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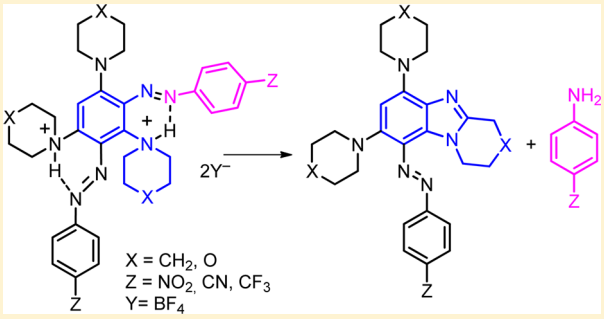
Ring Closure of Azo Compounds to 1,2-Annulated Benzimidazole Derivatives and Further Evidence of Reversibility of the Azo-Coupling Reaction

Erminia Del Vecchio, Carla Boga,* Luciano Forlani, Silvia Tozzi, Gabriele Micheletti, and Silvia Cino

Department of Industrial Chemistry 'Toso Montanari', Alma Mater Studiorum, Università di Bologna, Viale del Risorgimento, 4, 40136 Bologna, Italy

Supporting Information

ABSTRACT: The reaction between 1,3,5-tris(*N*,*N*-dialkylamino)-benzene derivatives and 2 equiv of *p*-substituted benzenediazonium salts gives dicationic species which collapse to new benzimidazole derivatives with expulsion of *p*-substituted anilines. The presence of electron-withdrawing groups on the benzenediazo moiety of the dicationic species plays a key role in this unexpected ring closure reaction. The observed chemical behavior has been rationalized in terms of the already reported reversibility of azo coupling reactions and provided further evidence for it.



INTRODUCTION

Our interest was piqued concerning the chemical reactivity of very electron-rich benzene systems bearing symmetrically substituted (1,3,5) amino groups, i.e., 1,3,5-tris(*N*,*N*-dialkylamino)benzenes **1**−**3**, where the *N*,*N*-dialkylamino substituents are cyclic amines: piperidine, morpholine, or pyrrolidine, as originally studied by Effenberger.[1] These compounds exhibit very high reactivity and are thus referred to as "carbon supernucleophiles". Their reactions with electrophilic reagents have been very helpful in elucidation of the mechanism of the electrophilic aromatic substitution reaction S_EAr.[2−4] Their reactivity permitted the isolation and characterization by spectroscopic means of several intermediates in the S_EAr reaction such as Wheland σ complexes[2,3,5] and zwitterionic Wheland−Meisenheimer complexes.[6−8]

Particular attention was paid to the azo-coupling reaction between 1,3,5-tris(*N*-piperidinyl)benzene (**1**) or 1,3,5-tris(*N*-morpholinyl)benzene (**2**) with benzenediazonium salts, shown in Scheme 1.

In particular, we studied the formation and characterization of the Wheland intermediates (**W** in Scheme 1) and the subsequent step (the rearomatization reaction) and found, in contrast to what is generally thought, that (1) proton departure from the Wheland complex is the rate-determining step of the reactions in Scheme 1 and (2) that the reaction is reversible.[3,4]

Contained in the older literature, benzenediazonium cations have generally not been considered strong electrophilic reagents. In the recent Mayr classification, they are considered very strong electrophilic reagents; for example, Mayr's electrophilicity parameter for the 4-nitrobenzenediazonium cation ($E = -5.1$)[9] is very close to that of 4,6-dinitrobenzofuroxan ($E = -5.06$),[10] a carbon neutral superelectrophile that, when coupled with triaminobenzenes **1**−**3**, permitted us to characterize, for the first time, Wheland−Meisenheimer intermediates.[6]

In the course of these investigations, we noted that in some cases, among the products arising from the azo coupling reaction between **1** or **2** and benzenediazonium salts, substituted tricyclic benzimidazoles derived from a ring closure reaction were formed. This unexpected finding prompted us to study the reaction in detail owing also to the importance of benzimidazole derivatives in many areas of applied chemistry. Actually, they are versatile compounds especially for use in agro-alimentary, pharmaceutical, textile, and cosmetic industries,[11,12] and their synthesis covers a myriad of literature reports.[13−15] Tricyclic benzimidazoles have been synthesized from *o*-phenylendiamine or its derivatives under different conditions, such as in the presence of Hg(II)EDTA,[16] metals,[17] or under radical conditions.[18,19] Oxidative cyclization in the presence of strong acids[20,21] or multistep transformations of aromatic azides[22−24] has also resulted in the formation of benzimidazoles. Moreover, cyclization reactions involving azo compounds have been reported by Price[25] and Meth-Cohn and Suschitzky[26] in the presence of $CoCl_2$ or of acids as catalyst, respectively.

Herein, we report results obtained regarding the ring-closure reaction, observed under mild conditions, from dicationic species derived from an azo coupling reaction leading to new benzimidazole derivatives containing the *N*-piperidinyl or *N*-morpholinyl moiety as fused ring.

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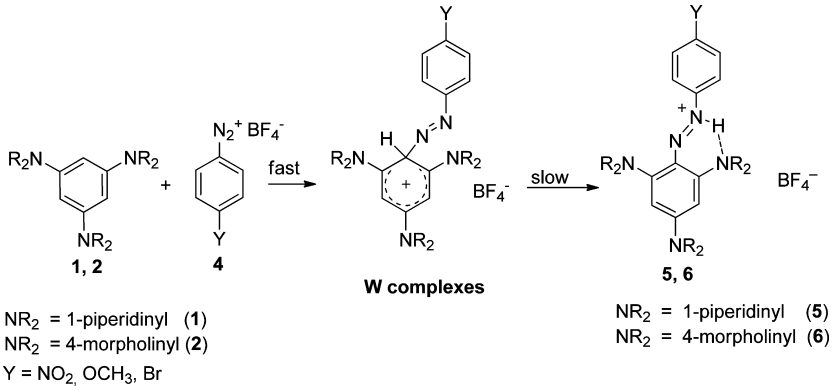
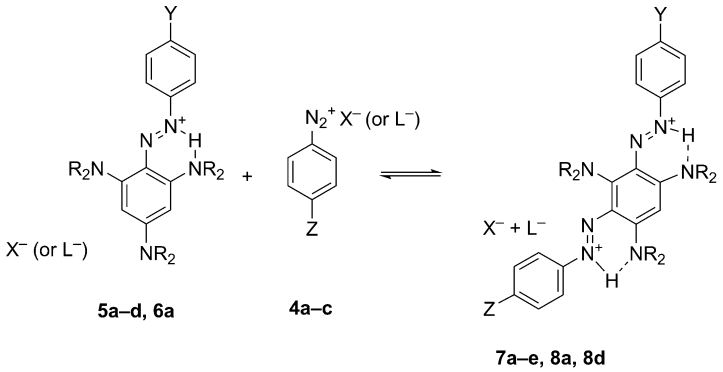
Scheme 1. Azo Coupling Reaction between 1,3,5-Tris(*N*,*N*-dialkylamino)benzenes 1 and 2 and Benzenediazonium Salts

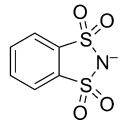


Scheme 2. Formation of Diprotonated Species by Reaction between Triaminobenzenes 1 and 2 and Benzenediazonium Salts 4



NR_2 = 1-piperidinyl **5**
NR_2 = 4-morpholinyl **6**
5a: Y = NO_2, $X^- = BF_4^-$
5b: Y = CN, $L^- = C_6H_4(SO_2)_2N^-$
5c: Y = CF_3, $L^- = C_6H_4(SO_2)_2N^-$
5d: Y = OCH_3, $X^- = BF_4^-$
6a: Y = NO_2, $X^- = BF_4^-$
4a: Z = NO_2, $X^- = BF_4^-$
4b: Z = CN, $L^- = C_6H_4(SO_2)_2N^-$
4c: Z = CF_3, $L^- = C_6H_4(SO_2)_2N^-$

$C_6H_4(SO_2)_2N^-$ =



NR_2 = 1-piperidinyl **7**
7a: Y = Z = NO_2, $X^- = L^- = BF_4^-$
7b: Y = Z = CN, $X^- = L^- = C_6H_4(SO_2)_2N^-$
7c: Y = Z = CF_3, $X^- = L^- = C_6H_4(SO_2)_2N^-$
7d: Y = OCH_3; Z = NO_2, $X^- = L^- = BF_4^-$
7e: Y = CN; Z = NO_2, $X^- = BF_4^-$, $L^- = C_6H_4(SO_2)_2N^-$
NR_2 = 4-morpholinyl **8**
8a: Y = Z = NO_2, $X^- = L^- = BF_4^-$
8d: Y = OCH_3; Z = NO_2, $X^- = L^- = BF_4^-$

RESULTS AND DISCUSSION

Triaminobenzenes **1** or **2** and diazonium salts **4a–c**, bearing electron-withdrawing groups (namely, 4-NO_2, 4-CN, and 4-CF_3, respectively) that enhance the reactivity of the diazonium salt, quickly afforded the dicationic species **7** and **8**, according to Scheme 2.

Previously, we have found[3] that compounds **7a** and **8a** are the main reaction products even when the ratio between **1** (or **2**) and the diazonium salt is 1:1; in this case, **1** (or **2**) may be recovered unreacted. Clearly, the second attack giving the diprotonated azo compounds **7** or **8** (Scheme 2) is a faster process than the first attack depicted in Scheme 1. These data are further complicated by the solubility of reagents and products; however, the fact that, as previously reported,[3] compounds **5** and **6** may be obtained from **7** and **8** (in the presence of **1** or **2**) is an indication of the reversibility of the second attack. The latter probably occurs on the deprotonated form of **5** (surely a more able nucleophilic reagent than its salt), even if the positive charge in **5** is supported by both amino and azo nitrogen atoms, thus reducing its electron-withdrawing power.

Compounds **7a–c** and **8a** can be also obtained by reaction (CH_3CN at −30 °C) of **1** (or **2**) with 2 equiv of the diazonium salt **4a**, **4b**, or **4c**. These products usually precipitated from the reaction mixture and have been isolated as coral-red solids. In some cases, a simple workup of species **7** and **8** (for instance, to obtain the corresponding free bases), or attempts to solubilize them in usual organic solvents, produced relevant amounts of substituted aniline **11** and of compounds **9a–c** and **10a** (Scheme 3) which are new benzimidazole derivatives. The reaction to form **10a** is slower than that to form compounds **9** from **7**.

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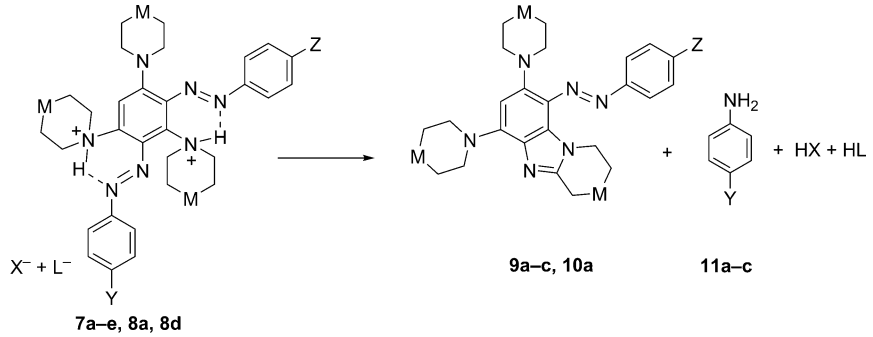
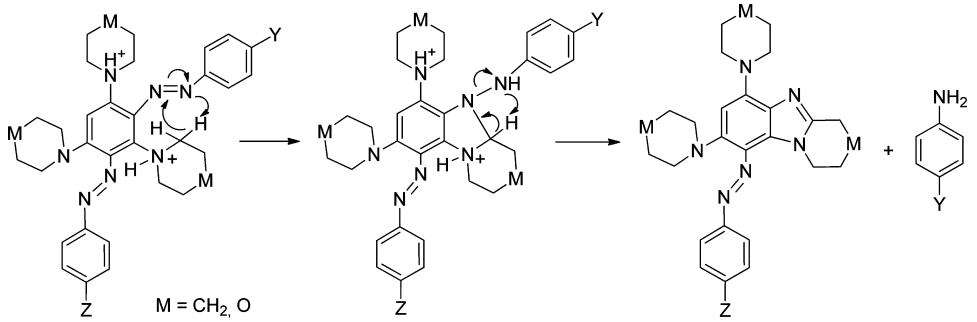
Scheme 3. Formation of New Benzimidazoles from Dicationic Species 7 and 8



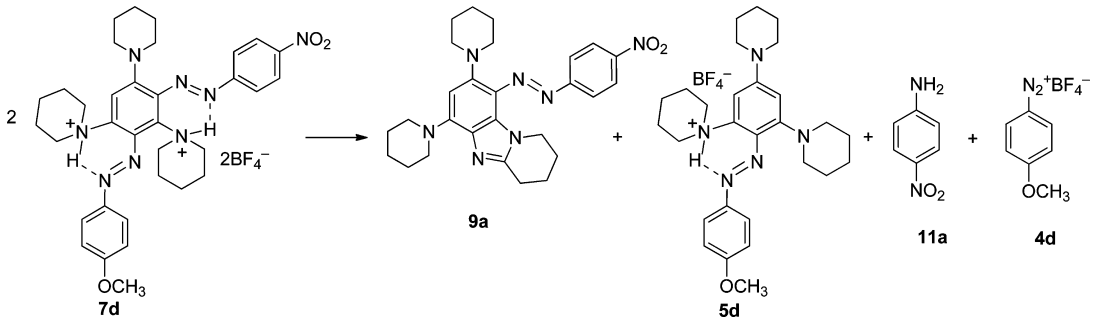
7a: M = CH_2; Y = Z = NO_2; $X^- = L^- = BF_4^-$
7b: M = CH_2; Y = Z = CN; $X^- = L^- = C_6H_4(SO_2)_2N^-$
7c: M = CH_2; Y = Z = CF_3; $X^- = L^- = C_6H_4(SO_2)_2N^-$
7d: M = CH_2; Y = OCH_3; Z = NO_2; $X^- = L^- = BF_4^-$
7e: M = CH_2; Y = CN; Z = NO_2; $X^- = BF_4^-$, $L^- = C_6H_4(SO_2)_2N^-$
8a: M = O; Y = Z = NO_2; $X^- = L^- = BF_4^-$
8d: M = O; Y = OCH_3; Z = NO_2; $X^- = L^- = BF_4^-$

9a: M = CH_2; Z = NO_2
9b: M = CH_2; Z = CN
9c: M = CH_2; Z = CF_3
10a: M = O; Z = NO_2
11a: Y = NO_2
11b: Y = CN
11c: Y = CF_3

Scheme 4. Proposed Mechanism for the Formation of Benzimidazoles 9 and 10



Scheme 5. Evolution of Compound 7d, Bearing Two Groups of Different Electronic Ability, and Products Observed in the Reaction Mixture



Compounds **9a–c** and **10a** were isolated by percolation of compounds **7a–c** and **8a** on silica gel column with different eluents, and their structures were ascertained by usual spectroscopic methods (see Experimental Section). Alumina columns may be also used, but in this case, the yields were lower than those obtained using silica gel column due to the recovery of free bases of **7** and **8**; attempts to obtain free bases by addition of a base to solutions of **7a** or **8a** produced very complicated reaction mixtures containing (as tested by ^{1}H NMR spectral data) the required free bases, 4-nitroaniline, **9** (or **10**) and other unidentified products.

With respect to the benzimidazole ring formation there is the cleavage of a N=N double bond of **7** (or **8**) and subsequent formation of a C=N new double bond involving one of the α carbon atoms of the cyclic amino substituents of the starting dicationic species **7** or **8**.

The observed cyclization leading to benzimidazoles from azo-compounds **7** and **8**, with an aromatic ring bearing in adjacent position a cyclic amine and an azo group, is reminiscent of a process in which the so-called "tert-amino effect" is operative.[26−29]

The term, which was coined by Meth-Cohn and Suschizky in 1972,[26] generalizes the cyclization reactions of tertiary anilines bearing double bonds in the ortho-position. The cyclization proceeds with formation of a new bond affording a five- or six-membered fused-ring system and represents a convenient

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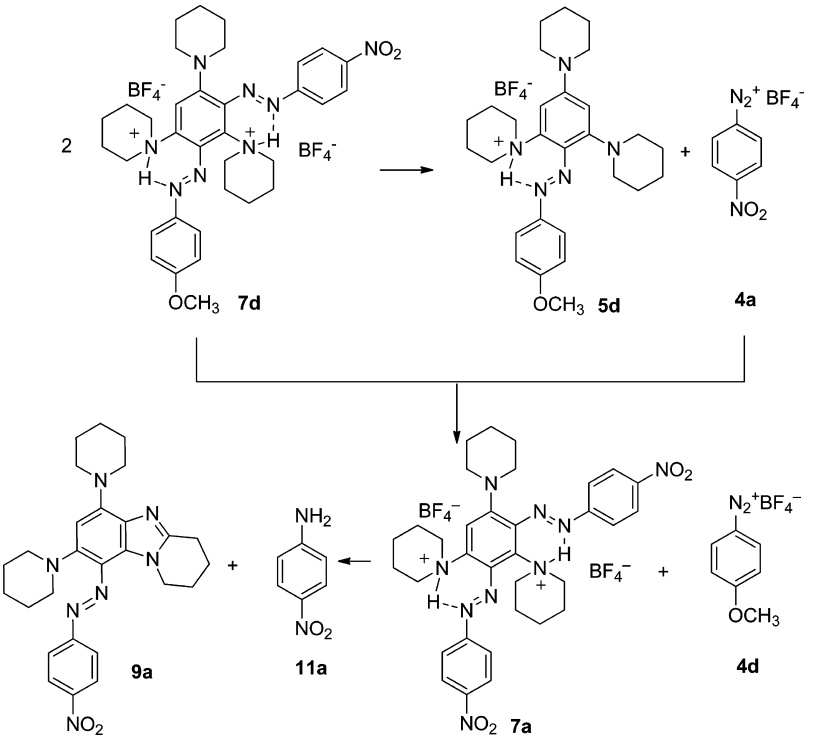
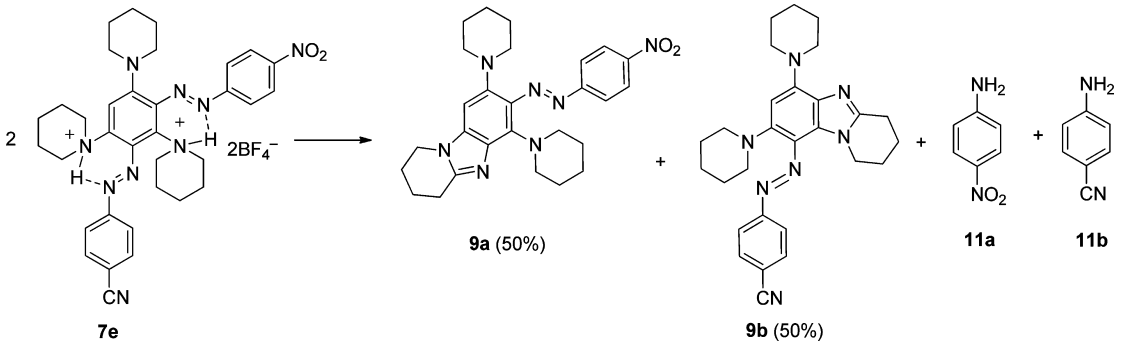
Scheme 6. Tentative Pathway for the Reaction Shown in Scheme 5



Scheme 7. Evolution of Compound 7e, Bearing Two Different Electron-Withdrawing Groups



method for the synthesis of a number of nitrogen-containing heterocycles otherwise obtained with great difficulty. The first instance of such cyclization was originally reported in 1895[30] when 1,2-dimethylbenzimidazole was unexpectedly obtained by prolonged reflux of *o*-aminodimethylaniline in acetic anhydride. The formation of benzimidazole derivatives from azo compounds has been reported in a few cases[25,26,31] beginning with *N*,*N*-dialkylamino ortho-substituted azobenzenes: also in these cases the tert-amino effect is operative.

In this context, formation of benzimidazoles from azoderivatives **7** and **8** represents a further extension of this cyclization, and a possible reaction pathway involving a proton transfer or internal (intramolecular) salification (Scheme 4), in which both ammonium ions are proximal to the diazo group that is being cleaved, thus favoring the cleavage.

Meth-Cohn reported the mechanism of the cyclization of *N*-(*o*-acylaminophenyl)pyrrolidine by peroxy-acid catalysis, involving the formation of *N*-oxide species.[32] In the present case, acid catalysis is operative to favor both the C−H bond breaking with formation of a new C−N bond formation.

In the case of the mixed dicationic species **7d**, **7e**, and **8d**, the reaction behavior is complicated by the presence, in the reaction mixture, of different compounds, as indicated in Schemes 5 and 7.

Scheme 5 illustrates the presence on **7d** of two groups of opposite electronic demand: a strongly electron withdrawing group (NO_2) and a strongly electron releasing group (OCH_3). The reaction product **9a** contains the azo moiety bearing the nitro group. The ^1H NMR spectrum of the crude reaction mixture showed presence of **9a** in yields not exceeding 50% together with the remaining material **5d**, *p*-nitroaniline **11a**, and other signals that are consistent with the presence of **4d**.

It should be noted that the reaction depicted in Scheme 5 is indirect evidence for the reversibility of the azo coupling reaction[3,4] and suggests that the benzimidazole so formed bears an azo moiety with the electron-withdrawing group. Scheme 6 shows a reasonable mechanistic pathway to explain the reaction in Scheme 5 which is consistent with previously reported observations.[3,4]

Due to the reversible character of the azo coupling reaction, the *p*-nitrobenzenediazonium salt **4a** ($E_{Mayr} = -5.1$)[9] is expelled

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from **7d** and then reacts with a second molecule of **7d** to replace its *p*-methoxybenzenediazo moiety (E_{Mayr} = −8.4),[9] thus producing **4d** and **7a**, which is the precursor of **9a**. We had previously determined that the benzenediazonium salt bearing the electron-donating group is replaced by the more powerful electrophile.[3]

When the two different groups bound to the benzenediazonium salt moiety of dicationic species are both electron-withdrawing groups, such as in the case of compound **7e**, in the reaction mixture both benzimidazole derivatives **9a** and **9b** are present in 1:1 relative amount together with the respective released substituted anilines **11a** and **11b**, as reported in Scheme 7.

This finding supports the above discussion highlighting the importance of the presence of an electron-withdrawing substituents, not only on the leaving aniline, but also in the remaining diazo moiety, to obtain benzimidazole derivatives. The importance of an electron-withdrawing group on the leaving aniline favors the breaking of the N−N bond thus facilitating the departure of the substituted aniline.

In other words, the presence of two electron-withdrawing groups on both azo moieties (**Z** and **Y** in Scheme 4) is a fundamental condition to realize the ring closure reaction.

CONCLUSIONS

The reaction between equimolar amounts of triaminobenzene derivatives **1** or **2** and *p*-substituted benzenediazonium salts, bearing substituents with different electronic demands, gave the salt of the diazo compound deriving from the attack of the neutral carbon atom of the nucleophile to the electrophile. If additional quantities of the same (or a different) benzenediazonium salt is added to the former, a dicationic species can be obtained. This latter can be recovered by filtration from the crude reaction mixture when the reaction is carried out in a 1:2 molar ratio between the nucleophile and the electrophilic species. When the dicationic species bears electron-withdrawing groups on the benzenediazonium moiety, new benzimidazole derivatives can be isolated after workup or percolation on silica gel column. The formation of the reported new benzimidazole derivatives confirms the reversible character of the azo coupling reaction, owing to the ability of the more reactive electrophilic benzenediazonium salt (bearing electron-withdrawing group, such as nitro group) to replace the less powerful electrophilic benzenediazonium salt, bearing electron donor substituents (e.g., *p*-methoxy group).

EXPERIMENTAL SECTION

The ^{1}H and ^{13}C NMR spectra were recorded at 300, 400, or 600 MHz (^{1}H NMR) and 75.46, 100.56, or 150.80 MHz (^{13}C NMR), respectively. *J* values are given in hertz (Hz). Signal multiplicities were established by DEPT-135 experiments. Chemical shifts were referenced to the solvent [(δ =7.27 and 77.0 ppm for $CDCl_3$), (δ = 2.0 and 0.3 ppm for CD_3CN), (δ = 4.3 and 57.3 ppm for CD_3NO_2) for ^{1}H and ^{13}C NMR, respectively]. Chromatographic purifications were carried out on silica gel or aluminum oxide (activated, basic, Brockmann I, standard grade ca. 150 mesh) columns at medium pressure. In the Supporting Information, copies of the ^{1}H and ^{13}C NMR spectra of all new compounds are provided; some of the compounds presented difficulties in obtaining mass spectra/elemental analysis, due to reduced stability. 1,3,5-Tris(dialkylamino)benzenes **1** and **2** were prepared as described previously.[2] The arenediazonium tetrafluoroborate salts **4a** and **4d** were commercially available; 4-cyanobenzenediazonium benzo[*d*][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide (**4b**) and 4-(trifluoromethyl)benzenediazonium benzo[*d*][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide (**4c**) were prepared as previously described.[33] Compounds **5a**, **5d**, **6a**, **7a**, **7d**, **8a**, and **8d** were prepared as described previously[2,3] and their spectral data agree with those previously described.[2,3]

General Procedure for the Synthesis of Compounds 5 and 6. 1,3,5-Tris(*N*,*N*-dialkylamino)benzene (0.092 mmol) was dissolved in CH_3CN (2 mL) and cooled to −30 °C; then the arenediazonium salt (0.092 mmol) was added. Immediately after mixing, a yellow color developed and the solution was stirred for 20 min; in this interval the color turned to red. TLC analysis (eluent: light petroleum/diethyl ether, 50:50) showed the disappearance of the starting 1,3,5-tris(*N*,*N*-dialkylamino)benzene. After removal of the solvent *in vacuo*, the crude product was dissolved in CH_2Cl_2 (2 mL) and the compounds **5** and **6** were precipitated by adding Et_2O. The products were isolated as dark-red solids in 80−90% yield and, except **5b** and **5c**, crystallized from CH_2Cl_2 and *n*-hexane. Compounds **5a**, **5d**, **6a**, and **6d** were prepared as previously described,[2] and their characterization data agree with those previously reported.[2]

*1-(2-((4-Cyanophenyl)diazenyl)-3,5-di(piperidin-1-yl)phenyl)-piperidin-1-ium Benzo[d][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide (**5b**).* Red solid 0.056 g (90%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ (ppm): 1.40−2.00 (m, 18 H, $NCH_2CH_2CH_2$), 2.90−3.05 (m, 2 H, NCH_2), 3.40−3.50 (m, 2 H, NCH_2), 3.61 (m, 4 H, NCH_2), 3.81 (m, 4 H, NCH_2), 5.72 (d, 1 H, *J* = 2 Hz, H-4 or H-6), 6.18 (d, 1 H, *J* = 2 Hz, H-4 or H-6), 7.34 (d, 2 H, *J* = 8.8 Hz, CHCN=N), 7.50−7.58 (m, 2 H), 7.60 (d, 2 H, *J* = 8.8 Hz, CHCCN), 7.70−7.77 (m, 2 H), 11.94 (bs, 1 H, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz, 25 °C) δ (ppm): 23.4 ($NCH_2CH_2CH_2$), 23.9 ($NCH_2CH_2CH_2$), 24.1 ($NCH_2CH_2CH_2$), 25.7 (NCH_2CH_2), 26.2 (NCH_2CH_2), 26.4 (NCH_2CH_2), 50.3 (NCH_2), 51.4 (NCH_2), 52.0 (NCH_2), 91.2 (CH, C-4 or C-6), 98.9 (CH, C-4 or C-6), 106.3, 115.2 (CH), 119.0, 121.0 (CH), 128.7, 131.8 (CH), 133.8 (CH), 142.6, 145.6, 151.6, 159.3, 159.7.

*1-(2-((4-Trifluoromethylphenyl)diazenyl)-3,5-di(piperidin-1-yl)-phenyl)piperidin-1-ium Benzo[d][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide (**5c**).* Dark-red solid 0.030 g (45%). ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C) δ (ppm): 1.50−2.00 (m, 18 H, $NCH_2CH_2CH_2$), 2.93−3.07 (m, 2 H, NCH_2), 3.36−3.46 (m, 2 H, NCH_2), 3.57−3−67 (m, 4 H, NCH_2), 3.76−3.89 (m, 4 H, NCH_2), 5.75 (d, 1 H, *J* = 2.4 Hz, H-4 or H-6), 6.23 (d, 1 H, *J* = 2.4 Hz, H-4 or H-6), 7.34 (br.d, 2 H, *J* = 8.5 Hz), 7.54 (dd, J_1 = 6.1 Hz, J_2 = 3.2 Hz, 2 H), 7.34 (br.d, 2 H, *J* = 8.5 Hz), 7.76 (dd, J_1 = 6.1 Hz, J_2 = 3.2 Hz, 2 H), 12.06 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75.5 MHz, 25 °C) δ (ppm): 23.4 ($NCH_2CH_2CH_2$), 23.9 ($NCH_2CH_2CH_2$), 24.1 ($NCH_2CH_2CH_2$), 25.8 (NCH_2CH_2), 26.2 (NCH_2CH_2), 26.4 (NCH_2CH_2), 50.2 (NCH_2), 51.5 (NCH_2), 52.1 (NCH_2), 91.4 (CH, C-4 or C-6), 98.9 (CH, C-4 or C-6), 114.9 (CH), 120.9 (CH), 127.6, 127.0 (q, $^3J_{CF}$ = 3.8 Hz), 131.6 (CH), 142.8, 144.8, 151.7, 159.1, 159.8.

Preparation of Compounds 7b and 7c. To a magnetically stirred solution of **1** in acetonitrile (0.092 mmol in 2 mL of solvent), cooled at −30 °C, the arenediazonium salt **4** (0.184 mmol) was added. Immediately the color of the obtained solution became yellow. In case **b**, after 20 min a coral-red solid precipitated. After filtration, compound **7b** was isolated as coral red solid in 85% yield. Compound **7b** can be obtained also by addition of an equimolar amount of diazonium salt **4b** to a cooled (−30 °C) solution in acetonitrile of compound **5b**. Compound **7c** did not precipitated and was not isolated but the reaction mixture obtained after addition of 2 equiv of **4c** to 1 equiv of **1** was subjected to column chromatography to give benzimidazole derivative **9c**.

*1,1′-{2,4-Bis[(4-cyanophenyl)diazenyl]-5-piperidin-1-yl-1,3-phenylene}dipiperidinium Di(benzo[d][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide) (**7b**).* Yield, 0.07 g (74%). ^{1}H NMR (CD_3NO_2, 600 MHz, −30 °C) δ (ppm): 1.55−2.50 (m, 18 H, $NCH_2CH_2CH_2$), 3.45−4.70 (m, 12 H, NCH_2), 6.45 (br s, 1 H, H-6), 7.55 (d, 4 H, *J* = 8.1 Hz), 7.70−7.77 (m, 12 H), 10.31 (br s, 2 H, NH). ^{13}C NMR (CD_3NO_2, 100.56 MHz, −30 °C) δ (ppm): 18.4 (CH_2), 18.9 (CH_2), 20.9 (2C, CH_2), 22.4 (CH_2), 23.0 (CH_2), 45.6 (CH_2), 49.3 (CH_2), 54.9 (CH_2), 89.4 (CH, C-6), 103.4, 111.9 (CH), 114.7, 116.6 (CH), 121.4, 124.1, 128.6 (CH), 129.6 (CH), 137.3, 140.4, 150.9, 157.5.

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Preparation of Compound 7e. To a solution of salt **5b** (0.074 mmol in 2 mL of CH_3CN), cooled at −30 °C, was added 0.0176 g (0.074 mmol) of 4-nitrobenzenediazonium tetrafluoborate (**4a**). After magnetic stirring for 20 min, a solid precipitated. After filtration, the solid was washed with dichloromethane, then the crude product **7e** was characterized by ^{1}H and ^{13}C NMR and subjected to column chromatography without further purification.

*1,1′-{4-[(4-Cyanophenyl)diazenyl]-2-[(4-nitrophenyl)diazenyl]-5-piperidin-1-yl-1,3-phenylene}dipiperidinium Tetrafluoroborate (Benzo[d][1,3,2]dithiazol-2-ide 1,1,3,3-tetraoxide) (**7e**).* Orange solid 0.040 g (60%). ^{1}H NMR (CD_3NO_2 600 MHz, −28 °C) δ (ppm): 1.55−2.45 (m, 18 H, $NCH_2C\underline{H}_2C\underline{H}_2$), 3.00−4.70 (m, 12 H, NCH_2), 6.45 (s, 1 H, H-6), 7.53−7.64 (m, 4 H), 7.70−7.76 (m, 6 H), 8.23 (br.d, 2 H, J = 7.9 Hz), 10.2 (bs, 1 H, NH), 10.3 (bs, 1 H, NH); ^{13}C NMR (CD_3NO_2, ref at 62.95 ppm, 150 MHz, −28 °C) δ = 24.0 (CH_2), 24.4 (CH_2), 26.4 (CH_2), 28.1 (CH_2), 28.7 (CH_2), 51.2 (CH_2), 55.0 (CH_2), 55.4 (CH_2), 59.5 (CH_2), 60.6 (CH_2), 95.1 (CH, C-6), 109.3, 117.2, 117.5, 120.2, 122.1, 126.8, 127.6, 134.1, 135.2, 143.0, 145.6, 145.8, 147.5, 156.4, 163.1.

Synthesis of Compounds 9a−c and 10a: General Procedure. Compound **1** or **2** (0.092 mmol) was dissolved in acetonitrile (2 mL). The solution was cooled at −30 °C, and then the arenediazonium salt **4** (0.184 mmol) was added. Immediately, the solution became yellow, and after magnetic stirring for 20 min, the color turned orange-red. After removal of the solvent, the crude residue was treated with water, extracted with dichloromethane (3 × 1 mL) and subjected to chromatography on silica gel (ethyl ether/light petroleum or ethyl acetate−hexane: 7/3). It is possible to isolate compounds **9** and **10** also by percolation of **7** and **8** on silica gel column. Compounds **9** and **10**, dark-purple in color, were unstable to the usual crystallization techniques. Compounds **11** were also recovered, and their spectral data agree with those of authentic commercial samples.

*9-((4-Nitrophenyl)diazenyl)-6,8-di(piperidin-1-yl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (**9a**).* Yield, 0.034g (76%). ^{1}H NMR ($CDCl_3$, 600 MHz, 25 °C) δ (ppm): 1.20−2.10 (m, 16 H, CH_2), 3.00−3.20 (m, 6 H, CH_2), 3.88−4.01 (m, 4 H, CH_2), 4.42−4.52 (m, 2 H, $CH_2C{=}N$), 6.13 (s, 1 H, H-6), 7.73 (d, 2 H, J = 9.4 Hz, $CHCN{=}N$), 8.28 (d, 2 H, J = 9.4 Hz, $CHCNO_2$). ^{13}C NMR ($CDCl_3$, 75.5 MHz, 25 °C) δ (ppm): 20.4 (CH_2), 23.8 (CH_2), 24.3 (CH_2), 24.7 (CH_2), 26.0 (2C, CH_2), 26.1 (CH_2), 48.4 (CH_2), 50.4 (CH_2), 54.1 (CH_2), 97.2 (CH, C-6), 121.1 (CH), 124.9 (CH), 127.2, 127.9, 136.9, 144.4, 145.2, 147.7, 148.0, 159.2. MS (EI, 70 eV). m/z (%): 487 (0.2, M^+), 349 (100), 266 (52), 138 (26). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $[M + H]$ $C_{27}H_{34}N_7O_2$, 488.2774; found, 488.2774.

*4-((6,8-Di(piperidin-1-yl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo-[1,2-a]pyridin-9-yl)diazenyl)benzonitrile (**9b**).* Yield, 0.034 g (79%). ^{1}H NMR ($CDCl_3$, 600 MHz, −30 °C): δ (ppm): 1.50−2.40 (m, 16 H, CH_2), 3.04−3.13 (m, 6 H, CH_2), 3.80−3.90 (m, 4 H, CH_2), 4.41−4.48 (m, 2 H, $CH_2C{=}N$), 6.16 (s, 1 H, H-6), 7.70 (d, 2 H, J = 8.44 Hz,), 7.74 (d, 2 H, J = 8.44 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz, −25 °C) δ (ppm): 20.1 (CH_2), 22.8 (CH_2), 23.6 (CH_2), 24.1 (CH_2), 24.5 (CH_2), 25.8 (CH_2), 26.0 (CH_2), 48.3 (CH_2), 50.3 (CH_2), 53.8 (CH_2), 97.8 (CH, C-6), 108.6, 119.9, 121.6 (CH), 126.5, 128.7, 133.1 (CH), 135.7, 142.0, 147.5, 148.8, 159.2. MS (EI, 70 eV). m/z (%): 467 (3, M^+), 350 (100), 266 (37), 175 (11), 118 (32). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{34}N_7$ $[M + H]$, 468.28757; found, 468.2876.

*6,8-Di(piperidin-1-yl)-9-((4-(trifluoromethyl)phenyl)diazenyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (**9c**).* Yield, 0.018 g (38%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ (ppm): 1.50−2.20 (m, 16 H, CH_2), 3.03−3.23 (m, 6 H, CH_2), 3.78−3.90 (m, 4 H, CH_2), 4.40−4.52 (m, 2 H, $CH_2C{=}N$), 6.22 (s, 1 H, H-6), 7.68 (d, 2 H, J = 8.3 Hz), 7.79 (d, 2 H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 100.56 MHz, 25 °C): δ (ppm): 20.4 (CH_2), 23.8 (CH_2), 24.3 (CH_2), 24.7 (CH_2), 25.9 (CH_2), 26.1 (CH_2), 26.2 (CH_2), 48.3 (CH_2), 50.5 (CH_2), 54.4 (CH_2), 98.2 (CH, C-6), 121.4 (CH), 124.4 (q, $^1J_{CF}$ = 127.0 Hz, CF_3), 126.0 (q, $^3J_{CF}$ = 3.8 Hz, CH), 126.9, 128.4 (q, $^2J_{CF}$ = 32.5 Hz), 129.5, 136.2, 143.1, 146.8, 148.2, 157.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{34}F_3N_6$ $[M + H]$ 511.27971; found, 511.2797.

*7,9-Dimorpholino-6-((4-nitrophenyl)diazenyl)-3,4-dihydro-1H-benzo[4,5]imidazo[2,1-c][1,4]oxazine (**10a**).* Yield, 0.032 g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C) δ (ppm): 3.19−3.24 (m, 4 H, NCH_2), 3.88−4.01 (m, 12 H, CH_2), 4.13 (t, 2 H, J = 5.3 Hz, CH_2), 4.54 (t, 2 H, J = 5.3 Hz, OCH_2), 5.02 (s, 2 H, $OCH_2C{=}N$), 6.17 (s, 1 H, H-6), 7.74 (d, 2 H, J = 9.1 Hz, $CHCN{=}N$), 8.33 (d, 2 H, J = 9.1 Hz, $CHCNO_2$). ^{13}C NMR ($CDCl_3$, 100.56 MHz, 25 °C): δ (ppm): 47.6 (CH_2), 49.2 (CH_2), 53.2 (CH_2), 64.5 (CH_2), 65.8 (CH_2), 66.8 (CH_2), 67.0 (CH_2), 97.2 (CH, C-6), 121.5 (CH), 125.0 (CH), 127.3, 129.4, 136.2, 143.1, 145.0, 144.0, 147.2, 158.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}N_7O_5$ $[M + H]$ 494.21519; found, 494.2152.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the ^{1}H and ^{13}C NMR spectra for all new compounds and of HRMS (ESI-TOF) spectra for compounds **9a−c** and **10a**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: carla.boga@unibo.it.

Notes

The authors declare no competing financial interest.

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