THE STRUCTURE OF THE PRODUCTS OF THE OPENING OF THE PYRONE RING OF CHROMONES BY AMINES

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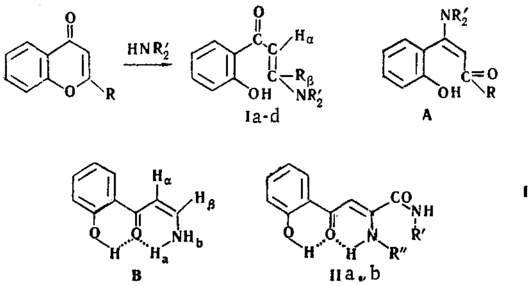
The fine structure of the products of the opening of the pyrone ring of chromones by amines – 2-(β-aminoacryloyl)phenols – has been determined.

The products of the cleavage of the pyrone ring of chromones by primary and secondary amines are usually ascribed the structure of β-aminovinyl ketones (I) (see [1-4]). The possible isomeric structure (A) has also been considered [5], since it was assumed that the pyrone ring is cleaved not by a molecule of amine but by a hydroxyl ion present in the water-containing reaction mixture. The production of identical substances by the reaction of amines with chromones and by the reaction of the same amines with the corresponding β-dicarbonyl compounds [5-7] is of little significance for a choice between the isomeric enamines mentioned, since the structure of the enamines synthesized by the second method has still been demonstrated insufficiently strictly. It is just for this reason that attempts were made – unfortunately unsuccessful [8] – to synthesize the enamine (Ia) from 1-β-diethylaminoacryloyl-2-methoxybenzene, the structure of which is known definitively.



Ia $R=H, R'=C_2H_5$;
b $R=H, NR'_2=$piperidine
c $R=R'=H$;
d $R=H, NR_2=NHCH_2C_6H_5$.
II a $R'=R''=n\text{-}C_4H_9$;
b $R'+R''=CH_2CH_2$

The choice between the structures I and A when R = H can be made without difficulty by means of the NMR spectra. Thus, in the NMR spectrum of compound Ib there is no signal of the proton of an aldehyde group, which should have appeared in the form of a doublet in the 9-10 ppm region, and at 5.83 ppm there is the doublet signal of H_α. The corresponding signal of H_β with δ 7.83 ppm falls partially in the region of the protons of the benzene ring. The narrow signal of the chelated hydroxyl has a chemical shift of 13.94 ppm. The spin-spin coupling constant of the H_α and H_β vinyl protons is 12.2 Hz (in D_6-DMSO solution, 15.5 Hz), which shows the trans configuration of Ib (with respect to the hydrogen atoms). In the IR spectrum of Ib (in $CHCl_3$) at 990 cm^{-1} there is a fairly strong band of the nonplanar deformation vibrations of the CH bonds of a trans CH = CH grouping. The fact that Ia belongs to the trans series has been reported previously [8].

The question of the fine structure of aminovinyl ketone I with primary and secondary amino groups and the possibility of prototropic tautomerism for these compounds has not hitherto been considered. It has been reported only that the phenolic hydroxyl forms an intramolecular hydrogen bond with the carbonyl

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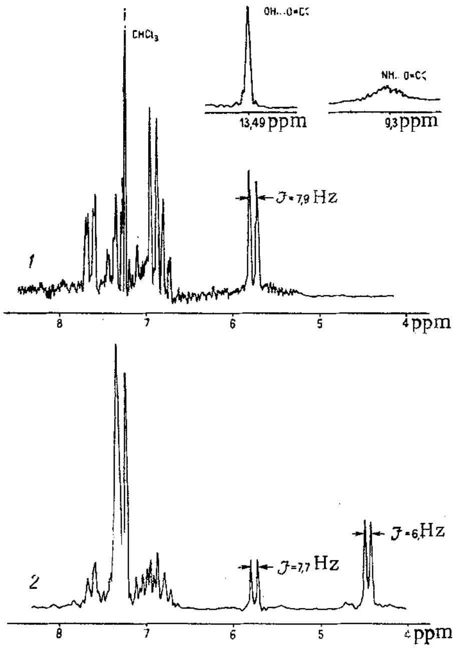

Fig. 1. NMR spectra: 1) 2-β-aminoacryloylphenol (Ic); 2) 2-β-benzylaminoacryloylphenol (Id).

group [2,8-10]. We have studied the NMR spectra of compounds Ic,d. In the spectrum of Ic (Fig. 1, curve 1) at 5.77 ppm there is the doublet signal of H_α with J 7.9 Hz (on the interpretation of the NMR spectra of β-aminovinyl carbonyl compounds see [11-14]). Consequently, the cis configuration (formula C) must be adopted for compound Ic. The multiplet signal of H_β is masked by the signals of the C_6H_4 protons. A fairly narrow signal with an intensity of 1 proton unit at δ 13.49 ppm must be ascribed to the proton of the phenolic OH group chelated with the carbonyl. The narrow signal at 9.3 ppm is due to the NH_a proton, forming a hydrogen bond with the carbonyl. In the 5.1-5.9 ppm region there is a very broad signal with an area of approximately 1 proton unit of the NH_b proton, which does not form a hydrogen bond; this signal is not sufficiently well identified, since it is overlapped by the doublet signal of H_α. The addition of CD_3OD to the solution causes the disappearance of all the signals of the OH and NH_2 groups. The IR spectrum of Ic in CCl_4 also agrees with this structure; in the 900-1010 cm^{-1} region there are no trans-CH = CH bands. At 2400-3200 cm^{-1} there are low-intensity diffuse bands of a chelated hydroxyl. The NH_2 group is characterized by stretching vibrations at 3515 cm^{-1} (free NH_b) and at 3308 cm^{-1} (bound NH_a; for the assignment of the bands in the IR spectra of β-aminovinyl ketones, see [15]). The intensity of the ν_{NH_2} bands and the values of their frequencies do not change on passing from a concentration of 0.01 to 0.002 M in CCl_4 solution. The saturation of such solutions with water has no effect on the appearance of these bands, but after a solution in CCl_4 has been shaken with deuterium oxide they disappear, and ν_{ND_2} vibrations appear at 2636 and 2435 cm^{-1}. At the same time it can be seen that the broad bands of a chelated OD group are located in the 2000-2400 cm^{-1} region. The NMR spectrum of Id (Fig. 1, curve 2) has a doublet signal with J 6.1 Hz at 4.48 ppm (determined at field frequencies of 100 and 60 MHz) with an intensity of 2 proton units caused by the protons of the benzyl CH_2 group, interacting with NH proton. A doublet with J 7.7 Hz from H_α is located at 5.77 ppm. A broad signal at 10.21 ppm and a narrower signal at 13.78 ppm relate respectively, to NH and OH groups participating in the formation of hydrogen bonds with the carbonyl. Hence, it follows that Id exists in the form of the enamino ketone and not in the other possible tautomeric forms. In the IR spectrum of Id in CCl_4 solution at concentrations of 0.05 and 0.002 M, the bands of the stretching vibrations of a free NH group are absent, and there is a broad band of low intensity in the 3200-3300 cm^{-1} region fusing with the broad band of the chelated hydroxyl at 2500-3200 cm^{-1}.

Thus, the products of the opening of the chromone ring by secondary amines contain a β-aminovinyl ketone fragment with the trans configuration (with respect to the hydrogen atoms of the vinyl group or the amino and CO groups), and the corresponding compounds with a primary or secondary amino group have the cis configuration stabilized by an intramolecular hydrogen bond between NH and CO groups, this bond being formed in spite of the fact that the carbonyl probably takes part simultaneously in the formation of a chelate hydrogen bond with the OH group. A similar phenomenon has been observed recently in the related compounds obtained by the reactions of amines with 1-(o-hydroxyphenyl)alkane-1,3-diones [16-17]. Other structures with intramolecular hydrogen bonds can be envisaged, but they are less probable, since they require a disturbance of the coplanarity of the systems of double conjugated bonds or the conversion of the benzene structure into a quinoid structure.

By analogy it may be considered that other compounds with a secondary amino group — for example, 2-(β-butylamino-β-n-butylaminocarbonylacryloyl)phenol (IIa) [4] and 3-(2-hydroxybenzoylmethylene) piperazin-2-one (IIb) [3] — have the cis configuration (with respect to the NH and CO groups). In the NMR spectrum of IIb in DMSO, the chemical shift of the signal of the vinyl proton is 6.75 ppm, and the signals of the protons of the C_6H_4 group are located in the 6.8-8.1 ppm region. The signals of the protons of the HN-C=O, HN-C=C, and OH groupings have chemical shifts of 8.69, 10.49 and 13.37 ppm. On the addition of CD_3-OD to a solution of this substance in DMSO, the signal with δ 8.69 disappears most rapidly. The products of the reaction of 2-alkoxycarbonylchromones with secondary amines – for example, 2-(β-piperidino-β-piperidinocarbonylacryloyl)phenol (III) [2] have not yet been assigned to the cis or trans series.

EXPERIMENTAL

2-(β-Piperidinoacryloyl)phenol (Ib) was obtained by the action of piperidine on chromone [9]. IR spectrum ($CHCl_3$, c 0.1 M, d 0.16 mm), cm^{-1}: 2300-3300 (chelated hydroxyl), 1627 (very strong band), 1581 (strong), 1541 (very strong). In CCl_4 solution (c 0.1 M, d 0.16 mm), the chelated hydroxyl gives weak bands at 2500-3100 cm^{-1}.

2-(β-Aminoacryloyl)phenol (Ic). This was obtained by the action (20°C, 60 hr) of dry ammonia on chromone in absolute ethanol: mp 101.5-102.5°C. Found, %: C 66.2; H 5.5; N 8.8. Calculated for $C_9H_9NO_2$, %: C 66.2; H 5.6; N 8.6. IR spectrum (in CCl_4), cm^{-1}: 1634 (very strong, C=O), 1585 (medium intensity), and 1520 (strong).

2-(β-Benzylaminoacryloyl)phenol (Id) was obtained by the action of benzylamine on chromone [6].

2-(β-n-Butylaminocarbonylacryloyl)phenol (IIa) was obtained by the reaction of n-butylamine with 2-ethoxycarbonylchromone [4]. IR spectrum ($CHCl_3$,c 0.05 M, d 0.16 mm), cm^{-1}: 3420 (amide NH), 2500-3300 (broad bands, bound NH of an enamine and chelate OH), 1677 (amide C=O), 1600, 1577, 1530.

3-(2-Hydroxybenzoylmethylene)piperazin-2-one (IIb) was synthesized by the reaction of ethylenediamine with 2-ethoxycarbonylchromone [3]. IR spectrum ($CHCl_3$, c 0.05 M, d 0.166 mm) cm^{-1}: 3415 (amide NH), 2500-3420 and 3100 (broad bands, bound NH of an enamine and chelate OH), 1690 (C = O),. 1615, 1590, 1555.

2-(β-Piperidino-β-piperidinocarbonylacryloyl)phenol (III) was obtained by the action of piperidine on 2-ethoxycarbonylchromone [2]. IR spectrum ($CHCl_3$, c 0.05 M, d 0.16 mm) cm^{-1}: 2500-3200 (chelate OH), 1640 (very strong broad band with an inflection at 1620, amide and ketone C = O groups), 1575, 1534.

The IR spectra were taken on a UR-10 instrument. The NMR spectra were taken in $CDCl_3$ relative to TMS (Ic,d) or HMDS (Ib) on RS-60 and JEOL instruments with working frequencies of 60 MHz (Ib, d) or a JNM 44-100 instrument with a working frequency of 100 MHz (Ic).

LITERATURE CITED

1. W. Baker and V. Butt, J. Chem. Soc., 2142 (1949).
2. Z. Jerzmanovska and K. Kostka, Roczn. Chem., 37, 413 (1963).
3. V. A. Zagorevskii and D. A. Zykov, ZhOKh, 30, 3579 (1960).
4. V. A. Zagorevskii, D. A. Zykov, and E. K. Orlova, ZhOKh, 34, 539 (1964).
5. G. Wittig and H. Blumenthal. Ber., 60, 1085 (1927).
6. K. Kostka, Roczn. Chem., 40, 1683 (1966).
7. K. Kostka, Roczn. Chem., 40, 1661 (1966).
8. I. Lockhart and E. Tanner, J. Chem. Soc., 3611(1965).
9. D. A. Zykov, Investigations in the 2-and 4-Benzopyran Series [in Russian], Dissertation, Moscow, 1964.
10. P. W. Feit, Acta Chem. Scand., 18, 2401 (1964).
11. J. O. Dudek and R. H. Holm, J. Am. Chem. Soc., 83, 2099 (1961); 84, 269 (1962).
12. J. O. Dudek and G. P. Volpp, J. Am. Chem. Soc., 85, 694, 2697 (1963).
13. J. Dabrowski, J. Terpinski,and K. Kamienska-Trela, Roczn. Chem., 39, 769 (1965).
14. H. E. A. Kramer, Ann., 696, 15 (1966).
15. J. Dabrowski, Spectrochim. Acta, 19, 475 (1963).
16. G. Dudek and E. P. Dudek, Tetrah., 23, 3245 (1967).
17. R. A. Coburn and G. Dudek, J. Am. Chem. Soc.,90, 4756 (1968).