2. V. I. Markov, S. I. Burmistrov, and D. A. Danileiko, Khim. Tekhnol., 21, 97 (1971).
3. V. I. Markov, S. I. Burmistrov, and V. A. Doroshenko, Ukr. Khim. Zh., 33, 495 (1967).
4. V. I. Markov and S. I. Burmistrov, Zh. Obshch. Khim., 35, 158 (1965).

CONDENSATION OF o-DIAMINO DERIVATIVES OF ANTHRAQUINONE AND NAPHTHOQUINONE WITH MESITYL OXIDE

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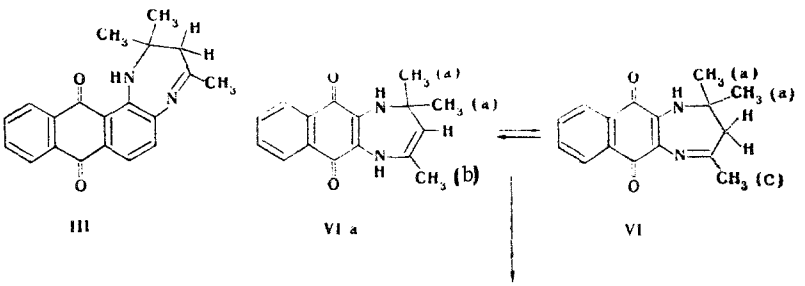
Anthraquinone- and naphthoquinonediazepines are formed by the reaction of 1,2- and 2,3-diamino-9,10-anthraquinones and 2,3-diamino-1,4-naphthoquinones with mesityl oxide. It was shown by spectral methods that naphthoquinonediazepine exists in two tautomeric forms.

It is known that 2,2,4-trimethyl-1,5-benzodiazepine is formed in the reaction of o-phenylenediamine with mesityl oxide [1, 2] or with acetone in acidic media [3, 4]. In order to synthesize heterocyclic derivatives of quinones we carried out the condensation of mesityl oxide with o-diamino derivatives of anthra- and naphthoquinones.

At room temperature 1,2- and 2,3-diaminoanthraquinones (I and II) react with mesityl oxide to give diazepines III and IV (in 60-70% yields), the structures of which were confirmed by spectral data. Thus, in addition to the signals of six aromatic protons (7.37, 7.66, 7.70, and 8.17 ppm), the PMR spectrum of III contains singlets of nine protons of methyl groups (1.44 and 2.29 ppm, intensity ratio 6:3) and two protons of a methylene group (2.52 ppm). The shift of the signal of the proton of the NH group to weak field (9.15 ppm) as compared with the position of the same protons in the spectrum of diazepine IV (4.34 ppm) is in agreement with the presence in the IR spectrum of III of two frequencies corresponding to $\nu_{C=O}$ vibrations (1665 and 1630 cm^{-1}) and also with the position of the frequency of the stretching vibrations of the N–N bond and its independence of dilution; this constitutes evidence for linkage of the NH group by an intramolecular hydrogen bond with the carbonyl group and confirms the structure of diazepine III.

2,3-Diamino-1,4-naphthoquinone (V) reacts with mesityl oxide to give diazepine VI, which can be isolated from the reaction mixture in the form of a salt or the free base. The formation of diazepines is also observed in the reaction of diamines I, II, and V with acetone in acidic media (acetone forms mesityl oxide under these conditions), but this method is less convenient because of the low yields of reaction products.



III VI a VI

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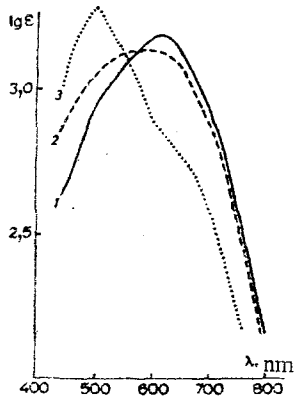
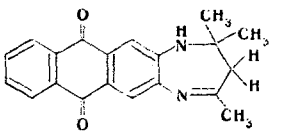
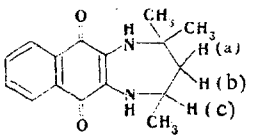


Fig. 1. Electronic absorption spectra of naphthoquinonediazepine VI in alcohol recorded immediately after preparation of the solution (1) and after 1 h (2) and 6 h (3).



IV



VII

Thus IV was obtained in [5] in 10% yield by reaction of diamine II with acetone in the presence of $SnCl_2$.

A characteristic property of 1,5-benzodiazepine derivatives is their tendency to undergo tautomeric transformations [6, 7]. We have established that naphthoquinonediazepine also exists in two tautomeric forms (VIa and VIb), whereas this phenomenon is not observed for anthraquinonediazepines III and IV.

The tautomeric transformations of VI can be observed on sorbents and in some solvents [alcohol, chloroform, and dimethyl sulfoxide (DMSO)]. Thus the long-wave absorption maximum in alcohol 6 h after preparation of the solution is shifted from 610 to 500 nm (Fig. 1). A solution of naphthoquinonediazepine VI in CCl_4 is blue (λ_{max} 600 nm), whereas in $CHCl_3$ the initially blue coloration changes to red-violet after 1-2 min.* The electronic spectrum of a solution in $CHCl_3$ is characterized by the presence of two absorption bands of equal intensity with maxima at 510 and ∿ 615 nm. A frequency corresponding to $\nu_{C=N}$ vibrations (1565 cm^{-1}) is present in the IR spectrum of diazepines VI in $CHCl_3$,† whereas frequencies of 1665 and 1635 cm^{-1} (in place of the one broad band with a maximum at 1640 cm^{-1} in CCl_4 solution) correspond to vibrations of the C=O groups; this constitutes evidence for the presence of free and hydrogen-bonded carbonyl groups. In conformity with this, there are two bands (3330 and 3365 cm^{-1}), the position of which does not change on dilution, in the region of stretching vibrations of the N–H bonds in CCl_4 solution, whereas one broad band at 3220-3270 cm^{-1} is observed in the case of $CHCl_3$ solution.

The data from the absorption spectra make it possible to assume that enamine form VIa predominates in $CCCl_4$ solution, whereas a mixture of tautomers VIa and VIb in a ratio of ∿ 1:1 is presented in $CHCl_3$. The structures of the tautomeric forms are confirmed by the PMR spectra. In addition to four aromatic protons (7.49 and 7.94 ppm), the PMR spectrum of a CCl_4 solution contains singlets of nine protons of methyl group (1.37 and 1.96 ppm with an intensity ratio of 6:3) and broad signals of equal intensity of protons of CH‡ and NH groups (4.64, 5.12, and 6.64 ppm). Singlets of protons of methyl groups at 1.40 and 1.42 CH_2 (CH_3^a), 1.96 (CH_3^b), and 2.38 ppm (CH_3^c) and a singlet of protons of a CH_2 group (2.62 ppm) are visible in the spectrum of a $CDCl_3$ solution, in addition to signals of aromatic protons (7.64 and 7.94 ppm). There are broad signals of equal intensity corresponding to a methylidyne proton (4.64 ppm) and the protons of three NH groups (5.04, 6.04, and 6.70 ppm) in the medium-field region. Disappearance of the signals of the NH, CH, CH_2, and CH_3^c (partially) groups is observed on deuteration.

*The same changes in the color of the solution are observed after the solvent is removed by distillation and the residue is subsequently dissolved in chloroform.

†According to the data in [8], the frequencies corresponding to the stretching vibrations of the C=N bond in naphthoquinonequinoxalines are found in 1516-1540 cm^{-1}.

‡The signal of the methylidyne protons is apparently broadened due to coupling with the proton of the imino group.

The similarity between the IR spectra of a CCl_4 solution of VI and a KBr pellet of it makes it possible to assume that naphthoquinonediazepine also exists in enamine form VIa in the crystalline state.

The increased stability of the enamine form and the absence of such ability in the case of anthraquinonediazepines (III, IV) are evidently associated with the possibility of its fixation due to the formation of a hydrogen bond between the adjacent NH and CO groups. A similar (with respect to its formal characteristics) solvent effect has been noted [7] for tautomeric forms of 8-nitro-4-methyl-1,5-benzo-2-diazepinone.

Naphthoquinonediazepine VI is reduced by tin in hydrochloric acid or by sodium hydrosulfite to dihydro derivative VII.

The anthra- and naphthoquinonediazepines react with hydrohalic acids to give salts that are readily hydrolyzed by water to the starting bases.

EXPERIMENTAL*

The IR spectra of CCl_4 solutions of the compounds were recorded with an UR-20 spectrometer. The electronic absorption spectra of ethanol solutions (c $0.5 \cdot 10^{-4}$ M, cuvette thickness 1 and 5 cm) or of solutions in a 0.1 N alcohol solution of HCl (for the hydrochlorides) were recorded with a Specord UV-vis spectrophotometer.

The PMR spectra were obtained from 3-5% solutions of the compounds in deuterochloroform with a Varian A-56/60A spectrometer at 60 MHz (with hexamethyldisiloxane as the internal standard). Chromatography was accomplished with activity II Al_2O_3 and silica gel (the 0-140 mm fraction was elutriated and dried at 130° for 24 h).

1H-2,3-Dihydro-2,2,4-trimethylanthra[1,2-b]-1,4-diazepine-8,13-dione (III). A mixture of 0.3 g (1 mmole) of diamine I, 0.8 ml (7 mmole) of mesityl oxide, and 4 ml of 6% HCl in 8 ml of DMSO was stirred at 20-25° for 4 h, after which it was poured into water (200 ml), and the aqueous mixture was extracted with chloroform. The chloroform extract was chromatographed on Al_2O_3 (elution with benzene) to give 0.25 g (63%) of a product with R_f 0.1 and mp 136-139° (reprecipitation from benzene by addition of petroleum ether). UV spectrum, λ_{max}, nm (log ε): 257 (3.57), 324 i† (3.72), and 530 (3.86). Found: C 75.9; H 5.7; N 8.6% $C_{20}H_{18}N_2O_2$. Calculated: C 75.5; H 5.7; N 8.8%.

1H-2,3-Dihydro-2,2,4-trimethylanthra[2,3-b]-1,4-diazepine-7,12-dione (IV). A mixture of 1 g (4 mmole) of diamine II, 1 ml (8 mmole) of mesityl oxide, and 8 ml of 10% HCl in 30 ml of DMSO was stirred at 20-25° for 1 h, after which it was poured into water (500 ml), and the precipitate was removed by filtration and chromatographed on activity IV Al_2O_3 (elution with benzene) to give 1 g (75%) of a product with R_f 0.05 and mp 220-222° (from benzene). UV spectrum, λ_{max}, nm (log ε): 246 (4.37), 270 i (4.21), 323 (4.38), and 445 (5.53). PMR spectrum δ, ppm: 1.42 (6H, CH_3), 2.39 (3H, CH_3), 2.47 (2H, CH_2), 4.34 (1H, NH), 7.57, 7.74, 8.07, and 8.26 (6H, aromatic protons). Found: C 75.0; H 5.8; N 8.7%. $C_{20}H_{18}N_2O_2$. Calculated: C 75.5; H 5.7; N 8.8%. The hydrochloride of diazepine IV was obtained by bubbling dry HCl through a solution of 0.1 g of IV in 10 ml of benzene. The hydrochloride was obtained in 70% yield and had mp 166-170° (dec., from methanol). UV spectrum, λ_{max}, nm (log ε): 246 (4.36), 294 (4.35), and 373 (3.86). Found: C 67.3; H 5.3; Cl 10.0; N 7.7%. $C_{20}H_{18}N_2O_2 \cdot HCl$. Calculated: C 67.7; H 5.3; Cl 10.0; N 7.9%.

1H-2,5-Dihydro-2,2,4-trimethylnaphtho[2,3-b]-1,4-diazepine-6,11-dione (VI). A) A solution of 0.1 g (0.5 mmole) of diamine V and 0.2 g of $SnCl_2 \cdot 2H_2O$ in 10 ml of acetone and 2 ml of concentrated HCl was refluxed for 4 h, after which it was poured into water (200 ml), and the aqueous mixture was neutralized with ammonia and extracted with benzene. Chromatography of the extract on Al_2O_3 (elution with chloroform) gave two principal zones — a blue zone and a red zone (R_f 0.4 and 0.25) — which were collected together to give 0.06 g (43%) of VI with mp 125-128° (reprecipitation from benzene by the addition of petroleum ether). The individual substances could not be isolated from either fraction. Rechromatography separated each fraction again into two zones — a blue and a red zone. UV spectrum,

*With the participation of A. Z. Dzhumanazarova.
†Inflection.

λ_{max}, nm (log ε): in CCl_4 284 i (4.13), 308 i (4.22), 319 (4.30), 600 (3.30); in $CHCl_3$ 308 i (4.21), 322 (4.26), 510 (3.08), and 615 (3.06). Found: C 71.9; H 5.9; N 10.3%. $C_{16}H_{16}N_2O_2$. Calculated: C 71.6; H 6.0; N 10.4%. The hydrochloride of diazepine VI, with mp ∿ 150° (dec., from methanol), was obtained in 72% yield. UV spectrum, λ_{max}, nm (log ε): 294 (4.06), 326 (3.97), and 431 (3.43). Found: C 63.1; H 5.7; Cl 11.7; N 9.2%. $C_{16}H_{16}N_2O_2 \cdot HCl$. Calculated: C 63.1; H 5.6; Cl 11.7; N 9.2%.

B) A solution of 1 g (5 mmole) of diamine V, 1 ml (8 mmole) of mesityl oxide, and 0.5 ml of 50% HBr in 40 ml of methanol was refluxed for 2 h, after which it was evaporated to a volume of 5-10 ml. The mixture was then worked up either as in the preceding experiment to give 1.4 g (98%) of diazepine VI, or it was poured into ether (40 ml) to give 1.4 g (84%) of the hydrobromide as yellow plates with mp ∿ 170° (dec., from methanol). Found: C 55.1; H 5.0; Br 23.5; N 7.8%. $C_{16}H_{16}N_2O_2 \cdot HBr$. Calculated: C 55.0; H 5.0; Br 22.9; N 8.0%.

1H-2,3,4,5-Tetrahydro-2,2,4-trimethylnaphthol[2,3-b]-1,4-diazepine-6,11-dione (VII). A mixture of 0.1 g (0.35 mmole) of diazepine VI, 1 g (9 mmole) of tin, and 5 ml of concentrated HCl was stirred at 60° for 2 h, after which it was filtered, and the filtrate was poured into water. The aqueous mixture was extracted with benzene, and the extract was chromatographed on SiO_2 (elution with benzene) to give 0.06 g (57%) of tetrahydro derivative VII with mp 75-77° (from petroleum ether). UV spectrum, λ_{max}, nm (log ε): 234 (4.12), 268 (4.11), 302 (4.28), and 584 (3.26). IR spectrum, cm^{-1}: 3335 (NH), 2878-2975 (CH), and 1640 (CO). PMR spectrum, δ, ppm (in CCl_4): 1.23 (3H, CH_3), 1.28 (3H, J = 5.5 Hz, CH_3—CH), 1.38 (3H, CH_3), 1.71 (2H, J = 7 Hz, CH_2*), 3.56 (1H, J = 7 and 5.5 Hz, CH), ∿4.12 (2H, NH), and 7.46 and 7.82 (4H, aromatic protons). Found: C 71.0; H 6.6; N 10.6%. $C_{16}H_{18}N_2O_2$. Calculated: C 71.1; H 6.7; N 10.4%. The hydrochloride of diazepine VII, with mp 118-120° (from methanol), was obtained in 70% yield. UV spectrum, λ_{max}, nm (log ε): 266 (4.20), 296 (4.00), and 440 (3.27). Found: Cl 11.2; N 8.7%. $C_{16}H_{18}N_2O_2 \cdot HCl$. Calculated: Cl 11.6; N 9.2%.

LITERATURE CITED

1. L. K. Mushkalo and V. A. Chuiguk, Ukr. Khim. Zh., 35, 740 (1969).
2. W. Ried and E. Torinus, Ber., 92, 2902 (1959).
3. A. N. Kost, Z. F. Solomko, L. N. Polovina, and L. G. Gergel', Khim. Geterotsikl. Soedin., 553 (1971).
4. Dang Quoc Quan, Raymond Caujolle, and Thi Bang Tam Dan, Compt. Rend., C, 272, 1518 (1971).
5. V. A. Loskutov, T. I. Kruglyak, A. V. Konstantinova, and E. P. Fokin, Izv. Sibirsk. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 2, 128 (1975).
6. J. A. Moore and E. Mitchell, Heterocyclic Compounds, 9, 224 (1967).
7. A. N. Kost, Z. F. Solomko, V. A. Budylin, and T. S. Semenova, Khim. Geterotsikl. Soedin., 696 (1972).
8. G. A. Efimova and L. S. Éfros, Zh. Organ. Khim., 2, 531 (1966).
9. P. W. W. Hunter and G. A. Webb, Tetrahedron, 29, 147 (1973).

*The AB spectrum was obtained for the CH_2 group from a benzene solution (Varian HA-100 spectrometer). The spin—spin coupling constants found by the double-resonance method (J_{ab} = 15, J_{ac} = 10, and J_{bc} = 2.5 Hz) are in good agreement with the constants presented in [9] for 1H-2,3,4,5-tetrahydro-2,2,4-trimethyl-1,5-benzodiazepine.