Tetrahedron: *Asymmetry* 19 (2008) 2616–2619

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Facile enantiospecific synthesis of (−)-muricatacin

Kavirayani R. Prasad *, Vasudevarao Gandi

Department of Organic Chemistry, Indian Institute of Science, Bangalore, Karnataka 560 012, India

ARTICLE INFO

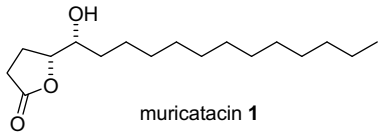
Article history:
Received 24 October 2008
Accepted 7 November 2008

ABSTRACT

A facile approach for the enantiospecific synthesis of the bioactive butanolide (−)-muricatacin from L-(+)-tartaric acid is presented. Pivotal reaction sequence includes the elaboration of γ-hydroxy amide derived from tartaric acid and ring-closing metathesis.

1. Introduction

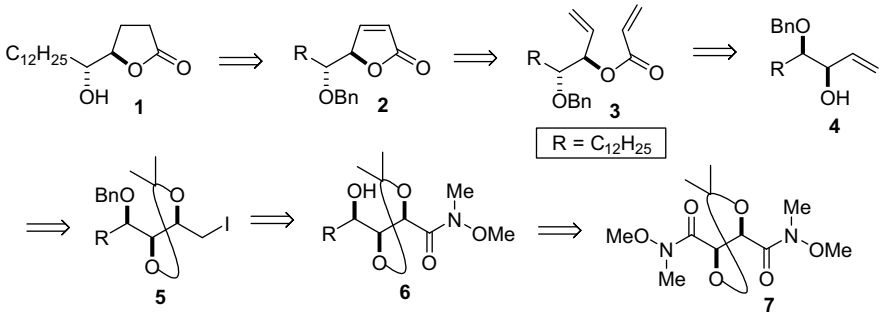
Annonaceae acetogenins from the *Annonaeceae* plants are shown to possess diverse biological profile including cytotoxic activity.[1] Muricatacin **1**, isolated as a mixture of enantiomers from the seeds of *Anona muricata* L.,[2] is a simple butanolide possessing potent cytotoxicity toward several human tumor cell lines. While the diastereomers of muricatacin had no significant effect on bioactivity, it was shown that altering the alkyl side chain influenced the activity.[3] Several syntheses of muricatacin and its congeners were developed in recent years.[4]



muricatacin **1**

2. Results and discussion

We have recently demonstrated the use of novel building block γ-hydroxy butyramides derived from tartaric acid in the total synthesis of natural products.[5] Herein, we report the facile synthesis of (−)-muricatacin which is general and applicable for the synthesis of a number of analogues. Our approach toward the synthesis of muricatacin is depicted in Scheme 1. It is based on the hydrogenation of butenolide **2**, the synthesis of which is anticipated by ring-closing metathesis of the acrloyl ester **3** derived from the allylic alcohol **4**. The formation of **4** is envisaged via Boord type fragmentation of the isopropylidinedioxy iodide **5**. γ-Hydroxy amide **6** was identified as the ideal precursor for the synthesis of **5**. The synthesis of **6** from the bis-Weinreb amide **7** of tartaric acid involving a combination of controlled addition of Grignard reagent and stereoselective reduction is a procedure established in our laboratory.[6]



Scheme 1. Retrosynthesis for the synthesis of (−)-muricatain.

* Corresponding author. Tel.: +91 80 22932524; fax: +91 80 23600529.
E-mail address: prasad@orgchem.iisc.ernet.in (K. R. Prasad).

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.11.004

Accordingly, the synthesis of muricatacin commenced with the controlled addition of *n*-dodecylmagnesium bromide to the bis-Weinreb amide **7**[7] resulting in the formation of the mono keto amide **8** in 82% yield. Stereoselective reduction of the keto group in **8** with K-Selectride furnished alcohol **6** in 93% yield. The protection of the hydroxyl group in **6** as the corresponding benzyl ether **9** was accomplished in 71% yield (94% yield based on recovery of the starting compound) by treating with $BnBr/Ag_2O$. Reduction of the Weinreb amide in **9** with $NaBH_4$ afforded the primary alcohol **10** in 92% yield. Reaction of the primary alcohol **10** with PPh_3/I_2 provided the iodide **5** in 86% yield. Refluxing an ethanol solution of iodide **5** with activated Zn cleanly produced the allylic alcohol **4** in 99% yield. Acrloylation of **4** afforded ester **3** in 88% yield, which on ring-closing metathesis with Grubbs second generation catalyst (10 mol %) furnished the butenolide in 91% yield. Hydrogenation of **2** with Pd/C afforded muricatacin **1** in 97% yield, the physical and spectroscopic data of which are in complete agreement with those reported in the literature.[8]

3. Conclusion

In conclusion, a facile synthesis of bioactive lactone, (−)-muricatacin, was accomplished from the chiral pool material L-(+)-tartaric acid. The synthetic sequence presented is highly diastereoselective and is amenable to the synthesis of a number of functionalized and non-functionalized derivatives of muricatacin (Scheme 2).

4. Experimental

4.1. General procedures

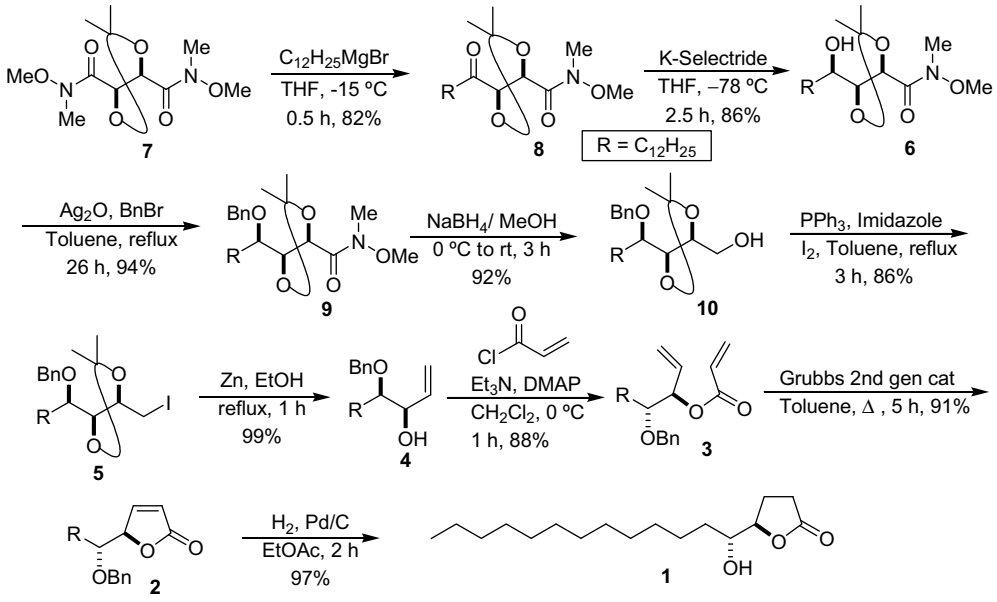
Column chromatography was performed on silica gel, Acme grade 100–200 mesh. TLC plates were visualized either with UV, in an iodine chamber, or with phosphomolybdic acid spray, unless noted otherwise. Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. THF was freshly distilled over Na-benzophenone ketyl. Melting points are uncorrected. Unless stated otherwise, all the reactions were performed under an inert atmosphere. Optical rotations were measured on a JASCO DIP-370 digital polarimeter measured at 25 °C.

4.1.1. Preparation of (4*R*,5*R*)-*N*-methoxy-*N*,2,2-trimethyl-5-tridecanoyl-1,3-dioxolane-4-carboxamide 8

In a two-necked 50 mL, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed **7** (0.5 g, 1.81 mmol), which was dissolved in 6 mL of THF and cooled to −15 °C. A freshly prepared THF solution of dodecylmagnesium bromide (7.2 mL of 0.5 M solution in THF, 3.6 mmol) was added at a rate that the internal temperature did not rise above −10 °C. The progress of the reaction was monitored by TLC and after the reaction was complete (0.5 h), it was cautiously quenched by addition of saturated solution of NH_4Cl (5 mL). It was then poured into water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined ethyl acetate extracts were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether/EtOAc (70:30) as eluent yielded **8** (0.57 g, 82%) as a colorless oil. $[\alpha]_D = +4.4$ (*c* 1.1, $CHCl_3$); IR (neat) 2926, 1721, 1675, 1378, 1082, 863 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.03 (d, *J* = 5.6 Hz, 1H), 4.81 (d, *J* = 5.6 Hz, 1H), 3.70 (s, 3H), 3.22 (s, 3H), 2.74–2.51 (m, 2H), 1.61–1.51 (m, 2H), 1.49 (s, 3H), 1.43 (s, 3H), 1.29–1.22 (m, 18H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.5, 169.8, 112.7, 82.3, 73.9, 61.7, 39.3, 32.5, 31.9, 29.62, 29.6, 29.46, 29.38, 29.3, 29.1, 26.7, 26.2, 23.1, 22.7, 14.1; HRMS for $C_{21}H_{39}NO_5$ + Na (M+Na) calcd 408.2726; found 408.2734.

4.1.2. Preparation of (4*R*,5*S*)-5-((*R*)-1-hydroxytridecyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide 6

To a pre-cooled solution of **8** (0.5 g, 1.3 mmol) in THF(4 mL) at −78 °C was added K-Selectride (2 mL, 1 M solution in THF, 2 mmol) dropwise over a period of 10 min, under an argon atmosphere and stirred at the same temperature. The progress of the reaction was monitored by TLC and after the reaction was complete (0.5 h), it was cautiously quenched by the dropwise addition of water (2 mL) at −78 °C and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the resulting residue with petroleum ether/EtOAc (1:1) as eluent afforded **6** (0.43 g, 86%) as a colorless oil; $[\alpha]_D = -4.3$ (*c* 1.1, $CHCl_3$); IR (neat) 3454, 2925, 2853, 1667, 1594, 1378, 1068 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.76 br s, 1H), 4.36 (br s, 1H), 3.73 (s, 3H), 3.62–3.55 (m, 1H), 3.22 (br s, 3H), 1.96 (d, *J* = 8.8 Hz, 1H), 1.75–1.38 (m, 8 H), 1.37–1.17 (br s,



Scheme 2. Synthesis of (−)-muricatacin.

20H) 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 111.0, 80.9, 73.8, 70.3, 61.7, 34.6, 32.4, 31.9, 29.67 (2xC), 29.64, 29.59, 29.5, 29.3, 27.0, 26.1, 25.8, 25.6, 22.7, 14.1; HRMS calcd for $C_{21}H_{41}NO_5$+Na (M+Na) 410.2882; found 410.2887.

4.1.3. Preparation of (4*R*,5*S*)-5-((*R*)-1-(benzyloxy)tridecyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide 9

To a solution of **8** (0.15 g, 0.38 mmol) in toluene (3 mL) was added Ag_2O (0.18 g, 0.77 mmol) under an argon atmosphere at room temperature. The reaction mixture was stirred at reflux for 1 h, and then cooled to room temperature. Benzyl bromide (0.07 mL, 0.57 mmol) was then introduced into the reaction mixture, and was allowed to reflux for additional 23 h. Progress of the reaction was monitored by TLC and after the reaction was complete, the reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (2 × 5 mL). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether/EtOAc (70:30) as an eluent furnished **9** 0.14 g as a colorless oil; $[\alpha]_D = +6.5$ (c 1.4, $CHCl_3$); IR (neat) 3031, 2926, 2851, 1671, 1376, 1070 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 m, 5H), 4.76–4.70 (m, 2H), 4.64 and 4.59 (AB q, J = 11.5 Hz, 2H), 3.65 (s, 3H), 3.57 (dd, J = 10.7, 6.2 Hz, 1H), 3.18 (s, 3H), 1.57 (q, J = 7.2 Hz, 2H), 1.48 (s, 3H), 1.47 (s, 3H), 1.30–1.22 (m, 20H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 138.6, 128.2, 127.9, 127.7, 127.5, 110.1, 80.3, 79.2, 78.0, 72.2, 61.7, 32.3, 31.9, 30.1, 29.67, 29.61, 29.58, 29.38, 27.1, 26.2, 25.8, 22.7, 14.1; HRMS calcd for $C_{28}H_{47}NO_5$+Na 500.3352; found 500.3338.

4.1.4. Preparation of (4*S*,5*S*)-5-((*R*)-1-(benzyloxy)tridecyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol 10

In a single-necked round-bottomed flask equipped with a magnetic stir bar and guard tube was placed a solution of **9** (0.150 g, 0.31 mmol) in MeOH (2 mL). $NaBH_4$ (0.024 g, 0.62 mmol) was introduced into the solution at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred for 3 h at the same temperature. After the reaction was complete (TLC), most of the methanol was removed under reduced pressure and water (3 mL) was added to the reaction mixture and extracted with ethyl acetate (2 × 10 mL). The combined organic layers were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ethyl acetate (7:3) as eluent furnished **10** (0.12 g, 92%) as a colorless oil; $[\alpha]_D = +9.7$ (c 1.5, $CHCl_3$); IR(neat) 3467, 3031, 2925, 2856, 1459, 1374, 1070 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 m, 5H), 4.63 (s, 2H), 4.2–3.96 (m, 2H), 3.73–3.50 (m, 3H), 2.39 (t, J = 4.2 Hz, 1H), 1.42 (s, 3H), 1.40 (m, 2H), 1.78–1.37 (m, 2H), 1.37–1.20 (m, 22H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 138.0, 128.4, 128.2, 128.0, 127.9, 108.8, 78.8, 78.2, 77.2, 73.0, 62.8, 31.9, 30.3, 29.70, 29.67, 29.61, 29.60, 29.38, 27.1, 26.1, 22.7, 14.1. HRMS for $C_{26}H_{44}O_4$+Na calcd 443.3137; found 443.3127.

4.1.5. Preparation of (4*S*,5*R*)-4-((*R*)-1-(benzyloxy)tridecyl)-5-(iodomethyl-2,2-dimethyl-1,3-dioxolane 5

To a solution of **10** (0.12 g, 0.28 mmol), in dry toluene (6 mL), was added PPh_3 (0.23 g, 0.85 mmol), imidazole (0.058 g, 0.85 mmol), and iodine (0.066 g, 0.52 mmol), under argon atmosphere at room temperature. The reaction mixture was then stirred at reflux for 1 h. After the reaction was complete (TLC), it was cooled to room temperature and poured into water (5 mL) and extracted with ether (2 × 10 mL). The combined ethereal layers were washed with brine (5 mL) followed by saturated solution of sodium thiosulfate (5 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ether (95:5) as eluent afforded **5** (0.13 g, 84%) as a colorless oil; $[\alpha]_D = -7.4$ (c 2, $CHCl_3$); IR (neat) 3032, 2925, 2854, 1458, 1373, 1068, 883 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 5H), 4.63 (m, 2H), 3.92 (dd, J = 7.5, 3.9 Hz, 1H), 3.85 (td, J = 7.5, 2.9 Hz, 1H), 3.55 (td, J = 8.8, 4.2 Hz, 1H), 3.34 (dd, J = 10.7, 4.2 Hz, 1H), 3.22 (dd, J = 10.7, 5.1 Hz, 1H), 1.68–1.52 (m, 2H), 1.47 (s, 3H), 1.43 (s, 3H), 1.38–1.24 (m, 20H), 0.89 (t, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 128.4, 128.1, 127.8, 109.3, 81.8, 77.8, 75.5, 72.8, 31.9, 30.4, 29.69, 29.66, 29.60, 29.59, 29.40, 27.5, 27.3, 26.0, 22.7, 14.1, 7.5 HRMS calcd for $C_{26}H_{43}IO_3$+Na 553.2155; found 553.2150.

4.1.6. Preparation of (3*R*,4*R*)-4-(benzyloxy)hexadec-1-en-3-ol 4

To a solution of the iodide **5** (0.12 g, 0.22 mmol) was added activated zinc dust (0.12 g, 1.8 mmol) in absolute ethanol (4 mL) at room temperature and stirred for 1 h at 80 °C. Progress of the reaction was followed by TLC. After completion of the reaction, it was filtered through a short pad of Celite and the Celite pad was washed with Et_2O (2 × 5 mL). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ethyl acetate (9:1) as eluent furnished **4** (0.076 g, 99%) as a colorless oil. $[\alpha]_D = -3.6$ (c 1.7, $CHCl_3$); IR (neat) 3465, 2925, 2855, 1460, 1219, 1099 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.24 m, 5H), 5.88 (ddd, J = 16.8 Hz, 10.5 Hz, 6.3 Hz, 1H), 5.36 (dt, J = 17.1 Hz, 1.5 Hz, 1H), 5.22 (dt, J = 10.5 Hz, 1.5 Hz, 1H), 4.64 and 4.54 (AB q, J = 11.4 Hz, 2H), 4.0–4.2 (m, 1H), 3.35 (dd, J = 11.1 Hz, 6.0 Hz, 1H), 2.49 (d, J = 4.5 Hz, 1H), 1.68–1.48 (m, 3 1.47–1.24 (m, 19H), 0.88 (t, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3; 137.7, 128.4, 127.9, 127.8, 116.8, 82.4, 74.4, 72.6, 31.9, 30.4, 29.9, 29.70, 29.66, 29.61, 29.60, 29.4, 25.1, 22.7, 14.1 HRMS calcd for M+Na ($C_{23}H_{38}O_2$+Na) 369.2770; found 369.2751.

4.1.7. Preparation of (3*R*,4*R*)-4-(benzyloxy)hexadec-1-en-3-yl acrylate 3

To an ice-cold solution of **4** (0.03 g, 0.08 mmol) in CH_2Cl_2 (2 mL) was added DMAP (0.01 g, 0.08 mmol) and Et_3N (0.03 mL, 0.26 mmol) and stirred for 15 min at the same temperature. Acryloyl chloride (0.02 mL, 0.26 mmol) was added to the reaction mixture at 0 °C and stirred at the same temperature for 1 h. After the reaction was complete (TLC), it was poured into water (5 mL) and extracted with ethyl acetate (2 × 5 mL). The combined organic layers were washed with brine (5 mL) followed by saturated sodium bicarbonate solution (5 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ethyl acetate (95:5) as eluent resulted in the acryloyl ester **3** (0.028 g, 88%) as a colorless oil; $[\alpha]_D = +21.6$ (c 0.8, $CHCl_3$); IR (neat) 3090, 3033, 2925, 1730, 1635, 1404, 1265, 1099 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 6.45 (dd, J = 17.3, 1.39 Hz, 1H), 6.17 (dd, J = 17.2, 10.3 Hz, 1H), 5.93–5.87 (m, 1H), 5.86 (dd, J = 10.3, 1.4 Hz, 1H), 5.55–5.50 (m, 1H), 5.36–5.23 (m, 2H), 4.65 and 4.58 (AB q, J = 11.5 Hz, 2H), 3.52 (dd, J = 12.1, 5.4 Hz, 1H), 1.56–1.41 (m, 4H), 1.39–1.15 (m, 18H), 0.88 (t, J = 6.6 Hz, 3H);^{13}CNMR (100 MHz, $CDCl_3$) δ 165.3, 138.4, 133.0, 131.0, 128.5, 128.3, 128.0, 127.7, 118, 79.8, 75.4, 72.8, 31.9, 30.4, 29.69, 29.66, 29.62, 29.6, 29.5, 29.4, 25.4, 22.7, 14.1. HRMS calcd for $C_{26}H_{40}O_3$+Na 423.2875; found 423.2874.

4.1.8. Preparation of (*R*)-5-(*R*-1-(benzyloxy)tridecyl)furan-2(5*H*)-one 2

A mixture of the diene **3** (0.02 g, 0.05 mmol) and Grubbs 2nd generation catalyst (0.004 g, 0.005 mmol, 10 mol %) in 1 mL of toluene was stirred at reflux for 4 h. It was then cooled to room temperature and most of the toluene evaporated off. Column chromatography of the resultant residue using petroleum ether/ethyl acetate (9:1) as eluent afforded **2** in 91% (0.017g) yield $[\alpha]_D = +104.5$ (c 1.1, $CHCl_3$); IR (neat) 2924, 2853, 1783, 1757, 1160, 1070, 823, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd,

J = 5.7 Hz, 1.4 Hz, 1H), 7.38–7.24 (m, 5H), 6.17 (dd, J = 5.7 Hz, 1.7 Hz, 1H), 5.14–5.08 (m, 1H), 4.69 and 4.61 (AB q, J = 11.5 Hz, 2H), 3.68–3.59 (m, 1H), 1.50–1.34 (m, 4H), 1.32–1.15 (m, 18H), 0.88 (t, J = 6.5 Hz, 3H);^{13}CNMR (100 MHz, $CDCl_3$) δ 172.9, 154.0, 137.8, 128.5, 128.0, 122.7, 84.6, 78.8, 73.4, 31.9, 30.6, 29.7, 29.65, 29.62, 29.56, 29.49, 29.4, 25.6, 22.7, 14.1; HRMS calcd for $C_{24}H_{36}O_3$+Na 395.2562; found 395.2548.

4.1.9. Preparation of muricatacin 1

To a solution of **2** (0.016 g, 0.04 mmol) in 1 mL of EtOAc at room temperature was added 10% activated Pd/C (50 mg). The reaction mixture was stirred for 2 h under a hydrogen atmosphere (balloon) at the same temperature. After the reaction was complete (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (2 × 5 mL). The residue obtained after evaporation of the solvent was purified by column chromatography using petroleum ether/ethyl acetate (1:1) as eluent to yield muricatacin **1** (0.011 g, 97%) as a white solid. mp 67–69 °C; lit.[8] mp 67–68 °C $[\alpha]_D = -23.9$ (c 0.8, $CHCl_3$); lit.[8] $[\alpha]_D = -23.3$ (c 1.8, $CHCl_3$); IR (KBr) 3441, 3401, 2956, 1743, 1471, 1196 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (td, J = 7.2 Hz, 4.4 Hz, 1H), 3.62–3.53 (br m, 1H), 2.68–2.45 (m, 2H), 2.28–2.21 (m, 1H), 2.16–2.06 (m, 1H)1.89 (br s, 1H), 1.61–1.46 (m, 2H), 1.41–1.24 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 83.0, 73.7, 33.0, 31.9, 29.66, 29.64, 29.57, 29.50, 29.3, 28.7, 25.5, 24.1, 22.7, 14.1; Anal. calcd for $C_{17}H_{32}O_2$: C, 71.79; H, 11.34. Found: C, 71.70: H, 11.10.

Acknowledgments

We thank DST and DBT, New Delhi, for funding of this project. V.G. thanks CSIR for a junior research fellowship.

References

1. (a) Bermejo, A.; Figadere, B.; Zafra-Polo, M.-C.; Barrachina, I.; Estornell, E.; Cortes, D. *Nat. Prod. Rev.* **2005**, *22*, 269; (b) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504; (c) Cave, A.; Figadere, B.; Laurens, A.; Cortes, D.. In *Progress in the Chemistry of Organic Natural Products: Acetogenins from Annonaceae*; Herz, W., Ed.; Springer, 1997; Vol. 70, pp 81–288.
2. Reiser, M. J.; Kozlowski, J. F.; Wood, K. V.; McLaughlin, J. L. *Tetrahedron Lett.* **1991**, *32*, 1137.
3. (a) Cave, A.; Chaboche, C.; Figadere, B.; Harmange, J. C.; Laurens, A.; Peyrat, J. F.; Pichon, M.; Szlosek, M.; Cotte-Lafitte, J.; Quero, A. M. *Eur. J. Med. Chem.* **1997**, *32*, 617; (b) Yoon, S.-H.; Moon, H.-S.; Hwang, S.-K.; Choi, S. R.; Kang, S.-K. *Bioorg. Med. Chem.* **1998**, *6*, 1043.
4. For recent syntheses of muricatacin see: (a) Ferrie, L.; Reymond, S.; Capdevielle, P.; Cossy, J. *Synlett* **2007**, 2891; (b) Yokoyama, T.; Kutsumura, N.; Ohgiya, T.; Nishiyama, S. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 578; (c) Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2006**, *16*, 2465; (d) Popsavin, V.; Krstic, I.; Popsavin, M.; Sreco, B.; Benedekovic, G.; Kojic, V.; Bogdanovic, G. *Tetrahedron* **2006**, *62*, 11044; (e) Ahmed, Md. M.; Cui, H.; O'Doherty, G. A. *J. Org. Chem.* **2006**, *71*, 6686; (f) Dhotare, B.; Chattopadhyay, A. *Tetrahedron Lett.* **2005**, *46*, 3103.
5. (a) Prasad, K. R.; Swain, B. *Tetrahedron: Asymmetry* **2008**, *19*, 1134; (b) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2008**, *73*, 2; (c) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2008**, *73*, 2916; (d) Prasad, K. R.; Dhaware, M. G. *Synthesis* **2007**, 3697; (e) Prasad, K. R.; Chandrakumar, A. *J. Org. Chem.* **2007**, *72*, 6312; (f) Prasad, K. R.; Gholap, S. L. *Tetrahedron Lett.* **2007**, *48*, 4679; (g) Prasad, K. R.; Dhaware, M. G. *Synlett* **2007**, 1112; (h) Prasad, K. R.; Anbarasan, P. *Synlett* **2006**, 2087; (i) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2006**, *71*, 3643; (j) Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2006**, *17*, 1146; (k) Prasad, K. R.; Anbarasan, P. *Tetrahedron* **2006**, *62*, 8303; (l) Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2006**, *17*, 850; (m) Prasad, K. R.; Anbarasan, P. *Tetrahedron Lett.* **2006**, *47*, 1433; (n) Prasad, K. R.; Gholap, S. L. *Synlett* **2005**, 2260.
6. Prasad, K. R.; Chandrakumar, A. *Tetrahedron* **2007**, *63*, 1798.
7. (a) Nugiel, D. A.; Jakobs, K.; Worley, T.; Patel, M.; Kaltenbach, R. F., III.; Meyer, D. T.; Jadhav, P. K.; De Lucca, G. V.; Smyser, T. E.; Klabe, R. M.; Bacheler, L. T.; Rayner, M. M.; Seitz, S. P. *J. Med. Chem.* **1996**, *39*, 2156–2169; (b) McNulty, J.; Grunner, V.; Mao, J. *Tetrahedron Lett.* **2001**, *42*, 5609.
8. Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1994**, *59*, 4122.