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A study of the tendency of organic bases towards cationic heteroconjugation in polar non-aqueous solvents

Ewa Kaczmarczyk, Danuta Augustin-Nowacka, Mariusz Makowski, Anna Kozak and Lech Chmurzyński *

Department of General Chemistry, University of Gdańsk, Sobieskiego 18, 80-952 Gdańsk, Poland. E-mail: lech@chemik.chem.univ.gda.pl; Fax: +48 58 341 0357; Tel: +48 58 345 0392

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By using the potentiometric method, cationic heteroconjugation constants, $ssK_{BHB_1^+}$, were determined in systems involving a cation of protonated 4-*N′*,*N′*-dimethylaminopyridine *N*-oxide and *N*-oxides of 4-methylpyridine, 3-methylpyridine, 2-methylpyridine, unsubstituted pyridine, as well as protonated trimethylamine *N*-oxide and 4-*N′*,*N′*-dimethylaminopyridine *N*-oxide in polar non-aqueous solvents, protophobic aprotic acetone and amphiprotic methanol. In order to estimate the influence of the basicity of the proton donors and proton acceptors on the cationic heteroconjugation constants, their values determined in the *N*-oxide systems studied were compared with the previously determined ones for other *N*-oxide systems in the two above-mentioned solvents. Furthermore, to evaluate the influence of the medium on the tendency towards cationic heteroconjugation, all the determined heteroconjugation constant values in acetone and methanol were compared with those determined in other polar solvents, such as nitromethane, nitrobenzene, acetonitrile, propylene carbonate, *N*,*N*-dimethylformamide and dimethyl sulfoxide. Moreover, a comparison of the constant values obtained in the *N*-oxide systems (with $[OHO]^+$ bridges) with those determined in the heterocyclic *N*-base systems (with $[NHN]^+$ bridges) and in systems involving both kinds of bases (with mixed $[NHO]^+$–$[OHN]^+$ bridges) provided a basis for discussion of the influence of the types of H-bonded bridges on their stability.

Introduction

In systems involving organic bases (amines or their *N*-oxides) and conjugate acids of these bases, apart from the dissociation equilibria of the protonated bases [eqn. (1) and (2)], consecutive acid–base equilibria, *i.e.* those of cationic homo- [eqn. (3) and (4)] and heteroconjugation [eqn. (5)], are likely to be present. Consequently, the following scheme of the acid–base equilibria attained in these solutions can be envisaged,

$$BH^+ \rightleftharpoons B + H^+ \qquad (1)$$

$$B_1H^+ \rightleftharpoons B_1 + H^+ \qquad (2)$$

$$BH^+ + B \rightleftharpoons BHB^+ \qquad (3)$$

$$B_1H^+ + B_1 \rightleftharpoons B_1HB_1^+ \qquad (4)$$

$$BH^+ + B_1 \rightleftharpoons BHB_1^+ \qquad (5)$$

where B and B_1 are organic bases, BH^+ and B_1H^+ are cationic acids conjugated to base B and B_1, respectively, BHB^+ and $B_1HB_1^+$ are homocomplexed cations and BHB_1^+ is a heterocomplexed cation. Consecutive acid–base equilibria [eqn. (3)–(5)] are established in polar non-aqueous solvents by virtue of their strong differentiating properties and mostly weak acid–base properties.[1,2]

As seen in eqn. (5), cationic heteroconjugation is a reaction wherein a cationic acid BH^+ reacts with a base B_1 conjugated to acid B_1H^+ to afford a hydrogen-bonded complex, BHB_1^+. Bases B and B_1 in this complex are bonded with an asymmetric hydrogen bond and the location of the proton within the hydrogen bridge depends on the difference in basicities of the bases. When $sspK_a(BH^+) < sspK_a(B_1H^+)$ a proton is transferred from base B onto base B_1. Eqn. (5) defines the cationic heteroconjugation equilibrium in which BH^+ acts as a proton donor and B_1 as a proton acceptor. However, one can write down an equation equivalent to eqn. (5) defining the heteroconjugation equilibrium in which B_1H^+ acts as a proton donor and B as a proton acceptor (resulting in the formation of the same heterocomplex ion BHB_1^+). Therefore, we will assume in all subsequent considerations that B in its protonated form acts as a proton donor. Moreover, it is assumed that B is a stronger base than B_1. These assumptions rule out the proton transfer equilibrium in further considerations, because as demonstrated previously,[3] the proton transfer equilibria present in experimental heteroconjugating systems make difficult a precise determination of the cationic heteroconjugation constants.

Heteroconjugation equilibria have mostly been studied in classic Brönsted (B + HA) acid–base systems, where B was an aliphatic or aromatic amine and HA was a carboxylic acid or phenol.[4–10] Less frequently anionic heteroconjugation leading to AHA_1^- anions was studied in non-aqueous solvents,[11–13] and still less frequently the cationic heteroconjugation affording BHB_1^+ cations. Those studies were usually concerned with $[NHN]^+$ bridges, *i.e.* those formed by organic *N*-bases.[14–17] Much less attention[18] has been focused on the $[OHO]^+$ bridges formed by amine *N*-oxides and on the mixed $[NHO]^+$–$[OHN]^+$ bridges. But even with the relatively well experimentally surveyed $[NHN]^+$ systems, evaluation of the cationic heteroconjugation constant values determined in non-aqueous solvents is not straightforward due to a diversity of experimental methods used for deriving the constants[14–17] and the variety being studied, involving aliphatic, cyclic and aromatic *N*-bases.[19–22] Nonetheless, the results have shown that the $[NHN]^+$ bridges[23–25] are less stable than the $[NHO]^+$–$[OHN]^+$ bridges,[26,27] in which one of the bases is replaced by its *N*-oxide, as well as the $[OHO]^+$ bridges.[3]

The relatively high cationic heteroconjugation constant values of the $[OHO]^+$ bridges, prompted us to comprehensively

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survey these equilibria in polar aprotic and amphiprotic solvents in systems involving substituted pyridine *N*-oxides and trimethylamine *N*-oxide. Studies in nitromethane,[28] nitrobenzene,[29] acetonitrile,[30] propylene carbonate,[31] acetone,[3] *N*,*N*-dimethylformamide[28] and methanol[3] revealed a complex nature of these equilibria. In the $[OHO]^+$ systems, the constant values have been found to increase with increasing proton acceptor basicity and decreasing basicity of the proton donor.[28,29] Another factor affecting the tendency towards cationic heteroconjugation in the $[OHO]^+$ systems was their capacity for hydrogen bonding.[30]

Having in hand experimental data concerning the $[OHO]^+$ bridges, we have recently embarked on issues of cationic heteroconjugation equilibria set up in non-aqueous solvents in $[NHN]^+$ and $[NHO]^+$–$[OHN]^+$ systems. With the $[NHN]^+$ ones, preliminary investigations in systems containing free and protonated substituted pyridines carried out in nitromethane, acetonitrile and acetone have shown that the tendency towards cationic heteroconjugation is rather weak.[32–34] An unexpectedly strong tendency was found in the amphiprotic methanol,[34] which has been considered as a rather unfavourable solvent for conjugation equilibria.

The main objective of this contribution was to collect and supplement cationic heteroconjugation constant values referring to the $[OHO]^+$, $[NHN]^+$ and $[NHO]^+$–$[OHN]^+$ systems in polar non-aqueous solvents in order to provide a sound basis for discussion of the tendency towards cationic heteroconjugation in these systems. The non-aqueous solvents of interest were polar protophobic aprotic ones, nitromethane (NM), nitrobenzene (NB), acetonitrile (AN) and acetone (AC); polar protophilic aprotic solvents, *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), as well as the amphiprotic methanol (MeOH).

Experimental

Chemicals

Pyridine (PyO) and 4-*N*′,*N*′-dimethylaminopyridine ($4NMe_2$-PyO) *N*-oxides were prepared and purified by the methods of Ochiai[35] and Katritzky,[36] respectively. 4-Methoxy-2,6-dimethylpyridine *N*-oxide ($Me_2MeOPyO$) monohydrate was prepared from 2,6-dimethylpyridine *via* 4-nitro-2,6-dimethylpyridine *N*-oxide by standard methods. The anhydrous *N*-oxide was obtained by sublimation. 2-Methylpyridine (2PicO) and 3-methylpyridine (3PicO) *N*-oxides were purified by vacuum distillation. 4-Methylpyridine (4PicO) and trimethylamine *N*-oxides (Me_3NO) were crystallised twice from 3 : 1 acetone–methanol and methanol, respectively. Perchlorates of *N*-oxides were obtained by a modified version of Szafran's procedure.[37,38] Equivalent quantities of a 72% aqueous perchloric acid and *N*-oxide were mixed together in a small amount of methanol. The mixture was concentrated *in vacuo*. The residue was filtered off, washed twice with chloroform and dried *in vacuo* over P_2O_5. Picric acid was purified by triple crystallisation from ethanol. Tetra-*n*-butylammonium picrate was obtained by mixing together equimolar quantities of the purified picric acid with 25% tetra-*n*-butylammonium hydroxide in methanol. Tetra-*n*-butylammonium perchlorate was obtained by mixing together equimolar quantities of 72% aqueous $HClO_4$ solution with 25% tetra-*n*-butylammonium hydroxide in methanol. Both salts were crystallised twice from ethanol. Tetra-*n*-butylammonium chloride was purified by triple crystallisation from a 1 : 1 mixture of acetonitrile and ethyl acetate. 2,6-Dinitrophenol was purified by crystallisation from ethanol. Tetra-*n*-butylammonium 2,6-dinitrophenolate was prepared by reacting equimolar quantities of 2,6-dinitrophenol and tetra-*n*-butylammonium hydroxide. Thus, the 2,6-dinitrophenol was dissolved in methanol and a 55% aqueous solution of tetra-*n*-butylammonium hydroxide was added. The solvents (methanol and water) were then evaporated under reduced pressure and the residue was crystallised twice from ethyl acetate. The purity of all obtained and purified chemicals were tested by elemental analysis.

Solvents

Methanol in the first step was dried over freshly calcined sodium sulfate for 2–3 days. After decantation, *ca.* 100 cm^3 of the solvent was refluxed over 10 g of magnesium and 2 g of iodine until discoloration. After addition of 900 cm^3 of methanol the refluxing was continued for the next 30 min. The solvent was then distilled over a Vigreaux column. A fraction boiling at 64.5 °C was collected and further redistilled over tartaric acid (0.4 g dm^{-3} of methanol). The purified solvent had a specific conductivity of $1–3 \times 10^{-7}$ S cm^{-1}.

Acetone in the first step was refluxed with additions of small portions of $KMnO_4$ until the violet colour persisted. Then the solution was filtered and the solvent was dried over anhydrous $CaSO_4$. After decantation, acetone was distilled twice over the Vigreaux column and a fraction boiling at 56.5 °C was collected. The purified solvent had a specific conductivity of 2×10^{-7} S cm^{-1}.

The remaining solvents were purified as described elsewhere.[28–31,39]

Experimental procedures

The cationic heteroconjugation constants of amine *N*-oxides in non-aqueous solvents were determined by a potentiometric titration method. The electromotive force (emf) measurements of the *N*-oxide perchlorate–*N*-oxide systems were run at a constant ionic strength. The solution containing base perchlorate ($BHClO_4$) at a concentration of about 10^{-3} mol dm^{-3} was titrated with the solution containing the base B_1 at a concentration of about 10^{-2} mol dm^{-3} and $BHClO_4$ (where B and B_1 are the *N*-oxides studied) at the same concentration as that of the titrand (to keep the formal ionic strength constant for all titration points). The emf was recorded for each titration point, after electrode relaxation (*i.e.* when the measured potential was stable). Each titration consisted of approximately 30 titration points and was repeated at least twice. If necessary, *i.e.* in the case of divergent results, a third titration was carried out. The same potentiometric-titration procedure was applied in electrode calibration, with tetra-*n*-butylammonium picrate (tetra-*n*-butylammonium 2,6-dinitrophenolate) in the titrand and a mixture of this salt and picric acid (2,6-dinitrophenol) in the titrant in the case of acetone (methanol) solutions.

The emf measurements of the cell: indicator glass electrode| system studied||modified calomel electrode were run by means of a CX-731 (Elmetron) multifunctional computer-aided instrument with accuracy of ±0.1 mV. An OP-7183 (Radelkis) indicator glass electrode and an OP-08303 (Radelkis) reference calomel electrode were used. The reference calomel was modified by replacing the aqueous KCl solution by a 0.1 mol dm^{-3} tetraethylammonium chloride solution in non-aqueous solvent. In the case of measurements in methanol solutions the same solvent was used in the calomel electrode whereas for the measurements in acetone medium another aprotic non-aqueous solvent—acetonitrile—was used instead of acetone. This replacement was caused by poor solubility of the tetraalkylammonium salts in acetone. The modified electrode was incorporated in a salt bridge filled with a 0.01 mol dm^{-3} tetra-*n*-butylammonium perchlorate in appropriate solvent (acetone or methanol). The glass electrode was checked against a standardising system consisting of tetra-*n*-butylammonium picrate and picric acid. The literature pK_a value for picric acid in acetone[40] is 6.3. In methanol, the electrode was checked against a standardising system consisting of tetra-*n*-butylammonium 2,6-dinitrophenolate and 2,6-dinitrophenol. The literature pK_a value for 2,6-dinitrophenol in methanol[41] is 7.8.

Solutions for potentiometric measurements were prepared on a volume basis. All the measurements were carried out at 298.1 ± 0.1 K.

Calculations

The acidic dissociation and cationic homo-and heteroconjugation constants were calculated by using the STOICHIO computer program based on the general method of Kostrowicki and Liwo.[42–44] Parameters s (slope of the response of the glass electrode) and E° (standard emf), obtained from potentiometric titrations in standardising systems together with the results of the potentiometric titrations performed in the systems BH^+–B, served as a basis for the determination of the acidic dissociation and cationic homoconjugation constants. The values of cationic heteroconjugation constants were calculated based on an equilibrium model accounting for the equilibria of dissociation of cationic acids [eqn. (1) and (2)], the cationic homoconjugation eguilibria [eqn. (3) and (4)] and the equilibrium of cationic heteroconjugation without proton transfer [eqn. (5)]. Previously determined acidity and cationic homoconjugation constant values used in calculations were not treated as unknown parameters, but considered as known parameters charged with errors equal to their standard deviation values.

Results and discussion

All the cationic heteroconjugation constant values considered in this work were determined in the BH^+–B_1 systems without proton transfer, for which the condition $\mathrm{ss}pK_a(BH^+) < \mathrm{ss}pK_a(B_1H^+)$ was satisfied. These were the systems of protonated 4-N',N'-dimethylaminopyridine N-oxide ($4NMe_2PyO$) as the proton donor and the N-oxides of 4-methylpyridine (4PicO), 3-methylpyridine (3PicO), 2-methylpyridine (2PicO) and pyridine (PyO) as proton acceptors, as well as, respectively, the systems of protonated trimethylamine N-oxide (Me_3NO) and 4-N',N'-dimethylaminopyridine N-oxide in acetone and methanol. Due to its lack, the cationic homoconjugation constant value of 4-N',N'-dimethylaminopyridine N-oxide in methanol was also determined.

Cationic heteroconjugation constant values determined in the amine N-oxide systems in acetone and methanol are collected in Table 1. All were derived from measurements on the pH scale specific to the selected solvent and, therefore, have been noted as $\mathrm{ss}K_{BHB_1^+}$.[45] They are relatively low, ranging between 0.86 and 2.36 on the logarithmic scale for systems of substituted pyridine N-oxides (for the protonated trimethylamine N-oxide system in acetone the value is much higher—$\log \mathrm{ss}K_{BHB_1^+} = 3.89$), and very low in methanol, where the constant values were determined in one substituted pyridine N-oxide system only and in the trimethylamine N-oxide system with respective $\log \mathrm{ss}K_{BHB_1^+}$ values of 1.34 (0.38) and 1.04 (0.30).

Cationic heteroconjugation constant values in amine N-oxide systems studied in both solvents in Table 2 are supplemented with the previously determined[3] ones in other N-oxide systems. For the sake of comparison, and to provide the basis for discussing the stability of the $[OHO]^+$ bridges in polar non-aqueous solvents, included are also constants in other solvents,[28–31,46,47] namely aprotic protophobic nitromethane, nitrobenzene, acetonitrile, propylene carbonate and acetone, aprotic protophilic N,N-dimethylformamide and the amphiprotic methanol.

Table 1 Cationic heteroconjugation constants, $\mathrm{ss}K_{BHB_1^+}$, of the amine N-oxide systems determined in acetone (AC) and methanol (MeOH) at 298.1 K

	$\log \mathrm{ss}K_{BHB_1^+}$ [a]	
BH^+–B_1 system [b]	AC	MeOH
$4NMe_2PyOH^+$–4PicO	2.36 (0.08)	[c]
$4NMe_2PyOH^+$–3PicO	1.88 (0.13)	0.52 [d]
$4NMe_2PyOH^+$–2PicO	1.86 (1.08)	[c]
$4NMe_2PyOH^+$–PyO	1.54 (0.18)	1.34 (0.38)
Me_3NOH^+–$4NMe_2PyO$	3.89 (0.06)	1.04 (0.30)

[a] Values in parentheses are standard deviations. [b] N-oxide name abbreviations: $4NMe_2PyO$, 4-N',N'-dimethylaminopyridine N-oxide; 4PicO, 4-methylpyridine N-oxide; 3PicO, 3-methylpyridine N-oxide; 2PicO, 2-methylpyridine N-oxide; PyO, pyridine N-oxide; Me_3NO, trimethylamine N-oxide. [c] Heteroconjugation constant value could not be determined from potentiometric measurements. [d] Large standard deviation (greater than heteroconjugation constant value determined).

When estimating the influence of solvent on the cationic heteroconjugation constant values in all the media studied, it can be concluded that the tendency towards cationic heteroconjugation in the systems of N-oxides significantly declines on moving from protophobic aprotic solvents to the protophilic aprotic and the amphiprotic MeOH. A comparison of the constants in particular acid–base systems, BH^+–B_1, in the two last mentioned solvents shows that the constants are in most cases higher in DMF than in MeOH. However, the constants determined in DMF are burdened with much larger standard deviations[39] than those determined in MeOH. This means that the true values of the constants in DMF, falling in the range of $K_{BHB_1^+} \pm 3\sigma$ may be lower than those determined in methanol. Furthermore, the number of the constants determined in MeOH is greater than that determined in DMF. In addition, bearing in mind the finding that in neither of the acid–base systems involving amine N-oxides in another protophilic aprotic solvent, dimethyl sulfoxide, the heteroconjugation equilibria do not exist, the classes of the polar solvents can be arranged in the following series of declining tendency towards cationic heteroconjugation of the $[OHO]^+$ type: protophobic aprotic >> amphiprotic > protophilic aprotic. Identical rank order has been found in the case of the $[OHO]^+$ cationic homoconjugation.[48] A closer look at the constant values reveals their relevance to solvent basicity expressed by the donicity number (DN). The series of solvents arranged by increasing basicity (DN) as shown in eqn. (6) with respective donicity numbers[49]

$$\mathrm{NM} < \mathrm{NB} < \mathrm{AN} < \mathrm{PC} < \mathrm{AC} < \mathrm{MeOH} < \mathrm{DMF} < \mathrm{DMSO} \qquad (6)$$

of 2.7, 4.4, 14.9, 15.1, 17.0, 19.1, 26.6 and 29.8; a declining tendency to cationic heteroconjugation can be seen as expressed by both the cationic heteroconjugation constants and the number of systems in which the constant values can be determined.

A closer look at the heteroconjugation constant values in systems involving the amine N-oxides in the non-aqueous solvents considered (Table 2) supports a hypothesis drawn from investigations of some media[29,30] according to which in the substituted pyridine N-oxide systems containing one proton donor and different proton acceptors, the constants increase with increasing proton acceptor basicity. Again, in systems with a given proton acceptor and various proton donors, the constants increase with decreasing basicity of the proton donor. These regularities are distinct in protophobic aprotic solvents, being less applicable to the protophilic DMF and aprotic MeOH, probably owing to low values of the constants on one hand, and their large standard deviations, on the other. As a consequence of the N-oxide systems obeying these rules, there is a strong tendency towards formation of heterocomplex $[OHO]^+$ bridges by N-oxides of comparable basicities. It should also be stated that those involving trimethylamine N-oxide as a proton donor do not obey the rule of the variation of the constants in systems with a fixed proton acceptor.

Another factor affecting the stability of the heterocomplexed cations of the $[OHO]^+$ type emerging from the study in

Table 2 Cationic heteroconjugation constants, ss$K_{BHB_1^+}$, of the amine N-oxide systems ([OHO$^+$] bridges) in polar non-aqueous solvents—nitromethane (NM), nitrobenzene (NB), acetonitrile (AN), propylene carbonate (PC), acetone (AC), methanol (MeOH) and N,N-dimethylformamide (DMF) at 298.1 K

	Log ss$K_{BHB_1^+}$[a]						
BH^+–B_1 system[b]	NM[28]	NB[29]	AN[30]	PC[31]	AC[3]	DMF[28]	MeOH[3]
$4NMe_2PyOH^+$–4PicO	2.82 (0.09)	4.77 (0.05)	2.63 (0.11)	3.93 (0.02)	2.36 (0.08)	[c]	[c]
$4NMe_2PyOH^+$–3PicO	2.79 (0.12)	4.06 (0.01)	2.00 (0.20)	3.17 (0.01)	1.88 (0.13)	[c]	0.52[d]
$4NMe_2PyOH^+$–2PicO	2.75 (0.13)	3.80 (0.01)	1.71 (0.26)	3.34 (0.03)	1.86 (1.08)	[c]	[c]
$4NMe_2PyOH^+$–PyO	[c]	3.47 (0.05)	2.50 (0.13)	3.36 (0.04)	1.54 (0.18)	2.50 (0.13)	1.34 (0.38)
$Me_2MeOPyOH^+$–4PicO	3.57 (0.05)[45]	—	3.16 (0.02)[46]	—	2.82 (0.04)[45]	[c]	1.41 (0.43)[45]
$Me_2MeOPyOH^+$–3PicO	3.42 (0.09)[45]	—	2.77 (0.13)[46]	—	2.49 (0.02)[45]	[c]	2.22 (0.13)[45]
$Me_2MeOPyOH^+$–2PicO	3.34 (0.06)[45]	—	2.47 (0.04)[46]	—	2.31 (0.06)[45]	[c]	2.30 (0.10)[45]
$Me_2MeOPyOH^+$–PyO	3.22 (0.08)[45]	—	1.85 (0.38)[46]	—	2.00 (0.08)[45]	2.37 (0.78)[45]	2.10 (0.10)[45]
$4PicOH^+$–3PicO	3.85 (0.25)	3.04[d]	3.60 (0.04)	—	2.44 (0.21)	3.27 (0.56)	2.59 (0.20)
$4PicOH^+$–2PicO	3.25 (0.27)	3.05[d]	3.44 (0.03)	—	2.23 (0.18)	3.42 (0.42)	2.66 (0.18)
$4PicOH^+$–PyO	3.21 (0.25)	3.06[d]	3.35 (0.03)	—	2.63 (0.04)	2.86 (0.63)	2.18 (0.27)
Me_3NOH^+–4NMe$_2$PyO	3.56 (0.09)	3.00[d]	4.48 (0.04)	4.28 (0.07)	3.89 (0.06)	5.12 (0.63)	1.04 (0.30)
Me_3NOH^+–4PicO	3.10 (0.04)	4.00 (0.03)	1.99 (0.23)	2.42 (0.09)	2.35 (0.15)	1.98 (0.23)	1.97 (0.62)
Me_3NOH^+–3PicO	3.04 (0.09)	3.76 (0.01)	1.87 (0.15)	2.42 (0.06)	2.82 (0.03)	1.76 (0.31)	[c]
Me_3NOH^+–2PicO	2.50 (0.02)	3.53 (0.02)	[c]	2.30 (0.05)	1.97 (0.36)	[c]	[c]
Me_3NOH^+–PyO	2.45 (0.03)	—	[c]	2.62 (0.03)	2.62 (0.10)	[c]	[c]

[a] Values in parentheses are standard deviations. [b] N-oxide name abbreviations: 4NMe$_2$PyO, 4-N',N'-dimethylaminopyridine N-oxide; 4PicO, 4-methylpyridine N-oxide; 3PicO, 3-methylpyridine N-oxide; 2PicO, 2-methylpyridine N-oxide; PyO, pyridine N-oxide; Me$_3$NO, trimethylamine N-oxide. [c] Heteroconjugation constant value could not be determined from potentiometric measurements. [d] Large standard deviation (greater than heteroconjugation constant value determined).

acetonitrile[30] is the ability of hydrogen bond formation by the acid–base components of the bridge, defined as the arithmetic mean of the cationic homoconjugation constants of the N-oxide constituents of the bridge. Thus a relationship derived and tested[30] for the [OHO$^+$] type asymmetric bridge including the arithmetic mean of the homoconjugation constants and the difference in basicities of the N-oxides constituting the bridge is given in eqn. (7).

$$\log ssK_{BHB_1^+} - 0.5(\log ssK_{BHB^+} + \log ssK_{B_1HB_1^+}) = a\Delta sspK_a + b \quad (7)$$

Having in hand the values of cationic heteroconjugation constants in a number of non-aqueous solvents, the applicability of eqn. (7) was then explored in relation to the solvents studied. Coefficients a and b in eqn. (7), obtained by the linear regression method, together with the correlation coefficients are collected in Table 3. In this Table included are both the coefficients calculated for all the heteroconjugation constants in particular solvents listed in Table 2 and for those remaining after rejection of one or two values deviating most from those on the straight line (numbers in square brackets). In the case when the rejection of the data point deviating most did not improve the correlation, only the coefficients determined on the basis of all data points were included. A closer inspection of the data shows that linear correlations with coefficients R oscillating around −0.9 (ranging from −0.861 for acetone to −0.933 for acetonitrile) were obtained for all the aprotic solvents studied. For the protophilic DMF the coefficient was distinctly lower (−0.7828), while for the amphiprotic MeOH there was no correlation (R = −0.3290). After rejection of one (AN) or two (AC and DMF) data points the correlation coefficients appreciably increased up to a level of 0.97 (95% of explained variance). Only with the amphiprotic MeOH could a correlation coefficient as high as −0.8770 be achieved after rejection of three data points. Further, taking nitromethane as an example, the effect of the limitation of the number of the systems to those with the same proton donor on the value of the correlation coefficient was checked. After consideration of all 15 systems with four different proton donors (4NMe$_2$PyOH$^+$, Me$_2$MeOPyOH$^+$, 4PicOH$^+$ and Me$_3$NOH$^+$), the R-value was −0.8639, whereas in systems with Me$_3$NOH$^+$ as the proton donor the R-value was −0.9800. An example of the graphical presentation of the correlation line in the case of acetone is presented in Fig. 1. The negative slope of line supports the preliminary conclusion that the cationic heteroconjugation constants in the [OHO$^+$] systems increase with decreasing difference in basicity of the N-oxides of B and B$_1$. The foregoing considerations lead to the conclusion that in all the polar solvents studied, eqn. (7) is obeyed for heteroconjugation reactions affording [OHO]$^+$ bridges and can provide a general measure of the tendency towards cationic heteroconjugation in non-aqueous solvents of this type. Moreover, this correlation allows expression of the heteroconjugation constants by quantities characteristic of the reacting N-oxides. One of its practical uses may be, for instance, prediction of the cationic heteroconjugation constant values in those cases where they are too small to be measured directly.

Table 3 Listing of coefficients a, b and R[a] in the linear correlation equation $y = ax + b$ described by eqn. (7) for non-aqueous solvents

Solvent	a	b	R
NM	−0.25 (0.05)	0.33 (0.22)	−0.8639
	[−0.51 (0.05)]	[1.94 (0.30)]	(−0.9800)
NB	−0.28 (0.06)	0.12 (0.29)	−0.9046
AN	−0.35 (0.04)	0.05 (0.17)	−0.9332
	[−0.36 (0.03)]	[0.16 (0.13)]	(−0.9670)
PC	−0.39 (0.06)	0.82 (0.36)	−0.9202
AC	−0.17 (0.03)	−0.57 (0.35)	−0.8612
	[−0.23 (0.02)]	[−0.42 (0.12)]	(−0.9656)
DMF	−0.52 (0.17)	3.06 (0.47)	−0.7828
	[−0.68 (0.09)]	[3.13 (0.21)]	(−0.9679)
MeOH	−0.17 (0.17)	0.99 (0.36)	−0.3290
	[−0.35 (0.09)]	[1.80 (0.18)]	(−0.8770)

[a] Values in parentheses are standard deviations.

Table 4 summarises cationic heteroconjugation constant values determined in systems without proton transfer formed by protonated and free derivatives of pyridine, *i.e.*, organic N-bases producing [NHN]$^+$ bridges in polar non-aqueous solvents, namely aprotic protophobic nitromethane,[32] acetonitrile,[33] acetone,[34] the amphiprotic methanol[34] and aprotic protophilic dimethyl sulfoxide.[50] As seen, their values are much lower as compared with those of the [OHO]$^+$ bridges and range

Table 4 Cationic heteroconjugation constants, $ssK_{BHB_1^+}$, of the substituted pyridine systems[a] in nitromethane (NM), acetonitrile (AN), acetone (AC), methanol (MeOH) and dimethyl sulfoxide (DMSO) at 298.1 K

	$\log ssK_{BHB_1^+}$[b]				
BH^+–B_1 system	NM[32]	AN[33]	AC[34]	MeOH[34]	DMSO[50]
$4NH_2PyH^+$–4Pic	[c]	2.11 (0.17)	2.13 (0.01)	2.29 (0.11)	2.73 (0.03)
$4NH_2PyH^+$–3Pic	[c]	[c]	[c]	1.94 (0.25)	1.91 (0.06)
$4NH_2PyH^+$–2Pic	[c]	[c]	[c]	1.58 (0.65)	1.45 (0.28)
$4PicH^+$–3Pic	2.56 (0.47)	[c]	0.99 (1.00)	[c]	2.91 (0.11)
$4PicH^+$–2Pic	[c]	[c]	[c]	[c]	2.23 (0.44)
$4PicH^+$–Py	[c]	[c]	[c]	1.74 (0.26)	3.20 (0.05)

[a] Amine name abbreviations: $4NH_2Py$, 4-aminopyridine; 4Pic, 4-methylpyridine; 3Pic, 3-methylpyridine; 2Pic, 2-methylpyridine; Py, pyridine. [b] Values in parentheses are standard deviations. [c] The heteroconiugation constant could not be determined from potentiometric measurements.

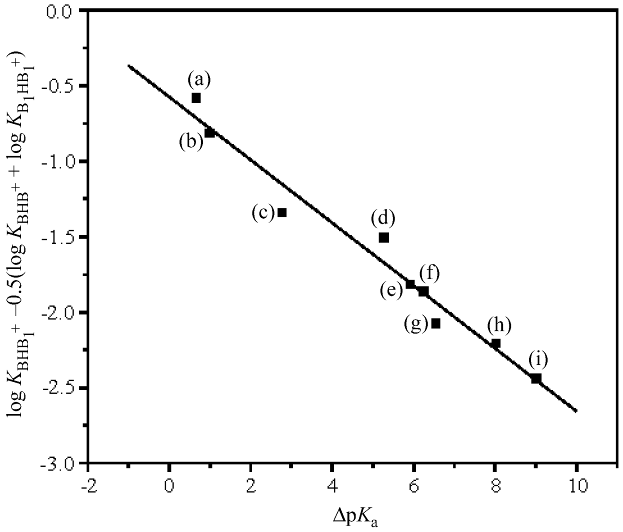

Fig. 1 Correlation between the difference in basicity (ΔpK_a) and the equation: $\log K_{BHB_1^+} - 0.5(\log K_{BHB^+} + \log K_{B_1HB^+_1})$ in acetone. The following labels are assigned to respective *N*-oxide systems: (a) $4PicOH^+$–3PicO; (b) $4PicOH^+$–2PicO; (c) Me_3NOH^+–$4NMe_2PyO$; (d) $4NMe_2PyO$–4PicO; (e) $4NMe_2PyO$–3PicO; (f) $4NMe_2PyO$–4PicO; (g) $4NMe_2PyO$–PyO; (h) Me_3NOH^+–4PicO; (i) Me_3NOH^+–2PicO.

from 0.99 to 3.20 on the logarithmic scale and could be determined potentiometrically for a half of the systems studied (more exactly, for 14 out of a total of 30). Based on the number of the constant values determined one may conclude that the tendency towards cationic heteroconjugation within the class of the *N*-bases studied increases on moving from aprotic protophobic solvents over the amphiprotic MeOH to the protophilic aprotic DMSO This order is the reverse of that observed in amine *N*-oxides systems. Moreover, the constant values determined in each solvent studied are comparable. Thus, the influence of the basicity of solvent is rather insignificant as far as the formation of the $[NHN]^+$ bridges are concerned. Furthermore, systems involving $4NH_2PyH^+$ as the proton donor in DMSO and MeOH support the hypothesis that the cationic heteroconjugation constant values increase with increasing proton acceptor basicity at a fixed basicity of the proton donor. The constants increase on moving from the least basic 2Pic to 3Pic to the strongest base of these series, 4Pic (after consideration of standard deviation values of the constants). The constants in DMSO in systems where 3Pic and 2Pic were proton acceptors and protonated $4NH_2Py$ and 4Pic were used as proton donors can serve as confirmation of the rule that the constant values in systems with a fixed proton acceptor and different proton donors increase with declining basicity of the latter. To generalise both conclusions it can be stated that the available limited experimental evidence suggests that the same rules relating the heteroconjugation constant values to basicities of the proton donors and acceptors are as applicable to systems of substituted pyridines forming $[NHN]^+$ bridges, as those involving $[OHO]^+$ bridges. On the contrary, in systems of organic *N*-bases, the ability to form hydrogen bonding defined as the arithmetic mean of the cationic homoconjugation constants of the *N*-bases cannot be applied. The main reason is that for most of the *N*-bases forming systems for which the heteroconjugation constants were determinable in a particular solvent, the homoconjugation constants could not be determined, thus precluding applicability of eqn. (7).

In Table 5 collected are cationic heteroconjugation constant values (in systems without proton transfer) in acid–base systems containing both heterocyclic *N*-base (pyridine) and some amine *N*-oxide bridges in polar non-aqueous solvents, aprotic protophobic nitromethane,[28] nitrobenzene,[29] acetonitrile,[30] and acetone;[3] the amphiprotic methanol,[3] as well as aprotic protophilic *N*,*N*-dimethylformamide[28] and dimethyl sulfoxide.[51] The constant values related both to experimental $[NHO]^+$ systems in which protonated pyridine was a proton donor and the *N*-oxides were proton acceptors, and to the $[OHN]^+$ systems where the protonated *N*-oxides were proton donors and pyridine was proton acceptor are presented. A closer inspection of these constants shows that the values of constants are determinable for the mixed $[NHO]^+$–$[OHN]^+$ bridges, similar to the case of organic *N*-bases, in almost a half of the systems studied and that they are slightly higher than those determined for organic *N*-bases, ranging from 1.94 to 3.14 on the logarithmic scale.

As far as the influence of solvent on the heteroconjugation constants in these systems is concerned, a preliminary conclusion can be drawn from the available constant values that, similar to the *N*-oxide systems, they decline with increasing solvent basicity. Moreover, a careful inspection of the cationic heteroconjugation constant values leads to a conclusion that with mixed bridges, none of the rules applying to the $[OHO]^+$ bridges is obeyed. In particular, the constant values for a given proton donor do not increase with increasing basicity of proton acceptor, and for a given proton acceptor they do not decline with increasing proton donor basicity. Also eqn. (7) is not applicable here due, amongst other reasons, to indeterminability of the cationic homoconjugation constants of the *N*-bases constituting the heterocomplexed bridges.

Conclusions

To sum up the above considerations, the following conclusions can be formulated.

1. There is a tendency towards cationic heteroconjugation of organic bases in polar solvents and the factors affecting this tendency depend primarily on the nature of the hydrogen bridge formed ($[OHO]^+$, $[NHN]^+$ or $[NHO]^+$–$[OHN]^+$).

2. With the $[OHO]^+$ bridges formed by *N*-oxides of substituted pyridines and trimethylamine, the factors affecting the constants can unambiguously be specified. These are as follows. (a) Solvent basicity. The constants decline with increasing solvent basicity. The polarity of solvent is of minor importance. (b) Basicity of proton acceptor (at a fixed basicity of *N*-oxide

Table 5 Cationic heteroconjugation constants, ss$K_{BHB_1^+}$, of the organic bases systems ([OHN^+–NHO^+] bridges) in nitromethane (NM), nitrobenzene (NB), acetonitrile (AN), acetone (AC), methanol (MeOH), *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) at 298.1 K

	Log ss$K_{BHB_1^+}$ [a]						
BH^+–B_1 system [b]	NM[28]	NB[29]	AN[30]	AC[3]	MeOH[3]	DMSO[51]	DMF[28]
PyH^+–4PicO	2.16 (0.47)	—	2.62 (0.25)	[c]	0.84 [d]	[c]	[c]
PyH^+–3PicO	2.36 (0.28)	—	2.68 (0.19)	[c]	2.43 (0.15)	[c]	[c]
PyH^+–2PicO	3.06 (0.13)	—	2.69 (0.18)	[c]	2.49 (0.10)	[c]	[c]
PyH^+–PyO	2.69 (0.19)	—	2.68 (0.17)	[c]	2.04 (0.18)	[c]	[c]
$4Me_2NPyOH^+$–Py	1.94 (0.78)	3.01 (0.01)	1.33 (0.83)	[c]	[c]	[c]	[c]
$Me_2MeOPyOH^+$–Py	3.05 (0.13)	—	—	2.18 (0.23)	[c]	3.14 (0.46)	2.77 (0.42)
Me_3NOH^+–Py	2.86 (0.02)	2.52 (0.02)	[c]	[c]	[c]	2.57 (0.21)	2.57 (0.16)

[a] Values in parentheses are standard deviations. [b] Organic base name abbreviations: Py, pyridine; 4PicO, 4-methylpyridine *N*-oxide; 3PicO, 3-methylpyridine *N*-oxide; 2PicO, 2-methylpyridine *N*-oxide; PyO, pyridine *N*-oxide; $4NMe_2PyO$, 4-*N′*,*N′*-dimethylaminopyridine *N*-oxide; $Me_2MeOPyO$, 4-methoxy-2,6-dimethylpyridine *N*-oxide; Me_3NO, trimethylamine *N*-oxide. [c] Heteroconjugation constant value could not be determined from potentiometric measurements. [d] Large standard deviation (greater than heteroconjugation constant value determined).

of proton donor). The constants increase with increasing basicity of proton acceptor. (c) Basicity of proton donor (at a fixed basicity of proton acceptor). The constants decline with increasing basicity of proton donor. (d) Ability of hydrogen bond formation by *N*-oxides constituting the $[OHO]^+$ bridge, defined as the arithmetic mean of cationic homoconjugation constants of the *N*-oxides. The heteroconjugation constants increase with increasing "mean" value of the cationic homoconjugation constant. (e) For the $[OHO]^+$ bridges the tendency towards cationic heteroconjugation in polar non-aqueous solvents can be expressed by a linear relationship [eqn. (7)] between cationic heteroconjugation constant value and the difference in basicities of the proton donor and acceptor and their ability to form hydrogen bonding. (f) The stability of the $[NHN]^+$ bridges formed by heterocyclic *N*-bases (substituted pyridines) depends in the same manner on the basicity of the proton donor and acceptor as does the stability of the $[OHO]^+$ bridges. (g) Similarly to the $[OHO]^+$ bridges, solvent basicity affects the stability of the $[NHO]^+$–$[OHN]^+$ bridges formed by substituted pyridines and amine *N*-oxides. (h) The tendency towards heteroconjugation in the $[NHN]^+$ and $[NHO]^+$–$[OHN]^+$ bridges cannot be determined by correlations derived for the $[OHO]^+$ bridges.

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