On the Amination of Tetraazafulvalenes

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Abstract: The palladium catalyzed amination of tetraazafulvalenes is described. Starting from either the tetraalkylated compounds **7** or their vinylogous derivatives **8**, substitution of the aryl bromide by different amines was realized. The synthesis of compounds which possess four primary amino groups as well as four hydrazino residues by employing a one-pot, two-step method is also described. Bichromophores are accessible as demonstrated by the introduction of the phenoxazine system into tetraazafulvalenes.

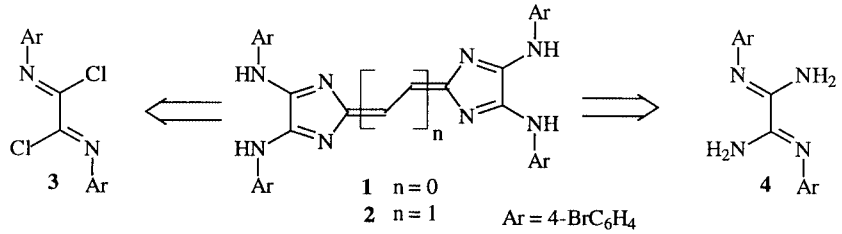
Key words: aminations, arenes, cross-coupling, heterocycles, palladium, tetraazafulvalenes

Numerous syntheses of 1,4,5,8-tetraazafulvalenes of type **1** and **2** have been previously described.[1-4] Due to their redox properties as well as their multifunctionalities, these electron deficient heterofulvalenes offer the possibility of constructing functional dyes and dentritic structures. In particular, the introduction of amino groups into the aromatic residues of tetraazafulvalenes should be of interest. Protonation and alkylation reactions should thus afford water soluble derivatives. In addition, the auxochromic NR_2-substructures should lead to a bathochromic shift of the long wavelength absorption maxima of compounds **1** and **2**.

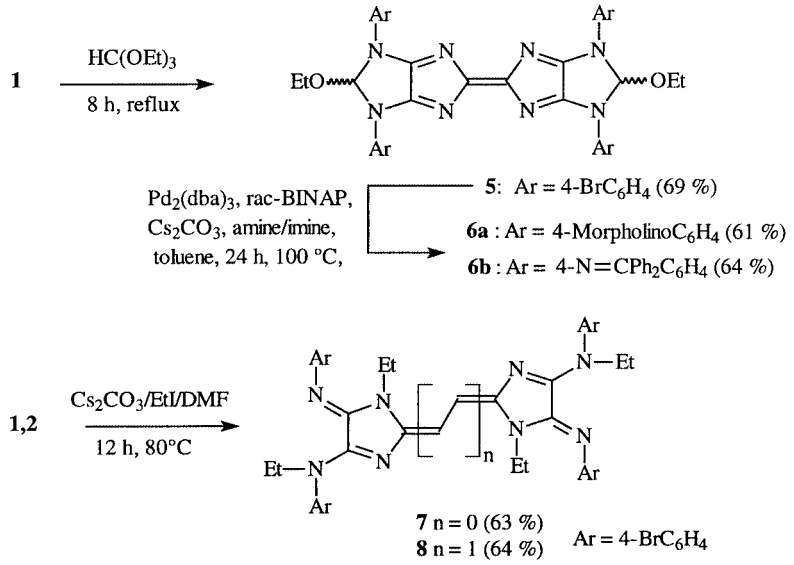
All attempts to synthesize derivatives which possess amino groups (**1**, **2** with Ar = 4-$R_2NC_6H_4$) at the aromatic residues have failed to date because the corresponding educts **3** and **4** are not accessible. Reduction of the less soluble 4-nitro derivatives of compounds **1** and **2** (Ar = 4-$O_2NC_6H_4$) did not give the desired amino derivatives either. We now report that metal catalyzed amination allows the synthesis of these compounds. Thus, under palladium[5] or nickel catalysis[6], aromatic halogen atoms in **1** and **2** can be replaced by amino groups under mild conditions. Encouraged by the results reported in the literature, we started from easily accessible tetraazafulvalenes **1** and **2** bearing a bromine atom in para position of the aryl group. However, in our first experiments, no substitution reaction could be observed. This is probably due to the fact that the vicinal diamino substructure in the educts **1** and **2** forms a new complex with the metal which is then inactivated and unable to participate in the catalytic cycle.

The solution to this problem results in a previous cyclization of **1** with orthoformate[2] leading to a 1:1 *syn/anti* mixture of compound **5**. Initial studies using morpholine or diphenylketimine in the presence of a palladium catalyst (Pd_2dba_3/*rac*-BINAP) confirmed this. The amination of **5** to products **6a** and **6b** was then easily realized. It is noteworthy to mention that in the case of the conversion of **5** to **6a**,**b** only cesium carbonate as a weak base led to an amino transfer reaction whereas sodium *tert*-butoxide and LiHMDS were inactive. Both of the new amino derivatives **6a,b** could be isolated and structurally characterized. However, due to their poor solubility, a further derivatization seemed to be useless. Another pathway to derivatives showing a good solubility and unable to complex the metal is the alkylation of heterofulvalenes **1** and **2**.[2] Thus, treatment of **1** and **2**, with ethyl iodide in the presence of a base lead to the tetraalkylated compounds **7** and **8**, respectively in a smooth reaction (Scheme 2). Subsequently, **7** and **8** were converted into different amino aryl heterofulvalenes **9**, **10** (Scheme 3).

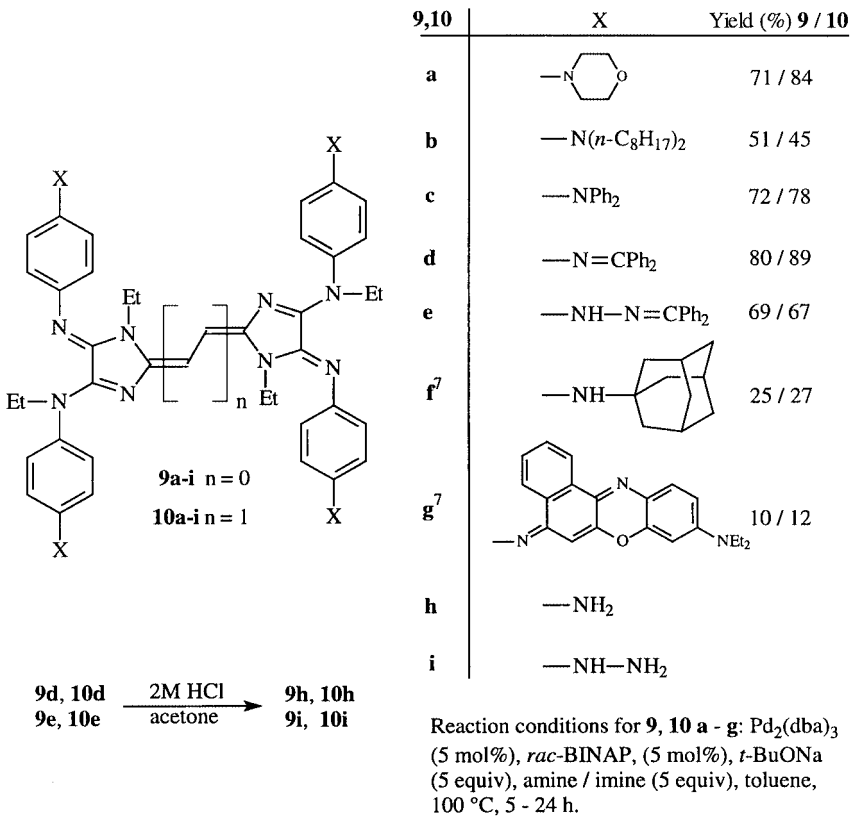
The direct metal catalyzed substitution of bromine by ammonia leading to primary amino groups was not successful.[7] We therefore employed the coupling reaction of bromo derivatives **7** and **8** with benzophenone imine.[8] Final treatment of the amination products **9d,10d** with hydrochloric acid formed the desired primary amines **9h,10h** under cleavage of benzophenone. In an analogous manner, the hydrazino derivatives **9e,10e** were synthesized via the hydrazones **9i,10i**. Moreover, with the substitution of bromine by the phenoxazine fragment to **9g,10g**, an easy access to bichromophoric systems is obtained.[9]



Scheme 1



Scheme 2



Scheme 3

In the UV/Vis spectra of derivatives **9a-c** and **10a-c,** the longest wavelength absorption maxima are bathochromically shifted only about 10 nm as compared to the halogenated educts. A much stronger influence was obtained with the diphenylketimine substructure (**9d**: λ_{max} = 586 nm, **10d**: λ_{max} = 606 nm) which was further increased by cleavage of benzophenone: the hydrochloride of **9h** absorbs at λ_{max} = 632 nm and that of **10h** at λ_{max} = 658 nm. In addition to the typical absorption for tetraazafulvalenes at about 570 nm, the phenoxazine dye in **9g** is characterized by a second strong absorption at 635 nm.

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References and Notes

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(7) With these primary amines, mainly the disubstitution products were formed even at longer reaction times.

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(9) Typical procedure for alkylation of tetraazafulvalenes: A mixture of **2** (0.83 g, 1 mmol), cesium carbonate (1.62 g, 5 mmol) and ethyl iodide (0.78g, 5 mmol) in 20 mL of anhyd DMF was heated to 50 °C for 12 h. After addition of 10 mL of water, the precipitate was filtered off and the crude product was purified by column chromatography (alumina, toluene/heptane 1/1). **8**: (0.61 g, 64%). ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 7.22 (d, 4 H), 7.13 (d, 4 H), 6.67 (d, 4 H), 6.47 (s, 2 H), 6.30 (d, 4 H), 3.94 (q, 4 H), 3.43 (q, 4 H), 1.21 (t, 6 H), 1.10 (t, 6 H). UV/Vis (DMSO): λ_{max} (lg ε) = 557 nm (4.8). MS (DCI with H_2O): m/z = 954 (100), 951, 873, 632.
Typical procedure for amination reactions: A schlenk tube was charged with $Pd_2(dba)_3$ (20 lmol), rac-BINAP (20 lmol), sodium *tert*-butoxide (for **6a**,**b**: cesium carbonate) (0.5 mmol), tetraazafulvalenes **5**, **7** or **8** (0.1 mmol), amine (0.5 mmol) and 10 mL toluene under argon. The mixture was heated to 100 °C with stirring until completion of the reaction (TLC). The reaction mixture was then cooled to r.t., taken up in diethyl ether, washed with water, dried over Na_2SO_4 and evaporated in vacuo. Column chromatography of the residue on alumina gave pure products.
Selected data for **6b**: *from **5** and benzophenone imine*. Mp 280 °C (dec.). ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 7.78 (d, (16 H), 7.47 (m, 10 H), 7.32 (d, 16 H), 7.15 (m, 8 H), 6.85 (d, 8 H), 3.32 (q, 4 H), 1.00 (t, 6 H). MS (ESI in $CHCl_3$/MeOH): m/z = 1325.6. **9a**: *from **7** and morpholine*. (71 mg, 74%), mp 318 °C. MS (ESI in $CHCl_3$/MeOH): m/z = 949.2. ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 7.02 (m, 8 H), 6.56 (m, 8 H), 4.52 (q, 4 H), 3.89 (q, 4 H), 3.78 (m, 16 H), 3.10 (m, 16 H), 1.21 (t, 6 H), 1.14 (t, 6 H). UV/Vis (DMSO): λ_{max} (lg ε) = 552 nm (4.8). **10a**: *from **8** and morpholine*. (82mg, 84%), mp 309 °C. ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 6.61 (m, 12 H), 6.46 (d, 4H), 6.32 (s, 2H), 3.96 (q, 4 H), 3.81 (m, 16 H), 3.67 (q, 4 H), 3.05 (m, 16 H), 1.24 (t, 6 H), 1.15 (t, 6H). ^{13}C NMR (62 MHz, CD_2Cl_2): δ = 149.1, 148.1, 146.8, 146.2, 144.3, 136.8, 126.1, 121.4, 116.0, 97.9, 67.4, 67.2, 51.0, 50.0, 48.9, 36.8, 13.9, 13.0. UV/Vis (DMSO): λ_{max} (lg ε) = 561 nm (4.9). **10b**: *from **8** and dioctylamine*. (72 mg, 45%), mp 120 °C. MS (DCI with water): m/z = 1592 (M^+), 1522, 520, 364, 102. UV/Vis (DMSO): λ_{max} (lg ε) = 566 nm (4.9). **10c**: *from **8** and diphenylamine*. (102 mg, 78%), mp 93 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.35 (m, 22 H), 7.02 (m, 18 H), 6.86 (m, 8 H), 6.47 (m, 8 H), 6.25 (s, 2 H), 3.98 (q, 4 H), 3.74 (q, 4 H), 1.29 (t, 6 H), 1.16 (t, 6 H). MS (ESI in $CHCl_3$/MeOH): m/z = 1303.7. **10d**: *from **8** and benzophenone imine*. (121 mg, 89%), mp 268 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.72 (m, 8H), 7.45 (m, 4H), 7.39 (m, 8H), 7.29 (m, 8 H), 7.15 (m, 8 H), 7.08 (m, 4 H), 6.74 (m, 4 H), 6.53 (m, 8 H), 6.31 (m, 4 H), 6.22 (s, 2 H), 3.95 (q, 4H), 3.40 (q, 4 H), 1.17 (t, 6 H), 0.93 (t, 6 H). ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 168.1, 167.5, 148.8, 146.4, 145.9, 145.0, 140.4, 140.2, 139.9, 137.4, 136.5, 130.9, 130.8, 129.9, 129.8, 129.6, 129.4, 129.0, 128.7, 128.4, 128.3, 128.2, 125.9, 121.8, 121.5, 120.6, 97.5, 48.6, 37.1, 13.9, 13.0. UV/Vis (DMSO); λ_{max} (lg ε) = 360 nm (4.4), 606 (4.7). MS (ESI in $CHCl_3$/MeOH); m/z = 1351.7. **10e**: *from **8** and benzophenone hydrazone*. (96 mg, 67%), mp 199 °C. ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 7.56 (d, 16 H), 7.30 (m, 20 H), 7.27 (m, 10 H), 6.84 (m, 10 H), 6.47 (s, 2 H), 4.02 (q, 4 H), 3.61 (q, 4 H), 1.06 (t, 6 H), 0.86 (t, 6 H). MS (ESI in $CHCl_3$/MeOH): m/z = 1411.8. **10f**: *from **8** and 1-aminoadamantane*. (33 mg, 27%), mp 132 °C. MS (DCI with water): m/z = 1232 (M^+). UV/Vis (DMSO): λ_{max} (lg ε) = 567 nm (4.8). **10g**: *from **8a** and nile blue*. (30 mg, 12%), mp > 350 °C. ^{1}H NMR (250 MHz, CD_2Cl_2): δ = 8.43 (m, 10 H), 7.56 (m, 22 H), 7.24 (m, 42 H), 6.86 (m, 12 H), 6.4 (m, 8 H), 6.02 (s, 2 H), 4.12 (q, 4 H), 3.82 (q, 4 H), 3.21 (q, 8 H), 3.11 (q, 8 H), 1.21 (m, 24 H), 1.04 (t, 6 H), 1.01 (t, 6 H). UV/Vis (DMSO): λ_{max} (lg ε) = 568 nm (4.8), 638 (4.7).
The cleavage of the imine **10d** or hydrazone **10e** was realized in acetone as solvent by addition of a few drops of 2 M HCl. The precipitation was filtered off and recrystallized from ethanol. **10h**: mp 255 °C. MS (DCI with H_2O): m/z = 695 (M^+), 627, 503, 245, 102. UV/Vis (DMSO): λ_{max} (lg ε) = 658 nm (4.7). **10i**: mp 265 °C. MS (DCI with H_2O): m/z = 755 (M^+), 687, 512, 102.

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