Chemistry of Natural Compounds, Vol. 45, No. 2, 2009

MODIFIED COUMARINS. 29. SYNTHESIS OF STRUCTURAL ANALOGS OF NATURAL 6-ARYLFURO[3,2-*g*]CHROMEN-7-ONES

M. M. Garazd,[1*] Ya. L. Garazd,[2] A. S. Ogorodniichuk,[1] and V. P. Khilya[2]

UDC 547.814.5

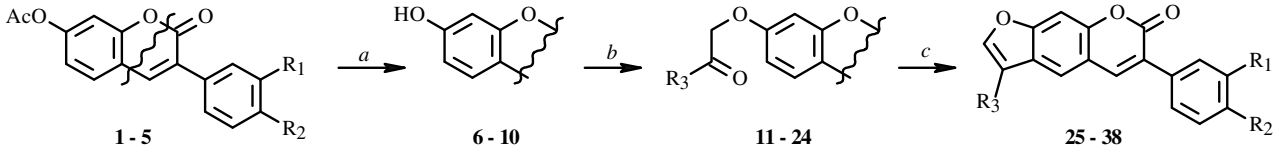
3-Substituted 6-arylfuro[3,2-g]chromen-7-ones, structural analogs of natural furocoumarins, were synthesized by linear annelation of a furan fragment to a 3-arylcoumarin system.

Key words: coumarins, 3-arylcoumarins, furocoumarins, psoralene.

Furocoumarins are structurally varied natural compounds that are mostly derivatives of the linear furocoumarin psoralene [1]. The heightened interest in furocoumarins is due to the important role that they play in the life processes of plants and animals and their high and varied biological activity [2]. In most instances furocoumarins are unsubstituted in the 2- and 3-positions of the pyran-2-one ring. However, compounds containing aryl substituents in these positions have been isolated from natural sources. Examples of such secondary metabolites based on the 3-arylcoumarin core are pachyrrhizin {6-(6-methoxy-1,3-benzodioxol-5-yl)furo[3,2-*g*]chromen-7-one}, which was isolated from the plants *Pachyrrhizus erosus* [3-5], *P. tuberosus* [6], *Neorautassenia pseudopachyrriza* [7], and *N. edulis* [8-10]; neofolin {9-methoxy-6-(6-methoxy-1,3-benzodioxol-5-yl)furo[3,2-*g*]chromen-7-one}, which was isolated from *Neorautanenia ficifolia* [11]; and 6-(2,4,5-trimethoxyphenyl)furo[3,2-*g*]chromen-7-one, which is produced by *P. tuberosus* [6].

We synthesized substituted 6-arylfuro[3,2-*g*]chromen-7-ones, structural analogs of natural furocoumarins, based on the 3-arylcoumarin core.

7-Acetoxycoumarins **1**-**5** were prepared by a Perkin—Oglialoro reaction [12] of 2,4-dihydroxybenzaldehyde and substituted phenylacetic acids in acetic anhydride in the presence of pyridine. Acidolysis of **1**-**5** formed 7-hydroxy-3-arylcoumarins **6**-**10** that were required for further transformations.



a. EtOH, H_2SO_4; *b.* R_3COCH_2Hal, K_2CO_3; *c*. 1. NaOH, 2. H_2SO_4

1, 6: $R_1 = R_2 = H$; **2, 7:** $R_1 = H$, $R_2 = F$; **3, 8:** $R_1 = H$, $R_2 = Cl$; **4, 9:** $R_1 = H$, $R_2 = OMe$; **5, 10:** $R_1 = R_2 = OMe$
11, 25: $R_1 = R_2 = H$, $R_3 = CH_3$; **12, 26:** $R_1 = H$, $R_2 = F$, $R_3 = CH_3$; **13, 27:** $R_1 = H$, $R_2 = Cl$, $R_3 = CH_3$
14, 28: $R_1 = H$, $R_2 = OMe$, $R_3 = CH_3$; **15, 29:** $R_1 = R_2 = OMe$, $R_3 = CH_3$; **16, 30:** $R_1 = R_2 = H$, $R_3 = (CH_3)_3C$
17, 31: $R_1 = H$, $R_2 = F$, $R_3 = (CH_3)_3C$; **18, 32**: $R_1 = H$, $R_2 = OMe$, $R_3 = (CH_3)_3C$; **19**, **33**: $R_1 = H$, $R_2 = Cl$, $R_3 = Ph$
20, 34: $R_1 = R_2 = OMe$, $R_3 = Ph$, **21, 35:** $R_1 = R_2 = H$, $R_3 = 4$-Me-Ph; **22, 36:** $R_1 = H$, $R_2 = OMe$, $R_3 = 4$-F-Ph
23, 37: $R_1 = R_2 = H$, $R_3 = 3$-MeO-Ph; **24, 38:** $R_1 = H$, $R_2 = Cl$, $R_3 = 3$-MeO-Ph

The reaction of hydroxycoumarins **6**-**10** with α-haloketones under Williamson conditions produced the corresponding substituted oxoethers **11**-**24**. The alkylating agents in these syntheses were chloroacetone (**11**-**15**), 1-chloropinacolone (**16**-**18**), phenacylbromide (**19** and **20**), 4-methylphenacylbromide (**21**), 4-fluorophenacylchloride (**22**), and 3-methoxyphenacylbromide (**23** and **24**).

1) Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine, 02094, Ukraine, Kiev, ul. Murmanskaya, 1, e-mail: gmm@i.com.ua; 1) Taras Shevchenko Kiev National University, 01033, Ukraine, Kiev, ul. Vladimirskaya, 64. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 140-144, March-April, 2009. Original article submitted November 6, 2007.

 0009-3130/09/4502-0158

Ketones **11**-**24** under MacLeod cyclization conditions [13] upon heating with NaOH solution (1 N) and subsequent acidolysis were cyclized smoothly and in high (69-89%) yields to 3-substituted-6-arylfuro[3,2-*g*]chromen-7-ones (**25**-**38**).

Linear annelation of the furan ring at the 6,7-positions of the 3-arylcoumarin was confirmed by PMR spectroscopy. The PMR spectra of **25**-**38** showed a simplified splitting pattern for the aromatic protons compared with the starting ketones due to decoupling of the 6-proton of the 3-arylcoumarin ring. Protons H-4 and H-9 in 3-substituted 6-arylfuro[3,2-*g*]chromen-7-ones resonated as singlets at 7.82-8.34 and 7.60-7.71 ppm, respectively. Furthermore, PMR spectra of 6-arylfuro[3,2-*g*]chromen-7-ones **25**-**38** exhibited a singlet for proton H-2, a characteristic feature of annelation of the furocoumarin ring. The singlet of proton H-2 was located at 7.56-7.97 ppm with alkyl substituents (**25**-**32**) in the 3-position of the 6-arylfuro[3,2-*g*]chromen-7-one. Aryl substituents in the 3-position (**33**-**38**) shifted the resonance of H-2 to weaker (8.37-8.48 ppm) field.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Merck 60 F254 plates with $CHCl_3$:CH_3OH (9:1 and 19:1) as eluents. Melting points were determined on a Kofler block. PMR spectra were recorded on Varian VXR-300 and Mercury 400 spectrometers at 300 and 400 MHz, respectively, relative to TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

7-Acetoxy-3-arylcoumarins 1-5. A mixture of 2,4-dihydroxybenzaldehyde (13.8 g, 0.1 mol), the appropriate arylacetic acid (0.1 mol), freshly distilled acetic anhydride (30 mL), and anhydrous pyridine (30 mL) was refluxed for 12 h and cooled. The resulting precipitate was filtered off and crystallized from propanol-2.

7-Acetoxy-3-phenylchromen-2-one (1): yield 56%, mp 187-188°C (lit. [14] 182-183°C, [15] 182-184°C, [16] 184-185°C, [17] 185-187°C, [18] 186°C), $C_{17}H_{12}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.33 (3H, s, CH_3COO-7), 7.18 (1H, dd, J = 2.0, 8.0, H-6), 7.32 (1H, d, J = 2.0, H-8), 7.44 (3H, m, H-3′, H-4′, H-5′), 7.72 (2H, d, J = 8.0, H-2′, H-6′), 7.82 (1H, d, J = 8.0, H-5), 8.26 (1H, s, H-4).

3-(4-Fluorophenyl)-7-acetoxychromen-2-one (2): yield 67%, mp 203-204°C (lit. [12] 208°C), $C_{17}H_{11}FO_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.31 (3H, s, CH_3COO-7), 7.19 (1H, dd, J = 2.0, 8.0, H-6), 7.28-7.33 (3H, m, H-8, H-3′, H-5′), 7.77 (2H, m, H-2′, H-6′), 7.80 (1H, d, J = 8.0, H-5), 8.26 (1H, s, H-4).

3-(4-Chlorophenyl)-7-acetoxychromen-2-one (3): yield 71%, mp 206-207°C (lit. [12] 202°C), $C_{17}H_{11}ClO_4$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.36 (3H, s, CH_3COO-7), 7.08 (1H, dd, J = 2.1, 8.1, H-6), 7.16 (1H, d, J = 2.1, H-8), 7.42 (2H, d, J = 8.1, H-3′, H-5′), 7.55 (1H, d, J = 8.1, H-5), 7.64 (2H, d, J = 8.1, H-2′, H-6′), 7.80 (1H, s, H-4).

7-Acetoxy-3-(4-methoxyphenyl)chromen-2-one (4): yield 64%, mp 181-182°C (lit. [19] 178°C, [20] 177-178°C), $C_{18}H_{14}O_5$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.35 (3H, s, CH_3COO-7), 3.85 (3H, s, CH_3O-4′), 6.98 (2H, d, J = 8.7, H-3′, H-5′), 7.08 (1H, dd, J = 2.1, 8.1, H-6), 7.14 (1H, d, J = 2.1, H-8), 7.52 (1H, d, J = 8.1, H-5), 7.66 (2H, d, J = 8.7, H-2′, H-6′), 7.74 (1H, s, H-4).

7-Acetoxy-3-(3,4-dimethoxyphenyl)chromen-2-one (5): yield 68%, mp 179-180°C (lit. [17] 173-175°C), $C_{19}H_{16}O_6$.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.35 (3H, s, CH_3COO-7), 3.93 and 3.95 (6H, 2s, CH_3O-3′, CH_3O-4′), 6.94 (1H, d, J = 8.4, H-5′), 7.07 (1H, dd, J = 2.1, 8.1, H-6), 7.15 (1H, d, J = 2.1, H-8), 7.26-7.30 (2H, m, H-2′, H-6′), 7.54 (1H, d, J = 8.1, H-5), 7.77 (1H, s, H-4).

7-Hydroxy-3-arylcoumarins 6-10. A suspension of acetate **1**-**5** (50 mmol) in ethanol (50 mL) was treated with H_2SO_4 (20 mL, 20%), refluxed for 5-10 h (end of reaction determined by TLC), and cooled. The resulting solid was filtered off.

7-Hydroxy-3-phenylchromen-2-one (6): yield 86%, mp 205-206°C (lit. [21] 204-205°C, [15] 206-208°C, [22] 207-208°C, [23] 209°C, [14, 18, 24] 209-210°C, [25] 211-212°C, [26] 212-213°C), $C_{15}H_{10}O_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.76 (1H, d, J = 2.0, H-8), 6.80 (1H, dd, J = 2.0, 8.0, H-6), 7.38-7.46 (3H, m, H-3′, H-4′, H-5′), 7.61 (1H, d, J = 8.0, H-5), 7.69 (2H, d, J = 8.0, H-2′, H-6′), 8.16 (1H, s, H-4), 10.63 (1H, br.s, OH-7).

3-(4-Fluorophenyl)-7-hydroxychromen-2-one (7): yield 89%, mp 238-239°C (lit. [12] 245°C), $C_{15}H_9FO_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.76 (1H, d, J = 2.0, H-8), 6.83 (1H, dd, J = 2.0, 8.0, H-6), 7.23 (2H, t, J = 8.8, H-3′, H-5′), 7.60 (1H, d, J = 8.0, H-5), 7.75 (2H, m, H-2′, H-6′), 8.16 (1H, s, H-4), 10.47 (1H, br.s, OH-7).

3-(4-Chlorophenyl)-7-hydroxychromen-2-one (8): yield 91%, mp 271-272°C (lit. [27] 280-282°C, [23] 289°C, [12] 295°C), $C_{15}H_9ClO_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.76 (1H, d, J = 2.0, H-8), 6.84 (1H, dd, J = 2.0, 8.0, H-6), 7.50 (2H, d, J = 8.4, H-3′, H-5′), 7.60 (1H, d, J = 8.0, H-5), 7.74 (2H, d, J = 8.4, H-2′, H-6′), 8.20 (1H, s, H-4), 10.65 (1H, br.s, OH-7).

7-Hydroxy-3-(4-methoxyphenyl)chromen-2-one (9): yield 82%, mp 215-216°C (lit. [28] 210-212°C, [19] 232°C, [12] 240°C), $C_{16}H_{12}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.80 (3H, s, CH_3O-4′), 6.75 (1H, d, J = 2.0, H-8), 6.82 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (2H, d, J = 8.4, H-3′, H-5′), 7.58 (1H, d, J = 8.0, H-5), 7.66 (2H, d, J = 8.4, H-2′, H-6′), 8.08 (1H, s, H-4), 10.55 (1H, br.s, OH-7).

7-Hydroxy-3-(3,4-dimethoxyphenyl)chromen-2-one (10): yield 87%, mp 219-220°C (lit. [17] 221-223°C), $C_{17}H_{14}O_5$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.80 and 3.18 (6H, 2s, CH_3O-3′, CH_3O-4′), 6.75 (1H, d, J = 2.0, H-8), 6.83 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 8.4, H-5′), 7.30 (2H, m, H-2′, H-6′), 7.57 (1H, d, J = 8.0, H-5), 8.11 (1H, s, H-4), 10.56 (1H, br.s, OH-7).

Ketones 11-24. A hot solution of coumarins **5**-**10** (4 mmol) in anhydrous acetone (30 mL) was treated with freshly calcined potash (1.38 g, 10 mmol), stirred vigorously and heated (50-56°C), treated with the appropriate α-haloketone (4.2 mmol), held for 1-5 h with heating, stirred vigorously (course of reaction monitored by TLC), and poured into H_2SO_4 solution (100 mL, 1 N). The resulting precipitate was filtered off and crystallized from propanol-2.

7-(2-Oxopropoxy)-3-phenylchromen-2-one (11): yield 78%, mp 179-180°C, $C_{18}H_{14}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.18 (3H, s, CH_3-3″), 5.00 (2H, s, CH_2-1″), 6.98 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 2.0, H-8), 7.37-7.46 (3H, m, H-3′, H-4′, H-5′), 7.67-7.71 (3H, m, H-5, H-2′, H-6′), 8.20 (1H, s, H-4).

3-(4-Fluorophenyl)-7-(2-oxopropoxy)chromen-2-one (12): yield 85%, mp 193-194°C, $C_{18}H_{13}FO_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.18 (3H, s, CH_3-3″), 5.00 (2H, s, CH_2-1″), 6.98 (1H, dd, J = 2.0, 8.0, H-6), 7.01 (1H, d, J = 2.0, H-8), 7.28 (2H, t, J = 8.8, H-3′, H-5′), 7.68 (1H, d, J = 8.0, H-5), 7.78 (2H, m, H-2′, H-6′), 8.20 (1H, s, H-4).

3-(4-Chlorophenyl)-7-(2-oxopropoxy)chromen-2-one (13): yield 88%, mp 216-217°C, $C_{18}H_{13}ClO_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.18 (3H, s, CH_3-3″), 5.01 (2H, s, CH_2-1″), 6.97 (1H, dd, J = 2.0, 8.0, H-6), 7.01 (1H, d, J = 2.0, H-8), 7.52 (2H, d, J = 8.8, H-3′, H-5′), 7.70 (1H, d, J = 8.0, H-5), 7.74 (2H, d, J = 8.8, H-2′, H-6′), 8.25 (1H, s, H-4).

3-(4-Methoxyphenyl)-7-(2-oxopropoxy)chromen-2-one (14): yield 81%, mp 191-192°C, $C_{19}H_{16}O_5$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.18 (3H, s, CH_3-3″), 4.98 (2H, s, CH_2-1″), 3.18 (3H, s, CH_3O-4′), 6.95 (2H, d, J = 8.4, H-3′, H-5′), 6.98 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 2.0, H-8), 7.64 (2H, d, J = 8.4, H-2′, H-6′), 7.69 (1H, d, J = 8.0, H-5), 8.21 (1H, s, H-4).

3-(3,4-Dimethoxyphenyl)-7-(2-oxopropoxy)chromen-2-one (15): yield 89%, mp 196-197°C, $C_{20}H_{18}O_6$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.18 (3H, s, CH_3-3″), 4.98 (2H, s, CH_2-1″), 3.81 and 3.82 (6H, 2s, CH_3O-3′, CH_3O-4′), 6.95 (1H, d, J = 8.4, H-5′), 6.97 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 2.0, H-8), 7.28 (2H, m, H-2′, H-6′), 7.70 (1H, d, J = 8.0, H-5), 8.24 (1H, s, H-4).

7-(3,3-Dimethyl-2-oxobutoxy)-3-phenylchromen-2-one (16): yield 76%, mp 185-186°C, $C_{21}H_{20}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.20 [9H, s, $(CH_3)_3$], 5.18 (2H, s, CH_2-1″), 6.97 (1H, dd, J = 2.0, 8.0, H-6), 7.01 (1H, d, J = 2.0, H-8), 7.37-7.46 (3H, m, H-3′, H-4′, H-5′), 7.66-7.70 (3H, m, H-5, H-2′, H-6′), 8.19 (1H, s, H-4).

7-(3,3-Dimethyl-2-oxobutoxy)-3-(4-fluorophenyl)chromen-2-one (17): yield 87%, mp 198-199°C, $C_{21}H_{19}FO_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.19 [9H, s, $(CH_3)_3$], 5.19 (2H, s, CH_2-1″), 6.98 (1H, dd, J = 2.0, 8.0, H-6), 7.01 (1H, d, J = 2.0, H-8), 7.29 (2H, t, J = 8.8, H-3′, H-5′), 7.68 (1H, d, J = 8.0, H-5), 7.78 (2H, m, H-2′, H-6′), 8.19 (1H, s, H-4).

7-(3,3-Dimethyl-2-oxobutoxy)-3-(4-methoxyphenyl)chromen-2-one (18): yield 79%, mp 187-188°C, $C_{21}H_{19}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.20 [9H, s, $(CH_3)_3$], 5.21 (2H, s, CH_2-1″), 3.81 (3H, s, CH_3O-4′), 6.95 (2H, d, J = 8.4, H-3′, H-5′), 6.97 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 2.0, H-8), 7.65 (2H, d, J = 8.4, H-2′, H-6′), 7.69 (1H, d, J = 8.0, H-5), 8.21 (1H, s, H-4).

3-(4-Chlorophenyl)-7-(2-oxo-2-phenylethoxy)chromen-2-one (19): yield 78%, mp 239-240°C, $C_{23}H_{15}ClO_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 5.70 (2H, s, CH_2-1″), 7.01 (1H, dd, J = 2.1, 8.1, H-6), 7.10 (1H, d, J = 2.1, H-8), 7.45 (2H, d, J = 8.7, H-3′, H-5′), 7.56 (3H, t, J = 7.5, H-3‴, H-4‴, H-5‴), 7.67 (1H, d, J = 8.0, H-5), 7.73 (2H, d, J = 8.8, H-2′, H-6′), 8.04 (2H, d, J = 8.7, H-2‴, H-5‴), 8.21 (1H, s, H-4).

3-(3,4-Dimethoxyphenyl)-7-(2-oxo-2-phenylethoxy)chromen-2-one (20): yield 87%, mp 226-227°C, $C_{25}H_{20}O_6$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.82 and 3.83 (6H, 2s, CH_3O-3′, CH_3O-4′), 5.68 (2H, s, CH_2-1″), 6.96 (1H, d, J = 8.4, H-5′), 6.99 (1H, dd, J = 2.1, 8.1, H-6), 7.08 (1H, d, J = 2.1, H-8), 7.28 (2H, m, H-2′, H-6′), 7.56 (2H, t, J = 7.5, H-3‴, H-5‴), 7.63 (1H, d, J = 8.1, H-5), 7.68 (1H, m, H-4‴), 8.04 (2H, d, J = 7.2, H-2‴, H-6‴), 8.10 (1H, s, H-4).

7-[2-(4-Methylphenyl)-2-oxoethoxy]-3-phenylchromen-2-one (21): yield 83%, mp 228-229°C, $C_{24}H_{18}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.40 (3H, s, Me-4‴), 5.72 (1H, s, CH_2-1″), 6.98 (1H, dd, J = 2.0, 8.0, H-6), 7.00 (1H, d, J = 2.0, H-8), 7.37-7.46 (5H, m, H-3′, H-4′, H-5′, H-3‴, H-5‴), 7.67-7.71 (3H, m, H-5, H-2′, H-6′), 7.94 (2H, d, J = 7.6, H-2‴, H-6‴), 8.20 (1H, s, H-4).

7-[2-(4-Fluorophenyl)-2-oxoethoxy]-3-(4-methoxyphenyl)chromen-2-one (22): yield 91%, mp 233-234°C, $C_{24}H_{17}FO_5$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.81 (3H, s, CH_3O-4′), 5.63 (2H, s, CH_2-1″), 6.95 (2H, d, J = 8.7, H-3′, H-5′), 6.97 (1H, dd, J = 2.1, 8.1, H-6), 7.06 (1H, d, J = 2.1, H-8), 7.33 (2H, t, J = 8.7, H-3‴, H-5‴), 7.62 (1H, d, J = 8.1, H-5), 7.64 (2H, d, J = 8.7, H-2′, H-6′), 8.03 (1H, s, H-4), 8.13 (2H, m, H-2‴, H-6‴).

7-[2-(3-Methoxyphenyl)-2-oxoethoxy]-3-phenylchromen-2-one (23): yield 85%, mp 241-242°C, $C_{24}H_{18}O_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.85 (3H, s, OCH_3-3‴), 5.62 (2H, s, CH_2-1″), 6.98 (1H, dd, J = 2.1, 8.1, H-6), 7.00 (1H, d, J = 2.1, H-8), 7.22 (1H, dd, J = 2.7, 8.4, H-4‴), 7.37-7.41 (3H, m, H-3′, H-4′, H-5′), 7.45 (1H, t, J = 8.4, H-5‴), 7.51 (1H, dd, J = 2.7, 2.7, H-2‴), 7.62 (1H, d, J = 8.4, H-6‴), 7.67-7.71 (3H, m, H-5, H-2′, H-6′), 8.20 (1H, s, H-4).

3-(4-Chlorophenyl)-7-[2-(3-methoxyphenyl)-2-oxoethoxy]chromen-2-one (24): yield 92%, mp 248-249°C, $C_{24}H_{17}ClO_5$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.85 (3H, s, OCH_3-3‴), 5.62 (2H, s, CH_2-1″), 6.97 (1H, dd, J = 2.1, 8.1, H-6), 7.01 (1H, d, J = 2.1, H-8), 7.22 (1H, dd, J = 2.7, 8.4, H-4‴), 7.45 (1H, t, J = 8.4, H-5‴), 7.50 (1H, dd, J = 2.7, 2.7, H-2‴), 7.52 (2H, d, J = 8.7, H-3′, H-5′), 7.62 (1H, d, J = 8.4, H-6‴), 7.70 (1H, d, J = 8.1, H-5), 7.74 (2H, d, J = 8.7, H-2′, H-6′), 8.21 (1H, s, H-4).

3-Substitited 6-Arylfuro[3,2-*g*]chromen-7-ones 25-38. A solution or suspension of ketones **11-24** (2 mmol) in propanol-2 (10 mL) was treated with NaOH solution (10 mL, 1 N), heated for 3-4 h (course of reaction monitored by TLC), and poured into H_2SO_4 solution (100 mL, 1 N). The resulting precipitate was filtered off and crystallized from propanol-2.

3-Methyl-6-phenylfuro[3,2-*g*]chromen-7-one (25): yield 69%, mp 219-220°C, $C_{18}H_{12}O_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-3), 7.47 (3H, m, H-3′, H-4′, H-5′), 7.71 (1H, s, H-9), 7.73 (2H, d, J = 7.6, H-2′, H-6′), 7.90 (1H, s, H-2), 8.01 (1H, s, H-4), 8.37 (1H, s, H-5).

6-(4-Fluorophenyl)-3-methylfuro[3,2-*g*]chromen-7-one (26): yield 83%, mp 224-225°C, $C_{18}H_{11}FO_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-3), 7.31 (2H, t, J = 8.0, H-3′, H-5′), 7.60 (1H, s, H-9), 7.78 (2H, m, H-2′, H-6′), 7.94 (1H, s, H-2), 7.82 (1H, s, H-4), 8.37 (1H, s, H-5).

6-(4-Chlorophenyl)-3-methylfuro[3,2-*g*]chromen-7-one (27): yield 89%, mp 233-234°C, $C_{18}H_{11}ClO_3$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-3), 7.51 (2H, d, J = 8.0, H-3′, H-5′), 7.65 (1H, s, H-9), 7.76 (2H, d, J = 8.0, H-2′, H-6′), 7.97 (1H, s, H-2), 7.86 (1H, s, H-4), 8.36 (1H, s, H-5).

6-(4-Methoxyphenyl)-3-methylfuro[3,2-*g*]chromen-7-one (28): yield 78%, mp 229-230°C, $C_{19}H_{14}O_4$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-3), 3.82 (3H, s, CH_3O-4′), 7.04 (2H, d, J = 8.8, H-3′, H-5′), 7.69 (1H, s, H-9), 7.70 (2H, d, J = 8.8, H-2′, H-6′), 7.90 (1H, s, H-2), 7.99 (1H, s, H-4), 8.30 (1H, s, H-5).

6-(3,4-Dimethoxyphenyl)-3-methylfuro[3,2-*g*]chromen-7-one (29): yield 81%, mp 221-222°C, $C_{20}H_{16}O_5$.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-3), 3.82 and 3.83 (6H, 2s, CH_3O-3′, CH_3O-4′), 7.04 (1H, d, J = 8.8, H-5′), 7.34 (2H, m, H-2′, H-6′), 7.68 (1H, s, H-9), 7.88 (1H, s, H-2), 7.96 (1H, s, H-4), 8.33 (1H, s, H-5).

3-*t*-Butyl-6-phenylfuro[3,2-*g*]chromen-7-one (30): yield 75%, mp 196-197°C, $C_{21}H_{18}O_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.44 [9H, s, $(CH_3)_3$], 7.43 (3H, m, H-3′, H-4′, H-5′), 7.58 (1H, s, H-2), 7.70 (1H, s, H-9), 7.73 (2H, d, J = 7.8, H-2′, H-6′), 8.23 (1H, s, H-4), 8.37 (1H, s, H-5).

3-*t*-Butyl-6-(4-fluorophenyl)furo[3,2-g]chromen-7-one (31): yield 83%, mp 205-206°C, $C_{21}H_{17}FO_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.44 [9H, s, $(CH_3)_3$], 7.24 (2H, t, J = 8.1, H-3′, H-5′), 7.58 (1H, s, H-2), 7.70 (1H, s, H-9), 7.78 (2H, m, H-2′, H-6′), 8.22 (1H, s, H-4), 8.38 (1H, s, H-5).

3-*t*-Butyl-6-(4-methoxyphenyl)furo[3,2-*g*]chromen-7-one (32): yield 87%, mp 219-220°C, $C_{22}H_{20}O_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.44 [9H, s, $(CH_3)_3$], 3.82 (3H, s, CH_3O-4′), 7.00 (2H, d, J = 8.7, H-3′, H-5′), 7.56 (1H, s, H-2), 7.68 (2H, d, J = 8.7, H-2′, H-6′), 7.69 (1H, s, H-9), 8.19 (1H, s, H-4), 8.30 (1H, s, H-5).

6-(4-Chlorophenyl)-3-phenylfuro[3,2-*g*]chromen-7-one (33): yield 81%, mp 246-247°C, $C_{23}H_{13}ClO_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.40-7.54 (5H, m, H-3′, H-5′, H-3″, H-4″, H-5″), 7.69 (1H, s, H-9), 7.76 (4H, d, J = 8.1, H-2′, H-6′, H-2″, H-6″), 8.32 (1H, s, H-4), 8.38 (1H, s, H-5), 8.43 (1H, s, H-2).

6-(3,4-Dimethoxyphenyl)-3-phenylfuro[3,2-*g*]chromen-7-one (34): yield 86%, mp 232-233°C, $C_{25}H_{18}O_5$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.82 and 3.83 (6H, 2s, CH_3O-3′, CH_3O-4′), 7.00 (1H, d, J = 8.7, H-5′), 7.33 (2H, m, H-2′, H-6′), 7.41 (1H, m, H-4″), 7.52 (2H, t, J = 7.5, H-3″, H-5″), 7.70 (1H, s, H-9), 7.77 (2H, d, J = 7.5, H-2″, H-6″), 8.31 (1H, s, H-4), 8.34 (1H, s, H-5), 8.38 (1H, s, H-2).

3-(4-Methylphenyl)-6-phenylfuro[3,2-*g*]chromen-7-one (35): yield 78%, mp 239-240°C, $C_{24}H_{16}O_3$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.40 (3H, s, CH_3-4″), 7.32 (2H, d, J = 8.1, H-3″, H-5″), 7.43 (3H, m, H-3′, H-4′, H-5′), 7.64 (2H, d, J = 8.1, H-2′, H-6′), 7.69 (1H, s, H-9), 7.73 (2H, d, J = 8.1, H-2″, H-6″), 8.31 (1H, s, H-4), 8.33 (1H, s, H-5), 8.39 (1H, s, H-2).

3-(4-Fluorophenyl)-6-(4-methoxyphenyl)furo[3,2-*g*]chromen-7-one (36): yield 75%, mp 246-247°C, $C_{24}H_{15}FO_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.82 (3H, s, CH_3O-4′), 7.00 (2H, d, J = 8.7, H-3′, H-5′), 7.31 (2H, t, J = 8.7, H-3″, H-5″), 7.68 (2H, d, J = 8.7, H-2′, H-6′), 7.71 (1H, s, H-9), 7.78 (2H, m, H-2″, H-6″), 8.29 (1H, s, H-4), 8.30 (1H, s, H-5), 8.37 (1H, s, H-2).

3-(3-Methoxyphenyl)-6-phenylfuro[3,2-*g*]chromen-7-one (37): yield 83%, mp 247-248°C, $C_{24}H_{16}O_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.87 (3H, s, CH_3O-3″), 6.96 (1H, dd, J = 2.1, 8.7, H-4″), 7.27-7.32 (2H, m, H-2″, H-6″), 7.42 (1H, t, J = 8.7, H-5″), 7.47 (3H, m, H-3′, H-4′, H-5′), 7.71 (1H, s, H-9), 7.73 (2H, d, J = 8.7, H-2′, H-6′), 8.34 (1H, s, H-4), 8.40 (1H, s, H-5), 8.43 (1H, s, H-2).

6-(4-Chlorophenyl)-3-(3-methoxyphenyl)furo[3,2-*g*]chromen-7-one (38): yield 79%, mp 254-255°C, $C_{24}H_{15}ClO_4$.

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.87 (3H, s, CH_3O-3″), 6.96 (1H, dd, J = 2.1, 8.7, H-4″), 7.27-7.32 (2H, m, H-2″, H-6″), 7.42 (1H, t, J = 8.7, H-5″), 7.48 (2H, d, J = 8.7, H-3′, H-5′), 7.71 (1H, s, H-9), 7.77 (2H, d, J = 8.7, H-2′, H-6′), 8.34 (1H, s, H-4), 8.41 (1H, s, H-5), 8.48 (1H, s, H-2).

ACKNOWLEDGMENT

We thank OAO Eximed (Kiev, Ukraine) for help in performing the work.

REFERENCES

1. R. D. H. Murray, *The Naturally Occurring Coumarins*, Springer, Vienna-New York (2002).
2. L. Santana, E. Uriarte, F. Roleira, N. Milhazes, and F. Borges, *Curr. Med. Chem.*, **11**, 3239 (2004).
3. L. B. Norton and R. Hansberry, *J. Am. Chem. Soc.*, **67**, 1609 (1945).
4. E. Simonitsch, H. Frei, and H. Schmid, *Monatsh. Chem.*, **88**, 541 (1957).
5. A. Phrutivorapongkul, V. Lipipun, N. Ruangrungsi, T. Watanabe, and T. Ishikawa, *Chem. Pharm. Bull.*, **50**, 534 (2002).

6. A. F. Magalhaes, B. H. L. N. Sales, E. G. Magalhaes, and I. F. M. Valio, *Phytochemistry*, **31**, 1831 (1992).
7. L. Crombie and D. A. Whiting, *J. Chem. Soc.*, 1569 (1963).
8. B. L. Van Duuren and P. W. G. Groenewoud, *J. S. Afr. Chem. Inst.*, **3**, 29 (1950).
9. C. Abrams, C. van der M. Brink, and D. H. Meiring, *J. S. Afr. Chem. Inst.*, **15**, 78 (1962).
10. B. L. Van Duuren, *J. Org. Chem.*, **26**, 5013 (1961).
11. C. van der M. Brink, W. Nel, G. J. H. Rall, J. C. Weitz, and K. G. R. Rachler, *J. S. Afr. Chem. Inst.*, **19**, 24 (1966).
12. S. Kirkiacharian, A. T. Lormier, M. Resche-Rigon, F. Bouchoux, and E. Cerede, *Ann. Pharm. Fr.*, **61**, 51 (2003).
13. J. K. MacLeod, B. R. Woth, and R. J. Wells, *Aust. J. Chem.*, **31**, 1533 (1978).
14. A. K. Das Gupta, K. R. Das, and A. Das Gupta, *Indian J. Chem.*, **10**, 32 (1972).
15. G. Bargellini, *Gazz. Chim. Ital.*, **57**, 461 (1927).
16. W. Baker, *J. Chem. Soc.*, 2898 (1927).
17. G. N. Walker, *J. Am. Chem. Soc.*, **80**, 645 (1958).
18. B. B. Dey and K. K. Row, *J. Indian Chem. Soc.*, **1**, 117 (1923/1924).
19. P. R. Bhandari, J. L. Bose, and S. Siddiqui, *J. Sci. Ind. Res., Sect. B*, **8**, 189 (1949).
20. N. R. Krishnaswamy, T. R. Seshadri, and B. R. Sharma, *Indian J. Chem.*, **4**, 120 (1966).
21. A. K. Das Gupta and M. S. Paul, *J. Indian Chem. Soc.*, **47**, 1017 (1970).
22. V. F. Traven, L. I. Vorobjeva, T. A. Chibisova, E. A. Carberry, and N. J. Beyer, *Can. J. Chem.*, **75**, 365 (1997).
23. Ng. Ph. Buu-Hoi, B. Ekert, and R. Royer, *J. Org. Chem.*, **19**, 1548 (1954).
24. I. C. Badhwar, W. Baker, B. K. Menon, and K. Venkatraman, *J. Chem. Soc.*, 1541 (1931).
25. P. L. Sawhney and T. R. Seshadri, *J. Sci. Ind. Res., Sect. B*, **13**, 316 (1954).
26. S. Neelakantan, P. V. Raman, and A. Tinabaye, *Indian J. Chem., Sect. B*, **21**, 256 (1982).
27. H. Meerwein, E. Buechner, and K. van Emster, *J. Prakt. Chem.*, **152**, 237 (1939).
28. B. Vittal Rao and V. V. Somayajulu, *Indian J. Chem., Sect. B*, **19**, 232 (1980).