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PREPARATION OF SALTS OF 3-(1,4-BENZODIOXANE-6-YL) CHROMONES, SOLUBLE IN WATER

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Abstract. This paper describes the preparation of novel isoflavones—derivatives of 1,4-benzodioxane analogs of pseudobaptigenin—bearing methoxycarbonylmethoxy and carboxymethoxy substituents at the 7-position. Water-soluble diethanolamine salts of these 3-(1,4-benzodioxan-6-yl) chromones were synthesized, which is of significant importance for conducting pharmacological studies. The physical constants of the compounds were determined, and their structures were confirmed by ^{1}H NMR spectroscopy.

Keywords: synthesis, 3-(1,4-benzodioxan-6-yl) chromone, diethanolamine salts, water-soluble salts.

Introduction

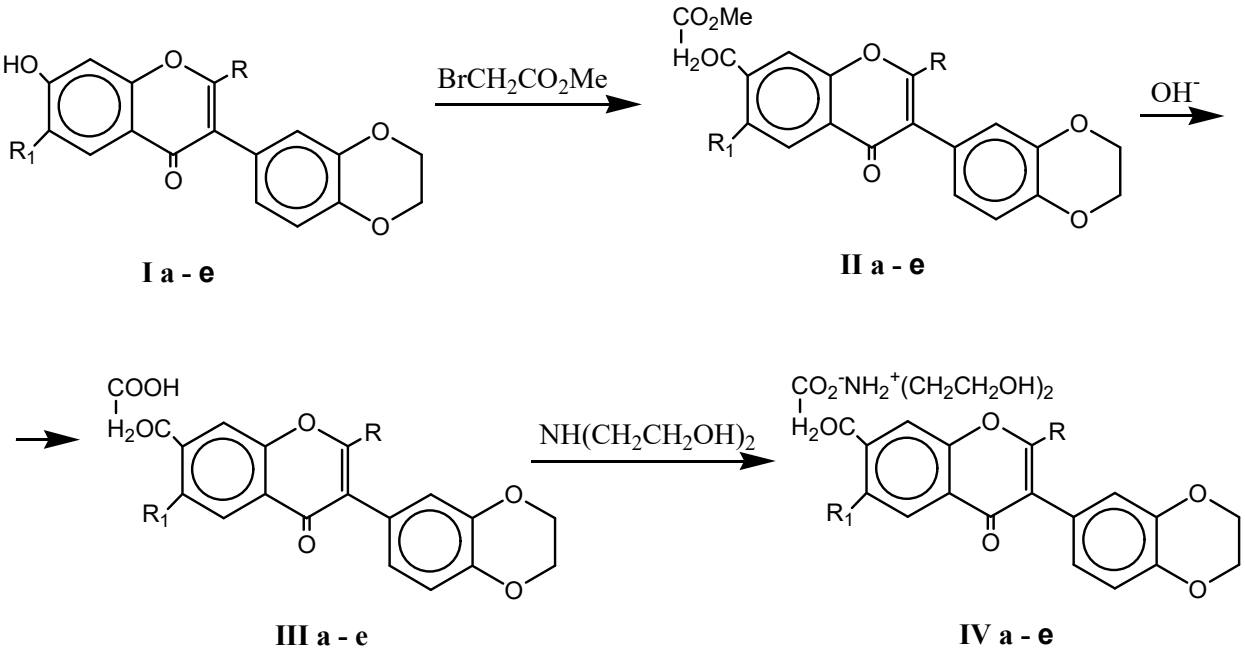
Isoflavones, as well as their heterocyclic analogs, are attracting the attention of scientists from various fields as physiologically active substances with a diverse spectrum of action.

In a previous study on the synthesis of 3-alkoxycarbonylchromones and 3-alkoxalylchromones, their biological activities were investigated, including antitumour activity, inhibition of HIV-1 integrase, low photochemical activity, and high activity as selective phosphatase inhibitors [1]. Furthermore, 7-carboxymethoxyisoflavone derivatives are analogues of the pharmaceutical agent Ipriflavone, which is used to regulate bone and cartilage metabolism [2].

For this purpose, the synthesis of 7-alkoxycarbonylmethoxy derivatives of isoflavones is of increased interest.

Materials and Methods

In this context, the synthesis of 7-alkoxycarbonylmethoxy derivatives of isoflavones is of particular interest. 7-Methoxycarbonylmethoxy derivatives of 3-(1,4-benzodioxan-6-yl) chromones **(II a – e)** are readily obtained in good yields by refluxing the corresponding 7-hydroxyisoflavones **(I a – e)** [3 – 7] with methyl bromoacetate in acetone in the presence of potassium carbonate (scheme 1).



(I) – (IV) a: R=R₁=H; **b:** R=H, R₁=Et; **c:** R=H, R₁=Pr; **d:** R=Me, R₁=H; **e:** R=Me, R₁=Et.

Scheme 1. Synthesis of 3-(1,4-benzodioxan-6-yl) chromones (IV a – e) as diethanolamine salts.

Results

Most organic compounds are insoluble in water. For the study of the biological properties of substances, it is particularly important to convert them into water-soluble compounds.

To obtain water-soluble derivatives, compounds **(II a – e)** were subjected to alkaline hydrolysis to yield the corresponding free acids **(III a – e)**. These were then converted into water-soluble diethanolamine salts **(IV a – e)** by heating them to 70 – 75°C in the presence of diethanolamine. The mixture was subsequently cooled in a refrigerator (using isopropyl alcohol as a solvent), and the resulting precipitate was filtered off and washed with the cold solvent (iso-PrOH).

Discussion

The synthesized diethanolamine salts **(IV a – e)** are colorless crystalline substances that are readily soluble in water, which is particularly important for physiological tests.

The physical constants and yields of compounds **(II) – (IV)** are presented in table 1.

In the proton nuclear magnetic resonance (^{1}H NMR) spectra of compounds **(II)** and **(III)**, the signals corresponding to phenolic hydroxyl protons, which are present in the spectra of the starting compounds, are absent. Instead, signals attributable to methoxy groups appear at 3.8–3.9 ppm, while signals assigned to carboxylic acid protons are observed in the range of 13.0–16.2 ppm. The remaining proton signals of the synthesized compounds occur in chemical shift regions characteristic of the corresponding signals in the starting compounds [3 – 5].

Table 1. Characterization of Compounds (II) – (IV)

Compound	M.p. (°C)	Molecular formula	Yield (%)
(II) a	187-188	$C_{20}H_{16}O_7$	100
b	156-157	$C_{21}H_{20}O_7$	84
c	121-122	$C_{23}H_{22}O_7$	96
d	174-175	$C_{21}H_{18}O_7$	95
e	151-152	$C_{23}H_{22}O_7$	75
(III) a	242-243	$C_{19}H_{14}O_7$	95
b	213-214	$C_{21}H_{18}O_7$	92
c	222-223	$C_{22}H_{20}O_7$	89
d	217-218	$C_{20}H_{16}O_7$	90
e	238-239	$C_{22}H_{20}O_7$	98
(IV) a	167-168	$C_{23}H_{25}NO_9$	77
b	141-142	$C_{25}H_{29}NO_9$	90
c	143-145	$C_{26}H_{31}NO_9$	75
d	148-149	$C_{24}H_{27}NO_9$	97
e	146-148	$C_{26}H_{31}NO_9$	89

Conclusion

Studies on the physiological activity of the newly synthesized compounds **(IV a – e)** have revealed that some of them are capable of accelerating the body's recovery. These compounds serve as analogs to various existing medicinal drugs and also provide a means to obtain novel, original compounds containing specific structural fragments that are significant for pharmacological testing.

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