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RESEARCH ARTICLE

Strain-induced Reactivity Effects in the Reaction of 2,5-Dihydroxy-[1,4]-benzoquinone with Diamines

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Abstract: The regioselectivity of the reaction of 2,5-dihydroxy-[1,4]-benzoquinone (DHBQ) with diamines could not be explained satisfactorily so far. In general, the reaction products can be derived from the tautomeric *ortho*-quinoid structure of a hypothetical 4,5-dihydroxy-[1,2]-benzoquinone. However, both aromatic and aliphatic 1,2-diamines form phenazines, in some cases, formally by diimine formation on the quinoid carbonyl groups, and in other cases, the corresponding 1,2-diamino-[1,2]-benzoquinones by nucleophilic substitution of the OH groups; the regioselectivity apparently does not follow any discernible pattern. The reactivity was now explained by an adapted theory of strain-induced bond localization (SIBL). Here, the preservation of the "natural" geometry of the two quinoid C–C double bonds (C3=C4 and C5=C6) as well as the N–N distance of the co-reacting diamine are crucial. A decrease of the annulation angle sum (N–C4–C5 + C4–C5–N) is tolerated well and the 4,5-diamino-*ortho*-quinones, having relatively short N–N spacings, are formed. An increase in the angular sum is energetically unfavorable, so that diamines with a larger N–N distance afford the corresponding *ortho*-quinone imines. Thus, for the reaction of DHBQ with diamines, exact predictions of the regioselectivity and the resulting product structure can be made on the basis of simple computations of bond spacings and product geometries.

Keywords: Amines, benzoquinones, diamines, DHBQ, regioselectivity, SIBL theory.

1. INTRODUCTION

2,5-Dihydroxy-[1,4]-benzoquinone (DHBQ, **1**) is a popular component of supramacromolecular structures such as MOFs [1-4], organic ferroelectric materials [5], being easily deprotonated to the very stable aromatic dianion [6]. It also appears as one of the key chromophores in the aging and yellowing of cellulosic materials [7]. The reaction of DHBQ with mono-amines follows a consistent pattern and does not really hold any surprises (Scheme **1**) [6, 8, 9]. Primary amines react either at DHBQ's quinoid keto groups (C-1 and C-4) and form quinone diimines (**2**) *via ipso*-substitution at C-2 and C-5 hydroxy groups resulting in 2,5-bis(alkylamino)-[1,4]-benzoquinones (**3**). Secondary amines react only at C-2 and C-5 by respective substitution to 2,5-bis(dialkylamino)-[1,4]-benzoquinones (**4**), and not at the quinoid keto groups, whereas tertiary amines do not react at all in substitution reactions. In the reaction of DHBQ with primary and secondary monoamines, the fundamental *para*-quinoid structure is maintained throughout (Scheme **1**).

For the reaction with diamines, mostly aromatic 1,2-diamines (1,2-phenylenediamines) are used, which react with DHBQ to form phenazine heterocycles (**5**) [10-13], as shown in Scheme **2a**. It is assumed that a quinone imine is formed first, followed by ring closure through the reaction of the second amino group with the adjacent OH group. The last step is then re-aromatization, which also represents the thermodynamic driving force of the overall reaction.

The reaction with diamines thus differs from the reaction of monoamines in that the products are derived from an *ortho*-quinoid structure, the tautomeric 4,5-dihydroxy-[1,2]-benzoquinone, which, however, does not exist as a free compound. If an excess of phenylenediamine is used, the further reaction in a double aza-Michael process can lead to dihydrotetraazapentacenes (**6**) (Scheme **2a**) [14].

2. RESULTS AND DISCUSSION

While according to literature, the reaction with *ortho*-phenylenediamines proceeds unambiguously giving only the *ortho*-quinone diimine, the reaction with the aliphatic ethylenediamine resulted in a mixture of the *ortho*-quinone diimine (2,3-dihydroquinoxaline-6,7-diol, **7**) and the respective 4,5-diamino-substituted *ortho*-quinone (1,2,3,4-tetrahydroquinoxaline-6,7-dione, **8**), as shown in Scheme **2b** [6, 15, 16].

Follow-up studies to our investigations on DHBQ in the chromophore chemistry of cellulosic fibers [17, 18] showed that DHBQ and urea formed 1*H*-benzo[*d*]imidazole-2,5,6(3*H*)-trione (**9**) with the two quinone-carbonyls remaining non-derivatized. Thus, the formation of an aromatic or conjugated system could not be the decisive factor, otherwise urea would rather have formed the corresponding – hypothetical – *ortho*-quinone diimine structure. Most

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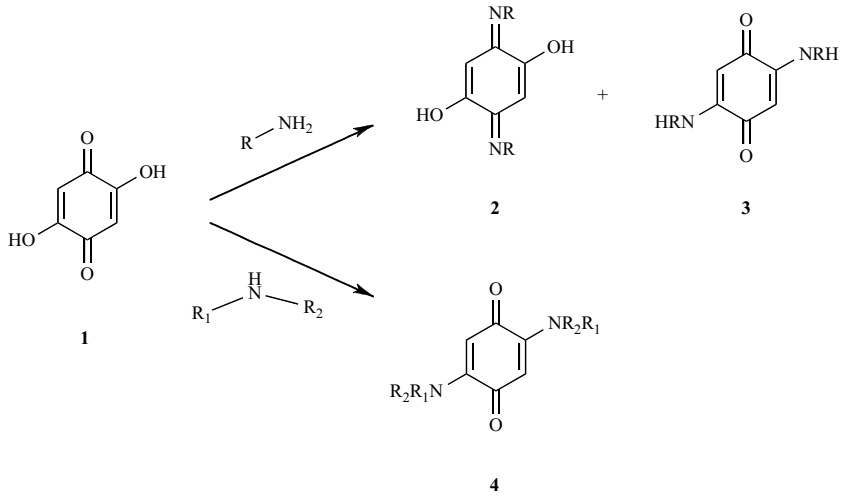
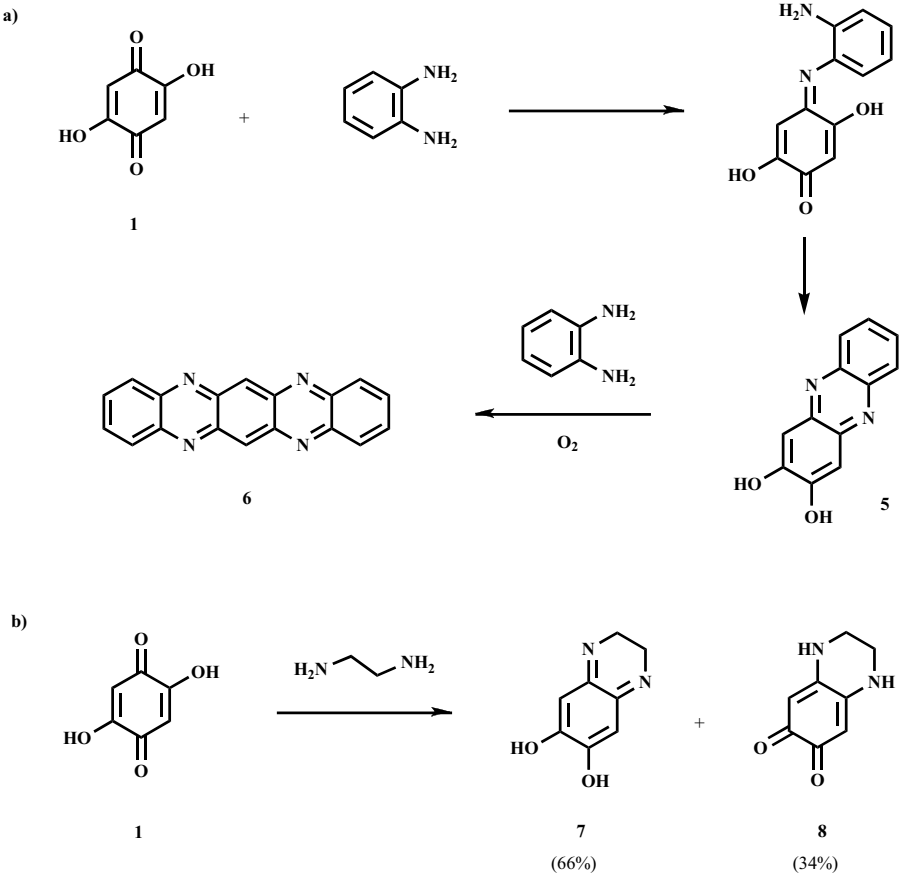


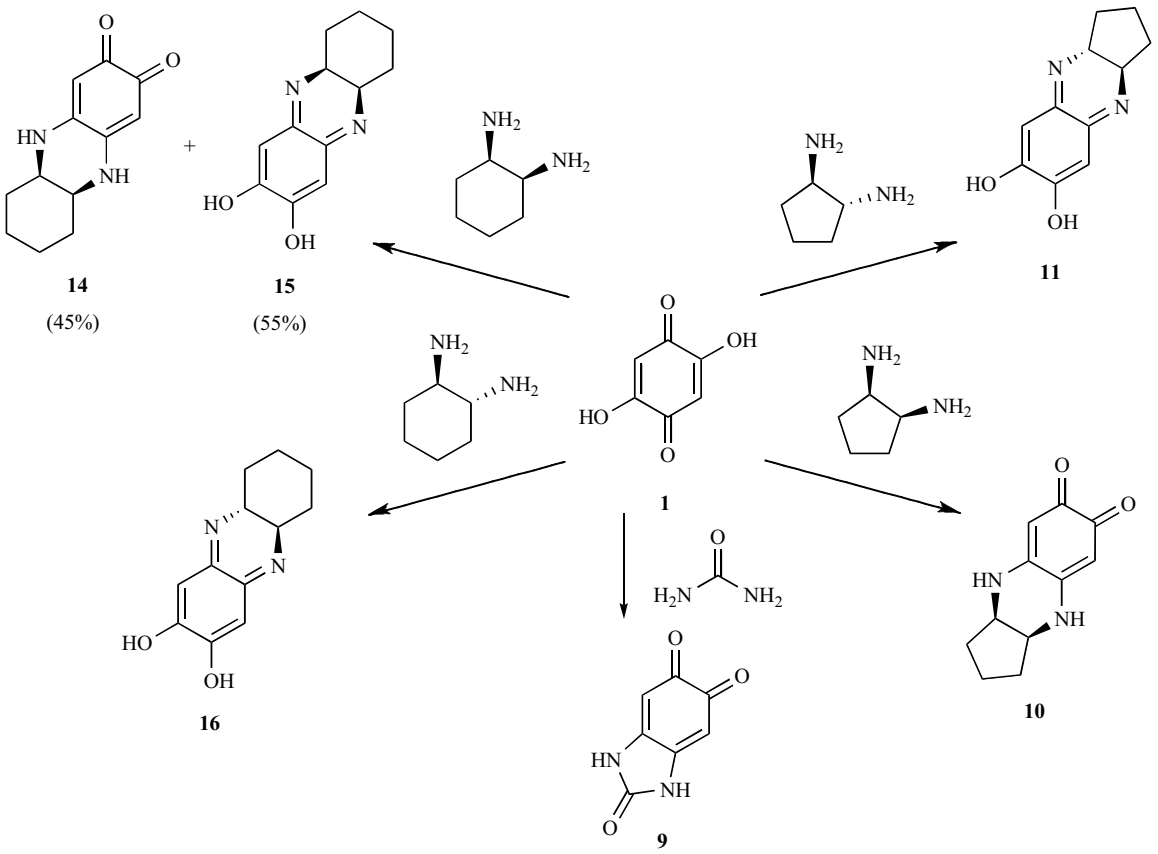
Scheme 1. Reaction of 2,5-dihydroxy-[1,4]-benzoquinone (**1**) with aliphatic primary and secondary monoamines, R=Me, Et, Ph.



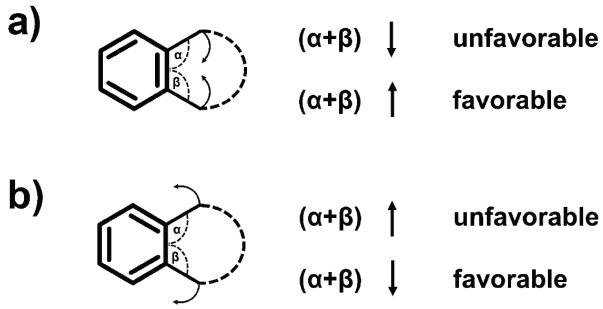
Scheme 2. Reaction of 2,5-dihydroxy-[1,4]-benzoquinone (**1**) with (**a**) *ortho*-phenylene diamine; and (**b**) with ethylene diamine (1,2-diaminoethane) [10-14].

puzzling, in the beginning at least, was the result of the reaction with the two isomeric 1,2-diaminocyclopentanes: the *cis*-compound afforded exclusively the diamino-*ortho*-quinone **10** while *trans*-1,2-diaminocyclopentane gave the *ortho*-quinone diimine product **11**, as shown in Scheme **3**. This outcome was impossible to explain just by conventional aromaticity, conjugation or general reactivity considerations.

Reaction of DHBQ with other compounds having two primary amino groups (Table **1**) led us to the conclusion that the reactivity of DHBQ towards diamines can be well explained by adapting the theory of strain-induced bond localization (SIBL) [19-22], which was developed from original observations often called "Mills-Nixon effect" [23, 24]. The original theory states that the ring tension imposed by an annulated single-bond (σ-bond) ring system can cause localization of the double bonds in an aromatic (π-bond) system. In general, a reduction of the angle between the (*exo*-)substituent and the adjacent double bond in the aromatic ring, *i.e.* a "bending" of the substituent towards the double bond, is energetically less favorable than an increase of the angle (a "bending" away from the double bond). The aromatic/quinoid system evades in a way that minimizes unfavorable strain, and the double bonds are "placed" accordingly (Scheme **4**).



Scheme 3. Surprising selectivity effects in the reaction of 2,5-dihydroxy-[1,4]-benzoquinone (**1**) with different aliphatic diamines.



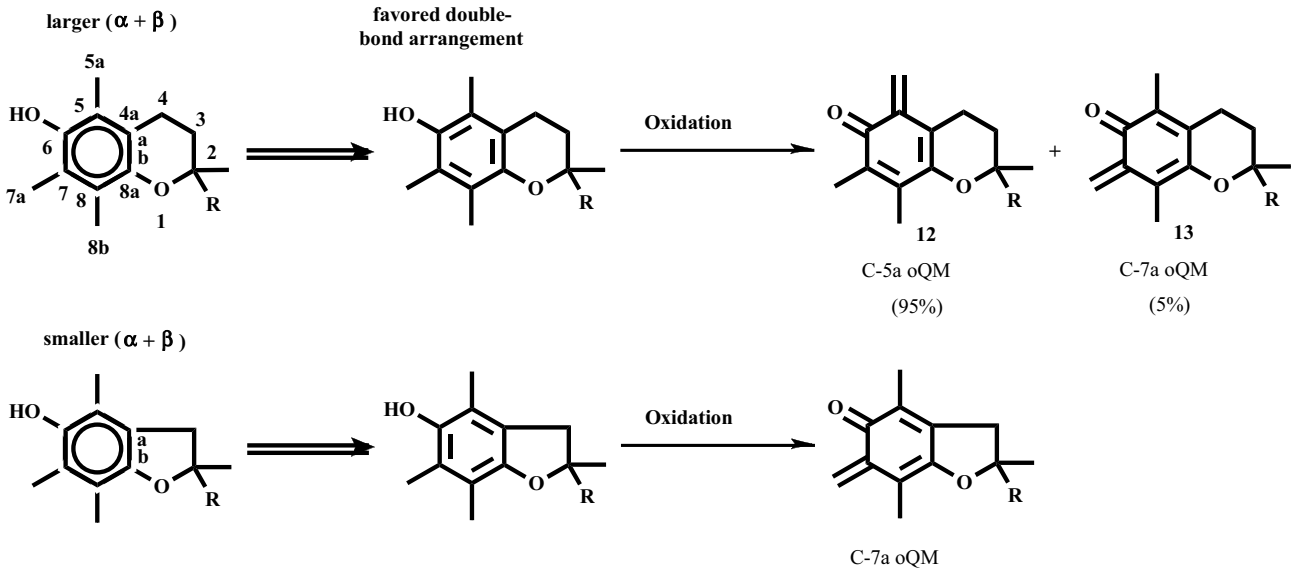
Scheme 4. Schematic representation of strain-induced bond localization (SIBL) [24], based on the Mills-Nixon theory [25].

This SIBL behavior has been studied very well for the example of the *ortho*-quinone methide (oQM) derived from α-tocopherol (**12**), the main component of vitamin E (Scheme **5**) [25]. Two-electron oxidation of this compound under aprotic conditions leads to a mixture of two oQMs at room temperature which is formed under the involvement of C-5a (**12**, 95%) and C-7a (**13**, 5%). If the sum of the annulation angles (α+β) is increased only slightly by fusing "larger" rings, complete C-5a selectivity is observed, while a gradual reduction of the annulation angle sum increasingly favors the formation of the oQM at C-7a. When the annulated ring is "opened", *i.e.* replaced by two non-linked substituents, the molar ratio of the two possible oQMs is 1:1.

An annulated ring changes the "*quasi*-natural" angle sum which these two independent substituents at the aromatic ring would assume, and the ring imposes σ-strain on the aromatic π-system, which reacts by "localizing" the double bonds (Scheme **4**). This positioning, in the case of α-tocopherol as an example, occurs in a way that larger angle sums (α+β) favor the C-5a oQM, while smaller sums favor the formation of the C-7a oQM counterpart. The "size" of the annulated ring determines the position of the double bonds in the *ortho*-quinoid system. Once again, a decrease of the angle between the two σ-bonds extending from an sp^2-carbon (a carbon involved in the double bond) is better tolerated than an increase, and the double bonds arrange themselves in a way that results in the least unfavorable angle deformation (strain).

The same general explanation can be applied to the case of the reaction of DHBQ with primary aliphatic diamines (Scheme **6**). Apparently, the geometries of the two conjugated quinoid double bonds (C3=C4 and C5=C6) are decisive here. Co-reacting diamines with more "distant" amino groups would cause a large sum of annulation angles (α+β), or in other words, smaller (α′+ β′) angles between substituent and adjacent double bond. Since this is unfavorable according to the SIBL theory, the reaction forms the *ortho*-quinone diimine, thus avoiding this strain. Diamine substituents with "close by" amino groups, in contrast, result in a small sum of annulation angles (α+β) at C4 and C5 (= larger angles (α′+ β′) between the substituent and double bonds), which is more favorable in terms of energy, so that the reaction gives the respective diamino-*ortho*-quinone.

Table **1** shows the products of the reaction of DHBQ with various diamines, the N–N distances in the product as predicted by fast geometry computations on the DFT level (B3LYP/6-31G*), the ^{13}C NMR data of the products (as the ^{1}H data are not informative, see below) and the overall relative yield. The two possible product tautomers can be easily distinguished by their ^{13}C NMR resonances (see experimental part); in the *ortho*-quinones, the resonances of the

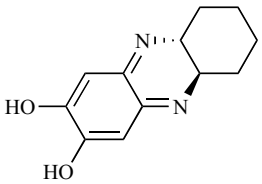
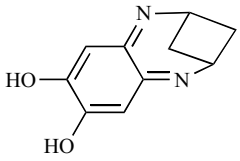
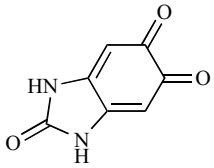
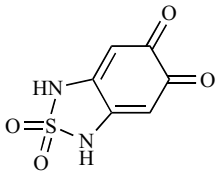
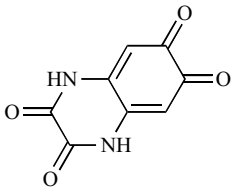
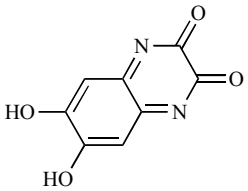
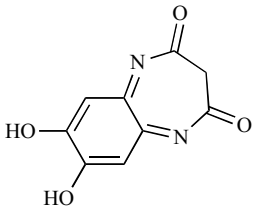
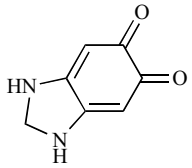


Scheme 5. Strain-induced bond localization (SIBL) [25] explained by the example of α-tocopherol oxidation chemistry: regioselectivity of oQM formation dependent on the size of the annulated ring.

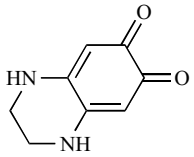
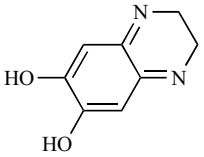
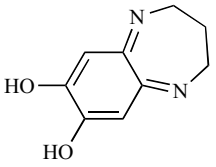
Table 1. Reaction of DHBQ (1) with diamines: product selectivity (product tautomers and yields) and N–N distances.

Diamine co-reactant	Diamino-*ortho*-quinone product *	*ortho*-Quinone diimine product *	N–N distance in product (Å)
cis-1,2-Diaminocyclopentane	**10**, 100 %	0 %	2.80
trans-1,2-Diaminocyclopentane	0 %	**11**, 100 %	2.98
cis-1,2-Diaminocyclohexane	**14**, 45 %	**15**, 55 %	2.84/2.85

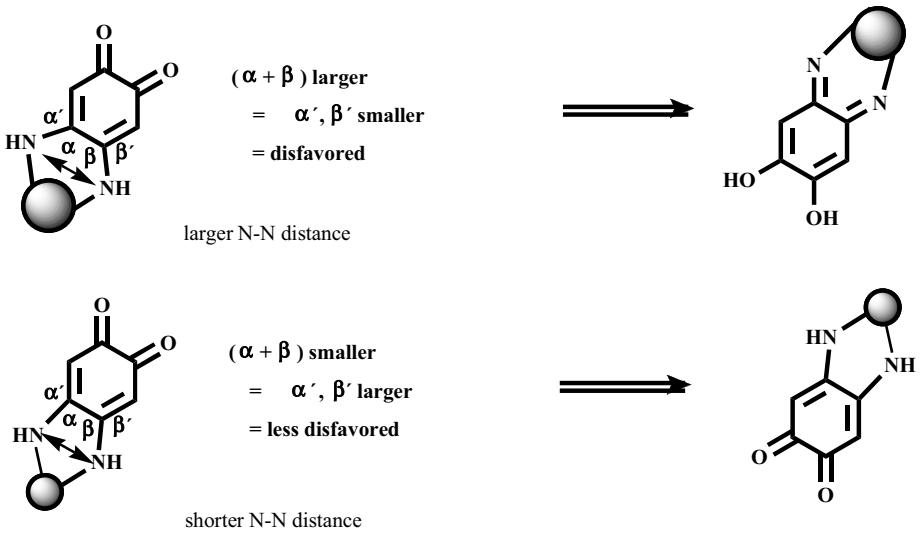
(Table 1) contd….

trans-1,2-Diaminocyclohexane	0 %	 **16**, 100 %	2.96
cis-1,3-Diaminocyclobutane	0 %	 **17**, 100 %	2.97
Urea	 **9**, 100 %	0 %	2.31
Sulfamide	 **18**, 100 %	0 %	2.54
Oxalamide	 **19**, 88 %	 **20**, 12 %	2.85/2.88
Malonamide	0 %	 **21**, 100 %	3.02
1,1-Methylenediamine**	 **22**, 100 %	0 %	2.45

(Table 1) contd….

1,2-Ethylenediamine	 **8**, 34 %	 **7**, 66 %	2.77/2.91
1,3-Propylenediamine	0 %	 **23**, 100	3.22

*For the ring structures R, see diamine co-reactants in column 1. For the atom numbering (a, b, c) *cf.* the ^{13}C NMR resonances in the experimental part.
** Hexamethylenetetramine (0.4 eq.) used as amine co-reactant.



Scheme 6. Outcome of the reaction of DHBQ with aliphatic primary diamines explained according to the SIBL theory. The strain effects imposed by the annulated ring on the double bonds determine which tautomer (quinone imine *vs.* diamino *ortho*-quinone) is formed and thus formally the regioselectivity of the diamine reaction towards DHBQ can be obtained; for the co-reacting diamines and products, see Table **1**.

C=O (quinone carbonyls C1 and C2) appear around 176-182 ppm and the C–N (amino-carrying carbons C4 and C5) at around 145-148 ppm, while in the *ortho*-quinone imines, the C=N (imino carbons at C1 and C2) are found at around 158-163 ppm and the C–OH (hydroxyl-carrying carbons C4 and C5) at around 149-154 ppm.

In most cases, there was a complete selectivity for either the amino-*ortho*-quinone or the *ortho*-quinone imine. The case of 1,2-diaminocyclopentane was especially instructive, with the *cis*-diamine giving only diamino-*ortho*-quinone **10** and the *trans*-compound only *ortho*-quinone diimine **11**. In fact, it is possible to cleanly separate a mixture of *cis*- and *trans*-1,2-diaminocyclopentane *via* temporary derivatization with DHBQ. The N–N distances in the diamines allow an estimation of a "threshold" up to which diamino-*ortho*-quinones are formed (1,2-elimination pathway in Scheme **7**) and above which length, the *ortho*-quinone diimine compounds are generated (1,4-elimination path in Scheme **7**). *cis*-1,2-Diaminocyclohexane was the compound that obviously lay exactly on this threshold of about 2.85 Å, because in the special case of this compound, both the *ortho*-quinone **14** (N–N: 2.85 Å) and the quinone diimine **15** (N–N: 2.86 Å) were formed in a nearly equimolar ratio (Table **1**). With this distance threshold, the puzzling reactivity difference between *cis*- and *trans*-diaminocyclopentane can also be smoothly explained: the *cis*-isomer (2.80 Å in **10**) lies below the limit of approx. 2.85 Å, resulting in diamino-*ortho*-quinone formation, and the *trans*-isomer (2.98 Å in **11**) is above this threshold so that the *ortho*-quinone diimine is formed. Alternatively, the reaction outcome can be imagined as two product tautomers, the equilibrium of which is determined by the N–N distance (Scheme **7**). At about 2.85 Å, both tautomers are formed, and a shorter distance shifts the equilibrium strongly towards the diamino-*ortho*-quinone, a larger distance shifts it towards the *ortho*-quinone diimines.

trans-1,2-Diaminocyclohexane with its larger N–N distance (2.96 Å) afforded only the *ortho*-quinone diimine **16**. The same is true for *cis*-1,3-diaminocyclobutane with its very similar N–N distance (2.97 Å) in the corresponding *ortho*-quinone diimine **17**. This example nicely confirmed that the N–N distance can indeed be taken as the decisive factor that determines product formation; no matter what the configuration of the cyclic diamine was (*cis* or

trans) or whether a 1,2-diamine (*trans*-1,2-diaminocyclohexane) or a 1,3-diamine (*cis*-1,3-diaminocyclobutane) was employed, when the N–N distance was similar, the same kind of product was formed.

Bisamides underwent the same reaction with DHBQ as diamines, with the N–N distance also determining the product in this case. Urea and sulfamide provided the corresponding diamino-*ortho*-quinones **9** (2.31 Å) and **18** (2.54 Å), respectively, while oxalamide afforded both the diamino-*ortho*-quinone **19** and the *ortho*-quinone diimine; the N–N spacings of both were close to the "threshold" (2.85 Å and 2.88 Å, respectively). Malonamide afforded only the *ortho*-quinone diimine **21** with the long N–N spacing of 3.02 Å.

Both the alicyclic diamines and the amides represented rather stiff systems in which the N–N distances, predetermined by the geometry, were fixed and rather "inflexible". The comparison with aliphatic diamines becomes interesting in this context because in these compounds, the N–N spacing can vary quite widely by conformational changes. This is not yet the case for 1,1-methylenediamine which exclusively gives the diamino-*ortho*-quinone derivative **22**, with its small N–N distance of 2.45 Å. However, 1,2-ethylenediamine (Scheme **2b**) is flexible enough and can thus adopt different product geometries, affording both the diamino-*ortho*-quinone derivative **8** (2.77 Å) and the *ortho*-quinone diimine **7** (2.91 Å). In the case of 1,3-propylenediamine, by contrast, only the *ortho*-quinone diimine **23** (3.22 Å) is found because the three-ring carbons enforce a long N–N distance that allows only this product geometry, despite their conformational flexibility in the starting diamine. The series 1,1-methylenediamine, 1,2-ethylenediamine and 1,3-propylenediamine is thus another good illustration of how the product system tries to avoid unfavorable ring strain. From the examples in Table **1**, it is evident that the adapted SIBL reasoning explained the observed regioselectivities really well. Aromaticity considerations, as involved in the case of aromatic diamine co-reactants, are not required.

The agreement of the observed product formation with the SIBL prediction can also be understood by considering the key addition intermediate in the DHBQ + diamine reaction (Scheme **7**), which cannot be isolated and thus remains hypothetical. If 1,4-elimination of water would generate ring double bonds that suffer from imposed strain (diamino-*ortho*-quinones), the system rather undergoes 1,2-elimination to the *ortho*-quinone imines to avoid this strain. Alternatively, the two corresponding products are tautomers, and the stability of the tautomers can be seen as being determined by the SIBL-predicted ring strain.

3. MATERIALS AND METHODS

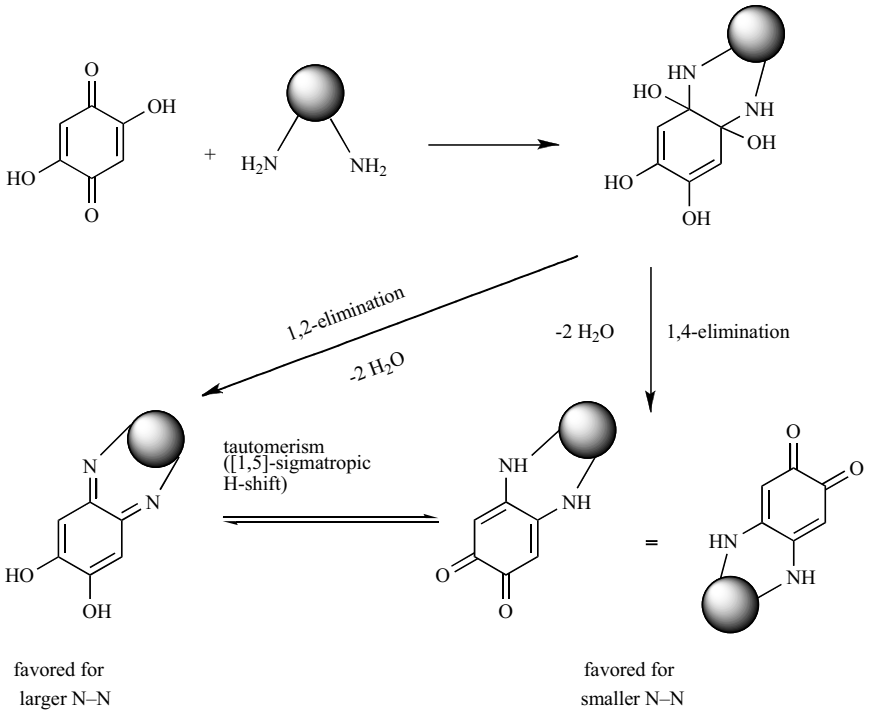
3.1. General

Commercially available chemicals and reagents (DHBQ, diamines) as well as solvents were purchased from Sigma-Aldrich (Schnelldorf, Germany) or ABCR (Karlsruhe, Germany). Chemicals were of the highest grade available and used without further purification.

TLC was performed with Merck silica gel 60 F_{254} pre-coated plates. Flash chromatography was performed with Baker silica gel (40 μm particle size). All products were purified to homogeneity as checked by TLC/GC-MS analysis. Melting points (ambient conditions) are uncorrected. All given yields refer to isolated, pure products.

3.2. NMR Spectroscopy

The NMR experiments were performed on a Bruker Avance II 400 instrument (^{1}H resonance at 400.13 MHz, ^{13}C resonance at 100.61 MHz) with a 5 mm broadband probe head (BBFO) equipped with z-gradient with standard Bruker pulse programs. All data were collected with 32k data points and apodized with a Gaussian win-



Scheme 7. Reaction of DHBQ with aliphatic primary diamines. The alternative placement of double bond systems can be envisaged by either 1,2- or 1,4-elimination of water from the primary addition intermediate or by the formation of either two tautomers. For co-reacting diamines and products, see Table **1**.

dow function (GB = 0.3) prior to FT. Enhancement of signal-to-noise was achieved by multiplication of the FID with an exponential window function (lb = 1Hz). Bruker TopSpin 3.5 (3.0) software was used for data processing. Chemical shifts are given in ppm, referencing to residual solvent signals.

3.3. GCMS Analysis

GC-MS was performed on a GC 6890N/MSD 5973B instrument with a fused silica HP-5ms (30 m, 0.25 mm, 25 μm) column and helium as a carrier gas. The total flow was 27.5 mL min^{-1} at 46.9 kPa carrier gas pressure and the resulting column flow was 0.9 mL min^{-1}. The temperature programs were as follows: 100°C (5 min), 10°C min^{-1} to 280°C (20 min). Aliquots (0.2 μL) of the dissolved samples were injected at 230°C inlet temperature in split mode (25:1). Ionization was performed in EI(+) mode at 70 eV.

3.4. General Procedure for the Reaction of DHBQ (1) with Diamines

DHBQ was recrystallized from glacial acetic acid (commercially available DHBQ may contain up to 30% of its salts, mostly in the sodium form). DHBQ (5 mmol, 0.70 g) was dissolved in 2-propanol (50 mL). Under stirring at 40°C, the co-reacting diamine (5 mmol) dissolved in 2-propanol (10 mL) was added slowly over 15 min at 40°C. The mixture was refluxed for 5 min, cooled to r.t., filtered through a layer of basic aluminum oxide (Brockmann grade III, 10 g), and evaporated *in vacuo*. The solid residue was recrystallized from dioxane. When TLC analysis indicated the formation of more than one product, the residue from evaporation was dissolved in ethyl acetate and chromatographed on silica gel (ethyl acetate/toluene, v/v=4:3). The combined fractions were evaporated and the solid residue was recrystallized from dioxane.

3.5. Analytical Data

The structure of the compounds was characterized by their ^{13}C NMR spectra (solvent $CDCl_3$), with full assignment of all resonances. In the compounds listed below, "Ca" denotes the sp^2-hybridized carbon (C=O or C=N), "Cb" the methine carbon (CH) and "Cc" the sp^3-carbon with OH or NH-substituent. All of these three resonances have a double intensity as they originate from three magnetically equivalent carbon atoms in the symmetric DHBQ moiety. Note that the ^1H NMR spectra are not conclusive; the only proton resonance of the DHBQ moiety, coming from the two equivalent methine protons, appears as a broad singlet at about 5.7±0.15 ppm for all products (in $CDCl_3$ or DMSO-d_6) and additionally undergoes H-D exchange in protic NMR solvents.

MS (EI+) spectra of the compounds give clear molecular ion peaks (M^+ or MH^+) but are otherwise poor in fragmentation signals. While all the *ortho*-quinones showed a characteristic strong [M-28] peak (loss of CO) along with a weaker [M-56] signal (loss of 2×CO), the quinone imines did not show such an analogous fragmentation.

The purity of the compounds was confirmed by GC-MS (>99.5% in all cases) and additionally checked by TLC (ethyl acetate/toluene, v/v=4:3 or v/v=4:1). Note that elemental analysis is not meaningful in the present cases because it cannot distinguish between the two possible tautomeric reaction products, which have the same elemental composition.

3.6. Reaction with *cis*-1,2-diaminocyclopentane

(*R,S*)-2,3,3a,4,9,9a-Hexahydro-1*H*-cyclopenta[b]quinoxaline-6,7-dione (**10**), red powder, m.p. (decomp.) = 176-177°C, yield 92%, purity (GCMS): 99.8%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.31. ^1H NMR: δ 1.58-1.84 (m, 6H, CH_2), 2.52 (m, 2H, N-CH), 5.78 (s, 2H, HCb).^{13}C NMR: δ Ca: 178.6, Cb: 105.8, Cc: 145.6, 54.0 (CH-N), 32.4 (CH_2), 22.9 (CH_2).

3.7. Reaction with *trans*-1,2-diaminocyclopentane

(*R,R*)-2,3,3a,9a-Tetrahydro-1*H*-cyclopenta[b]quinoxaline-6,7-diol (**11**), yellow powder, m.p. (decomp.) = 184-186°C, yield 98.2%, purity (GCMS): 99.6%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.44. ^1H NMR: δ 1.60-1.82 (m, 6H, CH_2), 2.58 (m, 2H, N-CH), 5.76 (s, 2H, HCb). ^{13}C NMR: δ Ca: 162.6, Cb: 109.5, Cc: 148.9, 59.3 (CH-N), 26.2 (CH_2), 20.2 (CH_2).

3.8. Reaction with *cis*-1,2-diaminocyclohexane

(*R,S*)-5,5a,6,7,8,9,9a,10-Octahydrophenazine-2,3-dione (**14**), red powder, m.p. (decomp.) = 185°C, yield 94.4% (together with **15**), purity (GCMS, sum with **15**): 100.0%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.24. ^1H NMR: δ 1.12-1.21 (m, 4H, N-CH-CH_2-C$\underline{H}_2$), 1.32-1.50 (m, 2H, N-CH-C$\underline{H}_A$), 1.66-1.70 (m, 2H, N-CH-C$\underline{H}_B$), 2.58 (m, 2H, N-CH), 5.74 (s, 2H, HCb). ^{13}C NMR: δ Ca: 181.7, Cb: 109.7, Cc: 147.8, 55.1 (CH-N), 31.8 (CH_2), 23.9 (CH_2).

(*R,S*)-5a,6,7,8,9,9a-Hexahydrophenazine-2,3-diol (**15**), yellow powder, m.p. (decomp.) = 192-194°C, yield 94.4% (together with **14**), purity (GCMS, sum with **14**): 100.0%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.46. ^1H NMR: δ 1.12-1.21 (m, 4H, N-CH-CH_2-C$\underline{H}_2$), 1.32-1.49 (m, 2H, N-CH-C$\underline{H}_A$), 1.66-1.70 (m, 2H, N-CH-C$\underline{H}_B$), 2.59 (m, 2H, N-CH), 5.70 (s, 2H, HCb).^{13}C NMR: δ Ca: 158.5, Cb: 110.4, Cc: 150.3, 55.5 (CH-N), 30.2 (CH_2), 24.8 (CH_2).

3.9. Reaction with *trans*-1,2-diaminocyclohexane

(*R,R*)-5a,6,7,8,9,9a-Hexahydrophenazine-2,3-diol (**16**), pale yellow powder, m.p. (decomp.) = 162-165°C, yield 96.4%, purity (GCMS): 99.8%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.54. ^1H NMR: δ 1.08-1.20 (m, 4H, N-CH-CH_2-C$\underline{H}_2$), 1.36-1.52 (m, 2H, N-CH-C$\underline{H}_A$), 1.66-1.72 (m, 2H, N-CH-C$\underline{H}_B$), 2.58 (m, 2H, N-CH), 5.78 (s, 2H, HCb). ^{13}C NMR: δ Ca: 159.1, Cb: 109.2, Cc: 149.8, 60.8 (CH-N), 35.6 (CH_2), 28.0 (CH_2).

3.10. Reaction with *cis*-1,3-diaminocyclobutane

(*R,R*)-3,4-Dihydro-2*H*-2,4-methanobenzo[*b*][1,4]-diazepine-7,8-diol (**17**), yellow powder, m.p. (decomp.) = 132-133°C, yield 68.2%, purity (GCMS): 99.5%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.58. ^1H NMR: δ 2.02-2.05 (m, 2H, $CH_{2(A)}$), 2.12-2-16 (m, 2H, $CH_{2(B)}$), 3.18 (m, 2H, CH-N), 5.80 (s, 2H, HCb). ^{13}C NMR: δ Ca: 162.3, Cb: 106.9, Cc: 153.8, 52.9 (CH-N), 42.6 (CH_2).

3.11. Reaction with Urea

1*H*-Benzo[*d*]imidazole-2,5,6(3*H*)-trione (**9**), orange-red crystals, m.p. = 156-157°C, yield 98.5%, purity (GCMS): 100.0%. TLC (ethyl acetate/toluene, v/v=4:1): R_f = 0.45. ^1H NMR: δ 5.90 (s, 2H, HCb). ^{13}C NMR: δ Ca: 176.6, Cb: 105.8, Cc: 146.6, 155.4 (N-CO-N).

3.12. Reaction with Sulfamide

Benzo[*c*][1,2,5]thiadiazole-5,6(1*H*,3*H*)-dione 2,2-dioxide (**18**), orange crystals, m.p. = 180-181°C, yield 99.3%, purity (GCMS): 99.8%. TLC (ethyl acetate/toluene, v/v=4:1): R_f = 0.60. ^1H NMR: δ 5.86 (s, 2H, HCb). ^{13}C NMR: δ Ca: 178.4, Cb: 104.5, Cc: 145.0.

3.13. Reaction with Oxalamide

Quinoxaline-2,3,6,7(1*H*,4*H*)-tetraone (**19**), red needles, m.p. = 140-144°C, yield 88.3% (together with **20**), purity (GCMS, sum

with **20**): 99.7%. TLC (ethyl acetate/toluene, v/v=4:1): R_f = 0.36. ^{1}H NMR: δ 5.86 (s, 2H, HCb). ^{13}C NMR: δ Ca: 177.4, Cb: 110.1, Cc: 145.7, 158.7 (N-CO).

6,7-Dihydroxyquinoxaline-2,3-dione (**20**), yellow plates, m.p. (decomp.) = 148-149°C, yield 88.3% (together with **19**), purity (GCMS, sum with **19**): 99.7%. TLC (ethyl acetate/toluene, v/v=4:1): R_f = 0.47. ^{1}H NMR: δ 5.88 (s, 2H, HCb). ^{13}C NMR: δ Ca: 162.2, Cb: 114.5, Cc: 150.7, 167.3 (N-CO).

3.14. Reaction with Malonamide

7,8-Dihydroxy-2*H*-benzo[*b*]-[1,4]diazepine-2,4(3*H*)-dione (**21**), yellow crystals, m.p. = 162-164°C, yield 94.9%, purity (GCMS): 99.9. TLC (ethyl acetate/toluene, v/v=4:1): R_f = 0.50. ^{1}H NMR: δ 2.99 (s, 2H, CH_2), 5.86 (s, 2H, HCb). ^{13}C NMR: δ Ca: 160.9, Cb: 110.4, Cc: 152.8, 169.6 (N-CO), 51.4 (CH_2).

3.15. Reaction with 1,1-methylenediamine

2,3-Dihydro-1*H*-benzo-[*d*]imidazole-5,6-dione (**22**), yellow-green powder, m.p. (decomp.) = 192-193°C, yield 74.2%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.28. ^{1}H NMR: δ 5.01 (s, 2H, N-CH_2-N), 5.74 (s, 2H, HCb). ^{13}C NMR: δ Ca: 176.9, Cb: 107.7, Cc: 145.4, 79.1 (CH_2).

3.16. Reaction with 1,2-ethylenediamine

1,2,3,4-Tetrahydro-quinoxaline-6,7-dione (**7**), pale reddish powder, m.p. (decomp.) = 184-185°C, yield 98.3% (together with **8**), purity (GCMS, sum with **8**): 100.0%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.32. ^{1}H NMR: δ 3.38 (s, 4H, N-CH_2), 5.74 (s, 2H, HCb). ^{13}C NMR: δ Ca: 180.0, Cb: 105.1, Cc: 144.9, 41.4 (CH_2).

2,3-Dihydroquinoxaline-6,7-diol (**8**), yellow-orange powder, m.p. (decomp.) = 192-193°C, yield 98.3% (together with **7**), purity (GCMS, sum with **7**): 100.0%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.50. ^{1}H NMR: δ 3.37 (s, 4H, N-CH_2), 5.78 (s, 2H, HCb). ^{13}C NMR: δ Ca: 158.3, Cb: 108.8, Cc: 149.7, 44.2 (CH_2).

3.17. Reaction with 1,3-propylendiamine

3,4-Dihydro-2*H*-benzo[*b*][1,4]diazepine-7,8-diol (**23**), pale yellow-gray powder, m.p. (decomp.) = 148-150°C, yield 99.0%, purity (GCMS): 99.7%. TLC (ethyl acetate/toluene, v/v=4:3): R_f = 0.50. ^{1}H NMR: δ 1.56 (m, 2H, N-CH_2-$C\underline{H}_2$), 3.25 (m, 4H N-CH_2), 2.99 (s, 2H, CH_2), 5.74 (s, 2H, HCb). ^{13}C NMR: δ Ca: 162.1, Cb: 110.7, Cc: 148.9, 51.8 (N-CH_2), 35.6 (CH_2).

CONCLUSION

In summary, the rather simple approach of strain-induced bond localization (SIBL) can excellently explain the hitherto puzzling results regarding the reaction between DHBQ and primary aliphatic diamines. It observes the possible tension applied to the double bonds in the *ortho*-quinoid product system. The system evades the smallest constraint, so that "smaller rings" (smaller sum of annulation angles due to smaller N–N distance) give the *ortho*-quinones with 4,5-annulated diaza rings, while "larger rings" (larger sum of annulation angles due to larger N–N distances) are annulated through the nitrogens of the *ortho*-quinone diimines formed. The strain exerted on the double bonds in the ortho-quinoid system determines which of the two alternative tautomeric products is formed, and this strain is simply related to the N–N distance in the co-reacting diamine. These results also allow robust predictions of the outcome of DHBQ reactions with other diamines based on the computationally modeled product structures and their N–N distances.

LIST OF ABBREVIATIONS

DHBQ = 2,5-dihydroxy-[1,4]-benzoquinone

oQM = *ortho*-quinone Methide

SIBL = Strain-Induced Bond Localization

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of this article is available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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