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N-Methylated 1,8-Diaminonaphthalenes as Bifunctional Nucleophiles in Reactions with α,ω-Dihalogenoalkanes: A Facile Route to Heterocyclic and Double Proton Sponges

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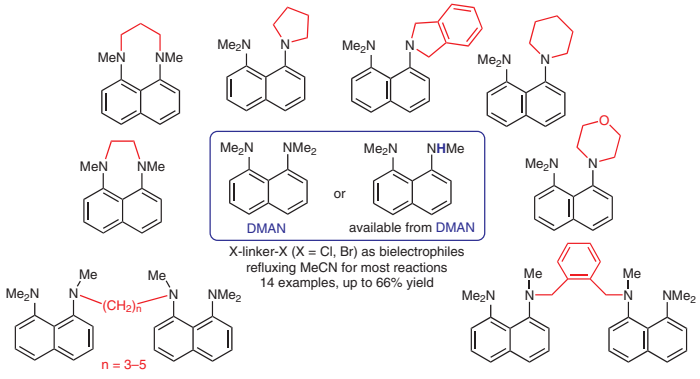

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Abstract The reaction of 1-dimethylamino-8-(methylamino)naphthalene with 1,3-dibromopropane chemoselectively leads to the product of *N*,*N*′-heterocyclization, while in the case of 1,4-dibromobutane and 1,2-bis(bromomethyl)benzene the process results in heterocyclization onto the same nitrogen atom with the formation of previously unknown 1-dimethylamino-8-pyrrolidino- and 1-dimethylamino-8-isoindolino-naphthalenes. The same reactions conducted without adding any auxiliary base lead to the formation of *N*,*N*′-linked double proton sponges as a new type of polynitrogen organic receptor. Proceeding as a sequence of quaternization–demethylation–cyclization steps, this heterocyclization process can also be used to construct six-membered rings (piperidino, morpholino), albeit in lower yields. The ability of 1,2-dibromoethane to brominate *N*-alkylated 1,8-diaminonaphthalenes is also described. It is shown for the first time that a commercially available 1,8-bis(dimethylamino)naphthalene (DMAN) can be used as a starting material in a heterocyclization reaction, which via a one-pot approach and in a short time can be converted into 1,5-dimethylnaphtho[1,8-*bc*]-1,5-diazacyclooctane or 1-dimethylamino-8-(pyrrolidin-1-yl)naphthalene.

Key words 1,8-diaminonaphthalenes, *N*,*N*′-linked double proton sponges, NHN$^+$ hydrogen bonding, heterocyclization, *N*-demethylation

Since its discovery in 1968, 1,8-bis(dimethylamino)naphthalene (DMAN) (**1**) has become a textbook compound due to its exceptionally high basicity, its unusual structural and nucleophilic properties and its ability to form short, strong, low-barrier N–H···N intramolecular hydrogen bonds (IHBs) on protonation.[1–7] IHBs attract special attention from physical organic chemists and biologists because they are instructive in modeling enzyme catalysis.[8–11] It is no exaggeration to say that the ideas connected with DMAN have largely stimulated the development of the 'host–guest' concept, thus accelerating the appearance of supramolecular chemistry, e.g., cryptands, cavitands and other guest structures.[12–14] Surprisingly, until recently, DMAN itself had been infrequently used to design supramolecular systems. Among the rare examples that can be mentioned are naphthyl-linked double DMANs (e.g., **2**),[15] the proton sponge analogue **3** of Tröger's base,[16] and the recently synthesized acetylene oligomers of type **4** (Figure 1).[17] Apart from their great importance for the development of acid–base theory, these types of compounds contribute to 'host–guest' chemistry, the design of electron- and proton-conducting materials (if partially protonated), and conducting and semi-conducting polymers.[17,18] As our research

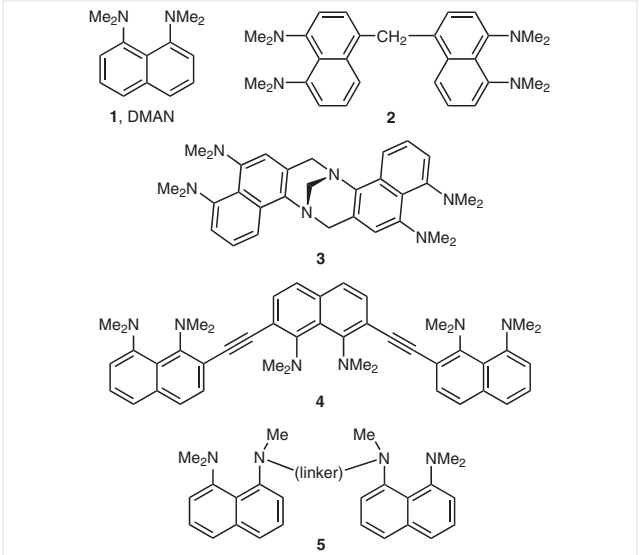

Figure 1 DMAN and examples of its C- and N-linked derivatives

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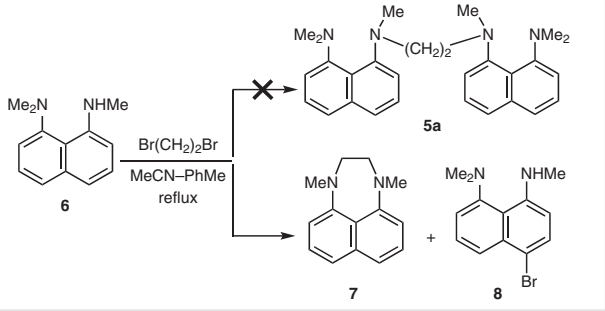
group has been continuously involved in extensive studies on the chemistry of DMANs, including those with modified dialkylamino functions,[6,19–22] the original aim of the present work was the preparation of novel nitrogen-linked double proton sponges such as **5**. We reasoned that the presence of a flexible linker in **5** would provide a higher degree of freedom between the DMAN subunits, thus rendering these bifunctional bases with the potential for the solvation and recognition of dicarbonic acids.[23,24]

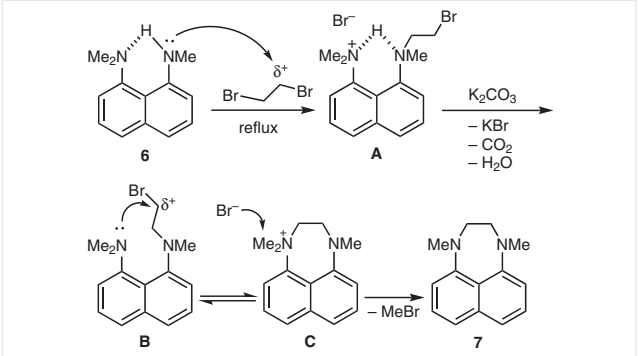
Previously, it was reported that DMAN undergoes *mono*-demethylation under protic or Lewis catalysis conditions to produce 1-dimethylamino-8-(methylamino)naphthalene (**6**) in high yield. The most practical method seems to be our protocol consisting of heating DMAN in a HBr–KI–DMF system.[25] Thus, starting from **6** and the corresponding organic dihalides, we anticipated being able to obtain a series of double sponges **5**. Unexpectedly, on heating **6** with 1,2-dibromoethane in a MeCN–PhMe mixture in the presence of K_2CO_3 or Et_3N, the only products that could be isolated were 1,4-diazacycloheptane derivative **7** (15–27% yield) and bromide **8** (up to 33% yield), but not the *N*,*N*′-linked double sponge **5a** (Scheme 1).



Scheme 1 Anticipated synthesis of dimer **5a**

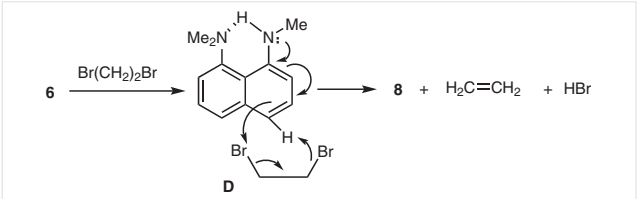
It should be noted that compounds of type **7** were obtained previously by reacting rather poorly accessible 1,8-bis(methylamino)naphthalene with α,ω-dihalogenoalkanes in the presence of carbonates or NaH.[26] Obviously, in our case, utilizing the more readily available trimethyl derivative **6** resulted in reactions proceeding via a somewhat different pathway consisting of several steps, including *N*-demethylation. Presumably, the whole process involves three successive S_N2 reactions at a saturated carbon atom proceeding via intermediates **A**–**C** (Scheme 2). Formally, the final product **7** can be considered as a good leaving group.

The driving force for the heterocyclization is probably the entropy factor, which always favors the intramolecular process, especially when unstrained rings are formed. As for the bromination reaction, we did not find examples of the direct bromination of activated aromatic substrates (which include *N*-alkylated 1,8-diaminonaphthalenes) with dibromoethane. Perhaps the reaction proceeds through a



Scheme 2 Reaction mechanism leading to **7**

cyclic transition state **D** with subsequent electrophilic bromination and the elimination of ethylene and hydrogen bromide (Scheme 3). In addition, the partial possibility of an ion-radical mechanism should not be excluded as 1,8-diaminonaphthalenes possess extremely high C-nucleophilicity and very low ionization potentials.[6,27]

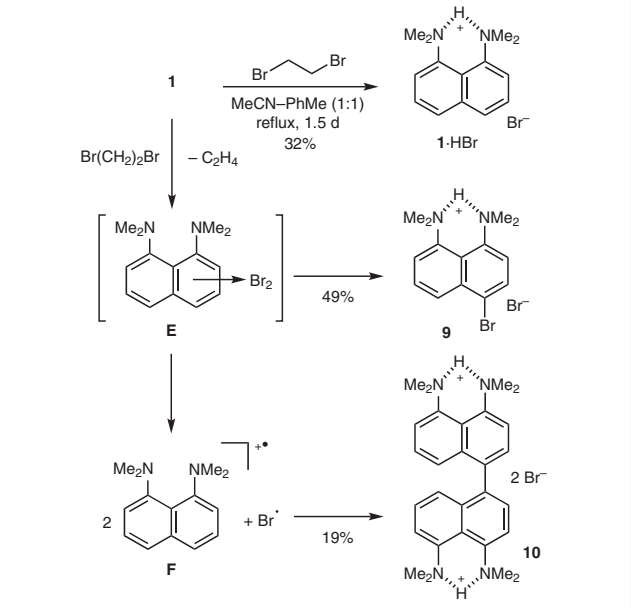


Scheme 3 Proposed route to bromide **8**

A model experiment conducted between 1,2-dibromoethane and proton sponge **1** (prolonged boiling in an acetonitrile–toluene mixture) showed that DMAN was indeed brominated with 1,2-dibromoethane, and that this reaction was the major process leading to compound **9**, although not the only one occurring (Scheme 4).

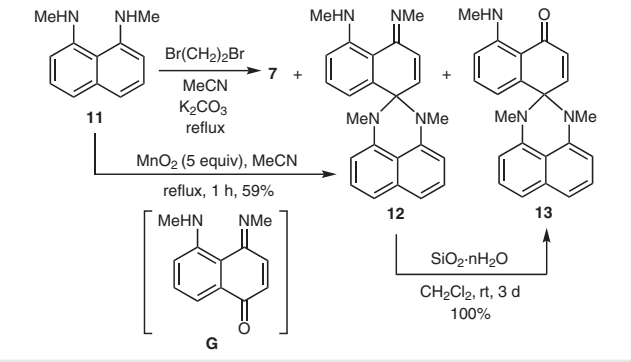
NMR analysis of the reaction mixture (see SI-1 in the Supporting Information; hydrobromides **1**·**HBr**, **9**, and **10** could be easily identified by their ^{1}H NMR spectra without separation) showed that the bromination occurred with almost 50% yield (presumably through intermediates of types **D** or **E**), while the dibromoethane dehydrobromination proceeded in 32% yield under the action of diamine **1** as a strong base (this causes the formation of the salt **1**·**HBr**). An ion-radical process is also realized to a small extent, ending with the dehydrodimerization of the starting compound through radical cation **F** under the influence of molecular bromine (the latter acts as a single-electron oxidant).[28]

Interestingly, the reaction of 1,2-dibromoethane with diamine **11** was also accompanied by oxidative transformations. Thus, during prolonged heating in acetonitrile, along with the expected product **7** (up to 33% yield according to NMR data), two additional previously unknown products were formed with variable yields: spiroimine **12** and



Scheme 4 Model experiment with DMAN (**1**)

spiroketone **13**, resulting from the oxidative dimerization (self-condensation) of the initial diamine **11** via the transient quinoneimine **G** (Scheme 5). As can be seen, dibromoethane is both an electrophile and an oxidant in this reaction.



Scheme 5 Cyclization and oxidation of diamine **11**

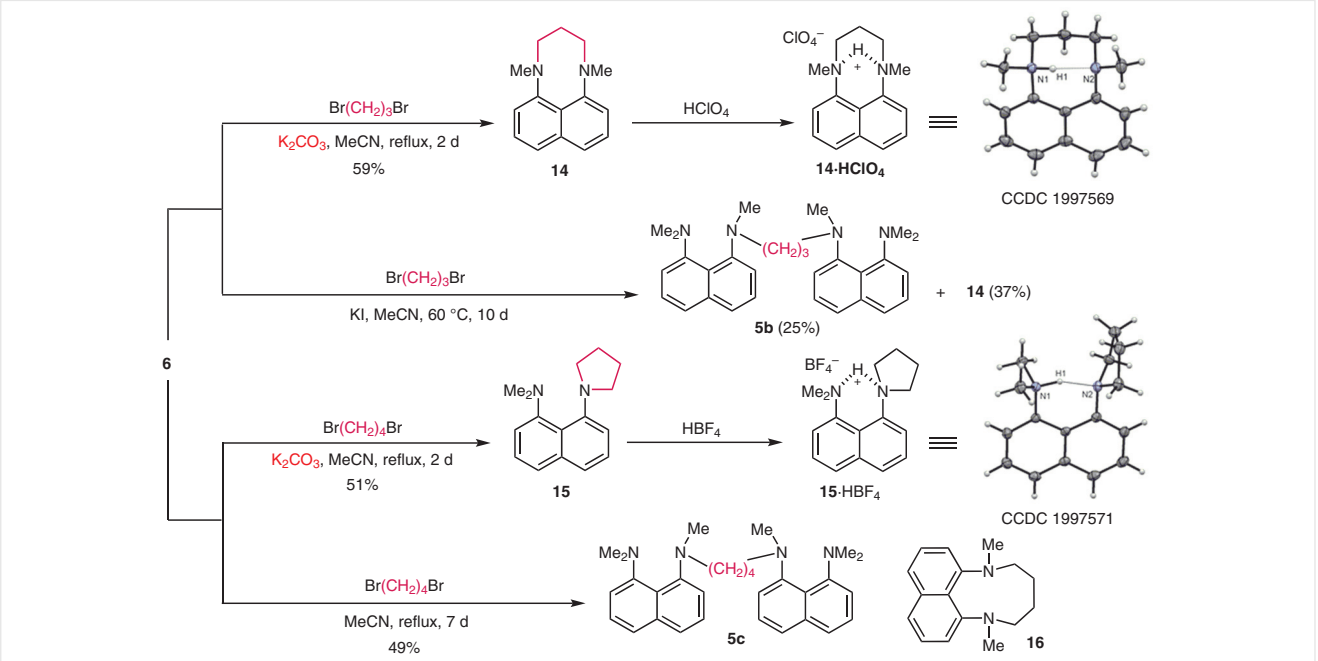
Brief heating of diaminonaphthalene **11** in the presence of activated manganese dioxide results in conversion into compound **12** in a good yield. Imine **12** is relatively stable during storage, but gradually transforms into ketone **13** as a result of hydrolysis. This process proceeds quantitatively on silica gel with simple stirring of the reagents in dichloromethane (Scheme 5). The structures of heterocyclic compounds **12** and **13** were proved by ^{1}H and ^{13}C NMR spectroscopy, as well as by mass spectrometry. Interestingly, both substances contain IHBs, which manifest themselves in the ^{1}H NMR spectra in the form of a broadened one-proton signal located at 9.4–10.6 ppm. Spiroheterocycles **12** and **13** differ from simple diaminonaphthalenes in their yellow and red–orange colors, respectively.

The reactions of *N*,*N*,*N*′-trimethyl-1,8-diaminonaphthalene (**6**) with 1,3-dibromopropane and 1,4-dibromobutane in the presence of K_2CO_3 proceed smoothly and chemoselectively, giving heterocycles **14** and **15** as the only products (Scheme 6). As can be seen, the extension of the dibromopropane carbon chain by just one carbon atom changes the topology of heterocyclization, and the formation of the pyrrolidine ring is preferred compared to that of the nine-membered macrocycle (no signs of isomeric compound **16** were found). Fortunately, on performing the synthesis without the addition of any auxiliary base (K_2CO_3), we were able to isolate *N*,*N*′-dimeric compounds **5b** and **5c** for the first time (Scheme 6).

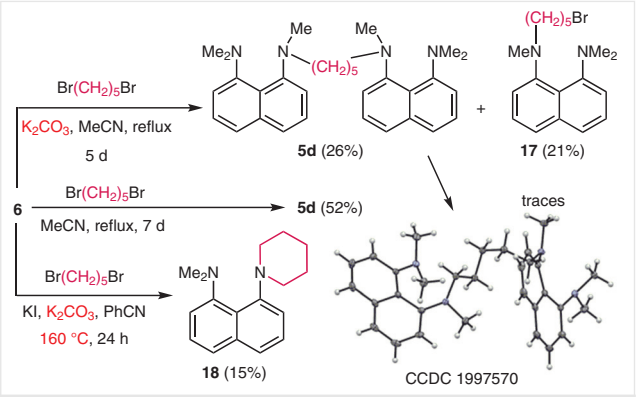
In general, the use of 1,4-dibromobutane allows compounds **15** and **5c** to be obtained very selectively depending on whether potash is present or absent from the reaction mass. The structures of the new products were confirmed by spectral methods, and additionally for compounds **14** and **15**, by XRD analyses (in the form of the corresponding protic salts, Scheme 6, and SI-2 and SI-3 in the Supporting Information). In contrast to heterocycles **14** and **15**, double proton sponges **5b** and **5c** differ in their low chromatographic mobility and signal broadening in the ^{1}H NMR spectra, possibly due to their large molecular weight combined with their structural flexibility and bond inversion at the chiral nitrogen atoms.

It was expected that the reaction of diamine **6** with 1,5-dibromopentane in the presence of a base would give the previously unknown piperidine derivative **18**. However, under standard conditions, only dimer **5d** and bromide **17** were isolated along with some unreacted starting compound. The same reaction without K_2CO_3 gave a 52% yield of dimeric product **5d** (Scheme 7). Thus, as in the case of 1,4-dibromobutane, there were no signs of the intramolecular alkylation of the second amino group in **17**, which would have produced the ten-membered analogue of **16**.

After the synthesis was carried out under more severe conditions (160 °C, with the addition of equimolar amounts of KI and K_2CO_3), product **18** was successfully isolated, but the yield did not exceed 15% (Scheme 7). The structures of the new compounds were confirmed by NMR and mass spectrometry, and for double proton sponge **5d**, by XRD analysis (Scheme 7 and SI-4 in the Supporting Information). As is typical of (poly)cyclic compounds, the main peak (100%) in the EI mass spectrum of piperidinonaphthalene **18** is due to a molecular ion with m/z = 254 that distinguishes it from acyclic analogues **5d** and **17**, which are easily fragmented in the gas phase, affecting primarily the pentamethylene chain.



Scheme 6 Synthesis of heterocycles **14** and **15**, and dimers **5b**,**c**



Scheme 7 Reactions of **6** with 1,5-dibromopentane

The conditions outlined above for the synthesis of **18** turned out to be applicable for the formation of morpholine derivative **19** (14–18% yield). At the same time, utilizing bis(chloroethyl) ether as the solvent (150 °C, in the presence of K_2CO_3 and an inert atmosphere) afforded a 61% yield of chloride **20** as the only product (Figure 2).

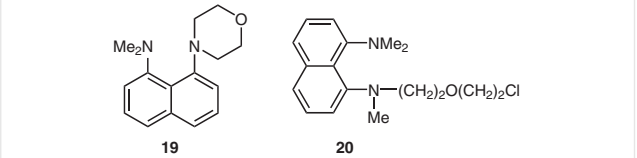
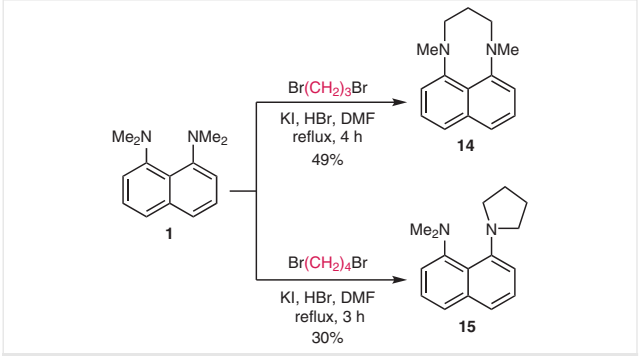


Figure 2 New products derived from bis(chloroethyl) ether

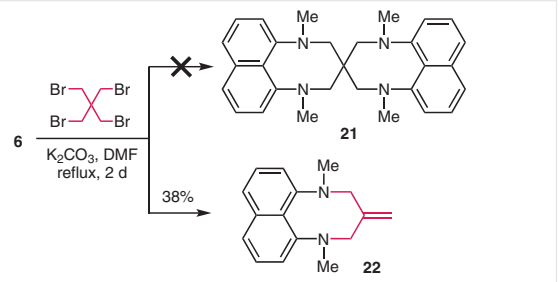
Next, we investigated the possibility of the formation of heterocycles **14**, **15**, and **18** directly from commercially available 1,8-bis(dimethylamino)naphthalene (**1**). To this end, compound **1** was reacted with an excess of the corresponding dibromoalkane in DMF in the presence of KI and a 37% HBr solution (1 equiv) for several hours, thus combining demethylation and heterocyclization processes (Scheme 8).



Scheme 8 Direct conversion of DMAN (**1**) into heterocycles **14** and **15**

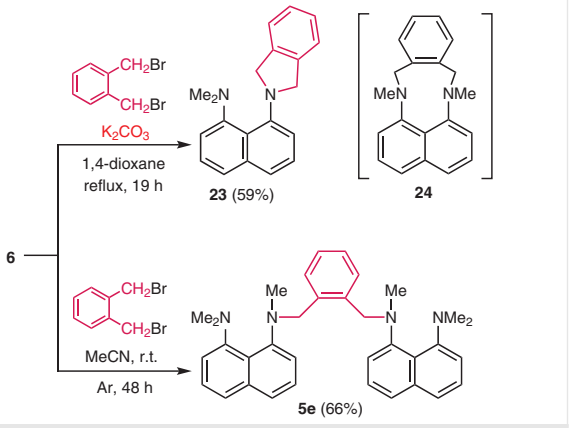
As in the case of diamine **6**, six-membered heterocycle **18** was not formed under the indicated conditions, while compounds **14** and **15** were still obtained by this protocol. Despite the fact that the yields of **14** and **15** were somewhat lowered, this one-pot approach significantly reduced the time of the whole process.

To synthesize spiro-dimer **21**, we attempted the reaction of **6** with pentaerythritol tetrabromide. Due to the sterically demanding nature of the binucleophile and the congested structure of the tetraelectrophile, no reaction occurred in hot THF, acetonitrile or acetonitrile–toluene mixture in the presence of K_2CO_3 or NaH. The reaction only took place in boiling DMF but was accompanied by a change in the residue of the electrophile, and the only product obtained was the alkene derivative **22** (Scheme 9). Notably, when we used **11** as a simpler nucleophile, the reaction did not take place at all, giving rise to neither **21** nor **22**, and leaving **11** unchanged.



Scheme 9 Reaction of **6** with $C(CH_2Br)_4$

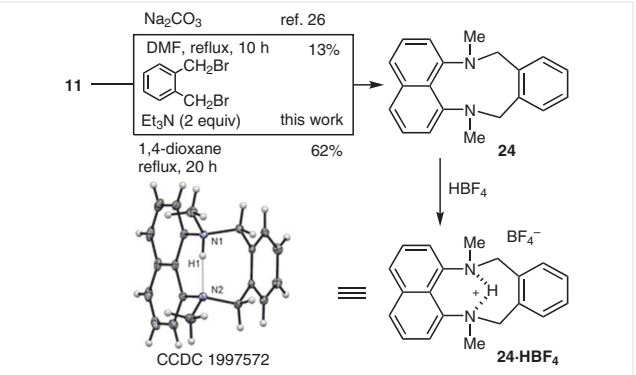
The reaction of *o*-xylylene dibromide with diaminonaphthalene **6** displays the classical ambiguity associated with the topology (structural organization) of the products. Both the isoindoline derivative **23** and the earlier described bridged compound **24** could be obtained (Scheme 10).[26] However, conducting the reaction in acetonitrile, DMF, or in a mixture of acetonitrile–toluene led to the formation of complex mixtures that were difficult to separate, in which isoindoline heterocycle **23** (≤9%) and dimer **5e** were present in small quantities. The situation was restored to control by using 1,4-dioxane as the solvent. This time, heating in the presence of K_2CO_3 led to the formation of previously unpublished compound **23** in a reasonable 59% yield.



Scheme 10 Synthesis of isoindoline **23** and DMAN dimer **5e**

When carrying out the reaction in acetonitrile at room temperature, only dimer **5e** was isolated in 66% yield (Scheme 10). Thus, if diaminonaphthalene **6** is used as the nucleophile, macrocyclic compound **24**, isomeric to isoindoline derivative **23**, is not formed.

To gain insights into the structure and properties of bridged heterocycle **24**, as well as to reliably distinguish it from isomeric structure **23**, and, therefore, exclude its formation in the reaction shown in Scheme 10, we synthesized it under milder conditions and with a higher yield than those published earlier (Scheme 11).[26]



Scheme 11 Modified synthesis of bridged structure **24**

NMR spectroscopy showed that compound **24** was a mixture of *cis*/*trans* isomers with a 38:62 ratio (see SI-6 in the Supporting Information), a fact not mentioned in the original work.[26] Base **24** was converted into tetrafluoroborate salt **24·HBF$_4$**, in the cationic part of which, as shown by X-ray diffraction, the benzo-1,5-diazacyclononane fragment is exclusively in the *cis*-configuration relative to the naphthalene ring plane (Scheme 11, and SI-5 in the Supporting Information). The *cis*/*trans* assignment mentioned above was made possible based on a comparison with a close but more expanded analogue of 1,6-diazacyclononane **24**, which in solution and in the solid form exists only as a *trans*-isomer, and in mono-protonated form it converts into the *cis*-isomer.[21]

It is quite logical that when using organic dihalides with a less flexible organic linker, which excludes the formation of heterocyclic products, double proton sponges will be the only result of the reactions. Thus, a short period of heating trimethyl derivative **6** with *p*-xylylene dibromide in MeCN–DMF gave only dimeric compound **5f** in good yield, which is isomeric with dimer **5e**. The hypothetical heterocyclic structure **25** would be extremely strained in this case (Figure 3).

Finally, we have shown that isoindoline **23** undergoes selective *N*-demethylation to furnish methylamino derivative **26**. As can be seen, the isoindoline ring is not affected (Scheme 12). This circumstance was used to synthesize a

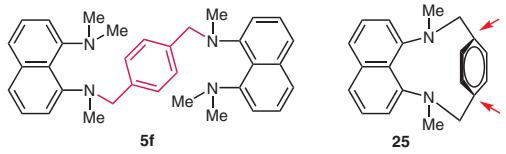
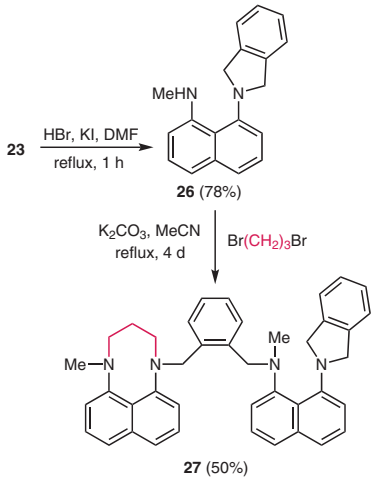


Figure 3 *p*-Xylylene derivatives **5f** and **25**

dimeric proton sponge with heterocyclic DMAN residues linked by a trimethylene bridge. Quite surprisingly, prolonged heating of diamine **26** in acetonitrile with 1,3-dibromopropane resulted in a compound with a molecular weight that matched that of the expected dimer, while its NMR spectrum was indicative of asymmetric structure **27**.

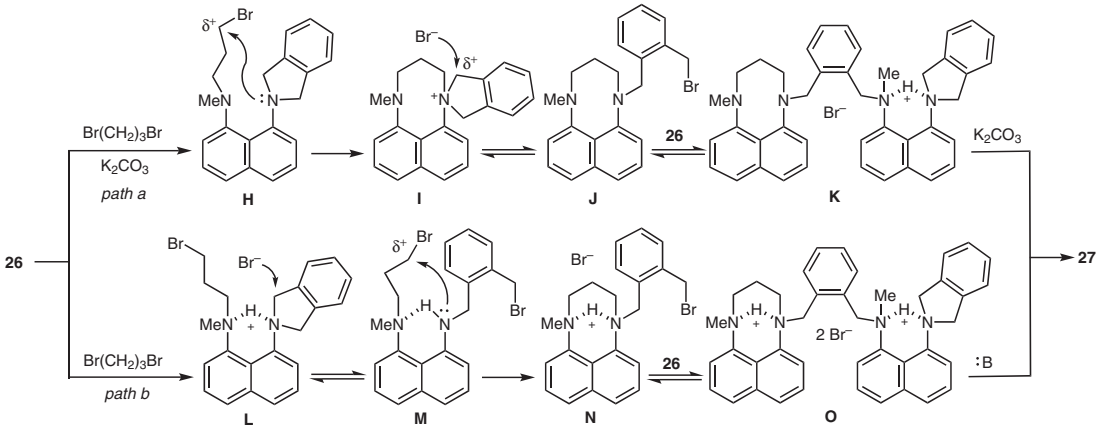


Scheme 12 Synthesis of mixed dimer **27**

The accuracy of the proposed structure was confirmed by a comparison of the NMR spectra of compound **27** with those of simpler molecules **5e**, **14** and **23**, having similar structural fragments, as well as through a number of experimental observations. These included the low sensitivity of the reaction to the presence or absence of K_2CO_3 (although in the presence of potash the process ran more smoothly), the amount of dibromopropane (0.5 and 1 equiv were tried), and the absence of intermediate compounds in the reaction mass as observed by chromatography (only **26** and **27** were detected). This suggests the following two pathways for transforming isoindoline **26** into dimer **27** (Scheme 13).

Path *a* implemented in the presence of potash includes the formation of bromide **H**, which undergoes intramolecular cyclization to give spiro salt **I**, and ring opening to bromide **J**, which then reacts with starting compound **26** to give salt **K** and, ultimately, dimer **27**. Path *b* assumes equilibrium opening of quaternary salt **L** to give dibromide **M**, which undergoes cyclization to give salt **N** and then a reaction with **26** to form double salt **O**. Finally, isolation of the product via alkalization gives compound **27**. The stages leading to compounds **H** and **L** are limiting, whereas their subsequent conversions, in particular quaternization of the methylamino group in **26** by S_N1-active bromides **J** and **N**, proceed quickly, preventing the accumulation of any intermediate products in noticeable quantities in the reaction mixture.

In conclusion, we have proposed a two-stage approach for the synthesis of heterocyclic naphthalene proton sponges possessing saturated hetero-fragments. The process involves modification of the dimethylamino groups in the parent proton sponge [1,8-bis(dimethylamino)naphthalene] via simple realkylation facilitated by the proximity of the nitrogen atoms. The ability of 1,2-dibromoethane to brominate *N*-alkylated 1,8-diaminonaphthalenes is also discussed. Utilizing appropriate organic α,ω-dihalides and readily available 1-dimethylamino-8-(methylamino)naphthalene, naphtho-fused or naphthyl-substituted azacycles with 2, 3, 4 or 5 atomic fragments can be synthesized. Using this approach, it was possible to isolate for the first time double proton sponges crosslinked through the nitrogen atoms by various organic bridges. Factors contributing to the



Scheme 13 Reaction mechanism leading to **27**

heterocyclization and/or dimerization have been identified. This, as well as the search for conditions leading to selective heterocyclization or dimerization processes are other outcomes of the present study.

The solvents were purified and dried by standard methods. The progress of the reactions and the purities of the products were monitored by TLC on Al_2O_3 plates (developed with iodine vapor or UV light). Column chromatography was carried out on Al_2O_3 (Brockmann activity III) or silica gel (70–230 mesh, Aldrich). Melting points were measured in sealed capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-250 (250 MHz) spectrometer with the solvent residual peaks as the internal standard (Scientific and Educational Laboratory of Resonance Spectroscopy, Department of Natural and High Molecular Compounds Chemistry, Southern Federal University). In some cases a Bruker Avance 600 (600 MHz) or a Varian Unity-300 (300 MHz) spectrometer was used. Mass spectra were obtained using a Finnigan MAT INCOS 50 instrument (electron impact, 70 eV). The HR-ESI mass spectra were obtained on a BRUKER maXis spectrometer equipped with an electrospray ionization (ESI) source; methanol was used as the solvent (Chemical Analysis and Materials Research Centre, St. Petersburg State University). The instrument was operated in positive mode using an *m*/*z* range of 50–1200. The capillary voltage of the ion source was set at 4000 V. The nebulizer gas pressure was 1.0 bar, and the drying gas flow was set to 4.0 L/min. Elemental analyses were obtained using a PerkinElmer 2400 analyzer instrument.

X-ray Structure Determination

CCDC 1997569 (**14**·$HClO_4$), 1997571 (**15**·HBF_4), 1997570 (**5d**) and 1997572 (**24**·HBF_4) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures. See also SI-7 in the Supporting Information for additional details.

4-Bromo-8-dimethylamino-1-(methylamino)naphthalene (8)

A solution of 1-dimethylamino-8-(methylamino)naphthalene (**6**)[25] (100 mg, 0.50 mmol), 1,2-dibromoethane (0.22 mL, 2.50 mmol) and triethylamine (0.70 mL, 5.00 mmol) in a mixture of toluene (3 mL) and acetonitrile (3 mL) was refluxed for 51 h. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (silica gel, CH_2Cl_2) to afford bromide **8** (46 mg, 33%) as a pale yellow oil (first mobile fraction with blue fluorescence under UV light), followed by compound **7** (16 mg, 15%) as a pale beige solid (mp 88–90 °C).[26]

^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.19 (br s, 1 H, NH), 7.98 (dd, *J* = 8.6, 1.2 Hz, 1 H), 7.57 (d, *J* = 8.4 Hz, 1 H), 7.42 (dd, *J* = 8.6, 7.5 Hz, 1 H), 7.21 (dd, *J* = 7.5, 1.2 Hz, 1 H), 6.27 (d, *J* = 8.4 Hz, 1 H), 2.94 (s, 3 H, NMe), 2.72 (s, 6 H, NMe_2).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 152.1, 148.0, 134.2, 131.0, 126.5, 124.5, 119.3, 115.8, 106.8, 102.9, 45.9 (NMe_2), 30.3 (NMe).

MS (EI): *m*/*z* (%) = 280 (94), 278 [M]$^+$ (95), 263 (18), 248 (94), 246 (69), 200 (23), 183 (19), 168 (96), 154 (49), 140 (34), 126 (56), 111 (37), 97 (51), 85 (51), 71 (68), 57 (100), 43 (84).

Anal. Calcd for $C_{13}H_{15}BrN_2$: C, 55.93; H, 5.42; N, 10.03. Found: C, 55.98; H, 5.33; N, 10.19.

1′,3′-Dimethyl-5-methylamino-4-methylimino-1′,3′-dihydro-4*H*-spiro[naphthalene-1,2′-perimidine] (12)

A mixture of 1,8-bis(methylamino)naphthalene (**11**)[29] (93 mg, 0.50 mmol) and MnO_2 (217 mg, 2.50 mmol) in acetonitrile (5 mL) was refluxed for 1 h. Upon completion of the reaction, the mixture was filtered, the residue washed with dichloromethane and the solvents were evaporated to dryness. Recrystallization from *n*-octane gave **12** (54 mg, 59%) as yellow crystals (mp 180–182 °C).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 10.57 (br s, 1 H, NH), 7.33–7.39 (m, 3 H), 7.24 (br d, *J* = 7.9 Hz, 2 H), 7.14 (br d, *J* = 7.3 Hz, 1 H), 6.88 (d, *J* = 10.5 Hz, 1 H), 6.72 (br d, *J* = 8.1 Hz, 1 H), 6.54 (br d, *J* = 7.5 Hz, 2 H), 6.14 (d, *J* = 10.5 Hz, 1 H), 3.51 (s, 3 H), 2.98 (s, 3 H), 2.54 (s, 6 H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 160.7, 150.7, 141.6, 140.9, 134.0, 133.3, 131.6, 127.2, 119.2, 117.3, 115.5, 114.8, 112.4, 110.0, 104.2, 74.2, 37.5 and 34.1 (NMe), 29.6.

MS (EI): *m*/*z* (%) = 369 (28), 368 [M]$^+$ (100), 183 (20), 169 (26), 168 (40), 154 (16).

Anal. Calcd for $C_{24}H_{24}N_4$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.29; H, 6.42; N, 15.30.

1′,3′-Dimethyl-5-methylamino-1′,3′-dihydro-4*H*-spiro[naphthalene-1,2′-perimidin]-4-one (13)

A mixture of **12** (74 mg, 0.20 mmol) and silica gel (300 mg) in CH_2Cl_2 (5 mL) was stirred for 3 d at 25 °C. Upon completion of the reaction, the adsorbent was filtered off and then washed with dichloromethane and acetone. Evaporation of the solvents gave **13** (71 mg, 100%) as orange-red crystals [mp 250–252 °C (*n*-octane)].

^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.35 (br q, *J* = 5.2 Hz, 1 H, NH), 7.47 (t, *J* = 8.2 Hz, 1 H), 7.34 (t, *J* = 8.0 Hz, 2 H), 7.24 (dd, *J* = 8.4, 1.0 Hz, 2 H), 7.09 (dd, *J* = 7.6, 0.9 Hz, 1 H), 6.72 (dd, *J* = 8.5, 0.9 Hz, 1 H), 6.55 (br d, *J* = 7.1 Hz, 2 H), 6.47 (d, *J* = 10.1 Hz, 1 H), 6.34 (d, *J* = 10.1 Hz, 1 H), 2.97 (d, *J* = 5.2 Hz, 3 H, NMe), 2.54 (s, 6 H, 2 NMe).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 186.5 (C=O), 152.5, 145.1, 141.1, 140.6, 135.6, 133.9, 131.5, 127.2, 117.9, 115.2, 114.6, 112.3, 111.1, 104.7, 73.8, 34.0, 29.6.

MS (EI): *m*/*z* (%) = 356 (24), 355 [M]$^+$ (100), 354 (83), 169 (20), 168 (33), 154 (17), 127 (20).

Anal. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82. Found: C, 77.84; H, 6.03; N, 11.78.

Compounds 14 and 15; General Procedure

Route 1

A mixture of diamine **6** (100 mg, 0.50 mmol), α,ω-dibromoalkane (1.5 equiv) and K_2CO_3 (53 mg, 0.38 mmol) in acetonitrile (6 mL) was refluxed for 48 h. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, CH_2Cl_2).

1,5-Dimethylnaphtho[1,8-*bc*]-1,5-diazacyclooctane (14)

Yield: 67 mg (59%); beige solid; mp 77–79 °C.[26]

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.46 (br d, *J* = 8.0 Hz, 2 H), 7.33 (dd, *J* = 8.0, 7.6 Hz, 2 H), 7.06 (br d, *J* = 7.6 Hz, 2 H), 2.92–2.97 (m, 10 H), 1.59 (quin, *J* = 5.8 Hz, 2 H).

General procedure for preparation of proton complexes

These were prepared by mixing equimolar amounts of appropriate bases and 60% aqueous $HClO_4$ or 40% aqueous HBF_4 in a minimum volume of EtOAc followed by 3-fold dilution with Et_2O. The residue thus formed was washed with Et_2O and vacuum-dried to give the desired salts in high yield.

Perchlorate 14·$HClO_4$

Yield: 85% (28 mg from 23 mg of 14); colorless crystals with mp 175–176 °C. Crystals suitable for XRD analysis were obtained from acetone.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 14.51 (br s, 1 H), 8.01 (dd, *J* = 8.1, 1.4 Hz, 2 H), 7.76 (dd, *J* = 7.8, 1.4 Hz, 2 H), 7.68 (dd, *J* = 8.1, 7.8 Hz, 2 H), 3.70–3.78 (m, 2 H), 3.19 (d, *J* = 2.4 Hz, 6 H, 2 NMe), 3.04–3.12 (m, 2 H), 1.73–1.79 (m, 1 H), 1.22–1.30 (m, 1 H).

1-Dimethylamino-8-(pyrrolidin-1-yl)naphthalene (15)

Yield: 61 mg (51%); pale beige oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.25–7.35 (m, 4 H), 6.87–6.89 (m, 2 H), 3.16–3.25 (m, 4 H), 2.80 (s, 6 H, NMe_2), 1.89–1.94 (m, 4 H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 150.7, 147.5, 137.7, 125.6, 125.4, 121.1, 120.5, 120.2, 111.9, 110.6, 51.8, 44.2 (NMe_2), 24.7.

MS (EI): *m*/*z* (%) = 240 $[M]^+$ (48), 212 (18), 209 (16), 208 (28), 197 (20), 196 (23), 183 (21), 182 (36), 181 (23), 171 (17), 170 (34), 169 (26), 168 (87), 167 (57), 166 (24), 154 (44), 140 (17), 128 (24), 127 (54), 115 (22).

Anal. Calcd for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39; N, 11.66. Found: C, 80.02; H, 8.44; N, 11.43.

Tetrafluoroborate 15·HBF_4

Yield: 76% (25 mg from 24 mg of **15**); colorless crystals, mp 146–147 °C. Crystals suitable for XRD analysis were obtained by diffusion of Et_2O into a MeOH–CH_2Cl_2 solution.

^{1}H NMR (250 MHz, CD_3CN): δ = 18.90 (br s, 1 H), 8.02–8.07 (m, 2 H), 7.83–7.90 (m, 2 H), 7.67–7.73 (m, 2 H), 3.78–3.87 (m, 2 H), 3.35–3.49 (m, 2 H), 3.07 (d, *J* = 2.1 Hz, 6 H), 2.31–2.44 (m, 2 H), 2.19–2.29 (m, 2 H).

^{13}C NMR (62.9 MHz, CD_3CN): δ = 145.2, 141.5, 135.2, 129.5, 129.0, 127.1, 122.4, 121.7, 120.4, 58.3, 45.7, 24.4.

Route 2

A mixture of 1,8-bis(dimethylamino)naphthalene (DMAN) (**1**) (54 mg, 0.25 mmol), α,ω-dibromoalkane (5.0 equiv), KI (125 mg, 0.75 mmol) and 37% aq HBr (0.04 mL, 0.25 mmol) in DMF (3 mL) was refluxed for 3–4 h. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with ethyl acetate (3 × 7 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, $CHCl_3$).

1,5-Dimethylnaphtho[1,8-*bc*]-1,5-diazacyclooctane (14)

Yield: 28 mg (49%).

The data are identical with the sample described above.

1-Dimethylamino-8-(pyrrolidin-1-yl)naphthalene (15)

Yield: 18 mg (30%).

The data are identical with the sample described above.

***N*,*N*′-Dimethyl-*N*,*N*′-[8-bis(dimethylamino)naphth-1-yl]-1,3-diaminopropane (5b)**

A mixture of diamine **6** (100 mg, 0.50 mmol), KI (249 mg, 1.50 mmol) and 1,3-dibromopropane (0.03 mL, 0.25 mmol) in acetonitrile (10 mL) was stirred for 10 d at 60 °C. Upon completion of the reaction, the resulting mixture was poured into water (45 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, $CHCl_3$) to afford **5b** (pale yellow oil, 27 mg, 25%) followed by **14** (less mobile fraction, 21 mg, 37%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.33–7.37 (m, 4 H), 7.23–7.29 (m, 4 H), 6.85–6.91 (m, 4 H), 2.79–3.04 (m, 10 H), 2.63 (br s, 12 H, 2 NMe_2), 1.69–1.95 (m, 2 H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 150.8, 150.4, 137.9, 125.4 (2 C), 122.1, 122.0, 120.9, 114.2, 112.8, 55.8, 44.5, 40.6, 40.3, 24.6.

MS (EI): *m*/*z* (%) = 440 $[M]^+$ (11), 227 (18), 213 (16), 200 (36), 198 (52), 197 (85), 196 (100), 183 (23), 182 (31), 169 (19), 168 (48).

Anal. Calcd for $C_{29}H_{36}N_4$: C, 79.05; H, 8.24; N, 12.72. Found: C, 79.12; H, 8.19; N, 12.74.

Compounds 5c and 5d; General Procedure

A solution of diamine **6** (100 mg, 0.50 mmol) and α,ω-dibromoalkane (0.5 equiv) in acetonitrile (6 mL) was refluxed for 7 d. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, $CHCl_3$).

***N*,*N*′-Dimethyl-*N*,*N*′-[8-bis(dimethylamino)naphth-1-yl]-1,4-diaminobutane (5c)**

Yield: 56 mg (49%); beige solid; mp 102–103 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.41 (br d, *J* = 8.0 Hz, 4 H), 7.31–7.34 (m, 4 H), 6.95–6.97 (m, 4 H), 3.00–3.19 (m, 2 H), 2.83–2.89 (m, 8 H), 2.76 (br s, 12 H, NMe_2), 1.45–1.52 (m, 4 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.7, 150.3, 137.8, 125.27, 125.26, 122.0, 120.9, 114.0, 112.7, 57.2, 45.4 and 43.8 (NMe_2), 40.5 (NMe), 25.1.

MS (EI): *m*/*z* (%) = 454 $[M]^+$ (6), 213 (23), 200 (31), 199 (18), 198 (41), 197 (69), 184 (36), 183 (55), 182 (65), 170 (25), 169 (28), 168 (100), 167 (24), 154 (27), 127 (23), 84 (15), 44 (35), 42 (26), 32 (15).

Anal. Calcd for $C_{30}H_{38}N_4$: C, 79.25; H, 8.42; N, 12.32. Found: C, 79.14; H, 8.44; N, 12.27.

***N*,*N*′-Dimethyl-*N*,*N*′-[8-bis(dimethylamino)naphth-1-yl]-1,5-diaminopentane (5d)**

Yield: 61 mg (52%); beige solid; mp 81–83 °C. Crystals suitable for XRD analysis were obtained from DMF.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (br d, *J* = 8.0 Hz, 4 H), 7.36–7.39 (m, 4 H), 7.01–7.04 (m, 4 H), 3.07–3.21 (m, 2 H), 2.75–2.95 (m, 20 H), 1.58–1.66 (m, 4 H), 1.19 (quin, *J* = 7.6 Hz, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.7, 150.3, 137.8, 125.27, 125.26, 122.0, 120.9, 114.0, 112.7, 57.2, 45.4 and 43.8 (NMe_2), 40.5 (NMe), 25.1.

MS (EI): *m*/*z* (%) = 468 $[M]^+$ (4), 199 (15), 198 (25), 197 (39), 184 (24), 183 (31), 182 (33), 170 (15), 169 (18), 168 (100).

Anal. Calcd for $C_{31}H_{40}N_4$: C, 79.44; H, 8.60; N, 11.95. Found: C, 79.60; H, 8.65; N, 12.01.

N^1-(5-Bromopentyl)-N^1,N^8,N^8-trimethylnaphthalene-1,8-diamine (17)

A mixture of diamine **6** (100 mg, 0.50 mmol), K_2CO_3 (53 mg, 0.38 mmol) and 1,5-dibromopentane (0.14 mL, 1.00 mmol) in acetonitrile (6 mL) was refluxed for 5 d. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, $CHCl_3$) to afford **17** (36 mg, 21%) as a dark beige oil followed by dimer **5d** (31 mg, 26%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35 (br d, *J* = 8.1 Hz, 2 H), 7.24–7.32 (m, 2 H), 6.88–6.99 (m, 2 H), 3.33 (t, *J* = 6.7 Hz, 2 H), 3.05–3.07 (m, 1 H), 2.83 (s, 3 H, NMe), 2.68–2.80 (m, 7 H), 1.70–1.85 (m, 2 H), 1.45–1.68 (m, 2 H), 1.28–1.36 (m, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.8, 150.4, 137.8, 125.3, 122.1, 122.0, 114.0, 112.8, 57.2, 45.5 and 43.8 (NMe_2), 40.5 (NMe), 33.8, 32.7, 26.3, 26.1.

MS (EI): *m*/*z* (%) = 350 $[M + 2]^+$ (^{81}Br) (16), 348 $[M]^+$ (^{79}Br) (18), 213 (37), 199 (26), 198 (21), 197 (27), 184 (33), 183 (31), 182 (52), 170 (30), 169 (29), 168 (82), 167 (21), 154 (24), 127 (16), 99 (17), 42 (18), 41 (23).

Anal. Calcd for $C_{18}H_{25}BrN_2$: C, 61.89; H, 7.21; N, 8.02. Found: C, 61.92; H, 7.14; N, 8.11.

1-Dimethylamino-8-(piperidin-1-yl)naphthalene (18)

A mixture of diamine **6** (100 mg, 0.50 mmol), KI (166 mg, 1.00 mmol), K_2CO_3 (53 mg, 0.38 mmol) and 1,5-dibromopentane (0.10 mL, 0.75 mmol) in benzonitrile (5 mL) was stirred for 24 h at 160 °C. Upon completion of the reaction, the solvent was removed and the residue was dissolved in dichloromethane (10 mL), treated with water (25 mL) and basified with aq KOH to pH 10–11. The mixture was extracted with dichloromethane (2 × 10 mL), then the solvent was evaporated and the crude product was purified by column chromatography [Al_2O_3 (calcined at 600 °C), $CHCl_3$] to afford **18** (19 mg, 15%) as a light-beige, waxy solid (mp 69–72 °C).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.37 (dd, *J* = 8.3, 1.3 Hz, 1 H), 7.28–7.32 (m, 2 H), 6.95–6.97 (m, 2 H), 3.35–3.37 (m, 2 H), 2.81 (s, 6 H, NMe_2), 2.50–2.54 (m, 2 H), 1.68–1.85 (m, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 151.4, 150.7, 137.7, 125.5, 125.3, 122.6, 122.3, 121.3, 113.7, 113.1, 54.6, 45.2 (NMe_2), 26.3, 24.7.

MS (EI): *m*/*z* (%) = 254 $[M]^+$ (100), 239 (17), 223 (33), 222 (28), 210 (21), 184 (24), 183 (23), 182 (26), 171 (17), 170 (25), 169 (19), 168 (46), 154 (22), 127 (21), 84 (20).

Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.31; H, 8.84; N, 10.95.

Tetrafluoroborate 18·HBF_4

Yield: 70% (11 mg from 12 mg of **18**); colorless solid; mp 229–231 °C.

^{1}H NMR (300 MHz, CD_3CN): δ = 18.77 (br s, 1 H), 8.08 (dd, *J* = 5.1, 1.0 Hz, 1 H), 8.05 (dd, *J* = 5.1, 1.0 Hz, 1 H), 7.92 (dd, *J* = 7.8, 1.0 Hz, 1 H), 7.87 (dd, *J* = 7.6, 1.0 Hz, 1 H), 7.68–7.75 (m, 2 H), 3.37–3.45 (m, 4 H), 3.09 (d, *J* = 2.4 Hz, 6 H, NMe_2), 2.07–2.13 (m, 2 H), 1.79–1.90 (m, 4 H).

1-Dimethylamino-8-morpholinonaphthalene (19)

A mixture of diamine **6** (100 mg, 0.50 mmol), KI (166 mg, 1.00 mmol), K_2CO_3 (53 mg, 0.38 mmol) and bis(chloroethyl) ether (0.09 mL, 0.75 mmol) in benzonitrile (5 mL) was stirred for 24 h at 160 °C. Upon completion of the reaction, the solvent was removed and the residue was dissolved in dichloromethane (10 mL), treated with water (25 mL) and basified with aq KOH to pH 10–11. The mixture was extracted with dichloromethane (2 × 10 mL), then the solvent was evaporated and the crude product was purified by column chromatography [Al_2O_3 (calcined at 600 °C), $CHCl_3$] to afford **19** (23 mg, 18%) as a beige solid (mp 140–142 °C).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.42 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.31–7.35 (m, 2 H), 7.00 (dd, *J* = 7.5, 1.2 Hz, 1 H), 6.96 (dd, *J* = 7.5, 1.2 Hz, 1 H), 3.87–3.91 (m, 4 H), 3.19–3.21 (m, 2 H), 2.83–2.86 (m, 2 H), 2.81 (s, 6 H, NMe_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.3, 149.7, 137.7, 125.53, 125.52, 123.4, 122.7, 120.9, 113.8, 113.4, 67.2, 53.6, 45.2 (NMe_2).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{21}N_2O$: 257.1648; found: 257.1642.

Tetrafluoroborate 19·HBF_4

Yield: 72% (12 mg from 13 mg of **19**); colorless solid; mp 231–234 °C.

^{1}H NMR (300 MHz, CD_3CN): δ = 18.41 (br s, 1 H), 8.12 (dd, *J* = 8.4, 1.0 Hz, 1 H), 8.07 (dd, *J* = 8.2, 1.0 Hz, 1 H), 7.96 (dd, *J* = 7.8, 1.0 Hz, 1 H), 7.93 (dd, *J* = 7.6, 1.0 Hz, 1 H), 7.71–7.76 (m, 2 H), 4.11–4.17 (m, 2 H), 3.82–3.91 (m, 2 H), 3.38–3.48 (m, 2 H), 3.19–3.31 (m, 8 H).

N^1-[2-(2-Chloroethoxy)ethyl]-N^1,N^8,N^8-trimethylnaphthalene-1,8-diamine (20)

A mixture of diamine **6** (50 mg, 0.25 mmol) and K_2CO_3 (104 mg, 0.75 mmol) in bis(chloroethyl) ether (2 mL) was stirred for 35 h under an argon atmosphere at 150 °C. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 7 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, CH_2Cl_2) to afford **20** (47 mg, 61%) as a beige solid (mp 49–50 °C).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.34–7.40 (m, 2 H), 7.24–7.32 (m, 2 H), 7.00 (dd, *J* = 7.4, 1.1 Hz, 1 H), 6.92 (dd, *J* = 7.4, 1.1 Hz, 1 H), 3.47–3.67 (m, 6 H), 3.19–3.28 (m, 2 H), 2.95 (s, 3 H, NMe), 2.75 (br s, 6 H, NMe_2).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 150.6, 149.7, 137.8, 125.4, 125.3, 122.4, 122.1, 120.8, 114.5, 113.0, 70.9, 69.9, 56.2, 45.8 and 43.5 (NMe_2), 42.9, 41.2 (NMe).

MS (EI): *m*/*z* (%) = 308 $[M + 2]^+$ (^{37}Cl) (27), 306 $[M]^+$ (^{35}Cl) (80), 227 (46), 214 (17), 213 (85), 199 (40), 198 (100), 197 (98), 195 (15), 184 (25), 183 (32), 182 (58), 170 (26), 169 (24), 168 (70), 154 (16), 127 (15).

Anal. Calcd for $C_{17}H_{23}ClN_2O$: C, 66.55; H, 7.56; N, 9.13. Found: C, 66.54; H, 7.51; N, 9.23.

1,5-Dimethyl-3-methylene-2,3,4,5-tetrahydro-1*H*-naphtho[1,8-*bc*][1,5]diazocine (22)

A mixture of diamine **6** (57 mg, 0.28 mmol), pentaerythritol tetrabromide (110 mg, 0.28 mmol) and K_2CO_3 (39 mg, 0.28 mmol) in DMF (6 mL) was refluxed for 48 h. Upon completion of the reaction, the resulting mixture was poured into water (40 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, CH_2Cl_2) to afford **22** (25 mg, 38%) as a dark-beige solid (mp 58–61 °C).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.44 (br d, *J* = 7.7 Hz, 2 H), 7.29–7.32 (m, 2 H), 7.07 (br d, *J* = 7.4 Hz, 2 H), 4.622–4.624 (m, 2 H), 3.55 (s, 4 H), 2.93 (s, 6 H, NMe_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.6, 144.1, 136.3, 126.4, 125.5, 124.0, 117.0, 116.7, 65.6, 43.36 (NMe_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{19}N_2$: 239.1543; found: 239.1543.

1-Dimethylamino-8-(isoindolin-2-yl)naphthalene (23)

A mixture of diamine **6** (100 mg, 0.50 mmol), K_2CO_3 (69 mg, 0.50 mmol) and *o*-xylylene dibromide (158 mg, 0.60 mmol) in 1,4-dioxane (12 mL) was stirred at reflux for 19 h. Upon completion of the reaction, the solvent was removed and the residue was dissolved in ethyl acetate (10 mL), treated with water (25 mL) and basified with aq KOH to pH 10–11. The mixture was extracted with ethyl acetate (2 × 10 mL), then the solvent was evaporated and the crude product was purified by column chromatography (silica gel, CH_2Cl_2; after isolation of mobile precursors, the solvent was changed to ethyl acetate–CH_2Cl_2, 1:1) to afford **23** (85 mg, 59%) as a dense yellow gum.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.22–7.38 (m, 8 H), 7.08 (dd, *J* = 7.1, 1.7 Hz, 1 H), 6.91 (dd, *J* = 6.8, 1.9 Hz, 1 H), 4.67 (br s, 4 H), 2.74 (s, 6 H, NMe_2).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 150.6, 146.4, 139.9, 137.8, 126.6, 125.63, 125.60, 122.1, 121.6, 121.1, 120.2, 112.3, 112.0, 56.9, 44.1 (NMe_2).

MS (EI): *m*/*z* (%) = 288 [M]$^+$ (30), 242 (20), 171 (16), 170 (34), 168 (34), 154 (18), 128 (24), 127 (34), 126 (15), 118 (27), 91 (21), 90 (18), 89 (31), 78 (19), 77 (33), 65 (19), 63 (28), 51 (28), 45 (37), 44 (78), 42 (100), 39 (42).

Anal. Calcd for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71. Found: C, 83.33; H, 7.04; N, 9.86.

N^1,*N*$^{1'}$-[1,2-Phenylenebis(methylene)]bis(*N*^{1},*N*^{8},*N*^{8}-trimethylnaphthalene-1,8-diamine) (5e)

A solution of diamine **6** (100 mg, 0.50 mmol) and *o*-xylylene dibromide (66 mg, 0.25 mmol) in acetonitrile (5 mL) was stirred for 48 h under an argon atmosphere at 25 °C. Upon completion of the reaction, diethyl ether (6 mL) was added resulting in the formation of a precipitate. The precipitate was washed with diethyl ether (3 × 10 mL) and dissolved in water (25 mL), then the solution was basified with aq KOH to pH 10–11. The product was extracted with ethyl acetate (3 × 10 mL) and the solvent was evaporated to afford dimer **5e** (83 mg, 66%) as a beige solid (mp 116–117 °C).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.13–7.35 (m, 12 H), 6.90 (br d, *J* = 7.3 Hz, 2 H), 6.63 (br d, *J* = 7.6 Hz, 2 H), 3.83 (br s, 4 H), 2.65 (br s, 12 H, 2 NMe_2), 2.63 (br s, 6 H, 2 NMe).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 150.9, 149.9, 137.8, 136.9, 129.4, 125.9, 125.4, 122.1, 121.9, 120.4, 114.4, 112.7, 57.7, 46.1 (NMe_2), 39.8 (NMe).

MS (EI): *m*/*z* (%) = 502 [M]$^+$ (7), 287 (23), 271 (18), 258 (19), 257 (18), 200 (32), 199 (32), 198 (47), 197 (52), 184 (67), 183 (100), 182 (53), 170 (47), 169 (36), 168 (76), 154 (19), 140 (16), 128 (46), 127 (77), 115 (35), 105 (18), 103 (18), 99 (15), 91 (23), 78 (26), 77 (59), 63 (28).

Anal. Calcd for $C_{34}H_{38}N_4$: C, 81.24; H, 7.62; N, 11.15. Found: C, 81.35; H, 7.54; N, 11.23.

N,*N*′-Dimethylbenzo[*c*]naphtho[1,8-*gh*]1,6-diazacyclononane (24)

A solution of diamine **11** (50 mg, 0.27 mmol), *o*-xylylene dibromide (84 mg, 0.32 mmol) and triethylamine (0.08 mL, 0.54 mmol) in 1,4-dioxane (6 mL) was refluxed for 20 h. Upon completion of the reaction, the resulting mixture was poured into water (30 mL), basified with aq KOH to pH 10–11 and extracted with $CHCl_3$ (3 × 7 mL). The solvent was evaporated and the crude product was purified by column chromatography [Al_2O_3 (calcined at 600 °C), $CHCl_3$] to give **24** (48 mg, 62%) as a pale beige solid (mp 62–64 °C); the physical appearance was not reported in the literature.[26]

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (br d, *J* = 7.9 Hz, 2 H), 7.34–7.37 (m, 2 H), 7.24–7.32 (m, 4 H), 7.10 (br d, *J* = 7.5 Hz, 2 H), 5.52 (br s, 1 H), 4.75 (br s, 1 H), 3.94 (br s, 1 H), 3.73 (br s, 1 H), 2.72 (s, 6 H, 2 NMe).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.3, 139.2, 130.4, 129.5, 127.1, 126.8, 125.7, 125.3, 123.1, 122.2, 117.2, 116.3, 61.8, 39.8 and 38.6 (NMe).

Tetrafluoroborate 24·HBF_4

Yield: 77% (20 mg from 20 mg of **24**); pale pink solid; mp 227–228 °C (dec.) (Lit.[26] 232–235 °C). Crystals suitable for XRD analysis were obtained from EtOH.

^{1}H NMR (250 MHz, CD_3CN): δ = 19.85 (br s, 1 H), 7.77–7.80 (m, 4 H), 7.57 (dd, *J* = 7.3, 1.2 Hz, 2 H), 6.92–7.03 (m, 4 H), 5.03 (br d, *J* = 12.3 Hz, 2 H), 4.22 (dd, *J* = 12.6, 4.4 Hz, 2 H), 3.35 (d, *J* = 2.7 Hz, 6 H, 2 NMe).

N^1,*N*$^{1'}$-(*p*-Xylylene)bis[8-dimethylamino-1-(methylamino)naphthalene] (5f)

A solution of diamine **6** (100 mg, 0.50 mmol) and *p*-xylylene dibromide (66 mg, 0.25 mmol) in a mixture of DMF (1.5 mL) and acetonitrile (4.5 mL) was refluxed for 3 h. Upon completion of the reaction, the resulting mixture was poured into water (25 mL), basified with aq KOH to pH 10–11 and extracted with dichloromethane (3 × 10 mL). The solvent was evaporated and the crude product was purified by column chromatography (Al_2O_3, *n*-hexane–CH_2Cl_2, 3:1) to afford **5f** (57 mg, 45%) as shiny pale beige crystals [mp 150–152 °C ($CHCl_3$/EtOH, 1:3)].

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.43–7.46 (m, 4 H), 7.28–7.38 (m, 4 H), 7.00 (br d, *J* = 7.3 Hz, 2 H), 6.87–6.90 (m, 6 H), 4.19 (br s, 4 H), 2.81 (br s, 12 H, 2 NMe_2), 2.75 (s, 6 H, 2 NMe).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 151.0, 149.8, 137.9, 136.9, 128.2, 125.5, 125.4, 122.19, 122.16, 120.5, 114.6, 112.9, 61.6, 39.7; the signal for the NMe_2 groups was not evident due to very strong broadening (see the ^{13}C NMR spectrum of the salt sample below).

MS (EI): *m*/*z* (%) = 502 [M]$^+$ (10), 209 (16), 199 (44), 197 (19), 184 (77), 183 (100), 169 (19), 168 (73), 154 (29), 127 (18).

Anal. Calcd for $C_{34}H_{38}N_4$: C, 81.24; H, 7.62; N, 11.15. Found: C, 81.29; H, 7.53; N, 11.27.

Bis(tetrafluoroborate) 5f·2HBF_4

Yield: 98% (33 mg from 25 mg of **5f**); Pale pink crystals; mp 278–280 °C.

^{1}H NMR (250 MHz, CD_3CN): δ (diastereomeric mixture, 39:61) = 17.56 and 17.28 (both br s, 0.78 and 1.24 H, 2 NHN^+), 7.93–8.00 (m, 5.33 H), 7.83 (dd, *J* = 7.5, 0.9 Hz, 0.84 H), 7.56–7.73 (m, 4.97 H), 7.30 (dd, *J* = 7.7, 0.9 Hz, 1.26 H), 6.89–6.90 (m, 4.00 H), 4.28–4.40 (m, 4.00 H), 3.02–3.04 (m, 6.07 H, NMe_2), 2.97 and 2.93 (both d, *J* = 3.2 and 3.3 Hz, 2.47 and 4.08 H, NMe_2), 2.53 and 1.74 (both d, *J* = 3.3 and 3.5 Hz, 3.26 and 3.78 H, 2 NMe).

^{13}C NMR (62.9 MHz, CD_3CN): δ (diastereomeric mixture, 39:61) = 142.84, 142.77, 142.5, 142.3, 135.2, 135.1, 134.5, 134.3, 131.2, 130.9, 129.9, 129.7, 129.1, 129.0, 127.1, 127.0, 126.9, 126.8, 123.6, 123.4, 120.9, 120.8, 120.2, 120.1, 60.8, 60.1, 47.3, 47.0, 46.8, 45.7, 45.0, 44.8.

8-(Isoindolin-2-yl)-1-(methylamino)naphthalene (26)

A mixture of **23** (61 mg, 0.21 mmol), KI (174 mg, 1.05 mmol) and 37% aqueous HBr (0.03 mL, 0.21 mmol) in DMF (3 mL) was refluxed for 1 h. Upon completion of the reaction, the resulting mixture was poured into water (30 mL) and extracted with *n*-hexane (3 × 6 mL). The solvent was evaporated and the crude product was purified by column chromatography (silica gel, CH_2Cl_2) to afford **26** (45 mg, 78%) as a pale yellow solid (mp 101–102 °C); its solutions possess blue fluorescence under UV light.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.06 (br s, 1 H, NH), 7.59 (dd, *J* = 6.8, 2.6 Hz, 1 H), 7.33–7.39 (m, 7 H), 7.10 (br d, *J* = 8.1 Hz, 1 H), 6.47 (br d, *J* = 7.6 Hz, 1 H), 4.67 (dd, *J* = 15.0, 3.2 Hz, 2 H), 4.46 (dd, *J* = 15.0, 3.2 Hz, 2 H), 2.89 (s, 3 H, NMe).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 148.3, 148.2, 139.3, 137.0, 127.3, 127.2, 126.3, 125.5, 122.4, 119.8, 117.9, 115.0, 102.7, 60.5, 30.5 (NMe).

MS (EI): *m*/*z* (%) = 274 $[M]^+$ (100), 272 (16), 271 (14), 257 (20), 256 (40), 242 (26), 183 (51), 169 (12), 168 (28), 127 (15), 118 (34).

Anal. Calcd for $C_{19}H_{18}N_2$: C, 83.18; H, 6.61; N, 10.21. Found: C, 83.27; H, 6.53; N, 10.15.

8-(Isoindolin-2-yl)-*N*-methyl-*N*-{2-[(5-methyl-2,3,4,5-tetrahydro-1*H*-naphtho[1,8-*bc*][1,5]diazocin-1-yl)methyl]benzyl}naphthalen-1-amine (27)

A mixture of methylamino-naphthalene **26** (41 mg, 0.15 mmol), 1,3-dibromopropane (0.02 mL, 0.15 mmol) and K_2CO_3 (15 mg, 0.11 mmol) in acetonitrile (4 mL) was refluxed for 4 d. The resulting mixture was poured into water (20 mL), basified with aq KOH to pH 10–11 and extracted with ethyl acetate (3 × 7 mL). The solvent was evaporated and the crude product was purified by column chromatography (silica gel, $CHCl_3$, after isolation of mobile **26**, the solvent was changed to EtOAc) to afford **27** (22 mg, 50%) as a pale yellow solid (mp 96–98 °C).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 (br d, *J* = 7.6 Hz, 1 H), 7.50 (dd, *J* = 8.1, 1.1 Hz, 1 H), 7.46 (dd, *J* = 8.1, 1.0 Hz, 1 H), 7.44 (br d, *J* = 7.4 Hz, 1 H), 7.30–7.38 (m, 4 H), 7.26–7.28 (m, 2 H), 7.20–7.23 (m, 2 H), 7.12 (t, *J* = 7.7 Hz, 1 H), 7.07–7.10 (m, 2 H), 7.03 (br d, *J* = 7.6 Hz, 1 H), 6.98 (dd, *J* = 7.5, 1.0 Hz, 1 H), 6.77 (t, *J* = 7.4 Hz, 1 H), 6.72 (br d, *J* = 7.5 Hz, 1 H), 6.60 (br d, *J* = 7.3 Hz, 1 H), 4.34–4.95 (m, 6 H), 3.57–3.79 (m, 2 H), 2.82 (s, 3 H, NMe), 2.72–2.74 (m, 2 H), 2.67 (s, 3 H, NMe), 2.60–2.63 (m, 2 H), 1.42–1.45 (m, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.1, 149.3, 148.6, 146.7, 139.7, 138.5, 137.8, 136.7, 135.9, 131.2, 129.5, 129.4, 126.6, 126.1, 126.0, 125.8, 125.7, 125.6, 125.5, 124.4, 123.4, 122.1, 121.6, 121.2, 120.0, 119.7, 116.4, 114.0, 111.6, 68.1, 58.5, 57.5, 57.2, 55.1, 44.1, 40.4, 25.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{41}H_{41}N_4$: 589.3326; found: 589.3316.

HRMS (ESI): *m*/*z* $[M + 2H]^{2+}$ calcd for $C_{41}H_{42}N_4$: 295.1699; found: 295.1702.

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Supporting Information

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