Chromones from the Branches of *Harrisonia perforata*

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Four new chromones, perforamone A, B, C, and D have been isolated together with six known compounds, peucenin-7-methyl ether, *O*-methylalloptaeroxylin, perforatic acid, eugenin, saikochromone A and greveichromenol, from the branches of *Harrisonia perforata* (Simaroubaceae). The structures were identified by spectroscopic data. The compounds were tested for antimycobacterial and antiplasmodial activities.

Key words *Harrisonia perforata*; Simaroubaceae; chromone

The leaves, wood and root-bark of *Harrisonia perforata* (Family: Simaroubaceae) have been used medically.[1)] The extracts of the leaves and the branches showed *in vitro* antimalarial activity against *Plasmodium falciparum*.[2,3)] Several chromones, peucenin-7-methyl ether, *O*-methylalloptaeroxylin (perforatin A), perforatin B, perforatic acid, perforatic acid methyl ester and perforatin C—G and two limonoids, perforatin and perforatinolone, have been isolated from the roots,[4,5)] leaves,[6,7)] branches[8)] and wood[9)] of *H. perforata*. From our ongoing study on the biologically active constituents of *H. perforata*, we now report the isolation of four new chromones, perforamone A, B, C, and D (**4**—**6**, **9**) together with six known chromones, compounds **1**—**3**,[8)] eugenin (**7**),[10)] saikochromone A (**8**)[11)] and greveichromenol (**10**)[12)] from the branches of this plant. Compounds **1**—**10** were tested for antimycobacterial and antiplasmodial activities.

The EtOAc-soluble fraction of the ethanolic extract was subjected to successive CC and prep. TLC on silica gel. Three major chromone derivatives, peucenin-7-methyl ether (**1**), *O*-methylalloptaeroxylin (**2**) and perforatic acid (**3**) and seven minor ones, perforamone A, B, C, and D (**4**—**6**, **9**), eugenin (**7**), saikochromone A (**8**), and greveichromenol (**10**) were isolated. Compounds **4**—**6** and **9** are new natural products.

Perforamone A (**4**) was isolated as colorless needles, which was shown to be optically active ($[\alpha]_D^{25}$ −19.4°, *c*=0.07). The compound gave a parent ion by HR-MS at *m*/*z* 290.1151, corresponding to a molecular formula $C_{16}H_{18}O_5$. Its IR spectrum showed absorption bands corresponding to the hydroxyl group and an aryl ketone at 3413 and 1666 cm^{-1}, respectively. The ^{1}H-NMR spectrum (Table 1) revealed signals of two singlets at δ 1.30 (3H) and 1.44 (3H), and an ABX system at δ 2.87 (1H, dd, *J*=7.2, 13.2 Hz), 3.10 (1H, dd, *J*=4.2, 13.2 Hz) and 2.95 (1H, dd, *J*=4.2, 7.2 Hz), which are due to the presence of a 2,3-epoxy-4-methylbutyl group. This was consistent with the ^{13}C-NMR data (Table 2) of **4**, which exhibited two methyl carbons at δ 19.1 (C-4′) and 24.8 (C-5′), a methylene carbon atom at δ 22.3 (C-1′), an oxymethine carbon atom at δ 63.2 (C-2′) and a quaternary carbon atom at δ 59.5 (C-3′). The signal at δ 12.90 (1H, s) in the ^{1}H-NMR spectrum was ascribed to a phenolic group hydrogen bonded to a carbonyl group. Two singlets of three hydrogens each at δ 2.39 and 3.91 and two singlets of one hydrogen each at δ 6.05 and 6.42 were assigned to an olefinic methyl (2-Me), a methoxyl (7-OMe) and two hydrogens at positions 3 and 6 of the chromone nucleus, respectively. The ^{13}C-NMR spectrum of **4** (Table 2) showed 16 signals which were assigned by the DEPT, 2D HMQC and 2D HMBC spectra.

The position of the phenolic at C-5 was established by 2D HMBC correlations between phenolic proton OH-5 and C-5,

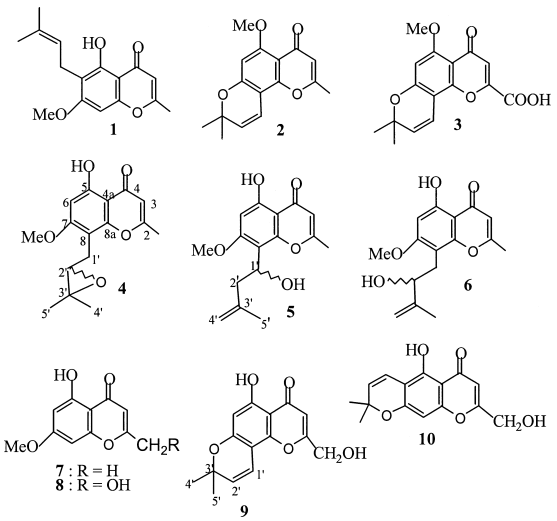

Table 1. ^{1}H-NMR Spectral Data of Compounds **4**—**6**, **9** and **10**

H	4	5	6	9	10
3	6.05, br s	6.05, br s	6.05, br s	6.34, br s	6.32, br s
6	6.42, s	6.41, s	6.42, s	6.26, s	—
8	—	—	—	—	6.30, s
1′	2.87, dd (7.2, 13.2)	4.56, dd (6.0, 7.5)	2.99, dd (7.8, 13.7)	6.63, d (10.0)	6.69, d (10.0)
	3.10, dd (4.2, 13.2)	—	3.09, dd (5.3, 13.7)	—	—
2′	2.95, dd (4.2, 7.2)	2.97, dd (6.0, 13.8)	4.31, dd (5.3, 7.8)	5.57, d (10.0)	5.62, d (10.0)
		3.08, dd (7.5, 13.8)			
4′	1.30, s	4.88, br s	4.82, br s	1.47, s	1.45, s
		4.96, br s	4.89, br s		
5′	1.44, s	1.87, s	1.87, s	1.47, s	1.45, s
2-CH_3	2.39, s	2.38, s	2.39, s	—	—
2-CH_2	—	—	—	4.58, s	4.49, s
7-OCH_3	3.91, s	3.93, s	3.92, s	—	—
OH	12.90, s	12.85, s	12.82, s	12.66, s	12.85, s

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Table 2. ^{13}C-NMR Spectral Data of Compounds **4**—**7**, **9** and **10**

C	4	5	6	7	9	10
2	166.8	166.5	166.6	166.8	167.3	167.5
3	108.5	108.4	108.4	108.8	106.9	106.7
4	183.0	182.0	182.9	182.5	182.5	182.5
4a	104.5	104.5	104.5	105.2	105.5	105.6
5	161.0	161.0	161.1	162.2	161.9	157.1
6	95.1	95.1	95.1	97.8	100.4	105.7
7	163.2	163.0	163.2	165.4	159.7	159.7
8	103.8	104.0	104.8	92.5	101.1	95.5
8a	154.5	155.2	155.4	158.1	159.7	156.5
1′	22.3	88.1	29.3	—	114.6	115.4
2′	63.2	24.4	75.5	—	127.6	128.2
3′	59.5	143.7	147.0	—	78.1	78.1
4′	19.1	113.5	110.7	—	28.2	28.3
5′	24.8	18.0	17.9	—	28.2	28.3
2-CH_3	20.6	20.5	20.5	20.5	—	—
2-CH_2	—	—	—	—	61.3	61.4
7-OCH_3	56.0	56.2	56.1	55.7	—	—

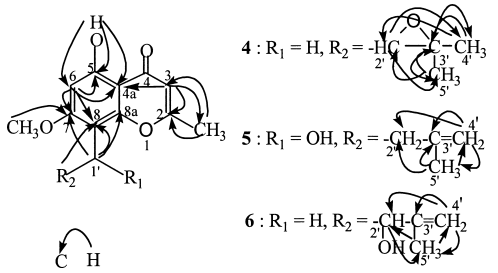

Fig. 1. 2D HMBC Correlations of **4**—**6**

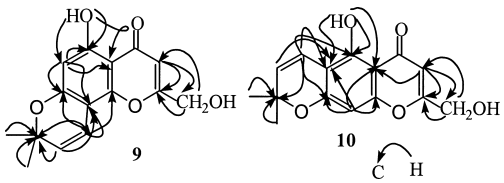

Fig. 2. 2D HMBC Correlations of **9** and **10**

C-6 and C-4a (Fig. 1). The 2,3-epoxy-4-methylbutyl substituent attached to C-8 was apparent from the long-range correlations between the H-1′ signals at δ 2.87 and 3.10 and C-8, C-7 and C-8a and the H-2′ signal at δ 2.95 and C-8 (Fig. 1). H-6 (δ 6.42) correlated with C-5, C-7, C-4a and C-8, H-3 (δ 6.05) with C-2, C-4a and 2-Me, the methoxy signal (δ 3.91) with C-7 and the 2-methyl group (δ 2.39) with C-2. On the basis of the above evidence, perforamone A was characterized as 5-hydroxy-7-methoxy-2-methyl-8-(2,3-epoxy-3-methylbutyl)chromone (**4**).

Perforamone B (**5**) was isolated as colorless needles. Compound **5** has a molecular formula of $C_{16}H_{18}O_5$ determined by HR-MS. The UV, IR, ^{1}H- (Table 1) and ^{13}C-NMR (Table 2) spectra of **5** were almost identical with those of compound **4**, except in regard to the signals of the substituent at C-8. In compound **5**, proton signals appeared at δ 2.97 (1H, dd, J=6.0, 13.8 Hz), 3.08 (1H, dd, J=7.5, 13.8 Hz), 4.56 (1H, dd, J=6.0, 7.5 Hz), 4.88 (1H, br s), 4.96 (1H, br s) and 1.87 (3H, s) and carbon signals at δ 88.1 (C-1′), 24.4 (C-2′), 143.7 (C-3′), 113.5 (C-4′) and 18.0 (C-5′) due to the presence of a 1-hydroxy-3-methyl-3-butenyl group. The 2D HMBC data (Fig. 1) revealed three- and two-bond correlations between the OH-5 proton and C-6, C-4a and C-5, between the proton signal of H-1′ and C-7, C-8a and C-8 and between the proton signal of H-2′ and C-8. On the basis of the above evidence, perforamone B was assigned as 5-hydroxy-7-methoxy-2-methyl-8-(1-hydroxy-3-methyl-3-butenyl)chromone (**5**).

Perforamone C (**6**) was crystallized from MeOH/H_2O as pale yellow rhombs. The UV, IR, HR-MS and EI-MS data for **6** closely resembled those for **5**. Compound **6** showed ^{1}H- (Table 1) and ^{13}C-NMR (Table 2) spectral data that were different from those of **5** only in the signals of the C5 unit at C-8. Compound **6** showed proton signals at δ 2.99 (1H, dd, J=7.8, 13.7 Hz), 3.09 (1H, dd, J=5.3, 13.7 Hz), 4.31 (1H, dd, J=5.3, 7.8 Hz), 4.82 (1H, br s), 4.89 (1H, br s) and 1.87 (3H, s) and carbon signals at δ 29.3 (C-1′), 75.5 (C-2′), 147.0 (C-3′), 110.7 (C-4′) and 17.9 (C-5′) which indicated a 2-hydroxy-3-methyl-3-butenyl group. The HMBC data (Fig. 1) supported the positions of the phenolic OH and 2-hydroxy-3-methyl-3-bytenyl group at C-5 and C-8, respectively. On the basis of the above evidence, therefore, perforamone C was characterized as 5-hydroxy-7-methoxy-2-methyl-8-(2-hydroxy-3-methyl-3-butenyl)chromone (**6**).

Compound **7** was identified to be the known compound eugenin, by comparison with the ^{1}H-NMR spectral data previously reported.[10] The ^{13}C-NMR spectral data of **7** (not reported in the literature) were assigned by a combination of DEPT, 2D HMQC and 2D HMBC experiments (Table 2). Compound **8** was identified as saikochromone A by comparison the spectral data with those reported in the literature.[11]

Perforamone D (**9**) was crystallized from MeOH/H_2O as pale yellow rhombs. The compound gave a parent ion by HR-MS at m/z 274.0842 corresponding to a molecular formula $C_{15}H_{14}O_5$. The IR spectrum of **9** resembled those of compounds **4**—**6**. The ^{1}H-NMR spectrum (Table 1) revealed signals of one singlet of six hydrogens at δ 1.47 and two doublets of one hydrogen each at δ 5.57 (J=10.0 Hz) and 6.63 (J=10.0 Hz) established the presence of a 2,2-dimethylchromene ring. The signal at δ 12.66 (1H, s) was ascribed to a phenolic group hydrogen bonded to an acyl group. Two singlets of one hydrogen each at δ 6.34 and 6.26 and the presence of one singlet of two hydrogens at δ 4.58 were identified to H-3, H-6 and a hydroxymethyl group at C-2 of the chromone nucleus, respectively. The ^{13}C-NMR spectrum of **9** (Table 2) showed 15 signals which were assigned by the DEPT, 2D HMQC and 2D HMBC spectra.

The position of the phenolic group at C-5 in **9** was established by the 2D HMBC correlation (Fig. 2) of the phenolic OH-5 to C-6, C-4a and C-5. The long-range correlations (Fig. 2) of H-1′ (δ 6.63) to C-7, C-8a and C-8 and H-2′ (δ 5.57) to C-8 were observed in **9**. Additionally, H-6 (δ 6.26) showed correlations with the carbon signals of C-4a, C-8, C-5 and C-7. These results clearly indicated that the chromene ring located between C-7 and C-8 in **9**. On the basis of the above evidence, therefore, perforamone D was assigned as 2-hydroxymethylalloptaeroxylin (**9**).

Greveichromenol (**10**) was crystallized as pale yellow needles and has previously been deduced as structure **10**,[12] mainly from chemical evidence; the ^{1}H- and ^{13}C-NMR spectra were not measured. The ^{1}H- (Table 1) and ^{13}C-NMR

Table 3. *In Vitro* Antiplasmodial and Antimycobacterial Activity of Compounds **1**—**10**

Compound	Antiplasmodial EC_{50} (μg/ml)	Antimycobacterial MIC (μg/ml)
1	>20 (inactive)	50
2	10.5	100
3	>20 (inactive)	>200 (inactive)
4	>20 (inactive)	200
5	>20 (inactive)	25
6	>20 (inactive)	200
7	>20 (inactive)	100
8	>20 (inactive)	>200 (inactive)
9	>20 (inactive)	25
10	>20 (inactive)	50

(Table 2) data of **10** were almost identical with those of compound **9**. The 2D HMBC data (Fig. 2) supported the chromene ring located between C-6 and C-7 and the phenolic hydroxyl group attached to C-5. Therefore structure **10** was identified for greveichromenol.

The spectral data (^{1}H-, ^{13}C-NMR and MS) of chromones **1**, **2** and **3** were identical with the reported ones.[8)]

The antiplasmodial and antimycobacterial activity of compounds **1**—**10** have been tested (Table 3).

Experimental

Melting points are uncorrected. Optical rotations were determined with a Jasco digital polarimeter. UV spectra were recorded with a Shimadzu UV-240 spectrophotometer. IR spectra were recorded with a Jasco A-302 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$ or $CDCl_3$/DMSO-d_6 on a Bruker Avance 400 (400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR) spectrometer. Chemical shifts are given in δ (ppm) with tetramethylsilane as an internal standard. MS were recorded on a VG 7070 mass spectrometer operating at 70 eV with VG Quattro triple quadrupole mass spectrometer for the electrospray mass spectra. Column chromatography was carried out on Kieselgel 60 (Merck, 70—230 mesh or 230—400 mesh). TLC and PLC were performed on precoated silica gel 60 F_{254} plates (Merck); spots were detected by UV or spraying with 1% $CeSO_4$ in 10% aq. H_2SO_4 following by heating. A voucher specimen (Bansiddhi 91-08) of the plant material has been deposited at the Herbarium, the Division of Medicinal Plant Research and Development, Department of Medical Science, Nonthaburi, Thailand.

Extraction and Isolation The branches of *H. perforata* (5.1 kg) were extracted with 95% EtOH at room temperature. The ethanolic extract was filtered and evaporated to a dark brown viscous oil (186.3 g). The extract was partitioned between water (500 ml) and EtOAc (3×500 ml) and the water layer was further extracted with *n*-BuOH (3×400 ml). After evaporation, the EtOAc-, *n*-BuOH- and water-soluble fractions gave a brown viscous oil (69.8 g), a dark brown viscous oil (25.7 g) and a light brown viscous oil (50.8 g), respectively.

A portion (38.7 g) of the EtOAc-soluble fraction was separated by flash column chromatography using silica gel [Merck, 230—400 mesh, diameter×height (13.0 cm×5.0 cm)]. The column was eluted with 500 ml each fraction of hexane, gradient of hexane/EtOAc, EtOAc, gradient of EtOAc/MeOH and MeOH to gave 16 fractions.

Fr. 3 (1st column, 40% EtOAc in hexane) (6.15 g) was chromatographed on a column of silica gel (Merck, 70—230 mesh, 400 g) using hexane, gradient of hexane/EtOAc, EtOAc, gradient of EtOAc/MeOH and MeOH to give 12 fractions. Fr. 4 (2nd column, 30% EtOAc in hexane) (674 mg) was further separated on a column of silica gel (Merck, 70—230 mesh, 60 g) and eluted with hexane, gradient of hexane/EtOAc, EtOAc and 1% MeOH in EtOAc to give peucenin-7-methyl ether (**1**) as a pale yellow solid (416 mg) and a mixture of **1**, perforamone A (**4**), B (**5**) and C (**6**) as a yellow oil (36 mg). The mixture was separated by preparative TLC using hexane/EtOAc (2 : 1) to give **1** (3.8 mg), **4** (7.6 mg), **5** (3.8 mg) and **6** (2.0 mg). Similarly, fr. 5 (2nd column, 35—40% EtOAc in hexane) (1.04 g) was separated by column chromatography and preparative TLC gave **1** (801 mg), **4** (7.8 mg), **5** (16.1 mg) and **6** (9.0 mg). Compound **5**, a pale yellow wax (13.9 mg), was further purified by preparative TLC using hexane/EtOAc (1 : 1, 2 runs) as the developing solvent to give **5** as a pale yellow wax (6.1 mg) which was crystallized from MeOH/CH_2Cl_2 as colorless needles.

Fr. 4 (1st column, 60% EtOAc in hexane) (3.2 g) was separated on a column of silica gel (Merck, 70—230 mesh, 250 g) using hexane/EtOAc (60 : 1), gradient of hexane/EtOAc, EtOAc, gradient of EtOAc/MeOH and MeOH to give 13 fractions. Fr. 8 (2nd column, hexane/EtOAc, 1 : 1) was a yellow viscous oil (165 mg); a portion (44 mg) of the oil was separated by preparative TLC using benzene/hexane (5 : 1, 6 runs) to give compound **7** as a pale yellow wax (8 mg).

Fr. 5 (1st column, 80% EtOAc in hexane) (4.0 g) was chromatographed on a column of silica gel (Merck, silica gel 70—230 mesh, 250 g) using hexane and gradient of hexane/EtOAc to give 13 fractions. Fr. 7 (2nd column, hexane/EtOAc, 50 : 1 and 25 : 1), a brown oil (106 mg), was purified by preparative TLC using benzene/EtOAc (4 : 1) as the developing solvent to give greveichromenol (**10**) as a pale yellow wax (27 mg). Fr. 9 (2nd column hexane/EtOAc, 10 : 1) (308 mg) was separated by column chromatography using silica gel (Merck, 70—230 mesh, 25 g) using gradient of hexane/EtOAc, EtOAc and EtOAc/MeOH (100 : 1) as the eluent to give compound **6** as a pale yellow wax (28 mg) and a mixture of compounds **6** and perforamone D (**9**) as a yellow oil (110 mg). The mixture was further purified by preparative TLC using CH_2Cl_2/MeOH (40 : 1, 2 runs) to give **6** (18 mg) and **9** (25 mg). Fr. 10 (2nd column, hexane/EtOAc, 7 : 1) (425 mg) was purified by column chromatography using silica gel (Merck, 70—230 mesh, 40 g) and gradient of hexane/EtOAc as the eluent to give compound **8** as a yellow solid (148 mg) which was crystallized from CH_2Cl_2/MeOH (1 : 1) to give colorless needles.

Fr. 6 (1st column, EtOAc), a dark brown oil (3.5 g), was separated by column chromatography using silica gel (Merck, 70—230 mesh, 250 g) and gradient of hexane/EtOAc, EtOAc and gradient of EtOAc/MeOH to give *O*-methylalloptaeroxylin (**2**) as a yellow solid (375 mg) which was crystallized from MeOH/H_2O as yellow rhombs, mp 153—155°C.

Fr. 14 (1st column, 60% MeOH in EtOAc) (1.8 g) and Fr. 15 (1st column, 80% MeOH in EtOAc) (0.5 g) were combined and chromatographed on a column of silica gel (Merck, 70—230 mesh, 225 g) and CH_2Cl_2/MeOH/H_2O (15 : 3 : 1, 10 : 3 : 1, 7 : 3 : 1 and 6.5 : 3.5 : 1) as the eluent to give perforatic acid (**3**) as a brown solid (710 mg), which was crystallized from Et_2O/MeOH as a yellow powder, mp >325°C.

Peucenin-7-methyl Ether (1) Compound **1** was crystallized from MeOH as pale yellow needles, mp 105—106°C.[8,13)] *O*-Methylalloptaeroxylin (**2**), yellow rhombs, mp 153—155°C.[8,12,14)] Perforatic acid (**3**), a yellow powder, mp >325°C.[8)]

5-Hydroxy-7-methoxy-2-methyl-8-(2,3-epoxy-3-methylbutyl)chromone (Perforamone A) (4) Compound **4** was crystallized from MeOH/CH_2Cl_2 as colorless needles, mp 119—120°C; $[\alpha]_D^{25}$ −19.4° (c=0.07, MeOH). λ_{max}^{MeOH} (log ε) nm: 202 (4.02), 225 (3.82), 251 (3.90), 258 (3.91), 294 (3.29), 325 (3.18). ν_{max}^{Nujol} cm^{-1}: 3413, 1666, 1622, 1592, 1423, 1385, 1330, 1268, 1203, 1178, 1125, 1084. MS *m*/*z* (rel. int.): 290 (M^+, 3%), 247 (54), 219 (100), 189 (43), 149 (37), 121 (20), 77 (14), 69 (43). HR-MS *m*/*z*: Calcd for $C_{16}H_{18}O_5$: 290.1153. Found: 290.1151. ^{1}H- and ^{13}C-NMR, see Tables 1 and 2, respectively.

5-Hydroxy-7-methoxy-2-methyl-8-(1-hydroxy-3-methyl-3-butenyl)-chromone (Perforamone B) (5) Compound **5**, colorless needles, mp 162—163°C; $[\alpha]_D^{25}$ −18.2° (c=0.12, MeOH). λ_{max}^{MeOH} (log ε) nm: 204 (4.02), 225 (sh) (3.85), 252 (3.94), 258 (3.95), 295 (3.34), 325 (3.25). ν_{max}^{Nujol} cm^{-1}: 3424, 1660, 1619, 1590, 1421, 1383, 1330, 1272, 1206, 1179, 1123, 1083. MS *m*/*z* (rel. int.): 290 (M^+, 4.5%), 219 (100), 205 (4.5), 189 (18), 149 (13), 121 (10), 83 (8), 69 (18). HR-MS *m*/*z*: Calcd for $C_{16}H_{18}O_5$: 290.1153. Found: 290.1156. ^{1}H- and ^{13}C-NMR, see Tables 1 and 2, respectively.

5-Hydroxy-7-methoxy-2-methyl-8-(2-hydroxy-3-methyl-3-butenyl)-chromone (Perforamone C) (6) Compound **6** was crystallized from MeOH/H_2O as pale yellow rhombs, mp 104—105°C; $[\alpha]_D^{25}$ −70.6° (c=0.10, MeOH); λ_{max}^{MeOH} (log ε) nm: 204 (4.32), 225 (sh) (4.14), 252 (4.22), 259 (4.24), 296 (3.59), 327 (3.51); ν_{max}^{Nujol} cm^{-1}: 3412, 1658, 1619, 1586, 1423, 1383, 1329, 1270, 1203, 1182, 1119, 1080; MS *m*/*z* (rel. int.): 290 (M^+, 4%), 219 (100), 205 (3), 189 (13), 149 (5), 121 (5), 71 (5). HR-MS *m*/*z*: Calcd for $C_{16}H_{18}O_5$: 290.1153. Found: 290.1154. ^{1}H- and ^{13}C-NMR, see Tables 1 and 2, respectively.

Eugenin (**7**): Pale yellow plates, mp 107—108°C.[10)] ^{13}C-NMR see Table 2. Saikochromone A (**8**): Colorless needles, mp 196—198°C.[11)]

2-Hydroxymethylalloptaeroxylin (Perforamone D) (9) Compound **9** was crystallized from MeOH/H_2O as pale yellow rhombs, mp 139—140°C; λ_{max}^{MeOH} (log ε) nm: 223 (3.96), 237 (3.91), 265 (4.12), 302 (sh) (3.36), 347 (3.04); ν_{max}^{Nujol} cm^{-1}: 3389, 1662, 1614, 1583, 1424, 1371, 1329, 1290, 1172,

1124, 852; MS *m*/*z* (rel. int.): 274 (M^+, 11%), 259 (100), 219 (11), 203 (8), 135 (6), 115 (6), 73 (7). HR-MS *m*/*z*: Calcd for $C_{15}H_{14}O_5$: 274.0840. Found: 274.0842. ^{1}H- and ^{13}C-NMR, see Tables 1 and 2, respectively.

Greveichromenol (10) Compound **10** was crystallized from MeOH/H_2O as pale yellow needles, mp 173—175°C.[12] λ_{max}^{MeOH} (log ε) nm: 229 (4.25), 229 (4.25), 236 (sh) (4.19), 248 (4.15), 277 (4.44), 295 (sh) (4.15); ν_{max}^{Nujol} cm^{-1}: 3333, 1660, 1627, 1581, 1450, 1413, 1325, 1302, 1169, 1153, 1125, 1092, 1020, 853; MS *m*/*z* (rel. int.): 274 (M^+, 29%), 259 (100), 115 (3), 69 (3). ^{1}H- and ^{13}C-NMR, see Tables 1 and 2, respectively.

Antimycobacterial Assay The antimycobacterial activity was assessed against *Mycobacterium tuberculosis* H37Ra using the Microplate Alamar Blue Assay (MABA).[15] Standard drugs, isoniazide (MIC of 0.040—0.090 μg/ml) and kanamycin sulfate (MIC of 2.0—5.0 μg/ml) were used as reference compounds for the assay.

Antiplasmodial Assay The *Plasmodium falciparum* (K1, multidrug resistant strain) was cultured continuously according to the method of Trager and Jensen.[16] The quantitative assessment of the antiplasmodial activity *in vitro* was performed by means of the microculture radioisotope technique based upon the method described by Desjardins *et al*.[17] Standard sample, chloroquin diphosphate (IC_{50} value of 0.16 μg/ml, 0.31 μM) was used as reference compound for the assay.

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