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H-Bond-Assisted Intramolecular Nucleophilic Displacement of the 1-NMe_2 Group in 1,8-Bis(dimethylamino)naphthalenes as a Route to Multinuclear Heterocyclic Compounds and Strained Naphthalene Derivatives

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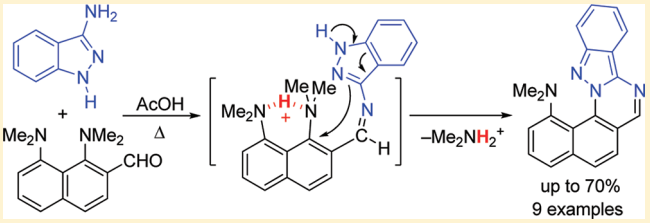
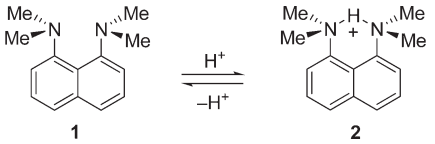
Supporting Information

ABSTRACT: It has been shown that azomethines, hydrazones, and oximes derived from 2(7)-carbonyl derivatives of 1,8-bis(dimethylamino)naphthalene can undergo acid-catalyzed heterocyclization leading to a nucleophilic displacement of the 1-NMe_2 group. The process is believed to be directly connected with the proton sponge nature of the substrates, in which 1-NMe_2, being a poor leaving group, is preliminary activated via the formation of a chelated protonated form. A number of difficult to access derivatives of benzo[*g*]indazole, benzo[*g*]quinazoline, naphtho[2,1-*d*]isoxazole, and 8-dimethylamino-1-naphthol have been prepared in moderate to high yields.



INTRODUCTION

Discovery of the abnormally high basicity of 1,8-bis(dimethylamino)naphthalene (**1**),[1] widely known as 'proton sponge', has raised a great interest in the nature of intramolecular hydrogen bonding (IHB) of its cation **2**. In dozens of papers such properties of the IHB such as symmetry and geometry,[2−5] energy,[6−8] the barrier and mechanism for proton transfer,[9−12] unusually strong deshielding of the chelated NH proton (δ 18−20 ppm),[13] etc., have been investigated (see reviews[14−19] for a general survey of the topic). As a result, it was concluded that the IHB strength in **2** after electrostatic and steric destabilization of the free base **1** is, by importance, a second factor contributing to the proton sponge basicity.[1,6,14−17] Due to the unique shortness of the IHB ($r_{N\cdots N}$ = 2.52−2.57 Å),[8,15−18] the proton sponge cations have also attracted considerable attention for proton transfer modeling in enzymatic reactions.[20]



For a long time, one question concerning the IHB in cations of type **2**, namely its influence on proton sponge reactivity, remained largely unexplored. However, even scarce information on this account reveals that such an influence is rather significant and can be displayed in specific forms.[21] For example, upon heating with mild nucleophiles (PhS^-, $PhSe^-$, SCN^-, I^-), protonated proton sponges lose one of the *N*-methyl groups, producing *N*,*N*,*N*′-trimethyl-1,8-diaminonaphthalene **3** or its derivatives in high yield.[22−24] The reaction is thought to occur via a classical S_N2 mechanism and is assisted by IHB, making compound **3** a good leaving group (Scheme 1). Interestingly, that *N*-ethyl group, e.g., in cation **5**, is almost inert to elimination, and the ease of removing the methyl attached to the same nitrogen atom as the ethyl is somewhat higher than that of methyls in the NMe_2 group. This circumstance was used for exhaustive realkylation of proton sponge **1** into its tetraethyl and tetrapropyl counterparts **4** that has no analogy in the arylamine series.[24]

RESULTS AND DISCUSSION

In the present work, we report for the first time that the IHB in proton sponge cations can promote not only nucleophilic replacement of the *N*-methyl group but the whole NMe_2 group as well. The process normally operates for proton sponge derivatives containing a nucleophilic center in the ortho-functionality and is accompanied by heterocyclization. Thus, after heating aldehyde **6**[25] with hydrazine monohydrobromide (1.2 equiv) in ethanol for 1 h, we have obtained hydrazone **7** and 9-dimethylaminobenzo[*g*]indazole **8** in 41% and 22% yields, respectively; a trace amount of azine **9** has also been isolated (Scheme 2).

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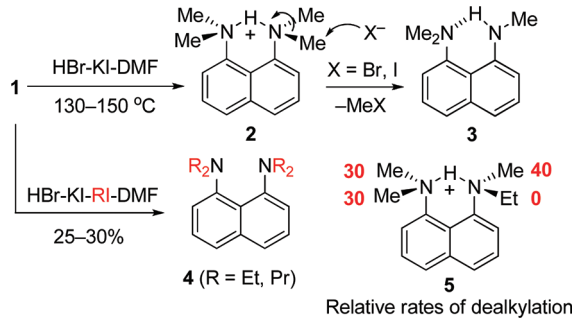
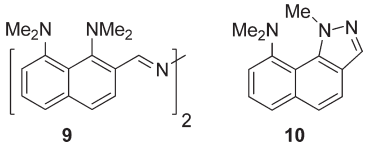
Scheme 1

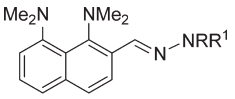


Owing to the enhanced basicity of proton sponges, the process most likely proceeds via cationic intermediate $7H^+$ equilibrating with σ-complex 7S, thus furnishing the elimination of dimethylamine in the form of dimethylammonium cation as a good leaving group in an S_N2Ar reaction. After the reaction time was increased to 3 h, the products **8** and **9** were obtained in 63% and 6% yields, respectively, while hydrazone **7** was not detected in the reaction mixture at all. Replacing ethanol by acetic acid (reflux, 1 h) dropped the yield of **8** to 6% due to acetylation of the hydrazone NH_2 group with the formation of compound **11a** (54%); azine **9** was not formed in this case. In contrast, **9** became the only isolable product in 45% or 99% yield when 1.2 equiv of hydrazine hydrate (24 h) or 0.5 equiv of hydrazine monohydrobromide (12 h) was used in EtOH at room temperature. Similar to that for hydrazine hydrobromide, heating aldehyde **6** with methylhydrazine hydrosulfate (1.2 equiv, EtOH, 5 h) gave 1-methylbenzo[*g*]indazole **10** in 67% yield. Use of AcOH as a solvent led in this case to the formation of commeasurable amounts of **10** (30%) and **11b** (33%).



9 **10**

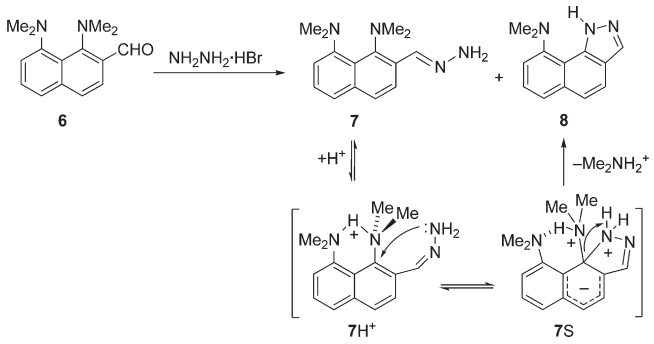
We had also prepared phenyl- and 2,4-dinitrophenylhydrazones **11c,d**, which failed to cyclize upon heating in acidic media (AcOH, HCl) probably due to their lowered nucleophilicity and sterics.



11a R = H, R^1 = COMe
11b R = Me, R^1 = COMe
11c R = H, R^1 = Ph
11d R = H, R^1 = 2,4-$(NO_2)_2C_6H_3$

In accordance with X-ray measurements, benzoindazole **8** exists in the solid state as the 1*H*-tautomer (Figure 1a,b). Though the N(1)···N(2) distance in molecule **8** (2.800 Å) is exactly the same as in the base **1**,[26] it is considerably larger than in proton sponge cations (see above). Besides, the N—H proton practically

Scheme 2



6 **7** **8** **7H+** **7S**

resides on pyrazole fragment [N(1)···H(2N) = 2.38 Å]. Thus, there is no substantial IHB in **8** between the N(1) and N(2) atoms. Instead, intermolecular hydrogen pairing is realized between molecules of **8** via the heterocyclic N(3) atom [N(3)···H(2N) = 2.20 Å] (Figure 1b, cf., ref 27). Apparently, in solution the NH proton in **8** is also located almost entirely at the N(2) nitrogen, because it resonates at δ = 12 ppm ($CDCl_3$), which is close to that of indazole (13.1 ppm in DMSO-d_6) and strongly differs from that of proton sponge cations (18—20 ppm).

Another kind of heterocyclization with the replacement of the 1-NMe_2 group was observed at interaction of aldehyde **6** with 3-aminoindazole in acetic acid or a ethanol—hydrochloric acid mixture (Scheme 3). This gave benzo[*h*]quinazoline derivative **13** as a single product in good yield in both cases. Obviously, the N(2) atom of the indazole system acts here as a nucleophile, and the cyclization is promoted by IHB in the protonated azomethine intermediate **12**. Having changed 3-aminoindazole for 2-aminobenzimidazole, we observed no reaction upon heating in acidic media (AcOH or EtOH—HCl). However, to our satisfaction, aldehyde **6** reacted with 2-aminobenzimidazole without any solvents upon melting at 135 °C for 10 min to give highly strained and likely helical isomeric derivative **15** in a moderate yield (Scheme 3).[28]

X-ray analysis of perchlorate **13**·$HClO_4$ has shown that the N(2)···N(4) distance (2.550 Å) in the seven-membered chelate is practically the same as in most proton sponge cations (Figure 2). It is therefore not surprising that the NH proton in the ^{1}H NMR spectrum of the salt resonates at δ 18.15 ppm (CD_3CN). At the same time, the IHB thus formed is highly asymmetric with the NH proton predominantly located on the NMe_2 group: the N(4)—H(4N) and N(2)···H(4N) distances are equal to 0.96 Å and 1.61 Å, respectively. As a consequence of this asymmetry, which is coupled with rather poor basicity of **13**, cation **13**·H^+ undergoes easy deprotonation not only in rather basic DMSO-d_6 but even in wet CD_3CN.

In the ^{1}H NMR spectrum ($CDCl_3$, 20 °C), benzoindazolo quinazoline **13** displays strong dynamics, showing a very diffuse signal from the NMe_2 group at δ 0.9—4.0 ppm; upon cooling to −50 °C, molecular movement is frozen and peaks from two magnetically unequal N—Me groups are distinctly separated (δ_H 1.48 and 3.46 ppm), indicating their asymmetrical disposition relative to the aromatic ring plane. In contrast to **13**, its benzimidazole counterpart **15** already reveals two magnetically unequal N—Me groups at room temperature (δ_H 1.45 and 2.61 ppm), reflecting more hindered dynamics of the NMe_2 group in this case that are apparently due to the nonflat, helical-like structure of **15** (see Supporting Information for peak assignments).

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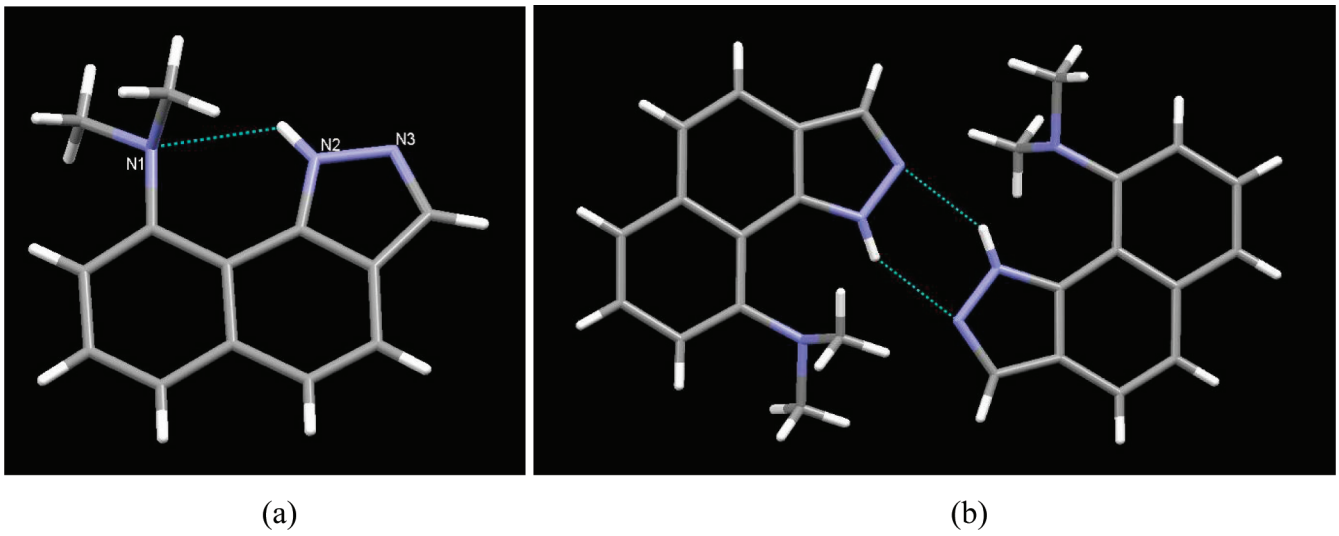
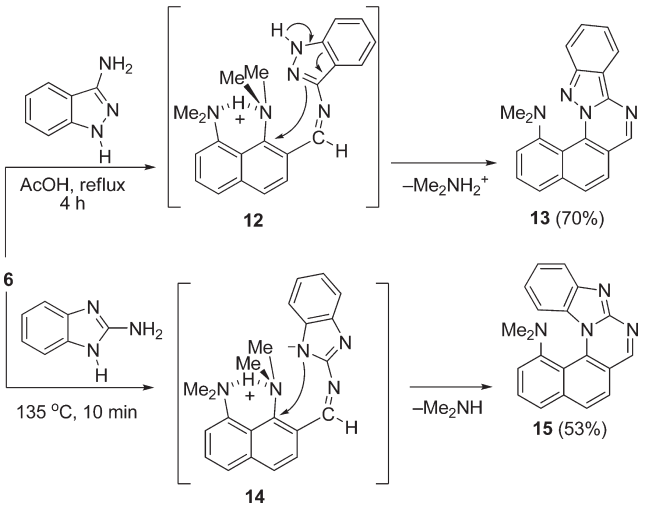


Figure 1. Molecular structure of compound **8** showing (a) weak H-bonding between the NMe_2 and pyrazole units and (b) pairing of **8** in crystals at 120 K.

Scheme 3



Interaction of aldehyde **6** with 5-aminotetrazole in boiling AcOH proceeds in a more complex manner than that with 3-aminoindazole and 2-aminobenzimidazole and gives 1-amino-10-dimethylaminobenzo[*h*]quinazolin-2-one **18** in 35% yield (Scheme 4). We suggest, that initially formed cyclization product **16** undergoes acid-catalyzed covalent hydration with subsequent elimination of a N_2 molecule from the intermediate **17**. The structure of **18**, apart from the high-resolution mass spectrum, is proved by the presence in its ^{1}H NMR spectrum of an exchangeable two-proton peak of the NH_2 group at δ 5.26 ppm ($CDCl_3$) or 6.72 ppm (DMSO-d_6). In the IR spectrum of **18**, absorption bands of the NH_2 and C=O groups are exhibited at ν_{max} 3324, 3183 cm^{-1} and 1653 cm^{-1}, respectively.[30]

We then reasoned that by analogy with hydrazone **7** the intramolecular replacement of the 1-NMe_2 group could be also possible for aldoxime **19**. In this case, naphtho[2,1-*d*]-isoxazole derivative **20** would be the expected reaction product. However, after melting the solid **19** at 120−130 °C for 12 h, we only isolated naphthonitriles **21** and **22**, in ~30% yield each (Scheme 5).

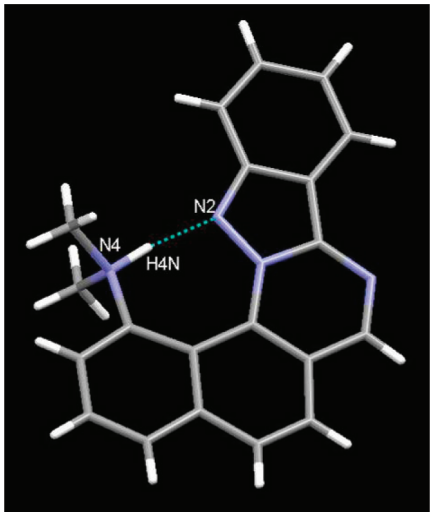


Figure 2. Molecular structure of salt **13**·$HClO_4$ at 120 K (anion ClO_4^- is omitted) showing intramolecular NHN bonding.

Whereas the formation of **22** can be treated as ordinary oxime dehydration, naphthol **21** may arise from the base-catalyzed[31] and well-known[32] isoxazole izomerization **20** → **21**. In special experiments (refluxing bases **19** and **22** or their hydrochlorides in water for 6 h or treatment of **19** and **22** with KOH in DMSO at 120 °C for 15 min), we have proved that the alternative formation of naphthol **21** via direct substitution of the dimethylamino group by an external hydroxylic nucleophile[33] does not occur.

Remarkably, the transformation of **19** in DMSO at 140−150 °C goes much faster (2 h against 12 h than that for the melt), giving naphthol **21** with almost perfect selectivity in more than 95% yield. In the ^{1}H NMR spectrum of the crude reaction mixture, only signals of **21** and dimethylamine (δ = 2.3 ppm) were seen. This observation in combination with several other facts may shed some light on the mechanism of the conversion **19** → **21**. We suggest that three main events should occur in the coversion of **19** to **21** (Scheme 6). The first one is the cleavage of aldoxime dimer **23**, to produce free **19** (see the

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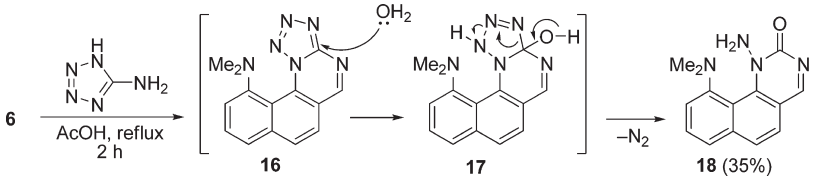
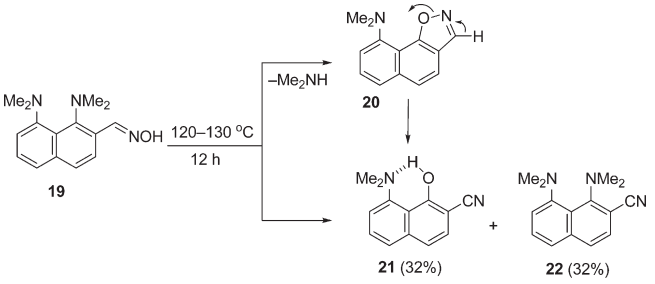
Scheme 4



Scheme 5



Supporting Information for X-ray structure of **19**); such dimers are typical for most oximes[36] and are usually rather stable.[37] Presumably, polarity (μ = 3.9 D) and basicity (pK_a = 0) of DMSO are high enough to disrupt the dimer structure, at least partially.

Because the *E*-form **19a**, arising from the dimer disruption, is stereochemically unready for cyclization, the second event should be the $E \rightarrow Z$ isomerization (**19a** → **19b**). This process also demands polar media and elevated temperature,[38] which are likely provided by using DMSO. The third event, namely the nucleophilic substitution of the 1-NMe_2 group, appears to be the most complex and unclear stage. We have come to a conclusion that both the nucleophilic group (OH) and the electrophilic center (C_1-atom) should be activated for the transformation **19** → **20** → **21**. Indeed, acidic ionization of the oxime group upon heating **19** in the KOH−DMSO system, where **19** exists exclusively as *O*-anion **26** (see Experimental Section for ^{1}H NMR data), is itself insufficient for heterocyclization and yields nitrile **22** as a sole product. Obviously, the capability of the CH═N−O^- group in **26** to act as a nucleophile in the heterocyclization reaction is considerably lowered owing to conjugation between the negatively charged oxygen atom and the ring π-system (Scheme 7).

On the other hand, prolonged reflux of the oxime hydrochloride **19**·HCl in EtOH or THF produces only traces of the naphthol **21** while melting of **19**·HCl leads to complete tarring. At the same time, naphthol **21** was obtained in 18% yield upon reflux of **19** in AcOH for 4 h, demonstrating once again that an enhanced temperature is an essential factor for the heterocyclization.[39] Thus, we have hypothesized that the *Z*-form self-stabilizes via the formation of hydrogen out-chelate **19b**,[25,40] which then rearranges[41] into zwitterionic chelate **24a**. A great advantage of the latter mechamsim is the simultaneous activation of the nucleophilic center (OH → O^-) and the enhancement of the leaving ability of the 1-NMe_2 group (bifunctional catalysis). Dimethyl sulfoxide is thought to play a key role as a polar media and proton-transfer carrier in the whole process; it may also more strongly accelerate the heterocyclization reaction (**19** → **20**) if compared with the dehydration of **19** into nitrile **22**.

For more evidence in favor of the involvement of zwitterion **24a**, we have measured by a NMR competitive method[42] the pK_a values of aldoxime **19** as a nitrogen base and a OH-acid. In the first case, the ^{1}H NMR spectrum of the equilibrating 1:1 mixture of **19** and **1**·$HClO_4$ has revealed that **19** (pK_a = 7.3, DMSO-d_6, 25 °C) is ca. 0.2 pK_a units less basic than the parent sponge **1** (see Supporting Information).[43] In the case of OH-acidity, no visible proton transfer occurred in DMSO-d_6 between **19** and **1**. At the same time, a strongly shifted equilibrium is established between **19** and its anion **26** in the presence of much more basic 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene (pK_a = 11.5, DMSO-d_6, 25 °C) (see Supporting Information).[44] The observed concentration of anion **26** (~1.5%) allowed us to estimate that the OH-acidity of **19** lies near pK_a = 15.1. Such a large difference between the pK'_as of the peri-nitrogen center and the OH group corresponds to a concentration of **24a** on the level of 10^{-7}−10^{-6} M. At first glance, this value is negligible, but one cannot exclude that the cyclization may still proceed via equilibrium quantities of the zwitterion species due to their high activity.[45] It is also known[46] that zwitterions are commonly strongly stabilized by the close proximity of the opposite charges as in the case of **24a**.

In light of the recent report that about 20% of hydroxylamine exists in water as ammonia oxide, NH_3^+−O^-,[47] we wonder if the related zwitterionic form **27** can contribute in the heterocyclization reaction (Scheme 8). In this case, the process could develop as a more complex version of the proton translation mechanism **19** → **27a** → **27b** → **24b** with the final $E \rightarrow Z$ isomerization into **24a**. Although the reliable choice between both pathways is difficult, Scheme 6 seems more preferable because the nitrogen basicity of hydroxylamine (pK_a = 5.7, in H_2O)[47] is much smaller than that of the proton sponges **1** and **19** (pK_a ~12).

Next, we have found that thermolysis of 2,7-dioxime **28** results in intramolecular substitution of only one NMe_2 group, furnishing compounds **30** and **31** in 32% and 20% yield, respectively (Scheme 9). This experiment can be considered as additional support in favor of the bifunctional catalysis, because the formation of OH···N hydrogen bonding in the primarily formed naphthol **29** should hamper the subsequent proton transfer from the remaining oxime group thus preventing its activation.

As expected, thermolysis of ketoximes **33a** and **33b** produces exclusively isoxazoles **34a** and **34b** in 64% yield each. Interestingly, unlike aldoximes **19** and **28**, we could not obtain ketoximes **33a** and **33b** directly by oximation of the corresponding 2-aroyl-1,8-bis(dimethylamino)naphthalenes[25] with hydroxylamine. Fortunately, this could be easily done from ketone imines **32a** and **32b** by their treatment with hydroxylamine hydrochloride (Scheme 10). The success of the latter protocol seems to consist of acid catalysis, allowing easier protonation of the imino function and therefore higher activity of an iminium group in nucleophilic addition as compared with the C═O group. Previously unknown

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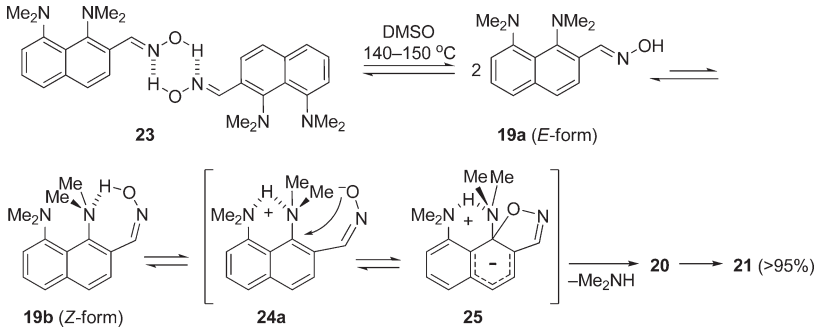
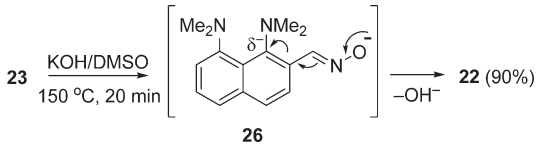
Scheme 6



Scheme 7



and unexpectedly stable imines **32** were prepared upon treatment of 2-lithio-1,8-bis(dimethylamino)naphthalene[25] with the corresponding benzonitriles (see Experimental Section for details).

Note that 2-dimethylaminobenzophenone oxime, as we have found, does not undergo reaction similar to that for **35** → **36**, and it remains unchanged upon heating at 120−130 °C (Scheme 11). This experiment gives further support to the main idea of the present work that the disclosed heterocyclizations of the above proton sponge substrates are promoted by acidic catalysis via chelation of the *peri*-NMe_2 groups.

CONCLUSIONS

In summary, in the present work we have demonstrated for the first time that naphthalene proton sponges with an appropriate nucleophilic ortho-functionality, such as the hydrazone, azomethine, or oxime group, can undergo intramolecular displacement of the nearest NMe_2 group, resulting in heterocyclization. The method is useful for the preparation of a number of naphthalene-based heterocycles and peri-substituted naphthalene derivatives, including strained molecules, which are obtainable with difficulty by other ways. The success of these transformations seems to originate from the proton sponge nature of the above substrates, which are strongly activated under conditions of acid or bifunctional acid−base catalysis or autocatalysis due to intramolecular H-bonding.

EXPERIMENTAL SECTION

1,8-Bis(dimethylamino)-2-(hydrazonomethyl)naphthalene (7). A solution of **6**[25] (100 mg, 0.41 mmol) and hydrazine hydrobromide (56 mg, 0.49 mmol) in ethanol (10 mL) was refluxed for 1 h. After evaporation of volatiles to dryness, the residue was treated with a 5% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 3 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3, first with $CHCl_3$ elution and then with Et_2O−*n*-hexane (1:1) to yield **7** (43 mg, 41%), **8** (19 mg, 22%), and a trace amount of **9**. Light-beige crystals, mp 171−173 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.90 (9H, s), 3.12 (3H, s), 4.57 (2H, br s), 7.03 (1H, dd, J = 7.3, 1.4 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.26−7.53 (3H, m), 7.94 (1H, s). Anal. Calcd for $C_{15}H_{20}N_4$: C, 70.28; H, 7.86; N, 21.86. Found: C, 70.29; H, 7.98; N, 21.91.

9-Dimethylamino-1*H*-benzo[*g*]indazole (8). A solution of **6** (100 mg, 0.41 mmol) and hydrazine hydrobromide (56 mg, 0.49 mmol) in ethanol (10 mL) was refluxed for 3 h. After evaporation of volatiles to dryness, the residue was treated with a 5% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 3 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3, first with $CHCl_3$ elution and then with Et_2O−*n*-hexane (1:1) to yield **8** (55 mg, 63%) and **9** (6 mg, 6%). Colorless crystals, mp 131−133 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.87 (6H, s), 7.38−7.57 (3H, m), 7.70 (2H, m), 8.11 (1H, s), 12.15 (1H, br s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 46.3, 117.6, 117.7, 119.8, 120.2, 122.7, 125.3, 126.9, 134.4, 134.9, 137.0, 151.3. EI MS: m/z (I, %) 211 $[M]^+$ (100), 196 (54), 181 (23), 168 (45), 140 (31), 115 (16), 44 (16). Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.85; H, 6.30; N, 19.92.

1,8-Bis(dimethylamino)naphthalene-2-carbaldehyde Azine (9). A solution of **6** (100 mg, 0.41 mmol) and hydrazine hydrobromide (24 mg, 0.21 mmol) in ethanol (10 mL) was kept at room temperature for 12 h. After evaporation of the volatiles to dryness, the residue was treated with a 5% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 3 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ to yield **9** (97 mg, 99%) as orange crystals with mp 165−166 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.77 (12H, s), 3.16 (12H, s), 7.05 (2H, dd, J = 7.1, 1.3 Hz), 7.27−7.43 (4H, m), 7.46 (2H, d, J = 8.5 Hz), 8.06 (2H, d, J = 8.5 Hz), 9.02 (2H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 46.0, 46.4, 115.2, 123.2, 124.5, 124.7, 125.7, 127.3, 128.2, 139.5, 152.1, 152.9, 162.6. EI MS: m/z (I, %) 240 $[M/2]^+$ (49), 225 (91), 210 (82), 196 (92), 181 (82), 168 (100), 154 (50), 141 (18), 127 (37), 115 (20), 58 (98), 44 (72). Anal. Calcd for $C_{30}H_{36}N_6$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.82; H, 7.39; N, 17.61.

9-Dimethylamino-1-methylbenzo[*g*]indazole (10). A solution of **6**[25] (100 mg, 0.41 mmol) and methylhydrazine hydrosulfate (71 mg, 0.49 mmol) in ethanol (10 mL) was refluxed for 5 h. After evaporation of volatiles to dryness, the residue was treated with a 5% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 3 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3, first with $CHCl_3$ elution and then with *n*-hexane to yield **10** (62 mg, 67%) as a pale-yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.98 (6H, s), 4.26 (3H, s), 7.23 (1H, dd, J = 6.5, 2.5 Hz), 7.34 (1H, d, J = 8.9 Hz), 8.11 (1H, s), 7.40−7.49 (2H, m), 7.52 (1H, d, J = 8.9 Hz), 7.85 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 40.7, 45.8, 115.7, 118.8, 120.4, 120.7, 123.2, 123.7, 124.8, 126.6, 135.2, 144.9, 151.0. EI MS: m/z (I, %) 225 $[M]^+$ (91), 211 (20), 210 $[M - Me]^+$ (100), 196 (43), 195 (25), 181 (25), 140 (18), 57 (26), 55 (19), 43 (34), 42 (42), 41 (29). Anal. Calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.72; H, 6.80; N, 18.61.

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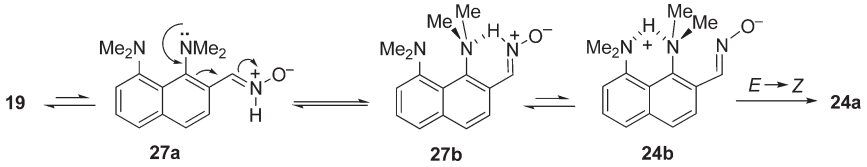
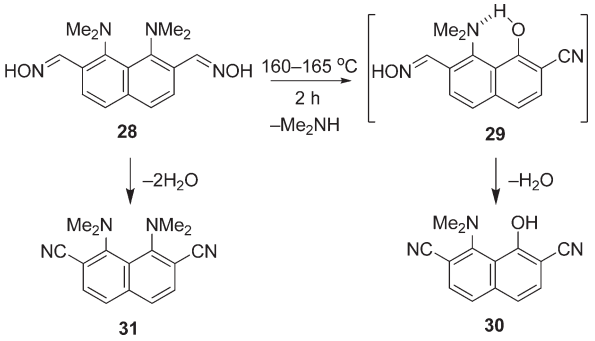
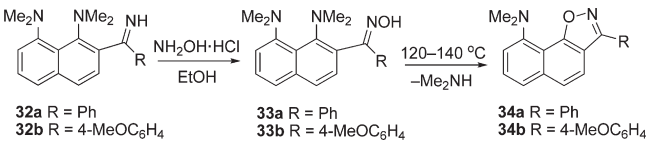
Scheme 8



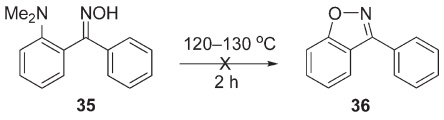
Scheme 9



Scheme 10



Scheme 11



***N′*-[(1,8-Bis(dimethylamino)naphthalen-2-yl)methylene]-acetohydrazide (11a).** A solution of **6** (100 mg, 0.41 mmol) and hydrazine hydrobromide (56 mg, 0.49 mmol) in AcOH (10 mL) was refluxed for 1 h. After evaporation of volatiles to dryness, the residue was treated with a 10% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 4 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **11a** as yellow crystals (66 mg, 54%) with mp 198−200 °C (*n*-hexane−$CHCl_3$, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.39 (3H, s), 2.74 (6H, s), 3.06 (6H, s), 7.07 (1H, d, J = 7.0 Hz), 7.25−7.47 (3H, m), 7.81 (1H, d, J = 8.5 Hz), 8.02 (1H, s), 9.00 (1H, br s). Anal. Calcd for $C_{17}H_{22}N_4O$: C, 68.43; H, 7.43; N, 18.78. Found: C, 68.52; H, 7.56; N, 18.83.

***N′*-[(1,8-Bis(dimethylamino)naphthalen-2-yl)methylene]-*N*-methylacetohydrazide (11b).** A solution of **6** (100 mg, 0.41 mmol) and methylhydrazine hydrosulfate (71 mg, 0.49 mmol) in AcOH (10 mL) was refluxed for 2 h. After evaporation of volatiles to dryness, the residue was treated with a 10% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 4 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **11b** (42 mg, 33%) and **10** (28 mg, 30%). Yellow crystals, mp 114−116 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.50 (3H, s), 2.75 (6H, s), 3.08 (6H, s), 3.40 (3H, s), 7.09 (1H, dd, J = 7.0, 1.2 Hz), 7.31 (1H, t, J = 7.7 Hz), 7.39 (1H, dd, J = 7.9, 1.2 Hz), 7.46 (1H, d, J = 8.6 Hz), 7.86 (1H, d, J = 8.6 Hz), 7.96 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 22.2, 27.9, 45.8, 46.3, 115.7, 123.6, 124.6, 125.0, 125.3, 126.9, 129.2, 138.7, 140.2, 150.0, 152.7, 173.3. Anal. Calcd for $C_{18}H_{24}N_4O$: C, 69.20; H, 7.74; N, 17.93. Found: C, 69.38; H, 7.67; N, 18.00.

General Procedure for Preparation of 11c and 11d. A solution of **6** (100 mg, 0.41 mmol), corresponding arylhydrazine (0.41 mmol), and 38% HCl (0.033 mL, 0.41 mmol) in EtOH (10 mL) was refluxed for 1 h. After evaporation of volatiles to dryness, the residue was treated with a 5% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 4 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **11c** or **11d**.

1,8-Bis(dimethylamino)-2-((2-phenylhydrazono)methyl)naphthalene (11c). Yield 25%. Light-beige crystals, mp 136−139 °C (decomp, *n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.75 (6H, s), 3.07 (6H, s), 6.85 (1H, t, J = 7.3 Hz), 7.05−7.19 (3H, m), 7.23−7.33 (3H, m), 7.40 (1H, d, J = 7.9 Hz), 7.48 (1H, d, J = 8.7 Hz), 7.68 (1H, br s), 8.20 (2H, m). Anal. Calcd for $C_{21}H_{24}N_4$: C, 75.87; H, 7.28; N, 16.85. Found: C, 75.79; H, 7.30; N, 16.74.

1,8-Bis(dimethylamino)-2-((2-phenylhydrazono)methyl)naphthalene hydrochloride (**11c**·HCl) was prepared in MeOH upon addition of 1 equiv of 38% aqueous HCl; yellow crystals, mp 280−283 °C (decomp, MeOH), yield 96%. ^{1}H NMR (250 MHz, DMSO-d_6): δ 3.24 (6H, s), 3.30 (6H, d, J = 3.2 Hz), 6.85 (1H, t, J = 7.1 Hz), 7.16 (2H, m), 7.29 (2H, m), 7.70 (1H, t, J = 7.9 Hz), 7.99−8.16 (3H, m), 8.35 (1H, d, J = 8.8 Hz), 8.58 (1H, s), 11.02 (1H, s), 18.56 (1H, br s). Anal. Calcd for $C_{21}H_{24}N_4$·HCl: C, 68.37; H, 6.83; Cl, 9.61; N, 15.19. Found: C, 68.47; H, 6.95; Cl, 9.54; N, 15.24.

1,8-Bis(dimethylamino)-2-(2-(2,4-dinitrophenyl)hydrazono)-methylnaphthalene (11d). Yield 52%. Wine-red crystals, mp 201−203 °C (EtOH). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.72 (6H, s), 3.11 (6H, s), 7.10 (1H, dd, J = 7.0, 1.3 Hz), 7.27−7.54 (3H, m), 7.91 (1H, d, J = 8.5 Hz) 8.11 (1H, d, J = 9.8 Hz), 8.35 (2H, m), 9.14 (1H, d, J = 2.5 Hz), 11.34 (1H, br s). Anal. Calcd for $C_{21}H_{22}N_6O_4$: C, 59.71; H, 5.25; N, 19.89. Found: C, 59.79; H, 5.30; N, 19.83.

***N*,*N*-Dimethylbenzo[*h*]indazolo[2,3-*a*]quinazolin-1-amine (13).** A solution of **6** (100 mg, 0.41 mmol) and 3-aminoindazole (55 mg, 0.41 mmol) was refluxed in AcOH (10 mL) for 4 h or in EtOH (10 mL) for 12 h with addition of aqueous 38% HCl (0.033 mL, 0.41 mmol). After evaporation of volatiles to dryness, the residue was treated with a 10% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 5 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **13** as orange crystals (90 mg, 70%) with mp 129−132 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$, ^{1}H−^{1}H COSY): δ 0.9−4.0 (6H, br s), 7.29−7.43 (3H, m), 7.65 (2H, m), 7.80 (2H, m), 7.95 (1H, d, J = 8.53 Hz), 8.47 (1H, d, J = 8.21 Hz), 9.80 (1H, s). ^{1}H NMR (250 MHz, $CDCl_3$, −50 °C): δ 1.48 (3H, br s), 3.46 (3H, br s), 7.30−8.09 (8H, m), 8.46 (1H, br d, J = 7.9 Hz), 9.09 (1H, s). ^{1}H NMR (250 MHz, CD_3OD): δ 1.00−3.90 (6H, very br s), 7.38−7.58 (3H, m), 7.73 (2H, m), 7.95 (1H, d, J = 8.5 Hz), 8.02 (2H, m), 8.46 (1H, d, J = 8.4 Hz), 9.24 (1H, s). ^{1}H NMR (250 MHz, DMSO-d_6): δ 1.40−3.20 (6H, very br s), 7.33−7.51 (3H, m), 7.69

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(2H, m), 7.93 (1H, d, J = 8.7 Hz), 8.02 (1H, d, J = 8.5 Hz), 8.09 (1H, d, J = 8.7 Hz), 8.38 (1H, d, J = 8.2 Hz), 9.32 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 41.0, 110.0, 114.3, 115.1, 116.2, 117.5, 118.5, 121.2, 121.6, 123.2, 128.4, 129.1, 130.1, 134.8, 138.6, 142.1, 144.7, 150.6, 151.7. EI MS: m/z (I, %) 312 $[M]^+$ (51), 297 (100), 269 (16), 193 (22), 148 (11), 44 (11). Anal. Calcd for $C_{20}H_{16}N_4$: C, 76.90; H, 5.16; N, 17.94. Found: C, 76.87; H, 5.11; N, 18.00.

N,N-Dimethylbenzo[*h*]indazolo[2,3-*a*]quinazolin-1-amine perchlorate (**13**·$HClO_4$) was prepared in MeOH upon addition of 1 equiv of 40% aqueous $HClO_4$; beige crystals, mp 264−267 °C (decomp, dry MeCN). ^{1}H NMR (250 MHz, CD_3CN): δ 3.29 (6H, s), 7.64 (1H, t, J = 7.4 Hz), 7.96 (1H, m), 8.15 (1H, d, J = 8.8 Hz), 8.25 (1H, t, J = 8.1 Hz), 8.40−8.60 (5H, m), 9.63 (1H, s), 18.15 (1H, br s). Anal. Calcd for $C_{20}H_{16}N_4$·$HClO_4$: C, 58.19; H, 4.15; Cl, 8.59; N, 13.57. Found: C, 58.21; H, 4.23; Cl, 8.52; N, 13.64.

N,N-Dimethylbenzo[*h*]benzimidazolo[2,3-*a*]quinazolin-1-amine (15). A mixture of **6** (100 mg, 0.41 mmol) and 2-aminobenzimidazole (55 mg, 0.41 mmol) was heated in an argon atmosphere at 135 °C for 10 min. The fused mixture was cooled to 20 °C and chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **15** as orange crystals (68 mg, 53%) with mp 109−111 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$, ^{1}H−^{1}H COSY): δ 1.45 (3H, s), 2.61 (3H, s), 7.15−7.31 (3H, m), 7.46−7.58 (2H, m), 7.73 (1H, t, J = 7.8 Hz), 7.84 (2H, m), 8.03 (1H, d, J = 8.4 Hz), 9.22 (1H, s). ^{1}H NMR (250 MHz, $CDCl_3$ + 3CF_3COOH, crimson-colored solution): δ 1.59 (3H, s), 2.69 (3H, s), 7.45 (3H, m), 7.71 (1H, d, J = 7.5 Hz), 7.82 (1H, m), 7.93−8.07 (3H, m), 8.15 (1H, d, J = 8.8 Hz), 9.57 (1H, s), 9.75 (1H, br s). EI MS: m/z (I, %) 312 $[M]^+$ (100), 311 (64), 297 (15), 268 (33), 267 (17), 44 (16), 42 (30). Anal. Calcd for $C_{20}H_{16}N_4$: C, 76.90; H, 5.16; N, 17.94. Found: C, 76.98; H, 5.23; N, 17.89.

1-Amino-10-dimethylaminobenzo[*h*]quinazolin-2(1*H*)-one (18). A solution of **6** (100 mg, 0.41 mmol) and 5-aminotetrazole (35 mg, 0.41 mmol) was refluxed in AcOH (10 mL) for 4 h. After evaporation of volatiles to dryness, the residue was treated with a 10% solution of NH_4OH (5 mL) and then extracted with $CHCl_3$ (3 × 10 mL). The solvent was evaporated to dryness, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution to yield **18** as yellow crystals (37 mg, 35%) with mp 159−160 °C (*n*-octane). IR (ν/cm^{-1}) (KBr): 3324, 3183 (NH_2), 1653 (C=O). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.95 (6H, br s), 5.26 (2H, br s), 7.19 (1H, d, J = 6.5 Hz), 7.32−7.61 (4H, m), 8.88 (1H, s). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.86 (6H, s), 6.72 (2H, br s), 7.12 (1H, dd, J = 7.9, 1.1 Hz), 7.35 (1H, dd, J = 7.9, 1.1 Hz), 7.43 (1H, d, J = 8.9 Hz), 7.52 (2H, m), 8.92 (1H, s). ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 45.6, 115.2, 117.5, 120.5, 120.9, 124.4, 125.2, 130.2, 139.9, 153.1, 153.3, 160.6, 161.4. CI MS: m/z (I, %) 478 $[2M + 2H]^{2+}$ (2.8), 255 $[M + H]^+$ (0.7), 239 $[M - NH_2 + H]^+$ (100). EI MS: m/z (I, %) 238 $[M - NH_2]^+$ (20), 223 (43), 296 (55), 195 (21), 168 (38), 152 (19), 140 (61), 126 (37), 119 (25), 113 (18), 75 (17), 63 (22), 42 (100). Anal. Calcd for $C_{14}H_{14}N_4O$: C, 66.13; H, 5.55; N, 22.03. Found: C, 66.21; H, 5.48; N, 22.07.

General Procedure for Preparation of 19 and 28. A mixture of NH_2OH·HCl (100 mg, 1.5 mmol) and K_2CO_3 (220 mg, 1.6 mmol) in EtOH (10 mL) was stirred for 15 min at 20 °C. Then a solution of **6** (150 mg, 0.65 mmol) or 1,8-bis(dimethylamino)-2,7-diformylnaphthalene[25] (90 mg, 0.33 mmol) in EtOH (2 mL) was added, and the stirring was continued for 2 h. The resulting mixture was filtered, the solvent was evaporated to dryness, and the residue was recrystallized from *n*-hexane to give **19** or from *n*-octane to give **28**.

(*E*)-1,8-Bis(dimethylamino)naphthalene-2-carbaldehyde Oxime (19). Yield 80%. Golden-yellow crystals, mp 109−110 °C (*n*-hexane). IR (ν/cm^{-1}) (KBr): 3150−3450 (OH). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.69 (6H, s), 2.97 (6H, s), 7.09 (1H, br d, J = 7.3 Hz), 7.32 (1H, t, J = 7.9 Hz), 7.40−7.50 (m, 2H), 7.66 (1H, d, J = 8.5 Hz), 8.29 (1H, s), 11.15 (1H, s). ^{1}H NMR (250 MHz, DMSO-d_6 + 1 equiv KOH, *O*-anion **26**): δ 2.69 (6H, s), 2.89 (6H, s), 7.00 (1H, br d, J = 7.0 Hz), 7.12 (1H, t, J = 7.5 Hz), 7.25−7.34 (m, 2H), 8.08 (1H, d, J = 8.8 Hz), 8.13 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 46.2, 46.4, 116.2, 124.2, 125.7, 125.8, 125.9, 127.1, 127.8, 139.8, 151.0, 152.2, 153.7. EI MS, m/z (I, %): 257 $[M]^+$ (67), 241 (20), 240 $[M - OH]^+$ (100), 225 (24), 224 (29), 212 (22), 211 (26), 209 (32), 197 (49), 196 (52), 195 (35), 193 (24), 182 (33), 181 (22), 168 (33), 167 (23). UV−vis (MeCN): λ_{max} (log ε) 224 (4.49), 266 (4.60), 338 (3.95). Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33. Found: C, 70.29; H, 7.47; N, 16.39.

1,8-Bis(dimethylamino)naphthalene-2,7-dicarbaldehyde Dioxime (28). Yield 78%. Yellow crystals, mp 160−162 °C (from *n*-octane). IR (ν/cm^{-1}) (KBr): 3430−3105 (br, OH). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.95 (12H, s), 7.59 (2H, d, J = 8.5 Hz), 7.73 (2H, d, J = 8.5 Hz), 8.27 (2H, s), 11.33 (2H, s). ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 46.6, 126.3, 127.7, 131.9, 132.6, 139.4, 149.1, 150.7. EI MS, m/z (I, %): 300 $[M]^+$ (61), 283 (74), 265 (35), 251 (31), 238 (87), 236 (48), 223 (43), 222 (68), 221 (46), 220 (39), 210 (29), 209 (29), 208 (31), 207 (42), 206 (28), 194 (27), 193 (38), 167 (28), 58 (64), 44 (100), 42 (50), 40 (36), 36 (77). UV−vis (MeCN): λ_{max} (log ε) 273 (5.04), 341 (4.15). Anal. Calcd for $C_{16}H_{20}N_4O_2$: C, 63.98; H, 6.71; N, 18.65. Found: C, 63.72; H, 6.74; N, 18.72.

General Procedure for Preparation of 32a and 32b. A solution of the corresponding nitrile (benzonitrile for **32a** (0.49 mL, 0.5 mmol) or *p*-methoxybenzonitrile for **32b** (67 mg, 0.5 mmol)) in absolute Et_2O (10 mL) was added to a cold (−20 °C) solution of 2-lithio-1,8-bis(dimethylamino)naphthalene[25] (100 mg, 0.45 mmol) in absolute Et_2O (10 mL) under argon atmosphere. The resulting mixture was kept at −20 °C for 30 h and quenched with water (10 mL). The organic layer was separated, and the water layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were evaporated to dryness, and the residue was chromatographed on Al_2O_3 with Et_2O−hexanes (2:1) elution to yield **32a** or **32b**.

1,8-Bis(dimethylamino)-2-(imino(phenyl)methyl)naphthalene (32a). Yield 65%. Yellow crystals, mp 113−114 °C (*n*-hexane). IR (ν/cm^{-1}) (paraffin oil): 3250 (NH). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.54 (6H, s), 2.70 (6H, s), 7.03 (1H, dd, J = 7.6, 1.0 Hz), 7.07−7.19 (1H, very br d), 7.30−7.55 (8H, m), 10.25 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 45.0, 45.6, 115.2, 123.3, 124.0, 124.3, 127.6, 128.4, 129.3, 129.4, 131.8, 133.8, 139.8, 141.0, 148.7, 153.5, 181.9. EI MS, m/z (I, %): 317 $[M]^+$ (100), 302 (41), 301 (70), 286 (68), 273 (41), 240 (28), 168 (36), 127 (28), 104 (38), 77 (60), 44 (35), 42 (37). Anal. Calcd for $C_{21}H_{23}N_3$: C, 79.46; H, 7.30; N, 13.24. Found: C, 79.14; H, 7.33; N, 13.29.

1,8-Bis(dimethylamino)-2-(imino(*p*-methoxyphenyl)methyl)-naphthalene (32b). Yield 60%. Yellow crystals, mp 108−109 °C (*n*-hexane). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.58 (6H, s), 2.71 (6H, s), 3.77 (3H, s), 6.93 (2H, d, J = 8.9 Hz), 7.02 (1H, dd, J = 7.4, 1.3 Hz), 7.08 (1H, d, J = 8.4 Hz), 7.33 (1H, t, J = 7.9 Hz), 7.38−7.58 (4H, m), 9.96 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 45.1, 45.5, 56.1, 114.5, 115.1, 123.2, 123.8, 124.1, 127.5, 128.3, 131.3, 133.4, 133.8, 139.7, 148.5, 153.5, 163.0, 180.9. EI MS, m/z (I, %): 347 $[M]^+$ (100), 332 (48), 331 (98), 316 (54), 303 (28), 168 (34). Anal. Calcd for $C_{22}H_{25}N_3O$: C, 76.05; H, 7.25; N, 12.09. Found: C, 76.35; H, 7.22; N, 12.14.

General Procedure for Preparation of 33a and 33b. Solid imines (**32a** (230 mg, 0.73 mmol) or **32b** (250 mg, 0.72 mmol)) were added to a solution of NH_2OH·HCl (100 mg, 1.5 mmol) in EtOH (10 mL). The resulting dark red mixture was refluxed for 4 h. The solvent was evaporated, and the residue was neutralized with a 5% NH_4OH solution (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The solvent was evaporated to dryness, and the residue was recrystallized from benzene−*n*-hexane (for **33a**) or methanol−water (for **33b**) to give an inseparable mixture of syn- and anti-forms of the corresponding oximes (2:1 for **33a** and 3:1 for **33b**).

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(1,8-Bis(dimethylamino)naphthalen-2-yl)(phenyl)methanone Oxime (33a). Yield 71%. Yellow crystals, mp 120−122 °C (C_6H_6−*n*-hexane). IR (ν/cm^{-1}) (paraffin oil): 3430−3105 (br, OH). ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.49−2.80 (12H, m), 6.96−7.07 (2H, m), 7.20−7.53 (8H, m), 11.27 (0.65H, s), 11.38 (0.35H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 43.8, 44.4, 44.7, 45.9, 46.1, 47.3, 114.8, 115.2, 123.3, 123.6, 123.9, 124.3, 125.2, 126.0, 127.4, 127.5, 128.3, 128.7, 129.0, 129.4, 129.6, 130.4, 130.7, 131.3, 131.9, 135.5, 138.5, 139.8, 149.6, 150.0, 153.3, 153.5, 159.6, 161.4. EI MS, *m*/*z* (*I*, %): 333 [M]$^+$ (44), 316 [M − OH]$^+$ (58), 289 (40), 288 (100), 273 (87), 258 (27), 193 (27), 182 (33), 168 (95), 167 (47), 154 (35), 128 (29), 127 (51), 115 (35), 91 (38), 77 (92), 51 (41), 44 (62), 42 (56). Anal. Calcd for $C_{21}H_{23}N_3O$: C, 75.65; H, 6.95; N, 12.60. Found: C, 75.55; H, 6.98; N, 12.55.

(1,8-Bis(dimethylamino)naphthalen-2-yl)(*p*-methoxyphenyl)-methanone Oxime (33b). Yield 70%. Yellow crystals, mp 126−129 °C (MeOH−H_2O). IR (ν/cm^{-1}) (paraffin oil): 3430−3134 (br, OH). ^{1}H NMR (DMSO-d_6): δ 2.55−2.90 (12H, m), 3.76 (3H, s), 6.88−6.94 (∼2H, m), 6.98−7.70 (∼2H, m), 7.22 (2H, d, *J* = 9.0 Hz), 7.25−7.55 (∼3H, m), 11.08 (0.75H, s), 11.30 (0.25H, s). EI MS, *m*/*z* (*I*, %): 363 [M]$^+$ (40), 346 [M − OH]$^+$ (53), 319 (32), 318 (73), 303 (100), 168 (49), 127 (27), 121 (58), 115 (26), 92 (35), 77 (56), 64 (32), 63 (28), 44 (55), 42 (47). Anal. Calcd for $C_{22}H_{25}N_3O_2$: C, 72.70; H, 6.93; N, 11.56. Found: C, 72.99; H, 6.96; N, 11.61.

General Procedure for Preparation of 21 and 22, 30 and 31, 34a and 34b. A solid compound [**19** (100 mg, 0.39 mmol) or **28** (100 mg, 0.33 mmol) or **33a** (100 mg, 0.30 mmol) or **33b** (100 mg, 0.28 mmol)] was kept for 12 h at 120−130 °C (for **19**), 2 h at 160−165 °C (for **28**), 2 h at 120−130 °C (for **33a**), or 3 h at 130−140 °C (for **33b**) with stirring under argon atmosphere. The fused mixture was cooled to 20 °C and chromatographed on Al_2O_3/Et_2O−*n*-hexane (1:1) (for **21** and **22**), Al_2O_3/$CHCl_3$−*n*-hexane (1:1) (for **30** and **31**), or Al_2O_3/$CHCl_3$ (for **34a** and **34b**), correspondingly. The solvents were evaporated to yield the products.

2-Cyano-8-dimethylamino-1-naphthol (21). Yield 32%. Beige crystals, mp 105−106 °C (*n*-hexane). IR (ν/cm^{-1}) (paraffin oil): 2220 (C≡N). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.84 (6H, s), 7.18 (1H, d, *J* = 8.6 Hz), 7.37 (1H, d, *J* = 8.6 Hz), 7.43 (1H, d, *J* = 7.4, 1.1 Hz), 7.52 (1H, t, *J* = 7.7 Hz), 7.65 (1H, d, *J* = 8.0 Hz), 16.53 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 46.9, 94.0, 118.9, 119.1, 119.2, 128.3, 129.2, 130.1, 138.7, 151.4, 164.8. EI MS: *m*/*z* (*I*, %) 212 [M]$^+$ (55), 197 (33), 140 (72), 115 (61), 114 (54), 113 (51), 98 (37), 89 (28), 88 (40), 87 (33), 77 (31), 76 (32), 75 (45), 74 (27), 71 (38), 64 (34), 63 (88), 62 (45), 52 (33), 51 (49), 50 (36), 44 (97), 43 (34), 42 (100). UV−vis (MeCN): λ_{max} (log ε) 348 (3.94), 333 (3.86), 316 (3.74), 228 (4.50). Fluorescence (MeCN): λ_{max} 347 (excitation), 446 (fluor.). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.27; H, 5.72; N, 13.16.

2-Cyano-1,8-bis(dimethylamino)naphthalene (22). Yield 32%. Yellow oil. IR (ν/cm^{-1}) (liquid film): 2209 (C≡N). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.80 (6H, s), 3.19 (6H, s), 7.00 (1H, br d, *J* = 7.4 Hz), 7.28−7.44 (4H, m). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 45.0, 45.3, 101.1, 115.3, 121.9, 112.4, 123.4, 129.7, 129.9, 141.1, 153.5, 156.5. EI MS: *m*/*z* (*I*, %) 239 [M]$^+$ (70), 224 (22), 209 (31), 208 (75), 207 (67), 195 (72), 194 (34), 193 (100), 179 (26), 152 (29), 44 (60). UV−vis (MeCN): λ_{max} (log ε) 388 (3.62), 342 (3.65), 259 (4.36), 216 (4.25). Anal. Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.28; H, 7.13; N, 17.49.

Alternatively, this compound may be prepared as follows. A mixture of **19** (100 mg, 0.39 mmol) and KOH (22 mg, 0.39 mmol) in DMSO (5 mL) was kept for 20 min at 150 °C. The solvent was evaporated, and the residue was chromatographed on Al_2O_3 with $CHCl_3$ elution. The solvent was evaporated to yield 84 mg (90%) of **22** with properties identical to those for the sample described above.

2,7-Dicyano-8-dimethylamino-1-naphthol (30). Yield 32%. Yellow crystals, decomp above 180 °C (*n*-hexane). IR (ν/cm^{-1}) (paraffin oil): 2263 (C≡N). ^{1}H NMR (250 MHz $CDCl_3$): δ 3.15 (6H, d, *J* = 0.6 Hz), 7.24 (1H, d, *J* = 8.7 Hz), 7.56 (1H, d, *J* = 8.5 Hz), 7.62 (1H, d, *J* = 8.5 Hz), 7.76 (1H, d, *J* = 8.5 Hz), 16.60 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 44.1, 96.6, 106.8, 117.8, 118.2, 119.2, 119.7, 129.8, 132.4, 132.8, 140.4, 154.7, 166.2. EI MS, *m*/*z* (*I*, %): 237 [M]$^+$ (23), 222 (19), 139 (21), 44 (72), 42 (100). UV−vis (MeCN): λ_{max} (log ε) 360 (3.90), 343 (3.82), 262 (4.52), 226 (4.49). Fluorescence (MeCN): 338 nm (excitation), 421 nm (fluor.). Anal. Calcd for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.59; H, 4.65; N, 17.66.

2,7-Dicyano-1,8-bis(dimethylamino)naphthalene (31). Yield 20%. Yellow crystals, mp 194−196 °C (*n*-octane). IR (ν/cm^{-1}) (paraffin oil): 2196 (C≡N). ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.15 (12H, s), 7.21 (2H, d, *J* = 8.9 Hz), 7.39 (2H, d, *J* = 8.9 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 45.5, 101.8, 121.7, 122.7, 133.4, 143.3, 157.0. EI MS, *m*/*z* (*I*, %): 264 [M]$^+$ (58), 249 (17), 233 (81), 232 (83), 220 (47), 219 (39), 218 (100), 44 (78), 41 (29). UV−vis (MeCN): λ_{max} (log ε) 405 (4.09), 378 (4.18), 271 (4.73), 228 (4.68). Anal. Calcd for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.99; H, 6.12; N, 21.13.

9-Dimethylamino-3-phenylnaphtho[2,1-*d*]isoxazole (34a). Yield 64%. Beige crystals, mp 111−112 °C (*n*-hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.01 (6H, s), 7.23 (1H, dd, *J* = 8.2, 1.1 Hz), 7.49−7.58 (5H, m), 7.67 (1H, d, *J* = 8.7 Hz), 7.79 (1H, d, *J* = 8.7 Hz), 7.99 (2H, dd, *J* = 7.7, 1.9 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 40.0, 116.7, 117.3, 117.7, 119.6, 123.3, 127.3, 129.5, 129.5, 130.4, 130.6, 131.2, 137.5, 151.8, 158.6, 163.1. EI MS, *m*/*z* (*I*, %): 288 [M]$^+$ (100), 287 (15), 273 (64), 140 (25), 115 (33), 77 (59), 51 (35). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.82; H, 5.57; N, 9.70.

9-Dimethylamino-3-(*p*-methoxyphenyl)naphtho[2,1-*d*]isoxazole (34b). Yield 64%. Beige crystals, mp 126−127 °C (*n*-heptane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.99 (6H, s), 3.84 (3H, s), 7.06 (2H, d, *J* = 8.9 Hz), 7.20−7.24 (1H, m), 7.48−7.58 (2H, m), 7.66 (d, 1H, *J* = 8.5 Hz), 7.78 (1H, d, *J* = 8.5 Hz), 7.92 (2H, d, *J* = 8.9 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 46.0, 56.1, 115.7, 116.6, 117.3, 117.7, 119.7, 122.9, 123.3, 127.1, 129.4, 130.8, 137.4, 151.8, 158.2, 162.5, 163.0. EI MS, *m*/*z* (*I*, %): 318 [M]$^+$ (100), 304 (21), 303 (97), 211 (16), 140 (15), 115 (20), 92 (22), 77 (19), 64 (13). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.15; H, 5.72; N, 8.76.

Attempted Preparation of Compound 36. (2-Dimethylaminophenyl)(phenyl)methanone oxime[48] (**35**) (100 mg, 0.42 mmol) was kept for 2 h at 120−130 °C with stirring under argon atmosphere. The fused mixture was cooled to 20 °C, and the starting oxime **35** was recovered almost quantitatively.

X-ray Crystallography. Atomic coordinates, bond lengths, bond angles, and thermal parameters for **8**, **13**·$HClO_4$, and **19** have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge via www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ; fax: +44 1223 335 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference numbers.

Crystal Data for 8. Obtained from MeCN: $C_{13}H_{13}N_3$, *M* = 211.26, space group *Pbca* (orthorhombic), *a* = 7.4737(14), *b* = 12.984(2), *c* = 23.026(4) Å, *V* = 2234.4(7) Å^3, *Z* = 8, D_c = 1.256 g cm^{-3}, μ(Mo K$_\alpha$) = 0.077 mm^{-1}, 120 K, 19782 reflections collected, 2420 unique (R_{int} = 0.0730), 1850 reflections with $I > 2\sigma(I)$, 145 parameters, R_1 = 0.0676, wR_2 (all data) = 0.1087. CCDC reference number 828288.

Crystal Data for 13·$HClO_4$. Obtained from dry MeCN: $C_{20}H_{17}ClN_4O_4$, *M* = 412.83, space group $P\bar{1}$ (triclinic), *a* = 8.9925(16), *b* = 9.4538(17), *c* = 11.710(2) Å, α = 109.472(4)°, β = 105.396(4)°, γ = 90.581(4)°, *V* = 899.5(3) Å^3, *Z* = 2, D_c = 1.524 g cm^{-3}, μ(Mo K$_\alpha$) = 0.251 mm^{-1}, 120 K,

8606 reflections collected, 3874 unique (R_{int} = 0.0305), 2621 reflections with $I > 2\sigma(I)$, 285 parameters, R_1 = 0.0771, wR_2 (all data) = 0.1092. CCDC reference number 828289.

Crystal Data for 19. Obtained from *n*-hexane: $C_{15}H_{19}N_3O$, M = 257.33, space group $P\bar{1}$ (triclinic), a = 8.3498(11), b = 10.0042(13), c = 17.756(2) Å, V = 1390.2(3) Å^3, Z = 4, D_c = 1.229 g cm^{-3}, μ(Mo K$_\alpha$) = 0.079 mm^{-1}, 120 K, 14373 reflections collected, 6637 unique (R_{int} = 0.0368), 3325 reflections with $I > 2\sigma(I)$, 351 parameters, R_1 = 0.1132, wR_2 (all data) = 0.1210. CCDC reference number 828290.

■ ASSOCIATED CONTENT

Supporting Information. ORTEP structures of compounds **8**, **13**·$HClO_4$, and **19**; selected structural parameters of oxime **19**; ^{1}H and ^{13}C NMR spectra of all new compounds; COSY data for **13** and **15**; ^{1}H NMR spectra of competitive transprotonation mixtures for oxime **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) Apparently, the inertness of 2-aminobenzimidazole toward aldehyde **6** in acidic media results from its considerably higher basicity (pK_a = 7.54, H_2O, 25 °C) in comparison with 3-aminoindazole (pK_a = 3.15).[29] Consequently, under acidic conditions, the imidazole ring can be protonated with complete loss of nucleophilicity. Upon melting, the cyclization may proceed via zwitterionic form **14** in which the anionic imidazole ring should be strongly nucleophilic. Apparently, in the absence of external protons, the zwitterionic motif may be a widespread phenomenon in such transformations: see data below on similar reactions of proton sponge-based aldoximes.
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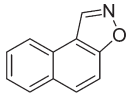
(30) 5-Aminotetrazole and 2-aminobenzimidazole can be considered as cyclic guanidine derivatives. However, we were unsuccessful in conducting the same reaction with the parent guanidine, probably owing to its much higher basicity and existing under employed acidic conditions solely as a non-nucleophilic protonated form. The same may be applied for benzamidine, while urea did not react with **6** in either acidic or neutral media.
(31) Most likely, the 8-NMe_2 group acts as a basic catalyst for transformation **20** → **21**. The participation of dimethylamine, evolving during the reaction, seems less probable in light of the stability of isomeric naphtho[1,2-*d*]isoxazole **A** in the presence of Et_3N: Dale, T. G.; Sather, A. C.; Rebek, J., Jr. *Tetrahedron Lett.* **2009**, *50*, 6173.



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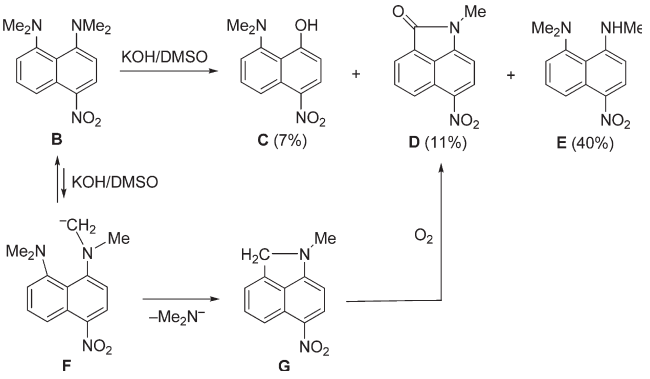
(33) The only known example of nucleophilic displacement of the NMe_2 group with an external nucleophile in the proton sponge series is the formation of naphthol **C** and lactam **D** along with demethylation product **E** upon treatment of compound **B** with a KOH−DMSO mixture.[34] Evidently, the reaction in this case is facilitated by a *p*-nitro group and use of a superbasic reagent. The formation of lactam **D** is thought to result from acidic ionization of the N−CH_3 group and intramolecular substitution of the 8-NMe_2 group by carbanionic nucleophile **F** followed by auto-oxidation of pyrroline intermediate **G**. Nucleophilic substitution of the NMe_2 group in ordinary dimethylaminonaphthalenes normally demands the presence in a substrate of several strongly activating groups and also proceeds with anionic nucleophiles.[35]



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