

Total synthesis of the putative structure of the marine alkaloid haliclorensins

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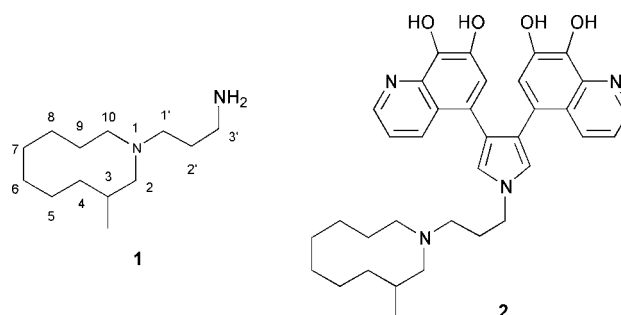
Received (in Montpellier, France) 8th June 2001, Accepted 21st August 2001

First published as an Advance Article on the web 9th October 2001

Compound **1**, the structure of which has been assigned to the marine natural product haliclorensins, was prepared by an unambiguous synthetic pathway and subjected to spectroscopic analysis. The derived data do not match those reported for the natural product.

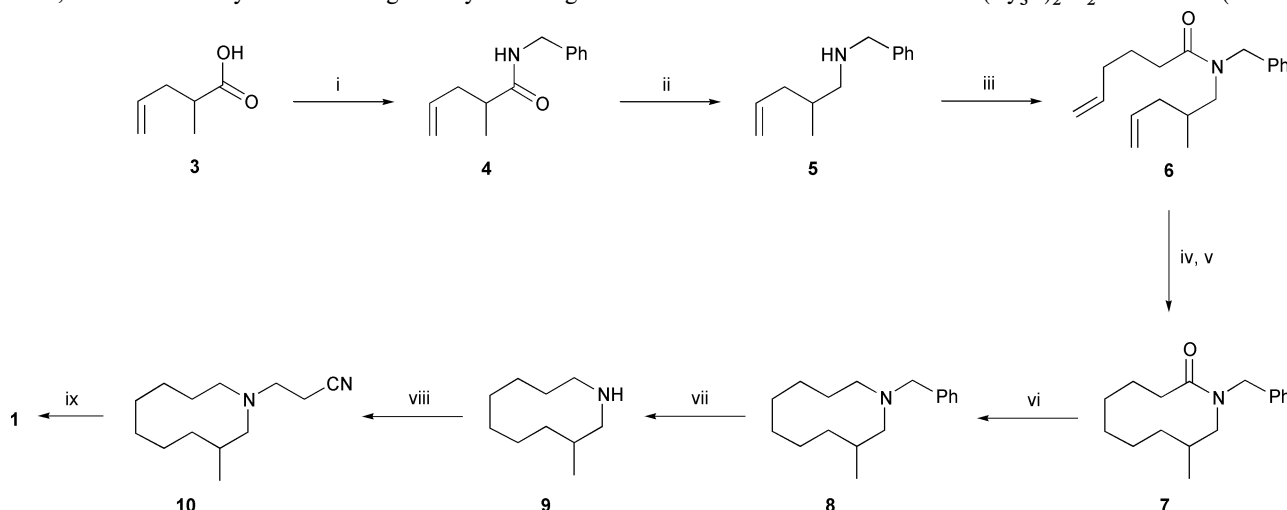
The natural products haliclorensins¹ and halitulin² were isolated by Kashman and co-workers from the marine sponge *Haliclona tulearensis*, collected in Sodwana Bay, Durban, South Africa. The structures of these compounds were assigned as **1** and **2**, respectively, using a combination of spectroscopic studies and biosynthetic considerations. The absolute stereochemistry associated with the single stereogenic centre incorporated in these structures was not assigned. While no significant biological activity has been ascribed to haliclorensins, halitulin was found to be cytotoxic against several tumour cell lines (*e.g.*, P-388, A-549, HT-29 and MEL-28) with IC₅₀ values in the 12–25 ng ml⁻¹ range. Such properties, coupled with the novel structure assigned to halitulin, prompted a patent filing³ (jointly with PharmaMar S. A., Madrid) claiming 3,4-bis(7,8-dihydroxyquinolin-5-yl)pyrroles as antitumour agents.

Our continued interest in developing total syntheses of biologically active, pyrrole-containing marine natural products^{4–6} prompted us to undertake the preparation of the racemic modification of compound **1** as a prelude to the assembly of the structurally more challenging congener **2**. Herein, we detail the synthesis of target **1** by unambiguous



means and report that it does not correspond to the natural product haliclorensins.⁷

The synthesis of compound **1** is shown in Scheme 1. The key step involves a ring-closing metathesis (RCM) step for construction of the azacyclodecane ring,⁸ a protocol that has been applied to the preparation of a number of other prominent and structurally related marine alkaloids, including manzamine C.⁹ Thus, condensation of the commercially available acid **3** with benzylamine using DMTMM¹⁰ afforded amide **4** (100%), which was reduced to the *N*-benzylamine **5** (100%) with lithium aluminium hydride. DMTMM-mediated condensation of the latter compound with 5-hexenoic acid then gave the doubly unsaturated amide **6** (40%), which was obtained as a *ca.* 1 : 1 and chromatographically distinguishable mixture of rotamers. In keeping with the studies of Weiler *et al.*,¹¹ compound **6** participated in a RCM reaction when treated with 15 mol% of (Cy₃P)₂Cl₂Ru=CHPh (Grubbs'



Scheme 1 Reagents and conditions: (i) benzylamine (1.2 mol equiv.), DMTMM (1 mol equiv.), THF, 18 °C, 16 h; (ii) LiAlH₄ (2 mol equiv.), THF, 0–18 °C, 16 h; (iii) 5-hexenoic acid (1 mol equiv.), DMTMM (1.5 mol equiv.), THF, 18 °C, 16 h; (iv) (Cy₃P)₂Cl₂Ru=CHPh (*ca.* 15 mol%), CH₂Cl₂, reflux, 48 h; (v) H₂ (1 atm.), 10% Pd on C (50% by wt.), MeOH, 18 °C, 24 h; (vi) LiAlH₄ (2 mol equiv.), THF, 18 °C, 16 h; (vii) H₂ (1 atm.), 20% Pd(OH)₂ on C, CH₂Cl₂, 18 °C, 24 h; (viii) acrylonitrile (excess), AcOH (2 mol equiv.), reflux, 16 h; (ix) NaBH₄ (25 mol equiv.), MeOH, 18 °C, 2 h. DMTMM = 4-{4,6-dimethoxy[1,3,5]triazin-2-yl}-4-methylmorpholinium chloride.

catalyst)¹² in refluxing dichloromethane, although it was clear that one rotameric form reacted more rapidly than the other in this process. The resulting *ca.* 3 : 1 mixture of *E*- and *Z*-alkenes (76%) was immediately subjected to hydrogenation with dihydrogen in the presence of 10% palladium on carbon and, in this manner, the corresponding saturated lactam **7** (100%) was obtained and the structure determined by single-crystal X-ray analysis (Fig. 1 and Experimental).

Lithium aluminum hydride-promoted reduction of the latter compound then afforded the *N*-benzylated amine **8** (100%), which was reacted with hydrogen in the presence of 20% Pd(OH)₂ on carbon to give 3-methylazadodecane (**9**). This latter compound was not characterized but immediately subjected to treatment with excess acrylonitrile in the presence of acetic acid and, in this manner, the expected Michael addition product **10** (36% from **8**) was obtained. Treatment of compound **10** with sodium borohydride in the presence of cobalt(II) chloride hexahydrate¹³ then gave the target diamine **1** in 90% yield. NMR spectroscopic and mass spectrometric analysis of this material gave data completely consistent with structure **1** but these did not match those reported¹ for the natural product (Table 1 and Experimental). Our data do, however, match those reported⁷ by Heinrich and Steglich for their synthetically-derived samples of compound **1**.

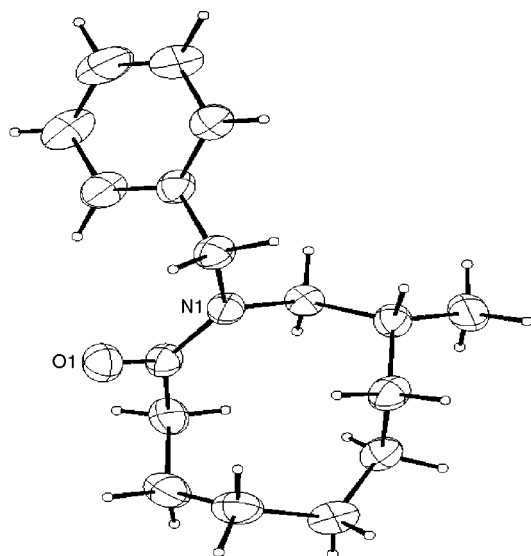


Fig. 1 Diagram derived from single-crystal X-ray analysis of compound **7**.

Table 1 Comparison of ¹³C NMR spectral data derived from compound **1** with those reported¹ for haliclorensine^a

Carbon no.	Compound 1 (at 125 MHz)	Haliclorensine	Calc. ^b
2	60.3(CH ₂)	48.5(t)	61.1
3	29.4(CH)	26.5(d)	31.7
4	31.6(CH ₂)	30.3(t)	34.7
5	21.7(CH ₂)	22.6(t)	27.5
6	26.1(CH ₂)	24.3(t)	30.6
7	24.2(CH ₂)	24.1(t)	30.0
8	24.0(CH ₂)	22.3(t)	28.0
9	25.4(CH ₂)	21.5(t)	30.0
10	52.8(CH ₂)	42.4(t)	54.5
11	19.4(CH ₃)	17.7(q)	17.8
1'	52.4(CH ₂)	41.3(t)	51.6
2'	30.0(CH ₂)	19.2(t)	34.1
3'	40.3(CH ₂)	41.2(t)	40.0

^a Both spectra recorded in DMSO-*d*₆. ^b Generated using the NMR chemical shift calculation package associated with ChemDraw Ultra™ 6.0 (PC Version).

On the basis of the foregoing, we conclude that the structure for haliclorensine has been incorrectly assigned. These observations also call into question the structure assigned to halituline. Synthetic and spectroscopic studies designed to establish the structures of haliclorensine and halituline are now underway in our laboratories and results will be reported in due course.

Experimental

Unless otherwise specified, ¹H and ¹³C NMR spectra were recorded on a Varian Gemini 300 spectrometer using deuteriochloroform as solvent. The 500 MHz ¹H NMR spectra and the 150 MHz ¹³C NMR spectrum were obtained on the corresponding Varian Inova spectrometers. Infrared spectra were recorded on either a Perkin–Elmer 683 or 1800 FTIR instrument. Unless otherwise specified, mass spectral analyses were carried out in electron-impact mode and on a VG Micromass 7070F double-focussing spectrometer. Thin layer chromatographic analyses were carried out on aluminium-backed 0.2 mm thick silica gel 60 GF₂₅₄ plates supplied by Merck while flash chromatographic purifications were conducted according to the method of Still *et al.*¹⁴ and using Merck silica gel 60 (230–400 mesh) as adsorbent. All solvents and common reagents were purified by established procedures.¹⁵

Syntheses

(±)-2-Methylpent-4-enoic acid benzylamide (4). DMTMM (9.09 g, 32.96 mmol) was added in portions to a magnetically stirred solution of benzylamine (2.94 g, 27.46 mmol) and 2-methylpent-4-enoic acid (3.14 g, 27.46 mmol) in THF (125 ml) maintained at 0 °C under a nitrogen atmosphere. The resulting mixture was allowed to warm to 18 °C over *ca.* 1 h, stirred at this temperature for a further 15 h, then poured into water (150 ml) and extracted with diethyl ether (3 × 200 ml). The combined ethereal extracts were washed with HCl (2 × 400 ml of a 2 M aq. solution), NaHCO₃ (2 × 400 ml of a saturated aq. solution) and brine (1 × 400 ml) before being dried (Na₂SO₄), filtered and concentrated under reduced pressure to afford a dark yellow oil. Subjection of this material to flash chromatography (silica gel, 2 : 3 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (*R*_f 0.6) afforded amide **4**¹⁶ (4.95 g, 89%) as a pale yellow oil. HRMS: *m/z* 203.1316 (*M*⁺); C₁₃H₁₇NO requires 203.1310; *ν*_{max} 3286, 3076, 3030, 2971, 2931, 1643, 1548, 1454, 1250, 993, 914, 730, 697 cm⁻¹; *δ*_H 7.34–7.26 (m, 5H), 5.83–5.69 (complex m, 2H), 5.11–5.01 (complex m, 2H), 4.48 (dd, *J* 14.7 and 5.6 Hz, 1H), 4.42 (dd, *J* 14.7 and 5.6 Hz, 1H), 2.44 (m, 1H), 2.25 (m, 1H), 2.18 (m, 1H), 1.18 (d, *J* 6.2 Hz, 3H); *δ*_C 175.8 (CO), 138.4 (C), 135.7 (CH), 128.3 (2 × CH), 127.4 (2 × CH), 127.1 (CH), 116.5 (CH₂), 43.0 (CH₂), 40.7 (CH), 38.2 (CH₂), 17.2 (CH₃); *m/z* 203 (*M*⁺, 47%), 188 [(*M* – CH₃)⁺, 22], 162 [(*M* – C₃H₅)⁺, 33], 91 (100).

(±)-Benzyl(2'-methylpent-4'-enyl)amine (5). Lithium aluminium hydride (13.7 ml of a 1.0 M solution in THF, 13.7 mmol) was added, dropwise, to a magnetically stirred solution of amide **4** (1.39 g, 6.86 mmol) in THF (50 ml) maintained at 0 °C under a nitrogen atmosphere. The resulting mixture was allowed to warm to 18 °C over *ca.* 1 h, stirred at this temperature for a further 15 h then quenched with ethyl acetate (20 mL). The resulting mixture was treated with sodium hydroxide (20 ml of a 2 M aq. solution) and the ensuing precipitate filtered through Celite™. The filtrate was treated with water (100 ml) and ethyl acetate (100 ml) and the separated aqueous phase extracted with ethyl acetate (3 × 100 ml). The combined organic extracts were then dried (Na₂SO₄), filtered and concentrated under reduced pressure to afford the title amine **5**¹⁷ (1.33 g, 99%) as a pale yellow oil. HRMS: *m/z*

174.1283 ($M - CH_3$)⁺; $C_{12}H_{16}N$ requires 174.1283; ν_{max} 3063, 3026, 2954, 2905, 2813, 1639, 1494, 1453, 1118, 993, 910, 734, 697 cm^{-1} ; δ_H 7.33–7.21 (complex m, 5H), 5.78 (m, 1H), 5.05–4.96 (complex m, 2H), 3.78 (s, 2H), 2.56 (dd, J 11.6 and 6.3 Hz, 1H), 2.43 (dd, J 11.6 and 6.9 Hz, 1H), 2.16 (m, 1H), 1.91 (m, 1H), 1.73 (m, 1H), 1.37 (br s, 1H), 0.91 (d, J 6.7 Hz, 3H); δ_C 140.5 (C), 137.0 (CH), 128.1 (2 \times CH), 127.8 (2 \times CH), 126.6 (CH), 115.7 (CH₂), 55.2 (CH₂), 53.9 (CH₂), 39.2 (CH₂), 33.0 (CH), 17.8 (CH₃); m/z 189 (M^+ , 58%), 188 [($M - H$)⁺, 67], 174 [($M - CH_3$)⁺, 22], 120 [($M - C_5H_9$)⁺, 92], 91 (100). This material was used without further purification in the next step of the reaction sequence.

(±)-Hex-5-enoic acid benzyl(2'-methylpent-4'-enyl)amide (6). DMTMM (2.77 g, 10.02 mmol) was added, in portions, to a magnetically stirred solution of amine **5** (1.26 g, 6.68 mmol) and 5-hexenoic acid (0.76 g, 6.68 mmol) in THF (60 ml) maintained at 0°C under a nitrogen atmosphere. The reaction mixture was allowed to warm to 18°C over *ca.* 1 h, stirred at this temperature for a further 15 h then poured into water (60 ml) and extracted with diethyl ether (3 \times 100 ml). The combined ethereal extracts were washed with HCl (2 \times 200 ml of a 2 M aq. solution), NaHCO₃ (2 \times 200 ml of a saturated aq. solution) and brine (1 \times 200 ml), then dried (Na₂SO₄), filtered and concentrated under reduced pressure to afford a dark yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 4 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.4) afforded amide **6** (800 mg, 42%) as a pale yellow oil and a *ca.* 1 : 1 mixture of rotamers (as judged by ¹³C NMR analysis). HRMS: m/z 285.2093 (M^+); $C_{19}H_{27}NO$ requires 285.2093; ν_{max} 2957, 2925, 1642, 1451, 1421, 911, 698 cm^{-1} ; δ_H 7.38–7.12 (complex m, 5H), 5.82–5.67 (complex m, 2H), 5.06–4.91 (complex m, 4H), 4.71–4.54 (complex m, 2H), 3.56–2.94 (complex m, 2H), 2.35 (dt, J 19.3 and 7.5 Hz, 2H), 2.18–2.00 (complex m, 3H), 2.00–1.70 (m, 4H), 0.89 (apparent t, J 6 Hz, 3H); δ_C 173.5 (C), 173.2 (C), 138.0 (CH), 137.7 (C), 137.0 (C), 136.6 (CH), 135.8 (CH), 128.8 (2 \times CH), 128.4 (2 \times CH), 127.8 (2 \times CH), 127.3 (CH), 127.1 (CH), 126.0 (2 \times CH), 116.8 (CH₂), 116.1 (CH₂), 115.1 (CH₂), 115.0 (CH₂), 52.3 (CH₂), 51.6 (CH₂), 51.5 (CH₂), 48.3 (CH₂), 38.8 (CH₂), 38.6 (CH₂), 33.2 (CH₂), 33.1 (CH₂), 32.4 (CH₂), 32.3 (CH₂), 32.1 (CH), 31.5 (CH), 24.9 (CH₂), 17.2(9) (CH₃), 17.2(6) (CH₃) (one signal due to CH and one due to CH₂ carbon are overlapping or obscured); m/z 285 (M^+ , 26%), 244 [($M - C_3H_5$)⁺, 26], 216 (27), 188 (28), 120 (100), 91 (94).

(±)-1-Benzyl-9-methylazacyclodecan-2-one (7). A solution of Grubbs' catalyst [(Cy₃P)₂Cl₂Ru=CHPh] (205 mg, 0.25 mmol) in CH₂Cl₂ (5 ml) was added dropwise (in two aliquots over 24 h) to a magnetically stirred solution of diene **6** (475 mg, 1.66 mmol) in CH₂Cl₂ (600 ml) maintained under a nitrogen atmosphere at 18°C. The resulting mixture was heated at reflux for 48 h, then cooled and concentrated under reduced pressure to give a light orange oil. This material was subjected to flash chromatography (silica gel, 1 : 5 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.3) gave an inseparable and *ca.* 3 : 1 mixture (as judged by NMR analysis) of the *E* and *Z* isomers of the expected unsaturated lactam (325 mg, 76%) as a pale yellow oil. This material was used immediately in the next step of the reaction sequence.

A magnetically solution of the above-mentioned lactam (325 mg, 1.26 mmol) in methanol (20 ml) containing 10% Pd on C (160 mg) was maintained under a hydrogen atmosphere at 18°C for 24 h. The resulting mixture was filtered through a short pad of Celite™ which was washed with methanol (150 ml). The combined filtrates were concentrated under reduced

pressure to afford a light yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 5 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.5) gave the saturated lactam **7** (325 mg, 99%) as crystalline masses, m.p. 46–49°C. HRMS: m/z 259.1934 (M^+); $C_{17}H_{25}NO$ requires 259.1936; ν_{max} 2930, 1632, 1450, 1144, 740, 700 cm^{-1} ; δ_H 7.30–7.10 (complex m, 5H), 5.37 (br d, J 14.2 Hz, 1H), 3.80 (br d, J 14.2 Hz, 1H), 3.40 (t, J 13.5 Hz, 1H), 2.90 (m, 2H), 2.20–1.96 (complex m, 3H), 1.60–1.10 (complex m, 9H), 0.76 (d, J 6.9 Hz, 3H); δ_C 173.9 (C), 137.6 (C), 128.4 (2 \times CH), 128.2 (2 \times CH), 127.1 (CH), 50.7 (CH₂), 46.8 (CH₂), 30.0 (CH₂), 29.0 (CH), 27.4 (CH₂), 26.0 (CH₂), 23.9 (CH₂), 21.0 (CH₂), 20.3 (CH₂), 15.8 (CH₃); m/z 259 (M^+ , 35%), 140 (35), 120 (100), 91 (100).

(±)-1-Benzyl-3-methylazacyclodecane (8). Lithium aluminum hydride (690 μ l of a 1.0 M solution in THF, 0.69 mmol) was added dropwise to a magnetically stirred solution of the lactam **7** (89 mg, 0.34 mmol) in THF (5 ml) maintained at 18°C under a nitrogen atmosphere. After the addition was complete stirring was continued for a further 16 h, then the reaction mixture was quenched with ethyl acetate (3 ml) and then diluted with water (40 ml) and CHCl₃ (40 ml). The separated aqueous phase was extracted with CHCl₃ (3 \times 40 ml) and the combined organic extracts dried (MgSO₄), filtered and concentrated under reduced pressure to give a light yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 5 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.5) gave the title amine **8** (84 mg, 99%) as a clear colourless oil. HRMS: m/z 245.2140 (M^+); $C_{17}H_{27}N$ requires 245.2144; ν_{max} 2922, 1477, 1451, 734, 697 cm^{-1} ; δ_H 7.40–7.20 (complex m, 5H), 3.84 (d, J 13.5 Hz, 1H), 3.10 (d, J 13.5 Hz, 1H), 2.77 (m, 1H), 2.40 (t, J 12.1 Hz, 1H), 2.20 (dt, J 12.1 and 5.0 Hz, 1H), 2.10 (dd, J 12.1 and 5.0 Hz, 1H), 2.02–1.56 (complex m, 6H), 1.54–1.30 (complex m, 7H), 0.80 (d, J 6.0 Hz, 3H); δ_C 139.9 (C), 129.2 (CH), 128.0 (CH), 126.5 (CH), 60.1(5) (CH₂), 60.0(8) (CH₂), 52.7 (CH₂), 31.8 (CH₂), 29.5 (CH), 26.1 (CH₂), 25.6 (CH₂), 25.1 (CH₂), 24.3 (CH₂), 22.5 (CH₂), 19.4 (CH₃); m/z 245 (M^+ , 35%), 244 [($M - H$)⁺, 30], 154 [($M - C_7H_7$)⁺, 72], 120 (77), 91 (100).

(±)-3-(3'-Methylazacyclodecan-1'-yl)propionitrile (10). Palladium hydroxide (120 mg of 20 wt% on carbon) was added to a solution of amine **8** (120 mg, 0.49 mmol) in CH₂Cl₂ (10 ml) maintained under an atmosphere of hydrogen (1 atm) and the resulting suspension stirred at 18°C for 24 h. The reaction mixture was then filtered through a pad of Celite™ and the residue washed with a solution of CH₂Cl₂ [pretreated with aqueous NH₄OH then dried (Na₂SO₄)] (3 \times 30 ml). The filtrate was concentrated under reduced pressure to afford (±)-3-methylazecane (**9**) as a dark green oil. This material was immediately dissolved in acrylonitrile (10 ml) containing acetic acid (50 μ l) and the resulting mixture heated at reflux for 16 h. The cooled reaction mixture was concentrated under a stream of nitrogen and the residue subjected to flash chromatography (silica gel, 1 : 19 v/v ethyl acetate–hexane elution). Concentration of the appropriate fractions (R_f 0.4) afforded nitrile **10** (37 mg, 36% from **8**) as a pale yellow oil. HRMS: m/z 208.1938 (M^+); $C_{13}H_{24}N_2$ requires 208.1939; ν_{max} 2924, 2850, 2804, 2246, 1457, 1377, 1124, 1079 cm^{-1} ; δ_H 2.89 (dt, J 13.2 and 7.6 Hz, 1H), 2.78–2.59 (complex m, 2H), 2.46 (m, 2H), 2.40–2.24 (complex m, 3H), 1.96–1.30 (complex m, 13H), 0.82 (d, J 6.7 Hz, 3H); δ_C 119.4 (C), 59.9 (CH₂), 52.5 (CH₂), 50.2 (CH₂), 31.8 (CH₂), 30.0 (CH), 26.6 (CH₂), 25.8 (CH₂), 24.4 (CH₂), 24.2 (CH₂), 22.0 (CH₂), 19.3 (CH₃), 14.7 (CH₂); m/z 208 (M^+ , 18%), 168 [($M - C_2H_2N$)⁺, 100], 149 (30), 126 (30), 97 (49), 83 (67).

(\pm)-3-(3'-Methylazacyclodecan-1'-yl)propylamine (1). Sodium borohydride (38 mg, 1.00 mmol) was added in portions to a magnetically stirred solution of nitrile **10** (8 mg, 0.04 mmol) and cobalt(II) chloride hexahydrate (23 mg, 0.10 mmol) in methanol (2 ml) maintained at 18 °C under a nitrogen atmosphere. After 2 h HCl (5 ml of a 2 M aq. solution) was added and the resultant mixture concentrated under reduced pressure. The residue thus obtained was then dissolved in NH₄OH (20 ml of a concentrated aq. solution) and CHCl₃ (20 ml) and the separated aqueous phase extracted with CHCl₃ (3 \times 20 ml). The combined organic extracts were dried (Na₂SO₄), filtered and concentrated under reduced pressure to afford a tan oil. Subjection of this material to flash chromatography (silica gel, 3 : 2 v/v methanol–chloroform elution) and concentration of the appropriate fractions (*R_f* 0.4) afforded the title amine **1**⁷ (6 mg, 90%) as a pale yellow oil. HRMS: *m/z* 212.2253 (*M*⁺); C₁₃H₂₈N₂ requires 212.2252; ν_{\max} 2947, 2923, 2867, 2849, 2792, 1578, 1473, 1455 cm⁻¹; δ_{H} 2.90 (br s, 2H), 2.69 (ddd, *J* 12.8, 10.6 and 4.0 Hz, 1H), 2.58 (br s 2H), 2.52–2.44 (complex m, 1H), 2.32 (dd, *J* 13.0 and 11.5 Hz, 1H), 2.15 (dt, *J* 13.0 and 4.5 Hz, 1H), 2.10–2.05 (complex m, 2H), 1.90–1.70 (complex m, 3H), 1.68–1.26 (complex m, 12 H), 0.78 (d, *J* 7.0 Hz, 3H); δ_{C} see Table 1; *m/z* 212 (*M*⁺, 7%), 182 [(*M* – CH₂NH₂)⁺, 13], 168 [(*M* – C₂H₄NH₂)⁺, 100], 154 (23), 126 (31).

Crystal data and refinement details for lactam **7**

Data collection and reduction. Crystallographic data for the title compound are given in Table 2. Intensity data were collected (from a plate only 0.017 mm thick) on a Nonius Kappa CCD diffractometer using graphite monochromated Mo-K α radiation (λ = 0.71073 Å) to a maximum 2θ value of 55°. Data were extracted from diffraction images *via* the DENZO¹⁸ package and an analytical absorption correction was applied.

Table 2 Crystallographic data for lactam **7**

Formula	C ₁₇ H ₂₅ NO
FW	259.393
Crystal system	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>a</i>
<i>a</i> /Å	8.6690(2)
<i>b</i> /Å	15.7588(3)
<i>c</i> /Å	11.4462(2)
β /°	102.0894(11)
<i>U</i> /Å ³	1529.02(5)
<i>Z</i>	4
<i>T</i> /K	200(±1)
μ /mm ⁻¹	0.069
No. of reflections	26911
Unique reflections	3513 (<i>R</i> _{int} = 0.072)
<i>R</i>	0.0372
<i>R_w</i>	0.0395

Structure solution and refinement. The structure was solved by direct methods¹⁹ and expanded using Fourier techniques.²⁰ The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at geometrically

determined positions riding on the carbon of attachment. The final cycle of full-matrix least squares refinement²⁰ was based on 1892 observed reflections [*I* > 3.0 σ (*I*)] and 173 variable parameters.

CCDC reference number 170402. See <http://www.rsc.org/suppdata/nj/b1/b105045c/> for crystallographic data in CIF or other electronic format.

Acknowledgements

We thank the Institute of Advanced Studies for financial support and the Australian Research Council for providing an APA(I) (to D. J. W.). Professor Wolfgang Steglich (Ludwig-Maximilians-Universität, München) is thanked for providing a preprint of his paper on the synthesis of compounds (+)- and (–)-**1**.

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