STUDIES OF PYRANS AND RELATED COMPOUNDS

XLIV.* STRUCTURES OF THE PRODUCTS OF THE OPENING OF THE PYRONE RING OF 4-PYRONES BY AMINES

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The fine structures of the products of the cleavage of the heterorings of chromones and 4-pyrones by ammonia and primary and secondary amines, i.e., 2-β-aminoacrylylphenols (I) and di(β-aminovinyl) ketones (II), were studied by means of IR and PMR spectra, and it was established that I and II, which contain amino groups with a hydrogen atom attached to the nitrogen, exist in the cis form with double intramolecular (chelate) bonding between one carbonyl and two proton-containing groups.

The β-aminovinyl ketone structure is usually given to the products of the opening of the pyrone ring of chromones by primary and secondary amines (for examples, see [1-4]). The fine structures of these compounds and the possibility for their prototropic tautomerism have, until recently, been given virtually no consideration. It has been noted only that a phenolic hydroxyl group forms an intramolecular hydrogen bond with the carbonyl group [2, 5-7] (from the IR spectra) and that Ib has the trans configuration (from the PMR spectrum [5]). A structure with double intramolecular hydrogen bonding of the OH and NH groups with the carbonyl group was recently [8,9] assigned to the similarly constructed β-aminovinyl ketones obtained by the reaction of the appropriate o-hydroxyphenyl-β-dicarbonyl compounds with amines.

We have studied the detailed structures of a number of products (I) of the cleavage of chromone and flavone by primary and secondary amines† using IR and PMR spectroscopy. To begin with, we were able, by means of PMR spectra, to reject without difficulty the possible aminovinyl ketone structure in which the amino group would be closer to the benzene ring (for a discussion of this possibility, see [5, 11], for example). Thus, the signal of the proton of an aldehyde group is absent from 9-10 ppm in the PMR spectrum of Ia (in $CDCl_3$), and there is a doublet at δ 5.88 ppm from the $C_\alpha H$ proton. The reciprocal doublet of the $C_\beta H$ proton is located at 7.88 ppm. The spin–spin splitting constant (J) for these protons is about 12 Hz (15.5 Hz in D_6-dimethyl sulfoxide), which indicates a trans configuration for Ia (with respect to the hydrogen atoms). A rather intense band from the out-of-plane vibrations of the CH bonds in trans-CH=CH appears at 990 cm^{-1} in the IR spectrum of Ia (in $CHCl_3$).

Compounds Ic-e, obtained by the reaction of chromone with ammonia or primary amines, are cis isomers with J 7.7-7.9 Hz (determined from the splitting of the signals of the $C_\alpha H$ protons; the $C_\beta H$ signals fall into the aromatic proton region). No bands are observed in the 900-1010 cm^{-1} region in the IR spectrum of Ic (Fig. 1, curve 1). (Bands which are hard to identify are found in this region for the other cis compounds.)

From the IR and PMR spectral data (Tables 1 and 2), Ia-f do not have a free OH group, and there is an intramolecular chelate hydrogen bond between the phenolic hydroxyl group and the carbonyl group. At

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*See [27] for communication XLIII.

†See [10] for a preliminary communication.

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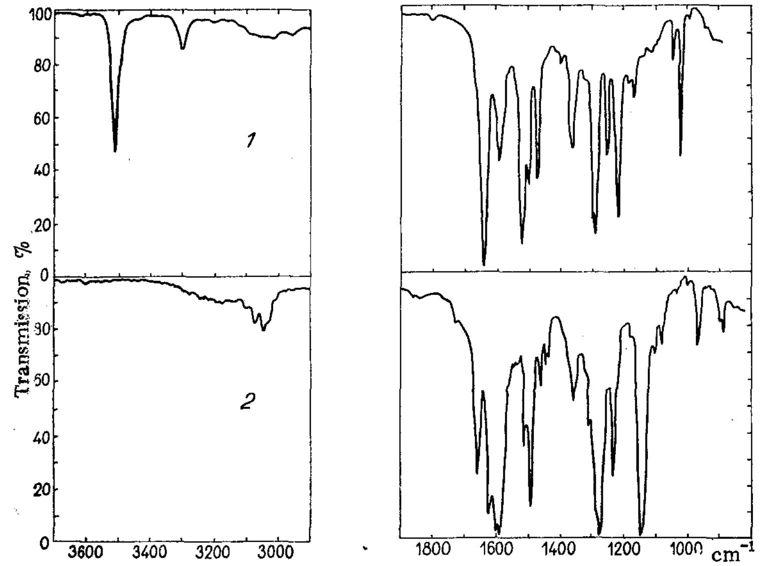


Fig. 1. IR spectra (in CCl_4, c ~ 0.05 M, d ~ 0.25 mm): 1) 2-β-aminoacrylylphenol (Ic); 2) 1,5-dianilino-1,4-pentadien-3-one (IIa).

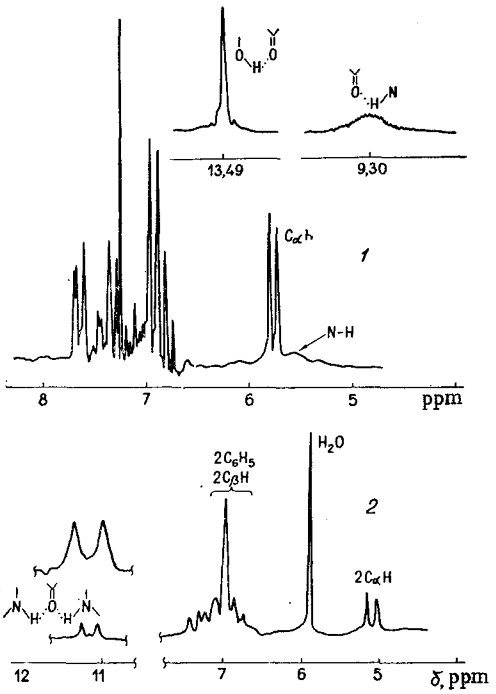
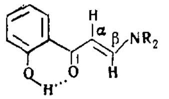
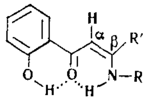


Fig. 2. PMR spectra: 1) 2-β-aminoacrylylphenol (Ic); 2) 1,5-dianilino-1,4-pentadien-3-one (IIa) in dimethyl sulfoxide.

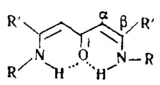
the same time, in the case of Ic-f, which have primary or secondary amino groups, one does not observe the valence vibrations of a free NH group, except for Ic, in the spectrum of which there is a narrow band from the free NH of the $-NH_2$ fragment (Fig. 1, curve 1) at 3516 cm^{-1} in addition to the band at 3310 cm^{-1} (bonded NH). The δ_{NH_2} vibrations do not appear at 1600-1650 cm^{-1}, as established by deuteration (see [12-14], for example, for the assignment of bands in the IR spectra of β-aminovinyl ketones).



Ia,b



Ic-i



IIa,b

Ia $NR_2 = NC_5H_{10}$; b $R = C_2H_5$; c $R = R' = H$; d $R = CH_2C_6H_5$, $R' = H$; e $R = C_6H_5$, $R' = H$; f $R = CH_2C_6H_5$, $R' = C_6H_5$; g $R = n\text{-}C_4H_9$, $R' = CONHC_4H_9\text{-}n$; h $R + R' = CH_2CH_2NHCO$; i $R = NC_5H_{10}$, $R' = CONC_5H_{10}$,
IIa $R = C_6H_5$, $R' = H$; b $R = R' = CH_3$

TABLE 1. IR Spectra of I and II

Comp.	Solvent*	Valence vibrations, cm^{-1}		Frequencies from 1500 to 1800 cm^{-1}
		OH	NH (or NH_2)	
Ia	$CHCl_3$	2400—3300		1626, 1588, 1540
Ic†	CCl_4	2400—3250	3516, 3310	1633, 1584, 1515
Id	CCl_4	2500—3200	3200—3350	1632, 1582, 1552, 1503
Ie	CCl_4	2700—3400		1630, 1603, 1580, 1555
If	CCl_4	2600—3300		1600 (inflect. 1610), 1572, 1528
If	C_6H_6	2600—3300		1600, 1568, 1530
Ig	$CHCl_3$	2500—3330	3420 (NH amide)	1677 (CO amide), 1600, 1577, 1530
Ih	$CHCl_3$	2500—3420, 3100	3415 (NH amide)	1690 (CO amide), 1615, 1590, 1555
Ii	$CHCl_3$	2500—3200		1640 (broad with an inflection at 1620, CO amide and ket.), 1575, 1534
IIa	CCl_4		3100—3350	1650, 1612, 1595, 1582, 1507
IIb	CCl_4		3050—3350‡	1635, 1585, 1540, 1505
IIb	C_6H_6		3100—3350	1627, 1580, 1540, 1505

*For solutions in $CHCl_3$ with c 0.05 M and d 0.16 mm; for CCl_4 with c 0.05 M and d 0.25 mm; for C_6H_6 with c = 0.06-0.07 M and d 0.07 mm.

†The OH bands vanish during deuteration (by shaking the same solution with D_2O), and a broad ν_{OD} band appears at 1960-2400 cm^{-1}; ν_{ND_2} bands appear at 2630 and 2430 cm^{-1} in place of the ν_{NH_2} band; the band at 1633 cm^{-1} is shifted to 1623 cm^{-1} but remains just as intense. In a control determination, the character of the bands at 2400-3550 cm^{-1} does not change during saturation of the CCl_4 solution with water.

‡This band vanishes during deuteration, and a broad band appears at 2200-2500 cm^{-1}.

The intensities and positions of the ν_{OH} and ν_{NH} bands do not change on passing from 0.05 to 0.002 M solutions in CCl_4. The PMR spectra of Ic-f (see [15-18] for the interpretation of the PMR spectra of β-aminovinylcarbonyl compounds) also attest to the presence of a rather strong intramolecular hydrogen bonding (δ 9.22-11.72 ppm) with the participation of an NH group. The broad signal at 5.2-6.0 ppm in the spectrum of Ic (Fig. 2, curve 1) with an intensity of about one proton unit is related to the NH proton that does not form a hydrogen bond. This signal is overlapped by the doublet of the $C_{\alpha}H$ proton but is readily identified upon the addition of CD_3OD. (All of the NH_2 signals and the OH signal vanish.) The data presented above indicate that intramolecular hydrogen bonding is most likely realized in molecules of Ic-f simultaneously between one carbonyl group and two hydrogen atoms of the NH and OH groups. One can also conceive of other structures with intramolecular hydrogen bonds, but they are less preferable, since they must be constructed with disruption of the coplanarity of the systems of conjugated double bonds and with removal from the plane of conjugation of the p electrons of the nitrogen atom or with conversion of the o-hydroxyphenyl residue to a quinoid system. A substantial confirmation of the structure of I is the large J constant (~ 13 Hz) for the H—N—C—H grouping in Ie, which attests to the trans orientation of the protons. (The fine structure of the signals of the NH groups in the spectra of Ic and Id is not resolved.) In order to exclude the assumption of the possibility of the existence of associated molecules in the solutions, the molecular weight of If was determined cryoscopically in benzene. For the same concentration of a solution of If in benzene, free OH and NH groups (broad band at 2600-3300 cm^{-1}) are not displayed in the IR spectrum, while the OH signal is found at 13.9 ppm in the PMR spectrum. By analogy, it should be supposed that the other products of the cleavage of substituted chromones by primary amines, for example, 2-(β-n-butylamino-β-n-butylaminocarbonylacrylyl)phenol (Ig) and 3-(2-hydroxybenzoylmethylidene)-2-piperazinone (Ih), have the cis configuration (with respect to the NH and CO groups). The chemical shift of the $C_{\alpha}H$ proton in the PMR spectrum of Ih in dimethyl sulfoxide is 6.80 ppm, while the C_6H_4 signals are situated at 6.8-8.2 ppm. The signals of the protons of the HN—C=O, HN—C=C, and OH groupings are found at 8.74, 10.54, and 13.42 ppm, respectively. The signal at 8.74 ppm vanishes most rapidly when CD_3OD is added. The cis or trans form cannot yet be assigned with certainty, however, to the products of the reaction of 2-carboalkoxychromone with secondary amines, for example, 2-(β-piperidino-β-piperidinocarbonylacrylyl)phenol (Ii), but there is no doubt that there is a chelated hydroxyl group in this compound: the IR spectrum ($CHCl_3$, c 0.05 M, d 0.16 mm) contains a broad band at 2500-3200 cm^{-1} as well as bands at 1640 (broad with a shoulder at 1620 cm^{-1}), 1575, and 1534 cm^{-1}.

TABLE 2. PMR Spectra of I and II

Compound	Spectroscopic conditions	δ, ppm (relative to TMS)		
		OH	NH	other protons
Ia	$CDCl_3$	13,99[b]		$C_\alpha H$: 5,88 (d^c; $J_{C_\alpha H, C_\beta H}$ 12,2 Hz); $C_\beta H$: 7,88 (d; $J_{C_\beta H, C_\alpha H}$ 12,2 Hz); C_6H_4 : 6,3—7,5
Ib	$CDCl_3$	13,99		$C_\alpha H$: 5,80 (d; $J_{C_\alpha H, C_\beta H}$ 12,2 Hz); $C_\beta H$: 7,89 (d; $J_{C_\beta H, C_\alpha H}$ 12,2 Hz)
Ib	Dioxane	12,75		
Ic	DMSO	13,41		
Ic	$CDCl_3$	13,34	9,22 ; 5,2—6,0	$C_\alpha H$: 5,82 (d; $J_{C_\alpha H, C_\beta H}$ 7,9 Hz); C_6H_4 and $C_\beta H$: 6,3—7,5
Id	$CDCl_3$	13,44	10,22	$C_\alpha H$: 5,79 (d; $J_{C_\alpha H, C_\beta H}$ 7,7 Hz); CH_2 : 4,47 (d; $J_{CH_2, NH}$ 6,1 Hz); C_6H_4, C_6H_5 and $C_\beta H$: 6,7—7,6
Ie	$CDCl_3$ (sat. solution)	13,16	11.72 (d, poorly resolved)	$C_\alpha H$: 5,95 (d; $J_{C_\alpha H, C_\beta H}$ 7,7 Hz); C_6H_4, C_6H_5; and $C_\beta H$: 6—7,7
Ie	DMSO + dioxane (about 1 : 1)	13,13	11.65 (d, $J_{NH, C_\beta H}$ 12.9 Hz)	$C_\alpha H$: 6,12 (d; $J_{C_\alpha H, C_\beta H}$ 9 Hz)
Ie	Dioxane[e]	13,10	11.75 (d, $J_{NH, C_\beta H}$ 12.8 Hz)	$C_\alpha H$: 6,05 (d; $J_{C_\alpha H, C_\beta H}$ 8,7 Hz)
If	CCl_4	13,15	11,2	$C_\alpha H$: 5,73 (s^f); CH_2 : 4,41 (d; $J_{CH_2, NH}$ 6,2Hz); C_6H_4 и C_6H_5 : 6,5—7,4
IIa	$CDCl_3$		11.60 (d, $J_{NH, C_\beta H}$ 12.6 Hz[d])	$C_\alpha H$: 5,10 (d; $J_{C_\alpha H, C_\beta H}$ 8,2 Hz); C_6H_5 and $C_\beta H$: 6,4—7,8
IIa	DMSO		11.58 (d, $J_{NH, C_\beta H}$ 11.4 Hz)	$C_\alpha H$: 5,35 (d; $J_{C_\alpha H, C_\beta H}$ 7,6 Hz)
IIb	CCl_4		9,88	$C_\alpha H$: 4,33 (s); CH_3—N : 2,86 (d; $J_{CH_3, NH}$ 5,2Hz); CH_3—C_β : 1,80 (s)

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[a] In all cases at ~20°. For Ia-d, c is 0.36 M.

[b] In d_6-dimethyl sulfoxide, δ 10.04.

[c] d is doublet.

[d] Determined with 60 and 100 MHz spectrometers.

[e] With a 100 MHz spectrometer.

[f] s is singlet.

Note: δ = 13.8 ppm for 2-β-morpholinoacrylylphenol (in $CDCl_3$, c 0.36 M).

We also note that the two strong bands in the IR spectra of I at 1610-1635 and 1520-1555 cm^{-1}, like those in the usual β-aminovinyl ketones [13-14], must most likely be assigned to the subordinate vibrations of the double bonds of the N−C=C−C=O system, which absolutely unambiguously establishes the tautomerism of the enamine-ketone form of I in a number of cases by means of PMR spectra (particularly for Id-f).

From an examination of the chemical shifts of the protons of the chelated hydroxyl groups in compounds of the I type, for example Ia-d, in comparison with the chemical shifts of related compounds – o-hydroxyacetophenone and salicylaldehyde (11.64 and 10.58 ppm, respectively; the spectra were recorded under the same conditions as the spectra of Ia-d) – it is easy to conclude that the signals of I are situated at weaker fields. This is undoubtedly associated with the fact that the electron density on the oxygen atom of the carbonyl group of β-aminovinylcarbonyl compounds is raised considerably as a consequence of conjugation with the amino group. The location of the OH group signals of Ia,b at weaker fields than those of Ic,d is apparently explained by the participation of the carbonyl groups of Ic,d in the formation of two hydrogen bonds simultaneously, as a result of which relatively less electron density of the oxygen atom of the CO group goes into the hydrogen bond between OH and CO. It should be noted, however, that Ic,d are cis isomers, while Ia,b are trans isomers, and the effectiveness of the conjugation of the amino and carbonyl groups and, consequently, the strength of the hydrogen bond between the OH and C=O groups may depend on the configuration.

In connection with the fact that the formation of double hydrogen bonding between one electron donor and two proton-containing groups is a comparatively rare phenomenon but, at the same time, is attracting the attention of research workers in attempts to explain the fine structure peculiarities of such important components of animate nature as water [19], polypeptides [20], or substances of the antibiotic type [21], we became interested in the fine structure of the products of the cleavage of monocyclic pyrones by primary amines in the case of di(β-aminovinyl) ketones (IIa, b). A structure with two intramolecular hydrogen bonds has been described for IIb [22], but sufficiently rigorous proof was not presented. We have considered it probable that more definite information would be obtained by studying the IR and PMR spectra of IIa, since it has two pairs of vicinal vinyl protons and two NH groups in the H–N–C–H system, and the characteristic spin–spin splitting of the corresponding protons may therefore appear. In fact, the cis configuration of the vinylene grouping is readily established in the PMR spectrum (Table 2 and Fig. 2, curve 2): there is a doublet at 5-6 ppm from the two equivalent $C_{\alpha}H$ with J ~ 8 Hz (the $C_{\beta}H$ signal is located in the region of the C_6H_5 signals). The two equivalent NH protons give a doublet at 11.6 ppm with $J_{NH,C_{\beta}H}$ 12 Hz (determined at 60 and 100 MHz), which attests to the trans configuration of the H–N–C–H fragment. Vibrations of free NH groups are absent in the IR spectrum of Ia (Table 1 and Fig. 1, curve 2) in CCl_4. The valence vibrations of two chelated NH groups, the intensities and shapes of which do not change when the concentration is varied from 0.05 to 0.002 M, appear at 3100-3350 cm^{-1} as a broad band.

Complete equivalency of the protons of identical groupings – two vinyl protons (narrow singlet), two CH_3–C methyl groups (singlet), and two CH_3–N groups (narrow doublet) with $J_{CH_3,NH}$ 5.2 Hz – is observed in the PMR spectrum of IIb (Table 2) in CCl_4. An unresolved multiplet in the form of a broad symmetrical signal of two NH is found at 9.88 ppm. The spin–spin relationship of N–CH_3 and N–H was established by means of double resonance (by the conversion of the doublet from CH_3 to a singlet). Just as for IIa, vibrations of free NH groups (in CCl_4, c 0.05-0.002 M) do not appear in the IR spectrum of IIb (Table 1). The determination of the molecular weight by cryoscopy in benzene demonstrated that IIb exists as a monomer in this solution, and vibrations of free NH groups are absent in the IR spectrum of the same solution, while a doublet CH_3–N signal (2.25 ppm) appears in the PMR spectrum in addition to CH_3–C (1.42 ppm) and $C_{\alpha}H$ (5.0 ppm) singlets; the NH signal is masked by the signals of the solvent protons. It is interesting that, because of hindered exchange of the protons of the NH groups of IIb, the addition of water to a solution of IIb in $CHCl_3$–CCl_4 (~1 : 1) does not induce conversion of the doublet from CH_3–N (2.86 ppm) to a singlet, nor does it cause an appreciable change in the chemical shift of the NH signal (9.78 ppm); the signal of the water protons appears as an isolated band at 4.7 ppm. Retention of a solution of IIb in CCl_4 containing CD_3OD (~1 h) results in the disappearance of the CH_3–N doublet (2.88 ppm) and the NH and $C_{\alpha}H$ signals.

Thus, one can state with sufficient confidence that, in the planar and symmetrical IIa,b molecules, there is double hydrogen bonding of the chelate type with the participation of one carbonyl and two NH groups. The assumption that structure II corresponds to the form with intramolecular bonds between two NH groups (four-membered ring) in the presence of a free carbonyl group is rejected even by a simple examination of Stuart–Briegleb and Dreiding molecular models, according to which the two NH groups in this form are not equivalent, and the dihedral angles between the H–N and C–R' bonds in the two H–N–C–R' groups are substantially different. In addition, the carbonyl group in this system turns out to be almost perpendicular to the plane of the double bonds and, consequently, ought to have a frequency substantially higher than 1635 cm^{-1} in the IR spectrum.

EXPERIMENTAL

The IR spectra were obtained with a UR-10 spectrometer, and the PMR spectra were obtained with an RS-60 or JNM-4H-100 spectrometers with operating frequencies of 60 and 100 MHz, respectively.

2-β-Aminoacrylylphenol (Ic). This was obtained by the action of excess dry ammonia on chromone in absolute alcohol at 20°C for 60 h and had mp 101.5-102.5°. Found %: C 66.2; H 5.5; N 8.8. $C_9H_9NO_2$. Calculated %: C 66.2; H 5.6; N 8.6.

2-β-Morpholinoacrylylphenol [23], 2-β-piperidinoacrylylphenol (Ia) [24], 2-β-diethylaminoacrylylphenol (Ib) [5], 2-β-benzylaminoacrylylphenol (Id) [23], 2-β-anilinoacrylylphenol (Ie) [24], 2-(β-benzylamino-β-phenylacrylyl)phenol (If) [25], 2-(β-n-butylamino-n-butylaminocarbonylacrylyl)phenol (Ig) [4], 3-(2-hydroxybenzoylmethylidene)-2-piperazinone (Ih) [3], and 2-(β-piperidino-β-piperidinocarbonylacrylyl)phenol (Ii) [2] were obtained by the reaction of the appropriate chromones with amines, while 1,5-di(anilino)-1,4-pentadien-3-one (IIa) [26] and 2,6-di(methylamino)-2,5-heptadien-4-one (IIb) [22] were synthesized by the action of aniline of 4-pyrone and methylamine on dehydroacetic acid, respectively.

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