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SYNTHESIS OF 9-ARYLIDENE DERIVATIVES OF DEOXYVASICINONE

Kh. M. Shakhidoyatov and I. K. Kaisarov

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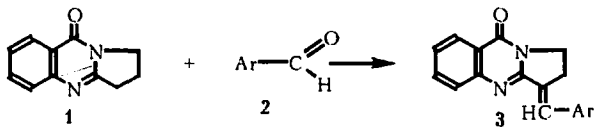
A simple method has been developed for obtaining 9-arylidenedeoxyvasicinones by condensing deoxyvasicinone with aromatic aldehydes in the presence of glacial acetic acid. The yields of reaction products amount to 69-95%.

The methylene protons in the 9-position of the alkaloid deoxyvasicinone are mobile [1]. They can be replaced by a bromine atom or atoms [1, 2]. The formylation [3-5] and acylation [1] reactions of this compound also take place at the α-methylene group [1]. It reacts with aromatic and heterocyclic aldehydes [1, 6]. Deoxyvasicinone and also deoxypeganine react with benzaldehyde to form benzylidene derivatives [7, 8]. The condensation of deoxyvasicinone with aromatic and heterocyclic aldehydes takes place under severe conditions (fusion at 150-180°C) and leads either to ylidene derivatives or to substituted 9-α-hydroxybenzylidenedeoxyvasicinones. Which of these products is formed depends both on the nature of substituents in the aromatic aldehyde and on the reaction temperature. In order to find a simpler and more convenient method of obtaining 9-arylidenedeoxyvasicinones, we have studied the condensation of deoxyvasicinone with aromatic aldehydes in the presence of acids.

It is known that the reaction of 2-methyl-3-arylquinazol-4-ones with aromatic aldehydes takes place more readily when perchloric acid is used as a condensing agent [9]. We used acetic acid. As the aldehyde components we took benzaldehyde (**2a**), *m*- and *p*-nitrobenzaldehydes (**2**b and c), *p*-dimethylaminobenzaldehyde (**2d**), salicylaldehyde (**2e**), 5-bromosalicylaldehyde (**2f**), and *o*-vanillin (**2g**).

The reaction was performed by heating equimolar amounts of (**1**) and (**2**) in glacial acid for 2-4 h. The reaction products were obtained with high yields (Table 1).



1 **2** **3**

Ar = C_6H_5 (a); m-O_2N-C_2H_4 (b); p-O_2N-C_6H_4 (c); $(CH_3)_2NC_6H_4$ (d); o-HOC_6H_4 (e); 2-HO-,5-BrC_6H_3 (f); 2-HO-,3-CH_3O-C_6H_3 (g)

It must be emphasized that on the reaction of deoxyvasicinone with *p*-dimethylaminobenzaldehyde by this method the yield of product rises sharply as compared with the method described in [6] (69% in place of 17%). This fact is apparently explained by the possibility of the protonation of the nitrogen atom of dimethylamino group. In view of its strong attraction of electrons, the ammonium cation so formed increases the positive charge on the carbon atom of the carbonyl group, and this facilitates the condensation process.

In [6] it was shown that *m*- and *p*-nitrobenzaldehydes react with deoxyvasicinone in two directions: with the formation of *m*- and *p*-nitrobenzylidenedeoxyvasicinones (**3**b and c) or of 9-α-hydroxy-*m*- and -*p*-nitrobenzyldeoxyvasicinones (**4**b and c). Which of these compounds is formed depends on the temperature of the reaction: at a relatively low temperature, compounds (**4**b and c) are obtained. At 190-200°C they are converted into compounds (**3**b and c). In contrast to [6], when glacial acetic acid is used only compounds (**3**b and c) are obtained. This fact is apparently explained by the facilitation of the

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 40 64 75. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 79-81, January-February, 1998. Original article submitted June 30, 1997.

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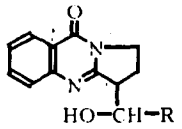
TABLE 1. Yields and Some Physicochemical Characteristics of the Compounds Obtained

Initial aldehyde	Reaction product	Yield (%) by method		mp, °C	R_f*
		A*	B†		
2a	3a	95	66	179–180	0.82
2b	3b	90	91	244–245	0.74
2c	3c	88	60	240–241	0.72
2d	3d	69	17	230–231	0.23
2e	3e	90	86	275–276	0.55
2f	3f	92	90	290–291	0.46
2g	3g	91	81	247–248	0.35

*This reaction was conducted in glacial acetic acid. R_f values were determined on Silufol plates with the solvent benzene–chloroform–methanol (5:3.5:1.5).

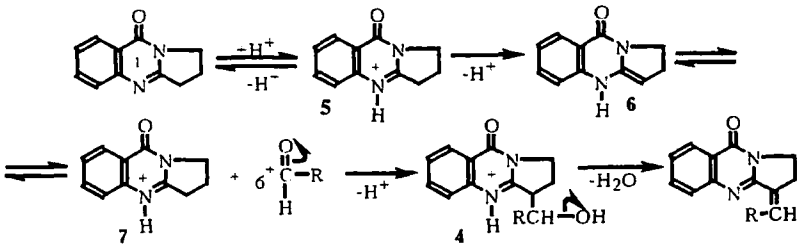
†This reaction was conducted by fusing a mixture of the two reactants.

splitting out of the hydroxy group in the 9-α-hydroxy-*m*- and -*p*-nitrobenzyldeoxyvasicinones (4b and c) formed as intermediates.



4a R= m-$C_6H_4NO_2$
4b R=.p-$C_6H_4NO_2$

The catalyzing role of acetic acid consists in the fact that the nitrogen atom in position 1 of deoxyvasicinone undergoes protonation, while it does not do so when the mixture of reactants is fused [6].



In the quaternary salt formed (5) isomerization of the N^1-C^2 double bond to the C^9 atom takes place with the formation of the enamine (6), existing in equilibrium with the anion (7). Attack of the carbonyl group by this anion leads to the 9-α-hydroxy derivative (4), the splitting out of water from which gives the expected product.

The structures of the compounds synthesized were confirmed by spectral methods and a comparison of their physicochemical characteristics with those of authentic specimens (see Table 1).

EXPERIMENTAL

Deoxyvasicinone was synthesized by the method of [5].

Its elementary analysis corresponded to the calculated values.

Condensation of *p*-Nitrobenzaldehyde with Deoxyvasicinone. A solution of 0.93 g (5 mmole) of deoxyvasicinone in 10 ml of glacial acetic acid was treated with 0.8 g (5.3 mmole) of *p*-nitrobenzaldehyde. The reaction mixture was boiled for 2 h, the acetic acid being distilled off. The residue was recrystallized from benzene, to give 1.4 g of 9-*p*-nitrobenzylidenedeoxyvasicinone (3c) with mp 240-241°C.

Compounds (3a, b, and d-g) were obtained analogously.

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