Ligand Design

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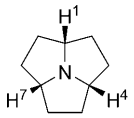
Azatriquinane as a Platform for Tripodal Metal Complexes and Calixiform Scaffolds**

*Martyn Jevric, Tao Zheng, Nabin K. Meher, James C. Fettinger, and Mark Mascal**

Azatriquinane **1** is a bowl-shaped tricycle featuring an apical, acutely pyramidalized nitrogen.[1,2] The trefoil fusion of three five-membered rings in **1** results in an averaged C_{3v}-symmetric platform, which presents the opportunity to build out from the sites α to the nitrogen (C-1, 4, and 7) to position substituents in an array with a conic focus. Herein, we report a synthetic approach to substitution at these sites, leading both to a novel, conformationally fixed tripodal ligand system and calix-like derivatives with a basic nitrogen at the bottom of the cavity.



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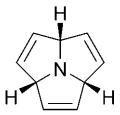

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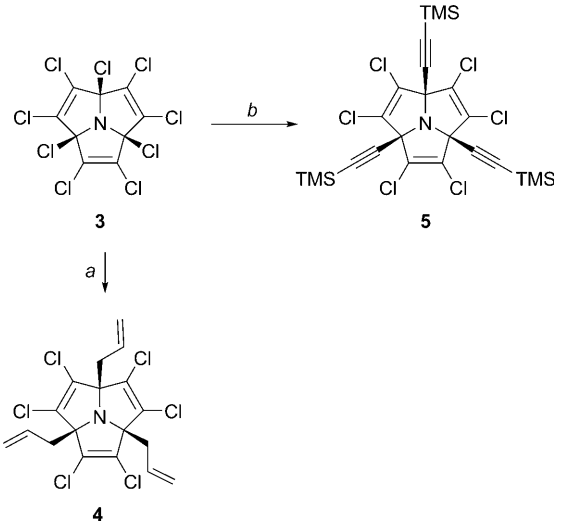
The centerpiece of this chemistry is perchloroazatriquinacene **3**, a synthetic precursor to the parent azatriquinacene **2**. It can be produced in a single step and high yield by photochemical chlorination of **1** with SO_2Cl_2, and is available in multigram quantities.[1] The presence of doubly allylic α chloroamine functions in **3** suggested the potential to generate cationic intermediates which could alkylate electron-rich π systems. Thus, the Lewis acid catalyzed reaction of **3** with either allyltrimethylsilane or bis(trimethylsilyl)acetylene led to the corresponding triallyl **4** or triyne **5** derivatives in good yields (Scheme 1). Although a number of opportunities for further elaboration present themselves in **4** and **5**, we were first attracted to the prospect of applying the azatriquinane framework as a scaffold for tripodal ligands. To this end, we envisaged a threefold "click" reaction[3,4] with the alkyne functions in **5** to give a tris(1,2,3-triazole) similar to the Sharpless TBTA ligand,[5] but with the nitrogen sites preorganized in a trigonal-pyramidal arrangement. This was accomplished as shown in Scheme 2. Desilylation of **5** with fluoride gave **6**, and subsequent dehalogenation with lithium in *tert*-butanol gave triethynylazatriquinacene **7**. Reaction of **7**



Scheme 1. Reagents and conditions: a) $H_2CCHCH_2SiMe_3$, $AlCl_3$, CH_2Cl_2, 16 h, 90%; b) $Me_3SiCCSiMe_3$, $AlCl_3$, CH_2Cl_2, 10 h, 68%.

with phenyl azide provided the tris(1,2,3-triazole) derivative **8**, which could be hydrogenated to the ligand **9**.

Simple mixing of **9** with either Zn^{II} acetate or Co^{II} acetate in methanol gave rise to metal complexes, and X-ray quality crystals of both could be obtained by capping the metals with a terminal chloride ligand and exchanging the counterion for PF_6^-. In each case, the coordination geometry is pseudo-trigonal-bipyramidal, with the axial N–M bond longer than the equatorial N–M bonds. For example, in the Co^{II} complex (Figure 1), the former is 2.382(2) Å and the latter are 2.012(2), 2.020(2), and 2.030(2) Å. As noted above, an attractive characteristic of this host is its degree of preorganization, compared to flexible tris(2-aminoethyl)amine (tren)-based ligands.[6,7]

The reaction of **3** with aromatic rings gave rise to triaryl-substituted hexachloroazatriquinacenes **10** (Scheme 3). X-ray

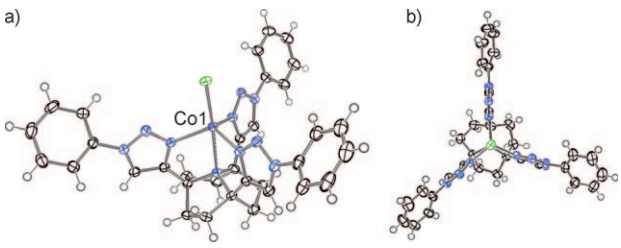


Figure 1. ORTEP[8] views of the X-ray crystal structure of the [**9**-CoCl]PF_6 complex (counterion omitted for clarity). Thermal ellipsoids are drawn at the 60% probability level.

[*] Dr. M. Jevric, Dr. T. Zheng, Dr. N. K. Meher, Dr. J. C. Fettinger, Prof. M. Mascal
Department of Chemistry, University of California Davis
1 Shields Avenue, Davis, CA 95616 (USA)
E-mail: mascal@chem.ucdavis.edu

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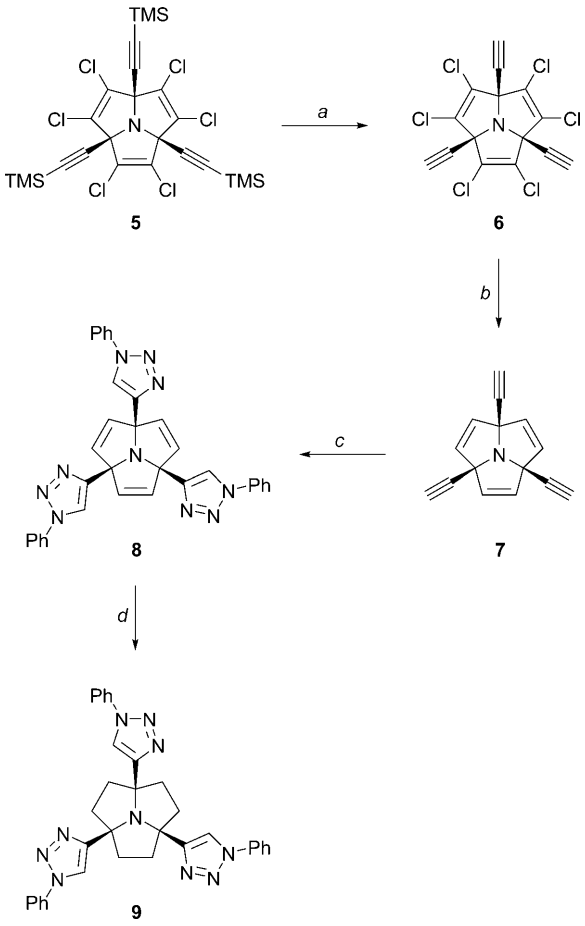


Scheme 2. Reagents and conditions: a) KF, MeOH, 16 h, 99%; b) Li, *t*BuOH/THF, reflux, 1 h, 44%; c) PhN_3, sodium ascorbate, $CuSO_4$, *t*BuOH/H_2O, 80°C, 6 h, 96%; d) H_2, Pd/C, MeOH, 48 h, 98%.

crystal structures of these derivatives reveal them to be calix shaped (Figure 2a). In order to take advantage of the basic nitrogen site at the base of the cavity, the electron-withdrawing chlorine substituents have to be removed. As above, this could be accomplished by reduction with an active metal to give azatriquinacenes **11**. Likewise, these could also be hydrogenated to the corresponding azatriquinanes **12**. Interestingly, in the case of **12c**, the aromatic rings turn to occupy the cavity in the solid state, probably due in part to weak $C_{Ar}H\cdots N$ hydrogen bonding with the now basic nitrogen (Figure 2b).

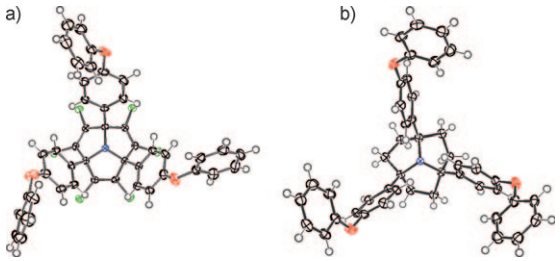
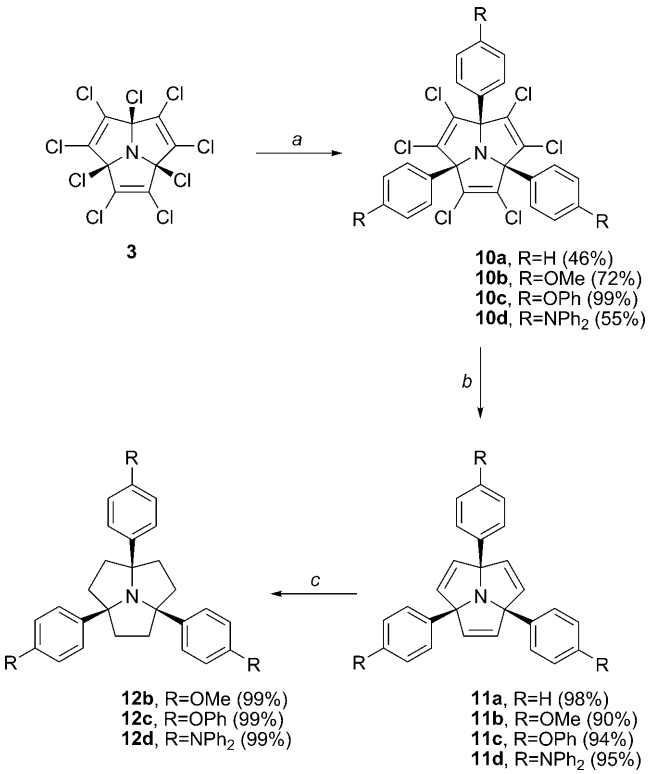
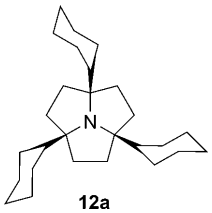


Figure 2. ORTEP[8] views of the a) X-ray crystal structure of **10c**; b) X-ray crystal structure of **12c**. Thermal ellipsoids are drawn at the 60% probability level.



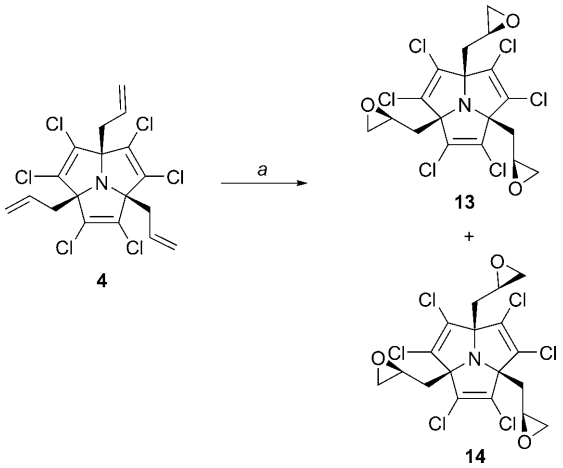
Scheme 3. Reagents and conditions: a) RAr, $AlCl_3$, CH_2Cl_2; b) Na, *i*PrOH, THF; c) H_2, Rh/Al_2O_3, EtOAc.

An unexpected but certainly interesting outcome of the hydrogenation reaction of **11a** was the complete saturation of the molecule to give tricyclohexylazatriquinane **12a**. This occurred under the same conditions as the reduction of **11b–d** (5% Rh on Al_2O_3, 1 atm H_2), which otherwise gave the expected products **12b–d** (Scheme 3).



There is remarkably little in the way of prior work on conformationally fixed amines with threefold symmetry to be found in the literature. The only systems conceptually analogous to 1,4,7-trisubstituted azatriquinanes are the correspondingly substituted 1-azaadamantanes or quinuclidines. Although none of the former have been described, Canary[9] and Corey[10] have both published work on the latter. In these papers, the main point is the chirality of the ring framework, an issue that does not have to be confronted in the synthesis of substituted analogues of **1** and **2** since the α-positions do not become chiral centers. For our part, we can introduce chiral C_3 symmetry into the system by the addition across the double bonds of triallyltriquinacene **4**. For example, treatment of **4** with *m*-chloroperbenzoic acid (MCPBA) gives a separable mixture of the C_3-symmetric tris-epoxide **13** and asymmetric isomer **14** in good overall yield (Scheme 4).

In summary, we have described the application of the azatriquinane ring system as a novel, rigid, threefold symmetric molecular scaffold, and demonstrate this by the synthesis of a preorganized tripodal transition-metal host



Scheme 4. Reagents and conditions: a) MCPBA, $CHCl_3$, 24 h, **13** (24%), **14** (70%).

and a series of triaryl derivatives with calix-like structures. We look forward to investigating the diverse opportunities in molecular architecture that triallyl, triethynyl, and triaryl azatriquinanes have to offer.

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Keywords: calixarenes · fused-ring systems · tripodal ligands · triquinacenes · triquinanes

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