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Steric hindrance to the syntheses and stabilities of 1,5- and 2,6-naphthalene N-permethylated diammonium salts

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Steric hindrance to the syntheses and stabilities of 1,5- and 2,6-naphthalene *N*-permethylated diammonium salts

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ABSTRACT

A series of naphthalene-1,5- and 2,6-diamines and their *N*-methyl derivatives were synthesized and characterized. ¹H NMR spectroscopy showed that an aqueous solution of naphthalene-2,6-di(NMe₃I) (**2**) underwent considerable demethylation over a 24 hour period after its initial preparation. Exchange of the iodide nucleophilic anion by the triflate non-nucleophilic counterion afforded a stable quaternary aminium salt. H/D α -position exchange in D₂O solutions of naphthalene-2,6-di(NH₂MeCl) (**3**•HCl) and naphthalene-2,6-di(NHMe₂Cl) (**4**•HCl) with acidic ¹NH protons was observed, but not in those of naphthalene-2,6-di(NMe₃I) or triflate (**2** or **5**). Exhaustive per-*N*-methylation of naphthalene-1,5-di(NMe₂) (**7**) afforded only the mixed naphthalene-1-NMe₃I-5-NHMe₂I quaternary aminium-tertiary ammonium salt due to severe 1,8-type *peri*-strain.

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1. Introduction

The ultra high binding of diamantane-4,9-di(NMe₃I) **1** to a cucurbit[7]uril host (with a $K_a = 7.2 \times 10^{17} \text{ M}^{-1}$ association constant in pure D₂O, and $K_a = 2.1 \times 10^{15} \text{ M}^{-1}$ in 50 mM NaO₂CCD₃ buffered D₂O at pD 4.74)¹ was the impetus to prepare other rigid-skeleton bisquaternary aminium guests with similar N⁺...N⁺ distances, but different space filling capabilities within the binding cavity. Naphthalene-2,6-di(NMe₃I) **2** was deemed to be a particularly auspicious candidate for synthesis since its 7.87(9) Å N⁺...N⁺ mean distance calculated from eight crystal structures in the Cambridge Structural Database (CSD) compared quite favorably with the 7.82(3) Å mean distance for **1** and its derivatives, while its planar skeleton differs greatly from that of cylindrical **1**. K_a binding constants and BLYP-D3/def2TZVPP quantum mechanical calculations of cucurbit[7]uril complexes of naphthalene, 4,4'-bipiperidine, and diamantane quaternary diaminium salts have recently been reported by us.²

The naphthalene compounds are of on-going interest in our group.³ It is well known that naphthalene amines have many applications and they are useful in many fields, such as in assisted laser desorption/ionization mass spectrometry for imaging of small molecules in tissues,⁴ as a part of conducting polymer as a matrix for biomolecule immobilization,⁵ in the preparation of functionalized Pt nanoparticles for study of electrochemical activity and redox chemistry occurring on one surface,⁶ in naphthylamine-based organic photovoltaic cells,⁷ as well as for reductive electron transfer to DNA.⁸ For these reasons we believe that it is important to improve known, or develop new, synthetic methods to make these compounds easily accessible.

Although the synthesis of 1,5- and 2,6-dimethylaminonaphthalenes was previously described,^{9,10} their *N*-permethylated derivatives are unknown in the literature, which is not surprising because the synthesis of naphthalene quaternary ammonium salts was not an easy task. The facile demethylation of initially formed naphthalene-2,6-di(NMe₃I) prompted us to also study steric factors in the more spatially challenged 1,5-naphthalene analogue.

In this paper we report simple methods for the synthesis of secondary to quaternary ammonium salts of 1,5- and 2,6-

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diaminonaphthalenes. These procedures are based upon the standard reductive amination using formaldehyde/H₂/PtO₂, which can be easily scaled-up if necessary. Permethylation using methyl iodide and methyl triflate as methylating agents is described as well.

2. Results and discussion

2.1. Synthesis of compounds

The synthesis of 2,6- and 1,5-substituted naphthalene derivatives **2-5**, **6-9**, and **15-16**, was based upon the corresponding dibromo or diamino derivatives as shown in Schemes 1, 2, and 3, respectively.

The methylamino derivative **3** was obtained by an Ullmann reaction¹¹ between 2,6-dibromonaphthalene and methylamine (78% yield). It was then converted to the corresponding **3**·HCl salt upon addition of HCl/Et₂O solution. To avoid permethylation, the reductive amination of naphthalene derivative **3** was utilized to prepare bis(dimethylamino)-naphthalene derivative **4**, which was then converted to the hydrochloride salt **4**·HCl. The permethylated derivative **2** (42% yield) was synthesized by methylation of **3** with an excess of MeI under basic conditions (CaCO₃), see Scheme 1. ¹H NMR spectra (D₂O) recorded immediately after isolation of salt **2**, compared to those recorded after 24 h in solution, showed that demethylation of compound **2** had occurred in the aqueous medium over a period of time (see Supporting Information, Fig. S12 and S13).

Scheme 1. (a) CH₃NH₂(aq), 10 mol% Cu, Δ, η = 78%; (b) HCl/Et₂O, η = quant.; (c) CH₂O(aq), H₂/PtO₂, EtOH, rt, 16 h, η = 55%; (d) MeI, CaCO₃, MeOH/H₂O, Δ, 16 h, η = 42%; (e) MeOTf, K₂CO₃, CH₃CN, Δ, 16 h, η = 75%.

A search of the CSD afforded 27 Ph-N⁺Me₂H tertiary ammonium substructures where the ⁺N—H bond eclipses a C_{Ar}(non-protonated)—C_{Ar}(methine) bond. Six of these structures exhibited ±3(2)° *synperiplanar* H—N—C_{Ar}(non-protonated)—C_{Ar}(methine) torsion angles. In these six structures, the two more sterically demanding ⁺N—C(methyl) bonds are *staggered* to the second C_{Ar}(non-protonated)—C_{Ar}(methine) bond [e.g. ±63(4)° *synclinal* C(methyl)—N—C_{Ar}(non-protonated)—C_{Ar}(methine) torsion angles]. Another characteristic feature of these aromatic amines is their 106.8(3)° H—N—C_{Ar}(non-protonated) and 112.3(6)° C(methyl)—N—C_{Ar}(non-protonated) bond angles. The *N,N,N*-trimethyl-aniline **10** (Refcode ICOVIG⁶) C_s-symmetry quaternary aminium cation occupies a special crystallographic position of crystallographic mirror symmetry within the *P*2₁/*m* lattice. This crystal structure is an appropriate model to discuss the situation when a more sterically demanding ⁺N—Me bond

ideally eclipses a C_{Ar}(non-protonated)—C_{Ar}(methine) bond, and the two other ⁺N—Me bonds each exhibit ±59.6° *synclinal* C(methyl)—N—C_{Ar}(non-protonated)—C_{Ar}(methine) torsion angles. The result of this steric challenge is a more opened 113.3° C_{Me}(eclipsed)—N—C_{Ar}(non-protonated) bond angle and two correspondingly compressed 109.8° C_{Me}(staggered)—N—C_{Ar}(non-protonated) bond angles (Figure 1). Furthermore, **10**'s angular compression is further exacerbated by its shorter 1.495 Å C(sp²)—⁺NMe₃ bond length⁶ versus the longer 1.596 Å C(sp³)—⁺NMe₃ bonds⁷ in the diamantane-4,9-di(NMe₃)I, **1** crystal structure (Refcode TOCMEF), see Figure 1. Now, C(sp³)-hybridization at the bridgehead-C(4 or 9) of crystalline **1** enabled all three N—CH₃ bonds to be *staggered* relative to the three vicinal C_{Diam}(sp³-quat)—C(methylene) bonds, and thereby produced more stable 111.4(5)° C_{Me}(staggered)—N—C_{Diam}(quat.) bond angles.⁷ The putative strain in the C_{Me}(eclipsed)—N—C_{Ar}(non-protonated) and C_{Me}(staggered)—N—C_{Ar}(non-protonated) bond angles in naphthalene-2,6-di(NMe₃)I (**2**) is likely to be a dominant factor behind its aqueous solution decomposition in the presence of the iodide nucleophilic anion over a period of time. This instability was overcome by permethylation with methyl triflate which afforded a stable bis-quaternary aminium salt **5** (75% yield) having triflate non-nucleophilic anions.

Fig. 1. Left: Strained 113.3° C(sp²)-N—C_{Me}(eclipsed) and one of the two 109.8° C(sp²)-N—C_{Me}(staggered) unequal bond angles within a fragment of crystalline *N,N,N*-trimethyl-aniline **10**. Right: Two of the three equal 111.4° C(sp³)-N—C(methyl) less-strained bond angles in a *N,N,N*-trimethylammonium-segment of crystalline diamantane-4,9-di(NMe₃)I, **1**.

Since we noticed steric problems in the stability of the 2,6-diaminonaphthalene permethylated quaternary ammonium salts, we were stimulated to investigate the preparation of the corresponding 1,5-diaminonaphthalene permethylated quaternary ammonium salts where we expected even greater steric interactions to be present.

The permethylation of readily available 1,5-di(NH₂)-naphthalene (**6**) with MeI resulted in formation of dimethylamino derivative **7**, which was further reacted to give mono salt **8a** (Scheme 2). Salt **9** was obtained by addition of hydroiodic acid to the methanolic solution of salt **8a**. Our attempts to achieve permethylation using dimethyl sulfate as the methylating agent only provided a mixture of bis-tertiaryammonium tetra-*N*-methyl **7** and penta-*N*-methyl **8b**, with no observed permethylated product. Isolation of product **8b** turned out to be very difficult due to contamination with inorganic byproducts (probably NaMeSO₄). We decided next to perform the permethylation reaction with methyl triflate as the methylating agent because methyl triflate generates triflate non-nucleophilic anions. All hexa-*N*-permethylation attempts of naphthalene-1,5-diamine with methyl triflate were unsuccessful since only the penta-*N*-methyl compound **8c** was produced.

Scheme 2. (a) HCl/Et₂O, $\eta = 90\%$; (b) CH₂O(aq), H₂/PtO₂, EtOH, rt, 16 h, $\eta = 95\%$; (c) HCl/Et₂O, $\eta = 93\%$; (d) MeI, CaCO₃, MeOH/H₂O, Δ , 16 h; (e) Me₂SO₄, Na₂CO₃, MeOH, Δ , 16 h; (f) MeOTf, K₂CO₃, CH₃CN, Δ , 16 h; (g) HI(aq)/MeOH, $\eta = 39\%$.

A search of the CSD produced no crystal structures with either a 1-mono- or 1,5-di(*N,N,N*-trimethyl)aminium substituted naphthalene skeleton. Therefore, 1,8-type *peri*-strain was studied with BLYP-D3/def2SVP geometry optimized models for tetra-*N*-methyl (**11** and **12**), penta-*N*-methyl (**13**), and hexa-*N*-methyl (**14**) substituted naphthalene 1,5-diamine cations. These correspond to **6**·HCl, **8**, and its permethylated derivative, respectively (Figure 2). The same sterically favored ⁺NH₃-synperiplanar-to-H(4 or 8) conformation (found twice in model-**11** and once in model-**13**), is also apparent in the naphthalene-1,5-di(*i*Pr) carbon analogue Refcode PAZLUZ crystal structure,¹⁴ see **12**. Since the constitutions of the calculated DFT models all differed, one should not compare their calculated energies. However, a structural comparison of their optimized geometries is certainly possible. The transition from tertiary ammonium ⁺NHMe₂ to quaternary aminium ⁺NMe₃ in the naphthalene-1,5-diamine models seem to engender considerable bond-angle strain which results in conformational change. This is readily observed by a change of the ⁺NH₃-synperiplanar relationship to H(4 or 8) tertiary ammonium conformation in **11**, **12**, **13** to one in which H(4) or H(8) now become staggered (i.e. a *synclinal* relationship) to their two immediate *N*-methyl neighbors in the quaternary substituent of **13**, **14** due to the well-known 1,8-*peri*-interaction in naphthalene. This concurrently also produces an increase in angles involving the ordinarily parallel C(1)—X and C(8)—X bonds [corresponding C(4)—X and C(5)—X] for X = H *peri*-substituents. In the tertiary ammonium *peri*-interaction, the N(1)—C(1)···C(8) and opposite H(8)—C(8)···C(1) angles are 91.2(9)° and 92.6(3)°, respectively. These open up due to lateral strain so that the N(1)—C(1)···C(8) and opposite H(8)—C(8)···C(1) angles now become 93.8(3)° and 94.1(7)° for quaternary aminium *peri*-substituents. The above measurements appear to afford a rationale for the observation of only one quaternary trimethylammonium *peri*-substituent on the 1,5-disubstituted naphthalene skeleton.

Figure 2. Non-bonding angles [N(1)—C(1)···C(8)], [N(2)—C(5)···C(4)], [H(4)—C(4)···C(5)], and [H(8)—C(8)···C(1)] open up due to lateral (1,8)-*peri*-strain in BLYP-D3/def2SVP models of *N,N,N*-trimethyl quaternary nitrogen disubstituted naphthalene-1,5-diamine.

Permethylated 2,6-bis(aminomethyl)naphthalene derivative **16** was prepared starting from 2,6-dibromonaphthalene as shown in Scheme 3. The Grignard reagent prepared from 2,6-dibromonaphthalene was reacted with DMF to afford dialdehyde **15** which was subsequently converted to **16** in 9% overall yield via a reductive amination and permethylation reaction sequence.

Scheme 3. (a) Mg/THF, Δ , $\eta = 15\%$; (b) DMF; (c) H₃O⁺; (d) Me₂NH, H₂/PtO₂, MeOH, rt, 16 h; (e) MeI, Na₂CO₃/MeOH, Δ , 16 h, $\eta = 62\%$ (2 steps).

2.2. H/D Exchange NMR studies

In the initial ¹H NMR spectrum of the bis-secondary ammonium salt **3**·HCl measured in D₂O, the integral of the aromatic-H signal at 8.05 ppm did not correspond to the 2 protons that are commonly assigned to the H(1) and H(5) *peri*-protons on naphthalene-2,6-disubstituted rings. Therefore, we decided to investigate possible H/D exchange (Scheme 4).

Scheme 4. Deuterium incorporation at positions 1- and 8- in 2,6-substituted naphthalene salts **3•HCl** and **4•HCl**.

The low-intensity or missing signal was now visible when the solvent was changed from D₂O to DMSO-*d*₆ or H₂O with benzene as a spin lock (see Supporting information, Fig. S4, S6 and S7). This observation was consistent with deuterium-exchange of the *peri*-protons. A second finding of deuterium-exchange arises from the ¹H NMR (CDCl₃) spectrum of naphthalene-2,6-di(NHMe) **3** free base measured before and after addition of a drop of D₂O (see Supporting information, Fig. S1 and S2). Twenty-four hours after D₂O addition, the H(1)/H(5) fine structure at 6.84±0.02 ppm was still present, but the integral intensity decreased. A similar H/D exchange at naphthalene-1,5-positions was also found to take place for the **4•HCl** bistertiary ammonium salt, but did not take place in the bisquaternary aminium salts (**2** and **5**). However, it is known from the literature that C-protonation, rather than N-protonation in 1,8-diaminonaphthalenes occurs in solvents which can act as hydrogen-bond acceptors, resulting in incorporation of deuterium into the naphthalene moiety.¹⁵ H/D exchange also takes place in pure naphthalene by acid-catalyzed reaction.¹⁶ Exchange at the α-position of naphthalene is faster than that at the β-position by a factor of ca. 10, and our results [the exchange observed in naphthalene 2,6-substituted derivatives (at the naphthalene α-position)] are in good agreement with those previously reported. Furthermore, exchange in 1,5-substituted derivatives was not observed due to its slower kinetic rate (at naphthalene β-position). We can conclude that ⁺NH protonated 2,6-naphthalenes (such as **3•HCl** and **4•HCl**)-catalyze H/D exchange at the α-positions of naphthalene in D₂O solution. Lack of an exchangeable ⁺NH proton in the bisquaternary aminium salts **2** and **5** is in complete accord with the absence of H/D exchange observed for these compounds.

3. Conclusions

Simple procedures for the synthesis of secondary to quaternary ammonium salts of 1,5- and 2,6-diaminonaphthalene **2-9** and **16** were reported. Analyses of DFT calculated models (BLYP-D3/def2SVP) were in accordance with experimental observations that bisquaternization of 1,5-diaminonaphthalene is unfavorable due to strong (1,8)-*peri* steric hindrance. Bisquaternary iodide salt **2** was unstable in solution due to reaction with its iodide nucleophilic counterion. However, bis-quaternary salt **5**, which has a triflate non-nucleophilic counterion, is stable in solution.

H/D exchange was observed in **3•HCl** and **4•HCl** in D₂O solution. It was found that H/D exchange at the α-positions of naphthalene in D₂O solution was catalyzed by ⁺NH.

4. Experimental section

4.1. General information

¹H and ¹³C spectra were recorded on a Bruker AV-300 or 600 MHz NMR spectrometer in solvents: D₂O (using dioxane as a reference in ¹³C spectra), DMSO-*d*₆ or CDCl₃ and are reported in ppm. Melting points were determined using an original Köfler Mikroheiztisch apparatus (Reichter, Wien) and are uncorrected. IR spectra were recorded on a FT-IR-ABB Bomem MB 102 spectrophotometer in KBr plates. HRMS were recorded only for new compounds. MALDI-TOF HRMS were obtained on an Applied Biosystems 4800 Plus MALDI TOF/TOF instrument (AB, Foster City, CA). Compounds 1,5-diaminonaphthalene, 2,6-dibromonaphthalene and 40% aqueous methylamine were purchased from commercial sources and were used as received. Solvents for chromatographic separations and recrystallizations (hexane, ethyl acetate, methanol, ethanol, diethyl-ether, and acetone) were used as received (p.a. grade purity) or purified by distillation (CH₂Cl₂).

No negative vibrational frequencies were found for the BLYP-D3/def2SVP calculated molecular models **11**, **13**, and **14**.

4.2. 2,6-Bis(methylamino)naphthalene **3**

A mixture of 2,6-dibromonaphthalene (500 mg, 1.75 mmol), 30% aqueous methylamine solution (10 mL, 87 mmol), and copper powder (32 mg, 0.5 mmol) were placed in a screw-cap pressure tube (50 mL) with a stirring bar, and stirred overnight on an oil bath at 100 °C. The color changed from light blue to dark blue during the reaction, and finally to black. After completion of the reaction, the reaction mixture was cooled to RT and the product was extracted with CH₂Cl₂ (3×20 mL). The combined extracts were dried over anhydrous MgSO₄ and the solvent was removed under reduced pressure. The crude product was purified on a column of silica gel using ethyl acetate/hexane (3:7) as the eluent to afford pure product **3** (342 mg, 78%) as a yellow crystalline solid; MP=126–128 °C; ν_{max} (KBr/cm⁻¹) 3402 (m), 3051 (w), 2922 (w), 1608 (s), 1522 (s), 1254 (s); δ_H (300 MHz, CDCl₃) 7.47 (d, *J* = 8.7 Hz, 2H), 6.83 (dd, *J* = 8.7, 2.0 Hz, 2H), 6.75 (d, *J* = 2.0 Hz, 2H); δ_C (150 MHz, CDCl₃) 144.4 (s), 128.9 (s), 126.9 (d), 118.1 (d), 104.9 (d), 31.0 (q); HRMS (MALDI): calcd. for [C₁₂H₁₄N₂]⁺ requires 186.1150; found 186.1153.

4.3. 2,6-Bis(methylamino)naphthalene dihydrochloride **3•HCl**

HCl/Et₂O was added dropwise to an ethereal solution of **3** (342 mg, 1.84 mmol) until complete precipitation was achieved. The solvent was removed by rotary evaporation to obtain pure **3•HCl** (477 mg, 100%) as a white solid; MP=225–228 °C; ν_{max} (KBr/cm⁻¹) 3431 (w), 2062 (s), 2762 (s), 2664 (s), 2428 (s), 1616 (w), 1525 (m), 1458 (m); δ_H (300 MHz, DMSO-*d*₆) 7.78 (d, *J* = 8.8 Hz, 2H), 7.43 (br. s, 2H, exchangeable), 7.34 (d, *J* = 8.8 Hz, 2H), 2.88 (s, 6H); δ_C (150 MHz, DMSO-*d*₆) δ: 128.3 (d), 128.1 (s), 123.1 (d), 121.7 (s), 120.4 (d), 33.5 (q).

4.4. 2,6-Bis(dimethylamino)naphthalene **4**

2,6-Bis(methylamino)naphthalene **3** (62 mg, 0.33 mmol) and 36% aqueous formaldehyde (1 mL) were dissolved in absolute ethanol (15 mL) in a round-bottomed flask and stirred vigorously overnight. The *in situ* formed Schiff base underwent reductive amination under a hydrogen atmosphere (balloon, 1 atm) and PtO₂ catalyst (10 mg, 0.04 mmol). The mixture was then filtered, and solvent removed on a rotary evaporator to afford a brown oil. The product was purified on a short column of silica gel using hexane/ethyl acetate (9:1) as the eluent to afford pure **4** (39 mg, 55%) as a light yellow solid, MP=150–151 °C [lit 148–150 °C];¹⁰

δ_{H} (300 MHz, CDCl_3) 7.56 (d, $J = 8.9$ Hz, 2H), 7.13 (dd, $J = 8.9$, 2.5 Hz, 2H), 6.90 (br. s, 2H), 2.98 (br. s, 12H); δ_{C} (75 MHz, CDCl_3) 146.7 (s), 128.3 (s), 127.1 (d), 117.6 (d), 107.5 (d), 41.4 (q).

4.5. 2,6-Bis(dimethylamino)naphthalene dihydrochloride **4**·HCl

Amine **4** (39 mg, 0.21 mmol) was converted to the corresponding **4**·HCl salt by adding a saturated solution of ethereal HCl to a Et_2O solution of **4** until complete precipitation was achieved. The crude product was recrystallized three times from ethanol/acetone (7:3) to obtain pure **4**·HCl (45 mg, 47%) as a white solid; MP=210–213 °C dec.; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3437 (w), 3020 (w), 2847 (w), 2536 (m), 2359 (s), 1618 (w), 1527 (m), 1475 (w); δ_{H} (300 MHz, D_2O) 8.28–8.22 (m, 4H), 7.83 (d, $J = 8.8$ Hz, 2H), 3.41 (s, 12H); δ_{C} (150 MHz, D_2O) 141.7 (s), 133.2 (s), 132.1 (d), 120.0 (d, 2C), 46.8 (q).

4.6. *N,N,N,N',N',N'*-hexamethylnaphthalene-2,6-diaminium diiodide **2**

2,6-Bis(methylamino)naphthalene **3** (62 mg, 0.33 mmol), CaCO_3 (62 mg, 0.67 mmol) and MeI (180 μL , 2.8 mmol) were mixed in MeOH/ H_2O (4:1, 400 μL) and the resulting suspension was refluxed overnight. Most of the CaCO_3 dissolved as the reaction proceeded. The resulting solution was filtered while hot, and the solvent was removed on a rotary evaporator. The solid residue was washed with hot acetone (5×10 mL) to afford a white powder, which was recrystallized three times from ethanol/acetone (3:7) to obtain pure **2** (70 mg, 42%) in the form of white crystals; MP=252–254 °C dec.; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3446 (s), 3030 (m), 3011 (m), 2918 (w), 1630 (s), 1606 (s), 1514 (s), 1472 (m), 1389 (m), 945 (s); δ_{H} (300 MHz, D_2O) 8.54 (d, $J = 2.8$ Hz, 2H), 8.36 (d, $J = 9.2$ Hz, 2H), 8.12 (dd, $J = 9.2$, 2.8 Hz, 2H), 3.81 (s, 18H); δ_{C} (75 MHz, D_2O) 146.2 (s), 132.9 (s), 132.8 (d), 124.3 (s), 119.8 (d), 119.6 (d), 57.6 (q); HRMS (MALDI): calcd. for $[\text{C}_{16}\text{H}_{24}\text{N}_2\text{I}]$ requires 371.0984; found 371.1010.

4.7. *N,N,N,N',N',N'*-hexamethylnaphthalene-2,6-diaminium triflate **5**

In a round-bottomed two-necked flask equipped with reflux condenser (all under N_2 -atmosphere), diamine **4** (40 mg, 0.19 mmol) was dissolved in anhydrous CH_3CN (8 mL) and K_2CO_3 was added. Methyl triflate (212 μL , 1.87 mmol) was slowly added with a microliter syringe. The resulting solution was refluxed overnight under N_2 , then cooled to RT, and diethyl-ether was added dropwise until complete precipitation occurred. The resulting white solid was washed with diethyl ether (5×5 mL) and then recrystallized three times from methanol/ether (9:1) to afford pure **5** (76 mg, 75%) as a white crystals; MP>320 °C; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3454 (w), 3088 (w), 3055 (w), 1608 (m), 1490 (s), 1255 (s), 1157 (s), 1030 (s), 638 (s); δ_{H} (300 MHz, D_2O) 8.57 (d, $J = 2.8$ Hz, 2H), 8.41 (d, $J = 9.2$ Hz, 2H), 8.16 (dd, $J = 9.2$, 2.8 Hz, 2H), 3.85 (s, 18H); δ_{C} (75 MHz, D_2O) 146.3 (s), 132.9 (d), 132.8 (s), 120.3 (q, $^1J_{\text{CF}} = 318$ Hz), 119.7 (d), 119.6 (d), 57.6 (q); HRMS (MALDI): calcd. for $[\text{C}_{15}\text{H}_{21}\text{N}_2\text{CF}_3\text{SO}_3]^+$ requires 393.1454; found 393.1458.

4.8. Naphthalene-1,5-diammonium dichloride **6**·HCl

1,5-Diaminonaphthalene **6** (164 mg, 1 mmol) was dissolved in Et_2O (20 mL) and a saturated solution of ethereal HCl was added until complete precipitation was achieved. The resulting grey precipitate was recrystallized from methanol/ether to afford pure **6**·HCl (208 mg, 90%) in the form of a greyish-white powder; MP=266–269 °C dec.; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3440 (w), 3022 (m), 2818 (s), 2590 (m), 1620 (m), 1577 (m), 1533 (s), 1414 (m); δ_{H} (300 MHz, D_2O) 8.08 (dd, $J = 6.8$, 2.5 Hz, 2H), 7.84–7.75 (m, 4H); δ_{C}

(75 MHz, D_2O) 128.1 (s), 128.0 (d), 127.92 (d), 127.90 (d), 127.7 (s).

4.9. 1,5-Bis(dimethylamino)naphthalene **7**

1,5-Diaminonaphthalene (164 mg, 1 mmol) and 36% aqueous formaldehyde (1 mL) were dissolved in abs. ethanol (20 mL) in a round-bottomed flask and stirred vigorously overnight. The *in situ* formed Schiff base underwent reductive amination under a hydrogen atmosphere (balloon, 1 atm) and PtO_2 catalyst (15 mg, 0.07 mmol). The mixture was filtered and solvent was then removed on rotary evaporator to afford crude product (378 mg) in the form of a brown-yellowish oil. The product was purified on a short column of silica gel using hexane/ethyl acetate (9:1) as eluent to afford pure **7** (204 mg, 95%) in the form of white solid; MP=88–89 °C [lit. 87–88 °C];¹⁰ δ_{H} (300 MHz, CDCl_3) 7.93 (d, $J = 8.8$ Hz, 2H), 7.42–7.34 (m, 2H), 7.05 (dd, $J = 7.4$, 0.6 Hz, 2H), 2.88 (s, 12H); δ_{C} (75 MHz, CDCl_3) 151.1 (s), 130.2 (s), 124.8 (d), 118.9 (d), 113.7 (d), 45.2 (q).

4.10. 1,5-Bis(dimethylamino)naphthalene dihydrochloride **7**·HCl

Compound **7** (204 mg, 0.95 mmol) was dissolved in Et_2O (20 mL) and saturated solution of ethereal HCl was added until complete precipitation was achieved. The salt was recrystallized three times from ethanol/acetone (7:3) to obtain pure product **7**·HCl (268 mg, 93%) in the form of white crystals; MP=214–216 °C dec.; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3431 (s), 3022 (w), 2850 (w), 2615 (s), 2434 (m), 1618 (w), 1520 (m), 1473 (s); δ_{H} (300 MHz, D_2O): 8.34 (d, $J = 8.7$ Hz, 2H), 8.13 (d, $J = 7.7$ Hz, 2H), 8.01–7.93 (m, 2H), 3.52 (s, 12H); δ_{C} (150 MHz, D_2O) 139.7 (s), 128.7 (d), 126.5 (s), 122.8 (d), 120.3 (d), 47.3 (q).

4.11. *N,N,N*-trimethylnaphthalen-1-aminium iodide-5-dimethylamine **8a**

MeI (2.6 mL, 41.8 mmol) was added to a suspension of 1,5-diaminonaphthalene (816 mg, 5 mmol) and CaCO_3 (1.12 g, 11.2 mmol) in MeOH/ H_2O (4:1, 10 mL). Following reflux (48 h) of the reaction mixture, the solvent was then removed by rotary evaporation to obtain a black thick oil. After three recrystallizations from ethanol/acetone (3:7) the free amine-quaternary salt **8a** (712 mg, 40%) was obtained in the form of a grayish-white solid; MP=173–174 °C; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3448 (w), 3105 (w), 2939 (m), 2842 (w), 1595 (s), 1454 (s), 793 (vs); δ_{H} (600 MHz, D_2O) 8.50 (d, $J = 8.6$ Hz, 1H), 8.16 (d, $J = 9.2$ Hz, 1H), 8.10 (d, $J = 8.6$ Hz, 1H), 7.78 (t, $J = 9.2$ Hz, 1H), 7.70 (t, $J = 8.2$ Hz, 1H), 7.47 (d, $J = 8.2$ Hz, 1H), 4.00 (s, 9H), 2.89 (s, 6H); δ_{C} (150 MHz, D_2O) 152.4 (s), 142.2 (s), 131.3 (s), 128.8 (d), 128.4 (d), 125.8 (s), 124.8 (d), 120.1 (d), 118.5 (d), 116.4 (d), 58.4 (q), 45.6 (q); HRMS (MALDI): calcd. for $[\text{C}_{15}\text{H}_{21}\text{N}_2]^+$ requires 229.1705; found 229.1709.

4.12. *N,N,N*-trimethylnaphthalen-1-aminium iodide-5-dimethylamine hydroiodide salt **9**

Compound **8a** (500 mg, 1.4 mmol) was dissolved in methanol and few drops of HI (conc.) was added. After evaporation of solvent and recrystallization from ethanol/acetone (3:7), pure **9** (270 mg, 39%) was obtained in the form of grayish-white crystals; MP=180–182 °C dec.; ν_{max} ($\text{KBr}/\text{cm}^{-1}$) 3418 (w), 3005 (m), 1616 (m), 1520 (m), 1472 (s); δ_{H} (300 MHz, D_2O) 8.70 (d, $J = 9.1$ Hz, 1H), 8.43 (d, $J = 8.8$ Hz, 1H), 8.29 (d, $J = 7.9$ Hz, 1H), 8.15 (d, $J = 7.9$ Hz, 1H), 8.05–7.89 (m, 2H), 4.03 (s, 9H), 3.52 (s, 6H); δ_{C} (150 MHz, D_2O) 142.9 (s), 140.8 (s), 128.4 (d), 128.3 (s), 127.7 (d), 126.0 (s), 125.6 (d), 124.5 (d), 121.6 (d), 119.8 (d), 58.8 (q), 47.4 (q); HRMS (MALDI): calcd. for $[\text{C}_{15}\text{H}_{21}\text{N}_2]^+$ requires 229.1705; found 229.1710.

4.13. Naphthalene-2,6-dicarbaldehyde **15**

The bis-Grignard reagent was prepared by adding the solution of 2,6-dibromonaphthalene (290 mg, 1 mmol) in dry THF (3 mL) to magnesium (97 mg, 4 mmol) in refluxing THF (dry, 7 mL). The reaction mixture was then cooled to RT and dry DMF (1 mL, 13 mmol) was added dropwise. After the resulting mixture was stirred 2 h at RT and 1 h at reflux, 1M HCl (15 mL) was slowly added, and stirring was continued overnight to completely convert the bis-Schiff base into the dialdehyde. The solvent was removed on a rotary evaporator, and the crude product was subjected to column chromatography on silica gel using CH₂Cl₂/hexane (1:1) as eluent to afford the dialdehyde product **15** (27 mg, 15%) in the form of an off-white solid; MP=170–172 °C [lit. 173.4–174.0 °C];¹⁷ $\nu_{\max}$ (KBr/cm⁻¹) 3448 (w), 2840 (m), 1687 (vs), 1333 (m), 1227 (m), 1111 (m); δ_{H} (300 MHz, CDCl₃) 10.22 (s, 2H), 8.40 (s, 2H), 8.15–8.03 (m, 4H); δ_{C} (75 MHz, CDCl₃) 191.6 (d), 136.1 (s), 135.6 (s), 133.5 (d), 130.5 (d), 124.0 (d).

4.14. 1,1'-(Naphthalene-2,6-diyl)-bis-(N,N,N-trimethylmethanaminium) diiodide **16**

Dialdehyde **15** (27 mg, 0.15 mmol) and 40% aqueous dimethyl amine (1 mL) were dissolved in absolute methanol (5 mL) in a round-bottomed flask. The *in situ* formed Schiff base underwent reductive amination under a hydrogen atmosphere (balloon, 1 atm) and PtO₂ catalyst (5 mg, 0.02 mmol) with vigorous stirring overnight. The mixture was filtered and the solvent was removed on rotary evaporator to afford the dimethylamino intermediate product (31 mg, 0.13 mmol) in the form of a white film on the walls of the flask. MeOH (10 mL) was added to dissolve the intermediate amine, followed by addition of Na₂CO₃ (20 mg, 0.2 mmol) and MeI (1 mL, 16 mmol). The resulting suspension was then refluxed overnight under N₂ atmosphere. The solvent was removed on a rotary evaporator and resulting yellow solid was washed with hot acetone (5×15 mL) until the yellow color was washed out. After drying, pure product **16** (49 mg, 62% over two steps) was obtained in the form of a white powder; MP>320 °C; $\nu_{\max}$ (KBr/cm⁻¹) 3427 (w), 2995 (m), 2966 (w), 1479 (s), 1402 (m), 877 (s); δ_{H} (300 MHz, DMSO-*d*₆) 8.23 (s, 2H), 8.16 (d, *J* = 8.5 Hz, 2H), 7.74 (dd, *J* = 8.5, 1.0 Hz, 2H), 4.76 (s, 4H), 3.12 (s, 18H); δ_{C} (75 MHz, DMSO-*d*₆) 132.6 (d), 129.8 (d), 128.8 (d), 127.2 (s, 2C), 67.8 (t), 52.0 (q); HRMS (MALDI): calcd. for [C₁₇H₂₅N₂]⁺ requires 257.2012; found 257.2016.

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