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Ab Initio Study of Energetics of Cationic Heteroconjugation in Pyridine *N*-Oxide and Its Derivatives Systems

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The energetics of formation of heterocomplexed cations formed by asymmetric O···H···O hydrogen bonding in systems of pyridine *N*-oxide and its derivatives was studied by means of restricted Hartree−Fock and Møller−Plesset ab initio calculations. The energy and Gibbs free energies of cationic heteroconjugation were calculated using the 6-31G* basis set in which a *d* polarization function is accounted for. The calculated energies, $\Delta E_{\mathrm{BHB}_1^+}$, and Gibbs free enthalpies, $\Delta G_{\mathrm{BHB}_1^+}$, of formation of the heterocomplexed cations in vacuo have been found to correlate very good with respective calculated energies and Gibbs free energies of protonation of both the proton acceptors (at a fixed pK_a value of the proton donor) and proton donors (at a fixed basicity of proton acceptor) and slightly worse with experimentally determined cationic heteroconjugation constants (expressed as log $K_{\mathrm{BHB}_1^+}$) determined on acetonitrile.

Introduction

A scheme of acid−base equilibria set up between acids (both molecular and cationic) and organic bases in nonaqueous media is very complicated and depends on the properties of the medium.[1−3] In systems consisting of pyridine *N*-oxide, its derivatives and cationic acids formed by protonation of the *N*-oxides in polar organic solvents, and particularly in polar aprotic ones, apart from the dissociation reactions of cationic acids BH^+ and BH_1^+, also equilibria of cationic homoconjugation[4−6] and heteroconjugation[7] with incomplete proton transfer are likely to occur. Conjugation processes occurring in the *homo* and *hetero* systems give rise to complexed cations with respectively symmetric and asymmetric hydrogen bonds (see an example of the structure of a heterocomplexed cation in Figure 1). These equilibria, nonobservable in aqueous solutions, are set up owing to strong differentiating properties and usually weak acid−base properties of these solvents.[4]

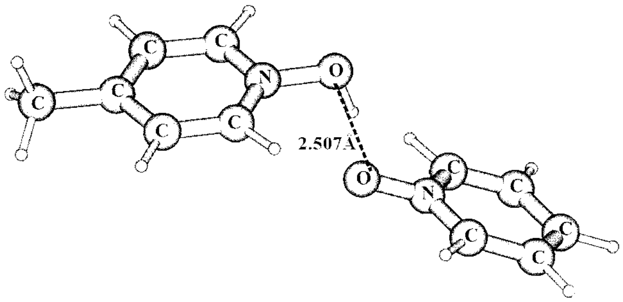

Figure 1. Example structure of heteroconjugated cation of (4PicO-HPyO)$^+$.

Acid dissociation, as well as homo- and heteroconjugation equilibria can be expressed as follows:

$$BH^+ \rightleftarrows B + H^+ \tag{1}$$

$$B_1H^+ \rightleftarrows B_1 + H^+ \tag{2}$$

$$BH^+ + B \rightleftarrows BHB^+ \tag{3}$$

$$B_1H^+ + B_1 \rightleftarrows B_1HB_1^+ \tag{4}$$

$$BH^+ + B_1 \rightleftarrows BHB_1^+ \tag{5}$$

where B and B_1 denote base molecules (pyridine *N*-oxide or its substituted derivatives), BH^+ and B_1H^+ are the protonated bases B and B_1, and BHB^+ and $B_1HB_1^+$ are homocomplexed and BHB_1^+ heterocomplexed (stabilized by asymmetric hydrogen bond) cations. As seen from eqs 3 and 4, cationic homoconjugation is a reaction whereby a cationic acid BH^+ (B_1H^+) reacts with the conjugate base B (B_1) to give a symmetric complex hydrogen-bonded ion BHB^+. Cationic heteroconjugation (eq 5) consists of a reaction of the cationic acid BH^+ with base B_1 to form an asymmetric complex ion BHB_1 held together by hydrogen bonding. Depending on the proton-donor properties of the reactants, either symmetric or asymmetric hydrogen bonds can be formed.

The corresponding equilibrium constants—acid dissociation (K_{BH^+} and $K_{\mathrm{BH}_1^+}$), cationic homoconjugation (K_{BHB^+} and $K_{\mathrm{B_1HB}_1^+}$), and heteroconjugation ($K_{\mathrm{BHB}_1^+}$)—are defined by eqs 6−10, respectively:

$$K_{\mathrm{BH}^+} = \frac{[B][H^+]}{[BH^+]} \tag{6}$$

$$K_{\mathrm{B_1H}^+} = \frac{[B_1][H^+]}{[B_1H^+]} \tag{7}$$

$$K_{\mathrm{BHB}^+} = \frac{[BHB^+]}{[B][BH^+]} \tag{8}$$

$$K_{\mathrm{B_1HB}_1^+} = \frac{[B_1HB_1^+]}{[B_1][B_1H^+]} \tag{9}$$

$$K_{\mathrm{BHB}_1^+} = \frac{[BHB_1^+]}{[B_1][BH^+]} \tag{10}$$

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Acid−base equilibria in nonaqueous media involving substituted pyridine *N*-oxides have been systematically studied by our research group.[5−14,16−18] Consequently, the acidity (pK_a) and cationic homoconjugation constants for a number of pyridine *N*-oxide derivatives in such polar nonaqueous solvents as acetone,[8] acetonitrile,[5,6] benzonitrile,[9] dimethylformamide,[10] dimethyl sulfoxide,[10] methanol,[11] nitromethane,[12] nitrobenzene,[13] and propylene carbonate[14] were determined. To check whether the experimentally determined values of the above-mentioned constants change in the same direction as values predicted on theoretical basis, the protonation and cationic homoconjugation energies and Gibbs free energies in vacuo were also calculated using ab initio methods.[15] It was found that the experimental values correlate well with those computed by theoretical methods.[15]

Recently, our interest was focused on cationic heteroconjugation equilibria taking place in polar aprotic solvents. Relevant studies carried out in acetonitrile,[16] acetone,[7] nitrobenzene,[17] and propylene carbonate[18] revealed the intricate nature of these equilibria. The results of these studies have shown that the values of the cationic homoconjugation constants depends, among other things, on the basicity of the proton donor and proton acceptor, as well as on concurrent cationic homoconjugation equilibria set up in particular acid−base systems.[16] Hence, the principal objective of this contribution was theoretical verification of the experimental results. Thus, by using the ab initio method, the energies ($\Delta E_{\mathrm{BHB}_1^+}$(RHF, MP2)) and Gibbs free energies ($\Delta G_{\mathrm{BHB}_1^+}$(RHF)) of formation of heterocomplexed cations in the gas phase were calculated and an attempt has been made to correlate the results with calculated basicities (expressed in terms of ΔE_{prot}(RHF, MP2) and ΔG_{prot}(RHF)) of proton donors and with experimental cationic heteroconjugation constants (log $K_{\mathrm{BHB}_1^+}$) in acetonitrile (AN) representing the class of polar nonaqueous solvents. In the next computational step, solvation effects were estimated by using a self-consistent reaction field (SCRF) model.

The systems for which the ab initio calculations were performed were selected based on experimentally determined pK_a and log $K_{\mathrm{BHB}_1^+}$ values of pyridine *N*-oxide derivatives in previously studied nonaqueous media.[5−14,16−18] The selected systems constitute classes with a fixed proton donor (BH^+) and a number of proton acceptors (B). The proton acceptors selected were those pyridine *N*-oxides which were weaker bases than the corresponding *N*-oxides whose protonated forms acted as proton donors. In other words, protonated acceptors had to exhibit lower pK_a values in acetonitrile than protonated *N*-oxides acting as proton donors. Satisfying this condition ensures that the composed acid−base systems were without the proton transfer. This is important, because, as it was found previously,[7] the proton-transfer reactions restrict, and in some cases even preclude, determination of correct values of the cationic heteroconjugation constants. From this point of view, it is mandatory to determine the constants in systems without proton transfer. Just under these experimental conditions were determined equilibrium constants used in this work.

As a consequence of ensuring these conditions, in the first class involving 4-*N′*,*N′*-(dimethylamino)pyridine *N*-oxide (4NMe$_2$PyOH$^+$) as a protonated compound, the following substituted pyridine *N*-oxides were used as proton acceptors: 2,6-dimethyl-4-methoxypyridine *N*-oxide (Me$_2$MeOPyO), 4-methoxypyridine *N*-oxide (4MeOPyO), 4-methylpyridine *N*-oxide (4PicO), 3-methylpyridine *N*-oxide (3PicO), 2-methylpyridine *N*-oxide (2PicO), pyridine *N*-oxide (PyO), and 4-nitropyridine *N*-oxide (4NO$_2$PyO). In the second class, 2,6-dimethyl-4-methoxypyridine *N*-oxide (Me$_2$MeOPyOH$^+$) was the proton donor, and the proton acceptors were 4MeOPyO, 4PicO, 3PicO, 2PicO, PyO, and 4NO$_2$PyO. In the third class, with protonated 4-methoxypyridine *N*-oxide (4MeOPyOH$^+$), 4PicO, 3PicO, 2PicO, PyO, and 4NO$_2$PyO were the proton acceptors. In the fourth class, with protonated 4-methylpyridine *N*-oxide as the proton donor, 3PicO, 2PicO, PyO, and 4NO$_2$PyO were proton acceptors, and in the fifth class, with protonated 3-methylpyridine *N*-oxide (3PicOH$^+$), only 2PicO, PyO, and 4NO$_2$PyO were the proton acceptors. Only these five representative classes of compounds underwent correlation analyses, because the remaining ones had an insufficient number of proton acceptors. For instance, in the class with protonated 2-methylpyridine *N*-oxide (2PicOH$^+$), only PyO and 4NO$_2$PyO were the proton acceptors, and with protonated pyridine *N*-oxide (PyOH$^+$), only 4NO$_2$PyO could act as the proton acceptor.

For the sake of comparison, calculations were accomplished also for one system with proton transfer, namely, that of 4NO$_2$PyOH$^+$/PyO. This is just a reverse system relative to that without proton transfer, namely, PyOH$^+$/4NO$_2$PyO.

Methods

Because it is recommended to employ optimized structures, especially in the case of gas-phase calculation of acid−base reactions,[19] optimization of the heterocomplexed systems was carried out at the RHF level using a GAMESS program[20] to an energy gradient of 0.0001 au/bohr (approximately 0.1 kcal mol^{-1}Å^{-1}). Geometric parameters corresponding to the lowest energy were considered as final ones. The 6-31G* basis set was used for the calculations. In this basis, *d*-type functions are included in orbitals of the *L* shell. This function, referred to as the polarization function, enables us to describe precisely the geometry of the systems, in particular those involving bonds between electronegative atoms, for instance, N−O. To express the energy of the systems more completely, translational, rotational, and vibrational contributions of particular species should be recognized. To do this, respective energy Hessians were calculated.

In view of the complexity of the systems considered and nonconvergence of the energy gradient, optimization at the MP2 level was impossible. However, to further improve the calculated electronic energies,[21] the dynamic correlation effect was calculated by single iteration for structures optimized at the RHF level.

The evaluation of the solvation contributions to the energy was performed by using the self-consistent reaction field (SCRF) model.[22−26] The SCRF model considers the solvent as a uniform polarizable medium with the solute molecule placed in a spherical cavity of a given radius prepared within the continuum, i.e., immersed in the dielectric of a fixed electric permeability corresponding to particular solvent. The radius of the cavity was assumed as a half of the largest interatomic distance in the molecule plus 1 Å, as recommended by the reported procedure.[24] The value of the relative permeability constants of acetonitrile adopted for calculations was[27] 35.94. In this model, the electric charge distribution of solute polarizes the medium (induce charge moments), which in turn acts back on the species, thereby creating an electrostatic stabilization. The solvation free energy can thus be[28] written as: $\Delta G_{\mathrm{solvation}} = \Delta G_{\mathrm{cavity}} + \Delta G_{\mathrm{dispertion}} + \Delta G_{\mathrm{electrostatic}}$.

The energy of formation of heterocomplexed cations, $\Delta E_{\mathrm{BHB}_1^+}$, was calculated as follows:

$$\Delta E_{\mathrm{BHB}_1^+} = E_{\mathrm{BHB}_1^+} - [E_{\mathrm{BH}^+} + E_{\mathrm{B}_1}] \qquad (11)$$

TABLE 1: Selected Geometric Parameters of Heterocomplexed Cations Formed in Systems with Substituted Pyridine *N*-Oxides (Bond Lengths in Å, Angles between Bonds in Degrees) Calculated in the 6-31G* Basis Set

BH^+/B_1 system	d(O···O)	d(O−H)	$d(N-O)^a$	$d(N-O)^b$	$d(N-O)^c$	$\Delta d(N-O)^b$	$(<CNC)^a$	$(<CNC)^b$	$<N^aONb$
$4NMe_2PyOH^+/Me_2MeOPyO$	2.529	1.000	1.351	1.329	1.303	0.026	121.30	121.88	115.21
$4NMe_2PyOH^+/4MeOPyO$	2.537	0.999	1.351	1.325	1.29^d	0.035	121.20	120.10	116.91
$4NMe_2PyOH^+/4PicO$	2.552	0.996	1.351	1.317	1.28^d	0.037	121.19	120.34	116.84
$4NMe_2PyOH^+/3PicO$	2.560	0.993	1.351	1.314	1.27^d	0.047	121.20	121.10	116.50
$4NMe_2PyOH^+/2PicO$	2.560	0.993	1.351	1.316	1.28^d	0.036	121.21	121.77	114.29
$4NMe_2PyOH^+/PyO$	2.562	0.994	1.351	1.314	1.28^d	0.034	121.18	120.90	119.26
$4NMe_2PyOH^+/4NO_2PyO$	2.621	0.982	1.352	1.299	1.25^d	0.049	121.34	121.04	119.23
$Me_2MeOPyOH^+/4MeOPyO$	2.545	0.998	1.352	1.326	1.29^d	0.036	123.77	120.08	117.54
$Me_2MeOPyOH^+/4PicO$	2.560	0.995	1.352	1.319	1.28^d	0.039	123.78	120.30	117.02
$Me_2MeOPyOH^+/3PicO$	2.570	0.991	1.353	1.314	1.27^d	0.044	123.80	121.03	114.64
$Me_2MeOPyOH^+/2PicO$	2.562	0.993	1.352	1.317	1.28^d	0.037	123.80	121.80	115.19
$Me_2MeOPyOH^+/PyO$	2.574	0.991	1.353	1.314	1.28^d	0.034	123.77	120.80	116.18
$Me_2MeOPyOH^+/4NO_2PyO$	2.623	0.979	1.354	1.299	1.25^d	0.049	123.94	121.05	114.16
$4MeOPyOH^+/4PicO$	2.535	1.003	1.350	1.328	1.28^d	0.048	122.15	120.44	113.63
$4MeOPyOH^+/3PicO$	2.527	0.997	1.350	1.319	1.27^d	0.049	122.07	120.45	115.69
$4MeOPyOH^+/2PicO$	2.530	1.003	1.350	1.319	1.28^d	0.039	122.02	121.89	117.15
$4MeOPyOH^+/PyO$	2.540	0.998	1.350	1.315	1.28^d	0.035	122.06	120.97	115.22
$4MeOPyOH^+/4NO_2P_yO$	2.591	0.985	1.351	1.301	1.25^d	0.051	122.19	121.15	114.77
$4PicOH^+/3PicO$	2.533	1.000	1.348	1.316	1.27^d	0.046	122.59	121.30	115.49
$4PicOH^+/2PicO$	2.517	1.008	1.347	1.320	1.28^d	0.040	122.44	121.93	117.21
$4PicOH^+/PyO$	2.507	1.003	1.348	1.318	1.28^d	0.038	123.28	121.11	116.07
$4PicOH^+/4NO_2P_yO$	2.580	0.989	1.349	1.302	1.25^d	0.052	122.58	121.16	114.62
$3PicOH^+/2PicO$	2.513	1.010	1.347	1.320	1.28^d	0.040	123.31	121.93	117.29
$3PicOH^+/PyO$	2.521	1.006	1.347	1.312	1.28^d	0.032	123.36	121.04	116.31
$3PicOH^+/4NO_2P_yO$	2.574	0.981	1.349	1.303	1.25^d	0.053	123.47	121.17	116.24
$2PicOH^+/PyO$	2.543	1.000	1.349	1.316	1.28^d	0.036	124.03	120.97	117.48
$2PicOH^+/4NO_2P_yO$	2.595	0.987	1.350	1.303	1.25^d	0.053	124.14	121.14	114.97
$PyOH^+/4NO_2P_yO$	2.568	0.991	1.348	1.303	1.25^d	0.053	123.24	121.20	113.95
$4NO_2PyOH^+/PyO$ (PT)	2.473	1.025	1.342	1.320	1.28^d	0.040	123.35	121.21	116.17

[a] Proton donor. [b] Proton acceptor. [c] Data for neutral *N*-oxide. [d] Reference 15.

where $E_{BHB_1^+}$ is the energy of heterocomplexed cation, E_{BH^+} is the energy of the proton donor, and E_{B_1} is the energy of the proton acceptor.

The Gibbs free energy of heteroconjugation, $G_{BHB_1^+}$, was calculated from the following expression:

$$\Delta G_{BHB_1^+} = E_{BHB_1^+} + E^o_{vib,BHB_1^+} + p\Delta V_{BHB_1^+} - T\Big[(S_{vib,BHB_1^+} + S_{rot,BHB_1^+}) - (S_{vib,BH^+} + S_{rot,BH^+} + S_{vib,B} + S_{rot,B}) - \frac{3}{2}R\Big] \quad (12)$$

where E^o_{vib,BHB_1^+} is the difference between the zero-point vibrational energies of the product and the reactant, p is the pressure, V is the volume of the system, S_{rot} and S_{vib} are, respectively, the rotational and vibrational entropies, and the $^3/_2R$ term refers to translational degrees of freedom of the system. A temperature of 298 K and a pressure of 1 atm were assumed for all calculations.

Results and Discussion

Selected calculated geometric parameters of the heterocomplexed cations of pyridine *N*-oxide derivatives calculated at the RHF level with the 6-31G* basis set are summarized in Table 1. As seen, the O···O bond length between the proton donor (cationic acid BH^+) and proton acceptor (base B_1) constituting the heterocomplexed cations in systems without proton transfer range from 2.507 to 2.623 Å. The bond elongates when ΔpK_a between the proton donor and acceptor increases. This is accompanied by the shortening of the O−H bond (from 1.000 to 0.979 Å). On the other hand, the N−O bond lengths for the proton donor oscillate around 1.35 Å (cf. Table 1). They become slightly elongated with $4NO_2PyO$ as the proton acceptor owing to strong electron attracting nature of the nitro group. Substituents in the remaining pyridine *N*-oxide derivatives donate electrons to the pyridine ring to produce the so-called positive inductive effect. In similar terms, i.e., by virtue of the negative induction effect of the nitro group, the shortening of the N−O bond in the nitro-substituted *N*-oxide can be explained when looking at the N−O bond of the proton acceptor. As expected, the bond is shorter (1.299−1.329 Å; Table 1) than that in the proton donors and it elongates with increasing proton-donor capacity of the ring substituent (i.e., with increasing basicity of the proton acceptor). Again, the gain in length of the N−O bond of the proton acceptor relative to the length of the bond in free *N*-oxide tends to decrease with increasing basicity of the acceptor down to limiting values of 0.053 Å for the least basic $4NO_2PyO$ and 0.026 Å for the most basic $4NMe_2PyO$.

The C−N−C bond angles of the pyridine ring are roughly equal for both the proton donor and acceptor, though for some systems, e.g., those involving $Me_2MeOPyOH^+$ and $4MeOPyOH^+$ as the proton donors, the angles are by 2−3° larger for the donors than for the acceptors. The values of this geometric parameter oscillate around 120°, this corresponding to sp^2 hybridization and the planar structure of this fragment of the system. The angles are slightly larger for the proton donors (Table 1). A comparison of the O···O and N−O bond lengths and the C−N−C angles with experimental ones for homocomplexed cations[15] shows that inclusion of the polarization function in ab initio calculations (the 6-31G* basis set) depicts reasonably well the geometry of the systems, in particular the bond lengths between such polar atoms as those of nitrogen and oxygen. The differences in geometric parameters among particular heterocomplexed cations are due to the occurrence of different substituents in the heterocyclic ring. The calculations also show that the rings of cationic acid BH^+ and base B_1 in systems linked with the O···H···O bridge are not coplanar.

In the proton-transfer system, $4NO_2PyOH^+/PyO$, there is a considerable, relative to the reverse system of $PyOH^+/4NO_2PyO$ without proton transfer, shortening of the O···O bond (by

TABLE 2: Energies of Formation of Heterocomplexed Cations Calculated at the RHF ($\Delta E_{\mathrm{BHB}_1^+}$(RHF)) and MP2 ($\Delta E_{\mathrm{BHB}_1^+}$(MP2)) Levels, Those Calculated with Accounting for Solvations Effects ($\Delta E_{\mathrm{BHB}_1^+}$(SCRF)) and Gibbs Free Energies of the Process Calculated at the RHF Level ($\Delta E_{\mathrm{BHB}_1^+}$(RHF)) in kcal/mol[a]

$\mathrm{BH^+/B_1}$ system	$\Delta E_{\mathrm{BHB}_1^+}$ (RHF)	$\Delta G_{\mathrm{BHB}_1^+}$ (RHF)	$\Delta E_{\mathrm{BHB}_1^+}$ (MP2)	$\Delta E_{\mathrm{BHB}_1^+}$ (SCRF)	ΔE_{prot} (RHF)	ΔG_{prot} (RHF)	ΔE_{prot} (MP2)	$\mathrm{p}K_{\mathrm{a}}^{\mathrm{AN}}$	$\log K_{\mathrm{BHB}_1^+}$
$\mathrm{4NMe_2PyOH^+/Me_2MeOPyO}$	−31.14	−22.58	−36.08	−13.62	−255.66	−246.88	−240.87	12.78	
$\mathrm{4NMe_2PyOH^+/4MeOPyO}$	−30.13	−21.55	−32.92	*b*	-250.38^{c}	-241.75^{c}	-236.37^{c}	12.21	
$\mathrm{4NMe_2PyOH^+/4Pic_O}$	−28.55	−22.15	−30.51	−7.22	-245.71^{c}	-237.31^{c}	-230.96^{c}	11.00	2.63
$\mathrm{4NMe_2PyOH^+/3PicO}$	−28.19	−19.97	−29.95	−7.40	-243.61^{c}	-235.50^{c}	-229.81^{c}	10.31	2.00
$\mathrm{4NMe_2PyOH^+/2PicO}$	−27.92	−15.66	−34.40	−10.68	-243.70^{c}	-235.40^{c}	-228.60^{c}	10.23	1.71
$\mathrm{4NMe_2PyOH^+/PyO}$	−27.92	−15.57	−28.77	−8.96	-241.24^{c}	-232.94^{c}	-226.76^{c}	10.04	*d*
$\mathrm{4NMe_2PyOH^+/4NO_2PyO}$	−18.71	−8.06	−20.34	−6.87	-223.38^{c}	-215.46^{c}	-211.10^{c}	5.64	
$\mathrm{Me_2MeOPyOH^+/4MeOPyO}$	−31.78	−22.32	−36.10	−27.07	-250.38^{c}	-241.75^{c}	-236.37^{c}	12.21	
$\mathrm{Me_2MeOPyOH^+/4PicO}$	−30.50	−20.29	−33.59	−23.08	-245.71^{c}	-237.31^{c}	-230.96^{c}	11.00	3.16
$\mathrm{Me_2MeOPyOH^+/3PicO}$	−29.48	−18.80	−33.03	−23.89	-243.61^{c}	-235.50^{c}	-229.81^{c}	10.31	2.77
$\mathrm{Me_2MeOPyOH^+/2PicO}$	−28.08	−18.41	−37.47	−26.56	-243.70^{c}	-235.40^{c}	-228.60^{c}	10.23	2.47
$\mathrm{Me_2MeOPyOH^+/PyO}$	−28.72	−18.04	−31.64	−25.22	-241.24^{c}	-232.94^{c}	-226.76^{c}	10.04	1.85
$\mathrm{Me_2MeOPyOH^+/4NO_2PyO}$	−19.97	−8.82	−22.96	−23.23	-223.38^{c}	-215.46^{c}	-211.10^{c}	5.64	
$\mathrm{4MeOPyOH^+/4PicO}$	−31.77	−20.76	−34.13	−11.15	-245.71^{c}	-237.31^{c}	-230.96^{c}	11.00	
$\mathrm{4MeOPyOH^+/3PicO}$	−32.47	−19.68	−33.06	−11.15	-243.61^{c}	-235.50^{c}	-229.81^{c}	10.31	
$\mathrm{4MeOPyOH^+/2PicO}$	−29.97	−18.89	−37.51	−14.04	-243.70^{c}	-235.40^{c}	-228.60^{c}	10.23	
$\mathrm{4MeOPyOH^+/PyO}$	−30.50	−17.73	−31.71	−12.96	-241.24^{c}	-232.94^{c}	-226.76^{c}	10.04	
$\mathrm{4MeOPyOH^+/4NO_2PyO}$	−20.74	−9.76	−22.91	*b*	-223.38^{c}	-215.46^{c}	-211.10^{c}	5.64	
$\mathrm{4PicOH^+/3PicO}$	−31.60	−22.73	−35.32	−5.90	-243.61^{c}	-235.50^{c}	-229.81^{c}	10.31	3.60
$\mathrm{4PicOH^+/2PicO}$	−31.25	−21.44	−38.71	−8.79	-243.70^{c}	-235.40^{c}	-228.60^{c}	10.23	3.44
$\mathrm{4PicOH^+/PyO}$	−31.02	−20.78	−33.00	−7.60	-241.24^{c}	-232.94^{c}	-226.76^{c}	10.04	3.35
$\mathrm{4PicOH^+/4NO_2PyO}$	−20.68	−11.92	−23.68	−5.00	-223.38^{c}	-215.46^{c}	-211.10^{c}	5.64	*d*
$\mathrm{3PicOH^+/2PicO}$	−30.78	−21.53	−39.00		−243.71	−235.40	−228.60	10.23	*d*
$\mathrm{3PicOH^+/PyO}$	−31.45	−21.44	−33.26		−241.24	−232.94	−226.76	10.04	*d*
$\mathrm{3PicOH^+/4NO_2PyO}$	−22.53	−10.31	−23.89		−223.38	−215.46	−211.10	5.64	1.32
$\mathrm{2PicOH^+/PyO}$	−31.40	−20.07	−34.45		−241.24	−232.94	−226.76	10.04	3.54
$\mathrm{2PicOH^+/4NO_2PyO}$	−21.96	−10.84	−24.79		−223.38	−215.46	−211.10	5.64	1.77
$\mathrm{PyOH^+/4NO_2PyO}$	−23.30	−11.34	−24.59		−223.38	−215.46	−211.10	5.64	*d*
$\mathrm{4NO_2PyOH^+/PyO}$ (PT)	−35.88	−27.39	−37.61		−241.24	−232.94	−226.76	10.04	
	-18.02^{e}	-9.91^{e}	-21.95^{e}						

[a] For comparison, also calculated ΔE_{prot}(RHF), ΔG_{prot}(RHF), and ΔE_{prot}(MP2) values are included as well as those of pK_{a} of proton acceptor (ref 6) and log $K_{\mathrm{BHB}_1^+}$ (ref 16) in acetonitrile. [b] Indeterminable quantity. [c] Reference 15. [d] The cationic heteroconjugation constant could not be determined from potentiometric measurements. [e] Energies (RHF and MP2) and free enthalpy (RHF) of formation of the hetereocomplexed cation (in the system without proton transfer) as calculated from eqs 68 and 69, respectively.

0.095 Å) and only a slight shortening of the N−O bond of the proton donor (by 0.006 Å) with accompanying elongation of the O−H (0.034 Å) and N−O bonds (0.017 Å) of the proton acceptor.

Table 2 summarizes calculated energies and Gibbs free energies of formation of the heterocomplexed cations ($\Delta E_{\mathrm{BHB}_1^+}$ and $\Delta G_{\mathrm{BHB}_1^+}$) at the RHF level, the energies of formation at the MP2 ($\Delta E_{\mathrm{BHB}_1^+}$) level, energies corrected for solvation effects (SCRF), experimental pK_{a} values for proton acceptors, and log $K_{\mathrm{BHB}_1^+}$ (logarithms of the formation constants of heterocomplexes) in acetonitrile. A comparison of the calculated energies and free energies at the RHF level shows that $\Delta G_{\mathrm{BHB}_1^+}$(RHF) is greater than $\Delta E_{\mathrm{BHB}_1^+}$(RHF) by almost a constant increment of approximately 10 kcal/mol for all of the chemical species considered. On the other hand, a comparison of the formation energies of the heterocomplexed cations at particular levels shows that the energies decline on moving from the RHF level to the MP2 level. Thus, $\Delta E_{\mathrm{BHB}_1^+}$(MP2) is the lowest energy at all. This can be explained in terms of considering electronic correlation in the Møller−Plesset perturbation theory. On the contrary, accounting for solvation effects contributes, as expected, to an increase in energy ($\Delta E_{\mathrm{BHB}_1^+}$(SCRF)) of formation of the heterocomplexes.

The calculated energies of formation of the heterocomplexes, at both the RHF and MP2 levels, and the free energies of the process calculated at the RHF level were correlated for each class of the pyridine *N*-oxide derivatives with fixed proton donor with the previously calculated[15] energies and Gibbs free protonation energies of the *N*-oxides acting as proton acceptors. These correlations seem worthwhile, because experiments carried out in nonaqueous media revealed the mounting tendency toward cationic heteroconjugation with increasing basicity of proton donors (at a fixed p$K_{\mathrm{a}}^{\mathrm{AN}}$ of the proton donor).[16] The calculation supported that conclusion by demonstrating that both the values calculated at the RHF level ($\Delta E_{\mathrm{BHB}_1^+}$(RHF) and $\Delta G_{\mathrm{BHB}_1^+}$(RHF) and at the MP2 level ($\Delta E_{\mathrm{BHB}_1^+}$(MP2)) can be presented as linear functions of respectively ΔE_{prot}, ΔG_{prot}, and ΔE_{prot}(MP2) of proton acceptor (at a fixed basicity of proton acceptor). The parameters *a* (the slope), *b* (the intercept), *R* (the correlation coefficient), and *σ* (the standard error of correlation) of these correlations together with the values of standard deviation of parameters *a* and *b* are listed in Table 3. Inspection of these parameters reveals good correlations between energies of formation of the heterocomplexes and the above-mentioned energetic parameters of proton acceptors. It is worth emphasizing that in all equations the values of the correlation coefficient, *R*, are close to unity, ranging from 0.978 to 0.996. The large values of the intercept in the correlations can be explained by the fact that the tendency toward heteroconjugation is not a simple function of protonation energy (pK_{a} value) of the proton acceptor or proton donor. For example, in nonaqueous solutions this tendency depends on the difference in the basicity of the proton donor and proton acceptor, ΔpK_{a}, and the arithmetic average of the logarithms of homoconjugation constants as a measure of the tendency of a proton donor and proton acceptor to form hydrogen bonds, as it has already been proven.[29] Figure 2 shows an example of the relationship between $\Delta E_{\mathrm{BHB}_1^+}$(RHF) and

TABLE 3: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between the Calculated $\Delta E_{BHB_1^+}$(RHF), $\Delta G_{BHB_1^+}$(RHF), and $\Delta E_{BHB_1^+}$(MP2) Values and Respectively Calculated ΔE_{prot}, ΔG_{prot}, and ΔE_{prot} (MP2) Values of Proton Acceptors (for a Fixed Proton Donor)[a]

proton donor	$\Delta E_{BHB_1^+}$(RHF)			$\Delta G_{BHB_1^+}$(RHF)			$\Delta E_{BHB_1^+}$(MP2)[b]			$\Delta E_{BHB_1^+}$(MP2)[c]		
	a	*b*	*R* *σ*	*a*	*b*	*R* α	*a*	*b*	*R* *σ*	*a*	*b*	*R* *σ*
$4NMe_2PyOH^+$	0.395	69	0.978	0.497	99	0.930	0.510	87	0.928	0.516	89	0.998
	(0.038)	(9)	0.931	(0.088)	(21)	2.107	(0.091)	(21)	2.095	(0.015)	(3)	0.347
$Me_2MeOPyOH^+$	0.444	79	0.988	0.511	101	0.997	0.544	91	0.911	0.526	88	0.999
	(0.035)	(8)	0.719	(0.019)	(4)	0.387	(0.123)	(28)	2.362	(0.013)	(3)	0.262
$4MeOPyOH^+$	0.510	93	0.979	0.486	95	0.995	0.614	106	0.920	0.556	94	0.999
	(0.061)	(15)	1.121	(0.027)	(6)	0.488	(0.151)	(34)	2.460	(0.014)	(3)	0.228
$4PicOH^+$	0.540	100	0.996	0.508	98	0.994	0.699	124	0.948	0.613	106	0.999
	(0.033)	(8)	0.559	(0.037)	(6)	0.620	(0.165)	(37)	2.502	(0.023)	(5)	0.322
$3PicOH^+$	0.441	76	0.984	0.590	117	0.994	0.760	137	0.958			
	(0.080)	(19)	1.248	(0.063)	(14)	0.969	(0.227)	(50)	3.084			

[a] Values of standard deviations of *a* and *b* in parentheses. [b] Including 2PicO as the proton acceptor. [c] After removing 2PicO.

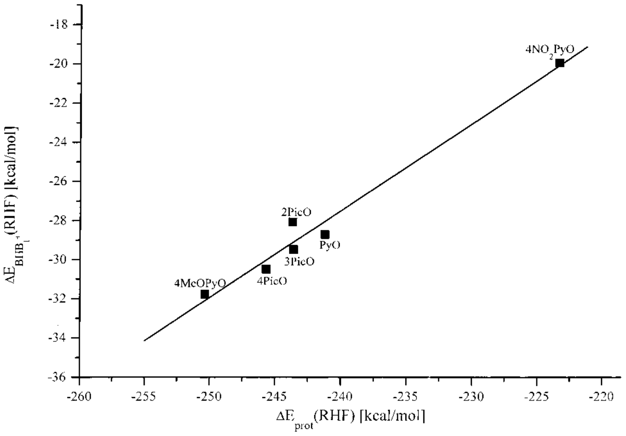

Figure 2. Plot of $\Delta E_{BHB_1^+}$(RHF) against ΔE_{prot}(RHF) of proton acceptors in the case of $Me_2MeOPyOH^+$ as the proton donor. Abbreviations for proton acceptors are given in the graph.

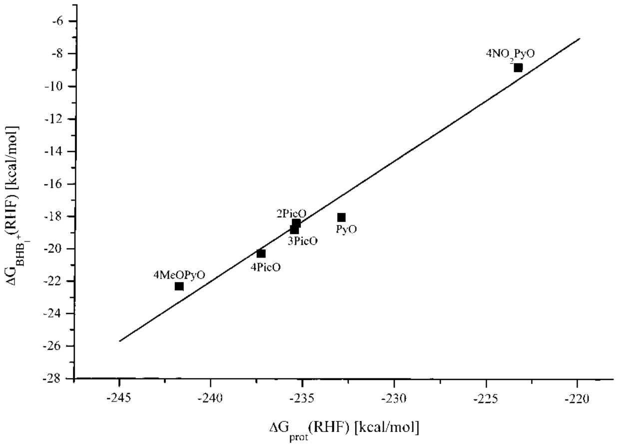

Figure 3. Plot of $\Delta E_{BHB_1^+}$(RHF) against ΔG_{prot}(RHF) of proton acceptors in the case of $Me_2MeOPyOH^+$ as the proton donor. Abbreviations for proton acceptors are given in the graph.

ΔE_{prot}(RHF) of proton acceptors for $Me_2MeOPyOH^+$ as the proton donor.

As in the case of the energies, also very good correlations (with the exception of systems involving $4NMe_2PyOH^+$ as the proton donor) were obtained for Gibbs free energies at the RHF level (see Table 3). It is worth noting that the correlation coefficients for the majority of these correlations are close to unity, ranging from 0.994 to 0.997, with the exception of systems with $4NMe_2PyOH^+$ as the proton donor where *R* is 0.930. This low correlation coefficient is due to the distinct deviation from linearity of the $\Delta G_{BHB_1^+}$ variations in systems involving 4PicO as the proton acceptor. In Figure 3 an exemplary relationship is presented between $\Delta G_{BHB_1^+}$(RHF) and ΔG_{prot} for proton acceptors with $Me_2MeOPyOH^+$ as the proton donor.

As mentioned, the $\Delta E_{BHB_1^+}$(MP2) values can also be linearly correlated with those of ΔE_{prot}(MP2) of proton acceptors. The obtained relationships are characterized by moderate correlation coefficients (ranging from 0.911 to 0.958), whereas slopes *a* and intercepts *b* are burdened with relatively large standard deviations (Table 3). However, a careful scrutiny of these relationships shows that in the considered series of proton donors, i.e., $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, $4MeOPyOH^+$, $4PicOH^+$, and $3PicOH^+$, significant deviations from linearity occur for systems containing 2PicO as the acceptor, this affecting parameters of straight line equations such as that of $\Delta E_{BHB_1^+}$(MP2) vs ΔE_{prot}(MP2) for proton acceptors. The deviations can be explained in terms of the so-called *ortho* effect. Namely, inspection of mesomeric structures of pyridine *N*-oxide[30] reveals that positions *ortho* and *para* are particularly prone to both electrophilic and nucleophilic substitutions. This contribution implies that the MP2 method is by far more sensitive to *ortho* effects than is the RHF method by which no deviations were noted for systems involving 2PicO as the proton acceptor.

After rejection of the data points referring to systems with 2PicO, a significant improvement of the correlations was obtained (see Table 3). For the system with $3PicOH^+$ as proton donor, no correlation is reported, because after rejection of 2PicO the correlation would have been constructed for two data points only. The correlation coefficients in these correlations are much higher (0.998−0.999) than those for ones involving systems with 2PicO, and parameters *a* and *b* are burdened with smaller standard deviations. For comparison, Figure 4 shows the relationships between $\Delta E_{BHB_1^+}$(MP2) and ΔE_{prot}(MP2) for $4NMe_2PyOH^+$ as the proton donor under consideration of all proton acceptors (solid line) and after rejection of 2PicO (dashed line).

As the energy (Gibbs free energy) of cationic heteroconjugation turned out to be linearly related to that of protonation of the proton acceptors and bearing in mind the linear relation of these energies (Gibbs free energies) against pK_a values in nonaqueous media (e.g., acetonitrile)[15] it can be envisaged that there would also exist linear correlations between the calculated energies (free enthalpies) of heterocomplexes and experimental pK_a^{AN} values (e.g., in acetonitrile) of the *N*-oxides acting as proton acceptors. As a matter of fact, such correlation would have rather limited theoretical background but could be useful

TABLE 4: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between the Calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) Values and Experimental pK_a Values of Proton Acceptors (for a Fixed Proton Donor)[a]

proton donor	$\Delta E_{\mathrm{BHB}_1^+}$(RHF)			$\Delta G_{\mathrm{BHB}_1^+}$(RHF)			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)[b]			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)[c]		
	a	*b*	*R* *σ*	*a*	*b*	*R* *σ*	*a*	*b*	*R* *σ*	*a*	*b*	*R* *σ*
$4NMe_2PyOH^+$	−1.73 (0.14)	−9.62 (1.43)	−0.985 0.766	−2.13 (0.35)	4.00 (3.71)	−0.938 1.994	−2.06 (0.38)	−9.20 (3.98)	−0.925 2.140	−2.07 (0.15)	−8.37 (1.56)	−0.990 0.835
$Me_2MeOPyOH^+$	−1.86 (0.12)	−9.69 (1.22)	−0.992 0.604	−2.08 (0.04)	2.86 (0.40)	−0.999 0.200	−2.08 (0.48)	−11.90 (4.86)	−0.907 2.404	−2.01 (0.08)	−11.70 (0.83)	−0.998 0.408
$4MeOPyOH^+$	−2.17 (0.25)	−8.60 (2.40)	−0.981 1.071	−2.02 (0.14)	1.73 (1.35)	−0.993 0.605	−2.31 (0.59)	−10.00 (5.69)	−0.914 2.547	−2.10 (0.09)	−11.06 (0.88)	−0.998 0.392
$4PicOH^+$	−2.33 (0.03)	−7.55 (0.26)	−0.999 0.111	−2.15 (0.18)	0.23 (1.71)	−0.993 0.730	−2.66 (0.69)	−8.60 (6.26)	−0.941 2.667	2.33 (0.32)	−10.50 (2.88)	−0.991 1.198
$3PicOH^+$	−1.90 (0.20)	−11.82 (1.77)	−0.995 0.730	−2.48 (0.07)	3.69 (0.65)	−0.999 0.270	−2.76 (1.00)	−8.21 (8.94)	−0.940 3.690			

[a] Values of standard deviations of *a* and *b* in parentheses. [b] Including 2PicO as the proton acceptor. [c] After removing of 2PicO

TABLE 5: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between Calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) Values and Experimental Acetonitrile log $K_{\mathrm{BHB}_1^+}$ Values of Proton Acceptors (for a Fixed Proton Donor)[a]

proton donor	$\Delta E_{\mathrm{BHB}_1^+}$(RHF)			$\Delta G_{\mathrm{BHB}_1^+}$(RHF)			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)		
	a	*b*	*R* *σ*	*a*	*b*	*R* *σ*	*a*	*b*	*R* *σ*
$(Me_2MeOPyOH^+)^b$	−1.40 (0.89)	−25.61 (2.33)	−0.742 0.855	−1.60 (0.55)	−14.78 (1.45)	−0.897 0.534	−1.00 (3.12)	−31.38 (8.12)	−0.221 2.982
$(Me_2MeOPyOH^+)^c$	−1.26 (0.41)	−26.29 (1.09)	−0.951 0.391	−1.56 (0.69)	−15.00 (1.82)	−0.915 0.652	−1.49 (0.02)	−28.88 (0.83)	−0.999 0.016
$4NMe_2PyOH^+$	−0.67 (0.09)	−26.81 (0.18)	−0.992 0.057	−6.47 (2.72)	−5.58 (5.84)	−0.922 1.808			
$4PicOH^+$	−0.0013 (0.0006)	−31.13 (0.12)	−0.919 0.163	−0.005 (0.002)	−21.09 (0.33)	−0.943 0.466			

[a] Values of standard deviations of *a* and *b* in parentheses. [b] Including 2PicO as the proton acceptor. [c] After removing 2PicO.

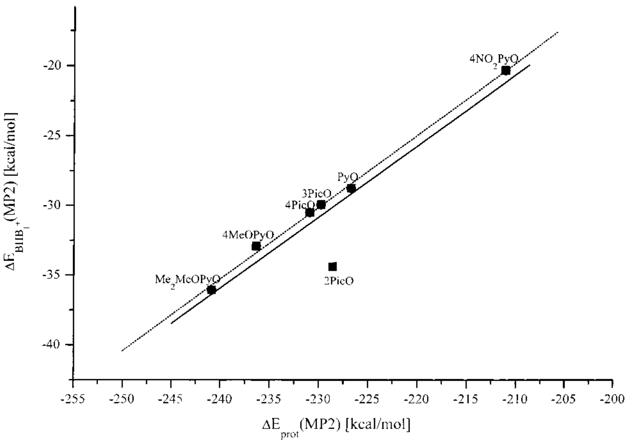

Figure 4. Plot of $\Delta E_{\mathrm{BHB}_1^+}$(MP2) against ΔE_{prot}(MP2) of proton acceptors in the case of $4NMe_2PyOH^+$ as the proton donor. Abbreviations for proton acceptors are given in the graph.

for experimental studies. The parameters of these correlations are listed in Table 4.

A direct verification of the consistence of experimental results with those obtained by the ab initio method would be possible by finding correlations between the calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) values and the determined cationic homoconjugation constants, log $\Delta K_{\mathrm{BHB}_1^+}$. Unfortunately, not for all of the systems for which the ab initio calculations were accomplished were the $\Delta K_{\mathrm{BHB}_1^+}$ values known. For a part of the systems the values were not determined because of experimental restrictions, for instance, for all systems with $4MeOPyOH^+$ as the proton donor and for 4MeOPyO as the acceptor. Furthermore, for some experimentally studied systems the equilibrium constants could not be determined from potentiometric titrations, because the equilibria were either not attained at all or were attained to a small extent only thus leading to equilibrium constants too small to be determined potentiometrically. Hence, it was impossible to construct linear correlations for all of the classes of compounds (rejected was the class with $4MeOPyOH^+$), whereas in the remaining three classes (with $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, and $4PicOH^+$ as the proton donors), the number of proton acceptors was also reduced. For this reason, from the statistical standpoint, as the most reliable can be considered correlations between theoretical $\Delta E_{\mathrm{BHB}_1^+}$ and $\Delta G_{\mathrm{BHB}_1^+}$ values on one hand and those of ΔE_{prot} and ΔG_{prot} of proton acceptors, on the other hand. As a matter of fact, these values are correlated only indirectly with cationic heteroconjugation constants. They were, however, previously determined[15] for all of the systems studied.

Nevertheless, by utilizing those systems for which experimental heteroconjugation constants were known correlations between theoretical and experimental values have been established. For systems with $Me_2MeOPyOH^+$ as the proton donor (there was the greatest number of experimental data for this species; the cationic heteroconjugation constants were determined for four proton acceptors), linear correlations have been found between the calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) values and those of log $\Delta K_{\mathrm{BHB}_1^+}$ in acetonitrile (Table 5). Very low correlation coefficients, in particular with the MP2 method, where there is no correlation between theoretical and experimental data points, are due to deviation from linearity of systems containing 2PicO (because of the mentioned *ortho* effect) as the proton acceptor. After rejection of these systems, the correlation coefficients increased significantly and the standard deviations of the *a* and *b* parameters markedly decreased (see Table 5). In Figure 5, relationships are shown between the calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF),

TABLE 6: Energies of Formation of the Heterocomplexed Cations Calculated at the RHF ($\Delta E_{\mathrm{BHB}_1^+}$(RHF) and $\Delta G_{\mathrm{BHB}_1^+}$(RHF)) and MP2 ($\Delta E_{\mathrm{BHB}_1^+}$(MP2)) Levels, as Well as Gibbs Free Energies of the Process Calculated at the RHF Level ($\Delta G_{\mathrm{BHB}_1^+}$(RHF)) in kcal/mol[a]

BH^+/B_1 system	$\Delta E_{\mathrm{BHB}_1^+}$ (RHF)	$\Delta G_{\mathrm{BHB}_1^+}$ (RHF)	$\Delta E_{\mathrm{BHB}_1^+}$ (MP2)	ΔE_{prot} (RHF)	ΔG_{prot} (RHF)	ΔE_{prot} (MP2)	pK_a^{AN}	$\log \Delta K_{\mathrm{BHB}_1^+}^{\mathrm{AN}}$
$4NMe_2PyOH+/4NO_2PyO$	−18.71	−8.06	−20.34	−260.10	−251.30	−247.42	15.63	
$Me_2MeOPyOH+/4NO_2PyO$	−19.97	−8.82	−22.96	−255.66	−246.88	−240.87	12.78	
$4MeOPyOH+/4NO_2PyO$	−20.74	−9.76	−22.91	−250.38	−241.75	−236.37	12.21	
$4PicOH+/4NO_2PyO$	−20.68	−11.92	−23.68	−245.71	−237.31	−230.96	11.00	
$3PicOH+/4NO_2PyO$	−22.53	−10.31	−23.89	−243.60	−235.50	−229.81	10.31	
$2PicOH+/4NO_2PyO$	−21.97	−10.84	−24.79	−243.71	−235.40	−228.60	10.23	
$PyOH+/4NO_2PyO$	−23.30	−11.34	−24.5	−241.24	−232.94	−226.76	5.64	
$4NMe_2PyOH+/PyO$	−27.92	−15.57	−28.77	−260.10	−251.30	−247.42	15.63	*b*
$Me_2MeOPyOH+/PyO$	−28.72	−18.04	−31.64	−255.66	−246.88	−240.87	12.78	1.85
4MeOPyOH+/PyO	−30.50	−17.73	−31.71	−250.38	−241.75	−236.37	12.21	
4PicOH+/PyO	−31.02	−20.78	−33.00	−245.71	−237.31	−230.96	11.00	3.35
3PicOH+/PyO	−31.45	−21.44	−33.26	−243.60	−235.50	−229.81	10.31	*b*
2PicOH+/PyO	−31.40	−20.07	−34.45	−243.71	−235.40	−228.60	10.23	3.54
$4NMe_2PyOH+/2PicO$	−27.92	−15.66	−34.40	−260.10	−251.30	−247.42	15.63	1.71
$Me_2MeOPyOH+/2PicO$	−28.08	−18.41	−37.47	−255.66	−246.88	−240.87	12.78	2.47
4MeOPyOH+/2PicO	−29.97	−18.89	−37.51	−250.38	−241.75	−236.37	12.21	
4PicOH+/2PicO	−31.25	−21.44	−38.71	−245.71	−237.31	−230.96	11.00	3.44
3PicOH+/2PicO	−30.78	−21.53	−39.00	−243.60	−235.50	−229.81	10.31	*b*
$4NMe_2PyOH+/3PicO$	−28.19	−19.97	−29.95	−260.10	−251.30	−247.42	15.63	2.00
$Me_2MeOPyOH+/3PicO$	−29.48	−18.80	−33.03	−255.66	−246.88	−240.87	12.78	2.77
4MeOPyOH+/3PicO	−32.47	−19.68	−33.06	−250.38	−241.75	−236.37	12.21	
4PicOH+/3PicO	−31.60	−22.73	−35.32	−245.71	−237.31	−230.96	11.00	3.60
$4NMe_2PyOH+/4PicO$	−28.55	−22.15	−30.51	−260.10	−251.30	−247.42	15.63	2.63
$Me_2MeOPyOH+/4PicO$	−30.50	−20.29	−33.69	−255.66	−246.88	−240.87	12.78	3.16
4MeOPyOH+/4PicO	−31.77	−20.76	−34.13	−250.38	−241.75	−236.37	12.21	

[a] For comparison, included are calculated ΔE_{prot}(RHF), ΔG_{prot}(RHF), and ΔE_{prot}(MP2) values and experimental pK_a of the proton donor (ref 6) and log $\Delta K_{\mathrm{BHB}_1^+}$ (ref 16) in acetonitrile. [b] Cationic heteroconjugation constant could not be determined from potentiometric measurements

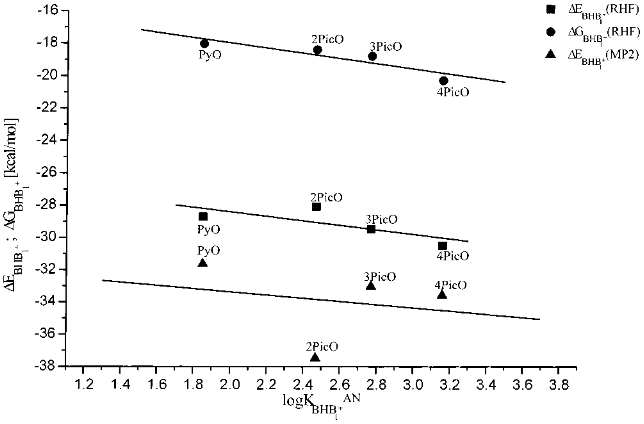

Figure 5. Plot of $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) against log $\Delta K_{\mathrm{BHB}_1^+}$ in acetonitrile in the case of $Me_2MeOPyOH^+$ as the proton donor. Abbreviations for proton acceptors are given in the graph.

$\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) values and those of log $\Delta K_{\mathrm{BHB}_1^+}$ in acetonitrile for the $Me_2MeOPyOH^+$ proton donor.

With the two remaining classes of compounds (containing $4NMe_2PyOH^+$ and $4PicOH^+$ as the proton donors) for which the number of experimental log $\Delta K_{\mathrm{BHB}_1^+}$ values was smaller (three only), good correlations were found at the RHF level only. There was no correlation between $\Delta E_{\mathrm{BHB}_1^+}$ (MP2) and log $\Delta K_{\mathrm{BHB}_1^+}$ (the correlation coefficients oscillated around −0.25). This lack of correlation can be present probably because of the presence of the *ortho* effect for considered 2PicO systems. Moreover, it is well-known that correlation between data in solution and gas phase is poor for 2-substituted derivatives.[31,32] The relationships between $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and log $\Delta K_{\mathrm{BHB}_1^+}$ for $4NMe_2PyOH^+$ and $4PicOH^+$ as proton donors, respectively, are also collected in Table 5. It is worth noting that in the above correlations the intercept values are much lower (in the range of units or tens) than in the case of correlations between the calculated heteroconjugation energies (free energies) and the calculated protonation energies (free energies); see Table 3. For such values of intercept, the entropy contributions[33] can be responsible.

Having in hand the results of calculations of the protonated *N*-oxide systems as the proton donors with nonconjugated *N*-oxides as the acceptors (Table 2), in the next step selected were five basic (i.e. those involving at least three proton donors) sets of systems with a fixed proton acceptor and various proton donors. In these sets as proton acceptors were 4PicO, 3PicO, 2PicO, PyO, and $4NO_2PyO$ and as proton donors were $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, and $4MeOPyOH^+$ in the case of 4PicO as proton acceptor; $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, and $4MeOPyOH^+$ with 3PicO as proton acceptor; $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, $4MeOPyOH^+$, $4PicOH^+$, and $3PicOH^+$ with 2PicO; $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, $4MeOPyOH^+$, $4PicOH^+$, $3PicOH^+$, and $2PicOH^+$ with PyO; $4NMe_2PyOH^+$, $Me_2MeOPyOH^+$, $4MeOPyOH^+$, $4PicOH^+$, $3PicOH^+$, $2PicOH^+$, and $PyOH^+$ with $4NO_2PyO$. To clarify the results, Table 6 summarizes the energies and Gibbs free energies of formation ($\Delta E_{\mathrm{BHB}_1^+}$ and $\Delta G_{\mathrm{BHB}_1^+}$, respectively) of the heterocomplexes at the RHF level, the formation energies ($\Delta E_{\mathrm{BHB}_1^+}$) at the MP2 level, and experimental pK_a values of proton donors, as well as log $\Delta K_{\mathrm{BHB}_1^+}$ values in acetonitrile. Obviously, all systems constituting these sets satisfied the conditions of the absence of the proton-transfer equilibria. In this way, foundations were laid for verification of experimental hypothesis that the tendency toward cationic heteroconjugation in nonaqueous media declines with increasing basicity of the proton donor at a fixed pK_a of proton acceptor.[7,16−18] To verify this hypothesis in depth, the energies of formation of the heterocomplexed cations, at both the RHF and MP2 levels, and Gibbs free energies of formation calculated at the RHF level were correlated respectively with the previously calculated[15] energies and Gibbs free energies of

TABLE 7: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between Calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) Values and Respectively Calculated ΔE_{prot}, ΔG_{prot}, and ΔE_{prot} (MP2) Values of Proton Donors (for a Fixed Proton Acceptor)[a]

proton donor	$\Delta E_{\mathrm{BHB}_1^+}$(RHF)			$\Delta G_{\mathrm{BHB}_1^+}$(RHF)			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)		
	a	*b*	*R* *σ*	*a*	*b*	R *σ*	*a*	*b*	R *σ*
4PicO	−0.328	−114	−0.985	0.139	13	0.688	−0.339	−115	−0.954
	(0.057)	(15)	0.391	(0.147)	(36)	0.992	(0.107)	(26)	0.840
3PicO	−0.275	−100	−0.881	−0.194	−68	−0.670	−0.305	−107	−0.964
	(0.104)	(26)	1.133	(0.142)	(35)	1.492	(0.059)	(14)	0.713
2PicO	−0.214	−83	−0.955	−0.360	−106	−0.973	−0.238	−94	−0.951
	(0.038)	(10)	0.526	(0.049)	(12)	0.650	(0.045)	(11)	0.652
PyO	−0.216	−84	−0.989	−0.314	−95	−0.931	−0.255	−92	−0.963
	(0.016)	(4)	0.252	(0.061)	(15)	0.901	(0.036)	(8)	0.591
$4NO_2PyO$	−0.211	−73	−0.939	−0.183	−54	−0.902	−0.186	−67	−0.946
	(0.035)	(9)	0.595	(0.039)	(9)	0.650	(0.029)	(7)	0.527

[a] Values of standard deviation of *a* and *b* in parentheses.

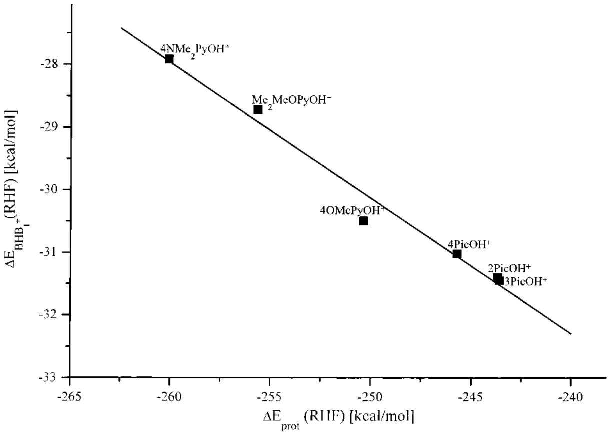

Figure 6. Plot of $\Delta E_{\mathrm{BHB}_1^+}$(RHF) against ΔE_{prot}(RHF) of proton donors in the case of PyO as the proton acceptor. Abbreviations for proton donors are given in the graph.

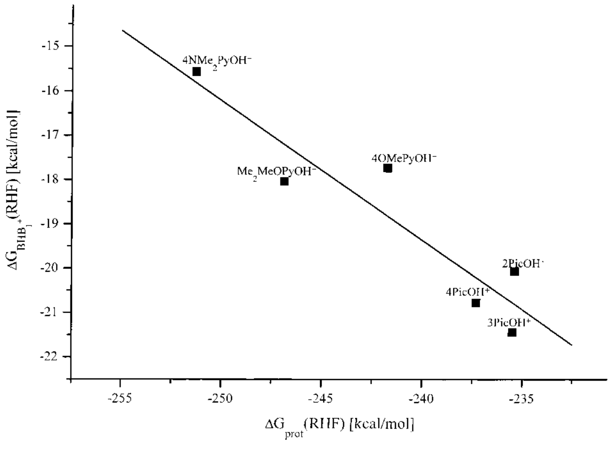

Figure 7. Plot of $\Delta G_{\mathrm{BHB}_1^+}$(RHF) against ΔG_{prot}(RHF) of proton donors in the case of PyO as the proton acceptor. Abbreviations for proton donors are given in the graph.

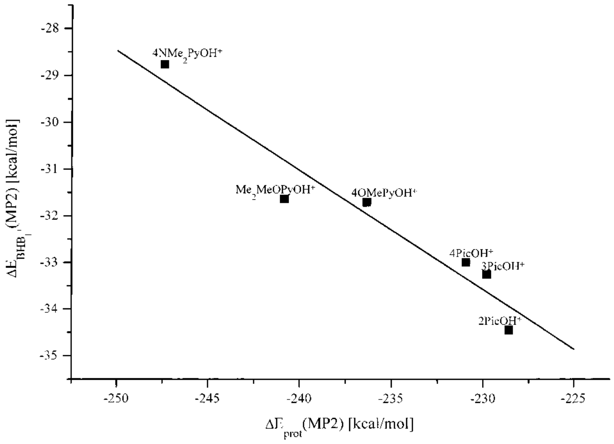

Figure 8. Plot of $\Delta E_{\mathrm{BHB}_1^+}$(MP2) against ΔE_{prot}(MP2) of proton donors in the case of PyO as the proton acceptor. Abbreviations for proton donors are given in the graph.

protonation of the *N*-oxides acting as proton donors for each set of pyridine *N*-oxide derivatives (with a fixed proton acceptor).

The results of correlation analyses supported that conclusion. It was found that the $\Delta E_{\mathrm{BHB}_1^+}$(RHF) and $\Delta G_{\mathrm{BHB}_1^+}$(RHF) values calculated at the RHF level, as well as those of $\Delta E_{\mathrm{BHB}_1^+}$(MP2) calculated at the MP2 level, can be represented as linear functions of respectively ΔE_{prot} and ΔG_{prot} of the proton donor (at a fixed basicity of proton acceptor). At the RHF level, when considering formation energies of the heterocomplexes, the correlations have been found to be linear functions described by the correlation parameters listed in Table 7. In these correlations, absolute values of slopes *a* and intercept *b* decreasegradually with decreasing ΔE_{prot} for proton donors. It is worth noting that the correlation coefficients, *R*, are close to unity (range from 0.953 to 0.989) with the exception of the equation for 3PicO (0.881). In Figure 6, an example is provided of the relationship between $\Delta E_{\mathrm{BHB}_1^+}$(RHF) and ΔE_{prot} (RHF) of the proton donors for PyO as the acceptor.

As in the case of energies, good correlations at the RHF level were obtained also with Gibbs free energies, with the exception of systems involving 4PicO and 3PicO, where the correlation coefficients oscillated around 0.7 (see Table 7) which proves the lack of linear relationships in these cases. In Figure 7, an example is provided of the relationship between $\Delta E_{\mathrm{BHB}_1^+}$(RHF) and ΔG_{prot} for the proton donors and PyO as the acceptor.

Also, the $\Delta E_{\mathrm{BHB}_1^+}$(MP2) values can be linearly correlated with those of ΔE_{prot}(MP2) of proton acceptors, the correlation coefficients being in the range of −0.946 to −0.964 (see Table 7). An example of the relationship between $\Delta E_{\mathrm{BHB}_1^+}$(MP2) and ΔE_{prot} of proton donors for PyO as the acceptor is shown in Figure 8.

As in the case of the classes with fixed proton donor, also in those with fixed proton acceptors, linear relationships have been established between the calculated energies (Gibbs free energies) of the heterocomplexes and experimental $\mathrm{p}K_{\mathrm{a}}^{\mathrm{AN}}$ values in acetonitrile for *N*-oxides functioning as proton donors. The parameters of these correlations are listed in Table 8. It should

TABLE 8: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between Calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) Values and Experimental Acetonitrile pK_a Values of Proton Donors (for a Fixed Proton Acceptor)[a]

proton acceptor	$\Delta E_{\mathrm{BHB}_1^+}$(RHF)			$\Delta G_{\mathrm{BHB}_1^+}$(RHF)			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)		
			R			R			R
	a	b	σ	a	b	σ	a	b	σ
4PicO	0.86	−41.90	0.970	−0.49	−14.49	0.920	1.08	−47.36	0.999
	(0.22)	(2.94)	0.559	(0.21)	(2.81)	0.535	(0.05)	(0.65)	0.124
3PicO	0.84	−41.19	0.837	0.42	−25.78	0.491	1.11	−47.11	0.984
	(0.38)	(5.01)	1.308	(0.53)	(6.94)	1.811	(0.14)	(1.83)	0.479
2PicO	0.64	−37.53	0.861	1.16	−33.58	0.982	0.88	−48.28	0.990
	(0.22)	(2.74)	0.901	(0.13)	(1.60)	0.526	(0.07)	(0.89)	0.291
PyO	0.69	−38.50	0.947	1.02	−31.22	0.940	0.94	−43.44	0.980
	(0.12)	(1.44)	0.538	(0.18)	(2.25)	0.843	(0.09)	(0.94)	0.433
4NO$_2$PyO	0.48	−26.51	0.935	0.35	−14.04	0.777	0.41	−27.83	0.840
	(0.08)	(0.94)	0.613	(0.13)	(1.46)	0.948	(0.12)	(1.35)	0.882

[a] Values of standard deviations of *a* and *b* in parentheses.

TABLE 9: Coefficients *a*, *b*, *R*, and *σ* in Linear Correlations between Calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) Values and Experimental Acetonitrile log $\Delta K_{\mathrm{BHB}_1^+}$ Values of Proton Donors (for a Fixed Proton Acceptor)[a]

proton acceptor	$\Delta E_{\mathrm{BHB}_1^+}$(RHF)			$\Delta G_{\mathrm{BHB}_1^+}$(RHF)			$\Delta E_{\mathrm{BHB}_1^+}$(MP2)		
			R			R			R
	a	b	σ	a	b	σ	a	b	σ
3PicO	−2.14	−23.80	−0.993	−1.76	−15.58	−0.700	−3.35	−23.42	−0.994
	(0.25)	(0.73)	0.287	(1.80)	(5.16)	2.039	(1.02)	(0.36)	0.405
2PicO	−1.99	−24.04	−0.917	−3.33	−10.04	−0.999	−2.44	−30.67	−0.952
	(0.87)	(2.28)	1.060	(0.14)	(0.37)	0.172	(0.78)	(2.06)	0.958
PyO	−1.57	−25.82	−0.999	−1.44	−15.43	−0.938	−1.37	−29.03	−0.905
	(0.04)	(0.13)	0.059	(0.53)	(1.61)	0.699	(0.65)	(1.94)	0.845

[a] Values of standard deviations of *a* and *b* in parentheses.

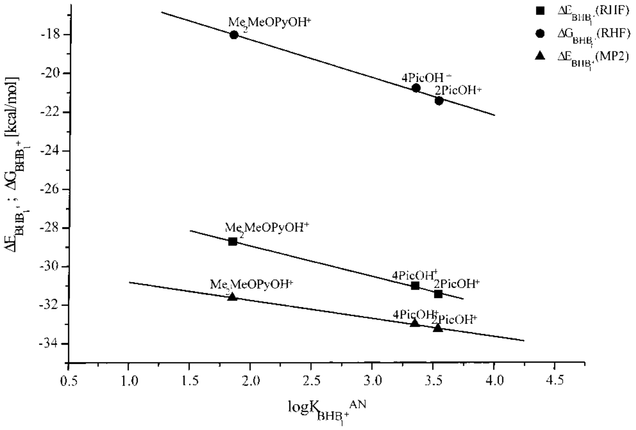

Figure 9. Plot of $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta E_{\mathrm{BHB}_1^+}$(RHF), and log $\Delta K_{\mathrm{BHB}_1^+}$-(MP2) against log $\Delta K_{\mathrm{BHB}_1^+}$ in acetonitrile in the case of PyO as the proton acceptor. Abbreviations for proton donors are given in the graph.

be emphasized that high correlation coefficients for all of the considered classes of compounds were obtained at the MP2 level only, unlike correlations for fixed donors where the coefficients were high both at the MP2 and the RHF levels.

By utilizing the limited number of available experimental cationic heteroconjugation constants in acetonitrile (under assumption that the minimal number of the data points used to establish the correlation is three, three sets were formed with fixed proton acceptor, namely, 3PicO, 2PicO, and PyO), an attempt was made to correlate theoretical $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) with those of log $\Delta K_{\mathrm{BHB}_1^+}$ (Figure 9). The correlation parameters are listed in Table 9. The values of correlation coefficients confirm existence of linear correlations between the calculated energies and Gibbs free energies of formation of the heterocomplexed cations, on the one hand, and experimental cationic heteroconjugation constants in nonaqueous media in systems with fixed basicity of proton acceptor and variable basicity of proton donors, on the other hand. Correlation coefficients in the majority of cases, with the exception of two relationships for 3PicO as the proton acceptor, are in excess of 0.9 and range from −0.917 to −0.999. Bearing in mind these findings and those referring to existing correlations between calculated $\Delta E_{\mathrm{BHB}_1^+}$(RHF), $\Delta G_{\mathrm{BHB}_1^+}$(RHF), and $\Delta E_{\mathrm{BHB}_1^+}$(MP2) values and those of pK_a^{AN}, it can be found that they all support the preliminary experimental hypothesis on the influence of the pK_a of proton donor on cationic heteroconjugation constants (at a fixed basicity of the proton acceptor) which states that the constants decline with increasing basicity of proton donors (at a fixed basicity of proton acceptor).

With a comparison of the efficiencies of the correlations between theoretically calculated energies and Gibbs free energies of formation of the heterocomplexed cations and analogous-magnitudes of protonation of the proton acceptor (at a fixed basicity of the proton donor), as well as of proton donors (at a fixed basicity of proton acceptor) on the one hand and experimental cationic heteroconjugation constants in acetonitrile on the other, a conclusion can be drawn that there is a better correlation between the theoretical magnitudes and the protonation energies (Gibbs free energies) than between them and the heteroconjugation constants determined in nonaqueous media. This is compatible with a previous conclusion stating that the cationic heteroconjugation constants are affected not only by the pK_a's of both the proton acceptor and donor but also by cationic homoconjugation constants of bases B and B$_1$ occurring in the heteroconjugating system.[16]

In Table 2 also, the results are shown of calculations of the energies (RHF and MP2) and Gibbs free energies (RHF) of formation of a heterocomplexed cation in a model system with proton transfer, 4NO$_2$PyOH$^+$/PyO. In such systems, the calculated $\Delta E_{\mathrm{BHB}_1^+}^{\mathrm{PT}}$ and $\Delta G_{\mathrm{BHB}_1^+}^{\mathrm{PT}}$ values are usually considered to be the sum of the energy (Gibbs free energy) of formation of the heterocomplexed cation and the energy (Gibbs free energy) of the proton transfer. The latter can be calculated from the following relationship:

$$\Delta E^{\mathrm{PT}} = \Delta E_{\mathrm{B_1H^+}} - \Delta E_{\mathrm{BH^+}} \tag{13}$$

$$\Delta G^{\mathrm{PT}} = \Delta G_{\mathrm{B_1H^+}} - \Delta G_{\mathrm{BH^+}} \tag{14}$$

For this reason, all magnitudes calculated for the system considered ($4NO_2PyOH^+/PyO$) should be appreciably higher than those for the reverse system ($PyOH^+/4NO_2PyO$). To verify this hypothesis, the previously calculated[15] energies and Gibbs free energies of protonation of PyO and $4NO_2PyO$ and the energy and Gibbs free energy of proton transfer were calculated from eqs 13 and 14 and then from the relationships:

$$\Delta E_{\mathrm{BHB_1^+}} = \Delta E^{\mathrm{PT}}_{\mathrm{BHB_1^+}} - \Delta E^{\mathrm{PT}} \tag{15}$$

$$\Delta E_{\mathrm{BHB_1^+}} = \Delta G^{\mathrm{PT}}_{\mathrm{BHB_1^+}} - \Delta G^{\mathrm{PT}} \tag{16}$$

calculated were the energies (Gibbs free energies) of formation of the heterocomplexed ion in a system without proton transfer (as also shown in Table 2). The results of these calculations are comparable with those calculated directly in the system without proton transfer, with the best coincidence being noted for the Gibbs free energy and the largest divergence for the energy of formation of the heterocomplexed cation at the RHF level.

The heteroconjugation energies ($\Delta E_{\mathrm{BHB_1^+}}$(SCRF)) calculated on the basis of the SCRF model are less negative than those calculated without accounting for solvation effects, thus, being in close agreement with the experiment. On the other hand, accounting for solvation does not improve the correlation between the calculated and experimental results. Just the reverse is seen: arrangement in series of the $\Delta E_{\mathrm{BHB_1^+}}$(RHF) values remains in only a rough relation to the series of experimental log $\Delta K_{\mathrm{BHB_1^+}}$ values, not permitting for construction of a linear relationship. It can thus be concluded that the SCRF model is not useful in the case chemical entities considered here. This can be explained in terms of a too poor conformity of the model of Onsager's spherical cavity to accommodate the heterocomplexes whose molecular surface departs much from spherical shape. To gain a better insight into energy variations of a chemical species caused by its interaction with solvent, one should probably utilize either the Monte Carlo method or that of molecular dynamics. This will be the objective of our further studies.

Conclusions

The calculations accomplished for 22 heterocomplexed cations lead to the following conclusions:

(1) Inclusion of the polarization function in calculations at the RHF level using the 6-31G* basis set enables allows for the meaningful calculation of the geometry of heterocomplexed cations formed by substituted pyridine *N*-oxide.

(2) Utilizing the relatively cheap calculations at the RHF level enables us to reproduce the sequence of changes of cationic heteroconiugation constants in nonaqueous media.

(3) Inclusion of electronic correlation to perturbation theory (MP2) allows us to far more precisely calculate energetic effects of specific processes, for instance, those accompanying the *ortho* effects.

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