A NEW CHROMENE GLYCOSIDE FROM *Tithonia diversifolia*

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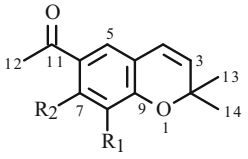
UDC 547.972

*A new chromene glycoside, 6-acetyl-2,2-dimethylchromene-8-*O-β-*D-glucoside, together with four known compounds were isolated from the aerial parts of* Tithonia diversifolia*. Their structures were established by* ^{1}H, ^{13}C *NMR, and HMQC together with the other physical and chemical investigations.*

Keywords*: Tithonia diversifolia*, chromene, 6-acetyl-2,2-dimethylchromene-8-*O*-*β*-D-glucoside.

Tithonia diversifolia (Hemsl.) A. Gray (Compositae), known as Mexican sunflower, is native to Mexico and Central America. Traditionally, *T. diversifolia* is used for the treatment of malaria [1] and other forms of fever. Presently, *T. diversifolia* has been introduced into other countries for ornamental purposes or for their pharmacological action and is widespread in the southern part of Asia, Africa, and the Pacific region. Now *T. diversifolia* is of particular interest for phytomedical and health care research. The extract and compounds isolated from the plant showed anti-inflammatory, analgesic, antimycotic, anti-HIV-1 [2], and antidiabetes mellitus properties [3]. Chemical studies on this species resulted in sesquiterpene lactones [4], such as tagitinin A–C and F, diversifol and tithonine chromene, and flavone derivatives [5, 6]. Here we investigate the aerial parts of *T. diversifolia* and report the isolation of one new natural compound, 6-acetyl-2,2-dimethylchromene-8-*O*-*β*-D-glucoside (**3**), together with other four known chromenes, 6-acetyl-2,2-dimethylchromene (**1**) [7], 6-acetyl-8-hydroxy-2,2-dimethyl-chromene (**2**) [8], 6-acetyl-7-hydroxy-2,2-dimethylchromene (**4**) [7], and 6-acetyl-7-methoxy-2,2-dimethylchromene (**5**) [9].



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1: $R_1 = R_2 = H$; **2:** $R_1 = OH$, $R_2 = H$
3: R_1 = O-Glc, $R_2 = H$; **4:** $R_1 = H$, $R_2 = OH$
5: $R_1 = H$, $R_2 = OCH_3$

The new compound **3** was obtained as colorless crystals with melting point 148–150°C and molecular formula $C_{19}H_{24}O_8$, as established by HR-ESI-MS *m/z* at 403.1374 $[M + Na]^+$ ($C_{19}H_{24}O_8Na^+$); calcd for $C_{19}H_{24}O_8$: 380.3906, which was supported by ^{13}C NMR. The EI-MS *m/z* ($I_{rel.}$, %) 218 (40), 203 (100), 164 (35), 43 (60), showed the presence of a sugar, and acid hydrolysis of **3** afforded D-glucose by GC analysis. The IR spectrum of compound **3** showed absorptions at 1676 and 1600 cm^{-1}, suggesting the presence of the carbonyl and phenyl groups. The ^1H NMR spectrum in MeOD exhibited signals for two similar methyl groups (s, 1.46; s, 1.48) and one acetoxyl group (s, 2.53); two meta aromatic hydrogens 7.44 (d, J = 1.8), 7.67 (d, J = 1.8); an alkenyl group 5.80 (d, J = 10.2 Hz), 6.43 (d, J = 10.2 Hz) flanked by the aromatic ring.

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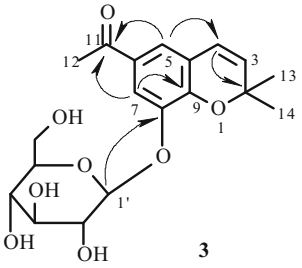

3

Fig. 1. HMBC correlations of **3**.

The ^{13}C NMR spectrum exhibited one acetoxy (199.27, C-11) and six aromatic carbon atoms; one alkenyl attached to the aromatic ring; one quaternary carbon (79.41, C-2) attached to oxygen. Based on the above spectral data, the skeleton of **3** was a chromene. The sequence and linkage position of the glucose moiety was subsequently deduced from the correlation between H-1′ of glucose and C-8 in the HMBC experiment (Fig. 1), and the β-D-glucosidic bond was deduced from the H-1′ (1H, d, J = 7.80 Hz); also, the position of the acetoxyl group was confirmed by the correlation between H-5 and C-11; the correlations between H-7 and C-9, C-11; H-4 and C-2 were also observed. Thus compound **1** was indentified as 6-acetyl-2,2-dimethylchromene-8-*O*-β-D-glucoside.

EXPERIMENTAL

General Methods. NMR spectra were obtained on a Bruker DRX-500 spectrometer at 500 MHz for ^1H and 125 MHz for ^{13}C. Chemical shifts are expressed in δ values with reference to DMSO-d_6 as internal standard, and coupling constants (J) are given in Hz; ESI-MS was recorded on a Varian MAT-212 mass spectrometer; melting point was measured on a ZMD83-1 electrothermal melting point apparatus and uncorrected; IR was recorded on a Bruker Vector 22 spectrometer with KBr pellet.

Plant Material. The aerial parts of *Tithonia diversifolia* (Hemsl.) A. Gray (Compositae) were collected in Mengzi, Yunnan province, P. R. China in September 2004 and were identified by Prof. Wansheng Chen. A voucher specimen was deposited in the Department of Pharmacognosy, Second Military Medical University, Shanghai, P. R. China.

Extraction and Isolation. The air-dried aerial parts of *Tithonia diversifolia* (70 kg) were percolated with 80% EtOH. The EtOH extract was concentrated to an aqueous residue and then suspended with water. The water layer was extracted with petroleum ether, CH_2Cl_2, EtOAc, and *n*-BuOH. The CH_2Cl_2-soluble part was evaporated to a black syrup (320 g), which was subjected to silica gel column chromatography with petroleum ether–EtOAc. 6-Acetyl-2,2-dimethylchromene (**1**) (20 mg), 6-acetyl-7-methoxy-2,2-dimethylchromene (**5**) (80 mg), 6-acetyl-7-hydroxy-2,2-dimethylchromene (**4**) (230 mg), 6-acetyl-8-hydroxy-2,2-dimethylchromene (**2**) (40 mg), and 6-acetyl-2,2-dimethylchromene-8-*O*-β-D-glucoside (**3**) (60 mg) were eluted with (50:1, 15:1, 5:1, 3:1) and purified by reversed-phase (RP-18) chromatography using silica gel and Sephadex LH-20.

6-Acetyl-2,2-dimethylchromene (1), white powder, $C_{13}H_{14}O_2$. EI-MS *m/z*: 203 $[M + H]^+$. ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 7.73 (1H, dd, J = 7.6, 1.8, H-7), 7.61 (1H, d, J = 7.6, H-8), 6.78 (1H, d, J = 1.8, H-5), 6.34 (1H, d, J = 10.2, H-4), 5.65 (1H, d, J = 10.2, H-3), 2.52 (3H, s, H-12), 1.45 (6H, s, H-13, 14); ^{13}C NMR ($CDCl_3$, δ): 196.6 (C-11), 157.4 (C-9), 131.2 (C-7), 129 (C-3), 126.9 (C-8), 120.6 (C-4), 113.9 (C-10), 99.6 (C-5), 76.8 (C-2), 28.3 (C-13,14), 26.2 (C-12).

6-Acetyl-7-hydroxy-2,2-dimethylchromene (2), white powder, $C_{13}H_{14}O_3$. EI-MS *m/z*: 219 $[M + H]^+$. ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 7.31 (1H, s, H-8), 6.33 (1H, s, H-5), 6.27 (1H, d, J = 10.2, H-4), 5.57 (1H, d, J = 10.2, H-3), 2.54 (3H, s, H-12), 1.45 (6H, s, H-13, 14); ^{13}C NMR ($CDCl_3$, δ): 203.1 (C-11), 160.7 (C-9), 129.7 (C-8), 129.1 (C-3), 121.4 (C-4), 114.6 (C-6), 165.1 (C-7), 114.0 (C-10), 104.5 (C-5), 78.2 (C-2), 28.4 (C-13, 14), 26.3 (C-12).

6-Acetyl-2,2-dimethylchromene-8-*O*-β-D-glucoside (3), colorless crystals, mp 148–150°C; $[\alpha]_D^{20}$ +20° (*c* 0.1, MeOH). UV (MeOH, λ_{max}, nm): 266; IR (KBr, ν_{max}, cm^{-1}): 3446, 2924, 1676, 1600, 1382, 1306, 1199, 1076. ^1H NMR (600 MHz, MeOD, δ, ppm, J/Hz): 1.46 (3H, s, H-13), 1.48 (3H, s, H-14), 2.53 (3H, s, H-12), 5.80 (1H, d, J = 10.2, H-3), 6.43 (1H, d, J = 10.2, H-4), 7.44 (1H, d, J = 1.8, H-5), 7.67 (1H, d, J = 1.8, H-7), 4.94 (1H, d, J = 7.80, H-1′), 3.45 (1H, m, H-2′), 3.40 (1H, m, H-3′) , 3.29 (1H, m, H-4′), 3.49 (1H, m, H-5′), 3.83 (1H, dd, J = 12.0, H-6′); ^{13}C NMR (150 MHz, MeOD, δ): 26.4 (C-12), 28.2 (C-14), 28.4 (C-13), 79.41 (C-2), 119.46 (C-3), 122.72 (C-5), 122.78 (C-10), 131.16 (C-6), 132.81 (C-4),

147.62 (C-8), 149.51 (C-9), 199.27 (C-11), 103.13 (C-1′), 77.99 (C-2′), 78.40 (C-3′), 71.36 (C-4′),74.96 (C-5′), 62.50 (C-6′). HR-ESI-MS *m/z*: 403.1374 $[M + Na]^+$ ($C_{19}H_{24}O_8Na^+$); calcd for $C_{19}H_{24}O_8$, 380.3906; EI-MS *m/z* ($I_{rel.}$, %): 218 (40), 203 (100), 164 (35), 43 (60).

6-Acetyl-8-hydroxy-2,2-dimethylchromene (4), white crystal, $C_{13}H_{14}O_3$. EI-MS *m/z*: 219 $[M + H]^+$. ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 7.45 (1H, d, J = 1.8, H-7), 7.28 (1H, d, J = 1.8, H-5), 6.38 (1H, d, J = 10.2, H-4), 5.69 (1H, d, J = 10.2, H-3), 2.55 (3H, s, H-12), 1.52 (6H, s, H-13, 14); ^{13}C NMR ($CDCl_3$, δ): 196.8 (C-11), 144.2 (C-6), 143.7 (C-8), 130.9 (C-3), 130.5 (C-9), 121.7 (C-4), 120.5 (C-10), 118.8 (C-5), 115.3 (C-7), 78.6 (C-2), 28.3 (C-13, 14), 26.3 (C-12).

6-Acetyl-7-methoxy-2,2-dimethylchromene (5), white powder, $C_{13}H_{16}O_3$. EI-MS *m/z*: 221 $[M + H]^+$. ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 7.53 (1H, s, H-5), 6.37 (1H, s, H-8), 6.29 (1H, d, J = 10.2, H-4), 5.51 (1H, d, J = 10.2, H-3), 3.87 (3H, s, O<u>Me</u>), 2.55 (3H, s, H-12), 1.43 (6H, s, H-13, 14); ^{13}C NMR ($CDCl_3$, δ): 197.5 (C-11), 161.8 (C-7), 158.4 (C-9), 129 (C-5), 128.3 (C-3), 121.6 (C-4), 113.4 (C-10), 99.6 (C-8), 76.8 (C-2), 55.5 (O<u>C</u>H_3), 28.3 (C-13, 14), 26.2 (C-12).

ACKNOWLEDGMENT

The work was supported by National Natural Science Foundation of China (20872177) and Program of Shanghai Science and Technology Commission (08DZ1971503).

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