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2-R-7-HYDROXY-8-METHYL-3-(2-QUINOLYL)CHROMONES

T. V. Shokol, A. V. Turov, and V. P. Khilya

By condensation of 2-methyl resorcinol with 2-quinolyl acetonitrile, we have synthesized α-(2-quinolyl)-2,4-dihydroxy-3-methylacetophenone, which when reacted with carboxylic acid anhydrides followed by hydrolysis yields 2-R-7-hydroxy-8-methyl-3-(2-quinolyl)chromones.

Keywords: 2-R-7-acyloxy-8-methyl-3-(2-quinolyl)chromones, 2-R-7-hydroxy-8-methyl-3-(2-quinolyl)-chromones, α-(2-quinolyl)-2,4-dihydroxy-3-methylacetophenone.

Flavonoids and isoflavonoids play a special role among biologically active substances of natural origin. Heterocyclic analogs of these compounds are not encountered in nature; they are obtained synthetically. Among the large number of diverse 2- and 3-hetarylchromones, there are substances having a broad spectrum of biological activity [1-3]. However, chromones with quinoline substituents have been little studied.

The starting compounds for synthesis of 2-quinolylchromones are 2-hydroxyacetophenones. 2-(2-Quinolyl)chromone is synthesized in low overall yield (11%) by condensation of 2-hydroxyacetophenone with quinaldic acid chloride followed by a Baker–Venkataraman rearrangement to the 1,3-diketone and cyclodehydration [4]. The yield could be considerably improved by replacing the 2-hydroxyacetophenone by its dilithium salt [5]. Condensation of 2-hydroxyacetophenone with 2-quinolinecarboxaldehyde has been used to synthesize quinolylacrylophenones, which are converted to 2-(2-quinolyl)chromones upon oxidation by selenium dioxide or hydrogen peroxide, yielding respectively 3-unsubstituted or 3-hydroxy derivatives [6].

The starting compounds for synthesis of 3-quinolylchromones are α-(quinolyl)-2-hydroxyacetophenones obtained by condensation of resorcinol, 4-methylresorcinol, or orcinol with 2- and 8-quinolylacetonitriles under modified Hoesch reaction conditions, where boron trifluoride etherate was used as both the solvent and the catalyst at the same time [7, 8]. Condensation of α-(quinolyl)-2-hydroxyacetophenones with acetic anhydride in pyridine has been used to obtain 7-acetyl-2-methyl-3-quinolyl-substituted chromones, and condensation with ethyl orthoformate in pyridine in the presence of catalytic amounts of piperidine has been used to obtain the 2-unsubstituted products [7, 8]. A convenient and highly efficient method for synthesis of the latter is condensation of the starting α-(quinolyl)-2-hydroxyacetophenones with acetoformic anhydride in the presence of bases (sodium formate, triethylamine) [9-14] (Scheme 1).

Compounds with useful properties have already been found among the 2- and 3-quinolylchromones. Derivatives of 2-(2-quinolyl)chromones are anticancer agents. In particular, 6-chloro-2-(2-quinolyl)chromone exhibits activity against sarcoma 180 [15], while 5-amino-2-quinolylchromones and their salts inhibit growth of adenocarcinoma MCF 7 cells [16]. Glycosides of 3-(2-quinolyl)chromones are promising anti-inflammatory drugs [2].

Taras Shevchenko Kiev National University, Kiev 01033, Ukraine; e-mail: shokol_tv@mail.univ.kiev.ua, vkhilya@mail.univ.kiev.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 407-415, March, 2005. Original article submitted March 1, 2002.

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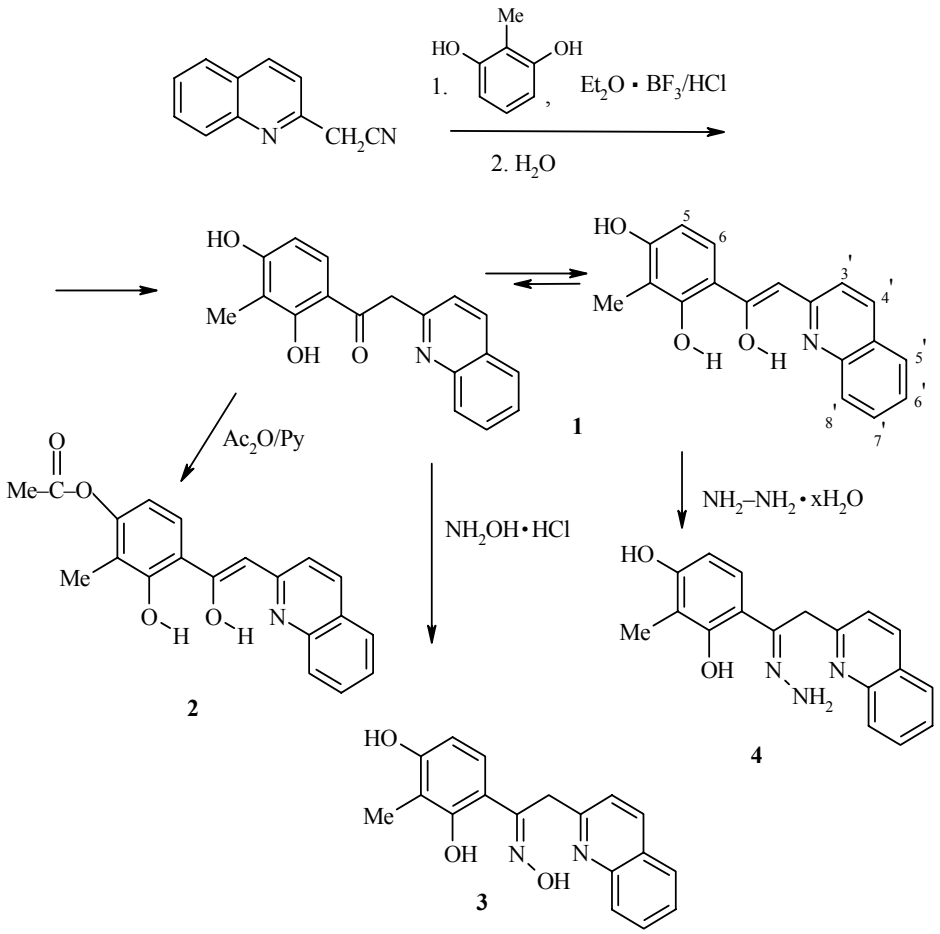
Scheme 1



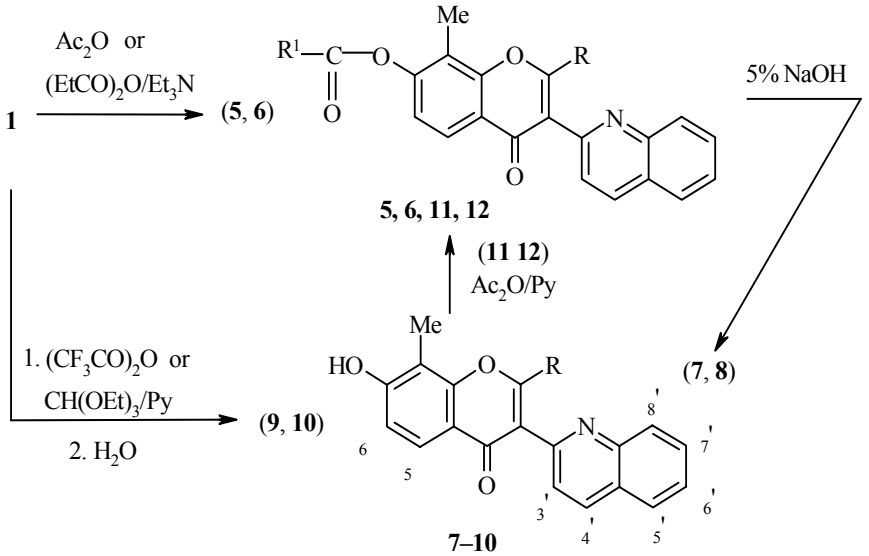
The facts indicated above encouraged us to continue a study of quinoline derivatives of chromones. This study has been devoted to synthesis of 2-R-8-methyl-3-(2-quinolyl)chromones. With this aim, we carried out a Hoesch reaction between 2-quinolylacetonitrile in boron trifluoride etherate and 2-methylresorcinol. After hydrolysis, we isolated the key product α-(2-quinolyl)-2,4-dihydroxy-3-methylacetophenone (**1**), which can exist in two forms: the ketone and the enol form.

In the ^{1}H NMR spectrum of compound **1**, the absence of a signal from the methylene group and the presence of a singlet from a methine proton in the 6.03 ppm region and a downfield singlet from an enol proton at 14.19 ppm suggest that this product exists in solution in exclusively the enol form. This is also typical of other α-(2-quinolyl)-2-hydroxyacetophenones with a similar structure [8, 12]. For the isomeric α-(8-quinolyl)-2-hydroxyacetophenones, the ketone form of the molecule is typical [7]. Such a difference is obviously due to stabilization of the enol form, owing to formation of a hydrogen bond between the enol hydroxyl and the favorably located nitrogen atom of the quinoline ring. The orange color of product **1** also suggests the presence of a longer conjugation chain, which is realized in the enol form, compared with the ketone form. The hydroxyl groups of the phenol portion of molecule **1** are not equivalent. In the ^{1}H NMR spectrum, they absorb in the region 14.08 ppm (C(2)OH) and 9.67 ppm (C(4)OH). The large difference in the chemical shifts is due to formation of an intramolecular bond between the hydrogen of the hydroxyl group in the 2 position of the phenyl radical and the enol oxygen.

For the same reason, acylation of product **1** by acetic anhydride in pyridine at low temperature occurs primarily at the hydroxyl group in the 4 position, with formation of a bright orange α-(2-quinolyl)-4-acetyl-2-hydroxy-3-methylacetophenone (**2**). In the ^{1}H NMR spectrum of this product, a singlet from the hydroxyl proton in the 2 position appears in the same region (14.33 ppm) as in the starting **1**, but there is no signal from the C(4)OH proton and a three-proton singlet appears from the acetyl group at 2.30 ppm. The presence of singlets from the enol proton at 14.45 ppm and from the methyl proton at 6.19 ppm suggests that compound **2** also exists exclusively in the enol form. In the IR spectrum of product **2**, we observe C=O stretching vibrations from the acetyl group at 1740 cm^{-1}.

Despite the existence of compound **1** in the enol form, it enters into reactions typical for the carbonyl group. When compound **1** was treated with hydroxylamine hydrochloride in pyridine and hydrazine hydrate in alcohol, oxime **3** and hydrazone **4** respectively were obtained in high yields. In the ^{1}H NMR spectra of these compounds, there is a two-proton singlet from the methylene group in the 4.40-4.49 ppm region, and also a singlet from the oxime proton at 11.95 ppm or a two-proton singlet from the amino group at 6.87 ppm. The protons of the C(4)OH group absorb at 9.31 ppm (oxime **3**) and 9.16 ppm (hydrazone **4**). The signals from protons of the hydroxyl group in the 2 position are located downfield (11.40 ppm for product **3** and 13.53 ppm for product **4**), since they participate in formation of an intramolecular hydrogen bond with the nitrogen atom. The same hydroxyl group participates in formation of a chelate complex with ferric chloride, which has the typical coloring: dark-brown for the starting ketone **1**, blue for the acetyl derivative **2**, blue-green for oxime **3**, and blue for hydrazone **4**.

When we boiled the starting ketone **1** in excess acetic or propionic anhydride in the presence of triethylamine, colorless crystalline products **5** and **6** were obtained respectively. Under the given conditions, the reaction does not stop at the step of acylation of the hydroxy group, but rather is accompanied by cyclodehydration with formation of 7-acyl-2-alkyl-8-methyl-3-(2-quinolyl)chromones **5** and **6**. Boiling them briefly in dilute alkali leads to the target 2-alkyl-7-hydroxy-8-methyl-3-(2-quinolyl)chromones **7** and **8**. When product **1** is reacted with trifluoroacetic anhydride in pyridine at low temperature followed by treatment with water, 7-hydroxy-8-methyl-3-(2-quinolyl)-2-trifluoromethylchromone (**9**) is immediately formed. 7-Hydroxy-8-methyl-3-(2-quinolyl)chromone (**10**) is formed in high yield when the starting **1** is boiled with ethyl orthoformate in pyridine in the presence of catalytic amounts of piperidine. Compounds **9** and **10** are smoothly acylated by acetic anhydride in pyridine at low temperature, yielding 7-acetyl derivatives **11** and **12** (Table 1).



5 R = R^1 = Me, **6** R = R^1 = Et, **7** R = Me, **8** R = Et, **9** R = CF_3, **10** R = H, **11** R = CF_3, R^1 = Me, **12** R = H, R^1 = Me

TABLE 1. Characteristics of Compounds **1-12**

Compound	Empirical formula	Found, % / Calculated, %	mp, °C (solvent)	Yield, %
1	$C_{18}H_{15}NO_3$	5.15 / 4.78	229 (aq. EtOH)	54
2	$C_{20}H_{17}NO_4$	4.18 / 4.18	219 (*n*-BuOH)	95
3	$C_{18}H_{16}N_2O_3$	9.23 / 9.09	238 (Dioxane)	92
4	$C_{18}H_{17}N_3O_2$	13.81 / 13.67	176 (EtOH)	79
5	$C_{22}H_{17}NO_4$	4.09 / 3.90	182 (EtOH)	61
6	$C_{24}H_{21}NO_4$	3.45 / 3.62	167 (MeOH)	60
7	$C_{20}H_{15}NO_3$	4.67 / 4.41	316 (EtOH)	98
8	$C_{21}H_{17}NO_3$	4.00 / 4.23	268 (MeOH)	98
9	$C_{20}H_{12}F_3NO_3$	3.98 / 3.77	278 (MeCN)	68
10	$C_{19}H_{13}NO_3$	4.90 / 4.62	310 (*n*-BuOH)	73
11	$C_{22}H_{14}F_3NO_4$	3.65 / 3.39	163 (MeCN)	70
12	$C_{21}H_{15}NO_4$	4.20 / 4.06	196 (MePh)	84

A characteristic feature of the ^{1}H NMR spectra for all chromones **7-10** is the presence of a singlet from the C(8)Me group in the 2.28-2.32 ppm region and a downfield singlet from the C(7)OH group in the 10.40-10.86 ppm. Furthermore, the spectra have signals from the substituent in the 2 position (see Table 2). In the IR spectra of compounds **7-10**, the stretching vibrations of the C=O group are observed in the 1640-1620 cm^{-1} region, and the stretching vibrations of the O–H group are observed at 3500-3200 cm^{-1}.

The ^{1}H NMR spectra of 7-acetyl derivatives **5, 11**, and **12** differ from the spectra of the 7-hydroxychromones in the absence of a signal from the hydroxyl group, instead of which we see a three-proton singlet from the acetyl group in the 2.37-2.41 ppm region. The positions of the rest of the signals are given in Table 2. In the IR spectra, we observe the stretching vibrations of the C=O acyl groups of compounds **5, 6, 11,** and **12** in the 1770-1750 cm^{-1} region. There is no absorption above 3040 cm^{-1}.

In chromones **5-12**, as in the acyclic products **1-4**, there are eight aromatic protons which cannot be assigned in the ^{1}H spectrum. To solve this problem, we used two-dimensional COSY spectroscopy. Fig. 1 shows as an example the COSY-90 spectrum of product 1. Judging from the positions of the cross-peaks in the spectrum, the signal furthest downfield in the aromatic region, a doublet from the γ-quinoline proton with δ 7.75 ppm, is coupled with a doublet at 6.95 ppm, i.e., the latter signal is assigned to the β-quinoline proton. The triplet (δ 7.24 ppm) from the quinoline proton C(6')H is coupled with the doublet at 7.44 ppm (assigned to the C(5')H proton) and the triplet at δ 7.53 ppm (C(7')H). In the absorption region of the latter, there is a doublet coupled with the doublet at δ 6.31 ppm, which are assigned to protons of the phenol moiety C(6)H and C(5)H respectively. The doublet at δ 7.61 ppm belongs to the C(8')H proton.

From the COSY spectrum of oxime **3** it follows that the doublet that is furthest upfield in the aromatic region (6.24 ppm), belonging to the C(5)H proton of the phenol moiety, is coupled with the adjacent doublet at 7.23 ppm which consequently is assigned to the C(6)H proton of the same moiety. The doublet furthest downfield in the aromatic region at δ 8.15 ppm, belonging to the γ-quinoline proton, is coupled with the doublet

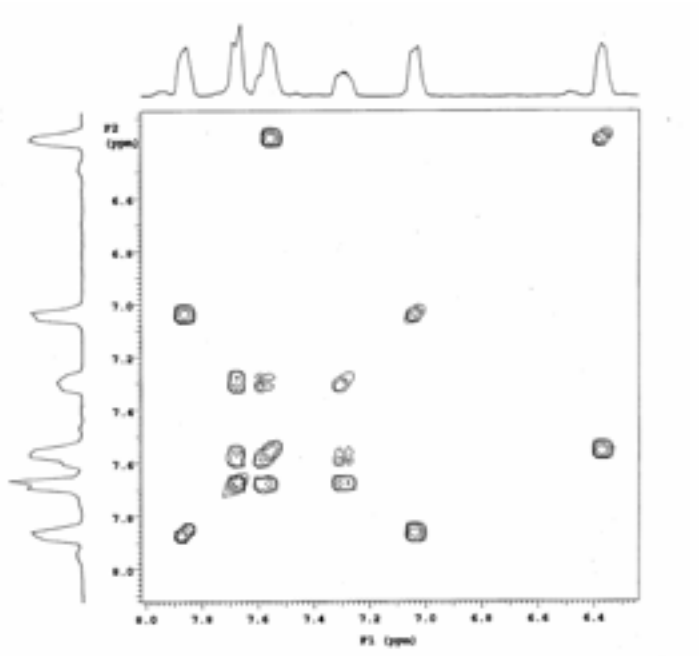


Fig. 1. COSY-90 spectrum of α-(2-quinolyl)-2,4-dihydroxy-3-methylacetophenone (**1**), recorded in DMSO-d_6.

at 7.38 ppm, which is the signal from the β-quinoline proton. The triplet further upfield at δ 7.49 is coupled with the triplet at 7.68 ppm and the doublet at 7.83 ppm. We assign these signals respectively to the 6'-, 7', and 5'-quinoline protons. Consequently, the other doublet in the aromatic region at δ 7.93 ppm belongs to the C(8')H proton of the quinoline ring.

From the COSY spectrum of 2-trifluoromethylchromone **9** it follows that the doublet furthest downfield, for the γ-quinoline proton at δ 8.38 pm, is coupled with the doublet for the β-quinoline proton at δ 7.50 ppm. The doublet furthest upfield at δ 7.07 is coupled with the doublet at δ 7.82 ppm. These signals are assigned respectively to the C(6)H and C(5)H protons of the chromone ring. The C(6')H and C(7')H protons of the quinoline ring are represented by triplets at 7.63 ppm and 7.77 ppm, while the signals from the C(5')H and C(8')H protons coincide and give a two-proton doublet at 8.00 ppm.

According to the COSY spectrum of 7-acetylchromone **12**, the two doublets furthest downfield at δ 8.36 ppm and 8.30 ppm belong to the γ- and β-quinoline protons respectively. The doublet furthest upfield at δ 7.25 ppm, belonging to the C(6)H proton of the chromone ring, is coupled with the doublet at 8.10 ppm, which is accordingly the signal from the C(5)H proton of the same ring, while the doublets for the C(8')H and C(5')H protons of the quinoline ring are found further upfield compared with the signals at 7.99 ppm and 7.90 ppm respectively. The same pattern is also observed in the spectrum of 7-hydroxychromone **10**. The significant downfield shift of the signal from the β-quinoline proton in the 2-unsubstituted products **10** and **12** compared with the rest of the chromones **5-9** and **11** is obviously due to the fact that the quinoline ring is found in the plane of the chromone ring, and the β-quinoline proton falls within the region of deshielding by the oxygen atom of the carbonyl group. In the remaining cases, a bulky substituent in the 2 position brings the quinoline ring away from the plane of the chromone molecule, which leads to an upfield shift of the signal from this proton to the 7.50-7.63 ppm region.

Thus based on compound **1**, we have synthesized a series of 7-hydroxy-8-methyl-3-(2-quinolyl)chromones with different substituents in the 2 position of the molecule as well as their 7-acyl derivatives.

TABLE 2. ^{1}H NMR Spectra of Compounds **1-12**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
1	1.94 (3H, s, CH_3); 6.03 (1H, s, =CH); 6.31 (1H, d, *J* = 8, C(5)H); 6.95 (1H, d, *J* = 8, C(3')H); 7.24 (1H, t, *J* = 8, C(6')H); 7.44 (1H, d, *J* = 8, C(5')H); 7.53 (2H, m, C(6)H + C(7')H); 7.61 (1H, d, *J* = 8, C(8')H); 7.75 (1H, d, *J* = 8, C(4')H); 9.67 (1H, s, C(4)OH); 14.08 (1H, s, C(2)OH); 14.19 (1H, s, =C–OH)
2	1.98 (3H, s, C(3)CH_3); 2.30 (3H, s, CH_3C=O); 6.19 (1H, s, CH=); 6.50 (1H, d, *J* = 8, C(5)H); 7.05 (1H, d, *J* = 8, C(3')H); 7.31 (1H, t, *J* = 8, C(6')H); 7.60 (1H, t, *J* = 8, C(7')H); 7.65 (3H, t, *J* = 8, C(6)H + C(5')H + C(8')H); 7.91 (1H, d, *J* = 8, C(4')H); 14.33 (1H, s, C(2)OH); 14.45 (1H, s, =C–OH)
3	1.95 (3H, s, CH_3); 4.49 (2H, s, CH_2); 6.24 (1H, d, *J* = 8, C(5)H); 7.23 (1H, d, *J* = 8, C(6)H); 7.38 (1H, d, *J* = 8, C(3')H); 7.49 (1H, t, *J* = 8, C(6')H); 7.68 (1H, t, *J* = 8, C(7')H); 7.83 (1H, d, *J* = 8, C(5')H); 7.93 (1H, d, *J* = 8, C(8')H); 8.15 (1H, d, *J* = 8, C(4')H); 9.31 (1H, s, C(4)OH); 11.41 (1H, s, C(2)OH); 11.95 (1H, s, N–OH)
4	1.97 (3H, s, CH_3); 4.41 (2H, s, CH_2); 6.28 (1H, d, *J* = 8, C(5)H); 6.88 (2H, br. s, NH_2); 7.25 (1H, d, *J* = 8, C(6)H); 7.52 (2H, t, *J* = 8, C(3')H + C(6')H); 7.70 (1H, t, *J* = 8, C(7')H); 7.87 (1H, d, *J* = 8, C(5')H); 7,94 (1H, d, *J* = 8, C(8')H); 8.23 (1H, d, *J* = 8, C(4')H); 9.17 (1H, s, C(4)OH); 13.53 (1H, s, C(2)OH)
5	2.32 (3H, s, C(8)CH_3); 2.37 (3H, s, CH_3C=O); 2.47 (3H, s, C(2)CH_3); 7.17 (1H, d, *J* = 8, C(6)H); 7.56 (1H, d, *J* = 8, C(3')H); 7.57 (1H, t, *J* = 8, C(6')H); 7.71 (1H, t, *J* = 8, C(7')H); 7.92 (1H, d, *J* = 8, C(5)H); 7.97 (2H, d, *J* = 8, C(5')H + C(8')H); 8.28 (1H, d, *J* = 8, C(4')H)
6	1.27 (3H, t, *J* = 7, C$\underline{H}_3$$CH_2$); 1.36 (3H, t, *J* = 7, C$\underline{H}_3$$CH_2$C=O); 2.34 (3H, s, C(8)$CH_3$); 2.74 (4H, m, 2$CH_2$); 7.19 (1H, d, *J* = 8, C(6)H); 7.55 (1H, d, *J* = 8, C(3')H); 7.61 (1H, t, *J* = 8, C(6')H); 7.75 (1H, t, *J* = 8, C(7')H); 7.99 (3H, t, *J* = 8, C(5)H + C(5')H + C(8')H); 8.33 (1H, d, *J* = 8, C(4')H)
7	2.29 (3H, s, C(8)CH_3); 2.43 (3H, s, C(2)CH_3); 6.95 (1H, d, *J* = 8, C(6)H); 7.55 (1H, d, *J* = 8, C(3')H); 7.59 (1H, t, *J* = 8, C(6')H); 7.73 (1H, t, *J* = 8, C(7')H); 7.76 (1H, d, *J* = 8, C(6)H); 7.95 (1H, d, *J* = 8, C(5')H); 7.99 (1H, d, *J* = 8, C(8')H); 8.30 (1H, d, *J* = 8, C(4')H); 10.42 (1H, s, OH)
8	1.34 (3H, t, *J* = 7, C$\underline{H}_3$$CH_2$); 2.31 (3H, s, C(8)$CH_3$); 2.71 (2H, q, *J* = 7, CH_2); 6.95 (1H, d, *J* = 8, C(6)H); 7.53 (1H, d, *J* = 8, C(3')H); 7.58 (1H, t, *J* = 8, C(6')H); 7.73 (1H, t, *J* = 8, C(7')H); 7.76 (1H, d, *J* = 8, C(5)H); 7.95 (1H, d, *J* = 8, C(5')H); 7.98 (1H, d, *J* = 8, C(8')H); 8.30 (1H, d, *J* = 8, C(4')H); 10.40 (1H, s, OH)
9	2.32 (3H, s, C(8)CH_3); 7.07 (1H, d, *J* = 8, C(6)H); 7.50 (1H, d, *J* = 8, C(3')H); 7.63 (1H, t, *J* = 8, C(6')H); 7.77 (1H, t, *J* = 8, C(7')H); 7.82 (1H, d, *J* = 8, C(5)H); 8.00 (2H, d, *J* = 8, C(5')H + C(8')H); 8.38 (1H, d, *J* = 8, C(4')H); 10,86 (1H, s, OH)
10	2.28 (3H, s, C(8)CH_3); 7.00 (1H, d, *J* = 8, C(6)H); 7.53 (1H, t, *J* = 8, C(6')H); 7.70 (1H, t, *J* = 8, C(7')H); 7.89 (2H, t, *J* = 8, C(5')H + C(8')H); 7.98 (1H, d, *J* = 8, C(5)H); 8.30 (1H, d, *J* = 8, C(3')H); 8.35 (1H, d, *J* = 8, C(4')H); 8.93 (1H, s, C(2)H); 10.51 (1H, s, OH)
11	2.33 (3H, s, C(8)CH_3); 2.41 (3H, s, CH_3C=O); 7.42 (1H, d, *J* = 8, C(6)H); 7.63 (1H, d, *J* = 8, C(3')H); 7.69 (1H, t, *J* = 8, C(6')H); 7.82 (1H, t, *J* = 8, C(7')H); 8.02 (1H, t, *J* = 8, C(5)H); 8.07 (2H, d, C(5')H + C(8')H); 8.49 (1H, d, C(4')H)
12	2.31 (3H, s, C(8)CH_3); 2.38 (3H, s, CH_3C=O); 7.25 (1H, d, *J* = 8, C(6)H); 7.55 (1H, t, *J* = 8, C(6')H); 7.71 (1H, t, *J* = 8, C(7')H); 7.90 (1H, d, *J* = 8, C(5')H); 7.99 (1H, d, *J* = 8, C(8')H); 8.10 (1H, d, *J* = 8, C(5)H); 8.30 (1H, d, *J* = 8, C(3')H); 8.36 (1H, d, *J* = 8, C(4')H); 9.03 (1H, s, C(2)H)

EXPERIMENTAL

The homogeneity of the synthesized compounds was monitored by TLC on Silufol UV-254 plates in a chloroform–methanol system, 9:1. The ^{1}H NMR spectra were recorded in DMSO-d_6 on a Varian Mercury 400 spectrometer (400 MHz), internal standard TMS.

α-(2-Quinolyl)-2,4-dihydroxy-3-methylacetophenone (1). A stream of dry hydrogen chloride was passed with stirring for 8 hours through a suspension (heated up to 50°C) of 2-quinolylacetonitrile (42 g, 250 mmol) and 2-methylresorcinol (31 g, 250 mmol) in boron trifluoride etherate (250 ml). After 3 days, the etherate was decanted from the precipitate. The precipitate was transferred in portions into hot water (500 ml) and boiled for 1 h with sulfuric acid (1 ml). The mixture was filtered hot. The precipitate was boiled for another

16 h, adding ammonia in portions up to pH 7. The crude product was reprecipitated from a 5% NaOH solution with 20% acetic acid.

α-(2-Quinolyl)-4-acetoxy-2-hydroxy-3-methylacetophenone (2). A solution of compound **1** (1.47 g, 5 mmol) in a mixture of acetic anhydride (2.55 g, 25 mmol) and triethylamine (2.53 g, 25 mmol) was held for 24 h at room temperature; the precipitate that formed was filtered out. The mother liquor was poured into water and an additional amount of product was filtered out.

α-(2-Quinolyl)-2,4-dihydroxy-3-methylacetophenone Oxime (3). A solution of compound **1** (1.47 g, 5 mmol) and hydroxylamine hydrochloride (1.04 g, 15 mmol) in absolute pyridine (6 ml) was boiled for 1 h. The mixture was held for 12 h at room temperature, and the precipitate formed was filtered out.

α-(2-Quinolyl)-2,4-dihydroxy-3-methylacetophenone Hydrazone (4). A solution of compound **1** (1.47 g, 5 mmol) and hydrazine hydrate (0.32 g, 10 mmol) in ethanol (25 ml) was boiled for 1 h. The mixture was cooled down and the alcohol was evaporated under vacuum. The residue was triturated in water (50 ml) and the precipitate was filtered out.

7-Acyloxy-2-alkyl-8-methyl-3-(2-quinolyl)chromones (5, 6). A solution of compound **1** (2.93 g, 10 mmol) in a mixture of acetic or propionic anhydride (50 mmol) and triethylamine (5 g, 50 mmol) was boiled for 2 h. The mixture was cooled down and the precipitate was filtered out.

2-Alkyl-7-hydroxy-8-methyl-3-(2-quinolyl)chromones (7, 8). 5% NaOH solution (2 ml) and water (20 ml) were added to a solution of the corresponding 7-acyloxy derivative **5, 6** (2 mmol) in ethanol (30 ml). The mixture was boiled for 5 min, then another 30 ml of water was added, the solution was neutralized with hydrochloric acid to pH 7, and the precipitate formed was filtered out.

7-Hydroxy-8-methyl-3-(2-quinolyl)-2-trifluoromethylchromone (9). Trifluoroacetic anhydride (4.2 g, 20 mmol) was added dropwise with stirring to a solution of compound **1** (1.47 g, 5 mmol) in pyridine (5 ml) that had been cooled down to 0°C. The mixture was held at room temperature for 48 h. The precipitate was filtered out and washed with water. The mother liquor was poured into water, and an additional amount of precipitate was filtered out.

7-Hydroxy-8-methyl-3-(2-quinolyl)chromone (10). A solution of compound **1** (1.47 g, 5 mmol) in a mixture of ethyl orthoformate (4.4 g, 30 mmol), pyridine (5 ml), and piperidine (0.33 g, 3.8 mmol) was boiled for 8 h and then cooled down and the precipitate was filtered out.

2-R-7-Acetoxy-8-methyl-3-(2-quinolyl)chromones (11, 12). A solution of the corresponding 7-hydroxy product **9, 10** (3 mmol) in a mixture of pyridine (2 ml) and acetic anhydride (1.22 g, 12 mmol) was held at room temperature for 48 h, and the precipitate formed was filtered out.

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