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SYNTHESIS OF PSEUDOBAPTIGENIN ANALOGS

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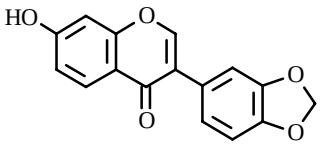
Homologs of the natural isoflavonoid pseudobaptigenin containing benzodioxane and benzodioxepane fragments were synthesized. Methanesulfonyl, carbamoyl, aminomethyl, and coumarin-containing isoflavone derivatives were prepared.

Key words: isoflavonoids, alkylation, acylation, aminomethylation, 4-chloromethylcoumarins, urethanes.

We carried out alkylation, acylation, and aminomethylation of isoflavones **1a-j** in order to modify pseudobaptigenin **1** [1, 2].



1

We used substituted 4-chloromethylcoumarins, derivatives of which exhibited antifungal properties, as the alkylating reagents [3]. The starting 4-chloromethylcoumarins were prepared by reaction of 4-chloroacetoacetic ester with substituted phenols in the presence of conc. H_2SO_4 (Pechmann reaction).

New isoflavones **2a-e**, which contain chromone and coumarin fragments, were synthesized by alkylation in a DMF—acetone mixture in the presence of potash.

One of the methods for modifying the synthesized isoflavones **1a-j** was Mannich aminomethylation. The Mannich bases prepared from the isoflavones are central-nervous-system and respiratory-pathway regulators. They exhibit anticonvulsive, antiallergic, and analgesic activities [4, 5]. Mannich bases based on the natural flavolignan silybin possess hepatoprotective and hypocholesteric activities [6]. Therefore, it seemed interesting to synthesize analogs that contain benzodioxane and benzodioxepane fragments.

The desired Mannich bases **3a-f**, **4a-e**, and **5a** and **b** were prepared according to the literature [7] using various aminals.

We found that reaction of equivalent amounts of aminal and isoflavone in boiling dioxane leads to aminomethylation of the chromone ring at the 8-position. It should be noted that isoflavones containing an ester in the second position are easily aminomethylated whereas aminolysis by the amine does not occur. This feature can be used for further modification of the isoflavones and to open a promising route to the preparation of aminomethyl derivatives with labile substituents.

Derivatives of sulfonic acids exhibit a wide spectrum of biological activity, for example, sulfamide preparations are used as chemotherapeutic antibacterial agents. Therefore, it was interesting to synthesize analogous modified isoflavones **6a-c**. Derivatives of sulfonic acids of isoflavones were prepared from the corresponding 7-hydroxyisoflavones **1e**, **f**, and **i** by reaction with methtanesulfonyl chloride in pyridine.

It was interesting to prepare urethanes during the study of the reactivity of phenolic hydroxyls of isoflavones. However, we did not find conditions for the reaction of 7-hydroxyisoflavones with isocyanates, which may be due to the insignificant reactivity of the hydroxyl and the reversibility of the reaction. We achieved the goal by reacting N,N-disubstituted carbamoyl chlorides. As it turned out, their reaction with 7-hydroxyisoflavones proceeds readily in pyridine at room temperature to form **7a-l**.

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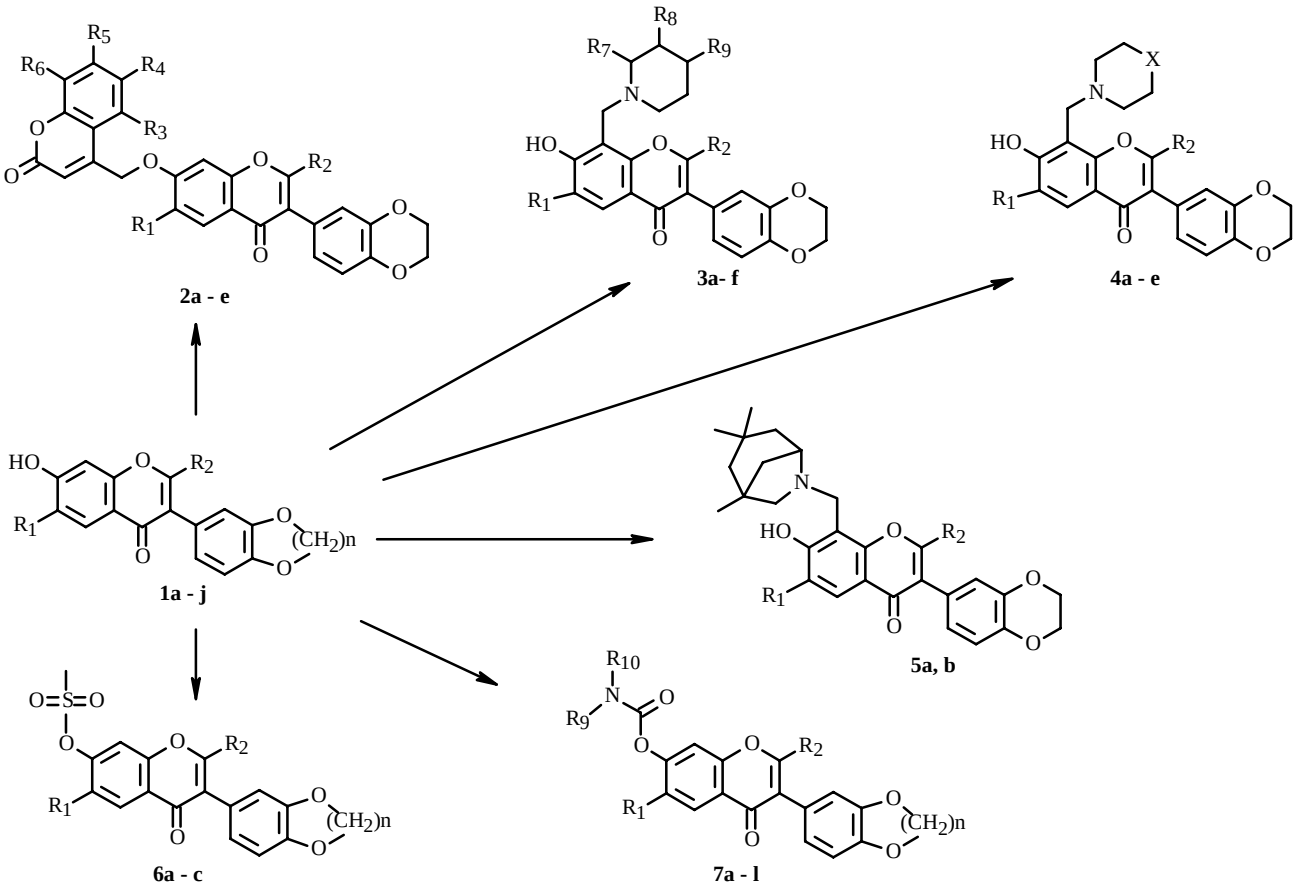

1a-f, **6a**,**b**, **7a**,**b**,**e**,**f**,**i**,**j**: n =2; **1g-j**, **6c**, **7c**,**d**,**g**,**h**,**k**,**l**: n = 3

1a, **2a**,**c**,**3a**,**d**,**f**, **4a**,**c**,**e**, **5a**: R_1 = H; **1b - d**,**g**,**h**, **2d**, **3b**,**c**,**e**, **4b**, **d**, **5b**, **7a**,**c**,**g**,**h**,**i**,**k**: R_1 = Et;
1e,**f**,**i**,**j**, **2b**,**e, 6a - c**, **7b**, **d - f**, **j**,**l**: R_1 = Pr;
2a,b: $R_3 = R_5$ = Me, $R_4 = R_6$ = H; **2c**: $R_3 = R_5$ = H, $R_4 = R_6$ = Me; **2d,e**: $R_3 = R_4 = R_6$ = H, R_5 = OMe;
3a - c: R_7 = Me, $R_8 = R_9$ = H; **3d,e**: $R_7 = R_9$ = H, R_8 = Me; **3f**: $R_7 = R_8$ = H, R_9 = Me;
4a: X = bond; **4b**: X = NMe; **4c,d**: X = NCH_2CH_2OH; **4e**: X = CH_2CH_2;
7a - d: $R_9 = R_{10}$ = Me, **7e-h**: $R_9 = R_{10}$ = Ph, **7i-l**: R_9R_{10} = $CH_2CH_2OCH_2CH_2$;
1a,b,e,g,i, 2a - e, **3a,b,d,f**, **4a,c,e**, **5a**, **6a,c**, **7e,g**, **i - l**: R_2 = Me;
1c,f,h,j, **6b,7a - d**, **f**, **h**: R_2 = Me; **1d, 3c,e**, **4b**,**d**, **5b**: R_2 = CO_2Et

EXPERIMENTAL

The course of reactions and purity of compounds were monitored by TLC on Sorbfil UV-254 (Russia) and Merk (Germany) plates. The eluent was a $CHCl_3$:CH_3OH (95:5) mixture. PMR spectra (δ, ppm, J/Hz) were measured on VXR-300 and Mercury 400 instruments (Varian, 300 and 400 MHz, respectively) in DMSO-d_6 and $CDCl_3$ relative to TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

Starting isoflavones **1a-j** were prepared as before [1, 2].

General Method for Preparing 7-Coumarylmethoxyisoflavonoes 2a-e. A hot solution of the appropriate 7-hydroxychromone (10 mmol) in absolute acetone (15 mL) and DMF (15 mL) was treated with freshly calcined K_2CO_3 (2.1 g, 15 mmol), stirred and heated to 60°C, treated with the appropriate 4-chloromethylcoumarin (12 mmol), left for 20 h (completion of the reaction determined by TLC), and poured into acidic ice water (100 mL). The resulting precipitate was filtered off and crystallized from propan-2-ol.

4-[3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-4*H*-chromen-7-yloxymethyl]-5,7-dimethylchromen-2-one (2a), mp 285-286°C. PMR spectrum: 4.28 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.07 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.15 (d, H-2′, ^4J = 2.4), 7.39 (1H, d, H-8, ^4J = 2.0), 7.29 (1H, dd, H-6, ^3J = 8.4, ^4J = 2.0), 8.10 (1H, d, H-5, ^3J = 8.4), 8.44 (1H, s, H-2), coumarin protons: 2.37, 2.72 (3H, 3H, 2s, CH_3-5 and CH_3-7), 5.69 (2H, s, CH_2O-4), 6.58 (1H, s, H-3), 7.08 (1H, br.s, H-8), 7.15 (1H, br.s, H-6).

4-([3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl]oxymethyl)-5,7-dimethyl-2*H*-chromen-2-one (2b), mp 226-227°C. PMR spectrum: 0.94 (3H, t, ^3J = 7.6), 1.65 (2H, m, ^3J = 7.6), 2.7 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$, 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.06 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.14 (d, H-2′, ^4J = 2.4), 7.34 (1H, s, H-8), 7.92 (1H, s, H-5), 8.44 (1H, s, H-2); coumarin protons: 2.38, 2.74 (3H, 3H, 2s, CH_3-5 and CH_3-7), 5.72 (2H, s, CH_2O-4), 6.52 (1H, s, H-3), 7.08 (1H, br.s, H-8), 7.15 (1H, br.s, H-6).

4-[3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-4*H*-chromen-7-yloxymethyl]-6,8-dimethylchromen-2-one (2c), mp 294-295°C. PMR spectrum: 4.28 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.07 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.15 (d, H-2′, ^4J = 2.4), 7.53 (1H, d, H-8, ^4J = 2.0), 7.32 (1H, dd, H-6, ^3J = 8.4, ^4J = 2.4), 8.08 (1H, d, H-5, ^3J = 8.4), 8.46 (1H, s, H-2); coumarin protons: 2.36, 2.38 (3H, 3H, 2s, CH_3-6 and CH_3-8), 5.53 (2H, s, CH_2O-4), 6.63 (1H, s, H-3), 7.37 (1H, br.s, H-5), 7.58 (1H, br.s, H-7).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-(7-methoxy-2-oxo-2*H*-chromen-4-ylmethoxy)-chromen-4-one (2d), mp 241-242°C. PMR spectrum: 1.24 (3H, t, ^3J = 7.8), 2.77 (2H, q, ^3J = 7.8), 6-CH_3CH_2; 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.02 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.15 (d, H-2′, ^4J = 2.4), 7.54 (1H, s, H-8), 7.91 (1H, s, H-5), 8.45 (1H, s, H-2); coumarin protons: 3.89 (3H, s, 7-MeO), 5.53 (2H, s, CH_2O-4), 6.43 (1H, s, H-3), 7.02 (1H, dd, H-6, ^3J = 8.8, ^4J = 2.4), 7.06 (1H, d, H-8, ^4J = 2.4), 7.88 (1H, d, H-5, ^3J = 8.8).

3-(2,3-Dihydrobenzo[1,4]diioxan-6-yl)-7-(7-methoxy-2-oxo-2*H*-chromen-4-ylmethoxy)-6-propylchromen-4-one (2e), mp 233-234°C. PMR spectrum: 0.94 (3H, t, ^3J = 7.6), 1.63 (2H, m, ^3J = 7.6), 2.72 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 4.27 [4H, m, $O(CH_2)_2O$], 6.89 (1H, d, H-5′, ^3J = 8.4), 7.06 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.14 (d, H-2′, ^4J = 2.4), 7.52 (1H, s, H-8), 7.87 (1H, s, H-5), 8.43 (1H, s, H-2); coumarin protons: 3.87 (3H, s, 7-MeO), 5.49 (2H, s, CH_2O-4), 6.39 (1H, s, H-3), 7.01 (1H, dd, H-6, ^3J = 8.8, ^4J = 2.4), 7.04 (1H, d, H-8, ^4J = 2.4), 7.85 (1H, d, H-5, ^3J = 8.8).

General Method for Preparing 8-Dialkylaminomethylisoflavones 3a-f, 4a-e, and 5a and b. A boiling solution of the appropriate isoflavone (10 mmol) in absolute dioxane (20 mL) was treated with aminal (15 mmol), boiled for 3-4 h (completion of the reaction determined by TLC), cooled. The dioxane, released amine, and unreacted aminal were evaporated in vacuum. The solid was recrystallized from propan-2-ol.

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-(2-methylpiperidin-1-ylmethyl)-chromen-4-one (3a), mp 179-180°C. PMR spectrum: 1.21, 1.12-3.26 (3H, d, 9H, m, piperidine protons), 3.88, 4.27 (2H, 2d, ^2J = 15.3, CH_2-8), 4.28 [4H, m, $0(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.84 (1H, d, ^3J = 9.0, H-6), 8.09 (1H, d, ^3J = 9.0, H-5), 7.85 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-8-(2-methylpiperidin-1-ylmethyl)-chromen-4-one (3b), mp 143-144°C. PMR spectrum: 1.26 (3H, t, ^3J = 7.8), 2.69 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.20, 1.12-3.26 (3H, m, 9H, m, piperidine protons), 3.75-4.50 (2H, m, CH_2-8), 4.28 [4H, m, $O(CH_2)_20$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 7.96 (1H, d, ^3J = 9.0, H-5), 7.84 (1H, s, H-2).

Ethyl 3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-8-(2-methylpiperidin-1-ylmethyl)-4-oxo-4*H*-chromen-2-carboxylate (3c), mp 155-156°C. PMR spectrum: 1.06 (3H, t, ^3J = 7.8), 2.69 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.25 (3H, t, ^3J = 8.0), 4.17 (2H, q, ^3J = 8.0) 2-CH_3CH_2OOC; 1.19, 1.33-3.19 (3H, m, 9H, m, piperidine protons), 3.80-4.53 (2H, m, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.88 (1H, d, H-5′, ^3J = 8.4), 6.74 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.83 (d, H-2′, ^4J = 2.4), 7.88 (1H, d, ^3J = 9.0, H-5).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-(3-methylpiperidin-1-ylmethyl)-chromen-4-one (3d), mp 183-184°C. PMR spectrum: 0.92, 0.76-3.13 (3H, d, 9H, m, piperidine protons), 3.98 (2H, s, CH_2-8), 4.28 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.86 (1H, d, ^3J = 9.0, H-6), 8.12 (1H, d, ^3J = 9.0, H-5), 7.85 (1H, s, H-2).

Ethyl 3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-8-(3-methylpiperidin-1-ylmethyl)-4-oxo-4*H*-chromen-2-carboxylate (3e), mp 204-205°C. PMR spectrum: 1.07 (3H, t, ^3J = 7.8), 2.70 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.26 (3H, t, ^3J = 8.0), 4.17 (2H, q, ^3J = 8.0) 2-CH_3CH_2OOC; 0.92, 0.88-3.19 (3H, m, 9H, m, piperidine protons), 4.04 (2H, s, CH_2-8),

4.28 [4H, m, $O(CH_2)_2O$], 6.89 (1H, d, H-5′, ^3J = 8.4), 6.75 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.83 (d, H-2′, ^4J = 2.4), 7.91 (1H, d, ^3J = 9.0, H-5).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-(4-methylpiperidin-1-ylmethyl)-chromen-4-one (3f), mp 190-191°C. PMR spectrum: 0.97, 1.21-3.16 (3H, d, 9H, m, piperidine protons), 3.99 (2H, s, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.02 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.86 (1H, d, ^3J = 9.0, H-6), 8.10 (1H, d, ^3J = 9.0, H-5), 7.85 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-pyrrolidin-1-ylmethylchromen-4-one (4a), mp 206-207°C. PMR spectrum: 1.82-2.00, 2.65-2.85 (4H, 4H, 2m, pyrrolidine protons), 4.15 (2H, s, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.86 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.87 (1H, d, ^3J = 9.0, H-6), 8.11 (1H, d, ^3J = 9.0, H-5), 7.86 (1H, s, H-2).

Ethyl 3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-8-(4-methylpiperazin-1-ylmethyl)-4-oxo-4*H*-chromen-2-carboxylate (4b), mp 200-201°C. PMR spectrum: 1.08 (3H, t, ^3J = 7.8), 2.70 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.25 (3H, t, ^3J = 8.0), 4.18 (2H, q, ^3J = 8.0) 2-CH_3CH_2OOC; 2.00-3.17 (8H, m, piperazine protons), 2.34 (3H, s, NCH_3), 4.07 (2H, s, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.88 (1H, d, H-5′, ^3J = 8.4), 6.73 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.82 (d, H-2′, ^4J = 2.4), 7.91 (1H, d, ^3J = 9.0, H-5).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-[4-(2-hydroxyethyl)-piperazin-1-ylmethyl]-chromen-4-one (4c), mp 174-175°C. PMR: 2.20-3.20 (8H, m, piperazine protons), 2.60, 3.64 (4H, m, NCH_2CH_2O), 4.04 (2H, s, CH_2-8), 4.28 [4H, m, $O(CH_2)_2O$], 6.90 (1H, d, H-5′, ^3J = 8.4), 7.02 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.88 (1H, d, ^3J = 9.0, H-6), 8.12 (1H, d, ^3J = 9.0, H-5), 7.87 (1H, s, H-2).

Ethyl 3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-8-[4-(2-hydroxyethyl)-piperazin-1-ylmethyl]-4-oxo-4*H*-chromen-2-carboxylate (4d), mp 210-211°C. PMR spectrum: 1.08 (3H, t, ^3J = 7.8), 2.69 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.25 (3H, t, ^3J = 8.0), 4.18 (2H, q, ^3J = 8.0) 2-CH_3CH_2OOC; 2.20-3.20 (8H, m, piperazine protons), 2.61, 3.64 (4H, m, NCH_2CH_2O), 4.08 (2H, s, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.89 (1H, d, H-5′, ^3J = 8.4), 6.74 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.82 (d, H-2′, ^4J = 2.4), 7.96 (1H, d, ^3J = 9.0, H-5).

8-Azepan-1-ylmethyl-3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxychromen-4-one (4e), mp 196-197°C. PMR spectrum: 1.57-1.90, 2.69-2.94 (8H, 4H, 2m, azepan protons), 4.10 (2H, s, CH_2-8), 4.28 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 6.87 (1H, d, ^3J = 9.0, H-6), 8.12 (1H, d, ^3J = 9.0, H-5), 7.85 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-7-hydroxy-8-(1,3,3-trimethyl-6-aza-bicyclo[3.2.1]oct-6-ylmethyl)-chromen-4-one (5a), mp 200-201°C. PMR spectrum: 0.84-3.33 (18H, m, base protons), 3.98, 4.26 (2H, 2d, ^2J = 11.4, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.03 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.09 (d, H-2′, ^4J = 2.4), 8.12 (1H, d, ^3J = 9.0, H-5), 7.85 (1H, s, H-2).

Ethyl 3-(2,3-dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-7-hydroxy-4-oxo-8-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-ylmethyl)-4*H*-chromen-2-carboxylate (5b), mp 158-159°C. PMR spectrum: 1.07 (3H, t, ^3J = 7.8), 2.71 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 1.25 (3H, t, ^3J = 8.0), 4.17 (2H, q, ^3J = 8.0) 2-CH_3CH_2OOC; 0.91-3.36 (18H, m, base protons), 4.00, 4.30 (2H, 2d, ^2J = 14.0, CH_2-8), 4.27 [4H, m, $O(CH_2)_2O$], 6.88 (1H, d, H-5′, ^3J = 8.4), 6.74 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.82 (d, H-2′, ^4J = 2.4), 7.91 (1H, d, ^3J = 9.0, H-5).

General Method for Synthesizing 6a-c and 7a-l. A solution of the appropriate 7-hydroxyisoflavone (10 mmol) in the minimal amount of absolute pyridine was treated with the acid chloride (12 mmol). The reaction mixture was held for 1 d at room temperature and then poured into icewater. The resulting precipitate was filtered off and crystallized from alcohol (**6a-c**) or propan-2-ol (**7a-c**).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl methanesulfonate (6a), mp 148-149°C (ethanol). PMR spectrum: 0.93 (3H, t, ^3J = 7.6), 1.63 (2H, m, ^3J = 7.6), 2.75 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 3.63 (3H, s, 7-CH_3SO_2O), 4.27 [4H, m, $O(CH_2)_2O$], 6.92 (1H, d, H-5′, ^3J = 8.4), 7.06 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.13 (d, H-2′, ^4J = 2.4), 7.75 (1H, s, H-8), 8.07 (1H, s, H-6), 8.52 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-2-methyl-4-oxo-6-propyl-4*H*-chromen-7-yl methanesulfonate (6b), mp 123-124°C. PMR spectrum: 0.92 (3H, t, ^3J = 7.6), 1.62 (2H, m, ^3J = 7.6), 2.74 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 2.29 (3H, s, 2-CH_3), 3.62 (3H, s, 7-CH_3SO_2O), 4.28 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 6.72 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.78 (d, H-2′, ^4J = 2.4), 7.72 (1H, s, H-8), 7.97 (1H, s, H-6).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl methanesulfonate (6c), mp 112-113°C. PMR spectrum: 0.93 (3H, t, ^3J = 7.6), 1.63 (2H, m, ^3J = 7.6), 2.76 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 3.63 (3H, s, 7-CH_3SO_2O), 4.16 (4H, m), 2.13 (2H, m) $O(CH_2)_3O$; 7.02 (1H, d, H-5′, ^3J = 8.4), 7.18 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.24 (d, H-2′, ^4J = 2.4), 7.76 (1H, s, H-8), 8.04 (1H, s, H-6), 8.55 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-2-methyl-4-oxo-4*H*-chromen-7-yl dimethylcarbamate (7a), mp 218-219°C. PMR spectrum: 1.17 (3H, t, ^3J = 7.8), 2.632 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 2.27 (3H, s, 2-CH_3), 2.96, 3.11 [6H, 2s, 7-$(CH_3)_2NCOO$], 4.28 [4H, m, $O(CH_2)_2O$], 6.90 (1H, d, H-5′, ^3J = 8.4), 6.72 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.78 (d, H-2′, ^4J = 2.4), 7.43 (1H, s, H-8), 7.90 (1H, s, H-6).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-2-methyl-4-oxo-6-propyl-4*H*-chromen-7-yl dimethylcarbamate (7b), mp 214-215°C. PMR spectrum: 0.89 (3H, t, ^3J = 7.6), 1.57 (2H, m, ^3J = 7.6), 2.60 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 2.27 (3H, s, 2-CH_3), 2.96, 3.10 [6H, 2s, 7-$(CH_3)_2NCOO$], 4.27 [4H, m, $O(CH_2)_2O$], 6.90 (1H, d, H-5′, ^3J = 8.4), 6.72 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.78 (d, H-2′, ^4J = 2.4), 7.44 (1H, s, H-8), 7.88 (1H, s, H-6).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-6-ethyl-2-methyl-4-oxo-4*H*-chromen-7-yl dimethylcarbamate (7c), mp 161-162°C. PMR spectrum: 0.93 (3H, t, ^3J = 7.6), 1.63 (2H, m, ^3J = 7.6), 2.76 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 2.27 (3H, s, 2-CH_3), 2.95, 3.10 [6H, 2s, 7-$(CH_3)_2NCOO$], 4.18 (4H, m), 2.12 (2H, m) $O(CH_2)_3O$; 7.01 (1H, d, H-5′, ^3J = 8.4), 6.85 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.89 (d, H-2′, ^4J = 2.4), 7.44 (1H, s, H-8), 7.90 (1H, s, H-6).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-2-methyl-4-oxo-6-propyl-4*H*-chromen-7-yl dimethylcarbamate (7d), mp 152-153°C. PMR spectrum: 1.17 (3H, t, ^3J = 7.8), 2.63 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 2.27 (3H, s, 2-CH_3), 2.95, 3.10 [6H, 2s, 7-$(CH_3)_2NCOO$], 4.18 (4H, m), 2.12 (2H, m) $O(CH_2)_3O$; 7.01 (1H, d, H-5′, ^3J = 8.4), 6.85 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.89 (d, H-2′, ^4J = 2.4), 7.44 (1H, s, H-8), 7.90 (1H, s, H-6).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl diphenylcarbamate (7e), mp 95-96°C. PMR spectrum: 0.78 (3H, t, ^3J = 7.6), 1.32 (2H, m, ^3J = 7.6), 2.49 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 4.26 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.05 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.13 (d, H-2′, ^4J = 2.4), 7.28-7.60 (10H, m, Ph_2NCOO-7), 7.72 (1H, s, H-8), 7.95 (1H, s, H-6), 8.46 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-2-methyl-4-oxo-6-propyl-4*H*-chromen-7-yl diphenylcarbamate (7f), mp 176-177°C. PMR spectrum: 0.78 (3H, t, ^3J = 7.6), 1.32 (2H, m, ^3J = 7.6), 2.48 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 2.27 (3H, s, 2-CH_3), 4.27 [4H, m, $O(CH_2)_2O$], 6.89 (1H, d, H-5′, ^3J = 8.4), 6.72 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.78 (d, H-2′, ^4J = 2.4), 7.32-7.53 (10H, m, Ph_2NCOO-7), 7.69 (1H, s, H-8), 7.85 (1H, s, H-6).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-6-ethyl-4-oxo-4*H*-chromen-7-yl diphenylcarbamate (7g), mp 93-94°C. PMR spectrum: 0.99 (3H, t, ^3J = 7.8), 2.56 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 4.16 (4H, m), 2.12 (2H, m) $O(CH_2)_3O$; 7.01 (1H, d, H-5′, ^3J = 8.4), 7.17 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.24 (d, H-2′, ^4J = 2.4), 7.28-7.60 (10H, m, Ph_2NCOO-7), 7.74 (1H, s, H-8), 7.98 (1H, s, H-6), 8.51 (1H, s, H-2).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-6-ethyl-2-methyl-4-oxo-4*H*-chromen-7-yl diphenylcarbamate (7h), mp 140-141°C. PMR spectrum: 0.99, J/Hz (3H, t, ^3J = 7.8), 2.55 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 2.28 (3H, s, 2-CH_3), 4.17 (4H, m), 2.12 (2H, m) $O(CH_2)_3O$; 7.00 (1H, d, H-5′, ^3J = 8.4), 6.85 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 6.89 (d, H-2′, ^4J = 2.4), 7.32-7.52 (10H, m, Ph_2NCOO-7), 7.69 (1H, s, H-8), 7.87 (1H, s, H-6).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-6-ethyl-4-oxo-4*H*-chromen-7-yl morpholine-4-carboxylate (7i), mp 216-217°C. PMR spectrum: 1.19 (3H, t, ^3J = 7.8), 2.65 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 3.40-3.55, 3.55-3.80 [8H, m, $N(CH_2CH_2)_2O$], 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.05 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.13 (d, H-2′, ^4J = 2.4), 7.54 (1H, s, H-8), 8.01 (1H, s, H-6), 8.47 (1H, s, H-2).

3-(2,3-Dihydrobenzo[1,4]dioxan-6-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl morpholine-4-carboxylate (7j), mp 194-195°C. PMR spectrum: 0.91 (3H, t, ^3J = 7.6), 1.57 (2H, m, ^3J = 7.6), 2.61 (2H, q, ^3J = 7.6) 6-$CH_3CH_2CH_2$; 3.42-3.50, 3.61-3.72 [8H, m, $N(CH_2CH_2)O$], 4.27 [4H, m, $O(CH_2)_2O$], 6.91 (1H, d, H-5′, ^3J = 8.4), 7.05 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.13 (d, H-2′, ^4J = 2.4), 7.54 (1H, s, H-8), 7.99 (1H, s, H-6), 8.46 (1H, s, H-2).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-6-ethyl-4-oxo-4*H*-chromen-7-yl morpholine-4-carboxylate (7k), mp 162-163°C. PMR spectrum: 1.19 (3H, t, ^3J = 7.8), 2.66 (2H, q, ^3J = 7.8) 6-CH_3CH_2; 3.42-3.50, 3.62-3.72 [8H, m, $N(CH_2CH_2)O$], 4.16 (4H, m), 2.13 (2H, m) $O(CH_2)_3O$; 7.02 (1H, d, H-5′, ^3J = 8.4), 7.18 (1H, dd, H-6′, ^3J = 8.4, ^4J = 2.4), 7.25 (d, H-2′, ^4J = 2.4), 7.55 (1H, s, H-8), 8.01 (1H, s, H-6), 8.50 (1H, s, H-2).

3-(3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepan-7-yl)-4-oxo-6-propyl-4*H*-chromen-7-yl morpholine-4-carboxylate (7l), mp 187-188°C. PMR spectrum: 0.91 (3H, t, ^{3}J = 7.6), 1.57 (2H, m, ^{3}J = 7.6), 2.62 (2H, m, ^{3}J = 7.6) 6-$CH_3CH_2CH_2$; 3.42-3.52, 3.58-3.75 [8H, m, $N(CH_2CH_2)O$], 4.16 (4H, m), 2.13 (2H, m) $O(CH_2)_3O$; 7.02 (1H, d, H-5′, ^{3}J = 8.4), 7.18 (1H, dd, H-6′, ^{3}J = 8.4, ^{4}J = 2.4), 7.24 (d, H-2′, ^{4}J = 2.4), 7.56 (1H, s, H-8), 7.99 (1H, s, H-6), 8.49 (1H, s, H-2).

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