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A NOVEL EXAMPLE OF A NATURAL 2,5-DIHYDROXYFLAVANONE FROM *UNONA LAWII*

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Key Word Index—*Unona lawii*; Anonaceae; 3-formyl-2,4,6-trihydroxy-5-methyldibenzoylmethane; 6 (or 8)-formyl-2,5,7-trihydroxy-8 (or 6)-methylflavanone; 3-formyl-2,6-dihydroxy-4-methoxy-5-methyldibenzoylmethane; synthesis.

Abstract—3-Formyl-2,4,6-trihydroxy-5-methyldibenzoylmethane from *Unona lawii* has been shown to exist in a cyclic hemiketal form whereas 3-formyl-2,6-dihydroxy-4-methoxy-5-methyldibenzoylmethane from the same plant mainly exists in the enolic ring opened form, owing to chelation of both hydroxyl groups. The flavonoid pattern of *Unona lawii* suggests the biogenetic scheme : flavanone → 2-hydroxyflavanone → flavone. 3-Formyl-2,4,6-trihydroxy-5-methyldibenzoylmethane has been synthesized by Baker–Venkataraman rearrangement of 3-formyl-2,4,6-trihydroxy-5-methylacetophenone benzoate.

INTRODUCTION

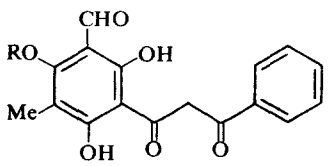
Two new dibenzoylmethanes have recently been isolated from the stem of *Unona lawii* and their structures derived from spectral and synthetic evidence as 3-formyl-2,4,6-trihydroxy-5-methyl- and 3-formyl-2,6-dihydroxy-4-methoxy-5-methyldibenzoylmethanes **1** and **2** [1]. Both compounds being 2,6-dihydroxydibenzoylmethanes are capable of existing in the cyclic hemiketal form, as 2,5-dihydroxy-flavanones, previously demonstrated for 2,6-dihydroxy-4-methoxydibenzoylmethane [2] and later generalized to other compounds of this type [3]. Therefore, their NMR spectra were reexamined in the light of this possibility. Indeed, **1** was shown to exist in the cyclic hemiketal forms **3** and **4**, but **2** in the ring opened enolic form. This striking difference has been ascribed to the chelation of both *o*-hydroxyl groups in **2** since several synthetic 2,6-dihydroxydibenzoylmethanes bearing a 2′-hydroxyl group have been found to exist mainly in the open diketo form stabilized by the chelation of both carbonyl groups [4].

Together with the 4-glucosyloxy and 4-methoxy-2,6-dihydroxydibenzoylmethanes from *Malus* leaves [5] and *Populus nigra* buds [6] respectively, **1** is the third natural dibenzoylmethane occurring in cyclic hemiketal form. All are characterized by the absence of hydroxyl or methoxyl groups in the B-ring and this feature is significant in view of the extreme ease of dehydration observed with synthetic 2,5-dihydroxyflavanones bearing such substituents in the B-ring [3].

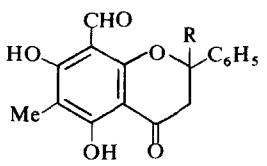
RESULTS AND DISCUSSION

The low temperature (−30, −40 and −60°) NMR spectra of **1** in d_6-acetone immediately showed the characteristic features of a 2,5-dihydroxyflavanone spectrum, i.e. presence of a D_2O-exchangeable doublet (J = 2Hz) near δ 7.5 ppm corresponding to the axial 2-OH, long range coupled with the axial 3-H which appears near δ 3.5 ppm as a quadruplet (J = 2 Hz, J' = 17 Hz), owing to the geminal coupling with the equatorial 3-H, seen as a doublet (J = 17 Hz) near δ 3.1 ppm. However each of these characteristic signals appeared as a pair, as do the singlets of the chelated phenolic hydroxyls 5-OH and 7-OH near δ 13.5, and with the same ratio, about 3:2, in each pair. On the other hand, the methyl and formyl groups gave rise to single peaks. Such a spectrum might be expected since cyclization of **1** can give rise to two Wessely–Moser isomers: 8-formyl-2,5,7-trihydroxy-6-methylflavanone **3** and 6-formyl-2,5,7-trihydroxy-8-methylflavanone **4** and that a previous work [7] on 2,5,7-trihydroxy-6 (or 8)-methoxyflavanones has shown them to exist as an equilibrium mixture of such isomers, too easily interconvertible to be separated. Moreover the magnetic equivalence of the 6 (or 8)-methyl and formyl groups in **3** and **4** may be compared with the equivalence of 6-H and 8-H in synthetic 2,5,7-trihydroxyflavanones [3].

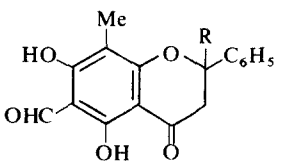
A tentative assignment of the signals to **3** or **4** could be proposed by comparison with the NMR spectra of the corresponding flavanones. Lawinal, 6-formyl-5,7-dihy-



1 R = H
2 R = Me



3 R = OH
5 R = H



4 R = OH
6 R = H

droxy-8-methylflavanone **6** co-occurs with **3** and **4** in *Unona lawii* extracts and has been synthesized, as well as its Wessely–Moser isomer, 8-formyl-5,7-dihydroxy-6-methylflavanone **5** which may be called isolawinal [8]. The chelated phenolic hydroxyl groups of the latter exhibited larger chemical shifts than those of lawinal. If this is assumed to be unaffected by the replacement of 2-H by 2-OH, the lower field signals, corresponding to the more abundant isomer, may be assigned to **3**. This assignment would be in agreement with the ratios 3:2 of the corresponding flavones, unonal and isounonal, in *Unona lawii* extracts [1].

Unlike **1**, **2** did not show in its NMR spectrum any signal around δ 3 ppm and therefore could not exist in cyclic hemiketal form. A weak singlet at δ 4.72 ppm, integrating for about 0.2 proton, could be ascribed to the methylene group of the diketo form and a singlet at δ 7.68 ppm integrating for about one proton, to the vinyl proton of the enol form which thus represents 90% of the mixture. The enol hydroxyl group appeared as a singlet at δ 15.23 ppm. All these characteristic signals showed chemical shifts in good agreement with the values found by Wagner *et al.* [9] for *o*-hydroxydibenzoylmethanes [9], but this may be ascribed to the conjugation appeared as two singlets at δ 14.72 and 14.33 ppm, instead of about 13.0 ppm in *o*-hydroxydibenzoylmethanes [9], but this may be ascribed to the conjunction of each hydroxyl group with two carbonyl groups, as in 3-formyl 2,4,6-trihydroxy-5-methylacetophenone, of which the three hydroxyl groups afforded a single broad signal at δ 14.3 [1].

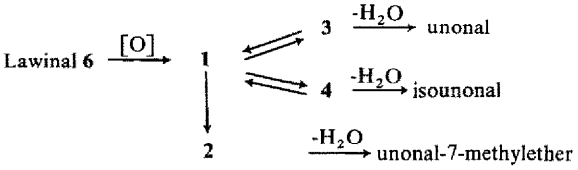
Thus, NMR spectra clearly showed that **1** exclusively exists in cyclic hemiketal form as an equilibrium mixture (3:2) of inseparable Wessely–Moser isomers, unlike **2** which exclusively exists in open form as an equilibrium mixture (9:1) of enol and diketo tautomers.

This striking difference resulting from methylation of the 4-OH can be easily explained if ring closure of 2,6-dihydroxydibenzoylmethanes requires availability (i.e. no extra chelation) of both phenolic *o*-hydroxyl and β-keto carbonyl groups. This requirement is satisfied in **1** where the 3-formyl group is chelatable by the 4-OH group, leaving 2-OH and 6-OH groups available for the β-keto carbonyl groups. In **2**, the 3-formyl group is chelated by the 2-OH group, which becomes unavailable for ring closure; therefore **2** behaves like *o*-monohydroxydibenzoylmethanes which exist in open form only [9].

A similar behaviour has previously been observed [4] with synthetic 2,2',6-trihydroxy, 2,2',4,6-tetrahydroxy- and 2,2',6-trihydroxy-4-methoxydibenzoylmethanes, which appear as mixtures of cyclic hemiketal and open diketo forms, the latter being preponderant. In these compounds, chelation of one of the β-keto carbonyl groups by the 2'-OH group reduces its availability for ring closure and its enolizability in the open form. The two 2,6-dihydroxydibenzoylmethanes from *Unona lawii* thus afford a new interesting example of the structural requirements which must be satisfied for ring closure to 2,5-dihydroxyflavanones.

Until now, nothing is known about the biogenesis of 2,5-dihydroxyflavanones and they can be equally regarded as precursors or as metabolites of flavones, since they are easily dehydrated into 5-hydroxyflavones and the latter can alternatively be hydrated to 2,5-dihydroxyflavanones [3]. In *Populus nigra* buds, 2,5-dihydroxy-7 methoxyflavanone was found to occur with the corresponding 5-hydroxy-7-methoxyflavanone and flavone, and both hypotheses are possible.

In *Unona lawii* stems, some indications favouring the precursor role of 2,5-dihydroxyflavanones can be derived from the flavonoid pattern which includes, at the flavanone stage, only one of the two Wessely–Moser isomers, lawinal **6**, and at the flavone stage, on the one hand the two isomers, unonal and isounonal, in the same ratio as the corresponding 2-hydroxyflavanones **3** and **4** derived from **1**, and on the other hand unonal-7-methyl ether, but no isounonal-7-methyl ether. This same flavone pattern would result from simple dehydration of the co-occurring dibenzoylmethanes **1** and **2**, since, as previously observed [1], unonal-7-methyl ether is the only dehydration product of **2** whereas both unonal and isounonal are produced from **1**. These data strongly support the biogenetic scheme: flavanone → 2-hydroxyflavanone → flavone (Scheme 1), since 7-*O*-methylation



Scheme 1. Biogenesis of *Unona flavonoids*

at the flavone stage would be expected to give both unonal-7-methyl ether and isounonal-7-methyl ether.

Finally, **1** was synthesized from 3-formyl-2,4,6-trihydroxy-5-methylacetophenone [1] by Baker–Venkataraman rearrangement of the crude benzoate, using the modified technique of Hauteville *et al.* [3]. The synthetic crystalline product showed the same mp, mmp, IR spectrum and chromatographic properties as the natural one.

EXPERIMENTAL

3-Formyl-2,4,6-trihydroxy-5-methyl dibenzoylmethane **1** = *8-formyl-2,5,7-trihydroxy-6-methyl flavanone* **3** + *6-formyl-2,5,7-trihydroxy-8-methyl flavanone* **4**. NMR (60 MHz, CD_3COCD_3, −60°) $\delta^{10^{-6}}_{TMS}$ 13.63 (0.6H, *s*, D_2O -exchanged) OH-5 (or 7) of **3**; 13.50 (0.6H, *s*, D_2O-exch.) OH-7 (or 5) of **3**; 13.44 (0.4H, *s*, D_2O-exch.) OH-5 (or 7) of **4**; 13.35 (0.4H, *s*, D_2O-exch.) OH-7 (or 5) of **4**; 10.34 (1H, *s*) CHO; 8.1–7.8 (2H, *m*) H-2', 6'; 7.8–7.6 (3.4H, *m*) H-3', 4', 5' + OH-2 of **4**; 7.47 (0.6H, *d*, 2Hz) OH-2 of **3**; 3.58 (0.6H, *dd*, 2 and 17 Hz; + D_2O : *d*, 17 Hz) H-3 ax of **3**; 3.50 (0.4H, *dd*, 2 and 17 Hz; + D_2O :*d*, 17 Hz) H-3ax of **4**; 3.14 (0.4H, *d*, 17 Hz) H-3 eq of **4**; 3.09 (0.6H, *d*, 17 Hz) H-3 eq of **3**; 1.99 (3H, *s*) Me. NMR (60 MHz, CD_3COCD_3, −40°) $\delta^{10^{-6}}_{TMS}$ 7.51 (0.4H, *d*, 2 Hz) OH-2 of **4**; 7.42 (0.6H, *d*, 2Hz) OH-2 of **3**; 3.54 (0.6H, *dd*, 2 and 17 Hz) H-3 ax of **3**; 3.48 (0.4H, *dd*, 2 and 17 Hz) H-3 ax of **4**; 3.13 (0.4H, *d*, 17 Hz) H-3 eq of **4**; 3.10 (0.6H, *d*, 17 Hz) H-3 eq of **3**. NMR (60 MHz, CD_3COCD_3, −30°) $\delta^{10^{-6}}_{TMS}$ 7.42 (0.4H, *d*, 2 Hz) OH-2 of **4**; 7.33 (0.6H, *d*, 2 Hz) OH-2 of **3**; 3.52 (0.6H, *dd*, 2 and 17 Hz) H-3 ax of **3**; 3.46 (0.4H, *dd*, 2 and 17 Hz) H-3 ax of **4**; 3.11 (0.4H, *d*, 17 Hz) H-3 eq of **4**; 3.07 (0.6H, *d*, 17 Hz) H-3 eq of **3**.

3-Formyl-2,6-dihydroxy-4-methoxy-5-methyldibenzoylmethane **2**. NMR (FT 90 MHz, $CDCl_3$, ord. temp.) $\delta^{10^{-6}}_{TMS}$ 15.23 (*s*) OH enol; 14.72 (*s*) OH-2 (or 6); 14.33 (*s*) OH-6 (or 2); 10.01 (*s*) CHO-3; 8.07–7.9 (2H, *m*) H-2', 6'; 7.68 (*s*) = CH-enol; 7.6–7.46 (3H, *m*) H-3', 4', 5'; 4.72 (*s*) $COCH_2CO$; 3.91 (*s*) OMe-4; 2.10 (*s*) Me-5.

Synthesis of **1**. 3-Formyl-2,4,6-trihydroxy-5-methylaceto-

phenone (150 mg) and benzoyl chloride (500 mg) in dry Py were left at room temp. during 24 hr. The mixture was poured on ice, HCl added until pH6 and extracted with EtOAc. After washing with aq. $NaHCO_3$ and H_2O, evapn of the extract led to an oily, chromatographically homogeneous benzoate (375 mg) which was dissolved in DMSO (10 ml) Powdered NaOH (800 mg) was added, the mixture shaken during 5 min before addition of ice, left at room temp. for 30 min, neutralized with HOAc and extracted with EtOAc. After washing with $NaHCO_3$ and H_2O, evapn left a brown residue which was dissolved in C_6H_6. Impurities were pptd by hexane, filtered and the crude product separated by further addition of hexane After successive crystallizations in MeOH–H_2O, Et_2O–hexane and C_6H_6, 38 mg (17%) colorless crystals were obtained, mp 165–167° (lit. 166–167°) undepressed by mixing with natural 3-formyl-2,4,6-trihydroxy-5-methyldibenzoylmethane. IR spectra (KBr) were superimposable and both products gave only one spot (bright yellow under UV, orange with diazotized benzidine without spraying Na_2CO_3) and the same R_f on TLC

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HESPERETIN 7-RHAMNOSIDE FROM *CORDIA OBLIQUA*

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Key Word Index—*Cordia obliqua*; Boraginaceae, hesperetin 7-rhamnoside, flavanone

The ethanolic extract of the roots of *Cordia obliqua* (Boraginaceae) yielded hesperetin 7-*O*-α-L-rhamnopyranoside. The species is commonly known as 'Lasora' in Hindi and various parts of the plant are used medicinally. Although hesperetin is a well known flavanone, its 7-rhamnoside has not previously been reported in plants.

EXPERIMENTAL

The powdered roots of the *Cordia obliqua* were extracted exhaustively with hot EtOH which on concn and keeping at 0 for 2 days deposited white crystals which are being further studied. The filtrate was diluted with H_2O and the insoluble portion was extracted with EtOAc to give the reported glycoside, which was crystallised from EtOAc–petrol and shown to be homogeneous by PC and TLC. The glycoside was a yellowish-brown solid, $C_{22}H_{24}O_{10}$, (C = 58.90; H = 5.33; Calc. C = 58.92; H = 5.35%). Acid hydrolysis afforded hesperetin, $C_{16}H_{14}O_6$, mp 222–223° (*d*) (UV, IR, acetate, methoxyl, alkaline degradation) and L-rhamnose (mp, mmp, PC and osazone). The location of the sugar linkage was established by spectral means and by specific colour reactions

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