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QUINAZOLINES. 13.* SOME REACTIONS OF 2,3-POLYMETHYLENE-3,4-DIHYDRO-4-QUINAZOLONES WITH ELECTROPHILIC REAGENTS

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2,3-Polymethylene-3,4-dihydro-4-quinazolones react with bromine and sulfur trioxide to give complexes involving the nitrogen atom, while bromination in acidic media and Vilsmeier—Haack formylation lead to replacement of the hydrogen atoms of the carbon atom in the α position. Their nitration and chlorosulfonation give 6-nitro- and 6-chlorosulfonyl-2,3-polymethylene-3,4-dihydro-4-quinazolones. Some of the chemical transformations of the synthesized compounds were studied.

We have previously developed a method for the synthesis of 2,3-polymethylene-3,4-dihydro-4-quinazolones (I) and quinazolines [2].

Continuing our systematic studies of quinazolines [3, 4] in order to synthesize pesticides we have studied several electrophilic substitution reactions of I: bromination, reaction with sulfur trioxide, chlorosulfonation, and Vilsmeier—Haack formulation.

It is known that in the nitration of quinazoline and 4-quinazolone the nitro group enters the 6 position of the aromatic ring [5, 6]. There are no other data available with regard to this problem.

The direction of bromination of 2,3-poly(tri-, tetra-, and penta-)methylene-3,4-dihydro-4-quinazolones (Ia-c) and their 6-nitro derivatives (IIa-c) depends on the conditions: Perbromides IIIa-c and IVa-c, respectively, were obtained from I and II in various solvents (chloroform, glacial acetic acid, concentrated H_2SO_4, and 80% methanol) in the cold in the presence of catalysts (iron filings of mixture of iron filings and iodine, as well as alumi-

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*See [1] for Communication 12.

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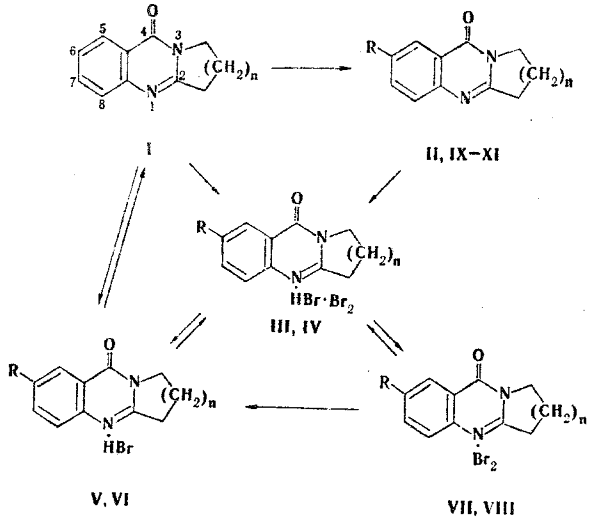
num chloride) or when no catalysts were present. Compound IIIa was also synthesized from Ia, hydrogen bromide, and bromine, as well as from VII and hydrobromic acid. Perbromides

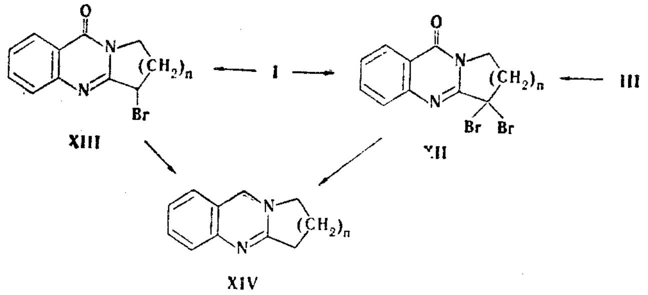


a n=1; b n=2; c n=3; II, IV, VI, VIII R=NO_2; III, V, VII R=H; IXa R=SO_2Cl; Xa R=SO_2NH_2; XIa R=$SO_2N(CH_3)_2$

III and IV lose a molecule of bromine and are converted to the hydrobromides of the starting 2,3-polymethylene-3,4-dihydro-4-quinazolones (VI) when they are heated in solutions and when they are allowed to stand; hydrobromides VI were also obtained from the reaction mixture after isolation of perbromides III and IV.

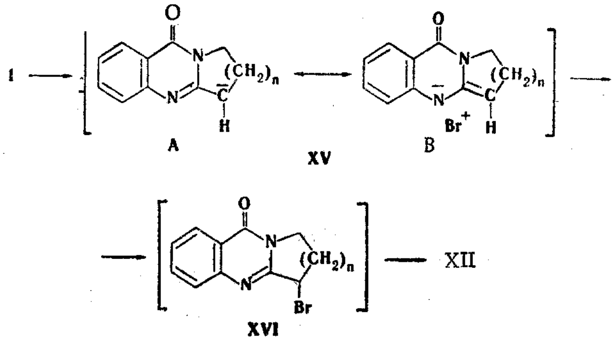
Molecular complexes VII and VIII are formed when III and IV are treated with a 5% aqueous solution of sodium bicarbonate. These molecular complexes, like III and IV, react with acetone or acetophenone and are converted to salts V and VI and bromoacetone (bromoacetophenone).

However, the bromination of I by heating in 75% acetic acid gives α,α-dibromo-2,3-polymethylene-3,4-dihydro-4-quinazolones (XII). It is interesting to note that α-monobromo-2,3-polymethylenes-3,4-dihydro-4-quinazolones (XIII) are not formed in this case. They were obtained from I and N-bromosuccinimide (NBS) in the presence of benzoyl peroxide. Compound XII is also formed by heating perbromide III and a mixture of III with I in 75% acetic acid.



It must be noted that we could not carry out the bromination of I in the aromatic ring even when we used ferrous chloride, aluminum chloride, iron filings, and iron and iodine as the catalysts or when we carried out the reaction in the presence of pyridine.

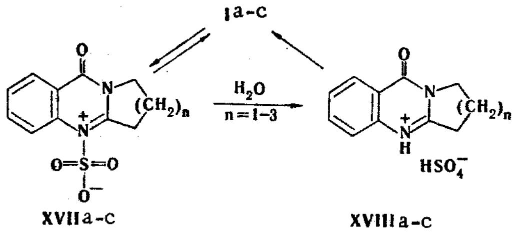
The formation of dibromides XII evidently proceeds in accordance with the scheme presented below. The "pyridine" nitrogen atom imparts lability to the hydrogen atoms of the methylene group in the α position, as in the case of 2,3-polymethylenequinaldines [7]. The detachment of a proton from the α-carbon atom leads to carbanion XV, which can exist in forms A ⇔ B. Its attack by the bromine cation leads to the formation of intermediate XVI. The subsequent XVI → XII conversion proceeds rapidly, since the detachment of a second proton is facilitated under the influence of the bromine atom that is incorporated in the ring. The latter explains why intermediate XVI cannot be isolated despite the presence of excess I.



The fact that 2,3-trimethylene-3,4-dihydro-4-quinazolone reacts with aromatic and heterocyclic aldehydes and forms α-ylidene- or α-hydroxy-α-arylmethylidene derivatives [8, 9] also constitutes evidence in favor of this scheme.

The reduction of α-bromo- and α,α-dibromo-2,3-polymethylene-3,4-dihydro-4-quinazolones under the conditions described in [2] leads to splitting out of bromine to give 2,3-polymethylene-3,4-dihydroquinazolines (XIV).

The reaction of Ia-c with sulfur trioxide was studied: N-sulfotrioxides (XVIIa-c) of Ia-c are formed in this case.



Compounds XVIIa-c are readily converted to 2,3-polymethylene-3,4-dihydro-4-quinazolone sulfates (XVIIIa-c) in aqueous solution. We were unable to introduce a sulfo group in the aromatic ring of 2,3-polymethylene-3,4-dihydro-4-quinazolones under the conditions described for nitrogen-containing heterocyclic compounds [10, 11] starting with N-sulfotrioxides XVIIa-c. No reaction occurred when the latter were heated to 210°C, and the starting Ia-c were recovered; resinification occurred under more severe conditions.

In contrast to bromination and sulfonation, the nitration and chlorosulfonation of I lead to the formation of electrophilic substitution products. Thus treatment of I with a nitrating mixture gives 6-nitro-2,3-polymethylene-3,4-dihydro-4-quinazolones (IIa-c), while 6-chlorosulfonyl-2,3-trimethylene-3,4-dihydro-4-quinazolone (IXa) was obtained by reaction of Ia with chlorosulfonic acid. The corresponding derivatives — 6-sulfonamido- and 6-N,N-dimethylsulfonamido-2,3-trimethylene-3,4-dihydro-4-quinazolones (Xa and XIa) — were obtained from IXa by the action of ammonia or dimethylamine.

In the PMR spectra of IIa and Xa the methylene protons attached to C_9—C_{11} are characterized by signals with coinciding chemical shifts — two-proton triplets at 3.40 and 4.18 ppm and a multiplet at 2.25 ppm, respectively. In the region of aromatic protons the spectrum of IIa contains three one-proton signals: 7.61 (d, J = 8.5 Hz, 8-H), 8.39 (dd, J_{ortho} = 8.5 Hz, J_{meta} = 2.5 Hz, 7-H), and 8.81 ppm (d, J_{meta} = 2.5 Hz, 5-H). The signals from the indicated protons with the same spin—spin coupling constants (SSCC) in the case of Xa have chemical shifts of 7.56, 8.11, and 8.52 ppm.

In order to synthesize 6-formyl-2,3-polymethylene-3,4-dihydro-4-quinazolones we studied the Vilsmeier—Haack formylation of Ia-c. The formylation of aromatic and heterocyclic compounds proceeds with replacement of one of the hydrogen atoms of the aromatic ring by a formyl group [12, 13]. Data on the formylation of the side chain of condensed lactams are available [14].

Depending on the conditions, a product of formylation of the carbon atom in the α position — α-hydroxyformylidene-Ia (XIX) — or α-dimethylaminoformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolone (XX) are formed in the reaction of Ia with a mixture of $POCl_3$ and dimethylformamide (DMF). Compound XIX was obtained by treatment of the reaction mixture with a saturated solution of sodium acetate, while XX was obtained with concentrated ammonium hydroxide.

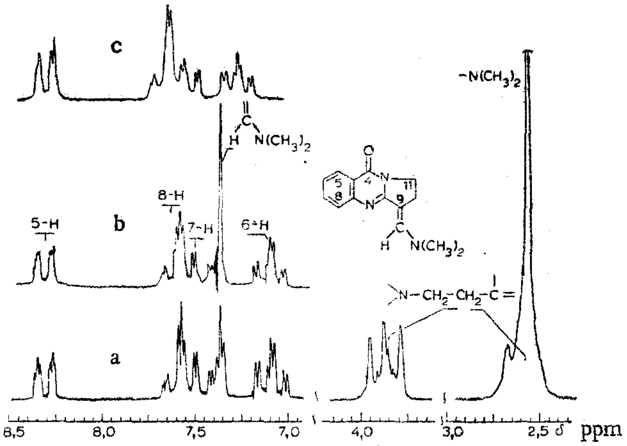
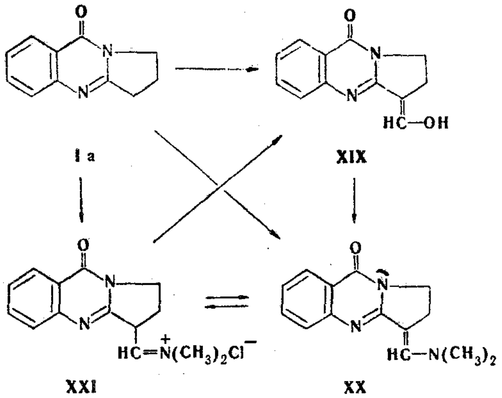


Fig. 1. Monoresonance spectra of XXa (a) and Ia (c) and double-resonance spectra of XX (b) in deuteropyridine.

Compounds XIX and XX are formed through intermediate immonium salt XXI, which can be isolated in individual form. It was also obtained from XX and hydrogen chloride. Treatment of XXI with a saturated solution of sodium acetate at room temperature leads to XIX, whereas treatment with ammonia leads to XX. Compound XIX is converted to XX by mixing it with an aqueous solution of dimethylamine at room temperature.



Ia

XIX

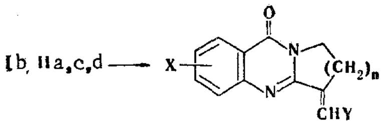
XXI

XX

The complete PMR spectrum of XX is presented in Fig. 1. The one-proton triplet at 7.36 ppm with J^4 = 1.7 Hz belongs to the olefin proton of the $=CHN(CH_3)_2$ grouping, since it becomes a singlet (Fig. 1) in the case of saturation of the resonance transitions of the 10-H nuclei by an additional radio-frequency field. In addition, the absence of the signal under consideration in the spectrum of Ia (Fig. 1) provides evidence for this.

Only α-hydroxyformylidene-Ib (XXII) is formed in the formylation of Ib under similar conditions. Compound Ic does not undergo formylation.

We also studied the formylation of 6- and 7-nitro-2,3-trimethylene-3,4-dihydro-4-quinazolones (IIa, d), for which one might have expected activation of the α position under the influence of the nitro group. These compounds react with the Vilsmeier reagent to give only 6- or 7-nitro-α-dimethylaminoformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolones (XXIII and XXIV), respectively, and the formation of α-hydroxyformylidene derivatives is not observed.



XXII–XXV

XXII X=H, n=2, Y=OH; XXIII X=6-NO_2, n=1, Y=$N(CH_3)_2$; XXIV X=7-NO_2, n=1, Y=$N(CH_3)_2$; XXV X=6-NO_2, n=3, Y=OH

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C*	Found; %			Empirical formula	Calc., %			R_f†	Yield, %
		C	H	N		C	H	N		
IIa	187—188	57,1	3,9	18,2	$C_{11}H_9N_3O_3$	57,0	3,9	18,2	0,78	73
IIb	179—180	58,6	4,6	17,0	$C_{12}H_{11}N_3O_3$	58,8	4,5	17,1	0,64	54
IIc	164—165	60,3	5,2	16,3	$C_{13}H_{13}N_3O_3$	60,2	5,0	16,2	0,64	57
IIIa	155—157	30,8	2,6	6,2	$C_{11}H_{11}Br_3N_2O$	30,9	2,6	6,5	—	75
IIIb	127—128	32,7	2,9	6,3	$C_{12}H_{13}Br_3N_2O$	32,6	3,0	6,3	0,66	83
IIIc	119—121	34,3	3,4	6,2	$C_{13}H_{15}Br_3N_2O$	34,3	3,3	6,1	—	80
IVa	220—223	27,9	2,2	8,7	$C_{11}H_{10}Br_3N_3O_3$	28,0	2,1	8,9	—	77
Va	304	50,0	4,2	10,8	$C_{11}H_{11}BrN_2O$	49,9	4,1	10,5	—	83
Vb	296—298	51,3	4,6	9,8	$C_{12}H_{13}BrN_2O$	51,2	4,6	10,0	0,66	100
Vc	254—256	52,9	5,0	9,6	$C_{13}H_{15}BrN_2O$	52,8	5,1	9,5	—	92
VIa	295—297	42,3	3,3	13,3	$C_{11}H_{10}BrN_3O_3$	42,3	3,2	13,4	—	99
VIIa	105—107	38,2	2,8	8,0	$C_{11}H_{10}Br_2N_2O$	38,1	2,9	8,1	—	74
VIIb	96—97	40,1	3,2	7,7	$C_{12}H_{12}Br_2N_2O$	40,0	3,3	7,8	0,68	63
VIIc	76—78	41,7	3,8	7,4	$C_{13}H_{14}Br_2N_2O$	41,7	3,7	7,5	—	60
VIIa	189—191	33,8	2,2	10,6	$C_{11}H_9Br_2N_3O_3$	33,7	2,3	10,7	—	60
IXa	195—197	46,4	3,2	9,6	$C_{11}H_9ClN_2O_3S$	46,5	3,1	9,8	At the start	60
Xa	266—268	49,9	4,2	15,7	$C_{11}H_{11}N_3O_3S$	50,0	4,1	15.8	0,2	77
XIa	204—205	53,3	5,1	14,3	$C_{13}H_{15}N_3O_3S$	53,2	5,1	14,3	0,83	44
XIIa	189—191	38,4	2,4	8,2	$C_{11}H_8Br_2N_2O$	38,3	2,3	8,1	0,77	50
XIIb	148—149	40,3	2,7	7,6	$C_{12}H_{10}Br_2N_2O$	40,2	2,8	7,8	0,97	35
XIIc	166—167	41,8	3,2	7,3	$C_{13}H_{12}Br_2N_2O$	41,9	3,2	7,5	—	36
XIIIa	145—147	49,6	3,4	10,4	$C_{11}H_9BrN_2O$	49,8	3,4	10,5	0,67	24
XIIIb	144—146	51,5	3,8	10,3	$C_{12}H_{11}BrN_2O$	51,6	3,9	10,1	0.85	72
XIIIc	122—123	53,2	4,4	9,3	$C_{13}H_{13}BrN_2O$	53,2	4,4	9,5	0,69	14
XVIIa	210—213	49,4	3,5	10,3	$C_{11}H_{10}N_2O_4S$	49,6	3,8	10,5	—	99
XVIIb	220—223	51,5	4.2	10,2	$C_{12}H_{12}N_2O_4S$	51,4	4,3	10,0	—	71
XVIIc	257—260	52,8	4,9	9,3	$C_{13}H_{14}N_2O_4S$	53,0	4,8	9,5	—	61
XIX	205—206	63,6	4,8	13,0	$C_{12}H_{10}N_2O_2$	63,7	4,7	13,1	0,48	68
XX	177—179	69,7	6,1	17,5	$C_{14}H_{15}N_3O$	69,7	6,2	17,4	0,68	65
XXI	285—287	60,7	5,7	14,9	$C_{14}H_{16}ClN_3O$	60,6	5,8	15,1	0,62	73
XXII	199—201	68,3	5,3	12,4	$C_{13}H_{12}N_2O_2$	68,4	5,2	12,3	0,91	88
XXIII	316—318	58,7	4,8	19,8	$C_{14}H_{14}N_4O_3$	58,8	4,9	19,6	0,81	89
XXIV	234—236	58,9	4,7	19,7	$C_{14}H_{14}N_4O_3$	58,8	4,9	19,6	0,86	93
XXV	179—181	58,6	4,6	14,5	$C_{14}H_{13}N_3O_4$	58,5	4,5	14,6	At the start	6

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*The compounds were recrystallized: IIa, b and Xa from methanol; IIc from aqueous methanol; XIa from ethyl acetate; IIIa-c and XXI from glacial acetic acid; Va-c, XIIa, and XIIIa-c from alcohol; XIIb, c from aqueous alcohol; and XIX, XX, and XXII-XXV from acetone. †The R_f values for IIa-c, XIIb, XIIIa, b, and XXV were determined in a chloroform-ether (1:1) system (on aluminum oxide); the R_f values for IXa, Xa, and XIa were determined with a chloroform-methanol (9:1) system (on aluminum oxide); the R_f values for IIIb, Vb, VIIb, and XIIa were determined with ether (on aluminum oxide); the R_f value for XIIIc was determined with a chloroform-methanol (25:1) system; and the R_f values for XIX-XXIV were determined with a chloroform-methanol (10:1) system (on Silufol).

The yields of the reaction products are higher for XXIII and XXIV than for XXI (Table 1); this is evidently explained by the electron-acceptor effect of the nitro group in the 6 or 7 position. This is also responsible for the occurrence of the Vilsmeier-Haack reaction with 6-nitro-2,3-pentamethylene-3,4-dihydro-4-quinazolone (IIc), in which case 6-nitro-α-hydroxyformylidene-2,3-pentamethylene-3,4-dihydro-4-quinazolone (XXV) is obtained in low yield.

The IR spectra of II, X-XIII, XIX, XX, and XXII-XXV contain absorption bands at 1600-1620 cm^{-1} (C=N), and the amide carbonyl group in the indicated compounds absorbs at 1660-1690 cm^{-1}. The spectra of IX-XI contain absorption bands of a sulfo group at 1350-1355 and 1185-1190 cm^{-1}, the sulfoamido group of X absorbs at 3308 cm^{-1}, and the hydroxy group absorbs at 3300-3600 cm^{-1}.

The intensities of the molecular-ion peaks in the mass spectra of Xa, XIIIa-c, XIX, and XXII range from 73 to 95%, and the most intense ion peaks are those with m/e 185 for Xa, XIIIa, and XIX, those with m/e 199 for XIIIb and XXII, and the peak with m/e 213 for XIIIc. The mass spectra of XX, XXIII, and XXIV are characterized by the presence of M — 15 (30-36%), M — 30 (11-14%), M — 42 (17-32%), and M — 44 (20-72%) ion peaks; the intensities of the molecular-ion peaks for the indicated compounds and for XXV are 100%.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The mass spectra were recorded with an MKh-1303 spectrometer. The PMR spectra of solutions of IIa and Xa (in CF_3COOH) and XX (in deuteropyridine) were recorded with a HNM-4H-100 spectrometer with hexamethyldisiloxane as the internal standard.

Reaction of 2,3-Trimethylene-3,4-dihydro-4-quinazolones with Bromine. A) A 5-g sample (30 mmole) of Ia was dissolved in 110 ml of chloroform, and the solution was cooled with ice and treated dropwise with a solution of 3.2 ml of bromine in 110 ml of chloroform. The reaction mixture was then stirred at room temperature for 2 h, and the resulting precipitate was removed by filtration and washed with chloroform and absolute ether to give 8.56 g (75%) of IIIa with mp 155-157°C (from glacial acetic acid). When the mother liquor was allowed to stand, 1.36 g (19%) of 2,3-trimethylene-3,4-dihydro-4-quinazolone hydrobromide (Va), with mp 304°C, precipitated.

Complexes IIIb, c and IVa were similarly obtained.

B) A 1.86-g (10 mmole) sample of Ia was dissolved in 10 ml of glacial acetic acid, and 4 ml of a 20% solution of bromine in glacial acetic acid was added with stirring and cooling to 5°C, as a result of which an orange precipitate formed. The reaction mixture was stirred at 10°C for 1 h, after which it was allowed to stand in a refrigerator for 24 h. The resulting crystals were removed by filtration, washed with ether, and dried to give 1.8 g (43%) of IIIa with mp 154-156°C (from glacial acetic acid). The filtrate after separation of IIIa was diluted with water, made alkaline with ammonium hydroxide, and extracted with chloroform. The extract was dried with Na_2SO_4, the solvent was removed by distillation, and the crystals were recrystallized from hexane to give 0.8 g of starting Ia with mp 110-111°C.

Reaction of IIIa with Acetone. A 0.2-g (0.5 mmole) sample of IIIa was dissolved in 3 ml of absolute acetone, 2 min after which colorless acicular crystals of hydrobromide Va precipitated and were washed with absolute acetone to give 0.1 g (83%) of a product with mp 304°C (from alcohol).

Compounds Vb, c and VIa were similarly obtained.

A 0.1-g (0.38 mmole) sample of hydrobromide Va was dissolved in 2 ml of water, and the solution was made alkaline with 25% ammonium hydroxide and extracted with chloroform. The organic layer was dried, the solvent was removed by distillation, and the residue was crystallized from hexane to give 68 mg (98%) of Ia with mp 109-110°C.

Molecular Complex of 2,3-Trimethylene-3,4-dihydro-4-quinazolone with Bromine (VIIa). A 15-ml sample of a 5% solution of sodium bicarbonate was added to 0.3 g (0.75 mmole) of IIIa; the reaction mixture became colorless when it was shaken. The yield of complex VIIa, with mp 103-104°C, was 0.18 g (74%).

Compounds VIIb, c and VIIIa were similarly obtained.

α,α-Dibromo-2,3-trimethylene-3,4-dihydro-4-quinazolone (XIIa). A solution of 0.5 g (1.25 mmole) of IIIa in 10 ml of 75% acetic acid was heated at 90-95°C for 1 h, after which it was allowed to stand overnight and diluted with a threefold volume of water. The resulting white precipitate of XIIa was removed by filtration, washed with water, and dried to give 0.2 g (50%) of product with mp 189-191°C (from alcohol).

α,α-Dibromo-2,3-tetra- and -pentamethylene-3,4-dihydro-4-quinazolones (XIIb, c) were similarly synthesized.

Bromination of Ic in Acetic Acid. A solution of 0.45 ml of bromine in 14 ml of 75% acetic acid was added in portions with stirring to a mixture of 0.9 g (4.2 mmole) of Ic in 14 ml of 75% acetic acid, and the mixture was heated at 80-90°C for 1 h. It was then cooled, and the resulting precipitate was removed by filtration and washed with 75% acetic acid and water. When the precipitate was treated with ammonia, it gave starting Ic. The yield was 0.1 g. The filtrate was diluted with water, and the precipitate was removed by filtration, dried, and recrystallized from aqueous alcohol to give 0.56 g (36%) of XIIc with mp 166-167°C.

The bromination of 2,3-tri- and -tetramethylene-3,4-dihydro-4-quinazolones was carried out similarly.

α-Bromo-2,3-tetramethylene-3,4-dihydro-4-quinazolone (XIIIb). A mixture of 0.2 g (1 mmole) of Ib, 0.18 g (1 mmole) of N-bromosuccinimide (NBS), 0.02 g of benzoyl peroxide, and 5 ml of absolute carbon tetrachloride was heated on a water bath for 7 h, after which it was cooled, and the precipitated succinimide was separated and washed with a small amount of carbon tetrachloride. The solvent was removed by distillation to give 0.2 g (72%) of XIIIb with mp 144-146°C (from aqueous alcohol).

Compounds XIIIa, c were similarly synthesized.

2,3-Trimethylene-3,4-dihydro-4-quinazolone N-Sulfotrioxide (XVIIb). A 0.28-g (0.34 mmole) sample of a 9.8% solution of sulfur trioxide in dry dichloroethane was added with cooling and vigorous stirring to a solution of 0.05 g (0.25 mmole) of Ib in 0.25 ml of dry dichloroethane, 5 min after which white crystals began to precipitate. The mixture was stirred at room temperature for 1 h, after which the solid material was removed by filtration, washed with dichloroethane and acetone, and dried in a vacuum desiccator. The yield of XVIIb, with mp 220-223°C, was 0.05 g (71%).

Compounds XVIIa, c were similarly obtained.

Conversion of XVIIa to Ia. A 0.1-g (0.38 mmole) sample of XVIIa was dissolved in 2 ml of water, 10 min after which the mixture was made alkaline with ammonium hydroxide and extracted with chloroform. The precipitate obtained after drying and removal of the solvent by distillation was crystallized from hexane to give 55 mg (79%) of Ia with mp 109-110°C. No melting-point depression was observed for a mixture of this product with a genuine sample.

6-Nitro-2,3-trimethylene-3,4-dihydro-4-quinazolone (IIa). A 2.5-g (13 mmole) sample of Ia was dissolved with stirring and cooling to 0°C in 21 ml of concentrated H_2SO_4, after which a nitrating mixture consisting of 1.25 ml of nitric acid (sp. gr. 1.5) and 1.75 ml of sulfuric acid (sp. gr. 1.84) was added in portions with vigorous stirring at such a rate that the temperature of the reaction mixture was below 2°C. The mixture was then stirred at 5°C for 1 h and at 20°C for 1 h, after which it was poured over ice. The resulting precipitate was removed by filtration, washed thoroughly with water, and recrystallized from methanol to give 2.26 g (73%) of 6-nitro-2,3-trimethylene-3,4-dihydro-4-quinazolone (IIa) with mp 187-188°C.

The nitration of 2,3-tetra- and -pentamethylene-3,4-dihydro-4-quinazolones was carried out similarly.

6-Chlorosulfonyl-2,3-trimethylene-3,4-dihydro-4-quinazolone (IXa). A 0.67-g (3.5 mmole) sample of Ia was added at 0°C to 2 ml of chlorosulfonic acid, and the resulting solution was heated at 110-120°C for 3 h. It was then poured over ice, and the aqueous mixture was allowed to stand at 0°C for 2 h. The precipitate was removed by filtration, washed with water, and dried to give 0.6 g (60%) of IXa with mp 195-197°C.

6-Sulfonamido-2,3-trimethylene-3,4-dihydro-4-quinazolone (Xa). An aqueous solution of 6-chlorosulfonyl-2,3-trimethylene-3,4-dihydro-4-quinazolone, obtained by the method described above from 1.35 g (7 mmole) of Ia and 4 ml of chlorosulfonic acid, was added with cooling to 15 ml of 25% ammonium hydroxide, and the mixture was maintained at 0°C for 16 h. The precipitate was removed by filtration and washed successively with water and boiling methanol. The yield of Xa was 1.46 g (77%). The colorless crystals, with mp 266-268°C (from methanol), were only slightly soluble in chloroform, methanol, and ether and insoluble in water.

6-N,N-Dimethylsulfonamido-2,3-trimethylene-3,4-dihydro-4-quinazolone (XIa). An aqueous solution of 6-chlorosulfonyl-2,3-trimethylene-3,4-dihydro-4-quinazolone, obtained by the method described above from 0.67 g (3.5 mmole) of Ia and 2 ml of chlorosulfonic acid, was poured into 8 ml of a 33% aqueous solution of dimethylamine. After 24 h, the precipitated crystals were removed by filtration and washed successively with water and ether to give 1 g (44%) of XIa with mp 204-205°C (from ethyl acetate).

α-Dimethylaminoformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolone Immonium Salt (XXI). A 1.7-g (11 mmole) sample of phosphorus oxychloride and 0.93 g (5 mmole) of Ia were added in portions to 4.89 g (67 mmole) of absolute dimethylformamide (DMF) with vigorous stirring and cooling, after which the reaction mixture was stirred at room temperature and allowed to stand overnight. It was then heated on a water bath for 2 h, cooled, and treated with water. A saturated solution of sodium acetate was added up to pH 5-6; and the white precipitate was removed by filtration, washed with water, and dried. The yield of salt XXI, with mp 285-287°C (from acetic acid), was 1.02 g (73%).

B) A stream of hydrogen chloride was bubbled into a solution of 0.5 g (2 mmole) of XX in 5 ml of absolute chloroform for 10 min, and the precipitated crystals were separated. The yield was 0.5 g. Another 0.05 g of reaction product precipitated when ether was added to the filtrate for an overall yield of 0.55 g (96%) of XXI with mp 284-286°C (from acetic acid). No melting-point depression was observed for a mixture of this product with a sample obtained by method A.

α-Dimethylaminoformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolone (XX). A) The reaction was carried out as in the preceding experiment. After treatment with water, the reaction mixture was made alkaline to pH 8-9 with 25% ammonium hydroxide. The resulting brown precipitate was removed by filtration, washed with water, and dried. A total of 1.6 g (65%) of XX, with mp 177-179°C (from acetone), was obtained from 2.4 g (33 mmole) of absolute DMF, 5.13 g (33 mmole) of phosphorus oxychloride, and 1.9 g (10 mmole) of Ia.

B) A mixture of 0.1 g (0.47 mmole) of XIX and 0.2 ml of a 33% aqueous solution of dimethylamine was allowed to stand for 10 min, after which it was treated with ether; and the precipitated crystals were separated, washed with ether, and dried to give 0.11 g (97%) of XX with mp 177-179°C. No melting-point depression was observed for a mixture of this product with a sample obtained by method A.

C) A 0.56-g (2 mmole) sample of XXI was dissolved in 10 ml of water, and the solution was made alkaline to pH 8-9 with 25% ammonium hydroxide. It was then stirred at room temperature for 1 h, and the resulting precipitate was removed by filtration, washed with water, and dried. The yield of XX, with mp 177-179°C (from acetone), was 0.34 g (70%).

α-Hydroxyformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolone (XIX). A) A 3.4-g (22 mmole) sample of phosphorus oxychloride was added with vigorous stirring and cooling with ice to 1.74 g (24 mmole) of absolute DMF, after which the mixture was stirred for 15 min, and 1.86 g (10 mmole) of Ia was added in portions. The reaction mixture was then stirred at room temperature for 1 h and allowed to stand overnight. It was then heated on a water bath for 2 h, cooled, treated with water, and neutralized with a saturated solution of sodium acetate. The resulting white precipitate was removed by filtration, washed with water, and dried to give 0.9 g (68%) of α-hydroxyformylidene-2,3-trimethylene-3,4-dihydro-4-quinazolone (XIX) with mp 205-206°C (from acetone).

B) A 0.56-g (2 mmole) sample of XXI was dissolved in 10 ml of water, and the solution was neutralized with a saturated solution of sodium acetate and stirred at room temperature for 5 h. The white precipitate was removed by filtration, washed with water, and dried. The yield of XIX, with mp 205-206°C (from acetone) was 0.23 g (53%).

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COMPARATIVE CHARACTERISTICS OF THE ELECTRONIC STRUCTURES OF PERIMIDINE AND NAPHTHIMIDAZOLES WITHIN THE FRAMEWORK OF THE CNDO-2 (COMPLETE NEGLECT OF DIFFERENTIAL OVERLAP) METHOD

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The 1H-naphth[1,2-d]imidazole, 3H-naphth[1,2-d]imidazole, and 1H-naphth[2,3-d]-imidazole molecules were calculated by the CNDO-2 method. The dipole moments of N-methyl derivatives of perimidine and linear naphthimidazole were measured. The π-donor character of N-methyl derivatives of perimidine and naphthimidazoles with respect to 1,3,5-trinitrobenzene was also measured. The study showed that the CNDO-2 method, except for individual details associated with the distribution of the σ electrons, leads to the same conclusions relative to the overall pattern of the effective charges on the atoms in the perimidine and naphthimidazole molecules as the π-approximation methods.

It has been previously shown that the perimidine molecule (I) has an extremely peculiar set of physicochemical properties, the principal feature of which is the simultaneous manifestation of clearly expressed π-surplus character and π-deficient character [1]. Since perimidine is formally peri-naphthimidazole, it also seems of interest to compare it with other naphthimidazoles. The goal of the present research was to compare the electronic characteristics of perimidine and both angular (II and III) and linear (IV) naphthimidazoles within the framework of the CNDO-2 (complete neglect of differential overlap) method, i.e., with the inclusion of all of the valence electrons.

The I molecule was calculated by the CNDO-2 method in [2]. We calculated the naphthimidazole molecules from a similar program with a BÉSM-6 computer with the use of the parameters in [3]. In view of the lack of experimental data on the geometry of the II-IV molecules, the benzene and imidazole rings in them were considered to be regular hexagons and pentagons with internal angles of 120 and 108°, respectively. The C—C and C—N bond lengths were assumed to be 1.39 Å, and the C—H bond length was assumed to be 1.07 Å. The numbering of the atoms and the selection of the system of coordinates are indicated in the formulas.

The Δq^{σ} and Δq^{π} values and the total charges on the atoms of the I-IV molecules presented in Table 1 make it possible to draw the following conclusions.

1. In all four compounds there is a shift of the π-electron density from the heteroring to the naphthalene system. The overall π charges on the nonbridged C atoms of the naphthalene ring in I-IV are, respectively, − 0.3335, − 0.0848, − 0.0879, and − 0.1654. Thus the intensity of the shift of the π-electron cloud is maximal in perimidine and minimal in the isomers of angular naphthimidazole. The linear naphthimidazole molecule occupies an intermediate position. A similar regularity was observed in calculations of the I-IV molecules within the framework of the Hückel MO method [4]. It should be noted that one can arrive at the same conclusions by analyzing the total charges on the atoms of the I-IV mole-

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