PERGAMON

Phytochemistry 53 (2000) 511–513

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

A chalcone and a dihydrochalcone from *Uvaria dulcis*

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Received 30 April 1999; received in revised form 16 July 1999

Abstract

2′,3′-Dihydroxy-4′,6′-dimethoxychalcone and the corresponding dihydrochalcone were isolated from the leaves of *Uvaria dulcis* and characterized by chemical and spectral methods. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: *Uvaria dulcis*; Annonaceae; Chalcone; Dihydrochalcone; Flavanone

1. Introduction

The genus *Uvaria* has been a rich and varied source of new compounds as is evidenced by the isolation of alkaloids (Panichpol, Waigh & Waterman, 1977; Achenbach & Roffelsberger, 1979) flavonoids (Cole, Torrance, Wiedhopf, Arora & Bates, 1976; Lasswell & Hufford, 1977; Okorie, 1977; Tammami, Torrance, Fabela, Wiedhopf & Cole, 1977; Hufford, Lasswell, Hirotsu & Clardy, 1979; Hufford & Oguntimcin, 1982), cyclohexene oxides (Holbert et al., 1979; Schulte, Ganem, Chantrapromma, Kodpinid & Subsuansri, 1982) and aromatic oils (Kodpinid, Thebtaranonth & Thebtaranonth, 1985). In continuation of our studies on the genus *Uvaria* (Holbert et al., 1979; Schulte et al., 1982; Chantrapromma, Pakawatchai, Shelton, White & Worapatamasri, 1989), we further examined the leaves of *U. dulcis* Dunal. We now report on the chemical examination of the leaves which gave a chalcone **1** and its corresponding new dihydrochalcone **2** together with flavanone **3** and benzyl benzoate.

2. Results and discussion

Hot hexane extract of the leaves of *U. dulcis* afforded a gum which was chromatographed on silica gel using increasing percentages of chloroform in hexane to give three compounds. The first, an oil, MS gave M.W 212 analysing for $C_{14}H_{12}O_2$ was found to be benzyl benzoate by detailed examination of IR, NMR, MS spectral data and by comparison with an authentic sample. The second compound, mp 124–126°C, was obtained as red crystals and identified as 2′,3′-dihydroxy-4′,6′-dimethoxychalcone **1** on the basis of UV, NMR, MS data and chemical interconversions. The UV spectrum in MeOH supports a chalcone structure of the compound (Panichpol et al., 1977; Mabry, Markham & Thomas, 1970), λ_{max} 240, 290 and 346 nm. The lack of a shift in Band II in NaOAc indicates that the A-ring 4′ position is substituted. A bathochromic shift of Band I in $AlCl_3$ relative to the MeOH spectrum of 34 nm (from 346 to 380 nm) suggests a free hydroxyl group at the 6′ position in the A-ring. NMR data establish an unsubstituted B-ring; a multiplet at δ 6.85–7.75 integrating for five aromatic protons which can be assigned to the B-ring and at δ 7.90 to the α- and

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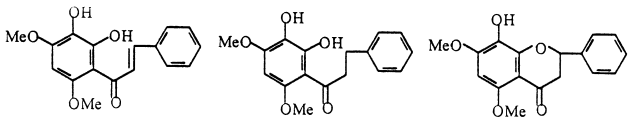
0031-9422/00/$ - see front matter
PII: S0031-9422(99)00477-X

β-protons. One aromatic signal at δ 5.91 can be attributed to a proton at either C-3 or C-5. Two methoxyl groups at δ 3.86 and 3.93 are assigned to the A — ring 4 and 6-positions. The hydrogen-bonded phenolic-OH at 14.06 in the NMR would then be placed in the C-2 position, making chalcone **1** a 2-hydroxychalcone. A strong molecular ion at m/z 300 confirms the molecular formula of $C_{17}H_{16}O_5$. That the chalcone contains a 2′-hydroxyl group was confirmed by a trace of the flavanone **3** were present in all samples of the chalcone **1**, and could be separated by silica gel TLC as 5,7-dimethoxy-8-hydroxyflavanone, an expected cyclization product from the chalcone **1**. Fragments for the chalcone **1** were at m/z 300 (100%), 269 (13%), 223 (22%), 196 (88%), 178 (75%), 150 (66%), 131 (13%), 103 (22%), 77 (44%). On treatment with acid (1 h 5% aqueous H_2SO_4) chalcone **1** gave a pale yellow crystalline flavanone **3** (mp 166–168°C), which was identified as 5,7-dimethoxy-8-hydroxyflavanone. The flavanone **3** was fully characterized by a combination of spectral data and X-ray crystallography (Chantrapromma, Seechamnanturakit, Pakawatchai, Chantrapromma, Chinnakali & Fun, 1998).

The third compound, light yellow crystals, mp 141–142°C gave a brown color with ethanolic $FeCl_3$ indicating the phenolic nature and a negative Shinoda reaction (Shinoda, 1928) suggesting absence of flavone or flavanone nucleus. The molecular formula was established by MS, m/z 302, $C_{17}H_{18}O_5$. The IR spectrum (3480 and 1635 cm^{-1}) indicated the presence of at least one phenolic hydroxyl group and a conjugated ketone group. The ^{1}H-NMR spectrum displayed ethylene proton signals of an A_2B_2 system centred at δ 3.05 and 3.35; two methoxyl groups at δ 3.84 and 3.95, one proton singlet at δ 6.00 and a five proton multiplet at δ 7.01–7.60. It also showed one proton broad singlet at δ 5.10 (lost on deuteration) assignable to phenolic-OH and a one proton sharp singlet at δ 13.80 (exchangeable with D_2O) attributable to a hydrogen bonded phenolic-OH. These data suggested that this compound is a 2′-hydroxydihydrochalcone with two methoxyl groups and two hydroxyl groups on the A-ring. The identification of H-6 of dihydrochalcone **2** was determined by NOE difference spectra. Irradiation of the H-6 signal showed a strong enhancement of the two methoxyl groups, thus indicating that it definitely has two methoxyl groups next to the H-6. In addition, irradiation of **2** at both the methoxyl signals showed only the enhancement of the H-6. Dihydrochalcone **2** was also suspected to be a dihydro derivative of the chalcone **1**. Indeed, catalytic hydrogenation of the chalcone **1** gave 2′,3′-dihydro-4′,6′-dimethoxydihydrochalcone **2**, which was indistinguishable from the natural product in all respects.



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3. Experimental

3.1. General experimental procedures

All mp's are uncorrected. CC was run on Merck Si gel 60 (70–230 mesh). TLC was performed on glass plates precoated with Kieselgel 60 F_{254} (Merck). MS were recorded on a Varian Saturn GC/MS 4D spectrometer. IR spectra were obtained on a Perkin-Elmer IR 783 spectrophotometer and UV spectra on a UV-160 A (SHIMADZU) spectrophotometer. ^{1}H-NMR were recorded at 60 MHz on a JEOL-PMx 60 and on a with TMS as an internal standard. Chemical shifts are quoted in ppm (δ). The NOE difference spectra were performed on a Varian INOVA 500 MHz nuclear magnetic resonance.

3.2. Plant material

Leaves of *U. dulcis* were collected at Phrae province, Thailand, in July 1990. A voucher specimen has been deposited at the Herbarium of the Forest Institute of Thailand.

3.3. Extraction and isolation

The air-dried ground leaves of *U. dulcis* (800 g) were extracted with hexane. Evaporation of the hexane extract in vacuo at 40° yielded a gum (85 g) and chromatographed on a column of Si gel (250 g) eluting with increasing percentages of $CHCl_3$–hexane. Hexane–$CHCl_3$ (9:1) eluted benzylbenzoate (0.07 g). Hexane–$CHCl_3$ (4:1) fraction furnished dihydrochalcone **2** as light yellow crystals mp 141–142°C (0.45 g). UV: λ_{max} 208, 240, 290 nm; IR: λ_{max} cm^{-1}; 3480, 1635; ^{1}H-NMR ($CHCl_3$): δ 3.86, 3.93 (2*s*, 6H, 2*x*OCH_3); 5.97 (*s*, 1H, 5-Ar-H), 6.85–7.75 (*m*, 5H, B-ring-H), 7.90 (*s*, 2H, α, β-H), 14.06 (*s*, 1H, 2-OH). MS: m/z 300 (M^+, 100%), 269 (12.5%), 223 (21.9%), 207 (12.5%), 197 (18.8%), 196 (87.5%), 178 (75%), 165 (12.5%), 131 (12.5%), 103 (22%), 77 (43.8%). Hexane–$CHCl_3$ (7:3) eluates afforded chalcone **1** as red crystal (0.08 g), mp 124–126°. UV: λ_{max} (MeOH): 208, 240, 290 nm; IR: λ_{max} cm^{-1} 3480, 1680, NMR ($CDCl_3$): δ 3.05 (*t*, 2H, J_{AB} 7.7 Hz, 2*x* β-H), 3.35 (*t*, 2H, J_{AB} 7.7 Hz, 2*x* α-H), 3.86, 3.93 (2*s*, 6H, 2*x*OMe), 5.10 (*s*, 1H, OH, lost on deuteration), 5.91 (*s*, 1H, AR-H), 7.01–7.60 (*m*, 5H, B-

ring-H), 13.80 (*s*, 1H, Ar–OH, disappearing with D_2O). MS: *m/z* 302 (M^+, 37%), 202 (14.8%), 197 (100%), 182 (17%), 105 (10.6%), 91 (37.7%).

3.4. Conversion of chalcone **1** to flavanone **3**

To a solution of chalcone **1** (0.102 g, 0.341 mmol) in ethanol (5 ml) was added dropwise a solution of 5% H_2SO_4 in ethanol (15 ml) in an atmosphere of nitrogen at 0°C, and the mixture was heated under reflux for 12 h. The cooled reaction mixture was then evaporated under reduced pressure to remove the ethanol. The residue was dissolved in chloroform and the organic layer was washed with water and brine, and dried (Na_2SO_4). Evaporation of the chloroform extract under reduced pressure afforded the crude flavanone **3** which was purified by preparative TLC with 30% ethyl acetate in chloroform as eluent. The first band (*Rf* = 0.38) yielded flavanone **3** (0.053 g, 54%) as pale yellow crystals, mp 166–168°C. This product was identical by TLC, UV, IR, ^{1}H-NMR and mass spectra to the natural 5,7-dimethoxy-8-hydroxyflavanone (Chantrapromma et al., 1998).

3.5. Catalytic reduction of chalcone **1**

A suspension of chalcone **1** (40 mg) and 10% Pd/C (20 mg) in methanol (3 ml) was stirred under an H_2 atmosphere until uptake had ceased. The reaction mixture was filtered off and evaporated to dryness to give pale yellow crystals (40 mg) mp 140–142°C. All the spectral data of this compound were indistinguishable from those of natural dihydrochalcone **2**.

Acknowledgements

The authors would like to thank the International Foundation for Science and Thailand Toray Science Foundation for financial support of this work.

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