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Ground States of Conjugated Molecules. XIX.[1] Tautomerism of Heteroaromatic Hydroxy and Amino Derivatives and Nucleotide Bases

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Abstract: The semiempirical SCF MO π approximation described in part XII of this series has been used to study tautomerism in a number of hydroxy and amino derivatives of heteroaromatic compounds containing five- and six-membered rings, including cytosine, uracil, adenine, and guanine. Bond lengths and other properties are also reported. The results agree well with the available evidence.

The prototropic tautomerism of heteroaromatic compounds containing hydroxy or amino groups has long been of interest to chemists and has attracted further attention in recent years through the realization that such processes may be of biological importance. Thus the production of spontaneous mutations has been attributed to the presence in DNA of nucleotide bases in abnormal tautomeric forms at the time of replication and attempts have been made on theoretical grounds to predict which base is most likely to be involved in such a process.[4]

Previous papers of this series have described the development of a semiempirical SCF MO treatment of conjugated molecules, using the Hückel σ,π approximation, which gives very good estimates of the heats of formation of compounds containing carbon, hydrogen, nitrogen, and oxygen. Here we wish to report a discussion of prototropic tautomerism in corresponding hydroxy and amino derivatives of a number of such systems in terms of the latest[5,6] version of this theoretical approach.

Theoretical Method

The calculations were carried out by the method of part XII,[6] using the variable β approximation and including σ polarization.

In calculating heats of atomization (ΔH_a) we used an average value (4.2018 eV) for the pyrrole-type NH bond energy,[7] increased (*cf.* Cox[7c]) to 4.3753 eV in the case of imino (=N—H)-type bonds. The latter value was also used for amides, where experimental data are lacking, on the grounds that the CN bonds in them have significant π character and the nitrogen atoms carry positive charges. The OH bond energy was assumed to have the value (4.439 eV) determined spectroscopically.[8]

In the case of five-membered rings, certain of the keto and imino tautomers are nonaromatic and contain methylene groups; *e.g.*

(1) Part XVIII: M. J. S. Dewar and N. Trinajstic, *Tetrahedron*, in press.
(2) Robert A. Welch Postdoctoral Fellow.
(3) On leave of absence from The Chemical–Pharmaceutical Research Institute, Cluj, Romania.
(4) See B. Pullman and A. Pullman, "Quantum Biochemistry," Interscience Publishers, New York, N. Y., 1963.
(5) M. J. S. Dewar and C. de Llano, *J. Amer. Chem. Soc.*, **91**, 789 (1969).
(6) M. J. S. Dewar and T. Morita, *ibid.*, **91**, 796 (1969).
(7) (a) C. T. Mortimer, "Reaction Heats and Bond Strengths," Pergamon Press, New York, N. Y., 1962, p 141; (b) J. A. Kerr, R. C. Sekhar, and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 3217 (1963); (c) J. D. Cox, *Tetrahedron*, **19**, 1175 (1963).
(8) (a) R. F. Barrow and A. R. Downie, *Proc. Phys. Soc.*, **A69**, 179 (1956); (b) H. W. Goldstein, P. N. Walsh, and D. White, *J. Phys. Chem.*, **65**, 1400 (1961).

Table I. Heats of Atomization of Tautomeric Forms of Hydroxy and Amino Derivatives of Heteroaromatic Compounds Containing Six-Membered Rings

Tautomer A	ΔH_a(A), eV	Tautomer B	ΔH_a(B), eV	ΔH_a(A) − ΔH_a(B), eV	ΔH_a(A,B) − H^+, eV
Ia	59.661	Ib	59.007	0.654	64.575
IIa	59.361	IIb	57.178	2.182	63.937
IIIa	59.455	IIIb	58.674	0.781	64.252
IVa	56.325	IVb	56.841	−0.516	61.607
Va	56.045	Vb	54.712	1.333	60.745
VIa	56.109	VIb	56.208	−0.099	60.852
VIIa	60.546	VIIb	61.031	−0.485	66.070
		VIIc	60.898	−0.352	
VIIIa	60.563	VIIIb	61.022	−0.459	
		VIIIc	62.291	−1.728	
IXa	89.796	IXb	90.630	−0.834	
Xa	89.409	Xb	88.225	1.184	
XIa	89.565	XIb	90.063	−0.498	
XIIa	89.531	XIIb	89.394	0.137	
XIIIa	89.495	XIIIb	87.924	1.571	
XIVa	89.517	XIVb	89.266	0.251	
XVa	89.468	XVb	88.092	1.376	
XVIa	89.782	XVIb	90.648	−0.866	
XVIIa	89.737	XVIIb	89.923	−0.187	
XVIIIa	89.472	XVIIIb	88.367	1.105	
XIXa	89.472	XIXb	87.939	1.433	
XXa	89.509	XXb	89.180	0.329	
XXIa	89.486	XXIb	87.848	1.638	
XXIIa	89.524	XXIIb	89.350	0.174	
XXIIIa	122.747	XXIIIb	123.183	−0.336	
XXIVa	122.810	XXIVb	121.510	1.300	
XXVa	122.832	XXVb	123.048	−0.216	
XXVIa	122.773	XXVIb	121.623	1.150	
XXVIIa	122.790	XXVIIb	123.918	−1.128	

(1)

The calculations in such cases were carried out for the corresponding open-chain compound derived by removing CH_2 (*i.e.*, CH_2=CHOCHO in the case indicated above) and corrected by appropriate group values for CH_2. The group value (E_C) for C—CH_2—C was found by comparing the heats of atomization of cyclopentadiene (49.198 eV[9]) and *cis*-1,3-butadiene (41.959 eV[10]). The group values for O-CH_2-C (E_O) and N-CH_2-C (E_N) are given in terms of E_C and bond energies (E_{XY}) by

$$E_O = E_C + (E_{CH} - E_{OH}) + (E_{CO} - E_{CC}(sp^2\text{–}sp^3)) \quad (2)$$

$$E_N = E_C + (E_{CH} - E_{NH}) + (E_{CN} - E_{CC}(sp^2\text{–}sp^3)) \quad (3)$$

Using appropriate values[11] for the bond energies, the following group values (eV) were obtained.

$$E_C = 7.239 \qquad E_O = 7.617 \qquad E_N = 7.201 \quad (4)$$

Results and Discussion

Table I lists the results for tautomeric forms of compounds containing six-membered rings. As in previous papers of this series, heats of atomization (ΔH_a) are treated as positive quantities. The heat of atomization of the hydroxy or amino tautomer (A) is listed first, of the corresponding keto or imino tautomer (B) second, and the difference between them third. A positive value for the difference implies that the hydroxy or amino tautomer is the more stable, a negative one that the keto or imino tautomer is the more stable. As a further check on the validity of the variable β procedure, calculations were also carried out for protonated forms in which protons were present at both positions, using initial geometries corresponding to A and B; the results agreed to within ±0.02 eV, showing that even in this extreme case the neglect of changes in integrals between nonbonded atoms is not important. An average of the two values is shown in the last column of the table.

It will be seen that the amino tautomers are in all cases predicted to be more stable than their imino counterparts; this is in agreement with the available experimental evidence. Thus it has been shown by uv spectroscopy[12] that the amount of imino tautomer present in equilibrium with Ia or IIIA is less than 0.1%, and studies of acid dissociation constants have indicated[13] that the equilibrium constants for Ia ⇌ Ib and IIIa ⇌ IIIb are approximately 200,000 and 2000, respectively. The corresponding free energies of isomerization (7.3 and 4.5 kcal, respectively) are less than the energy differences listed in Table I (15 and 18 kcal/mol, respectively); this discrepancy may be at least partly due to the fact that the calculations refer to the gas phase, whereas the pK_a measurements were carried out

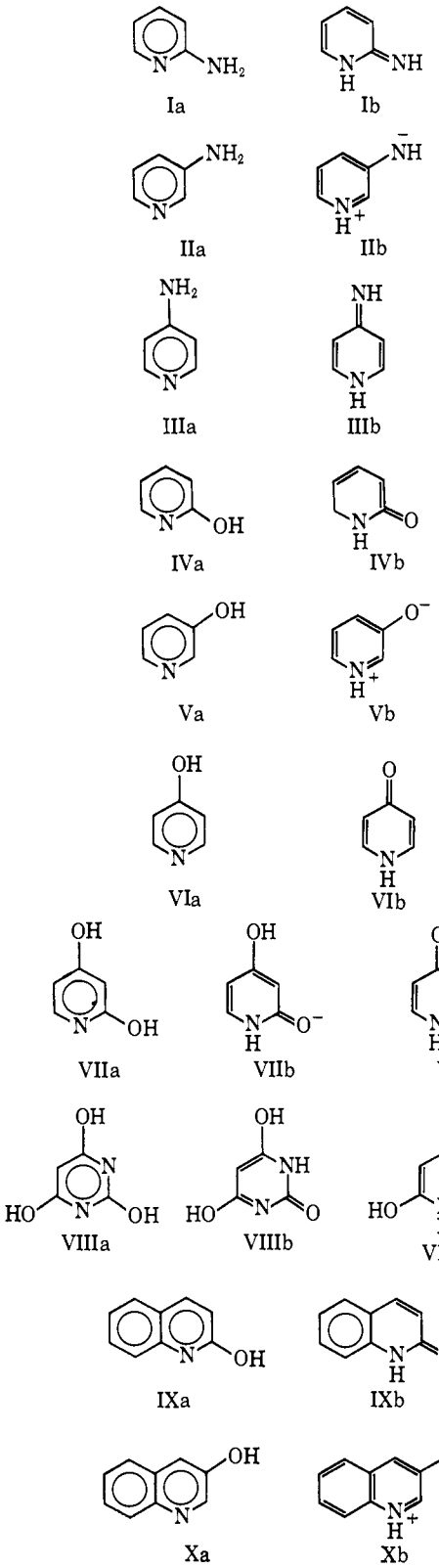
(9) Obtained using ΔH_a of *trans*-butadiene ("Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," American Petroleum Institute Research Project 44, Carnegie Press, Pittsburgh, Pa., 1953) and the heat of isomerization of *cis* → *trans*-butadiene; see N. C. Baird and M. J. S. Dewar, *J. Chem. Phys.*, **50**, 1262 (1969).

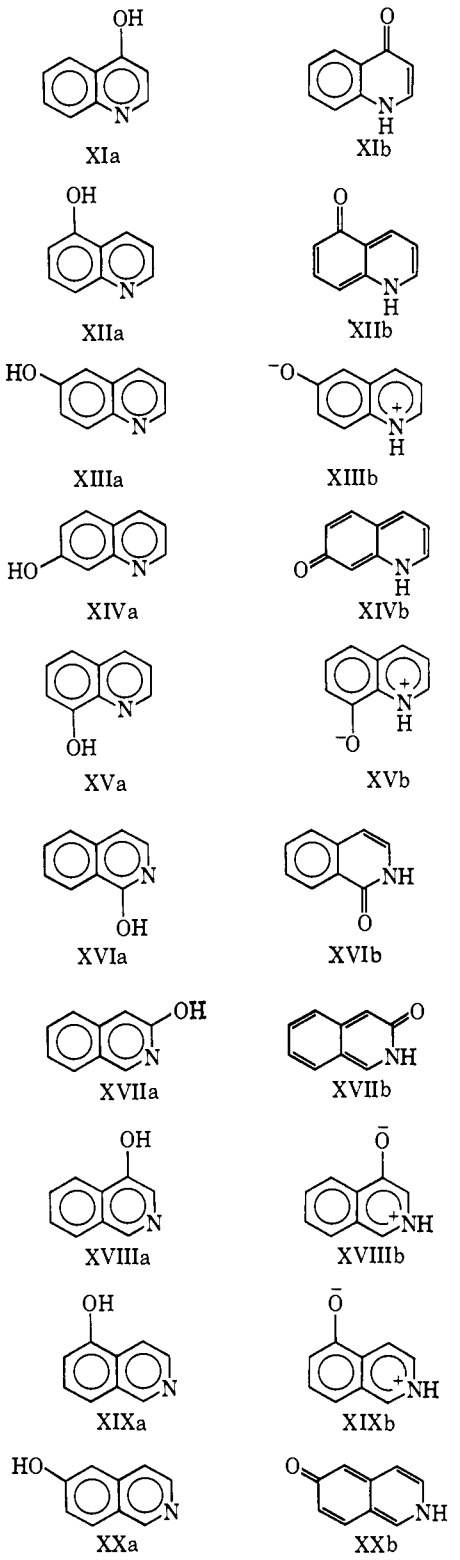
(10) Calculated from the heat of hydrogenation in C. T. Mortimer, "Reaction Heats and Bond Strengths," Pergamon Press, New York, N. Y., 1962, and the experimental ΔH_f for cyclopentane.

(11) See ref 5 and 7 and 8, respectively.

(12) L. C. Anderson and N. V. Seeger, *J. Amer. Chem. Soc.*, **71**, 340 (1949).

(13) S. J. Angyal and C. L. Angyal, *J. Chem. Soc.*, 1461 (1952).





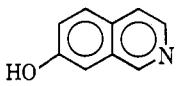
in aqueous solution. The energies of solvation of the tautomers in water could well differ considerably.

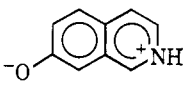
On the other hand the equilibrium in the case of compounds with hydroxyl α to nitrogen is expected to favor the lactam tautomer almost equally greatly; in the case of the γ-hydroxy derivatives, the oxodihydro tautomer is also favored but to a much smaller extent. This again seems to be in agreement with the available experimental evidence. Derivatives of α- and γ-hydroxypyridines have been shown to exist predominantly as the corresponding pyridones, both by uv[14] and ir[15] spectroscopy, while the greater tendency for ketonization of hydroxy groups α to nitrogen is indicated by the fact[16] that 2,4-dihydroxypyridine (VIIa) exists, as predicted (Table I), predominantly as the lactam VIIb rather than the γ-pyridone VIIc.

(14) S. F. Mason, *J. Chem. Soc.*, 5010 (1957), and references cited therein.

(15) (a) J. A. Gibson, W. Kynaston, and A. S. Lindsey, *ibid.*, 4340 (1955); (b) S. F. Mason, *ibid.*, 4874 (1957), and references cited therein.

(16) H. J den Hertog and D. J. Buurman, *Rec. Trav. Chim. Pays-Bas*, **75**, 257 (1956).


XXIa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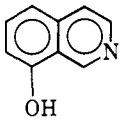
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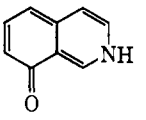
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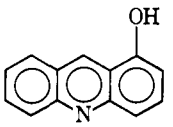
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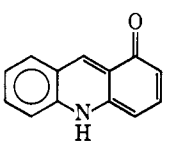
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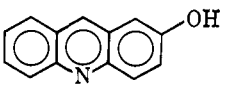
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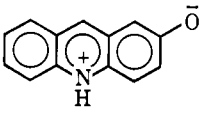
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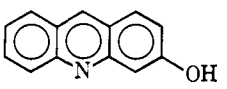
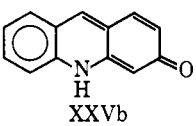
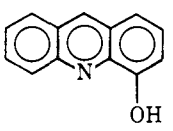

XXVa


XXVb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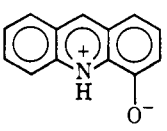
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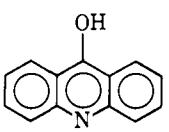
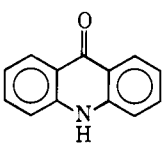
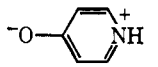

XXVIIa


XXVIIb

Compounds with more than one N=COH moiety are correctly predicted to exist mainly as polyamides; thus the preferred form of barbituric acid is, as predicted, the bisamide VIIIc.[17] The third hydroxyl remains as such since ketonization would destroy the aromaticity of the ring.

Similar relationships are predicted to hold in the case of benzo derivatives of α- and γ-hydroxypyridine; the available evidence[14,15] suggests that such compounds (*e.g.*, IX, XI, XVI, XVII, XXVII) do indeed exist preferentially as pyridone derivatives. On the other hand compounds with hydroxyl β to nitrogen (*e.g.*, IIa) are correctly predicted to exist as phenols; here of course it is impossible to write a pyridone structure, so the oxodihydro derivative would be either zwitterionic or nonaromatic. Similar considerations apply to hydroxy derivatives of quinoline, isoquinoline, and acridine, where the hydroxyl is separated from nitrogen by an even number of bonds.

Another factor of apparent importance is the effect of bond fixation in the oxodihydro tautomers. These would be fully aromatic only if they existed as zwitterions, *e.g.*



In practice the separation of charge is much less than this, the structure approaching that expected for the corresponding uncharged oxodihydro system. The resulting bond fixation leads to a loss of resonance energy; this indeed is why 2- and 4-aminopyridine exist as such rather than in the iminodihydro forms. In the case of the hydroxy derivatives, the loss of resonance energy is offset by the greater stability to be expected for a classical ketonic structure, as indicated by summing bond energies for single classical structures of ketonic and enolic type; if the loss of resonance energy is not too great, the ketonic (*i.e.*, oxodihydro) tautomer can then predominate.

In the pyridones (IVb and VIb) bond fixation affects the aromaticity of one ring only; the effect is greater in VIb where delocalization would require a greater separation of charge (since it involves transfer of electrons from nitrogen to oxygen). This is why the pyridone structure is less favored in the case of VIb. Similar considerations apply to the quinolones (IXb and XIb), isoquinolone (XVIb), and acridone (XXVIIb); since, moreover, the loss of resonance energy is less in quinolone or isoquinolone than in pyridone, and less again in acridone,[18] the oxodihydro tautomers are progressively favored in this order.

A different situation arises when the hydroxy group is in the benzenoid ring, as in 5- or 7-hydroxyquinoline (XIIb or XIVb) or 3-hydroxyisoquinoline (XVIIb); here only a quinonoid uncharged classical structure is possible in which bonds are fixed in two rings. Here the loss of resonance energy should be much greater than for the cases considered above, so the oxodihydro structure should be less favored. Indeed, the Bz-OH derivatives of quinoline and isoquinoline are predicted, apparently correctly,[14,15] to exist as such; the resonance energy of quinoline or isoquinoline is of course greater than that of pyridine. In the case of 3-hydroxyisoquinoline (VVIIa) the effect is much less since delocalization involves a much smaller separation of charge; XVII is predicted, apparently correctly,[14,15] to exist predominantly as the isoquinolone, but the ratio of tautomers should be much less than in XVI. There is no evidence concerning this.

In 1- and 3-hydroxyacridine (XXIII and XXV, respectively) the loss of resonance energy or ketonization is less than in the analogous hydroxyquinolines or hydroxyisoquinolines since the difference in resonance energy between acridine and benzene is less than the overall resonance energy of quinoline or isoquinoline (*cf.* ref 18); here the corresponding acridones are predicted to predominate, again correctly,[14,15] although the estimated differences in energy are small.

Table II shows the results of similar calculations for compounds containing five-membered rings. Here the imino and oxo tautomers are of two distinct types; those in which the hydrogen is transferred to a pyridine-type nitrogen atom in the ring, the resulting structure being isoconjugate with the original amine or hydroxy deriva-

(17) R. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," Interscience Publishers, New York, N. Y., 1960.

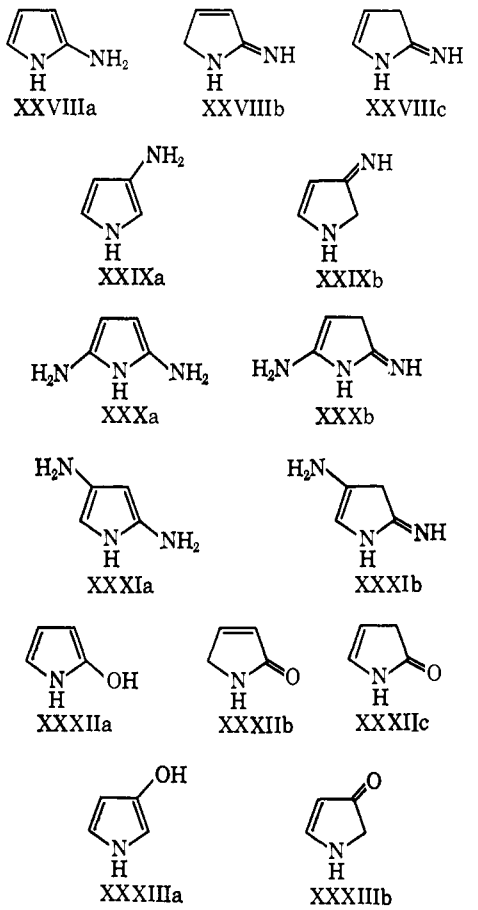
(18) The difference in resonance energy between quinoline or isoquinoline and benzene is less than the resonance energy of pyridine, and the difference between acridine and 9,10-dihydroacridine less again; this follows from the fact that the resonance energies of azines are similar to those of the isoconjugate hydrocarbons.[19]

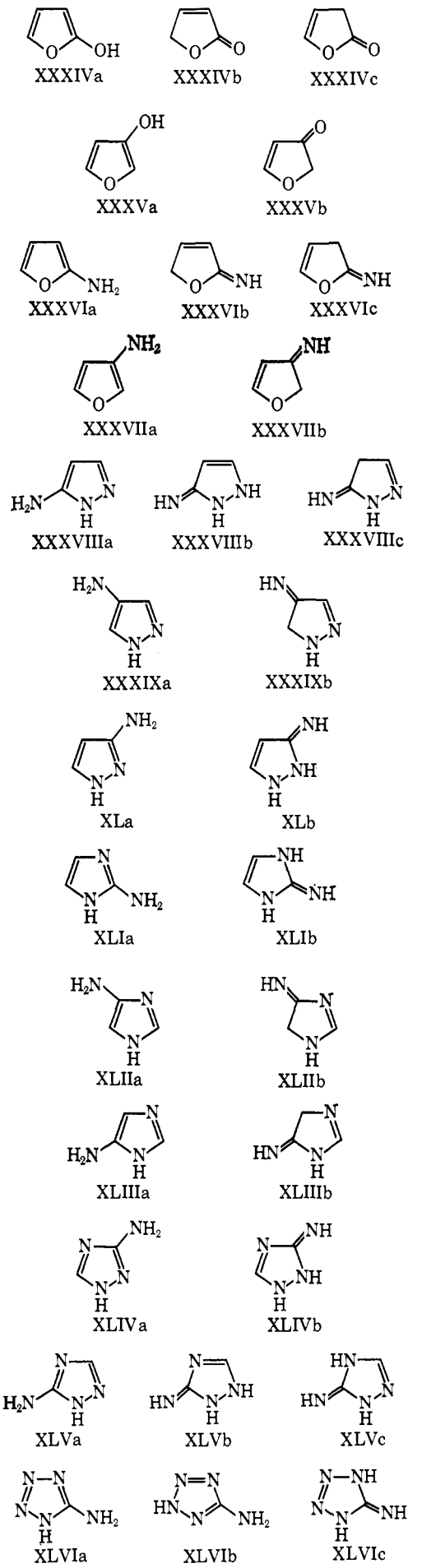
(19) See M. J. S. Dewar, *J. Amer. Chem. Soc.*, 74, 3345 (1952).

Table II. Heats of Atomization of Tautomeric Forms of Hydroxy and Amino Derivatives of Heteroaromatic Compounds Containing Five-Membered Rings

Tautomer A	ΔH_a(A), eV	Tautomer B	ΔH_a(B), eV	ΔH_a(A) − ΔH_a(B), eV
XXVIIIa	52.854	XXVIIIb	52.372	0.482
		XXVIIIc	51.900	0.954
XXIXa	52.589	XXIXb	52.125	0.354
XXXa	60.586	XXXb	59.620	0.966
XXXIa	60.360	XXXIb	59.408	0.952
XXXIIa	49.801	XXXIIb	50.202	−0.401
		XXXIIc	49.738	0.063
XXXIIIa	49.466	XXXIIIb	49.861	−0.395
XXXIVa	46.514	XXXIVb	47.180	−0.666
		XXXIVc	46.631	−0.117
XXXVa	45.725	XXXVb	46.580	−0.755
XXXVIa	49.584	XXXVIb	49.315	0.269
		XXXVIc	48.673	0.911
XXXVIIa	49.085	XXXVIIb	49.024	0.061
XXXVIIIa	47.538	XXXVIIIb	47.032	0.506
		XXXVIIIc	46.189	1.349
XXXIXa	47.160	XXXIXb	46.366	0.794
XLa	47.424	XLb	47.030	0.394
XLIa	48.181	XLIb	47.938	0.243
XLIIa	47.775	XLIIb	47.186	0.589
XLIIIa	47.753	XLIIIb	47.601	0.152
XLIVa	42.923	XLIVb	42.273	0.650
XLVa	43.080	XLVb	42.498	0.582
		XLV	42.267	0.813
XLVIa	36.491	XLVIc	36.429	0.062
XLVIb	36.804	XLVIc	36.429	0.375

tive (*cf.* Ia and Ib), and those where the hydrogen is transferred to a methine group, the aromaticity of the ring being destroyed. In cases where there is a choice between the two types of tautomerism, the former is favored (*cf.* XXXVIIIb with XXXVIIIc), as one would





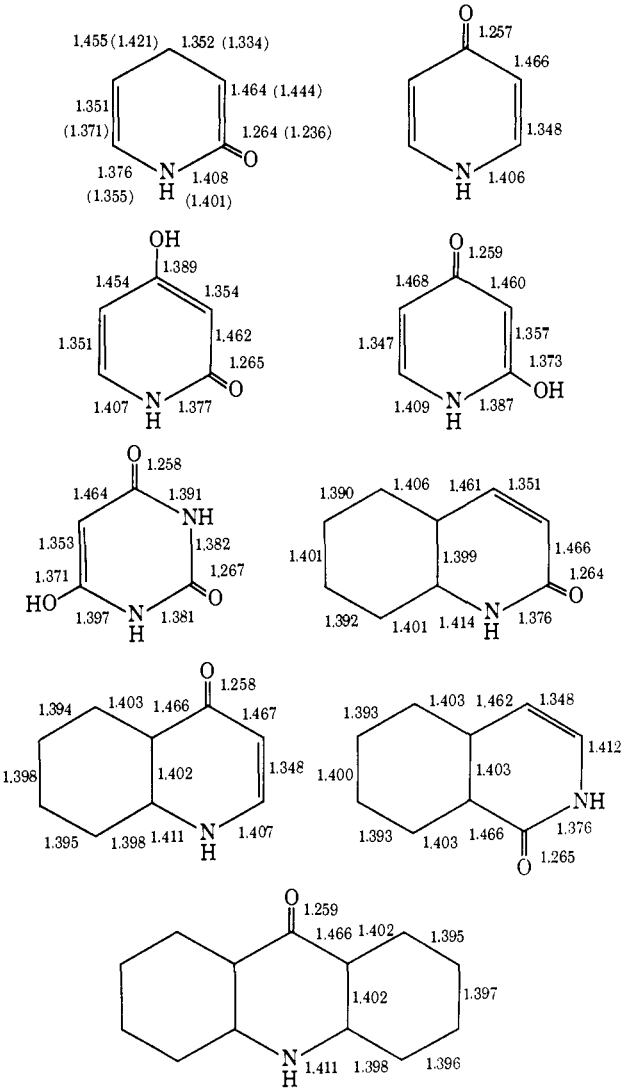


Figure 1. Calculated (observed) bond lengths (Å) in pyridones and related compounds.

expect, since in tautomers of the former type the aromaticity of the ring is not completely destroyed.

The calculations for amino compounds in Table II imply that these should all be stable with respect to tautomeric imines, although the margin of stability is quite small in the case of the aminofurans. The available evidence seems to support these predictions. Thus the ir spectrum of 2-amino-4-cyanopyrrole shows no bands characteristic of the imino group,[20] the uv spectrum of XXXa indicates that it exists exclusively as the diamine,[21] and detailed studies have shown aminotetrazole (XLVIa) to exist as such, both in the crystalline state and in solution.[22] On the other hand the chemical instability of the aminofurans seem to suggest that they undergo facile decomposition *via* the imino tautomers; for example, 2-aminofuran (XXXVIa) cannot be obtained by reduction of the corresponding nitro compound,[14] and 3-aminofuran (XXXVIIa) seems to exist in equilibrium with the corresponding imine (XXXVIIb) which may indeed predominate.[14]

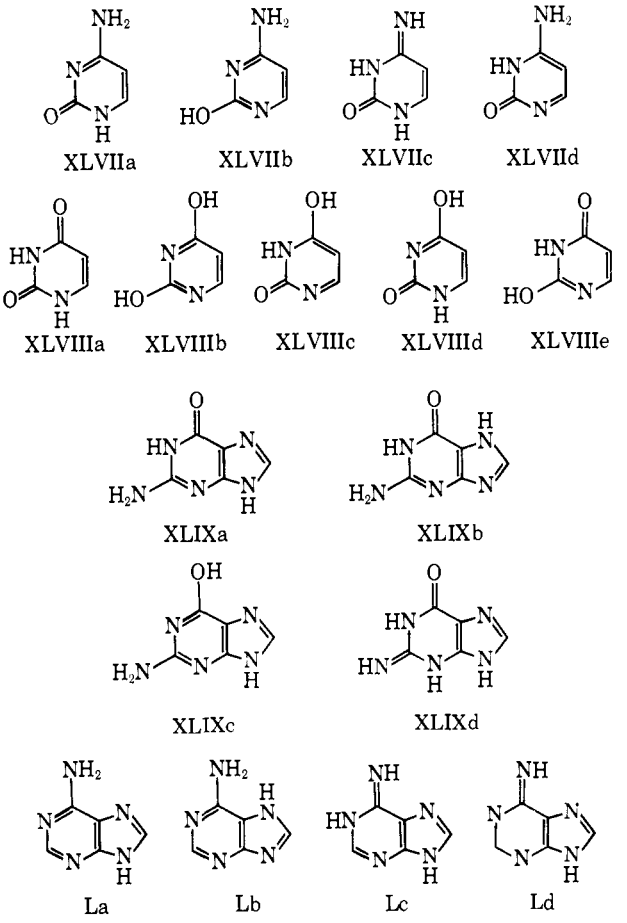
(20) C. A. Grob and H. Utzinger, *Helv. Chim. Acta*, 37, 1256 (1954).
(21) See ref 17.
(22) (a) D. B. Murphy and I. P. Picard, *J. Org. Chem.*, **19**, 1807 (1954); (b) V. P. Shchipanov, S. L. Portnova, V. A. Krasnova, Yu. N. Sheinker, and I. Ya. Postovskii, *Zh. Org. Khim.*, **1**, 2236 (1965).

The hydroxy derivatives on the other hand are all predicted to exist preferentially as ketonic tautomers; here again the available evidence supports our prediction. Thus 2-hydroxypyrrole seems[23] to exist as the lactam XXXIIb, while the 2- and 4-ethoxycarbonyl[24] and 5-carboxy[25] derivatives of XXXIII also seem to exist preferentially as the ketonic tautomers. The same is true of 2- and 3-hydroxyfurans,[21] all of which occur in ketonic forms (*e.g.*, XXXIVb and XXXVb).

Note that the preferred position of the double bond in the nonaromatic tautomers is predicted to be adjacent to the keto or imino group; this of course would be expected since the resonance energies of α,β-unsaturated ketones and imines are greater than those of vinyl ethers or amines.

Our procedure[5,6] automatically gives estimates of bond lengths; some values for pyridones and related compounds are shown in Figure 1. In the one case where experimental values are available[26] for comparison (*i.e.*, IVb) the agreement is reasonably satisfactory; the experimental values are shown in parentheses.

Having established the general validity of this treatment of tautomerism, we next applied it to the nucleotide bases XLVII–L. Calculations were carried out for uracil (XLVIII) rather than thymine (LI) since methyl groups cannot be included in our approximation and since the methyl group in LI should not significantly



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alter the equilibrium between the various tautomers. Calculations were carried out for the tautomers XLVIIa–d, XLVIIIa–e, XLIXa–d, and La–d; the corresponding heats of atomization are listed in Table III.

Table III. Heats of Atomization of Nucleotide Bases

Base	Heat of atomization of tautomer (a–e), eV a	b	c	d	e
Cytosine (XLVII)	59.707	59.503	59.612[a]	59.675	
Uracil (XLVIII)	57.601	56.151	56.568	56.310	56.826
Guanine (XLIX)	76.500	76.663	76.043	76.184	
Adenine (L)	71.322	71.302	70.391	70.185	

[a] Assuming that one ring NH is of amide type, the other of pyrrole type, since only one carbonyl group is present.

The results again imply that the bases should exist predominantly as lactams and amines rather than as hydroxy or imino derivatives, a conclusion which seems to be in agreement with the available chemical evidence. Thus while Blout and Fields[27] concluded on the basis of its ir spectrum that cytosine exists as XLVIIIb, subsequent studies by ir[28] and uv[29] spectroscopy and by X-ray crystallography[30] have shown that it in fact exists predominantly as XLVIIa, in agreement with our predictions. Recently Kokks, *et al.*,[31] concluded from its nmr spectrum that cytosine exists as a zwitterion in dimethyl sulfoxide, a conclusion severely criticized by Katritzky and Waring[32] and by Brown and Lyall[33] on the basis of ionization constants and uv spectral data.

In agreement with our calculations, uracil has been shown conclusively to exist predominantly as XLVIIIa by ir,[34] uv,[29,34] and X-ray[35] studies. An earlier investigation of uracil by Austin[36] has led to the conclusion that it exists predominantly as XLVIIIe, which is predicted by our calculations to be less stable than XLVIIIa by 17.8 kcal/mol.

Guanine has been shown by ir[28] and uv[37] spectroscopy and by X-ray crystallography[30] to exist predominantly in the keto-amino form. Our calculations confirm these experimental findings, predicting tautomeric exchange of hydrogen between the two imidazole nitrogens, with the 7-H tautomer being the more stable by 3.75 kcal/mol.

Ir[28], uv,[37] and X-ray[30] studies on adenine have shown it to exist in the amino form, 6-amino-9H-purine, in agreement with our prediction.

According to the Crick–Watson theory[4] of spontaneous mutations, these arise through one of the nucleotide bases being in an abnormal tautomeric form when DNA is being replicated. Given that one of the labile hydrogen atoms in each base is replaced by a sugar moiety, the tautomerism in question is that between XLVIIa and XLVIIc, XLVIIIa and XLVIIIc, XLIXa and XLIXc, or La and Lc. On this basis the results in Table I indicate that the ease with which the abnormal isomer should be formed is cytosine > guanine > adenine > uracil, the heat of isomerization being 2.2, 10.5, 21.5, and 23.8 kcal/mol, respectively. If therefore any reliance can be placed on these calculations, the tautomerism in question must be confined to cytosine. This conclusion had also been reached by the Pullmans and their collaborators[4,38] on the basis of MO calculations; however, the procedures used by them are known to give unsatisfactory estimates of heats of formation so the results reported here provide a much more reliable prediction. It should be added that the differences in heats of atomization between the isomers of XLVII–L cannot be used to estimate corresponding energy differences during replication since these must also involve contributions from hydrogen bonding to the conjugate base. Since cytosine and guanine in DNA are linked by three strong hydrogen bonds while adenine and thymine are linked only by two, the link between adenine and the abnormal form (XLVIIc) of cytosine, or thymine and the abnormal form (XLIXc) of guanine, should be weaker than that between the normal forms (XLVIIa and XLIXa) of cytosine and guanine. The difference in the energy of replication for the normal and abnormal forms of cytosine should therefore exceed that (2.2 kcal/mol) calculated for the isolated base by the energy of the additional hydrogen bond holding the bases together during normal replication. The rate of spontaneous mutation is about 10^{-4}–10^{-6} per nucleotide base per generation,[39] corresponding to a difference in free energy of 5–8 kcal/mol; the difference between this and the calculated difference in energy between XLVIIa and XLVIIc is just the expected contribution for an additional hydrogen bond.

Table IV compares calculated and observed bond lengths for the normal forms of the four bases. The agreement is reasonably good, given that the measurements refer to the crystal in which the molecules are linked by strong hydrogen bonds; these should alter

Table IV. Calculated (Observed)[a] Bond Lengths (Å) in Nucleotide Bases

Bond	XLVIIa	XLVIIIa	XLIX	La
1–2	1.380 (1.389)	1.379 (1.371)	1.383 (1.378)	1.350 (1.339)
2–3	1.398 (1.358)	1.386 (1.374)	1.314 (1.318)	1.333 (1.316)
3–4	1.310 (1.340)	1.390 (1.385)	1.394 (1.362)	1.364 (1.352)
4–5	1.456 (1.430)	1.470 (1.435)	1.373 (1.370)	1.393 (1.370)
5–6	1.352 (1.343)	1.346 (1.333)	1.459 (1.421)	1.419 (1.401)
1–6	1.403 (1.361)	1.414 (1.374)	1.391 (1.400)	1.344 (1.350)
2–7	1.266 (1.238)	1.265 (1.224)		
6–8	1.380 (1.337)	1.256 (1.233)		
5–7			1.379 (1.388)	1.389 (1.379)
7–8			1.300 (1.315)	1.298 (1.308)
8–9			1.375 (1.375)	1.380 (1.366)
4–9			1.386 (1.377)	1.387 (1.384)
2–11			1.377 (1.336)	
6–10			1.262 (1.232)	1.382 (1.334)

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Table V. π Electron Densities in Nucleotide Bases

Atom	XLVIIa	XLVIIc	XLVIIIa	XLVIIIc	XLIXa	XLIXc	La	Lc
1	1.834	1.849	1.852	1.420	1.822	1.550	1.516	1.843
2	0.602	0.675	0.682	0.613	0.720	0.565	0.539	0.706
3	1.447	1.835	1.824	1.791	1.478	1.566	1.512	1.386
4	0.671	0.778	0.669	0.821	0.927	0.758	0.780	0.967
5	1.100	1.034	1.047	1.120	1.083	1.175	1.150	1.033
6	0.884	0.966	0.950	0.631	0.653	0.583	0.650	0.750
7	1.560	1.553	1.529	1.549	1.317	1.325	1.344	1.335
8	1.889	1.311	1.448	1.980	0.826	0.817	0.801	0.813
9					1.792	1.815	1.810	1.788
10					1.507	1.972	1.898	1.380
11					1.876	1.876		

Table VI. Ionization Potentials and Electron Affinities of Nucleotide Bases

Compound	Ionization potential Vertical[a]	Ionization potential Adiabatic[b]	Electron affinity,[a] eV
XLVIIa	9.95	9.68	1.17
XLVIIc	10.61	10.15	1.20
XLVIIIa	11.27	10.90	1.33
XLVIIIc	9.24	8.82	−0.86
XLIXa	8.77	8.27	0.16
XLIXc	8.53	8.03	−0.66
La	8.91	8.46	0.12
Lc	8.72	8.36	0.39

[a] From Koopmans' theorem. [b] Calculated by the "half-electron" method.[41]

the geometry very significantly since they will facilitate mesomerism involving charge separation.[40] Note that the agreement is very good for the one compound (*i.e.*, adenine) where such hydrogen bonding should have relatively little effect.

Since hydrogen bonding plays such a fundamental role in nucleotide chemistry, and since the strengths of such hydrogen bonds depend on the formal charges of the atoms concerned, we are also listing (Table V) calculated π electron densities for the forms a and c of each base.

Two further properties of interest are the ionization potentials and electron affinities of the bases, since it has been suggested[4] that charge transfer processes involving them may be important. Table VI shows vertical ionization potentials and electron affinities, estimated from Koopmans' theorem, and adiabatic ionization potentials, calculated by the "half-electron" method,[41] for the normal (a) and abnormal (c) forms of each base.

The results in Table VI predict that ionization potential should fall along the series uracil > cytosine > adenine > guanine, in agreement with conclusions drawn from the charge transfer spectra of complexes formed by the bases with chloranil, bromanil, and *p*-benzoquinone in dimethyl sulfoxide.[42] The results in Table VI also imply that the pyrimidine bases should be better electron acceptors than the purines, again in agreement with the Pullmans and their collaborators.[43] It is true that our predicted order of decreasing electron affinity (uracil > cytosine > guanine > adenine) is not in agreement with the observed order of polarographic reduction potentials.[44] This, however, is not surprising since the reductions are irreversible processes involving species which are possibly protonated and certainly strongly hydrogen bonded to the solvent.

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