Conjugated, cross-conjugated, and pseudo-cross-conjugated derivatives of a pyridinium alkaloid from *Punica granatum*

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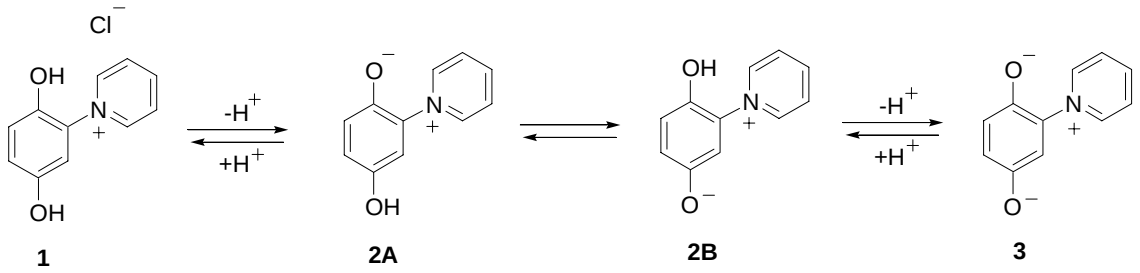
Abstract
A series of substituted N-(2′,5′-dihydroxyphenyl)pyridinium salts which are able to form mesomeric betaines have been prepared starting from *p*-benzoquinone. Depending on the substitution pattern these compounds form conjugated, cross-conjugated, or pseudo-cross-conjugated tautomers.

Keywords: Heterocyclic mesomeric betaines, hydroquinones, pyridinium-olates

Introduction

In 1994 the pyridinium substituted hydroquinone **1** (Scheme 1) was isolated as chloride from the leaves of pomegranates (*Punica granatum* L.).[1] Although this molecule had already been described as early as 1901[2] and since then several syntheses have been published,[3] it represents an unique structure within the class of alkaloids.[4] Its relationship to plastoquinol which plays key roles in photosynthesis, however, is apparent. Pyridinium substituted hydroquinones have attracted interest as partial structure of modified rifamycins with antibacterial activities.[5] Related structures are antifungal benzopyranylpyridinium-olates[6] and the alkaloid Ipohardine (*Ipomoea violacea*) which is an example of a phenolic pyridinium compound.[7] An interesting feature of alkaloid **1** is its ability to exist as heterocyclic mesomeric betaine after deprotonation of one of the hydroxy groups, forming either a conjugated mesomeric betaine **2A** or a cross-conjugated mesomeric betaine **2B**. In continuation of our work on betainic[8] and oligocationic structures[9] we started a spectroscopic reinvestigation of this compound,[10] because molecules which are interconvertible between the distinct classes of conjugated (CMB), cross-conjugated (CCMB), and pseudo-cross-conjugated mesomeric betaines (PCCMB) are very seldom.[11] The alkaloids Neooxygambirtannine,[12] Protopapaverinium betaine,[13] Dehydrodiscretamine,[14] and a red compound isolated from an *Aristolochia* species[15] are examples of natural mesomeric betaines

with interesting tautomeric forms.[4] Twofold deprotonation of **1** yields a stable anionic tripole **3** with two negative and one positive charge within a common π-electron system which supplements our cationic tripoles ("betainium salts") which we described earlier.[16]



Scheme 1

According to the valence bond approach the charges in conjugated mesomeric betaines (CMB) are in mutual conjugation and common atoms for either the positive and negative charges exist (Figure 1). By contrast, cross-conjugated mesomeric betaines (CCMB) consist of positively charged and negatively charged partial structures which are exclusively delocalized in separated parts of the molecules.

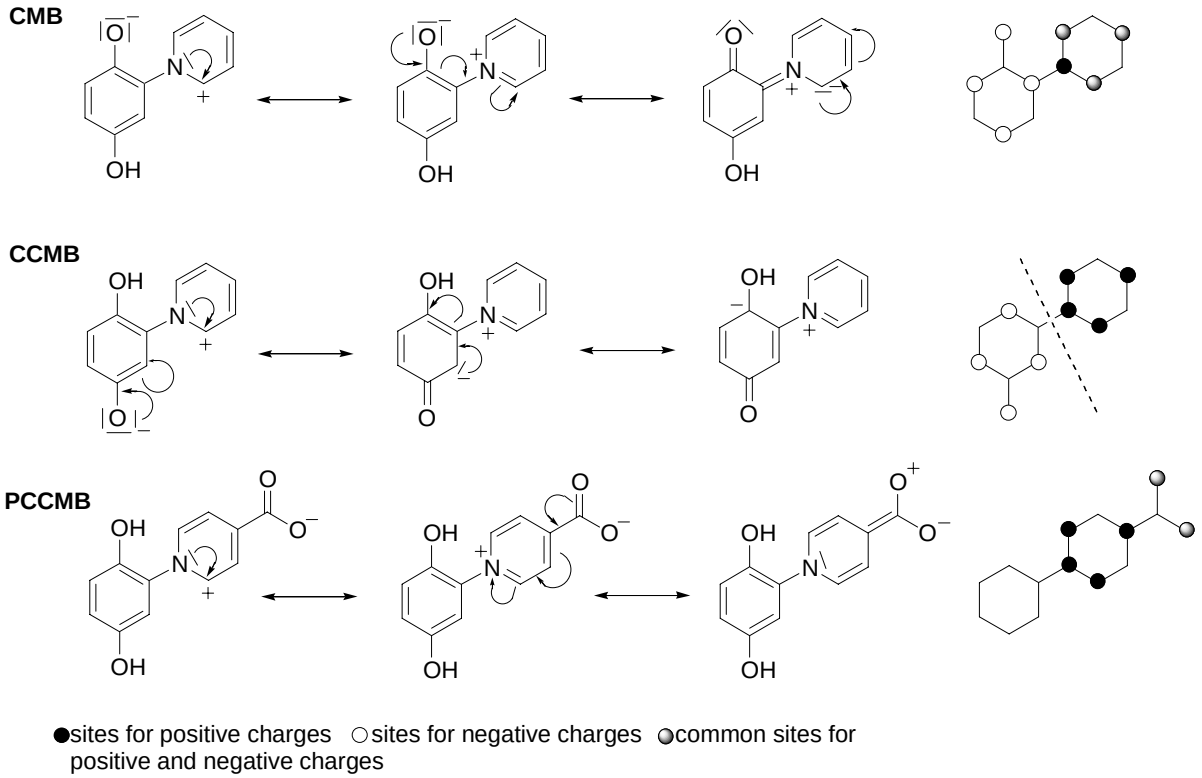


Figure 1

Electron sextet structures without internal octet stabilization can be formulated of pseudo-cross-conjugated mesomeric betaines (PCCMB) which are therefore hybrids between CMB and CCMB. According to this approach, the charges are effectively but not exclusively delocalized in separated parts of the molecule.[17]

The frontier orbital profiles and isoconjugate equivalents yield additional informations about the electronic differences of the distinct classes of MB.[18] Regardless of the predominant tautomer, the anionic partial structure of the betaines **2** is the phenolate **I** which is isoconjugate to the benzyl anion **II**, the HOMO of which **III** is depicted in Figure 2. Bonds to the cationic increment through active positions of the HOMO - starred atoms in **IV** - give conjugated mesomeric betaines (CMB), whereas bonds through inactive positions which are unstarred atoms in **IV** give cross-conjugated mesomeric betaines (CCMB).

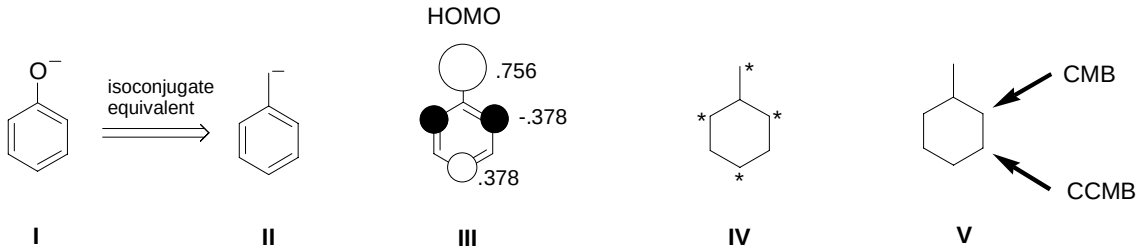


Figure 2

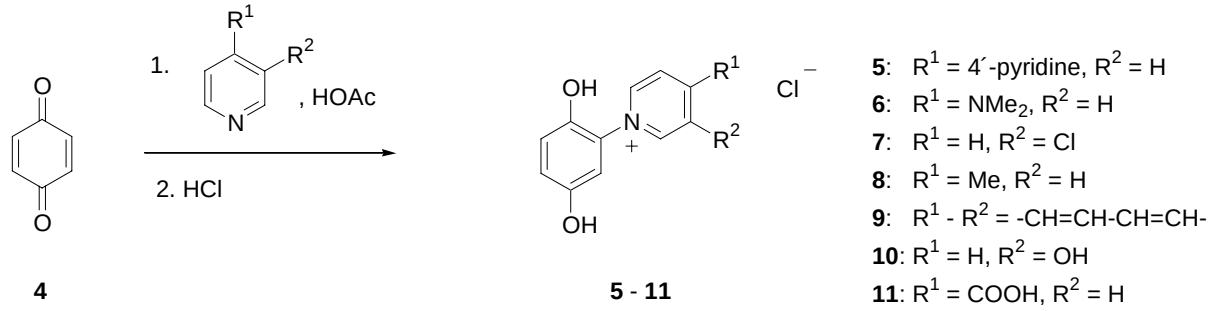
We report here the syntheses and the structures of derivatives of the *Punica* alkaloid **1**, which combine the structure elements of all three major classes of heterocyclic mesomeric betaines, *i.e.* conjugated (CMB), cross-conjugated (CCMB), and pseudo-cross-conjugated mesomeric betaines (PCCMB). We examined basic, neutral, and acidic substituents on the pyridinium moiety which give rise to the formation of tautomers which are members of the aforementioned distinct classes of heterocyclic mesomeric betaines.

Results and Discussion

The *N*-(2′,5′-dihydroxyphenyl)-pyridinium chlorides **5**, **7**, **8**, **10**, and **11** and the isochinolinium derivative **9** were formed on treatment of *p*-benzoquinone **4** in concentrated acetic acid with the substituted pyridines and isoquinoline, respectively, and subsequent addition of excess hydrochlorid acid. The 4-(dimethylamino)pyridine derivative **6** resulted from a reaction of *p*-benzoquinone and DMAP in water over a period of three hours, followed by acidification with excess hydrochlorid acid (Scheme 2).

With exception of the 4,4′-bipyridine derivative **5** (*vide infra*), all salts **6** – **11** are yellow to greenish-yellow in color. In ^{1}H NMR spectroscopy in DMSO-d_6 the hydroxy groups of the hydroquinone moieties of **6** – **11** are detectable between δ = 9.98 ppm and 10.55 ppm (5'-OH) and δ = 9.48 and 9.85 ppm (2'-OH), respectively. The assignments of the hydroxy groups were

confirmed by a HH-COSY NMR measurement of the natural product **1** which clearly indicated that the 5′-hydroxy group causes the more downfield shifted resonance frequency. An NMR titration revealed that the 5′-hydroxy group of **1** is the most acidic one in polar solvents and that the alkaloid forms a mixture between **2A** and **2B** in DMSO-d_6. The aromatic protons of the hydroquinone moities of **6** – **11** appear between δ = 6.84 ppm and 7.12 ppm, depending on the substitution pattern of the hetarenium substituents. Concentrated aqueous solutions of **5** – **11** are acids. The salts have two pK_a values at approximately 7 and 10, respectively, unless they possess an additional acidic functional group. Table 1 collects the pK_a values, the dissociation constants K_c and the degrees of dissociation α.



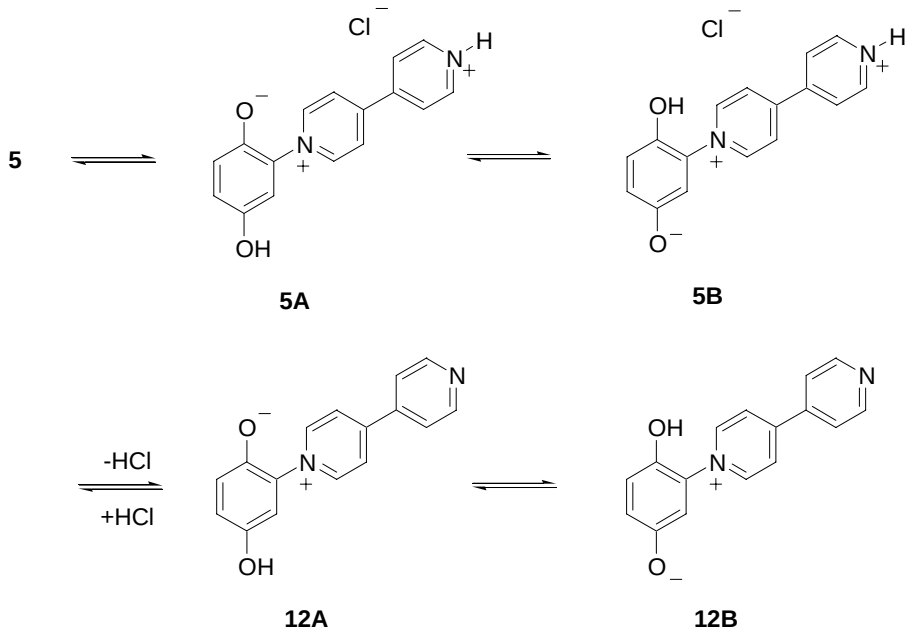
Scheme 2

Table 1. Acid-base properties of the salts **5** – **11**

Compound	pH of a conc. solution (c_0)	c_0 [mmol/L]	pK_a (1)	pK_a (2)	pK_a (3)	K_C	α
1	4.45	28.0	10.2	6.9	-	$4.5*10^{-8}$	$1.3*10^{-3}$
5	4.50	14.0	10.1	7.0	n.d.	$7.1*10^{-8}$	$2.3*10^{-3}$
6	6.30	4.0	10.5	7.5	-	$6.3*10^{-11}$	$1.3*10^{-4}$
7	6.10	1.3	9.5	6.6	-	$4.8*10^{-10}$	$6.1*10^{-4}$
8	4.30	28.0	10.2	7.1	-	$9.0*10^{-8}$	$1.8*10^{-3}$
9	2.70	12.0	10.2	7.0	-	$4.0*10^{-4}$	0.166
10	3.20	33.0	(12)	8.9	4.0	$1.2*10^{-5}$	0.019
11	1.70	24.2	10.5	8.0	1.7	0.094	0.825

A concentrated aqueous solution of the 4,4′-bipyridine substituted derivative **5** has a pH of 4.50. We determined the pK_a values of **5** by titration of an aqueous solution at rt to be 7.0 and 10.1. The third pK_a value, attributable to the 4′-pyridine substituent, could not be determined. The color of **5** hints at the formation of tripolar tautomers in equilibrium, possessing partial structures of a CMB (**5A**) or a CCMB (**5B**) plus one cationic substituent. This assumption is supported by the following additional observations: In contrast to the salts **6** - **11**, but in agreement to all mesomeric betaines (*vide infra*), the hydroxy group protons are not detectable in ^{1}H NMR spectroscopy in DMSO-d_6 at room temperature. The resonance frequencies of the α-

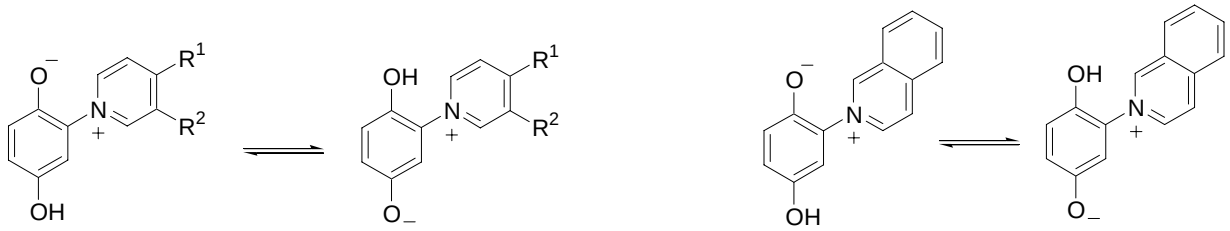
and β-positions of the 4′-pyridine substituent are slightly shifted downfield in DMSO-d_6 in comparison to non-protonated 4′-pyridine substituents. On addition of hydrochloric acid to an aqueous solution of **5** the color changes from brown to yellowish orange, and this hypsochromic shift seemingly is characteristic for the formation of protonated hydroquinone moieties (*cf*. MB **17**). In agreement to this, the mesomeric betaine **12** was obtained as dark violet crystals on treatment of an aqueous solution of **5** with sodium carbonate to pH 8 and subsequent crystallization of the deprotonated species. It was not possible, however, to differentiate between the CMB **12A** and the CCMB **12B** by spectroscopic methods, as only one set of NMR signals is observable in DMSO-d_6 at room temperature. On betaine formation, the resonance frequencies of the hydroquinone protons shift upfield [e.g. -Δδ(3-*H*) = 0.16 ppm]. In accordance with the formulation of a charge-separation in the ground-state of the molecules the betaine **12** displays a strong effect of negative solvatochromism.[19] Thus, the UV-VIS absorption maxima shift from 398 nm in DMSO (E_T^N = 0.444),[20] 308 nm in 2-propanol (E_T^N = 0.546), 302 nm in ethanol (E_T^N = 0.654), 272 nm in glycerine (E_T^N = 0.812) to 202 nm in water (E_T^N = 1.000).



Scheme 3

The 4-(dimethylamino)pyridinium-substituted hydroquinone **6**, which is slightly beige in color, is a weak acid. As expected, no hints at the formation of tripolar tautomers analogous to **5** were observable in the spectra. We were not able to isolate a stable mesomeric betaine **13** (Scheme 4) on deprotonation of **6**, although the titration curve as well as the changing color of the solution of **6** from intensely yellow to dark green (pH 8) with increasing pH indicates its existence. By contrast, the mesomeric betaine **14**, which is dark red in color, and **15**, which is almost black, were obtained on deprotonation of the yellow salts **7** and **8** either with the anion exchange resin Amberlite IRA-402 in its hydroxy form or with sodium carbonate in water. The

isoquinolinium derivative **9** is a strong acid in comparison to the other derivatives with neutral substituents. Its mesomeric betaine **16** was isolated as intensely red solid in quantitative yield. On betaine formation, the resonance frequencies of 1-*H* and 3-*H* of the isochinolinium ring shift 0.31 ppm and 0.14 ppm to upper field, respectively. All betaines **14**, **15**, and **16** show the effect of negative solvatochromism. The absorption maxima differences $\Delta\lambda_{max}$ are 48 nm for **15** on changing the solvent from toluene (E_T^N = 0.099) to water (E_T^N = 1.000), and approximately 100 nm for **14** and **16** on changing the solvent from acetone (E_T^N = 0.355) to water (E_T^N = 1.000). Additional absorption maxima are presented in the experimental section. The effect of negative solvatochromism of **16** is shown in Figure 2.



13: $R^1 = NMe_2$, R^2 = H
14: R^1 = H, R^2 = Cl
15: R^1 = Me, R^2 = H

16

Scheme 4

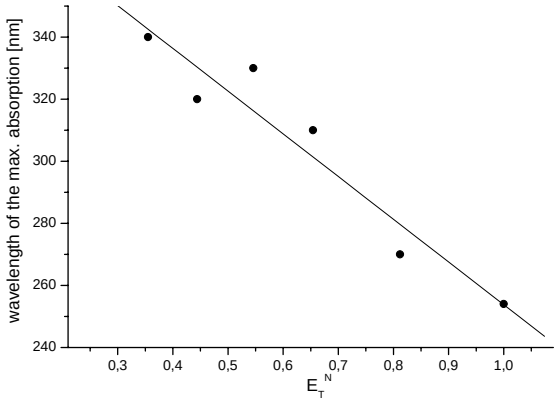


Figure 2. Effect of negative solvatochromism of betaine **16**.

Next we focussed our interest on acidic substituents on the pyridinium ring. The titration curve of the 3-hydroxypyridinium salt **10**, which is depicted in Figure 3, shows two pK_a values at 4.0 and 8.9, and one additional buffer area at approximately pK_a 12.

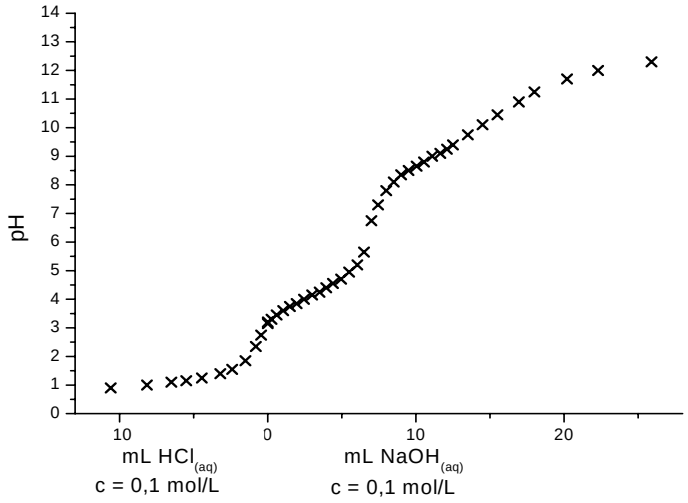
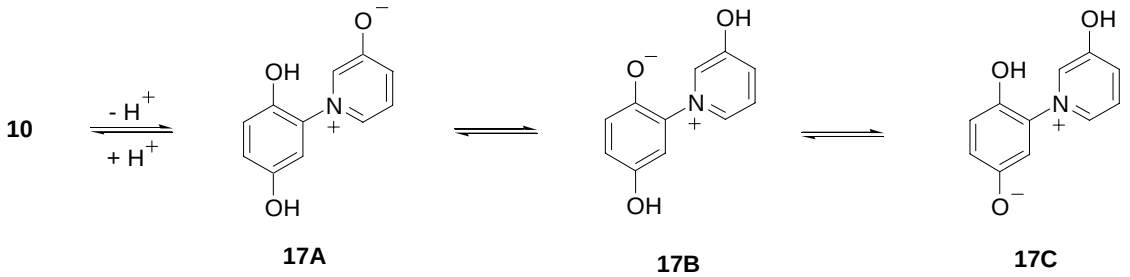


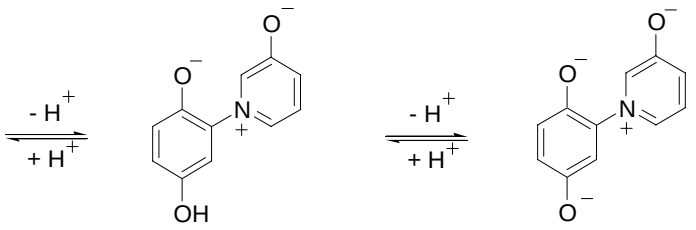
Figure 3. Titration curve of **10**.

A concentrated aqueous solution of **10** has a pH value of 3.2, so that deprotonated species such as the mesomeric betaine **17** exist in solution (Scheme 5). In principle, **17** can adopt two tautomers **17A** and **17B** which belong to the class of conjugated mesomeric betaines (CMB), and one tautomer **17C** in which the charges are in cross-conjugation (CCMB). A comparison of 1-methyl-pyridinium-3-olate (pK_a = 4.96)[21] and the alkaloid **1** (pK_a = 6.9 / 10.0) hint at the predominant formation of tautomer **17A** in aqueous solution. Indeed, Amberlite IRA-402 in its hydroxy form converted the cation **10** into the mesomeric betaine **17A**. Its slightly yellow color correspond well to the formulated structure. In ^{1}H NMR spectroscopy in DMSO-$_6$ the pyridinium resonance frequencies appear at δ = 8.09, 7.94, 7.32, and 7.30 ppm and are in total agreement to a pyridinium-3-olate moiety **17A**.[22]



Scheme 5

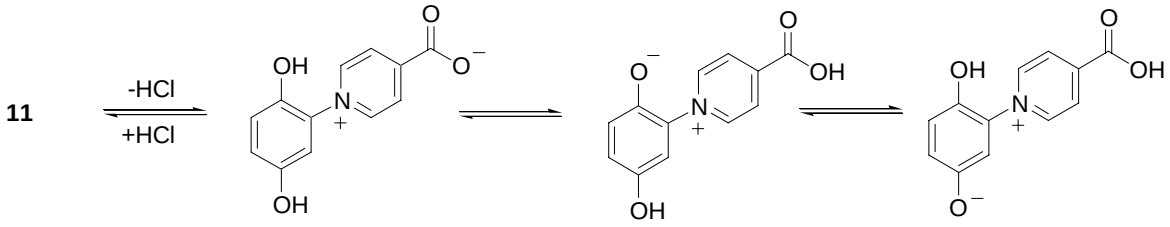
The anionic tripole **18** (pK_a 8.9; only one tautomer shown), and the dianionic tetrapole **19** (pK_a 12) could not be isolated.



18 **19**

Scheme 6

The pH value of a concentrated solution of the isonicotinic acid derivative **11**, which is yellow in color, is 1.7, thus indicating the existence of a mesomeric betaine **20** in solution (Scheme 7). The formation of a pseudo-cross-conjugated tautomer **20A** is unambiguously proved by the clear signals of the hydroxy groups at δ = 10.47 ppm and 9.70 ppm in ^{1}H NMR spectroscopy in DMSO-d_6, the absence of the resonance frequencies of the carboxylic acid group, and the color of the solution. The carboxyl carbon atom appears at δ = 163.5 ppm in the ^{13}C NMR spectra under these conditions. Although stable in the solid state, the salt **11** decomposes slowly in solution under decarboxylation to form pyridine and hydroquinone. Under the conditions of the electron impact mass spectrometry (EIMS) a decarboxylated product was detected at *m/z* = 186 amu. Attempts to isolate the mesomeric betaine **20**, however, failed.



20A **20B** **20C**

Scheme 7

In summary, the type of conjugation identified in our model compounds depends on the substitution pattern of the pyridinium ring. Even in dipolar solvents such as DMSO tautomers predominate which form conjugated (**17A**) and pseudo-cross-conjugated (**20A**) mesomeric betaines.

Experimental Section

General Procedures. Melting points are uncorrected. NMR spectra were recorded at 400 MHz and 200 MHz (^{1}H NMR), and 100 MHz and 50 MHz, respectively, in DMSO-d_6 (^{13}C NMR) with TMS as internal reference. The IR spectra were taken with a Vektor 22 FTIR (KBr pellets). The

mass spectra were measured with a Hewlett-Packard/Agilent LCMSD 1100 Series at 300°C drying gas temperature and 0 V fragmentor voltage (ESIMS), or with a Hewlett-Packard HP 5989B (EIMS).

General procedure for the synthesis of the *N*-(2′,5′-dihydroxyphenyl)-pyridinium chlorides (5 and 6 – 11)

2.7 g (25.0 mmol) of *p*-benzoquinone were suspended in 8 mL of concentrated acetic acid and treated slowly with 25.0 mmol of the substituted pyridines, unless otherwise noted. The resulting dark mixtures were diluted with 4 mL of water, heated and treated with 8 mL of 18% hydrochlorid acid. On cooling, solids precipitated which were filtered off, recrystallized from water and dried *in vacuo*.

***N*-(2′,5′-Dihydroxyphenyl)-4-(4′-pyridine)-pyridinium chloride (5).** 3.9 g of 4,4′-bipyridine were used to yield 4.2 g (14.0 mmol; 56%) of a brown solid, mp. 128 °C. IR: 3423, 2580, 1632, 1605, 1511, 1209, 818 cm^{-1}. UV (MeOH): λ_{max} = 295, 392 nm. ^1H NMR: δ = 9.27 (d, *J* = 7.0 Hz, 2H), 8.90 (dd, *J* = 1.5 Hz, *J* = 4.6 Hz, 2H), 8.69 (d, *J* = 7.0 Hz, 2H), 8.10 (dd, *J* = 1.5 Hz, *J* = 4.6 Hz, 2H), 7.12 (d, *J* = 2.6 Hz, 1H), 7.07 (s, 1H), 7.00 (d, *J* = 2.6 Hz, 1H) ppm. ^{13}C NMR: δ = 149.4, 147.8, 146.4, 144.9, 142.1, 125.8, 124.7, 117.6 ppm. ESIMS: *m/z* = 263 (M^+, 20), 110 (75), 156 (100) amu. Anal. Calcd. for $C_{16}H_{13}ClN_2O_2$ (300,07) · H_2O: C: 60.29; H: 4.74; N: 8.79. Found: C: 61.50; H: 4.66; N: 8.77.

***N*-(2′,5′-Dihydroxyphenyl)-4-(dimethylamino)pyridinium chloride (6).** 0.85 g (7.0 mmol) of *p*-benzoquinone were suspended in 25 mL of water and treated slowly with a concentrated solution of 0.75 g (7.0 mmol) of 4-(dimethylamino)pyridine in water. The mixture was then heated over a period of 3 h at reflux temperature. After cooling to rt concentrated hydrochloric acid was added until a red solid precipitated which was filtered off, washed with ethanol, and dried *in vacuo*. 0.9 g (3.4 mmol; 48%) of the salt were isolated, mp. 264 °C. IR: 3441, 3211, 1632, 1651, 1578, 1512, 1409, 1313, 1203, 1184, 819, 766 cm^{-1}. UV (MeOH): λ_{max} = 300 nm. ^1H NMR: δ 9.98 (s, 1H), 9.48 (s, 1H), 8.32 (d, *J* = 6.6 Hz, 2H), 7.08 (d, *J* = 6.6 Hz, 2H), 6.97 (m, 1H), 6.84 (m, 2H), 3.26 (s, 6H) ppm. ^{13}C NMR: δ 162.0, 155.8, 150.2, 143.0, 129.1, 117.7, 112.6, 107.2 ppm. The signals of the methyl group are overlapped by the signals of DMSO; EIMS: *m/z* = 231 (M^+, 100) amu. Anal. Calcd. for $C_{13}H_{17}ClN_2O_3$ (284,09) · H_2O: C: 54.84; H: 6.02; Cl: 12.45; N: 9.84; O: 16.86. Found: C: 54.75 ; H: 5.95; Cl: 12.40; N: 9.48; O: 17.42.

***N*-(2′,5′-Dihydroxyphenyl)-3-chloropyridinium chloride (7).** 10.0 g (9.3 mmol) of *p*-benzoquinone and 0.8 mL (0.93 mmol) of 3-chloropyridine were used. 0.24 g (0.9 mmol; 10 %) of a yellow solid were obtained, mp. 224 °C. IR: 3414, 3028, 1512, 1468, 1437, 1341, 1217, 1200, 860, 821, 796, 777 cm^{-1}. UV (MeOH): λ_{max} = 285, 370 nm. ^1H NMR: δ = 10.42 (s, 1H), 9.69 (s, 1H), 9.62 (t, *J* = 1.6 Hz, 1H), 9.18 (dt, *J* = 1.0 Hz, *J* = 6.0 Hz, 1H), 8.93 (ddd, *J* = 1.0 Hz, *J* = 1.6 Hz, *J* = 9.5 Hz, 1H), 8.30 (dd, *J* = 6.0 Hz, *J* = 9.5 Hz, 1H), 7.02 (m, 3H) ppm. ^{13}C NMR: δ = 150.1, 146.4, 145.5, 142.4, 133.9, 129.5, 128.3, 117.9, 112.6 ppm. ESIMS: *m/z* = 220 (M^+, 100) amu. Anal. Calcd. for $C_{11}H_{11}Cl_2NO_3$ (275,01) · H_2O: C: 47.85; H: 4.02; Cl: 25.68; N: 5.07; O: 17.38. Found: C: 48.07; H: 3.98; Cl: 25.67; N: 4.80; O: 17.48.

***N*-(2′,5′-Dihydroxyphenyl)-4-methyl-pyridinium chloride (8).** 2 mL (25.0 mmol) of 4-

methylpyridine were used. 4.25 g (18.0 mmol; 72 %) of a yellow solid were obtained, mp. 258 °C. IR: 3394, 3173, 1637, 1519, 1459, 1400, 1350, 1329, 1280, 1216, 827, 792 cm^{-1}. UV (MeOH): λ_{max} = 250, 315, 385 nm. ^{1}H NMR: δ 10.29 (s, 1H), 9.64 (s, 1H), 8.99 (d, *J* = 6.7 Hz, 2H), 8.08 (d, *J* = 6.7 Hz, 2H), 7.00 (m, 3H), 2.70 (s, 3H) ppm.^{13}C NMR: δ 160.2, 150.2, 145.2, 142.6, 128.0, 119.0, 118.0, 112.6, 21.6 ppm. EIMS: *m/z* = 201 (M^+, 75), 110 (100), 93 (60) amu. Anal. Calcd. for $C_{12}H_{14}ClNO_3$ (255,07) · H_2O: C: 56.37; H: 5.52; Cl: 13.87; N: 5.48; O: 18.77. Found: C: 56.09; H: 5.46; Cl: 13.83; N: 5.11; O: 19.51.

***N*-(2′,5′-Dihydroxyphenyl)-isoquinolinium chloride (9).** 3.23 g (25 mmol) of isoquinoline were used. 1.75 g (7.0 mmol; 26 %) of a yellow solid were isolated, mp. 143 °C. IR: 3431, 3189, 3064, 1641, 1516, 1506, 1392, 1326, 1202, 837, 789, 753 cm^{-1}. UV (MeOH): λ_{max} = 305, 405 nm. ^{1}H NMR: δ 10.55 (s 1H), 10.28 (s, 1H), 9.85 (s, 1H), 8.85 (d, *J* = 7.1 Hz, 1H), 8.69 (d, *J* = 7.1 Hz, 1H), 8.63 (d, *J* = 8.2 Hz, 1H), 8.45 (d, *J* = 8.2 Hz, 1H), 8.34 (t, *J* = 7.1 Hz, 1H), 8.12 (t, *J* = 7.1 Hz, 1H), 7.12 (m, 3H) ppm. ^{13}C NMR: δ 151.7, 150.3, 142.8, 140.2, 137.5, 137.1, 136.5, 131.2, 130.9, 130.1, 127.2, 125.2, 119.2, 118.1, 112.8 ppm. EIMS: *m/z* = 236 (M^+, 100) amu. Anal. Calcd. for $C_{15}H_{14}ClNO_3$ (291,07) · H_2O: C: 61.76; H: 4.84; Cl: 12.15; N: 4.80; O: 16.45. Found: C: 61.67; H: 4.82; Cl: 12.25; N: 4.52; O: 16.74.

***N*-(2′,5′-Dihydroxyphenyl)-3-hydroxy-pyridinium chloride (10).** 2.4 g (25.0 mmol) of 3-hydroxypyridine were used. 3.6 g (14.5 mmol; 58%) of a yellow solid were obtained, mp. 185 °C. IR: 3241, 1582, 1516, 1489, 1334, 1199, 827, 787 cm^{-1}; UV (MeOH), λ_{max} = 310 nm; ^{1}H NMR: δ = 12.46 (s, 1H), 10.36 (s, 1H), 9.71 (s, 1H), 8.49 (m, 1H), 8.45 (dt, *J* = 0.9 Hz, *J* = 5.6 Hz, 1H), 8.05 (dq, *J* = 0.9 Hz, *J* = 8.8 Hz, 1H), 7.95 (dd, *J* = 5.6 Hz, *J* = 8.8 Hz, 1H), 6.99 (m, 3H) ppm; ^{13}C NMR: δ = 158.1, 150.1, 142.5, 135.9, 134.3, 132.4, 130.2, 128.0, 119.0, 118.0, 112.4 ppm; EIMS: *m/z* = 203 (M^+, 13), 110 (100), 95 (26) amu. Anal. Calcd. for $C_{11}H_{10}ClNO_3$ (239,03) · H_2O: C: 51.27; H: 4,69; N: 5.44. Found: C: 51.04; H: 4.64; N: 5.11.

***N*-(2′,5′-Dihydroxyphenyl)-pyridinium-4-carboxylic acid chloride (11).** 3.08 g (25.0 mmol) of isonicotinic acid were used. 4.7 g (20.5 mmol; 82 %) of an orange solid were obtained, mp. 263 °C. IR: 3144, 3063, 1729, 1641, 1611, 1611, 1525, 1513, 1433, 1361, 1270, 1250, 1214, 1197, 850, 792, 773 cm^{-1}. UV (MeOH): λ_{max}: 290, 400 nm. ^{1}H NMR: δ 10.47 (s, 1H), 9.70 (s, 1H), 9.27 (d, *J* = 6.8 Hz, 2H), 8.47 (d, *J* = 6.8 Hz, 2H), 7.00 (m, 3H) ppm. ^{13}C NMR: δ 163.4, 150.3, 147.4, 142.4, 129.6, 126.6, 119.6, 118.1, 112.6 ppm. EIMS: *m/z* = 230 (M^+, 10), 186 (15), 123 (100), 110 (75) amu. Anal. Calcd. for $C_{12}H_{10}ClNO_4$ (267,66): C: 53.85; H: 3.77; N: 5.23. Found: C: 53.27; H: 3.75; N: 4.90.

General procedure for the preparation of the mesomeric betaines

Method A. A column was filled with 20 mL of Amberlite IRA-402 and washed with 400 mL of distilled water. Then, the resin was treated with 25 mL of a 4 % sodium hydroxide solution. After 15 minutes, the anion exchange resin was washed with water until the elute had pH 7, and then with 40 mL of a water/ethanol mixture (3:1). The pyridinium salts were dissolved in the same solvent mixture, added to the resin and eluted immediately. The elute was evaporated to dryness, and the dark residue was dissolved in ethanol. Insoluble precipitates were filtered off, and the filtrate was concentrated *in vacuo* again to crystallize the solids.

Method B. Aqueous solutions of the salts were treated with sodium carbonate to pH 8. The water was distilled off, the residue was taken up in ethanol, and insoluble residues were filtered off. The compounds crystallized on concentrating the solutions.

1-Hydroxyphenyl-2-(4′-pyridine)-pyridinium-4-olate (12a) / 4-hydroxyphenyl-2-(4′-pyridine)-pyridinium-1-olate (12b). Method B, yield: 80 % of dark violet crystals, mp. 230°C. IR: 3425, 1635, 1598, 1412, 1385, 805 cm^{-1}. ^1H NMR: δ 9.31 (d, *J* = 7.1 Hz, 2H), 8.87 (dd, *J* = 1.5 Hz, *J* = 4.6 Hz, 2H), 8.65 (d, *J* = 7.1 Hz, 2H), 8.09 (dd, *J* = 1.5 Hz, *J* = 4.6 Hz, 2H), 6.96 (m, 3H) ppm. ^{13}C NMR: δ 151.0, 148.8, 146.3, 144.6, 142.5, 126.6, 124.5, 117.3 ppm. ESIMS: *m/z* = 265 (100) amu. HR-ESITOFMS: Calcd. for $C_{16}H_{13}N_2O_2$ ($M+H^+$): 265.0977 amu. Found: 265.0971 amu.

1-Hydroxyphenyl-2-(3-chloro-pyridinium)-4-olate (14a) / 4-hydroxyphenyl-2-(3-chloro-pyridinium)-1-olate (14b). Method B. The substance was isolated as blackish red solid, yield 85%, mp. 201 °C. IR: 3425, 1619, 1561, 1475, 1264, 1207, 1124, 803, 771; 678 cm^{-1}. UV (Me_2CO): λ_{max} = 345 nm; UV (EtOH): λ_{max} = 298 nm; UV (glycerine): λ_{max} = 274 nm; UV (water): λ_{max}: 255 nm. ^1H NMR: δ 9.62 (s, 1H), 9.18 (d, *J* = 6.6 Hz, 1H), 8.93 (m, 1H), 8.30 (d, *J* = 6.6 Hz, 1H), 7.0 (m, 3H) ppm. ^{13}C NMR: δ 148.2, 148.0, 145.6, 145.4, 133.8, 129.5, 128.3, 119.8, 118.5, 112.3 ppm. ESIMS: *m/z* = 222.1 (100) amu. Anal. Calcd. for $C_{11}H_{12}ClNO_4 \cdot 2\ H_2O$ (257.05): C: 51.27; H: 4.69; N: 5.44. Found: C: 51.85; H: 4.19; N: 4.69.

1-Hydroxyphenyl-2-(4-methyl-pyridinium)-4-olate (15a) / 4-hydroxyphenyl-2-(4-methyl-pyridinium-1-olate (15b). Method A. The betaine was obtained as black solid in 18 % yield, mp. 274°C. IR: 3423, 1638, 1454, 1267, 1201, 1182, 797 cm^{-1}. UV (PhMe): λ_{max} = 288 nm; UV ($CHCl_3$): λ_{max} = 267 nm; UV (DMSO): λ_{max} = 270 nm; UV (*i*PrOH): λ_{max} = 250 nm; UV (glycerine): λ_{max} = 250 nm; UV (water): λ_{max} = 240 nm; ^1H NMR: δ 8.99 (d, *J* = 6.3 Hz, 2H), 7.95 (d, *J* = 6.3 Hz, 2H), 6.72 (m, 3H), 2.65 (s, 3H) ppm. ^{13}C NMR: δ 157.8, 149.3, 144.4, 142.1, 127.1, 117.4, 116.4, 111.9 ppm. ESIMS: *m/z* = 202 (100) amu. HR-ESITOFMS: Calcd. for $C_{12}H_{12}NO_2$ ($M+H^+$): 202.0868. Found: 202.0878.

1-Hydroxyphenyl-2-isoquinolinium-4-olate (16a) / 4-hydroxyphenyl-2-isoquinolinium-1-olate (16b). Method B. A red solid was isolated in quantitative yield, mp. 134 °C. IR: 3440, 2361, 2342, 1641, 1516, 1392, 1202, 837, 799, 753 cm^{-1}. UV (EtOH): λ_{max}: 310 nm. ^1H NMR: δ 9.97 (s, 1H), 8.71 (d, *J* = 6.5 Hz, 1H), 8.52 (s, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 8.28 (d, *J* = 6.5 Hz, 1H), 8.07 (m, 1H), 7.00 (m, 3H) ppm. ^{13}C NMR: δ 151.6, 150.3, 142.9, 137.5, 137.1, 136.5, 131.2, 130.9, 130.1, 127.3, 127.2, 125.2, 119.2, 118.1, 112.8 ppm. ESIMS: *m/z* = 238 (100) amu. HR-ESITOFMS Calcd. for $C_{15}H_{12}NO_2$: 238.0868 ($M+H^+$). Found: 238.0872.

***N*-(2′,5′-Dihydroxyphenyl)-pyridinium-3-olate (17a).** Method A. A slightly yellow solid was obtained, yield 30%. IR (KBr): 3442, 1558, 1490, 1441, 1348, 1275, 1017, 843, 778 cm^{-1}. UV (MeOH): λ_{max}: 285 nm. ^1H NMR: δ 8.09 (d, *J* = 6.3 Hz, 1H), 7,94 (d, *J* = 6.3 Hz, 1H), 7.32 (s, 1H), 7.30 (s, 1H), 7.13 (m, 3H) ppm. ESI-MS: *m/z* = 204 amu. Anal. Calcd. for $C_{11}H_{13}NO_5$ (239.08): C: 55.23; H: 5.48; N: 5.86. Found: C: 55.73; H: 4.35; N: 5.65.

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