INTRAMOLECULAR HYDROGEN BONDING WITH THE PARTICIPATION OF THE NITROGEN ATOM OF FIVE- AND SIX-MEMBERED HETEROCYCLES

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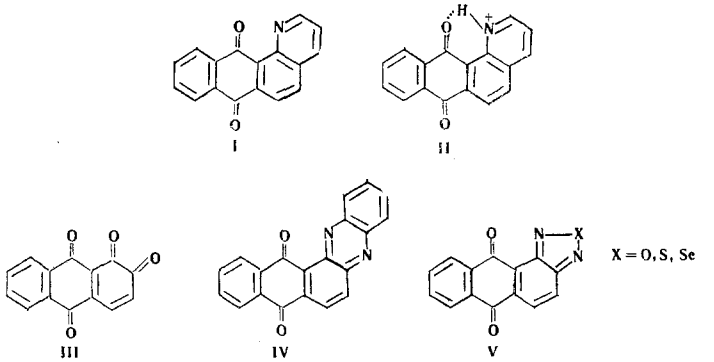
UDC 541.571.9:547.655.1'72/8:543.422

A comparison of the frequencies of the valence vibrations of the OH group and of the chemical shifts of the protons of the hydroxyl groups in α-naphthol derivatives containing the nitrogen atom of the condensed ring of pyridine, pyrazine, 1,2,5-selenadiazole, 1,2,5-thiadiazole, 1,2,5-oxadiazole, and imidazole in the peri position to the hydroxyl group is indicative of the decisive effect of the molecular geometry on intramolecular hydrogen bonding in systems with rigidly fixed configurations. All conditions being equal, the intramolecular hydrogen bond is considerably weaker when the nitrogen atom is part of a five-membered rather than a six-membered heterocycle. This is explained not only by an increase in the distance between the proton donor and acceptor (which may be the same in some cases), but also by the greater deviation of the orbital of the unshared electron pair of the nitrogen of the five-membered heterocycle from the O...N line and, thus, by its greater distance from the hydrogen atom. For the same favorable molecular geometry, the OH...N bond is stronger than the OH...O bond because of the high basicity of the nitrogen atom.

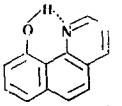
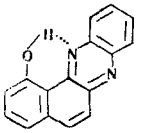
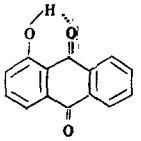
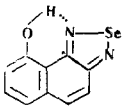
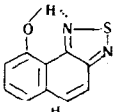
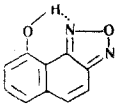
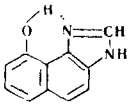
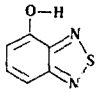
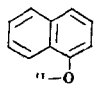
Intramolecular hydrogen bonds with the participation of a nitrogen atom as a proton acceptor have received much less study than hydrogen bonds with the participation of a carbonyl oxygen, which have served as the chief objects in the creation of modern concepts of intramolecular hydrogen bonding. Data on six-membered chelate rings with OH...N bonds involve primarily o-hydroxyazo compounds and o-hydroxyazomethines, i.e., systems with relatively flexible configurations which permit distortion of the valence angles during closing of the hydrogen bonds.

In an investigation of naphtho[2,3-h]quinoline-7,12-dione (I) we advanced the assumption of the acid catalysis of nucleophilic addition reactions through the formation of an intramolecular hydrogen bond in



Scientific-Research Institute of Organic Intermediates and Dyes. L. Ya. Karpov Physicochemical Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 238-244, February, 1971. Original article submitted September 8, 1969.

TABLE 1. Intramolecular Hydrogen Bond Characteristics*

Compound	Structural formula [reference for the synthesis]	IR spectrum (in CCl_4)				PMR spectrum (in $CDCl_3$), ppm	
		ν_{OH}, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	A_{OH}	δ_{OH}†	$\Delta\delta_{OH}$
VI	 [9]	~2800	~800			14,93	10,03
VII	 [10]	~2900	~700			14,30	9,40
—		3025[12]	580			12,53[13]	7,62
VIII	 [11]	3215	387	60	3,1	11,22	6,32
IX	 [11]	3332	270	60	2,2	10,04	5,14
X	 [6]	3445	157	62	1,6	7,79	2,89
XI	 [11]	3250	352	120	—	—	—
XII	 [14]	3550	52	22	0,9	6,35‡	1,45
—		3602[15]	0	22	1,4	4,90	0

* Symbols: ν_{OH} is the frequency of the valence vibrations of the O–H bond, $\Delta\nu_{OH}$ is the shift in the band of the O–H bond with respect to the band of α-naphthol, $\Delta\nu_{1/2}$ is the half-width of the O–H band, A_{OH} is the integral intensity of the O–H band (10^4 liter-mole^{-1}-cm^{-2}), δ_{OH} is the chemical shift of the proton of the hydroxyl group, and $\Delta\delta_{OH}$ is the shift in the signal of the proton of the hydroxyl group as compared with α-naphthol.
† Relative to tetramethylsilane.
‡ Extrapolation to infinite dilution.

the protonated molecule (II) [1, 2]. 9,10-Anthraquinone derivatives which contain a carbonyl group (III) [3], a pyrazine nitrogen atom (IV) [4], a 1,2,5-oxadiazole [5, 6], 1,2,5-thiadiazole [7], or a 1,2,5-selenadiazole [8] grouping (V) in the α-position have similar reactivities with respect to nucleophilic agents.

To solve the problem of the role of the tendency for chelate formation in these compounds it is necessary to have data on the strength of the hydrogen bond involving the nitrogen of the appropriate heterocycle in systems with rigidly fixed, three-dimensional structures. A study of the effect of the molecular geometry on the hydrogen bond is also of independent interest.

Angularly condensed α-naphthol derivatives (VI–XI) which contain a hydroxyl group in the peri position to the nitrogen of the heterocycle (Table 1) are suitable models. Compounds with pyridine (VI) [9] and

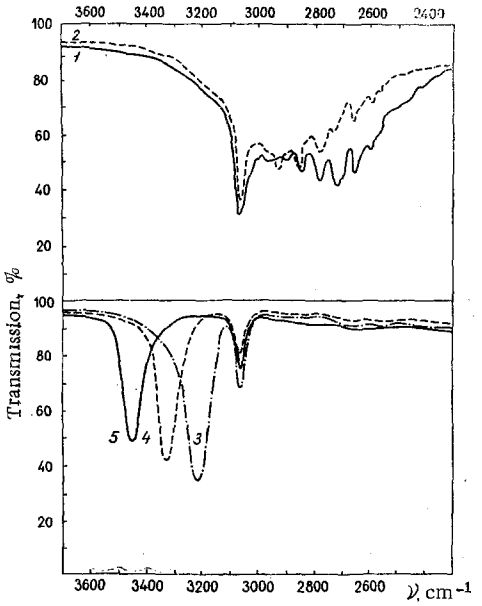


Fig. 1. IR spectra (in carbon tetrachloride): 1) 10-hydroxybenzo[h]-quinoline (VI); 2) 1-hydroxybenzo[a]-phenazine (VII); 3) 9-hydroxynaphtho-[1,2-c][1,2,5]selenadiazole (VIII); 4) 9-hydroxynaphtho[1,2-c][1,2,5]thiadiazole (IX); 5) 9-hydroxynaphtho[1,2-c]-[1,2,5]oxadiazole (X). Concentrations: 1), 3), 4), and 5): $3.2 \cdot 10^{-3}$ M; 2) $6.2 \cdot 10^{-3}$ M. Layer thickness: 1) and 2) 9.99 mm; 3), 4), and 5) 20.06 mm.

pyrazine (VII) [10] rings are described in the literature, but there are no quantitative characteristics for the hydrogen bonds in them. We synthesized naphthols with the nitrogen of the five-membered ring in the peri position to the hydroxyl group especially for this study [11].

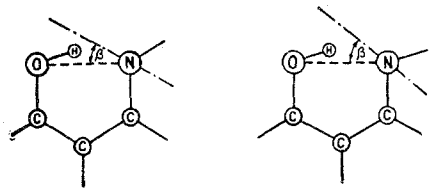
We used IR and PMR spectroscopy to study the hydrogen bonds. The frequencies of the O–H valence vibrations and the chemical shifts of the protons of the hydroxyl groups were measured. As seen from the results of measurements presented in Table 1, the ν_{OH} band in the IR spectra of VI-XI is shifted to lower frequencies, while the PMR signals of the phenolic protons (δ_{OH}) are shifted to weak field, which indicates the presence of a hydrogen bond. The absence of a concentration dependence indicates that it is intramolecular in nature. Unsubstituted α-naphthol was taken as the comparison sample in the calculation of the shifts ($\Delta\nu = \nu_0 - \nu$ and $\Delta\delta = \delta - \delta_0$) which characterize the hydrogen bond. The structural similarity of the objects makes it possible to relate the differences in the chemical shifts and the symbatically related altered frequencies due to the change in the hydrogen bond energy. The correction to δ_{OH} due to differences in the ring currents [16] in the most unfavorable case can scarcely exceed 0.5 ppm and, thus, does not change the overall picture. An approximate evaluation of the hydrogen bond energy from the formula [17] $E_H = (\Delta\nu / k \cdot \nu_0) \cdot 10^2$, starting from k = 1.98, calculated on the basis of data on the interaction of phenol with pyridine [18], gives a range of 2.2 to 10 kcal/mole.

Hydroxybenzoquinoline (VI) and hydroxybenzophenazine (VII), whose $\Delta\nu_{OH}$ and $\Delta\delta_{OH}$ values (Table 1) exceed those of 1-hydroxyanthraquinone and similar hydroxyquinones, have the strongest hydrogen bonds. The greater strength of the OH...N bond as compared with the OH...O bond is natural in view of the significant difference in the basicity of the proton acceptor. The basicities of the nitrogen in quinolines and phenazines [19] are ~ 12 and eight orders of magnitude higher, respectively, than the basicity of the carbonyl oxygen in anthraquinone [20]. The IR spectra of VI and VII, like the spectra of hydroxyquinones, contain a markedly diffuse band at 2400-3400 cm^{-1} (Fig. 1, curves 1 and 2) which is characteristic for compounds with a strong intramolecular hydrogen bonding.

A different picture is observed in the group of 1,2,5-diazoles (VIII-X), where the sp^2-hybridized nitrogen atom also serves as the proton acceptor. As seen from the $\Delta\nu_{OH}$ and $\Delta\delta_{OH}$ values, the hydrogen bond in diazoles VIII-X is weaker than in 1-hydroxyanthraquinone. The band of the O–H valence vibration in the IR spectra appears as a distinctly expressed peak with a half-width of 60-80 cm^{-1} (Fig. 1, curves 3-5). There is no direct dependence between the electronegativity of heteroatom X, which determines the basicity of the 1,2,5-X-diazoles and the characteristics of the hydrogen bond; while the weak hydrogen bond in oxadiazole X corresponds to the high electronegativity of oxygen, the hydrogen bond in selenadiazole VIII is appreciably stronger than that in thiadiazole IX although the electronegativities of selenium and sulfur atoms are about the same [21].

The sharp difference in the characteristics of the hydrogen bond in the hydroxy derivatives of pyridine (VI) and pyrazine (VII), on the one hand, and of 1,2,5-diazoles VIII-X, on the other, merits discussion.

The rings of 1,2,5-oxa-, -thia-, and -selenadiazoles are planar aromatic systems with equalized bonds [22-24], and these compounds are the electronic analogs of pyrazine, just as furan, thiophene, and selenophene are the electronic analogs of benzene. Quantum-chemical calculations indicate [25] that the π-electron density on the nitrogen atom and the C–N bond order, which are important for π conjugation through the hydrogen bond [26], are no less in 1,2,5-benzothiadiazole and 1,2,5-benzoselenadiazole than in quinoline and phenazine. There are no direct measurements of the basicities of 1,2,5-diazoles, but data



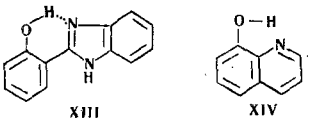
1 2

Fig. 2. Schematic depiction of the direction of the axis of the orbital of the unshared electron pair of the nitrogen atom of a six-membered heterocycle (1) and of a five-membered heterocycle (2) during the formation of an intramolecular hydrogen bond.

which demonstrate the similarity of 1,2,5-thia- and -selenadiazoles to pyrazine [27] make it possible to assume that the difference in basicity between 1,2,5-X-diazoles (X = S, Se) and pyrazines should not be significant. In any case, it is less than the difference between pyrazines and pyridines, which is ~ 4 pK_a units [19], but has little effect on the hydrogen bond in VI and VII. In the 1,2,5-diazole series the CCN angle, which is 119 deg in selenadiazole [24], 114 deg in thiadiazole [23], and 109 deg in oxadiazole [22], decreases with decreasing heteroatom (X) size. The decrease in the CCN angle entails an increase in the O...N distance and, correspondingly, the H...N distance in hydroxynaphthodiazoles, which explains the more rapid decrease in the hydrogen bond energy in naphthothiadiazole IX and naphthoxadiazole X than might have been expected from the electronegativity of heteroatom X. In selenadiazole, however, the CCN angle reaches about the same value as in pyridine or pyrazine.

The weakening of the hydrogen bond in selenadiazole VIII as compared with pyrazine VII cannot be explained by either a decrease in basicity or by an increase in the distance between the proton donor and acceptor, or by deterioration of the conditions for π conjugation through the hydrogen bridge. In our opinion, the reason for the differences in VII and VIII consists in the different orientation of the orbital of the unshared electron pair of the nitrogen which is a part of the six- and five-membered heterocycle (Fig. 2). As a consequence of interelectronic repulsion, the axis of this orbital is situated close to the bisector of the angle formed by the nitrogen bond and the adjacent atoms and is 120 deg in pyridines and pyrazines and 105 deg in 1,2,5-selenadiazole [24]. As a result, the axis of the sp^2-hybrid orbital of nitrogen in hydroxynaphthoselenadiazole VIII deviates more markedly from the O...N line (Fig. 2, angle β), which results in a decrease in the overlap with the orbital of the hydrogen atom and a decrease in the hydrogen bond energy. In thiadiazole IX and oxadiazole X, as in the majority of other similar compounds, this factor acts in conjuction with the increase in the distance between the proton donor and acceptor.

Hydrogen bonding involving the participation of the nitrogen atom of imidazole can serve as an illustration of what has been stated. The IR spectrum of 9-hydroxynaphth[1,2-d]imidazole (XI) (the PMR spectrum could not be measured because of its low solubility) contains a narrow band from the free NH group at 3465 cm^{-1} which is not shifted on dilution (Table 1). This indicates that the NH group, as was assumed, is in the β-position of the naphthalene ring in naphth[1,2-d]imidazoles [28], while the hydroxyl group participates in intramolecular bonding, whose strength considerably exceeds that of the hydrogen bond in benzoquinoline VI, whose basicity is close to that of these compounds. At the same time, judging from the character of the IR spectra (diffuse ν_{OH} band at 2400-3400 cm^{-1}), there is a very stable chelate ring in 2-(o-hydroxyphenyl)benzimidazole (XIII) [29]. The absence of hydrogen bonds in XI and XIII is apparently explained by the fact that, in the latter, steric hindrance (the increase in the O...N distance and deviation of the orbital of the unshared electron pair of nitrogen) is eliminated owing to flexible fusion of the phenyl residue to the benzimidazole ring. One should also take into account the fact that an imidazole C–N bond which has a higher order is included in the chelate ring of XIII.



XIII XIV

Sharp deterioration in the conditions for closing of a hydrogen bond occurs on passing from a six-membered chelate ring to the more strained five-membered ring. Judging from the dependence of δ_{OH} on the solution concentration, there is no clearly expressed intramolecular hydrogen bond even in 8-hydroxyquinoline (XIV) [30], which contains the nitrogen of a six-membered heterocycle, although the shifts in the IR spectra ($\Delta\nu$) [31] and in the PMR spectra ($\Delta\delta$) are extremely significant. The formation of a five-membered chelate ring in a condensed system with the participation of a five-membered heterocycle is even more hindered. An example of this is 4-hydroxybenzo[c][1,2,5]thiadiazole (XII), where the absence of intra-

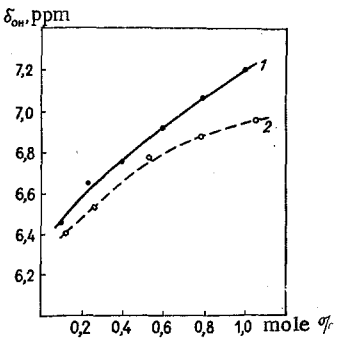
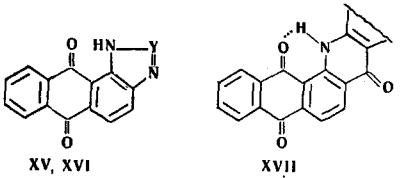


Fig. 3. Dependence of the chemical shifts of the protons of the OH groups of 4-hydroxybenzo[c][1,2,5]thiadiazole (XII) on the solution concentration: 1) in deuterochloroform; 2) in carbon tetrachloride.

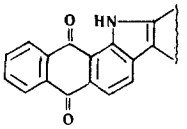
molecular hydrogen bonding is indicated by both the character of the concentration dependence in the PMR spectra (Fig. 3) and the small shifts, widths, and intensities of the OH band in the IR spectra (Table 1).

This comparison of model compounds leads to the conclusion that the tendency for closing of an intramolecular hydrogen bond in the protonated forms of quinones I and III-V should decrease in the order: I ≥ IV > III ≫ V. The hindrance to formation of a chelate bridge with the participation of the nitrogen of a five-membered heterocycle in anthraquinone derivatives should be still greater than in hydroxy compounds VIII-XI as a consequence of the more rigid attachment of the carbonyl oxygen as compared with the phenolic oxygen. In fact, intramolecular hydrogen bonding like that in α-aminoanthraquinones [32] and phthaloylacridones (XVII) [33] is completely absent in anthraquinoneimidazole XV and anthraquinonetriazole XVI. In contrast to α-aminoanthraquinones and XVII, there is no splitting of the carbonyl band (ν_{CO} 1672 cm^{-1}) in the IR spectra of XV and XVI, and a ν_{NH} band is observed at 3440-3460 cm^{-1}. The same picture was noted for diphthaloylcarbazoles (XVIII) [34].



XV, XVI

XVII



XVIII

XV Y=CH; XVI Y=N

In contrast to quinones I, III, and IV, it is apparent that the development of a hydrogen chelate bridge during protonation is energetically unfavorable for anthraquinonediazoles V and therefore cannot play an important role. The high reactivity of anthraquinonediazoles with respect to nucleophilic agents is chiefly due to the increased polarizability of the π-electron system of the ring adjoining the heterocycle, which is caused by the disruption of the equalization of the bonds with partial localization of the diene structure [35].

EXPERIMENTAL

The IR spectra of carbon tetrachloride solutions (chloroform solution for XI) were recorded with a UR-20 spectrometer for concentrations of $1 \cdot 10^{-1}$ to $2 \cdot 10^{-4}$ M and layer thicknesses of 0.1 to 5 cm at ~ 35 deg. The integral intensities were determined by the Burzhen method [36]. The accuracy in the measurements in the frequencies was ± 5 cm^{-1}, while that in the measurements of the integral intensities was 10%. The IR spectra of XV and XVI were obtained from KBr pellets.

The PMR spectra of deuterochloroform solutions were measured with an RS-60 spectrometer (60 MHz) [37] for concentrations of ~ 1 mole % at room temperature with cyclohexane as the internal standard. The results were converted to the tetramethylsilane standard by adding 1.43 ppm. The accuracy of the measurements was ± 0.05 ppm.

The references for the methods for preparing VI-XII are indicated in Table 1. Anthra[1,2-d]imidazole-6,11-dione (XV) and anthra[1,2-d]triazole-6,11-dione (XVI) were prepared according to [38] and [39], respectively.

LITERATURE CITED

1. M. V. Gorelik, M. I. Evstratova, and I. Ya. Koshcheeva, Zh. Organ. Khim., 4, 1465 (1968).
2. M. V. Gorelik and M. I. Evstratova, Zh. Organ. Khim., 5, 758 (1969).
3. M. V. Gorelik, Zh. Organ., Khim., 4, 509 (1968).
4. M. V. Gorelik and T. F. Bezrukova, Zh. Organ. Khim., 5, 1840 (1969).
5. M. V. Gorelik, T. P. Kononova, and N. S. Dokunikhin, Khim. Geterotsikl. Soedin., 545 (1967); 463 (1968).
6. M. V. Gorelik, B. E. Zaitsev, T. P. Kononova, and N. S. Dokunikhin, Khim. Geterotsikl. Soedin., 780 (1968).
7. M. V. Gorelik and S. B. Lantsman, Khim. Geterotsikl. Soedin., 447, 453 (1968).

8. M. V. Gorelik, Khim. Geterotsikl. Soedin., 541 (1967).
9. H. and M. Schenkel-Rudin, Helv. Chim. Acta, 27, 1456 (1944).
10. Aktien Gesellschaft für Anilin-Fabrikation, German Patent No. 394,195 (1924); Frdl., 14, 772.
11. T. Kh. Gladysheva and M. V. Gorelik, Khim. Geterotsikl. Soedin., 554 (1970).
12. A. Foldes and C. Sandorfy, J. Mol. Spectr., 20, 262 (1966).
13. N. N. Shapet'ko and D. N. Shigorin, Zh. Strukt. Khim., 8, 538 (1967).
14. L. S. Éfros, R. P. Polyakova, and M. G. Argitti, Zh. Obshch. Khim., 32, 516 (1962).
15. St. C. Flett, Spectrochim. Acta, 10, 21 (1957).
16. J. W. Emsley, J. Finney, and L. Sutcliffe High-Resolution Nuclear Magnetic Resonance Spectroscopy, Pergamon.
17. N. D. Sokolov, in: The Hydrogen Bond [in Russian], (1964), p. 7.
18. H. Fritsche, Ber. Bunsen Gesellschaft Phys., 68, No. 3, 459 (1964).
19. A. Albert, in: Physical Methods in Heterocyclic Chemistry, Academic Press (1971).
20. A. M. Arnett, in: Modern Problems of Physical Chemistry [Russian translation], Moscow (1967), p. 324.
21. A. L. Allred, J. Inorg. Nucl. Chem., 17, 215 (1961).
22. E. Saegebarth and A. P. Cox, J. Chem. Phys., 43, 166 (1965).
23. F. A. Momany and R. A. Bonham, J. Am. Chem. Soc., 86, 162 (1964).
24. V. Luzzatti, Acta Cryst., 4, 193 (1951).
25. J. Fajer, B. H. Bielski, and R. H. Felton, J. Phys. Chem., 72, 1281 (1968).
26. D. N. Shigorin, in: The Hydrogen Bond [in Russian], Nauka (1964), p. 195.
27. L. M. Weinstock, Advances in Heterocyclic Chemistry, 9, 107 (1968).
28. T. J. Lane and K. P. Quinlan, J. Am. Chem. Soc., 82, 2997 (1960).
29. V. I. Minkin, Yu. A. Zhandov, I. D. Sadekov, Yu. A. Ostroumov, N. E. Shelepin, and O. A. Raevskaya, Dokl. Akad. Nauk SSSR, 169, 1095 (1966).
30. L. W. Reeves and K. O. Stroemme Can. J. Chem., 39, 2318 (1961).
31. G. M. Badger and A. C. Moritz, J. Chem. Soc., 3437 (1958).
32. D. N. Shigorin and N. S. Dokunikhin, Zh. Fiz. Khim., 29, 1958 (1955).
33. T. Hayashi and J. Maehare, Bull. Chem. Soc. Japan, 35, 1690 (1962).
34. J. Arient, J. Knižek, J. Marhan, and V. Slavik, Coll. Czech. Chem. Commun., 33 3280 (1968).
35. M. V. Gorelik, O. S. Zhdamarov, É. S. Levin, and L. A. Chetkina, Zh. Organ. Khim., (1971, in press).
36. D. A. Ramsey, J. Am. Chem. Soc., 74, 72 (1952).
37. A. N. Lyubimov, A. F. Varenik, and A. V. Kessenikh, Zh. Strukt. Khim., 6, 694 (1966).
38. A. Schaarschmidt, Ann., 487, 185 (1915).
39. H. Waldmann and K. G. Hindenburg, Ber., 71, 371 (1938).