These compounds exhibited antipyretic action lowering the body temperature of a rat with milk fever. Most active were the 2,4-di(o-carboxyphenylamino)pyrimidines. In this group of compounds, preparation Ie — 2,4-di(o-carboxyphenylamino)-6-chloropyrimidine had the greatest antipyretic effect.

Thus, compounds Ia-f are less toxic than sodium mefenamate or brufen, and exhibit anti-inflammatory, analgesic, and antipyretic action.

LITERATURE CITED

1. T. Ueda and J. Fox, J. Med. Chem., 6, 697-701 (1963).
2. E. Falch, J. Wels, and J. Natvig, J. Med. Chem., 11, 608-611 (1968).
3. C. Völcker, M. Schönfeld, and H. Beyer, Z. Chem., 8, 103-104 (1968).
4. M. Yanai and T. Kuraishi, Kagaku Zasshi, 80, 1181-1183 (1959).
5. FRG Patent No. 2735919 (1977).
6. V. K. Karp, V. A. Portnyagina, and I. S. Barkova, Khim. Geterotsikl. Soedin., No. 9, 1252-1254 (1977).
7. E. Komlos and M. Porzasz, Acta Physiol. Acad. Sci. Hung., 1, 77-83 (1950).
8. F. P. Trinus, N. A. Mokhort, and B. M. Klebanov, Nonsteroid Antiinflammatory Agents [in Russian], Kiev (1975).

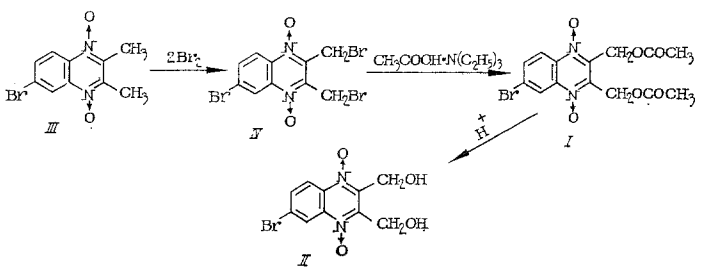
BROMINE ANALOGS OF QUINOXIDINE, DIOXIDINE, AND AMIDES OF DI-N-OXIDES OF 3-HYDROXYMETHYLQUINOXALINE-2-CARBOXYLIC ACID

I. S. Musatova, A. S. Elina,
N. P. Solov'eva, L. M. Polukhina,
N. Yu. Moskalenko, and G. N. Pershin

UDC 615.281:547.863.11].021.1

We investigated the synthesis of bromine analogs of the biologically-active quinoxaline derivatives quinoxidine, dioxidine, and amides of di-N-oxides of 3-hydroxymethylquinoxaline-2-carboxylic acid [1-3] in order to study their biological activity.

The bromine analogs of quinoxidine [2,3-bis(acetoxymethyl)-7-bromoquinoxaline-di-N-oxide (I)] and dioxidine [2,3-bis(hydroxymethyl)-7-bromoquinoxaline-di-N-oxide (II)] were synthesized as indicated in the scheme below from 2,3-dimethyl-7(6)-bromoquinoxaline-di-N-oxide (III) by means of the intermediate 2,3-bis(bromomethyl)-7(6)-bromoquinoxaline-di-N-oxide (IV).



Amides of 3-hydroxymethyl-7-bromoquinoxaline-2-carboxylic acid di-N-oxide (XXIIIa-i) were synthesized from 2-carbethoxy-3-methyl-7-bromoquinoxaline-di-N-oxide (V), which was in turn prepared by a known method: the reaction of 5(6)-bromobenzofuroxane (VI) with esters of acetoacetic acid in the presence of various basic reagents [4, 5]. These authors recommended the use of the 7- and 6-bromo isomers of 2-carbalkoxy-3-methylquinoxaline-di-N-oxide

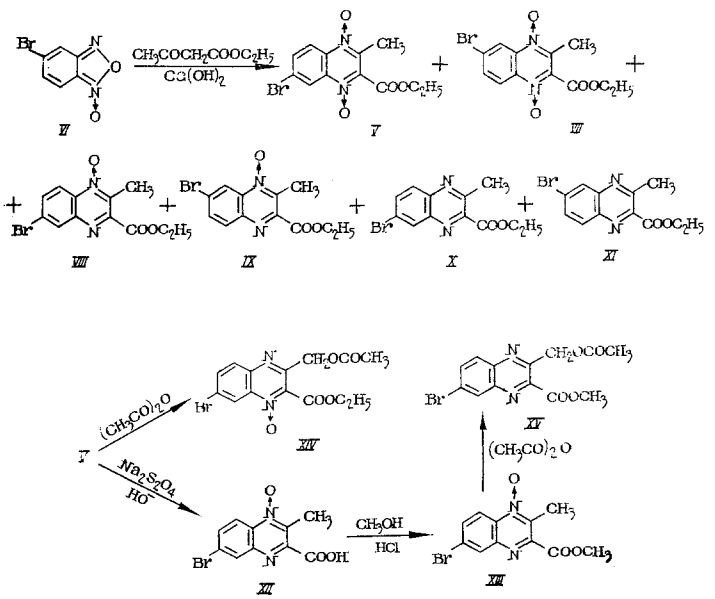
S. Ordzhonikidze All-Union Scientific-Research Institute of Pharmaceutical Chemistry, Moscow. Translated from Khimiko-farmatsevticheskii Zhurnal, Vol. 17, No. 11, pp. 1307-1312, November, 1983. Original article submitted February 28, 1983.

0091-150X/83/1711-0779$07.50

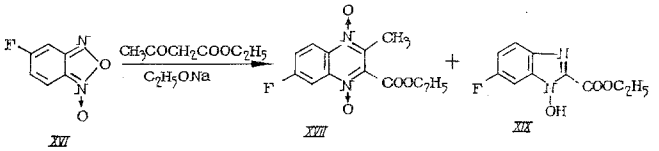
without isolation of either of the two pure isomers. The experiments also included the reaction of compound VI with the t-butyl ester of acetoacetic acid (using n-butylamine as the basic reagent), to give 2-tert-buryloxycarbonyl-3-methyl-7-bromoquinoxaline-di-N-oxide (41.5% yield) and 15.6% yield of a mixture of the corresponding 7- and 6-bromo isomers in a ratio of 1:1 [6].

We have studied the reaction of VI with ethyl acetoacetate. It was shown that in the presence of n-butylamine, this reaction did not reach completion and was accompanied by considerable tar. The most suitable basic reagent proved to be calcium oxyhydrate. From the reaction a 40% yield was isolated of the di-N-oxide of V containing an admixture (ca. 7%) of 2-carboethoxy-3-methyl-6-bromoquinoxaline-di-N-oxide (VII), which could be separated by repeated crystallization. From the mother liquor after concentration and fractionation with a silica gel column, a mixture (12.1%) of the bromo isomers V and VII with a predominance (67%) of the 6-isomer was isolated. Further, products of both partial and complete N-deoxygenation of both bromo isomers in the form of a mixture of VIII and XI also were isolated.

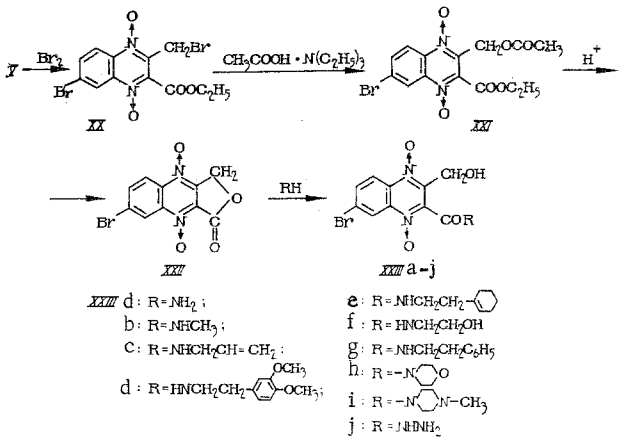
The structure of the reaction products and the composition of the mixtures were established by comparison of their PMR spectra with those of model compounds synthesized from dioxide V by successive deoxygenation of both cyclic nitrogen atoms (compounds XII-XV). The use of the PMR spectral features of condensed aromatic heterocyclic N-oxides allows the deduction that the signals of protons situated in the para-position to the oxygens on the cyclic nitrogen atoms are displaced to stronger field [7, 8]. Upon deoxygenation of N_1 in the dioxide V (compound XIII), the signal for the C_8-proton appears as a split signal ($^4J_{8,6}$ = 2 Hz) shifted to stronger field ($\Delta\delta_{8-H}$ = 0.4 ppm), and the position of the signal for the C_5-proton doublet ($^3J_{5,6}$ = 8 Hz) is practically unchanged. On passing from the mono-N-oxide XIII to the completely deoxygenated quinoxaline derivative (XV), obtained from XIII by the Boekelheide reaction, the C_5-proton signal is shifted to stronger field ($\Delta\delta_{5-H}$ = 0.47 ppm) coincident with the C_6-proton signal. This data indicates that in dioxide V, the bromine is in position 7. This conclusion was confirmed by comparison of the spectra of dioxide V and the 1-N-oxide (XIV) prepared from V by the Boekelheide reaction. In the spectra of compound XIV, the signal for the C_8-proton remains unchanged, and the signal for the C_5-proton shifts to stronger field ($\Delta\delta_{5-H}$ = 0.53 ppm). The determination of the composition of the mixtures obtained and the original structure of their ingredients was carried out by this method, i.e., comparison of their spectra with the spectra of the model compounds XIII-XV.



To carry out the analogous reaction with 5(6)-fluorobenzofuroxan (XVI), the most favorable basic reagent was sodium ethylate. The reaction gave 2-carboethoxy-3-methyl-7-fluoroquinoxaline-di-N-oxide (XVII), the structure of which also was proven by comparison of its PMR spectrum with that of 2-carboethoxy-3-acetoxymethyl-7-fluoroquinoxaline-1-N-oxide (XVIII). A compound was isolated from the mother liquor, to which, in correspondence with mass-spectral and IR data, was attributed the structure 1-hydroxy-2-carboethoxy-6-fluorobenzimidazole (XIX).



From the dioxide V through the intermediates 3-bromomethyl- and 3-acetoxymethyl-2-carboethoxy-7-bromoquinoxaline-di-N-oxide (XX and XXI), the amides (XXIIIa-i) and the hydrazide XXIIIj were synthesized by the scheme shown:



EXPERIMENTAL CHEMISTRY

IR spectra were determined on a Perkin-Elmer model 457 (Sweden) in mineral oil. Mass spectra were obtained on a Varian MAT-112 chromatomass-spectrometer (FRG) with ionizing electron energy 70 eV, ionization chamber temperature 180°C, and direct sample introduction into the ion source. PMR spectra were determined on a Varian XL-100 apparatus (Switzerland) in $CDCl_3$ with tetramethyl silane as internal standard.

2,3-Bis(bromomethyl)-7(6)-bromoquinoxaline-di-N-oxide (IV). To 1.5 g (5.6 mmoles) of III in 1.6 ml of methylene chloride and 1.6 ml of DMF was gradually added 0.8 ml (1.56 mmoles) of bromine at 55-65°C. The mixture was stirred for 2 h at 65°C, cooled, poured into 6 ml of water and the precipitate was filtered off to give 2.3 g (96.6%) of IV, mp 203-204°C (from acetic acid). Found, %: C 28.1; H 1.9; N 6.6. $C_{10}H_7Br_3N_2O_2$. Calculated, %: C 28.1; H 1.7; N 6.6.

2,3-Bis(acetoxymethyl)-7(6)-bromoquinoxaline-di-N-oxide (I). To 0.8 ml of acetic acid and 0.95 ml of triethylamine in 9.5 ml of acetone was added 1 g of IV. The mixture was boiled for 1.5 h, then concentrated in vacuum, and the residue was neutralized with a sodium bicarbonate solution to give 0.76 g (84.5%) of I, mp 170-171°C (from alcohol). Found, %: C 43.6; H 3.2; N 7.3. $C_{14}H_{13}BrN_2O_6$. Calculated, %: C 43.6; H 3.4; N 7.3.

2,3-Bis(hydroxymethyl)-7(6)-bromoquinoxaline-di-N-oxide (II). A mixture of 33 ml of alcohol, 49 ml of 1 N sulfuric acid and 3.6 g (9.4 mmoles) of I was boiled for 25 min, cooled, neutralized with 2.5 ml of 1 N sodium hydroxide to give 2.46 g (87.6%) of II, mp 123-124°C (from alcohol). Found, %: C 39.7; H 3.2. $C_{10}H_9BrN_2O_4$. Calculated, %: C 39.9; H 3.0. Mass spectrum, m/e 301 (M^+).

Reaction of 5-Bromobenzofuroxane (VI) with Acetoacetic Ester. A mixture of 16.33 g (76 mmoles) of VI, 9.65 ml (76 mmoles) of acetoacetic ester and 0.59 g (8 mmoles) of calcium oxyhydrate in 117 ml of anhydrous isopropyl alcohol was stirred for 30 min without heating (spontaneous temperature increase to 45°C), and then at 40-45°C for 4 h, followed by 20-23°C for 18 h. The mixture was cooled, the precipitate was separated, dissolved in chloroform and filtered. The chloroform was removed under vacuum, and the residue was recrystallized from alcohol to give 10 g (~40%) of a mixture of V (93%) and VII (7%), mp 179-181°C. Found, %: C 44.3; H 3.2; N 8.5. $C_{12}H_{11}BrN_2O_4$. Calculated, %: C 44.1; H 3.4; N 8.6. IR spectrum, cm^{-1}: 1748 (C=O). PMR spectra, δ, ppm: V, 8.48 d ($^3J_{5,6}$ = 8 Hz, 5-H), 7.95 d* (6-H), 8.75

*Here and below: doublet, split as a result of meta-interaction with the aromatic ring, ^4J = 2 Hz.

s† (8-H), 2.56 (CH_3), 1.47 and 4.58 (OCH_2CH_3); VII, 8.80 s† (5-H), 7.92 d* ($^3J_{7,8}$ = 8 Hz, 7-H), 8.44 d (8-H), 2.59 (CH_3), 1.47 and 4.58 (OCH_2CH_3).

The alcohol solution from the recrystallization of the mixture of V and VII was concentrated under vacuum, combined with the residue from concentration of the basic reaction solution and transferred in a small amount of chloroform to a column prepared from 174 g of silica gel. Benzene–alcohol (98:2) eluted 3 g (12.1%) of a mixture of V (33%) and VII (67%). The fractions eluted with benzene–alcohol (99:1) were combined and treated three times on silica gel, eluting with benzene–alcohol (99.5:0.5) to give 0.46 g (∿2%) of a mixture of VIII (30%) and IX (70%), mp 112-117°C. Found, %: C 46.2; H 3.5; N 8.8. $C_{12}H_{11}BrN_2O_3$. Calculated, %: C 46.3; H 3.6; N 9.0. PMR spectra, δ, ppm: VIII, 8.47 d ($^3J_{5,6}$ = 9 Hz, 5-H), 7.86 d* (6-H), 8.39 s† (8-H), 2.77 (CH_3), 1.49 and 4.56 (OCH_2CH_3); IX, 8.69 s‡ (5-H), 7.90 (7-H, 8-H). Mass spectrum, m/e: 310 (M^+), and 0.31 g (ca. 1.4%) of a mixture of X (40%) and XI (60%), mp 69-69.5°C (from hexane). Found, %: C 49.0; H 3.9; N 9.4. $C_{12}H_{11}BrN_2O_2$. Calculated, %: C 48.7; H 3.8; N 9.5. PMR spectra, δ, ppm: X, 8.05 d ($^3J_{5,6}$ = 9 Hz, 5-H), 7.89 d* (6-H), 8.24 s† (8-H), 2.95 (CH_3), 1.49 and 4.56 (OCH_2CH_3); XI, 8.37 s‡ (5-H), 7.91 (7-H, 8-H), 2.93 (CH_3), 1.49 and 4.56 (OCH_2CH_3).

2-Carboxy-3-methyl-7-bromoquinoxaline-4-N-oxide (XII). To 5 g (15.3 mmoles) of V in 100 ml of 1 N sodium hydroxide was added 3.5 g of sodium hydrosulfite dihydrate and the mixture was stirred at 22-25°C for 3 h and filtered. To the filtrate was added 2.5 N sulfuric acid to pH 1.0 to give 2.6 g (60%) of XII, mp 160.5-161°C (decomp. from anhydrous alcohol). Found, %: C 42.3; H 2.3; N 9.8. $C_{10}H_7BrN_2O_3$. Calculated, %: C 42.4; H 2.5; N 9.9.

2-Carbomethoxy-3-methyl-7-bromoquinoxaline-4-N-oxide (XIII). Into a solution of 2.56 g XII in 50 ml of methanol was passed a stream of dry hydrogen chloride for 2 h. The solution was concentrated under vacuum and the residue was neutralized with aqueous sodium bicarbonate and extracted with chloroform to give 2.1 g (78.3%) of XIII, mp 162-163°C (from anhydrous alcohol). Found, %: C 44.7; H 3.1; N 9.3. $C_{11}H_9BrN_2O_2$. Calculated, %: C 44.5; H 3.1; N 9.4. PMR spectrum, δ, ppm: 8.43 d ($^3J_{5,6}$ = 9.3 Hz, 5-H), 7.86 d* (6-H), 8.35 s† (8-H), 2.77 (CH_3), 4.08 (OCH_3).

2-Carbomethoxy-3-acetoxymethyl-7-bromoquinoxaline (XV). A mixture of 30 ml of acetic anhydride, 20 ml of acetic acid, and 3 g (10 mmoles) of XIII was boiled for 7 h. The solution was concentrated under vacuum, and the residue was recrystallized from anhydrous alcohol to give 1.7 g (49.6%) of XV, mp 108-109°C. Found, %: C 46.4; H 2.95; N 8.0. $C_{13}H_{11}\cdot BrN_2O_4$. Calculated, %: C 46.1; H 3.2; N 8.2. PMR spectrum, δ, ppm: 8.42 s†† (6-H), 7.96 (5-H, 6-H), 2.20 ($COCH_3$), 4.08 (OCH_3), 5.69 (CH_2).

2-Carboethoxy-3-acetoxymethyl-7-bromoquinoxaline-1-N-oxide (XIV). A mixture of 80 ml of acetic anhydride, 50 ml of acetic acid, and 10 g (30.6 mmoles) of V was boiled for 4 h. The solution was concentrated under vacuum and the residue was recrystallized from alcohol to give 7.34 g (65%) of XIV, mp 127-127.5°C. PMR spectrum, δ, ppm: 8.70 s†† (8-H), 7.95 (5-H, 6-H), 2.14 ($COCH_3$), 5.32 (CH_2), 1.46 and 4.55 (OCH_2CH_3).

Reaction of 5-Fluorobenzofuroxan (XVI) with Acetoacetic Ester. To a solution of 1.6 g (12.3 mmoles) of acetoacetic ester in 5 ml of anhydrous alcohol was added an alcoholic solution of sodium ethoxide prepared from 0.06 g (2.6 mmoles) of sodium and 2.3 ml of anhydrous alcohol, followed by 1.82 g (11.8 mmoles) of XVI added at a temperature of less than 35°C. The mixture was stirred for 18 h to give 1.06 g of XVII, and additional 0.64 g of XVII for a total yield of 1.7 g (54%). Recrystallization from anhydrous alcohol gave mp 146.5-147.5°C. Found, %: C 54.2; H 4.2; N 10.5. $C_{12}H_{11}FN_2O_4$. Calculated, %: C 54.1; H 4.2; N 10.5. PMR spectrum, δ, ppm: 8.64 q ($^4J_{F,5\text{-}H}$ = 5 Hz, $^3J_{5,6}$ = 9 Hz), 8.22 q ($^3J_{F,8\text{-}H}$ = 8.4 Hz, $^4J_{8\text{-}H,6\text{-}H}$ = 2.8 Hz, 8-H), 7.61 ($^3J_{F,6\text{-}H}$ = 7.4 Hz, $^3J_{6,5}$ = 9 Hz, $^4J_{6,8}$ = 2.8 Hz, 6-H), 2.56 (CH_3), 1.47 and 4.58 (OCH_2CH_3). Mass spectrum, m/e = 266 (M+). The solutions from the isolation and recrystallization of XVII were combined and concentrated under vacuum. The residue was treated with chloroform to give 0.93 g of an insoluble precipitate which was dis-

†Here and below: singlet, split as a result of meta-interaction with the aromatic ring, ^4J = 2 Hz.

‡Here and below: singlet, split as a result of virtual interaction with H-7 and H-8, the chemical shift of which coincides, ^4J = 2 Hz.

††Here and below: singlet, split as a result of virtual interaction with H-5 and H-6, the chemical shift of which coincides, ^4J = 2 Hz.

TABLE 1. Properties of the Amides XXIIIb-j

Compound	mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
XXIIIb	191-192 (decomp., from ethanol)	$C_{11}H_{10}BrN_3O_4$	40,1	3,2	12,8	40,3	3,1	12,8	97,5
XXIIIc	126-127 (decomp., from ethanol)	$C_{13}H_{12}BrN_3O_4$	43,7	3,5	11,8	44,1	3,4	11,9	83
XXIIId	192.5-193.5 (from anh. ethanol)	$C_{20}H_{20}BrN_3O_6$	50,3	4,4	8,4	50,3	4,2	8,8	96,4
XXIIIe	185-186 (decomp., from anh. ethanol)	$C_{18}H_{20}BrN_3O_4$	51,2	4,8	9,9	51,2	4,8	10,0	90
XXIIIf	190-191 (from anh. ethanol)	$C_{12}H_{12}BrN_3O_5$	40,1	3,4	11,7	40,3	3,4	11,7	87,6
XXIIIf	176.5-177.5 (from anh. ethanol)	$C_{18}H_{16}BrN_3O_4$	51,4	3,9	9,7	51,8	3,9	10,0	96,2
XXIIIg	186-187 (decomp., from water)	$C_{14}H_{14}BrN_3O_5$	43,7	3,7	11,0	43,8	3,7	10,95	85,6
XXIIIh	153-154 (from ethyl acetate)	$C_{15}H_{17}BrN_4O_4$	45,1	4,3	14,1	45,4	4,3	14,1	97,6
XXIIIi	170.5-171 (decomp., from 50% ethanol)	$C_{10}H_9BrN_4O_4$	36,4	2,9	16,9	36,5	2,8	17,05	89

solved in 2.5 N sodium hydroxide, filtered, and treated with 2.5 N hydrochloric acid to give 0.5 g (19%) of XIX, mp 141-142°C (from 50% alcohol). IR spectrum, cm^{-1}: 1730 (C=O), 2400-2500 (broad, assoc. OH). Mass spectrum, m/e: 224 (M+).

2-Carboethoxy-3-acetoxymethyl-7-fluoroquinoxaline-1-N-oxide (XVIII). A mixture of 0.5 g XVII, 2.5 ml of acetic anhydride and 2.5 ml of acetic acid was stirred at 80°C for 7 h. The solution was evaporated under vacuum and the residue was crystallized from hexane to give 0.44 g (76.3%) of XVIII, mp 77.5-78.5°C. Found, %: C 54.5; H 4.0; N 9.5. $C_{11}H_{13}FN_2O_5$. Calculated, %: C 54.6; H 4.3; N 9.1. PMR spectrum, δ, ppm: 8.20 q ($^3J_{F,8-H}$ = 8.4 Hz, $^3J_{6,8}$ = 2.8 Hz, 8-H), 8.14 q ($^4J_{F,5-H}$ = 5.5 Hz, $^3J_{5,6}$ = 9 Hz, 5-H), 7.64 m (6-H), 2.14 ($COCH_3$), 1.46 and 4.55 (OCH_2CH_3), 5.34 (CH_2).

2-Carboethoxy-3-bromomethyl-7-bromoquinoxaline-di-N-oxide (XX). To a solution of 5.33 g (16.3 mmoles) of V in 4.7 ml of methylene chloride and 4.7 ml of DMF at 55°C was added 1.1 ml (21.5 mmoles) of bromine in portions at 55-65°C. The mixture was stirred at 60-65°C for 3 h and then poured into water to give 6.4 g (97%) of XX, mp 167.5-168.5°C (from alcohol). Found, %: C 35.8; H 2.7; N 7.0. $C_{12}H_{10}Br_2N_2O_4$. Calculated, %: C 35.5; H 2.5; N 6.9.

2-Carboethoxy-3-acetoxymethyl-7-bromoquinoxaline-di-N-oxide (XXI). To a mixture of 3.35 ml of acetic acid and 3.94 ml of triethylamine in 36 ml of acetone was added 4.43 g of XX. After stirring at 35-40°C for 2.5 h, the solvents were removed and the residue was neutralized with aqueous sodium bicarbonate to give 3.4 g (93%) of XXI, mp 127.5-128.5°C (from alcohol). Found, %: C 43.5; H 3.5; N 7.3. $C_{14}H_{13}BrN_2O_6$. Calculated, %: C 43.6; H 3.4; N 7.3.

Lactone of 2-Carboxy-3-hydroxymethyl-7-bromoquinoxaline-di-N-oxide (XXII). A mixture of 3.8 g of XXI and 12 ml of concentrated hydrochloric acid was kept at 22-25°C for 18 h, water was added until no more turbidity, and the resulting precipitate was washed with water to give 2.15 g (93%) of XXII, mp 210-211°C (decomp. from acetic acid). Found, %: C 40.5; H 1.7; N 9.4. $C_{10}H_5BrN_2O_4$. Calculated, %: C 40.5; H 1.7; N 9.4.

2-Carboxamido-3-hydroxymethyl-7-bromoquinoxaline-di-N-oxide (XXIIIa). A mixture of 5 g of XXII and 28 ml of 14% alcoholic ammonia was kept at 22-25°C for 18 h to give 5.12 g (97.1%) of XXIIIa, mp 180-181°C (decomp. from 50% DMF). Found, %: 38.1: H 2.8; N 13.4. $C_{10}H_8 \cdot BrN_3O_4$. Calculated, %: C 38.3; H 2.6; N 13.4.

Compounds XXIIIb-j. These were prepared analogously (cf. Table 1). For compounds XXIIIc, d, e, f, h, 1.7 moles of ammonia per mole of XXII were used, and for compounds XXIIIg, i, j, 2 moles of ammonia per mole of XXII. All compounds were prepared in anhydrous alcohol except for XXIIh, for which benzene was used.

EXPERIMENTAL BIOLOGY

The antimicrobial activity of the synthesized compounds was studied in experiments *in vitro* against 4 species of gram-positive and 5 species of gram-negative bacteria, 3 spe-

cies of microbacteria, and 5 species of pathogenic fungi. The minimum concentration for suppression of growth of the microorganisms (MSG) was determined by the twofold serial dilution method in the liquid nutrient medium described earlier [9]. The majority of the compounds studied showed activity with respect to gram-positive bacteria and acid-resistant microbacteria. The activity of these compounds with regard to gram-negative bacteria and pathogenic fungi was less. Bromine analog II retained activity against gram-negative bacteria, as did bromine analog I, but compounds III and IV at a concentration of 250 μg/ml did not suppress the bacterial growth. Compound V possessed a wide spectrum of action against both gram-positive and gram-negative bacteria. Among the bromo analogs of 2-carboxamido-3-hydroxymethylquinoxaline-di-N-oxide, the most active against the indicated bacteria were compounds XXIIIb, f. The MSG for several species of bacteria was 15.6 μg/ml or less.

In animal experiments, the antibacterial activity of the studied compounds was shown to be below and more narrow in spectrum than that of quinoxidine, dioxidine, and 2-carboxamide-3-hydroxymethylquinoxaline-di-N-oxide.

All of the studied compounds showed significant antitubercular activity. The most effective against *M. tuberculosis* strain $H_{37}Rv$ were compounds XXI, XXIIIb, c, g, the minimal tuberculostatic concentrations of which were 0.5 μg/ml in Soton medium without protein stress.

These derivatives of quinoxaline also showed weak antitrichomonadal (compounds I, II, XXIIId, e, g, h) and antiamebic (compounds I, II, XXIIIa, d, e, g) action, suppressing the growth of pathogenic protozoa at a concentration of 100 μg/ml.

LITERATURE CITED

1. A. S. Elina, L. G. Tsyrul'nikova, and O. Yu. Magidson, Inventor's Certificate No. 207917 (USSR). Otkryt. Izobret., Prom. Obraztsy, Tovarnye Znaki, No. 3, 19 (1968).
2. K. A. Belozerova, A. S. Elina, O. Yu. Magidson, et al., Inventor's Certificate No. 428626 (USSR). ibid., No. 18, 151 (1975).
3. FRG Patent No. 1813918 (1978).
4. Fr. Patent No. 2132378 (1972).
5. UK Patent No. 1134729 (1968).
6. W. Dürckheimer, Justus Liebigs Ann. Chem., 765, 145 (1972).
7. Y. Morita, Chem. Pharm. Bull. (Tokyo), 14, 419-426 (1966).
8. W. W. Paudler, D. J. Pokorny, and S. J. Cornrich, J. Heterocycl. Chem., 7, 291-295 (1970).
9. G. N. Pershin (ed.), Methods of Experimental Chemotherapy [in Russian], Moscow (1971), pp. 103, 318.