Novel Dihydropyrazines and their Double ortho-Annulation to Hexaaazapentacenes

Rainer Strathausena,b, Rainer Beckerta, Jan Fleischhauera, Dirk Müllerc, and Helmar Görlsd

a Institut für Organische Chemie und Makromolekulare Chemie, Friedrich-Schiller-Universität Jena, Humboldtstr. 10, D-07743 Jena, Germany
b Present address: Biomolecular Photonics Group, Jena University Hospital, Nonnenplan 4, D-07743 Jena, Germany
c Klinikum Bad Berka, Department of Molecular Radiotherapy / Center for Molecular Imaging, D-99437 Bad Berka, Germany
d Institut für Anorganische und Analytische Chemie, Friedrich-Schiller-Universität Jena, Lessingstr. 8, D-07743 Jena, Germany

Reprint requests to Prof. Dr. R. Beckert. E-mail: Rainer.Beckert@uni-jena.de

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Dedicated to Professor Peter Metz, Dresden, on the occasion of his 60th birthday

The cycloacylation of oxalic amidines 7 with bis-imidoylchlorides 6 furnished the dihydropyrazine derivatives 8. Due to their vicinal amino-imino substructures, they provide good preconditions for a double intramolecular ring closure reaction. An alternative synthesis for hexaaaza-pentacenes 1 was developed using potassium carbonate as the base and lead tetraacetate as the oxidizing agent.

Key words: Hexaaazapentacenes, Dihydropyrazines, ortho-Annulation, Amidines, Fluorophores

Introduction

Acenes, particularly pentacene, have attracted significant interest in organic electronic devices; however, they become increasingly unstable with increasing size [1]. Whereas one approach to the stabilization of higher acenes involves their substitution at selected positions, the other involves the exchange of CH atoms with heteroatoms, such as nitrogen. The resulting aza-acenes [2 – 5] are of particular interest since they possess different electronic and physical properties, and they also introduce new possibilities for chemical modification at the nitrogen atoms. Linear systems, such as “pyrazinacenes” 1 [6], offer by far the most opportunities for derivatization and applications have been reported as solvatochromic dyes [7, 8], redox-switchable chromophores/fluorophores [9, 10] and liquid crystalline materials [11]. Their most important application, as easily processable organic derivatives, is established in organic thin-film field effect transistors (OTFTs) [12 – 18]. Recent reviews [19] emphasize that aza-acenes are underrepresented in charge transport materials, and there is a high need for research activities in this field.

We recently reported syntheses of novel hexaaaza-pentacenes 1 and 2, via aminolysis reaction of tetrachloropyrazine 3 with 2-aminophenyl(phenyl)-amine [20] (Scheme 1). At the beginning, product 3 has only been available by a tedious chlorination of pyrazine-2,3-dicarboxylic acid or pyrazine itself, and an alternative synthesis is desirable. In addition, pyrazines such as 3 have a high oxidation potential and, therefore, are able to oxidize vicinal diamines to undesirable by-products very easily.

The starting point for a new synthetic approach was the observation of highly fluorescent octaaza-hexacenes 5 as by-products during the derivatization reactions of pyrazino[2,3-b]pyrazines 4 [21] (Scheme 2). For the formation of 5, we first postulated a cycloaddition-redox sequence, however, this reaction is based on a different reaction type: an ortho-annulation reaction primarily via radical cations. Consequently, the prototropic form 4′, which possesses a vicinal amino-imino substructure, plays the key role in
Double ortho-Annulation

Scheme 1. Retrosynthetic approach to hexaazapentacenes of types 1 and 2.

Scheme 2. Pyrazino[2,3-b]pyrazines 4 and 4′ as starting point for a cascade reaction to give octaazahexacenes 5.

Generally, benzannulation of aromatics and heteroaromatics forms an important basis for the syntheses of new molecules, mainly for material chemistry. Modern organic chemistry offers an arsenal of methods using [4+2]-cycloaddition reactions of o-quinodimethanes [26, 27] or appropriately structured heterocycles (isobenzofurans, isoquinolinium systems) [28, 29], benzynes/pyrydynes [30–32], and 3,3-benzannulation reactions [33].

We have previously demonstrated that other vicinal amino imines also allow an oxidative ring closure reaction. Applying 4H-imidazoles [34] and 3,4-bis(arylamino)-substituted pyrroles as model compounds [35], new ring-fused derivatives were synthesized and characterized. Based on quantum-chemical calculations [35], we showed that a multi-step process with a radical cation as the key intermediate most likely takes place. The fact that during the formation of 5 from 4, a double ortho-annulation process took place prompted us to re-examine this reaction. Derivatives 8 (Scheme 3) provide ideal conditions to test this hypothesis and are easily accessible starting from common C2 building blocks.

Results and Discussion

As depicted in Scheme 3, derivatives 8 were synthesized by simple cycloacetylation of amidines 7 with bis-imidoyl chlorides 6. The only weakly electrophilic, but selective C2 building blocks of type 6 have already been used frequently for syntheses which take place via cyclization-tautomerism sequences [36–39]. Accordingly, the dihydropyrazines 8 were successfully synthesized. The reaction was carried out by fast addi-
tion of one equivalent of 6 to a dioxane solution containing the deprotonated amidine 7 (base: NaHMDS). The new products, which contain two linked oxamidine substructures, were isolated as orange crystalline compounds in good yields. They form equilibria consisting of different prototropic forms in common solvents, as indicated by broad signals in their NMR spectra. Starting from the $^{15}$N-labelled bis-imidoyl chloride 6e, a doublet ($\text{J} = 89 \text{ Hz, } ^{15}\text{N–H}$) was detected besides a singlet for the unlabelled NH in the NMR spectrum of its cyclization product 8e. This experimental finding is a clear indication of the coexistence of at least one other prototropic isomer 8e’. The structure of the latter, being a donor-substituted diaza-quinone-diamine, easily explains the strong absorption bands ($\lambda_{\text{max}} = 430-450 \text{ nm, } \varepsilon = 4.2$) in the UV/Vis spectra. We succeeded in obtaining single crystals suitable for X-ray structure analysis. The structure determined of the derivative 8b confirms the preference of the prototropic form 8b’ (Fig. 1).

The molecule crystallizes in space group $P2_1/m$ and has a twofold rotation axis perpendicular to the pyrazine ring, which, together with the nitrogen atoms, forms a plane. Both of the exocyclic imino substructures exhibit Z-configuration in the crystal. The aromatic rings bonded to the nitrogen atoms N2 and N3 are twisted out of the plane. The torsion angles between C2–C3–C8–N2 and between C1–N3–C9–C14 are 29.3$^\circ$ and 52.5$^\circ$, respectively; the smaller torsion angle is caused by the double bond. The proton on the nitrogen atom N3 is connected via a hydrogen bond to a methoxy group of a neighboring molecule, thus forming a ladder-type structure. Compared to the bond between C1 and N3 (1.341 (2) Å), the bond length between N2 and C2 (1.294 (2) Å) is, therefore, significantly reduced – a further indication for the preference of the prototropic form 8’ in Scheme 3.

In the first oxidation test, derivative 8a was reacted under the conditions (CAN in the presence of K$_2$CO$_3$ in acetonitrile) used successfully for ortho-annulation reactions already reported [34]. After a short time, the formation of a strongly yellow-fluorescent substance was detected by TLC. The chromatographic isolation yielded a black, amorphous substance; the MS data (M$^+$ $m/e = 494$) suggested the presence of structure 1a (Ar = 4-toly). Optimization reactions for derivative 1a showed that potassium carbonate as a base and lead tetraacetate as the oxidizing agent gave the best results.
Scheme 4. Double oxidative ortho-annulation to give leuco forms of 1 and 2 which were immediately oxidized by air to give regioisomeric hexaazapentacenes 1 and 2.

(Scheme 4, 1a: 24% yield). Traces of a strongly red-fluorescent compound were always isolated as a by-product, the MS data of which were similar to those of compound 1a. The $^1$H NMR spectrum clearly showed two singlets for two different tolyl groups ($\delta = 2.11$ and 2.43 ppm). However, no exact assignment was possible in the region of aromatic protons; the integrals were consistent with the number of protons expected. The molecular structure of 2a was confirmed by X-ray structure analysis. The poor quality of the crystals did not allow a satisfactory refinement. From these data, it is evident that, in this case, a double ortho-annulation also took place which led to the mesoionic regioisomer 2a.

Because no single crystals could be obtained, the further characterization of 1a proved to be problematic. Furthermore, all attempts to obtain suitable crystals by salt formation/N-methylation also failed. Suitable data could only be obtained from the UV/Vis fluorescence spectra. The absorption spectrum revealed a well-structured pattern with a maximum at 518 nm, while the emission spectrum is nearly congruent with an intense emission at 525 nm. The very small Stokes shift of only 7 nm comprises a very small difference between ground and excited state. The derivative 1c was isolated in very low yields starting from 8c and was characterized by MS ([M]$^+$, $m/e = 662$). All attempts to involve derivative 8b in oxidative ortho-annulation led only to decomposition reactions with the formation of inseparable mixtures of polymeric products, obviously due to the strong influence of the donor methoxy groups. Derivative 8d as a precursor gave better results. With a reaction time of 5 h, the derivative 1d (yield up to 45%) was obtained and characterized. Interestingly, the sequence cyclization/oxidation (starting from 6d and 7d via 8d) was successfully realized in a one-pot synthesis, and gave comparable yields. The hexaaza-pentacene 1d was obtained after purification by column chromatography as an amorphous, black solid, which showed decomposition upon heating above 400 °C. A molecular ion at $m/e = 708$ in its mass spectrum confirmed the proposed structure. The UV/Vis and the fluorescence spectra are almost identical to that of derivative 1a and again show a very small Stokes shift of only 7 nm (Fig. 2).

Despite the testing of other oxidizing agents, the yields for derivatives 1 could not be increased; instead, a series of highly fluorescent substances was formed as by-products. An interesting result was found when potassium ferricyanide was used as an oxidant. In this case, a non-fluorescent iron complex was first formed, which decomposed after some time to give the starting material and small amounts of 1a and 2a. Further studies with metal complexes as oxidizing agents are planned, and the results will be the subject of a separate publication.

Based on our previous work and the findings of the present studies, we postulate the following mechanism (Scheme 5) for the formation of hexaaza-pentacenes of types 1 and 2. First, the oxidation of the secondary amine group in 8 takes place under the intermediary formation of the radical cation A. A relatively strong
Fig. 2. UV/Vis and fluorescence spectrum of 1d in THF (normalized).

Scheme 5. Proposed mechanism for the double ortho-annulation sequence.

Acidity has been predicted for these types [40–42] and, consequently, deprotonation may result in the aminyl radical B. Radical cation A as well as radical B are able to substitute the attached aromatic ring intramolecularly to give the leuco-semi form C. Due to the bifunctionality of 10, the same reaction subsequently can form Leuco-1 and Leuco-2, which are transformed by oxygen from air in a final oxidation step into 1 and 2, respectively. The mechanism, in which the key intermediates are radical cations/aminyl radicals A/B, is supported by the following experimental facts. Generally, anilines can easily be oxidized, and the radical cations thus formed tend toward a fast deprotonation. It is noteworthy, however, that kinetic studies revealed that cyclization reactions of aminyl radical cations are much faster than those of the corresponding neutral radicals [43, 44]. Despite the fact that some methods for the generation of aminyl radicals are described in the literature [45–48], reactions of nitrogen-centered radicals are less well developed than
those of the analogous carbon species. In addition, only a few data for intramolecular cyclization reactions with aminyl radicals/radical cations exist [43–45], among which the Hoffman-Löffler-Freytag reaction is the oldest known reaction involving aminium cation radicals [49]. Whereas aminyl radicals are nucleophilic, ammonium cation radicals and their metal complexes render the nitrogen atom more electrophilic.

The oxidative cyclization of aryl-substituted amidines, which have a similar substructure as aminyl cation radicals and their metal complexes exist [43–45], among which the Hoffman-Löffler-Freytag reaction is the oldest known reaction involving aminium cation radicals [49]. Whereas aminyl radicals are nucleophilic, ammonium cation radicals and their metal complexes render the nitrogen atom more electrophilic. Because the interconversion of A to B is very fast, we are not able to determine the key intermediate.

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Transformation of derivatives 8a and 8d to hexaaazapentacenes 1a and 1d

In a 100 mL two-necked flask, a mixture consisting of 1 mmol of a dihydroazepine 8, 1.4 g (10 mmol) of potassium carbonate and 3.6 g (12 mmol) of Pb(OAc)₄ in 10 mL of dioxane was heated at 80 °C. The temperature was maintained for 5 h, and then unreacted Pb(OAc)₄ was reduced to Pb(OAc)₂ by adding 2 mL of ethylene glycol. The crude product was precipitated by adding 50 mL of water and filtered off. The solid was washed with 100 mL of dioxane-water (1/1) and finally, 10 mL of diethyl ether. The azacene was extracted with methylene chloride, then the extract was evaporated in vacuo and finally, the product was purified by column chromatography (silica gel 60, CHCl₃-acetone).

5,12-Bis-(4-toly)-3,10-dimethyl-5,12-dihydro[5,6,7,12,13,14]hexaaazapentacene (1a)

Black solid; yield 25%. – M. p. > 400 °C (dec.). – UV (CHCl₃): λmax (lg ε) = 272 (4.8), 403 (4.3), 428 (3.9), 454 (4.4), 486 (4.8), 520 nm (4.9). – Emission (CHCl₃): λ = 528, 570, 617 nm, fluorescence quantum yield (ΦA) = 0.95(±0.05). – 1H NMR (250 MHz, CDCl₃+ CF₃COOD): δ = 7.53 (m, 8H, aryl), 7.17 (d, J = 8.1 Hz, 4H, aryl), 6.9 (s, 1H, aryl), 6.78 (s, 1H, aryl), 5.05 (s, 2H, NH), 2.54 (s, 6H, CH₃), 2.11 ppm (s, 6H, CH₃). – C₂₃H₂₈N₂O (494.60): calcld. C 77.71, H 5.30; found C 77.54, H 5.20. N 16.85.

3-(n-Butyl)-5-(4-butylphenyl)-10-bromo-12-(4-bromo-phenyl)-dihydro[5,6,7,12,13,14]hexaaazapentacene (1d)

Black solid; yield 45%. – M. p. > 400 °C (dec.). – UV (CHCl₃): λmax (lg ε) = 272 (4.8), 431 (4.0), 458 (4.5), 488 (4.9), 524 nm (5.0). – Emission (CHCl₃): λ = 535, 576, 623 nm, fluorescence quantum yield (ΦA) = 0.95(±0.05). – 1H NMR (250 MHz, CDCl₃): δ = 7.41 (m, 14H, aryl), 2.27 (m, 4H, CH₂), 1.63 (m, 4H, CH₂), 1.03 (d, J = 3.7 Hz, 6H, CH₃), 0.88 ppm (q, J = 7.3 Hz, 4H, CH₃). – MS (EI): λ / z (%): 172 (50%, 665), 105 (398), 90, 171 (93), 132 (24). – C₂₆H₂₂Br₂N₂O (708.50): calcld. C 61.03, H 4.55; Br 22.56, N 11.86; found C 60.95, H 4.46, Br 22.40, N 11.71.

5,7-Bis-(4-toly)-3,9-dimethyl-5,12-dihydro[5,6,7,12,13,14]hexaaazapentacene (2a)

In a 25 mL flask a mixture consisting of 100 mg (0.2 mmol) of dihydroazepine 8a, 111 mg (0.8 mmol) of potassium carbonate and 263 mg (0.8 mmol) of K₃[Fe(CN)₆] in 5 mL of DMSO was heated at 75 °C. After 5 h the reaction was complete and the crude product was precipitated by addition of 10 mL of water. The precipitate was filtered off and washed with 10 mL DMSO-water (1/3). The product was purified by column chromatography (silica gel 60, CHCl₃-acetone).

Bluish-black crystals; yield 5%. – M. p. > 400 °C (dec.). – UV (CHCl₃): λmax (lg ε) = 375 (4.2), 409 (4.0), 525 (4.2), 564 (4.1), 609 nm (4.5). – Emission (CHCl₃): λ = 644 nm, fluorescence quantum yield (ΦA) = 0.55(±0.05). – 1H NMR (250 MHz, CDCl₃): δ = 7.11 (d, J = 8.0 Hz, 4H, aryl), 6.88 (d, J = 7.9 Hz, 8H, aryl), 6.16 (s, 2H, aryl), 2.43 (s, 6H, CH₃), 2.11 ppm (s, 6H, CH₃). – MS (EI): λ / z (%): 494 (66), 403 (10), 247 (14), 133 (35), 106 (100). – C₂₆H₂₂Br₂N₂O (708.50): calcld. C 61.03, H 4.55; Br 22.56, N 11.86; found C 60.95, H 4.46, Br 22.40, N 11.71.

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Crystal structure determinations

The intensity data for the compounds were collected on a Nonius KappaCCD diffractometer using graphite-monochromated MoKα radiation. Data were corrected for Lorentz and polarization but not for absorption effects [53, 54]. The structures were solved by Direct Methods (SHELXS-97 [55]) and refined by full-matrix least-squares techniques against $F^2$ (SHELX-97 [55]). The hydrogen atoms of 8b were located by difference Fourier synthesis and refined isotropically. All non-disordered, non-hydrogen atoms were refined anisotropically [55].

Crystals of 2a were extremely thin and of low quality, resulting in a substandard data set (triclinic, space group $P1\_1\_1$), $a = 8.7540(4)$, $b = 12.0801(9)$, $c = 14.6555(11)$ Å, $\alpha = 84.264(3)$, $\beta = 87.387(4)$, $\gamma = 81.701(4)^{\circ}$, $V = 1525.14(18)$ Å$^3$, $Z = 2$. The structure refinement was sufficient, however, to confirm the connectivity and overall geometry despite high final $R$ values. For the latter reason the crystallographic data will not be deposited at The Cambridge Crystallographic Data Centre.

Crystal data of 8b: $C_{12}H_{16}N_4O_4$, $M = 562.62$ g mol$^{-1}$, red-brown prisms, size 0.05 $\times$ 0.05 $\times$ 0.05 mm$^3$, monoclinic, space group $P2_1/n$, $a = 6.3256(3)$, $b = 10.8267(4)$, $c = 19.9198(7)$ Å, $\beta = 92.302(2)^{\circ}$, $V = 1563.11(9)$ Å$^3$, $T = -140^\circ$C, $Z = 2$, $\rho_{\text{calc}} = 1.37$ g cm$^{-3}$, $\mu$ (MoKa) = 1.9 cm$^{-1}$, $F(000) = 592$ e, 9389 reflections in $h(-7/8)$, $k(-14/13)$, $l(-25/25)$, measured in the range 3.42$^\circ$ $\leq \theta \leq$ 27.45$^\circ$, completeness to $\theta_{\text{max}}$ = 99.7%, 9389 measured reflections, 3112 independent reflections, $R_{\text{int}}$ = 0.0574, 2189 reflections with $F_o > 4\sigma(F_o)$, 250 refined parameters, no restraints, $R_{\text{1 obs}}$ = 0.0429, $wR_{\text{2 obs}}$ = 0.1018, $R_{\text{1 all}}$ = 0.0716, $wR_{\text{2 all}}$ = 0.1146, GoF = 1.024, largest difference peak and hole 0.18/−0.23 e Å$^{-3}$.

CCDC 974508 (8b) 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.


