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REACTIVITY OF CONDENSED ISOFLAVONE DERIVATIVES FOR HYDRAZINE

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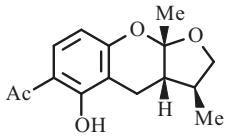
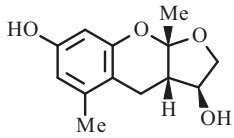
*Recyclization by hydrazine of furo[3,2-*b*]pyrano[2,3-*f*]chromen-4-ones, dipyrano[2,3-*b*:2′,3′-*f*]chromen-4-ones, and pyrano[2,3-*a*]xanthen-4-ones derived from natural isoflavonoids and their analogs was studied. The reaction was shown to proceed selectively with opening of the chromone ring. Several substituted 4-arylpyrazoles containing furo[3,2-*b*]chromen-5-ol, pyrano[2,3-*b*]chromen-6-ol, and xanthen-8-ol fragments were synthesized.*

Keywords: isoflavone, pyrazole, furo[3,2-*b*]chromen-5-ol, pyrano[2,3-*b*]chromen-6-ol, xanthen-8-ol.

2,3-Condensed chromone derivatives occur among secondary metabolites of plants and fungi and are interesting subjects in the chemistry of natural compounds. Unique xyloketals A-H in addition to widely distributed xanthone derivatives were isolated from mangrove fungus *Xylaria* sp. [1–4]; alboatrin, from *Verticillium albo-atrum* [5]. These contained furo[3,2-*b*]chromane moieties. Various methods for synthesizing the xyloketal core and its analogs have now been developed based on construction of pyran and furan rings [6–10].



Xyloketal D



Alboatrin

Benzopyrone derivatives can be precursors for synthesizing substituted pyrazoles [11, 12], pyrimidines [13, 14], or isoxazoles [15, 16] because nucleophiles tend to cleave the chromone core. This prompted us to study the preparation of 4-arylpyrazoles containing xyloketal or analogous cores.

Condensed derivatives of natural isoflavonoids and their analogs were synthesized via an inverse electron-demand Diels–Alder heteroreaction [17] and contained two substituted heterocyclic systems that could react with hydrazine or its derivatives. Thus, furo[3,2-*b*]pyrano[2,3-*f*]chromen-4-ones **3a**, **c**–**e**, **g**–**i**, and **h** and dipyrano[2,3-*b*:2′,3′-*f*]chromen-4-ones **4a** and **4b**, which were produced via condensation of the Mannich bases of isoflavones **2a**–**j** with 2,3-dihydrofuran or 3,4-dihydro-2*H*-pyran, contained a chromone fragment and an acetal that could react with hydrazine. Nucleophilic attack by hydrazine of 3-aryl-8,9,10,12-tetrahydro-4*H*,11*H*-pyrano[2,3-*a*]xanthen-4,11-diones **5a**–**c**, **f**–**h**, and **j** could occur at various positions of the heterocyclic system, i.e., at the 4- or 11-carbonyls to form hydrazones and at heterocyclic 2- and 7a-ketones resulting from opening of the pyrone rings.

As it turned out, the course of the reaction under the given conditions of the chromone derivatives with hydrazine was not affected by the acetal moiety in **3** and **4**. The stability of the acetals under weakly basic conditions may have been responsible for this. As a result, the reaction afforded high yields of pyrazolyl-substituted 2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ols **6a**, **c**–**e**, **g**–**i**, and **h** and 3,4,4a,10a-tetrahydro-2*H*,5*H*-pyrano[2,3-*b*]chromen-6-ols **7a** and **7b**.

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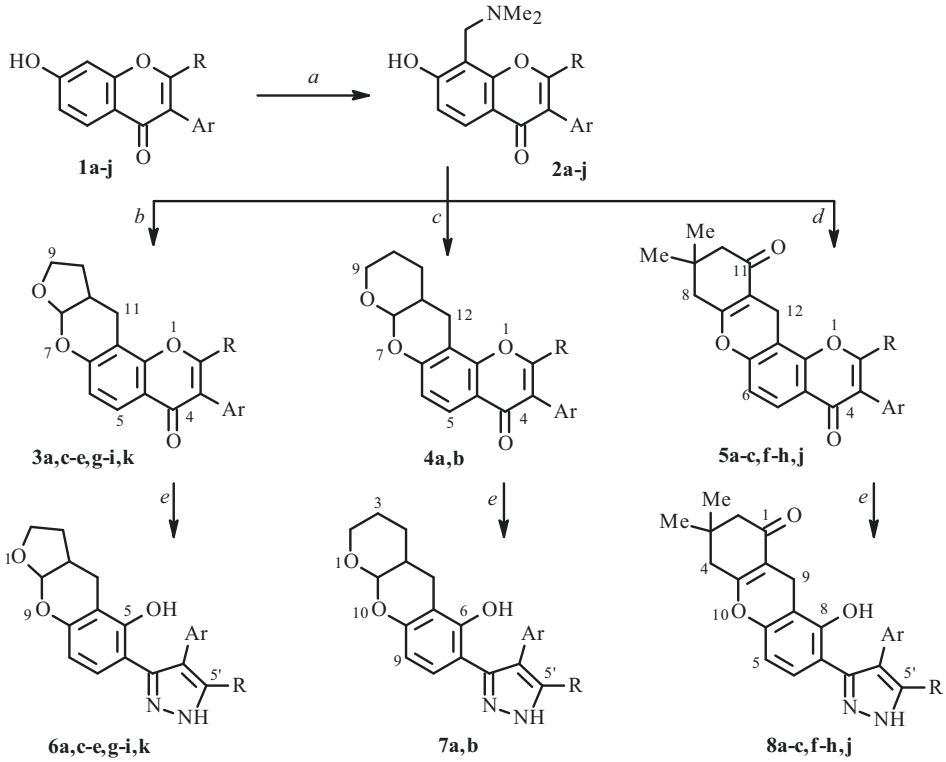

a: R = H, Ar = C_6H_4OMe-4; **b:** R = H, Ar = $C_6H_3(OMe)_2$-3,4; **c:** R = H, Ar = $C_6H_3(OCH_2O)$-3,4
d: R = H, Ar = C_6H_4Cl-4; **e:** R = H, Ar = $C_6H_3(OCH_2CH_2O)$-3,4; **f:** R = H, Ar = C_6H_4F-2; **g:** R = Me, Ar = Ph
h: R = Me, Ar = C_6H_4OMe-4; **i:** R = Me, Ar = $C_6H_3(OMe)_2$-3,4; **j:** R = Me, Ar = C_6H_4F-4; **k:** R = Me, Ar = C_6H_4Cl-4

a. $CH_2(NMe_2)_2$, *i*-PrOH; *b*. 2,3-dihydrofuran, DMF; *c*. 3,4-dihydro-2*H*-pyran, DMF;
d. 3-(*N*,*N*-dimethylamino)-5,5-dimethyl-2-cyclohexen-1-one, DMF; *e*. N_2H_4, EtOH

Reaction of hydrazine with 3-aryl-8,9,10,12-tetrahydro-4*H*,11*H*-pyrano[2,3-*a*]xanthene-4,11-diones **5a**–**c**, **f**–**h**, and **j** under these same conditions gave the major products 8-hydroxy-3-[4-arylpyrazol-3-yl]-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-ones **8a**–**c**, **f**–**h**, and **j**. Moreover, prolonged heating of compounds **5** with hydrazine formed insignificant quantities of the hydrazones of **8**, as confirmed by HPLC-MS.

As noted in our previous work, the reactivity toward binucleophiles decreased noticeably for natural isoflavone derivatives with electron-donating methoxyls on ring B, especially 2-methyl-substituted isoflavones **3g**–**i** and **k** and **5g**, **h**, and **j**, recyclization of which by hydrazine took several hours.

The pyrazole structure of **6**–**8** was confirmed by PMR and ^{13}C NMR spectroscopy. PMR spectra of **6**–**8** exhibited diamagnetic shifts by 0.7–0.8 and 1.2–1.3 ppm for the protons of the oxygen-containing aromatic heterocycle as compared with the positions of these proton resonances in starting compounds **3**–**5**. However, the positions and SSCCs of acetal protons in **6** and **7** were practically unchanged. Also, prototropic tautomerism of the pyrazole ring broadened resonances in both the PMR and ^{13}C NMR spectra.

The ^{13}C NMR spectrum of **8b** can be used as examples to demonstrate the presence of a xanthenone fragment. Thus, the resonance at 196.78 ppm was indicative of a carbonyl; a weak-field resonance at 163.99 ppm, to C-4a.

Thus, polycyclic oxygen-containing heterocycles prepared under inverse electron-demand Diels–Alder reaction conditions via cycloaddition of electron-rich dienes to *o*-quinone methides could be convenient intermediates for preparing derivatives of natural compounds.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Silufol UV-254_f plates (Merck, Germany) using CH_2Cl_2–MeOH (9:1, 95:5). PMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 vs. TMS internal standard on the δ-scale on Varian M400 (400 and 100 MHz, respectively) and Bruker 500 instruments (500 and 125 MHz,

respectively). GC-MS used an Agilent 1100 Series HPLC-MS equipped with an Agilent LC\MSD SL mass-selective diode-array detector and chemical ionization at atmospheric pressure (APCI). Elemental analyses of all compounds agreed with those calculated.

General Method for Preparing 8-Dimethylaminomethyl-7-hydroxyisoflavones 2a–j. A suspension of 7-hydroxyisoflavone (**1a**–**j**, 2 mmol) in *i*-PrOH (20 mL) was stirred, refluxed, treated with bis(dimethylamino)methane (2.4 mmol), refluxed for 6–8 h until the starting isoflavone was completely dissolved (end of reaction determined by TLC), and cooled. The precipitated Mannich base was filtered off, rinsed with hexane, and dried. If crystallization did not occur, the solvent and excesses of reagents were evaporated at reduced pressure. The solid was crystallized from *i*-PrOH–hexane. Data for synthesized Mannich bases **2a**–**e**, **g**–**i**, and **k** were reported by us earlier [17, 18].

7-Hydroxy-8-[(dimethylamino)methyl]-3-(2-fluorophenyl)-4*H*-chromen-4-one (2f). Yield 73%, $C_{18}H_{16}FNO_3$, mp 165–167°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.43 (6H, s, $N(CH_3)_2$), 3.99 (2H, s, H-8), 6.90 (1H, d, J = 8.8, H-6), 7.12–7.23, 7.31–7.40, 7.46–7.53 (2H, 1H, 1H, 3m, 3-C_6H_4F-*o*), 7.94 (1H, s, H-2), 8.12 (1H, d, J = 8.8, H-5), 10.60 (1H, s, 7-OH). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 44.60, 55.16, 107.61, 115.74, 115.78 (d, J(C/F) = 22.4), 116.91, 119.61 (d, J(C/F) = 14.9), 119.64 (d, J(C/F) = 1.3), 124.00 (d, J(C/F) = 3.7), 126.79, 129.93 (d, J(C/F) = 8.2), 132.14 (d, J(C/F) = 3.1), 153.34 (d, J(C/F) = 3.5), 155.01, 160.26 (d, J(C/F) = 247.4), 164.29, 175.03. ^{19}F NMR spectrum (377 MHz, $CDCl_3$, δ, ppm): 115.17. MS (CI) *m/z* 314.0 (MH^+, 100).

7-Hydroxy-8-[(dimethylamino)methyl]-3-(4-fluorophenyl)-2-methyl-4*H*-chromen-4-one (2j). Yield 69%, $C_{19}H_{18}FNO_3$, mp 160–162°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.24 (3H, s, H-2), 2.35 (6H, s, $N(CH_3)_2$), 3.94 (2H, s, H-8), 6.83 (1H, d, J = 8.8, H-6), 7.19–7.39 (4H, m, H-2′, 3′, 5′, 6′), 7.80 (1H, d, J = 8.8, H-5). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm, J/Hz): 19.14, 44.04, 53.30, 108.19, 114.67, 114.90 (d, J(C/F) = 21.1), 114.97, 120.96, 125.56, 129.63 (d, J(C/F) = 3.3), 132.61 (d, J(C/F) = 8.1), 154.68, 161.52 (d, J(C/F) = 243.8), 162.25, 163.86, 174.88. ^{19}F NMR spectrum (377 MHz, DMSO-d_6, δ, ppm): –115.06. MS (CI) *m/z* 328.2 (MH^+, 100).

9,9-Dimethyl-3-(2-fluorophenyl)-8,9,10,12-tetrahydro-4*H*,11*H*-pyrano[2,3-*a*]xanthene-4,11-dione (5f). A solution of Mannich base (314 mg, 1 mmol) and 3-(dimethylamino)-5,5-dimethylcyclohex-2-en-1-one (344 mg, 2 mmol) in DMF (10 mL) was refluxed for 4-6 h, cooled, and evaporated at reduced pressure. The solid was triturated with MeOH. The resulting precipitate was filtered off and crystallized from MeOH–MeCN. Yield 330 mg (85%), $C_{24}H_{19}FO_4$, mp 285–287°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.15 (6H, s, CH_3-9), 2.37 (2H, s, H-10), 2.49 (2H, s, H-8), 3.64 (2H, s, H-12), 7.05 (1H, d, J = 8.8, H-6), 7.11–7.28, 7.32–7.42, 7.42–7.51 (2H, 1H, 1H, 3m, 3-C_6H_4F-*o*), 8.05 (1H, s, H-2), 8.13 (1H, d, J = 8.8, H-5). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 16.63, 28.52, 32.31, 41.24, 50.68, 108.39, 110.21, 114.71, 115.98 (d, J(C/F) = 22.2), 119.27 (d, J(C/F) = 14.9), 120.67, 121.01, 124.21 (d, J(C/F) = 3.6), 125.75, 130.37 (d, J(C/F) = 8.3), 132.04 (d, J(C/F) = 3.0), 153.35, 154.40 (d, J(C/F) = 3.1), 154.79, 160.38 (d, J(C/F) = 247.9), 164.37, 174.96, 197.80. MS (CI) *m/z* 391.2 (MH^+, 100).

2,9,9-Trimethyl-3-(4-fluorophenyl)-8,9,10,12-tetrahydro-4*H*,11*H*-pyrano[2,3-*a*]xanthene-4,11-dione (5j) was prepared analogously to **5f**. Yield 85%, $C_{25}H_{21}FO_4$, mp 271–273°C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.16 (6H, s, CH_3-9), 2.33 (3H, s, CH_3-2), 2.38 (2H, s, H-10), 2.49 (2H, s, H-8), 3.64 (2H, s, H-12), 7.00 (1H, d, J = 8.7, H-6), 7.06–7.17 (2H, m, H-3″, 5″), 7.20–7.30 (2H, m, H-2″, 6″), 8.06 (1H, d, J = 8.7, H-5). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 16.59, 19.65, 28.54, 32.32, 41.34, 50.76, 108.45, 109.73, 114.23, 115.58 (d, J(C/F) = 21.4), 120.04, 122.93, 125.64, 128.78 (d, J(C/F) = 3.4), 132.24 (d, J(C/F) = 8.3), 153.17, 154.40, 162.53 (d, J(C/F) = 246.9), 163.52, 164.55, 176.15, 197.95. MS (CI) *m/z* 405.1 (MH^+, 100).

General Method for Preparing Pyrazoles 6–8. A hot solution of the appropriate polycyclic **3**–**6** (1 mmol) in the minimal amount of EtOH was treated with hydrazine hydrate (0.5 mL, 10 mmol), refluxed for 0.5–2 h (end of reaction determined by TLC), poured into H_2O (100–150 mL), and acidified to pH 7. The resulting precipitate was filtered off and crystallized from MeOH–H_2O.

6-[4-(4-Methoxyphenyl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6a). Yield 73%, $C_{21}H_{20}N_2O_4$, mp 206–208°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.40–1.59 (1H, m, H-3α), 1.95–2.12 (1H, m, H-3β), 2.60–2.70 (1H, m, H-3a), 2.79 (1H, dd, J = 17.2, 6.1, H-4α), 2.86 (1H, dd, J = 17.2, 2.5, H-4β), 3.76 (3H, s, 4″-OCH_3), 3.79–3.87 (1H, m, H-2α), 3.87–3.97 (1H, m, H-2β), 5.53 (1H, d, J = 4.4, H-9a), 6.15 (1H, d, J = 8.6, H-8), 6.87–6.95 (3H, m, H-7, 3″, 5″), 7.22 (2H, d, J = 8.6, H-2″, 6″), 7.88 (1H, s, H-5′). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 20.37, 28.22, 36.65, 55.48, 67.73, 100.60, 107.43, 108.41, 110.57, 114.40, 118.89, 126.19, 130.18, 130.71, 130.83, 146.29, 153.38, 154.65, 158.70. MS (CI) *m/z* 365.2 (MH^+, 100).

6-[4-(1,3-Benzodioxol-5-yl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6c). Yield 62%, $C_{21}H_{18}N_2O_5$, mp 105–107°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.41–1.59 (1H, m, H-3α), 1.96–2.11 (1H, m, H-3β), 2.60–2.70 (1H, m, H-3a), 2.79 (1H, dd, J = 17.1, 6.1, H-4α), 2.83–2.91 (1H, m, H-4β), 3.78–3.88 (1H, m, H-2α), 3.87–3.97 (1H, m, H-2β), 5.54 (1H, d, J = 4.4, H-9a), 6.01 (2H, s, OCH_2O), 6.20 (1H, d, J = 8.6, H-8), 6.77 (1H, d, J = 8.0, H-7″), 6.82 (1H, s, H-6″), 6.84–6.94 (2H, m, H-7, 4″), 7.87 (1H, s, H-5′). MS (CI) *m/z* 379.2 (MH^+, 100).

6-[4-(4-Chlorophenyl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6d). Yield 69%, $C_{20}H_{17}ClN_2O_3$, mp 238–240°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.41–1.58 (1H, m, H-3α), 1.97–2.13 (1H, m, H-3β), 2.59–2.72 (1H, m, H-3a), 2.73–2.92 (2H, m, H-4), 3.78–3.89 (1H, m, H-2α), 3.87–3.97 (1H, m, H-2β), 5.54 (1H, s, H-9a), 6.11–6.25 (1H, m, H-8), 6.85 (1H, d, J = 8.5, H-7), 7.19–7.47 (4H, m, H-2″, 3″, 5″, 6″), 8.01 (1H, s, H-5′), 10.86 (1H, s, 5-OH), 13.35 (1H, s, NH-1′). MS (CI) *m/z* 369.2 (MH^+, 100).

6-[4-(2,3-Dihydro-1,4-benzodioxan-6-yl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6e). Yield 74%, $C_{22}H_{20}N_2O_5$, mp 109–111°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm): 1.43–1.55 (1H, m, H-3α), 1.99–2.14 (1H, m, H-3β), 2.62–2.71 (1H, m, H-3a), 2.74–2.95 (2H, m, H-4), 3.78–3.87 (1H, m, H-2α), 3.87–4.00 (1H, m, H-2β), 4.24 (4H, s, OCH_2CH_2O), 5.54 (1H, s, H-9a), 6.16 (1H, s, H-8), 6.67–7.01 (4H, m, H-7, 5″, 7″, 8″), 7.90 (1H, s, H-5′), 11.15 (1H, s, 5-OH), 13.25 (1H, s, NH-1′). MS (CI) *m/z* 393.2 (MH^+, 100).

6-(5-Methyl-4-phenyl-1*H*-pyrazol-3-yl)-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6g). Yield 85%, $C_{21}H_{20}N_2O_3$, mp 263–265°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.41–1.57 (1H, m, H-3α), 1.95–2.09 (1H, m, H-3β), 2.15 (3H, s, CH_3-5′), 2.59–2.67 (1H, m, H-3a), 2.78 (1H, dd, J = 17.3, 6.0, H-4α), 2.85 (1H, dd, J = 17.3, 2.5, H-4β), 3.77–3.86 (1H, m, H-2α), 3.87–3.95 (1H, m, H-2β), 5.50 (1H, d, J = 4.4, H-9a), 6.02 (1H, d, J = 8.6, H-8), 6.70 (1H, d, J = 8.6, H-7), 7.24 (2H, d, J = 6.8, H-3″, 5″), 7.32–7.48 (3H, m, H-2″, 4″, 6″), 11.67 (1H, s, 5-OH), 13.05 (1H, s, NH-1′). MS (CI) *m/z* 349.2 (MH^+, 100).

5-Methyl-6-[4-(4-methoxyphenyl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6h). Yield 91%, $C_{22}H_{22}N_2O_4$, mp 213–215°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.39–1.61 (1H, m, H-3α), 1.94–2.10 (1H, m, H-3β), 2.13 (3H, s, CH_3-5′), 2.58–2.71 (1H, m, H-3a), 2.78 (1H, dd, J = 17.3, 6.0, H-4α), 2.81–2.92 (1H, m, H-4β), 3.79 (3H, s, 4″-OCH_3), 3.80–3.87 (1H, m, H-2α), 3.86–3.97 (1H, m, H-2β), 5.49 (1H, d, J = 4.3, H-9a), 6.04 (1H, d, J = 8.7, H-8), 6.76 (1H, d, J = 8.7, H-7), 6.99 (2H, d, J = 8.1, H-3″, 5″), 7.15 (2H, d, J = 8.1, H-2″, 6″), 11.71 (1H, s, 5-OH), 13.04 (1H, s, NH-1′). MS (CI) *m/z* 379.2 (MH^+, 100).

6-[4-(3,4-Dimethoxyphenyl)-5-methyl-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6i). Yield 89%, $C_{23}H_{24}N_2O_5$, mp 231–233°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.42–1.57 (1H, m, H-3α), 1.94–2.10 (1H, m, H-3β), 2.15 (3H, s, CH_3-5′), 2.58–2.69 (1H, m, H-3a), 2.78 (1H, dd, J = 17.3, 6.1, H-4α), 2.81–2.90 (1H, m, H-4β), 3.67 (3H, s, 3″-OCH_3), 3.79 (3H, s, 4″-OCH_3), 3.79–3.88 (1H, m, H-2α), 3.86–3.95 (1H, m, H-2β), 5.50 (1H, d, J = 4.3, H-9a), 6.07 (1H, d, J = 8.7, H-8), 6.66–6.90 (3H, m, H-7, 2″, 6″), 7.00 (1H, d, J = 8.2, H-5″), 11.74 (1H, s, 5-OH), 13.03 (1H, s, NH-1′). MS (CI) *m/z* 409.2 (MH^+, 100).

6-[5-Methyl-4-(4-chlorophenyl)-1*H*-pyrazol-3-yl]-2,3,3a,9a-tetrahydro-4*H*-furo[2,3-*b*]chromen-5-ol (6k). Yield 90%, $C_{21}H_{19}ClN_2O_3$, mp 245–247°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.41–1.58 (1H, m, H-3α), 1.94–2.10 (1H, m, H-3β), 2.16 (3H, s, CH_3-5′), 2.57–2.70 (1H, m, H-3a), 2.72–2.89 (2H, m, H-4), 3.78–3.87 (1H, m, H-2α), 3.86–3.97 (1H, m, H-2β), 5.50 (1H, d, J = 4.3, H-9a), 6.08 (1H, d, J = 8.6, H-8), 6.69 (1H, d, J = 8.6, H-7), 7.26 (2H, d, J = 7.9, H-3″, 5″), 7.47 (2H, d, J = 7.9, H-2″, 6″), 11.46 (1H, s, 5-OH), 13.15 (1H, s, NH-1′). MS (CI) *m/z* 383.0 (MH^+, 100).

7-[4-(4-Methoxyphenyl)-1*H*-pyrazol-3-yl]-3,4,4a,10a-tetrahydro-2*H*,5*H*-pyrano[2,3-*b*]chromen-6-ol (7a). Yield 59%, $C_{22}H_{22}N_2O_4$, mp 245–247°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.45–1.70 (4H, m, H-3, 4), 2.03–2.17 (1H, m, H-4a), 2.57 (1H, dd, J = 17.2, 5.0, H-5α), 2.74 (1H, dd, J = 17.1, 6.4, H-5β), 3.54–3.65 (1H, m, H-2α), 3.62–3.89 (4H, m, 4″-OCH_3, H-2β), 5.26 (1H, d, J = 2.3, H-10a), 6.15 (1H, d, J = 8.6, H-9), 6.90 (1H, d, J = 8.6, H-8), 6.95 (2H, d, J = 8.3, H-3″, 5″), 7.23 (2H, d, J = 8.3, H-2″, 6″), 7.91 (1H, s, H-5′), 11.24 (1H, s, 6-OH), 13.26 (1H, s, NH-1′). MS (CI) *m/z* 379.2 (MH^+, 100).

7-[4-(3,4-Dimethoxyphenyl)-1*H*-pyrazol-3-yl]-3,4,4a,10a-tetrahydro-2*H*,5*H*-pyrano[2,3-*b*]chromen-6-ol (7b). Yield 90%, $C_{23}H_{24}N_2O_5$, mp 170–172°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.42–1.70 (4H, m, H-3, 4), 2.05–2.16 (1H, m, H-4a), 2.57 (1H, dd, J = 17.3, 5.1, H-5α), 2.74 (1H, dd, J = 17.3, 6.3, H-5β), 3.56–3.65 (1H, m, H-2α), 3.67 (3H, s, 3″-OCH_3), 3.77 (3H, s, 4″-OCH_3), 3.80–3.88 (1H, m, H-2β), 5.26 (1H, s, H-10a), 6.18 (1H, d, J = 8.6, H-9), 6.73–7.07 (4H, m, H-8, 2″, 5″, 6″), 7.93 (1H, s, H-5′), 11.24 (1H, s, 6-OH), 13.25 (1H, s, NH-1′). MS (CI) *m/z* 409.2 (MH^+, 100).

8-Hydroxy-7-[4-(4-methoxyphenyl)-1*H*-pyrazol-3-yl]-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8a). Yield 89%, $C_{25}H_{24}N_2O_4$, mp 252–254°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm): 1.05 (6H, s, CH_3-3), 2.27 (2H, s, H-4), 2.43 (2H, s, H-2), 3.26 (2H, s, H-9), 3.77 (3H, s, 4″-OCH_3), 6.31–6.44 (1H, m, H-5), 6.83–7.04 (3H, m, H-6, 3″, 5″), 7.14–7.30 (2H, m, H-2″, 6″), 7.95 (1H, s, H-5′), 11.40 (1H, s, 8-OH), 13.37 (1H, s, NH-1′). MS (CI) *m/z* 417.2 (MH^+, 100).

8-Hydroxy-3,3-dimethyl-7-[4-(3,4-dimethoxyphenyl)-1*H*-pyrazol-3-yl]-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8b). Yield 89%, $C_{26}H_{26}N_2O_5$, mp 252–254°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.26 (2H, s, H-4), 2.43 (2H, s, H-2), 3.25 (2H, s, H-9), 3.66 (3H, s, 3″-OCH_3), 3.76 (3H, s, 4″-OCH_3), 6.43 (1H, d, J = 8.7, H-5), 6.79–6.92 (2H, m, H-2″, 6″), 6.95 (1H, d, J = 8.2, H-5″), 7.06 (1H, d, J = 8.7, H-6), 7.95 (1H, s, H-5′). ^{13}C NMR spectrum (125 MHz, DMSO-d_6, δ, ppm): 16.80, 27.77, 31.74, 40.25, 49.98, 55.38, 55.46, 106.38, 107.72, 108.77, 111.93, 112.63, 113.56, 119.07, 120.86, 125.74, 126.57, 130.75, 144.02, 147.82, 148.58, 149.33, 154.14, 163.99, 196.78. MS (CI) *m/z* 447.1 (MH^+, 100).

7-[4-(1,3-Benzodioxol-5-yl)-1*H*-pyrazol-3-yl]-8-hydroxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8c). Yield 88%, $C_{25}H_{22}N_2O_5$, mp 272–274°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.26 (2H, s, H-4), 2.43 (2H, s, H-2), 3.25 (2H, s, H-9), 6.02 (2H, s, OCH_2O), 6.36–6.49 (1H, m, H-5), 6.70–6.94 (3H, m, H-4″, 6″, 7″), 7.01 (1H, d, J = 8.7, H-6), 7.89–8.00 (1H, s, H-5′), 11.29 (1H, s, 5-OH), 13.37 (1H, s, NH-1′). MS (CI) *m/z* 431.1 (MH^+, 100).

8-Hydroxy-3,3-dimethyl-7-[4-(2-fluorophenyl)-1*H*-pyrazol-3-yl]-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8f). Yield 82%, $C_{24}H_{21}FN_2O_3$, mp 284–286°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.26 (2H, s, H-4), 2.42 (2H, s, H-2), 3.26 (2H, s, H-9), 6.39 (1H, d, J = 8.6, H-5), 6.86 (1H, d, J = 8.6, H-6), 7.19–7.32, 7.31–7.48 (2H each, m, 4′-C_6H_4F-*o*), 8.03 (1H, s, H-5′). MS (CI) *m/z* 405.1 (MH^+, 100).

8-Hydroxy-3,3-dimethyl-7-(5-methyl-4-phenyl-1*H*-pyrazol-3-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8g). Yield 63%, $C_{25}H_{24}N_2O_3$, mp 292–294°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.17 (3H, s, CH_3-5′), 2.26 (2H, s, H-4), 2.41 (2H, s, H-2), 3.24 (2H, s, H-9), 6.28 (1H, d, J = 8.7, H-5), 6.80 (1H, d, J = 8.7, H-6), 7.25 (2H, d, J = 7.3, H-3″, 5″), 7.32–7.49 (3H, m, H-6, 2″, 6″), 11.80 (1H, s, 5-OH), 13.23 (1H, s, NH-1′). MS (CI) *m/z* 401.1 (MH^+, 100).

8-Hydroxy-5-methyl-7-[4-(4-methoxyphenyl)-1*H*-pyrazol-3-yl]-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8h). Yield 58%, $C_{26}H_{26}N_2O_4$, mp 251–253°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.14 (3H, s, CH_3-5′), 2.26 (2H, s, H-4), 2.42 (2H, s, H-2), 3.24 (2H, s, H-9), 3.80 (3H, s, 4″-OCH_3), 6.32 (1H, d, J = 8.7, H-5), 6.86 (1H, d, J = 8.7, H-6), 7.00 (2H, d, J = 8.0, H-3″, 5″), 7.16 (2H, d, J = 8.0, H-2″, 6″), 11.89 (1H, s, 5-OH), 13.18 (1H, s, NH-1′). MS (CI) *m/z* 431.1 (MH^+, 100).

8-Hydroxy-3,3-dimethyl-5-methyl-7-[4-(4-fluorophenyl)-1*H*-pyrazol-3-yl]-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (8j). Yield 47%, $C_{25}H_{23}FN_2O_3$, mp 284–286°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.04 (6H, s, CH_3-3), 2.16 (3H, s, CH_3-5′), 2.26 (2H, s, H-4), 2.41 (2H, s, H-2), 3.24 (2H, s, H-9), 6.33 (1H, d, J = 8.6, H-5), 6.77 (1H, d, J = 8.6, H-6), 7.14–7.40 (4H, m, 4′-C_6H_4F-*p*), 11.71 (1H, s, 5-OH), 13.24 (1H, s, NH-1′). MS (CI) *m/z* 419.1 (MH^+, 100).

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