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# SHORT REPORT

## CHROMONES FROM *HARRISONIA PERFORATA* (BLANCO.) MERR.

SOMKIAT THADANITI, WANDEE ARCHAKUNAKORN,
PITTAYA TUNTIWACHWUTTIKUL AND JOHN B. BREMNER*

*Department of Chemistry, Faculty of Science, Silpakorn University, Nakorn Pathom 73000, Thailand; *Department of Chemistry, University of Wollongong, NSW 2522, Australia.*

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### ABSTRACT

*Peucenin 7-methyl ether* ***1****, O-methylalloptaeroxylin* ***2*** *and perforatic acid* ***3*** *were isolated from the branches of* Harrisonia perforata *(Blanco.) Merr. (Simaroubaceae). The structures of* ***1-3*** *were assigned on the basis of their spectroscopic data and also by a chemical conversion in the case of* ***3****.*

### INTRODUCTION

*Harrisonia perforata* (Blanco.) Merr. is a native of Southeast Asia, and its leaves, wood and root-bark have been used medicinally[1].

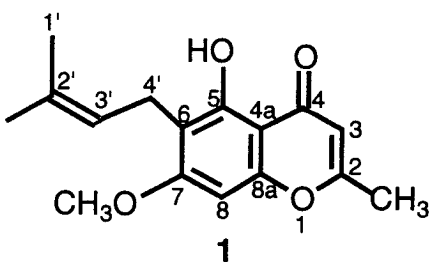
The *in vitro* antimalarial activity against *Plasmodium falciparum* of extracts of the leaves and the branches of *Harrisonia perforata* have been reported[2,3]. *O*-Methylalloptaeroxylin **2** and perforatic acid **3** and the limonoid, perforatin, have been isolated previously from the roots[4,5] and the leaves[6] of this plant, respectively. We now report the chemical investigation of the branches of *Harrisonia perforata.* Extraction of dried, ground branch material with chloroform, followed by extensive chromatography of the extract, led to the isolation of three chromones, which have been identified as peucenin 7-methyl ether **1**, *O*-methylalloptaeroxylin **2** and perforatic acid **3**. The structures were assigned on the basis of their spectroscopic data and also by an esterification in the case of **3**.

### RESULTS AND DISCUSSION

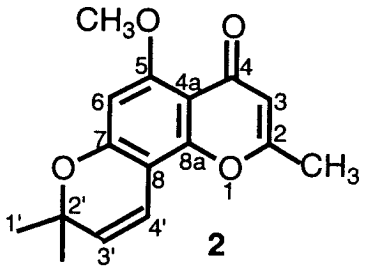
High resolution MS on **1-2** and **4**, the methyl ester of **3**, confirmed the molecular formulae. The UV, IR and $^1$H NMR spectral data of **1** and **2** are in close agreement with the data reported for peucenin 7-methyl ether[7-9] and *O*-methylalloptaeroxylin[10,11], respectively. The assignments of the $^1$H NMR signals and IR absorption bands for **1** and **2** were based on the previously published data[7-11]. Compounds **1** and **2** were therefore identified as peucenin

7-methyl ether and O-methylalloptaeroxylin, respectively. Compound **1** has never been isolated from *Harrisonia perforata* before and **1** appears to occur rarely in nature. An isomeric structure was noted previously for **1**[3], but this is now revised.

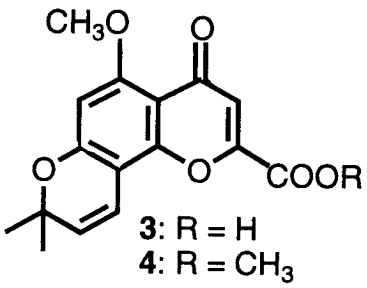
The structure of **3** was confirmed by comparison of its spectral data with those of **1** and **2**. Esterification of **3** gave the methyl ester analogue **4**. The $^{13}C$ NMR chemical shifts and assignments of compounds **1-4** are shown in Table 1.




**1**




**2**




**3**: R = H
**4**: R = $CH_3$

## EXPERIMENTAL

Melting points were measured with a micro-melting point apparatus. IR spectra were obtained on nujol mulls with a Jasco A-302 spectrophotometer. UV spectra in MeOH solutions, unless otherwise stated, were measured with a Jasco Univex-650 spectrophotometer. $^1H$ NMR spectra in $CDCl_3$ or in $CDCl_3$+$CD_3OD$ solutions were recorded at 300 MHz with a Bruker AM300 spectrometer and with TMS as internal standard. The $^{13}C$ NMR spectra of $CDCl_3$ solutions were obtained at 75.5 MHz.The NOESY spectrum was run with a Varian Unify 400 spectrometer.The mass spectra were determined with a VG7070 mass spectrometer, operating at 70 eV, with a source temperature of 200° (direct insertion) or with a VG Quattro triple quadrupole mass spectrometer for the electrospray mass spectrum. Plates for thin-layer chromatography (t.l.c.) or preparative layer chromatography (p.l.c.) were prepared from Merck silica gel PF254 and activated by drying at 100° for 2 h. Silica gel 70-230 mesh (Merck) was used for column chromatography.

An authentic specimen (Voucher Number Bansiddhi 91-08) of *Harrisonia perforata* (Blanco) Merr. has been deposited in the Herbarium at the Division of Medicinal Plant

**Table 1** $^{13}C$ NMR Chemical Shifts of Compounds **1-4**.

| Carbon | Compounds | | | |
|---|---|---|---|---|
| | **1** | **2** | **3** | **4** |
| 2 | 167.4 | 163.3 | 159.8 | 161.1 |
| 3 | 108.8 | 112.3 | 113.1 | 115.6 |
| 4 | 183.6 | 178.3 | 179.5 | 177.6 |
| 4a | 108.2 | 103.0 | 102.5 | 103.3 |
| 5 | 155.3 | 155.0 | 153.6 | 154.8 |
| 6 | 105.2 | 97.0 | 96.4 | 97.6 |
| 7 | 161.1 | 158.0 | 155.5 | 154.8 |
| 8 | 95.5 | 109.0 | 108.2 | 110.1 |
| 8a | 163.2 | 161.0 | 158.4 | 159.2 |
| 1' | 21.2 | 28.8 | 27.4 | 28.6 |
| 2' | 132.3 | 78.5 | 77.9 | 79.0 |
| 3' | 122.6 | 115.8 | 114.6 | 117.1 |
| 4' | 22.2 | 127.9 | 126.8 | 128.1 |
| $CH_3$-2' | 26.4 | 28.8 | 27.4 | 28.6 |
| $CH_3$-2 | 18.4 | 20.2 | - | - |
| $OCH_3$ | 58.5 | 57.0 | 55.4 | 57.0 |
| COOR | - | - | 165.5 | 161.4 |
| $COOCH_3$ | - | - | - | 53.6 |

Research and Development, Department of Medical Science, Nonthaburi 11000, Thailand. Branch material obtained from Sermsuk Osud, Nakorn Pathom, Thailand was comfirmed as coming from *Harrisonia perforata* by morphological inspection, and a sample is included with the voucher specimen.

*Extraction and Isolation.* The milled, dried, leaf-free branches (1.8 kg) of *H. perforata* obtained from Sermsuk Osod, Nakorn Pathom were extracted exhaustively with $CHCl_3$ in a Soxhlet apparatus. The extract was filtered and evaporated to a dark brown viscous oil (32.0 g). A portion (10.0 g) of the viscuos oil was chromatographed on a column of silica gel (400 g). Successive fractions obtained by gradient elution with MeOH/$CHCl_3$ (5%-100% MeOH v/v) were combined on the basis of their behaviour on t.l.c. ($Et_2O$) to give chromone **1** (fraction 1) (290 mg) as a slightly yellow solid, a mixture of **1** and **2** (fraction 2) as a yellow solid (751 mg) and a brown solid (1.34 g) (fraction 3) containing mainly chromone **3**.

The $CHCl_3$ extract of branch material of a separate authentic sample of *H. perforata* collected from Korat, Thailand contained the same components as above by t.l.c. analysis.

*Peucenin 7-Methyl Ether (**1**).* The slightly impure sample of **1**(fraction 1) was purified by p.l.c. on silica gel with $CH_2Cl_2$ as the mobile phase; the solid obtained was crystallized from MeOH to give the chromone **1** as slightly yellow needles, m.p. 105-106° [lit.[7] m.p. 108-109°, lit.[9] m.p.106-107°).(Found [M$^+$],274.1210. Calc. for $C_{16}H_{18}O_4$ 274.1204). UV $\lambda_{max}$ nm:330(log ε 3.30), 295(3.35), 258(4.05), 250sh(4.03), 225sh(3.93), 215sh(3.98). IR $\nu_{max}$ cm$^{-1}$: 1660, 1615, 1585, 1320, 1260, 1160, 1100, 1090. $^1$H NMR : δ 1.79, 1.67, *both s,* 2x$CH_3$; 2.36, *s,* $CH_3$-2; 3.38, *d, J* 9.0 Hz, $CH_2$-4'; 3.68, *s,* $OCH_3$; 5.15, *t, J* 9.0 Hz, H3'; 6.00, *s,* H3; 6.36, *s,* H8; 12.78, *s,* OH. MS : *m/z* 274(M$^+$, 60%), 259(100), 219(20), 206(55), 189(18).

*O-Methylalloptaeroxylin (**2**).* The mixture of **1** and **2** (751 mg) (fraction 2) was separated by p.l.c. on silica gel with diethyl ether as the mobile phase to give further compound **1** (303 mg) and compound **2** as a slightly yellow solid (214 mg). This solid was crystallized from MeOH/$H_2O$ to give the chromone **2** as yellow rhombs, m.p. 153-155° (lit.[10] m.p. 155-157°; lit.[11] m.p. 155-157°). (Found [M$^+$] 272.1040. Calc. for $C_{16}H_{16}O_4$ 272.1047). UV $\lambda_{max}$ nm : 330(log ε 3.36), 295(3.36), 260(4.34), 255sh(4.29), 237sh(4.04), 220(3.91). IR $\nu_{max}$ cm$^{-1}$ : 1660, 1620, 1565, 1330, 1210, 1200, 1168, 1150, 1120, 1080. $^1$H NMR : δ 1.48, *s,* 2x$CH_3$; 2.29, *s,* $CH_3$-2; 3.92, *s,* $OCH_3$; 5.57, *d, J* 10.3 Hz, H3'; 6.00, *s,* H3; 6.29, *s,* H6; 6.70, *d, J* 10.3 Hz, H4'. MS : *m/z* 272 (M$^+$, 54%), 257(100), 243(10), 228(16), 217(31), 202(10), 43(13), 28(16).

*Perforatic Acid (**3**).* A portion of **3** (262 mg) (fraction 3) was purified by p.l.c. on silica gel with $CH_2Cl_2$/MeOH/$H_2O$ (7:3:1, lower layer) as the mobile phase; the solid (70 mg) obtained was crystallized from diethyl ether/MeOH to give the acid as a yellow powder, m.p.>325°. (Found [MH$^+$], 303.3, electrospray MS. Calc. for $C_{16}H_{14}O_6$+H, 303.29). UV $\lambda_{max}$ nm : 340 (log ε 3.58), 305 sh(3.66). 275sh(4.44), 265(4.49), 225(4.45), 218sh(4.41). IR $\nu_{max}$ cm$^{-1}$ : 3400(broad), 1580-1700(broad), 1330, 1190, 1150, 1130, 1110, 1060. $^1$H NMR : δ 1.43, *s,* 2x$CH_3$; 3.89, *s,* $OCH_3$; 5.54, *d, J* 10.0 Hz, H3'; 6.29, *s,* H6; 6.88, *d, J* 10.0 Hz, H4'; 6.89, *s,* H3. A NOESY spectrum (400 MHz; $CD_3OD$) on **3** showed an nOe between the methoxyl group and H6, and no nOe from H4' to the methoxyl group.

*Esterification of* ***3***. Compound **3** (162 mg) was esterified with MeOH and conc. $H_2SO_4$ (few drops). On evaporation of the solvent, water (10 ml) was added to the residue and the mixture extracted with $CHCl_3$(3x10 ml). Removal of the $CHCl_3$ *in vacuo* gave the crude ester as a yellow solid (160 mg). The solid was purified by p.l.c. on silica gel with $CHCl_3$/EtOAc/MeOH(4:4:2) as the mobile phase to give the methyl ester **4** as a yellow solid (86 mg) which was crystallized from MeOH to give yellow needles, m.p. 207-208°. (Found [$M^+$], 316.095. Calc. for $C_{17}H_{16}O_6$316.0945).UV $\lambda_{max}^{EtOH}$nm :356(log ε 3.26), 324(3.43), 277sh(4.21), 271(4.23), 230(4.28), 215sh(4.22). IR $\nu_{max}$ $cm^{-1}$ : 1740, 1653, 1590, 1244, 1128. $^1$H NMR : δ 1.49, *s,* 2x$CH_3$; 3.94, *s,* $OCH_3$; 3.98, *s,* $COOCH_3$; 5.61, *d, J* 10.0 Hz, H3'; 6.33, *s,* H6; 6.82, *d, J* 10.0 Hz, H4'; 6.94, *s,* H3. MS : *m/z* 316 ($M^+$, 20%), 301(100), 287(40), 272(7), 258(5), 243(8), 229(5), 217(10), 213(12).

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## บทคัดย่อ

การศึกษาทางเคมีของส่วนสกัดของกิ่งของสีฟันคนทา *Harrisonia perforata* (Blanco.) Merr. พบ peucenin 7-methyl ether **1**, *O*-methyl-alloptaeroxylin **2** และ perforatic acid **3** พิสูจน์สูตรโครงสร้างของ **1-3** ด้วยเทคนิกสเปคโตร-สโคปีและปฏิกิริยาเคมี