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Stereoselective synthesis of tuberculostatic agent (*S*,*S*)-Ethambutol

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Abstract: A simple and efficient asymmetric synthesis of (*S*,*S*)-Ethambutol has been carried out using a chiral butanediol. The synthesis was completed within six steps with an overall yield 53% and the enantiomeric purity of final product was 98%. All the reactions were very clean and the yields are excellent.

Keywords: Ethambutol; butanediol; protection**;** tuberculosis; oxalylchloride; reduction.

1. Introduction

Tuberculosis (TB) is an infectious disease caused by various strains of bacterium, particularly *Mycobacterium tuberculosis* and *Mycobacterium bovis*. Usually the bacteria spread through air and attack the lungs but can also affect other parts of the body.[1-3] TB is known since ancient times, around 460 BC, Hippocrates identified phthisis and it is the most widespread diseases of the times, which was almost always fatal and infecting millions of people worldwide today. Isoniazid, Pyrazinamide, Rifampicin and Ethambutol are the front-line agents that are recommended by World Health Organization for the treatment of tuberculosis (Figure 1).[4] In 1961 Wilkinson and colleagues was reported,[5-10] (*S*,*S*)-Ethambutol is the most effective agent against almost all the strains of *Mycobacterium sps.* The biological activity of ethambutol has been attributed to its inhibition of mycobacterial arabinosyl transferases involved in bacterial cell wall biosynthesis.[11] The (*S*,*S*)-enantiomer of ethambutol is 200-500 times more potent than the (*R*,*R*)-enantiomer and the *meso*-isomer.[12] Pharmaceutical importance of the Ethambutol, attracted many researchers and it leads to the synthesis of this molecule in different ways, which involve in the resolution of racemic 2-amino-1-butanol,[13] palladium catalyzed regio and stereoselective epoxide opening as the key step,[14] a chiral pool approach by using amino alcohols as the chiral material[15,16] and proline catalysed α-aminooxylation and α-amination.[17]

In continuation of our research program, in design and the synthesis of biologically active compounds,[18-23] herein we report a potentially significant antituberculosis agent, **1** (*S*,*S*)-ethambutol using a chiral diol.

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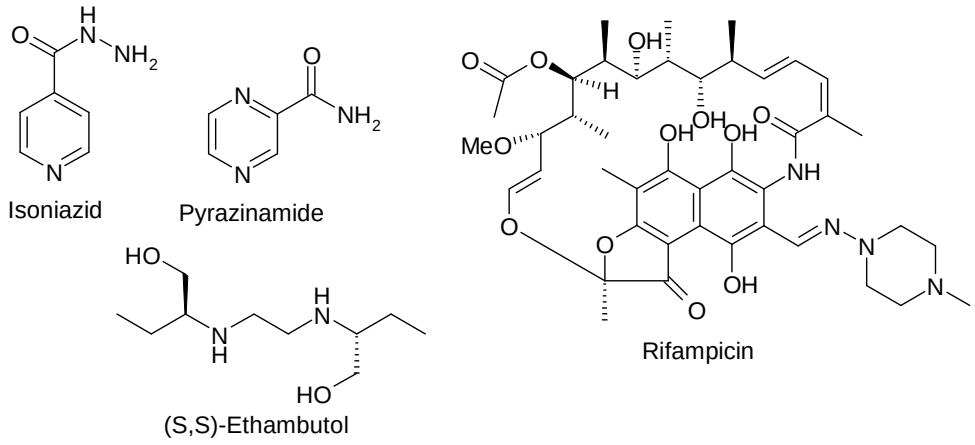

Figure 1. Isoniazid, Pyrazinamide, Rifampicin and Ethambutol are the front-line agents for the treatment of tuberculosis

2. Results and discussion

As shown in the Figure 2, (*R*)-butane-1,2-diol (**2**)[24,25] was treated with tertiarybutyldi methylsilylchloride and imidazole in CH_2Cl_2 to furnish, (*R*)-1-(*tert*-butyldimethyl silyloxy)-butan-2-ol **3**[26] in 91% yield; $[\alpha]^{21}_D$ = -9.3 (*c* 1, $CHCl_3$). Mesylation was carried with methane sulfonyl chloride and triethylamine[27] in CH_2Cl_2 to afford, (*R*)-1-(*tert*-butyldimethylsilyloxy)-butan-2-yl-methanesulfonate **4** in 90% yield; $[\alpha]^{21}_D$ = -6.5 (*c* 1, $CHCl_3$). Compound **4** on reaction with sodium azide in dimethylformamide at 60 ^{0}C to give the corresponding product, (*S*)-(2-azidobutoxy)(*tert*-butyl) dimethylsilane **5** in 83% yield; $[\alpha]^{21}_D$ = 19.3 (*c* 1, $CHCl_3$) with inversion of configuration. The azide compound **5** on hydrogenation[28] over Pd/C (10%) under hydrogen atmosphere furnished, (*R*)-1-(*tert*-butyldimethylsilyloxy) butan-2-amine **6** in 93% yield; $[\alpha]^{21}_D$ = 12.7 (*c* 1, $CHCl_3$).

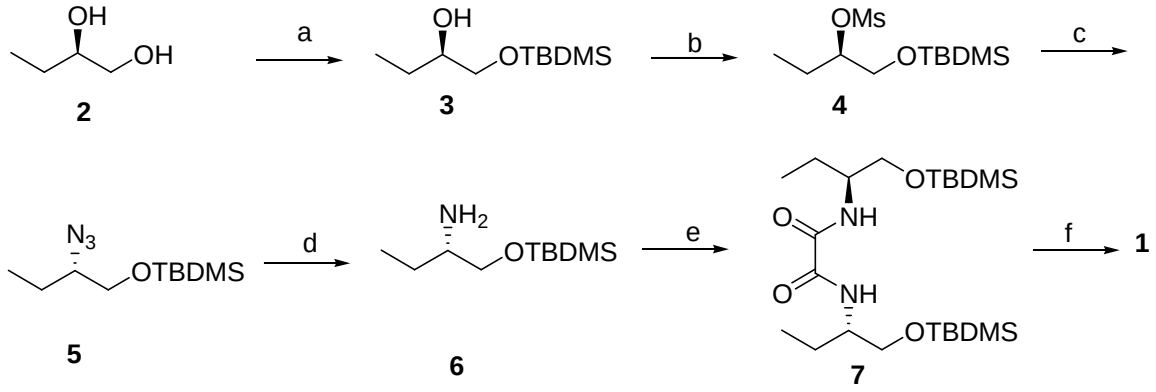

Figure 2. Synthesis of N^1-[(*R*)-1-(*tert*-butyldimethylsilyloxy) butan-2-yl]-N^2-[(*S*)-1-(*tert*-butyldimethylsilyloxy) butan-2-yl] oxalamide 7

Reaction conditions and reagents: (a) TBDMS-Cl, Imidazole, DCM, rt, 3h, 91%. (b) Methane sulfonyl chloride, DCM, TEA, rt, 4h, 90%. (c) NaN_3, DMF, 60 ^{0}C, 24h, 83%. (d) Pd/C, CH_3OH, H_2-atmosphere, 5h, rt, 93%. (e). Oxalyl chloride, pyridine, DCM, rt, 8h, 91%. (f) LAH, THF, reflux, 24h, 92%.

Subsequent treatment of amine compound **6** with oxalylchloride and pyridine in CH_2Cl_2 yielded a dimer product, N^1-[(*R*)-1-(*tert*-butyldimethylsilyloxy) butan-2-yl]-N^2-[(*S*)-1-(*tert*-butyldimethylsilyloxy) butan-2-yl] oxalamide **7** in 91%; $[\alpha]^{21}_D$ = 58.5 (*c* 1, $CHCl_3$). Finally, the protected hydroxyl groups and keto functionalities were treated with four equivalents of lithium aluminum hydride in THF at reflux to afford the target molecule (*S,S*)-Ethambutol (**1**) in very good

yields and the optical rotation of compound observed is $[\alpha]^{21}_{D} = 14.5$ (*c* 1, $CHCl_3$). All the products were confirmed by their ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopy analysis.

3. Conclusion

In summary, we have described a concise asymmetric synthesis of tuberculostatic agent (*S,S*)-ethambutol. The chiral starting material, (*R*)-butane1,2-diol **2** was turned in to (*S,S*)-ethambutol in six steps with an overall yield 53% and the enantiomeric purity of final product was 98%. The synthetic pathway is very simple, easy isolation of products and the yields of products were excellent.

4. Experimental

All the solvents and chemicals or reagents used were purchased from standard commercial suppliers and used as such. NMR spectra (^{1}H and ^{13}C at 300MHz) were recorded on Brucker-300 spectrometer with chemical shifts (δ) reported in ppm relative to tetramethylsilane (TMS) for ^{1}H and $CDCl_3$ for ^{13}C as internal standards. IR spectra were recorded on Perkin-Elmer Fourier transform (FT)-IR 240C spectrophoto meter. Mass spectra were recorded on Finnigan MAT 1020 mass spectro meter operating at 70 eV. Melting points were recorded in a Buchi capillary melting-point (R-535) apparatus. Optical rotations were measured on a Rudolph AUTOPOL IV automatic polarimeter.

General procedure and data of all compounds:

4.1.(R)-1-(Tert-butyldimethylsilyloxy)-Butan-2-ol (3): To a stirred solution of (*R*)-butane-1,2-diol (1 g, 11.1 mmol) in CH_2Cl_2 (30 mL) was added imidazole (1.13 g, 16.6 mmol) at 0 ^{0}C. After stirring for 10 minutes was added TBDMSCl (1.66 g, 11.1 mmol) and continued stirring for 3 hours at room temperature. After completion of reaction as monitored by TLC, the reaction mixture was poured into water and extracted with CH_2Cl_2 (3x30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) by eluting with ethyl acetate-hexane mixture (2:98). Pure product was obtained as colorless liquid; yield: 2.06 g (91%); $[\alpha]^{21}_{D} = -9.3$ (*c* 1, $CHCl_3$). IR (neat): υ 3446, 2956, 2929, 2858, 1637, 1465, 1388, 1254, 1095, 981, 837, 777 cm.$^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01 (s, 6H), 0.08-0.96 (m, 12H), 1.33-1.50 (m, 2H), 2.30 (brs, 1H, OH), 3.38-3.41 (m, 1H), 3.50-3.65 (m, 2H).; ^{l3}C NMR ($CDCl_3$): δ 73.1, 66.8, 25.7, 18.1, 9.8, -3.7, -5.5.; EIMS *m/z* (%): 204 (m^{+1}22), 188 (21), 187 (100), 145 (10), 133 (10), 115 (10), 108 (10), 93 (10), 73 (10).

4.2.(R)-1-(Tert-butyldimethylsilyloxy)butan-2-ylmethanesulfonate (4): To a stirred solution of (*R*)-1-(*tert*-butyldimethylsilyloxy)-butan-2-ol (2,03 g, 10.09 mmol) in dry CH_2Cl_2 (20 mL) was added triethylamine (4.2 mL, 29.85 mmol) at 0 ^{o}C and stirred for half an hour followed by the addition of methanesulfonyl chloride (1.2 mL, 15.14 mmol). The reaction mixture was allowed to stir at room temperature for 4 hours. After completion of the reaction as monitored by TLC, water (20 mL) was added to the reaction mixture and extracted with ethyl acetate (2x20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) by eluting with ethyl acetate-hexane mixture (3:97). Pure product obtained as thick yellow colour syrup; yield: 2.52 g (90%); $[\alpha]^{21}_{D} = -6.5$ (*c* 1, $CHCl_3$). IR (neat): υ 3455, 2933, 2887, 2858, 1631, 1466, 1352, 1255, 1175, 1102, 1044, 1009, 966, 921, 836, 776 cm.$^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.91 (s, 9H), 1.01 (t, 3H, *J* = 7.8 Hz), 1.65-1.79 (m, 2H), 3.01 (s, 3H), 3.69-3.77 (m, 2H), 4.52-4.59 (m, 1H).; ^{l3}C NMR ($CDCl_3$): δ 85.1, 64.2, 38.2, 25.6, 24.2, 18.1, 9.2, -5.7.; EIMS *m/z* (%): 305 (m^{+23}100), 283 (10), 263 (15), 235 (10), 234 (10), 233 (55), 209 (22), 191 (25), 71 (10).

4.3.(S)-(2-Azidobutoxy)(tert-butyl)dimethylsilane (5): To a stirred solution of (*R*)-1-(*tert*-butyl dimethylsilyloxy)butan-2-ylmethanesulfonate (2.52 g, 8.93 mmol) in DMF (10 mL) was added sodium azide (1.74 g, 26.8 mmol) and a catalytic amount of DMAP. The resulting reaction mixture was stirred at 60 ^{o}C for 24 h. After completion of the reaction (monitored by TLC), the reaction mixture

was poured into 20ml water and extracted with diethyl ether (3x20 mL) to obtain the crude product. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) by eluting with only hexane. The pure product was obtained as thick colorless syrup; yield: 1.69 g (83%); $[\alpha]^{21}_D$ = 19.3 (*c* 1, $CHCl_3$). IR (neat): υ 3384, 2966, 2933, 2882, 2098, 1719, 1463, 1342, 1259, 1053, 915, 776 cm.$^{-1;}$ ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.91 (s, 9H), 1.00 (t, 3H, *J* = 7.5 Hz), 1.40-1.60 (m, 2H), 3.18-3.28 (m, 1H), 3.56-3.64 (m, 1H), 3.66-3.74 (m, 1H).; ^{l3}C NMR ($CDCl_3$): δ 66.0, 65.2, 26.0, 23.4, 18.1, 10.5, -5.6.; EIMS *m/z* (%): 247 (m^{+18}50), 241 (18), 239 (20), 229 (10), 225 (100), 205 (18), 204 (60), 187 (40), 163 (18), 149 (10), 71 (10).

4.4.[(S)-2-Aminobutoxy](tert-butly) dimethylsilane (6): To a solution of (*S*)-(2-azido butoxy) (*tert*-butyl) dimethylsilane (1.69 g, 7.3 mmol) in methanol (10 mL) was carefully added Pd/C (10%) and followed by the addition of 5-6 drops of Et_3N. The reaction mixture was then stirred under hydrogen atmosphere (25 psi) for 5 hours. After completion of the reaction (monitored by TLC), the reaction mixture was filtered on celite-bed, the filtrate was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using neutral Al_2O_3 by eluting with ethyl acetate-hexane mixture (3:7). The pure product was obtained as pale yellow syrup; yield: 1.4 g (93%); $[\alpha]^{21}_D$ = 12.7 (*c* 1, $CHCl_3$). IR (neat): υ 3379, 2927, 2861, 1610, 1510, 1453, 1379, 1298, 1245, 1175, 1112, 1042, 1013, 915, 811, 739 cm.$^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.82-0.98 (m, 12H), 1.16-1.48 (m, 2H), 1.73 (brs, 2H, NH), 2.60-2.78 (m, 1H), 3.22-3.27 (m, 1H), 3.45-3.63 (m, 1H).; ^{l3}C NMR ($CDCl_3$): δ 68.0, 54.4, 26.5, 25.8, 18.3, 10.5, -5.4.; EIMS *m/z* (%): 204 (m^{+1}100), 114 (10).

4.5.(S,S)-N^1,N^2-Bis(1-tert-butyldimethylsilyloxybutan-2-yl)-oxamide (7): To a stirred solution of [(*S*)-2-aminobutoxy] (*tert*-butly) dimethyl silane (1.4 g, 6.89 mmol) in dry CH_2Cl_2 (20 mL) was added pyridine (1.8 mL, 34.4 mmol). The reaction mixture was cooled to 0 ^{o}C and added oxalyl chloride (0.3 mL, 3.5 mmol) slowly which was dissolved in CH_2Cl_2 (2 mL) with constant stirring, after 15 minutes, cooling was removed and continued stirring at room temperature for 10 hours. After completion of the reaction (monitored by TLC), the reaction was quenched by adding water (ml) and the reaction was extracted with ethyl acetate (2x20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) while eluting with ethyl acetate- hexane mixture (2:8). Pure product obtained as a white solid; yield: 2.8 g (91%). Mp. 85 ^{o}C; $[\alpha]^{21}_D$ = 58.5 (*c* 1, $CHCl_3$). IR (KBr): υ 3450, 3281, 2956, 2930, 2857, 1653, 1518, 1465, 1385, 1253, 1217, 1110, 1005, 837, 774 cm.$^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.05 (s, 12H), 0.90 (s, 18H), 0.95 (t, 6H, *J* = 7.8 Hz), 1.54-1.72 (m, 4H), 3.59-3.72 (m, 4H), 3.74-3.83 (m, 2H), 7.45-7.50 (d, 2H, *J* = 7.8 Hz).; ^{l3}C NMR ($CDCl_3$): δ 159.4, 64.0, 53.0, 29.6, 25.8, 24.2, 10.5, -5.5.; EIMS *m/z* (%): 483 (m^{+23}100), 461 (75), 416 (10), 353 (10), 329 (18), 228 (30), 227 (95), 202 (28), 201 (60), 179 (37), 137(100), 121 (25), 119(65), 79 (25).

4.6.(S,S)-Ethambutol (1): To a stirred solution of lithium aluminium hydride (1.42 g, 37.5 mmol) in dry THF (10 mL) at 0 ^{o}C was carefully added (*S,S*)-N^1,N^2-bis(1-*tert*-butyl dimethylsilyloxybutan-2-yl) oxamide (2.8 g, 6.26 mmol) which was dissolved in dry THF (20 mL) after 15 minutes stirring, cooling was removed and continued stirring for 24 hours at reflux condition. After completion of the reaction (monitored by TLC), the reaction was quenched by adding 10% NaOH solution (1.4 ml) and water (1.4 mL). The precipitate formed was filtered off and washed with ethyl acetate (2x20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product, which obtained was recrystallized with ethyl acetate to furnish (*S,S*)-Ethambutol as white solid; yield: 1.14 g (92%). Mp. 87-88 ^{o}C (lit. mp 87.5-88.5 ^{o}C); $[\alpha]^{21}_D$ = 14.5 (*c* 1, $CHCl_3$) (98% ee). {lit.$[\alpha]^{21}_D$ = 13.6 (*c* 2, H_2O)}.; IR (KBr): υ 3414, 2928, 1644, 1552, 1463, 1258, 1051, 781 cm.$^{-1}$;^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (t, 6H, *J* = 7.0 Hz), 1.40-1.60 (m, 4H), 2.58-2.68 (m, 2H), 2.70-2.88 (m, 4H), 3.51-3.60 (m, 2H), 3.65-372 (m, 2H).; ^{l3}C NMR ($CDCl_3$): δ 61.3, 57.7, 40.6, 20.3, 8.9.; EIMS *m/z* (%): 205 (m^{+1}65), 116 (100), 90 (10).

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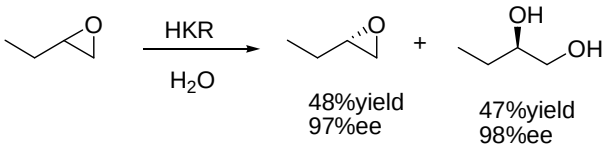
References

[1] De Souza, M. V. N. Promising drugs against tuberculosis, recent pat. Anti-infect. *Drug Discov*. **2006**, *1*, 33-44.
[2] World Health Organization, Report on Global Tuberculosis control. **2003** Geneva & anti-tuberculosis drug resistance in the world: report 3. Document no. (WHO/ HTM/ TB/ 2004. 343). **2004**.
[3] Shah, N. S.; Wright, A.; Bai, G. H.; Barrera, L.; Boulahbal, F.; Martin, C. N.; Drobniewski, F.; Gilpin, C.; Havelkova, M.; Lepe, R.; Lumb, R.; Metchock, B.; Portaels, F.; Rodrigues, M. F.; Rusch, G. S.; Van, D. A.; Vincent, V.; Laserson, K.; Wells, C.; Cegielski, J. P.Worldwide emergence of extensively drug-resistant tuberculosis. *Emerging Infect. Dis*. **2007**, *13*, 380-387.
[4] Mendez, P. A.; Ravigilone, M. C.; Laszlo, A.; Binkin, N.; Reider, H. L.; Bustero, F.; Cohn, D. L.; Weezenbeek, C.S. L.; Kim, S. J.; Chavlet, P.; Nunn, P. Global surveillance for antituberculosis drug resistance 1994-1997. *N. Engl. J. Med.* **1998**, *338*, 1641-1649.
[5] Wilkinson, R.G.; Shepherd, R. G.; Thomas, J. P.; Baughn, C. Stereospecificity in a new type of synthetic antituberculosis agents. *J. Am. Chem. Soc.* **1961**, *83*, 2212-2213.
[6] Shepherd, R. G.; Wilkinson, R. G. Antituberculosis agents.II. *N*,*N*'-diisopropyl ethylene diamine & analogs. *J. Med. Chem*. **1962**, *5*, 823-835.
[7] Wilkinson, R. G.; Cartrall, M.; Shepherd, R. G. Antituberculosis agents. III. (+)-2,2-(ethylenediimino)-di-1-butanol & some analogs. *J. Med. Chem.* **1962**, *5*, 835-845.
[8] Blessington, B. *Chem. Anal*. (New York) **1997**, *142*, 235.
[9] Periasamy, M.; Kumar, S. S.; Reddy, M. New convenient methods of synthesis &resolution of 1,2-amino alcohols. *Synthesis* **2003**, *13*, 1965-1967.
[10] Svedas, V. K.; Guranda, D. T.; Khimiouk, A. I.; Sheldon, R. A.; Van, R. F.; Van, L. Lukas, M. *PTC Int. Appl*. **2002**, WO 2002020821, A2 20020314.
[11] Takayama, K.; Armstrong, E. L.; Kunugi, K. A.; Kilburn, J. O. Inhibition by ethambutol of mycolic acid transfer into the cell wall of mycobacterium smegmatis. *Antimicrob. Agents Chemother*. **1979**, *16*, 240-242.
[12] Hausler, H.; Kawakami, R. P.; Mlaker, E.; Severn, W. B.; Stutz, A. E. Ethambutol analogues as potential antimycobacterial agents. *Bioorg. Med. Chem. Lett*. **2001**, *11*, 1679-1681.
[13] Bevinakatti, H. S.; Newadkar, R. V. Lipase catalyzed kinetic resolution of *N*,*O*-diacetyl-2-amino-1-butanol in diisopropyl ether. *Tetrahedron: Asymm.* **1990**, *1*, 583-586.
[14] Trost, B. M.; Bunt, R. C.; Lemoine, R. C.; Calkins, T. L. Dynamic kinetic asymmetric transformation of diene monoepoxides: a practical synthesis of vinylglycinol, vigabatrin and ethambutol. *J. Am. Chem. Soc*. **2000**, *122*, 5968-5976.
[15] Stauffer, C. S.; Datta, A. Efficient synthesis of (S,S) ethambutol from L-methionine. *Tetrahedron* **2002**, *58*, 9765-9767.
[16] Yendapally, R.; Lee, R. E. Design, synthesis and evaluation of novel ethambutol analogues. *Bioorg. Med. Chem. Lett*. **2008**, *18*, 1607-1611.
[17] Shriram, P. K.; Sudalai, A. Enantioselective synthesis of (S,S)-ethambutol using proline-catalyzed asymmetric α-aminoxylation and α-amination. *Tetrahedron: Asymm.* **2006**, *17*, 1738-1742.
[18] Wadavrao, S. B.; Ghogare, R. S.; Narsaiah, A. V. Stereoselective synthesis of Oxylipin-3: [(6*R*,9*R*,10*R*,7*E*)-6,9,10-trihydroxyoctadec-7-enoic acid]. *Tetrahedron Lett*. **2012**, *53*, 3955-3958.
[19] Narsaiah, A. V.; Narsimha, P. Efficient synthesis of antihistamines Clocinizine and Chlorcyclizine. *Med. Chem. Res.* **2012**, *21*, 538-541.
[20] Narsaiah, A. V.; Nagaiah, B.; Karuna Devi, B. CNS-Agent precursor: a simple and efficient synthesis of an antipsychotic drug Fluanisone. *J. Heterocyclic Chem.* **2012**, *49*, 829-832.
[21] Narsaiah, A. V.; Kumar, J. K. A novel asymmetric synthesis of (*S*)-Esmolol using Hydrolytic Kinetic Resolution. *Synth. Commum.* **2011**, *41*, 1603-1608.
[22] Narsaiah, A. V.; Ghogare, R. S. An expedient stereoselective synthesis of the antifungal agent (6*S*)-6-[(2*R*)-2-hydroxy-6-phenylhexyl]-5,6dihydro-2*H*-pyran-2-one. *Synthesis* **2011**, 3271-3276.
[23] Narsaiah, A. V.; Kumar, J. K. A simple and efficient synthesis of Calcium channel blocker Flunarizine. *Int. J. Ind. Chem.* **2011**, 3, 154-157.
[24] Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. Asymmetric catalysis with water : efficient kinetic resolution of terminal epoxides by means of catalytic hydrolysis. *Science* **1997**, *277*, 936-938.

[25] Kumar, P.; Naidu, V.; Gupta, P. Application of hydrolytic kinetic resolution (HKR) in the synthesis of bioactive compounds. *Tetrahedron* **2007**, *63*, 2745-2894.



[26] Corey, E.; Venkateswarlu, A. Protection of hydroxyl groups as tert-butyldimethyl silyl derivatives. *J. Am. Chem. Soc*. **1972**, *94*, 6190-6191.

[27] Crossland, R. K.; Servis, K. L. Facile synthesis of methanesulfonate esters. *J. Org. Chem*. **1970**, *35*, 3195-3196.

[28] Scriven, E. F. V.; Tumbull, K. Azides: their preparation and synthetic use. *Chem. Rev*. **1988**, *88*, 297-368.