Synthetic Studies on (+)-Biotin, Part 15[1]: A Chiral Squaramide-Mediated Enantioselective Alcoholysis Approach toward the Total Synthesis of (+)-Biotin

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An efficient stereocontrolled total synthesis of (+)-biotin (1) has been achieved *via* the intermediacy of Roche's lactone 5 starting from *cis*-1,3-dibenzyl-2-imidazole-4,5-dicarboxylic acid (2). The bifunctional cinchona alkaloid-derived squaramide-promoted enantioselective alcoholysis was utilizing as a tool for the construction of two contiguous stereocenters of C-3a and C-6a in biotin molecular with excellent enantioselectivity. In addition, the 4-carboxybutyl side chain was assembled by first using C4+C1 approach *via* a novel tricyclic thiophanium salt intermediate.

Key words (+)-biotin; cinchona alkaloid-derived squaramide; enantioselective alcoholysis; tricyclic thiophanium salt

Over the past two decades, significant progress in organocatalysis has been achieved by mark advances in the enantioselective desymmetrization of *meso* and other prochiral compounds. Well known in the respect is the catalytic asymmetric desymmetrization of *meso*-cyclic anhydride *via* the addition of an alcohol nuclophile, which represents a simple and elegant method for the preparation of synthetically pliable hemiester with the generation of either single or multiple stereocenters with high levels of enantiocontrol in one symmetry-breaking operation.[2—13] While naturally-occurring cinchona alkaloids such as quinine, quinidine and their variants have been demonstrated to serve as practical organocatalysts for the enantioselective alcoholysis of five- and six-membered *meso*-cyclic anhydrides since the pioneering works by Oda and colleagues[14,15] in the late 1980s.

In recent years, our group has made many significant efforts to explore the utility of various chiral amine (**I**—**III**, Fig. 1)-mediated enantioselective methanolysis[8,16,17] as a more effective strategy for the preparation of (3a*S*,6a*R*)-lactone (Roche's lactone, **5**) from the *meso*-cyclic anhydride **3** along Hoffmann Roche lactone-thiolactone route developed by Goldberg and Sternbach in 1949 to complete the stereocontrolled total synthesis of (+)-biotin **1**.[18,19] However, despite the indisputable advances that have been made, these methods for the enantioselective desymmetrization of **3** appling methanol as nuclophiles frequently suffer from one or more of the following problems: extended reaction times at reduced temperature, lower enantioselectivity and difficulties with organocatalyst preparation *etc.* The finding of novel catalysts and new protocols for the enantioselective methanolysis of **3** into the key intermediate (3a*S*,6a*R*)-lactone **5** to complete the commercial asymmetric total synthesis of **1** still remains challenge. Our continued interest in the development of practical asymmetric total synthesis of **1** based upon the chiral Lewis acid-catalyzed enantioselective anhydride desymmetrization has prompted us to investigate an facile organocatalytic enantioselective methanolysis approach toward **1** starting from *cis*-1,3-dibenzyl-2-imidazole-4,5-dicarboxylic acid (**2**) by utilizing our newly developed bifunctional cinchona alkaloid-derived squaramide **IV**[20]-promoted enantioselective methanolysis of **3** for the construction of **5** and a novel C4+C1 strategy for the introduction of the 4-carboxybutyl side chain at C-4 position of (3a*S*,6a*R*)-thiolactone **6**. Herein, we reported the details of our investigations on this subject.

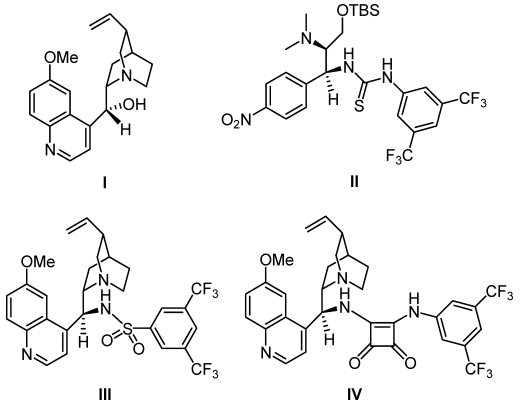

Fig. 1. Structure of Chiral Amine Organocatalysts

Results and Discussion

Our stereocontrolled total synthesis of (+)-biotin (**1**) was undertaken starting from *cis*-1,3-dibenzyl-2-imidazoledone-4,5-dicarboxylic acid (**2**) as outlined in Chart 1. Treatment of **2** in boiling toluene in the presence of a catalytic amount of $MeSO_3H$ with azeotropic removal of water for 4 h led to the desired *meso*-cyclic anhydride **3** in almost quantitatively yield.

We next set out to prepare the key chiral intermediate (4*S*,5*R*)-hemiester **4** from *meso*-cyclic anhydride **3** by a catalytic enantioselective methanolysis strategy using a bifunctional cinchona alkaloid-based squaramide **IV**. In our initial studies, the asymmetric desymmetrization of **3** upon treatment with 3 eq of methanol in the presence of 5 mol% catalyst **IV** in methyl *tert*-butyl ether (MTBE) at room temperature resulted in (4*S*,5*R*)-hemiester **4** in excellent yield with very low enantioselectivity (only 50% ee, Table 1, entry 1). It has been reported that the stoichiometric amount of organo-

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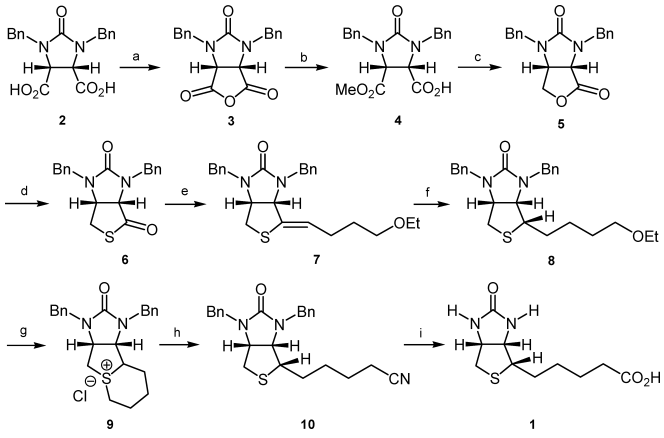
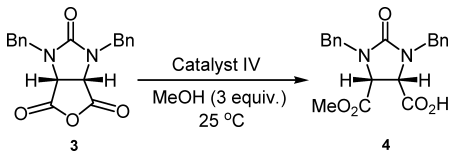


Reagents and conditions: a) $MeSO_3H$, toluene, reflux, 4 h, 98%; b) MeOH, catalyst **VI** (110 mol%), r.t., 24 h, 96%, 99% ee; c) BER, $CaCl_2$, EtOH, r.t., 24 h; then 5% HCl, 55 °C, 0.5 h, 95% (over two steps); d) PhCOSK, DMF, 150 °C, 2 h, 85%; e) $BrMg(CH_2)_4OEt$, THF, reflux, 2 h; then 30% H_2SO_4, reflux, 3 h, 95%; f) H_2, 10% Pd/C, iso-PrOH, 110 °C, 60 atm, 12 h, 98%; g) conc. HCl, 88% HCO_2H, reflux, 5 h, 90%; h) NaCN, DMSO, 90 °C, 3 h, 95%; i) 48% HBr, reflux, 10 h, 80%.

Chart 1. The Synthetic Route to (+)-Biotin **1**

Table 1. Optimization of Reaction Conditions in the Asymmetric Methanolysis of **3** Catalyzed by Chiral Squaramide **IV**[a)]



Entry	Catalyst loading (%)	Solvent	Yield[b)] (%)	ee[c)] (%)
1	5	MTBE	95	50
2	30	MTBE	96	60
3	50	MTBE	97	70
4	80	MTBE	96	74
5	110	MTBE	98	96
6	110	Et_2O	97	80
7	110	THF	96	85
8	110	Toluene	96	63
9	110	CH_2Cl_2	97	65

a) Unless otherwise noted, all reactions were performed with 5 mmol of **3** and 15 mmol of methanol in 1.65 l solvents. *b*) Yield of isolated product **4**. *c*) Determined by chiral HPLC analysis using chiralcel OJ-H column (hexane/IPA/TFA = 92/8/0.2, λ = 220 nm, 0.5 ml/min)

catalyst has found to constitute the key features for a highly efficient methanolytic desymmetrization of *meso*-cyclic anhydride in complex total synthesis due to the bulky size and the presence of multiple polar and basic functionalities of anhydrides.[8,10)] We also observed that anhydride **3** reacted very well leading to the corresponding product **4** in 98% yield with 96% ee when the catalyst loading increased from 5 to 110 mol% (Table 1, entries 1 and 5). The stereochemistry of **4** was confirmed by comparision with the specific optical rotation value reported in our laboratory.[21)] It is noteworthy that the stereochemical outcome of the methanolysis is strongly affected by the solvent used in the anhydride desymmetrization. A low enantioselectivity was obtained in the anhydride desymmetrization when other solvents including Et_2O, tetrahydrofuran (THF), toluene and CH_2Cl_2 was used instead of methyl *tert*-butyl ether (MTBE) (Table 1, entries 6—9). In addition, the catalyst **IV** was easily recovered quantitatively and no significant loss in the catalysis activity and enantioselectivity was observed when it was reused up to ten times.

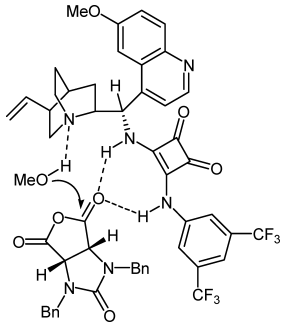


Fig. 2. The Proposed Transition-State Model for the Squaramide Mediated Enantioselective Methanolysis Reaction

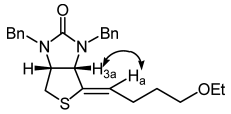


Fig. 3. The NOE Observed for **7** in the NOESY Spectrum

To account for the observed stereochemical outcome of this reaction, a transition state model was proposed and is depicted in Fig. 2. The NH group of the squaramide **IV** moiety are expected to form hydrogen-bonding interaction with the carbonyl group to active the electrophile (anhydride **3**) and the quinuclidine group is believed to simultaneously act as a general base to active the nucleophile (methanol).

The resulting chiral hemiester **4** was subjected to regioselective reduction with Borohydride anion exchange resin (BER, 3.3 mmol $BH4^-$/g) in the presence of anhydrous $CaCl_2$ in EtOH for 18 h, subsequent acid-catalyzed lactonization with 5% HCl for 30 min at 55 °C to furnish the desired (4*S*,5*R*)-lactone **5** in 95% overall yield with 98.5% enantiomeric excess. The resin could be recovered from reaction mixture by simple filtration followed by washing with 5% aq. NaOH and H_2O after the reduction went to completion. It is well documented that the recovered resin in this reaction could be regenerated to the original BER (3.3 mmol $BH4^-$/g) without much loss of activity upon treatment of KBH_4 in H_2O according to the BER preparation procedure.[22)] The conversion of **5** into the desired (3a*S*,6a*R*)-thiolactone **6** was achieved in 85% yield *via* a thiolactonization by heating of potassium benzothioate (PhCOSK) in anhydrous dimethylformamide (DMF) at 150 °C for 2 h.

With the (3a*S*,6a*R*)-thiolactone **6** in hand, installation of C4 side chain at C-4 position of **6** was efficiently carried out by the reaction of **6** with Grignard reagent derived from 1-bromo-4-ethoxybutane in anhydrous tetrahydrofuran (THF) and subsequent dehydration with 30% H_2SO_4 at refulxing temperature for 3 h, affording (*Z*)-alkene ether **7** in an overall yield of 95%. The (*Z*)-configuration of **7** was unequivocally characterized by nuclear Overhauser effect spectroscopy (NOESY) experiment, which showed the NOE correlation between H_{3a} and H_a, as depicted in Fig. 3.

The resulting unsaturated ether **7** further on high pressure hydrogenation (60 atm) at 110 °C for 12 h by the use of a catalytic amount of 10% Pd/C in iso-PrOH provided (3a*S*,4*S*,6a*R*)-saturated ether **8** in almost quantitative yield. Tricyclic thiophanium salt **9** was formed in 90% isolated yield *via* the

cleavage/chlorination/cyclization/salt fromation in a one-pot procedure upon treatment of **8** with concentrated HCl in formic acid at reflux for 5 h. Treatment of **9** with sodium cyanide in dimethyl sulfoxide (DMSO) at 90 °C for 3 h allowed the direct conversion into the desired (3a*S*,4*S*,6a*R*)-nitrile **10** in 95% yield. The absolute configuration of **10** was validated by comparison with the reported values of the specific rotation.[23] Final one-pot hydrolysis and debenzylation of **10** was effected in 48% HBr for 10 h to provide (+)-biotin (**1**) in 80% yield, which is identical in all respects with our previous reported values.[24]

In conclusion, we have developed a novel highly enantioselective organocatalytic approach to the total synthesis of (+)-biotin (**1**) in an overall yield of 48% starting from the known *cis*-1,3-dibenzyl-2-imidazoledone-4,5-dicarboxylic acid (**2**), which exhibit advantages over the existing synthetic routes to **1** in terms of the high enantioselectivity, overall yield and the practicality on large-scale production.

Experimental

General Procedures ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 400 spectrometer (400, 100 MHz, respectively) in $CDCl_3$ or DMSO-d_6 using tetramethylsilane (TMS) or DMSO (^{1}H δ 2.49) and $CDCl_3$ (^{13}C δ 77.0) or DMSO-d_6 (^{13}C δ 39.5) as internal standards. IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. Mass spectra were recorded on a Waters Quattro Micromass instrument using electrospray ionization (ESI) techniques. Optical rotations were obtained on a JASCO P1020 digital polarimeter. Melting points were measured with a WRS-1B digital melting point apparatus and are uncorrected. Unless otherwise notes all reactions were conducted in oven dried glassware under inert atmosphere of dried Ar or N_2. THF was distilled from sodium/benzophenone, toluene, CH_2Cl_2 from calcium hydride and DMF from calcium hydride under reduced pressure. The alcohols used were purified accorded to standard methods,[25] other reagents were obtained from commercial sources and used as received.

Procedure for the Synthesis of 3 A mixture of **2** (10 g, 28 mmol), CH_3SO_3H (0.04 g, 0.42 mmol), toluene (200 ml) was stirred under reflux with azeotropic removal of water for 4 h. After cooled to room temperature, the precipitated colorless crystals was filtered and dried at 70 °C *in vacuo* for 4 h to give the pure product **3** as a white powder (9.22 g, 98% yield). mp 237.1—237.6 °C [lit.[1] mp 237.1—237.8 °C]. IR (KBr) ν: 1805, 1740, 1687, 1227 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.15 (s, 2H), 4.18 (s, 2H), 4.22 (d, 1H, J=14.8 Hz), 5.15 (d, 1H, J=14.8 Hz), 7.15—7.35 (m, 10H). MS (ESI) m/z: 337.4 $(M+1)^+$.

Procedure for the Synthesis of 4 Methanol (0.5 g, 15 mmol) was added dropwise into a suspension of **3** (1.68 g, 5 mmol) and catalyst **VI** (3.5 g, 5.5 mmol) in MTBE (1.65 l) at 25 °C under argon atmosphere. Upon completion of the addition the reaction mixture was stirred for 24 h at room temperature and then evaporated *in vacuo*. The residue was washed with 10% aq. Na_2CO_3 (3×10 ml) and the organic phase was dried over Na_2SO_4 and concentrated to recover the catalyst **VI**. The combined aqueous phases was adjusted to pH 5 use 2 M HCl, then extracted with AcOEt (3×10 ml). The combined organic phases was dried over Na_2SO_4, filtred and concentrated *in vacuo* to yield the crude product, which was then purified by recrystallization from AcOEt to give the methyl monoester **4** as a white solid (1.77 g, 96% yield); ee=99%. mp 149.7—150.4 °C; $[\alpha]_D^{25.2}$ +7.22 (c=1.0, DMF) [lit.[21] mp 150—151 °C; $[\alpha]_D^{25}$ +7.31 (c=1.0, DMF)]. IR (KBr) ν: 3258, 2943, 1756, 1713, 1449, 1411, 1252, 968, 799, 598, 458 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.63 (s, 3H), 4.13—4.04 (m, 4H), 4.98 (d, 1H, J=14.8 Hz), 5.09 (d, 1H, J=14.8 Hz), 6.85 (br s, 1H), 7.36—7.19 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 46.80, 46.89, 52.6, 56.7, 57.3, 127.93, 127.98, 128.56, 128.64, 128.79, 128.85, 135.52, 135.57, 159.5, 168.5, 171.7. MS (ESI) m/z: 391.1 $(M+Na)^+$.

Procedure for the Synthesis of 5 To a stirred solution of **4** (3.68 g, 10 mmol) and anhydrous $CaCl_2$ (1.11 g, 10 mmol) in anhydrous ethanol (52 ml) was added BER (6.7 g, 20 mmol) at 0 °C. Stirring was continued at the same temperature for 1 h, the reaction mixture was allowed to warm up to room temperature and stirred for another 18 h at 25 °C. The resulting mixture was filtred and the filtrate was concentrated. The residue was treated with 5% aq. HCl (37 ml) at 55 °C. After 30 min at this temperatue, the solution was extracted with CH_2Cl_2 (3×30 ml). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* to afford **5** as a white solid (3.06 g, 95% yield). mp 119.4—120.1 °C; $[\alpha]_D^{25.3}$ +61.2 (c=2.0, $CHCl_3$) [lit.[26] mp 120—121 °C; $[\alpha]_D^{25}$ +61.5 (c=2.0, $CHCl_3$)]. IR (KBr) ν: 3031, 2919, 1775, 1706, 1415, 1365, 1237, 1209, 1146, 970, 754, 700, 639, 527 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.92 (d, 1H, J=8.0 Hz), 4.09—4.16 (m, 3H), 4.37 (dd, 2H, J=10.4, 15.2 Hz), 4.63 (d, 1H, J=15.2 Hz), 5.05 (d, 1H, J=15.2 Hz), 7.24—7.36 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 45.2, 46.9, 52.4, 54.3, 70.1, 127.8, 128.0, 128.2, 128.7, 128.8, 129.0, 135.9, 136.0, 158.1, 172.7. MS (ESI) m/z: 345.2 $(M+Na)^+$.

Procedure for the Synthesis of 6 A mixture of **5** (3.22 g, 10 mmol), potassium benzothioate (1.92 g, 12 mmol) and anhydrous DMF (30 ml) was stirred at 150 °C under argon atmosphere for 2 h. After cooling to room temperature, the resulting mixture was poured into H_2O (30 ml) and extracted three times with CH_2Cl_2 (3Å×30 ml). The combined organic phases were washed successively with brine (30 ml) and H_2O (30 ml), dried over Na_2SO_4, and evaporated the solvent to give the crude product which was then purified by recrystallization from iso-propanol to afford the pure **6** as a white solid (2.87 g, 85% yield). mp 125.5—126.2 °C; $[\alpha]_D^{25.3}$ +90.1 (c=1.0, $CHCl_3$) [lit.[23] mp 125—126 °C; $[\alpha]_D^{25}$ +90.2 (c=1.0, $CHCl_3$)]. IR (KBr) ν: 3030, 2934, 2889, 1703, 1697, 1453, 1412, 1361, 1218, 1148, 1051, 997, 903, 808, 698, 647, 581, 485 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.28 (dd, 1H, J =12.4, 2.0 Hz), 3.37 (dd, 1H, J=12.4, 5.6 Hz), 3.81 (d, 1H, J=8.0 Hz), 4.15—4.11 (m, 1H), 4.36 (d, 1H, J=14.8 Hz), 4.37 (d, 1H, J=15.6 Hz), 4.68 (d, 1H, J=15.6 Hz), 5.03 (d, 1H, J=14.8 Hz), 7.37—7.26 (m, 10H). ^{13}C-NMR ($CDCl_3$) δ: 33.0, 45.2, 46.5, 55.8, 62.1, 127.73, 127.91, 128.0, 128.66, 128.78, 128.87, 136.2, 136.4, 158.2, 203.4. MS (ESI) m/z: 361.1 $(M+Na)^+$.

Procedure for the Synthesis of 7 To a suspension of Magnesium powder (2.9 g, 120 mol) in anhydrous THF (20 ml) was added a catalytic amount of iodine under nirogen atmosphere and the mixture was heated to reflux. The soloution of 1-bromo-4-ethoxybutane (21.4 g, 120 mmol) in anhydrous THF (20 ml) was added dropwise and the resulting mixture was kept stirring at reflux for 1 h. The solution of compound **6** (20 g, 59 mmol) in anhydrous THF (200 ml) was added into the reaction mixture at 25 °C. After stirring for 2 h at reflux, the mixture was cooled to 0 °C before 30% H_2SO_4 (100 ml) was added. After further stirring at reflux for 3 h, the mixture was extracted with CH_2Cl_2 (3×60 ml). The combined organic phases were washed successively with brine (30 ml), sat. aq $NaHCO_3$ (30 ml) and H_2O (30 ml), dried over Na_2SO_4, and evaporated the solvent to give the crude product which was then purified by chromatography on a silica gel column (AcOEt/petroleum ether (PE)=1/1) to give **7** as a yellow oil (23.7 g, 95% yield). IR (KBr) ν: 3062, 3028, 2929, 1700, 1604, 1448, 1357, 1114, 1076, 750, 701 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (t, 3H, J=7.0 Hz), 1.64 (m, 2H, J=6.99 Hz), 2.13 (m, 2H), 2.95 (m, 2H), 3.37 (t, 2H, J=6.49 Hz), 3.43 (q, 2H, J=7 Hz), 4.02 (m, 1H), 4.02, 4.22, 4.80, 4.96 (dddd, 4H, J=15.71, 15.29 Hz), 4.27 (d, 1H, J=7.70 Hz), 5.48 (t, 1H, J=7.19 Hz), 7.21—7.36 (m, 10H). MS (ESI) m/z: 422.1 $(M+1)^+$.

Procedure for the Synthesis of 8 A suspension of compound **7** (29.5 g, 70 mmol), 10% Pd/C (7 g) in iso-propanol (160 ml) was stirred at 110 °C under hydrogen pressure of 60 atm for 12 h, and then filtred through Celite. The filtrate was evaporated under reduced pressure to give the crude product, which was purified by recrystallization from CCl_4/cyclohexane to afford pure **8** (29.1 g, 98% yield). mp 62—63 °C; $[\alpha]_D^{25}$ −27.6 (c=1.0, EtOH). IR (KBr) ν: 1679, 1462, 1452, 1425, 1236, 1105, 700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.21 (t, 3H, J=7.04 Hz), 1.54 (m, 6H), 2.65 (dddd, 1H, J=3.16, 5.84 Hz), 3.05 (m, 1H), 3.38 (m, 2H), 3.45 (q, 2H, J=7.05 Hz), 3.80 (dd, 1H, J=5.40 Hz), 3.93 (m, 1H), 3.93, 4.10, 4.70, 5.10 (dddd, 4H, J=15.21, 15.17 Hz), 7.14—7.32 (m, 10H). MS (ESI) m/z: 424 $(M+1)^+$.

Procedure for the Synthesis of 9 A mixture of compound **8** (12.7 g, 30 mmol), conc. HCl (18 g) and 88% aq. HCO_2H (40 ml) was heated to reflux for 5 h and then evaporated under reduced pressure. The residue was purified by recrystallization from acetone to get **9** as a white solid (11.2 g, 90% yield). IR (KBr) ν: 3447, 2931, 1683, 1608, 1443, 1067 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.6—2.2 (m, 6H), 4.0—4.1 (m, 2H), 3.45—3.6 (m, 1H), 4.3—4.35 (m, 1H), 4.48 (dd, 1H, J=5.97 Hz), 4.44 (dd, 1H, J=6.99 Hz), 4.95 (dd, 1H, J=6.02 Hz), 3.95, 4.15, 4.92, 5.2 (dddd, 4H, J=15.21, 15.17 Hz), 7.1—7.32 (m, 10H). MS (ESI) m/z: 414 $(M+1)^+$.

Procedure for the Synthesis of 10 A mixture of compound **9** (8.29 g, 20 mmol), NaCN (2.45 g, 50 mmol) and DMSO (100 ml) was stirred at 90 °C for 3 h. After cooling to room temperature, the reaction mixture was extracted with Toluene (3×30 ml). The combined organic phases was washed successively with brine and H_2O and dried over Na_2SO_4. Evaporation of the solvent gave the crude product, which was purified by recrystallization from iso-PrOH to obtain pure **10** as a white solid (7.70 g, 95% yield). mp 93—94 °C; $[\alpha]_D^{25}$ −67.1 (c=1.0, DMSO) [lit.[23] mp 93—94 °C;

$[\alpha]_D^{25}$ −67.3 (c=1.0, DMSO)]. IR (KBr) ν: 1679, 2270, 1451, 1237, 701 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.58—1.75 (m, 6H), 2.34 (t, 2H), 2.71 (dddd, 2H, J=2.34, 4.39 Hz), 3.06 (m, 1H), 3.89 (dd, 1H, J=5.56 Hz), 3.96 (m, 1H), 4.03, 4.15, 4.75, 5.00 (dddd, 4H, J=15.07, 15.08 Hz), 7.22—7.38 (m, 10H). MS (ESI) m/z: 405 $(M+1)^+$.

Procedure for the Synthesis of 1 A mixture of compound **8** (12 g, 30 mmol) and 47% aq HBr (300 ml) was heated to reflux with vigorous stirring. After 10 h the reaction mixture was extracted with toluene (3×30 ml), the aqueous phase was separated and concentrated *in vacuo* to get the crude product. The residue was purified by recrystallization from H_2O to give pure **1** as a white crystalline powder (5.8 g, 80% yield). mp 231.1—232.0 °C; $[\alpha]_D^{25}$ +91.3 (c=1.0, 0.1 N NaOH) [lit.[27] mp 232—233 °C; $[\alpha]_D^{21.9}$ +91.2 (c=1.0, 0.1 N NaOH)]. IR (KBr) ν: 3359, 3308, 2961, 2469, 1941, 1707, 1480, 1318, 1270, 1154, 1015, 842, 753, 651 cm^{-1}. ^{1}H-NMR (DMSO) δ: 1.37—1.30 (m, 2H), 1.62—1.41 (m, 4H), 2.20 (t, 2H, J=7.6 Hz), 2.57 (d, 1H, J =12.4 Hz), 2.82 (dd, 1H, J =12.4, 5.2 Hz), 3.12—3.07 (m, 1H), 4.15—4.11 (m, 1H), 4.30 (dd, 1H, J =7.6, 5.2 Hz), 6.33 (s, 1H), 6.40 (s, 1H), 11.9 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 25.0, 28.52, 28.57, 33.9, 40.0, 55.8, 59.6, 61.5, 163.1, 174.8. MS (ESI) m/z: 267 $(M+Na)^+$.

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