The Palladium Way to N-Heteroacenes

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Abstract: Novel synthetic methodologies allow increasingly efficient access to known organic materials, as well as the preparation of otherwise inaccessible species. Pd-catalyzed coupling of aromatic dihalides to ortho-diaminoaracenes furnishes embedded stable N,N'-dihydropyrazines expediently and in often excellent yields. The embedded N,N'-dihydropyrazines can then be oxidized by MnO₂ to give substituted azatetracenes, azapentacenes, azahexacenes, and azaseptacontacenes, which are soluble, processable, and stable. This powerful Pd-catalyzed methodology allows the preparation of azacenes, including diaza-, tetraaza- and hexaazacenes. In combination with a suitable Pd precursor, Buchwald-type biarylphosphines have been shown to give excellent results. Activated dihalides such as 2,3-dihaloquinoloxalines are coupled easily under simplified conditions, whereas 2,3-dibromoacenes require more stringent conditions and advanced catalyst precursors. Pd catalysts effect the assembly of azacenes with otherwise difficult to obtain substitution patterns. High yields and flexibility make this method most attractive.

Introduction

The development of new synthetic methodologies is critical in organic materials science, as, besides allowing increasingly efficient access to known key compounds, they enable the preparation of new classes of materials, with both issues being important. In recent years, we have tackled this task for the synthesis of larger azacenes by developing Pd-catalyzed coupling reactions of aromatic ortho-dihalides to aromatic ortho-diamines.

N-Heteroacenes

Acenes massively impact organic electronics, particularly as charge transport layers in organic thin-film transistors. Pentacene and its stabilized and substituted derivatives are heavily deployed in this field. Moreover, since Anthony’s TIPSpen (2) is commercially available, both vacuum-processed and solution-processed organic field effect transistors (OFETs) of this material are easily prepared. Pentacene (3) and its derivatives are hole transporters, as oxidation of the pentacene nucleus is much easier than its reduction, which is necessary for the generation of negative charge carriers in the organic semiconducting materials. Problems with water, oxygen, and trap states render difficult the use of pentacenes for electron transport.

Charge transport is, in a simplified way, proportional to the rate of degenerate charge transfer between two identical neighboring molecules (Figure 1).

Figure 1. Schematic view of an organic thin-film transistor with simplified charge (electron) transport in the film.

The charge transfer rate is dependent upon the transfer integral \( t \), which denotes the electronic overlap of two neighboring molecules and the reorganization energy \( \lambda \), defined as the energy gain of a radical anion or a radical cation upon structural relaxation from the equilibrium structure in the uncharged state to the equilibrium structure in its charged state. To optimize charge carrier mobility \( \mu \), \( t \) should be maximized, whereas \( \lambda \) should be minimized [Eq. (1)]. Generally, both factors can be favorable in larger acenes; particularly the rigid structure, but also the size of the acenes minimizes \( \lambda \).

\[
\mu \approx k_{ET} \approx \frac{1}{\sqrt{T}} e^{-\frac{\lambda}{kT}}
\]

Here \( \mu \) = charge carrier mobility, \( k_{ET} \) = charge transfer rate constant, \( T \) = temperature, \( k \) = Boltzmann constant, \( \tau = \) transfer integral, and \( \lambda \) = reorganization energy.

As the “normal” pentacenes are poor electron transport materials, one has to modify their structure. Lowering the energetic cost of electron injection and uptake, that is, increasing electron affinities, yet still retaining the superb properties of pentacenes would be desirable. Several groups have exploited the attachment of halogen atoms to pentacene. The alternative is the introduction of electronegative atoms directly into the perimeter of the acenes, as is the case in N-heteroacene 1. In the solid state, 1 packs in a similar manner to TIPS-pentacene 2 (Figure 2).
In 2007, Winkler and Houk calculated that several N-heteropentacenes display small reorganization energies and frontier orbital positions that should make them useful as electron transport materials. Several years later, Miao et al. reported the preparation of compound 1, which exhibited spectacular electron transporting properties with mobilities of up to $3.3 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$. Compound 1 is now a state-of-the-art electron-transport material.

Buchwald–Hartwig amination for cyclizing C–N bond formation

The Buchwald–Hartwig amination is an established and important reaction that forms $sp^2$ C–N bonds with a variety of different catalysts and Pd precursors. Many variants of this coupling have been developed. The synthesis of five-membered rings, such as those of the indole type, have been described and the Pd-catalyzed synthesis of acridines has also been reported, but the use of Pd catalysis of other six-membered N-heterocycles is a much less explored area. The Pd-catalyzed synthesis of $N,N'$-dihydropyrazines was unexplored before we started to investigate this area.

Figure 2. Packing of compound 1 in the solid state. This tetraazapentacene shows electron mobilities of up to $\mu_{\text{el}} = 3.3 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$ with $\eta_{\text{on}}/\eta_{\text{off}} = 6 \times 10^6$.

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Scheme 1. Classic synthetic approaches towards azaacenes.
diamines. Although they are more reactive than the dihydroxy compounds, ortho-quinones are often (not always) more sensitive and therefore harder to synthesize, but also more reactive and can lead to azacenes and various extended azaarenes. Mastalerz and co-workers assembled aromatic systems consisting of up to 11 fused six-membered rings by using this condensation strategy. The direct formation of azatetracenes by deploying ortho-quinones worked well, but for azapentacenes yields were variable. Very recently, Zhang and co-workers synthesized hexaazaazapentacenes by condensation of tetraaminophenazine with various diketones.

A variant of this condensation (Scheme 2) is the nucleophilic reaction of the diamine 12 in the presence of sodium amide with hexafluorobenzene to give the tautomerized N,N'-dihydro compound 13 in 24% yield. 13 is oxidized in good yields to give tetraazaacene 14.

Extension of this concept generates the N,N'-dihydro compounds 17 and 18 in reasonable yields (Scheme 3). For 18, oxidation is no longer possible, due to its low-lying HOMO, whereas for 17 only the dimer 19 is formed upon oxidation with MnO₂, probably via the fleeting intermediate tetrafluorotetraazahexacene.

Harnessing quinones, we treated the aromatic diamines 20–22 with naphthalene-1,2-dione. 1,2-Naphthoquinone is stable and condenses in high yields to give bent, phenanthrene-like azaarenes 23a–c in good to excellent yields (Scheme 4). A critical way to introduce substituents into azacenes is the alkylation of para-quinones structures such as 24 (Scheme 5). This works well for 1, if one uses a magnesium acetylide and then deoxygenates with tin chloride. Oxidation of the intermediate furnishes 1, which is obtained by oxidative oxidation of N,N'-dihydroazaacenes.

However, this arsenal of established methods can fail in the synthesis of substituted azacenes. The harsh conditions do not allow the coupling of alkynylated diamines 20–22 to dichloroquinoxaline 9a in boiling Hünig’s base. Upon changing the catalyst system into [Pd₂(db)₃] as a Pd source and RuPhos as ligand, we obtained the coupling product 25a in good yields (> 75%; Scheme 6). We also tested other Buchwald-type ligands, most of which also worked satisfactorily. In an extension of this concept, we also treated substituted dichloroquinoxalines 9b and c with 21, to give substituted, stable tetraazaazapentacenes 26b and c as stable compounds in good yields after coupling and oxidation.

In the coupling of 21 with the tetrachloride 9b, only two of the four chloride substituents participate, that is, only the activated chlorides react. 5-Nitro-2,3-dichloroquinoxaline 9c
also couples easily with diamine 21. The coupling reactions proceed smoothly in Hünig’s base (14–18 h) at its boiling temperature. In each case, 5 mol% of catalyst was used.

The isolated \(N,N’\)-dihydro tetraazapentacenes were all easily oxidized by MnO\(_2\). This approach provides access to tetraazatetracenes (Scheme 7). Although the Pd-catalyzed coupling of 5 to dichloropyrazines worked only in traces, the diaminobenzene 20, obtained through reduction of diethynylbenzothiadiazole (27) coupled to dichloroquinolines 9a–d to give the \(N,N’\)-dihydro tetraazatetracenes 28a–d; one of the few cases where \(N,N’\)-dihydroazatetracenes were isolated. MnO\(_2\) then oxidized 28a–d to give the tetraazatetracenes 29a–d.

This reaction cascade was extended to the synthesis of the first azahexacenes (Scheme 8).\(^\text{[18]}\) Both tetraaza- and hexaazahexacenes were obtained by Pd-catalyzed coupling of the substituted diaminoanthracene (22) or -phenazine (12) with activated dichloroquinolines 9a–c (Scheme 8). Although all
of the possible six \(N,N\)-dihydroazahexacenes 30a-f were obtained in high yields, only the derivatives 30a-d, leading to 31a-d, could be oxidized by \(MnO_2\). The other two dihydro derivatives (30e and f) had HOMOs that were energetically too low-lying, and could not be oxidized into azahexacenes 31.

**The Problem of Coupling Deactivated Dihalides\(^{[19]}\)**

The Pd-catalyzed coupling of 20–22 to activated ortho-dihalides is facile and furnishes the coupling products in good to excellent yields. However, the coupling to unactivated aromatic halides, such as 2,3-dibromonaphthalene (34) or 2,3-dibromoanthracene (43), was not yet possible. Therefore, we carefully optimized the reaction to find conditions under which we could couple the unactivated ortho-dihalides.

While the choice of the phosphane ligand was relatively clear, as the Buchwald-type ligands were by far the best systems we had tested and most such ligands worked, the Pd source \([Pd_2(dbca)]_3\) was not ideal (Scheme 9). In a first experiment, coupling of 12 to 32 under modified standard conditions furnished the monoarylated species 33 in 63% yield (Scheme 9), without any ring-closed products. A cyclometalated Pd complex with a RuPhos ligand was the most suitable system (Scheme 10). Good results were achieved with 5 mol% of Pd–RuPhos precatalyst, whereas lower loadings of Pd–RuPhos led to decreased yields and 10 mol% of the precatalyst increased the yield only slightly. As base/solvent combination, we could either employ Cs\(_2\)CO\(_3\) in dioxane or NaOtBu in toluene, both under microwave irradiation at temperatures of 120–150°C.

There are limits to this approach. We were never able to couple 12 with dichloro- (32) or dibromobenzene (37) to form the cyclic product. In the best cases, monoarylated products were isolated. If strong bases were used, catalyst decomposition was observed, whereas weak bases did not give any reaction. Bidentate and sterically encumbered phosphine ligands worked best, but only gave low conversions with dibromides. Ortho-dichlorobenzene worked best with a highest monoarylated open product yield of 63%. We assumed the superiority of chlorides to be due to steric effects, indicating that the reaction proceeded via a sterically crowded intermediate.

**Azapentacenes**

The diamine 21 reacted with dibromonaphthalene 34 to form 35 in 53% yield under the optimized reaction conditions (Scheme 11). The choice of base and temperature is critical for the formation of dihydro azapentacenes. When strong bases and temperatures over 120°C were applied, catalyst poisoning was observed. We believe that the catalyst poisoning was due to the oxidation of the formed dihydro azacene 35. Strong bases increase this tendency by deprotonation of 35, forming an even stronger reductant at these high temperatures. Oxidation of 35 with \(MnO_2\) gave the azacene 36 in 92% yield. An X-ray crystal structure of 36 was obtained (Figure 3). According to a similar reaction scheme, dibromobenzene 37 was coupled to the diaminoanthracene 22 to furnish 39 in 53%
yield (Scheme 12). However, some monoa rylated product was always formed, even when benzoquinone was employed to re-oxidize the Pd catalyst. These modified conditions provide a powerful strategy to access azapentacenes that are otherwise available only with difficulty. This Pd-catalyzed coupling was also employed by Müller and co-workers to prepare some attractive bisanthracenothiadiazoles.[20]

**Azahexacenes and Azaheptacenes**

Could one make diazahexacenes and possibly diazaheptacenes using Pd-catalyzed coupling sequences (see above)? Although we had previously prepared tetraaza- and hexaa zahexacenes, diazahexacenes and diazaheptacenes were unknown at the beginning of our synthetic endeavor. With the experience of the synthesis of the diazapentacenes, we coupled 22 to 34 and obtained the N,N'-dihydrodiazahexacene 40 in 49% yield (Scheme 13). More forcing conditions were applied in this case, as N,N'-dihydrodiazahexacenes are more resistant towards oxidation, in contrast to N,N'-dihydrodiazapentacenes (see above) during the Buchwald–Hartwig cyclization step. Oxidation of 40 with MnO2 gave the diazahexacene 41 in 81% yield (Scheme 13). The diazahexacene 41 is stable in solution, but attempts to obtain a single crystal X-ray structure of 41 failed and we isolated the butterfly dimer 42, the structure of which was solved and is analogous to that of the dimerization products formed from Anthony’s hexacenes (Figure 4).[21]

By employing the same strategy (Scheme 14), we coupled 2,3-dibromoanthracene 43 to the diamine 22. The N,N'-dihydrodiazaheptacene 44 was formed in 74% yield (Scheme 14). However, oxidation of 44 by MnO2 only produced the butterfly dimer 46. The preceding diazaheptacene 45 was elusive, going undetected even by UV/Vis spectroscopy of the reaction solu-
tion. Diazaheptacene 45 was apparently too reactive and immediately dimerized. We could, however, ascertain the structure of the butterfly dimer 46 by a single-crystal X-ray structure (Figure 5), which adopts the same topology that the analogous hydrocarbon-based heptacenes incur when they dimerize, as reported by Anthony and co-workers.\cite{21}

What would be the solution to the problem of dimerization of the azaheptacenes?\cite{22} The introduction of a second set of triisopropylsilyl (TIPS)-ethynyl groups might stabilize an azaheptacene sufficiently to allow its isolation. The two positions that participate in the cycloadditions are those closest to the central pyrazine ring. Blocking these sites in 41 or 45 should result in stabilization of such a large diazaacene. Retrosynthetic analysis suggested 48 and 49 as coupling partners (Scheme 15), but neither of these building blocks were known.

Reduction of the anthracenothiadiazoles 50\textsubscript{a–c} (Scheme 16), obtained from their respective quinones, furnished the diamines 48\textsubscript{a–c}. The best yield (64\%) was obtained for R = iPr. For the sterically more encumbered derivatives, the yields were lower. In the case of the dibromides 49\textsubscript{a–c}, the yields were variable but less afflicted by steric bulk. Surprisingly, the stability of the anthracenothiadiazoles 50 and their reduced diamines 48\textsubscript{a–c} was much decreased in comparison to the isomeric structure (22).

Coupling of 48 to 49 under optimized Pd catalysis conditions rendered the \(N,N'\)-dihydrodiazaheptacenes 52\textsubscript{a–d} in yields ranging from traces to 63\% (Scheme 17). The higher the steric burden on the starting materials, the lesser the yield of the coupling. For R and R’ = sec-Bu, practically acceptable coupling yields were still obtained. The formed \(N,N'\)-dihydrodiazaheptacenes 52 are easily oxidized by MnO\textsubscript{2} to give the diazaheptacenes in less than a minute (!) reaction time. Only the diazaheptacene 53 is reasonably stable and persists in solution for some time. For smaller substituents, the diazaheptacenes dimerize quickly to form structures 54 and 55.

Time-dependent NMR spectroscopy measurements (Figure 6) revealed that 53 is stable in moderately concentrated solution, barely having started to form the butterfly dimers 54 and 55 after several hours.

We obtained a \(^{13}C\) NMR spectrum of 53, and, in comparison to its \(N,N'\)-dihydro-precursor 52\textsubscript{c}, all of the signals had shifted to lower field, when oxidizing to 53 (Figure 7).

The diazaheptacene 53 is the largest linearly annulated azaacene reported to date, but its stability is only moderate. It is not clear whether larger N-heteroacenes will be sufficiently stable to be isolated. This problem could be overcome if synthetic routes towards sterically overloaded azaacenes evolve from the currently employed strategies. Until then, diazaheptacene 53 will remain the largest isolable representative.

The situation is entirely different if one introduces, for example, pyrene units, which enforce electronic separation of...
the aromatic units through the presence of more than one Clar sextet (Figure 8). Under such conditions, one can make considerably larger N-heteroarenes. However, these materials then do not show the extremely redshifted absorption bands that are so prominent in the “real” azaacenes. If one allows N,N'-dihydropyrazine rings embedded into the system, the size limitation of seven rings is also not an issue. Interestingly, it is not known whether band structures containing N,N'-dihydropyrazine units at certain intervals would present stable and persistent materials.23

Conclusion

N-Heteroacenes have come a long way from the backwaters of organic chemistry to high-performance materials for organic electronics. The substitution of an electron-accepting nitrogen group into the acene framework leads to changes with respect to both their synthesis and their properties. Our group and others have mostly concentrated on the introduction of pyrazine units into azaacenes. Pyrazines are—from a retrosynthetic point of view—modularized into azaacenes, as they can be quickly built up by the combination of an aromatic ortho-diamine with an aromatic ortho-dielectrophile. When employing aromatic ortho-dihalides as electrophiles, Pd-catalyzed coupling with ortho-diamines is a powerful new method to build up such N,N'-dihydroazaacenes. The accessibility of different aromatic ortho-dihalides, coupled with the modules 12 and 20–22, makes series of different azaacenes easily available in a construction-set type approach.

Recently, Koert and co-workers reported the use of 2,3-diaminonaphthalene as coupling partner for different dibromonaphthalenes,24 giving rise to interesting diazapentacenes, including the dicyanodiazapentacene 56 and other,
flourinatedazaacenes. These elegant coupling reactions were successful, as the authors employed Pd-RuPhos-G2 as the active catalyst precursor.

Questions regarding the synthesis of larger heteroacenes remain and it is, for example, not clear if long-term stableazaheptacenes and stableazaoctacenes can be prepared. It might remain and it is, for example, not clear if long-term stable aza-acenes and their derivatives remain stable. This powerful methodology enables access to molecular topologies that can otherwise not be simply achieved.

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