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Intermolecular interactions of punicin derivatives

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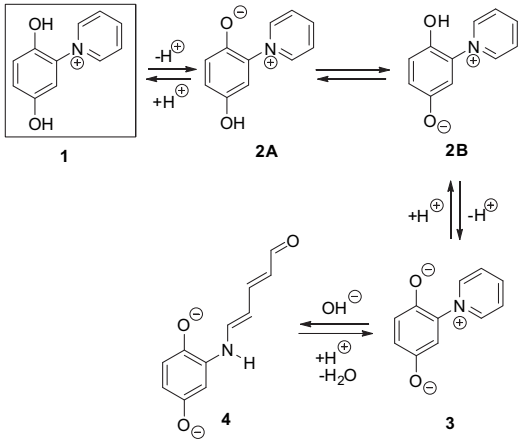
ABSTRACT

The 2- and 4-methyl derivates of punicin [*N*-(2′,5′-dihydroxyphenyl)-pyridinium chloride] were subjected to Knoevenagel reactions. Starting materials as well as reaction products were examined with respect to homo and hetero-intermolecular interactions. It was found that *N*-(2′,5′-dihydroxyphenyl)-2-methylpyridinium chloride forms a stable 2:1 complex to hydroquinone. Decomplexation can be accomplished by anion exchange to tetraphenylborate, or by competing complexation with *p*-benzoquinone. Results of three single crystal X-ray analyses as well as NMR titrations and dilution experiments are presented.

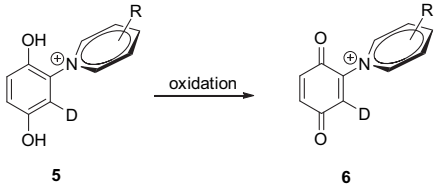
1. Introduction

Punicin **1** is a yellow alkaloid from the leaves of *Punica granatum* L.,[1] which possesses an astonishing variety of properties (Scheme 1). In aqueous solution, it forms an orange-colored mixture of two tautomeric heterocyclic mesomeric betaines, which differ in their type of conjugation.[2] Thus, betaine **2A** belongs to the class of conjugated mesomeric betaines[3] (CMB), whereas its tautomer **2B** is a member of the class of cross-conjugated mesomeric betaines (CCMB). Deprotonation of these betaines by the addition of bases yields the red monoanionic species **3**. Hydroxide-induced pericyclic ring cleavage of **3** yields **4**, which is reddish-black in color. These processes are reversible on addition of acids.[4]



Scheme 1. The alkaloid punicin.

Pyridinium substituted quinones obviously are only stable when they are substituted with additional olate groups,[5] amines,[6] chlorine,[7] or DMAP.[8] We found that substitution of punicin by the electron-donating group propenolate (D in **5**), give stable, intensively dark blue colored species **6** on oxidation.[9] These can be used in organic synthesis as oxidizing agents. 3-Substituted pyridines as partial structures result in the formation of atropisomers of **5** and **6**[9] (Scheme 2).



Scheme 2. Quinones of substituted punicins.

Moreover, punicin and its derivatives form persistent radical cations, such as **7** and radical anions, such as **8** depending on the reaction conditions and the methods of stabilization. Accordingly, punicin as well as its derivatives are redoxactive compounds. As an example, punicin attached to a polymer backbone stabilizes the radical cation species **7**.

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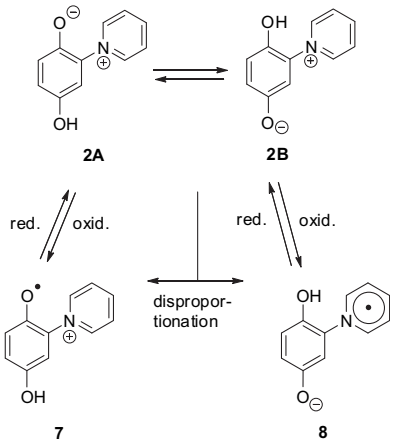
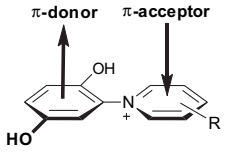
Radical anions such as **8** can be used in reversible photocatalytic electron-transfer reactions employing a sensitizer and a sacrificial donor such as EDTA. Under these conditions, oxygen is converted into hydroxide and H_2O_2. The radicals were characterized by ESR and solid-state ENDOR spectroscopy (Scheme 3).[10] These results were used to prepare new photoresponsive materials.[11]



Scheme 3. Radicals from punicin.

During the last decades much attention has also been devoted to the synthesis and characterisation of charge-transfer complexes (CT) of pyridinium salts with different molecules, such as iodide,[12] tetrafluoroborate,[13] and aromatic organic donors.[14] Especially supramolecular cyclophane systems based on bispyridinium salts with crown ether structures have been widely explored, as these complexes are interesting building blocks for the preparation of molecular switches or complexation reagents.[15] Resulting from their remarkable optical and electrochemical properties CT complexes have found applications as photoinitiators[16] for polymerisation reactions, fluorescent dyes,[17] and molecular nanoparticles.[18] These properties prompted us to examine intermolecular interactions of punicin which possesses π-donor and π-acceptor properties in different parts of the molecule (Scheme 4). We examined complexes in the solid state as well as in solution by X-ray single crystal analyses and by NMR titrations, respectively.



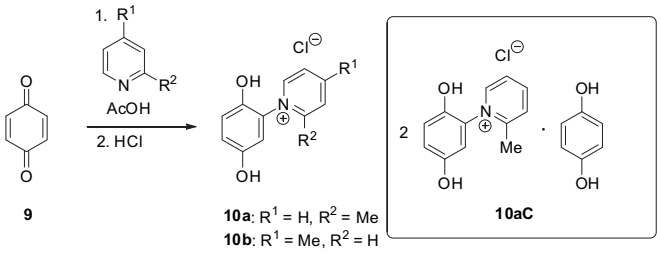
Scheme 4. Complexing partial structures of punicin derivatives.

2. Results and discussion

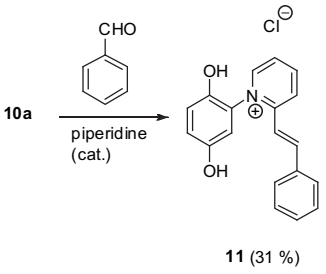
2.1. Syntheses of model compounds

It is known that *p*-benzoquinone reacts with pyridines in acidic medium to punicin derivatives.[19] We chose 2-methylpyridine and 4-methylpyridine as reaction partners, because they allow Knoevenagel reactions to larger π-conjugated systems. Thus, **10a** and **10b** were prepared in 57% and 79% yield, respectively. As a matter of fact, compound **10a** was isolated as a complex (**10aC**) of two molecules of the pyridinium salt and one molecule of hydroquinone.

Knoevenagel reaction of punicin derivative **10aC** with benzaldehyde resulted in the formation of the styrylpyridinium compound **11** in moderate yield (Scheme 6).

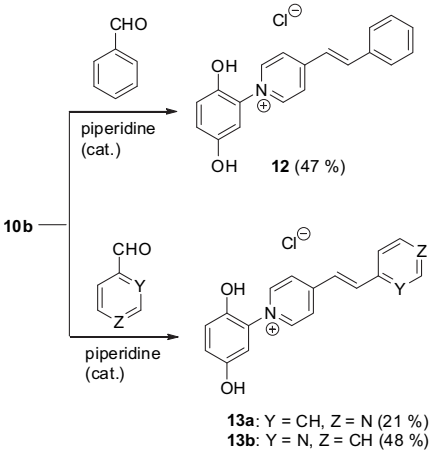


Scheme 5.



Scheme 6.

The 4-methylpyridinium derivative **10b** reacted with benzaldehyde in the presence of catalytic amounts of piperidine to give the *trans*-1-(2′,5′-dihydroxyphenyl)-4-styrylpyridinium salt **12**. Likewise, isonicotinaldehyde and picolinaldehyde reacted to afford the 4-(2-(pyridinyl)vinyl)pyridinium salts **13a**,**b** (Scheme 7).



Scheme 7.

The punicin derivatives **11**–**13** were obtained after chromatographic work-up and subsequent precipitation from a methanolic solution as yellow to light red solids. In all compounds, the trans configuration of the double bond was proved by a coupling constant of 16–17 Hz in the ^{1}H NMR spectra, and the results of X-ray analyses (vide infra). On deprotonation with bases, all punicin derivatives **10**–**13** form intensively red to dark brown colored mesomeric betaines similar to **2A**/**B** shown in Scheme 1. Characteristically, ^{1}H NMR resonance frequencies of starting material **10b**, which is the best soluble compound of the series, taken in DMSO-d_6 shift by 0.1 ppm (pyridinium protons) and 0.4 ppm (protons of the hydroquinone) upfield on deprotonation. Similar values were obtained for compound **12**. All other betaines are sparsely soluble and could therefore neither be purified nor characterized completely.

2.2. Intermolecular interactions

We started our studies with a single crystal X-ray analysis of compound **12**. Single crystals were obtained by slow evaporation of a solution of **12** in diluted HCl. The compound crystallized with one molecule of water of crystallization. Hydrogen bonds are formed between both hydroxyl groups of the hydroquinone and the chloride ion and the water of crystallization (not shown for clarity) with angles of 155.9° and 171.8°, respectively. Additional information concerning hydrogen-bond distances and angles is presented in Table 1. Vertical interactions with a distance of 3.902 Å between the hydroquinone rings of each molecule can be observed. This value is larger than the van-der-Waals distance (3.4 Å). The dihedral angles C2–N1–C7–C12 and C5–N1–C7–C8 were determined to be −52.771(18)° and −53.343(18)°, respectively (crystallographic numbering). The torsion angle between the pyridine and the benzene ring connected by the double bond is 13.192° (Fig. 1).

Table 1
Hydrogen-bond distances (Å) and angles (°) for $C_{15}H_{15}ClNO_3$ (**10aC**) and $C_{19}H_{18}ClNO_3$ (**12**)

D–H···A	D–H	H···A	D···A	D–H···A
$C_{15}H_{15}ClNO_3$				
O(8)–H(8) ···Cl	0.771	2.328	3.082	165.9
O(14)–H(14) ···Cl	0.749	2.377	3.108	165.6
$C_{19}H_{18}ClNO_3$				
O(11)–H(11) ···Cl	0.955	2.184	3.079	155.9
O(1)–H(1) ···Cl	0.831	2.309	3.104	160.4
O(8)–H(8) ···O(1)	0.884	1.725	2.603	171.8

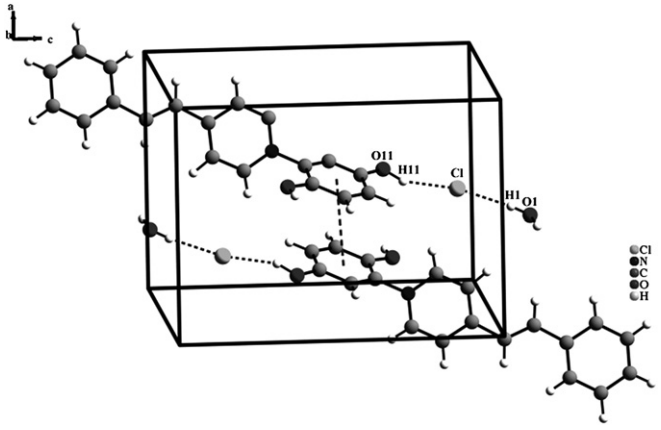


Figure 1. Molecular drawing of **12**.

Next, we turned our attention to complex formation with hydroquinone. As already mentioned, compound **10a** formed a stable π-complex **10aC** (cf. Scheme 5) consisting of 2 equiv of the salt **10a** and 1 equiv of hydroquinone. This complex can be recrystallized. We were able to obtain suitable crystals for a single crystal X-ray analysis. The molecular drawings are shown in Figure 2. The punicin derivative adopts a non-planar conformation with dihedral angles C2–N1–C7–C12 of −90.371(10)° and C6–N1–C7–C8 of −85.055 (10)°. The molecular drawing shows a sandwich-type arrangement of the two pyridinium moieties and the hydroquinone, which is located at distances of 3.601 Å and 3.621 Å to the pyridinium rings, respectively. The pyridinium and hydroquinone ring adopt an angle of 13.499(47)° to each other. The hydroquinone moieties of each punicin derivative stack to another hydroquinone ring of a neighboring molecule. Hydrogen bonds are found between the chloride ion and the hydroxy group at the 8-position of the hydroquinone moiety of the punicin and the added hydroquinone (Table 1).

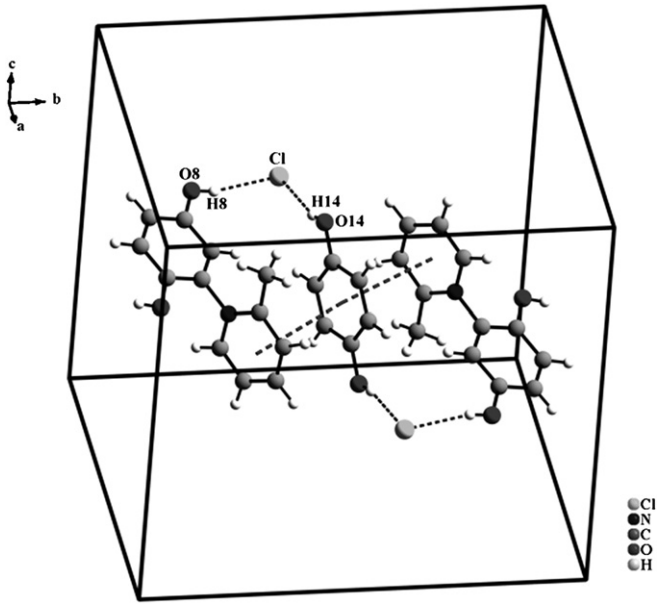
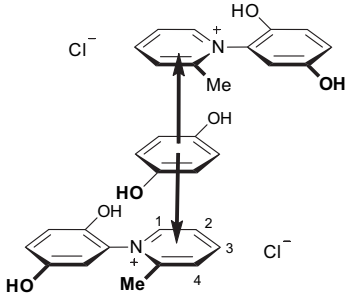


Figure 2. Sandwich-type arrangement of **10aC**.

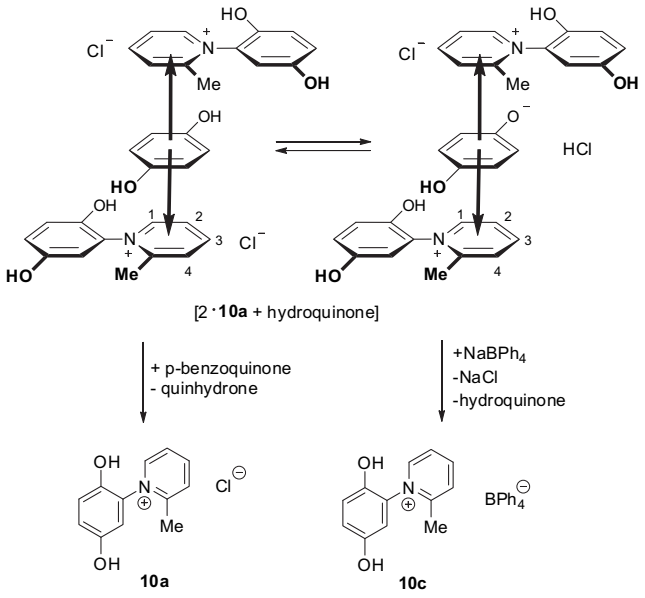
The π-stacking properties of **10a** and hydroquinone in solution were also examined. The comparison between the chemical shifts of probe protons provides a qualitative measure of the strengths of binding between the components of the complex. As expected, the ^{1}H NMR signals of the pyridinium protons of the complex [2·**10a**+hydroquinone] are the most affected. They shift to lower field on dilution of the complex in D_2O, whereas the resonance frequencies of the hydroquinone partial structure of the punicin remain virtually unchanged (Table 2).

Table 2
Dilution experiment of the complex [2 **10a**+hydroquinone]



Concentration of complex [2·**10a**+hydroquinone]	δ 1-*H*	δ 2-*H*	δ 3-*H*	δ 4-*H*
Saturated solution	8.47	7.84	8.41	7.92
150 mmol/L	8.48	7.85	8.42	7.92
100 mmol/L	8.54	7.87	8.44	7.95
50 mmol/L	8.58	7.89	8.46	7.97
5 mmol/L	8.63	7.91	8.47	8.00

In solution, Coulomb interactions between the positively charged pyridinium ring, its counterion, and the complexing hydroquinone as shown in Scheme 8 play an important role. In this case, the shape of the counterion has a direct influence of complex formation capabilities. As a matter of fact, anion exchange of the chloride to the sterically more demanding tetraphenylborate yields the pure salt **10c** without the presence of any complexing hydroquinone. Decomplexation of [2·**10a**+hydroquinone] can also be performed by addition of an excess of *p*-benzoquinone to an aqueous solution of complex **10aC**. On addition, a black solid spontaneously precipitated, which can be identified by NMR spectroscopy as quinhydrone.

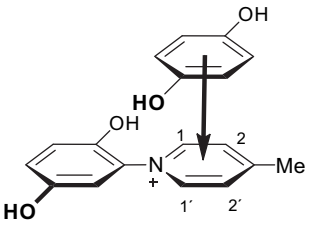


Scheme 8. Quinhydrone formation by addition of *p*-benzoquinone and anion exchange by $NaBPh_4$. Both methods result in decomplexation.

Extraction with dichloromethane to remove the remaining *p*-benzoquinone and evaporation of the aqueous phase resulted in compound **10a** in pure form. No change of the resonance frequencies can be observed by addition of *p*-benzoquinone to the purified punicin derivative **10a**, so that interactions between the π-accepting quinone and the π-donating hydroquinone partial structure of punicin can be excluded under these conditions.

Similarly to these observations, the resonance frequencies of the α- und β-protons of the pyridinium ring of **10b** (50 mmol/L solution in D_2O) shift upfield on addition of hydroquinone due to complex formation under these conditions. Our results are shown in Table 3.

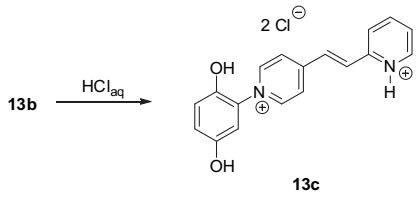
Table 3
NMR titration of **10b** with hydroquinone



Ratio **10b**:Hydroquinone	δ 1-*H*	δ 2-*H*
1:2	8.55	7.85
1:1	8.60	7.88
1:0.5	8.63	7.90
1:0.25	8.64	7.90
1:0.1	8.64	7.91
1:0	8.64	7.91

To gain more information about the π-complexes of the Knoevenagel products, compound **13b** was converted to its dicatonic salt **13c** by addition of concentrated hydrochloric acid to a suspension of **13b**. Precipitation resulted in the formation of the protonated punicin derivative **13c** in 55% yield, which has an increased solubility in protic solvents, such as methanol and water (Scheme 9).

Single crystals of this salt were obtained by slow evaporation of a diluted hydrochloric acid solution of **13c** (Fig. 3). The compound



Scheme 9. Formation of a stable salt **13c**.

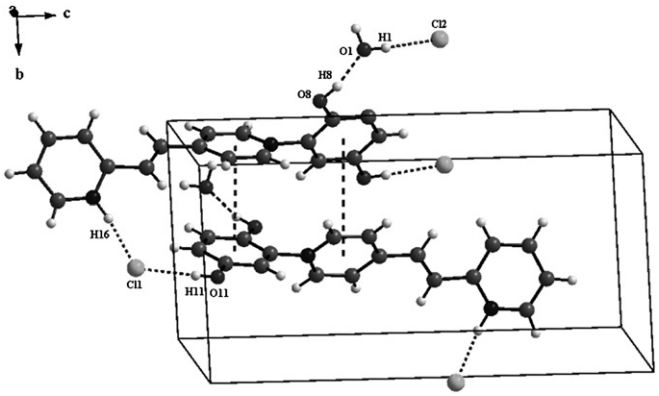


Figure 3. Molecular drawing of **13c**.

crystallizes with one molecule of water. A hydrogen bond is observed between the hydroxyl group of the hydroquinone moiety at the 8-position (crystallographic numbering) and the water of crystallization with an angle of 167.2°. Furthermore, a bridged hydrogen bond connection is formed between the other hydroxyl group (11-position), the chloride anion and the protonated nitrogen of the pyridinium ring with angles of 175.5° and 171.8°, respectively. Details are given in Table 4. The dihedral angles C2–N1–C7–C12 and C5–N1–C7–C8 were determined to be −60.204(21)° and −59.223(21)°, respectively. The torsion angle between the pyridine and the protonated pyridine ring connected by the double bond has a value of 51.659°. In contrast to compound **12**, in **13c** homo vertical interactions are formed between the hydroquinone moiety and the pyridinium ring of an adjacent molecule. The distances are 4.273 and 3.863 Å, respectively.

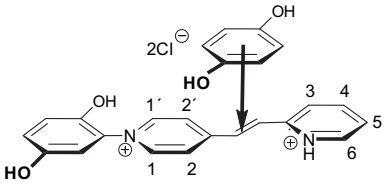
Table 4
Hydrogen-bond distances (Å) and angles (°) for $C_{18}H_{18}Cl_2N_2O_3$ (**13c**)

D–H···A	D–H	H···A	D···A	D–H···A
$C_{18}H_{18}Cl_2N_2O_3$				
O(11)–H(11) ···Cl(1)	0.821	2.255	3.074	175.5
N(16)–H(16) ···Cl(1)	0.946	2.080	3.019	171.8
O(8)–H(8) ···O(1)	0.862	1.777	2.625	167.2

Complex formation between **13c** and hydroquinone can also be observed in solution. NMR measurements of different ratios of **13c** (25 mmol/L in D_2O) and hydroquinone were performed. The results are shown in Table 5. Similar to the starting material **10b**, all protons of the two corresponding pyridine moieties shift upfield due to vertical interactions. The maximum change of the resonance frequencies can be observed for the two protons of the double bond, which appear in the same spectroscopic region. This indicates that the strongest binding interactions of **13c** with hydroquinone are localized in this part of the molecule. Similar results were also obtained for a protonated form of **13a**.

In summary, we present homo- as well hetero-intermolecular interactions of punicin derivatives, which supplement the broad variety of properties of this class of compounds. These results

Table 5
NMR titration of **13c** with hydroquinone



Ratio **13c**:Hydroquinone	δ 1-*H*	δ 2-*H*	δ 3-*H*	δ 4-*H*	δ 5-*H*	δ 6-*H*	δ C=C
1:2	8.83	8.24	8.25	8.48	7.90	8.67	7.77
1:1	8.86	8.27	8.28	8.50	7.91	8.69	7.82
1:0.5	8.87	8.28	8.29	8.50	7.92	8.69	7.84
1:0.25	8.88	8.29	8.30	8.51	7.92	8.70	7.85
1:0	8.89	8.30	8.31	8.51	7.93	8.70	7.87

could stimulate the design of larger supramolecular architectures, which take advantage of the complexing properties of punicin derivatives.

3. Experimental

3.1. General

The ^{1}H and ^{13}C NMR spectra were recorded on Bruker ARX-400 and DPX-200 spectrometers and were taken in DMSO-d_6 and D_2O at 200 and 400 MHz at 20 °C. As an internal standard the solvent signals of DMSO-d_6 at 2.50 ppm and D_2O at 4.72 ppm were used. The chemical shifts are reported in parts per million. Multiplicities are described by using the following abbreviations: s=singlet, d=doublet, t=triplet, m=multiplet, br=broad.

3.2. X-ray diffraction analysis

Suitable single crystals of the title compounds were selected under a polarization microscope and mounted in a glass capillary (d=0.3 mm). The crystal structures were determined by X-ray diffraction analysis using graphite monochromated Mo K_α radiation (0.71073 Å) [T=223(2) K], whereas the scattering intensities were collected with a single crystal diffractometer (STOE IPDS II). The crystal structures were solved by Direct Methods using SHELXS-97 and refined using alternating cycles of least squares refinements against F^2 (SHELXL-97). All non-H atoms were located in Difference Fourier maps and were refined with anisotropic displacement parameters. The H positions were determined by a final Difference Fourier Synthesis.

$C_{15}H_{15}ClNO_3$ (**10aC**) crystallized in the monoclinic space group $C2/c$ (no. 15), lattice parameters a=13.035(2) Å, b=15.153(2) Å, c=13.979(2) Å, β=91.07(1)°, V=2760.5(7) Å^3, Z=8, $d_{calc.}$= 1.409 g cm^{-3}, $F(000)$=1224 using 2444 independent reflections and 241 parameters. $R1$=0.0421, $wR2$=0.0924 [$I>2\sigma(I)$], goodness of fit on F^2=1.055, residual electron density=0.213 and −0.272 e Å^{-3}.

$C_{19}H_{18}ClNO_3$ (**12**) crystallized in the monoclinic space group $P2_1/c$ (no. 14), lattice parameters a=9.474(2) Å, b=14.172(2) Å, c=12.908(2) Å, β=90.22(1)°, V=1733.1(5) Å^3, Z=4, $d_{calc.}$= 1.318 g cm^{-3}, $F(000)$=720 using 3065 independent reflections and 290 parameters. $R1$=0.0670, $wR2$=0.0906 [$I>2\sigma(I)$], goodness of fit on F^2=1.127, residual electron density=0.188 and −0.198 e Å^{-3}.

$C_{18}H_{18}Cl_2N_2O_3$ (**13c**) crystallized in the monoclinic space group $P2_1/n$ (no. 14), lattice parameters a=14.262(3) Å, b=8.021(1) Å, c=16.610(1) Å, β=106.81(1)°, V=1819.0(5) Å^3, Z=4, $d_{calc.}$= 1.392 g cm^{-3}, $F(000)$=792 using 3203 independent reflections and 299 parameters. $R1$=0.0440, $wR2$=0.0903 [$I>2\sigma(I)$], goodness of fit on F^2=1.061, residual electron density=0.266 and −0.221 e Å^{-3}.

Further details on the crystal structure investigations may be obtained from Cambridge Crystallographic Data Centre CCDC, 12 Union Road, Cambridge CB2 1EZ, fax (+44) 1223 336 033, e-mail (deposit@ccdc.cam.ac.uk) on quoting the depository numbers CCDC-768706 for compound **$C_{15}H_{15}ClNO_3$**, CCDC-768707 for compound **$C_{19}H_{18}ClNO_3$**, and CCDC-774496 for compound **$C_{18}H_{18}Cl_2N_2O_3$**.

*3.2.1. N-(2′,5′-Dihydroxyphenyl)-2-methylpyridinium chloride **10a** and its complex with hydroquinone.* A solution of *p*-benzoquinone (5.4 g, 50 mmol) in 35 mL of concd acetic acid was treated with 2-methylpyridine (4.9 mL, 50 mmol). The mixture was then stirred for 24 h at rt, the resulting precipitate was filtered off, dissolved in water, and precipitated again by addition of concd HCl. By this way a complex of two molecules of **10a** and one molecule of hydroquinone is formed. Yield: 3.31 g (57%) of a pale brownish solid; mp 203–206 °C. ^{1}H NMR (DMSO-d_6): δ=10.30 (s, 2H, *OH*), 9.70 (s, 2H, *OH*), 8.97 (dd, J=6.2, 1.1 Hz, 2H), 8.65 (ddd+s, J=7.9, 6.2, 1.1 Hz, 2H+2H), 8.22 (d, J=7.5 Hz, 2H), 8.06 (m, 2H), 7.08 (m, 2H), 6.97 (m, 4H), 6.55 (s, 4H), 2.51 (s, 6H, *methyl*–H) ppm; ^{13}C NMR (DMSO-d_6): δ=156.4, 150.4, 149.7, 146.7, 146.6, 142.9, 129.2, 128.1, 125.5, 119.3, 118.0, 115.6, 112.4, 19.9 ppm; IR (KBr): 3166, 1629, 1524, 1514, 1453, 1337, 1267, 1199, 852, 776, 649, 629 cm^{-1}.

Decomplexation was achieved by addition of 4 equiv of *p*-benzoquinone (216 mg, 2 mmol) to an aqueous solution of complex **10a** (292 mg, 0.5 mmol). The mixture was stirred for 15 h at rt and the resulting solid was filtered off. The filtrate was extracted with five portions (50 mL) dichloromethane and the resulting aqueous phase was evaporated under reduced pressure to give the product as an orange colored waxy solid. Yield: 204 mg (86%). ^{1}H NMR (DMSO-d_6): δ=10.35 (s, 1H, *OH*), 9.73 (s, 1H, *OH*), 8.97 (dd, J=6.2, 1.1 Hz, 2H), 8.65 (ddd, J=7.9, J=6.2, 1.1 Hz, 1H), 8.22 (d, J=7.9 Hz, 1H), 8.06 (m, 1H), 7.10 (m, 1H), 6.98 (m, 2H), 2.51 (s, 3H, *methyl*–H) ppm.

*3.2.2. N-(2′,5′-Dihydroxyphenyl)-4-methylpyridinium chloride **10b**.* A solution of *p*-benzoquinone (5.4 g, 50 mmol) in 35 mL of concd acetic acid was treated with 4-methylpyridine (4.86 mL, 50 mmol). The mixture was stirred for 24 h at rt, then concd hydrochloric acid was added. The resulting solid was filtered off and washed subsequently with chloroform and ethyl acetate. Yield: 9.34 g (79%) of a pale brownish solid; dec 247–248 °C. ^{1}H NMR (DMSO-d_6): δ=10.19 (br s, 2H, *OH*–H), 8.99 (d, J=6.7 Hz, 2H), 8.08 (d, J=6.7 Hz, 2H), 7.13 (m, 1H), 6.99 (m, 2H), 2.69 (s, 3H, *methyl*–H) ppm; ^{13}C NMR (DMSO-d_6): δ=160.2, 150.3, 145.2, 142.7, 129.6, 128.1, 119.1, 118.0, 112.5, 21.7 ppm; IR (KBr): 3170, 1637, 1518, 1459, 1401, 1351, 1323, 1216, 827, 792, 652, 477 cm^{-1}. All spectroscopic data are in agreement with literature values.[4]

*3.2.3. trans-N-(2′,5′-Dihydroxyphenyl)-2-styrylpyridinium chloride **11**.* A solution of the complex of (2′,5′-dihydroxyphenyl)-2-methylpyridinium chloride **10a** with hydroquinone (672 mg, 2.3 mmol of the salt) in 30 mL of anhyd methanol was treated with benzaldehyde (0.25 mg, 2.5 mmol) and 10 drops of piperidine. The mixture was then heated at reflux temperature for 13 h. The solvent was then distilled off in vacuo and the residue was chromatographed (chloroform/MeOH=7:1). The resulting solid was dissolved in methanol and precipitated by the addition of chloroform. Yield: 235 mg (31%) of a yellow solid; dec 202 °C (DSC). ^{1}H NMR (200 MHz, DMSO-d_6): δ=10.32 (br s, 1H, *OH*–H), 9.81 (br s, 1H, *OH*–H), 8.95 (d, J=5.6 Hz, 1H), 8.73 (m, 2H), 8.12 (d, J=16.3 Hz, 1H), 8.03 (m, 1H), 7.44 (m, 5H), 7.08 (m, 3H), 6.74 (d, J=16.3 Hz, 1H) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): δ=152.5, 150.4, 146.5, 145.8, 143.5, 142.7, 134.5, 130.9, 129.3, 127.9, 127.5, 125.4, 124.7, 119.7, 118.0, 117.2, 113.1 ppm; IR (KBr): 3029, 1615, 1561, 1528, 1499, 1447, 1354, 1268,

1206, 1127, 974, 836, 798, 775, 685 cm^{-1}. HRESIMS: calcd for $C_{19}H_{16}NO_2^+$: 290.1180. Found: 290.1173.

3.2.4. trans-N-(2′,5′-Dihydroxyphenyl)-4-styrylpyridinium chloride ***12***. A solution of *N*-(2′,5′-dihydroxyphenyl)-4-methylpyridinium chloride **10b** (237 mg, 1 mmol) in 10 mL of anhyd methanol was treated with benzaldehyde (0.11 mL, 1.1 mmol) and three drops of piperidine. The mixture was then heated at reflux temperature for 24 h. After evaporation of the solvent in vacuo, the residue was chromatographed (silica gel; chloroform/MeOH=8:1). Recrystallization from chloroform/MeOH gave an orange-colored solid. Yield: 154 mg (47%); dec 272–273 °C. ^{1}H NMR (DMSO-d_6): δ=10.48 (br s, 1H, *OH*—H), 9.78 (br s, 1H, *OH*—H), 9.03 (d, *J*=6.4 Hz, 2H), 8.35 (d, *J*=6.4 Hz, 2H), 8.18 (d, *J*=16.3 Hz, 1H), 7.80 (m, 2H), 7.50 (m, 3H), 7.66 (d, *J*=16.3 Hz, 1H), 7.14 (d, *J*=8.8 Hz, 1H), 7.07 (d, *J*=2.6 Hz, 1H), 6.97 (dd, *J*=8.8 Hz, *J*=2.6 Hz, 1H) ppm; ^{13}C NMR (DMSO-d_6): δ=153.6, 150.4, 145.7, 142.7, 141.8, 135.2, 130.6, 129.6, 129.1, 128.3, 123.5, 123.4, 119.0, 118.1, 112.6 ppm; IR (KBr): 3057, 1614, 1507, 1455, 1339, 1270, 1189, 1119, 973, 825, 794, 767, 692 cm^{-1}. HRESIMS: [$C_{19}H_{16}NO_2^+$] calcd 290.1180. Found: 290.1181.

3.2.5. trans-N-(2′,5′-Dihydroxyphenyl)-4-(2-(pyridin-4-yl)vinyl)pyridinium chloride ***13a***. A solution of *N*-(2′,5′-dihydroxyphenyl)-4-methylpyridinium chloride **10b** (544 mg, 2.3 mmol) in 30 mL of anhyd methanol was treated with pyridine-4-carbaldehyde (0.24 mL, 2.5 mmol) and five drops of piperidine. After heating at reflux temperature for 15 h, the solvent was distilled off in vacuo and the resulting residue was chromatographed (chloroform/MeOH=7:1). The resulting solid was dissolved in methanol and precipitated by addition of chloroform. Yield: 160 mg (21%) of a red solid; dec 283 °C (DSC). ^{1}H NMR (200 MHz, DMSO-d_6): δ=10.52 (br s, 1H, *OH*—H), 9.82 (br s, 1H, *OH*—H), 9.12 (d, *J*=6.7 Hz, 2H), 8.70 (d, *J*=5.9 Hz, 2H), 8.42 (d, *J*=6.7 Hz, 2H), 8.15 (d, *J*=16.4 Hz, 1H), 7.92 (d, *J*=16.4 Hz, 1H), 7.72 (d, *J*=5.9 Hz, 2H), 7.15 (d, *J*=8.8 Hz, 1H), 7.08 (d, *J*=2.8 Hz, 1H), 6.98 (dd, *J*=8.8 Hz, *J*=2.7 Hz, 1H) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): δ=152.6, 150.5, 150.4, 146.1, 142.7, 142.2, 138.7, 129.6, 127.7, 124.2, 121.9, 119.2, 118.1, 112.5 ppm; IR (KBr): 3122, 3054, 1625, 1606, 1509, 1454, 1341, 1284, 1202, 1068, 1014, 977, 838, 805, 654, 564, 533 cm^{-1}. HRESIMS: Calcd for $C_{18}H_{15}N_2O_2^+$: 291.1134. Found: 291.1141.

3.2.6. trans-N-(2′,5′-Dihydroxyphenyl)-4-(2-(pyridin-2-yl)vinyl)pyridinium chloride ***13b***. Pyridine-2-carbaldehyde (0.24 mL, 2.5 mmol) and five drops of piperidine were added to a solution of *N*-(2′,5′-dihydroxyphenyl)-4-methylpyridinium chloride **10b** (544 mg, 2.3 mmol) in 30 mL of anhyd methanol. The mixture was then heated at reflux temperature for 15 h. Then, the solvent was distilled off in vacuo und the residue was chromatographed (chloroform/MeOH=7:1). The resulting solid was dissolved in methanol and precipitated from chloroform. Yield: 360 mg (48%) of a yellow solid; dec: 221 °C (DSC). ^{1}H NMR (200 MHz, DMSO-d_6): δ=10.51 (br s, 1H, *OH*—H), 9.80 (br s, 1H, *OH*—H), 9.08 (d, *J*=6.5 Hz, 2H), 8.71 (d, *J*=3.6 Hz, 1H), 8.47 (d, *J*=6.5 Hz, 2H), 8.20 (d, *J*=16.0 Hz, 1H), 7.95 (m, 2H), 7.73 (d, *J*=7.6 Hz, 1H), 7.45 (t, *J*=5.5 Hz, 1H), 7.15 (d, *J*=8.8 Hz, 1H), 7.07 (d, *J*=2.5 Hz, 1H), 6.98 (dd, *J*=8.8 Hz, *J*=2.5 Hz, 1H) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): δ=153.0, 152.8, 150.4, 150.2, 146.0, 142.7, 140.5, 137.4, 129.7, 126.5, 125.3, 124.7, 124.3, 119.1, 118.1, 112.6 ppm; IR (KBr): 3115, 3058, 1619, 1509, 1457, 1330, 1198, 1031, 972, 829, 770, 657, 524 cm^{-1}. HRESIMS: calcd for $C_{18}H_{15}N_2O_2^+$: 291.1134. Found: 291.1135.

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