In the case of the preparation of V the petroleum ether was removed by vacuum evaporation to dryness, and the residue was dissolved in methanol. The addition of water precipitated 0.02 g (1%) of 1-diethylamino-4,4,4-trichloro-1-buten-3-one with mp 55-56°C (55-56°C [3]).

4-Trichloroacetonylpyrimidine (VII). This compound was obtained by the method presented above. After separation of the triethylamine hydrochloride, the filtrate was evaporated, and the residue was dissolved in methanol and precipitated by the addition of water to give 1.4 g of VII.

N-Trichloroacetyl-4-methylene-6-trichloroacetonylpyrimidine (X). This compound was similarly obtained, but 60 mmole of trichloroacetyl chloride was used in the reaction. Workup of the reaction mixture gave 0.9 g of a mixture of V and X. Fractional reprecipitation from methanol by the addition of water gave 0.1 g of V and 0.7 g of X (Table 2). A 0.1 g sample of X was heated in petroleum ether for 3 h, after which the solution was evaporated in vacuum to give 0.07 g of V with mp 147-148°C.

The synthesized trichloro- and trifluoroacetonylpyrimidines were light-yellow crystalline substances.

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PYRIMIDINES.

LXIV.* STRUCTURE AND PROPERTIES OF 1,3-DIARYLDIHYDROBENZO[f]QUINAZOLINES

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It is shown that the 1,3-diaryldihydrobenzo[f]quinazolines that are formed in the condensation of β-naphthylamine, an aromatic aldehyde, and ammonia are 1,2-dihydro isomers. They readily form salts due to the developing stabilization of the molecule by resonance of the amidinium type. Thus 2,4-dialkylbenzo[f]quinazolinium iodides rather than monoalkyl derivatives were obtained in the case of alkylation with alkyl halides as a result of refluxing the reaction mixtures. The isomeric monoalkylbenzoquinazolinium iodides, the structure of which was proved by the formation of the known benzoquinazolines after treatment with alkali, were also obtained.

We have previously reported [2] that the reaction of β-naphthylamine, an aromatic aldehyde, and ammonia leads to the formation of dihydro derivatives of 1,3-diarylbenzo[f]quinazolines (I). The formation of dihydro derivatives rather than aromatic compounds is probably due to the peculiarities of the structure of the former: first, the presence of a bulky substituent in the 1 position of the benzoquinazoline hinders aromatization of the molecule under the reaction conditions [2], and, second, the existence of a saturated node

*See [1] for communication LXIII.

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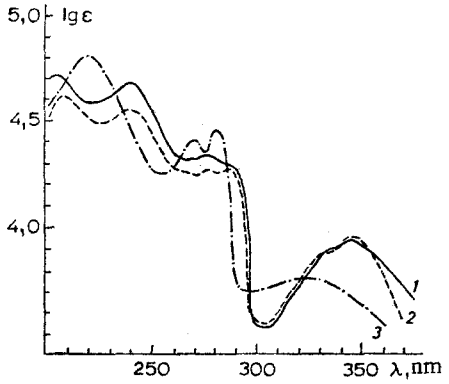
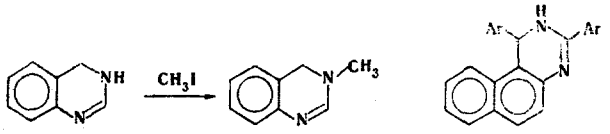


Fig. 1. UV spectra of benzo[f]quinazolines: 1) benzoquinazoline III; 2) methylbenzoquinazoline II; 3) methiodide IVa.

at $C_{(1)}$ decreases the steric strain of the molecule. These ideas are in good agreement with the data on the effect of the steric factor on the ease of formation of dihydro derivatives at the 3—4 bond in 4,5-dialkylquinazolines [3].

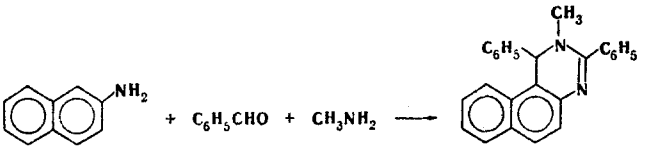
In the present research we examined the structure of dihydrobenzoquinazolines I and studied some possibilities for the preparation of other isomers.

Of the dihydro derivatives of condensed pyrimidines, dihydroquinazolines are closest to the compounds under examination. Dihydroquinazolines have been obtained in most cases from the corresponding aromatic derivatives of quinazolines [4-6]; they have also been obtained directly by cyclization from o-(chloromethyl)anilines and nitriles [7] and by reaction of o-(aminoalkyl)anilines with amidines [3, 8]. A study of the structure of N-unsubstituted dihydroquinazolines [3, 4, 6] showed that, despite the possibility of amidine isomerism, they exist in the form of 3,4-dihydro isomers, which are energetically more favorable than the 1,4-dihydro isomers.* In the case of dihydroquinazoline the 3,4-dihydro structure is in agreement with the fact that only 3-methyl-3,4-dihydroquinazoline was obtained by methylation [10].



Ia

On the basis of these data one might have assumed that the dihydrobenzo[f]quinazolines that we obtained most likely have the structure (Ia) of 1,2-dihydro derivatives. To ascertain their structure we synthesized a genuine sample of 2-methyl-1,3-diphenyl-1,2-dihydro-



II

benzo[f]quinazoline (II) and compared its UV spectrum with the UV spectrum of 1,3-diphenyldihydrobenzo[f]quinazoline (III) [2]. The similarity in the UV spectra of II and II (see Fig. 1) provides a basis for the assumption that the dihydrobenzo[f]quinazolines obtained by the reaction of β-naphthylamine, an aromatic aldehyde, and ammonia [2] have the structure of 1,2-dihydro derivatives.

An attempt to obtain an isomeric compound — 4-methyl-1,3-diphenyl-1,4-dihydrobenzo[f]quinazoline — by condensation of N-methyl-β-naphthylamine with benzaldehyde and ammonia was unsuccessful.

*This is in agreement with the data on the heats of hydrogenation of 1,2- and 1,4-dihydronaphthalenes, for which it has been shown that the heat of hydrogenation is lower for the 1,2 isomer [9].

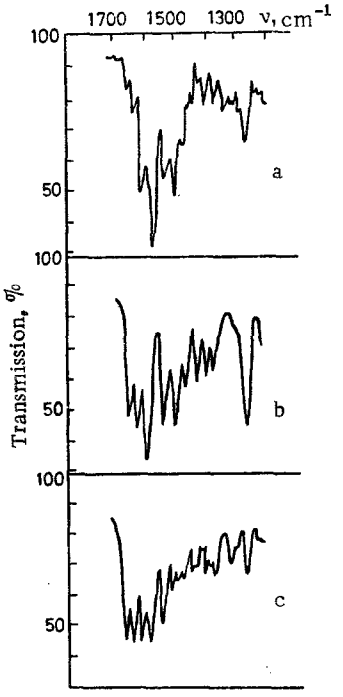


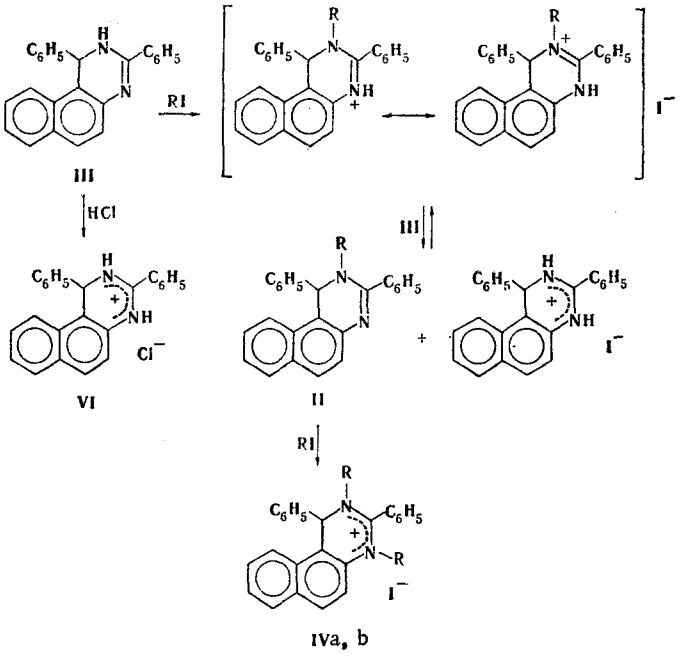
Fig. 2. IR spectra of benzoquinazolines (1% solutions in $CHCl_3$): a) benzoquinazoline III; b) methiodide IVa; c) reaction mixture (III + CH_3I).

In order to ascertain the possibility of the preparation of the isomeric 4-alkyl-substituted compound, we carried out the alkylation of benzoquinazoline III. The formation of an isomer in the alkylation reaction could not be excluded if one takes into account the fact that the 2-NH group in 1,3-diaryl-1,2-dihydrobenzo[f]quinazolines is sterically hindered. The methylation of benzoquinazoline III with trimethyl phosphate [11] and methyl p-toluenesulfonate [12] did not give positive results. We were able to accomplish alkylation only when we used alkyl halides. Methylation occurred in the reaction of quinazoline III with methyl iodide in the presence of NaH [13]; the process was monitored from the IR spectrum of the reaction product (IVa) (disappearance of the N—H vibrations) and by determination of the molecular weight by mass spectrometry. However, the PMR spectrum of IVa contained signals of two methyl groups (see the experimental section). (See scheme on following page).

The PMR spectrum of the reaction mixture (III + CH_3I) obtained by refluxing benzoquinazoline III with CH_3I in the absence of NaH contained precisely the same signals. The presence of two signals in the PMR spectra nevertheless did not constitute evidence for the formation of two isomeric compounds, since they were shifted to weak field as compared with the signal of the N—CH_3 group in benzoquinazoline II. A comparison of the IR spectrum of the reaction mixture (III + CH_3I) with the IR spectra of benzoquinazolines II, III, and IVa at 1400-1700 cm^{-1} demonstrated clearly (see Fig. 2) that the reaction mixture (III + CH_3I) contains only III and IVa. From the spectral data obtained and the literature data on the structure of amidinium salts [14] it may be concluded that quaternization to give 2,4-dimethyldihydrobenzoquinazolinium iodide (IVa) takes place along with alkylation in both cases. The reaction also proceeded similarly in the case of benzoquinazoline III and ethyl iodide.

The data in [6, 15], in which the PMR spectra of the substituted dihydroquinazolines and dihydroquinazolinium salts are presented, make it possible to assign the signals of the CH_3 groups in the PMR spectrum of IVa: the signal of the 2-CH_3 group is located at stronger field (3.27 ppm), and the weaker-field signal (3.60 ppm) is related, correspondingly, to the 4-CH_3 group.

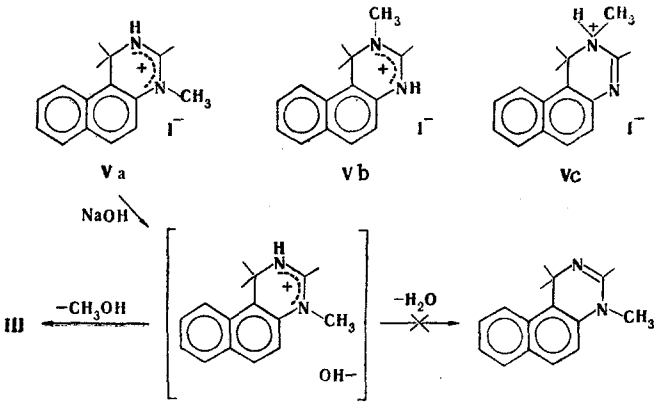
The facile and rapid formation of dialkyl-substituted IVa and the absence of monoalkylquinazoline II in the mixture were somewhat unexpected. An intense similar dialkylation in the reaction of 2,2-diethyl-1,2-dihydropyrimidine with methyl iodide at room tempera-



II, IV a R=CH_3; IV b R=C_2H_5

ture has been described [16], whereas only monomethylquinazolinium iodide was obtained in the reaction of 3,4-dihydroquinazoline with CH_3I at room temperature [10].

When a mixture of benzoquinazoline III and methyl iodide in alcohol is maintained at room temperature, a very intense band at 1555 cm^{-1}, which is characteristic for N-methyl-substituted II and IVa, appears in the IR spectrum of product V (a similar intense absorption band is also present in the IR spectra of N-methyldihydroquinazolines [6]); the PMR spectrum contains only one signal of the N—CH_3 group at 3.42 ppm, which is shifted to weak field as compared with the signal for methylquinazoline II. The additional presence of bands of N—H stretching vibrations at 3420 and 3250 cm^{-1} in the IR spectrum of V provided us with a basis for the assumption that it is methyldihydrobenzoquinazolinium iodide Va, Vb, or Vc.



Although structure Va [14] or Vb [10] is most likely according to the literature data, the IR spectrum of V at 1580-1650 cm^{-1} did not contain bands characteristic for amidinium salts [17] and differed from the IR spectrum of a genuine sample of Vb (from II and HI). On the other hand, it has been shown for structurally related dihydroquinazolinium salts that in the case of structures of the Vb and Vc type [18] treatment with alkali under mild conditions leads to N-methyl-substituted products; Vb also gave starting methylquinazoline II. However, in the case of the action of dilute NaOH on methylation product V under similar conditions, we obtained starting benzoquinazoline III rather than quinazoline II. On the basis of these results we can evidently assume that the compound obtained has structure Va and that treatment of it with alkali leads to the formation of the more favorable 1,2-dihydro isomer rather than the 1,4-dihydro isomer.

The ease of formation of quaternary salts IV is due to the resulting stabilization of th molecule by resonance of the amidinium type [14]. 2-Methylbenzoquinazoline II reacts smoothly with CH_3I to give dimethylquinazolinium iodide (IVa). In contrast to V, IV have high stabilities and are unaffected by treatment with dilute NaOH at room temperature.

The formation of stable pyrimidinium salts is characteristic for various types of dihydropyrimidines: the charge is delocalized over the amidine fragment [3, 19] or over the structural element of the type characteristic for cyclic vinamidinium salts [15, 20] (i.e., with breaking of the conjugation chain in the 4 or 2 position of the pyrimidine ring).

The dihydrobenzoquinazolines that we obtained in this research similarly formed the corresponding salts when they were treated with acids. For example, benzoquinazolinium chloride VI was obtained from benzoquinazoline III and dry HCl in alcohol.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra were recorded with a Varian A56/60A spectrometer with hexamethyldisiloxane as the internal standard. The molecular weights were determined with an MS-902 mass spectrometer with a system for the direct introduction of the samples at 120-140°C.

2-Methyl-1,3-dipehnyl-1,2-dihydrobenzo[f]quinazoline (II). A mixture of 2.75 g (0.019 mole) of β-naphthylamine, 4.1 g (0.038 mole) of benzaldehyde, 5.5 g (0.061 mole) of methylammonium acetate, and 4 ml of propionic acid was refluxed for 5 h, after which it was cooled and poured into 200 ml of water. The aqueous mixture was neutralized with dry sodium bicarbonate and extracted with chloroform. The chloroform was washed with water, dried with $MgSO_4$ and vacuum distilled. The residual oil was triturated with ether to give 2.3 g (34%) of methylbenzoquinazoline II with mp 182-185°C (from ethyl acetate). IR spectrum (in $CHCl_3$): 1555 (very intense absorption); 2820, 2920, and 2970 cm^{-1} (N—CH_3). UV spectrum, λ_{max} (log ε): 210, (4.56), 239 (4.49), 277 (4.26), 288 (4.28), and 343 nm (4.59). PMR spectrum (in $CDCl_3$): 2.87 (3H, s, N—CH_3), 5.9 (1H, s, 1-H), and 7.15-7.70 ppm (16H, m, H_{arom}). Found: C 86.0; H 5.7; N 8.3%; M 348. $C_{25}H_{20}N_2$. Calculated: C 86.3; H 5.7; N 8.1%; M 348. Recrystallization from alcohol gave a crystal solvate with mp 82-86°C. Found: C 82.3; H 6.7; N 7.7%; $C_{25}H_{20}N_2 \cdot C_2H_5OH$. Calculated: C 82.2; H 6.6; N 7.1%.

2,4-Dimethyl-1,3-diphenyl-1,2-dihydrobenzo[f]quinazolinium Iodide (IVa). A) A mixture of 1.65 g (4.9 mmole) of benzoquinazoline III, 0.14 g (5.8 mmole) of NaH, and 15 ml of absolute dimethylacetamide was stirred at room temperature for 15 min, and 3.5 ml (57 mmole) of methyl iodide was added slowly. The solution was filtered, and the solvent was removed from the filtrate by vacuum distillation. The residue, which began to crystallize, was triturated with ether, and the solid was removed by filtration and washed with water to give 1.7 g (70%) of salt IVa. Recrystallization from alcohol gave a crystal solvate with mp 210-212°C. Found: C 62.6; H 5.4; N 5.3%. $C_{26}H_{23}IN_2 \cdot C_2H_5OH$. Calculated: C 62.6; H 5.4; N 5.2%. An analytical sample of iodide IVa, with mp 260-263°C, was obtained by heating the crystal solvate in vacuo (∿ 10 mm) at 200°C for 8 h or by refluxing with ethyl acetate. IR spectrum (in $CHCl_3$): 1555 cm^{-1} (vs). PMR spectrum (in $CDCl_3$): 3.27 (3H, s, 2-CH_3), 3.60 (3H, s, 4-CH_3), 7.03 (1H, s, 1-H), and 7.23-8.03 ppm (16H, m, H_{arom}). Found: C 63.7; H 4.8; N 5.7%; M 348. $C_{26}H_{23}IN_2$. Calculated: C 63.6; H 4.7; N 5.7%; M 490 (348 + 142).

B) Methyl iodide (10 ml) was added to 0.4 g (1.15 mmole) of methylbenzoquinazoline II, and the mixture was refluxed for 2 h. The resulting precipitate was removed by filtration and washed with water to give 0.5 g (89%) of quinazolinium salt IVa with mp 262-265°C.

2,4-Diethyl-1,3-diphenyl-1,2-dihydrobenzo[f]quinazolinium Iodide (IVb). A mixture of 1.65 g (4.9 mmole) of benzoquinazoline III, 0.15 g (5.9 mmole) of NaH, and 15 ml of absolute dimethyl sulfoxide (DMSO) was stirred at room temperature for 15 min, and 4 ml (50 mmole) of ethyl iodide was added slowly. At the end of the addition, the solution was filtered, the solvent was removed from the filtrate by vacuum distillation, and the residual oil was triturated with water. The precipitated substance was removed by filtration and washed with water and hot ethyl acetate. The residue was recrystallized from alcohol and refluxed with ethyl acetate to give 0.7 g of diethyl derivative IVb with mp 262-264°C. UV spectrum, λ_{max} (log ε): 218 (4.75), 261 (4.19), 270 (4.33), 279 (4.37), and 325 nm (3.62). Found: C 65.1; H 5.1; N 5.6%; M 362. $C_{28}H_{27}IN_2$. Calculated: C 64.9; H 5.2; N 5.4%; M 518 (362 + 156).

1,3-Diphenyl-1,2-dihydrobenzo[f]quinazolinium Chloride (VI). Dry methanol (50 ml) was saturated with gaseous HCl, 0.33 g (0.01 mole) of benzoquinazoline III was added, and the mixture was stirred at room temperature for 1 h. The precipitate was removed by filtration and dried in a vacuum desiccator to give 0.23 g of chloride VI with mp 260-270°C. IR spectrum (in KBr): 1555, 1585, 1610, and 1640 cm^{-1}. Found: C 77.2; H 5.2; N 7.4%. $C_{24}H_{18}N_2 \cdot HCl$. Calculated: C 77.7; H 5.1; N 7.5%.

Reaction of 1,3-diphenyl-1,2-dihydrobenzo[f]quinazoline (III) with CH_3I at Room Temperature. A mixture of 0.7 g (0.02 mole) of benzoquinazoline III, 1 ml of methyl iodide, and 50 ml of dry methanol was stirred for 10.5 h, after which the precipitate was removed by filtration to give 0.79 g of V with mp 227-230°C. A 0.37 g sample of salt V was dissolved in 30 ml of $CHCl_3$, and the solution was shaken in a separatory funnel with 40 ml of a 5% solution of NaOH. The chloroform layer was washed with water, dried with $MgSO_4$, and evaporated to give 0.22 g of benzoquinazoline III with mp 225-228°C. The IR and PMR spectra were identical to the spectra of a genuine sample.

Preparation of 2-Methylbenzoquinazolium Iodide (Vb) and Its Decomposition with NaOH. A 0.2 g sample of quinazoline II was dissolved in 5 ml of methanol, three drops of concentrated HI were added, and the mixture was stirred at room temperature for 3 h. The solvent was removed by evaporation, and the residue was washed with water to give 0.23 g of salt Vb with mp 205-228°C. IR spectrum (in KBr): 1580, 1600, 1620, and 1650 cm^{-1}.

A 0.1 g sample of salt Vb was dissolved in 5 ml of $CHCl_3$, and the solution was shaken with 5% NaOH solution, washed with water, dried, and evaporated. The residue was triturated with water, and the solid was removed by filtration and dried to give 0.04 g of methylquinazoline II with mp 179-181°C. The IR spectrum of this product was identical to the IR spectrum of an authentic sample of benzoquinazoline II.

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