Mastigophorenes: Novel Dimeric Isocuparane-type Sesquiterpenoids from the Liverwort *Mastigophora diclados*

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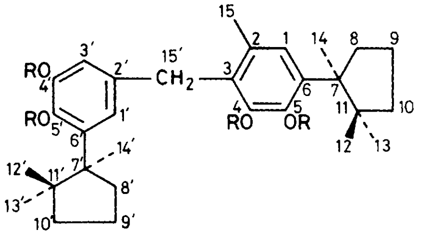
Mastigophorenes C and D, novel dimeric isocuparane-type sesquiterpenoids isolated from *Mastigophora diclados*, have been assigned structures on the basis of detailed spectroscopic analyses.

Here we report the isolation and structure of two novel dimeric isocuparane (herbertane)-type sesquiterpenoids, namely mastigophorenes C (**1**), and D (**2**), the polar constituents of the liverwort *Mastigophora diclados* (Brid.) Nees, and think they could be significant in relation to the biogenesis initiated by a phenolic oxidation from (−)-herbertenediol (**3**). The dried whole plant (220 g) of *M. diclados* (collected in Borneo) was extracted with ether. A combination of silica gel and Sephadex LH-20 chromatography of the extract has resulted in the isolation of mastigophorenes C (30 mg) and D (70 mg) along with the previously known (−)-herbertenediol (**3**) (1.3 g).[1,2]

The less polar compound, mastigophorene C (**1**) {oil, $[\alpha]_D^{20}$ −46.7° (*c* 0.4, $CHCl_3$); mass spec. *m/z* 466.3082 ($C_{30}H_{42}O_4$ requires 466.3083)} exhibited hydroxy and aromatic absorption bands at 3530 cm^{-1}, and 216 (ε 16300) and 280 (ε 3000) nm, in its i.r. and u.v spectra respectively. Acetylation of (**1**) with Ac_2O/pyridine led to a fully acetylated derivative (**1a**), the ^{1}H n.m.r. spectrum of which revealed the presence of four aromatic acetyl signals (δ 2.13, 2.17, 2.23, and 2.25), suggesting that compound (**1**) has four hydroxy groups. The ^{1}H and ^{13}C n.m.r. spectra of (**1**)† indicated the presence of a pair of three tertiary methyl groups, and one benzylic methylene group and a 1,3,4,5-tetrasubstituted benzene ring [H-1′ and H-3′ at δ 6.70 (d, *J* 1.8 Hz) and 6.51 (d, *J* 1.8 Hz) respectively], as well as a pentasubstituted benzene ring appended with a methyl group (H-15 at δ 2.32). These spectral features suggested that compound (**1**) was an unsymmetric dimer of (−)-herbertenediol (**3**), the main constituent of the title plant. In the long-range ^{13}C-{^{1}H} COSY spectrum of (**1**), the aromatic methyl proton signal (H-15) was correlated to the carbon signals at δ 122.33 (C-1), 126.73 (C-2), and 123.16 (C-3), and the benzylic proton signal (H-15′) showed clear correlations with the aromatic carbon signals at δ 121.16 (C-1′), 129.37 (C-2′), 112.40 (C-3′), and 123.16 (C-3). These spectral data indicated that the array of the substituents on the benzene ring not only corresponded to that of (−)-herbertenediol (**3**), but also that the C-15 methyl group of one molecule of (**3**) should be bonded to the C-3 position on the benzene nucleus of another molecule of (**3**). In addition, the 2-D NOESY spectrum of (**1**) substantiated the above mentioned assignment for (**1**).

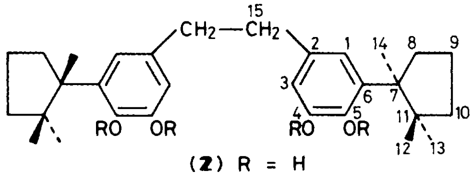
The slightly polar compound, mastigophorene D (**2**) {m.p. 201—203 °C, $[\alpha]_D^{23}$ −46.1° (*c* 0.5, $CHCl_3$)} has the same molecular formula $C_{30}H_{42}O_4$ as that of (**1**), based on its high resolution mass spectrum [*m/z* 466.3083 (calcd. 466.3083)]. The ^{1}H and ^{13}C n.m.r. spectra of (**2**),† however, resembled those of herbertenediol (**3**), the major difference being the observation of a benzylic methylene group (δ_H 2.80, δ_C 37.69) instead of the aromatic methyl group existing in (**3**). This spectral evidence, in conjunction with a base fragment ion at *m/z* 233 in its electron-impact mass spectrum, indicates that (**1**) has a symmetrical dimeric structure through the single bond formed between the C-15 aromatic methyl groups in (**3**). The 2-D ^{13}C-{^{1}H} and long-range ^{13}C-{^{1}H} COSYs of the acetate derivative (**2a**) (*m/z* 634) correlated the C-15 proton signal to the aromatic C-1, C-2, and C-3 carbon signals, whereas its NOESY analysis observed a nuclear Overhauser enhancement between the H-15 and the H-1, 3. These results fully corroborated the structure (**2**) for mastigophorene D.

Although various *ent*-cuparane and isocuparane (herbertane)-type sesquiterpenes are found in the liverworts (Hepaticae),[3—6] and are regarded as being biochemically significant,[1,4] the dimeric compounds such as (**1**) and (**2**) have not been recorded before. These dimeric isocuparenes are presumably biosynthesized *via* phenoxy radicals formed by



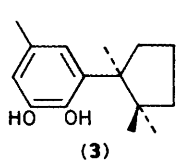
(1) R = H

(1a) R = Ac



(2) R = H

(2a) R = Ac



(3)

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† *Selected spectroscopic data for* (**1**): ^{1}H n.m.r. (400 MHz, $CDCl_3$) δ 0.72 (s, 3 H, H-13′), 0.76 (s, 3 H, H-13), 1.09 (s, 3 H, H-12′), 1.17 (s, 3 H, H-12), 1.38 (s, 3 H, H-14′), 1.41 (s, 3 H, H-14), 2.32 (s, 3 H, H-15), 2.49 (m, 1 H, H-8′β), 2.61 (m, 1 H, H-8β), 3.82 (s, 2 H, H-15′), 6.51 (d, 1 H, H-3′, *J* 1.8 Hz), 6.70 (d, 1 H, H-1′, *J* 1.8 Hz), 6.76 (s, 1 H, H-1); ^{13}C n.m.r. (100 MHz, $CDCl_3$) δ 19.78 (C-15), 20.25 (C-9′), 20.31 (C-9), 22.86 (C-14), 22.95 (C-14′), 25.20 (C-12′), 25.41 (C-12), 26.43 (C-13′), 26.89 (C-13), 32.16 (C-15′), 39.09 (C-8), 39.18 (C-8′), 40.71 (C-10′), 40.91 (C-10), 44.84 (C-11), 45.05 (C-11′), 50.97 (C-7), 51.21 (C-7′), 112.40 (C-3′), 121.16 (C-1′), 122.33 (C-1), 123.16 (C-3), 126.73 (C-2), 129.37 (C-2′), 131.12 (C-6), 133.91 (C-6′), 141.85 (C-5), 141.95 (C-5′), 142.20 (C-4), 143.85 (C-4′).

For (**2**): ^{1}H n.m.r. (400 MHz, $CDCl_3$) δ 0.73 (s, 3 H, H-13), 1.16 (s, 3 H, H-12), 1.39 (s, 3 H, H-14), 2.80 (s, 2 H, H-15), 4.95 (s, 1 H, OH), 5.37 (s, 1 H, OH), 6.49 (d, 1 H, H-3, *J* 2.0 Hz), 6.64 (d, 1 H, H-1, *J* 2.0 Hz); ^{13}C n.m.r. (50.3 MHz, $CDCl_3$) δ 20.33 (C-9), 22.93 (C-14), 25.39 (C-12), 26.79 (C-13), 37.69 (C-15), 39.23 (C-8), 40.91 (C-10), 44.91 (C-11), 51.18 (C-7), 112.93 (C-3), 121.93 (C-1), 132.33 (C-2), 133.38 (C-6), 141.39 (C-5), 143.26 (C-4).

one electron oxidation[7] from (−)-herbertenediol (**3**) co-existing in the plant.

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