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# MODIFIED COUMARINS. 34. SYNTHESIS AND TRANSFORMATIONS OF ANGULAR α-PYRONOFLAVANONES

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*Syntheses of angular α-pyronoflavanones were described. Their reactions with nucleophiles were studied.*

**Keywords:** coumarins, flavonoids, flavanones, α-pyronoflavanones, pyrazolines, heterocyclization.

Flavonoids are the most broadly distributed natural compounds of plant origin and occur in practically all species. The flavonoid class currently numbers about 6,500 natural compounds [1]. The heightened interest in flavonoids is due to the important role these compounds play in plant and animal metabolism and their high and varied biological activity [2]. Flavonoids are subdivided into several types, the most common of which are flavanones, the structures of which are based on the 2-arylchromane skeleton. The coumarin core is also included in the structures of many important natural compounds [3] and substances with high pharmacological activity [4]. Therefore, the combination in a single molecule of the flavanone and coumarin cores seems interesting for both flavonoid and coumarin chemistry and targeted synthesis of new biologically active compounds. Herein we present results for the synthesis of angular α-pyronoflavanones and the study of their reactions with nucleophiles.

5-Hydroxy-7-methylcoumarins **1**–**4** were required for further transformations and were prepared via a Pechmann reaction of orcinol and the appropriate ethylacylacetates in the presence of a condensing agent (conc. $H_2SO_4$). Acetylation of hydroxycoumarins **1**–**4** by acetic anhydride in Py formed 5-acetoxycoumarins **5**–**8**, Fries rearrangement of which in the presence of anhydrous $AlCl_3$ at 120–130°C afforded in high yields 6-acetylcoumarins **9**–**12**.

Reactions of **9**–**12** and aromatic aldehydes with heating in EtOH in the presence of catalytic amounts of pyrrolidine led to annelation of a 2-aryltetrahydropyran-4-one ring and formation of 2-aryl-10-alkyl-5-methyl-2,3-dihydropyrano [2,3-*f*]chromen-4,8-diones **13**–**35** [5, 6]. Obviously, the angular α-pyronoflavanones formed via the corresponding intermediate chalcones, which heterocyclized smoothly under the synthetic conditions. PMR spectra of **13**–**35** showed resonances for H-2 (5.59–6.16 ppm, dd, J = 2.4 and 13.6 Hz), equatorial H-3 (2.66–2.83 ppm, dd, J = 2.4 and 16.8 Hz), and axial H-3 (3.20–3.51 ppm, dd, J = 13.6 and 16.8 Hz), which were characteristic resonances for flavanone protons [7, 8].

Hydrazine is known to react with flavanones to give various compounds depending on the reaction conditions. In particular, the principal products can be hydrazones of flavanones, 3-(2-hydroxyphenyl)-5-phenylpyrazolines, or azines of flavanones [9, 10]. We found that the flavanone core recyclized upon heating EtOH solutions of **13**–**35** with a five-fold excess of hydrazine hydrate and formed 6-[5-aryl-4,5-dihydropyrazol-3-yl]-4-alkyl-5-hydroxy-7-methylcoumarins **36**–**47**, the PMR spectra of which contained resonances characteristic of the coumarin and pyrazoline moieties [11]. In particular, the methylene diastereotopic protons resonated at 3.09–3.45 and 3.72–3.88 ppm (dd, J = 10.4 and 16.4 Hz) whereas pyrazoline H-5 was observed as a multiplet at 4.75–5.43 ppm. A characteristic feature of the PMR spectra of **36**–**47** was the separate absorption of the NH and OH protons. The NH proton appeared as a doublet with SSCC J = 3.6 Hz in the range 7.60–7.82 ppm. The presence of the hydroxyl proton resonance at weak field (13.65–14.05 ppm) was indicative of an intramolecular interaction between it and the pyrazoline N atom. Compounds **36**–**47** gave a characteristic brownish-green chelate complex in an EtOH solution of $FeCl_3$ because of the coumarin phenol hydroxyl and the pyrazoline N atom.

The reaction of **25** and phenylhydrazine in EtOH did not involve recyclization even with prolonged heating but formed the corresponding phenylhydrazone of α-pyronoflavanone **48**.

The reaction of **25** and hydroxylamine in Py also did not involve recyclization but gave the corresponding oxime of α-pyronoflavanone **49**.

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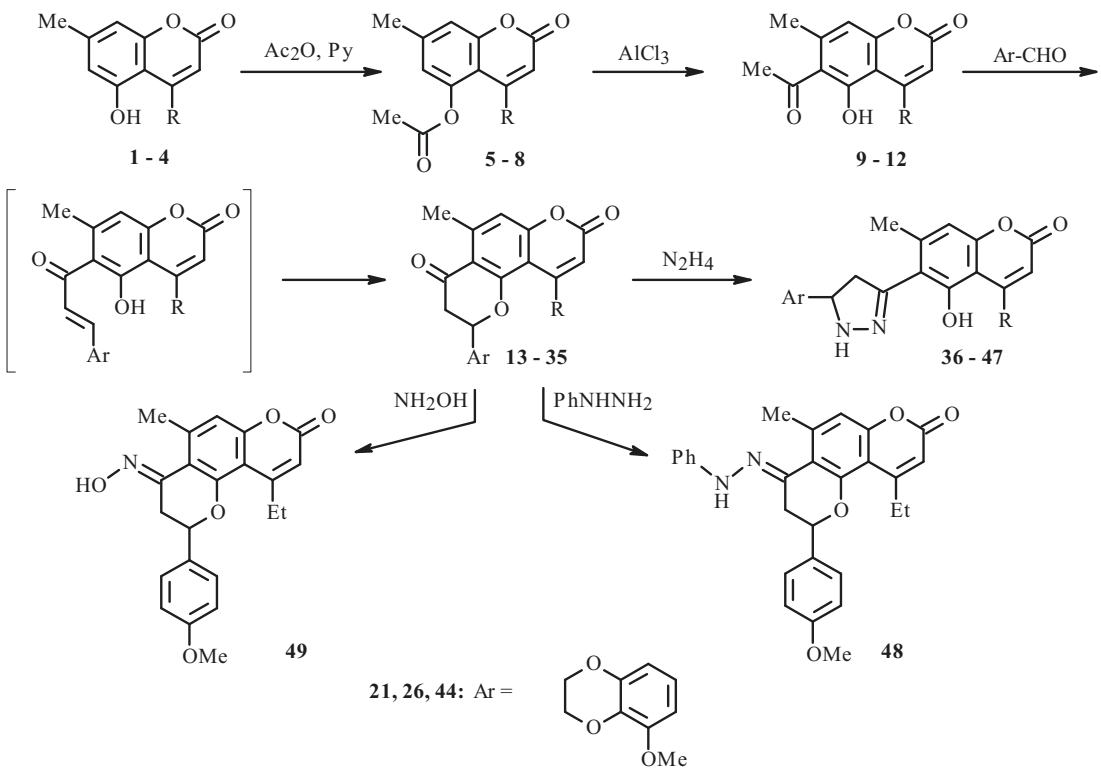


**1, 5, 9:** R = $CH_3$; **2, 6, 10:** R = $CH_2CH_3$; **3, 7, 11:** $CH_2CH_2CH_3$; **4, 8, 12:** $CH_2CH_2CH_2CH_3$; **13, 36**: R = $CH_3$, Ar = 4-$ClC_6H_4$
**14, 37:** R = $CH_3$, Ar = 4-$CH_3OC_6H_4$; **15, 38:** R = $CH_3$, Ar = 4-$(CH_3)_2NC_6H_4$; **16, 39:** R = $CH_3$, Ar = 2-$CH_3OC_6H_4$
**17, 40:** R = $CH_3$, Ar = 2,4-$(CH_3O)_2C_6H_3$; **18, 41:** R = $CH_3$, Ar = 2-Cl-6-$FC_6H_3$; **19, 42:** R = $CH_3$, Ar = 2,3,4-$(CH_3O)_3C_6H_2$
**20, 43:** R = $CH_3$, Ar = 2,4,5-$(CH_3O)_3C_6H_2$; **22, 45:** $CH_2CH_3$, Ar = 4-$ClC_6H_4$; **21, 44:** R = $CH_3$; Ar = X
**23, 46:** R = $CH_2CH_3$, Ar = 4-$CH_3OC_6H_4$ **24, 47:** R = $CH_2CH_3$, Ar = 4-$(CH_3)_2NC_6H_4$; **25:** R = $CH_2CH_3$, Ar = 3-HO-4-$CH_3OC_6H_3$
**26:** R = $CH_2CH_3$, Ar = X; **27:** $CH_2CH_2CH_3$, Ar = 4-$CH_3C_6H_4$ **28:** R = $CH_2CH_2CH_3$, Ar = 4-$CH_3OC_6H_4$
**29:** R = $CH_2CH_2CH_3$, Ar = 4-$(CH_3)_2NC_6H_4$; **30:** R = $CH_2CH_2CH_3$, Ar = 2,4-$(CH_3O)_2C_6H_3$
**31:** $CH_2CH_2CH_3$, Ar = 2,3,4-$(CH_3O)_3C_6H_2$; **32:** R = $CH_2CH_2CH_2CH_3$, Ar = 3,4-$(CH_3O)_2C_6H_3$;
**33:** R = $CH_2CH_2CH_2CH_3$, Ar = 4-HO-3-$CH_3OC_6H_3$ **34:** R = $CH_2CH_2CH_2CH_3$, Ar = 4-HO-3,5-$(CH_3O)_2C_6H_3$
**35:** R = $CH_2CH_2CH_2CH_3$, Ar = 2,3,4-$(CH_3O)_3C_6H_2$

## EXPERIMENTAL

**General.** 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). Melting points were measured on a Kofler apparatus. NMR spectra were recorded relative to TMS internal standard on a Varian Mercury 400 spectrometer at 400 MHz. Elemental analyses of all compounds agreed with those calculated.

Coumarins **1**–**12** were obtained as before [12].

**2-Aryl-10-alkyl-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-diones (13–35).** A mixture of 6-acetyl-5-hydroxycoumarin (**9**–**12**, 4 mmol) and the appropriate aromatic aldehyde (4.8 mmol) in EtOH was refluxed for 5–6 h in the presence of catalytic amounts (1–2 drops) of pyrrolidine (end of reaction determined by TLC). The reaction mixture was cooled. The resulting precipitate was filtered off and crystallized from EtOH.

**2-(4-Chlorophenyl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (13).** Yield 74%, mp 211–212°C, $C_{20}H_{15}ClO_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.42 (3H, s, $CH_3$-10), 2.65 (3H, s, $CH_3$-5), 2.83 (1H, dd, J = 2.4, 16.8, H-$3_{eq}$), 3.24 (1H, dd, J = 13.6, 16.8, H-$3_{ax}$), 5.78 (1H, dd, J = 2.4, 13.6, H-2), 6.23 (1H, s, H-9), 6.93 (1H, s, H-6), 7.53 (2H, d, J = 8.4, H-3′, 5′), 7.63 (2H, d, J = 8.4, H-2′, 6′).

**2-(4-Methoxyphenyl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (14).** Yield 63%, mp 197–197°C, $C_{21}H_{18}O_5$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.43 (3H, s, $CH_3$-10), 2.62 (3H, s, $CH_3$-5), 2.81 (1H, dd,

J = 2.4, 16.8, H-3$_{eq}$), 3.23 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.80 (3H, s, OCH$_3$-4′), 5.69 (1H, dd, J = 2.4, 13.6, H-2), 6.20 (1H, s, H-9), 6.90 (1H, s, H-6), 7.02 (2H, d, J = 8.4, H-3′, 5′), 7.52 (2H, d, J = 8.4, H-2′, 6′).

**2-[4-(Dimethylamino)phenyl]-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (15).** Yield 59%, mp 229–230°C, $C_{22}H_{21}NO_4$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.41 (3H, s, CH$_3$-10), 2.65 (3H, s, CH$_3$-5), 2.76 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 2.93 (6H, s, N(CH$_3$)$_2$), 3.21 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 5.59 (1H, dd, J = 2.4, 13.6, H-2), 6.17 (1H, s, H-9), 6.76 (2H, d, J = 8.0, H-3′, 5′), 6.87 (1H, s, H-6), 7.37 (2H, d, J = 8.0, H-2′, 6′).

**2-(2-Methoxyphenyl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (16).** Yield 62%, mp 188–189°C, $C_{21}H_{18}O_5$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.45 (3H, s, CH$_3$-10), 2.65 (3H, s, CH$_3$-5), 2.79 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.20 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.84 (3H, s, OCH$_3$-2′), 5.91 (1H, dd, J = 2.4, 13.6, H-2), 6.23 (1H, s, H-9), 6.93 (1H, s, H-6), 7.07 (1H, t, J = 7.6, H-5′), 7.12 (2H, d, J = 8.4, H-3′), 7.41 (1H, t, J = 7.6, H-4′), 7.59 (2H, d, J = 8.0, H-6′).

**2-(2,4-Dimethoxyphenyl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (17).** Yield 76%, mp 201–202°C, $C_{22}H_{20}O_6$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.44 (3H, s, CH$_3$-10), 2.67 (3H, s, CH$_3$-5), 2.79 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.26 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.82 and 3.84 (6H, two s, OCH$_3$-2′, 4′), 5.83 (1H, dd, J = 2.4, 13.6, H-2), 6.19 (1H, s, H-9), 6.61 (2H, dd, J = 2.4, 8.4, H-5′), 6.66 (2H, d, J = 2.4, H-3′), 6.90 (1H, s, H-6), 7.47 (2H, d, J = 8.4, H-6′).

**2-(2-Chloro-6-fluorophenyl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (18).** Yield 81%, mp 221–222°C, $C_{20}H_{14}ClFO_5$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.36 (3H, s, CH$_3$-10), 2.66 (3H, s, CH$_3$-5), 2.84 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.51 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 6.16 (1H, dd, J = 2.4, 13.6, H-2), 6.22 (1H, s, H-9), 6.95 (1H, s, H-6), 7.39–7.56 (3H, m, H-3′, 4′, 5′).

**5,10-Dimethyl-2-(2,3,4-trimethoxyphenyl)-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (19).** Yield 85%, mp 194–196°C, $C_{23}H_{22}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.43 (3H, s, CH$_3$-10), 2.67 (3H, s, CH$_3$-5), 2.70 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.25 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.80 and 3.85 (9H, two s, OCH$_3$-2′, 3′, 4′), 5.83 (1H, dd, J = 2.4, 13.6, H-2), 6.20 (1H, s, H-9), 6.91 (1H, s, H-6), 6.92 (2H, d, J = 8.8, H-5′), 7.32 (2H, d, J = 8.8, H-6′).

**5,10-Dimethyl-2-(2,4,5-trimethoxyphenyl)-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (20).** Yield 72%, mp 198–199°C, $C_{23}H_{22}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.45 (3H, s, CH$_3$-10), 2.65 (3H, s, CH$_3$-5), 2.68 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.24 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.74, 3.82 and 3.84 (9H, three s, OCH$_3$-2′, 4′, 5′), 5.83 (1H, dd, J = 2.4, 13.6, H-2), 6.22 (1H, s, H-9), 6.78 (2H, s, H-3′), 6.92 (1H, s, H-6), 7.20 (2H, s, H-6′).

**2-(8-Methoxy-1,4-benzodioxan-6-yl)-5,10-dimethyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (21).** Yield 74%, mp 201–202°C, $C_{23}H_{20}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.46 (3H, s, CH$_3$-10), 2.64 (3H, s, CH$_3$-5), 2.76 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 3.26 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.76 (3H, s, OCH$_3$-8′), 4.24 (4H, s, CH$_2$-2′, 3′), 5.60 (1H, dd, J = 2.4, 13.6, H-2), 6.22 (1H, s, H-9), 6.71 (2H, s, H-5′), 6.84 (2H, s, H-7′), 6.91 (1H, s, H-6).

**2-(4-Chlorophenyl)-10-ethyl-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (22).** Yield 71%, mp 191–192°C, $C_{21}H_{17}ClO_4$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.02 (3H, t, J = 7.2, CH$_3$-2′), 2.66 (3H, s, CH$_3$-5), 2.75–2.85 (3H, m, H-3$_{eq}$, CH$_2$-1′), 3.23 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 5.71 (1H, dd, J = 2.4, 13.6, H-2), 6.11 (1H, s, H-9), 6.86 (1H, s, H-6), 7.45 (2H, d, J = 8.4, H-3″, 5″), 7.58 (2H, d, J = 8.4, H-3″, 5″).

**10-Ethyl-2-(4-methoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (23).** Yield 63%, mp 159–160°C, $C_{22}H_{20}O_5$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, CH$_3$-2′), 2.68 (3H, s, CH$_3$-5), 2.74 (1H, dd, J = 2.8, 16.8, H-3$_{eq}$), 2.78–2.85 (2H, m, CH$_2$-1′), 3.21 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.82 (3H, s, OCH$_3$-4″), 5.60 (1H, dd, J = 2.8, 13.6, H-2), 6.08 (1H, s, H-9), 6.83 (1H, s, H-6), 6.95 (2H, d, J = 8.4, H-3″, 5″), 7.46 (2H, d, J = 8.4, H-3″, 5″).

**2-(4-Dimethylaminophenyl)-10-ethyl-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (24).** Yield 78%, mp 193–194°C, $C_{23}H_{23}NO_4$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.05 (3H, t, J = 7.2, CH$_3$-2′), 2.66 (3H, s, CH$_3$-5), 2.70 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 2.76–2.84 (2H, m, CH$_2$-1′), 2.97 (6H, s, (CH$_3$)$_2$N), 3.23 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 5.52 (1H, dd, J = 2.4, 13.6, H-2), 6.09 (1H, s, H-9), 6.72 (2H, d, J = 8.4, H-3″, 5″), 6.83 (1H, s, H-6), 7.34 (2H, d, J = 8.4, H-3″, 5″).

**10-Ethyl-2-(3-hydroxy-4-methoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (25).** Yield 56%, mp 210–211°C, $C_{22}H_{20}O_6$. $^1$H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, CH$_3$-2′), 2.66 (3H, s, CH$_3$-5), 2.70 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 2.76–2.84 (2H, m, CH$_2$-1′), 3.25 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.82 (3H, s, OCH$_3$-4″), 5.62 (1H, dd, J = 2.4, 13.6, H-2), 6.18 (1H, s, H-9), 6.91 (1H, s, H-6), 6.97–7.01 (3H, m, H-2″, 5″, 6″), 8.95 (1H, br.s, OH-3″).

**10-Ethyl-2-(8-methoxy-1,4-benzodioxan-6-yl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (26).** Yield 76%, mp 206–207°C, $C_{24}H_{22}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 1.07 (3H, t, J = 7.2, $CH_3$-2′), 2.65 (3H, s, $CH_3$-5), 2.70 (1H, dd, J = 2.4, 16.8, H-3$_{eq}$), 2.76–2.86 (2H, m, $CH_2$-1′), 3.25 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 3.79 (3H, s, $OCH_3$-8″), 4.25 (4H, s, $CH_2$-2″, 3″), 5.59 (1H, dd, J = 2.4, 13.6, H-2), 6.18 (1H, s, H-9), 6.71 (1H, s, H-5″), 6.83 (1H, s, H-7″), 6.90 (1H, s, H-6).

**5-Methyl-2-(4-methylphenyl)-10-propyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (27).** Yield 82%, mp 177–178°C, $C_{23}H_{22}O_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.58 (3H, t, J = 7.2, $CH_3$-3′), 1.35–1.45 (2H, m, $CH_2$-2′), 2.39 (3H, s, $CH_3$-4″), 2.62–2.70 (2H, m, $CH_2$-1′), 2.68 (3H, s, $CH_3$-5), 2.74 (1H, dd, J = 2.8, 16.8, H-3$_{eq}$), 3.21 (1H, dd, J = 13.6, 16.8, H-3$_{ax}$), 5.59 (1H, dd, J = 2.8, 13.6, H-2), 6.05 (1H, s, H-9), 6.84 (1H, s, H-6), 7.23 (2H, d, J = 8.4, H-3″, 5″), 7.42 (2H, d, J = 8.4, H-2″, 6″).

**2-(4-Methoxyphenyl)-5-methyl-10-propyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (28).** Yield 64%, mp 181–182°C, $C_{23}H_{22}O_5$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.50 (3H, t, J = 7.2, $CH_3$-3′), 1.40–1.48 (2H, m, $CH_2$-2′), 2.62–2.75 (3H, m, H-3$_{eq}$, $CH_2$-1′), 2.70 (3H, s, $CH_3$-5), 3.40 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.80 (3H, s, $OCH_3$-4″), 5.67 (1H, dd, J = 2.0, 13.6, H-2), 6.18 (1H, s, H-9), 6.94 (1H, s, H-6), 7.30 (2H, d, J = 8.8, H-3″, 5″), 7.54 (2H, d, J = 8.8, H-2″, 6″).

**2-(4-Dimethylaminophenyl)-5-methyl-10-propyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (29).** Yield 76%, mp 181–182°C, $C_{24}H_{25}NO_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.53 (3H, t, J = 7.2, $CH_3$-3′), 1.38–1.45 (2H, m, $CH_2$-2′), 2.62–2.75 (3H, m, H-3$_{eq}$, $CH_2$-1′), 2.65 (3H, s, $CH_3$-5), 2.93 (6H, s, $(CH_3)_2$N), 3.35 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 5.57 (1H, dd, J = 2.0, 13.6, H-2), 6.15 (1H, s, H-9), 6.77 (2H, d, J = 8.8, H-3″, 5″), 6.90 (1H, s, H-6), 7.39 (2H, d, J = 8.8, H-2″, 6″).

**2-(2,4-Dimethoxyphenyl)-5-methyl-10-propyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (30).** Yield 81%, mp 178–179°C, $C_{24}H_{24}O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.56 (3H, t, J = 7.2, $CH_3$-3′), 1.35–1.42 (2H, m, $CH_2$-2′), 2.65 (3H, s, $CH_3$-5), 2.65–2.75 (3H, m, H-3$_{eq}$, $CH_2$-1′), 3.42 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.81 and 3.82 (6H, two s, $OCH_3$-2″, 4″), 5.83 (1H, dd, J = 2.4, 13.6, H-2), 6.17 (1H, s, H-9), 6.62 (2H, dd, J = 2.4, 8.4, H-5″), 6.66 (2H, d, J = 2.4, H-3″), 6.92 (1H, s, H-6), 7.50 (2H, d, J = 8.4, H-6″).

**5-Methyl-10-propyl-2-(3,4,5-trimethoxyphenyl)- 2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (31).** Yield 81%, mp 172–173°C, $C_{25}H_{26}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.50 (3H, t, J = 7.2, $CH_3$-3′), 1.38–1.45 (2H, m, $CH_2$-2′), 2.63–2.78 (3H, m, H-3$_{eq}$, $CH_2$-1′), 2.65 (3H, s, $CH_3$-5), 3.46 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.68 (3H, s, $OCH_3$-4″), 3.81 (6H, s, $OCH_3$-3″, 5″), 5.63 (1H, dd, J = 2.4, 13.6, H-2), 6.19 (1H, s, H-9), 6.93 (1H, s, H-6), 6.96 (2H, s, H-2″, 6″).

**10-Butyl-2-(3,4-dimethoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (32).** Yield 59%, mp 169–170°C, $C_{25}H_{26}O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.65 (3H, t, J = 7.2, $CH_3$-4′), 0.76–0.95 (2H, m, $CH_2$-3′), 1.24–1.38 (2H, m, $CH_2$-2′), 2.66 (3H, s, $CH_3$-5), 2.67–2.78 (3H, m, H-3$_{eq}$, $CH_2$-1′), 3.48 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.78 and 3.79 (6H, two s, $OCH_3$-3″, 4″), 5.65 (1H, dd, J = 2.4, 13.6, H-2), 6.18 (1H, s, H-9), 6.95 (1H, s, H-6), 7.02 (1H, d, J = 8.0, H-5″), 7.02 (1H, dd, J = 2.0, 8.0, H-6″), 7.26 (1H, d, J = 2.0, H-2″).

**10-Butyl-2-(4-hydroxy-3-methoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (33).** Yield 68%, mp 178–179°C, $C_{24}H_{24}O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.66 (3H, t, J = 7.2, $CH_3$-4′), 0.75–0.92 (2H, m, $CH_2$-3′), 1.26–1.39 (2H, m, $CH_2$-2′), 2.66 (3H, s, $CH_3$-5), 2.66–2.75 (3H, m, H-3$_{eq}$, $CH_2$-1′), 3.46 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.80 (3H, s, $OCH_3$-3″), 5.62 (1H, dd, J = 2.4, 13.6, H-2), 6.18 (1H, s, H-9), 6.76 (1H, d, J = 8.4, H-5″), 6.94 (1H, s, H-6), 7.03 (1H, dd, J = 2.0, 8.4, H-6″), 7.21 (1H, d, J = 2.0, H-2″), 9.21 (1H, s, OH-4″).

**10-Butyl-2-(4-hydroxy-3,5-dimethoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (34).** Yield 72%, mp 187–188°C, $C_{25}H_{26}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.66 (3H, t, J = 7.2, $CH_3$-4′), 0.72–0.94 (2H, m, $CH_2$-3′), 1.29–1.39 (2H, m, $CH_2$-2′), 2.66 (3H, s, $CH_3$-5), 2.66–2.74 (3H, m, H-3$_{eq}$, $CH_2$-1′), 3.48 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.79 (6H, s, $OCH_3$-3″, 5″), 5.59 (1H, dd, J = 2.4, 13.6, H-2), 6.19 (1H, s, H-9), 6.94 (1H, s, H-6), 6.91 (2H, s, H-2″, 6″), 8.55 (1H, s, OH-4″).

**10-Butyl-5-methyl-2-(2,3,4-trimethoxyphenyl)-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione (35).** Yield 59%, mp 169–170°C, $C_{25}H_{26}O_7$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 0.64 (3H, t, J = 7.2, $CH_3$-4′), 0.78–0.92 (2H, m, $CH_2$-3′), 1.26–1.32 (2H, m, $CH_2$-2′), 2.66 (3H, s, $CH_3$-5), 2.66–2.75 (3H, m, H-3$_{eq}$, $CH_2$-1′), 3.42 (1H, dd, J = 14.0, 16.4, H-3$_{ax}$), 3.79, 3.83 and 3.84 (9H, three s, $OCH_3$-2″, 3″, 4″), 5.84 (1H, dd, J = 2.4, 13.6, H-2), 6.18 (1H, s, H-9), 6.93 (2H, d, J = 8.4, H-5″), 6.94 (1H, s, H-6), 7.36 (2H, d, J = 8.4, H-6″).

**6-[5-Aryl-4,5-dihydropyrazol-3-yl]-4-alkyl-5-hydroxy-7-methylchromen-2-ones (36–47).** A mixture of **13**–**35** (2 mmol) and hydrazine monohydrate (0.50 mL, 10 mmol) in EtOH was refluxed for 2–3 h (end of reaction determined by TLC). The reaction mixture was cooled. The resulting precipitate was filtered off and crystallized from EtOH.

**6-[5-(4-Chlorophenyl)-4,5-dihydropyrazol-3-yl]-5-hydroxy-4,7-dimethylchromen-2-one (36).** Yield 58%, mp 231–232°C, $C_{20}H_{17}ClN_2O_3$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.48 (3H, s, $CH_3$-7), 2.61 (3H, s, $CH_3$-4), 3.15 (1H, dd, J = 10.4, 16.4, H-4′a), 3.80 (1H, dd, J = 10.4, 16.4, H-4′b), 4.88 (1H, m, H-5′), 6.11 (1H, s, H-3), 6.71 (1H, s, H-8), 7.43 (2H, d, J = 8.4, H-3″, 5″), 7.47 (2H, d, J = 8.4, H-2″, 6″), 7.82 (1H, d, J = 3.6, NH), 13.65 (1H, s, OH-5).

**5-Hydroxy-6-[5-(4-methoxyphenyl)-4,5-dihydropyrazol-3-yl]- 4,7-dimethylchromen-2-one (37).** Yield 52%, mp 218–219°C, $C_{21}H_{20}N_2O_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.49 (3H, s, $CH_3$-7), 2.61 (3H, s, $CH_3$-4), 3.17 (1H, dd, J = 10.4, 16.4, H-4′a), 3.74 (3H, s, $OCH_3$-4″), 3.75 (1H, dd, J = 10.4, 16.4, H-4′b), 4.81 (1H, m, H-5′), 6.13 (1H, s, H-3), 6.72 (1H, s, H-8), 6.93 (2H, d, J = 8.8, H-3″, 5″), 7.35 (2H, d, J = 8.8, H-2″, 6″), 7.80 (1H, d, J = 3.6, NH), 13.90 (1H, s, OH-5).

**6-[5-(4-Dimethylaminophenyl)-4,5-dihydropyrazol-3-yl]-5-hydroxy-4,7-dimethylchromen-2-one (38).** Yield 63%, mp 235–236°C, $C_{22}H_{23}N_3O_3$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.50 (3H, s, $CH_3$-7), 2.62 (3H, s, $CH_3$-4), 2.88 (6H, s, $(CH_3)_2N$), 3.16 (1H, dd, J = 10.4, 16.4, H-4′a), 3.73 (1H, dd, J = 10.4, 16.4, H-4′b), 4.75 (1H, m, H-5′), 6.14 (1H, s, H-3), 6.72 (1H, s, H-8), 6.72 (2H, d, J = 8.8, H-3″, 5″), 7.23 (2H, d, J = 8.8, H-2″, 6″), 7.71 (1H, d, J = 3.6, NH), 13.95 (1H, s, OH-5).

**5-Hydroxy-6-[5-(2-methoxyphenyl)-4,5-dihydropyrazol-3-yl]- 4,7-dimethylchromen-2-one (39).** Yield 52%, mp 219–220°C, $C_{21}H_{20}N_2O_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.48 (3H, s, $CH_3$-7), 2.60 (3H, s, $CH_3$-4), 3.09 (1H, dd, J = 10.4, 16.4, H-4′a), 3.78 (1H, dd, J = 10.4, 16.4, H-4′b), 3.83 (3H, s, $OCH_3$-2″), 5.06 (1H, m, H-5′), 6.11 (1H, s, H-3), 6.70 (1H, s, H-8), 6.97 (1H, t, J = 7.6, H-5′), 7.03 (2H, d, J = 8.4, H-3′), 7.28 (1H, t, J = 7.6, H-4′), 7.42 (2H, d, J = 8.0, H-6′), 7.68 (1H, d, J = 3.6, NH), 13.90 (1H, s, OH-5).

**6-[5-(2,4-Dimethoxyphenyl)-4,5-dihydropyrazol-3-yl]-5-hydroxy-4,7-dimethylchromen-2-one (40).** Yield 57%, mp 228–229°C, $C_{22}H_{22}N_2O_5$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.48 (3H, s, $CH_3$-7), 2.60 (3H, s, $CH_3$-4), 3.09 (1H, dd, J = 10.4, 16.4, H-4′a), 3.72 (1H, dd, J = 10.4, 16.4, H-4′b), 3.76 and 3.80 (6H, two s, $OCH_3$-2″, 4″), 4.98 (1H, m, H-5′), 6.12 (1H, s, H-3), 6.52 (2H, dd, J = 2.0, 8.0, H-5″), 6.58 (2H, d, J = 2.0, H-3″), 6.70 (1H, s, H-8), 7.30 (2H, d, J = 8.0, H-6′), 7.60 (1H, d, J = 3.6, NH), 13.94 (1H, s, OH-5).

**6-[5-(2-Chloro-6-fluorophenyl)-4,5-dihydropyrazol-3-yl]-5-hydroxy-4,7-dimethylchromen-2-one (41).** Yield 49%, mp 237–238°C, $C_{20}H_{16}FClN_2O_3$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.49 (3H, s, $CH_3$-7), 2.63 (3H, s, $CH_3$-4), 3.45 (1H, dd, J = 10.4, 16.4, H-4′a), 3.88 (1H, dd, J = 10.4, 16.4, H-4′b), 5.43 (1H, m, H-5′), 6.13 (1H, s, H-3), 6.73 (1H, s, H-8), 7.21–7.41 (3H, m, H-3″, 4″, 5″), 7.74 (1H, d, J = 3.6, NH), 13.75 (1H, s, OH-5).

**5-Hydroxy-4,7-dimethyl-6-[5-(2,3,4-trimethoxyphenyl)-4,5-dihydropyrazol-3-yl]-chromen-2-one (42).** Yield 48%, mp 219–220°C, $C_{23}H_{24}N_2O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.50 (3H, s, $CH_3$-7), 2.62 (3H, s, $CH_3$-4), 3.13 (1H, dd, J = 10.4, 16.4, H-4′a), 3.75 (1H, dd, J = 10.4, 16.4, H-4′b), 3.78, 3.79 and 3.83 (9H, three s, $OCH_3$-2″, 3″, 4″), 4.99 (1H, m, H-5′), 6.14 (1H, s, H-3), 6.73 (1H, s, H-8), 6.82 (2H, d, J = 8.8, H-5″), 7.14 (2H, d, J = 8.8, H-6″), 7.65 (1H, d, J = 3.6, NH), 13.93 (1H, s, OH-5).

**5-Hydroxy-4,7-dimethyl-6-[5-(2,4,5-trimethoxyphenyl)-4,5-dihydropyrazol-3-yl]-chromen-2-one (43).** Yield 54%, mp 227–228°C, $C_{23}H_{24}N_2O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.49 (3H, s, $CH_3$-7), 2.62 (3H, s, $CH_3$-4), 3.15 (1H, dd, J = 10.4, 16.4, H-4′a), 3.72 (1H, dd, J = 10.4, 16.4, H-4′b), 3.70 and 3.80 (9H, two s, $OCH_3$-2″, 3″, 4″), 5.02 (1H, m, H-5′), 6.14 (1H, s, H-3), 6.73 (2H, s, H-8, 3″), 7.05 (1H, s, H-6″), 7.65 (1H, d, J = 3.6, NH), 13.89 (1H, s, OH-5).

**5-Hydroxy-6-[5-(8-methoxy-1,4-benzodioxan-6-yl)-4,5-dihydropyrazol-3-yl]-4,7-dimethylchromen-2-one (44).** Yield 50%, mp 230–231°C, $C_{23}H_{22}N_2O_6$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 2.49 (3H, s, $CH_3$-7), 2.61 (3H, s, $CH_3$-4), 3.16 (1H, dd, J = 10.4, 16.4, H-4′a), 3.74 (1H, dd, J = 10.4, 16.4, H-4′b), 3.76 (3H, s, $OCH_3$-8″), 4.21 (4H, s, $CH_2$-2″, 3″), 4.78 (1H, m, H-5′), 6.13 (1H, s, H-3), 6.54 (2H, s, H-5″), 6.66 (2H, s, H-7″), 6.71 (1H, s, H-8), 7.77 (1H, d, J = 3.6, NH), 13.92 (1H, s, OH-5).

**6-[5-(4-Chlorophenyl)-4,5-dihydropyrazol-3-yl]-4-ethyl-5-hydroxy-7-methylchromen-2-one (45).** Yield 69%, mp 223–224°C, $C_{21}H_{19}ClN_2O_3$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 1.27 (3H, t, J = 7.2, $CH_3$-2′), 2.48 (3H, s, $CH_3$-7), 3.05 (2H, q, J = 7.2, $CH_2$-1′), 3.20–3.30 (1H, m, H-4″a), 3.79 (1H, dd, J = 10.4, 16.4, H-4″b), 4.87 (1H, m, H-5″), 6.00 (1H, s, H-3), 6.63 (1H, s, H-8), 7.34 (2H, d, J = 8.4, H-3‴, 5‴), 7.45 (2H, d, J = 8.4, H-2‴, 6‴), 7.72 (1H, d, J = 3.6, NH), 13.93 (1H, s, OH-5).

**4-Ethyl-5-hydroxy-6-[5-(4-methoxyphenyl)-4,5-dihydropyrazol-3-yl]-7-methylchromen-2-one (46).** Yield 54%, mp 221–222°C, $C_{22}H_{22}N_2O_4$. $^1$H NMR spectrum (400 MHz, $CCl_4$, δ, ppm, J/Hz): 1.29 (3H, t, J = 7.2, $CH_3$-2′), 2.48 (3H, s, $CH_3$-7), 3.05 (2H, q, J = 7.2, $CH_2$-1′), 3.20 (1H, dd, J = 10.0, 16.4, H-4″a), 3.64 (1H, dd, J = 10.4, 16.4, H-4″b), 3.78 (3H, s, $OCH_3$-4‴), 4.80 (1H, m, H-5″), 5.75 (1H, br.s, NH), 5.93 (1H, s, H-3), 6.54 (1H, s, H-8), 6.80 (2H, d, J = 8.4, H-3‴, 5‴), 7.24 (2H, d, J = 8.4, H-3‴, 5‴), 13.37 (1H, s, OH-5).

**6-[5-(4-Dimethylaminophenyl)-4,5-dihydropyrazol-3-yl]-5-hydroxy-7-methyl-4-propylchromen-2-one (47).** Yield 54%, mp 237–238°C, $C_{24}H_{27}N_3O_3$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 1.00 (3H, t, J = 7.2, $CH_3$-3′), 1.63 (2H, m, $CH_2$-2′), 2.48 (3H, s, $CH_3$-7), 2.88 (6H, s, $(CH_3)_2$N), 2.96 (2H, m, $CH_2$-1′), 3.18 (1H, dd, J = 10.4, 16.4, H-4″a), 3.74 (1H, dd, J = 10.4, 16.4, H-4″b), 4.75 (1H, m, H-5″), 6.11 (1H, s, H-3), 6.72 (2H, d, J = 8.8, H-3‴, 5‴), 6.73 (1H, s, H-8), 7.24 (2H, d, J = 8.8, H-2‴, 6‴), 7.73 (1H, d, J = 3.6, NH), 14.05 (1H, s, OH-5).

**10-Ethyl-2-(4-methoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione 4-phenylhydrazone (48).** A mixture of **25** (0.73 g, 2 mmol) and phenylhydrazine (0.50 mL, 5 mmol) in EtOH (5 mL) was refluxed for 8 h (end of reaction determined by TLC). The reaction mixture was cooled. The resulting precipitate was filtered off and crystallized from EtOH. Yield 81%, mp 248–249°C, $C_{28}H_{26}N_2O_4$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 1.05 (3H, t, J = 7.2, $CH_3$-2′), 2.72–2.86 (3H, m, H-3a, $CH_2$-1′), 2.83 (3H, s, $CH_3$-5), 3.51 (1H, dd, J = 2.8, 17.6, H-3b), 3.83 (3H, s, $OCH_3$-4″), 5.04 (1H, dd, J = 2.8, 12.4, H-2), 6.01 (1H, s, H-9), 6.72 (1H, t, J = 7.2, H-4‴), 6.88 (1H, s, H-6), 6.97 (2H, d, J = 8.8, H-3″, 5″), 7.10–7.20 (4H, m, H-2‴, 3‴, 5‴, H-6‴), 7.48 (2H, d, J = 8.8, H-3″, 5″), 9.20 (1H, s, NH).

**10-Ethyl-2-(4-methoxyphenyl)-5-methyl-2,3-dihydropyrano[2,3-*f*]chromen-4,8-dione 4-oxime (49).** A mixture of **25** (0.73 g, 2 mmol) and hydroxylamine hydrochloride (0.35 g, 5 mmol) in anhydrous Py (5 mL) was heated at 90–100°C for 8 h (end of reaction determined by TLC). The reaction mixture was cooled, transferred into $H_2O$ (100 mL), and acidified to pH 6–7. The resulting precipitate was filtered off and crystallized from EtOH. Yield 72%, mp 203–204°C, $C_{22}H_{21}NO_5$. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm, J/Hz): 1.03 (3H, t, J = 7.2, $CH_3$-2′), 2.64 (3H, s, $CH_3$-5), 2.72–2.86 (3H, m, H-3a, $CH_2$-1′), 3.42 (1H, dd, J = 3.2, 17.6, H-3b), 3.81 (3H, s, $OCH_3$-4″), 5.04 (1H, dd, J = 3.2, 12.4, H-2), 6.01 (1H, s, H-9), 6.84 (1H, s, H-6), 6.93 (2H, d, J = 8.4, H-3″, 5″), 7.41 (2H, d, J = 8.4, H-3″, 5″), 11.23 (1H, s, NOH).

## REFERENCES


1. J. B. Harborne and C. A. Williamson, *Phytochemistry*, **55**, 481 (2000).
2. B. H. Havsteen, *Pharmacol. Ther.*, **96**, 67 (2002).
3. R. D. H. Murray, *Progress in the Chemistry of Organic Natural Products.* Vol. 83, *The Naturally Occurring Coumarins*, Springer, Vienna, New York, 2002, 673 pp.
4. R. O'Kennedy and R. D. Thornes, *Coumarins – Biology, Applications and Mode of Action*, John Wiley & Sons Ltd., Chichester, 1997, 358 pp.
5. M. S. Y. Khan and P. Sharma, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, **32**, 374 (1993).
6. M. S. Y. Khan and S. Bawa, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, **40**, 1207 (2001).
7. T. J. Mabry, K. R. Markham, and M. B. Thomas, *The Systematic Identification of Flavonoids*, Springer-Verlag, New York, 1970, pp. 33–354.
8. J. B. Harborne, T. J. Mabry, and H. Mabry (eds.), *The Flavonoids*, Chapman and Hall, London, 1975, pp. 45–77.
9. F. Kallay, G. Janzso, and I. Koczor, *Tetrahedron*, **21**, 19 (1965).
10. F. Kallay, G. Janzso, and I. Koczor, *Tetrahedron*, **21**, 3037 (1965).
11. A. Voskiene, V. Mickevicius, and G. Mikulskiene, *ARKIVOC*, **XV**, 303 (2007).
12. I. V. Nagorichna, A. A. Tkachuk, M. M. Garazd, Ya. L. Garazd, and V. P. Khilya, *Chem. Nat. Compd.*, **45**, 152 (2009).