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MODIFIED COUMARINS. 36. SYNTHESIS OF LINEAR AND ANGULAR DIHYDROPYRANOCOUMARINCARBOXYLIC ACIDS

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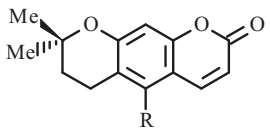
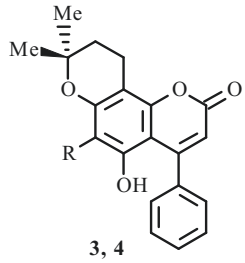
The syntheses of linear and angular dihydropyranocoumarincarboxylic acids, modified structural derivatives of dihydroxanthyletin and dihydroseselin, were described.

Keywords: coumarins, pyranocoumarins, dihydropyranocoumarins, dihydroxanthyletin, dihydroseselin.

The benzopyran-2-one moiety is a structural fragment of many important natural secondary metabolites [1] and compounds with potent pharmacological activity [2]. Pyranocoumarins are broadly distributed in nature and contain a 2,2-dimethylpyran ring annelated to benzopyran-2-one [1]. The majority of natural pyranocoumarins are derived from the linear pyranone xanthyletin. Pyranocoumarins also include coumarin derivatives containing an annelated 2,2-dimethyldihydropyran ring. Typical representatives of linear natural dihydropyranocoumarins are dihydroxanthyletin (**1**), which is produced by the plants *Cassia pumila* Lam. [3], *Seseli tortuosum* L.B.S. Eur. [4], *Ammi majus* [5], and *Ficus tsiangii* [6] and 5-methoxydihydroxanthyletin (dihydroxanthoxyletin) (**2**), which was isolated from *Glycyrrhiza uralensis* [7]. Angular dihydropyranocoumarins **3** and **4** were dihydroseselin derivatives and were isolated from leaves of *Marila pluricostata* [8].



1, 2



3, 4

1, 3: R = H; **2:** R = OMe; **4:** R = $C(O)CH_2CH_3$

It is also noteworthy that dihydropyranocoumarin derivatives inhibited acetylcholinesterase [9] and exhibited anticancer activity [10].

The goal of the present work was to functionalize the dihydropyranocoumarin system by adding a carboxylic acid to its structure.

2,2-Dimethylchroman-7-ol (**5**) that was required to synthesize the linear dihydropyranocoumarins was prepared by Kabbe condensation [11] of 2,4-dihydroxyacetophenone with acetone in the presence of pyrrolidine followed by Clemmensen reduction of the chromanone by Zn dust in HCl [12]. Pechmann condensation of chromanol **5** and the corresponding acetoacetic esters in the presence of conc. H_2SO_4 gave esters **6**–**8** of linear dihydropyranocoumaric acids. The splitting pattern of the aromatic protons in PMR spectra of **6**–**8** was simplified compared with that of the starting 2,2-dimethylchromane because proton H-6 did not couple with the dihydropyran ring. Protons H-5 and H-10 of the 8,8-dimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2-one system appeared as two 1H singlets at 7.44–7.57 and 6.70 ppm, respectively. The PMR spectrum of **8** also had a 1H singlet at 6.25 ppm for the dihydroxanthyletin H-3 proton. Furthermore, PMR spectra of **6**–**8** contained resonances characteristic of a 2,2-dimethyldihydropyran ring (a 6H singlet at 1.31 ppm and two triplets at 1.80 and 2.80 ppm with SSCC 6.4 Hz) and an ester.

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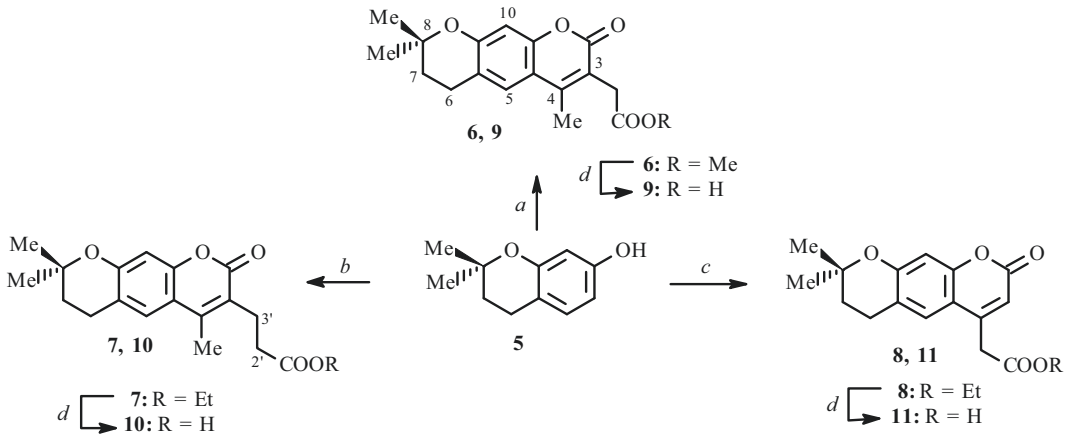
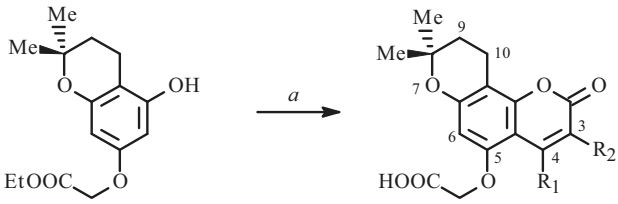


a. Dimethylacetylsuccinate, MeOH, H_2SO_4; *b*. diethyl 2-acetylglutarate, EtOH, H_2SO_4;
c. diethyl 1,3-diacetonedicarboxylate, EtOH, H_2SO_4; *d*. 1. NaOH (1 N), 2. H_2SO_4 (1 N)

Alkaline hydrolysis of **6**–**8** formed the corresponding linear dihydropyranocoumarincarboxylic acids **9**–**11**. Alkaline hydrolysis of **8** was associated with a side decarboxylation reaction that resulted in partial (at room temperature) or full (with heating) formation of 4,8,8-trimethyldihydropyrano[3,2-*g*]chromen-2-one. Therefore, alkaline hydrolysis of **8** was carried out with cooling (0–5°C). The ^{13}C NMR spectrum of **9** showed resonances at 174.92 and 160.29 ppm that were characteristic of a carboxylic acid and coumarin carbonyl [13], respectively, in addition to resonances of a linearly annelated 2,2-dimethyldihydropyran ring (74.98, 32.35, 26.67, 26.61, and 23.32 ppm).

Angular dihydropyranocoumarincarboxylic acids were synthesized from starting ethyl (5-hydroxy-2,2-dimethylchroman-7-yloxy)acetate (**12**), which was obtained via alkylation of 5,7-dihydroxy-2,2-dimethylchroman-4-one by ethylbromoacetate followed by Clemmensen reduction of the chromanone by Zn dust in HCl [14]. Pechmann condensation of **12** and the appropriate ethyl acetoacetates in the presence of conc. H_2SO_4 as a condensing agent and subsequent alkaline hydrolysis of the ester gave substituted [(8,8-dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic acids (**13**–**21**).

PMR spectra of **13**–**21** showed a simplified splitting pattern for the aromatic protons compared with starting 2,2-dimethylchromane because pyran proton H-6 did not couple. As a result, H-6 of 8,8-dimethyl-9,10-dihydropyrano[2,3-*f*]chromen-2-one was observed as a 1H singlet at 6.18–6.27 ppm. PMR spectra of **13**–**17** also exhibited 1H singlets at 5.86–5.96 ppm that belonged unambiguously to H-3 and were characteristic for a 4-substituted coumarin ring. Furthermore, PMR spectra of **13**–**21** contained resonances characteristic of a 2,2-dimethyldihydropyran ring, a hydroxyacetic group, and substituents of the synthesized coumarin ring. ^{13}C NMR spectra of **13** had resonances at 171.56 and 161.41 ppm that were characteristic of a carboxylic acid and coumarin carbonyl, respectively, in addition to resonances for an angular annelated 2,2-dimethyldihydropyran ring (75.96, 31.75, 26.56, 26.43, and 16.38 ppm) [8].

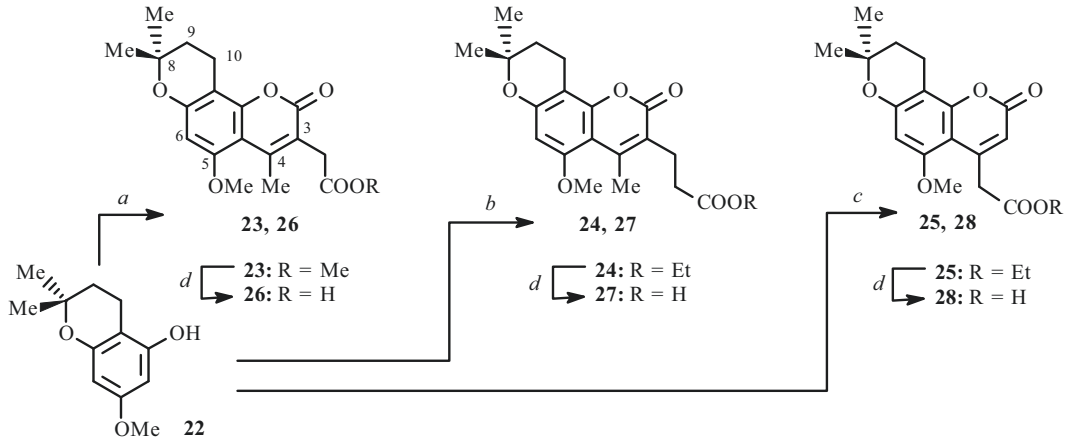


13: $R_1 = CH_3$, R_2 = H; **14:** $R_1 = CH_2CH_3$, R_2 = H; **15:** $R_1 = (CH_2)_2CH_3$, R_2 = H
16: $R_1 = (CH_2)_3CH_3$, R_2 = H; **17:** R_1 = Ph, R_2 = H; **18:** $R_1 = R_2 = CH_3$
19: $R_1 = CH_3$, $R_2 = CH_2Ph$; **20:** $R_1R_2 = (CH_2)_3$; **21:** $R_1R_2 = (CH_2)_4$

a. 1. R_1COCHR_2COOEt, H_2SO_4; 2. NaOH (1N) ; 3. H_2SO_4 (1N)

Angular dihydropyranocoumarincarboxylic acids were also synthesized using 7-methoxy-5-hydroxy-2,2-dimethylchromane (**22**) as starting material [12]. Pechmann condensation of chromanol **22** and the appropriate acetoacetic esters in the presence of conc. H_2SO_4 gave esters **23**–**25**, PMR spectra of the pyranocoumarins of which showed H-6 of the 8,8-dimethyl-9,10-dihydropyrano[2,3-*f*]chromen-2-one systems as 1H singlets at 6.32–6.34 ppm. The PMR spectrum of **25**

also had a 1H singlet at 6.11 ppm that was assigned unambiguously to H-3 and was a characteristic resonance for a 4-substituted coumarin ring. Furthermore, PMR spectra of **23**–**25** showed resonances characteristic of a 2,2-dimethyldihydropyran ring and an ester.



a. Dimethylacetylsuccinate, MeOH, H_2SO_4; *b*. diethyl 2-acetylglutarate, EtOH, H_2SO_4; *c*. diethyl 1,3-diacetonedicarboxylate, EtOH, H_2SO_4; *d*. 1. NaOH (1 N), 2. H_2SO_4 (1 N)

Alkaline hydrolysis of esters **23**–**25** gave the corresponding angular dihydropyranocoumarincarboxylic acids **26**–**28**. Alkaline hydrolysis of **25**, analogously to ester **8**, was also associated with a side decarboxylation reaction. Therefore, it was also hydrolyzed with cooling (0–5°C). The ^{13}C NMR spectrum of **26** had resonances at 175.06 and 161.53 ppm that were characteristic of carboxylic acid and coumarin carbonyl, respectively, in addition to resonances of an angular annelated 2,2-dimethyldihydropyran ring (75.98, 31.87, 26.69, 26.47, and 16.41 ppm).

The synthesized linear and angular dihydropyranocoumarincarboxylic acids are interesting as multi-faceted organic synthons because they act as an activated ester or carboxylic acid. This opens new possibilities for further modification of pyranocoumarin derivatives.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Merck 60 F254 plates using $CHCl_3$–MeOH (9:1 and 95:5) as eluents. Melting points were determined on a Kofler block. NMR spectra were measured on Varian VXR-300 and Mercury 400 spectrometers at 300 and 400 MHz, respectively, vs. TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

The syntheses of 2,2-dimethylchroman-7-ol (**5**), ethyl (5-hydroxy-2,2-dimethylchroman-7-yloxy)acetate (**12**), and 7-methoxy-5-hydroxy-2,2-dimethylchromane (**22**) were reported before [12, 14, 15].

4,8,8-Trimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromenes 6–8 and 5-Methoxy-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromenes 23–25. A cooled (0°C) solution of 2,2-dimethylchroman-7-ol (17.8 g, 0.1 mol, for **6**–**8**) or 7-methoxy-5-hydroxy-2,2-dimethylchromane (20.8 g, 0.1 mol, for **23**–**25**) and the appropriate acetoacetic ester (0.1 mol) in MeOH (30 mL) (for **6** and **23**) or EtOH (30 mL) (for **7**, **8**, **24**, and **25**) was stirred vigorously, cooled, treated dropwise with conc. H_2SO_4 (30 mL), stirred for 8 h, and left overnight at room temperature. The mixture was poured into ice water (500 mL). The resulting precipitate was filtered off and crystallized from aqueous MeOH (for **6** and **23**) or aqueous EtOH (for **7**, **8**, **24**, and **25**).

Methyl (4,8,8-Trimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-3-yl)acetate (6). $C_{18}H_{20}O_5$. Yield 74%, mp 172–173°C. ^1H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.57 (1H, s, H-5), 6.69 (1H, s, H-10), 3.64 (2H, s, CH_2-3), 3.61 (3H, s, $COOCH_3$), 2.82 (2H, t, J = 6.4, H-6), 2.35 (3H, s, CH_3-4), 1.81 (2H, t, J = 6.4, H-7), 1.31 (6H, s, CH_3-8).

Ethyl 3-(4,8,8-Trimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-3-yl)propionate (7). $C_{20}H_{24}O_5$. Yield 65%, mp 123–124°C. ^1H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.54 (1H, s, H-5), 6.68 (1H, s, H-10), 4.02 (2H, q, J = 7.2, H-1″), 2.81 (2H, t, J = 6.4, H-6), 2.76 (2H, t, J = 8.0, H-2′), 2.37 (2H, t, J = 8.0, H-3′), 2.35 (3H, s, CH_3-4), 1.81 (2H, t, J = 6.4, H-7), 1.31 (6H, s, CH_3-8), 1.15 (3H, t, J = 7.2, H-2″).

Ethyl (8,8-Dimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-4-yl)acetate (8). $C_{18}H_{20}O_5$. Yield 75%, mp 167–168°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.44 (1H, s, H-5), 6.71 (1H, s, H-10), 6.25 (1H, s, H-3), 4.12 (2H, q, J = 7.2, H-1′), 3.93 (2H, s, CH_2-4), 2.78 (2H, t, J = 6.4, H-6), 1.88 (2H, t, J = 6.4, H-7), 1.31 (6H, s, CH_3-8), 1.19 (3H, t, J = 7.2, H-2′).

Methyl (5-Methoxy-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-3-yl)acetate (23). $C_{19}H_{22}O_6$. Yield 78%, mp 183–184°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.32 (1H, s, H-6), 3.79 (3H, s, 5-OCH_3), 3.63 (2H, s, CH_2-3), 3.62 (3H, s, $COOCH_3$), 2.63 (2H, t, J = 6.4, H-10), 2.45 (3H, s, CH_3-4), 1.78 (2H, t, J = 6.4, H-9), 1.31 (6H, s, CH_3-8).

Ethyl 3-(5-Methoxy-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-3-yl)propionate (24). $C_{21}H_{26}O_6$. Yield 64%, mp 130–131°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.33 (1H, s, H-6), 4.04 (2H, q, J = 7.2, H-1″), 3.79 (3H, s, 5-OCH_3), 2.76 (2H, t, J = 8.0, H-2′), 2.64 (2H, t, J = 6.4, H-10), 2.47 (3H, s, CH_3-4), 2.40 (2H, t, J = 8.0, H-3′), 1.79 (2H, t, J = 6.4, H-9), 1.29 (6H, s, CH_3-8), 1.16 (3H, t, J = 7.2, H-2″).

Ethyl (5-Methoxy-8,8-dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-4-yl)acetate (25). $C_{19}H_{22}O_6$. Yield 73%, mp 172–173°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.34 (1H, s, H-6), 6.11 (1H, s, H-3), 4.07 (2H, q, J = 7.2, H-1′), 3.83 (2H, s, CH_2-4), 3.71 (3H, s, 5-OCH_3), 2.68 (2H, t, J = 6.4, H-10), 1.80 (2H, t, J = 6.4, H-9), 1.31 (6H, s, CH_3-8), 1.17 (3H, t, J = 7.2, H-2′).

Dihydropyranocoumarincarboxylic Acids 9, 10, 26, and 27. A solution of ester **6**, **7**, **23**, or **24** (50 mmol) in *i*-PrOH (50 mL) was treated with NaOH solution (150 mmol, 150 mL, 1 M), stirred vigorously, and heated for 1 h (course of reaction monitored by TLC). When the reaction was complete, the mixture was cooled, poured into water (200 mL) and acidified to pH 5–6. The resulting precipitate was filtered off and crystallized from aqueous *i*-PrOH.

(4,8,8-Trimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-3-yl)acetic Acid (9). $C_{17}H_{18}O_5$. Yield 88%, mp 181–182°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.27 (1H, br.s, COOH), 7.56 (1H, s, H-5), 6.69 (1H, s, H-10), 3.54 (2H, s, CH_2-3), 2.82 (2H, t, J = 6.4, H-6), 2.33 (3H, s, CH_3-4), 1.81 (2H, t, J = 6.4, H-7), 1.31 (6H, s, CH_3-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 174.92, 160.29, 158.41, 150.46, 149.15, 127.91, 122.06, 118.35, 114.65, 101.49, 74.98, 32.90, 32.35, 26.67, 26.61, 23.32, 15.24.

3-(4,8,8-Trimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-3-yl)propionic Acid (10). $C_{18}H_{20}O_5$. Yield 81%, mp 151–152°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.16 (1H, br.s, COOH), 7.51 (1H, s, H-5), 6.69 (1H, s, H-10), 2.73–2.81 (4H, m, H-2′, 6), 2.37 (3H, s, CH_3-4), 2.37 (2H, t, J = 8.0, H-3′), 1.81 (2H, t, J = 6.4, H-7), 1.30 (6H, s, CH_3-8).

(**5-Methoxy-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-3-yl)acetic Acid (26).** $C_{18}H_{20}O_6$. Yield 83%, mp 195–196°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.25 (1H, br.s, COOH), 6.30 (1H, s, H-6), 3.81 (3H, s, 5-OCH_3), 3.61 (2H, s, CH_2-3), 2.64 (2H, t, J = 6.4, H-10), 2.47 (3H, s, CH_3-4), 1.78 (2H, t, J = 6.4, H-9), 1.31 (6H, s, CH_3-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 175.06, 161.53, 160.13, 159.84, 154.57, 149.22, 121.16, 102.73, 99.29, 88.73, 75.98, 56.41, 32.77, 31.87, 26.69, 26.47, 16.41, 16.19.

(**5-Methoxy-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-3-yl)proprionic Acid (27).** $C_{19}H_{22}O_6$. Yield 75%, mp 149–150°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.17 (1H, br.s, COOH), 6.33 (1H, s, H-6), 3.80 (3H, s, 5-OCH_3), 2.74 (2H, t, J = 8.0, H-2′), 2.65 (2H, t, J = 6.4, H-10), 2.48 (3H, s, CH_3-4), 2.33 (2H, t, J = 8.0, H-3′), 1.79 (2H, t, J = 6.4, H-9), 1.30 (6H, s, CH_3-8).

Dihydropyranocoumarincarboxylic Acids 11 and 28. A solution of NaOH (150 mmol, 150 mL, 1 M) was cooled to 0–5°C, treated with a solution of ester **8** or **25** in *i*-PrOH (50 mL), held at 0–5°C, and stirred vigorously for 1 h (course of reaction monitored by TLC). When the reaction was finished, the mixture was cooled (0–5°C) and acidified to pH 5–6. The resulting precipitate was filtered off and crystallized from aqueous *i*-PrOH.

(8,8-Dimethyl-2-oxo-7,8-dihydropyrano[3,2-*g*]chromen-4-yl)acetic Acid (11). $C_{16}H_{16}O_5$. Yield 72%, mp 150°C (dec.).^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.20 (1H, br.s, COOH), 7.41 (1H, s, H-5), 6.70 (1H, s, H-10), 6.23 (1H, s, H-3), 3.85 (2H, s, CH_2-4), 2.77 (2H, t, J = 6.4, H-6), 1.86 (2H, t, J = 6.4, H-7), 1.30 (6H, s, CH_3-8).

(5-Methoxy-8,8-dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-4-yl)acetic Acid (28). $C_{17}H_{18}O_6$. Yield 68%, mp 165°C (dec.). ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.24 (1H, br.s, COOH), 6.29 (1H, s, H-6), 6.00 (1H, s, H-3), 3.75 (3H, s, 5-OCH_3), 3.74 (2H, s, CH_2-4), 2.72 (2H, t, J = 6.4, H-10), 1.82 (2H, t, J = 6.4, H-9), 1.33 (6H, s, CH_3-8).

[(8,8-Dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acids 13–21. A solution of chromanol **12** (21.02 g, 75 mmol) and the appropriate ethyl acetoacetate (75 mmol) in EtOH (20 mL) was cooled (0°C), stirred vigorously,

treated dropwise with conc. H_2SO_4 (50 mL), stirred for 8 h, left overnight at room temperature, and poured into ice water (500 mL). The resulting oily precipitate was dissolved in *i*-PrOH (100 mL), diluted with NaOH solution (9.6 g, 240 mmol) in H_2O (100 mL), stirred vigorously, and heated at 90–100°C for 2 h (course of reaction monitored by TLC). When the reaction was finished, the mixture was cooled to room temperature and acidified to pH 4. The resulting precipitate was filtered off and crystallized from aqueous EtOH.

[(4,8,8-Trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (13). $C_{17}H_{18}O_6$. Yield 76%, mp 192–193°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.02 (1H, br.s, COOH), 6.22 (1H, s, H-6), 5.91 (1H, s, H-3), 4.68 (2H, s, 5-OCH_2), 2.66 (2H, t, J = 6.8, H-10), 2.57 (3H, s, CH_3-4), 1.81 (2H, t, J = 6.8, H-9), 1.32 (6H, s, CH_3-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 171.56, 161.41, 160.12, 154.81, 154.52, 154.17, 111.67, 102.95, 99.63, 87.88, 75.96, 68.35, 31.75, 26.56, 25.43, 20.69, 16.38.

[(4-Ethyl-8,8-dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (14). $C_{18}H_{20}O_6$. Yield 72%, mp 185–186°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.95 (1H, br.s, COOH), 6.21 (1H, s, H-6), 5.91 (1H, s, H-3), 4.69 (2H, s, 5-OCH_2), 3.02 (2H, q, J = 7.2, H-1′), 2.71 (2H, t, J = 6.6, H-10), 1.82 (2H, t, J = 6.6, H-9), 1.33 (6H, s, CH_3-8), 1.19 (3H, t, J = 7.2, H-2′).

[(8,8-Dimethyl-2-oxo-4-propyl-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (15). $C_{19}H_{22}O_6$. Yield 65%, mp 174–175°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.98 (1H, br.s, COOH), 6.21 (1H, s, H-6), 5.88 (1H, s, H-3), 4.68 (2H, s, 5-OCH_2), 2.95 (2H, q, J = 7.2, H-1′), 2.71 (2H, t, J = 6.6, H-10), 1.82 (2H, t, J = 6.6, H-9), 1.53–1.66 (2H, m, H-2′), 1.33 (6H, s, CH_3-8), 0.97 (3H, t, J = 7.2, H-3′).

[(4-Butyl-8,8-dimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (16). $C_{20}H_{24}O_6$. Yield 68%, mp 162–163°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.09 (1H, br.s, COOH), 6.27 (1H, s, H-6), 5.96 (1H, s, H-3), 4.76 (2H, s, 5-OCH_2), 2.95 (2H, q, J = 7.6, H-1′), 2.67 (2H, t, J = 6.4, H-10), 1.79 (2H, t, J = 6.4, H-9), 1.50–1.55 (2H, m, H-2′), 1.30–1.39 (2H, m, H-3′), 1.30 (6H, s, CH_3-8), 0.87 (3H, t, J = 7.2, H-4′).

[(8,8-Dimethyl-2-oxo-4-phenyl-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (17). $C_{22}H_{20}O_6$. Yield 78%, mp 184–186°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.93 (1H, br.s, COOH), 7.29–7.36 (5H, m, Ph-4), 6.18 (1H, s, H-6), 5.86 (1H, s, H-3), 4.19 (2H, s, 5-OCH_2), 2.78 (2H, t, J = 6.6, H-10), 1.86 (2H, t, J = 6.6, H-9), 1.35 (6H, s, CH_3-8).

[(3,4,8,8-Tetramethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (18). $C_{18}H_{20}O_6$. Yield 81%, mp 195–196°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.06 (1H, br.s, COOH), 6.20 (1H, s, H-6), 4.67 (2H, s, 5-OCH_2), 2.70 (2H, t, J = 6.6, H-10), 2.59 (3H, s, CH_3-4), 2.06 (3H, s, CH_3-3), 1.81 (2H, t, J = 6.6, H-9), 1.32 (6H, s, CH_3-8).

[(3-Benzyl-4,8,8-trimethyl-2-oxo-9,10-dihydropyrano[2,3-*f*]chromen-5-yl)oxy]acetic Acid (19). $C_{24}H_{24}O_6$. Yield 65%, mp 159–160°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.90 (1H, br.s, COOH), 7.13–7.27 (5H, m, Ph), 6.27 (1H, s, H-6), 4.72 (2H, s, 5-OCH_2), 3.93 (2H, s, CH_2-3), 2.67 (2H, t, J = 7.2, H-10), 2.57 (3H, s, CH_3-4), 1.79 (2H, t, J = 7.2, H-9), 1.29 (6H, s, CH_3-8).

[(2,2-Dimethyl-6-oxo-3,4,6,7,8,9-hexahydrocyclopenta[*c*]pyrano[2,3-*h*]chromen-10-yl)oxy]acetic Acid (20). $C_{19}H_{20}O_6$. Yield 67%, mp 193–194°C. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.01 (1H, br.s, COOH), 6.19 (1H, s, H-11), 4.64 (2H, s, 10-OCH_2), 3.31 (2H, t, J = 7.2, H-7), 2.71 (2H, t, J = 7.2, H-2), 2.66 (2H, t, J = 7.2, H-9), 1.99–2.10 (2H, m, H-8), 1.81 (2H, t, J = 7.2, H-3), 1.32 (6H, s, CH_3-2).

[(2,2-Dimethyl-6-oxo-3,4,7,8,9,10-hexahydrobenzo[*c*]pyrano[2,3-*h*]chromen-11-yl)oxy]acetic Acid (21). $C_{20}H_{22}O_6$. Yield 76%, mp 181–182°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.09 (1H, br.s, COOH), 6.23 (1H, s, H-12), 4.74 (2H, s, 11-OCH_2), 3.07 (2H, m, H-7), 2.66 (2H, t, J = 7.2, H-3), 2.37 (2H, m, H-10), 1.78 (2H, t, J = 7.2, H-4), 1.64 (4H, m, H-8, 9), 1.28 (6H, s, CH_3-2).

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