SYNTHESIS OF SOME 4-METHYL- AND 4-PHENYL-3-HYDROXYCOUMARINS

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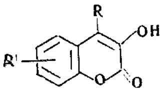
Some 4-methyl- and 4-phenyl-3-hydroxycoumarins were synthesized by the reaction of phenols with α-acetoxyacetyl- or α-acetoxybenzoylacetic esters.

It has been proposed that 3-hydroxycoumarins be obtained by the hydrolysis of the corresponding amino or acetamido derivatives [1-3], by cyclization of ethyl O-(acetoxyacetyl)salicylate [4,5], and by treatment of coumarandione with diazoalkanes [6]. We have obtained the following 3-hydroxycoumarins by the direct reaction of phenols or their acetate esters with α-acetoxyacetyl- and α-acetoxybenzoylacetic esters in the presence of sulfuric acid via the Pechmann reaction: 3-hydroxy-4,7-dimethylcoumarin (I), 3-hydroxy-4-methyl-7-methoxycoumarin (II), 3,7-dihydroxy-4-methylcoumarins (III), 3,5,7-trihydroxy-4-methylcoumarin (IV), 3,6,7-trihydroxy-4-methylcoumarin (V), 3,7,8-trihydroxy-4-methylcoumarin (VI), benzo[h]-3-hydroxy-4-methylcoumarin (VII), 3,6,7-trihydroxy-4-phenylcoumarin (VIII), and 3,7,8-trihydroxy-4-phenylcoumarin (IX) (Table 1). The yields of these products depend on the nature of the reagents and the acid concentration (see [7,8]).

The 3-hydroxycoumarins are colorless or slightly colored crystalline substances that melt with decomposition. Most of them are stable in air. Except for 3,6,7- and 3,7,8-trihydroxycoumarins, which precipitate silver from silver nitrate in neutral and weakly acidic media, these compounds reduce silver nitrate in alkaline sulfite solutions. Their aqueous and alcoholic solutions darken rapidly.

TABLE 1. 3-Hydroxycoumarins



Compound	Synthetic method	Decomposition temp. (crystallization solvent)	Empirical formula	Found, %		Calc., %		Yield, %
				C	H	C	H	
I	B	181—182 Benzene	$C_{11}H_{10}O_3$	69,50	5,30	69,46	5,30	28
II	A	201—203 Benzene	$C_{11}H_{10}O_4$	64,22	4,95	64,07	4,88	52
III	A	211—212 Water, benzene	$C_{10}H_8O_4$	62,78	4,64	62,52	4,19	77
IV	A	243—246 Water	$C_{10}H_8O_5 \cdot H_2O$	53,11	4,25	53,10	4,45	96
V	A*	285—291 Alcohol	$C_{10}H_8O_5$	57,78	3,75	57,70	3,87	72
VI	A	273—275 Alcohol	$C_{10}H_8O_5$	57,61	4,11	57,70	3,87	49
VII	B	252—254 Ethyl Acetate	$C_{14}H_{10}O_3$	74,22	4,57	74,33	4,45	24
VIII	A	263—265†	$C_{15}H_{10}O_5$	66,56	4,17	66,66	3,69	15
IX	A	245—250‡	$C_{15}H_{10}O_5$	66,50	4,12	66,66	3,69	14

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*Obtained from hydroxyhydroquinone triacetate.

† The wash solvent was alcohol—hydrochloric acid (1:3).

‡ The wash solvent was alcohol—hydrochloric acid (1:2).

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The compounds obtained may be of interest as developers and antifog agents in photography [9].

EXPERIMENTAL

3-Hydroxy-4-methyl- or 3-Hydroxy-4-phenylcoumarins. A. A mixture of 5 mole of the phenol or 10 mmole of its acetate, 10 mmole of α-acetoxyacylacetic ester, and 10 ml of 75-85% sulfuric acid was heated for 30 min at 40°, after which 100 ml of water was added. The resulting precipitate was washed with water until it gave a neutral reaction to Congo and was then crystallized from water, alcohol, or benzene. The readily oxidized 3-hydroxy-4-phenylcoumarins were purified by boiling in a mixture of alcohol and hydrochloric acid (sp. gr. 1.18), washing with water until they gave a weakly acidic reaction to Congo red and drying over alkali.

B. Sulfuric acid [10 ml (sp. gr. 1.84)] was added gradually with stirring to a mixture of 5 mmole of the phenol and 10 mmole of α-acetoxyacylacetic ester at 10-15 deg. The reaction mixture was allowed to stand for 24 h at 20-25 deg and was then stirred with 50 g of ice. The isolation and purification were similar to the procedures described in method A.

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