SUPPORTING INFORMATION

Diastereoselective Amidoalkylation of (3*S*, 7*aR*)-6-benzyl-7-hydroxy-3-phenyltetrahydro-5*H*-imidazo [1,5-*c*][1,3]thiazol-5-one: A Short and Highly Efficient Synthesis of (+)-Biotin

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General information:

All solvents were freshly distilled before use and dry solvents were distilled under argon from Na/benzophenone. Melting points are uncorrected. Chemical shifts in ^1H and ^{13}C NMR are reported relative to residual solvents. Abbreviations for ^1H NMR: s = singlet, d = doublet, m = multiplet. Progress of the reactions were monitored by TLC using Merck silica gel 60 F₂₅₄ pre-coated plates and visualized by fluorescence quenching or by charring after treatment with the mixture of p-anisaldehyde-H₂SO₄ in ethanol. The products were purified by column chromatography (SiO₂).

Analytical data of all known compounds were compared with the literature, and new compounds were fully characterized.

General procedure for C-C bond formation (compounds 5a to 5i): To a solution of compound (3*S*, 7*aR*)-6-benzyl-7-hydroxy-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (**4**) (1 mmol) in dichloromethane (10 mL) was added nucleophile (1.2 mmol) and the solution was cooled and stirred at 0 °C. Boron trifluoride etherate (BF₃·OEt₂) (1.1 mmol) was added drop wise. The reaction mixture was stirred at 0 °C for 10 min. and quenched with saturated ammonium chloride (10 mL). The organic layer was separated, dried over anhyd. Na₂SO₄. Concentration under reduced pressure and column purification (SiO₂) with ethyl acetate:pet.ether (15:85) provided 7-substituted imidazothiazolones as viscous liquids in near quantitative yield.

(3*S*,7*S*,7*aR*)-6-Benzyl-7-(2-oxocyclohexyl)-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5a): Highly viscous liquid; Optical Rotation: $[\alpha]_{\text{D}} = -246$ ($c=1.3$; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3143, 3112, 3085, 3062, 2935, 2862, 1715, 1701, 1492, 1439, 1352, 1129, 912. **^1H NMR** (CDCl₃, 200 MHz): 1.65 (m, 2H); 1.9-2.1 (m, 4H); 2.32 (t, $J = 9.3$ Hz, 2H); 2.56 (m, $J = 4.5, 6.7, 11.2$ Hz, 1H); 2.65 (dd, $J = 9, 10$ Hz, 1H); 3.33 (dd, $J = 6, 10$ Hz, 1H); 3.64 (dd, $J = 6.1, 7.6, 9$ Hz, 1H); 3.87 (dd, $J = 2, 4.7, 12.5$ Hz, 1H); 4.12 (d, $J = 15.12$ Hz, 1H); 4.70 (d, $J = 15.12$ Hz, 1H); 6.37 (s, 1H); 7.38 (m, 10H). **^{13}C NMR** (CDCl₃, 75.5 MHz): 24.2(t), 26.5(t), 26.9(t), 38.1(t), 42.0(t), 46.5(t), 50.5(d), 57.4(d), 63.5(d), 66.0(d), 125.3(d), 127.2(d), 127.5(d, 2C), 128.5(d), 128.1(d, 2C), 128.2(d), 128.5(d, 2C), 137.1(s), 146.3(s), 160.2(s, C=O), 208.7(s). **Mass** (m/z): 406(M⁺, 91), 373(92), 360(42), 332(10), 309(10), 281(8), 269(15), 263(32), 241(9), 132(17), 117(8), 106(11), 91(100), 83(11), 77(16), 65(8), 55(7). **Anal. calcd for C₂₄H₂₆N₂O₂S:** C 70.90; H 6.45; N 6.89; S 7.89; Found C 70.71; H 6.25; N 6.78; S 7.78.

(3*S*,7*R*,7*aR*)-6-Benzyl-7-(1-hydroxy-2-oxocyclohexyl)-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5b): Highly viscous liquid; Optical Rotation: $[\alpha]_{\text{D}} = -211$ ($c=1.18$; CHCl₃). **IR**

(CHCl₃, cm⁻¹): 3421, 2939, 2861, 1705, 1415, 1352, 1175, 1115, 1043, 839, 698. **¹H NMR** (CDCl₃, 200 MHz): 1.63 (m, 3H); 1.86 (m, 3H); 2.0-2.45 (m, 3H); 2.73 (m, 1H); 3.05 (m, 1H); 3.80 (m, 3H); 5.05 (dd, *J* = 15.6 Hz, 1H); 6.35 (s, 1/2H); 6.45 (s, 1/2H); 7.32 (m, 10H). **¹³C NMR** (CDCl₃, 75.5MHz): 20.2(t), 26.8(t), 34.8(t), 37.9(t), 38.3(t), 47.0(t), 60.3(d), 61.9(d), 64.9(d), 78.9(s), 125.8(d), 127.3(d), 127.6(d, 2C), 127.9(d, 2C), 128.3(d, 2C), 128.4(d), 128.5(d), 138.4(s), 141.7(s), 161.9(s, C=O), 211.5(s). **Mass** (m/z): 422(M⁺, 1), 405(1), 309(32), 263(23), 142(6), 132(7), 121(6), 91(100), 77(19), 65(5). **Anal. calcd for:** C₂₄H₂₆N₂O₃S: C 68.22, H 6.20, N 6.63, S 7.59 found C 68.05, H 6.40, N 6.42, S 7.69.

(3*S*,7*S*,7*aR*)-6-Benzyl-7-(2-oxo-2-phenylethyl)-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5c): [α]_D = -104.22 (*c* = 0.9; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3060, 3015, 2924, 1705, 1441, 1378, 1348, 1249, 1216, 698. **¹H NMR** (CDCl₃, 200 MHz): 2.66 (t, *J* = 9.3 Hz, 1H); 3.30 (m, 3H); 3.75 (dd, *J* = 5.9, 8.8 Hz 1H); 3.92 (dd, *J* = 3.9, 9.3 Hz, 1H); 4.14 (d, *J* = 15.2 Hz, 1H); 4.85 (d, *J* = 15.1 Hz, 1H); 6.44 (s, 1H); 7.39 (m, 13H); 7.85 (d, *J* = 8.8 Hz, 1H). **¹³C NMR** (CDCl₃, 75.5MHz): 37.2(t), 40.7(t), 45.5(t), 54.1(d), 65.6(d), 66.0(d), 126.3(d, 3C), 127.5(d, 3C), 127.8(d, 3C), 128.3(d, 3C), 128.7(d, 3C), 133.6(s), 136.6(s), 141.7(s), 160.1(s), 197.3(s). **Mass** (m/z) 428(M⁺, 6), 395(23), 382(34), 337(10), 323(10), 291(16), 277(81), 263(10), 214(10), 187(39), 144(39), 132(67), 121(25), 105(100), 91(25), 77(4). **Anal. calcd for:** C₂₆H₂₄N₂O₂S: C 72.84, H 5.64, N 6.54, S 7.48. Found C 72.77, H 5.34, N 6.24, S 7.58.

(3*S*,7*S*,7*aR*)-6-Benzyl-7-[2-(4-chlorophenyl)-2-oxoethyl]-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5d): Highly viscous liquid; [α]_D = -111.36 (*c*=1.2; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3063, 3031, 1699, 1688, 1588, 1447, 1421, 1381, 1220, 1209, 1090, 699. **¹H NMR** (CDCl₃, 200 MHz): 2.68 (dd, *J* = 9.3, 10.3 Hz, 1H); 3.09 (dd, *J* = 9.6, 17.5 Hz, 1H); 3.31 (dd, *J* = 4.6, 10.3 Hz, 1H); 3.43 (dd, *J* = 6.3, 9.1 Hz, 1H); 3.51 (m, 1H); 3.92 (dd, *J* = 3.9, 9.3 Hz, 1H); 4.16 (d, *J* = 15.14 Hz, 1H); 4.81 (d, *J* = 15.14 Hz, 1H); 6.45 (s, 1H); 7.26 (m, 10H); 7.39 (d, *J* = 8.8 Hz, 2H); 7.76 (d, *J* = 8.8 Hz, 2H). **¹³C NMR** (CDCl₃, 75.5MHz): 37.1(t), 40.3(t), 45.2(t), 55.3(d), 66.3(d), 66.8(d), 114.2(d), 126.1(d, 2C), 127.3(d), 127.5(d, 2C), 128.1(d, 2C), 128.5(d, 2C), 128.7(d, 2C), 129.3(s), 130.7(d, 2C), 137.1(s), 139.4(s), 142.4(s), 160.8(s), 196.8(s). **Mass** (m/z): 463(M⁺, 1), 35(5), 309(12), 308(36), 277(7), 187(10), 135(91), 121(15), 104(12), 91(100), 77(41), 65(17). **Anal. Calcd for:** C₂₆H₂₃ClN₂O₂S: C 67.45, H 5.01, N 6.05, S 6.93. found C 67.36, H 5.31, N 6.33, S 6.78

(3*S*,7*S*,7*aR*)-6-Benzyl-7-[2-(4-methoxyphenyl)-2-oxoethyl]-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5e): Highly viscous liquid; [α]_D = -105 (*c*=1; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3098,

3016, 2925, 1711, 1441, 1352, 1309, 1248, 1167. **¹H NMR** (CDCl₃, 200 MHz): 2.67 (dd, *J* = 8.7, 10.8 Hz, 1H); 3.15 (dd, *J* = 9.4, 17.4 Hz, 1H); 3.34 (m, 2H); 3.77 (m, 3H); 3.88 (s, 3H); 4.16 (d, *J* = 15.14 Hz, 1H); 4.86 (d, *J* = 15.14 Hz, 1H); 6.46 (s, 1H); 6.93 (d, *J* = 8.79 Hz, 2H); 7.31 (m, 10H); 7.83 (d, *J* = 8.79 Hz, 2H). **¹³C NMR** (CDCl₃, 75.5 MHz): 37.5(t), 40.7(t), 45.6(t), 54.6(d), 55.4(q), 65.9(d), 66.3(d), 113.9(d), 126.4(d, 2C), 127.6(d), 127.7(d, 2C), 128.1(d, 2C), 128.3(d, 2C), 128.7(d, 2C), 129.5(s), 130.3(d, 2C), 137.0(s), 142.0(s), 160.2(s), 163.9(s), 195.7(s). **Mass** (m/z) 458(M⁺, 1), 457(M⁺-1, 2), 425(6), 412(5), 335(2), 309(8), 308(24), 277(5), 187(8), 135(89), 121(11), 104(12), 91(100), 77(41), 65(17). **Anal. calcd for** C₂₇H₂₆N₂O₃S: C 70.72, H 5.71, N 6.11, S 6.99; Found C 71.52; H 5.62; N 6.33; S 6.70.

(3*S*,7*S*,7*aR*)-6-Benzyl-7-[4-(dimethylamino)phenyl]-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5f): Highly viscous liquid; Optical Rotation: [α]_D = -123.75 (*c* = 0.5 ; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3020, 2924, 2855, 1708, 1596, 1495, 1440, 1349, 698. **¹H NMR** (CDCl₃, 200 MHz): 2.61 (dd, *J* = 10.2 Hz, 1H); 2.85 (s, 6H); 3.16 (dd, *J* = 6, 10.2 Hz, 1H); 3.87 (d, *J* = 15.12 Hz, 1H); 3.92 (dd, *J* = 6, 9.3 Hz, 1H); 4.94 (d, *J* = 15.12 Hz, 1H); 5.03 (s, 1H); 6.47 (s, 1H); 6.73 (d, *J* = 8.9 Hz, 2H); 7.08 (m, 2H); 7.29 (m, 10H). **¹³C NMR** (CDCl₃, 75.5 MHz): 37.3(t), 45.2(t), 51.2(q), 51.5(q), 54.3(d), 66.1(d), 66.5(d), 113.3(d), 126.7(d, 2C), 127.6(d), 127.9(d, 2C), 128.5(d, 2C), 128.7(d, 2C), 128.9(d, 2C), 129.5(s), 130.3(d, 2C), 137.5(s), 138.3(s), 142.6(s), 160.5(s). **Mass** (m/z): 429(M⁺, 1), 414(1), 383(1), 354(2), 338(1), 309(1), 308(2), 254(2), 187(2), 106(100), 91(22), 77(35), 65(13). **Anal. calcd for**: C₂₆H₂₇N₃OS: C 72.69; H 6.34; N 9.78; S 7.46; Found C 72.50; H 6.53; N 10.12; S 7.38.

(3*S*,7*S*,7*aR*)-7-Allyl-6-benzyl-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one(5g): Highly viscous liquid; Optical Rotation: [α]_D = - 233.98 (*c* = 1.02 ; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3062, 3026, 2922, 1709, 1620, 1494, 1424, 1356, 1224, 1094, 1029. **¹H NMR** (CDCl₃, 200MHz): 2.44 (m, 2H); 2.55 (dd, *J* = 9, 10 Hz, 1H); 3.07 (dd, *J* = 6, 10 Hz, 1H); 3.35 (m, 1H); 3.8 (m, 1H); 4.08 (d, *J* = 15.14 Hz, 1H); 4.96 (d, *J* = 15.14 Hz, 1H); 5.18 (m, 2H); 5.76 (m, 1H); 6.46 (s, 1H); 7.32 (m, 10H). **¹³C NMR** (CDCl₃, 75.5 MHz): 35.9(t), 36.9(t), 44.7(t), 56.1(d), 63.9(d), 65.0(d), 118.8(t), 125.5(d), 127.1(d, 2C), 127.3(d, 2C), 127.6(d, 2C), 128.0(d, 2C), 128.4(d), 131.9(d), 136.2(s), 141.8(s), 159.7(s, C=O). **Mass** (m/z): 350(M⁺, 67), 309(77), 303(75), 277(13), 263(60), 213(9), 187(4), 170(4), 132(23), 117(9), 104(8), 91(100), 77(7), 65(6). **Anal. Calcd for**: C₂₁H₂₂N₂OS: C 71.97; H 6.33; N 7.97; S 9.15; Found C 72.21; H 6.62; N 7.72; S 8.84.

(3*S*,7*S*,7*aR*)-6-Benzyl-7-hex-1-yn-1-yl-3-phenyltetrahydro-5*H*-imidazo[1,5-*c*][1,3]thiazol-5-one (5h):M.P.: 54 °C; Optical Rotation: [α]_D = - 169.08 (*c* = 1 ; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3011, 2956,

2929, 2865, 2210, 2117, 1710, 1439, 1359, 1218. **¹H NMR** (CDCl₃, 200 MHz): 0.98 (t, *J* = 7.32 Hz, 3H); 1.50 (m, 4H); 2.27 (dt, *J* = 1.95, 6.8 Hz, 2H); 2.62 (dd, *J* = 10.3 Hz, 1H); 3.12 (dd, *J* = 6.3, 10.4 Hz, 1H); 3.96 (d, *J* = 1.5 Hz, 1H); 4.06 (dd, *J* = 6.3, 9.0 Hz, 1H); 4.10 (d, *J* = 14.7 Hz, 1H); 5.0 (d, *J* = 14.7 Hz, 1H); 6.46 (s, 1H); 7.32 (m, 10H). **¹³C NMR** (CDCl₃, 50 MHz): 14.0(q), 18.7(t), 22.3(t), 30.9(t), 37.0(t), 45.9(t), 49.3(d), 65.8(d), 66.6(d), 76.0(s), 87.5(s), 125.8(d), 126.5(d), 127.4(d), 127.8(d), 128.0(d), 128.2(d), 128.5(d), 128.7(d), 128.8(d), 129.1(d), 136.6(s), 142.1(s), 160.1(s, C=O). **Mass** (m/z): 390(M⁺, 14), 348(22), 269(13), 258(22), 211(15), 177(9), 166(9), 155(15), 132(41), 117(15), 105(54), 91(100), 77(28), 65(6). **Anal. calcd for** C₂₄H₂₆N₂OS: C 73.81; H 6.71; N 7.17; S 8.21; Found C 73.56; H 6.97; N 7.34; S 7.98.

Methyl 2-[(3*S*,7*S*,7*aR*)-6-benzyl-5-oxo-3-phenyltetrahydro-1*H*-imidazo[1,5-*c*][1,3]thiazol-7-yl]-2-methylpropanoate (5i). Highly viscous liquid; Optical Rotation: [α]_D = - 216.86 (*c* = 1.1; CHCl₃). **IR** (CHCl₃, cm⁻¹): 3022, 2982, 2946, 1711, 1439, 1417, 1359, 1138, 704. **¹H NMR** (CDCl₃, 200 MHz): 1.22 (s, 3H); 1.27 (s, 3H); 2.20 (dd, *J* = 9.52, 10.3 Hz, 1H); 2.91 (dd, *J* = 5.86, 10.3 Hz, 1H); 3.58 (s, 3H); 3.6 (m, 2H); 3.82 (d, *J* = 14.66 Hz, 1H); 5.07 (d, *J* = 14.66 Hz, 1H); 6.43 (s, 1H); 7.31 (m, 10H). **¹³C NMR** (CDCl₃, 75.5 MHz): 20.7(q), 21.3(q), 37.5(t), 46.1(s), 47.1(t), 51.8(d), 62.6(q), 62.6(d), 65.1(d), 125.5(d, 2C), 127.2(d, 2C), 127.5(d, 2C), 127.7(d), 128.0(d, 2C), 128.3(d), 136.1(s), 141.5(s), 161.5(s, C=O), 175.8(s, C=O). **Mass** (m/z): 410(M⁺, 7), 379(1), 364(3), 319(1), 309(19), 263(23), 187(4), 132(8), 117(14), 91(100), 65(6), 55(2). **Anal. calcd for:** C₂₃H₂₆N₂O₃S: C 67.29; H 6.38; N 6.82; S 7.81; Found C 67.13; H 6.68; N 7.13; S 7.54.

Methyl 6-[(3*S*,7*R*,7*aR*)-6-benzyl-5-oxo-3-phenyltetrahydro-1*H*-imidazo[1,5-*c*][1,3]thiazol-7-yl]-6-oxohexanoate (7): To an alkaline solution of methanol (0.336g, 6 mmol of KOH was dissolved in 10 mL of methanol) was added compound **5b** (0.844g, 2 mmol). The solution was cooled to 0 °C and then 70% t-butyl hydrogenperoxide (0.216g, 2.4 mmol) was added drop wise. The reaction mixture was stirred for an additional 30 min. After stirring for 30 min, the methanol was removed and the aqueous layer was extracted with ethyl acetate. The aqueous layer was acidified to pH 3 and extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with saturated sodium chloride solution (1 x 20 mL), dried with anhydrous sodium sulphate, filtered and the solvent was removed under reduced pressure. The residue thus obtained was taken in anhydrous ether (20 mL), and ethereal diazomethane was added drop wise until the yellow color persisted. Removal of the solvent on rotary evaporator furnished a residue, which upon purification by column chromatography on silica gel gave the compound **7** (0.630g, 75% yield.) Viscous liquid; Optical Rotation: [α]_D = - 162.5° (*c* = 1, CHCl₃); **IR** (CHCl₃, cm⁻¹): 3030, 2949, 1731, 1728, 1716, 1444, 1415, 1359, 1222, 1157, 914, 732. **¹H NMR** (CDCl₃, 200MHz): 1.55 (m, 4H); 2.27 (m, 2H); 2.44 (m, 2H); 2.58 (dd, *J* = 9.3, 10.3 Hz, 1H); 3.17

(dd, $J = 7.82, 11.2$ Hz, 1H); 3.66 (s, 3H); 3.75 (s, 1H); 3.80 (dd, $J = 6.3, 9.0$ Hz, 1H); 4.06 (d, $J = 14.65$ Hz, 1H); 4.98 (d, $J = 14.65$ Hz, 1H); 6.45 (s, 1H); 7.38 (m, 10H). ^{13}C NMR (CDCl_3 , 125 MHz): 22.4(t), 24.0(t), 33.4(t), 37.3 (t), 37.8(t), 46.7(t), 59.9(q), 61.8(d), 64.9(d), 65.2(d), 125.9(d), 127.6(d), 127.7(d), 127.9(d), 128.3(d, 2C), 128.5(d, 2C), 128.8(d, 2C), 135.5(s), 141.1(s), 160.0(s, C=O), 173.3s, C=O), 206.3(s, C=O). **Mass** (m/z): 452 (M+1); 421(3), 309(14), 263(7), 233(6), 187(5), 132(6), 121(5), 91(100), 77(10), 65(6), 55(5). **Anal. calcd for:** $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_4\text{S}$: C 66.34; H 6.23; N 6.19; S 7.08; Found C 66.01; H 6.43; N 6.21; S 7.36.

Methyl(5Z)-5-[(3aS,6aR)-1,3-dibenzyl-2-oxohexahydro-4H-thieno[3,4-d]imidazol-4-ylidene]pentanoate (8): The keto ester **7** (0.452g, 1 mmol) was dissolved in glacial acetic acid (10 mL), and zinc dust (0.975g, 15 mmol) was added in portions at room temperature under nitrogen atmosphere. After addition was complete, the reaction mixture was heated to 80°C for 5h. After completion of the reaction (monitored by TLC) the reaction mixture was filtered through celite and the filtrate was concentrated to 2 mL. To this solution, piperidine (0.176g, 1.5 mmol) was added and the reaction mixture was heated to 100°C for 90 min. After completion of reaction, the reaction mixture was quenched with dil. HCl (10 mL) and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhyd. Na_2SO_4 , filtered and concentrated under reduced pressure. Column chromatography of the residue over silica gel using ethyl acetate:pet.ether (35:65) mixture as eluent furnished the olefin **8** as pale yellow viscous liquid. Yield: (0.310 g, 70%); viscous liquid.; Optical Rotation: $[\alpha]_{\text{D}} = +194^\circ$ ($c=1$, CHCl_3) **IR** (cm^{-1} , in CHCl_3): 3032, 2928, 1743, 1701, 1634, 1440, 1415, 1342, 1219, 1143, 1079, 789. ^1H NMR (CDCl_3 , 200MHz): 1.72 (m, 2H); 2.12 (m, 2H); 2.31 (t, $J = 7.3$ Hz, 2H); 3.05 (dd, $J = 9.2, 10.2$ Hz, 1H); 3.12 (dd, $J = 4.4, 10.2$ Hz, 1H); 3.70 (s, 3H); 4.05 (d, $J = 15.4$ Hz, 1H); 4.10 (ddd, $J = 4.4, 7.3, 9.5$ Hz, 1H); 4.25 (d, $J = 15.1$ Hz, 1H); 4.30 (d, $J = 7.32$ Hz, 1H); 4.85 (d, $J = 15.4$ Hz, 1H); 5.01(d, $J = 16.0$ Hz, 1H); 5.54 (t, $J = 7.3$ Hz, 1H); 7.35 (m, 10H). **Mass** (m/z): 436(M+1, 1), 422(1), 405(1), 345(1), 309(45), 263(37), 187(6), 173(4), 158(4), 143(5), 132(17), 117(8), 105(25), 91(100), 77(10), 65(6).

Dibenzylbiotin methyl ester: A mixture of olefin **8** (0.220g, 0.50mmol) and 10% palladium on charcoal (36mg) in methanol (50mL) was hydrogenated (200psi) at 65°C for 8h. After cooling to room temperature, the catalyst was removed by filtration and the filtrate evaporated under reduced pressure to give the crude N,N'-dibenzyl biotin methyl ester (0.220g) which was subjected to debenzylation without further purification. M.p 78 °C; Optical Rotation $[\alpha]_{\text{D}} = -42.13^\circ$ ($c=1.05$, CHCl_3); **IR** (cm^{-1} , in CHCl_3): 3028, 2932, 2840, 1741, 1698, 1448, 1440, 1425, 1347, 1198, 1134, 1081, 792. ^1H NMR(CDCl_3 , 200MHz): 1.67 (m, 6H); 2.33 (t, 2H); 3.10 (m, 1H); 3.69 (s, 3H); 3.90 (m, 3H); 4.15 (d, $J = 15.4$ Hz, 1H); 4.75 (d, $J = 15.6$ Hz, 1H); 5.10 (d, $J = 15.4$ Hz, 1H); 7.32 (m, 10H); ^{13}C NMR (CDCl_3 , 125 MHz):

24.42(t), 28.14(t), 28.29(t), 33.65(t), 34.53(t),, 46.40(t), 47.76(t), 51.25(d), 54.05(d), 60.99(d), 62.46(q), 127.42(d, 2C), 128.04(d, 4C), 128.45(d, 4C), 136.79(s, 2C); 160.83(s, C=O), 173.66(s, C=O);

Mass (m/z): 438(M⁺, 8), 347(13), 277(31), 265(13), 240(9), 187(18), 149(4), 91(100), 77(3), 65(9).

d(+)-Biotin:

N, N'-Dibenzyl biotin methyl ester (0.2g, 0.456mmol) was added to a solution of 47% hydrobromic acid (10 mL). The reaction mixture was stirred under reflux for 5h. After cooling to room temperature, the reaction mixture was extracted with toluene (2x10 mL). The aqueous phase was concentrated under reduced pressure to dryness. The residue was dissolved in anhydrous methanol (5 mL) and refluxed for 2h in the presence of conc. H₂SO₄ (1drop). The reaction mixture was neutralized with solid NaHCO₃, filtered and concentrated under reduced pressure. Crude solid thus obtained was dissolved in methanol (10 mL) and charcoal was added to it and heated and filtered. The filtrate was concentrated under reduced pressure to furnish a residue which was chromatographed to furnish a white solid. The solid was heated on a water bath with 1N HCl (10 mL) and the progress of the reaction monitored by TLC. The solvent was reduced to 5 mL and neutralized with con HCl to pH 2. The white solid thus obtained was filtered and dried at 80 °C under vacuum to give pure **1** (0.087g, 78%). Mp. 230-231°C; [α]_D= +89.7 (c=1.01, 0.1 N NaOH) **IR** (KBr, cm⁻¹): 3308, 2929, 1701, 1672; **¹H NMR** (CDCl₃): δ 1.30–1.67 (m, 6H, 3×CH₂), 2.14 (t, 2H, J=7.3 Hz), 2.62 (dd, 1H, J=1.7, 12.5 Hz), 2.78 (dd, 1H, J=4.7, 12.5 Hz), 3.16 (m, 1H), 4.19 (m, 1H), 4.28 (m, 1H), 6.41 (s, 1H, NH), 6.52 (s, 1H).