QUINAZOLINES

XI. CONDENSATION OF DEOXYVASICINONE WITH ALDEHYDES

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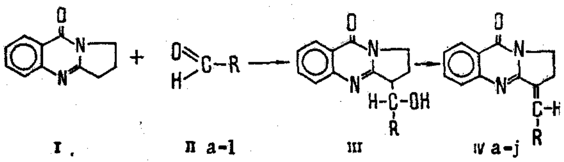
Deoxyvasicinone (I) and deoxypeganine react with benzaldehyde (IIa) to form benzylidene derivatives [1, 2]. Continuing an investigation of the synthesis and chemical transformations of 2,3-polymethylenequinazolin-4-ones and quinazolines [3, 4], we have studied the reaction of deoxyvasicinone (I) with aliphatic, aromatic, and heterocyclic aldehydes. The aldehydes used were: benzaldehyde (IIa), m- and p-nitrobenzaldehydes (IIb and c), p-bromobenzaldehyde (IId), p-dimethylaminobenzaldehyde (IIe), salicylaldehyde and 5-bromosalicylaldehyde (IIf and g), o-vanillin (IIh), furfural and 5-iodofurfural (IIi and j), and also nonanal (IIk) and crotonaldehyde (IIj).



I. II a-l III IV a-j

a) $R = C_6H_5$; b) $R = \text{м-}NO_2C_6H_4$; c) $R = \text{n-}NO_2C_6H_4$; d) $R = \text{n-}BrC_6H_4$; e) $R = \text{n-}N(CH_3)_2\ C_6H_4$; f) $R = 2-HO-C_6H_4$; g) $R = 2-HO-,\ 5-Br-C_6H_3$; h) $R = 2-HO-,\ 3-CH_3-C_6H_3$; i) $R = C_4H_3O$; j) $R = 5-J-C_4H_2O$, k) $R = C_8H_{17}$; l) $R = CH_3CH = CH$.

The reaction takes place when equimolar amounts of (I) and (II) are heated and gives condensation products with high yields (Table 1).

The course of the reaction depends both on the temperature at which it is performed and also on the nature of the substituents in the initial aldehyde. Aromatic aldehydes with strong electron-accepting groups (m- and p-NO_2 and -Br) give reaction products with (I) in higher yield than do aldehydes with electron-donating substituents. This is apparently explained by the fact that an electron-accepting substituent attracts the electrons of the carbon atoms of the carbonyl group through the π-bond of the aromatic ring, decreasing the electron density on it and thereby increasing its electrophilicity. In addition, p-nitrobenzaldehyde reacts with (I) under milder conditions than the metaisomer, which is in harmony with literature information on the reactivities of substituted benzaldehydes with rhodanine [6].

Strong electron-accepting substituents not only increase the yield of reaction products but also determine the structure of the compounds formed. Thus, under relatively mild conditions (150-160°C) the reaction of (I) with (IIb) gives the intermediate product (IIIb), and under more severe conditions (180-185°C, 4 h) it gives (IVb).

When compounds (IIIb, c) were heated at 190-200°C the products of their further transformation, (IVb, c), were obtained.

According to the literature [1], the product of the condensation of (I) with benzaldehyde (IIa) – 9-benzylidenedeoxyvasicinone – has mp 137-139°C. The (IVa) that we obtained melted at 178-179°C. We have been unable to obtain a product with mp 137-139°C under various conditions: at temperatures from 110 to 250°C with variations of the time. At lower temperatures (110-120°C) no reaction took place; the initial compounds were recov-

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TABLE 1

Initial compound	Reaction product	React. cond.		Yield, %	mp. °C	R_f,* (Al_2O_3)	Empirical formula
		temperature, °C	time, h				
IIa	IVa	180–190	4	66	178–179 (benzene)	0,63	$C_{18}H_{14}ON_2$
IIb	IIIb	150–160	1	30	170–172 (benzene)	0,14	$C_{18}H_{15}O_4H_3$
IIc	IIIc	120–130	3	61	188–189 (acetone)	0,14	$C_{18}H_{15}O_4N_3$
IIIb	IVb	190–200	0,5	78	245–246 (acetone)	0,44	$C_{18}H_{13}O_3N_3$
IIIc	IVc	190–200	0,5	76	239–241 (benzene)	0,41	$C_{18}H_{13}O_3N_3$
IIb	IVb	180–190	4	91	245–246 (acetone)	0,44	$C_{18}H_{13}O_3N_3$
IIc	IVc	150–160	1	60	239–241 (benzene)	0,41	$C_{18}H_{13}O_3N_3$
IId	IVd	150–160	4	98	199–201 (benzene)	0,56	$C_{15}H_{13}ON_2Br$
IIe	IVe	180–190	4	17	229–231 (benzene)	0,42	$C_{20}H_{19}ON_3$
IIf	IVf	180–190	4	86	273–275 (acetone)	—	$C_{18}H_{14}O_2N_2$
IIg	IVg	180–190	4	90	289–291 (acetone)	—	$C_{18}H_{13}O_2N_2Br$
IIh	IVh	150–160	4	81	247–248 (acetone)	—	$C_{19}H_{16}O_3N_2$
IIi	IVi	180–190	4	67	226–228 (benzene)	0,64	$C_{16}H_{12}O_2N_2$
IIj	IVj	150–160	1	61	245–246 (benzene)	0,73	$C_{16}H_{11}O_2N_2I$

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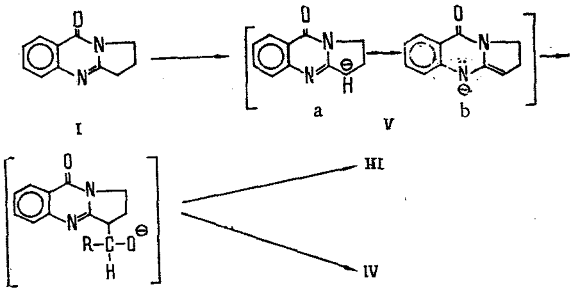
*The R_f values were determined in the following solvent systems: for compounds (IVa–c, i, IIIc), chloroform–ether (1:20); for (IIIb, IVd, e, j), chloroform–ether (1:1).

ered. With a rise in the temperature of the reaction mixture, the formation of product (IVa) began and at 180–190°C only (IVa) was obtained. The performance of the reaction under the conditions described in the literature also led to a mixture of (IVa) with the starting materials. According to the literature, the product obtained was recrystallized from petroleum ether. Since (I) also crystallizes well from this solvent, it is quite possible that the (IVa) described in this paper [1] was a mixture with (I) and therefore had a low melting point.

It was impossible to condense (I) with the aliphatic aldehyde (IIk) or with crotonaldehyde (IIj); this is connected with an increase in the electron density on the carbon atom of the carbonyl group because of the positive inductive effect of the alkyl radical.

The formation of compounds (III) and (IV) in the condensation of deoxyvasicinone with aldehydes takes place in accordance with the scheme given. The electronegative pyridine nitrogen atoms imparts mobility to the hydrogen atoms of the methylene group in the *a* position such as aldehydes, ketones, β-keto esters, esters of dicarboxylic acids, acid anhydrides, etc. [7]. An analogous phenomenon is observed in α-picoline, the methylene group of which reacts with benzaldehyde [8]. This is explained by the tautomeric transformation of 2,4-dihydroxyquinazolines into tetrahydroquinazoline-2,4-diones, and conversely [9]. Consequently, the splitting out of hydrogen in the form of a proton from the α-carbon atom of (I) takes place more readily. The carbanion (V) so produced can exist in the form of two resonance species (Va and Vb). The nucleophilic attack by the above-mentioned anion of the carbonyl group of the aldehyde leads to the intermediate addition product (VI). The latter is stabilized either by the addition of hydrogen and the formation of compounds of type (III) or by the splitting out of water, which leads to product (IV).



The scheme given explains why aromatic aldehydes take part in this reaction while aliphatic aldehydes do not. The structures of the compounds obtained were shown on the basis of the results of elementary analysis and their IR and mass spectra, and their individuality was shown by thin-layer chromatography. The IR spectrum of compounds of (IIIb, c) contain absorption bands of a hydroxy group in the 3390-3400 cm^{-1} region, while there is no such band in the spectra of compounds (IVa-c, i, j). Amide carbonyl absorbs at 1660-1670 cm^{-1} in (IIIb, c) and at 1680-1685 cm^{-1} in (IVa-j).

The mass spectrum of (IIIb) shows the molecular ion and also of ions with m/e 319 (M−18. 288 (M−49), 272 (M−65), 186 (M−151), 185 (M−152), 151 (M−186), 150 (M−187). In these compounds, the strongest peak is that of the ion with m/e 186, corresponding to deoxyvasicinone. In the spectrum of (IIIc) there is a metastable peak with m/e 232.6 (318 → 272). The mass spectra of (IVb, c) are characterized by the presence of the molecular ion (100%), the M − 1 ion (70-80%), and ions with m/e 272 (30-35%) and 271 (21-30%), and by the absence of fragments with m/e 186, 185.

EXPERIMENTAL

The IR spectra were taken on a UR-20 instrument and the mass spectra on a MKh-1303 spectrometer. The elementary analyses corresponded to the calculated figures.

9-Benzylidenedeoxyvasicinone (IVa). A mixture of 0.93 g (0.005 mole) of (I) and 0.64 g (0.006 mole) of (IIa) was heated in the oil bath at 180-190°C for 4 h. The solid mass was recrystallized from benzene. This gave 0.91 g (66%) of 9-benzyledenedeoxyvasicinone (IVa) with mp 178-179°C. IR spectrum: 1680 cm^{-1} (ν_{CO}).

The reaction of (I) with m- and p-nitro, p-bromo- and p-dimethylamino-p-methylaminobenzaldehydes (IIb, d, e), salicylaldehyde and 5-bromosalicylaldehyde (IIf, g) and with furfural (IIi) were performed similarly.

9-(α-Hydroxy-m-nitrobenzyl)deoxyvasicinone (IIIb). A mixture of 0.93 g (0.005 mole) of (I) and 0.91 g (0.006 mole) of (IIb) was kept at 150-160°C for an hour. Recrystallization of the reaction mixture from benzene gave 0.51 g (30%) of (IIIb) with mp 170-172°C. IR spectrum: 1670 cm^{-1} (ν_{CO}), 3410-3420 cm^{-1} (ν_{OH}).

Compound (IIIc) was obtain similarly.

Conversion of 9-(α-Hydroxy-p-nitrobenzyl)deoxyvasicinone (IIIc) into 9-(p-Nitrobenzylidene)deoxyvasicinone (IVc). Compound (IIIc) (0.19 g) was heated at 190-200°C for 30 min. After recrystallization of the solid residue from benzene, 0.14 g (78%) of (IVc) with mp 239-241°C was obtained. The products gave no depression of the melting point in admixture with (IVc) obtained from (I) and (IIc).

SUMMARY

In the reaction of deoxyvasicinone with aldehydes, depending on the nature of the substituents of aromatic and heterocyclic aldehydes, and also on the reaction conditions, 9-benzylidene or 9-α-hydroxybenzyl derivatives of deoxyvasicinone are obtained.

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