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AMOTIN AND AMOENIN, TWO SESQUITERPENES OF THE PICROTOXANE GROUP FROM *DENDROBIUM AMOENUM*

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Key Word Index—*Dendrobium amoenum*; Orchidaceae; sesquiterpenes; amotin; amoenin.

Abstract—Two new sesquiterpenes, amotin and amoenin, of the picrotoxane group were isolated from *Dendrobium amoenum*. The constitution of amoenin was evident from spectral investigations and by its conversion into α-dihydropicrotoxinin on oxidation with oxygen in the presence of platinum. The constitution of amotin was shown by its spectral properties and the conversion of aduncin into amotin by hydrogenolysis of its epoxide ring. That the configuration at C-4 in aduncin and amotin is *R* was supported by circular dichroism measurements on some derivatives of picrotoxinin and aduncin.

INTRODUCTION

The isolation and structure of aduncin (**4**), the first sesquiterpene of the picrotoxane group [1] isolated from the genera *Dendrobium*, was reported in a recent communication [2]. We now report the occurrence in *Dendrobium amoenum* of two new sesquiterpenes of this group. One of them, named amotin (**1**), differs from aduncin only in having a C-9 hydroxyl group instead of a C-8, C-9 epoxide function. The other, named amoenin (**2**), differs from α-dihydropicrotoxinin (**11**) in having hydroxylic groups at C-2 and C-11 instead of the lactone function.

RESULTS AND DISCUSSION

Amotin (**1**)

Elemental and spectral analyses showed amotin to have the molecular formula $C_{15}H_{20}O_6$. From the spectral similarities between amotin and aduncin it was concluded that the compounds were closely related. The ^{1}H NMR spectrum of amotin, compared with that of aduncin, suggested that the epoxide function in the former had been replaced by a C-9 hydroxyl function in the latter. That amotin indeed has the structure **1** was shown by the fact that it was formed upon hydrogenolysis of the epoxide ring in aduncin.

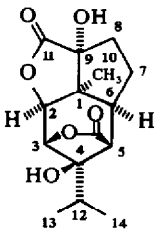
As a model compound for the hydrogenolysis of the epoxide ring, α-dihydropicrotoxinin (**11**) was used. The reaction, which was performed at 120 atm and 110° with palladium as a catalyst, gave **6**, **7** and **8** in the proportions 4.7:1.6:1.

Amoenin (**2**)

Elemental and spectral analyses showed that amoenin had the molecular formula $C_{15}H_{22}O_6$. Spectral analyses (IR, ^{13}C and ^{1}H NMR) showed amoenin to have only one γ-lactone function. The presence of an epoxide function, an isopropyl group and a methyl group was evident from its ^{1}H NMR spectrum. Furthermore the ^{1}H NMR spectrum showed, *inter alia*, a methine proton singlet at δ 4.49 ppm and an AX system at δ 4.10 and 5.16 ppm, J = 13 Hz. On acetylation, amoenin gave a diacetate (**3**), the ^{1}H NMR spectrum of which showed downfield shifts of the AX signals of 0.67 and 0.16 ppm, respectively, compared with that of amoenin. The methine proton signal was shifted downfield 1.13 ppm.

These results indicated the presence in amoenin of one primary and one secondary hydroxyl group. In addition to the spectral data above, decoupling experiments pointed to the structure **2** for amoenin. This structure was confirmed by the oxidation of amoenin to α-dihydropicrotoxinin (**11**), of known absolute configuration [1, 3, 4], using oxygen in the presence of platinum.

To gain evidence for the proposed [2] configuration at C-4 in aduncin (**4**), some derivatives of picrotoxinin (**10**)



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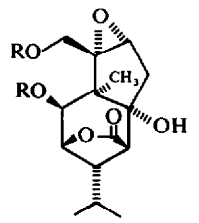
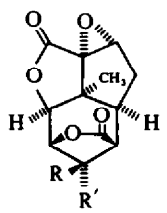
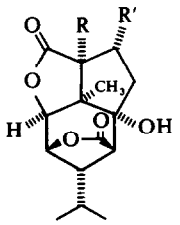


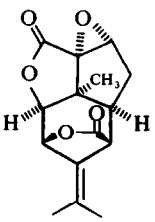
2 R = H
3 R = $COCH_3$



4 R = OH; R′ = $CH(CH_3)_2$
5 R = $CH(CH_3)_2$; R′ = H



6 R = OH; R′ = H
7 R = H; R′ = OH
8 R = R′ = H



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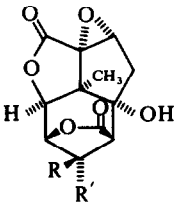
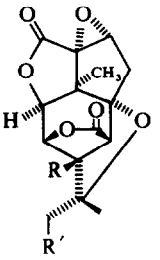


10 R = H; R′ = CH_2 = C—CH_3
11 R = H; R′ = $CH(CH_3)_2$
12 R = OH; R′ = CH_2 = C—CH_3
13 R = OH; R′ = $CH(CH_3)_2$
14 R = $CH(CH_3)_2$; R′ = H



15 R = OH; R′ = Br
16 R = H; R′ = Br
17 R = R′ = H

and aduncin (**4**) were synthesized and their CD spectra compared. Dehydration of aduncin (**4**) followed by catalytic hydrogenation gave **5**. The 4*R* configuration of **5** was confirmed by the fact that no coupling between H-3 and H-4 was observed in the ^{1}H NMR spectrum of **5** [2]. The compound **13** was produced by selenium dioxide oxidation of picrotoxinin (**10**) in water followed by catalytic hydrogenation. The oxidation step occurred with complete retention of the configuration at C-4 and no traces of the C-13 (14) hydroxylated isomer could be detected. The configuration at C-4 in the oxidation product (**12**) was shown by its reaction with bromine water to form the monobromo derivative **15**, analogous to the formation of β-bromopicrotoxinin (**16**) from picrotoxinin (**10**) under the same conditions [5, 6]. An acid catalysed isomerization at C-4 prior to cyclization seems improbable due to the fact that treatment of **12** with dil. HBr under the same conditions as used in the bromination step, gave a quantitative recovery of the starting material. The constitution of **15** was further supported by the similarities in the ^{1}H NMR spectra of **15**, **16** and **17**.

That the configuration at C-4 in aduncin (**4**) is *R* was supported by CD measurements on **4**, **5**, **11**, **13** and **14**, studying the Δε values at *ca* 228 nm. On comparing the CD spectra of **11** and **13** it was evident that replacement of the 4β hydrogen atom by a hydroxyl function had no influence on the Cotton effect. On the other hand, the CD curves of **5** and **14** showed that replacement of the C-6 hydroxyl function by a hydrogen atom resulted in a positive contribution of 1.0 units. On the basis of these results the calculated value for aduncin (**4**), with a 4*R* configuration, is −2.7 (starting from **13**: −3.7 + 1.0 = −2.7), a value in good agreement with the observed one (−2.8).

EXPERIMENTAL

Mps are corr. Elemental analyses were carried out at Alfred Bernhardt Mikroanalytisches Laboratorium, Elbach über Engelskirchen, West Germany. Plates precoated with Si gel F_{254} (Merck) were used for TLC and spots were visualized by I_2 vapor and by spraying with H_2SO_4 (8%) followed by heating to 120°. Optical rotations were measured in Me_2CO, NMR spectra in C_5D_5N with TMS as internal standard and CD spectra in MeOH unless otherwise stated.

Plant material. Dendrobium amoenum Wall. was delivered from Chandra Orchid & Bulb Nurseries, 8.5 miles P.O. Kalimpong, West Bengal, India.

Isolation of **1** *and* **2**. Fresh plants of *D. amoenum* (5.8 kg) were extracted with MeOH (15 l.). The extract was concd to 1 l. and diluted with H_2O (1 l.). After washing with $CHCl_3$ (3 × 400 ml), the soln was saturated with *n*-BuOH and extracted with *n*-BuOH saturated with H_2O (6 × 300 ml). The butanolic phase was washed with H_2O saturated with *n*-BuOH (75 ml) and evapd to dryness. A part (6.5 g) of the residue (21 g) was filtered through a column of Sephadex LH-20 (7.5 × 57 cm) using EtOH–H_2O (1:1) as eluent. The progress of the separation was followed by using a refractive index detector and by TLC ($CHCl_3$–MeOH–H_2O, 65:35:10 lower phase). The fraction containing **1** and **2** (0.6 g, R_f 0.8) was chromatographed on Si gel (2.6 × 25 cm) using EtOAc–toluene (5:1) as eluent to give **1** (90 mg, R_f 0.6) and a second fraction containing mainly **2** (100 mg, R_f 0.3). The latter fraction was submitted to PLC on Si gel using EtOAc–toluene–MeOH (10:4:1) as eluent giving **2** (57 mg, R_f 0.4).

Characterization of **1**. Prisms (EtOH), mp 255–256°; $[\alpha]_{578}^{21}$ −13° (*c* 1.9). (Found: C, 60.9; H, 6.8; O, 32.3. $C_{15}H_{20}O_6$ requires: C, 60.8; H, 6.8; O, 32.4%). IR ν_{max}^{KBr} cm^{-1}: 3650–3050 (s), 1785 (s), 1765 (s). CD, nm (Δε): $\lambda_{extrema}$ 204.5 (−0.08), 226 (+0.2). ^{1}H NMR: δ 1.22 (*d*, 6H, *J* = 6.5 Hz), 1.66 (*s*, 3H), 1.96–3.02 (7H), 2.93 (*d*, 1H, *J* = 5.5 Hz, H-5), 4.78 (*d*, 1H, *J* = 3.5 Hz, H-2), 4.98 (*s*, OH), 5.13 (*d*, 1H, *J* = 3.5 Hz, H-3). ^{13}C NMR: δ 16.1 (*q*), 16.9 (*q*), 25.8 (*q*), 28.9 (*d*), 30.4 (*t*), 38.1 (*t*), 47.4 (*d*), 50.8 (*s*), 52.2 (*d*), 81.7 (*s*), 83.5 (*d*), 84.2 (*d*), 85.8 (*s*), 178.4 (*s*), 178.8 (*s*). MS *m/e* (rel. int.) (165°): 296 (M^+, 0.5), 253 (0.5), 234 (1), 226 (1), 219 (5), 209 (12), 206 (6), 191 (42), 179 (11), 173 (15), 163 (21), 147 (82), 137 (19), 133 (18), 119 (28), 97 (39), 93 (28), 71 (26), 55 (29), 43 (100), 41 (60).

Characterization of **2**. Needles (EtOAc–hexane), mp 195–199° (d); $[\alpha]_{578}^{21}$ +55° (*c* 1.2). (Found: C, 60.3; H, 7.4; O, 32.3. $C_{15}H_{22}O_6$ requires: C, 60.4; H, 7.4; O, 32.2%). IR ν_{max}^{KBr} cm^{-1}: 3650–3060 (s), 3050 (w), 1780 (s), 1750 (s). CD, nm (Δε): $\lambda_{extremum}$ 222 (+1.1). ^{1}H NMR: δ 0.78 (*d*, 3H, *J* = 6.5 Hz), 1.06 (*d*, 3H, *J* = 6 Hz), 1.09 (*s*, 3H), 2.0–2.2 (*m*, 1H, H-4), 2.33 (*d*, 1H, *J* = 14 Hz, H-7$_\alpha$), 2.4–2.9 (*m*, 1H, H-12), 2.78 (*dd*, 1H, J_1 = 14 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 2.88 (*d*, 1H, *J* = 3.5 Hz, H-5), 3.70 (*d*, 1H, *J* = 3.5 Hz, H-8), 4.10 (*d*, 1H, *J* = 13 Hz, H-11), 4.49 (*s*, 1H, H-2), 4.98 (*d*, 1H, *J* = 5.5 Hz, H-3), 5.05 (*s*, OH), 5.16 (*d*, 1H, *J* = 13 Hz, H′-11). ^{13}C NMR: δ 20.1 (*q*), 20.5 (*q*), 22.1 (*q*), 26.7 (*d*), 42.9 (*t*), 53.6 (*d*), 53.6 (*s*), 54.3 (*d*), 61.0 (*d*), 64.7 (*t*), 72.3 (*d*), 74.5 (*s*), 85.1 (*d*), 87.5 (*s*), 176.5 (*s*). MS *m/e* (rel. int.) (160°): 298 (M^+, 2), 282 (1), 280 (2), 267 (3), 262 (6), 255 (2), 249 (3), 237 (11), 222 (10), 209 (16), 191 (27), 166 (43), 151 (24), 143 (77), 125 (79), 109 (49), 97 (96), 43 (96), 41 (100).

Amoenin diacetate (**3**). Amoenin (**2**, 10 mg) was treated with Ac_2O–C_5H_5N (1:1) at room temp. for 6 hr and the mixture was then evapd to dryness. Needles (toluene), mp 204–206°; $[\alpha]_{578}^{21}$ +8° (*c* 0.7). IR ν_{max}^{KBr} cm^{-1}: 3440 (s), 3040 (w), 1785 (s), 1750 (s), 1740 (s), 1715 (s). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (m), 3600–3300 (w), 1785 (s), 1740 (s). CD, nm (Δε) $\lambda_{extremum}$ 219 (+1.6). ^{1}H NMR: δ 1.06 (*d*, 3H, *J* = 6.5 Hz), 1.08 (*d*, 3H, *J* = 6 Hz), 1.59 (*s*, 3H), 2.01 (*s*, 3H), 2.14 (*s*, 3H), 1.9–2.3 (*m*, 1H, H-4), 2.30 (*d*,1H, *J* = 14 Hz, H-7$_\alpha$), 2.5–2.9 (*m*, 1H, H-12), 2.78 (*dd*, 1H, J_1 = 14 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 2.92 (*d*, 1H, *J* = 4 Hz, H-5), 3.72 (*d*, 1H, *J* = 3.5 Hz, H-8), 4.77 (*d*, 1H, *J* = 12.5 Hz, H-11), 4.92 (*d*, 1H, *J* = 5 Hz, H-3), 5.09 (*s*, OH), 5.32 (*d*, 1H, *J* = 12.5 Hz, H-11), 5.62 (*s*, 1H, H-2).

α-Dihydropicrotoxinin (**11**). Pictrotoxinin (**10**) was hydrogenated as described by ref. [7] to give **11**. Plates (EtOH), mp 259–260°; (Lit. [7] mp 252°). $[\alpha]_{578}^{21}$ −3° (*c* 0.6), (Lit. [2]

$[\alpha]_{578}^{23}$ −5° (*c* 0.5, Me_2CO). (Lit. [2] CD, nm (Δε): $\lambda_{extremum}$ (MeOH) 228 (−3.7)).

Oxidation of amoenin (**2**). Amoenin (**2**, 10 mg) was dissolved in EtOAc (3.5 ml) and Pt freshly prepared from PtO_2, 115 mg [8, 9] was added. The mixture was stirred under O_2 at room temp. for 1 hr, filtered and evapd to give **11** in a quantitative yield. Plates (EtOH), mp 259–261° $[\alpha]_{578}^{21}$ −3° (*c* 0.6). The IR, MS and ^1H NMR spectra were in accordance with those of α-dihydropicrotoxinin (**11**) derived from picrotoxinin (**10**).

Hydrogenolysis of α-dihydropicrotoxinin (**11**). α-Dihydropicrotoxinin (528 mg) was hydrogenated at 110 atm in H_2O (300 ml) with Pd (2 g, 10% on C) as catalyst. The suspension was heated to 125° (required time 6 hr). After 1 hr at 125° the heating was shut off and the hydrogenation was continued for 16 hr. After working up, the residue was chromatographed on Si gel (2.5 × 30 cm) using EtOAc–toluene (1:1) as eluent to give the starting material (24 mg, R_f 0.5), **7** (102 mg, R_f 0.2) and a fraction containing **6** and **8** (R_f 0.4). Further chromatography on Si gel (2.6 × 40 cm) using $CHCl_3$–MeOH (19:1) as eluent gave **8** (66 mg, R_f 0.5) and **6** (308 mg, R_f 0.3).

Characterization of **6**. Needles ($EtOH–H_2O$) mp 214–217° (d); $[\alpha]_{578}^{21}$ −2° (*c* 2.3). IR ν_{max}^{KBr} cm^{-1}: 3510 (s), 3380 (s), 1785 (s). CD, nm (Δε): $\lambda_{extremum}$ 227 (−0.5). ^1H NMR: δ 1.00 (*d*, 3H, *J* = 6 Hz), 1.18 (*d*, 3H, *J* = 5.5 Hz), 1.76 (*s*, 3H), 1.96–2.88 (7H, 6H on addition of H_2O), 3.10 (*d*, 1H, further coupled, *J* = 3 Hz, H-5), 4.66 (*d*, 1H, *J* = 3.5 Hz, H-2), 4.96–5.10 (*m*, 1H, H-3), 5.2 (*s*, OH).

Characterization of **7**. Long plates (H_2O), mp 216–220° (d); $[\alpha]_{578}^{21}$ −67° (*c* 2.2). IR ν_{max}^{KBr} cm^{-1}: 3500 (s), 3200 (m), 1770 (s). CD, nm (Δε): $\lambda_{extremum}$ 227 (+1.5). ^1H NMR ($C_5D_5N + D_2O$): δ 0.97 (*d*, 3H, *J* = 6 Hz), 1.15 (*d*, 3H, *J* = 5.5 Hz), 1.71 (*s*, 3H), 1.98–2.50 (2H, H-4 and H-12), 28.7 (*dd*, 1H, J_1 = 13 Hz, J_2 = 11 Hz, H-7$_\alpha$), 3.14 (*d*, 1H, *J* = 3.5 Hz, H-5), 3.30 (*d*, 1H, *J* = 7 Hz, H-9), 3.34 (*dd*, 1H, J_1 = 13 Hz, J_2 = 6.5 Hz, H-7$_\beta$), 4.62 (*d*, 1H, *J* = 3.5 Hz, H-2), 4.84–5.18 (2H, H-3 and H-8).

Characterization of **8**. Prisms (MeOH), mp 272–275°: $[\alpha]_{578}^{21}$ −44° (*c* 1.5). IR ν_{max}^{KBr} cm^{-1}: 3510 (s), 1785 (s), 1750 (s). CD, nm (Δε): $\lambda_{extremum}$ 227 (+1.4). ^1H NMR ($C_5D_5N + D_2O$): δ 0.95 (*d*, 3H, *J* = 6 Hz), 1.14 (*d*, 3H, *J* = 5.5 Hz), 1.59 (*s*, 3H), 1.72–2.90 (6H), 2.94–3.24 (2H), 4.64 (*d*, 1H, *J* = 3.5 Hz, H-2), 4.90–5.04 (*m*, 1H, H-3).

Hydrogenolysis of aduncin (**4**). Aduncin (16 mg) was hydrogenated at 110 atm in H_2O (50 ml) with Pd (1 g, 10% on C) as catalyst. The suspension was heated to 100° (required time 5 hr). After 1 hr at 100° the heating was shut off and the hydrogenation was continued for 12 hr. PLC on Si gel using $CHCl_3$–MeOH (19:1) as eluent gave **1** (7.6 mg, R_f 0.2). Prisms (EtOH), mp 254–255°; $[\alpha]_{578}^{21}$ −15° (*c* 0.8). The IR, MS and ^1H NMR spectra were in accordance with those of the natural product.

Dehydration of aduncin (**4**). Aduncin (26 mg) was dissolved in C_5H_5N (1.5 ml) at 0°. $POCl_3$ (0.07 ml) was added and the soln was allowed to stand at room temp. for 120 hr, cf. [10]. The reaction mixture was poured into ice-H_2O (4 ml) and then extracted with $CHCl_3$ (5 × 1 ml). The $CHCl_3$ phase was dried (Na_2SO_4), filtered and evapd to give **9** and starting material. Chromatography on Si gel (1.3 × 18 cm) using $CHCl_3$–MeOH (19:1) as eluent, followed by crystallization from EtOH gave **9** (10.2 mg). Needles, mp 287–289° $[\alpha]_{578}^{21}$ −1° (*c* 1.0). ^1H NMR: δ 1.22 (*s*, 3H), 1.66 (*s*, 3H), 1.69 (*s*, 3H), 2.11 (*dd*, 1H, J_1 = 15 Hz, J_2 = 7 Hz, H-7$_\alpha$), 2.47 (*dd*, 1H, J_1 = 7 Hz, J_2 = 6 Hz, H-6), 2.50 (*dd*,1H, J_1 = 15 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.38 (*d*, 1H, *J* = 6 Hz, H-5), 4.23 (*d*, 1H, *J* = 3.5 Hz, H-8), 4.70 (*d*, 1H, *J* = 4 Hz, H-2), 5.69 (*d*, 1H, *J* = 4 Hz, H-3).

Hydrogenation of **9**. **9** (10 mg) was dissolved in EtOAc (15 ml) and hydrogenated over Pd (88 mg, 10% on C) at room temp. and atm pres. for 3 hr to give **5**. Needles (EtOH), mp 195–197° $[\alpha]_{578}^{21}$ −33° (*c* 0.8). CD, nm (Δε): $\lambda_{extremum}$ 227.5 (−4.4). ^1H NMR: δ 0.87 (*d*, 3H, *J* = 6.5 Hz), 0.89 (*d*, 3H, *J* = 6.5 Hz), 1.33 (*s*, 3H), 1.4–1.86 (2H, H-4 and H-12), 2.12 (*dd*, 1H, J_1 = 15 Hz, J_2 = 7.5 Hz, H-7$_\alpha$), 2.32–2.60 (2H, H-6 and H-7$_\beta$), 2.68 (*d*, 1H, *J* = 6 Hz, H-5), 4.22 (*d*, 1H, *J* = 3.5 Hz, H-8), 4.74 (*d*, 1H, *J* = 3.5 Hz, H-2), 5.09 (*d*, 1H, *J* = 3.5 Hz, H-3).

Selenium dioxide oxidation of picrotoxinin (**10**). Picrotoxinin (300 mg) was dissolved in H_2O (15 ml) at 100°. SeO_2 (120 mg) in H_2O (3 ml) was added and the mixture was refluxed for 5 min, cooled and filtered through a Si gel column (5 × 13 cm) using EtOAc–toluene (1:1) as eluent. The fraction containing **12** (R_f 0.2) was evapd, dissolved in hot EtOH and filtered through finely divided Ag to remove traces of colloidal Se. Evapn gave crude **12** (150 mg). Recrystallization from H_2O gave **12** (55 mg). Needles (H_2O), mp 233–236° (d); $[\alpha]_{578}^{21}$ +95° (*c* 1.9). ^1H NMR: δ 1.51 (*s*, 3H), 2.33 (*s*, 3H), 2.40 (*d*, 1H, *J* = 15 Hz, H-7$_\alpha$), 3.24 (*dd*, 1H, J_1 = 15 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.40 (*s*, 1H, H-5), 4.16 (*d*, 1H, *J* = 3.5 Hz, H-8), 5.10 (*s*, OH), 5.22 (*br s*, 1H), 5.40 (*s*, 1H), 5.55 (*s*, 2H).

Hydrogenation of **12**. **12** (75 mg) was dissolved in MeOH (5 ml) and hydrogenated over Pd (50 mg, 10% on C) at room temp. and atm pres. for 4 hr to give **13**. Needles (H_2O), mp 250–256° (d): $[\alpha]_{578}^{21}$ +27° (*c* 1.7). CD, nm (Δε): $\lambda_{extremum}$ 230 (−3.7). ^1H NMR: δ 1.27 (*d*, 3H, *J* = 7 Hz), 1.41 (*d*, 3H, *J* = 6.5 Hz), 1.60 (*s*, 3H), 2.2–2.9 (*m*, 1H, H-12), 2.39 (*d*, 1H, *J* = 15 Hz, H-7$_\alpha$), 3.21 (*dd*, 1H, J_1 = 15 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.23 (*s*, 1H, H-5), 4.16 (*d*, 1H, *J* = 3.5 Hz, H-8), 5.04 (*s*, OH), 5.13 (*d*, 1H, *J* = 3 Hz, H-2), 5.30 (*d*, 1H, *J* = 3 Hz, H-3).

β-Dihydropicrotoxinin (**14**). Picrotoxinin (**10**) was hydrogenated as described by ref. [7] to give **14**. Prismatic needles (EtOAc), mp 257–260°; (Lit. [7] mp 256–257°). $[\alpha]_D^{21}$ −25°, $[\alpha]_{578}^{21}$ −26° (*c* 3.3), Lit. [7] $[\alpha]_D^{20}$ −24.69°). CD, nm (Δε): $\lambda_{extremum}$ 228 (−5.4).

Bromination of **12**. **12** (43 mg) was dissolved in H_2O (1 ml) at 100°. Bromine H_2O was added until the soln remained pale yellow. The soln was then allowed to cool to room temp. The needles were filtered off, washed with H_2O and dried to give crude **15** (45 mg). Needles ($EtOH–H_2O$), mp 214–220° (d); $[\alpha]_{578}^{21}$ −19° (*c* 2.0). ^1H NMR: δ 1.49 (*s*, 3H), 1.82 (*s*, 3H), 2.26 (*dd*, 1H, J_1 = 14 Jz, J_2 = 1.5 Hz, H-7$_\alpha$), 2.64 (*dd*, 1H, J_1 = 14 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.91 (*d*, 1H, *J* = 1.5 Hz, H-5), 4.03 (*s*, 2H, CH_2Br), 4.36 (*dd*, 1H, J_1 = 3.5 Hz, J_2 = 1.5 Hz, H-8), 5.1 (*s*, OH), 5.63 (*dd*, 1H, J_1 = 5 Hz, J_2 = 1.5 Hz, H-3), 5.76 (*d*, 1H, *J* = 5 Hz, H-2).

β-Bromopicrotoxinin (**16**). **16** was prepared as described by ref. [5]. Needles (EtOH), mp 263–269° (d); (Lit. [5] mp 259–260°). $[\alpha]_D^{21}$ −129°, $[\alpha]_{578}^{21}$ −135° (*c* 0.6, $CHCl_3$), (Lit. [5] $[\alpha]_D^{17}$ −132.5° ($CHCl_3$)). ^1H NMR: δ 1.41 (*s*, 3H), 1.59 (*s*, 3H), 2.26 (*dd*, 1H, J_1 = 14 Hz, J_2 = 1 Hz, H-7$_\alpha$), 2.58 (*dd*, 1H, J_1 = 14 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.5–3.7 (2H, H-4 and H-5), 3.80 and 3.85 (AB pattern, 2H, *J* = 11.5 Hz, CH_2Br), 4.35 (*dd*, 1H, J_1 = 3.5 Hz, J_2 = 1 Hz, H-8), 5.35–5.56 (2H, H-2 and H-3).

Anhydropicrotin (**17**). **17** was prepared as described by ref. [11]. Rhombs (AcOH), mp 328–331° (d); (Lit. [12] mp 322–324° (d)). $[\alpha]_D^{21}$ −99° (*c* 0.09, AcOH), (Lit. [12] $[\alpha]_D^{21}$ −99° (*c* 0.09, AcOH)). ^1H NMR: δ 1.32 (*s*, 6H), 1.40 (*s*, 3H), 2.21 (*d*, 1H, further coupled, *J* = 14 Hz, H-7$_\alpha$), 2.52 (*dd*, 1H, J_1 = 14 Hz, J_2 = 3.5 Hz, H-7$_\beta$), 3.24–3.50 (2H, H-4 and H-5), 4.32 (*dd*, 1H, J_1 = 3.5 Hz, J_2 = 1.5 Hz, H-8), 5.16–5.37 (2H, H-2 and H-3).

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