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tert-Amino effect in naphthalene proton sponges: a novel approach to benzo[*h*]quinoline and quino[7,8:7′,8′]quinoline derivatives

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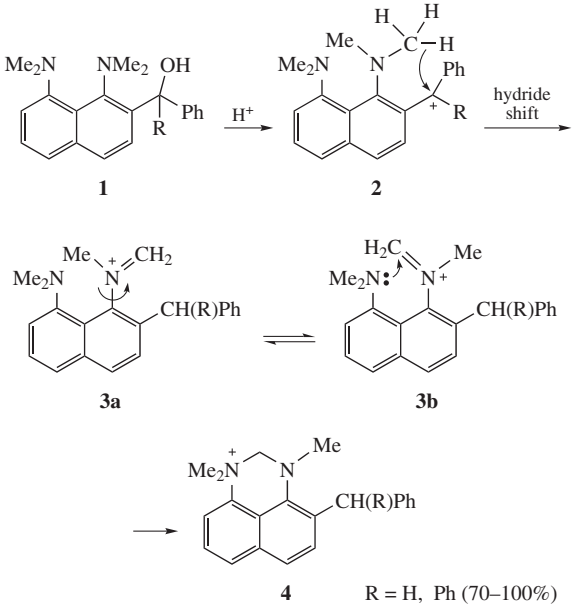
2-Vinyl- and 2,7-divinyl-1,8-bis(dimethylamino)naphthalenes with strong –M substituents in the β-positions of vinyl groups have been shown to undergo a *tert*-amino-type rearrangement providing a new and facile route to benzo[*h*]quinoline and quino[7,8:7′,8′]quinoline derivatives.

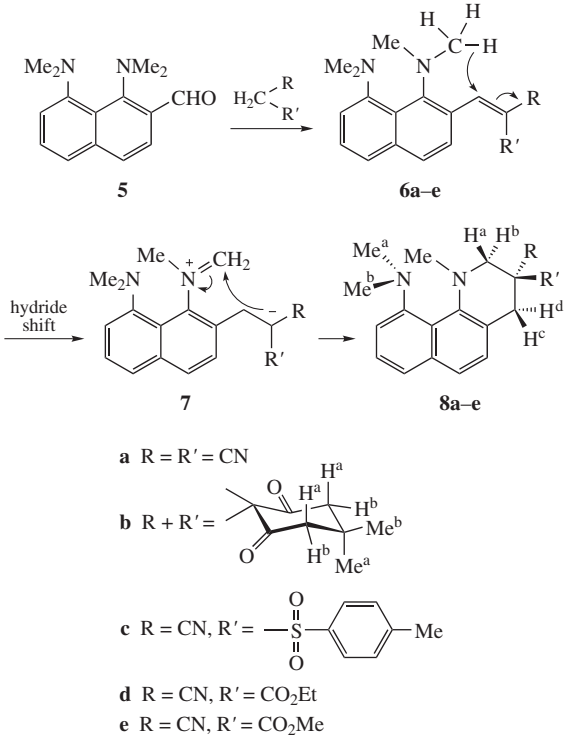
Recently, we have disclosed that acidic treatment of secondary and tertiary alcohols of type **1** on the basis of 1,8-bis(dimethylamino)naphthalene (proton sponge) generates naphthyl-2-methyl carbocations **2**, which then undergo a fast transformation into 1,1,3-trimethyl-2,3-dihydroperimidinium salts **4**.[1] The process involves hydride anion transfer from the neighbouring N–Me group to the carbenium centre followed by the *peri*-cyclization of intermediate methyleneimmonium salt **3** (Scheme 1). These were the first examples of the so-called *tert*-amino effect[2,3] in proton sponges.



Scheme 1

Here we report another kind of *tert*-amino effect in this series in which cyclization proceeds with the participation of an electron-deficient *ortho*-substituent instead of the *peri*-NMe_2 group, providing a new and convenient approach to inaccessible[4,5] benzo[*h*]quinoline and quino[7,8:7′,8′]quinoline systems. 2-Vinyl- and 2,7-divinyl-1,8-bis(dimethylamino)naphthalenes (**6** and **10**, respectively) were employed as starting compounds, which were prepared by the Knoevenagel condensation of earlier described[6] 2-formyl- and 2,7-diformyl-1,8-bis(dimethylamino)-naphthalenes (**5** and **9**, respectively) with malonodinitrile, dimedone, tosylacetonitrile and ethyl cyanoacetate (Schemes 2 and 3).

Monoaldehyde **5** has been shown to react easily with these methylene-active compounds in alcohol or toluene solution under ambient conditions. However, in the latter solvent, an addition of piperidine is needed whereas in EtOH an external catalyst is not necessary.† We were able to isolate in a pure state only alkenes **6c**,**d**. As regards alkenes **6a**,**b**, though their formation in the reaction mixture can be monitored spectrophotometrically, they are rapidly transformed into benzo[*h*]quinolines **8a**,**b**.‡ Thus, the presence of an electron-deficient α-carbon atom in the polarized vinyl group of compounds **6a**,**b** initiates spontaneous hydride transfer from the neighbouring *N*-methyl group followed by the tetrahydropyridine ring closure. Apparently, the way of cyclization of methyleneimmonium cation **7** is due to a higher nucleophilicity of the side-chain carbanionic centre as compared with the 8-NMe_2 group. Moreover, the *peri*-cycliza-



Scheme 2

† As reported earlier, both the parent proton sponge[7] and its derivatives[8] can effectively function as basic catalysts in the Knoevenagel reaction.

tion, similar to that depicted in Scheme 1, should only proceed after rotation of the $–N^+(Me)=CH_2$ function around the $C_{arom}–N$ bond (*cf.* **3a** → **3b**), that requires some extra energy.

We have found that the isomerization of alkenes **6c**,**d** into benzo[*h*]quinolines **8c**,**d** can be conducted almost quantitatively by simply heating the solid samples or by keeping their solutions in polar solvents such as DMSO or EtOH at room temperature. Interaction of aldehyde **5** with ethyl cyanoacetate in methanol (room temperature, 72 h) is accompanied by re-esterification yielding benzo[*h*]quinoline **8e**.

For dicyano-substituted benzo[*h*]quinoline **8a**, a single-crystal X-ray study has been performed confirming its structure (Figure 1).§ The naphthalene plane of **8a** is notably twisted [torsion C(2)–C(3)···C(7)–C(8) is 9.6°] with the amine nitrogens being out of the plane and 2.81 Å apart indicating that **8a** and its analogues are still sterically distorted molecules.

2,7-Dialdehyde **9** behaves towards the selected methylene-active reagents in a similar manner. Its interaction with malonodinitrile and ethyl cyanoacetate provides dialkenes **10a**,**c**,‡ which under above mentioned conditions are easily converted into quino[7,8:7′,8′]quinolines **11a**,**c**. Reaction of **9** with dimedone, as in the case of **5**, produces compound **11b** in a one-pot process. All yields are near 98%.

In summary, our study has disclosed an earlier unknown type of proton sponge reactivity reflecting a rather high hydride donor ability of the *peri*-NMe_2 groups. The suggested method is synthetically useful for the construction of benzo[*h*]quinolines, quino[7,8:7′,8′]quinolines and, possibly, other naphthalene-based heterocyclic systems, including chiral compounds.

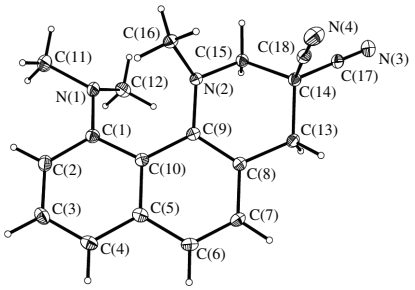
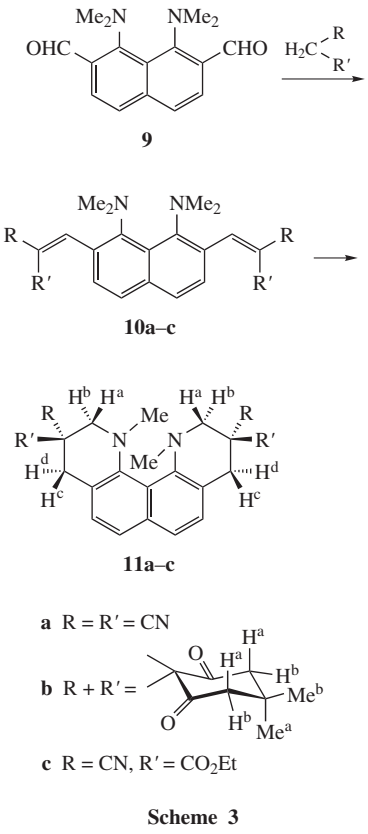


Figure 1 Molecular structure of **8a** in representation of atoms *via* thermal ellipsoids at $p = 30\%$. Selected bond lengths and distances (Å), valence and torsion angles (°): N(1)–C(1) 1.402(2), N(2)–C(9) 1.406(2), N(1)···N(2) 2.808(2); N(1)–C(1)–C(10) 120.87(14), N(2)–C(9)–C(10) 120.16(13), C(9)–C(10)–C(1) 125.31(14); N(1)–C(1)–C(2)–C(3) 174.30(15), C(7)–C(8)–C(9)–N(2) 171.46(13), C(6)–C(5)–C(10)–C(1) 169.07(14).



Scheme 3

‡ All new structures gave correct analytical and spectral data. Some experimental details and selected spectral characteristics [^{1}H NMR (250 MHz), IR (paraffin oil)] are as follows.

6c: A mixture of **5** (0.07 g, 0.29 mmol), tosylcyanomethane (0.057 g, 0.29 mmol) and piperidine (0.025 g, 0.29 mmol) in 4 ml of EtOH was kept at room temperature for 24 h. Wine-coloured solid (0.106 g, 87%) was filtered off, washed with cold EtOH and dried *in vacuo*. IR (ν/cm^{-1}): 2211 (C≡N). ^{1}H NMR ($CDCl_3$) δ: 2.44 (s, 3H, CMe), 2.73 (s, 6H, 8-NMe_2), 3.21 (s, 6H, 1-NMe_2), 7.03 (dd, 1H, H-7, ^3J 7.4 Hz, ^2J 1.4 Hz), 7.28–7.41 (m, 5H, H-3,5,6,3′,5′), 7.79 (d, 1H, H-4, ^3J 8.8 Hz), 7.89 (d, 2H, H-2′,6′, ^3J 8.4 Hz), 8.38 (s, 1H, –CH=). On heating the crystals are discoloured at 140–145 °C without melting due to a conversion into **8c**.

8c: Method A. A sample of **6c** (0.07 g, 0.17 mmol) was heated in an argon atmosphere at 140–180 °C until full discolouration. Slightly beige crystals, mp 219–221 °C (from MeOH). Yield 0.063 g (90%). IR (ν/cm^{-1}): 2231 (C≡N). ^{1}H NMR ($CDCl_3$) δ: 2.51 (s, 3H, 4′-Me), 2.63 (br. s, 3H, 10-NMe^a_2), 2.85 (br. s, 3H, 10-NMe^b_2), 2.99 (s, 3H, 1-NMe), 3.16 (dd, 1H, 4-CH^c_2, ^2J 16.4 Hz, ^4J 2.2 Hz), 3.75 (d, 1H, 4-CH^d_2, ^2J 16.4 Hz), 3.89 (br. d, 1H, 2-CH^a_2, ^2J 13.3 Hz), 4.03 (br. d, 1H, 2-CH^b_2, ^2J 13.3 Hz), 6.92–7.00 (m, 2H, H-5,9), 7.28–7.34 (m, 3H, H-6,7,8), 7.49 (d, 2H, H-3′,5′, ^3J 8.2 Hz), 7.97 (d, 2H, H-2′,6′, ^3J 8.2 Hz).

Method B. A solution of **6c** (0.07 g, 0.17 mmol) in DMSO (3 ml) was kept at room temperature for 48 h. After vacuum evaporation of the solvent, a pure sample of **8c** (0.07 g, 100%) was obtained.

10a: A mixture of dialdehyde **9** (0.07 g, 0.26 mmol), malonodinitrile (0.019 g, 0.29 mmol) and piperidine (0.022 g, 0.26 mmol) in PhMe (8 ml) was kept at room temperature for 24 h. The deposited wine-coloured crystals of **10a** (0.084 g, 88%) were filtered off and washed with cold (0 °C) toluene (3 ml) to give pure compound. IR (ν/cm^{-1}): 2219, 2193 (C≡N). ^{1}H NMR ($CDCl_3$) δ: 3.25 (s, 12H, NMe_2), 7.39 (d, 2H, H-3,6, ^3J 8.8 Hz), 7.85 (s, 2H, –CH=), 7.92 (d, 2H, H-4,5, ^3J 8.8 Hz). On heating the crystals are discoloured between 145–155 °C converting, without melting, into **11a**.

11a: Method A. Dialkene **10a** (0.07 g, 0.19 mmol) was heated under argon at 145–155 °C until full discolouration. This gave 0.067 g (96%) of **11a** with mp 251–253 °C (from MeOH). IR (ν/cm^{-1}): 2251 (C≡N). ^{1}H NMR ($CDCl_3$) δ: 3.03 (s, 6H, NMe), 3.66 (br. d, 4H, 4-CH_2, 9-CH_2, ^2J 13.3 Hz), 3.84 (m, 2H, 2-CH^a_2, 11-CH^a_2), 4.07 (m, 2H, 2-CH^b_2, 11-CH^b_2), 7.07 (d, 2H, H-5,8, ^3J 8.4 Hz), 7.38 (d, 2H, H-6,7, ^3J 8.4 Hz).

Method B. A solution of **10a** (0.07 g, 0.19 mmol) in 3 ml of DMSO was kept at room temperature for 48 h, providing after evaporation of the solvent pure **11a** (0.07 g, 100%).

For characteristics of compounds **6d**, **8a**,**b**,**d**,**e**, **10c** and **11b**,**c**, see Online Supplementary Materials.

§ *X-ray diffraction data*. Crystals of **8a** (obtained by slow evaporation of saturated solution of **8a** in *n*-hexane, $C_{18}H_{18}N_4$, $M = 290.36$) are monoclinic, space group $P2_1/c$, at 100 K: $a = 7.1632(5)$, $b = 12.3083(9)$ and $c = 17.4259(11)$ Å, $V = 1517.12(18)$ Å^3, $Z = 4$, $d_{calc} = 1.271$ Mg m^{-3}, μ(MoKα) = 0.078 mm^{-1}, $F(000) = 616$. Intensities of 4923 reflections were measured with a CAD4 Enraf-Nonius diffractometer [λ(MoKα) = 0.71072 Å, $\theta/2\theta$-scans, $2\theta_{max} = 27.99°$] and 4420 independent reflections ($R_{int} = 0.0294$) were used in a further refinement. The refinement converged to $wR_2 = 0.0911$ and GOF = 1.014 for all independent reflections [$R_1 = 0.0480$ was calculated against F for 2959 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0.

CCDC 758607 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2010.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2010.01.014.

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