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Synthesis of Modified Psoralen Analogues

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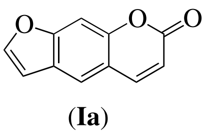
Abstract—Substituted 3-(5-methyl-7-oxofuro[3,2-*g*]chromen-6-yl)propanoic acids analogous to psoralen were synthesized by linear annulation of a furan moiety to the coumarin system.

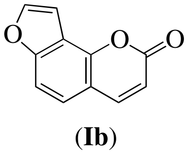
Key words: coumarins, furocoumarins, synthesis, psoralen

INTRODUCTION

One of the alternative ways for the design of new biologically active compounds is the synthesis of analogues of natural bioregulators, which can particularly be achieved by the formation of several pharmacophore centers in their molecules. The advantage of such compounds consists in that their structures are close to the biochemical structures of live organism and cause a considerably less number of side effects. Among the compounds exhibiting biological activities, an important place belongs to derivatives of heterocyclic systems. Especially interesting are the coumarin derivatives, since coumarin is the basis of a great variety of natural and synthetic biologically active compounds.

Furocoumarins are an important group of natural compounds isolated mainly from the higher plants belonging to the families of Rutaceae, Umbelliferae, Leguminosae, and Moraceae [1]. These compounds are the derivatives of psoralen (**Ia**), a linear furocoumarin, and its angular isomers angelicin (**Ib**) and allopsoralen (**Ic**).


(**Ia**)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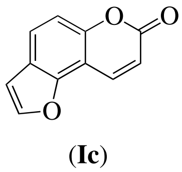
(**Ic**)

Natural furocoumarins and their synthetic analogues exhibit various biological activities. In particular, they have a photosensitizing action and can enhance the sensitivity of human and animal organisms to sun rays. In medicine, furocoumarins are used for the treatment of vitiligo (leukodermia), alopecia areata, and a number of other skin diseases [2]. 8-Methoxypsoralen is used for the treatment T-cellular lymphoma, one of the kinds of blood cancer [3]. Spasmolytic and coronary vessel dilatory properties are characteristic of the psoralen and angelicin derivatives, due to which they exhibit a papaverin-like mechanism of action on the muscles of viscera and coronary vessels [4]. Among furocoumarins, there are also found the compounds with anticonvulsive, sedative, hypotensive, contraceptive, estrogenic, bactericide, fungicide [1], antitumor [5], antihepatitive [6], antiinfectious [7], and anti-HIV activities [8, 9].

RESULTS AND DISCUSSION

The goal of this work was the modification of psoralen core by the introduction into it of an additional pharmacophore center, carboxyl group and substituents in positions 2, 3, and 9 of the furo[3,2-*g*]chromen-7-one cycle.

Numerous approaches to the formation of psoralen system are known [10–13]. Of them, we chose the MacLeod method [14, 15] that is based on the cyclization of 7-(2-oxoethyl)coumarins in alkaline medium, because it leads exclusively to linear furocoumarins of the psoralen type.

The Pechmann condensations of diethyl 2-acetylglutarate and resorcinol and 2-methylresorcinol in the presence of dry hydrogen chloride as a catalyst at 0°C [16] were used for the preparation of ethyl 3-(7-hydroxy-4-methyl-2-oxochromen-3-yl)propanoate (**II**) and ethyl 3-(7-hydroxy-4,8-dimethyl-2-oxochromen-3-yl)propanoate (**III**), necessary for the further conversions.

The Williamson reaction of 7-hydroxycoumarins (**II**) and ((**III**) with α-halogenoketones in the presence of potash led to the formation of corresponding substituted oxoethers (**IV**)–(**XXV**) in high yields (71–92%). The alkylating reagents in this reaction were bromoacetone for (**IV**) and (**V**), 1-chloropinacolon for (**VI**) and (**VII**), 3-chlorobutan-2-one for (**VIII**) and (**IX**), 2-bromopropiophenone for (**X**) and (**XI**), phenacyl bromide

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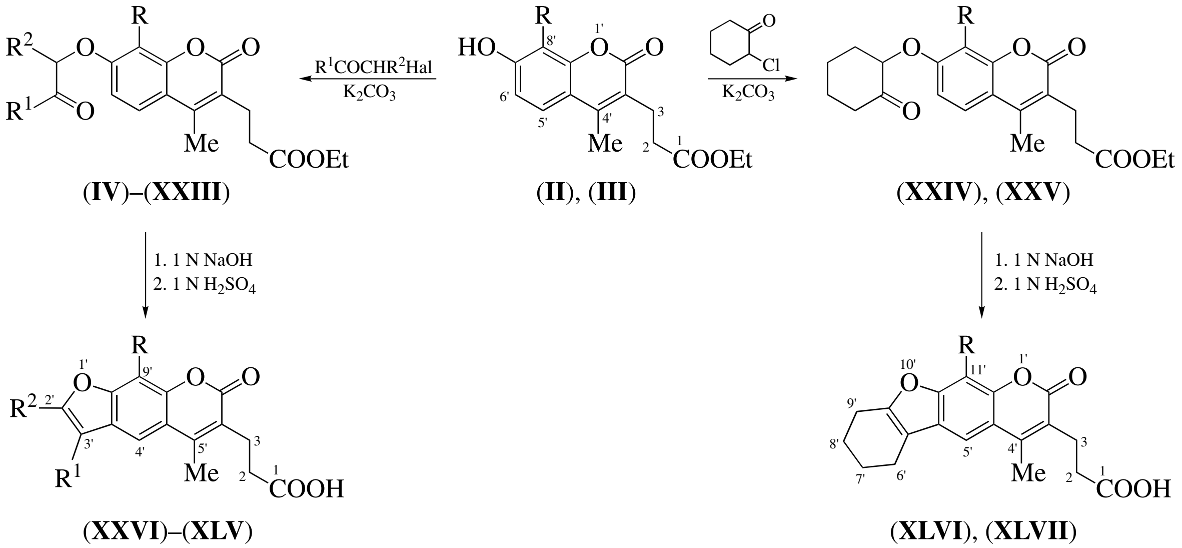

Compound	R	R^1	R^2	Compound	R	R^1
(**II**), (**XXIV**), (**XLVI**)	H	–	–	(**XIII**), (**XXXV**)	CH$_3$	Ph
(**III**), (**XXV**), **XLVII**)	CH$_3$	–	–	(**XIV**), (**XXXVI**)	H	4-F-Ph
(**IV**), (**XXVI**)	H	CH$_3$	H	(**XV**), (**XXXVII**)	CH$_3$	4-F-Ph
(**V**), (**XXVII**)	CH$_3$	CH$_3$	H	(**XVI**), (**XXXVIII**)	H	4-Cl-Ph
(**VI**), (**XXVIII**)	H	(CH$_3$)$_3$C	H	(**XVII**), (**XXXIX**)	CH$_3$	4-Cl-Ph
(**VII**), (**XXIX**)	CH$_3$	(CH$_3$)$_3$C	H	(**XVIII**), (**XL**)	H	4-Br-Ph
(**VIII**), (**XXX**)	H	CH$_3$	CH$_3$	(**XIX**), (**XLI**)	CH$_3$	4-Br-Ph
(**IX**), (**XXXI**)	CH$_3$	CH$_3$	CH$_3$	(**XX**), (**XLII**)	H	4-MeO-Ph
(**X**), (**XXXII**)	H	Ph	CH$_3$	(**XXI**), (**XLIII**)	CH$_3$	4-MeO-Ph
(**XI**), (**XXXIII**)	CH$_3$	Ph	CH$_3$	(**XXII**), (**XLIV**)	H	3-MeO-Ph
(**XII**), (**XXXIV**)	H	Ph	–	(**XXIII**), (**XLV**)	CH$_3$	3-MeO-Ph

Scheme

for (**XII**) and (**XIII**), 2-chloro-4'-fluoroacetophenone for (**XIV**) and (**XV**)**,** 2,4-dichloroacetophenone for (**XVI**) and (**XVII**), 4-bromophenacyl bromide for (**XVIII**) and (**XIX**), 4-methoxyphenacyl bromide for (**XX**) and (**XXI**), 2-bromo-3'-methoxyacetophenone for (**XXII**) and (**XXIII**), and 2-chlorocyclohexanone for (**XXIV**) and (**XXV**). The signals characteristic of the coumarin cycle and alkyl type substituents were registered in the ^{1}H NMR spectra of (**IV**)–(**XXV**) synthesized (Table 1). Their UV spectra exhibited the main intensive maximum at 202–206 nm, a maximum or an inflection at 219–224 nm, and a long-wave intensive maximum at 318–324 nm. The 7-(2-oxo-2-phenylethoxy)coumarins (**X**)–(**XXIII**) had an additional maximum at 243–284 nm, which was less intensive than the long-wave band. The IR spectra of oxoethers (**IV**)–(**XXV**) were characterized by two bands at 1694–1734 cm^{-1} assigned to the valent oscillations of the C=O bond of coumarin cycle and the carbonyl group of alkoxyl residue.

The ketones (**IV**)–(**XXV**) were cyclized in high yields (71–94%) into the correspondingly substituted 3-(5-methyl-7-oxofuro[3,2-*g*]chromen-6-yl)propanoic acids (**XXVI**)–(**XLVII**) at heating with 1 N NaOH (with the simultaneous saponification of ester grouping) and the subsequent acidolysis of the reaction mixture. The final construction of furan ring in the positions 6, 7 of coumarin system was confirmed by spectral data. The ^{1}H NMR spectra of the synthesized furocoumarins (**XXVI**)–(**XLV**) demonstrated a simplified pattern of spin–spin coupling in the area of aromatic protons in comparison with the starting ketones

Table 1. The ^{1}H NMR spectral data of ethyl 3-[4'-methyl-2'-oxo-7'-(2'-oxopropoxy)chromen-3'-yl]propanoates (**IV**)–(**XXV**)

Compound	Proton signal, δ, ppm, spin coupling constants, *J*, Hz								
	H2 2 H, t, *J* 7.2	H3 2 H, t, *J* 7.2	$CO_2CH_2C\underline{H}_3$ 3 H, t, *J* 7.2	$CO_2C\underline{H}_2CH_3$ 2 H, q	$C4'–C\underline{H}_3$ 3 H, s	H5' 1 H, d, *J* 8.4	H6'	C8'–R	$C7'–OCHR^2COR^1$
(**IV**)	2.47	2.81	1.17	4.03	2.40	7.72	6.95 (1 H, dd, *J* 2.4, 8.4)	6.93 (1 H, d, *J* 2.4)	2.17 (3 H, s, $COCH_3$), 4.97 (2 H, s, CH_2)
(**V**)	2.46	2.81	1.19	4.06	2.39	7.50	6.86 (1 H, d, *J* 8.7)	2.27 (3 H, s, CH_3)	2.19 (3 H, s, $COCH_3$), 4.90 (2 H, s, CH_2)
(**VI**)	2.46	2.81	1.17	4.04	2.40	7.63	6.90 (1 H, dd, *J* 2.4, 8.4)	6.86 (1 H, d, *J* 2.4)	1.20 (9 H, s, $COC(CH_3)_3$), 5.18 (2 H, s, CH_2)
(**VII**)	2.46	2.79	1.19	4.04	2.39	7.49	6.81 (1 H, d, *J* 8.7)	2.27 (3 H, s, CH_3)	1.21 (9 H, s, $COC(CH_3)_3$), 5.23 (2 H, s, $H1'''CH_2$)
(**VIII**)	2.47	2.78	1.19	4.06	2.40	7.66	6.88 (1 H, dd, *J* 2.4, 8.4)	6.83 (1 H, d, *J* 2.4)	1.48 (3 H, d, *J* 7.2, $CHC\underline{H}_3$), 2.18 (3 H, s, $COCH_3$), 5.04 (1 H, q, $C\underline{H}CH_3$)
(**IX**)	2.46	2.81	1.18	4.06	2.38	7.51	6.80 (1 H, d, *J* 8.7)	2.27 (3 H, c, CH_3)	1.47 (3 H, d, *J* 7.2, $CHC\underline{H}_3$), 2.18 (3 H, s, $COCH_3$), 5.06 (1 H, q, $C\underline{H}CH_3$)
(**X**)	2.47	2.78	1.19	4.05	2.40	7.68	6.88 (1 H, dd, *J* 2.4, *J* 8.4)	6.83 (1 H, d, *J* 2.4)	1.63 (3 H, d, *J* 7.2, $CHC\underline{H}_3$), 6.05 (1 H, q, $C\underline{H}CH'_3$), 7.54 (2 H, t, *J* 7.6, H3, H5–Ph), 7.64 (1 H, t, *J* 7.6, H4–Ph), 8.04 (2 H, d, *J* 7.6, H2, H6-Ph)
(**XI**)	2.45	2.80	1.18	4.03	2.35	7.48	6.81 (1 H, d, *J* 8.7)	2.27 (3 H, s, CH_3)	1.63 (3 H, d, *J* 7.2, $CHC\underline{H}_3$), 6.07 (1 H, q, $C\underline{H}CH_3$), 7.54 (2 H, t, *J* 7.5, H3, H5–Ph), 7.66 (1 H, t, *J* 7.5, H4–Ph), 8.04 (2 H, d, *J* 7.5, H2, H6–Ph)
(**XII**)	2.45	2.81	1.19	4.04	2.41	7.66	6.97 (1 H, dd, *J* 2.4, 8.4)	7.00 (1 H, d, *J* 2.4)	5.66 (2 H, s, CH_2), 7.54 (2 H, t, *J* 7.5, H3, H5–Ph), 7.66 (1 H, m, H4-Ph), 8.03 (2 H, d, *J* 7.5, H2, H6–Ph)
(**XIII**)	2.46	2.82	1.20	4.06	2.39	7.49	6.93 (1 H, d, *J* 8.7)	2.30 (3 H, s, CH_3)	5.68 (2 H, s, CH_2), 7.55 (2 H, t, *J* 7.5, H3, H5–Ph), 7.68 (1 H, t, *J* 7.5, H4–Ph), 8.01 (2 H, d, *J* 7.5, H2, H6–Ph)
(**XIV**)	2.48	2.81	1.19	4.04	2.41	7.66	6.97 (1 H, dd, *J* 2.4, 8.4)	7.01 (1 H, d, *J* 2.4)	5.63 (2 H, s, CH_2), 7.34 (2 H, t, *J* 7.5, H3, H5–Ph), 8.11 (2 H, m, H2, H6–Ph)

Table 1. (Contd.)

Compound	Proton signal, δ, ppm, spin coupling constants, *J*, Hz								
	H2 2 H, t, *J* 7.2	H3 2 H, t, *J* 7.2	$CO_2CH_2C\underline{H}_3$ 3 H, t, *J* 7.2	$CO_2C\underline{H}_2CH_3$ 2 H, q	C4'–$C\underline{H}_3$ 3 H, s	H5' 1 H, d, *J* 8.4	H6'	C8'–R	C7'–$OCHR^2COR^1$
(**XV**)	2.48	2.81	1.19	4.04	2.39	7.49	6.94 (1 H, d, *J* 8.7)	2.30 (3 H, s, CH_3)	5.66 (2 H, s, CH_2), 7.34 (2 H, t, *J* 7.5, H3, H5–Ph), 8.10 (2 H, m, H2'''', H6'''')
(**XVI**)	2.47	2.81	1.19	4.06	2.41	7.65	6.98 (1 H, dd, *J* 2.4, 8.4)	7.01 (1 H, d, *J* 2.4)	5.63 (2 H, s, 1'''CH_2), 7.59 (2 H, d, *J* 8.4, H3, H5–Ph), 8.03 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XVII**)	2.48	2.82	1.20	4.04	2.40	7.49	6.95 (1 H, d, *J* 8.7)	2.30 (3 H, s, CH_3)	5.66 (2 H, s, CH_2), 7.59 (2 H, d, *J* 8.4, H3, H5–Ph), 8.03 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XVIII**)	2.47	2.81	1.19	4.06	2.39	7.65	6.96 (1 H, dd, *J* 2.4, 8.4)	7.02 (1 H, d, *J* 2.4)	5.63 (2 H, s, CH_2), 7.74 (2 H, d, *J* 8.4, H3, H5–Ph), 7.96 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XIX**)	2.47	2.82	1.19	4.04	2.39	7.49	6.95 (1 H, d, *J* 8.7)	2.30 (3 H, s, CH_3)	5.65 (2 H, s, CH_2), 7.74 (2 H, d, *J* 8.4, H3, H5–Ph), 7.95 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XX**)	2.47	2.81	1.19	4.06	2.41	7.64	6.97 (1 H, dd, *J* 2.4, 8.4)	7.00 (1 H, d, *J* 2.4)	3.87 (3 H, s, $s\underline{H}_3OPh$), 5.57 (2 H, s, CH_2), 7.08 (2 H, d, *J* 8.4, H3, H5–Ph), 7.98 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XXI**)	2.48	2.81	1.19	4.06	2.38	7.49	6.90 (1 H, d, *J* 8.7)	2.29 (3 H, s, CH_3)	3.87 (3 H, s, $C\underline{H}_3OPh$), 5.60 (2 H, s, CH_2), 7.05 (2 H, d, *J* 8.4, H3, H5–Ph), 7.98 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XXII**)	2.47	2.81	1.19	4.06	2.41	7.65	6.98 (1 H, dd, *J* 2.4, 8.4)	7.01 (1 H, d, *J* 2.4)	3.85 (3 H, s, $C\underline{H}_3OPh$), 5.64 (2 H, s, CH_2), 7.22 (1 H, dd, *J* 2.7, 8.4, H4–Ph), 7.46 (1 H, t, *J* 8.4, H5–Ph), 7.51 (1 H, dd, *J* 2.7, 2.7, H2–Ph), 7.62 (1 H, d, *J* 8.4, H6–Ph)
(**XXIII**)	2.47	2.82	1.20	4.04	2.39	7.50	6.93 (1 H, d, *J* 8.7)	2.31 (3 H, s, CH_3)	3.85 (3 H, s, $C\underline{H}_3OPh$), 5.65 (2 H, s, CH_2), 7.22 (1 H, dd, *J* 2.7, 8.4, H4–Ph), 7.46 (1 H, t, *J* 8.4, H5–Ph), 7.51 (1 H, dd, *J* 2.7, 2.7, H2–Ph), 7.60 (1 H, d, *J* 8.4, H6–Ph)
(**XXIV**)	2.45	2.80	1.19	4.03	2.40	7.63	6.86 (1 H, dd, *J* 2.4, 8.4)	6.84 (1 H, d, *J* 2.4)	1.62–2.69 (8 H, m, 4CH_2), 5.13 (1 H, m, OCH)
(**XXV**)	2.46	2.81	1.19	4.04	2.39	7.44	6.81 (1 H, d, *J* 8.7)	2.24 (3 H, s, CH_3)	1.67–2.60 (8 H, m, 4CH_2), 5.14 (1 H, m, OCH)

due to the exclusion of coupling with H6 of coumarin cycle. In the case of 9-methylfurocoumarins, H4' was observed as a singlet at 7.54–7.94 ppm. The furocoumarins devoid of methyl group in position 9 exhibit the resonances of H4' and H9' in the form of singlets at δ 7.72–8.11 and 7.35–7.64 ppm. In addition, furocoumarins (**XXVI**)–(**XXIX**) and (**XXXIV**)–(**XLV**) containing no substituents in position 2' exhibit one-proton singlet of H2', which also indicates the formation of furocoumarin cycle. The presence of alkyl substituents in position 3' of (**XXVI**)–(**XXIX**) leads to the resonance of H2' at 7.68–7.84 ppm, whereas 3'-aryl substituents in the case of (**XXXIV**)–(**XLV**) defines the a downfield shift of H2' (8.22–8.40 ppm). The proton of free carboxyl group resonates as a broadened singlet at 12.05–12.13 ppm.

The UV spectra of the furocoumarins synthesized contain three intensive absorption maxima at 202–217, 245–255, and 291–308 nm. Note that the absorption band at 245–255 nm is more intensive than the long-wave band, which also confirms the formation of furan cycle [17].

EXPERIMENTAL

Analytical TLC was carried out on precoated Merck 60 F254 plates in 9 :1 and 95 : 5 chloroform–methanol systems. Melting points were determined on a Koffler apparatus. IR spectra were measured on a Nicolet FTIR Nexus 475 spectrometer in KBr pellets. UV spectra were registered on a Specord M40 spectrophotometer. ^{1}H NMR spectra were obtained on a Varian VXR-300 spectrometer in DMSO-d_6 at 300 MHz with Me_4Si as an internal standard. Chemical shifts are given in δ scale in ppm, and spin–spin coupling constants *J* in Hz.

Ethyl 3-(7'-hydroxy-4'-methyl-2'-oxochromen-3'-yl)propanoate (II). Dry HCl was blown through a cooled (0°C) solution of resorcinol (11.0 g, 0.1 mol) and diethyl 2-acetylglutarate (24.66 ml, 0.1 mol) in absolute ethanol (50 ml) at intensive stirring and cooling for 3 h. The reaction mixture was kept overnight at room temperature and poured into ice water (500 ml). The precipitated solid was filtered and recrystallized from 50% ethanol to give (**II**); yield 56%, mp 116–117°C; UV, EtOH, λ_{max}, nm logε): 204 (4.65), 222 (4.28), and 326 (4.24); IR (cm^{-1}): 3250, 1735, 1675, 1615, 1568, 1513, 1468, 1388, 1360, 1324, 1299, 1237, 1181, 1149, 1095, 853; ^{1}H NMR: 1.17 (3 H, t, *J* 7.2, $CO_2CH_2C\underline{H}_3$), 2.37 (3 H, s, 4'-CH_3), 2.47 (2 H, t, *J* 7.2, H2), 2.80 (2 H, t, *J* 7.2, H3), 4.04 (2 H, q, $CO_2C\underline{H}_2CH_3$), 6.68 (1 H, d, *J* 2.4, H8'), 6.81 (1 H, dd, *J* 2.4 and 8.4, H6'), 7.58 (1 H, d, *J* 8.4, H5'), 10.43 (1 H, s, OH). Found, %: C 65.56, H 6.01. $C_{15}H_{16}O_5$. Calculated, %: C 65.21, H 5.84.

Ethyl 3-(7'-hydroxy-4',8'-dimethyl-2'-oxochromen-3'-yl)propanoate (III) was similarly obtained from 2-methylresorcinol (12.4 g, 0.1 mol) and diethyl 2-acetylglutarate (24.66 ml, 0.1 mol); yield 18.02 g (62%); mp 163–165°C; UV, EtOH, λ_{max}, nm (logε): 205 (4.47), 224 (3.97), and 328 (4.05); IR (cm^{-1}): 3235, 1724, 1674, 1607, 1577, 1467, 1379, 1363, 1299, 1256, 1193, 1143, 1103, 810; ^{1}H NMR: 1.19 (3 H, t, *J* 7.2, $CO_2CH_2C\underline{H}_3$), 2.17 (3 H, s, 8'-CH_3), 2.36 (3 H, s, 4'-CH_3), 2.45 (2 H, t, *J* 7.2, H2, CH_2), 2.79 (2 H, t, *J* 7.2, H3), 4.06 (2 H, q, $CO_2C\underline{H}_2CH_3$), 6.82 (1 H, d, *J* 8.7, H6'), 7.39 (1 H, d, *J* 8.7, H5'), 10.12 (1 H, s, OH). Found, %: C 65.96, H 6.31. $C_{16}H_{18}O_5$. Calculated, %: C 66.19, H 6.25.

Ketones (IV)–(XXV). A hot solution of coumarin (**II**) or (**III**) (4 mmol) in anhydrous acetone (30 ml) was treated with freshly heated potash (1.38 g, 10 mmol) and then, at intensive stirring and heating (50–56°C), with the corresponding α-halogenoketone (4.2 mmol). The reaction mixture was kept under these conditions for 1–5 h at TLC monitoring and poured into 1 N H_2SO_4 (100 ml); the precipitated solid was filtered and recrystallized from aqueous ethanol.

Ethyl 3-(4'-methyl-2'-oxo-7'-(2'-oxopropoxy)chromen-3'-yl)propanoate (IV): yield 74%; mp 115–116°C; UV, EtOH, λ_{max}, nm (logε): 202 (4.53), 222 (4.17), and 321 (4.07); IR (cm^{-1}): 1726, 1696, 1612, 1565, 1430, 1384, 1372, 1336, 1304, 1209, 1180, 1156, 1095, 852. Found, %: C 65.26, H 5.92. $C_{18}H_{20}O_6$. Calculated, %: C 65.05, H 6.07.

Ethyl 3-(4',8'-dimethyl-2'-oxo-7'-(2'-oxopropoxy)chromen-3'-yl)propanoate (V): yield 78%; mp 142–143°C; UV, EtOH, λ_{max}, nm (logε): 206 (4.67), 223 (4.28), and 321 (4.19); IR (cm^{-1}): 1724, 1694, 1606, 1580, 1428, 1357, 1309, 1292, 1231, 1215, 1163, 1128. Found, %: C 65.66, H 6.52. $C_{19}H_{22}O_6$. Calculated, %: C 65.88, H 6.40.

Ethyl 3-[7'-(3',3'-dimethyl-2'-oxobutoxy)-4'-methyl-2'-oxochromen-3'-yl]propanoate (VI): yield 77%; mp 97–98°C; UV, MeCN, λ_{max}, nm (logε): 204 (4.97), 222 (4.49), and 319 (4.57); IR (cm^{-1}): 1731, 1707, 1610, 1422, 1393, 1372, 1282, 1192, 1164, 1088, 1006. Found, %: C 67.46, H 6.82. $C_{21}H_{26}O_6$. Calculated, %: C 67.36, H 7.00.

Ethyl 3-[7'-(3',3'-dimethyl-2'-oxobutoxy)-4',8'-dimethyl-2'-oxochromen-3'-yl]propanoate (VII): yield 82%; mp 141–142°C; UV, MeCN, λ_{max}, nm (logε): 205 (4.62), 224 (4.06), and 321 (4.21); IR (cm^{-1}): 1729, 1688, 1604, 1427, 1372, 1290, 1192, 1165, 1141, 1088, 1064, 990. Found, %: C 67.86, H 7.42. $C_{22}H_{28}O_6$. Calculated, %: C 68.02, H 7.27.

Ethyl 3-[4'-methyl-7'-(1'-methyl-2'-oxopropoxy)-2'-oxochromen-3'-yl]propanoate (VIII): yield 79%; mp 76–77°C; UV, dioxane, λ_{max}, nm (logε): 211 (4.55), 223 (4.37), 291 (4.03), and 321 (4.24); IR (cm^{-1}): 1728, 1694, 1614, 1563, 1435, 1377, 1349, 1330, 1298, 1193, 1160, 1123, 1099, 863. Found, %: C 65.76, H 6.22. $C_{19}H_{22}O_6$. Calculated, %: C 65.88, H 6.40.

Table 2. The ^{1}H NMR spectral data of 2-[5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl]propanoates (**XXVI**)–(**XLV**)

Compound	Proton signals, δ, ppm, spin coupling constants, Hz							
	COOH 1 H, br. s	H2 2 H, t, *J* 7.2	H3 2 H, t, *J* 7.2	H2' 1 H, s	H4' 1 H, s	C5'–CH_3 3 H, s	C9'–Rc	C3'–R
(**XXVI**)	12.13	2.44	2.84	7.84 (1 H, s, H)	7.98	2.53	7.58 (1 H, s, H)	2.27 (3 H, s, CH_3)
(**XXVII**)	12.09	2.41	2.82	7.73 (1 H, s, H)	7.68	2.52	2.45 (3 H, s, CH_3)	2.26 (3 H, s, CH_3)
(**XXVIII**)	12.11	2.42	2.85	7.68 (1 H, s, H)	7.98	2.56	7.51 (1 H, s, H)	1.44 (9 H, s, $C(CH_3)_3$)
(**XXIX**)	12.05	2.42	2.85	7.72 (1 H, s, H)	7.68	2.54	2.46 (3 H, s, CH_3)	1.45 (9 H, s, $C(CH_3)_3$)
(**XXX**)	12.08	2.41	2.81	2.39 (3 H, s, CH_3)	7.72	2.51	7.35 (1 H, s, H)	2.19 (3 H, s, CH_3)
(**XXXI**)	12.08	2.41	2.80	2.39 (3 H, s, CH_3)	7.54	2.48	2.44 (3 H, s, CH_3)	2.17 (3 H, s, CH_3)
(**XXXII**)	12.09	2.40	2.82	2.44 (3 H, s, CH_3)	7.76	2.48	7.53 (1 H, s, H)	7.42 (1 H, m, H4–Ph), 7.55 (4 H, m, H2, H3, H5, H6–Ph)
(**XXXIII**)	12.08	2.39	2.81	2.50 (3 H, s, CH_3)	7.59	2.56	2.42 (3 H, s, CH_3)	7.42 (1 H, m, H4–Ph), 7.52 (4 H, m, H2, H3, H5, H6–Ph)
(**XXXIV**)	12.07	2.43	2.86	8.32 (1 H, s, H)	8.11	2.57	7.63 (1 H, s, H)	7.40 (1 H, m, H4–Ph), 7.52 (2 H, t, *J* 7.5, H3, H5–Ph), 7.74 (2 H, d, *J* 7.5, H2, H6–Ph)
(**XXXV**)	12.05	2.42	2.84	8.28 (1 H, s, H)	7.88	2.51	2.51 (3 H, s, CH_3)	7.39 (1 H, m, H4–Ph), 7.50 (2 H, t, *J* 7.5, H3, H5–Ph), 7.72 (2 H, d, *J* 7.5, H2, H6–Ph)
(**XXXVI**)	12.11	2.42	2.83	8.32 (1 H, s, H)	8.09	2.57	7.64 (1 H, s, H)	7.30 (2 H, t, *J* 7.5, H3, H5–Ph), 7.80 (2 H, m, H2, H6–Ph)
(**XXXVII**)	12.07	2.40	2.85	8.33 (1 H, s, H)	7.93	2.55	2.55 (3 H, s, CH_3)	7.30 (2 H, t, *J* 7.5, H3, H5–Ph), 7.80 (2 H, m, H2, H6–Ph)
(**XXXVIII**)	12.10	2.43	2.85	8.39 (1 H, s, H)	8.08	2.56	7.64 (1 H, s, H)	7.53 (2 H, d, *J* 8.4, H3, H5–Ph), 7.79 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XXXIX**)	12.05	2.43	2.85	8.38 (1 H, s, H)	7.94	2.55	2.55 (3 H, s, CH_3)	7.53 (2 H, d, *J* 8.4, H3, H5–Ph), 7.78 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XL**)	12.12	2.43	2.85	8.41 (1 H, s, H)	8.09	2.56	7.64 (1 H, s, H)	7.67 (2 H, d, *J* 8.4, H3, H5–Ph), 7.73 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XLI**)	12.07	2.42	2.85	8.38 (1 H, s, H)	7.92	2.54	2.54 (3 H, s, CH_3)	7.66 (2 H, d, *J* 8.4, H3, H5–Ph), 7.71 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XLII**)	12.08	2.42	2.83	8.22 (1 H, s, H)	8.06	2.56	7.60 (1 H, s, H)	3.84 (3 H, s, $C\underline{H}_3$–OPh), 7.06 (2H, d, *J* 8.4, H3, H5–Ph), 7.67 (2 H, d, *J* 8.4, H2, H6–Ph)
(**XLIII**)	12.10	2.42	2.84	8.22 (1 H, s, H)	7.88	2.53	2.53 (3 H, s, CH_3)	3.83 (3 H, s, $C\underline{H}_3$–OPh), 7.05 (2 H, d, *J* 8.4, H3, H5–Ph), 7.63 (2 H, d, *J* 8.4, H2, H6'–Ph)
(**XLIV**)	12.09	2.42	2.84	8.34 (1 H, s, H)	8.09	2.53	7.62 (1 H, s, H)	3.83 (3 H, s, $C\underline{H}_3$–OPh), 6.95 (1H, dd, *J* 2.7, 8.4, H4–Ph), 7.24 (1 H, dd, *J* 2.7, 2.7, H2–Ph), 7.32 (1 H, d, *J* 8.4, H6–Ph), 7.43 (1 H, t, *J* 8.4, H5–Ph)
(**XLV**)	12.08	2.41	2.84	8.33 (1 H, s, H)	7.91	2.54	2.54 (3 H, s, CH_3)	3.86 (3 H, s, $C\underline{H}_3$–OPh), 6.94 (1 H, dd, *J* 2.7, 8.4, H4–Ph), 7.22 (1 H, dd, *J* 2.7, 2.7, H2–Ph), 7.31 (1 H, d, *J* 8.4, H6–Ph), 7.42 (1 H, t, *J* 8.4, H5–Ph)

Ethyl 3-[4',8'-dimethyl-7'-(1'-methyl-2'-oxopropoxy)-2'-oxochromen-3'-yl]propanoate (IX): yield 75%; mp 63–64°C; UV, EtOH, λ_{max}, nm (log ε): 203 (4.51), 224 (4.09), and 322 (4.13); IR (cm^{-1}): 1724, 1704, 1607, 1499, 1450, 1424, 1378, 1358, 1306, 1293, 1279, 1205, 1132, 1112. Found, %: C 66.45, H 6.81. $C_{20}H_{24}O_6$. Calculated, %: C 66.65, H 6.71.

Ethyl 3-[4'-methyl-7'-(1'-methyl-2'-oxo-2'-phenylethoxy)-2'-oxochromen-3'-yl)propanoate (X): The oil separated after the reaction mixture pouring into 1 N H_2SO_4 was extracted with ethyl acetate (50 ml). The extract was successively washed with 5% $NaHCO_3$ (25 ml), water (25 ml), 1 N H_2SO_4 (25 ml), water (25 ml), and saturated NaCl solution (25 ml); dried with anhydrous $MgSO_4$; and evaporated in a vacuum. The residue was triturated with petroleum ether, and the remaining yellow oil was dried in a vacuum; yield 71%. Found, %: C 70.66, H 5.82. $C_{24}H_{24}O_6$. Calculated, %: C 70.57, H 5.92.

Ethyl 3-[4',8'-dimethyl-7'-(1'-methyl-2'-oxo-2'-phenylethoxy)-2'-oxochromen-3'-yl)propanoate (XI): yield 80%; mp 113–114°C; UV, EtOH, λ_{max}, nm (log ε): 204 (4.80), 247 (4.28), and 323 (4.26); IR (cm^{-1}): 1734, 1694, 1600, 1580, 1449, 1354, 1304, 1272, 1248, 1226, 1139, 1110, 1063. Found, %: C 70.86, H 6.42. $C_{25}H_{26}O_6$. Calculated, %: C 71.07, H 6.20.

Ethyl 3-[4'-methyl-2'-oxo-7'-(2'-oxo-2'-phenylethoxy)chromen-3'-yl)propanoate (XII): yield 86%; mp 139–141°C; UV, EtOH, λ_{max}, nm (log ε): 204 (4.72), 223 (4.22), 243 (4.24), and 322 (4.21); IR (cm^{-1}): 1715, 1700, 1617, 1450, 1426, 1378, 1330, 1300, 1229, 1199, 1167, 1094. Found, %: C 69.86, H 5.49. $C_{23}H_{22}O_6$. Calculated, %: C 70.04, H 5.62.

Ethyl 3-[4',8'-dimethyl-2'-oxo-7'-(2'-oxo-2'-phenylethoxy)chromen-3'-yl)propanoate (XIII): yield 91%; mp 179–181°C; UV, EtOH, λ_{max}, nm (log ε): 204 (4.85), 225 (4.35), 244 (4.32), and 322 (4.28); IR (cm^{-1}): 1719, 1709, 1698, 1603, 1580, 1502, 1450, 1434, 1379, 1358, 1329, 1308, 1285, 1252, 1226, 1207, 1174, 1135, 1069, 978. Found, %: C 70.39, H 6.02. $C_{24}H_{24}O_6$. Calculated, %: C 70.57, H 5.95.

Ethyl 3-{7'-[2'-(4''-fluorophenyl)-2'-oxoethoxy]-4'-methyl-2'-oxochromen-3'-yl}propanoate (XIV): yield 89%; mp 141–142°C; UV, EtOH, λ_{max}, nm (log ε): 203 (4.77), 247 (4.33), and 322 (4.34); IR (cm^{-1}): 1722, 1709, 1698, 1618, 1598, 1508, 1424, 1336, 1303, 1273, 1230, 1179, 1161, 1093, 1068, 843. Found, %: C 67.16, H 5.02. $C_{23}H_{21}FO_6$. Calculated, %: C 66.98, H 5.13.

Ethyl 3-{7'-[2'-(4''-fluorophenyl)-2'-oxoethoxy]-4',8'-dimethyl-2'-oxochromen-3'-yl}propanoate (XV): yield 86%; mp 169–170°C; UV, EtOH, λ_{max}, nm (log ε): 204 (4.67), 223 (4.13), 245 (4.07), and 321 (4.09); IR (cm^{-1}): 1728, 1708, 1696, 1604, 1510, 1435, 1329, 1304, 1290, 1234, 1166, 1144, 985, 854. Found, %: C 67.76, H 5.52. $C_{24}H_{23}FO_6$. Calculated, %: C 67.60, H 5.44.

Ethyl 3-{7'-[2'-(4''-chlorophenyl)-2'-oxoethoxy]-4'-methyl-2'-oxochromen-3'-yl}propanoate (XVI): yield 87%; mp 152–153°C; UV, MeCN, λ_{max}, nm (log ε): 204 (4.89), 223 (4.29), 252 (4.39), and 319 (4.34); IR (cm^{-1}): 1727, 1701, 1616, 1591, 1424, 1376, 1331, 1300, 1226, 1201, 1167, 1094. Found, %: C 64.19, H 5.08. $C_{23}H_{21}ClO_6$. Calculated, %: C 64.41, H 4.94.

Ethyl 3-{7'-[2'-(4''-chlorophenyl)-2'-oxoethoxy]-4',8'-dimethyl-2'-oxochromen-3'-yl}propanoate (XVII): yield 92%; mp 200–201°C; UV, MeCN, λ_{max}, nm (log ε): 205 (4.91), 224 (4.28), 253 (4.38), and 319 (4.36); IR (cm^{-1}): 1725, 1711, 1609, 1589, 1432, 1379, 1289, 1225, 1208, 1143, 1092, 986. Found, %: C 64.16, H 5.12. $C_{24}H_{23}ClO_6$. Calculated, %: C 65.09, H 5.23.

Ethyl 3-{7'-[2'-(4''-bromophenyl)-2'-oxoethoxy]-4'-methyl-2'-oxochromen-3'-yl}propanoate (XVIII): yield 90%; mp 145–146°C; UV, MeCN, λ_{max}, nm (log ε): 203 (4.79), 222 (4.24), 258 (4.32), and 319 (4.24); IR (cm^{-1}): 1724, 1701, 1613, 1587, 1566, 1424, 1376, 1330, 1300, 1225, 1199, 1167, 1094, 1072, 997. Found, %: C 58.18, H 4.52. $C_{23}H_{21}BrO_6$. Calculated, %: C 58.36, H 4.47.

Ethyl 3-{7'-[2'-(4''-bromophenyl)-2'-oxoethoxy]-4',8'-dimethyl-2'-oxochromen-3'-yl}propanoate (XIX): yield 92%; mp 197–198°C; UV, MeCN, λ_{max}, nm (log ε): 206 (4.74), 256 (4.29), and 319 (4.20); IR (cm^{-1}): 1712, 1701, 1608, 1585, 1501, 1432, 1379, 1357, 1309, 1288, 1224, 1208, 1175, 1142, 1070, 984. Found, %: C 58.97, H 4.92. $C_{24}H_{23}BrO_6$. Calculated, %: C 59.15, H 4.76.

Ethyl 3-{7'-[2'-(4''-methoxyphenyl)-2'-oxoethoxy]-4'-methyl-2'-oxochromen-3'-yl}propanoate (XX): yield 86%; mp 127–128°C; UV, MeCN, λ_{max}, nm (log ε): 204 (4.77), 219 (4.47), 282 (4.40), and 319 (4.29); IR (cm^{-1}): 1728, 1709, 1695, 1615, 1602, 1511, 1424, 1378, 1330, 1298, 1265, 1238, 1188, 1166, 1096, 998. Found, %: C 67.96, H 5.62. $C_{24}H_{24}O_7$. Calculated, %: C 67.91, H 5.70.

Ethyl 3-{7'-[2'-(4''-methoxyphenyl)-2'-oxoethoxy]-4',8'-dimethyl-2'-oxochromen-3'-yl}propanoate (XXI): yield 91%; mp 173–174°C; UV, MeCN, λ_{max}, nm (log ε): 205 (4.77), 220 (4.44), 284 (4.40), and 322 (4.30); IR (cm^{-1}): 1728, 1711, 1700, 1603, 1577, 1430, 1379, 1311, 1289, 1263, 1241, 1209, 1175, 1141, 984. Found, %: C 68.36, H 6.06. $C_{25}H_{26}O_7$. Calculated, %: C 68.48, H 5.98.

Ethyl 3-{7'-[2'-(3''-methoxyphenyl)-2'-oxoethoxy]-4'-methyl-2'-oxochromen-3'-yl}propanoate (XXII): yield 88%; mp 101–102°C; UV, EtOH, λ_{max}, nm (log ε): 203 (4.68), 221 (4.53), 251 (4.01), and 322 (4.21); IR (cm^{-1}): 1730, 1711, 1698, 1615, 1583, 1458, 1426, 1329, 1302, 1289, 1264, 1199, 1179, 1162, 1094, 1008. Found, %: C 67.76, H 5.82. $C_{24}H_{24}O_7$. Calculated, %: C 67.91, H 5.70.

Ethyl 3-{7'-[2'-(3''-methoxyphenyl)-2'-oxoethoxy]-4',8'-dimethyl-2'-oxochromen-3'-yl}propanoate (XXIII): yield 81%; mp 165–167°C; UV, MeCN, λ_{max}, nm (logε): 206 (4.68), 219 (4.57), 249 (4.08), and 318 (4.25); IR (cm^{-1}): 1721, 1701, 1606, 1467, 1432, 1378, 1309, 1288, 1267, 1207, 1174, 1139. Found, %: C 68.56, H 6.01. $C_{25}H_{26}O_7$. Calculated, %: C 68.48, H 5.98.

Ethyl 3-[4'-methyl-2'-oxo-7-(2''-oxocyclohexyloxy)chromen-3''-yl}propanoate (XXIV): yield 71%; mp 158–159°C; UV, EtOH, λ_{max}, nm (logε): 205 (4.32), 224 (4.01), and 324 (3.98); IR (cm^{-1}): 1730, 1691, 1600, 1501, 1442, 1355, 1283, 1231, 1162, 1128, 1101. Found, %: C 67.56, H 6.66. $C_{21}H_{24}O_6$. Calculated, %: C 67.73, H 6.50.

Ethyl 3-[4',8'-dimethyl-2'-oxo-7'-(2''-oxocyclohexyloxy)chromen-3'-yl}propanoate (XXV): yield 78%; mp 172–173°C; UV, EtOH, λ_{max}, nm (logε): 206 (4.58), 224 (4.17), and 324 (4.15); IR (cm^{-1}): 1729, 1689, 1600, 1499, 1445, 1356, 1287, 1238, 1158, 1129, 1107. Found, %: C 68.19, H 6.96. $C_{22}H_{26}O_6$. Calculated, %: C 68.38, H 6.78.

3-(5'-Methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acids (XXVI)–(XLVII). Ten ml of 1 N NaOH were added to solutions or suspensions of ketones (**IV**)–(**XXV**) (2 mmol). The reaction mixture was heated for 3–4 h at TLC monitoring and then transferred into 1 N H_2SO_4 (100 ml). The precipitated solid was filtered and recrystallized from isopropanol.

3-(3',5'-Dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXVI): yield 82%; mp 215–216°C; UV, EtOH, λ_{max}, nm (logε): 211 (4.38), 249 (4.32), 296 (4.03), and 336 (3.89); IR (cm^{-1}): 3403, 2925, 1718, 1699, 1629, 1579, 1426, 1411, 1397, 1335, 1256, 1245, 1141, 1075, 960, 867. Found, %: C 66.95, H 5.06. $C_{16}H_{14}O_5$. Calculated, %: C 67.13, H 4.93.

3-(3',5',9'-Trimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXVII): yield 86%; mp 239–240°C; UV, EtOH, λ_{max}, nm (logε): 211 (4.25), 251 (4.12), 304 (3.87), and 342 (3.61); IR (cm^{-1}): 3382, 2928, 1719, 1700, 1620, 1596, 1449, 1426, 1395, 1356, 1299, 1213, 1121, 1070. Found, %: C 68.05, H 5.36. $C_{17}H_{16}O_5$. Calculated, %: C 67.99, H 5.37.

3-[3'-(*tert*-Butyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXVIII): yield 81%; mp 201–202°C; UV, dioxane, λ_{max}, nm (logε): 212 (4.65), 244 (4.53), 251 (4.52), 291 (4.23), 302 (4.18), and 327 (4.07); IR (cm^{-1}): 2966, 1706, 1627, 1581, 1430, 1392, 1341, 1305, 1216, 1136, 1086, 886, 804. Found, %: C 69.69, H 6.09. $C_{19}H_{20}O_5$. Calculated, %: C 69.50, H 6.14.

3-[3'-(*tert*-Butyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXIX): yield 84%; mp 196–197°C; UV, MeCN, λ_{max}, nm (logε): 210 (4.57), 245 (4.47), 250 (4.48), 298 (4.22), and 329 (4.03); IR (cm^{-1}): 2958, 1710, 1620, 1586, 1431, 1341, 1308, 1211, 1134, 1081, 886. Found, %: C 69.98, H 6.56. $C_{20}H_{22}O_5$. Calculated, %: C 70.16, H 6.48.

3-(2',3',5'-Trimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXX): yield 79%; mp 219–220°C; UV, EtOH, λ_{max}, nm (logε): 211 (4.12), 254 (4.10), 299 (3.78), and 336 (3.64); IR (cm^{-1}): 3506, 2925, 1721, 1707, 1671, 1642, 1627, 1579, 1440, 1400, 1294, 1209, 1177, 1159, 1128, 871. Found, %: C 70.15, H 5.36. $C_{17}H_{16}O_5$. Calculated, %: C 67.99, H 5.37.

3-(2',3',5',9'-Tetramethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXXI): yield 71%; mp 255–256°C; UV, EtOH, λ_{max}, nm (logε): 210 (4.08), 255 (4.02), 304 (3.78), and 340 (3.59); IR (cm^{-1}): 3376, 2924, 1719, 1695, 1641, 1594, 1423, 1407, 1355, 1298, 1210, 1153, 1130, 1111. Found, %: C 68.96, H 5.86. $C_{18}H_{18}O_5$. Calculated, %: C 68.78, H 5.77.

3-(2',5'-Dimethyl-7'-oxo-3-phenylfuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXXII): yield 76%; mp 208–210°C; UV, EtOH, λ_{max}, nm (logε): 202 (4.52), 211 (4.46), 254 (4.50), 295 (4.17), and 335 (3.90); IR (cm^{-1}): 3385, 2925, 1730, 1689, 1637, 1582, 1437, 1395, 1327, 1267, 1220, 1199, 1185, 1153, 1098. Found, %: C 73.08, H 5.09. $C_{22}H_{18}O_5$. Calculated, %: C 72.92, H 5.01.

3-(2',5',9'-Trimethyl-7'-oxo-3-phenylfuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXXIII): yield 83%; mp 268–269°C; UV, MeCN, λ_{max}, nm (logε): 204 (4.52), 210 (4.50), 255 (4.54), 298 (4.23), and 342 (3.82); IR (cm^{-1}): 3211, 2925, 1735, 1706, 1671, 1627, 1584, 1440, 1399, 1383, 1332, 1214, 1177, 1145. Found, %: C 73.21, H 5.42. $C_{23}H_{20}O_5$. Calculated, %: C 73.39, H 5.36.

3-(5'-Methyl-7'-oxo-3-phenylfuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXXIV): yield 82%; mp 200–201°C; UV, MeCN, λ_{max}, nm (logε): 203 (4.59), 226 (4.40), 250 (4.46), 298 (4.24), and 338 (3.89); IR (cm^{-1}): 3100, 2688, 1746, 1709, 1663, 1627, 1575, 1425, 1389, 1360, 1299, 1199, 1166, 1120, 1089, 853. Found, %: C 72.25, H 4.76. $C_{21}H_{16}O_5$. Calculated, %: C 72.41, H 4.63.

3-(5'9'-Dimethyl-7'-oxo-3-phenylfuro[3,2-*g*]chromen-6'-yl)propanoic acid (XXXV): yield 88%; mp 264–265°C; UV, EtOH, λ_{max}, nm (logε): 202 (4.37), 216 (4.29), 229 (4.18), 251 (4.16), and 304 (3.96); IR (cm^{-1}): 3424, 3095, 1743, 1707, 1661, 1608, 1591, 1566, 1387, 1355, 1341, 1301, 1169, 1132, 1106. Found, %: C 72.75, H 5.06. $C_{22}H_{18}O_5$. Calculated, %: C 72.92, H 5.01.

3-{3'-(4'-Fluorophenyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XXXVI): yield

81%; mp 199–200°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 203 (4.54), 213 (4.47), 226 (4.39), 250 (4.37), 301 (4.18), and 331 (3.97); IR (cm^{-1}): 3105, 1756, 1704, 1669, 1627, 1575, 1510, 1387, 1349, 1312, 1298, 1166, 1085, 854. Found, %: C 68.66; H 4.19. $C_{21}H_{15}FO_5$. Calculated, %: C 68.85, H 4.13.

3-{3'-(4'-Fluorophenyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XXXVII): yield 92%; mp 263–265°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 204 (4.55), 215 (4.51), 227 (4.41), 250 (4.42), 304 (4.23), and 342 (3.87); IR (cm^{-1}): 3100, 1753, 1705, 1669, 1612, 1588, 1570, 1510, 1388, 1347, 1314, 1298, 1236, 1168, 1134, 1107, 852. Found, %: C 69.32, H 4.59. $C_{22}H_{17}FO_5$. Calculated, %: C 69.47, H 4.50.

3-{3'-(4'-Chlorophenyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XXXVIII): yield 91%; mp 207–208°C; UV, MeCN, λ_{max}, nm ($\log\varepsilon$): 204 (4.71), 248 (4.59), 301 (4.34), and 335 (4.02).; IR (cm^{-1}): 3091, 1739, 1714, 1681, 1629, 1582, 1491, 1394, 1272, 1160, 1115, 1096, 832. Found, %: C 65.68; H 4.07. $C_{21}H_{15}ClO_5$. Calculated, %: C 65.89, H 3.95.

3-{3'-(4'-Chlorophenyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XXXIX): yield 88%; mp 269–270°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 207 (4.44), 216 (4.40), 250 (4.39), and 302 (4.19); IR (cm^{-1}): 3095, 1743, 1715, 1675, 1589, 1495, 1379, 1367, 1298, 1166, 1134, 1110, 842. Found, %: C 66.48, H 4.27. $C_{22}H_{17}ClO_5$. Calculated, %: C 66.59, H 4.32.

3-{3'-(4'-Bromophenyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XL): yield 92%; mp 224–225°C; UV, MeCN, λ_{max}, nm ($\log\varepsilon$): 202 (4.58), 248 (4.46), 295 (4.24), and 340 (3.81); IR (cm^{-1}): 3091, 1739, 1713, 1679, 1629, 1581, 1394, 1272, 1160, 1115, 1093, 1073, 873, 829. Found, %: C 59.18; H 3.57. $C_{21}H_{15}BrO_5$. Calculated, %: C 59.04, H 3.54.

3-{3'-(4'-Bromophenyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XLI): yield 94%; mp 277–278°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 206 (4.58), 217 (4.49), 251 (4.50), and 302 (4.28); IR (cm^{-1}): 3093, 1739, 1711, 1675, 1589, 1491, 1378, 1368, 1341, 1297, 1164, 1133, 1112, 1079, 841. Found, %: C 59.68; H 3.87. $C_{22}H_{17}BrO_5$. Calculated, %: C 59.88, H 3.88.

3-{3'-(4'-Methoxyphenyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XLII): yield 94%; mp 233–234°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 205 (4.57), 231 (4.40), 251 (4.39), 308 (4.16); IR (cm^{-1}): 3044, 1730, 1701, 1679, 1627, 1587, 1577, 1511, 1396, 1303, 1278, 1255, 1183, 1161, 1113, 1085, 1028. Found, %: C 69.69; H 4.87. $C_{22}H_{18}O_6$. Calculated, %: C 69.83, H 4.79.

3-{3'-(4'-Methoxyphenyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XLIII): yield 86%; mp 254–255°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 202 (4.82), 240 (4.66), 250 (4.68), 304 (4.43); IR (cm^{-1}): 3049, 1741, 1705, 1655, 1614, 1587, 1564, 1512, 1363, 1300, 1255, 1184, 1170, 1136, 1110, 1028, 820. Found, %: C 70.29; H 5.07. $C_{23}H_{20}O_6$. Calculated, %: C 70.40, H 5.14.

3-{3'-(3'-Methoxyphenyl)-5'-methyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XLIV): yield 87%; mp 200–201°C; UV, MeCN, λ_{max}, nm ($\log\varepsilon$): 213 (4.61), 251 (4.40), 298 (4.24), and 328 (3.92); IR (cm^{-1}): 2940, 1719, 1670, 1627, 1613, 1578, 1418, 1397, 1354, 1310, 1211, 1158, 1095, 857. Found, %: C 69.74; H 4.82. $C_{22}H_{18}O_6$. Calculated, %: C 69.83, H 4.79.

3-{3'-(3'-Methoxyphenyl)-5',9'-dimethyl-7'-oxofuro[3,2-*g*]chromen-6'-yl}propanoic acid (XLV): yield 79%; mp 234–235°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 214 (4.49), 251 (4.23), and 304 (4.11); IR (cm^{-1}): 2961, 1701, 1612, 1595, 1570, 1428, 1387, 1356, 1329, 1295, 1279, 1209, 1123, 1104, 1035. Found, %: C 70.24; H 5.21. $C_{23}H_{20}O_6$. Calculated, %: C 70.40, H 5.14.

3-{4'-Methyl-2'-oxo-6',7',8',9'-tetrahydrobenzo[4,5]furo[3,2-*g*]chromen-3'-yl}propanoic acid (XLVI): yield 85%; mp 247–248°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 211 (4.23), 255 (4.22), 298 (3.94), and 338 (3.80); IR (cm^{-1}): 3240, 2937, 1739, 1672, 1626, 1576, 1468, 1402, 1294, 1269, 1185, 1170, 1154, 1118, 863; ^{1}H NMR: 1.85 (2 H, m, H7'), 1.92 (2 H, m, H8'), 2.40 (2 H, t, *J* 7.2, H2), 2.50 (3 H, s, 4'-CH_3), 2.64 (2 H, m, H6'), 2.73 (2 H, m, H9'), 2.81 (2 H, t, *J* 7.2, H3), 7.40 (1 H, s, H11'), 7.73 (1 H, s, H5'), 12.05 (1 H, br. s, COOH). Found, %: C 70.09; H 5.67. $C_{19}H_{18}O_5$. Calculated, %: C 69.93, H 5.56.

3-{4',11'-Dimethyl-2'-oxo-6',7',8',9'-tetrahydrobenzo[4,5]furo[3,2-*g*]chromen-3'-yl}propanoic acid (XLVII): yield 81%; mp 245–246°C; UV, EtOH, λ_{max}, nm ($\log\varepsilon$): 211 (4.47), 256 (4.46), 302 (4.13), 340 (3.84); IR (cm^{-1}): 3387, 2944, 1730, 1703, 1681, 1639, 1591, 1442, 1412, 1339, 1275, 1188, 1142, 1094, 908, 783; ^{1}H NMR: 1.84 (2 H, m, H7'), 1.91 (2 H, m, H8'), 2.39 (2 H, t, *J* 7.2, H2), 2.45 (3 H, s, C11'-CH_3), 2.50 (3 H, s, C4'-CH_3), 2.62 (2 H, m, H6'), 2.74 (2 H, m, H9'), 2.80 (2 H, t, *J* 7.2, H3), 7.55 (1 H, s, H5'), 12.00 (1 H, br. s, COOH). Found, %: C 70.49; H 5.97. $C_{20}H_{20}O_5$. Calculated, %: C 70.57, H 5.92.

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