

Xanthenes from *Drimiopsis maculata*

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Received March 26, 2004

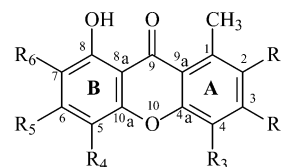
Six new xanthenes, drimiopsins A–F (**1**–**6**), have been isolated from the South African *Drimiopsis maculata*. The structures of these compounds were difficult to elucidate due to the lack of correlating protons seen in the NMR spectra, and INADEQUATE spectra were used to confirm the structures. Xanthenes have not previously been reported from the Hyacinthaceae.

The genus *Drimiopsis* Lindl. (Hyacinthoideae: Hyacinthaceae) is endemic to sub-Saharan Africa, where it is represented by approximately 20 species, at least five of which occur in southern Africa. *Drimiopsis maculata* Lindl., the only South African species from this genus reportedly employed in ethnomedicine, is found along the eastern coastal region. The plant is traded by the Zulu as “inJobo”¹ but is also known as “ucibicibane” (Zulu)² or “intshwilisa” (Xhosa).³ A warmed infusion of the bulbs is administered by the Zulu as an enema to children suffering from stomach complaints.² For the relief of constipation in children, the bulbs may also be chopped and ingested with food.³ A recipe for the mucilage-rich purging medicine prepared from the bulbs of *D. maculata* has been documented;⁴ this infusion was reportedly being used to treat an alleged Xhosa disease of newborn infants known as “ipleyiti”. Sheep toxicity tests using fresh plants in the flowering and seeding stages proved negative.⁵

Of the 14 genera belonging to the southern African Hyacinthoideae, only *Eucomis* L’Hérit and *Merwillia* Speta (syn. *Scilla* L.) have been extensively studied and have been found to typically contain 3-benzylchroman-4-ones (homoisoflavanones)⁶ and eucosterol derivatives.⁷ In a preliminary study of this *Drimiopsis maculata* species the known scillascillins, 5,3'-dihydroxy-4',7-dimethoxyspiro[2H-1-benzopyran-3(4H),7'-bicyclo[4.2.0]octa[1,3,5]-trien]-4-one and 5,7,3'-trihydroxy-4'-methoxyspiro[2H-1-benzopyran-3(4H),7'-bicyclo[4.2.0]octa[1,3,5]-trien]-4-one were isolated.⁸ As there appeared to be different types of interesting compounds present in small quantities, a second plant collection was made, and six new xanthenes, drimiopsins A–E (**1**–**6**), were also isolated. Structures were determined using NMR and MS techniques.

Previously, the dibenzo- α -pyranones, autumnariol and autumnariniol, were reported from the bulbs of *Eucomis autumnalis* (Mill.) Chitt. (Hyacinthoideae: Hyacinthaceae).⁹ However, NMR data in this publication were incomplete, and in light of our findings, it is likely that the structures of these compounds were incorrectly assigned and are actually the corresponding xanthenes.

The FABMS of drimiopsin A (**1**) gave a molecular ion peak at m/z 318.07411, indicating a molecular formula of C₁₆H₁₄O₇. The IR spectrum showed a strong carbonyl stretch at 1633 cm⁻¹. The ¹H NMR spectrum (Table 1)



	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆
1	H	OH	H	OCH ₃	OH	OCH ₃
2	H	OH	H	OCH ₃	OCH ₃	OCH ₃
3	H	OH	H	H	OH	OCH ₃
4	H	OH	OCH ₃	OCH ₃	OH	H
5	H	OH	H	OCH ₃	OH	H
6	H	OCH ₃	H	H	OH	OCH ₃

indicated the presence of two methoxy group proton resonances (δ 3.78, 3.73, 3H, each), an aromatic methyl group proton resonance (δ 2.70, 3H), and a pair of *meta*-coupled proton resonances at δ 6.62 ($J = 2.38$ Hz) and 6.67 ($J = 2.38$ Hz). The ¹³C NMR spectrum showed 12 resonances ascribable to aromatic carbons of two rings, two methoxy group carbon resonances (δ 61.7, 60.7), a methyl group carbon resonance (δ 23.7), and a carbonyl carbon resonance at δ 182.5. The chemical shift of this carbonyl resonance indicated a xanthone structure rather than an isomeric dibenzo- α -pyranone structure.¹⁰ The structure of ring A was determined using the COSY and NOESY spectra. The methyl group proton singlet (δ 2.70, 3H) showed correlations in the COSY and NOESY spectra with the proton resonance at δ 6.62 and so were placed at C-1 and C-2, respectively. The *meta*-coupled proton resonance at δ 6.67 was thus assigned as H-4. As no NOESY correlations were seen between either of the methoxy group proton resonances and H-2 or H-4, a hydroxy group was placed at C-3. The molecular formula indicated a fully substituted ring B, and an INADEQUATE NMR experiment was used to place the remaining two methoxy and two hydroxy groups on the ring and to confirm the xanthone structure. This experiment indicated that methoxy groups were present at C-5 and C-7 and hydroxy groups occurred at C-6 and C-8. The presence of a hydroxy group at C-8 was confirmed by the phenolic proton resonance at δ 13.23, indicative of a phenolic proton that is hydrogen bonded to the neighboring carbonyl group.¹¹ Thus, structure **1** was assigned to drimiopsin A. All ¹³C NMR resonances could be assigned using the INADEQUATE spectrum and are shown in Table 1.

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molecular formula indicated the presence of an additional hydroxyl group. The proton resonance was assigned as H-7, a hydroxyl group was placed at C-6, and the methoxy group was placed at C-5. The assignment of the proton resonance as H-7 was supported by the HMBC correlations seen from C-8 and C-8a to H-7. Methoxy groups with protons at one of the *ortho* positions occur at approximately 55 ppm. However, the methoxy group carbon resonance of drimiopsin E (**5**) occurred at δ 60.6, which confirmed a neighboring hydroxy group substituent, and the methoxy group was therefore placed at C-5.¹³ Thus, structure **5** was assigned to drimiopsin E.

Ring A of drimiopsin F (**6**), C₁₆H₁₄O₆, had the same substitution pattern as drimiopsins A–C (**1–3**) except that instead of a hydroxyl group, **6** has a methoxy group at C-3. This was indicated by the NOESY correlations seen between the protons of the methoxy group at δ 3.91 and the *meta*-coupled protons at δ 6.73 ($J = 2.56$ Hz) and 6.88 ($J = 2.56$ Hz). A hydroxy group was placed at C-8 due to the appearance of the carbonyl carbon of C-9 at δ 182.6,¹¹ as found for drimiopsins A–E (**1–5**). The single proton resonance was assigned to C-5 due to a HMBC correlation with C-4a. The remaining methoxy and hydroxy groups were placed at C-7 and C-6, respectively, since no correlations were seen in the NOESY spectrum between H-5 and the methoxy group proton resonance. Thus structure **6** was assigned to drimiopsin F.

Experimental Section

General Experimental Procedures. The melting points of the crystalline compounds were recorded on a Kofler micro-hot stage melting point apparatus. The ultraviolet absorption spectra were obtained on a Varian DMS 300 UV–visible spectrometer, and infrared spectra were recorded using a Nicolet Impact 400D Fourier transform infrared (FT-IR) spectrometer. NMR spectroscopy was carried out on a 400 MHz Varian UNITY-INOVA spectrophotometer, and INADEQUATE spectra were acquired for drimiopsins A (**1**) and B (**2**) in the Varian NMR Applications Laboratory in Darmstadt, Germany, using a 400 MHz Varian UNITY-INOVA spectrophotometer. FABMS were recorded on a Micromass 70-70E mass spectrometer, using a *m*-nitrobenzyl alcohol matrix and xenon as the bombardment gas, with peak matching for drimiopsins A, D, E, and F, while low-resolution mass spectra were obtained for the remaining samples.

Plant Material. The bulbs of *Drimiopsis maculata* Lindl., cultivated in Pretoria, South Africa, were harvested in January 2000, and a voucher was lodged for verification purposes (Crouch 1000, NH).

Extraction and Isolation. The material (2585.4 g) was extracted at room temperature for 24 h on a Labcon Mechanical shaker with methylene chloride, and the extract (1.25 g) was separated using gravity column chromatography over silica gel (Merck 9385, solvent MeCl₂/EtOAc) to yield the xanthenes drimiopsin A, **1** (7.2 mg), drimiopsin B, **2** (8.4 mg), drimiopsin C, **3** (5.7 mg), drimiopsin D, **4** (8.1 mg), drimiopsin E, **5** (9.1 mg), and drimiopsin F, **6** (5.6 mg). Compounds **1–4** were eluted using a ratio of 9:1 dichloromethane to ethyl acetate, and compounds **5** and **6** were eluted using a ratio of 8:2 dichloromethane to ethyl acetate.

Drimiopsin A (3,6,8-Trihydroxy-5,7-dimethoxy-1-methylxanthone) (1): yellow powder; mp 218–222 °C; UV (MeOH) λ_{\max} (log ϵ) 315 (3.48) nm; IR (NaCl) ν_{\max} 3404, 2931, 2858, 1633, 1596, 1463, 1324, 1185, 1052 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; FABMS m/z 318 [M⁺] (18), 279 (14),

217 (12), 154 (95), 136 (100), 107 (47), 77 (52); HRMS m/z 318.07411 (calcd for C₁₆H₁₄O₇, 318.07395).

Drimiopsin B (3,8-Dihydroxy-5,6,7-trimethoxy-1-methylxanthone) (2): fine, white powder; UV (MeOH) λ_{\max} (log ϵ) 310 (3.48) nm; IR (NaCl) ν_{\max} 3380, 2922, 2847, 1644, 1607, 1461, 1250, 1169, 1049 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; FABMS m/z 332 [M⁺] (12), 303 (17), 288 (70), 273 (72), 245 (100), 151 (25), 121 (36), 107 (11); FABMS m/z 332 (calcd for C₁₇H₁₆O₇, 332).

Drimiopsin C (3,6,8-Trihydroxy-7-methoxy-1-methylxanthone) (3): off-white powder; mp 222–225 °C; IR (NaCl) ν_{\max} 3387, 2918, 2848, 1630, 1622, 1467, 1273, 1158 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; HRMS m/z 288.06310 (calcd for C₁₅H₁₂O₆, 288.06339).

Drimiopsin D (3,6,8-Trihydroxy-4,5-dimethoxy-1-methylxanthone) (4): fine, white powder; mp 205–208 °C; UV (MeOH) λ_{\max} (log ϵ) 311 (3.94) nm; IR (NaCl) ν_{\max} 3396, 2921, 2850, 1651, 1614, 1456, 1320, 1168, 1100 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; FABMS m/z 318 [M⁺] (100), 303 (77), 287 (24), 260 (53), 107 (16), 77 (32); HRMS m/z 318.07411 (calcd for C₁₆H₁₄O₇, 318.07395).

Drimiopsin E (3,5,8-Trihydroxy-6-methoxy-1-methylxanthone) (5): brown, amorphous material; IR (NaCl) ν_{\max} 3429, 2914, 2846, 1644, 1613, 1276, 102 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; FABMS m/z 288 [M⁺] (69), 273 (100), 245 (91), 149 (25), 123 (55), 57 (43); HRMS m/z 288.06310 (calcd for C₁₅H₁₂O₆, 288.06339).

Drimiopsin F (6,8-Dihydroxy-3,7-dimethoxy-1-methylxanthone) (6): fine, white crystalline material; mp 214–216 °C; IR (NaCl) ν_{\max} 3328, 2923, 1625, 1597, 1507, 1413, 1157, 1035 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; FABMS m/z 302 [M⁺] (54), 287 (100), 259 (71), 216 (10); HRMS m/z 302.07911 (calcd for C₁₆H₁₄O₆, 302.07903).

Acknowledgment. The DEAT has generously funded the development of MEDBASE, the National Medicinal Plants Database for South Africa. We are grateful to Dr. and Mrs. R. Clark for providing the plant material, Mr. D. Jagjivan for running NMR spectra, Dr. P. Boshoff and Mr. John Hill for mass spectrometric analysis, and Mr. B. Parel for technical assistance. C.K. gratefully acknowledges the National Research Foundation (NRF) postgraduate bursaries. This research was funded by the NRF and University of Natal Research Fund.

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NP040076Z