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MODIFIED COUMARINS. 13. SYNTHESIS OF CYCLOPENTANE-ANNELATED PYRANOCOUMARINS

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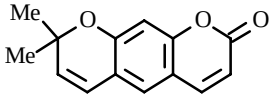
Modified pyranocoumarins containing a condensed cyclopentane fragment were synthesized by adjoining a 2,2-dimethyltetrahydropyran ring to a 2,3-dihydrocyclopenta[c]chromen-4-one system and annelation of a pyrone ring to a 2,2-dimethylchromane.

Key words: coumarins, pyranocoumarins, furocoumarins, chromanones, 2,3-dihydrocyclopenta[*c*]chromen-4-one.

Pyranocoumarins (chromeno-α-pyrones) are widely distributed in nature and contain a 2,2-dimethylpyran ring annelated to a benzopyran-2-one system at the 6,7; 5,6; or 7,8 positions [1]. Most natural pyranocoumarins are derivatives of the linear pyranone xantiletin (**1**) or its angular isomer seselin (**2**).



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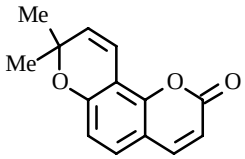

2

Pyranocoumarins also include coumarins with a condensed 2,2-dimethyldihydropyran ring or an annelated 2,2-dimethyltetrahydropryan-4-one moiety. Typical representatives of natural 8,8-dimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2-ones are dihydroxantiletin (**3**) isolated from *Seseli tortuosum* [2], *Ammi majus* [3], and *Cassia pumila* [4]; kanzonol Q (**4**) produced by *Glycyrrhiza uralensis* [5]; and isoglycycoumarin (**5**) isolated from *Glycyrrhiza aspera* [6, 7], *G. inflata*, *G. glabra*, and *G. uralensis* [8].

Examples of metabolites based on 8,8-dimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione are graveolone (**6**) produced by *Anethum graveolens* [9-12] and *Pituranthos tortuosus* [13] or clausenine (5-hydroxygraveolone) (**7**) isolated from *Clausena heptaphylla* and *C. excavata* [14-16].

Our goal was to modify the structure of 2,3-dihydrocyclopenta[*c*]chromen-4-one by adjoining a 2,2-dimethylpyran ring. The cyclopentane-annelated dihydropyranocoumarins were synthesized by two methods: 1) addition of a 2,2-dimethyltetrahydropyran ring to the coumarin and 2) annelation of a pyrone ring to the 2,2-dimethylchromane core.

Because they were necessary for further transformations, 7-hydroxy-6-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (**8**) and 9-hydroxy-7-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (**9**) were prepared by Pechmann condensation of 2-methylresorcinol and orcinol, respectively, with ethyl-2-oxocyclopentanecarboxylate in the presence of conc. H_2SO_4 [17]. Condensation of **8** and 3,3-dimethylallylbromide in the presence of *p*-toluenesulfonic acid [18] gave the linear dihydropyranocoumarin 6,8,8-trimethyl-2,3,9,10-tetrahydrocyclopenta[*c*]pyrano[3,2-*g*]chromen-4-one (**10**). Using **9** in this condensation forms the angular isomer 2,2,5-trimethyl-3,4,10,11-tetrahydrocylopenta[*c*]pyrano[2,3-*f*]chromen-8-one (**11**). The results were analogous if 3-methyl-2-buten-1-ol instead of 3,3-dimethylallylbromide was used as the alkylating agent. PMR spectra of **10** and **11** show simplified splitting patterns for the aromatic protons compared with the starting coumarins owing to a lack of coupling for the benzopyran H-6 proton. For **10**, H-11 is observed as a singlet at 6.99 ppm; for **11**, H-6 at 6.73 ppm.

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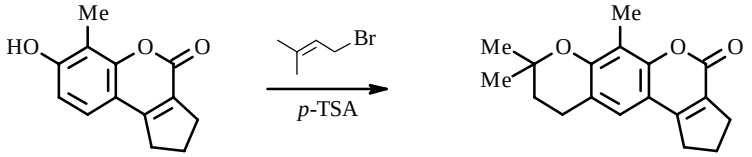
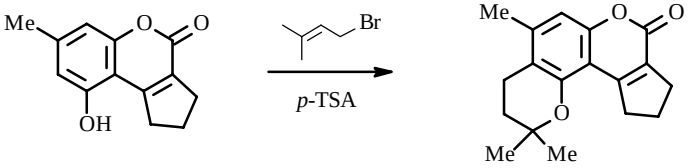
Furthermore, the PMR spectra of the compounds contain signals characteristic of a 2,2-dimethyltetrahydropyran ring [19]. It should be noted that using 7-hydroxy-2,3-dihydrocyclopenta[*c*]chromen-4-one in this condensation gave a difficultly separated mixture of 6,7-dihydropyranocoumarin and its 7,8-angular isomer in a 3:2 ratio according to PMR spectroscopy.

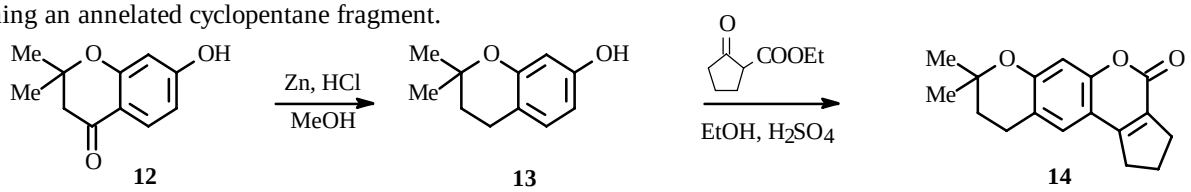


8 **10**



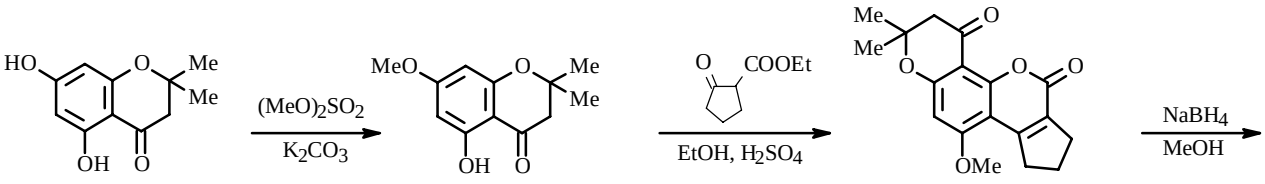
9 **11**

The starting compounds for synthesizing the dihydropyranocoumarins were also derivatives of 2,2-dimethyl-4-chromanone. Kabbe condensation [20] of 2,4-dihydroxyacetophenone and acetone in the presence of pyrrolidine gave 7-hydroxy-2,2,-dimethylchroman-4-one (**12**). Clemensen reduction of **12** by zinc dust in HCl gave 2,2-dimethylchroman-7-ol (**13**). Pechmann condensation of **13** and ethyl-2-oxocyclopentanecarboxylate in the presence of conc. H_2SO_4 formed 8,8-dimethyl-2,3,9,10-tetrahydrocyclopenta[*c*]pyrano[3,2-*g*]chromen-4-one (**14**), a modified analog of dihydroxantiletin containing an annelated cyclopentane fragment.

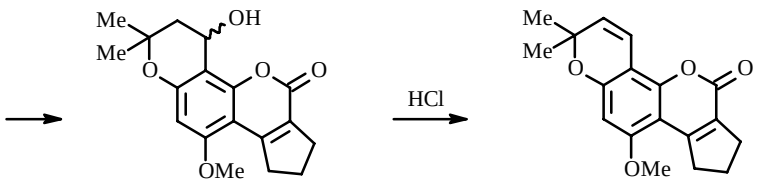


12 **13** **14**

5,7-Dihydroxy-2,2-dimethyl-4-chromanone (**15**) was synthesized by Friedel—Krafts acylation of floroglucinol with 3,3-dimethylacrylic acid in the presence of BF_3 etherate [21]. Selective methoxylation of the 7-phenol (the chromone 5-hydroxy group is bound by an intramolecular H-bond to the ketone) by a Williamson reaction using dimethylsulfate gave 2,2-dimethyl-5-hydroxy-7-methoxy-4-chromanone (**16**). Pechmann condensation of **16** with ethyl-2-oxocyclopentanecarboxylate in the presence of conc. H_2SO_4 completed the synthesis of 10-methoxy-2,2-dimethyl-8,9-dihydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-4,6-dione (**17**) in 48% yield. The PMR spectrum of **17** contains signals for the chromanone ring (6H singlet for two methyls and a singlet for the CH_2 protons), for the cyclopentane moiety, and a 1H singlet in the range of aromatic protons. Reduction of **17** by $NaBH_4$ in CH_3OH gave chromanol **18**, dehydration of which under acid-catalysis conditions formed 10-methoxy-2,2-dimethyl-8,9-dihydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (**19**) [22]. The PMR spectrum of **19** contains two doublets at 5.69 and 6.65 ppm with SSCC 9.6 Hz, characteristic of an annelated 2,2-dimethylpyran ring [19].

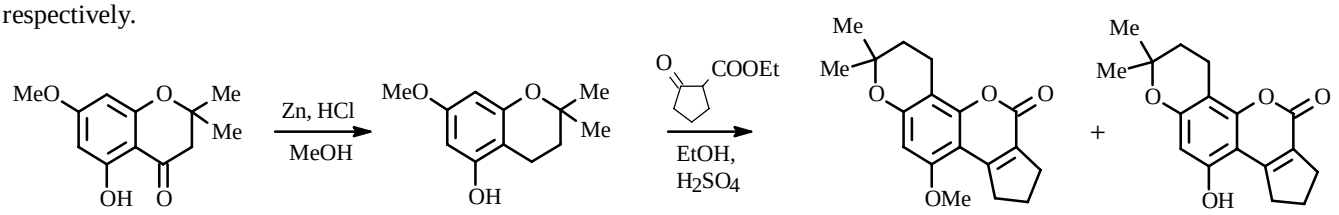


15 **16** **17**



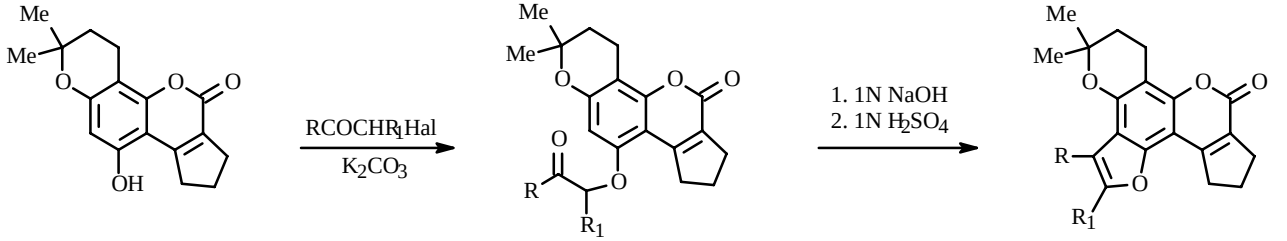
18 **19**

5-Hydroxychroman-4-one (**16**) was also used as starting material for synthesizing dihydropyranocoumarins that contain the 2,2-dimethyldihydropyran ring annelated at the 7,8-positions of the benzopyran-2-one. Clemensen reduction of **16** by zinc dust in HCl gave 7-methoxy-5-hydroxy-2,2-dimethylchromane (**20**). Pechmann condensation of **20** and ethyl-2-oxocyclopentanecarboxylate in the presence of conc. H_2SO_4 formed a mixture of 10-methoxy-2,2-dimethyl-3,4,8,9-tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (**21**) and its 10-demethoxylated derivative **22** in yields of 41 and 38%, respectively.



16 **20** **21** **22**

Hydroxycoumarin **22** was used as starting material to synthesize 5,5-dimethyl-6,7-dihydrofuro[2,3-*f*]pyrano[2,3-*h*]chromen-9-ones. The MacLeod method [23] was used to add the furan ring to the dihydropyranocoumarin system. Alkylation of hydroxycoumarin **20** under Williamson reaction conditions using chloroacetone and 3-chlorobutan-2-one gave oxoethers **23** and **24**, respectively. Heating **23** and **24** with NaOH solution (1 N) and subsequent acidolysis of the reaction mixture caused smoothly and with high yield cyclization to 5,5-dimethyl-6,7,11,12-tetrahydrocyclopenta[*c*]furo[2,3-*f*]pyrano[2,3-*h*]chromen-9-ones **25** and **26**, respectively.



22

23: R = CH_3, R_1 = H
24: R = R_1 = CH_3

25: R = CH_3, R_1 = H
26: R = R_1 = CH_3

EXPERIMENTAL

The course of reactions and purity of products were monitored using TLC on Merck 60 F254 plates using $CHCl_3$:CH_3OH (9:1) as eluent. Melting points were determined on a Kofler block. IR and UV spectra were measured on a Nicolet FTIR Nexus 475 spectrometer and a Specord M40 spectrophotometer, respectively. PMR specra were recorded on a Varian VXR-300 spectrometer at 300 MHz relative to TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

Hydroxycoumarins **8** and **9** were prepared as before [17].

6,6,8-Trimethyl-2,3,9,10-tetrahydrocyclopenta[*c*]pyrano[3,2-*g*]chromen-4-one (10). A mixture of **8** (2.16 g, 10 mmol), 3,3-dimethylallylbromide (1.75 mL, 15 mmol) or 3-methyl-2-buten-1-ol (1.52 mL, 15 mmol), and *p*-toluenesulfonic acid monohydrate (1.90 g, 10 mmol) in toluene (50 mL) was held at 100-110°C for 24 h (end of reaction determined using TLC). After the reaction was complete, the solvent was removed in vacuum in a rotary evaporator. The solid was dissolved in $CHCl_3$ (50 mL). The resulting solution was treated with NaOH solution (1 N, 2×50 mL) and saturated NaCl solution. Acidification of the combined extracts of the alkaline solution regenerated unreacted hydroxycoumarin. The organic layer was dried over anhydrous $MgSO_4$. The solvent was removed in vacuum in a rotary evaporator. The oily product was crystallized from hexane. Yield 68%, mp 140-141°C, empirical formula $C_{18}H_{20}O_3$. IR spectrum (KBr, cm^{-1}): 2972, 1710, 1614, 1580, 1396, 1162, 1122, 1104. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 211 (4.65), 225 (4.21), 329 (4.24).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.36 (6H, s, two CH_3-8), 1.84 (2H, t, J = 7.2, CH_2-9), 2.17 (2H, m, CH_2-2), 2.27 (3H, s, CH_3-6), 2.84 (2H, t, J = 7.2, CH_2-10), 2.92 (2H, m, CH_2-3), 3.01 (2H, m, CH_2-1), 6.99 (1H, s, H-11).

2,2,5-Trimethyl-3,4,10,11-tetrahydrocyclopenta[*c*]pyrano[2,3-*f*]chromen-8-one (11) was prepared analogously to **10** from **9** (2.16 g, 10 mmol). Yield 59%, mp 152-153°C, empirical formula $C_{18}H_{20}O_3$. IR spectrum (KBr, cm^{-1}): 1722, 1612, 1452, 1164, 1146, 1120, 1072. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 209 (4.61), 311 (4.20).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.36 (6H, s, two CH_3-2), 1.85 (2H, t, J = 7.2, CH_2-3), 2.10 (2H, m, CH_2-10), 2.23 (3H, s, CH_3-5), 2.63 (2H, t, J = 7.2, CH_2-4), 2.81 (2H, m, CH_2-9), 3.34 (2H, m, CH_2-11), 6.73 (1H, s, H-6).

7-Hydroxy-2,2-dimethylchroman-4-one (12). A solution of 2,4-dihydroxyacetophenone (15.22 g, 0.1 mol) absolute acetone (15 mL, 0.2 mol), and freshly distilled pyrrolidine (17 mL, 0.2 mol) in absolute CH_3CN (200 mL) was held at 40-50°C for 12 h (end of rection determined using TLC). After the reaction was complete, solvent was removed in vacuum in a rotary evaporator. The oily product was crystallized from hexane:propan-2-ol (9:1). Yield 74%, mp 181°C (lit. 169°C [24], 172-174°C [25]), empirical formula $C_{11}H_{12}O_3$. IR spectrum (KBr, cm^{-1}): 3124, 2968, 1644, 1582, 1572, 1484, 1372, 1330, 1312, 1256, 1170, 1126. UV spectrum (EtOH, λ_{max}, nm, log ε): 214 (4.39), 236 (4.14), 278 (4.23), 316 (3.99).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.38 (6H, s, two CH_3-2), 2.60 (2H, s, CH_2-3), 6.20 (1H, d, J = 2.1, H-8), 6.39 (1H, dd, J = 2.1, J = 8.4, H-6), 7.55 (1H, d, J = 2.1, H-8), 10.31 (1H, s, OH-7).

2,2-Dimethylchroman-7-ol (13). A solution of **12** (1.92 g, 10 mmol) in CH_3OH (20 mL) was vigorously stirred, treated with zinc dust (6.4 g, 100 mmol), dropwise with conc. HCl (20 mL), held at room temperature, and vigorously stirred for 2 h (end of reaction determined using TLC). After the reaction was complete, the solid of unreacted zinc was filtered off. The filtrate was treated with saturated NaCl solution (50 mL). The product was extracted with ethylacetate. The organic layer was dried over anhydrous $MgSO_4$. The solvent was removed in vacuum in a rotary evaporator. The chromanol was obtained in 95% yield as a light-yellow oil and was used in further transformations.

8,8-Dimethyl-2,3,9,10-tetrahydrocyclopenta[*c*]pyrano[3,2-*g*]chromen-4-one (14). A solution of **13** (0.89 g, 5 mmol) and ethyl-2-oxocyclopentanecarboxylate (0.74 mL, 5 mmol) in ethanol (5 mL) was vigorously stirred, treated with conc. H_2SO_4, (5mL) left overnight at room temperature, and poured into icewater (50 mL). The resulting solid was filtered off and crystallized from propan-2-ol. Yield 60%, mp 131-132°C, empirical formula $C_{17}H_{18}O_3$. IR spectrum (KBr, cm^{-1}): 1720, 1628, 1566, 1504, 1400, 1384, 1364, 1332, 1320, 1148, 1118, 1066. UV spectrum (EtOH, λ_{max}, nm, log ε): 208 (4.72), 223 (4.26), 333 (4.35).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.30 (6H, s, two CH_3-8), 1.80 (2H, t, J = 7.2, CH_2-9), 2.07 (2H, m, CH_2-2), 2.70 (2H, m, CH_2-3), 2.80 (2H, t, J = 7.2, CH_2-10), 3.00 (2H, m, CH_2-1), 6.71 (1H, s, H-6), 7.32 (1H, s, H-11).

5,7-Dihydroxy-2,2-dimethylchroman-4-one (15). A solution of floroglucinol dihydrate (6.48 g, 40 mmol) and 3,3-dimethylacrylic acid (4.80 g, 48 mmol) in BF_3 etherate (20 mL) was held at 70°C for 2 h (end of reaction determined using TLC). After the reaction was complete, the reaction mixture was cooled to room temperature and poured into icewater (500 mL). The resulting solid was filtered off and crystallized from CH_3CN. Yield 88%, mp 195-196°C (lit. 189-190°C [21], 194-195°C [26], 196-197°C [24], 197-198°C [27, 28], 198°C [29, 30], 198-199°C [31]), empirical formula $C_{11}H_{12}O_4$. IR spectrum (KBr, cm^{-1}): 3152, 1642, 1584, 1504, 1372, 1334, 1300, 1256, 1196, 1174, 1086. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 212 (4.31), 230 (4.15), 288 (4.22).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.37 (6H, s, two CH_3-2), 2.75 (2H, s, CH_2-3), 5.81 and 5.82 (two d, J = 2.1, H-6, H-8), 10.73 (1H, s, OH-7), 12.10 (1H, s, OH-5).

5-Hydroxy-7-methoxy-2,2-dimethylchroman-4-one (16). A mixture of **15** (5.20 g, 25 mmol) and anhydrous potash (6.9 g, 50 mmol) in absolute acetone (50 mL) was stirred at 50°C for 30 min and treated with dimethylsulfate (3.9 mL, 27.5 mmol). The reaction mixture was held at 50°C and vigorously stirred for 1 h (course of reaction monitored by TLC). After the reaction was complete, the mixture was cooled to room temperature, poured into icewater (300 mL), and acidified to pH 4. The resulting solid was filtered off and crystallized from propan-2-ol (50%). Yield 83%, mp 62-63°C (lit. 48-49°C [32], 61-64°C [33], 65-66°C [34], 69-70°C [31], 71-73°C [21]), empirical formula $C_{12}H_{14}O_4$. IR spectrum (KBr, cm^{-1}): 2968, 1640, 1580, 1518, 1444, 1360, 1314, 1282, 1252, 1200, 1160, 1090. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 215 (4.28), 229 (4.09), 288 (4.18).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.40 (6H, s, two CH_3-2), 2.81 (2H, s, CH_2-3), 3.78 (1H, s, CH_3O-7), 6.01 and 6.03 (two d, J = 2.1, H-6, H-8), 12.05 (1H, s, OH-5).

10-Methoxy-2,2-dimethyl-8,9-dihydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-4,6-dione (17). A solution of **16** (2.22 g, 10 mmol) and ethylcyclopentanone-2-carboxylate (1.5 mL, 10 mmol) in ethanol (5 mL) was treated dropwise with conc. H_2SO_4 (10 mL). The reaction mixture was held at 50°C for 8 h, left overnight at room temperature, and poured into icewater (100 mL). The resulting solid was filtered off and crystallized from propan-2-ol. Yield 48%, mp 262-263°C, empirical formula $C_{18}H_{18}O_5$. IR spectrum (KBr, cm^{-1}): 1726, 1712, 1688, 1656, 1620, 1582, 1478, 1458, 1390, 1280, 1232, 1168, 1094.

UV spectrum (EtOH, λ_{max}, nm, log ε): 221 (4.52), 287 (4.39), 321 (4.32).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.43 (6H, s, two CH_3-2), 2.00 (2H, m, CH_2-8), 2.64 (2H, m, CH_2-9), 2.74 (2H, s, CH_2-3), 3.15 (2H, m, CH_2-7), 3.90 (1H, s, OCH_3-10), 6.47 (1H, s, H-11).

4-Hydroxy-10-methoxy-2,2-dimethyl-3,4,8,9-tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (18). A solution of **17** (1.14 g, 4 mmol) in CH_3OH (10 mL) was treated in portions with $NaBH_4$ (0.46 g, 12 mmol). The reaction mixture was held at room temperature and stirred vigorously for 2 h (end of reaction determined using TLC). After the reaction was complete, the mixture was poured into saturated NaCL solution (100 mL) and extracted with ethylacetate (3×20 mL). The organic layer was dried over anhydrous $MgSO_4$. The solvent was removed in vacuum in a rotary evaporator. The solid was crystallized from CH_3OH. Yield 89%, mp 243-244°C, empirical formula $C_{18}H_{20}O_5$. IR spectrum (KBr, cm^{-1}): 3460, 2976, 1706, 1692, 1620, 1592, 1488, 1440, 1392, 1372, 1324, 1244, 1204, 1156, 1130, 1090. UV spectrum (EtOH, λ_{max}, nm, log ε): 212 (4.71), 252 (4.11), 262 (4.12), 329 (4.36).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.38, 1.43 (6H, two s, two CH_3-2), 1.86 (1H, dd, J = 12.0, J = 5.7, H-3α), 2.00 (2H, m, CH_2-8), 2.04 (1H, dd, J = 12.0, J = 2.4, H-3β), 2.64 (2H, m, CH_2-9), 3.17 (2H, m, CH_2-9), 3.80 (1H, s, OCH_3-10), 4.88 (1H, m, H-4), 4.97 (1H, d, J = 5.4, OH-4), 6.24 (1H, s, H-11).

10-Methoxy-2,2-dimethyl-8,9-dihydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (19). A solution of **18** (0.86 g, 3 mmol) in dioxane (10 mL) was treated with HCl (4 M, 10 mL). The reaction mixture was held at room temperature and vigorously stirred for 4 h (end of reaction determined using TLC). After the reaction was complete, solvent was removed in vacuum in a rotary evaporator. The solid was crystallized from CH_3OH. Yield 86%, mp 219-220°C, empirical formula $C_{18}H_{18}O_4$. IR spectrum (KBr, cm^{-1}): 1712, 1618, 1590, 1488, 1452, 1436, 1360, 1228, 1198, 1152, 1130, 1114, 1084. UV spectrum (EtOH, λ_{max}, nm, log ε): 226 (4.46), 283 (4.13), 294 (4.16), 329 (4.10).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.43 (6H, s, two CH_3-2), 2.02 (2H, m, CH_2-8), 2.64 (2H, m, CH_2-9), 3.19 (2H, m, CH_2-7), 3.83 (3H, s, CH_3O-10), 5.69 (1H, d, J = 9.6, H-3), 6.34 (1H, s, H-11), 6.65 (1H, d, J = 9.6, H-4).

7-Methoxy-2,2-dimethyl-chroman-5-ol (20) was prepared analogously to **13** from **16** (3.09 g, 14 mmol), zinc dust (9.0 g, 140 mmol), and conc. HCl (40 mL). Yield 93% as a light-yellow oil that was used for further transformations.

Tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-ones 21 and 22. A solution of **20** (2.70 g, 13 mmol) and ethyl-2-oxocyclopentanecarboxylate (1.9 mL, 13 mmol) in ethanol (10 mL) was stirred vigorously and treated dropwise with conc. H_2SO_4 (20 mL). The resulting mixture was held at 50°C for 4 h, left overnight at room temperature, and poured into icewater (100 mL). The resulting solid was dissolved in $CHCl_3$ (50 mL) and treated with NaOH solution (1 N, 2×50 mL) and saturated NaCl solution. The organic layer was dried over anhydrous $MgSO_4$. The solvent was removed in vacuum in a rotary evaporator. The oily product was crystallized from CH_3OH to give **21**. The combined extracts of the alkaline solution were acidified to pH 4. The resulting solid (**22**) was filtered off and crystallized from propan-2-ol.

10-Methoxy-2,2-dimethyl-3,4,8,9-tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (21). Yield 41%, mp 191-192°C, empirical formula $C_{18}H_{20}O_4$. IR spectrum (KBr, cm^{-1}): 1724, 1622. 1602, 1486, 1470, 1436, 1378, 1326, 1208, 1152, 1122, 1082. UV spectrum (EtOH, λ_{max}, nm, log ε): 209 (4.51), 264 (3.91), 333 (4.12).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.32 (6H, s, two CH_3-2), 1.83 (2H, t, J = 7.2, CH_2-3), 2.04 (2H, m, CH_2-8), 2.54 (2H, t, J = 7.2, CH_2-4), 2.71 (2H, m, CH_2-9), 3.21 (2H, m, CH_2-7), 3.79 (1H, s, CH_3O-10), 6.25 (1H, s, H-11).

10-Hydroxy-2,2-dimethyl-3,4,8,9-tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (22). Yield 38%, mp 224-225°C, empirical formula $C_{17}H_{18}O_4$. IR spectrum (KBr, cm^{-1}): 3236, 2972, 1704, 1668, 1612, 1572, 1440, 1406, 1368, 1282, 1256, 1160, 1120, 1064. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 212 (4.53), 324 (4.12).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.32 (6H, s, two CH_3-2), 1.76 (2H, t, J = 7.2, CH_2-3), 2.01 (2H, m, CH_2-8), 2.54 (2H, t, J = 7.2, CH_2-4), 2.61 (2H, m, CH_2-9), 3.22 (2H, m, CH_2-7), 6.30 (1H, s, H-11), 10.21 (1H, s, OH-10).

2,2-Dimethyl-10-(2-oxopropoxy)-3,4,8,9-tetrahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-6-one (23). A hot solution of **22** (1.14 g, 4 mmol) in absolute acetone (20 mL) was treated with freshly calcined potash (1.66 g, 10 mmol), vigorously stirred, heated to 50-56°C, treated with chloroacetone (0.35 mL, 4.4 mmol), and held for 3 h with heating and vigorous stirring (course of reaction monitored by TLC). After the reaction was complete, the mixture was cooled to room temperature, poured into icewater (100 mL), and acidified to pH 4. The solid was filtered off and crystallized from propan-2-ol (75%). Yield 86%, mp 190-191°C, empirical formula $C_{20}H_{22}O_5$. IR spectrum (KBr, cm^{-1}): 1720, 1614, 1438, 1396, 1160, 1122, 1054. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 214 (4.64), 322 (4.24).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.34 (6H, s, two CH_3-2), 1.80 (2H, t, J = 6.6, CH_2-3), 2.05 (2H, m, CH_2-8), 2.19 (3H, s, CH_3-3′), 2.65 (2H, m, CH_2-4, CH_2-7), 3.26 (2H, m, CH_2-9), 4.85 (3H, s, CH_2-1′), 6.44 (1H, s, H-11).

2,2-Dimethyl-10-(1-methyl-2-oxopropoxy)-3,4,8,9-tetrahydrocyclpenta[*c*]pyrano[2,3-*h*]chromen-6-one (24) was prepared analogously to **23** from **22** (1.14 g, 4 mmol) and 3-chloro-2-butanone (0.44 mL, 4.4 mmol). Yield 82%, mp 124-126°C, empirical formula $C_{21}H_{24}O_5$. IR spectrum (KBr, cm^{-1}): 1716, 1608, 1570, 1432, 1396, 1364, 1162, 1112, 1060. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 214 (4.65), 322 (4.26).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.33, 1.35 (6H, two s, two CH_3-2), 1.46 (3H, d, J = 6.6, CH_3-1′), 1.80 (2H, t, J = 6.6, CH_2-3), 2.04 (2H, m, CH_2-8), 2.18 (3H, s, CH_3-3′), 2.64 (2H, m, CH_2-4, CH_2-7), 3.26 (2H, m, CH_2-9), 5.01 (1H, q, J = 6.9, H-1′), 6.37 (1H, s, H-11).

3,5,5-Trimethyl-6,7,11,12-tetrahydrocyclopenta[*c*]furo[2,3-*f*]pyrano[2,3-*h*]chromen-9-one (25). A solution of **23** (0.85 g, 2.5 mmol) in propan-2-ol (10 mL) was treated with NaOH solution (1 N, 10 mL). The reaction mixture was heated for 3 h (end of reaction determined by TLC). After the reaction was complete, the mixture was cooled to room temperature, poured into icewater (100 mL), and acidified to pH 4. The solid was filtered off and crystallized from propan-2-ol (75%). Yield 91%, mp 247-249°C, empirical formula $C_{20}H_{20}O_4$. IR spectrum (KBr, cm^{-1}): 1710, 1620, 1540, 1428, 1156, 1110, 1092. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 211 (4.53), 231 (4.37), 259 (4.37), 273 (4.29), 314 (4.15).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.36 (6H, s, two CH_3-5), 1.85 (2H, t, J = 6.6, CH_2-6), 2.05 (2H, m, CH_2-11), 2.39 (3H, s, CH_3-3), 2.68 (2H, m, CH_2-10), 2.84 (2H, t, J = 6.6, CH_2-7), 3.32 (2H, m, CH_2-12), 7.55 (1H, s, H-2).

2,3,5,5-Tetramethyl-6,7,11,12-tetrahydrocyclopenta[*c*]furo[2,3-*f*]pyrano[2,3-*h*]chromen-9-one (26) was prepared analogously to **25** from **24** (0.89 g, 2.5 mmol). Yield 85%, mp 255-256°C, empirical formula $C_{21}H_{22}O_4$. IR spectrum (KBr, cm^{-1}): 1710, 1620, 1588, 1432, 1382, 1288, 1158, 1102, 1080. UV spectrum (EtOH, λ_{max}, nm, log ε): 212 (4.52), 230 (4.37), 252 (4.20), 258 (4.27), 278 (4.29), 319 (4.10).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.36 (6H, s, two CH_3-5), 1.85 (2H, t, J = 6.6, CH_2-6), 2.05 (2H, m, CH_2-11), 2.33, 2.34 (6H, two s, CH_3-2, CH_3-3), 2.83 (2H, m, CH_2-10), 2.83 (2H, t, J = 6.6, CH_2-7), 3.33 (2H, m, CH_2-12).

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