **4** (0.5 g, 2.1 mmol) was dissolved in dry pyridine (2 ml) and cooled to 0 °C in an ice-bath under argon atmosphere. Freshly distilled thionyl dichloride (0.46 g, 0.19 ml, 2.2 mmol) was added dropwise and the reaction mixture was stirred for 3 h. Ice-cold water was added to the reaction mixture, which was then extracted with ether. The ethereal layer was washed successively with dil. HCl, saturated aq. sodium bicarbonate and brine. The ether extract was dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was dissolved in 10 ml of dichloromethane and a 2.5 ml aliquot was purified by flash column chromatography using EtOAc–petroleum ether (1 : 9) to furnish a *light yellow oil* (0.138 g, 93%); $[\alpha]_D$ +12.05 (*c* 0.8, MeOH); IR (neat, cm^{-1}) 2930, 1440, 1390, 1235, 1195; ^1H NMR (200 MHz; $CDCl_3$) δ 1.5–1.9 (m, 6H), 1.9–2.1 (m, 2H), 3.3 (m, 1H), 4.1 (m, 1H), 4.4 (m, 2H), 4.7 (d, *J* 6.4 Hz, 1H), 4.9 (m, 1H), 5.35 (m, 1H), 6.85 (d, *J* 8.1 Hz, 1H), 7.0 (d, *J* 8.1 Hz, 1H), 7.2 (t, *J* 8.1 Hz, 1H), 7.3 (d, *J* 8.1 Hz, 1H); ^{13}C NMR (50.3 MHz; $CDCl_3$) δ_C 25.78, 33.13, 33.19, 39.51, 67.09, 69.01, 78.70, 121.95, 127.02, 127.36, 135.12, 156.07; MS (% rel. intensity) 282 (12), 218 (2), 160 (78), 145 (50), 131 (56), 121 (100), 107 (41), 91 (94), 77 (6) (Calc. for $C_{14}H_{18}O_4S$: C, 59.57; H, 6.38; S, 11.35. Found: C, 59.94; H, 6.42; S, 11.31%).

Preparation of cyclic sulfate 6

The crude cyclic sulfite **5** (0.41 g, 1.5 mmol) was dissolved in a mixture of 2 ml of acetonitrile and 2 ml of CCl_4 and the solution was cooled to 0 °C in an ice-bath. Sodium periodate (0.47 g, 2.2 mmol) was added to the cold solution followed by $RuCl_3$ (3 mg, 0.014 mmol) and 3 ml of water. The reaction mixture was filtered through a pad of Celite and evaporated. The residual mixture was extracted with ether, and this extract was dried over anhydrous sodium sulfate and evaporated to dryness. Purification by flash column chromatography of the crude product with EtOAc–petroleum ether (1 : 9) afforded a white solid (0.4 g, 91%), mp 89 °C; $[\alpha]_D$ +5.6 (*c* 1, MeOH); IR (Nujol, cm^{-1}) 2900, 1445, 1370, 1235, 1195; ^1H NMR (200 MHz; $CDCl_3$) δ 1.5–1.95 (m, 6H), 1.95–2.1 (m, 2H), 3.25–3.4 (m, 1H), 4.35 (d, *J* 6.4 Hz, 2H), 5.75–5.95 (m, 2H), 5.3 (m, 1H), 6.75 (d, *J* 8.1 Hz, 2H), 7.0 (t, *J* 8.1 Hz, 1H), 7.15 (t, *J* 8.1 Hz, 1H), 7.25 (d, *J* 8.1 Hz, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) δ_C 25.29, 32.88, 38.73, 65.95, 69.35, 79.00, 111.44, 122.03, 126.53, 127.03, 135.08, 155.14; MS (% rel. intensity) 298 (M^+, 15), 161 (26), 145 (100), 131 (150), 115 (23), 107 (12), 91 (18), 77 (10).

Procedure for the opening of cyclic sulfate 6 to give 1-(2-cyclopentylphenoxy)-3-[(1,1-dimethylethyl)amino]propan-2-ol [(*S*)-penbutolol] 1

A 25 ml round-bottomed flask was charged with cyclic sulfate **6** (200 mg, 0.67 mmol) in dry THF (10 ml) and freshly distilled *t*-butylamine in excess (5 ml) under nitrogen atmosphere. The reaction mixture was refluxed for 8 h. The solvent was evaporated under reduced pressure to give a wine-red, viscous residue. This residue was treated with 5 ml of 20% H_2SO_4 and 10 ml of

ether for 12 h. A white precipitate was formed. The reaction mixture as such was further treated with 20% aq. NaOH until pH 10 and was then stirred for 0.5 h, during which time the white precipitate disappeared. Thereafter, the reaction mixture was extracted with ether (3.20 ml) and then with ethyl acetate. The ether layer was discarded and the ethyl acetate layer was washed with brine and dried over Na_2SO_4. Removal of ethyl acetate gave almost pure product, which was recrystallized from hot heptane to afford 140 mg of (*S*)-penbutolol **1** (72%), mp 66–68 °C [lit.,[4b] 68–72 °C]; IR ($CHCl_3$, cm^{-1}) 3456, 3094, 2980, 2918, 2842, 1600, 1492, 1452, 1380, 1216, 1028, 918; $[\alpha]_D$ −10.9 (*c* 0.8, MeOH) [lit.,[4b] −11.5 (*c* 1, MeOH)]; ^{1}H NMR (300 MHz; $CDCl_3$) δ 1.9 (s, 9H), 1.5–1.9 (m, 6H), 1.9–2.1 (m, 2H), 3.3 (m, 1H), 3.45 (m, 2H), 4.1–4.3 (m, 3H), 5.1 (br s, 1H), 6.75 (d, *J* 8 Hz, 1H), 6.9 (t, 1H), 7.1 (t, *J* 8 Hz, 1H), 7.2 (d, *J* 8 Hz, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) δ_C 25.02, 25.45, 32.69, 38.84, 44.18, 57.62, 72.43, 111.32, 121.24, 126.46, 134.59, 155.21; MS (% rel. intensity) 291 (M^+, 2), 276 (5), 233 (3), 200 (3), 162 (13), 133 (29), 120 (16), 107 (16), 91 (13), 86 (100), 77 (4).

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References

1 (*a*) C. Barrett, *Br. J. Pharmacol.*, 1968, **34**, 43; (*b*) V. Hansteen, *Br. Med. J.*, 1982, **284**, 155; (*c*) J. D. Fitzgerald, in *Pharmacology of Antihypertensive Drugs*, ed. A. Scriabine, Raven Press, New York, 1980, p. 195.
2 (*a*) S. Howe, *Nature* (*London*), 1966, **210**, 1336; (*b*) M. Shiratsuchi, K. Kawamura, T. Akashi, H. Ishihama, M. Nakamura and F. Takenaka, *Chem. Pharm. Bull.*, 1987, **35**, 3691.
3 (*a*) W. L. Nelson, J. E. Wennerstrom and S. R. Sankar, *J. Org. Chem.*, 1977, **42**, 1006; (*b*) D. E. McClure, B. H. Arison and J. J. Baldwin, *J. Am. Chem. Soc.*, 1979, **101**, 3666; (*c*) T. Katsuki, *Tetrahedron Lett.*, 1984, **25**, 2821; (*d*) J. M. Klunder, S. Y. Ko and K. B. Sharpless, *J. Org. Chem.*, 1986, **51**, 3710; (*e*) A. V. R. Rao, M. K. Gurjar and S. V. Joshi, *Tetrahedron: Asymmetry*, 1990, **1**, 697; (*f*) Z.-M. Wang, X.-L. Zhang and K. B. Sharpless, *Tetrahedron Lett.*, 1993, **34**, 2267.
4 (*a*) H. Takahashi, S. Sakuraba, H. Takeda and K. Achiwa, *J. Am. Chem. Soc.*, 1990, **112**, 5876; (*b*) S. Sakuraba, H. Takahashi, H. Takeda and K. Achiwa, *Chem. Pharm. Bull.*, 1995, **43**, 738.
5 (*a*) S. Iriushijima and N. Kojima, *Agric. Biol. Chem.*, 1982, **46**, 1153; (*b*) K. Kan, A. Miyama, S. Hamaguchi, T. Ohashi and K. Watanabe, *Agric. Biol. Chem.*, 1985, **49**, 1669; (*c*) N. Matuso and N. Ohno, *Tetrahedron Lett.*, 1985, **26**, 5533; (*d*) S. Hamaguchi, T. Ohashi and K. Watanabe, *Agric. Biol. Chem.*, 1986, **50**, 375; (*e*) Y. Terao, M. Murata and K. Achiwa, *Tetrahedron Lett.*, 1988, **29**, 5173; (*f*) Y.-F. Wang, S. T. Chen, K. K.-C. Liu and C. H. Wong, *Tetrahedron Lett.*, 1989, **30**, 1917; (*g*) S.-H. Hsu, S.-S. Wu, Y.-F. Wang and C. H. Wong, *Tetrahedron Lett.*, 1990, **31,** 6406; (*h*) A. Kamal and M. V. Rao, *Tetrahedron: Asymmetry*, 1991, **2**, 751; (*i*) H. S. Bevinakatti and A. A. Banerji, *J. Org. Chem.*, 1991, **56**, 5372.
6 (*a*) Y. Tsuda, K. Yoshimoto and T. Nishikawa, *Chem. Pharm. Bull.*, 1981, **29**, 3593; (*b*) H. Sasai, T. Suzuki, N. Itoh and M. Shibasaki, *Appl. Organomet. Chem.*, 1995, **9**, 421; (*c*) C. del Campo, E. F. Llama and J. V. Sinisterra, *Tetrahedron: Asymmetry*, 1996, **7**, 2627.
7 (*a*) H. Ruschig, K. Schmitt, H. Lessenich and G. Haertfelder, *S. Afr. Pat.*, 6, 807, 915, 1969 (*Chem. Abstr.*, 1970, **72**, 90054j); (*b*) G. Haertfelder, H. Lessenich and K. Schmitt, *Arzneim.-Forsch.*, 1972, **22**, 930; (*c*) K. Kan, A. Miyama, S. Hamaguchi, T. Ohashi and K. Watanabe, *Agric. Biol. Chem.*, 1985, **49**, 207; (*d*) J. M. Klunder, T. Onami and K. B. Sharpless, *J. Org. Chem.*, 1989, **54**, 1295; (*e*) U. Ader and P. Schneider, *Tetrahedron: Asymmetry*, 1992, **3**, 521.
8 P. Phukan, S. Dalvoy and A. Sudalai (Indian patent applied for).
9 H. C. Kolb, M. S. van Nieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94** 2483.
10 B. B. Lohray and J. R. Ahuja, *J. Chem. Soc.*, *Chem. Commun.*, 1991, 95.

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