Supporting Information-1 (experimental procedures and spectral data)

A Simple Biomimetic Synthesis of \textit{dl}-Chamaejasmine, a Unique 3,3’-Biflavanone

Wei-Dong Z. Li* and Bao-Chun Ma

\textit{State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China}

Table of Contents

1. \textit{General} procedure .................................................................\textbf{S2}  
2. Typical procedures for the preparation of substituted chalcones and the corresponding flavanones ........................................\textbf{S2–S3}  
3. Typical procedures for the preparation of substituted 3-haloflanones ........\textbf{S3–S4}  
4. Physical and spectral data of substituted 3-haloflanones ....................\textbf{S5–S9}  
5. Typical procedures for the reductive dimerization of 3-iodoflanones ........\textbf{S9–S10}  
6. Physical and spectral data of 3,3’-biflavanones ................................\textbf{S10–S12}  
7. Global demethylation and synthesis of \textit{dl}-chamaejasmine (1) ...........\textbf{S12–S14}  
8. X-ray crystallographic data (Table 1) of tetramethyl ether \textit{dl}-13 ........\textbf{S15}  
9. High resolution FTMS (SIMS) data collection (Table 2) of some typical 3-haloflanones–observation of dehalogenative dimeric product formation ......\textbf{S16}  
10. FT-HRMS spectrum of 3-halogenated flavanone derivatives...............\textbf{S17–S23}
**Experimental**

**General**

For product purification by flash column chromatography, silica gel (200~300 mesh) and light petroleum ether (bp. 60~90 °C) are used. All solvents were purified and dried by standard techniques, and distilled prior to use. All organic extracts were dried over Na₂SO₄, unless otherwise noted. IR spectra were recorded on a Nicolet FT-170SX spectrometer as liquid film. \(^1\)H and \(^13\)C NMR spectra were taken on a Bruker AM-200, AM-400 and Varian mercury 300 MHz spectrometer with TMS as an internal standard and CDCl₃ as solvent unless otherwise noted. EI-MS was obtained on HP-5988A GC/MS instrument. FAB-MS was measured on VG ZAB-HS instrument. HRMS were determined on a Bruker Daltonics APEX II 47e FT-ICR spectrometer. For liquid secondary ion mass spectrometry (LSIMS), Cs⁺ ion beam (2 mA) was used at 10000 V and analytical cell vacuum was \(2 \times 10^{-9}\) mba. Preparative TLC purification was performed on silica gel GF₂₅₄ TLC plates (20 cm × 20 cm, 0.5–1.0 mm). Melting points were measured on Kofler hot stage and are uncorrected.

All moisture-sensitive reactions were performed in flame-dried glassware under stream of nitrogen. Other commercially obtained reagents and solvents were used as received without further purification unless indicated otherwise.

Substituted 2-hydroxyl chalcones and the corresponding flavanones were synthesized according to standard literature methods,\(^1\) or by the following general procedures, respectively.

*Typical procedure for the preparation of substituted 2-hydroxyl chalcones*

\[
\begin{align*}
\text{R_2-OH} & \quad \text{R_3} \\
\text{R_2} \quad \text{O} & \quad \text{R_1} \\
& \quad \text{CHO} & \quad \text{KOH} \\
\text{EtOH-H}_2\text{O} & \quad 75\% \\
& \quad \text{R_2} \quad \text{R_3} & \quad \text{OH} \\
& \quad \text{R_1} \quad \text{O} \\
\end{align*}
\]

A mixture of substituted acetylphenol substrate (10 mmol) and substituted benzaldehyde derivative (12 mmol) in 20 mL of EtOH was treated with a solution mixture of KOH (ca. 10 g) in H₂O (8 mL) and EtOH (10 mL) at 0 °C by dropwise

---

addition. The reaction mixture was stirred at rt. for 36 h, then poured onto ice-water (100 mL), acidified with conc. HCl to pH 2, the precipitates were filtered, and dried. Recrystallization of the crude product from EtOH gave the corresponding 2-hydroxy chalcone derivatives as colorless crystals in generally good yield (ca. 75%).

Typical procedure for the preparation of substituted flavanone derivatives from the corresponding chalcone precursors

A mixture of substituted 2-hydroxy chalcone (10 mmol) and anhydrous NaOAc (2.0 g) in 30 mL of 95% ethanol was brought to reflux for ca. 48 h. The reaction mixture was then cooled; 20 mL of water was added, and extracted with EtOAc (50 mL × 3). The organic layer was washed with water, brine and dried. Evaporation of the solvent followed by purification by silica gel chromatography gave flavanone as solids in ca. 60% yield (depending on the conversion of the starting chalcone employed).

Experimental procedures for the preparation of 3-halogenated flavanone derivatives

Method-A²

A representative procedure of this method is as follows:

To a solution of flavanone (5a, R₁ = R₂ = H, 1.56 g, 6.95 mmol) in anhydrous CH₃CN (10 mL) was added portionwise I₂ (0.77 g, 3.82 mmol, 0.55 equiv) and SeO₂ (0.42 g, 3.82 mmol, 0.55 equiv) successively at room temperature. The reaction mixture was then refluxed for ca. 8 h, cooled to rt., filtered through a pad of silica gel. The filtrate was taken in water and extracted with EtOAc (30 mL × 3). The organic layers were

combined, washed with aqueous Na$_2$S$_2$O$_3$, water, brine, and dried. Evaporation of the solvent in vacuo followed by silica gel chromatographic purification (Petrol. Ether : EtOAc 50:1) gave the corresponding 3-iodoflavanone 5 (cis and trans) as light-sensitive solids: trans isomer (0.55 g) and cis isomer (2.23 g) in an overall yield of 85% in a ratio of ca. 1 : 4.

3-Iodoflavanones 7 and 8 (cis and trans isomers)$^3$ were prepared by the above procedure, 3-iodoflavanone 9 (cis and trans isomers) was prepared by the following Method-B.

**Method-B$^4$**

A mixture of naringenin trimethyl ether (9a, 0.94 g, 3.0 mmol) and NIS (0.61 g, 2.7 mmol, 0.9 equiv) in anhydrous CCl$_4$ (50 mL) was refluxed for 6 h under N$_2$. The resulting reaction mixture was cooled and filtered through a pad of Celite. The filtrate was diluted with EtOAc (30 mL), then washed with water, brine, and dried. Evaporation of the solvent followed by silica gel chromatography purification (Petrol. Ether : EtOAc 20:1) gave 3-iodonaringenin trimethyl ethers 9: trans isomer (0.15 g) and cis isomer (0.77 g) as solids in an overall yield of 70% in a ratio of ca. 1 : 5.

**Method-C$^5$** (preparation of 3-bromoflavanone derivatives)

A representative procedure of this method is as follows:

---

$^3$ The isomeric ratio varies for different flavanone substrates, but cis isomer is predominated.


To a stirred mixture of the naringenin trimethyl ether (9a, R₁ = R₂ = R₃ = OMe, 0.315 g, 1.0 mmol) in 10 mL of ethyl acetate–chloroform (v/v, 3:2) was added cupric bromide (0.67 g, 3.0 mmol, 3 equiv) in one portion and the resulting mixture was brought to reflux for ca. 8 h, cooled to rt., filtered through a pad of Celite, and washed with ethyl acetate. The filtrate was evaporated under reduced pressure and followed by careful silica gel chromatography purification (Petrol. Ether : EtOAc 50:1) to give 3-bromonaringenin trimethyl ethers as light-sensitive solids: trans isomer (43 mg) and cis isomer (172 mg) in an overall yield of 55% in a ratio of 1 : 4.

\[
\text{cis-3-Iodoflavanone (cis-5), mp. 122–123 °C (EtOAc–petrol. Ether); IR (KBr, cm}^{-1}\text{) } \nu_{\text{max}} 2990, 1682, 1303, 1223, 757; ^1\text{H-NMR (200 MHz, CDCl}_3\text{) } \delta 4.66 (1H, d, J = 2.0 Hz, H-3); 4.86 (1H, d, J = 2.0 Hz, H-2); 7.05 (2H, dd, J = 8.0; 1.4 Hz); 7.65 (5H, m); 8.02 (2H, dd, J = 8.0; 1.4 Hz) ppm; ^13\text{C-NMR (50 MHz, CDCl}_3\text{) } \delta 35.4, 79.6, 118.1, 122.6, 125.5, 128.4, 128.5, 128.7, 136.6, 137.0, 160.2, 187.9 ppm. EIMS (m/z, %): 350 (M⁺, 10), 223 ([M-I]⁺, 100), 121(17); HRMS (SIMS) m/z 447.1569 ([2[M-I]+H]⁺); 350.9868 ([M+H]⁺, calcd for C₁₅H₁₂O₂I: 350.9876); 223.0750 ([M-I]⁺).
\]

\[
\text{trans-3-Iodoflavanone (trans-5), mp. 102–103 °C (EtOAc–petrol. Ether); IR (KBr, cm}^{-1}\text{) } \nu_{\text{max}} 2990, 1682, 1461, 1303, 1223, 757; ^1\text{H-NMR (200 MHz, CDCl}_3\text{) } \delta 5.32 (1H, d, J = 6.8 Hz, H-3); 5.63 (1H, d, J = 6.8 Hz, H-2); 7.05 (2H, dd, J = 8.0; 1.4 Hz); 7.36 (4H, m); 7.56 (2H, dd, J = 8.0; 1.4 Hz); 7.91 (1H, dd, J = 8.0; 1.4 Hz) ppm; EIMS (m/z, %): 350 (M⁺, 10), 223 ([M-I]⁺, 100), 121 (17); HRMS (SIMS) m/z 447.1596 ([2[M-I]+H]⁺); 350.9882 ([M+H]⁺, calcd for C₁₅H₁₂O₂I: 350.9876); 223.0754 ([M-I]⁺).
\]
cis-3-Bromoflavanone, mp. 109–111 °C (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) ν_max 2956, 1698, 1373, 1294, 1193, 848; ¹H NMR (200 MHz, CDCl₃) δ 4.57 (1H, d, J = 1.8 Hz, H-3); 5.43 (1H, s, br, H-2); 7.05 (2H, dd, J = 7.8; 1.6 Hz); 7.46 (6H, m); 7.95 (1H, dd, J = 8.0; 1.8 Hz) ppm; EIMS (m/z, %): 302 (M⁺, 8), 223 ([M–Br]⁺, 61), 121 (100).

trans-3-Bromoflavanone, mp. 90–92 °C (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) ν_max 2930, 1705, 1459, 1294, 1228, 763; ¹H NMR (200 MHz, CDCl₃) δ 5.01 (1H, d, J = 8.6 Hz, H-3); 5.59 (1H, d, J = 8.6 Hz, H-2); 7.08 (2H, d, J = 7.8 Hz); 7.41 (5H, m); 7.57 (1H, m, H-6); 7.94 (1H, d, J = 7.8 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ 51.5, 83.9, 118.0, 119.0, 122.4, 127.2, 128.1, 128.9, 129.3, 136.2, 137.0, 160.0, 185.3 ppm; HRMS (SIMS) m/z 447.1603 ([2[M–Br]+H]^+) ; 303.0020 ([M+H]^+, calcd for C₁₅H₁₂O₂Br: 303.0015); 223.0755 ([M–Br]^+).

cis-4’-Methoxy-3-iodoflavanone (cis-7), mp. 121–123 °C (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) ν_max 2924, 1686, 1462, 1254, 1179, 759; ¹H NMR (300 MHz, CDCl₃) δ 3.76 (3H, s, OCH₃); 4.57 (1H, s, br, H-3); 4.79 (1H, d, J = 2.2 Hz, H-2); 6.86 (2H, d, J = 8.8 Hz); 6.99 (2H, t, J = 8.8 Hz); 7.28 (2H, dd, J = 8.4; 2.0 Hz); 7.53 (1H, dd, J = 8.4; 2.0 Hz); 7.90 (1H, dd, J = 8.4; 2.0 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ 36.1, 55.2, 79.2, 113.8, 118.0, 122.4, 126.8, 128.3, 129.0, 136.4, 160.0, 188.0 ppm; EIMS (m/z, %): 380 (M⁺, 19), 253 ([M–I]⁺, 100), 121(33). HRMS (SIMS) m/z 507.1783 ([2[M–I]+H]^+); 380.9970 ([M+H]^+, calcd for C₁₆H₁₄O₃I: 380.9982); 253.0859 ([M–I]^+).

trans-4’-Methoxy-3-iodoflavanone (trans-7), mp. 106–108 °C (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) ν_max 2926, 1686, 1461, 1297, 1254, 758; ¹H NMR (200 MHz, CDCl₃) δ 3.79 (3H,
cis-4', 7-Dimethoxy-3-iodoflavanone (cis-8), mp. 138–140 °C (EtOAc–petrol. Ether); IR ((KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\) 2925, 1685, 1029, 759; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.54 (3H, s, OCH\(_3\)); 3.56 (3H, s, OCH\(_3\)); 4.59 (1H, s, br , H-3); 4.81 (1H, d, \(J = 2.1\) Hz, H-2); 6.98 (2H, d, \(J = 8.8\) Hz); 7.05 (2H, d, \(J = 8.8\) Hz); 7.42 (1H, d, \(J = 2.0\) Hz); 7.53 (1H, dd, \(J = 8.4; 2.0\) Hz); 7.94 (1H, dd, \(J = 8.4; 2.0\) Hz) ppm; EIMS (m/z, %): 380 (M\(^+\), 19), 253 ([M–I]\(^+\), 100), 121 (33).

trans-4', 7-Dimethoxy-3-iodoflavanone (trans-8), mp. 154–156 °C (EtOAc–petrol. Ether); IR ((KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\) 2924, 2362, 1687, 1028, 762; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.61 (3H, s, OCH\(_3\)); 3.62 (3H, s, OCH\(_3\)); 5.32 (1H, d, \(J = 7.4\) Hz, H-3); 5.58 (1H, d, \(J = 7.4\) Hz, H-2); 6.69 (2H, d, \(J = 8.8\) Hz); 7.08 (2H, d, \(J = 8.8\) Hz); 7.30 (1H, d, \(J = 2.0\) Hz); 7.56 (1H, dd, \(J = 8.4; 2.0\) Hz); 7.93 (1H, dd, \(J = 8.4; 2.0\) Hz) ppm; EIMS (m/z, %): 410 (M\(^+\), 12), 283 ([M–I]\(^+\), 100), 134 (66); HRMS (SIMS) \(m/z\) 567.1996 ([2[M–I]+H]\(^+\)); 411.0092 ([M+H]\(^+\), calcd for C\(_{17}\)H\(_{16}\)O\(_4\)I: 411.0088); 283.0968 ([M–I]\(^+\)).

cis-3-Iodonaringeninin trimethyl ether (cis-6), mp. 181–183 °C (EtOAc–petrol. Ether); IR (KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\) 2936, 1669, 1608, 1253, 1159, 831; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 3.78 (3H, s, OCH\(_3\)); 3.80 (3H, s, OCH\(_3\)); 3.85 (3H, s, OCH\(_3\)); 4.46 (1H, br s, H-3); 4.61 (1H, d, \(J = 1.8\) Hz S7
Hz, H-2); 6.09 (1H, d, J = 2.0 Hz); 6.20 (1H, br d, J = 2.0 Hz); 6.90 (2H, d, J = 8.8 Hz); 7.32 (2H, d, J = 8.8 Hz) ppm; $^{13}$C NMR (50 MHz, CDCl$_3$) δ 38.5, 56.1, 56.4, 56.6, 79.7, 94.4, 94.6, 103.4, 114.6, 115.0, 127.7, 128.5, 130.1, 164.1, 164.5, 167.2, 186.3 ppm; EIMS (m/z, %): 440 (M$^+$, 57), 313 ([M–I]$^+$, 80), 121 (100); HRMS (SIMS) m/z 627.2133 ([2[M–I]+H]$^+$); 441.0154 ([M+H]$^+$, calcd for C$_{18}$H$_{18}$O$_5$I: 441.0193); 313.1036 ([M–I]$^+$).

trans-3-Iodonaringenin trimethyl ether (trans-9), mp. 167–169 ºC (EtOAc–petrol. Ether); IR ((KBr, cm$^{-1}$) νmax 3935, 1670, 1607, 1250, 822; $^1$H NMR (200 MHz, CDCl$_3$) δ 3.71 (3H, s, OCH$_3$); 3.76 (3H, s, OCH$_3$); 3.79 (3H, s, OCH$_3$); 5.06 (1H, d, J = 5.8 Hz, H-3); 5.46 (1H, d, J = 5.8 Hz, H-2); 6.01 (1H, d, J = 1.8 Hz); 6.10 (1H, d, J = 1.8 Hz); 6.78 (2H, d, J = 8.6 Hz); 7.20 (2H, d, J = 8.6 Hz) ppm; $^{13}$C NMR (50 MHz, CDCl$_3$) δ 32.0, 55.2, 55.6, 56.1, 84.0, 93.4, 93.5, 103.4, 113.8, 126.8, 128.1, 128.6, 159.9, 162.7, 162.8, 166.6, 183.6 ppm; EIMS (m/z, %): 440 (M$^+$, 16), 313 ([M–I]$^+$, 100), 121 (90); HRMS (SIMS) m/z 627.1986 ([2[M–I]+H]$^+$); 441.0162 ([M+H]$^+$, calcd for C$_{18}$H$_{18}$O$_5$I: 441.0193); 313.1065 ([M–I]$^+$).

cis-3-Bromonaringenin trimethyl ether, mp. 139–141 ºC (EtOAc–petrol. Ether); IR ((KBr, cm$^{-1}$) νmax 2938, 1675, 1609, 1253, 1217, 834; $^1$H NMR (200 MHz, CDCl$_3$) δ 3.84 (3H, s, OCH$_3$); 3.86 (3H, s, OCH$_3$); 3.92 (3H, s, OCH$_3$); 4.39 (1H, d, J = 1.6 Hz, H-3); 5.35 (1H, s, br, H-2); 6.15 (1H, d, J = 2.2 Hz); 6.26 (1H, d, J = 2.2 Hz); 6.97 (2H, d, J = 8.8 Hz); 7.43 (2H, d, J = 8.8 Hz) ppm; $^{13}$C NMR (50 MHz, CDCl$_3$) δ 53.7, 55.2, 55.6, 56.2, 78.7, 93.4, 93.7, 102.8, 113.7, 127.3, 127.7, 159.8, 163.3, 163.8, 166.4, 183.7 ppm; EIMS (m/z, %): 392 (M$^+$, 29), 313 ([M–Br]$^+$, 100). HRMS (SIMS) m/z 627.1821 ([2[M–Br]+H]$^+$); 393.0292 ([M+Br]$^+$, calcd for C$_{18}$H$_{18}$O$_5$Br: 393.0332); 313.1053 ([M–Br]$^+$).
trans-3-Bromonaringenin trimethyl ether, mp. 177−179 °C (EtOAc−petrol. Ether); IR (KBr, cm⁻¹) ν max 2938, 1679, 1609, 1253, 1218, 821;¹H NMR (200 MHz, CDCl₃) δ 3.79 (3H, s, OCH₃); 3.83 (3H, s, OCH₃); 3.88 (3H, s, OCH₃); 4.81 (1H, d, J = 6.8 Hz, H-3); 5.52 (1H, d, J = 6.8 Hz, H-2); 6.10 (1H, d, J = 2.2 Hz); 6.16 (1H, d, J = 2.2 Hz); 6.88 (2H, d, J = 8.6 Hz); 7.29 (2H, d, J = 8.6 Hz) ppm;¹³C NMR (50 MHz, CDCl₃) δ 51.8, 55.3, 55.7, 56.2, 82.9, 93.5, 103.9, 114.2, 114.4, 128.3, 160.1, 162.8, 163.0, 166.7, 182.2 ppm; EIMS (m/z, %): 392 (M⁺, 41), 313 ([M−Br]⁺, 100). HRMS (SIMS) m/z 393.0376 ([M+H]⁺, calcd for C₁₈H₁₈O₅Br: 393.0332); 313.1053 ([M−Br]⁺).

Reductive dimerization of 3-iodoflavanone 5 to dl-6 mediated by metallic indium

\[
\begin{align*}
\text{5 (cis + trans)} & \quad \xrightarrow{\text{In, DMF, reflux ca. 3 – 5%}} \quad \text{dl-6} \\
\end{align*}
\]

A mixture of trans- and cis-3-iodoflavanones 5 (700 mg, 2.0 mmol) and indium powder (230 mg, 2.0 mmol) in dry DMF (5 mL) was brought to reflux under nitrogen for 6 h. The reaction mixture was diluted with EtOAc and filtered. The filtrate was washed successively with water, brine, and dried. Evaporation of the solvent followed by silica gel chromatography purification and further preparative TLC purification with benzene as solvent gave the dehalogenated dimer 3,3’-biflavanone dl-6 (23 mg, 0.052 mmol, ca. 5%), along with the corresponding flavanone (25 mg, 5%, reductive dehalogenation), flavone (90 mg, 20%, dehydrohalogenation), and chalcone (110 mg, 25%) derivatives.
Reductive dimerization of substituted 3-iodoflavanones 5, 7, 8 and 9 to the corresponding dl-3,3'-biflavanones 6, 10, 11 and 12 respectively induced by metallic lanthanum

Typical experimental procedure is as follows:

A mixture of trans- and cis-3-iodoflavanones 5 (1.05 g, 3.0 mmol) and lanthanum turnings (139 mg, 1.0 mmol) in anhydrous THF (3 mL) was refluxed under nitrogen atmosphere for 2 h. The reaction was then quenched by the addition of aqueous HCl (1 M, 3 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with water, brine, and dried over MgSO₄. The solvent was evaporated in vacuo and the residue was purified by silica gel chromatograph (Petrol. Ether : EtOAc 40:1) to give the corresponding reductive dimerization product dl-6 (135 mg, ca. 20%), along with the corresponding flavanone (35 mg, 5%), flavone (65 mg, 10%), and chalcone (164 mg, 25%) derivatives.⁶

Racemate (trans, trans, trans)-2, 2', 3, 3'-Tetrahydro-2, 2'-bis-phenyl-(3, 3'-Bi-4H-1-benzopyran)-4, 4'-dione (dl-6), mp. 199–201 °C (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) νmax 1728, 1689, 1649, 1607, 1376, 1270; ¹H NMR (300 MHz, CDCl₃) δ 2.82 (2H, d, J = 12 Hz, H-3, H-3'), 6.10 (2H, d, J = 12 Hz, H-2, H-2'), 7.10 (4H, m), 7.30 (10H, m), 6.94 (2H, dd, J = 8.0; 1.4 Hz), 7.92 (2H, dd, J = 8.0; 1.4 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ 51.3 (C-3, C-3'), 84.0 (C-2, C-2'), 117.9, 121.0, 121.6, 127.0, 127.5, 128.3, 128.9, 129.4, 136.2, 136.8, 161.3, 192.8 ppm; EIMS (m/z, %): 446 (M⁺, 1), 223 ([M/2]⁺, 100), 121 (36); FABMS

⁶ An adjusted yield of 33% for the dimeric product dl-6 was estimated based on the recovered corresponding flavanone, flavone and chalcone derivatives, which in principle could be converted readily to the starting 3-iodoflavanones.

Racemate (trans, trans, trans)-2, 2′, 3, 3′-Tetrahydro-2, 2′-bis(4-methoxyphenyl)-[3, 3′-Bi-4H-1-benzopyran]-4, 4′-dione (dl-10), yield 18% (30%), mp. 176–178 ºC (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) νmax 1725, 1681, 1606, 1513, 1465, 1253; ¹H NMR (300 MHz, CDCl₃) δ 2.83 (2H, d, J = 12 Hz, H-3, H-3′), 3.85 (6H, s, OMe), 6.06 (2H, d, J = 12 Hz, H-2, H-2′), 6.76 (4H, d, J = 9.3 Hz), 6.93 (2H, d, J = 8.1 Hz), 7.03 (2H, dd, J = 7.5; 1.8 Hz), 7.07 (4H, d, J = 9.3 Hz), 7.46 (2H, dd, J = 7.5; 1.8 Hz), 7.90 (2H, d, J = 7.5 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ 51.4 (C-3, C-3′), 55.4, 83.8 (C-2, C-2′), 114.2, 117.8, 121.0, 121.5, 127.4, 129.1, 129.2, 136.1, 160.3, 161.4, 193.0; EIMS (m/z, %): 506 (M⁺), 385, 372, 253 ([M/2]⁺, 100); HRMS (ESI, m/z): 507.1805 ([M+H]⁺, calcd for C₃₂H₂₇O₆: 507.1802); 253.0859 ([M/2]⁺).

Racemate (trans, trans, trans)-2, 2′, 3, 3′-Tetrahydro-7, 7′-dimethoxy-2, 2′-bis(4-methoxyphenyl)-[3, 3′-Bi-4H-1-benzopyran]-4, 4′-dione (dl-11), yield 15% (25%), mp. 165–167 ºC (EtOAc–petrol. Ether); IR ((KBr, cm⁻¹) νmax 1727, 1671, 1607, 1513, 1247, 1160; ¹H NMR (300 MHz, CDCl₃) δ 2.75 (2H, d, J = 12 Hz, H-3, H-3′), 3.76 (6H, s, OMe), 3.83 (6H, s, OMe), 6.68 (2H, d, J = 12 Hz, H-2, H-2′), 6.38 (2H, s), 6.58 (2H, d, J = 8.7 Hz), 6.87 (4H, d, J = 8.1 Hz), 7.08 (4H, d, J = 8.7 Hz), 7.84 (2H, d, J = 9.0 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ 50.9 (C-3, C-3′), 55.4, 55.6, 84.1 (C-2, C-2′), 100.6, 110.1, 114.2, 115.0, 128.3, 135.9 ppm.

⁷ Yield in parentheses refers to the adjusted yield (ref. 6).
129.1, 129.2, 160.3, 163.3, 166.1, 191.6 ppm; FABMS (m/z): 589.4 ([M+Na]+), 567.4 ([M+H]+), 417.3, 283.2 ([M/2]+); HRMS (SIMS, m/z): 567.2021 ([M+H]+, calcd for C_{34}H_{31}O_{8}: 567.2013); 283.0966 ([M/2]+). 

Racemate (trans, trans, trans)-2, 2′, 3, 3′-Tetrahydro-5, 5′, 7, 7′-tetramethoxy-2, 2′-bis(4-methoxyphenyl)-[3, 3′-Bi-4H-1-benzopyran]-4, 4′-dione (dl-chamaejasmine hexamethyl ether 12), yield 10% (17%), mp. 185–187 °C (EtOAc–petrol. Ether); IR ((KBr, cm\(^{-1}\)) \(\nu_{\text{max}}\) 1665, 1607, 1573, 1515, 1461, 1217; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 2.68 (2H, d, \(J = 12.3\) Hz, H-3, H-3′), 3.76 (6H, s, OMe), 3.85 (6H, s, OMe), 3.88 (6H, s, OMe), 6.03 (2H, d, \(J = 2.4\) Hz), 6.04 (2H, d, \(J = 12.3\) Hz, H-2, H-2′), 6.07 (2H, d, \(J = 2.4\) Hz), 6.86 (4H, d, \(J = 9.0\) Hz), 7.10 (4H, d, \(J = 8.7\) Hz) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 52.1 (C-3, C-3′), 55.3, 55.5, 56.1, 83.3 (C-2, C-2′), 93.1, 93.2, 106.3, 113.9, 129.3, 129.5, 160.0, 162.5, 164.7, 165.6, 190.1 ppm; FABMS (m/z): 627.2 ([M+H]+), 447.2, 312.9 ([M/2]+); HRMS (SIMS, m/z): 627.2215 ([M+H]+, calcd for C_{36}H_{35}O_{10}: 627.2224); 313.1060 ([M/2]+).

**Global demethylation of dl-12 to dl-chamaejasmine (I) and partial demethylation to dl-13**

To a stirred solution of BBr\(_3\) (0.5 mL, large excess) in 5 mL of freshly distilled CH\(_2\)Cl\(_2\) at −78 °C was added dropwise a solution of dl-12 (30 mg, 0.048 mmol) in 3 mL of CH\(_2\)Cl\(_2\). The resulting reaction mixture was allowed to warm up to room temperature gradually and stirred

---

Nyandat, E.; Hassanali, A.; De Vicente, Y.; Multrari, G.; Galeffi, C. *Phytochemistry* 1990, 29, 2361. A melting point of 117–119 °C (from n-hexane) was recorded for the partial racemate (enantiomeric ratio ca. 2:1) of (+)-(2\(S\), 3\(R\))-chamaejasmine hexamethyl ether therein.
for 24 h. The reaction was carefully quenched with 2 mL cold water and stirred vigorously for 2 h, extracted with EtOAc (20 mL x 6) and dried over MgSO$_4$. Evaporation of the solvent in vacuo, the residue was purified by flash chromatograph on silica gel eluting with acetone to give $dl$-chamaejasmine (1) as colorless solids (18 mg, yield 70%).

**Partially** demethylated product $dl$-13 was obtained (ca. 30%) when the reaction was quenched carefully at −78 ºC after 1 h of addition of BBr$_3$ and usual extractive workup and chromatographic purification on silica gel. The unreacted hexamethyl ether $dl$-12 (ca. 70%) was fully recovered.

Racemate ($trans$, $trans$, $trans$)-2, 2', 3, 3'-Tetrahydro-5, 5', 7, 7'-tetrahydroxy-2', 2'-bis (4-hydroxyphenyl)-[3, 3'-Bi-4H-1-benzopyran]-4, 4'-dione ($dl$-chamaejasmine, 1), mp. 293–295 ºC (acetone); $^9$ IR (KBr, cm$^{-1}$) $\nu_{\text{max}}$ 3198, 1688, 1636, 1515, 1643, 1158; $^1$H NMR (300 MHz, $d_6$-acetone) $\delta$ 2.94 (d, 2 H, $J$ = 12.3 Hz, H-3, H-3'), 5.86 (d, 2 H, $J$ = 12.3 Hz, H-2, H-2'), 5.88 (s, 2 H), 5.96 (2 H, $d$, $J$ = 1.8 Hz), 6.86 (4 H, $d$, $J$ = 8.4 Hz), 7.02 (4 H, $d$, $J$ = 8.4 Hz), 7.36 (s, OH), 8.70 (s, OH), 9.72 (s, OH), 11.92 (s, 2 H) ppm; $^{13}$C NMR (75 MHz, $d_6$-acetone) $\delta$ 49.9 (C-3, C-3'), 83.9 (C-2, C-2'), 95.2, 96.4, 102.6, 115.7, 127.8, 129.6, 158.6, 163.4, 164.7, 166.9, 197.2 ppm; FABMS ($m/z$): 543.2 ([M+H]$^+$), 271.1 ([M/2]$^+$). HRMS (SIMS) $m/z$ observed 543.1280 for [M+H]$^+$, calcd 543.1286 for C$_{30}$H$_{23}$O$_{10}$; observed 271.0619 for [M/2]$^+$, calcd 271.0603 for C$_{15}$H$_{11}$O$_5$.

---

$^9$ Huang, W. –K.; Zhang, Z. –J. Kexue Tongbao 1979, 24, 24; Chem. Abstr. 1979, 90, 135086m. A melting point of 309 ºC (uncorrected, crystallized from ethanol) was recorded therein.
Racemate (*trans*, *trans*, *trans*)-2, 2’, 3, 3’-Tetrahydro-5, 5’-dihydroxy-7, 7’-dimethoxy-2, 2’-bis(4-methoxyphenyl)-[3, 3’-Bi-4H-1-benzopyran]-4, 4’-dione (dl-13), mp. 118–120 °C (as trihydrate from petrol. Ether–acetone); IR (KBr, cm⁻¹) νmax 3118, 1700, 1574, 1514, 1251, 1155; ¹H NMR (300 MHz, CDCl₃) δ 2.82 (d, 2 H, J = 12 Hz, H-3, H-3’), 3.77 (s, 6 H, OMe), 3.85 (s, 6 H, OMe), 5.93 (d, 2 H, J = 12 Hz, H-2, H-2’), 5.94 (d, 2 H, J = 1.8 Hz), 6.06 (d, 2 H, J = 1.8 Hz), 6.87 (d, 4 H, J = 8.4 Hz), 7.04 (d, 4 H, J = 8.4 Hz); 11.87 (s, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 49.7 (C-3, C-3’), 55.4, 55.7, 83.5 (C-2, C-2’), 94.0, 95.2, 103.1, 114.3, 124.5, 129.2, 160.4, 162.6, 164.1, 167.9, 196.6 ppm; FABMS (m/z): 621.4 ([M+Na]+), 599.3 ([M+H]+), 299.1 ([M/2]⁺). HRMS (SIMS) m/z observed 599.1914 for [M+H]⁺, calcd 599.1912 for C₃₄H₃₁O₁₀; observed 299.0959 for [M/2]⁺, calcd 299.0917 for C₁₇H₁₅O₅.
### Table 1. X-ray crystallographic data of *dl-13*

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color/shape</td>
<td>Colorless/block</td>
</tr>
<tr>
<td>Crystal dimension (mm$^3$)</td>
<td>0.4×0.3×0.2</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>C$<em>{34}$H$</em>{30}$O$_{10}$·3H$_2$O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>652.63</td>
</tr>
<tr>
<td>Temperature (K)</td>
<td>293 (2)</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P1</td>
</tr>
<tr>
<td>Unit cell dimension (Å)</td>
<td>a = 11.143 (2) Å, b = 11.274 (2) Å, c = 14.362 (3) Å</td>
</tr>
<tr>
<td></td>
<td>α = 72.17 (3)$^\circ$, β = 74.90 (3)$^\circ$, γ = 76.96 (3)$^\circ$</td>
</tr>
<tr>
<td>Volume (Å$^3$)</td>
<td>1637.3 (5)</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
</tr>
<tr>
<td>Density (Mg/m$^3$)</td>
<td>1.324</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.102</td>
</tr>
<tr>
<td>Diffractometer</td>
<td>Enraf-Nonius CAD4</td>
</tr>
<tr>
<td>Scan</td>
<td>ω/2θ</td>
</tr>
<tr>
<td>θ range ($^\circ$)</td>
<td>1.52~18.50</td>
</tr>
<tr>
<td>Reflections measured</td>
<td>2595</td>
</tr>
<tr>
<td>Independent reflections (R$_{int}$)</td>
<td>2421 (0.1915)</td>
</tr>
<tr>
<td>Observed reflections (I &gt; 2σI)</td>
<td>687</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>2421/0/425</td>
</tr>
<tr>
<td>Extinction coefficient</td>
<td>0.0259 (16)</td>
</tr>
<tr>
<td>Goodness of fit on F$^2$</td>
<td>0.799</td>
</tr>
<tr>
<td>R$_1$ (I &gt; 2σ(I))</td>
<td>0.0523</td>
</tr>
<tr>
<td>WR$_2$ (all data)</td>
<td>0.1189</td>
</tr>
</tbody>
</table>
Table 2. HRMS (SIMS) data of a series of 3-haloflavanones measured on a *Bruker Daltonics* APEXII 47e FT-ICR spectrometer—observation of dehalogenative dimmers.

<table>
<thead>
<tr>
<th>entry</th>
<th>3-haloflavanones</th>
<th>[M+H]$^+$ (error, ppm)</th>
<th>[M−X]$^+$ (Br, I)</th>
<th>{2 [M−X]+H}$^+$ (error, ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td>350.9882 (1.7 ppm)</td>
<td>223.0754</td>
<td>447.1596 (1.1 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{15}$H$</em>{12}$O$_2$I</td>
<td></td>
<td>C$<em>{30}$H$</em>{23}$O$_4$</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Image" /></td>
<td>350.9868 (2.2 ppm)</td>
<td>223.0750</td>
<td>447.1569 (4.9 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{15}$H$</em>{12}$O$_2$I</td>
<td></td>
<td>C$<em>{30}$H$</em>{23}$O$_4$</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Image" /></td>
<td>303.0020 (1.6 ppm)</td>
<td>223.0755</td>
<td>447.1603 (2.7 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{15}$H$</em>{12}$O$_2$Br</td>
<td></td>
<td>C$<em>{30}$H$</em>{23}$O$_4$</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Image" /></td>
<td>380.9970 (3.1 ppm)</td>
<td>253.0859</td>
<td>507.1783 (3.8 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{16}$H$</em>{14}$O$_3$I</td>
<td></td>
<td>C$<em>{32}$H$</em>{27}$O$_6$</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Image" /></td>
<td>411.0092 (0.9 ppm)</td>
<td>283.0968</td>
<td>567.0996 (7.3 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{17}$H$</em>{16}$O$_4$I</td>
<td></td>
<td>C$<em>{34}$H$</em>{31}$O$_8$</td>
</tr>
<tr>
<td>6</td>
<td><img src="image6" alt="Image" /></td>
<td>441.0154 (8.8 ppm)</td>
<td>313.1036</td>
<td>627.2133 (14.6 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{18}$H$</em>{18}$O$_3$I</td>
<td></td>
<td>C$<em>{36}$H$</em>{35}$O$_{10}$</td>
</tr>
<tr>
<td>7</td>
<td><img src="image7" alt="Image" /></td>
<td>441.0085 (2.4 ppm)</td>
<td>313.1034</td>
<td>627.2274 (7.8 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{18}$H$</em>{18}$O$_3$I</td>
<td></td>
<td>C$<em>{36}$H$</em>{35}$O$_{10}$</td>
</tr>
<tr>
<td>8</td>
<td><img src="image8" alt="Image" /></td>
<td>393.0292 (10 ppm)</td>
<td>313.1053</td>
<td>627.1821 (64 ppm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C$<em>{18}$H$</em>{18}$O$_3$Br</td>
<td></td>
<td>C$<em>{36}$H$</em>{35}$O$_{10}$</td>
</tr>
</tbody>
</table>
positive-SIMS, $M+H=350.9876$, error=1.7ppm, November 21, 2001

positive-SIMS, $2H, M+H=350.9876$, error=2.2ppm, Oct.11, am, 2002
positive SIMS, M+H=441.0188, error=2 ppm, Oct 14, am, 2002

positive SIMS, M+H=441.0193, error=7 ppm, Oct 11, am, 2002
positive SIMS, M+H=441.0193, error=7ppm, Oct.11, am, 2002

positive - SIMS, Dec.17, 2002