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MODIFIED COUMARINS. 28. SYNTHESIS OF SPIROSUBSTITUTED PYRANOCOUMARINS

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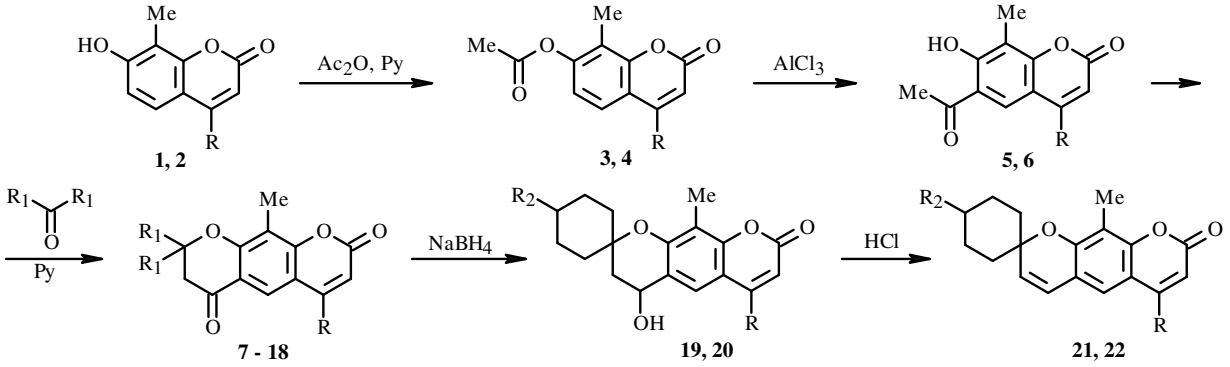
Spiropyranobenzopyrandiones were prepared, reduced, and dehydrated to form spirosubstituted pyranocoumarins.

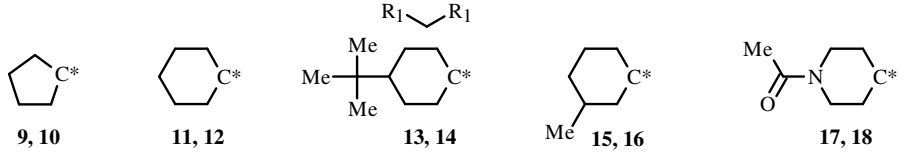
Key words: coumarins, pyranocoumarins, spiropyranocoumarins.

Pyranocoumarins (chromeno-α-pyrones) are widely distributed natural coumarins that contain a 2,2-dimethylpyran ring annelated to benzopyran-2-one [1]. Pyranocoumarins also include coumarin derivatives containing an annelated 2,2,-dimethyltetrahydropyran-4-one core. Thus, 8,8-dimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione (graveolone) was isolated from parsley [2], *Anethum graveolens* [3-6], and *Pituranthos tortuosus* [7] or clausenine (5-hydroxygraveolone) was isolated from *Clausena heptaphylla* and *C. excavata* [8-10].

We synthesized structural analogs of graveolone and spirosubstituted pyranocoumarins, which are presently practically unstudied [11-13].



1, 3, 5: R = $CH_2CH_2CH_3$; **2, 4, 6:** R = $CH_2CH_2CH_2CH_3$; **7:** R = $CH_2CH_2CH_3$, R_1 = CH_3
8: R = $CH_2CH_2CH_2CH_3$, R_1 = CH_3; **19, 21:** R = $CH_2CH_2CH_3$, R_2 = $(CH_3)_3C$
20, 22: R = $CH_2CH_2CH_2CH_2CH_3$, R_2 = H
9, 11, 13, 15, 17: R = $CH_2CH_2CH_3$; **10, 12, 14, 16, 18:** R = $CH_2CH_2CH_2CH_3$



9, 10 **11, 12** **13, 14** **15, 16** **17, 18**

C* - Spiroatom

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7-Hydroxy-8-methylcoumarins **1** and **2** that were required for further transformations were prepared by Pechmann condensation of 2-methylresorcinol with ethylbutyrylacetate or methyl-3-oxoheptanoate in the presence of conc. H_2SO_4 as condensing agent. Hydroxycoumarins **1** and **2** were acetylated by acetic anhydride in pyridine to form 7-acetoxycoumarins **3** and **4**. Fries rearrangement of **3** and **4** in the presence of anhydrous $AlCl_3$ at 120°C produced in high yields 6-acetylcoumarins **5** and **6**, convenient starting mateirals for annelation of the 2,2-dimethyltetrahydropyran-4-one core.

Kabbe condensation [14] of **5** and **6** with acetone in the presence of pyrrolidine formed 8,8,10-trimethyl-4-alkyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-diones **7** and **8**, structural analogs of the natural pyranocoumarin graveolone. The PMR spectra of **7** and **8** contained resonances characteristic of the coumarin system and an annelated chromanone ring, a 6H singlet for two methyls at 1.50 ppm and a singlet for CH_2 protons at 2.78 ppm. The ^{13}C NMR spectra of **7** and **8** exhibited a resonance for the spiroatom at 81.20-81.30 ppm.

Using cyclic ketones in the Kabbe condensation produced spiropyranobenzopyrandiones **9**-**18** in high yields. These were spiroanalogs of the natural pyranocoumarin graveolone. We used cyclopentanone (**9** and **10**), cyclohexanone (**11** and **12**), 4-*t*-butylcyclohexanone (**13** and **14**), 3-methylcyclohexanone (**15** and **16**), and 1-acetylpiperidin-4-one (**17** and **18**) in this reaction. The PMR spectra of the spirosubstituted pyranocoumarins showed resonances characteristic of the coumarin ring, the cycloalkyl spirosubstituent, and the formed methylene group at 2.70-3.00 ppm. The ^{13}C NMR spectra of spiropyranobenzopyrandiones **11**-**18** with a cyclohexyl spirosubstituent contained a resonance for the spiroatom at 80-84 ppm. The spiroatom in cyclopentanespiropyranocoumarin **10** resonated at weaker field at 92 ppm. Doubled proton resonances for the spirosubstituent and the dihydropyranobenzopyrandione system were noted in the NMR spectra of **15** and **16**, which contain a methyl substituent in the cyclohexane substituent. Obviously such splitting was due to the formation of a mixture of two diastereomers.

Reduction of **12** and **13** by $NaBH_4$ in CH_3OH produced chromanols **19** and **20**, dehydration of which under acid-catalysis conditions (HCl in dioxane) [15] formed spirosubstituted 4-alkylpyrano[3,2-*g*]chromen-2-ones **21** and **22**, spiroanalogs of natural linear pyranocoumarins. The PMR spectra of **21** and **22** contained two doublets at 5.73-5.76 and 6.48-6.54 ppm with SSCC J = 9.6 Hz that were characteristic of an annelated pyran ring [16]. The ^{13}C NMR spectra of **21** and **22** showed a resonance for the C spiroatom at 78.03-78.43 ppm.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Merck 60 F_{254} plates with elution by $CHCl_3$:CH_3OH (9:1 and 19:1). Melting points were determined on a Kofler block. NMR spectra were recorded on Varian VXR-300 Mercury 400 spectrometers at 300 and 400 MHz, respectively, vs. TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

7-Hydroxy-8-methyl-4-propylchrome-2-one (1). A cooled (0°C) solution of 2-methylresorcinol (12.41 g, 0.1 mol) and ethylbutyrylacetate (15.9 mL, 0.1 mol) in ethanol (20 mL) was stirred vigorously, cooled, and treated dropwise with conc. H_2SO_4 (40 mL). The mixture was stirred until thickened, left overnight at room temperature, and poured into icewater (500 mL). The resulting precipitate was filtered off and crystallized from aqueous propanol-2 to afford **1**, mp 172-173°C (lit. [17] 165-166°C), $C_{13}H_{14}O_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.00 (3H, t, J = 7.2, CH_3-3′), 1.67 (2H, m, CH_2-2′), 2.18 (3H, s, CH_3-8), 2.69 (2H, t, J = 7.2, CH_2-1′), 5.98 (1H, s, H-3), 6.83 (1H, d, J = 8.7, H-6), 7.38 (1H, d, J = 8.7, H-5), 10.24 (1H, s, OH-7).

7-Hydroxy-8-methyl-4-butylchromen-2-one (2) was prepared analogously to **1** from 2-methylresorcinol (12.41 g, 0.1 mol) and methyl-3-oxoheptanoate (15.9 mL, 0.1 mol). Yield 79%, mp 158-159°C, $C_{13}H_{14}O_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.92 (3H, t, J = 7.2, CH_3-4′), 1.37 (2H, m, CH_2-3′), 1.58 (2H, m, CH_2-2′), 2.16 (3H, s, CH_3-8), 2.72 (2H, t, J = 7.2, CH_2-1′), 6.07 (1H, s, H-3), 6.89 (1H, d, J = 8.1, H-6), 7.47 (1H, d, J = 8.1, H-5), 10.39 (1H, s, OH).

7-Acetoxy-8-methyl-4-propylchromen-2-one (3). A mixture of **1** (10.95 g, 50 mmol), freshly distilled acetic anhydride (9.5 mL, 100 mmol), and anhydrous pyridine (5 mL) was heated for 1 h and left overnight at room temperature. The resulting precipitate was filtered off and crystallized from propanol-2. Yield 76%, mp 114-116°C (lit. [17] 106-107°C), $C_{15}H_{16}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.98 (3H, t, J = 7.6, CH_3-3′, 1.64 (2H, m, CH_2-2′), 2.16 (3H, s, CH_3-8), 2.37 (3H, s, CH_3COO-7), 2.76 (2H, t, J = 7.6, CH_2-1′), 6.32 (1H, s, H-3), 7.14 (1H, d, J = 8.8, H-6), 7.70 (1H, d, J = 8.8, H-5).

7-Acetoxy-8-methyl-4-butylchromen-2-one (4) was prepared analogously to **3** from **2** (11.64 g, 50 mmol), acetic anhydride (9.5 mL, 100 mmol), and anhydrous pyridine (5 mL). Yield 66%, mp 89-90°C, $C_{16}H_{18}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.98 (3H, t, J = 7.2, CH_3-4′), 1.47 (2H, m, CH_2-3′), 1.68 (2H, m, CH_2-2′), 2.29 (3H, s, CH_3-8), 2.38 (3H, s, CH_3COO-7), 2.75 (2H, t, J = 7.2, CH_2-1′), 6.25 (1H, s, H-3), 7.02 (1H, d, J = 8.8, H-6), 7.49 (1H, d, J = 8.8, H-5).

6-Acetyl-7-hydroxy-8-methyl-4-propylchromen-2-one (5). A ground mixture of coumarin **3** (7.80 g, 30 mmol) and $AlCl_3$ (12.00 g, 90 mmol) was held at 120-130°C for 1 h, cooled, and diluted with HCl solution (100 mL, 1 N). The resulting precipitate was filtered off and crystallized from propanol-2. Yield 85%, mp 145-147°C, $C_{15}H_{16}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.00 (3H, t, J = 7.6, CH_3-3′), 1.66 (2H, m, CH_2-2′), 2.15 (3H, s, CH_3-8), 2.75 (3H, s, CH_3CO-6), 2.82 (2H, t, J = 7.6, CH_2-1′), 6.20 (1H, s, H-3), 8.11 (1H, s, H-5), 12.99 (1H, s, OH).

6-Acetyl-7-hydroxy-8-methyl-4-butylchromen-2-one (6) was prepared analogously to **5** from **4** (8.23 g, 30 mmol) and $AlCl_3$ (12.00 g, 90 mmol). Yield 76%, mp 123-125°C, $C_{15}H_{16}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.96 (3H, t, J = 7.6, CH_3-4′), 1.40 (2H, m, CH_2-3′), 1.61 (2H, m, CH_2-2′), 2.13 (3H, s, CH_3-8), 2.74 (3H, s, CH_3CO-6), 2.82 (2H, t, J = 7.6, CH_2-1′), 6.18 (1H, s, H-3), 8.08 (1H, s, H-5), 12.95 (1H, s, OH).

4-Alkyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-diones 7-18. A solution of 6-acetyl-7-hydroxycoumarin **5** or **6** (10 mmol) in CH_3CN (10 mL) was treated with pyrrolidine (25 mmol, 2.1 mL) and the appropriate ketone (25 mmol) and held at 45C for 8-20 h (end of the reaction determined by TLC). The solvent was removed in vacuo in a rotary evaporator. The solid was crystallized from propanol-2.

8,8,10-Trimethyl-4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione (7). Yield 72%, mp 119-121°C, $C_{18}H_{20}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, CH_3-3′), 1.49 (6H, s, 2 × CH_3-8), 1.73 (2H, m, CH_2-2′), 2.31 (3H, s, CH_3-10), 2.72 (2H, t, J = 7.6, CH_2-1′), 2.78 (2H, s, CH_2-7), 6.17 (1H, s, H-3), 8.07 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.87 (C-6), 159.98 (C-2, C-10a), 157.26 (C-4), 156.72 (C-9a), 121.02 (C-4a), 116.97 (C-5), 114.26 (C-5a), 113.37 (C-3), 111.89 (C-10), 81.27 (C-8), 48.26 (C-7), 33.38 (C-1′), 26.89 (CH_3-8), 21.70 (C-2′), 14.30 (C-3′), 8.71 (CH_3-10).

8,8,10-Trimethyl-4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione (8). Yield 65%, mp 176-177°C, $C_{19}H_{22}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.98 (3H, t, J = 7.2, CH_3-4′), 1.43 (2H, m, CH_2-3′), 1.51 (6H, s, 2 × CH_3-8), 1.67 (2H, m, CH_2-2′), 2.30 (3H, s, CH_3-10), 2.76 (2H, t, J = 7.6, CH_2-1′), 2.78 (2H, s, CH_2-7), 6.17 (1H, s, H-3), 8.07 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.83 (C-6), 159.95 (C-2, C-10a), 157.48 (C-4), 156.71 (C-9a), 120.99 (C-4a), 116.96 (C-5), 114.26 (C-5a), 113.32 (C-3), 111.81 (C-10), 81.25 (C-8), 48.26 (C-7), 31.19 (C-1′), 30.54 (CH_3-8), 26.89 (C-2′), 22.59 (C-3′), 14.34 (C-4′), 8.71 (CH_3-10).

Spiro[(4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-cyclopentane] (9). Yield 78%, mp 246-247°C, $C_{19}H_{20}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.05 (3H, t, J = 7,2, CH_3-3′), 1.60-2.15 (10H, CH_2-2′, CH_2-2′, CH_2-3′, CH_2-4′, CH_2-5′), 2.29 (3H, s, CH_3-10), 2.75 (2H, t, J = 7.5, CH_2-1′), 2.88 (2H, s, CH_2-7), 6.17 (1H, s, H-3), 8.07 (1H, s, H-5).

Spiro[(4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-cyclopentane] (10). Yield 68%, mp 168-169°C, $C_{20}H_{22}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.93 (3H, t, J = 7.2, CH_3-4′), 1.41 (2H, m, CH_2-3′), 1.50-2.00 (10H, CH_2-2′, CH_2-2′, CH_2-3′, CH_2-4′, CH_2-5′), 2.18 (3H, s, CH_3-10), 2.79 (2H, t, J = 7.6, CH_2-1′), 2.98 (2H, s, CH_2-7), 6.26 (1H, s, H-3), 7.98 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.63 (C-6), 160.54 (C-2), 160.00 (C-10a), 157.63 (C-4), 156.71 (C-9a), 121.25 (C-4a), 117.94 (C-5), 114.76 (C-5a), 111.93 (C-3), 110.06 (C-10), 91.79 (C-8), 46.57 (C-7), 37.60 (C-2″, C-5″), 31.09 (C-1′), 30.55 (C-3″, C-4″), 23.86 (C-2′), 22.28 (C-3′), 13.91 (C-4′), 8.21 (CH_3-10).

Spiro[(4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-cyclohexane] (11). Yield 73%, mp 197-199°C, $C_{20}H_{22}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, CH_3-3′), 1.23-2.15 (12H, CH_2-2′, CH_2-2″, CH_2-3″, CH_2-4″, CH_2-5″, CH_2-6″), 2.34 (3H, s, CH_3-10), 2.74 (2H, t, J = 7.6, CH_2-1′), 2.76 (2H, s, CH_2-7), 6.17 (1H, s, H-3), 8.05 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.61 (C-6), 159.98 (C-2), 159.73 (C-10a), 157.32 (C-4), 157.10 (C-9a), 121.03 (C-4a), 117.79 (C-5), 114.56 (C-5a), 113.68 (C-3), 111.98 (C-10), 81.91 (C-8), 48.10 (C-7), 34.76 (C-2″, C-6″), 33.35 (C-1′), 25.07 (C-4″), 21.69 (C-3″, C-5″), 21.59 (C-2′), 13.93 (C-3′), 8.25 (CH_3-10).

Spiro[(4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-cyclohexane] (12). Yield 82%, mp 200-201°C, $C_{21}H_{24}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.98 (3H, t, J = 7.2, CH_3-4′), 1.25-2.11 (14H, CH_2-2′, CH_2-3′, CH_2-2″, CH_2-3″, CH_2-4″, CH_2-5″, CH_2-6″), 2.36 (3H, s, CH_3-10), 2.74 (2H, s, CH_2-7), 2.76 (2H, t, J = 7.6, CH_2-1′), 6.17 (1H, s, H-3), 8.06 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.59 (C-6), 159.98 (C-2), 159.73 (C-10a), 157.61 (C-4), 157.10 (C-9a), 121.02 (C-4a), 117.80 (C-5), 114.57 (C-5a), 113.66 (C-3), 111.91 (C-10), 81.91 (C-8), 48.10 (C-7), 34.77 (C-2″, C-6″), 31.10 (C-1′), 30.56 (C-2′), 25.07 (C-4″), 22.29 (C-3′), 21.69 (C-3″, C-5″), 13.91 (C-4′), 8.25 (CH_3-10).

Spiro[(4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-(4-*t*-butylcyclohexane)] (13). Yield 81%, mp 231-232°C, $C_{24}H_{30}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.90 [9H, s, $(CH_3)_3$-4″], 1.06 (3H, t, J = 7.2, CH_3-3′), 1.37-2.20 (11H, CH_2-2′, CH_2-2″, CH_2-3″, H-4″, CH_2-5″, CH_2-6″), 2.36 (3H, s, CH_3-10), 2.72 (2H, s, CH_2-7), 2.74 (2H, t, J = 7.6, CH_2-1′), 6.17 (1H, s, H-3), 8.06 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.67 (C-6), 159.95 (C-2), 159.64 (C-10a), 157.30 (C-4), 157.10 (C-9a), 121.10 (C-4a), 117.89 (C-5), 114.51 (C-5a), 113.73 (C-3), 111.99 (C-10), 81.26 (C-8), 48.56 (C-7), 46.69 (C-4″), 34.81 (C-2″, C-6″), 33.35 (C-1′), 32.59 [C-$(CH_3)_3$], 27.77 [$(CH_3)_3$], 22.20 (C-3″, C-5″), 21.58 (C-2′), 13.92 (C-3′), 8.11 (CH_3-10).

Spiro[(4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-(4-*t*-butylcyclohexane)] (14). Yield 73%, mp 250-251°C, $C_{25}H_{32}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.90 [9H, s, $(CH_3)_3$-4″], 0.98 (3H, t, J = 7.2, CH_3-4′), 1.36-2.20 (13H, CH_2-2′, CH_2-3′, CH_2-2″, CH_2-3″, H-4″, CH_2-5″, CH_2-6″), 2.36 (3H, s, CH_3-10), 2.71 (2H, s, CH_2-7), 2.77 (2H, t, J = 7.6, CH_2-1′), 6.17 (1H, s, H-3), 8.06 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.61 (C-6), 159.98 (C-2), 159.68 (C-10a), 157.60 (C-4), 157.10 (C-9a), 121.11 (C-4a), 117.85 (C-5), 114.56 (C-5a), 113.73 (C-3), 111.93 (C-10), 81.29 (C-8), 48.59 (C-7), 46.70 (C-4″), 34.82 (C-2″, C-6″), 32.59 [C-$(CH_3)_3$], 31.10 (C-1′), 30.56 (C-2′), 27.79 [$(CH_3)_3$], 22.29 (C-3′), 22.21 (C-3″, C-5″), 13.92 (C-4′), 8.21 (CH_3-10).

Spiro[(4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-(3-methylcyclohexane)] (15). Yield 59%, mp 173-174°C, $C_{22}H_{26}O_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.86 (3H, d, J = 7.2, CH_3-3″), 0.99 (3H, t, J = 7.2, CH_3-3′), 1.05-2.00 (11H, CH_2-2′, CH_2-2″, CH_2-3″, H-3″, CH_2-5″, CH_2-6″), 2.20 and 2.24 (3H, 2s, CH_3-10), 2.77 (2H, t, J = 7.6, CH_2-1′), 2.82 and 3.00 (2H, s, CH_2-7), 6.25 (1H, s, H-3), 7.94 and 7.96 (1H, 2s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.86 (C-6), 159.99 (C-2), 159.36 (C-10a), 157.29 (C-4), 156.77 (C-9a), 121.01 (C-4a), 117.53 (C-5), 114.45 (C-5a), 113.47 (C-3), 111.98 (C-10), 83.60 and 82.19 (C-8), 48.61 and 42.86 (C-7), 33.97 and 33.74 (C-2″, C-6″), 33.41 (C-1′), 27.84 (C-4″), 22.75 (C-3″), 21.73 (CH_3-3″), 21.53 (C-2′, C-5″), 14.31 (C-3′), 8.63 (CH_3-10).

Spiro[(4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,1′-(3-methylcyclohexane)] (16). Yield 81%, mp 155-157°C, $C_{23}H_{28}O_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.91 (3H, d, J = 7.2, CH_3-3″), 0.98 (3H, t, J = 7.2, CH_3-4′), 1.20-2.15 (13H, CH_2-2′, CH_2-3′, CH_2-2″, CH_2-3″, H-3″, CH_2-5″, CH_2-6″), 2.30 and 2.35 (3H, 2s, CH_3-10), 2.71 and 2.90 (2H, s, CH_2-7), 2.77 (2H, t, J = 7.6, CH_2-1′), 6.17 (1H, s, H-3), 8.04 and 8.06 (1H, 2s, H-5).

^{13}C NMR spectrum (100MHz, DMSO-d_6, δ, ppm): 191.78 and 191.48 (C-6), 159.94 and 159.93 (C-2), 159.77 and 159.33 (C-10a), 157.48 and 156.79 (C-4), 156.73 (C-9a), 120.95 and 120.94 (C-4a), 117.49 and 117.29 (C-5), 114.44 (C-5a), 113.41 (C-3), 111.81 and 111.79 (C-10), 83.60 and 82.17 (C-8), 48.61 and 42.87 (C-7), 33.97 and 33.73 (C-2″, C-6″), 31.21 (C-1′), 30.56 (C-2′), 27.82 (C-4″), 22.56 (C-3′, C-3″), 21.53 (CH_3-3″, C-5″), 14.34 (C-4′), 8.59 (CH_3-10).

Spiro[(4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,4′-(1-acetylpiperidine)] (17). Yield 56%, mp 216-217°C, $C_{21}H_{23}NO_5$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, CH_3-3′), 1.58-1.80 (4H, m, CH_2-2′, H-3α″, H-5α″), 2.05-2.18 (2H, m, H-3β″, H-5β″), 2.13 (3H, s, CH_3CON-4″), 2.37 (3H, s, CH_3-10), 2.74 (2H, t, J = 7.6, CH_2-1′), 2.79 (2H, s, CH_2-7), 3.03 and 3.51 (2H, 2m, H-2α″, H-6α″), 3.69 and 4.47 (2H, 2m, H-3β″, H-5β″), 6.20 (1H, s, H-3), 8.08 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.30 (C-6), 168.85 (CO–CH_3), 159.93 (C-2), 159.01 (C-10a), 157.27 (C-4), 156.82 (C-9a), 121.11 (C-4a), 117.49 (C-5), 114.70 (C-5a), 113.75 (C-3), 112.16 (C-10), 80.15 (C-8), 47.34 (C-7), 42.09 (C-3″, C-5″), 34.61 (C-2″, C-6″), 33.40 (C-1′), 21.96 (C-2′), 21.75 (CO–CH_3), 14.30 (C-3′), 8.69 (CH_3-10).

Spiro[(4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2,6-dione)-8,4′-(1-acetylpiperidine)] (18). Yield 71%, mp 197-198°C, $C_{22}H_{25}NO_5$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.98 (3H, t, J = 7.2, CH_3-4′), 1.40-2.00 (8H, m, CH_2-2′, CH_2-3′, CH_2-3″, CH_2-5″), 2.03 (3H, s, CH_3CON-4″), 2.28 (3H, s, CH_3-10), 2.80 (2H, t, J = 7.6, CH_2-1′), 2.92 (2H, s, CH_2-7), 2.92 and 3.65 (2H, 2m, H-2α″, H-6α″), 3.72 and 4.21 (2H, 2m, H-3β″, H-5β″), 6.28 (1H, s, H-3), 7.99 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 191.56 (C-6), 168.81 (CO–CH_3), 159.98 (C-2), 159.72 (C-10a), 157.47 (C-4), 156.95 (C-9a), 121.10 (C-4a), 117.79 (C-5), 114.61 (C-5a), 113.71 (C-3), 111.96 (C-10), 80.95 (C-8), 47.34 (C-7), 42.11 (C-3″, C-5″), 34.65 (C-2″, C-6″), 31.10 (C-1′), 30.56 (C-2′), 22.29 (C-3′), 21.75 (CO–CH_3), 13.91 (C-4′), 8.25 (CH_3-10).

Spiro[(6-hydroxy-4-alkyl-7,8-dihydropyrano[3,2-*g*]chromen-2-one)-8,1′-cyclohexanes] 19 and 20. A solution of **12** or **13** (3 mmol) in CH_3OH (10 mL) was treated in portions with $NaBH_4$ (0.46 g, 12 mmol), held at room temperature and stirred for 2 h (end of reaction determined by TLC), poured into saturated NaCl solution (100 mL), and extracted with EtOAc (3 × 20 mL). The organic layer was dried over anhydrous $MgSO_4$. Solvent was removed in vacuo in a rotary evaporator. The solid was crystallized from CH_3OH.

Spiro[(6-hydroxy-4-propyl-7,8-dihydropyrano[3,2-*g*]chromen-2-one)-8,1′-(4-*t*-butylcyclohexane)] (19). Yield 71%, mp 194-195°C, $C_{24}H_{32}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.86 [9H, s, $(CH_3)_3$-4″], 0.98 (3H, t, J = 7.6, CH_3-3′), 1.00-2.05 (13H, CH_2-7, CH_2-2′, CH_2-2″, CH_2-3″, H-4″, CH_2-5″, CH_2-6″), 2.18 (3H, s, CH_3-10), 2.72 (2H, t, J = 7.6, CH_2-1′), 4.78 (1H, m, H-6), 5.63 (1H, d, J = 5.6, OH-6), 6.11 (1H, s, H-3), 7.74 (1H, s, H-5).

Spiro[(6-hydroxy-4-butyl-7,8-dihydropyrano[3,2-*g*]chromen-2-one)-8,1′-cyclohexane] (20). Yield 92%, mp 140-141°C, $C_{21}H_{26}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.93 (3H, t, J = 7.2, CH_3-4′), 1.25-2.15 (16H, CH_2-7, CH_2-2′, CH_2-3′, CH_2-2″, CH_2-3″, CH_2-4″, CH_2-5″, CH_2-6″), 2.19 (3H, s, CH_3-10), 2.74 (2H, t, J = 7.6, CH_2-1′), 4.76 (1H, m, H-6), 5.57 (1H, d, J = 5.6, OH-6), 6.11 (1H, s, H-3), 7.71 (1H, s, H-5).

Spiro[(4-alkylpyrano[3,2-*g*]chromen-2-one)-8,1′-cyclohexanes] 21 and 22. A solution of **19** or **20** (2 mmol) in dioxane (5 mL) was treated with HCl solution (5 mL, 4 M), held at room temperature and stirred for 4 h (end of reaction determined using TLC). Solvent was removed in vacuo in a rotary evaporator. The solid was crystallized from CH_3OH.

Spiro[(4-propylpyrano[3,2-*g*]chromen-2-one)-8,1′-(4-*t*-butylcyclohexane)] (21). Yield 84%, mp 168-169°C, $C_{24}H_{30}O_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.90 [9H, s, $(CH_3)_3$-4″], 0.99 (3H, t, J = 7.6, CH_3-3′), 1.10-2.00 (11H, CH_2-2′, CH_2-2″, CH_2-3″, H-4″, CH_2-5″, CH_2-6″), 2.21 (3H, s, CH_3-10), 2.71 (2H, t, J = 7.6, CH_2-1′), 5.73 (1H, d, J = 9.6, H-7), 6.12 (1H, s, H-3), 6.54 (1H, d, J = 9.6, H-6), 7.40 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 160.80 (C-2), 157.54 (C-10a), 153.80 (C-4), 152.99 (C-9a), 131.81 (C-7), 122.72 (C-6), 120.23 (C-4a), 11.78 (C-5), 113.16 (C-5a), 112.93 (C-3), 110.70 (C-10), 78.03 (C-8), 46.74 (C-4″), 36.27 (C-2″, C-6″), 33.48 (C-1′), 32.66 [C–$(CH_3)_3$], 27.80 [$(CH_3)_3$], 22.02 (C-3″, C-5″), 21.77 (C-2′), 13.97 (C-3′), 7.93 (CH_3-10).

Spiro[(4-butylpyrano[3,2-*g*]chromen-2-one)-8,1′-cyclohexane] (22). Yield 86%, mp 114-115°C, $C_{21}H_{24}O_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.95 (3H, t, J = 7.2, CH_3-4′), 1.20-1.90 (14H, CH_2-2′, CH_2-3′, CH_2-2″, CH_2-3″, CH_2-4″, CH_2-5″, CH_2-6″), 2.23 (3H, s, CH_3-10), 2.71 (2H, t, J = 7.5, CH_2-1′), 5.76 (1H, d, J = 9.6, H-7), 6.04 (1H, s, H-3), 6.48 (1H, d, J = 9.6, H-6), 7.29 (1H, s, H-5).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 160.78 (C-2), 157.80 (C-10a), 153.88 (C-4), 153.20 (C-9a), 131.43 (C-7), 122.48 (C-6), 120.24 (C-4a), 118.67 (C-5), 112.91 (C-5a), 112.86 (C-3), 110.51 (C-10), 78.43 (C-8), 36.60 (C-2″, C-6″), 31.41 (C-1′), 30.80 (C-2′), 25.25 (C-4″), 22.62 (C-3′), 21.61 (C-3″, C-5″), 14.38 (C-4′), 8.46 (CH_3-10).

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