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SYNTHETIC AND MODIFIED ISOFLAVONOIDS. II. SYNTHESIS OF NEW 2,6-DIALKYL-SUBSTITUTED ANALOGUES 0F PSEUDOBAPTIGENIN

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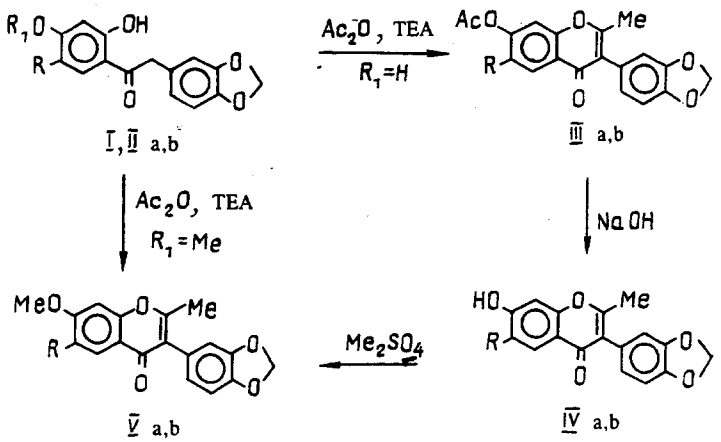
New 2,6-dialkyl-substituted isoflavone analogues of the natural isoflavone pseudobaptigenin have been synthesized. Their structures have been confirmed by IR and PMR spectroscopies.

In the development of investigations on the synthesis of analogues of pseudobaptigenin, we give the results of the preparation of 2,6-dialkyl-3′,4′- methylenedioxyisoflavones. As is known from literature sources [2], 2-alkylisoflavones are formed on the interaction of 2-hydroxydeoxybenzoins with carboxylic acid anhydrides in the presence of organic or inorganic bases. To synthesize pseudobaptigenin analogues containing a methyl group in position 2 and an ethyl or propyl group in position 6 of the chromone ring, ketones (I) [1] were heated in a mixture of acetic anhydride and triethylamine. The 7-acetoxy-2-methyl-6-alkylchromones (III) so formed were converted into the corresponding 7-hydroxychromones (IV) by brief heating with a 5% solution of alkali in alcohol. The resulting 7-hydroxy-2-methyl-6-alkylisoflavones were readily alkylated at the phenolic hydroxyl. The reaction of these compounds with dimethyl sulfate in boiling acetone in the presence of potash formed the 7-methoxy derivatives (V) with high yields (method B). The same compounds were also obtained by the cyclization of the 2-hydroxy-4-methoxyacetophenones (II) with acetic anhydride in the presence of triethylamine (method A). The two methods gave practically identical yields of the desired 7-methoxychromones (V).



To confirm the structures of the isoflavones (III-V), in addition to the analytical results we used spectral characteristics. The following absorption bands were found in the IR spectra of the 7-acetoxychromone (III): 1768 cm^{-1} (ν_{OAc}) and 1639 cm^{-1} ($\nu_{C=O}$). For the 7-hydroxychromones (IV) we observed the characteristic absorption bands of the stretching vibrations of a phenolic hydroxyl (3080-3180 cm^{-1}) of a carbonyl group of a pyrone ring (1633-1635 cm^{-1}), and of the skeletal vibrations of aromatic rings (1500-1580 cm^{-1}). The IR spectra of the 7-methoxyisoflavones (V), in contrast to those of the 7-hydroxy compounds (IV), lacked the absorption bands of hydroxy groups. Information on the IR spectra and on the yields and physical constants of compounds (III) and (IV) is given in Table 1, and details of their PMR spectra in Table 2.

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TABLE 1. Characteristics of Componds (III-V)

Compound	Yield, %	T. mp, °C	Empirical formula	IR spectrum, cm^{-1}		
				νOH	νOAc	νCO
III a	52	159	$C_{21}H_{18}O_6$	—	1768	1638
III b	98	124—125	$C_{22}H_{20}O_6$	—	1768	1639
IV a	97	238—239	$C_{19}H_{16}O_5$	3180	—	1635
IV b	99	229—230	$C_{20}H_{18}O_5$	3080	—	1633
V a	88* 92**	172—173	$C_{20}H_{18}O_5$	—	—	1640
V b	90* 92**	133—134	$C_{21}H_{20}O_5$	—	—	1643

*Yield by method A.

**Yield by method B.

In the PMR spectra of the 2-methylisoflavones (III-V), as compared with those of the initial ketones (I-II), the two-proton singlet of the methylene unit of the ketone and the weak-field peak of the proton of the OH group had disappeared and a three-proton singlet of a methyl group had appeared in the 2.2-2.3 ppm region. Another characteristic feature of the formation of the 2-methylchromone ring is the presence of a peak in the 7.7-8.1 ppm region assigned to the aromatic H-5 proton, which experiences the descreening influence of the neighboring carbonyl group.

The PMR spectra of the 7-methoxychromones (V) lacked the signal of the phenolic hydroxyl proton and had the three-proton singlet of the methoxy group.

As a result of the study of the biological activities of the new compound it was established that the 2-methyl analogues of pseudobaptigenin (IV) possess a considerable antiinflammatory activity.

Thus, the formation of synthetic analogues of pseudobaptigenin from benzodioxole derivatives of 2-hydroxyacetophenones in the reaction with a carboxylic acid anhydride takes place readily and with high yields.

EXPERIMENTAL

The course of the reactions and the purity of the compounds obtained were checked by the TLC method on Silufol UV-254 plates. A mixture of benzene and ethanol (9:1) was used as the eluent. PMR spectra were measured on a Bruker WP-100 SU spectrometer in DMSO-d_6 or $CDCl_3$ relative to DMS (internal standard). IR spectra were determined on a PAY Unicam SP_3-300 spectrometer (in KBr tablets). The results of the analysis of all the compounds corresponded to the calculated figures.

7-Acetoxy-3-(1,3-benzodioxol-5-yl)-2-methyl-6-alkylchromones (IIIa and b). A mixture of 50 mmole of a ketone (Ia or b), 23 ml (250 ml of acetic anhydride, and 28 ml (200 mmole) of triethylamine was heated at 120-130°C for 5-6 h. Then the reaction mixture was poured into cold water containing 2.5 ml of hydrochloric acid. The precipitate that deposited was filtered off and washed with water and, after drying, was crystallized from ethyl acetate.

3-(1,3-Benzodioxol-5-yl)-7-hydroxy-2-methyl-6-alkylchromones (IV a and b). A hot solution of 30 mmole of a 7-acetoxy-2-methylchromone (III a or b) in the minimum amount of ethanol was treated with 24 ml (30 mmole) of a 5% solution of caustic soda, and the mixture was boiled for 6 min. Then 20 ml of water was added and boiling was continued for another 10 min, after which the pH was brought to 7 with dilute hydrochloric acid. The resulting precipitate was filtered off and crystallized from alcohol.

3-(1,3-Benzodioxol-5-yl)-7-methoxy-2-methyl-6-alkylchromones (Va and b). Method A. A mixture of 40 mmole of a ketone (IIa or b), 44.8 ml (480 mmole) of acetic anhydride, and 49.6 ml (320 mmole) of triethylamine was heated at 120-130°C for 10 h. It was then poured into cold water containing 8 ml of hydrochloric acid. The resulting precipitate was filtered off, washed on the filter with water until the smell had disappeared, and crystallized from alcohol.

TABLE 2. Chemical Shifts in the PMR Spectra of the Pseudobaptigenin Derivatives (III-V) (δ, ppm)*

Compound	Chromone protons					Benzodioxole protons			
	Me-2, s	H-5, s	R-6	OAc-7, OH-7, OMe-7, s	H-8, s	H-4, d J=2 Hz	H-6, dd J=1,5 Hz J=8,3 Hz	H-7, d J=7,8 Hz	$-OCH_2O-$, s
IIIa	2.29	8.10	2.64 q; 1.24 t	2.37	7.20	6.74	6.69	6.88	5.99
IIIb	2.29	8.07	2.60 t; 1.64 m; 0.95 t	2.37	7.19	6.74	6.69	6.87	5.99
IVa	2.20	7.68	2.59 q; 1.14 t	10.69	6.82	6.79	6.67	6.93	6.02
IVb	2.23	7.69	2.58 t; 1.57 m; 0.90 t	10.70	6.84	6.81	6.69	6.95	6.05
Va	2.28	7.94	2.68 q; 1.22 t	3.92	6.77	6.75	6.70	6.86	5.98
Vb	2.28	7.92	2.65 t; 1.63 m; 0.95 t	3.91	6.77	6.76	6.70	6.87	5.98

*The PMR spectra of compounds (IVa and b) were measured in deuteromethyl sulfoxide and those of the other compounds in deuterochloroform.

Method B. A hot solution of 10 mmole of a 7-hydroxy-2-methylchromone (IVa or b) in the minimum amount of dry acetone was treated with 1.15 ml (10 mmole) of dimethyl sulfate and 4.14 g (30 mmole) of freshly calcined potash, and the mixture was boiled for 15-30 min. The inorganic residue was filtered off and was washed on the filter with a small amount of hot acetone. The acetone was distilled off in a water-pump vacuum and the residue was crystallized from ethanol.

REFERENCES

1. A. Aitmambetov and V. P. Khilya, Khim. Prir. Soedin., 669 (1993).
2. V. Sabo, L. G. Grishko, S. Borbei, and V. P. Khilya, Khim. Geterotsikl. Soedin., No. 2, 174-179 (1975).