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An alternative synthesis of benzobis(imidazolium) salts via a 'one-pot' cyclization/oxidation reaction sequence

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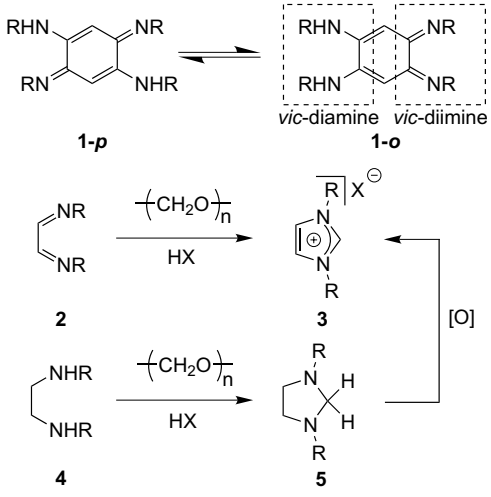
Abstract—Cyclization of *N*-aryl and *N*-alkyl 2,5-diamino-1,4-benzoquinonediimines using paraformaldehyde under acidic conditions followed by oxidation with catalytic amounts of $Pd(OAc)_2$ afforded their respective benzobis(imidazolium) salts in yields of 48–98%. A comparative solid-state study between a 2,5-diamino-1,4-benzoquinonediimine and its corresponding benzobis(imidazolium) dichloride was also performed.

We have recently reported a concise synthesis of a series of 1,2,4,5-tetrakis(*N*-alkyl and *N*-arylamino)benzenes[1] and demonstrated that they undergo formylative cyclization with triethylorthoformate to afford their respective benzobis(imidazolium) salts.[2] The electron-rich tetraaminobenzene intermediates were found to oxidize under aerobic conditions which necessitated the use of inert atmosphere or drybox techniques for their isolation and storage. In contrast, their oxidized products, namely azophenines[3] and related 2,5-diamino-1,4-benzoquinonediimines,[4] are robust and accessible via numerous synthetic protocols.[3–5] These quinone derivatives have found tremendous utility in coordination chemistry,[6] as pH-dependent chromophores,[7] and in theoretical studies.[8] In an effort to build upon our previous work and encompass new methodologies for preparing benzobis(imidazolium) salts using simple, bench-top procedures, we envisioned that azophenines and 2,5-diamino-1,4-benzoquinonediimines could function as a highly versatile class of appropriate starting materials.

As shown in Scheme 1, the *ortho*-quinoid tautomer[9] (**1**-*o*) of 2,5-diamino-1,4-benzoquinonediimine **1** displays vicinal diamino and diimino moieties which are independently known for undergoing dehydrative cyclizations. For example, treatment of 1,2-diimine **2** with paraformaldehyde affords imidazolium salt **3**[10] whereas the corresponding vicinal diamine **4** affords the cyclic *N*,*N*′-acetal **5**.[11] With these considerations in mind, we



Scheme 1. The *o*-tautomer of 2,5-diamino-1,4-benzoquinonediimine (**1**-*o*) exhibits vicinal diamino and diimino fragments which are independently known for undergoing dehydrative cyclizations with paraformaldehyde.

suspected analogous cyclization reactions with **1** should afford an annulated benzimidazolium/*N*,*N*′-acetal hybrid.[12] Oxidation of this intermediate using Thorn's recently reported[13] Pd-mediated process for efficiently generating hydrogen gas from phenylene diamine-derived *N*,*N*′-acetals should then afford the respective benzobis(imidazolium) salts. Furthermore, the apparent compatibility of the cyclization and oxidation reaction conditions suggested they could be performed successively in a single reaction vessel.

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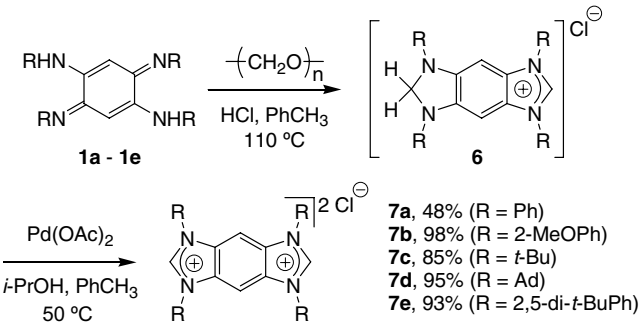

Scheme 2. Conversion of 2,5-diamino-1,4-quinonediimines to their respective benzobis(imidazolium) salts using a 'one-pot' cyclization/oxidation reaction sequence.

To test this hypothesis, azophenine **1a** was obtained via condensation of aniline with *o*-benzoquinone dioxime according to literature protocol.[5a] Related 2,5-diamino-1,4-quinonediimines **1b–e** were prepared via Pd-catalyzed aryl amination[14] of 1,2,4,5-tetrabromobenzene followed by an aerobic workup,[15] in analogy with our previously reported procedure. Confirmation of the 2,5-diamino-1,4-quinonediimine structure was determined through identification of the diagnostic chemical shift of the vinylic proton of the quinoid ring ($\delta =$ 5.5 ppm in $CDCl_3$) and single crystal X-ray analysis for **1b**.[16] As shown in Scheme 2, compounds **1** were each reacted with paraformaldehyde in $PhCH_3$ under acidic conditions at 110 °C.[17] Within 2–6 h, the intense colors associated with these quinone derivatives had dissipated and the reaction mixtures developed yellow-brown solids suggesting that a hybrid intermediate **6** had formed.[18] The reaction temperature was then reduced to 50 °C and, to facilitate dissolution of solids, *i*-PrOH (10% by volume) was added. Upon the addition of catalytic amounts of $Pd(OAc)_2$ (1 mol %), slow and persistent generation of gas was observed. Analysis of the crude reaction mixtures by ^{1}H NMR spectroscopy indicated the 2,5-diamino-1,4-benzoquinonediimines were cleanly converted to the desired benzobis(imidazolium) products (diagnostic signal: C–*H*, $\delta = 9$–11 ppm in DMSO-d_6) **7** in good to excellent yields (48–98%).[19]

Although ^{1}H NMR analyses of the products obtained above were strongly indicative of the desired benzobis(imidazolium) structure, they were further characterized by using X-ray analysis after quality crystals of benzobis(imidazolium) dichloride **7b** were obtained by slow cooling of a hot, saturated, DMSO solution.[16] As shown in Figure 1, the N1–C2–N2 bond angle (110.2°) was typical of annulated imidazolium compounds as were the imidazole bond lengths.[20] Furthermore, C–C bond lengths typical of arene rings were observed (1.38–1.41 Å) in the tetraaminoarene fragment, which indicated the parent quinone core was successfully reduced. The *N*-anisidyl rings were rotated out-of-plane with respect to the benzobis(imidazolium) core (dihedral angles ranged between 35° and 60°) suggesting that there was relatively minimal electronic overlap between the two moieties.

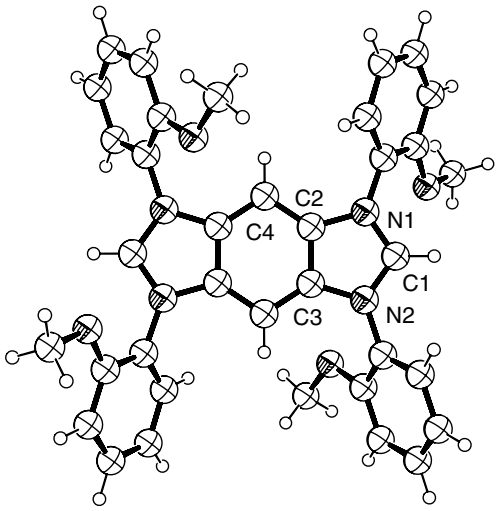

Figure 1. ORTEP drawing of **7b** (counterions have been removed for clarity). Selected bond lengths (Å) and angles (°): N1–C1, 1.3352(19); N2–C1, 1.3398(19); N1–C2, 1.4007(18); N2–C3, 1.3986(18); C2–C3, 1.4062(19); C2–C4, 1.384(2); N1–C1–N2, 110.21(13); C1–N1–C2, 108.55(11); N1–C2–C3, 106.37(12); C4–C2–N1, 130.60(13); C6–C5–N1–C2, 126.27(15); C3–N2–C12–C13, 59.12(19).

In summary, we have developed an alternative, 'one-pot' protocol for synthesizing a variety of benzobis(imidazolium) salts from readily available 2,5-diamino-1,4-benzoquinonediimines. In particular, the *o*-quinoid tautomers of 2,5-diamino-1,4-benzoquinonediimines were cyclized using paraformaldehyde to obtain benzimidazolium/*N*,*N*′-acetal hybrid intermediates which were subsequently oxidized to afford their respective bis(azolium) salts.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.05.076.

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15. General procedure for preparing compounds **1b**–**e**: A 20 mL vial charged with 1,3-bis(2,6-diisopropylphenyl)-imidazolium chloride (0.02 mmol), NaO*t*-Bu (0.02 mmol), $Pd(OAc)_2$ (0.01 mmol), and $PhCH_3$ (5 mL). After stirring the resulting mixture for 10 min, 1,2,4,5-tetrabromobenzene (1.00 mmol), amine (4.10 mmol), NaO*t*-Bu (4.20 mmol), and $PhCH_3$ (5 mL) were added. The resulting mixture was sealed under an atmosphere of nitrogen and stirred at 110 °C for 8 h. After cooling to ambient temperature, the resulting mixture was diluted with hexanes and precipitated solids were collected by filtration. Residual inorganic salts were removed by filtering $CHCl_3$ solutions of the products. Characterization data for new compounds: Azophenine **1b**: ^{1}H NMR ($CDCl_3$): δ 8.55 (s, 2H), 7.05–6.91 (m, 16H), 6.16 (s, 2H) 3.83 (s, 12H); ^{13}C NMR ($CDCl_3$): δ 150.4, 148.2, 134.4, 130.5, 121.0, 120.6, 119.1, 114.4, 111.3, 110.3, 93.1, 55.7, 55.5; HRMS: $[M]^+$ calcd for $C_{34}H_{32}N_4O_4$, 560.2424. Found: 560.2428. Spectral data of **1c** was consistent with its previously reported[1] value. Compound **1d**: ^{1}H NMR ($CDCl_3$): δ 6.69 (br, 2H), 5.77 (s, 2H), 2.10 (br, 12H), 1.97 (br, 24H), 1.68 (br, 24H); ^{13}C NMR ($CDCl_3$): δ (ca 138), 92.2, 52.7, 42.6, 36.9, 29.8; HRMS: $[M]^+$ calcd for $C_{46}H_{64}N_4$, 672.5131. Found: 672.5134. Azophenine **1e**: ^{1}H NMR ($CDCl_3$): δ 8.13 (s, 2H), 7.03 (s, 2H), 6.78 (br, 8H), 6.31 (s, 2H), 1.17 (s, 72H); ^{13}C NMR ($CDCl_3$): δ 151.4, 117.6, 90.7, 34.8, 31.4; HRMS: $[M+1]^+$ calcd for $C_{62}H_{88}N_4$, 889.7009. Found: 889.7089.
16. Crystal data for **1b**: $C_{34}H_{32}N_4O_4$–$2C_4H_8O$, $M = 704.84$, triclinic, $P\bar{1}$, $a = 12.5090(8)$, $b = 13.3300(9)$, $c = 14.2730(11)$ Å, $\alpha = 64.179(3)$, $\beta = 89.750(4)$, $\gamma = 64.058(5)°$, $V = 1874.8(2)$ Å^3, $Z = 2$, $D_c = 1.249$ g cm^{-3}, $\mu = 0.084$ mm^{-1}, $F_{(000)} = 752$, λ (Mo K$_\alpha$) = 0.71073 Å, large red prisms, crystal size $0.33 \times 0.30 \times 0.25$ mm, 10820 reflections measured ($R_{int} = 0.0499$), 6570 unique, $R1 = 0.1268$ for $I > 2\sigma(I)$ and 0.2564 for all data. There were two molecules of THF in the asymmetric unit, one of which was found to be disordered and could not be adequately modeled. Key bond lengths (Å) and angles (°): N1–C1, 1.301(5); N2–C2, 1.376(5); C1–C2, 1.493(6); C1–C3, 1.431(6); C2–C3, 1.340(6); C4–N1–C1–C2, 176.1(4). Crystal data for **7b**: $(C_{36}H_{32}N_4O_4)$ 2Cl–$4C_2H_6SO$, $M = 968.07$, triclinic, $P\bar{1}$, $a = 8.2689(2)$, $b = 11.4843(2)$, $c = 13.3347(3)$ Å, $\alpha = 112.090(1)$, $\beta = 96.690(1)$, $\gamma = 90.029(1)°$, $V = 1164.00(4)$ Å^3, $Z = 1$, $D_c = 1.381$ g cm^{-3}, $\mu = 0.375$ mm^{-1}, $F_{(000)} = 510$, λ (Mo K$_\alpha$) = 0.71073 Å, colorless prisms, crystal size $0.49 \times 0.31 \times 0.20$ mm, 7435 reflections measured ($R_{int} = 0.0162$), 5229 unique, $R1 = 0.0363$ for $I > 2\sigma(I)$ and 0.0460 for all data. The data were collected at 153(2) K using an Oxford Cryostream low temperature device. The structures were solved by direct methods and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97 (Sheldrick, G. M. University of Gottingen, Germany, 1994). Data for these structures have been deposited with the Cambridge Crystallographic Data Centre (12 Union Road, Cambridge CB2 1EZ, UK) as CCDC 603509 (**1b**) and 603510 (**7b**).
17. General procedure for preparing compounds **7**: A 50 mL flask was charged **1** (0.5 mmol), $PhCH_3$ (20 mL), paraformaldehyde (1.2 mmol), and concd HCl (1 drop). After stirring the mixture at 110 °C for 2–6 h, the temperature was reduced to 50 °C and *i*-PrOH (2 mL) was added to facilitate partial dissolution of solids. $Pd(OAc)_2$ (5 μmol) was then added and slow evolution of gas followed. The mixture was stirred for an additional 2–4 h and then concentrated to afford crude product. Note: this protocol was found to work equally well in other solvents (e.g., CH_3CN, DMF, DMSO, and EtOH). Spectral data of **7a**–**d** were in accord with their previously reported values.[1] Characterization data for **7e**: ^{1}H NMR ($CDCl_3$): δ 9.98 (br, 2H), 7.97 (br, 8H), 7.82 (br, 2H), 7.62 (s, 4H), 1.32 (s, 72H); ^{13}C NMR ($CDCl_3$): δ 154.0, 144.7, 132.1, 125.5, 120.7, 114.9, 99.6, 35.5, 31.4; HRMS: $[M]^+$ calcd for $C_{64}H_{88}N_4$, 912.7009. Found: 912.6983.
18. Subjecting *N*,*N*′,*N*″,*N*‴-tetra(*p*-chlorophenyl)-2,5-diamino-1,4-benzoquinonediimine[5a] to the cyclization–oxidation reaction sequence outlined in Scheme 2 afforded 1,3-di(*p*-chlorophenyl)-5,6-di(*p*-chlorophenyl-amino)benzimidazolium chloride (95% yield): ^{1}H NMR ($CDCl_3$): δ 10.14 (s, 1H), 7.97 (d, $J = 9.2$ Hz, 4H), 7.84 (d, $J = 9.2$ Hz, 4H), 7.49 (s, 8H), 7.13 (s, 2H), 5.95 (s, 2H).
19. It was also found that benzobis(imidazolium) salts **7** could be prepared via a one-pot, reduction–cyclization reaction sequence: Subjecting **1a**–**d** independently to standard hydrogenative conditions (10% Pd/C, 400 PSI H_2) in $HC(OEt)_3$ for 16–24 h followed by addition of acid (HCl or HBF_4) at 60–110 °C for 2–24 h afforded the respective benzobis(imidazolium) salts **7a**–**d** in 51–92% yields.
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