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TWO NEW DIHYDROCHALCONES FROM *MYRICA GALE**

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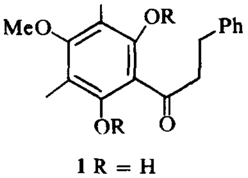
Abstract—From the fruits of *Myrica gale* the isolation of 2′,6′dihydroxy-4′-methoxy-3′,5′-dimethyldihydrochalcone and 4,4,6-trimethyl-2-(3-phenylpropionyl)-cyclohexane-1,3,5-trione is described. The constitutions have been deduced from spectroscopic data and confirmed by synthesis.

INTRODUCTION

In 1971 we described in a brief communication [1] the isolation of the three flavonoids **1–3** from *Myrica gale* L. and the elucidation of their constitutions by spectroscopic methods. In this paper it was suggested that **3** might be an artefact formed by extrusion of formaldehyde from **2**. We have now synthesized **1** and **2** and reextracted fruits of *M. gale* in order to verify the presence of **3**. In spite of several attempts we have not been able to reisolate **3** and it therefore seems likely that this compound is an artefact. However, the possibility that **3** is present in the plant at only certain times of the year cannot be excluded. In a recent communication Siaens *et al.* [2] have shown that oxidation of hexahydrocolupulone (**4**) in the presence of Cu (II) acetate affords the cyclopentenedione **5**. This corresponds to a similar loss of formaldehyde as in a supposed formation of **3** from **2**. However, the presence of **3** in our first extracts of fruits from *Myrica gale* cannot be doubted since **3** has recently been prepared [3] and the spectroscopic data of our **3** and synthetic **3** are identical. Attempts to prepare **3** from **2** by oxidation in the presence of Cu (II) acetate have not yet been successful.

Synthesis of 2′,6′-dihydroxy-4′-methoxy-3′,5′-dimethyldihydrochalcone (**1**) was performed by hydrogenation of 5-hydroxy-7-methoxy-6,8-dimethylflavanone (**6**) in methanol with 10% Pd/C as catalyst. The preparation of **6** is described elsewhere [4]. A marked increase in the yield of **1** was found when 0.5% KOH was added. This is presumably due to a greater tendency to form the corresponding chalcone in basic solution [5]. The spectroscopic properties of natural and synthetic **1** were identical. Acetylation of **1** furnished an oily diacetate $C_{22}H_{24}O_6$ (**10**). This compound is also obtained by hydrogenation of the diacetate of the corresponding chalcone (**11**). 4,4,6-Trimethyl-2-(3-phenylpropionyl)-cyclohexane-1,3,5-trione (**2**) was synthesized by methylation with MeI of 2′,4′,6′-trihydroxydihydrochalcone (**12**) [6]. All physical and spectroscopic data were identical with those of the natural compound. Further, vigorous methylation of **2** furnished a compound which had physical and spectroscopical data identical with the natural product grandiflorone (**7**) [7]. Also a Cu-complex



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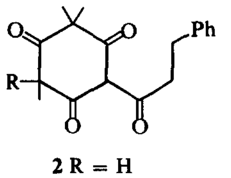

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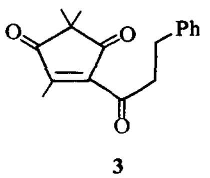

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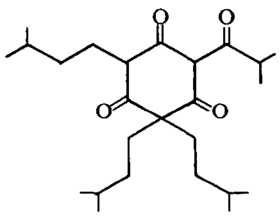

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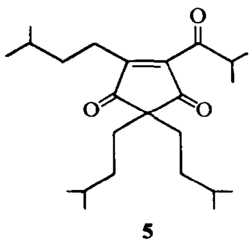

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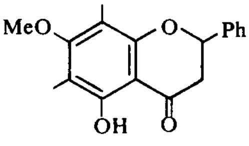
* Part 5 in the series: "Chemistry of *Myrica gale* L." For part 4 see ref. [4].



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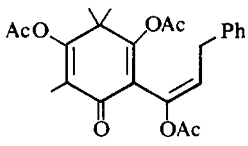

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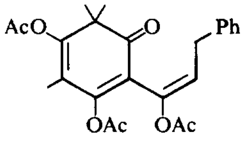

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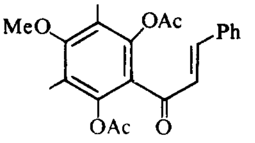

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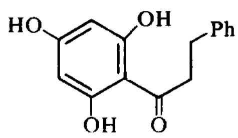

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and an imine had data in accordance with an earlier report [7].

Acetylation of **2** gave a colourless crystalline triacetate $C_{24}H_{26}O_7$, mp 97.5–98°. Its constitution had to be either as **8** or **9**. The UV spectrum, however, led to the choice of **8** as the triacetate, λ_{max} 212 nm is definitely not in accordance with a conjugated dienone as in **9**. The IR spectrum (ν_{max} 1648 cm^{-1}) also points to an $\alpha\beta$, $\alpha'\beta'$-unsaturated ketone such as **8**.

EXPERIMENTAL

Spectroscopy and chromatography were performed as described previously [4].

Plant material. Fruits of *Myrica gale* L. were collected in Bymarka, Trondheim and identified by Professor N. A. Sørensen of the University of Trondheim.

Isolation of 2′,6′-dihydroxy-4′-methoxy-3′,5′-dimethyldihydrochalcone (**1**) *and* 4,4,6-*trimethyl*-2-(3-*phenylpropionyl*)-*cyclohexane*-1,3,5-*trione* (**2**). Soxhlet extraction of air-dried fruits of *M. gale* (680 g) with Et_2O (1 l.) for 4 hr gave a brown oil (38 g). When the oil was left at room temp. **2** crystallized as pale yellow cubes (4 g), was washed with cold Et_2O and recrystallized from Et_2O–cyclohexane; mp 138–9°. M^+ 300.1365, calc for $C_{18}H_{20}O_4$ 300.1362. λ_{max} nm (log ε): 350 (4.30). ν_{max} cm^{-1}: 2930, 1665 (*s*), 1640, 1575 (*s*), 1518, 1472 (*s*), 1442 (*s*), 1385, 1375, 1328 (*s*), 1257 (*s*), 1248 (*s*), 1165 (*s*), 1038, 1000, 791, 755, 703, 642. PMR ppm (d_4-MeOH): δ 1.32 (6H, *s*), 1.80 (3H, *s*), 2.98, 330 (4H, AA′BB′-system), 7.20 (5H, narrow *m*). MS *m/e* (%): 300 (75, M), 285 (32, $M-CH_3$), 230 (22), 229 (9), 219 (20), 209 (4, $M-C_7H_7$), 201 (10), 196 (4, $M-C_6H_5CH{=}CH_2$), 195 (13, $M-C_6H_5CH_2$-CH_2), 168 (24, $M-C_6H_5CH{=}CHCO$), 133 (5, $C_6H_5CH_2CH_2$-CO) 105 (26, $C_6H_5CH_2CH_2$), 104 (9, $C_6H_6CH{=}CH_2$), 91 (61, C_7H_7). Repeated column chromatography of the remaining extract on SiO_2 with C_6H_6 and C_6H_6–$CHCl_3$ mixtures furnished needles of **1** (3 g) from cyclohexane, mp 117–117.5°. M^+ 300.1362 as calc. for $C_{18}H_{20}O_4$. λ_{max} nm (log ε): 223 sh (4.09), 281 (4.13), 350 (3.56), with NaOMe: 236 sh (4.17), 293 (4.07), 396 (3.51). ν_{max} cm^{-1}: 3445 (*s*), 2935, 1626 (*s*) 1597 (*s*), 1436 (*s*), 1124 (*s*), 902, 757, 702. PMR ppm: δ 2.11 (6H, *s*), 3.09, 3.38 (AA′BB′ system), 3.70 (3H, *s*), 7.24 (5H, narrow *m*), 9.36 (2H, *s*, disapp. with D_2O). MS *m/e* (%): 300 (69, M), 283 (10, M −OH), 195 (100, $M-C_6H_5CH_2CH_2$, *m**), 168 (20, $M-C_6H_5CH_2$-CH_2CO), 91 (12, C_7H_7). No trace of 2,2,5-trimethyl-4(3-phenylpropionyl)-cyclopent-4-ene-1,3-dione (**3**) was found in the extracts of *Myrica gale* fruits. However, a novel flavonoid,2′-hydroxy-4′,6′-dimethoxy-3′-methyldihydrochalcone [4] was isolated in small amount.

Synthesis of 2′,6′-*dihydroxy*-4′-*methoxy*-3′,5′-*dimethyl-dihydrochalcone* (**1**). The synthesis of 5-hydroxy-7-methoxy-6,8-dimethylflavanone (**6**) is described earlier [4]. Hydrogenation of **6** (57 mg) with 10% Pd/C (107 mg) in MeOH (50 ml) for 68 hr gave **1** (23 mg, 40%) in addition to unreacted **6**, (31 mg, 55%) separated on prep. TLC. Synthetic **1** was identical with the natural compound (mp, mmp, spectra). Hydrogenation in 0.5% methanolic KOH (50 ml) of **6** (55.5 mg, 103.8 mg Pd/C, 68 hr) yielded **1** (48.0 mg, 87%). No **6** was present. Hydrogenation in 0.5% methanolic HCl (50 ml) of **6** (52.0 mg, 97.2 mg Pd/C, 68 hr) gave 4.8 mg (9%) of **1** along with 35.1 mg (67%) of unreacted **6**. Acetylation of **1** (91.4 mg) in the usual way with Ac_2O/Py gave the diacetate **10**, 107.7 mg (92%), as a viscous, colourless oil from prep. TLC. M^+ 384.1565, calc. for $C_{22}H_{24}O_6$ 384.1571. λ_{max} nm (log ε): 248 (3.68). ν_{max} cm^{-1}: 3030, 2945, 1765 (*s*), 1699 (*s*), 1602 (*s*), 1498, 1455, 1430, 1372 (*s*), 1185 (*s*), 1125 (*s*), 1083 (*s*), 1007, 926, 702. PMR ppm: δ 2.03 (6H, *s*), 2.09 (6H, *s*), 2.99 (4H, narrow *m*), 3.70 (3H, *s*), 7.21 (5H, narrow *m*). MS *m/e* (%): 384 (23, M), 342 (25, $M-CH_2CO$, *m**), 300 (100, $M-2\times$ CH_2CO, *m**), 282 (10, *m/e* $300-H_2O$), 195 (66, *m/e* $300-C_6H_5CH_2CH_2$, *m**), 168 (17, *m/e* $300-C_6H_5CH{=}$ $CHCHO$, *m**), 105 (5, $C_6H_5CH_2CH_2$), 91 (25, C_7H_7). Hydrogenation of 2′,6′-diacetoxy-4′-methoxy-3′,5′-dimethylchalcone (**11**) [4] with 10% Pd/C (100 mg) in MeOH (50 ml) for 24 hr also gave **10** (33.6 mg from 35.2 mg, 95%).

Synthesis of 4,4,6-*trimethyl*-2-(3-*phenylpropionyl*)-*cyclohexane*-1,3,5-*trione* (**2**). Friedel-Crafts condensation of phloroglucinol (8.6 g) with dihydrocinnamoyl chloride (12.9 g) furnished 2′,4′,6′-trihydroxydihydrochalcone (**12**) [6], yield 5.4 g (31%), mp 139° (lit. [6] 137–8°). A soln of **13** (4.0 g) in MeOH (50 ml) was methylated with NaOMe (2.0 g) and MeI (8.8 ml) for 120 hr at 20°. The soln was neutralized with 1N H_2SO_4, taken to dryness, extracted with 50 ml 10% aq. $NaHCO_3$ × 4, and acidified to pH *ca* 3 with 1N H_2SO_4. Extraction with 25 ml Et_2O × 4 and recrystallization from $CHCl_3$–hexane gave **2**, 0.93 g (20%), identical with natural **2** (mp, mmp, UV, IR, NMR and MS). Acetylation of **2** (0.24 g) in the usual way with Ac_2O/Py gave a colourless oil purified by prep. TLC to give **8** (0.3 g, 88%). This oil was shown spectroscopically to be a triacetate of **2**. After standing for several months in a refrigerator, **8** crystallized. Recrystallization from MeOH gave colourless needles, mp 97.5–98°. M^+ 426.1678, calc. for $C_{24}H_{26}O_7$ 426.1677. λ_{max} nm (log ε): 212 (4.32), 218 sh (4.28), 242 sh (4.11). ν_{max} cm^{-1}: 3010, 1770 (*s*), 1648 (*s*), 1466, 1370, 1360, 1180 (*s*), 1126 (*s*), 1082 (*s*), 1005, 700. PMR ppm: δ 1.26 (6H, *s*), 1.70 (3H, *s*), 2.01 (3H, *s*), 2.13 (3H, *s*), 2.27 (3H, *s*), 3.42 (2H, *d*, $J = 8$ Hz), 5.57 (1H, *t*, $J = 8$ Hz), 7.21 (5H, narrow *m*). MS *m/e* (%): 426 (11, M), 384 (13, $M-CH_2CO$, *m**), 369 (10, $M-CH_2CO-CH_3$), 342 (17, $M-2$ × CH_2CO), 341 (37, $M-CH_2CO$–CH_3CO), 327 (20, $M-2$ × CH_2CO–CH_3), 300 (36, $M-3$ × CH_2CO, *m**), 299 (100, $M-2$ × CH_2CO–CH_3CO), 285 (28, *m/e* $300-CH_3$), 282 (21, *m/e* $300-H_2O$), 267 (7, *m/e* $300+H_2-CH_3$), 195 (20, *m/e* $300-C_6H$ CH_2CH_2, *m**), 168 (8, *m/e* $300-C_6H_5CH{=}$ $CHCHO$). 131 (7, $C_6H_5CH{=}CH{=}CO$, *m** from *m/e* 300), 91 (32, C_7H_7). Acetylation of natural **2** gave a compound identical with that from synthetic **2** (mp, mmp, UV, IR, NMR and MS).

Methylation of 4,4,6-*trimethyl*-2-(3-*phenylpropionyl*)-*cyclohexane*-1,3,5-*trione* (**2**). Methylation of (**2**) with NaOMe/MeI in MeOH gave grandifloron (**7**), 465 mg (85%), as colourless cubes from Et_2O/pentane, mp 31.5–32°. lit. [7] 32°. Spectral data identical with lit. [7]. The cupric salt of **7**, prepared according to [7], had a mp of 200.5–201° after recrystallization from MeOH and drying at 0.1 torr/90° for 1 hr (lit. [7] 201°). MS of the cupric salt showed M^+ 689.2178 (calc. for $C_{38}H_{42}O_8Cu$ 689.2176), thereby proving the structure to be a complex of one atom Cu and two molecules grandiflorone. The imine of **7**, prepared according to [7] had a mp of 148.5–149.5° (lit. [7] 149–150°).

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