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LETTERS

Heimiol A, a new dimeric stilbenoid from *Neobalanocarpus heimii*

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Abstract—A new stilbene dimer, heimiol A was isolated from the heartwood of *Neobalanocarpus heimii*, in addition to the four known oligostilbenoids, balanocarpol, copalliferol A, hopeaphenol and vaticaphenol A. The structures and relative configuration were established by means of 2D NMR spectroscopy including COSY, HMQC, HMBC and NOESY. © 2001 Published by Elsevier Science Ltd.

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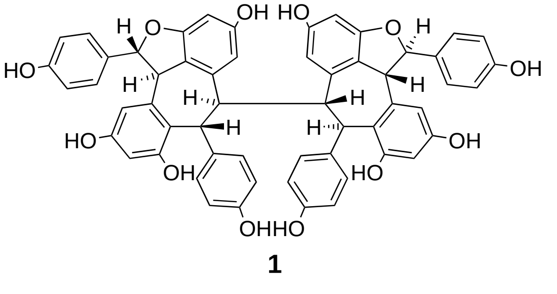
1. Introduction

In 1965, Coggon et al.[1] reported the first naturally occurring resveratrol tetramer, hopeaphenol, **1**, from the heartwood of a Dipterocarpaceae species, cengal, *Neobalanocarpus heimii*. The structure of **1** was elucidated by X-ray crystallography.[2] However, the then available isolation and spectroscopic techniques probably did not allow for a thorough chemical study. We undertook the reinvestigation of this valuable timber wood by applying the now well-established procedures used for the extraction and isolation of phenolics.

2. Results and discussion

In our study, the fractionation of the ethyl acetate extract of the heartwood of a sample of cengal wood and subsequent purification steps resulted in the isolation of five oligostilbenoids. Four of them were known, and include (−)-hopeaphenol **1**,[3] which has been reported as a single compound from this species by Coggon et al.[1,2] Another tetrameric species was also identified, vaticaphenol A **2**, which was recently isolated from *Vatica diospyroides*.[4] (+)-Copalliferol A **3** was also isolated for the second time, the first being from *Vatica copallifera*.[5] The major constituent of our sample was found to be a dimer, (−)-balanocarpol **4**. However, **4** is the enantiomer of the previously isolated (+)-balanocarpol.[6] In addition, we established the structure of a new dimer, heimiol A **5**, based on the following evidence. (−)-Heimiol A **5**, was obtained as a light brown residue (14 mg), $[\alpha]_D$ −37 (methanol). It gave a weak $[M+H]^+$ peak at *m*/*z* 471.08 in a positive ion mode MALDI-TOF, compatible with the molecular formula $C_{28}H_{22}O_7$ of a resveratrol dimer. Maxima of absorption were observed at 241 and 283 nm in the UV spectrum, attributable to the phenol rings. We could thus rule out the presence of the stilbene chromophore such as that of ε-viniferin.[7] No functional groups other than hydroxyls could be detected from the IR spectrum. The ^1H NMR (Table 1) and ^1H–^1H COSY spectra showed



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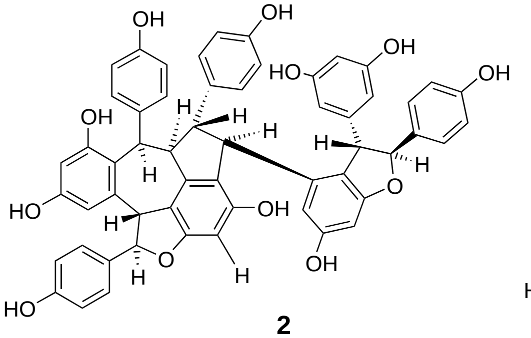

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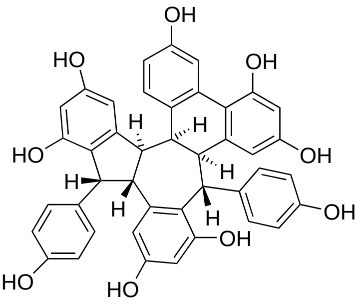

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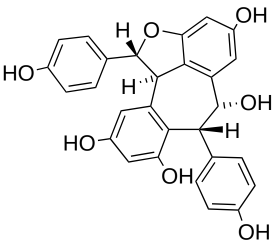

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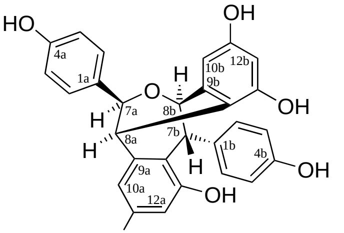
Table 1. ^1H (500 MHz) and ^{13}C (125 MHz) NMR data for **5** (CD_3OCD_3)

No	^1H δ ppm (J, Hz)	^{13}C δ ppm	No.	^1H δ ppm (J, Hz)	^{13}C δ ppm
1a		136.8	**1b**		136.9
2a(6a)	6.90 d (8.5)	127.8	**2b(6b)**	7.14 d (8.4)	160.1
3a(5a)	6.60 d (8.5)	115.1	**3b(5b)**	6.71 d (8.4)	115.2
4a		157.3	**4b**		156.9
7a	5.57 br s	81.5	**7b**	4.32 d (3.3)	50.8
8a	4.23 br s	46.8	**8b**	4.96 d (3.3)	81.4
9a		147.4	**9b**		142.6
10a	6.40 d (2.4)	107.2	**10b**	6.47 d (2.1)	104.6
11a		157.1	**11b**		158.0
12a	6.16 d (2.4)	101.9	**12b**	6.23 d (2.1)	126.0
13a		154.5	**13b**		156.1
14a		116.1	**14b**		116.7



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two sets of *ortho*-coupled aromatic protons in AA′BB′ spin systems assignable to two independent 4-hydroxyphenyl groups {δ (ppm) 6.60, 6.90 [2H each, d, $J=8.5$ Hz, H-3a(5a) and H-2a(6a)], 6.71, 7.14 [2H each, d, $J=8.4$ Hz, H-3b(5b) and H-2b(6b)]}, two sets of *meta*-coupled aromatic protons [δ (ppm) 6.40, 6.16 (1H each, d, $J=2.4$ Hz, H-10a and H-12a), 6.47, 6.23 (1H each, d, $J=2.1$ Hz, H-10b and H-12b)] assignable to two disubstituted resorcinol moieties. They also displayed two sets of coupled benzyl methine protons [δ 4.23 (br s, H-8a), 5.57 (br s, H-7a) and 4.32 (d, $J=3.3$ Hz, H-7b), 4.96 (d, $J=3.3$ Hz, H-8b)]. The large deshielding of H-7a and H-8b indicate that they might both be attached to benzylic carbons bearing an oxygen atom. Since the molecular formula includes seven oxygen atoms, it can be deduced that these two benzylic carbons are connected through an ether linkage. This hypothesis was further supported by the ^{13}C chemical shifts (Table 1). The connection between protons and their corresponding carbons was established by HMQC. Correlations from 2D long distance heteronuclear NMR spectrum (HMBC, Fig. 1) allowed the assignment of all proton and carbon signals. Observa-

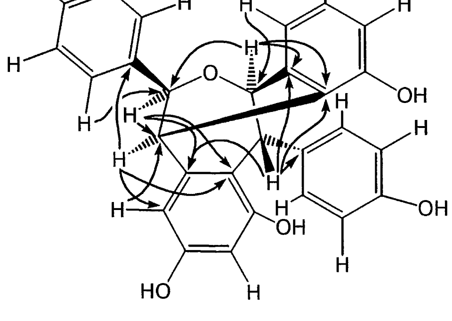

Figure 1. Main HMBC correlations in **5** (500 MHz, CD_3OCD_3).

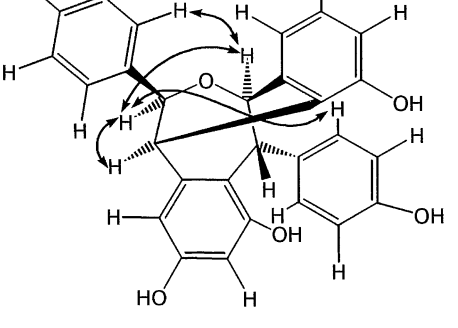

Figure 2. Main NOESY correlations in **5** (500 MHz, CD_3OCD_3).

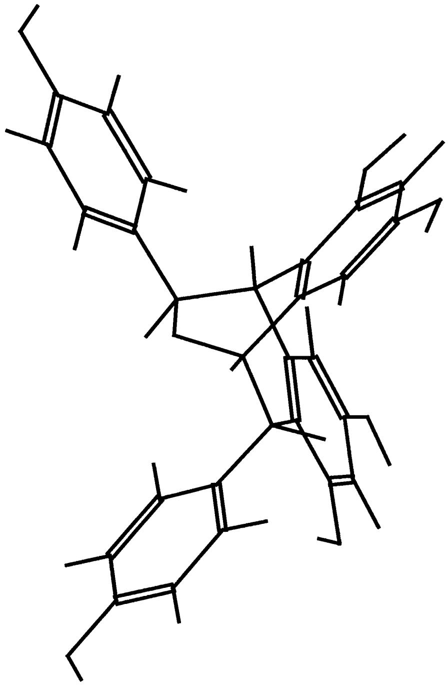

Figure 3. Computer modeling of **5**.

tion of a cross peak shown by H-2a with δ_C 81.5 (C-7a) confirmed that a 4-hydroxyphenyl group is attached to an oxygen bearing carbon. The signal of H-8b showed a cross peak with C-14b, which in turn coupled to H-7b. The signal of H-7b showed correlations with C-9b. These results, together with a correlation of H-7a/C-9a, led us to establish a fused benzopyran–benzooxepane structure. The relative configuration of **5** was deduced from the NOESY spectrum (Fig. 2). By definition, protons H-8a and H-8b are in a *syn* configuration. The *syn*-orientation of H-7a relative to H-8a was deduced from the NOE correlations H-8b/H-7a/H-8a. H-7b does not show any correlation, except with H-8b and H-2b/6b, its closest neighbors. In turn, H-2b/6b showed a strong NOE cross peak with H-7a, thus indicating that the 4-hydroxyphenyl group to which H-2b/6b are attached, is *syn* to H-7a, that is, orientated below the mean plane of the oxepane ring. Molecular modeling (Fig. 3) showed that the distance between H-2b/6b and H-7a can be as low as 2.5 Å. We conclude from the above that heimiol A has the structure shown in **5**.

3. Experimental

Optical rotations were measured using a Polartronic D, Schmidt+Haench digital polarimeter. UV spectra were recorded on a Shimadzu UV-300 spectrophotometer. IR spectra (KBr pellet) were run on a Perkin–Elmer 683. Mass data were collected either from a MALDI-TOF BIFLEX™ III Bruker or from a LCQ Finnigan MAT LCMS system. ^1H and ^{13}C NMR spectra were recorded in CD_3OCD_3 on BRUKER DRX spectrometer, at 500 and 125 MHz, respectively. Molecular modeling was performed by running MM2 calculation with Chem3D Pro v5.0 from CambridgeSoft.

Compound **1** *[(−)-hopeaphenol]*: brown solid (11 mg), physical and spectral data were comparable with literature values.[3]

Compound **2** *(vaticaphenol A)*: brown solid (6 mg), physical and spectral data were comparable with literature values.[4]

Compound **3** *[(+)-copalliferol A]*: brown solid (10 mg), physical and spectral data were comparable with literature values.[5]

Compound **4** *[(−)-balanocarpol]*: brown solid, (752 mg); $[\alpha]_D$ −84.5 (c=0.07, MeOH); other physical and spectral data were comparable with literature values for (+)-balanocarpol.[6]

Compound **5** *[(−)-heimiol A]*: light brown solid (14 mg). $[\alpha]_D$ −37 (c=0.13, MeOH). UV λ_{max}^{MeOH} (nm): 241 (log ε=3.75), 283 (log ε=3.67). IR (KBr) ν_{max}: 3380, 1612, 1513, 1458, 1339, 1296, 1143, 1071 and 840 cm^{-1}. MALDI-TOF $[M+Na+H]^+$: m/z 504.04. NMR: see Table 1.

Acknowledgements

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