SYNTHESIS OF ANALOGS OF NATURAL 2′-METHOXYISOFLAVONES

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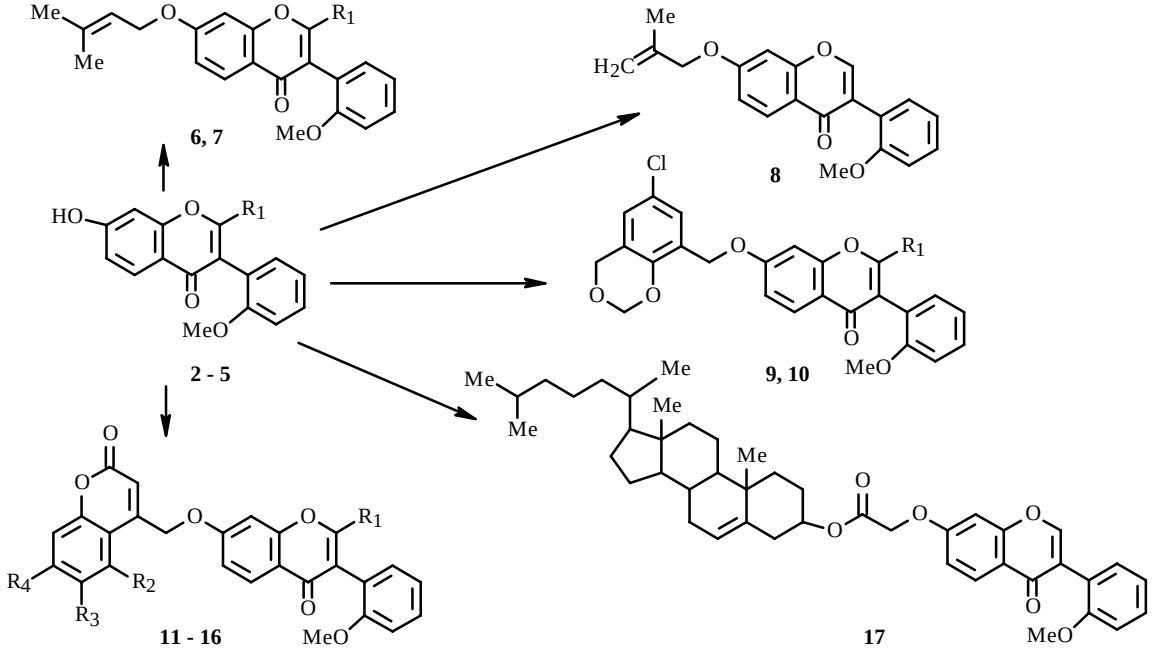
2-(Un)substituted-2′-methoxy-7-hydroxyisoflavones were synthesized. They were derivatized at the phenol hydroxyl using alkylation and acylation reactions and Mannich base formation.

Key words: isoflavonoids, alkylation, acylation, aminomethylation.

Flavonoids as a class are some of the most widely distributed compounds of plant origin. Representatives of them are present in practically all plant species [1]. Flavonoids are most frequently found as hydroxylated, methoxylated, and glycosylated derivatives. We reported previously on the isolation from plant material of the natural isoflavones teralin (7,4′-dihydroxy-2′-methoxyisoflavone) [2], milldurone (6,7,2′-trimethoxy-4′,5′-methylenedioxyisoflavone) [3], and irisolone (7,8,2′-trimethoxy-4′,5′-methylenedioxyisoflavone) [4]. Irilin C (5,2′-dimethoxy-6,7-methylenedioxyisoflavone) was recently isolated from *Iris bungei*, which is used in Mongolian folk medicine [5]; 2′-*O*-methyllabronisoflavone (2′-methoxy-5,7-dihydroxy-6-methylisoflavone), from *Mirabilis jalapa*, which exhibits high antifungicidal activity [6].

In continuation of research on the synthesis of natural alkoxyisoflavones (formononetin, orobol, biochanin A, pseudobaptigenin, cladrin) and their analogs [7-10] and considering the high and varied biological activity of these compounds, it was interesting to prepare analogs of natural 2′-methoxyisoflavones and their derivatives.

The starting compound for constructing the chromone nucleus was 2,4-dihydroxy-2′-methoxydeoxybenzoin (**1**) [11, 12], which was dictated by its availability and the preparative capabilities of converting it to isoflavones.



2, 6, 9, 11, 15: R_1 = H; **3, 7, 10, 13, 16:** R_1 = Me; **4, 12, 14:** R_1 = CF_3; **5:** R = COOEt
11, 12: R_2 = R_4 = Me, R_3 = H; **13, 14:** R_2 = R_3 = H, R_4 = OMe; **15, 16:** R_2 = H, R_3 = R_4 = Me

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2-Unsubstituted isoflavone **2** was synthesized by formylation of 2-hydroxydeoxybenzoin using Vilsmeier reagent with subsequent heterocyclization [12, 13]. Its 2-methyl derivative **3** was synthesized by the literature method [11].

Acid (chloro)anhydrides were used as acylating agents to prepare 2-substituted isoflavones **4** and **5** under Kostanetsky-Robinson conditions.

New derivatives of 7-hydroxyisoflavones **2-5** were prepared and their reactivities were investigated using reactions at the phenol hydroxyl and aminomethylation.

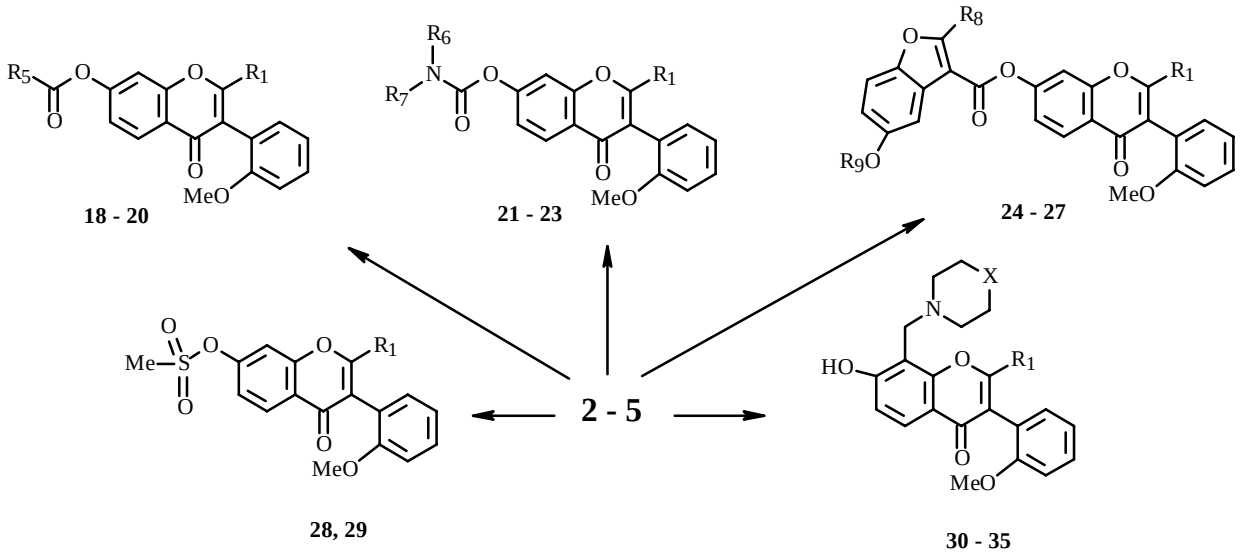
Natural isoflavones are frequently ethers of hydroxyisoflavones (e.g., maximaisoflavones A and B, xanthocercine, etc.). Therefore, considering the high and varied biological activity of natural isoflavonoids, the synthesis of alkoxy derivatives is especially interesting because the introduction of new pharmacophores into analogs of natural isoflavones can cause new valuable pharmacological properties to appear. For this reason we investigated the reaction of the prepared isoflavones with various alkylating reagents such as haloalkenes, compounds containing heterocyclic fragments (4-chloromethylcoumarins and 8-chloromethyl-6-chlorobenzo-1,3-dioxane), and chloroacetic ester with a steroid fragment.

We prepared 7-dimethylallyloxy- (**6** and **7**) and 7-methylallyloxyisoflavones (**8**) because allyl derivatives of isoflavones that are methoxylated on the B ring are insecticides [14].

Substituted 4-chloromethylcoumarins were used as the alkylating reagents to prepare analogs of natural bisbenzopyrones **11-16**. In this instance longer heating of the reaction mixture with an excess of alkylating reagent was required to complete the alkylation. This was due to the low stability of substituted 4-chloromethylcoumarins in alkaline media. Under these conditions they are known to rearrange into the corresponding substituted 3-benzofuranacetic acids [15].

Acylation of 7-hydroxyisoflavones proceeded readily in pyridine at room temperature. The acylating reagents were acid chlorides of substituted 3-benzofurancarboxylic and cyclopropane- and cyclohexanecaboxylic acids.

Compounds of the urethane type (**21-23**) were prepared for the first time as analogs of 2′-methoxyisoflavone using acylating reactions of *N*,*N*-disubstituted carbamoyl chlorides. Esters of methanesulfonic acid, isoflavones **28** and **29**, were synthesized using methanesulfonyl chloride.



23, 24, 28, 31 - 34: R_1 = H; **18, 25, 26, 35:** R_1 = Me; **19 - 22, 30:** R_1 = CF_3; **27, 29:** R_1 = COOEt; **18:** R_5 = Me
19: R_5 = cyclopropyl; **20:** R_5 = cyclohexyl; **21:** R_6R_7 = $(CH_2)_2O(CH_2)_2$; **22:** R_6 = R_7 = Ph; **23:** R_6 = R_7 = Et
24, 25: R_8 = Me, R_9 = Ac; **26, 27:** R_8 = Ph, R_9 = Et; **30:** X = bond; **31:** X = CH_2; **32:** X = CHMe
33: X = $N(CH_2)_2OH$; **34, 35:** X = NCH_3

Preparation of Mannich bases **30-35** is a variation of C-alkylation of the chromone nucleus. Aminomethyl derivatives of 7-hydroxyisoflavones were synthesized using aminals of secondary amines. Using an equivalent amount of aminal produced a chromone ring aminomethylated at the 8-position.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Sorbfil UV-254 (Russia) and Merck (Germany) plates with elution by $CHCl_3$:CH_3OH (95:5 and 9:1). PMR spectra were measured on a VXR-300 (Varian, 300 MHz) instrument in DMSO-d_6 (Mannich bases in $CDCl_3$) relative to TMS (internal standard) on the δ-scale. Analytical data for all compounds agreed with those calculated.

Synthesis of 2-Trifluoromethyl- and 2-Ethoxycarbonylisoflavones (4, 5). A cooled (0°C) solution of **1** (2.42 g, 10 mmol) in absolute pyridine (10 mL) was treated dropwise with trifluoroacetic anhydride or ethyloxalylchloride (20 mmol), left at room temperature for 1 d, and poured into icewater (100 mL) containing HCl (1 N, 1-3 mL). The precipitate was filtered off and crystallized from CH_3OH.

7-Hydroxy-3-(2-methoxyphenyl)-2-trifluoromethyl-4H-chromen-4-one (4). $C_{17}H_{11}F_3O_4$, yield 78%, mp 247-249°C (CH_3OH). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.70 (3H, s, OMe-2′), 6.96 (1H, d, H-8, ^4J = 2.1), 7.00 (1H, m, H-5′), 7.02 (1H, dd, ^3J = 8.8, ^4J = 2.1, H-6), 7.09 (1H, m, H-3′), 7.15 (1H, m, H-6′), 7.42 (1H, m, H-4′), 7.92 (1H, d, ^3J = 8.8, H-5), 11.13 (1H, s, HO-7).

Ethyl 7-hydroxy-3-(2-methoxyphenyl)-4-oxo-4H-chromen-2-carboxylate (5). $C_{19}H_{16}O_6$, yield 76%, mp 99-101°C (CH_3OH). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.91 (3H, t, ^3J = 7.2), 4.06 (2H, q, ^3J = 7.2) CH_3CH_2COO-2, 3.66 (3H, s, OMe-2′), 6.90 (1H, d, ^4J = 2.0, H-8), 6.97 (1H, m, H-5′), 6.98 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.04 (1H, m, H-3′), 7.12 (1H, m, H-6′), 7.36 (1H, m, H-4′), 7.92 (1H, d, ^3J = 8.8, H-5), 11.03 (1H, s, HO-7).

General Method for Preparing 7-Alkyloxyisoflavones (6-17). A hot solution of the appropriate 7-hydroxyisoflavone (**2-4**, 10 mmol) in absolute acetone (30 mL) was treated with fershly calcined potash (2.1 g, 15 mmol), stirred, boiled, treated with the appropriate alkylhalide (12 mmol), left for 1-4 h (completion of reaction determined by TLC), and poured into acidified icewater (100 mL). The resulting precipitate was filtered off and crystallized from a suitable solvent.

3-(2-Methoxyphenyl)-7-[3-methylbut-2-enyl)oxy]-4H-chromen-4-one (6). $C_{21}H_{20}O_4$, yield 84%, mp 135-136°C (ethanol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.72 (3H, s, OMe-2′), 6.99 (1H, m, H-5′), 7.07 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.08 (1H, m, H-3′), 7.16 (1H, d, ^4J = 2.4, H-8), 7.24 (1H, m, H-6′), 7.38 (1H, m, H-4′), 7.97 (1H, d, ^3J = 8.8, H-5), 8.25 (1H, s, H-2); alkyl-substituent protons 1.76 (6H, s, $2CH_3$), 5.48 (1H, d, ^3J = 6.8, CH), 4.69 (2H, d, ^3J = 6.8, CH_2O).

3-(2-Methoxyphenyl)-2-methyl-7-[(3-methylbut-2-enyl)oxy]-4H-chromen-4-one (7). $C_{22}H_{22}O_4$, yield 78%, mp 91-92°C (ethanol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.14 (3H, s, CH_3-2), 3.71 (3H, s, OMe-2′), 6.99 (1H, m, H-5′), 7.02 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.08 (1H, m, H-6′), 7.13 (1H, d, ^4J = 2.4, H-8), 7.14 (1H, m, H-3′), 7.37 (1H, m, H-4′), 7.89 (1H, d, ^3J = 8.8, H-5); alkyl-substituent protons 1.75 (6H, s, $2CH_3$), 5.48 (1H, d, ^3J = 7.2, CH), 4.68 (2H, d, ^3J = 7.2, CH_2O).

3-(2-Methoxyphenyl)-7-[(2-methylprop-2-enyl)oxy]-4H-chromen-4-one (8). $C_{20}H_{17}O_4$, yield 75%, mp 117-119°C (CH_3OH). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.71 (3H, s, OMe-2′), 6.99 (1H, m, H-5′), 7.08 (1H, m, H-3′), 7.11 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.17 (1H, d, ^4J = 2.4, H-8), 7.23 (1H, m, H-6′), 7.38 (1H, m, H-4′), 7.99 (1H, d, ^3J = 8.8, H-5), 8.26 (1H, s, H-2); alkyl-substituent protons 1.80 (3H, m, CH_3), 5.11, 5.01 (2H, m, $=CH_2$), 4.66 (2H, m, CH_2O).

7-[(6-Chloro-4H-1,3-benzodioxan-8-yl)methoxy]-3-(2-methoxyphenyl)-4H-chromen-4-one (9). $C_{25}H_{19}ClO_6$, yield 69%, mp 259-260°C (ethanol:DMF). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.73 (3H, s, OMe-2′), 7.00 (1H, m, H-5′), 7.09 (1H, m, H-3′), 7.16 (1H, m, H-6′), 7.23 (1H, d, ^4J = 2.0, H-8), 7.24 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.39 (1H, m, H-4′), 8.01 (1H, d, ^3J = 8,8, H-5), 8.27 (1H, s, H-2); alkyl-substituent protons 5.19 (2H, s, OCH_2O), 4.93 (2H, s, OCH_2-Ar), 7.43, 7.28 (2H, 2d, ^4J = 2.0, H-6, H-8), 5.36 (2H, s, CH_2O).

7-[(6-Chloro-4H-1,3-benzodioxan-8-yl)methoxy]-2-methyl-3-(2-methoxyphenyl)-4H-chromen-4-one (10). $C_{26}H_{21}ClO_6$, yield 69%, mp 252-253°C (ethanol:DMF). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.15 (3H, s, CH_3-2), 3.72 (3H, s, OMe-2′), 7.01 (1H, m, H-5′), 7.09 (1H, m, H-3′), 7.12 (1H, dd, ^3J = 8.8, ^4J - 2.0, H-6), 7.15 (1H, m, H-6′), 7.23 (1H, d, ^4J = 2.0, H-8), 7.39 (1H, m, H-4′), 7.93 (1H, d, ^3J = 8,8, H-5); alkyl substituent protons 5.19 (2H, s, OCH_2O), 4.93 (2H, s, OCH_2-Ar), 7.42, 7.14 (2H, 2d, ^4J = 2.0, H-6, H-8), 5.36 (2H, s, CH_2O).

4-({[3-(2-Methoxyphenyl)-4-oxo-4H-chromen-7-yl]oxy}methyl)-5,7-dimethyl-2H-chromen-2-one (11). $C_{28}H_{22}O_6$, yield 65%, mp 246-247°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.73 (3H, s, OMe-2′), 7.00 (1H, m, H-5′), 7.09 (1H, m, H-3′), 7.25 (1H, m, H-6′), 7.29 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.38 (1H, m, H-4′), 7.39 (1H, d,

^4J = 2.0, H-8), 8.06 (1H, d, ^3J = 8,8, H-6), 8.30 (1H, s, H-2); alkyl substituent protons 2.37 (3H, s, CH_3-7), 2.72 (3H, s, CH_3-5), 5.70 (2H, s, CH_2-4), 6.59 (1H, s, H-3), 7.07 (1H, d, ^4J = 2.0, H-8), 7.15 (1H, d, ^4J = 2.0, H-6).

4-({[3-(2-Methoxyphenyl)-4-oxo-2-(trifluoromethyl)-4H-chromen-7-yl]oxy}methyl)-5,7-dimethyl-2H-chromen-2-one (12). $C_{29}H_{21}F_3O_6$, yield 60%, mp 187-188°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.71 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.11 (1H, m, H-3′), 7.19 (1H, m, H-6′), 7.38 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.44 (1H, m, H-4′), 7.56 (1H, d, ^4J = 2.0, H-8), 8.05 (1H, d, ^3J = 8,8, H-5); alkyl substituent protons 2.38 (3H, s, CH_3-7), 2.74 (3H, s, CH_3-5), 5.77 (2H, s, CH_2-4), 6.54 (1H, s, H-3), 7.09 (1H, d, ^4J = 2.0, H-8), 7.16 (1H, d, ^4J = 2.0, H-6).

7-Methoxy-4-({[3-(2-methoxyphenyl)-2-methyl-4-oxo-4H-chromen-7-yl]oxy}methyl)-2H-chromen-2-one (13). $C_{28}H_{22}O_7$, yield 59%, mp 224-226°C (ethanol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.16 (3H, s, CH_3-2), 3.72 (3H, s, OMe-2′), 7.02 (1H, m, H-5′), 7.10 (1H, m, H-3′), 7.15 (1H, m, H-6′), 7.27 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.39 (1H, m, H-4′), 7.49 (1H, d, ^4J = 2.0, H-8), 7.97 (1H, d, ^3J = 8.8, H-5); alkyl substituent protons 3.89 (3H, s, CH_3O-7), 5.56 (2H, s, CH_2-4), 6.48 (1H, s, H-3), 7.03 (1H, dd, ^3J = 8,8, ^4J = 2.4, H-6), 7.07 (1H, d, ^4J = 2.4, H-8), 7.87 (1H, d, ^3J = 8.8, H-5).

7-Methoxy-4-({[3-(2-methoxyphenyl)-4-oxo-2-(trifluoromethyl)-4H-chromen-7-yl]oxy}methyl)-2H-chromen-2-one (14). $C_{28}H_{19}F_3O_7$, yield 69%, mp 235-236°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.72 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.12 (1H, m, H-3′), 7.19 (1H, m, H-6′), 7.39 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.45 (1H, m, H-4′), 7.70 (1H, d, ^4J = 2.0, H-8), 8.03 (1H, d, ^3J = 8.8, H-5); alkyl substituent protons 3.89 (3H, s, CH_3O-7), 5.60 (2H, s, CH_2-4), 6.50 (1H, s, H-3), 7.03 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.05 (1H, d, ^4J = 2.0, H-8), 7.88 (1H, d, ^3J = 8.8, H-5).

4-({[3-(2-Methoxyphenyl)-4-oxo-4H-chromen-7-yl]oxy}methyl)-6,7-dimethyl-2H-chromen-2-one (15). $C_{28}H_{22}O_6$, yield 74%, mp 275-277°C (ethanol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.73 (3H, s, OMe-2′), 7.01 (1H, m, H-5′), 7.10 (1H, m, H-3′), 7.26 (1H, m, H-6′), 7.33 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.40 (1H, m, H-4′), 7.59 (1H, d, ^4J = 2.0, H-8), 8.06 (1H, d, ^3J = 8.8, H-5), 8.31 (1H, s, H-2); alkyl substituent protons 2.23, 2.35 (6H, 2s, CH_3-6, CH_3-7), 5.56 (2H, s, CH_2-4), 6.58 (1H, s, H-3), 7.28 (1H, s, H-8), 7.70 (1H, s, H-5).

4-({[3-(2-Methoxyphenyl)-2-methyl-4-oxo-4H-chromen-7-yl]oxy}methyl)-6,7-dimethyl-2H-chromen-2-one (16). $C_{29}H_{24}O_6$, yield 70%, mp 283-284°C (ethanol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.16 (3H, s, CH_3-2), 3.72 (3H, s, OMe-2′), 7.02 (1H, m, H-5′), 7.10 (1H, m, H-3′), 7.15 (1H, m, H-6′), 7.29 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.39 (1H, m, H-4′), 7.51 (1H, d, ^4J = 2.0, H-8), 7.97 (1H, d, ^3J = 8.8, H-5); alkyl substituent protons 2.33, 2.35 (6H, 2s, CH_3-6, CH_3-7), 5.55 (2H, s, CH_2-4), 6.57 (1H, s, H-3), 7.28 (1H, s, H-8), 7.73 (1H, s, H-5).

Cholest-5-en-3-yl-{[3-(2-methoxyphenyl)-4-oxo-4H-chromen-7-yl]oxy}acetate (17). $C_{45}H_{58}O_6$, yield 59%, mp 156-157°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.81 (3H, s, OMe-2′), 6.85 (1H, d, ^4J = 2.0, H-8), 6.99 (1H, m, H-3′), 7.03 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.04 (1H, m, H-5′), 7.32 (1H, m, H-6′), 7.38 (1H, m, H-4′), 7.92 (1H, s, H-2), 8.23 (1H, d, ^3J = 8.8, H-5); cholestene protons 0.59-5.47; 4.71 (2H, s, CH_2O-7).

General Method for Preparing 7-Acyloxyisoflavones (18-29). A solution of the approprate 7-hydroxyisoflavone (**2-5**, 10 mmol) in the minimal amount of absolute pyridine was treated with the acid chloride (12 mmol). The reaction mixture was left for 1 d at room temperature and poured into icewater. The resulting precipitate was filtered off and crystallized from a suitable solvent.

3-(2-Methoxyphenyl)-2-methyl-4-oxo-4H-chromen-7-yl-acetate (18). $C_{19}H_{16}O_6$, yield 79%, mp 113-114°C (propan-2-ol). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.23 (3H, s, CH_3-2), 2.36 (3H, s, CH_3COO-7), 3.77 (3H, s, OMe-2′), 6.98 (1H, m, H-3′), 7.03 (1H, m, H-5′), 7.11 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.17 (1H, m, H-6′), 7.26 (1H, d, ^4J = 2.4, H-8), 7.37 (1H, m, H-4′), 8.24 (1H, d, ^3J = 8.8, H-5).

3-(2-Methoxyphenyl)-4-oxo-2-trifluoromethyl-4H-chromen-7-yl-cyclopropanecarboxylate (19). $C_{21}H_{15}F_3O_5$, yield 87%, mp 145-146°C (CH_3OH). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.71 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.12 (1H, m, H-3′), 7.20 (1H, m, H-6′), 7.42 (1H, dd, ^3J = 8.8, ^4J = 2.1, H-6), 7.44 (1H, m, H-4′), 7.76 (1H, d, ^4J = 2.1, H-8), 8.12 (1H, d, ^3J = 8.8, H-5); acyl protons 1.12 (4H, m, $2CH_2$), 1.90 (1H, m, CH).

3-(2-Methoxyphenyl)-4-oxo-2-trifluoromethyl-4H-chromen-7-yl-cyclohexanecarboxylate (20). $C_{24}H_{21}F_3O_5$, yield 78%, mp 106-107°C (CH_3OH). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.71 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.12 (1H, m, H-3′), 7.20 (1H, m, H-6′), 7.38 (1H, dd, ^3J = 8.8, ^4J = 2.1, H-6), 7.45 (1H, m, H-4′), 7.73 (1H, d, ^4J = 2.1, H-8), 8.13 (1H, d, ^3J = 8.8, H-5); acyl protons 1.17-2.76 (10H, m, $5CH_2$), 2.61 (1H, m, CH).

3-(2-Methoxyphenyl)-4-oxo-2-trifluoromethyl-4H-chromen-7-yl-morpholine-4-carboxylate (21). $C_{22}H_{18}F_3NO_6$, yield 87%, mp 138-139°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.71 (3H, s, OMe-2′), 7.03 (1H,

m, H-5′), 7.12 (1H, m, H-3′), 7.20 (1H, m, H-6′), 7.43 (1H, dd, ^3J = 8.8, ^4J = 2.1, H-6), 7.45 (1H, m, H-4′), 7.73 (1H, d, ^4J = 2.1, H-8), 8.11 (1H, d, ^3J = 8.8, H-5); morpholine protons 3.43-3.73 (8H, m, $4CH_2$).

3-(2-Methoxyphenyl)-4-oxo-2-trifluoromethyl-4H-chromen-7-yl-diphenylcarbamate (22). $C_{30}H_{20}F_3NO_5$, yield 76%, mp 189-190°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.70 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.11 (1H, m, H-3′), 7.20 (1H, m, H-6′), 7.29 (1H, dd, ^3J = 8.8, ^4J = 2.1, H-6), 7.45 (1H, m, H-4′), 7.87 (1H, d, ^4J = 2.1, H-8), 8.10 (1H, d, ^3J = 8.8, H-5); acyl protons 7.30-7.61 (10H, m, 2Ph).

3-(2-Methoxyphenyl)-4-oxo-4H-chromen-7-yl-diethylcarbamate (23). $C_{21}H_{21}NO_5$, yield 72%, mp 104-105°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.72 (3H, s, OMe-2′), 7.00 (1H, m, H-5′), 7.09 (1H, m, H-3′), 7.25 (1H, m, H-6′), 7.29 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.39 (1H, m, H-4′), 7.53 (1H, d, ^4J = 2.0, H-8), 8.09 (1H, d, ^3J = 8.8, H-5), 8.34 (1H, s, H-2); acyl protons 1.22, 1.14 (6H, 2t, ^3J = 7.6, $2CH_3$), 3.33, 3.43 (4H, 2q, ^3J = 7.6, $2CH_2$).

3-(2-Methoxyphenyl)-4-oxo-4H-chromen-7-yl-5-(acetyloxy)-2-methyl-1-benzofuran-3-carboxylate (24). $C_{28}H_{20}O_8$, yield 69%, mp 151-153°C (DMF:propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.82 (3H, s, OMe-2′), 7.00 (1H, m, H-3′), 7.04 (1H, m, H-5′), 7.32 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.35 (1H, m, H-6′), 7.39 (1H, m, H-4′), 7.46 (1H, d, ^4J = 2.0, H-8), 8.00 (1H, s, H-2), 8.34 (1H, d, ^3J = 8.8, H-5); benzofuran protons 2.34 (3H, s, CH_3COO-5), 2.87 (3H, s, CH_3-2), 7.07 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.49 (1H, d, ^3J = 8.8, H-7), 7.73 (1H, d, ^4J = 2.0, H-4).

3-(2-Methoxyphenyl)-2-methyl-4-oxo-4H-chromen-7-yl-5-(acetyloxy)-2-methyl-1-benzofuran-3-carboxylate (25). $C_{29}H_{22}O_8$, yield 76%, mp 219-220°C (DMF:propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.25 (3H, s, CH_3-2), 3.79 (3H, s, OMe-2′), 7.00 (1H, m, H-3′), 7.05 (1H, m, H-5′), 7.20 (1H, m, H-6′), 7.27 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.38 (1H, m, H-4′), 7.42 (1H, d, ^4J = 2.0, H-8), 8.31 (1H, d, ^3J = 8.8, H-5); benzofuran protons 2.34 (3H, s, CH_3COO-5), 2.87 (3H, s, CH_3-2), 7.07 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.49 (1H, d, ^3J = 8.8, H-7), 7.73 (1H, d, ^4J = 2.0, H-4).

3-(2-Methoxyphenyl)-2-methyl-4-oxo-4H-chromen-7-yl-5-ethoxy-2-phenyl-1-benzofuran-3-carboxylate (26). $C_{34}H_{26}O_7$, yield 57%, mp 152-154°C (DMF:propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.19 (3H, s, CH_3-2), 3.73 (3H, s, OMe-2′), 7.03 (1H, m, H-5′), 7.12 (1H, m, H-3′), 7.18 (1H, m, H-6′), 7.41 (1H, m, H-4′), 7.46 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.55 (1H, d, ^4J = 2.0, H-8), 8.10 (1H, d, ^3J = 8.8, H-5); benzofuran protons 1.38 (3H, t, ^3J = 6.8), 4.12 (2H, q, ^3J = 6.8) CH_3CH_2O-5, 7.09 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.54-8.10 (5H, m, Ph-2), 7.71 (1H, d, ^3J = 8.8, H-7), 7.76 (1H, d, ^4J = 2.0, H-4).

Ethyl7-{[(5-ethoxy-2-phenyl-1-benzofuran-3-yl)carbonyl]oxy}-3-(2-methoxyphenyl)-4-oxo-4H-chromen-2-carboxylate (27). $C_{36}H_{28}O_9$, yield 79%, mp 182-184°C (DMF:propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.94 [(3H, t, ^3J = 7.2), 4.09 (2H, q, ^3J = 7.2) CH_3CH_2COO-2], 3.69 (3H, s, OMe-2′), 7.00 (1H, m, H-5′), 7.07 (1H, m, H-3′), 7.19 (1H, m, H-6′), 7.40 (1H, m, H-4′), 7.53 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.54 (1H, d, ^4J = 2.0, H-8), 8.15 (1H, d, ^3J = 8.8, H-5); benzofuran protons 1.38 [(3H, t, ^3J = 6.8), 4.11 (2H, q, ^3J = 6.8) CH_3CH_2O-5], 7.08 (1H, dd, ^3J = 8.8, ^4J = 2.0, H-6), 7.54-8.11 (5H, m, Ph-2), 7.70 (1H, d, ^3J = 8.8, H-7), 7.89 (1H, d, ^4J = 2.0, H-4).

3-(2-Methoxyphenyl)-4-oxo-4H-chromen-7-yl-methanesulfonate (28). $C_{17}H_{14}O_6S$, yield 87%, mp 161-163°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.52 (3H, s, CH_3SO_2O-7), 3.72 (3H, s, OMe-2′), 7.01 (1H, m, H-5′), 7.09 (1H, m, H-3′), 7.26 (1H, m, H-6′), 7.40 (1H, m, H-4′), 7.49 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.77 (1H, d, ^4J = 2.4, H-8), 8.20 (1H, d, ^3J = 8.8, H-5), 8.40 (1H, s, H-2).

Ethyl 3-(2-methoxyphenyl)-7-[(methylsulfonyl)oxy]-4-oxo-4H-chromen-2-carboxylate (29). $C_{20}H_{18}O_8S$, yield 80%, mp 157-159°C (propan-2-ol). PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.94 (3H, t, ^3J = 7.2), 4.09 (2H, q, ^3J = 7.2) CH_3CH_2COO-2, 3.53 (3H, s, CH_3SO_2O-7), 3.67 (3H, s, OMe-2′), 7.00 (1H, m, H-5′), 7.06 (1H, m, H-3′), 7.16 (1H, m, H-6′), 7.39 (1H, m, H-4′), 7.52 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-6), 7.85 (1H, d, ^4J = 2.4, H-8), 8.18 (1H, d, ^3J = 8.8, H-5).

General Method for Preparing of 8-Dialkylaminomethylisoflavones (30-35). A boiling solution of the appropriate isoflavone (**2-4**, 10 mmol) in absolute dioxane (20 mL) was treated with the aminal (15 mmol), boiled for 1 h (completion of reaction determined by TLC), cooled, and evaporated in vacuo. The solid was crystallized from a suitable solvent.

7-Hydroxy-3-(2-methoxyphenyl)-8-(pyrrolidin-1-yl-methyl)-2-trifluoromethyl-4H-chromen-4-one (30). $C_{22}H_{20}F_3NO_4$, yield 89%, mp 150-151°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.76 (3H, s, OMe-2′), 4.18 (2H, s, CH_2-8), 6.90 (1H, d, ^3J = 8.8, H-6), 6.96 (1H, m, H-3′), 7.00 (1H, m, H-5′), 7.12 (1H, m, H-6′), 7.39 (1H, m, H-4′), 8.03 (1H, d, ^3J = 8.8, H-5), 11.13 (1H, s, HO-7); amine protons 1.94 (4H, m, $2CH_2$), 2.80 (4H, m, $2NCH_2$).

7-Hydroxy-3-(2-methoxyphenyl)-8-(piperidin-1-ylmethyl)-4H-chromen-4-one (31). $C_{22}H_{23}NO_4$, yield 79%, mp 132-134°C (ethylacetate:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.79 (3H, s, OMe-2′), 3.99 (2H, s,

CH_2-8), 6.86 (1H, d, ^3J = 8.8, H-6), 6.98 (1H, m, H-3′), 7.01 (1H, m, H-5′), 7.31 (1H, m, H-6′), 7.35 (1H, m, H-4′), 7.87 (1H, s, H-2), 8.09 (1H, d, ^3J = 8.8, H-5); amine protons 1.28-3.31 (10H, m, $5CH_2$).

7-Hydroxy-3-(2-methoxyphenyl)-8-[(4-methylpiperidin-1-yl)methyl)]-4H-chromen-4-one (32). $C_{23}H_{25}NO_4$, yield 75%, mp 177-179°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.80 (3H, s, OMe-2′), 4.00 (2H, s, CH_2-8), 6.86 (1H, d, ^3J = 8.8, H-6), 6.98 (1H, m, H-3′), 7.00 (1H, m, H-5′), 7.31 (1H, m, H-6′), 7.36 (1H, m, H-4′), 7.87 (1H, s, H-2), 8.09 (1H, d, ^3J = 8.8, H-5); amine protons 0.97 (3H, m, 4-CH_3), 1.23-3.16 (9H, m).

7-Hydroxy-8-{[4-(2-hydroxyethyl)piperazin-1-yl]methyl}-3-(2-methoxyphenyl)-4H-chromen-4-one (33). $C_{23}H_{26}N_2O_5$, yield 80%, mp 140-142°C (propan-2-ol). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.80 (3H, s, OMe-2′), 4.05 (2H, s, CH_2-8), 6.88 (1H, d, ^3J = 8.8, H-6), 6.98 (1H, m, H-3′), 7.01 (1H, m, H-5′), 7.31 (1H, m, H-6′), 7.36 (1H, m, H-4′), 7.89 (1H, s, H-2), 8.12 (1H, d, ^3J = 8.8, H-5); amine protons 2.61, 3.65 (4H, 2m, 4-NCH_2CH_2O), 2.09-3.22 (8H, m, $4CH_2$).

7-Hydroxy-3-(2-methoxyphenyl)-8-[(4-methylpiperazin-1-yl)methyl]-4H-chromen-4-one (34). $C_{22}H_{34}N_2O_4$, yield 76%, mp 164-165°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.81 (3H, s, OMe-2′), 4.04 (2H, s, CH_2-8), 6.88 (1H, d, ^3J = 8.8, H-6), 6.99 (1H, m, H-3′), 7.02 (1H, m, H-5′), 7.32 (1H, m, H-6′), 7.37 (1H, m, H-4′), 7.89 (1H, s, H-2), 8.12 (1H, d, ^3J = 8.8, H-5); amine protons 2.34 (3H, s, 4-NCH_3), 1.95-3.28 (8H, m, $4CH_2$).

7-Hydroxy-3-(2-methoxyphenyl)-2-methyl-8-[(4-methylpiperazin-1-yl)methyl]-4H-chromen-4-one (35). $C_{23}H_{24}N_2O_4$, yield 68%, mp 186-188°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.21 (3H, s, CH_3-2), 3.78 (3H, s, OMe-2′), 4.04 (2H, s, CH_2-8), 6.84 (1H, d, ^3J = 8.8, H-6), 6.98 (1H, m, H-3′), 7.02 (1H, m, H-5′), 7.16 (1H, m, H-6′), 7.35 (1H, m, H-4′), 8.05 (1H, d, ^3J = 8.8, H-5); amine protons 2.35 (3H, s, 4-NCH_3), 2.00-3.24 (8H, m, $4CH_2$).

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