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# TWO NEW $C_{15}$ ACETYLENES FROM THE MARINE RED ALGA *LAURENCIA OBTUSA*[1)]

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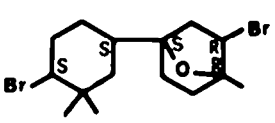
Abstract - Two new brominated $C_{15}$-nonterpenoids which are unusual oxolane derivatives possessing a propargylic bromide side chain have been isolated from the red alga L. obtusa and their structures were determined as 6 and 7. The $^1H$-NMR spectra of these new compounds are presented and assignments made.

Of the large number of metabolites isolated from the red alga of wide distribution Laurencia obtusa, most are halogenated sesquiterpenes[2)] and a smaller group consists of $C_{15}$ halogenated acetylenic ethers[3)]. In continuing our work on the yellowish-green coloured form of L. obtusa, collected at Graciosa Island (Canary Islands), we have recently reported[4)] the isolation and structural determination, including the absolute configuration, of the unique dibrominated sesquiterpene 1 and the crystalline tribrominated $C_{15}$ nonterpenoid 5. In this paper we wish to describe the structures of two further brominated $C_{15}$ acetylenes, compounds 6 and 7, which contain oxolane rings and propargylic bromide functionalities.

Hexane, ether and acetone extracts of powdered, air-dried L. obtusa were combined to yield a viscous oil (1.5% dry weight) which was chromatographed on silica gel, using a solvent gradient of increasing polarity from n-hexane to ethyl acetate. Selected fractions were rechromatographed to obtain individual compounds of which obtusin (5) (2.9% dry lipid weight) was the major metabolite. The least polar sesquiterpene metabolite was the dibrominated ether 1 which was isolated as a crystalline substance (0.42% of lipid weight), mp 100-102°C, $[\alpha]_D$-8.7° (c, 2.86, $CHCl_3$), and the structure and absolute configuration determined by x-ray crystallographic techniques[4)]. The remaining sesquiterpenes isolated were identified with the previously reported bromochlorinated ethers: caespitol (2)[5)] and isocaespitol (3)[6)], and the monocyclic farnesane derivative α-snyderol (4)[7)].

The nonterpenoid compounds isolated from the concentrated acetone extract of the alga possess a characteristic terminal acetylenic group. This common characteristic allowed them to be identified by infrared spectroscopy ($\nu_{C-H}$= 3300 $cm^{-1}$) in the mixtures enriched in these components. Although at least six compounds with this common characteristic were detected, only three of them could be isolated without decomposing and their structures be determined. Compound 5 which was isolated in greatest yield also proved to be the only crystallizable compound, its isolation and purification also proving comparatively easier. Recrystallizations of 5 from n-hexane gave long needles, mp 93-95°C, $[\alpha]_D$-107° (c, 0.84, $CHCl_3$). The high resolution mass



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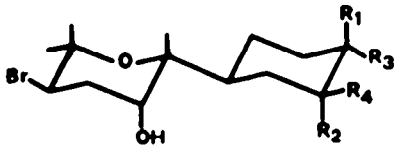
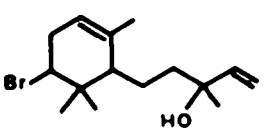


2: $R_1$=$CH_3$, $R_2$=H, $R_3$=Cl, $R_4$=Br

3: $R_1$=Br, $R_2$=Cl, $R_3$=$CH_3$, $R_4$=H



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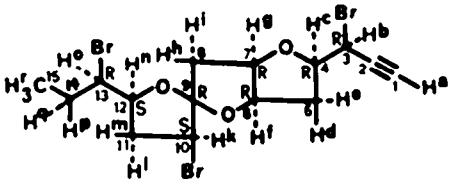

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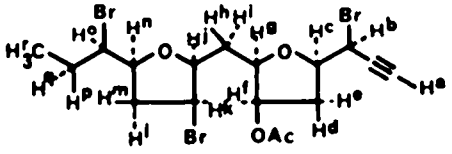

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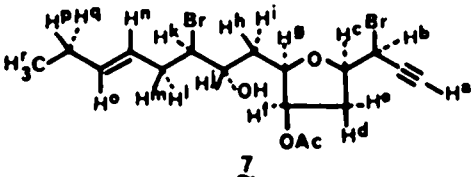

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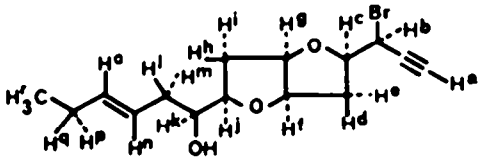

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spectrum of compound 5 indicated an elemental composition of $C_{15}H_{19}Br_3O_3$. The non-carbocyclic, although tricyclic nature of 5, and the presence of three ether bridges, were demonstrated from the absence of any further unsaturation beside the acetylenic moiety. The $^1$H-NMR spectrum of 5 (Table 1) presented signals which could be assigned to a monosubstituted acetylenic function, four α-ether protons and three α-halogen protons. The $^{13}$C-NMR spectrum confirmed that 5 was highly oxygenated as five carbon-oxygen, beside the three carbon-bromine, type resonances were discernible. The $^{13}$C-NMR spectrum showed the presence of one methyl at 11.7; four methylenes, 29.1, 37.5, 39.2, 40.0; eight methines, 40.4, 50.5, 61.5, 76.0, 80.8, 83.9, 84.6, 86.7; and two fully-substituted carbon atoms, 80.2, 115.5. The structure of 5, including the absolute configuration of its chiral centres, was determined by single x-ray diffraction studies[4].

In addition, two more polar halogenated acetylenes were identified in subsequent fractions of the lipid extract. From the n-hexane-ethyl acetate (4:1) eluent the tribrominated acetate 6 was isolated as a light mobile oil, $(\alpha)_D$-29.3 (c, 1.14, $CHCl_3$). Mass spectral analysis established that this new acetylenic ether has the elemental composition $C_{17}H_{23}Br_3O_4$. The IR spectrum [$\nu_{max}^{CHCl_3}$ 3300, 1730, 1430, 1250, 1070 $cm^{-1}$] showed the presence of an acetoxyl group. The $^1$H-NMR spectrum of 6 (Table 1) presented signals which could be assigned to a monosubstituted acetylenic side chain, four α-ether protons, one α-acetoxy proton, and three α-halogen protons. The $^{13}$C-NMR spectrum showed the presence of two methyls at 11.93, 21.08; four methylenes, 29.35, 32.41, 32.89, 38.21; nine methines, 39.07, 55.24, 61.33, 71.78, 73.11, 76.14, 80.96, 82.05; and two fully-substituted carbon atoms, 170.03, 80.09. Comperative analyses of the spectroscopic data

obtained for 5 and 6 allowed the structure proposed in 6 to be assigned to the latter.

Compound 7 was isolated also as a colourless oil, $[\alpha]_D$-14.5 (c, 0.62, $CHCl_3$). Mass spectral analysis gave the molecular formula of $C_{17}H_{24}Br_2O_4$, $M^+$ at *m/z* 450, 452, 454. The IR spectrum of 7 showed the presence of hydroxyl and acetoxyl groups ($\nu_{max}^{film}$ 3525, 3300, 2120, 1730, 1250, 965 $cm^{-1}$). The $^1$H-NMR spectrum (see Table 1) showed the presence of a bromo-propargylic and 2-hydroxy-3-bromo-trans-5-octenyl side chains. The $^{13}$C-NMR spectrum showed the presence of two methyls, 13.71, 21.19; four methylenes, 25.66, 32.22, 32.41, 38.48; nine methines, 38.04, 57.23, 72.05, 72.44, 76.61, 80.14, 81.29, 124.49, 136.33), and two fully-substituted carbons, 80.61, 170.73. Treatment of 7 with potassium carbonate in acetone gave an unstable epoxy-alcohol which it further rearranges to the more stable compound 8 containing a 2,6-dioxa-bicyclo|3.3.0|octane ring system. Detailed $^1$H-NMR spectrum of 8 is comparatively shown in Table 1. Related compounds possessing a bromoallene instead of the propargylic bromide moiety have been recently reported from the red alga Laurencia nipponica[8].

## EXPERIMENTAL

Mps were determined on a Kofler block and are uncorr. Infrared spectra were recorded on Perkin-Elmer Mod. 237 and Mod. 681 spectrophotometers. Optical rotations were determined for solutions in chloroform with a Perkin-Elmer 141 polarimeter. $^1$H-NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) and Bruker Mod. WM 360 spectrometers, chemical shifts are reported relative to $Me_4Si$ (δ0) and coupling constants are given in hertz. $^{13}$C-NMR spectra were obtained on a Bruker Mod. WM 360 and the chemical shifts are reported relative to $Me_4Si$ (δ0). Low and high resolution mass spectra were obtained from a VG Micromass ZAB-2F. Column and dry column chromatography were performed on silica gel 6, all Merck products. The TLC plates were developed by spraying with 6N-sulphuric acid and heating. All solvents were purified by standard techniques. Anhydrous sodium sulphate was used for drying solutions.

### Collection, extraction and chromatographic separation

Laurencia obtusa was collected in September 1981 by hand, using SCUBA (-3 to -10 m) in Graciosa Island; air-dried and ground in a Wiley mill to a 1 mm particle size. The dried alga (6.2 kg) was extracted in a Soxhlet apparatus for 24h each with hexane ( 5 L), diethyl ether (5 L), and acetone (5 L). The combined extracts were evaporated to leave a dark-green viscous oil (94.3 g, 1.5% dry weight). The crude extract (94.3 g) was added as a concentrated n-hexane solution to a column (90 x 7 cm) containing silica gel (980 g) in n-hexane). One-litre fractions were collected employing the following elution scheme: hexane, fractions 1-12; hexane/ethyl acetate (20/1), fractions 13-16; hexane/ethyl acetate (10/1), fractions 17-20; hexane/ethyl acetate (4/1), fractions 21-28; hexane/ethyl acetate (7/3), fractions 29-35; hexane/ethyl acetate (3/2), fractions 36-40; hexane/ethyl acetate (2/3), fractions 41-47; ethyl acetate, fractions 48-54. Fractions exhibiting similar t.l.c. profiles were combined. A portion of 1.06 g of combined fractions 2-12 (2.3 g) was chromatographed on 120 g of silica gel H using n-hexane as solvent and collecting 20 ml fractions. Fractions 7-12 yielded compound 1 (112 mg). Fractions 16-20 (1.77 g) was chromatographed on 200 g of silica gel H using n-hexane-ethyl acetate (10:1) as solvent and collecting 20 ml fractions; fractions 10-12 yielded isocaespitol (2) (23 mg) and fractions 14-18 yielded caespitol (3) (18 mg). A portion of 4.3 g of combined fractions 21-28 (6.5 g) was chromatographed on a column (30 x 2 cm) containing silica gel (35 g) in 5% ethyl acetate in n-hexane; fractions 2-7 yielded α-snyderol (3) (22 mg), and fractions 12-18 gave pure obtusin (5) 218 mg).

Fractions 29-36 (10.3 g) were rechromatographed on a column (40 x 5 cm) containing silica gel (60 g) in 20% ethyl acetate in n-hexane, which allowed isolation of compound 6 (fractions 7-12, 28 mg) and compound 7 (fractions 17-22, 62 mg).

Compound 1: was isolated as a crystalline substance, mp 100-102°C, $[\alpha]_D$-8.7 (c, 2.86, $CHCl_3$). IR $\nu_{max}^{KBr}$ 1450, 1380, 1220, 1105, 860 and 760 $cm^{-1}$. Mass measurement, $C_{15}H_{24}Br_2O$, $M^+$ at *m/z* 378, 380, 382; high resolution 364.0050 ($C_{15}H_{22}{}^{81}Br_2$; Δ-0.3), 323.9729 ($C_{12}H_{18}{}^{81}Br_2$; Δ+0.5), 202.0184 $C_9H_{13}{}^{81}Br$; Δ-0.4). $^1$H-NMR ($CDCl_3$, 360 MHz) 3.92 (1H, *dd*, *J*= 12.5, 4.3 Hz), 3.83 (1H, *d* of *dd*, *J*= 10.8, 8.4, 2.6 Hz), 2.54(1H, *d* of *dd*, *J*= 5.4, 3.4, 1.2 Hz), 2.30 (1H, *bt*, *J*= 12.5 Hz), 2.16 (1H, *dq*, *J*= 11.0, 3.4 Hz), 2.0 (2H, *m*), 1.5-1.8 (6H, *m*), 1.43 (3H, *q*), 1.1-1.2 (2H, *m*), and 1.06 (6H, *s*). $^{13}$C-NMR ($CDCl_3$) 89.0 (*s*), 86.1 (*s*), 65.8 (*d*), 52.2 (*d*), 44.4 (*t*), 41.6 (*t*), 37.9 (*d*), 36.5 (*s*), 33.9 (*t*), 33.7 (*t*), 32.0 (*t*), 31.8 (*q*), 29.3 (*t*), 20.5 (*q*), 18.8 (*q*).

TABLE 1: $^1$H-NMR spectra of compounds 5, 6, 7, 8 showing chemical shifts and multiplicities[a,b]

| Proton(s) at carbon no. | H | Compound 5 | | Compound 6 | | Compound 7 | | Compound 8 | |
|---|---|---|---|---|---|---|---|---|---|
| | | δ | Multiplicity, $J$(Hz) | δ | Multiplicity, $J$(Hz) | δ | Multiplicity, $J$(Hz) | δ | Multiplicity, $J$(Hz) |
| 1..... | $H^a$ | 2.65 | $d, J_{ab}$=2.4 | 2.63 | $d, J_{ab}$=2.5 | 2.69 | $d, J_{ab}$=2.2 | 2.67 | $d, J_{ab}$=2.4 |
| 2..... | - | - | - | - | - | - | - | - | - |
| 3..... | $H^b$ | 4.93 | $dd, J_{ba}$=2.4; $J_{bc}$=9.4 | 4.54 | $dd, J_{ba}$=2.5; $J_{bc}$=8.5 | 4.58 | $dd, J_{ba}$=2.2; $J_{bc}$=6.1 | 4.62 | $dd, J_{ba}$=2.4; $J_{bc}$=7.8 |
| 4..... | $H^c$ | 4.38 | $ddd, J_{cb}$=9.4; $J_{cd}$=3.4; $J_{ce}$=8.9 | 4.40 | $ddd, J_{cb}$=8.5; $J_{cd}$=2.6; $J_{ce}$=11.0 | 4.17 | $ddd, J_{cb}$=6.1; $J_{cd}$=3.2; $J_{ce}$=10.1 | 4.31 | $ddd, J_{cb}$=7.8; $J_{cd}$=7.4; $J_{ce}$=6.5 |
| 5..... | $H^d$ | undet.[c] | | 2.36 | $m$[c] | 2.45 | $m$[c] | 2.32 | $ddd, J_{dc}$=7.4; $J_{de}$=15.0; $J_{df}$=4.1 |
| | $H^e$ | undet.[c] | | 2.40 | | 2.45 | $m$[c] | 2.35 | $ddd, J_{ec}$=6.5; $J_{ed}$=15.0; $J_{ef}$=3.0 |
| 6..... | $H^f$ | 4.80 | $ddd, J_{fd}$=1; $J_{fe}$=1; $J_{fg}$=3.9 | 4.00 | $ddd, J_{fe}$=9.4; $J_{fd}$=5.9; $J_{fg}$=3.8 | 4.10 | $ddd, J_{fd}$=7.4; $J_{fe}$=3.4; $J_{fg}$=3.8 | 4.52 | $ddd, J_{fd}$=4.1; $J_{fe}$=3.0; $J_{fg}$=4.2 |
| 7..... | $H^g$ | 4.70 | $ddd, J_{gf}$=3.9; $J_{gh}$=1; $J_{gi}$=1 | 4.55 | $brs$[c] | 5.15 | $ddd, J_{gf}$=3.8; $J_{gh}$=1; $J_{gi}$=10.2 | 4.65 | $ddd, J_{gf}$=4.2; $J_{gh}$=6.4; $J_{gi}$=2.0 |
| 8..... | $H^h$ | undet.[c] | | 2.20 | $m$[c] | 2.00 | $m$[c] | 2.22 | $ddd, J_{hg}$=6.4; $J_{hi}$=15.0; $J_{hj}$=7.6 |
| | $H^i$ | undet.[c] | | 2.30 | | 2.00 | $m$[c] | 2.19 | $ddd, J_{ig}$=2.0; $J_{ih}$=15.0; $J_{ij}$=7.6 |
| 9..... | $H^j$ | - | | 4.53 | $brs$[c] | 3.75 | $ddd, J_{ji}$=6.3; $J_{jh}$=3.1; $J_{jk}$=3.1 | 3.90 | $ddd, J_{jh}$=7.6; $J_{ji}$=7.6; $J_{jk}$=7.4 |
| 10..... | $H^k$ | 3.98 | $dd, J_{kl}$=12.3; $J_{km}$=7.3 | 4.08 | $ddd$ $J_{kl}$=10.8; $J_{km}$=4.2; $J_{kj}$=4.2 | 4.27 | $ddd, J_{kj}$=3.1; $J_{km}$=3.1; $J_{kl}$=1 | 3.62 | $ddd, J_{kj}$=7.4; $J_{kl}$=6.2; $J_{km}$=5.5 |
| 11..... | $H^l$ | 2.38 | $ddd, J_{lk}$=12.3; $J_{lm}$=12.9; $J_{ln}$=9.5 | 1.84 | $ddd, J_{lk}$=10.8; $J_{lm}$=12.7; $J_{ln}$=2.5 | 2.50 | $m$[c] | 2.04 | $ddd, J_{lk}$=6.2; $J_{lm}$=14.5; $J_{ln}$=6.0 |
| | $H^m$ | 2.75 | $ddd, J_{mn}$=6.2; $J_{ml}$=12.9; $J_{mk}$=7.3 | 2.53 | $m$[c] | 2.50 | $m$[c] | 2.21 | $ddd, J_{mk}$=5.5; $J_{ml}$=14.5; $J_{mn}$=7.0 |
| 12..... | $H^n$ | 4.11 | $ddd, J_{no}$=9.5; $J_{nm}$=6.2; $J_{nl}$=9.5 | 4.35 | $ddd, J_{no}$=4.7; $J_{nm}$=2.5; $J_{nl}$=2.5 | 5.42 | $ddd, J_{nl}$=5.4; $J_{no}$=15.5; $J_{nm}$=5.4 | 5.42 | $ddd, J_{nl}$=6.0; $J_{nm}$=7.0; $J_{no}$=15.5 |
| 13..... | $H^o$ | 3.78 | $ddd, J_{oq}$=9.5; $J_{op}$=2.3; $J_{on}$=9.5 | 4.13 | $ddd, J_{on}$=4.7; $J_{op}$=7.3; $J_{oq}$=7.3 | 5.54 | $ddd, J_{on}$=15.5; $J_{op}$=7.1; $J_{oq}$=6.2 | 5.58 | $ddd, J_{on}$=15.5; $J_{op}$=5.7; $J_{oq}$=5.7 |
| 14..... | $H^p$ | 1.71 | $ddq, J_{pq}$=14.5; $J_{po}$=2.3; $J_{pr}$=7.3 | 1.96 | $ddq, J_{po}$=7.3; $J_{pq}$=14.5; $J_{pr}$=7.2 | 2.02 | $m$[c] | 2.02 | $m$[c] |
| | $H^q$ | 1.72 | $ddq, J_{qp}$=14.5; $J_{qo}$=9.5; $J_{qr}$=7.3 | 1.75 | $ddq, J_{qo}$=7.3; $J_{qp}$=14.5; $J_{qr}$=7.2 | 2.02 | $m$[c] | 2.02 | $m$[c] |
| 15..... | $H^r$ | 1.12 | $t, J_{rp}$=7.3; $J_{rq}$=7.3 | 1.05 | $t, J_{rp}$=7.2; $J_{rq}$=7.2 | 0.96 | $t, J_{rp}$=7.5; $J_{rq}$=7.5 | 0.98 | $t, J_{rp}$=7.5; $J_{rq}$=7.5 |
| Others | | | | 2.06 | $s$(3H) | 2.09 | $s$(3H) | | |

a) The spectra were recorded at 360 MHz in $CDCl_3$ solution; chemical shifts are reported in PPM relative to TMS (0).

b) Spin decoupling data support the proton assignments. c) Undetermined multiplicities.

Caespitol (2): was isolated as a crystalline substance; mp 109-11°C, $(\alpha)_D$ -12 (c, 0.19, $CHCl_3$). The physical and spectroscopic data (tlc, glc, IR, $^1$H-NMR, MS) were identical with those reported for caespitol[5].

Isocaespitol (3): was isolated as a crystalline substance; mp 92-93°C, $(\alpha)_D$ -13.6 (c, 1.12, $CHCl_3$). The physical and spectroscopic data (tlc, glc, IR, $^1$H-NMR, MS) were identical with those reported for isocaespitol[6].

α-Snyderol (4): was isolated as an oil, $(\alpha)_D$ +9.7 (c, 0.18, $CHCl_3$). The physical and spectroscopic data were identical with those reported for α-snyderol[7].

Compound 5: was crystallized from n-hexane: mp 93-95°C, $(\alpha)_D$ -107 (c, 0.84, $CHCl_3$); IR, $\nu_{max}^{KBr}$ 3300, 2110, 1445, 1430, 1330, 1195, 1130, 990, 910 and 885 cm$^{-1}$. High resolution electron impact (HREI) mass spectrometry established by peak matching the elemental composition $C_{15}H_{19}{}^{79}Br_2{}^{81}BrO_3$ (observed 485.8861; Δ=-0.3 mmμ), as well as fragment peaks at *m/z* 348.9430 ($C_{15}H_{15}{}^{79}Br_2O_2$; Δ=+0.8), 283.0238 ($C_{12}H_{15}{}^{79}BrO_3$; Δ=-0.1), and 247.1296 ($C_{15}H_{18}O_3$; Δ=-0.7).

Compound 6: was isolated as an oil, $(\alpha)_D$ -29.3 (c, 1.14, $CHCl_3$); IR (neat) 3300, 3010, 2960, 1730, 1430, 1370, 1250, 1070, 1030 cm$^{-1}$. High resolution mass spectrometry established the elemental composition as $C_{17}H_{23}Br_3O_4$; $M^+$ at *m/z* 528, 530, 532, 534; $C_{17}H_{23}{}^{79}Br^{81}Br_2O_4$ (observed 531.9097; Δ=-0.2); $M^+$-AcOH, $C_{15}H_{19}{}^{79}Br_2{}^{81}BrO_2$ (observed 469.8911; Δ=+0.2); $M^+$-$C_3H_2Br$, $C_{14}H_{21}{}^{79}Br^{81}BrO_4$ (observed 412.9783; Δ=+0.3); further peaks are found at *m/z* 389, 391, 393; 349, 351, 353; 307, 309, 311; 271, 273; 227, 229; 191.

Compound 7: was isolated as an oil, $(\alpha)_D$ -14.5 (c, 0.62, $CHCl_3$); IR (neat) 3525, 3300, 3000, 2960, 2120, 1730, 1450, 1370, 1250, 965 cm$^{-1}$. High resolution mass spectrometry established the elemental composition as $C_{17}H_{24}Br_2O_4$; $M^+$ at *m/z* 450, 452, 454, $C_{17}H_{24}{}^{79}Br^{81}BrO_4$ (observed 452.0011; Δ=-0.3); $M^+$-AcOH, $C_{15}H_{20}{}^{79}Br^{81}BrO_2$ (observed 391.9808; Δ=+0.4); $M^+$-HBr, $C_{17}H_{23}{}^{79}BrO_4$ (observed 370.0769; Δ=-0.4); $M^+$-$C_3H_2Br$, $C_{14}H_{22}{}^{79}BrO_4$ (observed 333.0690; Δ=-0.5); further peaks are found at *m/z* 327, 329; 311, 313; 293; 231.

Treatment of 7 with $K_2CO_3$. Compound 7 (53 mg) in acetone (15 ml) was treated at room temp. with anhydrous potassium carbonate (120 mg) for 12h. The solid was filtered off and the solution evaporated *in vacuo* and the residue taken up in water (20 ml) and extracted with ether (3 x 10 ml). The combined extracts were washed with dil HCl (3 x 10 ml) and water (2 x 10 ml), dried and evaporated *in vacuo* to yield a colourless oil (28 mg) which was purified by chromatography on silica gel (20 g) using n-hexane-ether gradient as eluent. Compound 8 was isolated as an oil (17 mg), $(\alpha)_D$-18.4 (c, 0.11, $CHCl_3$). IR (neat) 3530, 3300, 3040, 2960, 2125, 1440, 1380, 1230, 970, 860 cm$^{-1}$. High resolution mass spectrometry established the elemental composition as $C_{15}H_{21}BrO_3$, $M^+$ at *m/z* 328, 330, $C_{15}H_{21}{}^{79}BrO_2$ (observed 328.0664; Δ=+0.4); $M^+$-$H_2O$, $C_{15}H_{19}{}^{79}BrO_2$ (observed 211.1327; Δ=+0.2); further peaks are found at *m/z* 259, 261; 199, 201; 187; 163.

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