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Double head-to-tail direct arylation as a viable strategy towards aza-analog of dihydrocyclopenta[*hi*]aceanthrylene – intriguing antiaromatic heterocycle

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The first case of double head-to-tail direct arylation of aromatic compounds and the unusual photophysical properties of the resulting $2,2a^{1,5}b^{1,7}$ -tetraazacyclopenta[*hi*]aceanthrylene are reported. This molecule, comprising of two imidazo[1,2-*a*]pyridine units, is antiaromatic due to the changes in the efficiency of π -electron ring current and it belongs to a class of seldom encountered compounds with dark lowest electronically excited singlet state.

Polycyclic aromatic hydrocarbons (PAHs)¹ and their heterocyclic analogues possessing π -expanded structures² are of great significance in the field of organic electronics. The potential applications of materials possessing the heteroacene core in electronic devices such as organic light emitting diodes (OLEDs),^{3a} organic field effect transistors (OFETs)^{3b} as well as dye-sensitized solar cells⁴ have been widely studied in recent years. Most of the work in this area has focused on linear heteroacenes⁵ and ladder-type heterocycles.⁶ Although perylene is unique in the family of PAHs and has been extensively studied, the incorporation of heteroatoms into its skeleton is a difficult task. Only a few such perylene analogues are known⁷ because of the lack of general synthetic methods. Imidazo[1,2-a]pyridine is a prototypical heterocyclic system that is known to possess useful optical properties,⁸ and over the last five years, numerous papers have described advances in its synthesis.9 The development of suitable substrates to obtain heterocycles comprised of two imidazo[1,2-a]pyridine moieties that are fused at the 3,5 positions by using classical methods remains a difficult undertaking. Therefore, we aimed to develop an efficient synthesis of this compound through a different strategy.

Our initial strategy towards bis-imidazo[1,2-a]pyridine **4** was based on the assumption that singly-linked dimer **3**, obtained *via*

the direct C3-arylation,¹⁰ could be fused *via* dehydrogenative coupling reaction. The required substrates **1** and **2** were obtained in the condensation of 2-chloroacetaldehyde with 2-aminopyridine and with 2-amino-6-bromopyridine, respectively.¹¹ The compound **3** was synthesized *via* direct arylation of imidazo[1,2-*a*]pyridine (**1**) with substrate **2**, following the general procedure reported by Doucet *et al.*^{10e} (Scheme 1).



Scheme 1. Direct arylation of imidazo[1,2-*a*]pyridine and the synthesis of compound **4**.

Subsequently, singly-linked precursor **3** was subjected to the recently optimized anion-radical coupling conditions (K, toluene, 95 °C, air).¹² However, the expected bis-imidazo[1,2-*a*]pyridine **4** was not formed under these conditions. Moreover, neither Scholl reaction (AlCl₃, NaCl, 150 °C),¹³ nor oxidative coupling (PIFA, BF_3 ·Et₂O)¹³ afforded the desired product **4** (Scheme 1). In light of

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these results we decided to investigate an alternative strategy, namely double head-to-tail direct arylation. Thus, 5bromoimidazo[1,2-a]pyridine (2) was subjected to optimized conditions reported recently by Doucet and co-workers, (based on PdCl(C₃H₅)(dppb) as catalyst).¹⁴ To our delight, double direct arylation occurred, leading to compound 4 with 20% yield. This conversion constitutes the first case of double head-to-tail direct arylation ever reported. Careful optimization studies (ESI) allowed us to improve the yield of the formed bis-imidazo[1,2-a]pyridine 4 to 57% using Pd(OH)2/C, KOAc in DMA.15 Starting from 2bromo-4-methyl-6-aminopyridine we subsequently prepared analogous bis-imidazo[1,2-a]pyridine 5 (Fig. 1, details in ESI). It is important to add that substituted 2-bromo-6-aminopyridines are neither commercially available nor easy to synthesize, which somewhat limits the scope of this methodology. All attempts to obtain X-ray quality crystals of compounds 4 or 5 failed.



Fig. 1. ¹H NMR and ¹³C NMR assignment for compound **4** (a); and structure of compound **5** (b). ¹H and ¹³C shifts given in ppm.

Both confirmation of the structure and unambiguous signals assignment was performed based on additional 2D NMR-experiments, such as COSY, ¹³C¹H-HSQC and ¹³C¹H-HMBC (Fig. 1, details in ESI).

The analysis of the ¹H NMR spectrum of bis-imidazo[1,2*a*]pyridine $(2,2a^{1,5}b^{1,7}$ -tetraazacyclopenta[*hi*]aceanthrylene, **4**) revealed one striking observation. The protons of the sixmembered rings, which in the spectrum of imidazo[1,2*a*]pyridines are usually located around 7.12-8.13 ppm,¹⁶ were upfield shifted to 5.14-6.39 ppm. There is also the 0.35 ppm up-field shift of the Me groups in dye 5 compared to compound S2. This observations led us to analyze the changes of the extent of cyclic π -electron delocalization in this molecule. Initially, we used Nucleus Independent Chemical Shift,17 which we calculated at the ring centers (NICS) and 1Å above (NICS1) using GIAO/B3LYP/6-311+G** levels of theory.¹⁸ The values for 4 and 1 are given in Fig. 2. For the pyridine-type outer ring, NICS showed a very marked drop from -6.6 ppm (in the parent imidazo[1,2-a]pyridine) to +2.0 ppm in compound 4! The respective NICS(1) value changed from -7.9 to -0.6 ppm. In the five membered heterocyclic ring a similar, albeit smaller effect was observed: the NICS decreased here by 4 ppm. Topologically, this system resembles perylene, which has an outer naphthalene moiety that is less aromatic than in the parent molecule, whereas the central ring is strongly antiaromatic. Notably, here the NICS for the central ring was even more positive (NICS = +14.1, NICS(1) = +9.6) than in pervlene (NICS = +8, NICS(1) = +3).

Another case of antiaromaticity has been recently revealed by Tobe and co-workers.¹⁹ This unusual decline of aromaticity was also well reflected in the dramatic decrease of magnetic susceptibility exaltation of compound **4** as compared with the parent imidazo[1,2-*a*]pyridine system.



Fig. 2. The NICS values for 1 and 4. Values of NICS1 are given in parentheses.

Application of a simple homodesmotic approach²⁰ (bisimidazo[1,2-a]pyridine + 4 x ethene => 2 x imidazo[1,2-a]a)pyridine + 2 x butadiene), using the magnetic susceptibilities of the systems (calculated at CSGT/B3LYP/6-311+G** level of theory¹⁸) led to a reduction of 42 cgs ppm. This decrease is noteworthy, taking into account that the value of magnetic susceptibility for 4 is -92.6 cgs ppm, whereas a similar homodesmotic approach for perylene (perylene + 4 x ethene $\Rightarrow 2$ x naphthalene + 2 x butadiene) is only 16.5 cgs ppm. Importantly, this large change in magnetic structure was not accompanied by changes in either stability or geometry. Application of the homodesmotic approach (as above) using the total energies of the systems (fully optimized at B3LYP/6-311+G**, corrected for zero point energy correction; all species corresponded to minima on the potential energy surface with no imaginary frequencies¹⁸) of the compounds gave only 2 kcal/mol reduced stability of compound 4 as compared with imidazo[1,2-a] pyridine. Moreover, the geometry-based index of aromaticity HOMA²¹ gave almost the same values for the imidazo[1,2-a]pyridine moiety in 4 and in the parent heterocycle 1 (0.85 and 0.83, respectively). This result implies that the changes of the extent of π -electron delocalization due to coupling of two imidazo[1,2-a]pyridines are almost exclusively manifested in the magnetic properties. They are dominated by dramatic changes in the efficiency of the π -electron ring current.



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Fig. 3. Absorption spectrum of **4** in *n*-hexane and calculated energies of the electronic transitions $S_0 \rightarrow S_i$ (*black triangles*, details in ESI). Heights of the vertical lines indicate calculated oscillator strengths of the allowed transitions.

Having the desired molecule in hand, we conducted photophysical studies. The absorption spectrum of compound 4 in *n*-hexane (Fig. 3) revealed that the maximum of lowest energy absorption line was located at 420.9 nm. The spectrum is simple within the spectral range between 325 and 440 nm, and seems to be more complicated at higher energies (at wavelengths shorter than 325 nm). The above spectrum can be rationalized with the aid of quantum chemistry calculations. Results of calculations of So \rightarrow S_i transition energies and corresponding oscillator strengths with use of TD DFT/B3LYP/6-31G(d,p)//DFT B3LYP/6-31G(d,p) method are shown in Fig. 3 and presented with the description in Tabs.S20 of ESI. According to calculations (see Tab. S20) bands observed in the range 325-440 nm correspond to the $S_0 \rightarrow S_2$ transition. In the group symmetry C2h, to which molecule 4 belongs, it is the symmetry allowed $A_g \rightarrow B_u$ transition. Fig. 4 depicts both, the experimental absorption spectrum and the simulated spectrum in the $S_0 \rightarrow S_2$ region. The Franck-Condon (FC) factors for the vibronic transitions, given by the vertical lines, were calculated for the geometry of molecule 4 optimized in the S₂ state. A nearly perfect fit between the calculated and experimental spectra was obtained when we broadened the transition lines with the Gaussian distribution. Notably, the two main vibrations, 369 and 1608 cm⁻¹, can be characterized as stretching of molecule 4 along the C-C bonds connecting the two subunits 1 (see vibration vectors in the inset of Fig. 4). The relatively large values of the Franck-Condon factors for this vibration may be understood in terms of the large changes in the lengths of these C-C bonds when the molecule is excited from state S₀ to S₂ (by 0.03A; see Fig.S24 in ESI.

The transition $S_0(A_g) \rightarrow S_1(A_g)$ is symmetry forbidden. In the experimental absorption spectrum of compound **4** within the spectral range between 430 and 600 nm we observed only a weak structure (with the frequency ~1450 cm⁻¹) with two orders of magnitude lower intensity than that for the $S_0 \rightarrow S_2$ transition. We suppose that we are observing vibronically induced transitions, like in a case of $S_0(A_{1g}) \rightarrow S_1(B_{2u})$ transition in benzene and some other molecules.²² In this mechanism the intensity for the $S_0(A_g) \rightarrow S_1(A_g)$ transition is borrowed from other, symmetry allowed electronic transitions. As it was presented in Tab. S20, in molecule **4** there are several symmetry allowed transitions with high oscillator strength. All of them have symmetry B_u and these states can be mixed with the $S_1(A_g)$ state by b_u promoting vibrational modes.

Despite the use of different excitation wavelengths and a sensitive photon detection set-up, we were not able to monitor any fluorescence emission of **4**, neither from the S_1 nor from the S_2 state. The same optical properties have been observed for compound **5** (see ESI Tab. S26 and Fig. S27).

The group of molecules with a dark S_1 state has been extensively studied to extend our knowledge about the mechanisms of intermolecular coupling and the paths of excitation energy relaxation.²² An example of such compounds are diphenylpolyenes, molecules with the C_{2h} symmetry (like **4**), where the symmetry of the lowest excited singlet state is dependent on the chain length.²³⁻²⁵ Tetraazacyclopenta[*hi*]aceanthrylene bears some structural resemblance to s-indacenes, which are also non-fluorescent.²⁶ Conical intersection may contribute to fast depopulation of the S₂ state of compound **4**, and may explain the lack of radiative emission from this state. The S₁ \rightarrow S₀ transition is symmetry forbidden.



Fig. 4. Experimental absorption spectrum (red) observed over the range 370-430 nm, which is attributed to vibronic structure of the $S_0 \rightarrow S_2$ transition. Calculated FC factors for the vibronic transitions, shifted to coincide with the experimental spectrum, are given by the vertical lines. The simulated spectrum (black) was obtained when the lines were broadened with the Gaussian distribution, each with fwhm = 200 cm⁻¹.

Surprisingly, cyclic voltammetry studies revealed that they are not electrochemically active i.e. they undergo neither oxidation nor reduction in broad range of potentials. According to the DFT B3LYP/6-31G(d,p) calculations energies of frontier molecular orbitals of compound **4** are E(HOMO) = -4.98 eV and E(LUMO) = -1.85 eV respectively (all energies calculated for the geometry of **4** optimized in neutral state).

In conclusion, we have demonstrated that through careful design of the substrate, it is possible to fuse two molecules of heterocyclic bromoarene via double direct arylation. The prepared previously unknown π -expanded system, i.e., $2,2a^{1,5}b^{1,7}$ -tetraazacyclopenta[*hi*]aceanthrylene, is a compound with symmetry-forbidden transition between the ground state S_0 and the lowest electronically excited singlet state S_1 , which results in no fluorescence at all. Dramatic changes in the efficiency of the π -electron ring current, as exhibited by magnetic properties led to antiaromaticity of this compound (in sharp contrast with aromaticity of parent imidazo[1,2apyridine). Experimental absorption spectrum and TDDFT calculations gave compact picture of the electronic states of compound 4. We observed the large energy gap between the S_1 and S_2 states, what is the characteristic feature of antiaromatic molecules.23-25

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Notes and references

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[†] Electronic Supplementary Information (ESI) available: Experimental details for compounds **3-5**, ¹H NMR and ¹³C NMR, 2D NMR spectra, cyclic voltammetry as well as details of computational studies. For ESI see DOI: 10.1039/c000000x/

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Straightforwardly prepared head-to-tail bis-imidazo[1,2-*a*]pyridine displays antiaromaticity and no fluorescence due to the forbidden $S_0 \rightarrow S_1$ transitions.

