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SYNTHETIC AND MODIFIED ISOFLAVONOIDS. X. REACTION OF PSEUDOBAPTIGENIN ANALOGS WITH P_2S_5

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New 3′,4′-ethylenedioxy-4-thioxoisoflavones were synthesized. Their structures were confirmed by PMR spectra.

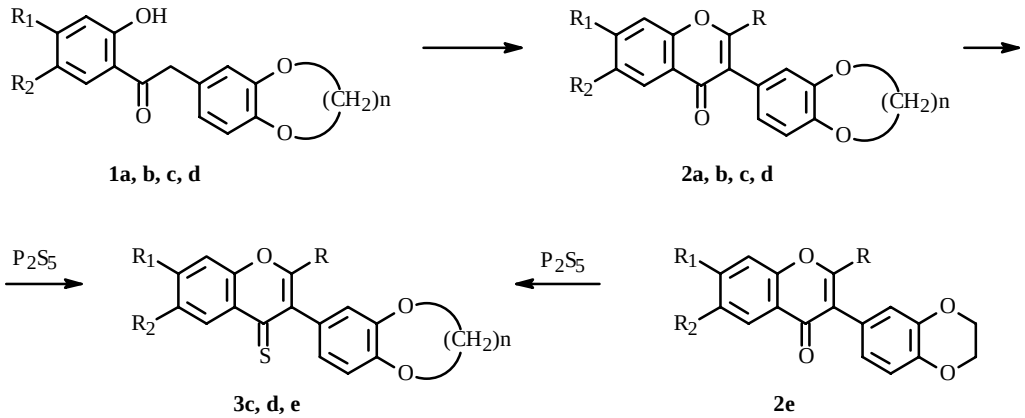
Key words: pseudobaptigenin, isoflavones, 4-thioxoisoflavones, biological activity.

Isoflavonoids with a benzodioxol group are often found among compounds isolated from plants. Pseudobaptigenin has been isolated from various plants [1, 2].

Compounds with pain-relieving [3], anti-allergic [4], carcinostatic, immunosuppressive [5, 6], and antiviral [7, 8] properties have been found.

Compounds based on 7-hydroxyisoflavones are used as medicinal preparations [9]. The natural isoflavones genistein, biochanin A, and 5,4′-dioxy-6,7-methylenedioxyisoflavone possess high antifungal [10, 11] and growth-inhibiting activities [11, 12]. Isoflavones with characteristic diuretic and hypotensive activities have been proposed in patents [13]. Preparations with isoflavones are known for treatment of cardiac diseases [12, 14, 15], with antitumor and immunostimulating [16], anti-inflammatory, analgesic, and anti-allergic activities [17].

The starting material for the synthesis of pseudobaptigenin, α-(1,3-benzodioxol-5-yl)-2,4-dihydroxyacetophenone (**1a**) [18], was prepared via condensation of resorcinol with 5-cyanomethyl-1,3-benzodioxol in a Hoesch reaction. The yield of **1a** reaches 53% upon condensation in dry benzene and ether in the presence of $ZnCl_2$. Performing this reaction using the literature conditions [19], in BF_3·etherate, which is also a catalyst, enables the yield of **1a** to be increased to 87%. The remaining starting ketones **1b-d** were prepared as before [19, 22].



a: R = R_2 = H, R_1 = OH, n = 1; **b:** R = R_2 = H, R_1 = OH, n = 2; **c:** R = Me, R_1 = OMe, R_2 = Pr, n = 1; **d:** R = Me, R_1 = OMe, R_2 = Pr, n = 2; **e:** R = R_1 = R_2 = H, n = 2

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Isoflavone **2e** was prepared by the literature method [23]; chromones **2c** and **d**, by reaction of **1c** and **d** with acetic anhydride in the presence of triethylamine [24, 25].

Isoflavonoids enter into various reactions owing to their polyfunctional nature: electrophilic substitution, oxidation, reduction, cycloaddition, condensation, recyclization, reactions with nucleophilic reagents, and many more.

We studied the reaction of 1,3-benzodioxole and 1,4-benzodioxane analogs of isoflavones with P_2S_5 as an example of reactions involving the carbonyl group of chromones. Heating **2c-e** with an excess of P_2S_5 in dry pyridine (method A) or toluene (method B) forms **3c-e** in high yields.

Thioxochromones **3c-e**, in contrast with the starting isoflavones, are bright red or orange compounds. The structures of **3c-e** were confirmed by elemental analyses and PMR spectra.

The PMR spectra of the thioxoisoflavones contain peaks corresponding to the chromone ring and the hetero groups. The signal for aromatic proton H-5 shifts to weak field by 0.5 ppm compared with the starting materials owing to the influence of the neighboring S atom.

A study of the biological activities of the synthetic pseudobaptigenin analogs showed that some of them possess hypolipidemic, hypoglycemic, anabolizing, and anti-inflammatory activities.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Silufol UV-254 plates using benzene:ethanol (9:1). PMR spectra were measured on a Bruker WP-100 SY instrument in $CDCl_3$ and DMSO-d_6 with TMS internal standard.

3-Hetaryl-4-thioxochromones 3c-e. Method A. A thoroughly ground mixture of the appropriate isoflavone (**2c-e**, 5 mmol) and P_2S_5 (0.074 g, 0.33 mmol) was dissolved in dry pyridine (65 mL), boiled for 3-3.5 h at 110-115°C, cooled to room temperature, and diluted with acetone (2-3 mL) and then water to form a precipitate. The product was filtered off and recrystallized from a suitable solvent.

Method B. A thoroughly ground mixture of the appropriate isoflavone (**2c-e**, 1 mmol) and P_2S_5 (0.148 g, 0.66 mmol) in absolute toluene (5 mL) was boiled for 45 min. The hot solvent was decanted. The oily residue was extracted with toluene (4×10 mL). The toluene solutions were combined and evaporated to dryness. The solid was recrystallized from a suitable solvent.

Compound 3c. Yield 79%, mp 193-194°C (ethylacetate).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): chromone protons: 2.21 (s, 3H, Me-2), 8.42 (s, 1H, H-5), 0.96; 1.65; 2.67 (m, 7H, J = 6.8, Pr-6), 3.94 (s, 3H, OMe-7), 6.79 (s, 1H, H-8); benzodioxole protons: 6.69 (d, 1H, J = 1.9, H-4), 6.65 (dd, 1H, J = 7.0, 1.9, H-6), 6.89 (d, 1H, J = 7.0, H-7), 6.01 (s, 2H, OCH_2O). Found, %: S 8.9. $C_{21}H_{20}O_4S$. Calc., %: S 8.7.

Compound 3d. Yield 74%, mp 185-186°C (ethylacetate).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): chromone protons: 2.19 (s, 3H, Me-2), 8.41 (s, 1H, H-5), 0.95; 1.65; 2.87 (m, 7H, J = 6.8, Pr-6), 3.93 (s, 3H, OMe-7), 6.78 (s, 1H, H-8); benzodioxane protons: 6.71 (d, 1H, J = 1.9 Hz, H-5), 6.67 (dd, 1H, J = 8.3, J = 1.9, H-7), 6.93 (d, 1H, J = 8.3, H-8), 4.29 (s, 4H, OCH_2CH_2O). Found, %: S 8.6. $C_{22}H_{22}O_4S$. Calc., %: 8.4.

Compound 3e. Yield 81.1%, mp 131-132°C (absolute alcohol).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): chromone protons: 7.81 (s, 1H, H-2), 8.67 (dd, 1H, J = 8.0, J = 2.0, H-5), 7.41 (1H, H-6), 7.68 (1H, H-7); 7.46 (dd, 1H, J = 8.0, J = 2.0, H-8); beznodioxane protons: 6.91 (d, 1H, H-5), 6.94 (H-7, H-8), 4.27 (s, 4H, $-OCH_2CH_2O$). Found, %: S 10.81. $C_{17}H_{21}O_3S$. Calc., %: S 10.82.

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