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The sulfinyl moiety as an intramolecular nucleophile. Part 3: Synthesis of (–)-muricatacin†

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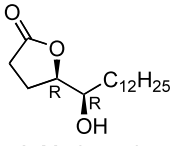
Abstract—A short, efficient and highly stereoselective synthesis of (–)-(*R*,*R*)-muricatacin is reported. The key steps include a highly diastereoselective reduction of a β-ketosulfoxide to a β-hydroxy sulfoxide, regio- and stereoselective bromohydration of an olefin employing the sulfinyl group as an internal nucleophile and chemoselective reduction of a double bond in the presence of a halogen atom.

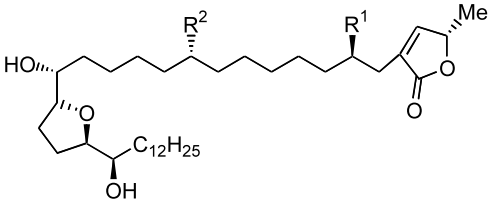
1. Introduction

The addition of nucleophiles to double bonds activated by complexation with electrophiles affords highly functionalized products. A substituent at the allylic or homoallylic position directs the regio- and stereochemistry of the reaction[1] and the steric[2] and/or stereoelectronic effects[3] from the substituent have been invoked to rationalize the outcome of such reactions. The asymmetric induction is also a function of the double bond geometry,[4] reaction conditions (thermodynamic versus kinetic control)[5] and whether the nucleophile attacks intramolecularly or intermolecularly[6] especially for electrophiles such as I_2, NBS (*N*-bromosuccinimide), $Hg(OAc)_2$ and PhSeCl. Substrates with an internal nucleophile have been shown to react with electrophiles via early transition states resembling π-complexes, while the reactions of substrates with external nucleophiles proceed via late transition states resembling onium ions. This difference affects the facial selectivity of electrophilic attack. We have been interested in the electrophile induced heterofunctionalisation of allylic olefins using the sulfinyl group as an internal nucleophile[7] and herein, we report a short, efficient and a highly stereoselective synthesis of (–)-muricatacin exploiting this methodology.

Muricatacin **1**, isolated from the seeds of *Annona muricata L.*[8] is probably a product of oxidative cleavage of its monotetrahydrofuranic acetogenin congeners[9] **2**–**7** (Fig. 1). The isolated sample is a mixture of enantiomers, with the (–)-(*R*,*R*) enantiomer predominating.



1, Muricatacin



2, $R^1 = R^2 = OH$, Annonacin
3, $R^1 = OH$, $R^2 = O$, Annonacinone
4, $R^1 = H$, $R^2 = OH$, Corrosolin
5, $R^1 = H$, $R^2 = O$, Corrosolone
6, $R^1 = OH$, $R^2 = H$, Murisolin
7, $R^1 = R^2 = H$, Solamin

Figure 1.

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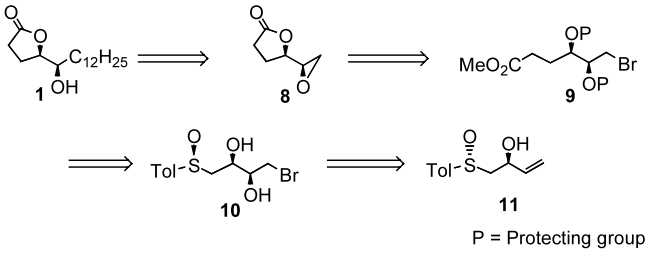
Muricatacin is a member of the hydroxy lactone class of compounds, that are notable for their biological activity[10] and as building blocks in the synthesis of both complex bioactive natural products[11] and synthetic compounds.[12] Muricatacin is biologically active showing cytotoxicity in KB and VERO cell lines. It has stimulated a great deal of attention due its biological activity and many syntheses[13] have been reported in the literature.

2. Results and discussion

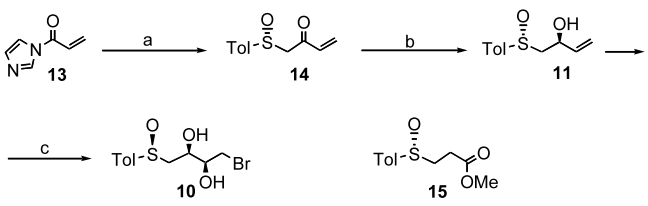
Retrosynthetic analysis (Scheme 1) shows that muricatacin **1** can be derived from the epoxy lactone **8**, which can be readily obtained from the bromoester **9**. The synthesis of **9** can be envisaged from the sulfoxide **10**, which in turn can be secured from the olefin **11**.

The synthesis began with the allyl alcohol **11**, which was obtained by diastereoselective reduction[14] (>95% de) of the β-ketosulfoxide **14** with DIBALH. Compound **14** was obtained by condensation of the anion of (*R*)-tolyl methyl sulfoxide **12**,[15] with 1-imidazolyl-2-propen-1-one **13**.[16] It is informative to note that the condensation of ethyl acrylate with the anion of tolyl methyl sulfoxide afforded predominantly the conjugate addition product **15** and none of the ketosulfoxide **14**. Treatment of the olefin **11** with NBS in the presence of water in toluene as the solvent afforded bromohydrin **10**[7a] stereospecifically (Scheme 2).

The formation of the bromohydrin **10** can be rationalized by the attack of bromonium ion on the olefin **11** in the depicted conformation[17] from the side of the hydrogen atom followed by intramolecular nucleophilic attack by the sulfinyl group in a 5-*exo* mode to afford the sulfonium salt followed by hydrolysis through attack of water on sulfur[18] (Fig. 2).



Scheme 1.



Scheme 2. *Reaction conditions*: (a) (*R*)-TolS(O)Me, LDA, THF, −30°C, −15°C, add **13**, 78%. (b) DIBAH, THF, −78°C, 93%. (c) NBS, H_2O, toluene, rt, 81%.

Treatment of the bromodiol **10** with 2,2-dimethoxypropane in the presence of catalytic CSA afforded the acetonide **16**, the ^{13}C spectrum of which revealed signals for the methyl groups at δ 27.1, 27.4 and for the quaternary carbon at δ 110.3 proving unambiguously[19] the *syn*-disposition of the hydroxy groups in **10**. Subjecting the acetonide **16** to Pummerer reaction[20] followed by aqueous $NaHCO_3$ workup of the intermediate, afforded the aldehyde which, without purification, was used directly in the next step. Thus, treatment of the aldehyde with methyl(triphenylphosphoranylidene)acetate in benzene afforded a mixture of the *cis*- and *trans*-olefins (**17** and **18**, respectively) in equimolar quantities. The *cis*- and *trans*-olefins were not separated (except for analytical purposes) and were subjected to hydrogenation over Pt/C in EtOAc as the solvent to yield the acetonide **19**. Deprotection of the acetonide by treatment with catalytic CSA in methanol led to concomitant cyclisation of the resulting hydroxy ester to afford the bromolactone **20**. Treatment of **20** with Ag_2O in acetonitrile afforded the epoxide **8** which was identical in all respects to the sample prepared by Depezay and co-workers.[13] Finally, reaction of the epoxy lactone **8** with an excess of undecylmagnesium bromide in the presence of Li_2CuCl_4 afforded (−)-muricatacin **1** (Scheme 3). It is instructive to note that starting from the diastereomer of **11** (that differs at the hydroxyl center) and using the above methodology, (+)-muricatacin can be elaborated.

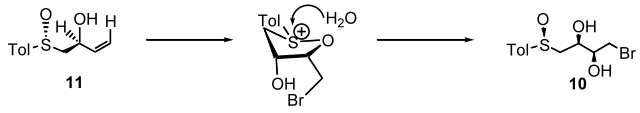
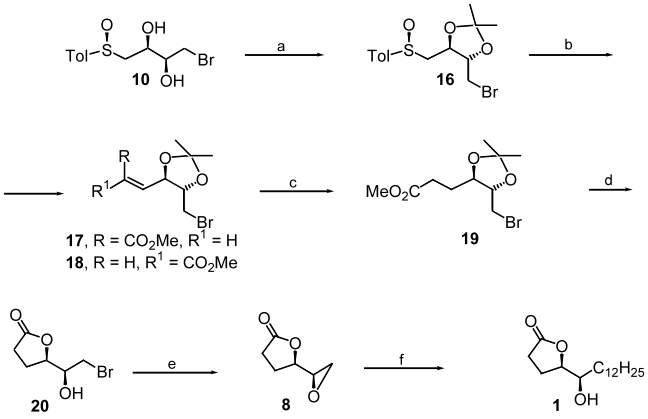


Figure 2.



Scheme 3. *Reaction conditions*: (a) 2,2-DMP, cat. CSA, acetone, rt, 92%. (b) (i) TFAA, Et_3N, CH_2Cl_2, 0°C, 15 min then aq. $NaHCO_3$; (ii) Ph_3PCHCO_2Me, PhH, rt, 1:1 of **17**:**18**, 58% for two steps. (c) H_2, Pt/C, EtOAc, rt, 94%. (d) Cat. CSA, MeOH, rt, 84%. (e) Ag_2O, CH_3CN, rt, 81%. (f) $C_{12}H_{25}MgBr$, Li_2CuCl_4, −78°C to rt 36 h, 72%.

In summary, we have devised a stereo- and regiospecific route to muricatacin from β-hydroxy sulfoxide **11**. The key steps include diastereoselective reduction of a β-keto sulfoxide, bromohydrin formation by neighbouring group participation from the sulfinyl moiety. This affords efficient 1,2-asymmetric induction and chemoselective reduction of the double bond of **17** and **18** in the presence of a labile halogen atom. The strategy adopted is flexible and should allow the synthesis of other members of the hydroxy lactone class of compounds.

3. Experimental

Melting points were recorded on Buchi R-535 apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Gemini-200 and Brucker 300 spectrophotometers in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan Matt 1200 mass spectrometer operating at 70 eV. Optical rotations were measured on a Jasco Dip 360 Digital polarimeter. Column chromatography was performed on silica gel (Merck, 100–200 mesh).

3.1. (1*R*)-(4-Methylphenylsulfinyl)-3-buten-2-one, 14

To a solution of acryloyl chloride (1.81 g, 20 mmol) in dry THF (40 mL) was added imidazole (2.72 g, 40 mmol) at 0°C and the mixture was stirred for 10 min. The salt was filtered and the filtrate (**13**) used directly in the next step: to a solution of diisopropyl amine (4.72 mL, 33.8 mmol) in dry THF (47 mL) at 0°C was added *n*-BuLi (1.6 M in hexanes, 21.1 mL, 33.8 mmol) dropwise and stirred for 10 min. LDA so generated was cooled to −30°C and a solution of (*R*)-tolyl methyl sulfoxide (3.47 g, 23 mmol) in dry THF (25 mL) was added dropwise and stirred for 20 min. The reaction mixture was then warmed to −15°C and the solution of **13** prepared above was added to it dropwise and stirred for 20 min. The reaction was quenched by adding saturated aq. ammonium chloride (10 mL). The reaction mixture was extracted with ether. The combined organic layers were washed with water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to yield the crude product mixture which was purified by column chromatography using 70% EtOAc/pet. ether as eluent to afford **14** (3.26 g, 78%). Viscous liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J=8.0 Hz, 2H), 7.25 (d, J=8.0 Hz, 2H), 6.30 (dd, J=17.6, 10.4 Hz, 1H), 6.15 (d, J=17.6 Hz, 1H), 5.90 (d, J=10.4 Hz, 1H), 4.05 (d, J=13.6 Hz, 1H), 3.85 (d, J=13.6 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.4, 142.3, 136.2, 131.6, 130.1, 124.2, 124.0, 65.8, 21.4. MS (EI) 208 (M^+). $[\alpha]_D$ +184.6 (*c* 1, $CHCl_3$).

3.2. (1*R*)-(4-Methylphenylsulfinyl)-(2*S*)-3-buten-2-ol, 11

To a solution of ketosulfoxide (**14**) (3.12 g, 15 mmol) in dry THF (65 mL) cooled at −78°C was added a solution of DIBAL (2 M in toluene, 7.5 mL) and stirred for 2 h. The reaction was quenched by the addition of methanol (60 mL) and allowed to attain rt. The solvents were removed under reduced pressure and the residue was treated with 10% aq. NaOH solution. The aq. layer was extracted with ether and the organic layer washed successively with water, brine and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by column chromatography using 30% EtOAc/pet. ether as eluent to afford **11** (2.92 g, 93%). Solid. Mp 81°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.52 (d, J=8.0 Hz, 2H), 7.32 (d, J=8.0 Hz, 2H), 5.80 (ddd, J=17.0, 10.3, 5.7 Hz, 1H), 5.34 (d, J=17.0 Hz, 1H), 5.12 (d, J=10.3 Hz, 1H), 4.70 (s, 1H), 4.40 (br s, 1H), 2.95 (dd, J=10.4, 6.0 Hz, 1H), 2.72 (dd, J=10.4, 1.5 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.2, 140.3, 138.6, 129.9, 123.9, 115.5, 66.7, 63.3, 21.3. MS (EI) 210 (M^+). $[\alpha]_D$ +134.0 (*c* 1, acetone).

3.3. 1-Bromo-(4*S*)-(4-methylphenylsulfinyl)-(2*S*,3*S*)-butane-2,3-diol, 10

To a solution of the unsaturated sulfoxide (**11**) (2.1 g, 10 mmol) in toluene (40 mL) was added water (0.27 mL, 15 mmol) followed by freshly recrystallized NBS (0.94 g, 12 mmol) and the mixture stirred at rt for 30 min. The reaction mixture was then diluted with ether and the organic layer washed successively with 5% aq. $NaHCO_3$, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to afford the crude product which was purified by column chromatography using 40% EtOAc/pet. ether as eluent to yield **10** (2.46 g) in 81% yield. Solid. Mp 108°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.54 (d, J=8.0 Hz, 2H), 7.35 (d, J=8.0 Hz, 2H), 4.70 (m, 1H), 3.54 (dd, J=10.3, 7.3 Hz, 1H), 3.40 (dd, J=10.3, 6.4 Hz, 1H), 3.02 (dd, J=13.7, 8.0 Hz, 1H), 2.89 (dd, J=13.7, 3.4 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 140.7, 140.0, 129.0, 123.0, 72.9, 64.8, 61.7, 33.3, 20.5. MS (FAB) 306 (M^++H). $[\alpha]_D$ −208.2 (*c* 0.5, MeOH).

3.4. 4-Bromomethyl-2,2-dimethyl-5-(4-methyl-(*S*)-phenylsulfinylmethyl)-(4*S*,5*S*)-1,3-dioxolane, 16

To the solution of the bromodiol (**10**) (1.83 g, 6.0 mmol) in acetone (15 mL) was added 2,2-dimethoxypropane (5 mL) and catalytic amounts of CSA and the mixture stirred at rt for 1 h. Et_3N, enough to neutralise CSA, was added and the volatiles were removed under reduced pressure. The residue was purified by column chromatography using 20% EtOAc/pet. ether as the eluent to afford **16** (1.92 g) in 92% yield. Solid. Mp 92°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.55 (d, J=8.0 Hz, 2H), 7.32 (d, J=8.0 Hz, 2H), 4.25 (ddd, J=6.9, 6.4, 5.5 Hz, 1H), 3.94 (q, J=6.4, 1H), 3.52 (dd, J=11.0, 5.5 Hz, 1H), 3.41 (dd, J=11, 6.9 Hz, 1H), 3.12 (d, J=6.4 Hz, 2H), 2.42 (s, 3H), 1.44 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.5, 130.0, 124.4, 110.3, 78.7, 75.3, 60.2, 31.3, 27.4, 27.1, 21.6. MS (EI) 346 (M^+). $[\alpha]_D$ −202.3 (*c* 1, $CHCl_3$).

3.5. Methyl 3-[5-bromomethyl-2,2-dimethyl-(4*R*,5*S*)-1,3-dioxolan-4-yl]-(*Z*)-2-propenoate, 17 and methyl 3-[5-bromomethyl-2,2-dimethyl-(4*R*,5*S*)-1,3-dioxolan-4-yl]-(*E*)-2-propenoate, 18

To the solution of the bromoacetonide (**16**) (1.74 g, 5 mmol) in dichloromethane (20 mL) cooled at 0°C was

added triethylamine (1.39 mL, 10 mmol) followed by trifluoroacetic anhydride (1.41 mL, 10 mmol) and stirred for 15 min. An aq. 5% $NaHCO_3$ solution (25 mL) was added at 0°C and stirred for another 20 min. The reaction mixture was then extracted into benzene (40 mL) and washed successively with water, brine and dried over Na_2SO_4. This benzene solution of the aldehyde was directly taken ahead to the next step and reacted with methyl(triphenylphosporanilidine)acetate (2.49 g, 6 mmol). The reaction was stirred at rt for 30 min. The solvent was removed under reduced pressure to afford a residue which was purified by column chromatography using 10% EtOAc/pet. ether as the eluent to afford an equimolar mixture of *cis*-(**17**) and *trans*-olefins (**18**) (0.81 g, 2.9 mmol) in 58% overall yield for two steps. A small amount of this mixture was separated to afford pure *cis*- and *trans*-isomers. The bulk sample was however used as a mixture of isomers in the next step. **17**: Viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.32 (dd, J=12.1, 7.7 Hz, 1H), 5.92 (d, J=12.1 Hz, 1H), 5.35 (t, J=7.7 Hz, 1H), 3.98 (td, J=7.7, 4.4 Hz, 1H), 3.76 (s, 3H), 3.62 (dd, J=12.1, 4.4 Hz, 1H), 3.50 (dd, J=12.1, 7.0 Hz, 1H), 1.41 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.6, 146.3, 122.5, 110.5, 80.9, 75.9, 51.6, 32.3, 27.3. MS (EI) 278 (M^+). $[\alpha]_D$ 118.5 (*c* 0.14, $CHCl_3$). **18**: Viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (dd, J=16.0 Hz, 6.1 Hz, 1H), 6.12 (d, J=16.0 Hz, 1H), 4.45 (t, J=6.1 Hz, 1H), 3.95 (m, 1H), 3.73 (s, 3H), 3.45 (d, J=6.1, 1H), 1.41 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 143.9, 122.7, 110.8, 79.4, 79.2, 51.8, 31.1, 27.0. $[\alpha]_D$ −9.2 (*c* 0.42, $CHCl_3$).

3.6. Methyl 3-[5-bromomethyl-2,2-dimethyl-(4*R*,5*S*)-1,3-dioxolan-4-yl]propanoate, 19

To a solution of the mixture of esters (0.70 g, 2.5 mmol) in EtOAc (10 mL) was added 5% Pt/C (70 mg) and the mixture was stirred at rt for 4 h under an atmosphere of hydrogen. The catalyst was removed by filtration and the filtrate evaporated in vacuo to dryness. The residue was purified by column chromatography using 20% EtOAc/pet. ether as the eluent to afford **19** (0.66 g, 2.35 mmol) in 94% yield. Viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90–3.81 (m, 2H), 3.67 (s, 3H), 3.48–3.36 (m, 2H), 2.58–2.40 (m, 2H), 2.05 (m, 1H), 1.81 (m, 1H), 1.38 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 109.3, 79.6, 79.3, 51.4, 31.7, 30.2, 28.7, 27.5, 27.2. MS (EI) 280 (M^+). $[\alpha]_D$ −15.7 (*c* 1.38, $CHCl_3$).

3.7. 5-[2-Bromo-1-hydroxy-(1*S*)-ethyl]-(5*R*)-2*H*,3*H*,4*H*-2-furanone, 20

To a solution of the bromoester **19** (0.63 g, 2.25 mmol) in methanol (2.3 mL) was added catalytic amounts of CSA and the mixture was stirred at rt for 2 h. Et_3N was added to neutralize the acid and methanol was removed under reduced pressure. The residue was purified by column chromatography using 40% EtOAc/pet. ether as the eluent to yield **20** (0.39 g, 1.89 mmol) in 84% yield. Viscous oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.68 (m, 1H), 3.78 (m, 1H), 3.45 (d, J=7.3 Hz, 2H), 2.62–2.40 (m, 2H), 2.40–2.20 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 79.5, 73.1, 33.5, 28.2, 24.0. MS (EI) 208 (M^+). $[\alpha]_D$ −35.6 (*c* 0.19, $CHCl_3$).

3.8. 5-[(2*R*)-Oxiran-2-yl]-(5*R*)-2*H*,3*H*,4*H*-2-furanone, 8

To a solution of bromohydrin **20** (0.418 g, 2 mmol) in CH_3CN (20 mL) was added Ag_2O (0.464 g, 2 mmol) at 0°C and the mixture was stirred under an atmosphere of nitrogen gradually allowing it to attain rt over 2 h. The reaction mixture was filtered and the filtrate evaporated in vacuo to afford the crude product. Column chromatography using 40% EtOAc/pet. ether as the eluent afforded **8** (0.208 g, 1.62 mmol) in 81% yield. Viscous liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.60 (m, 1H), 3.10 (m, 1H), 2.82–2.76 (m, 2H), 2.63 (m, 1H), 2.49 (m, 1H), 2.40 (m, 1H), 2.30 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 76.4, 53.0, 43.6, 27.5, 25.0. MS (EI) 128 (M^+). $[\alpha]_D$ −28.6 (*c* 1.64, $CHCl_3$).

3.9. 5-[1-Hydroxy-(1*R*)-tridecyl]-(5*R*)-2*H*,3*H*,4*H*-2-furanone, 1

To a stirred solution of Li_2CuCl_4 (0.1 M/THF, 7.5 mL, 0.75 mmol) cooled at −35°C was added undecyl magnesium bromide (1 M/THF, 7.5 mL, 7.5 mmol) and stirred for 30 min at the same temperature. This mixture was added to the solution of epoxy lactone **8** (0.192 g, 1.5 mmol) in anhydrous THF (7.5 mL) cooled at −78°C. The reaction mixture was gradually allowed to attain rt and stirred for 24 h. The reaction mixture was cooled to −78°C and another portion of the mixture of Li_2CuCl_4 and undecyl magnesium bromide was added and stirred for another 12 h allowing it to attain rt. The reaction was cooled to 0°C and quenched by the addition of aq. satd. NH_4OAc. The layers were separated and the aq. layer extracted with ether. The combined organic layers were washed successively with water, brine and dried over Na_2SO_4. The solvent was removed in vacuo and the residue purified by chromatography using 30% EtOAc/pet. ether as the eluent to afford **1** (0.305 g, 1.07 mmol) in 72% yield. Solid. Mp 72°C, lit. 71°C.[13o] ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.39 (m, 1H), 3.50 (m, 1H), 2.62–2.40 (m, 2H), 2.16 (m, 1H), 2.08 (m, 1H), 1.88 (m, 1H), 1.55 (m, 2H), 1.62–1.20 (m, 20H), 0.80 (t, J=6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 83.0, 73.5, 32.9, 31.8, 29.6, 29.5, 29.4, 29.3, 28.6, 25.4, 24.0, 22.6, 14.0. MS (FAB) 285 (M^++H). $[\alpha]_D$ −22.8 (*c* 1.0, $CHCl_3$), lit. −22.9 (*c* 1.1, $CHCl_3$).[13a]

Acknowledgements

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References

1. Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321 and references cited therein.
2. (a) Johnson, F. *Chem. Rev.* **1968**, *68*, 375; (b) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
3. Deslongchamps, P. In *Stereoelectronic Effects in Organic Chemistry*; 1st ed.; Baldwin, J. E., Ed.; Pergamon Press: Canada, 1983; Vol. 1.
4. (a) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1339; (b) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1345.
5. (a) Kinetic control: Jager, V.; Gunther, H. J. *Tetrahedron Lett.* **1977**, 2543; (b) Thermodynamic control: Bartlett, P. A.; Myerson, J. *J. Am. Chem. Soc.* **1978**, *100*, 3950.
6. Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672.
7. (a) Raghavan, S.; Rasheed, M. A.; Joseph, S. C.; Rajender, A. *J. Chem. Soc., Chem. Commun.* **1999**, 1845; (b) Raghavan, S.; Ramakrishna Reddy, S.; Tony, K. A.; Naveen Kumar, Ch.; Varma, A. K.; Nangia, A. K. *J. Org. Chem.* **2002**, *67*, 5838.
8. Rieser, M. J.; Kozlowski, J. F.; Wood, K. V.; McLaughlin, J. L. *Tetrahedron Lett.* **1991**, *32*, 1137.
9. (a) Myint, S. H.; Laurens, A.; Hocquemuller, R.; Cave, A.; Davoust, D.; Cortes, D. *Heterocycles* **1990**, *31*, 861; (b) Cortes, D.; Myint, S. H.; Laurens, A.; Hocquemuller, R.; Leboeuf, M.; Cave, A. *Can. J. Chem.* **1991**, *69*, 8; (c) Myint, S. H.; Cortes, D.; Laurens, A.; Hocquemuller, R.; Leboeuf, M.; Cave, A.; Colte, J.; Quero, A. M. *Phytochemistry* **1991**, *30*, 3335.
10. (a) Numata, A.; Hokimoto, K.; Takemura, T.; Katsuno, T.; Yamamoto, K. *Chem. Pharm. Bull. Jpn.* **1984**, *32*, 2815; (b) Cave, A.; Chaboche, C.; Figadere, B.; Harmange, J. C.; Laurens, A.; Peyrat, J. F.; Pichon, M.; Szosek, M.; Colte-Lafitte, J.; Quero, A. M. *Eur. J. Med. Chem.* **1997**, *32*, 617; (c) Schumacher, J. N.; Green, C. R.; Best, F. W.; Newell, M. P. *J. Agric. Food Chem.* **1977**, *25*, 310.
11. (a) Pearson, W. H.; Hembre, E. J. *J. Org. Chem.* **1996**, *61*, 7217; (b) Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 10012; (c) Avedissian, H.; Sinha, S. C.; Yazhak, A.; Sinha, A.; Neogi, P.; Sinha, S. C.; Keinan, E. *J. Org. Chem.* **2000**, *65*, 6035.
12. (a) Nishi, T.; Kataoaka, M.; Morisawa, Y. *Chem. Lett.* **1989**, 1193; (b) Gante, J.; Kahlenberg, H. *Chem.-Ztg.* **1991**, *115*, 215; (c) Chakraborty, T. K.; Gangakhedkar, K. K. *Tetrahedron Lett.* **1991**, *32*, 1897; (d) Harding, K. E.; Coleman, M. T.; Liu, L. T. *Tetrahedron Lett.* **1991**, *32*, 3795; (e) Ghosh, A. K.; McKee, S. P.; Thompson, W. J. *J. Org. Chem.* **1991**, *56*, 5600; (f) Poss, M. A.; Reid, J. A. *Tetrahedron Lett.* **1992**, *33*, 1141; (g) Askin, D.; Wallace, M. A.; Vacca, J. P.; Reamer, R. A.; Volante, R. P.; Shinkai, I. *J. Org. Chem.* **1992**, *57*, 2771.
13. (a) Scholz, G.; Tochtermann, W. *Tetrahedron Lett.* **1991**, *32*, 5355; (b) Figadere, B.; Harmange, J.-C.; Laurens, A.; Cave, A. *Tetrahedron Lett.* **1991**, *32*, 7539; (c) Tochtermann, W.; Scholz, G.; Bunte, G.; Wolff, C.; Peters, E.-M.; Peters, K.; VonSchnering, H. G. *Liebigs Ann. Chem.* **1992**, 1069; (d) Marshall, J. A.; Welmaker, G. S. *Synlett* **1992**, 537; (e) Kang, S.-K.; Cho, J.-S.; Kim, B.-K. *J. Carbohydr. Chem.* **1992**, *11*, 807; (f) Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B.; Sinha, S. C.; Sinha, A. B.; Kienan, E. *Tetrahedron Lett.* **1992**, *33*, 6407; (g) Liu, Z. Y.; Zhang, J. J.; Chen, W. *Chin. Chem. Lett.* **1993**, *4*, 663; (h) Pelletier, C. G.; Saniere, M.; Charvet, I.; Merrer, Y. L.; Depezay, J.-C. *Tetrahedron Lett.* **1994**, *35*, 115; (i) Tam, V. T.; Chaboche, C.; Figadere, B.; Chaphe, B.; Hiew, B. C.; Cave, A. *Tetrahedron Lett.* **1994**, *35*, 883; (j) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1994**, *59*, 4122; (k) Bonini, C.; Fedirici, C.; Rossi, L.; Righi, G. *J. Org. Chem.* **1995**, *60*, 4803; (l) Quayle, P.; Rahman, S.; Herbert, J. *Tetrahedron Lett.* **1995**, *36*, 8087; (m) Saniere, M.; Charvet, I.; Merrer, Y. L.; Depezay, J.-C. *Tetrahedron* **1995**, *51*, 1653; (n) Somfai, P. *J. Chem. Soc., Perkin Trans. 1* **1995**, 817; (o) VanAar, M. P. M.; Thijs, L.; Zwanenberg, B. *Tetrahedron* **1995**, *51*, 11223; (p) Rassu, G.; Pinna, L.; Spanu, P.; Zanardi, F.; Battistini, L.; Casiraghi, G. *J. Org. Chem.* **1997**, *62*, 4513; (q) Chang, S.-W.; Hung, C.-Y.; Liu, H.-H.; Uang, B.-J. *Tetrahedron: Asymmetry* **1998**, *9*, 521; (r) Szlosek, M.; Franck, X.; Figadere, B.; Cave, A. *J. Org. Chem.* **1998**, *63*, 5169; (s) Yoon, S.-H.; Moon, H.-S.; Hwang, S.-K.; Choi, S. R.; Kang, S.-K. *Bioorg. Med. Chem.* **1998**, *6*, 1043; (t) Solladie, G.; Hanquet, G.; Izzo, I.; Crumbie, R. *Tetrahedron Lett.* **1999**, *40*, 3071; (u) Couladoros, E. A.; Mihou, A. P. *Tetrahedron Lett.* **1999**, *40*, 4861; (v) Baylon, C.; Prestat, G.; Heck, M.-P.; Mioskowski, C. *Tetrahedron Lett.* **2000**, *41*, 3833; (w) Carda, M.; Rodriguez, S.; Gonzalez, F.; Castillo, E.; Villanueva, A.; Marco, J. A. *Eur. J. Org. Chem.* **2002**, 2649; (x) Chandrasekhar, M.; Chandra, K. L.; Singh, V. K. *Tetrahedron Lett.* **2002**, *43*, 2773.
14. (a) Solladie, G.; Demailly, G.; Greck, C. *Tetrahedron Lett.* **1985**, *26*, 435; (b) Solladie, G.; Frechou, C.; Demailly, G.; Greck, C. *J. Org. Chem.* **1986**, *51*, 1912; (c) Carreno, M. C.; Garcia Ruano, J. L.; Martin, A.; Pedregal, C.; Rodrigues, J. H.; Rubio, A.; Sanchez, J.; Solladie, G. *J. Org. Chem.* **1990**, *55*, 2120.
15. Solladie, G.; Hull, J.; Girardin, A. *Synthesis* **1987**, 173.
16. Solladie, G.; Demailly, G.; Greck, C. *J. Org. Chem.* **1985**, *50*, 1552.
17. Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819.
18. Khuddus, M. A.; Swern, D. *J. Am. Chem. Soc.* **1973**, *95*, 8393.
19. Dana, G.; Danechpajouh, H. *Bull. Soc. Chim. Fr.* **1980**, 395.
20. (a) Pummerer, R. *Chem. Ber.* **1909**, *42*, 2282; (b) Sugihara, H.; Tanikaga, R.; Kaji, A. *Synthesis* **1978**, 881; (c) Padwa, A.; Gunn, D. E., Jr.; Osterhout, M. H. *Synthesis* **1997**, 1353.