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Reactions of Amines with Zwitterionic Quinoneimines: Synthesis of New Anionic and Zwitterionic Quinonoids

Farba B. Tamboura,[a] Catherine S. J. Cazin,[a][‡] Roberto Pattacini,[a] and Pierre Braunstein*[a]

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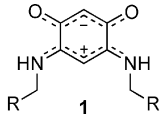
Following the discovery of an unprecedented transamination reaction between primary alkylamines and a quinonoid molecule of the type $[C_6H_2(=NHCH_2R)_2(=O)_2]$ (**1**), obtained from commercially available diaminoresorcinol·2HCl, we have extended this method to the use of primary arylamines, and found that, in contrast, secondary amines led to a different outcome. Whereas functionalized molecules of type **1**, which are best described as 6π + 6π zwitterions, were obtained with aniline or 4-methoxyaniline, no transmination was observed with *t*BuNH$_2$ in ethanol. In water, however, a reaction took place, but it afforded instead salt **6a**, which resulted from hydrolysis of the imine group and deprotonation. Under similar conditions, secondary amines led to comparable results. The cations associated with the anionic quinonoid are readily exchanged in the presence of a primary amine. Whereas for the transamination reaction basic amines react under mild conditions, slightly harsher conditions are needed for less basic amines such as piperidine, diisopropylamine, or diethylamine. Transamination reactions were also performed with bis(methylamino) quinoneimine **4c**, which is more soluble in organic solvents than **3**. This led to the first examples of quinonoidal zwitterions functionalized with different alkyl groups on the nitrogen atoms. A number of compounds were characterized by X-ray diffraction, which allowed a better understanding of their electronic situation, and in many cases, the presence of multiple hydrogen-bond donors and acceptors results in crystal packings dominated by these interactions.

Introduction

Organic compounds containing a quinonoid fragment are of great interest because of their intrinsic properties and their numerous applications in chemistry, physical chemistry, and biology.[1–33] In particular, benzoquinonemonoimines have been found to display unique properties in various areas such as color,[34] organic,[35,36] supramolecular,[37] coordination, and organometallic chemistry[37–44] and homogeneous catalysis.[39,43,45]



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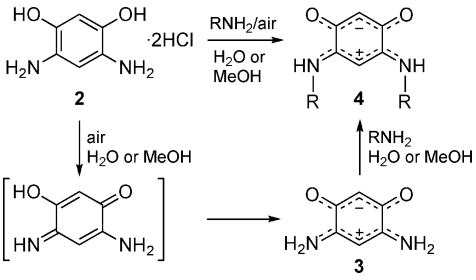
The first member of a new family of 12π-electron quinone-based zwitterions (**1**, R = *t*Bu) was reported in 2002.[36] Its original preparation involved the reaction of 1,2,4,5-tetraaminobenzene with *t*BuC(O)Cl in wet acetonitrile, which led to an aromatic diamidodiester derivative, which after reduction by $LiAlH_4$ followed by aerobic work up yielded quinonoid molecule **1**. Interestingly, **1** is a rare example of a zwitterion being more stable than its canonical forms, and its structure is best described as involving two chemically connected but electronically not conjugated 6π-electron subunits.[38] A more efficient synthesis was subsequently developed, which involved acylation of diaminoresorcinol followed by reduction with $LiAlH_4$ and aerobic work up.[20,38] However, only $–NCH_2R$ substituted derivatives could be obtained by using this procedure. This prompted us to develop a more versatile synthetic pathway for this new class of molecules. It consisted of an unprecedented, one-pot transamination reaction on a quinonoid fragment obtained after neutralization of commercially available diaminoresorcinol·2HCl, followed by air oxidation (Scheme 1).[40,46] Although this method allowed the synthesis of a range of new functionalized zwitterions, it was found to be efficient only for the transamination of nonsterically hindered primary alkylamines.

Considering the diverse areas in which benzoquinonemonoimines are involved, and the unique electronic structure of molecules such as **1** and **3**, which has aroused considerable theoretical interest,[38,47] it appeared important to explore the possibility of introducing various substituents R on the nitrogen atoms, which could influence the physical properties of these molecules, such as solubility in

[a] Laboratoire de Chimie de Coordination, Institut de Chimie (UMR 7177 CNRS),
Université de Strasbourg,
4 rue Blaise Pascal, 67070 Strasbourg, France
E-mail: braunstein@chimie.u-strasbg.fr
[‡] Present address: School of Chemistry, University of St Andrews,
North Haugh, St Andrews, KY16 9ST, UK

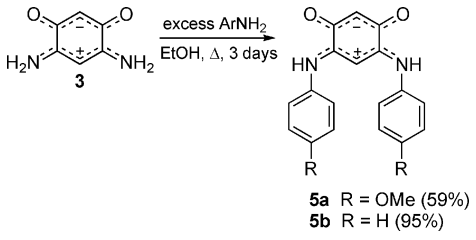


Scheme 1. Amination reactions on the parent quinonemonoimine zwitterion **3**.[40,46]

water and/or in organic solvents, and their electronic properties, as a result of a change in the nature of the R substituent. We thus investigated the behavior of a range of amines toward parent zwitterion **3**. Herein, we report that the scope of this transamination reaction can be extended to primary arylamines, and that, in contrast, secondary amines lead to a totally different outcome. In particular, ammonium salts of 2-amino-5-hydroxide-1,4-benzoquinone were obtained and structurally characterized for the first time, and these compounds are related to biologically active substituted aminobenzoquinones.[10,11,48]

Results and Discussion

The first primary arylamine selected for the synthesis of functionalized zwitterions was 4-methoxyaniline because of the electron-donor properties of the methoxy group, which should favor the transamination reaction. When the reaction was conducted under the conditions reported for the alkyl analogues,[46] it proved totally inefficient, but more forcing conditions resulted in the formation of desired product **5a**. When the same conditions (reflux in ethanol for 3 d) were applied to aniline and with the use of a much larger excess of the amine (50 equiv.), **5b** was isolated in 95% yield (Scheme 2). The ^{1}H NMR spectra of these products contain singlets at 5.15 and 5.77 ppm for **5a** and at 5.20 and 5.81 ppm for **5b**, which are characteristic of the CH groups of the quinonoid fragment (N–C=C*H* and O–C=C*H*, respectively). The ^{13}C{^{1}H} NMR spectroscopic data are also consistent with the structures illustrated in Scheme 2, with characteristic signals at 84.6, 98.0, 154.9, and 172.0 ppm for **5a** and at 85.2, 98.1, 155.5, and 171.8 ppm for **5b**, corresponding to the N–C=*C*, O–C=*C* and N–*C*, O–*C* carbon atoms, respectively.



Scheme 2. Synthesis of aryl-functionalized zwitterions.

Following these positive results with primary arylamines, we re-examined the initially unsuccessful reactions of sterically hindered alkyl congeners under these more forcing conditions. Gratifyingly, *i*PrNH$_2$ reacted in refluxing ethanol, within 1 h, to afford the corresponding functionalized zwitterion of type **4** (**4a**, R = *i*Pr, 91% yield). Its ^{1}H and ^{13}C{^{1}H} NMR spectroscopic data are consistent with the anticipated structure, which was unambiguously confirmed by single-crystal X-ray diffraction (Figure 1). All crystal structures determined in the course of this work are discussed in a separate paragraph (see below).

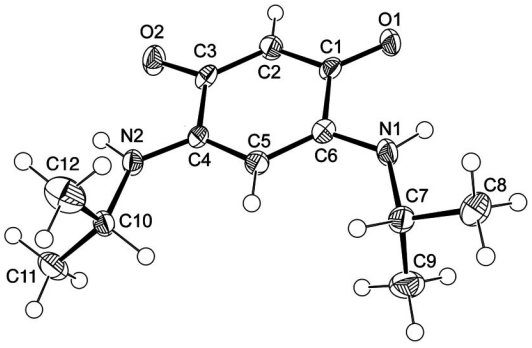
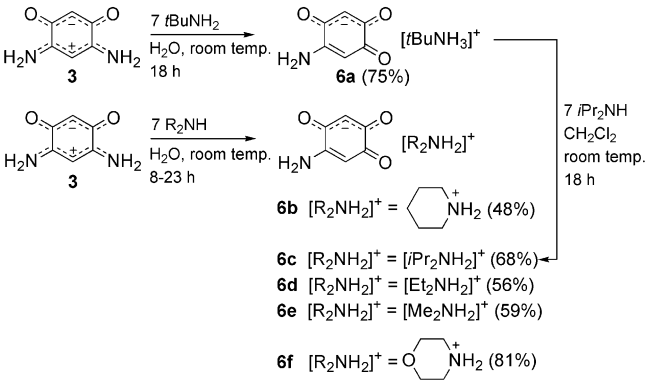


Figure 1. Molecular structure of **4a**. Ellipsoids include 50% of the electron density.

Surprisingly, when parent zwitterion **3** was treated with *t*BuNH$_2$, no transamination product was observed. In water, however, a reaction took place that afforded salt **6a** (Scheme 3). Hydrolysis of the imine group and deprotonation by the base account for the formation of this salt. The ^{1}H NMR spectrum of **6a** contains two singlets corresponding to the CH protons of the ring, upfield shifted with respect to the CH signals of *N*-functionalized zwitterions. The ^{13}C{^{1}H} NMR spectroscopic data show two signals for the CH groups, and the one corresponding to N–C=*C*H is shifted to 94.6 ppm, downfield with respect to that of the zwitterions. The O–C=*C*H resonance was found at 99.8 ppm. The quaternary carbon atoms give rise to four singlets, two of them corresponding to the two O–*C* carbon atoms with very close chemical shifts.



Scheme 3.

The use of secondary amines under comparable experimental conditions led to a similar outcome, and salts **6b–f** were obtained in good yields. Note that the ammonium cation of **6a** can be exchanged by an incoming amine, as exemplified by the synthesis of **6c** in 90% yield from the reaction of **6a** with *i*Pr_2NH (Scheme 3). ^1H and $^{13}C\{^1H\}$ NMR spectroscopic data for compounds **6b–f** are very similar to those obtained for **6a** (see Experimental Section). X-ray diffraction studies were performed on **6b**, **6c**, and **6d**·H_2O (Figures 2, 3, and 4).

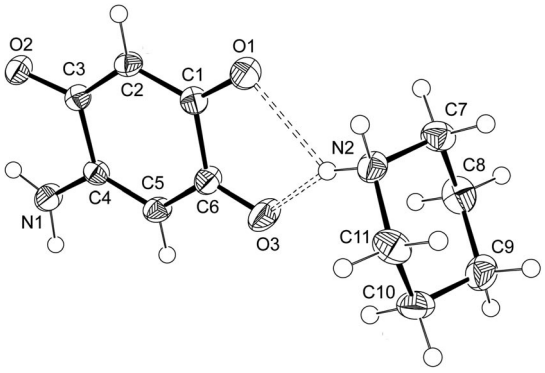


Figure 2. ORTEP plot of the molecular structure of **6b**, illustrating the H-bonding interactions between O1 and O3 of the anion and a NH proton of the piperidinium cation. Ellipsoids include 50% of the electron density.

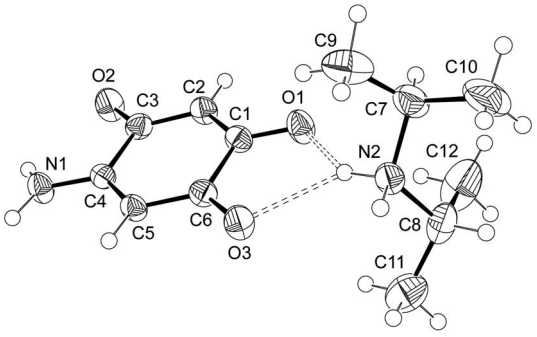


Figure 3. ORTEP plot of the molecular structure of **6c**, illustrating the H-bonding interactions between O1 and O3 of the anion and a NH proton of the diisopropylammonium cation. Ellipsoids include 50% of the electron density.

Interestingly, the more basic amines react under milder conditions, whereas slightly harsher conditions are needed for the less basic amines. Indeed, for piperidine, diisopropylamine, or diethylamine, the reaction was complete at room temperature within 8 h, whereas for dimethylamine the reaction time had to be increased to 23 h. For the much less basic morpholine, the reaction mixture had to be heated at reflux for 7 h to obtain **6f**.

When salts of type **6** were treated with two equivalents of the primary alkylamine $NH_2CH_2CH_2OH$, known functionalized zwitterionic product **4b** was obtained (Scheme 4).[46] The quinone function was thus transformed back into an imine group, which carries an additional donor function able to coordinate, for example, to Zn^{II} ions.[46]

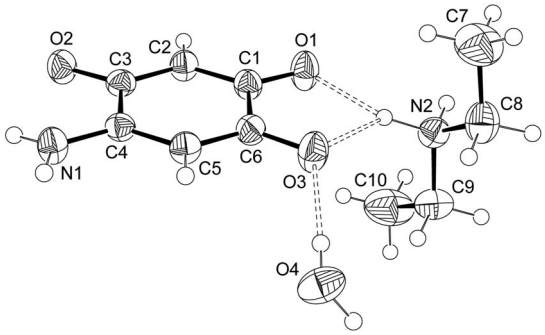
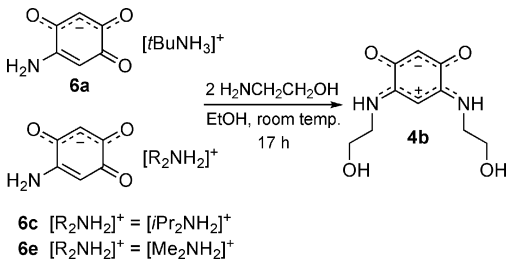
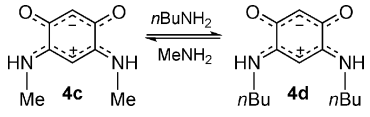


Figure 4. ORTEP plot of the molecular structure of **6d**·H_2O, illustrating the H-bonding interactions between O1 and O3 of the anion and a NH proton of the diethylammonium cation. In addition, O3 interacts with a proton of a water molecule. Ellipsoids include 50% of the electron density.



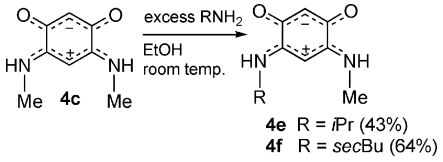
Scheme 4.

An alternative route for the synthesis of *N*-substituted zwitterions consists of performing a transamination reaction on the quinonoid ring of NMe derivative **4c** rather than on that of **3**, a compound that is less soluble in organic solvents (Scheme 5).[46] Such a pathway appears of great interest for two main reasons: (1) partial transamination could lead to *N*,*N*′-asymmetrically substituted zwitterions, and (2) it could provide a route to zwitterions bearing secondary amines, which would represent an interesting extension, as the synthetic strategy applied above had proven inefficient so far.



Scheme 5.

The first amine selected for this transamination reaction of **4c** was *i*$PrNH_2$, as we showed above that anticipated product **4a** could be obtained by reaction of zwitterion **3** with this amine. As shown in Scheme 6, reaction of **4c** with an excess amount of *i*$PrNH_2$ led to the formation of dissymmetric zwitterion **4e**, together with the symmetric product of double transamination, **4a** (Figure 1). Repeating the experiment with *sec*$BuNH_2$ led to the isolation of dissymmetric zwitterion **4f** in 64% yield (Scheme 6).



Scheme 6.

These are, to the best of our knowledge, the first examples of quinonoid zwitterions bearing different alkyl groups on the nitrogen atoms. The structure of **4e** was also unambiguously determined by single-crystal X-ray diffraction (Figure 5).

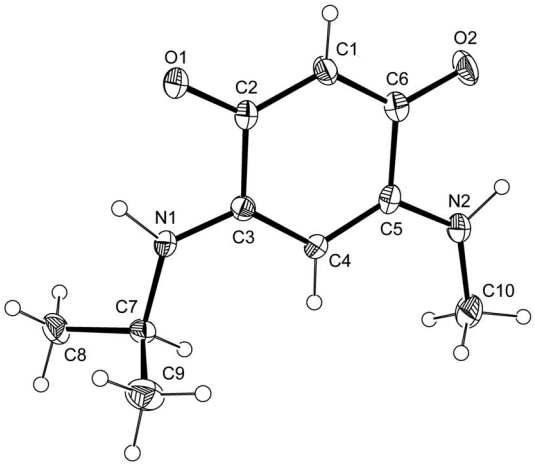
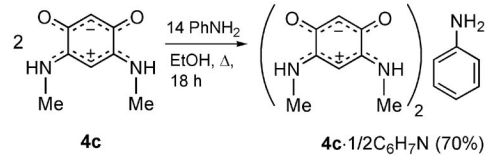


Figure 5. ORTEP plot of the molecular structure of **4e**. Ellipsoids include 50% of the electron density.

We then attempted to use primary arylamines to synthesize unsymmetrically substituted zwitterions having an alkyl or an aryl group on the nitrogen atoms. Surprisingly, the reaction of **4c** with aniline did not lead to transamination products, even under thermal conditions for many hours, but instead it afforded a dark brown product that was shown by X-ray diffraction to be an adduct between **4c** and aniline of the formula **4c**·1/2C_6H_7N (Scheme 7, Figure 6). The formation of the latter compound certainly does not require such harsh conditions but these emphasize the reluctance of aniline to undergo transamination with **4c**, in contrast to **3** (Scheme 2).



Scheme 7.

We also investigated whether or not the transamination reaction was possible on **4c** with the bulky, primary alkylamine $tBuNH_2$. Unsurprisingly, methyl-functionalized zwitterion **4c** reacted similarly to its parent zwitterion **3** when treated with $tBuNH_2$ (Scheme 3), as formation of salt **7a** occurred (Scheme 8). However, in this case, the ^1H NMR spectrum of the reaction mixture indicated the presence of

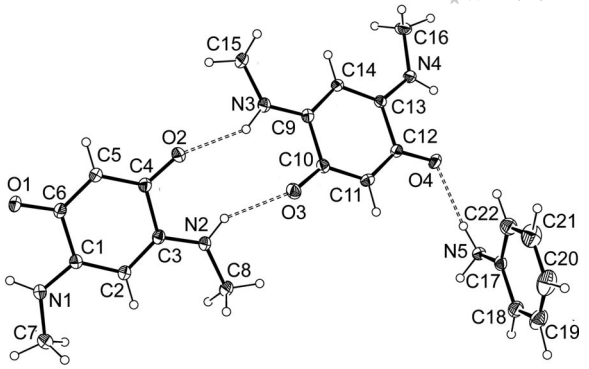
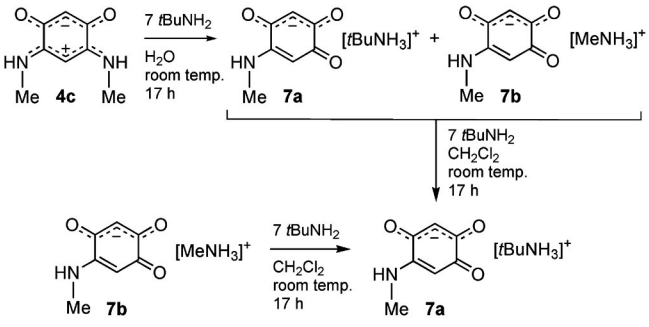


Figure 6. ORTEP plot of the molecular structure of **4c**·1/2C_6H_7N showing the intermolecular O···H–N interactions between two molecules of zwitterions **4c** and a molecule of **4c** and aniline. The plotted hydrogen bonds (dashed lines) correspond to those observed between the asymmetric unit molecules. Ellipsoids include 50% of the electron density.

a second product, **7b**, whose anionic part was the same as that in **7a**. When pure **7b** was treated with an excess amount of $tBuNH_2$ at room temperature in dichloromethane, exchange of the ammonium countercation occurred, leading to the quantitative formation of **7a** (Scheme 8). This cation exchange reaction is consistent with the stronger basicity of $tBuNH_2$ relative to that of $MeNH_2$. This methodology was thus applied to the reaction mixture of **7a** and **7b** to obtain pure **7a** in good yield. Single-crystal X-ray diffraction confirmed the structure of **7a** (Figure 7). Salts **7a** and **7b** clearly result from partial hydrolysis of **4c**, which transforms the cationic moiety $[MeNH{\cdots}C{\cdots}CH{\cdots}C{\cdots}NHMe]^+$ into the neutral fragment [MeNH–C=CH–C=O].



Scheme 8.

As in the case of parent zwitterions **3** (Scheme 3), secondary amines behaved similarly to $tBuNH_2$ when treated with **4c**. In this instance, products **7c**–**e** were formed, whereas **7b** results again from partial hydrolysis of **4c**. Mixtures of salts were obtained, and in the case of the piperidinium salt, the yield of **7e** was increased by further addition of piperidine to the reaction mixture (Scheme 9).

Finally, when salts of type **7** were treated with an excess amount of 2-aminoethanol, functionalized zwitterion **4b** was again formed (Scheme 10), similarly to the reaction starting from non *N*-substituted analogues **6** (Scheme 4).

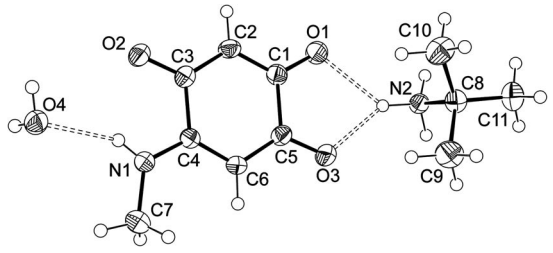
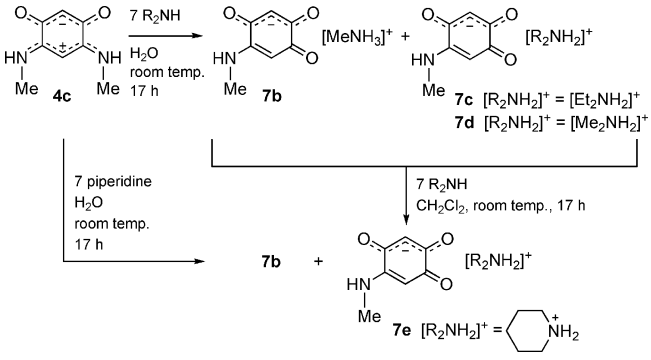
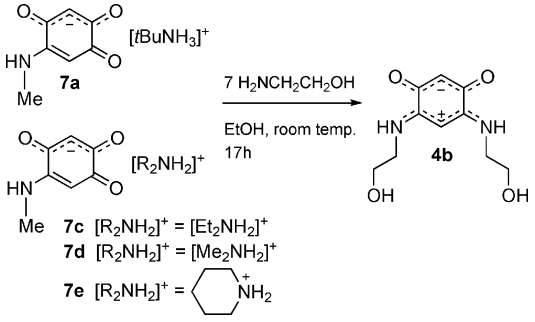


Figure 7. ORTEP plot of the molecular structure of **7a**·H_2O, illustrating the H-bonding interactions between O1 and O3 of the anion and a NH proton of the cation. In addition, the N1–H proton interacts with the oxygen atom of a water molecule. The plotted hydrogen bonds (dashed lines) correspond to those observed between the asymmetric unit molecules. Ellipsoids include 50% of the electron density.



Scheme 9.



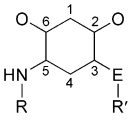
Scheme 10.

This product results from two consecutive reactions: a nucleophilic attack at the C=O group and a transamination at HNMe. Our efforts to isolate an intermediate resulting from one of these two steps and thus gain more insight into the reaction sequence involved were unsuccessful.

Discussion of the Crystal Structures

Selected bond lengths and angles for the crystal structures determined by X-ray diffraction are given in Table 1, which contains a unified labeling scheme to facilitate comparisons.

Table 1. Selected distances [Å] and angles for the crystal structures determined by X-ray diffraction. For **4c**·1/2C_6H_7N, only one crystallographically independent molecule is reported. The second displays similar metrical data.



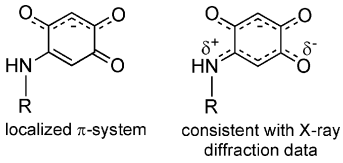
4a: E = NH; R = R′ = *i*Pr
4e: E = NH; R = *i*Pr; R′ = Me
4c: E = NH; R = R′ = Me
6b: ER' = O; R = H (monoanion)
6c: ER' = O; R = H (monoanion)
6d: ER' = O; R = H (monoanion)
7a: ER' = O; R = Me (monoanion)

	4a	**4c**·1/2C_6H_7N	**4e**	**6b**	**6c**	**6d**·H_2O	**7a**·H_2O
C1–C2	1.391(4)	1.400(2)	1.393(4)	1.389(2)	1.378(3)	1.393(3)	1.391(3)
C2–C3	1.526(5)	1.523(2)	1.524(4)	1.537(2)	1.532(3)	1.534(3)	1.537(3)
C3–C4	1.391(4)	1.388(2)	1.396(3)	1.413(2)	1.401(3)	1.395(3)	1.412(2)
C4–C5	1.387(4)	1.394(2)	1.384(4)	1.362(2)	1.364(3)	1.376(3)	1.371(2)
C5–C6	1.529(4)	1.525(2)	1.516(4)	1.525(2)	1.515(3)	1.523(3)	1.521(2)
C6–C1	1.390(4)	1.390(2)	1.383(3)	1.397(2)	1.404(3)	1.384(3)	1.392(2)
O1–C2	1.252(4)	1.254(1)	1.249(3)	1.262(2)	1.274(3)	1.257(2)	1.261(2)
O2–C6	1.253(4)	1.256(1)	1.264(3)	1.256(2)	1.243(3)	1.264(3)	1.260(2)
N–C5	1.316(4)	1.316(2)	1.318(3)	1.335(2)	1.323(3)	1.325(3)	1.331(2)
C3–E	1.316(4)	1.313(1)	1.320(3)	1.241(2)	1.254(3)	1.255(3)	1.248(2)

The structural parameters of **4a**, **4c**·1/2C_6H_7N, and **4e** are as expected, and similar to those reported elsewhere for other members of this family of zwitterions containing a fully delocalized π system within each of the O···C···C···C···O and N···C···C···C···N moieties.[38] The lengths of the carbon–carbon bonds connecting these two π systems correspond clearly to single bonds and indicate a lack of conjugation between the two "6π halves" of the ligand, which is thus best described as a zwitterionic 6π + 6π-electron molecule. In anionic **6b**, **6c**, **6d**·H_2O, and **7a**·H_2O, where one of the NHR moieties is replaced with an oxygen atom in the 3-position, the C3–C4 bonds are, as expected, longer than those in **4a**, **4c**·1/2C_6H_7N, and **4e**. This variation is, however, not significant (within the 3σ criterion) [mean C3–C4 distance for **4a**, **4e**, and **4c**·1/2C_6H_7N: 1.391(3) Å vs. 1.405(3) Å for **6b**, **6c**, **6d**·H_2O, and **7a**·H_2O], and the structural data indicate that a delocalization, similar to that observed in the zwitterionic species, exists. Consistently, the C4–C5 bond length is similar to that observed for the zwitterions and deviates significantly from that expected for a C=C bond [mean for **6b**, **6c**, **6d**·H_2O, and **7a**·H_2O: 1.378(3) Å]. These data indicate an extended delocalization within the anionic O–C–CH–C–O system, as reported in Scheme 11. The C2–C3 and C5–C6 bond lengths remain typical for C–C bonds.

To the best of our knowledge, no crystal structure on this class of anions has been previously reported, and only one crystal structure of a neutral, protonated derivative has been determined thus far, featuring R = CH_2–*t*Bu and an OH group in the 2-position.[20]

The presence of multiple hydrogen-bond donors and acceptors results in crystal packings dominated by these interactions. In zwitterions **4a**, **4c**·1/2C_6H_7N, and **4e** but also



Scheme 11.

in monoanionic **6c** and **6d**·H_2O, couples of molecules are connected as shown, for example, in Figure 6, through double NH···O hydrogen bonds. These interactions result in infinite chains in the case of **4a** and **4e** (see Figure 8 for **4e**). Other classical hydrogen bonds (e.g., NH···O and OH···O) are present, for example, in salts **6b**, **6c**, **6d**·H_2O, and **7a**·H_2O, where the cation interacts with the anion through bifurcated hydrogen bonds of the type shown in Figures 2–4 and 7. Other hydrogen bonds involve, when present, the cocrystallized molecules, such as aniline in **4c**·1/2C_6H_7N and water in **6d**·H_2O and **7a**·H_2O, contributing to the formation of extended 1D, 2D, and 3D networks.

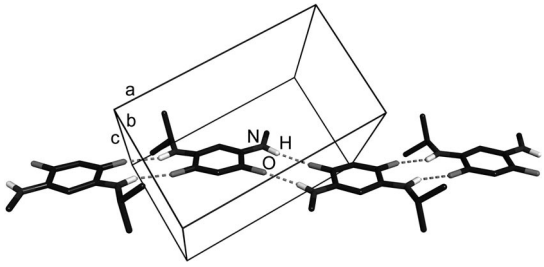


Figure 8. View of the crystal packing of **4e** displaying a section of the infinite net of molecules connected through double NH···O hydrogen bonds.

In addition to the hydrogen bonds mentioned above, columns formed by the stacking of four zwitterionic molecules are present in **4c**·1/2C_6H_7N, as shown in Figure 9.

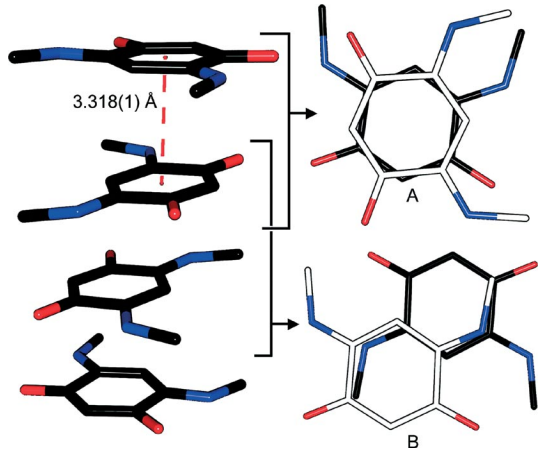


Figure 9. Partial view of the molecular stacking in crystals of **4c**·1/2C_6H_7N, in which columns formed by four molecules of the zwitterion are present. In A and B the view is perpendicular to the mean plane defined by the atoms forming the six-membered cycles of the molecule closest to the observer.

Pair A (Figure 9) displays the stacking of two zwitterionic molecules that are disposed in a mutual staggered arrangement. The distance between the centroids of the six-membered rings is 3.318(1) Å. The central pair (B, Figure 9) features a different arrangement, and the stacking involves the N=C–CH=C–N, formally cationic, moieties. Pairs of atoms lie almost on the same line perpendicular to the mean C_6 planes, namely, N3–C13 and C9–C14, together with their centrosymmetric counterparts. The distance between the atoms forming these couples is 3.519(2) Å. A stacking similar to that shown in Figure 9B involves centrosymmetric pairs of anions in **6d** (Figure 10).

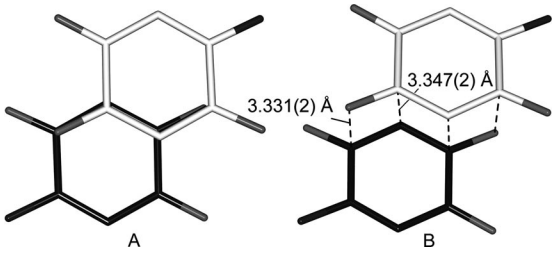


Figure 10. Partial view of the molecular stacking in crystals of **6d**·H_2O. In A the view is perpendicular to the mean plane defined by the atoms forming the six-membered cycles of the molecule closest to the observer. In B, the view is tilted by 20°.

It is worthy to note that the stacking observed in **6d**·H_2O involves two anions. Moreover, it involves the formally anionic group of the anion, which may be counterintuitive, in view of the expected electrostatic repulsion between the two moieties. Similarly, the stacking of **4c**·1/2C_6H_7N (Figure 9B) is observed between the cationic "halves" of the molecules.

Conclusions

We have shown that the scope of the reactions leading to the functionalization of zwitterionic quinoneimines can be extended to aryl groups. Furthermore, by performing a transamination reaction on zwitterions already bearing substituents on the nitrogen atoms, the first examples of dissymmetric quinonoid zwitterions were obtained. Further extension of the scope of these reactions to secondary amines proved impossible, as the zwitterions undergo partial hydrolysis, leading to a new series of salts. Finally, we showed that these salts react with primary alkylamines to regenerate a zwitterionic structure. A number of crystal structures were determined, which provide a firm basis for the description of the electronic situation in these molecules. In particular, ammonium salts of 2-amino-5-hydroxide-1,4-benzoquinone were obtained and structurally characterized for the first time, which has allowed a better understanding of the electronic situation in these molecules. Furthermore, it is interesting to recall that these compounds are related to neutral, biologically active, substituted 2-amino-5-hydroxy-1,4-benzoquinones, such as the marine quinone sesquiterpenes nakijiquinone A and smenospongidine or embelin derivatives.[10,11,48]

Experimental Section

General: ^{1}H NMR spectra were recorded at 300 MHz and $^{13}C\{^1H\}$ NMR spectra at 75.5 MHz with an FT Bruker Avance 300 instrument. Mass spectra were recorded with a Bruker Daltonics micro-TOF (ESI; positive mode; capillary voltage: 4.8 kV; nebulizer pressure: 0.2 bar; desolvation temperature: 180 °C; desolvation gas flow rate: 4.5 L min^{-1}).

Compound 4a: Isopropylamine (0.372 g, 6.28 mmol) was added to an ethanol (10 mL) suspension of parent zwitterion **3** (0.062 g, 0.45 mmol). The reaction mixture was heated to reflux for 1 h. The solvent was removed in vacuo, and the crude solid was washed with diethyl ether (2 × 10 mL). The product was obtained as a violet solid (0.090 g, 0.40 mmol, 88%). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of an ethanol solution of the product. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.24 (d, $^3J_{H,H}$ = 6.4 Hz, 12 H, CH$_3$), 4.06 (m, 2 H, C*H*CH$_3$), 4.98 (s, 1 H, N=C=C-H), 5.56 (s, 1 H, O=C=C-H), 8.64 (br. s, 2 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_6$]DMSO): δ = 21.1 (s, CH*C*H$_3$), 44.6 (s, *C*HCH$_3$), 81.2 (s, N=C=*C*H), 97.6 (s, O=C=*C*H), 154.7 (s, C=N), 172.0 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 223 (87) [M + H]$^+$, 245 (11) [M + Na]$^+$, 229 (2) [M + Li]$^+$. C$_{12}$H$_{18}$N$_2$O$_2$·1/3H$_2$O: calcd. C 63.13, H 8.24, N 12.27; found C 63.47, H 7.99, N 12.64.

Compound 4c·1/2C$_6$H$_7$N: To a solution of zwitterion **4c** (0.100 g, 0.60 mmol) dissolved in EtOH (10 mL) was added aniline (0.392 g, 4.21 mmol). The reaction mixture was heated to reflux for 18 h and cooled to room temperature, and after slow evaporation, dark brown crystals were obtained. These were washed with pentane (3 × 10 mL) and dried, and the compound was obtained as a brown solid (0.090 g, 70%). Crystals suitable for X-ray diffraction were obtained by slow evaporation of an ethanol solution of the compound. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.99 (d, $^3J_{H,H}$ = 5.4 Hz, 12 H, CH$_3$), 4.93 (s, 2 H, N=C=C-H), 5.32 (s, 2 H, O=C–C-H), 6.47 (m, 1 H, CH aromatic), 6.54 (m, 2 H, CH aromatic), 6.99 (m, 2 H, CH aromatic), 9.12 (br. s, 4 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_6$]DMSO): δ = 29.6 (s, CH$_3$), 81.3 (s, N=C–*C*H), 97.5 (s, O=C=*C*H), 113.8 (s, CH aromatic), 115.6 (s, CH aromatic), 128.8 (s, CH aromatic), 148.6 (s, C aromatic), 156.9 (s, C–N), 172.2 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 355 (33) [C$_{16}$H$_{20}$N$_4$NaO$_4$]$^+$, 333 (13) [C$_{16}$H$_{21}$N$_4$O$_4$]$^+$, 205 (11) [C$_8$H$_{10}$KN$_2$O$_2$]$^+$, 189 (16) [C$_8$H$_{10}$N$_2$NaO$_2$]$^+$, 167 (27) [C$_8$H$_{11}$N$_2$O$_2$]$^+$. C$_{22}$H$_{27}$N$_5$O$_4$ (425.49): calcd. C 62.10, H 6.40, N 16.46; found C 61.86, H 6.32, N 16.28.

Compound 4e: Isopropylamine (0.490 g, 8.28 mmol) was added to an ethanol (20 mL) suspension of zwitterion **4c** (0.100 g, 0.60 mmol). The reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo, and the crude solid was purified by preparative thin-layer chromatography (SiO$_2$; CH$_2$Cl$_2$/MeOH, 80:20). The product was obtained as a red solid (0.050 g, 43%). Single crystals suitable for X-ray diffraction were obtained after 2 d from an acetonitrile solution of the product in an NMR tube. ^{1}H NMR (300 MHz, [D$_3$]acetonitrile): δ = 1.30 (d, $^3J_{H,H}$ = 6.5 Hz, 1 H, CHC*H*$_3$), 3.05 (s, 3 H, NCH$_3$), 3.99 (m, 1 H, C*H*CH$_3$), 5.06 (s, 1 H, N=C=CH), 5.37 (s, 1 H, O=C=CH), 7.84 (br. s, 1 H, NH), 8.11 (br. s, 1 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_3$]acetonitrile): δ = 21.7 (s, CH*C*H$_3$), 30.2 (s, NCH$_3$), 46.2 (s, *C*HCH$_3$), 82.2 (s, N=C=*C*H), 98.1 (s, O=C=*C*H), 158.5 (s, C=N), 173.2 (s, C=O), 173.4 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 195 (20) [M + H]$^+$, 217 (80) [M + Na]$^+$.

Compound 4f: *sec*-Butylamine (0.620 g, 8.48 mmol) was added to an ethanol (20 mL) suspension of zwitterion **4c** (0.100 g, 0.60 mmol). The reaction mixture was stirred at room temperature for 3 d. The solvent was removed in vacuo, and the crude solid was purified by preparative thin-layer chromatography (SiO$_2$; CH$_2$Cl$_2$/MeOH, 80:20). The product was obtained as a red solid (0.080 g, 64%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.97 (t, $^3J_{H,H}$ = 7.4 Hz, 3 H, CH$_2$C*H*$_3$), 1.31 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CHC*H*$_3$), 1.69 (m, 2 H, C*H*$_2$CH$_3$), 3.10 (s, 3 H, NCH$_3$), 3.66 (m, 1 H, C*H*CH$_3$), 5.13 (s, 1 H, N=C=CH), 5.43 (s, 1 H, O=C=CH), 8.22 (br. s, 1 H, NH), 8.45 (br. s, 1 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, CDCl$_3$): δ = 10.6 (s, CH$_2$*C*H$_3$), 19.6 (s, CH*C*H$_3$), 29.2 (s, CH$_2$), 29.9 (s, NCH$_3$), 51.2 (s, NCH), 80.5 (s, N=C=*C*H), 99.0 (s, O=C=*C*H), 156.0 (s, C=N), 157.7 (s, C=N), 172.4 (s, C=O), 172.7 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 215 (80) [M + Li]$^+$.

Compound 5a: *p*-Methoxyaniline (0.750 g, 6.09 mmol) was added to an ethanol (20 mL) suspension of parent zwitterion **3** (0.120 g, 0.87 mmol). The reaction mixture was heated to reflux for 3 d. The crude solid was washed with diethyl ether (2 × 40 mL) and dichloromethane (20 mL). The product was obtained as a black solid (0.180 g, 59%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 3.75 (s, 6 H, OCH$_3$), 5.15 (s, 1 H, N=C=CH), 5.77 (s, 1 H, O=C=CH), 7.00 (d, $^3J_{H,H}$ = 7.2 Hz, 4 H, CH aromatic), 7.35 (d, $^3J_{H,H}$ = 7.2 Hz, 4 H, CH aromatic), 10.78 (br. s, 2 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_6$]DMSO): δ = 55.4 (s, OCH$_3$), 84.6 (s, N=C=*C*H), 98.0 (s, O=C=*C*H), 114.4 (s, CH aromatic), 126.0 (s, CH aromatic), 129.0 (s, C aromatic), 154.9 (s, C-N), 158.2 (s, 1 C), 172.0 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 351 (38) [M + H]$^+$. C$_{20}$H$_{18}$N$_2$O$_4$·2/3H$_2$O: calcd. C 66.29, H 5.38, N 7.73; found C 66.43, H 5.58, N 7.26.

Compound 5b: Aniline (3.370 g, 36 mmol) was added to an ethanol (20 mL) suspension of parent zwitterion **3** (0.100 g, 0.72 mmol). The reaction mixture was heated to reflux for 4 d. The mixture was cooled down to room temperature, and the crude solid was washed with diethyl ether (3 × 40 mL). The product was obtained as a black solid (0.200 g, 95%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 5.20 (s, 1 H, N=C=CH), 5.81 (s, 1 H, O=C=CH), 7.26–7.33 (m, 2 H, CH aromatic), 7.36–7.47 (m, 8 H, CH aromatic), 10.97 (br. s, 2 H, NH) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_6$]DMSO): δ = 85.2 (s, N=C=*C*H), 98.1 (s, O=C=*C*H), 124.8 (s, CH aromatic), 127.4 (s, CH aromatic), 129.2 (s, CH aromatic), 136.5 (s, C aromatic), 155.5 (s, C=N), 171.8 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 291 (80) [M + H]$^+$. C$_{18}$H$_{14}$N$_2$O$_2$·1/6H$_2$O: calcd. C 73.71, H 4.93, N 9.55; found C 73.72, H 5.23, N 9.77.

Compound 6a: *tert*-Butylamine (0.115 g, 1.57 mmol) was added to a water (10 mL) suspension of zwitterion **3** (0.031 g, 0.22 mmol). The reaction mixture was stirred at room temperature for 18 h and then washed with dichloromethane (3 × 10 mL). Removal of the solvent led to compound **6a** as a red solid (0.035 g, 75%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.23 (s, 9 H, *t*Bu), 4.85 (s, 1 H, NC=CH), 5.13 (s, 1 H, O=C=CH), 6.49 (br. s, 1 H, NH), 7.20 (br. s, 1 H, NH), 7.75 (br. s, 3 H, NH$_3$) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, [D$_6$]DMSO): δ = 28.1 (s, CH$_3$), 50.5 [s, *C*(CH$_3$)$_3$], 94.6 (s, NC=*C*H), 99.8 (s, O=C=*C*H), 155.7 (s, N*C*), 175.8 (s, C=O), 176.8 (s, C=O), 183.4 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 213 (97) [M + H]$^+$. C$_{10}$H$_{16}$N$_2$O$_3$·2H$_2$O: calcd. C 48.38, H 8.12, N 11.28; found C 48.3, H 7.2, N 11.8.

Compound 6b: Piperidine (0.133 g, 1.56 mmol) was added to a water (10 mL) suspension of zwitterion **3** (0.031 g, 0.22 mmol). The reaction mixture was stirred at room temperature for 8 h and then washed with dichloromethane (3 × 20 mL). The aqueous phase was filtered, and the solvent was removed in vacuo. The crude solid was washed with pentane (2 × 10 mL) and dichloromethane (1 × 10 mL), then dissolved in methanol (1 × 10 mL), and filtered. Removal of the solvents afforded compound **6b** as a red solid

(0.024 g, 48%). Crystals suitable for X-ray diffraction were obtained by slow diffusion of pentane into an ethanol solution of the compound. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.48–1.69 (m, 6 H, $CH_2CH_2CH_2$), 2.98 (br. m, 4 H, CH_2NCH_2), 4.85 (s, 1 H, NC=CH), 5.13 (s, 1 H, O=C=CH), 6.40 (br. s, 1 H, NH), 7.22 (br. s, 1 H, NH), 8.45 (br. s, 2 H, NH) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 22.0 (s, $CH_2CH_2CH_2$), 22.6 (s, $CH_2CH_2CH_2$), 43.9 (s, CH_2NCH_2), 94.6 (s, NC=CH), 99.7 (s, O=C=CH), 155.7 (s, NC), 175.6 (s, C=O), 177.0 (s, C=O), 183.5 (s, C=O) ppm. MS (MADI-TOF+): *m*/*z* (%) = 225 (24) [M + H]$^+$. $C_{11}H_{16}N_2O_3 \cdot 1/2\ H_2O$: calcd. C 56.64, H 7.35, N 12.01; found C 56.79, H 7.23, N 11.73.

Compound 6c: Diisopropylamine (0.158 g, 1.56 mmol) was added to a water (10 mL) suspension of zwitterion **3** (0.031 g, 0.22 mmol). The reaction mixture was stirred at room temperature for 8 h and then washed with dichloromethane (3 × 20 mL). The water was removed in vacuo. The crude product was dissolved in methanol (10 mL), and the solution was filtered. Removal of the solvent in vacuo led to the product as a red solid (0.036 g, 68%). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.28 (d, $^3J_{H,H}$ = 6.5 Hz, 12 H, CH_3), 3.42 (br. m, 2 H, $CHCH_3$), 5.30 (s, 1 H, NC=CH), 5.38 (s, 1 H, O=C–CH) ppm. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.20 (d, $^3J_{H,H}$ = 6.5 Hz, 12 H, CH_3), 3.35 (m, $^3J_{H,H}$ = 6.5 Hz, 2 H, $CHCH_3$), 5.04 (s, 1 H, NC=CH), 5.20 (s, 1 H, O=C=CH), 6.62 (br. s, NH), 7.31 (br. s, NH), 7.88 (br. s, NH) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]-DMSO): δ = 18.8 (s, CH_3), 46.1 [s, $CH(CH_3)_2$], 94.8 (s, NC=CH), 99.9 (s, O=C=CH), 155.3 (s, NC), 175.4 (s, C=O), 176.4 (s, C=O), 183.1 (s, C=O) ppm. MS (ESI–): *m*/*z* (%) = 138 (100) $[C_6H_4NO_3]^-$. MS (ESI+): *m*/*z* (%) = 241 (35) [M + H]$^+$, 102 (30) $[C_6H_{16}N]^+$. $C_{12}H_{20}N_2O_3 \cdot 1/2H_2O$: calcd. C 57.81, H 8.49, N 11.24; found C 57.95, H 8.35, N 11.48. It was observed that an alternative to the direct synthesis of **6c** reported above is the cation exchange reaction starting from **6a**.

Compound 6d: Diethylamine (0.115 g, 1.57 mmol) was added to a water (10 mL) suspension of zwitterion **3** (0.031 g, 0.22 mmol). The reaction mixture was stirred at room temperature for 8 h and then washed with dichloromethane (3 × 20 mL). The aqueous phase was filtered, and the solvent was removed in vacuo. The crude solid was washed with dichloromethane (2 × 10 mL), then dissolved in methanol and filtered. Removal of the solvent led to compound **6d** as a red solid (0.027 g, 56%). Crystals suitable for X-ray diffraction were obtained by slow diffusion of pentane into an ethanol solution of the compound. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.13 (t, $^3J_{H,H}$ = 7.2 Hz, 6 H, CH_3CH_2), 2.90 (q, $^3J_{H,H}$ = 7.2 Hz, 4 H, CH_3CH_2), 4.86 (s, 1 H, NC=CH), 5.14 (s, 1 H, O=C=CH), 6.53 (br. s, 1 H, NH), 7.20 (br. s, 1 H, NH), 8.40 (br. s, 2 H, NH_2) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 11.0 (s, CH_3), 41.3 (s, CH_2), 94.6 (s, N-C=CH), 99.8 (s, O=C=CH), 155.5 (s, N-C), 175.8 (s, C=O), 176.5 (s, C=O), 183.3 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 231 (24) [M + H_2O + H]$^+$. $C_{10}H_{16}N_2O_3 \cdot 1/2\ H_2O$: calcd. C 54.3, H 7.7, N 12.7; found C 53.9, H 7.0, N 12.7.

Compound 6e: Dimethylamine (0.105 g, 2.33 mmol) was added to a water (10 mL) suspension of zwitterion **3** (0.046 g, 0.33 mmol). The reaction mixture was stirred at room temperature for 23 h and then washed with dichloromethane (3 × 20 mL). The solvent was removed in vacuo, and the product was obtained as a red solid (0.036 g, 59%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.48 (s, 6 H, Me), 4.93 (s, 1 H, NC=CH), 5.19 (s, 1 H, O=C=CH), 6.66 (br. s, 1 H, NH), 7.44 (br. s, 1 H, NH), 9.08 (br. s, 2 H, NH_2) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 34. 3 (s, CH_3), 94.4 (s, NC=CH), 99.7 (s, O=C=CH), 155.6 (s, NC), 176.0 (s, C=O), 176.7 (s, C=O), 183.4 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 185 (73) $[C_8H_{13}N_2O_3]^+$, 184 (27) $[C_8H_{12}N_2O_3]$. $C_8H_{12}N_2O_3 \cdot 1/2H_2O$: calcd. C 49.7, H 6.8, N 14.5; found C 49.2, H 6.6, N 13.4.

Compound 6f: Morpholine (0.821 g, 9.42 mmol) was added to a water (30 mL) suspension of zwitterion **3** (0.186 g, 1.35 mmol). The reaction mixture was stirred at reflux for 8 h, cooled to room temperature, and washed with dichloromethane (4 × 10 mL). Removal of the solvent led to compound **6f** as a brown solid (0.248 g, 81%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 3.02 (br. s, 4 H, N-CH_2-), 3.71 (br. s, 4 H, OCH_2), 4.96 (s, 1 H, NC=CH), 5.18 (s, 1 H, O=C=CH), 6.63 (br. s, 1 H, NH), 7.36 (br. s, 1 H, NH), 8.93 (br. s, 2 H, NH) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 43.2 (s, NCH_2), 63.8 (s, OCH_2), 94.5 (s, NC=CH), 99.9 (s, O=C=CH), 155.7 (s, NC), 176.4 (s, C=O), 176.6 (s, C=O), 183.5 (s, C=O) ppm. MS (ESI+): *m*/*z* (%) = 179 (100). $C_{10}H_{14}N_2O_4 \cdot 1/2\ H_2O$: calcd. C 51.06, H 6.43, N 11.91; found C 51.39, H 6.61, N 11.30.

General Procedure for the Synthesis of 4b from Compounds of the Type 6 or 7: 2-Aminoethanol (1.0 or 3.5 mmol) was added to an ethanol (15 mL) solution of **6** or **7** (0.50 mmol). The reaction mixture was stirred at room temperature for 17 h. The solvent was removed in vacuo, and the crude product was washed with pentane (1 × 10 mL). The product was obtained as a red solid. NMR spectroscopic data were comparable to those published.[46]

Compound 7a, Starting from 4c: *tert*-Butylamine (0.308 g, 4.21 mmol) was added to a water (15 mL) solution of functionalized zwitterion **4c** (0.100 g, 0.60 mmol). The reaction mixture was stirred at room temperature for 17 h. The aqueous solution was washed with dichloromethane (3 × 20 mL) and water was removed in vacuo. The solid was washed with pentane (1 × 10 mL), and then dichloromethane (15 mL) and *tert*-butylamine (0.18 mL, 1.67 mmol) were added. The reaction mixture was stirred at room temperature overnight, and the solvent was removed in vacuo. The crude solid was washed with pentane (1 × 10 mL), and the product was obtained as a red solid (0.070 g, 52%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.25 [s, 9 H, $C(CH_3)_3$], 2.70 (d, $^3J_{H,H}$ = 5.0 Hz, 3 H, NCH_3), 4.90 (s, 1 H, NC=CH), 4.91 (s, 1 H, O=C=CH), 7.26 (br. s, 1 H, NH), 8.01 (br. s, 3 H, NH_3) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 27.1 [s, $C(CH_3)$], 28.6 (s, $HNCH_3$), 50.5 [$C(CH_3)$], 92.0 (s, NC=CH), 99.7 (s, O=C=CH), 154.4 (s, NC), 175.1 (s, C=O), 177.0 (s, C=O), 182.7 (s, C=O) ppm. $C_{11}H_{18}N_2O_3 \cdot 4/3H_2O$: calcd. C 52.8, H 8.3, N 11.2; found C 52.7, H 7.7, N 10.9. MS (ESI–): *m*/*z* (%) = 152 (88) $[C_7H_6NO_3]^-$.

Compound 7a, Starting from 7b (Ammonium Exchange): *tert*-Butylamine (0.280 g, 3.80 mmol) was added to a dichloromethane (10 mL) suspension of salt **7b** (0.100 g, 0.54 mmol). The reaction mixture was stirred at room temperature for 17 h. The solvent was removed in vacuo, and the crude product was washed with pentane (1 × 10 mL) and dried in vacuo. Compound **7a** was obtained as a red solid (0.095 g, 78%). Crystals of **7a**·H_2O suitable for X-ray diffraction were obtained by slow diffusion of pentane into an ethanol solution of the compound.

Compound 7c: Diethylamine (0.154 g, 2.11 mmol) was added to a water (5 mL) solution of functionalized zwitterion **4c** (0.050 g, 0.30 mmol). The reaction mixture was stirred at room temperature for 17 h and then washed with dichloromethane (3 × 20 mL). The aqueous phase was evaporated, and the crude product was washed with dichloromethane (1 × 20 mL) and dried in vacuo. The product was obtained as a pale-red solid (0.033 g, 48%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.15 (t, $^3J_{H,H}$ = 7.3 Hz, 6 H, CH_3), 2.69 (d, $^3J_{H,H}$ = 5.0 Hz, 3 H, CH_3), 2.92 (d, $^3J_{H,H}$ = 7.3 Hz, 4 H, CH_2), 4.95 (s, 1 H, NC=CH), 5.00 (s, 1 H, O=C=CH), 7.30 (br. s, 1 H, NH), 8.63 (br. s, 2 H, NH_2) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 11.0 (CH_2CH_3), 28.6 ($HNCH_3$), 41.3 (CH_2), 91.9

(s, NC=*C*H), 99.7 (s, O–C–*C*H), 154.4 (s, NC), 175.4 (s, C–O), 176.8 (s, C–O), 182.8 (s, C=O) ppm. $C_{11}H_{18}N_2O_3·H_2O$: calcd. C 54.08, H 8.25, N 11.47; found C 54.21, H 8.27, N 10.55. MS (ESI+): *m*/*z* (%) = 227 (100) $[M + H]^+$.

Compound 7d: Dimethylamine (0.074 g, 1.64 mmol) was added to an aqueous solution (5 mL) of functionalized zwitterion **4c** (0.039 g, 0.23 mmol). The reaction mixture was stirred at room temperature for 17 h and then washed with dichloromethane (3 × 20 mL). The solvent was removed in vacuo, and the solid was washed with dichloromethane (1 × 20 mL). The product was obtained as a red solid (0.032 g, 69%). ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 2.54 (s, 6 H, CH_3), 2.69 (d, $^3J_{H,H}$ = 4.6 Hz, 3 H, CH_3), 4.92 (s, 1 H, NC=CH), 4.93 (s, 1 H, O–C–CH), 7.28 (br. s, 1 H, NH), 8.47 (br. s, 2 H, NH_2) ppm. ^{1}H (300 MHz, D_2O): δ = 2.70 (s, 6 H, 2CH_3), 2.91 (d, 3 H, CH_3), 5.30 (s, 1 H, CH) ppm. [Note: the anionic part of this salt reacts with D_2O, which exchanges the H atom of the (O–C–CH) moiety for deuterium; this explains the appearance of the signal at δ = 5.30 ppm]. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]-DMSO): δ = 28.8 (CH_3), 34.4 (CH_3), 92.4 (s, NC=*C*H), 101.5 (s, O–C–*C*H), 152.4 (s, N-C), 169.6 (s, C–O), 178.9 (s, C–O), 180.6 (s, C=O) ppm. $C_9H_{14}N_2O_3·H_2O$: calcd. C 49.99, H 7.46, N 12.96; found C 49.71, H 6.89, N 11.89. MS (ESI+): *m*/*z* (%) = 199 (100) $[M + H]^+$.

Compounds 7e and 7b: Piperidine (0.301 g, 3.53 mmol) was added to a water (5 mL) solution of functionalized zwitterion **4c** (0.084 g, 0.50 mmol). The reaction mixture was stirred at room temperature for 17 h and then washed with dichloromethane (3 × 20 mL). The aqueous solution was evaporated to dryness, and the solid residue was suspended in dichloromethane (20 mL). Compound **7b** was collected by filtration, washed with dichloromethane (1 × 20 mL), and obtained as a red solid (0.035 g, 38%). The dichloromethane solutions were combined and the solvent evaporated to dryness, leading to compound **7e** as a red solid (0.062 g, 52%). Data for **7e**: ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.55 (br. m, 2 H, -CH_2-CH_2-CH_2-),1.65 (br. m, 4 H, -CH_2-CH_2-CH_2-), 2.72 (d, $^3J_{H,H}$ = 5.22 Hz, 3 H, CH_3), 2.98 (br. m, 4 H, CH_2NCH_2), 5.24 (s, 1 H, NC=CH), 5.73 (s, 1 H, O–C–CH), 7.80 (br. s, 1 H, NH), 8.78 (br. s, 2 H, NH_2) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, [D$_6$]DMSO): δ = 21.7 (s, $CH_2CH_2CH_2$), 22.1 (s, *C*H_2CH_2CH_2), 29.0 (s, CH_3), 43.5 (s, NCH_2), 92.8 (s, NC=*C*H), 103.4 (s, O–C–*C*H), 150.2 (s, N-*C*),

Table 2. Data collection and refinement parameters for all compounds.

	4a	**4c**·1/2C_6H_7N	**4e**	**6b**
Formula	$C_{12}H_{18}N_2O_2$	2($C_8H_{10}N_2O_2$)·C_6H_7N	$C_{10}H_{14}N_2O_2$	$C_5H_{12}N·C_6H_4NO_3$
M_r	222.28	425.49	194.23	224.26
Cell setting	orthorhombic	monoclinic	monoclinic	monoclinic
Space group	$P2_12_12_1$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a [Å]	5.6951(5)	11.5189(4)	12.744(1)	8.4333(3)
b [Å]	15.3531(11)	16.0820(7)	7.399(1)	12.6529(5)
c [Å]	14.0639(9)	11.6051(5)	10.838(1)	11.0569(5)
β [°]	90.00	92.498(2)	90.754(7)	108.824(2)
V [Å^3]	1229.71(16)	2147.77(15)	1021.9(2)	1116.73(8)
Z	4	4	4	4
D_x [Mg m^{-3}]	1.201	1.316	1.263	1.334
μ [mm^{-1}]	0.08	0.09	0.09	0.10
Crystal size [mm]	0.22 × 0.20 × 0.10	0.10 × 0.10 × 0.06	0.18 × 0.14 × 0.12	0.22 × 0.20 × 0.18
Measured, independent, observed reflections	12445, 1658, 1210	12483, 7437, 4371	3169, 1887, 838	4143, 2547, 1693
R_{int}	0.117	0.035	0.072	0.027
θ_{max} [°]	27.5	32.0	25.5	27.5
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.076, 0.116, 1.14	0.054, 0.142, 1.01	0.056, 0.121, 0.99	0.043, 0.122, 1.05
No. parameters	157	388	138	161
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [e Å^{-3}]	0.20, –0.19	0.31, –0.26	0.24, –0.28	0.21, –0.26
	6c	**6d**·H_2O	**7a**·H_2O	
Formula	$C_6H_4NO_3·C_6H_{16}N$	$C_4H_{12}N·C_6H_4NO_3·H_2O$	$C_{22}H_{38}N_4O_7$	
M_r	240.30	230.26	470.56	
Cell setting,	monoclinic	orthorhombic	monoclinic	
Space group	$P2_1/c$	*Pbca*	*C*2/*c*	
a [Å]	7.5733(8),	13.9133(6),	13.6464(10),	
b [Å]	14.247(1),	12.6639(6),	11.8438(10),	
c [Å]	12.3760(8)	14.9583(8)	17.2223(9)	
β [°]	95.566(6)	90.00	112.091(4)	
V [Å^3]	1329.0(2)	2635.6(2)	2579.2(3)	
Z	4	8	4	
D_x [Mg m^{-3}]	1.201	1.161	1.212	
μ [mm^{-1}]	0.09	0.09	0.09	
Crystal size [mm]	0.20 × 0.10 × 0.10	0.25 × 0.22 × 0.08	0.25 × 0.25 × 0.14	
Measured, independent, observed reflections	4528, 2607, 1305	5398, 2948, 1158	7780, 2950, 1735	
R_{int}	0.054	0.104	0.057	
θ_{max} [°]	26.0	27.5	27.5	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.058, 0.134, 1.07	0.052, 0.108, 0.96	0.058, 0.123, 1.01	
No. parameters	174	169	174	
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [e Å^{-3}]	0.23, –0.24	0.17, –0.19	0.17, –0.23	

162.0 (s, C=O), 178.3 (s, C=O), 182.5 (s, C=O) ppm. MS (ESI+): *m/z* (%) = 239 (100) $[M + H]^+$. $C_{12}H_{18}N_2O_3 \cdot H_2O$: calcd. C 56.23, H 7.87, N 10.93; found C 55.71, H 7.83, N 11.32. Data for **7b**: ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 2.37 (s, 3 H, CH_3), 2.70 (br. s 3 H, CH_3), 4.88 (s, 1 H, NC=CH), 4.90 (s, 1 H, O=C=CH), 7.22 (br. s, 1 H, NH), 7.79 (br. s, 3 H, NH_3) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, [D$_6$]DMSO): δ = 24.6 (s, CH_3), 28.6 (s, CH_3), 91.9 (s, NC=*C*H), 99.6 (s, O=C=*C*H), 154.5 (s, N-*C*), 175.2 (s, C=O), 177.1 (s, C=O), 182.8 (s, C=O) ppm. MS (ESI–): *m/z* (%) = 152 (100) $[M - H_3NMe]^-$. MS (ESI+): *m/z* (%) = 154 (47) $[M - H_3NMe + 2H]^+$.

X-ray Data Collection, Structure Solution, and Refinement for All Compounds: Suitable crystals for X-ray analysis were obtained as described above. The intensity data was collected at 173(2) K with a Kappa CCD diffractometer[49] (graphite monochromated Mo-K_α radiation, λ = 0.71073 Å). Crystallographic and experimental details for the structures are summarized in Table 2. The structures were solved by direct methods (SHELXS-97) and refined by full-matrix least-squares procedures (based on F^2, SHELXL-97)[50] with anisotropic thermal parameters for all the non-hydrogen atoms. The hydrogen atoms were introduced into the geometrically calculated positions (SHELXS-97 procedures) and refined riding on the corresponding parent atoms, except those on the nitrogen or oxygen atoms, which were found in the ΔF^2 maps and refined isotropically. CCDC-720164 (for **4a**), -720165 (for **4c**·1/2C_6H_7N), -720166 (for **4e**), -720167 (for **6b**), -720168 (for **6c**), -720169 (for **6d**·H_2O), and -720170 (for **7a**·H_2O) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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