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INTRAMOLECULAR CYCLIZATION OF 2-ARYL-3-AMINOACETYL-1,4-NAPHTHOQUINONES TO 3-BENZOCOUMARANONE DERIVATIVES*

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The isomerization of 2-aryl-3-(N-alkyl-N-arylamino)acetyl-1,4-naphthoquinones to 2-(N-alkyl-N-arylamino)-4-aryl-5-hydroxy-6,7-benzocoumaran-3-ones was studied. The structures of the compounds obtained were confirmed by the data from the UV, IR, mass and PMR spectra.

2-Aryl-3-(N-alkyl-N-arylamino)acetyl-1,4-naphthoquinones (I) are intramolecular donor-acceptor complexes (self-complexes) [2, 3]. Isomerization products in the form of yellow crystals that dissolve in aqueous alkalis to give red solutions and are isolated unchanged from them when the solutions are acidified were unexpectedly obtained during a study of their solubility in acetic acid. Benzocoumaranone structure II was established for the products of isomerization of aminoacetylnaphthoquinones I from the data from the UV, IR, mass, and PMR spectra (see Table 1 and the experimental section). The carbonyl bands of the five-membered ring are observed in the IR spectra of these compounds at 1705-1730 cm^{-1}; their assignment is in agreement with the data on the absorption of coumaranones [4, 5].

Benzocoumaranones II were characterized in the form of acetyl and benzoyl derivatives III and IV. Since the cyclization proceeds in the same way in all cases, it was subsequently more convenient to study it in the case of 2-(N-methylanilino)-4-phenyl-5-hydroxy-6,7-benzocoumaran-3-one (IIa).

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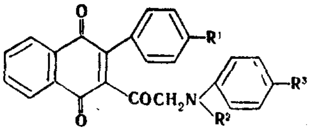
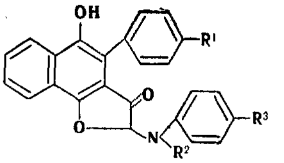
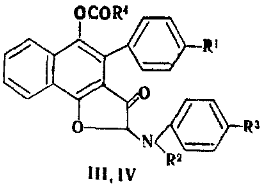


I



II



III, IV

III $R^4=CH_3$; IV $R^4=C_6H_5$; a $R^1=R^3=H$, $R^2=CH_3$; b $R^1=R^3=H$, $R^2=C_2H_5$; c $R^1=H$, $R^2=R^3=CH_3$; d $R^1=H$, $R^2=C_2H_5$, $R^3=CH_3$; e $R^1=H$, $R^2=CH_3$, $R^3=OCH_3$; f $R^1=H$, $R^2=C_2H_5$, $R^3=OCH_3$; g $R^1=OCH_3$, $R^2=C_2H_5$, $R^3=H$; h $R^1=OCH_3$, $R^2=R^3=CH_3$; i $R^1=OCH_3$, $R^2=C_2H_5$, $R^3=CH_3$; j $R^1=R^3=OCH_3$, $R^2=CH_3$; k $R^1=R^3=OCH_3$, $R^2=C_2H_5$; *l* $R^1=Br$, $R^2=CH_3$, $R^3=H$; m $R^1=Br$, $R^2=C_2H_5$, $R^3=H$; n $R^1=Br$, $R^2=R^3=CH_3$; o $R^1=Br$, $R^2=C_2H_5$, $R^3=CH_3$; p $R^1=Br$, $R^2=CH_3$, $R^3=OCH_3$; q $R^1=Br$, $R^2=C_2H_5$, $R^3=OCH_3$

The isomerization proceeds very readily in acetic acid and also on the surface of an adsorbent during chromatography of aminoacetylnaphthoquinones I on aluminum oxide or when the solid compounds are heated.

The starting compounds behave precisely like donor-acceptor systems in this reaction. The amine nitrogen atom is protonated in a strongly acidic medium or in the presence of mineral acids, the intramolecular charge-transfer band (CTB) vanishes, and isomerization does not take place. The model substances 2-aryl-3-acetyl-1,4-naphthoquinones also do not undergo cyclization under these conditions.

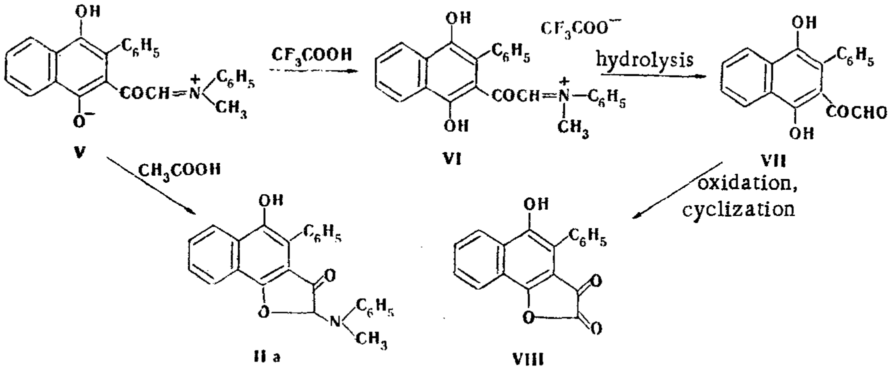
The isomerization should include a step involving intramolecular reduction of the 1,4-naphthoquinone ring of aminoacetylnaphthoquinone I and oxidation of the aminomethylene frag-

TABLE 1. Data from the IR and UV Spectra of II-IV

Compound	IR spectrum, ν, cm^{-1}								UV spectrum (ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$)
	in mineral oil				in dichloroethane				
	aromatic C=C	ring C=O	acyl C=O	OH	aromatic C=C	ring C=O	acyl C=O	OH	
IIa	1630 1602 1588	1705		3430	1635 1605 1580	1712		3545	223 (4,0), 242 (4,1), 278 (3,0), 410 (0,6)
IIf					1635 1590	1718		3550	219 (4,7), 244 (3,7), 278 (3,2), 407 (0,8)
IIg					1638 1612 1595	1717		3542	219 (5,2), 249 (4,4), 278 (3,2), 414 (0,5)
IIh					1637 1620 1593	1718		3545	220 (5,3), 249 (4,1), 280 (3,4), 415 (0,8)
II*l*	1605 1635	1710		3504	1605 1636	1718		3554	218 (4,6), 244 (4,6), 277 (4,2), 411 (0,9)
IIm					1635 1617	1719		3554	219 (4,6), 248 (4,3), 278 (3,8), 410 (0,8)
IIn					1638 1599	1719		3554	219 (5,1), 244 (4,7), 277 (3,8), 412 (0,9)
IIIa	1632 1605 1588	1717	1761		1635 1605 1580	1724	1772		212 (3,0), 247 (3,8), 272 (3,5), 380 (0,8)
IIIf					1636 1590	1723	1773		212 (3,4), 249 (3,0), 272 (3,0), 380 (0,6)
IIIg					1635 1615 1590	1723	1772		216 (3,8), 253 (3,7), 276 (3,0), 380 (0,6)
IIIm					1638 1617	1726	1775		216 (4,3), 251 (4,5), 272 (3,9), 375 (0,6)
IV	1632 1604 1588	1712	1737		1632 1604 1588	1720	1740		239 (4,9), 272 (2,5), 379 (0,6)

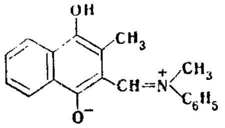
ment with simultaneous migration of one methylene proton and the formation of a dipolar ion of the V type.

Immonium-phenoxide dipolar ion V then undergoes cyclization to give the five-membered 3-benzocoumaranone (II). The reaction of dipolar ion V with a stronger protogenic agent



(trifluoroacetic acid) gives immonium salt VI, which is hydrolyzed to aldehyde VII by traces of moisture. Under the reaction conditions, aldehyde VII undergoes cyclization and oxidation to give 4-phenyl-5-hydroxy-6,7-benzocoumarin-2,3-dione (VIII) under extremely mild conditions, which is isolatable in pure form. Both air oxygen and a molecule of the starting naphthoquinone may act as the oxidizing agent. The structure of VIII was proved by physicochemical methods (see the experimental section).

In independent research together with V. Gailite and Ya. Dregeris it was shown that a similar immonium-phenoxide ion (IX) is formed during the photochemical isomerization of self-complexes of the 2-methyl-3-anilinomethyl-1,4-naphthoquinone series [6]. Under the influence of moisture, zwitterion IX also readily splits out an aniline residue to give 2-methyl-3-formyl-1,4-naphthoquinone, i.e., a close analog of keto aldehyde VII.



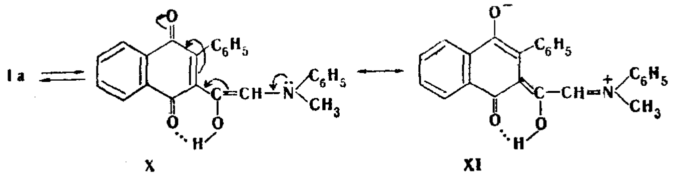
IX

A mechanism involving intramolecular hydride transfer is most likely for the intramolecular oxidation—reduction of aminoacetylnaphthoquinones I, since a total of two electrons and one proton is transferred. Using data from x-ray diffraction analysis [7], we calculated the closest intramolecular distance between the methylene hydrogen atom and the quinone carbonyl oxygen atom in the 2-phenyl-3-(N-methyl-p-anisidino)acetyl-1,4-naphthoquinone molecule (Ie) and found it to be extremely short (3.30 Å). This explains the fact that the cyclization of self-complexes I takes place even when the dry substances are heated.

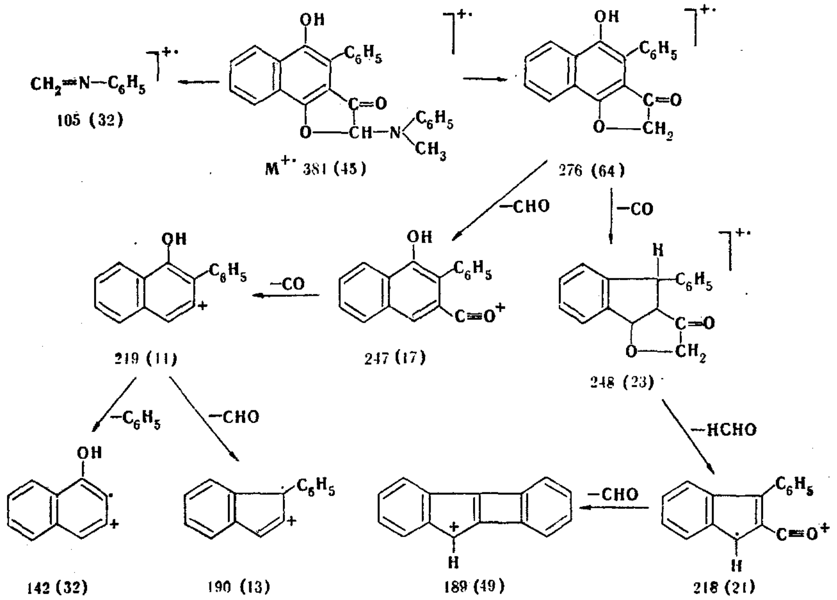
According to the literature data, the α-hydrogen atom in tertiary amines often has high hydride lability [8, 9], and quinone rings are strong hydride-ion acceptors [10]. The oxidation of amines by quinone derivatives is also explained by a hydride-transfer mechanism [11, 12]. Protonated quinones are even stronger hydride-ion acceptors [13]; the literature contains information regarding the hydride reduction of quinones in the presence of trifluoroacetic acid [14].

It has been previously shown that compounds of the "acceptor—CH_2NH" type under certain conditions can split out a molecule of hydrogen to give Schiff bases [15]. The possibility that hydride transfer as the first act in the conversion of a donor-acceptor system is characteristic for the isomerization of both aminoacetylnaphthoquinones I and the intermediates in the reaction of 9-halofluorenones or 2,4-dinitrobenzyl chloride with primary aromatic amines [15] cannot be excluded.

However, in solutions one also cannot exclude another oxidation scheme — reduction of aminoacetylnaphthoquinones I — which includes proton transfer in the conjugated polarized system formed as a result of the I→X(XI) tautomeric transformations. Quinone methides have often been included as intermediates in reaction schemes involving the oxidation and isomerization of quinone derivatives [16, 17].

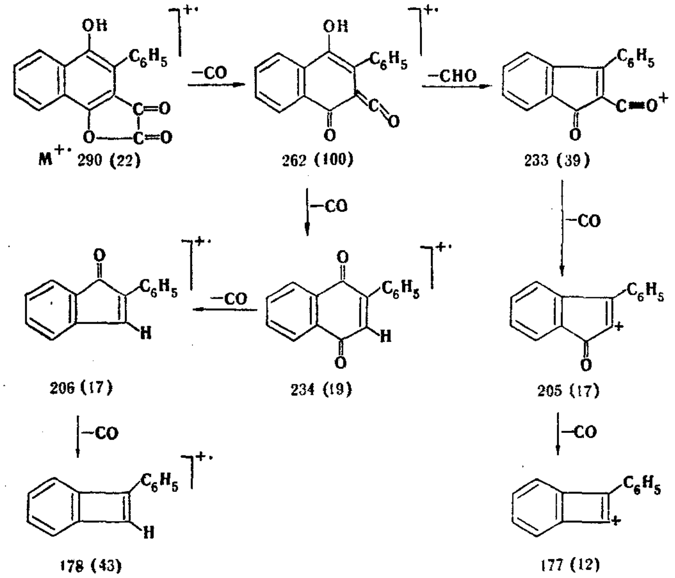


To establish their structures we studied the mass spectra of IIa and VIII. The peaks of the observed ions and their relative intensities are presented in the experimental section. The principal pathways of fragmentation of the compounds are shown in the following schemes:*



The sequence of the fragmentation of the molecular ions of Ia and VIII indicates that the single bonds of the five-membered heteroring are the most unstable bonds in the molecules as a result of electron impact.

In conclusion, we thank I. V. Dipan for recording the IR spectra.



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*The numbers under the structures of the ions are the mass-to-charge ratios (with the relative intensities in percent of the maximum peak given in parentheses).

TABLE 2. 2-(N-Alkyl-N-arylamino)-4-aryl-5-hydroxy-6,7-benzocoumaran-3-ones and Their Acyl Derivatives

Compound	mp, °C	Found, %			Empirical formula	Calculated, %		
		C	H	N		C	H	N
IIb	177	80,04	5,44	3,49	$C_{26}H_{21}NO_3$	78,98	5,35	3,54
IIc	178	78,61	5,36	3,63	$C_{26}H_{21}NO_3$	78,98	5,35	3,54
IId	152	79,03	5,78	3,54	$C_{27}H_{23}NO_3$	79,20	5,66	3,42
IIe	168	75,43	5,18	3,54	$C_{26}H_{21}NO_4$	75,89	5,15	3,41
IIf	160—161	76,21	5,59	3,45	$C_{27}H_{23}NO_4$	76,22	5,45	3,29
IIg	187—188	76,40	5,48	3,07	$C_{27}H_{23}NO_4$	76,22	5,45	3,29
IIh	192	76,49	5,51	3,11	$C_{27}H_{23}NO_4$	76,22	5,45	3,29
IIi	157—158	77,43	6,00	3,12	$C_{28}H_{25}NO_4$	76,52	5,73	3,19
IIj	198	72,98	5,25	3,59	$C_{27}H_{23}NO_5$	73,46	5,25	3,17
IIk	167—168	73,57	5,75	3,05	$C_{28}H_{25}NO_5$	73,83	5,53	3,08
IIl	195	65,38	4,00	3,45	$C_{25}H_{18}BrNO_3$	65,22	3,94	3,04
IIm	181	65,70	4,57	3,27	$C_{26}H_{20}BrNO_3$	65,83	4,25	2,95
IIn	193	65,01	4,18	3,29	$C_{26}H_{20}BrNO_3$	65,83	4,25	2,95
IIo	166—167	67,10	4,66	3,42	$C_{27}H_{22}BrNO_3$	66,39	4,54	2,87
IIp	224—225	63,50	3,76	3,02	$C_{26}H_{20}BrNO_4$	63,68	4,11	2,86
IIq	192—194	63,89	4,43	2,88	$C_{27}H_{22}BrNO_4$	64,30	4,40	2,78
IIIb	155—156	77,48	5,57	3,53	$C_{28}H_{23}NO_4$	76,87	5,30	3,20
IIIc	209	77,46	5,24	3,78	$C_{28}H_{23}NO_4$	76,87	5,30	3,20
IIIf	137	74,51	5,30	3,20	$C_{29}H_{25}NO_5$	74,50	5,39	3,00
IIIg	167	74,64	5,35	3,37	$C_{29}H_{25}NO_5$	74,50	5,39	3,00
IIIh	227	74,58	5,40	3,56	$C_{29}H_{25}NO_5$	74,50	5,39	3,00
IIIl	188	63,85	4,03	3,06	$C_{27}H_{20}BrNO_4$	64,55	4,01	2,79
IIIm	186	64,70	4,48	3,07	$C_{28}H_{22}BrNO_4$	65,13	4,30	2,71
IIIn	198—200	64,72	4,30	3,13	$C_{28}H_{22}BrNO_4$	65,13	4,30	2,71
IIIp	195—196	62,93	4,04	2,92	$C_{28}H_{22}BrNO_5$	63,17	4,17	2,63
IV	177	79,40	4,71	2,99	$C_{32}H_{23}NO_4$	79,16	4,78	2,89

EXPERIMENTAL

The UV spectra of $2\cdot10^{-5}$ M solutions of the compounds in a 1-cm thick cuvette were recorded with a Specord UV-vis spectrophotometer. The IR spectra were recorded with a UR-10 spectrometer. The PMR spectra were recorded with a Perkin—Elmer R 12A spectrometer (60 MHz) with cyclohexane and hexamethyldisiloxane as the internal standards. The mass spectra were obtained with an MS-50 AEI mass spectrometer with the use of a system for direct introduction of the substances into the ion source at a source temperature of 150°C and an ionizing-electron energy of 70 eV.

2-(N-Methylanilino)-4-phenyl-5-hydroxy-6,7-benzocoumaran-3-one (IIa). A) A 1.9-g (0.005 mole) sample of aminoacetylnaphthoquinone Ia was dissolved by heating in 15 ml of glacial acetic acid, and the mixture was maintained at room temperature for 24 h. The resulting precipitate was removed by filtration and recrystallized from ethanol to give 1.45 g (76%) of IIa in the form of yellow crystals with mp 157°C. PMR spectrum, δ ($CDCl_3$): 8.2-8.4 and 6.8-7.9 (2H and 7H, m, naphthalene and N-phenyl protons), 7.53 (5H, s, 4-C_6H_5), 5.97 (1H, s, CH), 5.8 (1H, s, OH), and 2.91 ppm (3H, s, NCH_3). Mass spectrum, m/e (principal ion peaks with relative intensities ≥ 10% of the maximum peak): 381 $M^{+\cdot}$ (45), 277 (12), 276 (64), 248 (23), 247 (17), 231 (18), 219 (11), 218 (21), 190 (13), 189 (49), 167 (31), 142 (32), 120 (33), 113 (43), 105 (32), 104 (45), 77 (21), 71 (100), 69 (71). Found: C 79.2; H 5.0; N 3.9%. $C_{25}H_{19}NO_3$. Calculated: C 78.7; H 5.0; N 3.7%.

B) A 0.38-g (0.001 mole) sample of Ia was chromatographed with a column filled with activity II (Brockmann) aluminum oxide (elution with chloroform), after which the solvent was removed by vacuum distillation, and the residue was recrystallized from ethanol. According to the results of analysis and its melting point, the product was identical to the product obtained by method A. The yield was 0.2 g (53%). Compound Ia did not undergo isomerization on the sorbent if aluminum oxide that had been previously treated with 10% acetic acid was used.

C) A 0.38-g (0.001 mole) sample of Ia was placed in an ampul, and the ampul was heated in an oil bath at 130-140°C for 3 h (the melting point of Ia is 177°C). The reaction mass was dissolved in chloroform, and the solution was chromatographed with a column filled with aluminum oxide that had been previously treated with acetic acid. Evaporation of the solvent and recrystallization of the residue from ethanol gave a substance with mp 157°C, which did not depress the melting point of the compound obtained by method A.

2-(N-Alkyl-N-arylamino)-4-aryl-5-hydroxy-6,7-benzocoumaran-3-ones (IIb-q). These compounds were obtained by method A in 70-80% yields. Their characteristics are presented in Table 2.

2-(N-Methylanilino)-4-phenyl-5-acetoxy-6,7-benzocoumaran-3-one (IIIa). A 0.2-g sample of benzocoumaranone IIa was dissolved in 5 ml of dry pyridine, and 2.3 ml of acetyl chloride was added with stirring. The reaction mixture was poured into water, and the precipitate was removed by filtration and recrystallized from ethanol to give a pale-yellow crystalline substance with mp 176-177°C. PMR spectrum, δ($CDCl_3$): 8.3-8.5 and 6.9-7.9 (2H and 7H, m, naphthalene and N-phenyl protons), 7.45 (5H, s, 4-C_6H_5), 6.08 (1H, s, CH), 2.92 (3H, s, NCH_3), and 2.12 ppm (3H, s, $OCOCH_3$). Found: C 75.9; H 5.0; N 3.0%. $C_{27}H_2NO_4$. Calculated: C 76.6; H 5.0; N 3.3%.

Other acylated benzocoumaranones III, the characteristics of which are given in Table 2, were similarly obtained.

4-Phenyl-5-hydroxy-5,7-benzocoumaran-2,3-dione (VIII). A 12-ml sample of trifluoroacetic acid was added to a solution of 1.9 g (0.005 mole) of aminoacetylnaphthoquinone Ia in 120 ml of acetone, and the mixture was allowed to stand at room temperature overnight. It was then evaporated in vacuo to 30 ml and worked up to give 1.1 g (76%) of VIII in the form of red crystals with mp 205°C. Recrystallization from ethanol—ether gave a product with mp 209-210°C. IR spectrum: in mineral oil: 3433 (OH); 1828 (CO); 1730 (CO); 1632 and 1590 cm^{-1} (aromatic C=C); in dichloroethane: 3540 (OH); 1830 (CO); 1735 (CO); 1636, 1615, and 1595 cm^{-1} (aromatic C=C). UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-4}$), in ethanol: 229 (2.75), 275 (1.83), and 421 nm (0.50). PMR spectrum, δ ($CDCl_3$): 8.34 and 8.16 (1H and 1H, dd, J = 8 and 2 Hz, α-naphthalene protons), 7.9 and 7.7 (2H, m, β-naphthalene protons), 7.3-7.7 (5H, m, 4-C_6H_5), and 5.8 ppm (1H, s, OH). Mass spectrum, m/e (principal ion peaks with relative intensities ≥10% of the maximum peak): 290 $M^{+\cdot}$ (22), 263 (21), 262 (100), 234 (19), 233 (39), 207 (21), 206 (17), 205 (17), 178 (43), 177 (12), 176 (22), 112 (34), 111 (53), 101 (10). Found: C 74.5; H 3.5%. $C_{18}H_{10}O_4$. Calculated: C 74.5; H 3.5%.

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