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REACTION OF ARYLIDENE-2-NAPHTHYLAMINES WITH THE ETHYL ESTER OF (2-QUINOLYL)-β-OXOPROPIONIC ACID

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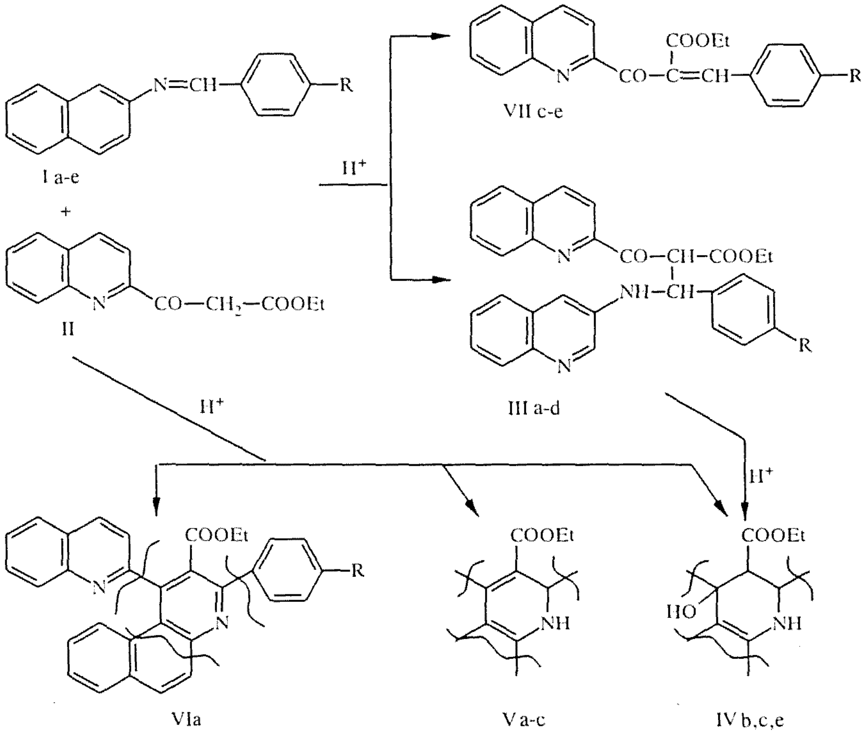
The reaction of arylidene-2-naphthylamines with the ethyl ester of (2-quinolyl)-β-oxopropionic acid results in the synthesis of ethyl esters of 1-(2-quinolyl)-3-arylbenzo[f]quinoline-2-carboxylic acids. All the theoretically possible intermediate reaction products were isolated: the amino esters of 2-quinoline-β-oxopropionic acid, the hydroxy esters of tetrahydro- and esters of dihydrobenzo[f]quinoline-2-carboxylic acid, as well as the by-products – the ethyl ester of 2-quinolyl-α-(R-benzylidene)-β-oxopropionic acid. The IR, UV, and mass spectra of the synthesized compounds are discussed.

We have previously studied the condensation of arylidene-2-naphthylamines with acetoacetic and furoylacetic esters [1, 2]. As the result we obtained the difficultly obtainable esters of 1,3-disubstituted benzo[f]fquinolines-2-carboxylic acids. To clarify the influence of substituents at the carbonyl group of the keto ester on the course of the reaction studied and in order to obtain new derivatives of benzo[f]quinoline-2-carboxylic acid, we carried out the condensation of arylidene-2-naphthylamines (Ia-e) with a qunioline analog of the above keto esters – the ethyl ester of (2-quinolyl)-β-oxopropionic acid (II).



I, III, IV–VIIa R=H, b R=F, c R=Br, d R=OMe, e R=NO$_2$

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Study of the reaction showed that under mild conditions (holding the reagents at room temperature for 10-20 min in an ethanol solution in the presence of hydrochloric acid) noncyclic aminoketo esters are formed – the ethyl esters of (2-quinolyl)-α-[(R-phenyl)(2-naphthylamino)]methyl-β-oxopropionic acid (IIIa-d), the composition and structure of which were confirmed by the data of elemental analysis, IR, UV and mass spectra.

In the IR spectra of compounds IIIa-d a characteristic band of the stretching vibrations of the NH group is observed at 3380-3375 cm^{-1}. The vibration bands of the CO of the ester group and the carbonyl group in the quinoline ring are present at 1720-1715 and 1695-1690 cm^{-1}, respectively.

The UV spectra of the aminoketo esters IIIa-d (Table 1) are similar to the spectrum of 2-naphthylamine. They contain two bands, characteristic for the local excitation of the phenyl chromophore, and one band due to the transfer of an electron of the quinoline ring nitrogen atom (the $n-\pi^*$–band) [3]. Introduction of substituents into the p-position of the phenyl ring leads to a small bathochromic shift of the long-wave band, without a change in the general pattern of the spectrum.

In the mass spectra of the aminoketo esters IIIa-d the peak intensity of the molecular ion (M^+) is low (12-25%). The fragmentary peaks corresponding to the starting compounds I and II and formed as the result of cleavage of the C–C bond, as well as the peaks of the $[M-C_{10}H_7NH_2]^+$ ions, are most intense.

On heating a mixture of Ib, c, e with II or aminoketo esters III at 80°C, or on prolonged (several days) holding at room temperature in ethanol or benzene in the presence of a catalyst (HCl, BF_3 etherate), cyclic products are formed – the ethyl esters of 1-hydroxy-1-(2-quinolyl)-3-aryl-1,2,3,4-tetrahydrobenzo[f]quinoline-2-carboxylic acid (IVb, c, e). Until this time this product has been isolated only by the condensation of benzylidene-2-napththylamine with cyclohexanone [4].

In the IR spectra of the cyclic hydroxy esters IVb, c, e, a diffused intense absorption band is observed in the 3600-3380 cm^{-1} region. When the spectrum is run in CCl_4 solution, the absorption in this region appears in the form of two bands: 3410 (v_{NH}) and 3605 (B_{OH}) cm^{-1}. The stretching vibrations of the ester group (v_{CO}) are observed at 1720 cm^{-1}. In the spectra of compounds IVb, c, e the stretching vibrations band of the keto group characteristic for the spectra of aminoketo esters IIIb, c, e is absent, which confirms the cyclization of the latter.

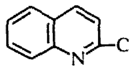
In the UV spectra of hydroxy esters IVb, c, e (Table 1) an increase in the intensity of the short-wave absorption band is observed in comparison with the spectra of IIIa-d. Moreover, in view of the transformation of the carbonyl group into a hydroxyl group, its influence on the quinoline ring is absent, and in the spectra of the hydroxy esters IVb, c, e an absorption band (316-317 nm) characteristic of the quinoline radical playing the role of an independent chromophore [5] can easily be ascertained. The long-wave band in the spectra of IVb, c, e has a lower intensity and is bathochromically shifted relative to the spectra of aminoketo esters IIIa-d.

In the mass spectra of compounds IVb, c, e there are peaks with a maximum intensity of the molecular ions, and fairly intense (45-60%) peaks of the $[M-18]^+$ ions, corresponding to the elimination of a water molecule from the molecular ion and confirming the presence of a hydroxyl group in the molecules of compounds IVb, c, e.

On prolonged heating of the starting reagents Ia-c and II in the presence of HCl in an ethanol or dimethylformamide solution the ethyl esters of 1-(2-quinolyl)-3-aryl-3,4-dihydrobenzo[f]-quinoline-2-carboxylic acids (Va-c) were obtained, which were formed as a result of dehydration of the cyclic hydroxy esters IV.

In the IR spectra of the dihydro derivatives Va-c there is a narrow mean intensity band at 3400 (v_{NH}(and an intense band (v_{CO}) of the ester group at 1700-1690 cm^{-1}.

In the mass spectra of compounds Va-c the peak of the molecular ion has the maximal intensity. There are fairly intense peaks (35-55%) of the fragmentary ions.

$[M-COOEt]^+$, $[M-C_6H_4R]^+$, [M–  –CH=CH–COOEt]$^+$.

In the UV spectra of the dihydro derivatives Va-c (Table 1), in comparison with the spectra of compounds III, IV, a decrease in the intensity of the second absorption maximum (232-235 nm) is observed as well as a considerable bathochromic shift of the long-wave band, possibly due to the influence of the ester group, drawn into conjugation with the quinoline and naphthalene rings as a result of the formation of a new double bond in the structure of benzo[f]quinoline.

When the reaction was carried out under rigorous conditions – heating of the reagents Ia and II in an ampule in a DMFA solution in the presence of HCl at 100°C, a dehydrogenation product of the dihydro derivative Va was obtained – the ethyl ester of 1-(2-quinolyl)-3-phenylbenzo[f]quinoline-2-carboxylic acid (VIa).

TABLE 1. Characteristics of Compounds IIIa-d, IVb, c, e, Va-c, VIa

Compound	Empirical formula	mp, °C	UV spectrum: λ_{max}, nm (log ε)	Yield, %
III a	$C_{31}H_{26}N_2O_3$	115...116	213(4,63), 224(4,65), 248(4,69), 270(4,48), 320(4,30)	79
III b	$C_{31}H_{25}FN_2O_3$	117...118	214(4,61), 228(4,63), 256(4,68), 286(4,48), 326(4,00)	58
III c	$C_{31}H_{25}BrN_3O_3$	121...122	215(4,62), 226(4,64), 249(4,66), 273(4,46), 280(4,46), 330(4,22)	64
III d	$C_{32}H_{28}N_4O_4$	103...104	214(4,65), 229(4,69), 238(4,65), 286(4,50), 326(4,32)	68
IV b	$C_{31}H_{25}FN_2O_3$	140...141	208(4,75), 235(4,83), 246(4,67), 284(4,10), 317(3,80), 349(3,60)	38
IV c	$C_{31}H_{25}BrN_2O_3$	218...220	208(4,76), 236(4,80), 249(4,63), 288(4,24), 316(3,84), 342(3,63)	29
IVe	$C_{31}H_{25}N_3O_5$	249...250	207(4,77), 235(4,81), 246(4,70), 281(4,30), 317(3,91), 347(3,60)	36
Va	$C_{31}H_{24}N_2O_2$	119...120	206(4,64), 239(4,59), 265(4,41), 317(3,92), 368(3,15)	63
V b	$C_{31}H_{23}FN_2O_2$	131...132	208(4,62), 235(4,56), 266(4,40), 415(3,88), 373(3,15)	34
V c	$C_{31}H_{23}BrN_2O_2$	207...208	206(4,63), 238(4,58), 270(4,43), 316(3,90), 440(3,60)	52
VIa	$C_{31}H_{22}N_2O_2$	187...188	209(4,70), 217(4,69), 234(4,69), 279(4,59), 318(4,10), 347(3,66), 361(3,61)	16

In the IR spectrum of compound VIa the characteristic stretching vibrations band of the NH group in the 3400 cm^{-1} region, which is present in the spectra of the dihydro derivatives V, is absent, but the vibration band (ν_{CO}) of the ester group at 1715 cm^{-1} is retained.

The mass spectrum of compound VIa confirms the stability of this compound on electron impact. It contains the peak with maximum intensity of the molecular ion and low-intensity peaks of the $[M-COOEt]^+$ and $[M-C_6H_5]^+$ ions.

The UV spectrum of the dehydrogenation product VIa (Table 1) differs from the spectra of tetrahydro- and dihydro derivatives of the esters of benzo[f]quinoline-2-carboxylic acids IV, V. The formation of a single closed system of conjugated bonds in the structure of benzo[f]quinoline makes it possible to compare the spectrum of compound VIa with the spectrum of phenanthrene [6] and to classify the bands present in it as β- (217, 234 nm) p- (279 nm) and α- (347, 361 nm) bands according to Clar. For the spectrum of compound VIa the resolution of the vibrational structure of the α-band is characteristic, as it happens in the spectra of previously studied benzo[f]quinolines [1, 2].

In the course of the investigation of the reaction of arylidene-2-naphthylamines (Ic-e) with the aminoketo ester II, together with above mentioned reaction products III-VI, by-products also have been obtained – the ethyl esters of (2-quinolyl)-α-(R-benzylidene)-β-oxopropionic acid (VIIc-e), in the IR spectra of which the bands at 1690-1680 ($\nu_{COOC2H5}$), 1600-1590 (ν_{CO}) and 1620 cm^{-1} ($\nu_{C=C}$) should be noted. Products with a similar structure were obtained in the reaction of aromatic aldehydes with the ethyl ester of 3-(pyridyl-β-oxopropionic acid [7], chloroacetic and cyanoacetic esters [8]. Taking into account the data of [7, 8] and the results of our previous investigations [5, 9], we believe that the formation of the unsaturated keto esters VIIc-e may occur, on the one hand, as a result of an aldol condensation of the aminoketo ester II with an aromatic aldehyde separating out as the result of the hydrolysis of the initial azomethine and, on the other hand, due to the hydraminic splitting off of the intermediate aminoketo ester III.

Thus, the investigation of the reaction of arylidene-2-naphthylamines with the aminoketo ester II showed that the cyclic products IV, V, VI are preceded by aminoketo esters III, the ability to undergo cyclization of which is dependent on the nature of substituent R. When R = H, NO_2, Br, F the cyclization process predominates over the splitting off of III. In the presence of a nitro group, the cyclization of the aminoketo ester proceeds as fast that it cannot be isolated. In the case the reaction product is the cyclic hydroxy ester IVe. On the contrary, the electron-donoric methoxy group shifts the reaction in the direction of splitting off of the aminoketo ester IIId, so that the corresponding cyclic products are not formed at all.

As far as the comparative analysis of the behavior of the arylidene-2-naphthylamines in the reaction with compound II, aceto- and furoylacetic esters [1, 2] is concerned, it is possible that the presence of a bulky quinoline substituent in the molecule of the aminoketo ester II leads to slowing down of the cyclization, dehydration and dehydrogenation processes of the intermediate compounds. This makes it possible, by varying the conditions, to stop the process at any stage and to obtain all the theoretically possible reaction products.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer in KBr tablets or in a CCl_4 solution. The mass spectra were obtained on a Varian Mat-311 spectrometer with a direct introduction of the materials into the ionic source at an energy of the ionizing radiation of 70 eV. The UV spectra were run on a Specord UV-vis spectrometer in ethanol. The ethyl ester of 2-quinoline-β-oxopropionic acid (II) was obtained according to [10].

The elemental analysis data for C, H, N correspond to the calculated values.

Ethyl Ester of 2-Quinolyl-α-[(R-phenyl)(2-naphthylamino)]methyl-β-oxopropionic Acid (IIIa-d). A solution of equimolar amounts (5 mmoles) of Ia-d and 11, 3 drops of a conc. HCl in 20 ml of ethanol was stirred for 10-20 min at 20°C. The precipitate that separated out was treated with an aqueous solution of NH_4OH, crystallized from ethanol and compounds IIIa-d were obtained (Table 1).

Ethyl Ester of 1-Hydroxy-1-(2-quinolyl)-3-aryl-1,2,3,4-tetrahydrobenzo[f]quinoline-2-carboxylic Acid (IVb, c, e). A solution of equimolar amounts (5 mmoles) of Ib, c, e and II or 2.5 mmoles of aminoketo esters IIIb, c, e in 20 ml of benzene with 5 drops of BF_3 etherate for Ib, c, IIIb, c or ethanol with 3 drops of conc. HCl for Ie was heated for 20 min at 80°C or allowed to stand for 72 h at 20°C. The reaction products were isolated as described for IIIa-d and compounds IVb, c, e were obtained (Table 1).

Ethyl Ester of 1-(2-Quinolyl)-3-aryl-3,4-dihydrobenzo[f]quinoline-2-carboxylic Acid (Va-c). A solution of equimolar amounts (5 mmoles) of Ia-c and II and 5 drops of a conc. HCl in 5 ml of DMFA for Ia or in 20 ml of ethanol for Ib, c was heated for 2.5 h at 80-1000°C. The solvent was evaporated twice. The resinous residue was treated with NH_4OH, hexane and compound Va was crystallized from isopropanol, Vb, c – from ethanol.

Ethyl Ester of 1-(2-Quinolyl)-3-phenylbenzo[f]quinoline-2-carboxylic Acid (VIa). A mixture of equimolar amounts (5 mmoles) of Ia and II, 5 ml of DMFA, and 1 ml of a conc. HCl was heated in an ampule for 3 h at 100°C. The resinous mixture obtained was allowed to stand for 2 days in air, treated with aqueous NH_4OH, ground with isopropanol, and crystallized from ethanol.

Ethyl ester of 2-quinoline-α-(R-benzylidene)-β-oxopropionic acid (VIIc-e) was obtained under the conditions of the synthesis of compounds IV, V by evaporating the mother liquor after the separation of the residues of IVc, e, Vc for VIIc, e and evaporation of the reaction solution to 1/3 volume for VIId. The resinous residues for VIIc, e and the precipitate for VIId were treated with aqueous NH_4OH, isopropanol, and compounds VIIc, d were crystallized from ethanol and VIIe from nitromethane. **Compound VIIc ($V_{21}H_{16}BrNO_3$).** Yield 11%, mp 149-150°C. **Compound VIId ($C_{22}H_{18}NO_4$).** Yield 54%, mp 128-129°C. **Compound VIIe ($C_{21}H_{16}N_2O_8$).** Yield 14%, mp 179-180°C.

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