σ^H-Adducts of 1-alkyl-1,4-diazinium salts as the sources of biradicals in the synthesis of tetraazaphenanthrenes

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O- and C-Adducts of 5-(het)aryl-2,3-dicyano-1-ethylpyrazinium salts are latent sources of biradicals capable of forming tetraazaphenanthrene derivatives *via* dimerization. The mechanisms of the reactions were examined using ESR spectroscopy. The stereochemistry of the resulting heterocyclic systems was studied by NMR spectroscopy. The crystallographic data on their three-dimensional structures were obtained.

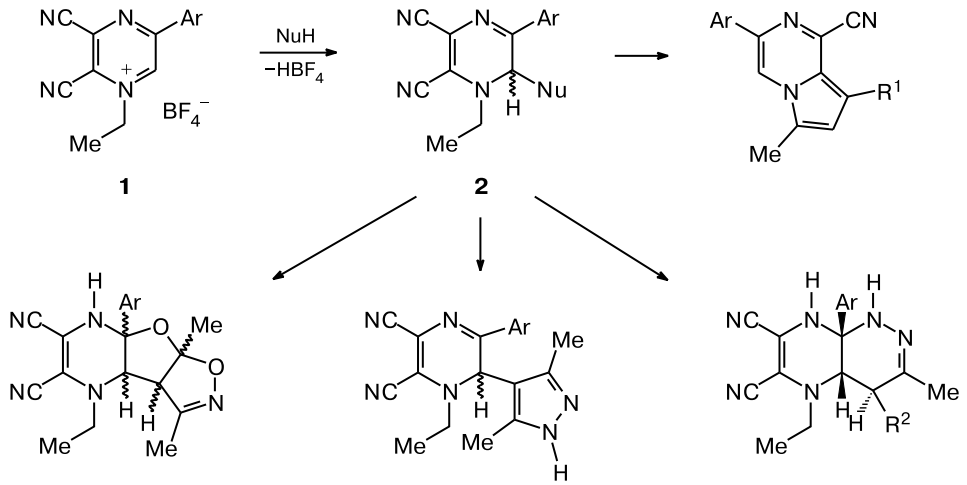
Key words: 2,3-dicyano-1-ethylpyrazinium salts, 1,2-dihydropyrazines, σ^H-adducts, biradicals, pyrrolo[1,2-*a*]pyrazines, 4a,4b,9,10-tetrahydro-3,6,8a,10a-tetraazaphenanthrenes.

σ^H-Adducts resulting from a direct nucleophilic attack on the unsubstituted C—H fragment of an aromatic ring are key intermediates in S_NH reactions.[1,2] The main pathways of their transformations include dissociation into the starting compounds, vicarious or oxidative aromatization,[1—3] and non-oxidative transformations into other cyclic systems, as recently shown for a number of 2,3-dicyanopyrazines (Scheme 1).[4—8]

The goal of the present work was to further study the properties of O- and C-adducts **2**. We found that reflux of σ^H-adducts **3a,b** and **4** (compounds **3a,b** were prepared from 5-(het)aryl-2,3-dicyano-1-ethylpyrazinium salts **1** and the acetylacetonate anion; compound **4** is the adduct of salt **1** and water) in *o*-xylene for 2 h gives tetraazaphenanthrenes **5a,b** (Scheme 2, Table 1).

Note that the dimerization of this type for 1,4-diazines is observed for the first time, though a similar transformation has been discovered earlier[9,10] in the series of *N*-alkyl-1,2,4-triazinium salts. In contrast to 1,2,4-triazine dimers isolated as the only diastereomer, the dimerization of

Scheme 1



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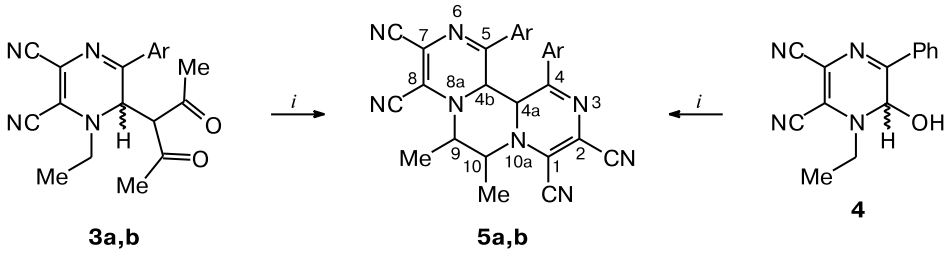
Scheme 2



i. Reflux, *o*-xylene.

Ar = Ph (**3a**, **5a**), 3-thienyl (**3b**, **5b**)

Table 1. Yields of compounds **5a,b** and the ratio of the diastereomers

Starting compound	Product	Yield (%)	Ratio of diastereomers **A** : **B**	
			Product[a]	Reaction mixture[b]
3a	**5a**	51	5 : 1	3 : 1
3b	**5b**	50	4 : 1	3.5 : 1
4	**5a**	73	5 : 1	2.5 : 1

[a] The product was isolated by filtration.
[b] For ^{1}H NMR studies, the reaction mixtures were concentrated and the residues were not subjected to any further treatment.

1,4-diazines yielded mixtures of two diastereomers (their ratios are specified in Table 1).

The structures and relative configurations of the asymmetric centers in compounds **5a,b** were proved by ^{1}H and ^{13}C NMR spectroscopy, 2D experiments (^{1}H—^{1}H COSY, ^{1}H—^{13}C HSQC, and ^{1}H—^{13}C HMBC), and X-ray diffraction.

The spectroscopic characteristics of the diastereomers differ noticeably (Fig. 1). The ^{1}H and ^{13}C NMR spectra of the major isomer containing two pairs of chemically equiv-

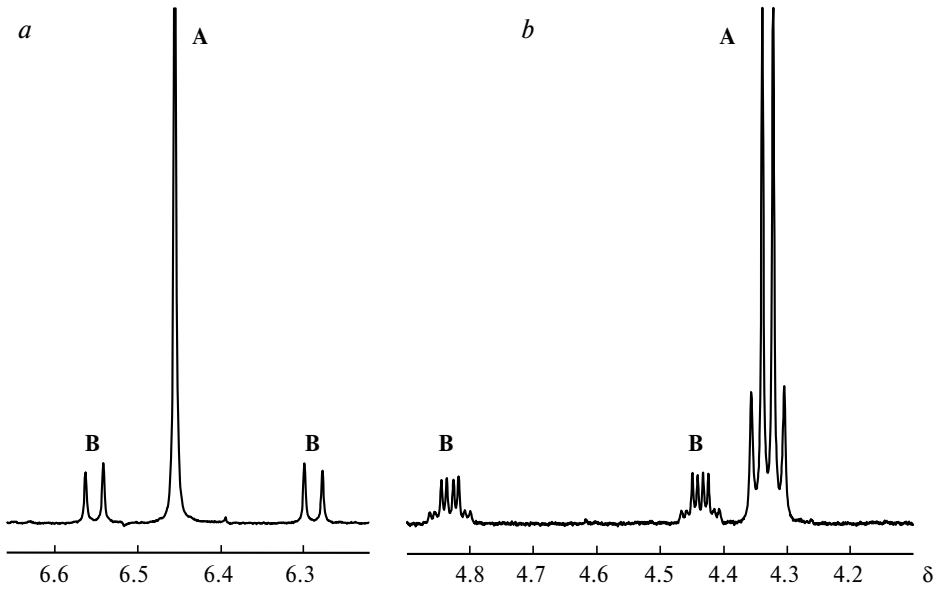


Fig. 1. Fragments of the ^{1}H NMR spectrum (400 MHz) of compound **5a**: the regions of the signals for the H(4a) and H(4b) protons (*a*) and the H(9) and H(10) protons (*b*).

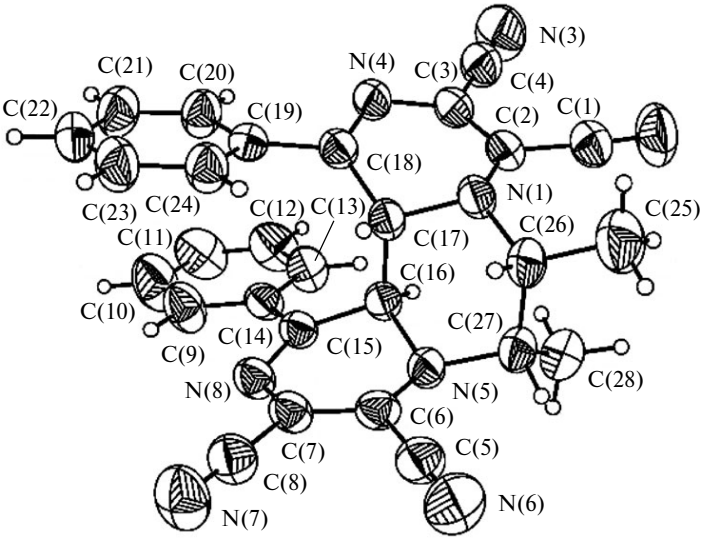
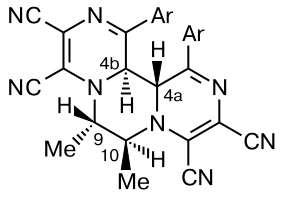


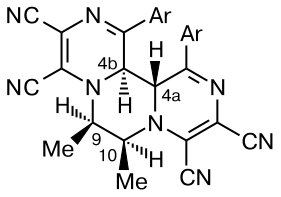
Fig. 2. Geometry of structure **5a** (isomer **B**) in the crystal.

alent carbon atoms (C(4a), C(4b) and C(9), C(10))[11] show one set of signals without a vicinal spin-spin coupling between the pairs of the corresponding protons (H(4a)—H(4b) and H(9)—H(10)). The ^{1}H and ^{13}C NMR spectra of the minor isomer contain a double set of signals with the constants $^3J_{H(4a),H(4b)} \approx 8.7$ Hz and $^3J_{H(9),H(10)} =$ = 3.2 Hz corresponding to the *ax—ax* and *ax—eq* couplings of the protons of the central piperazine ring.

The configurations and compositions of the diastereomers **A** and **B** of compounds **5a,b** were determined from the spectroscopic data (see Table 1). Major isomer **A** is a diastereomer of the tricyclic system, while minor isomer **B** is a *meso*-form.



A



B

The structure of the minor isomer of compound **5a** was determined by X-ray diffraction.

The general view of structure **5a** with the atomic numbering adopted in crystallographic experiments is shown in Fig. 2 (DMF molecules are omitted). The compound crystallizes from DMF in a centrosymmetric space group as a solvate with two DMF molecules.

The geometry of the dihydropyrazine rings in structure **5a** is close to that in the structures examined earlier.[4—7] The piperazine ring assumes the boat conformation. The endocyclic C—N bonds (N(1)—C(2) and N(5)—C(6)) and one methyl group, as well as the protons at the sp^3-hybridized C(16) and C(17) atoms of the dihydropyrazine rings, occupy axial positions, while the second methyl group and the C—C bonds of the dihydropyrazine rings (C(17)—C(18) and C(16)—C(15)) occupy equatorial positions. Thus, in the stereoisomer under consideration, the C(16) and C(17) atoms (according to the IUPAC nomenclature, these atoms should be designated as C(4) and C(4a), respectively) and the C(26) atom at the equatorial methyl group have a configuration opposite to that of the C(27) atom (at the axial group). This configuration is consistent with the ^{1}H NMR signals observed for the minor asymmetric isomer **B**. The crystal packing consists of layers of molecules along the plane [010], with interlaying solvent molecules (Fig. 3). The relative stability of the solvent-saturated packing is due to a very compact arrangement of DMF molecules and the formation of many shortened O...H—C contacts between the carbonyl group

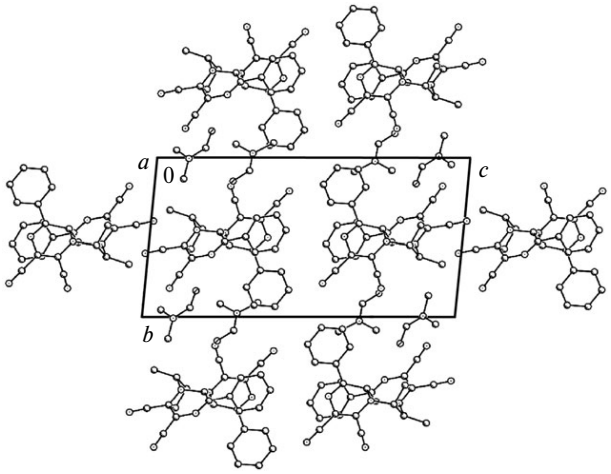
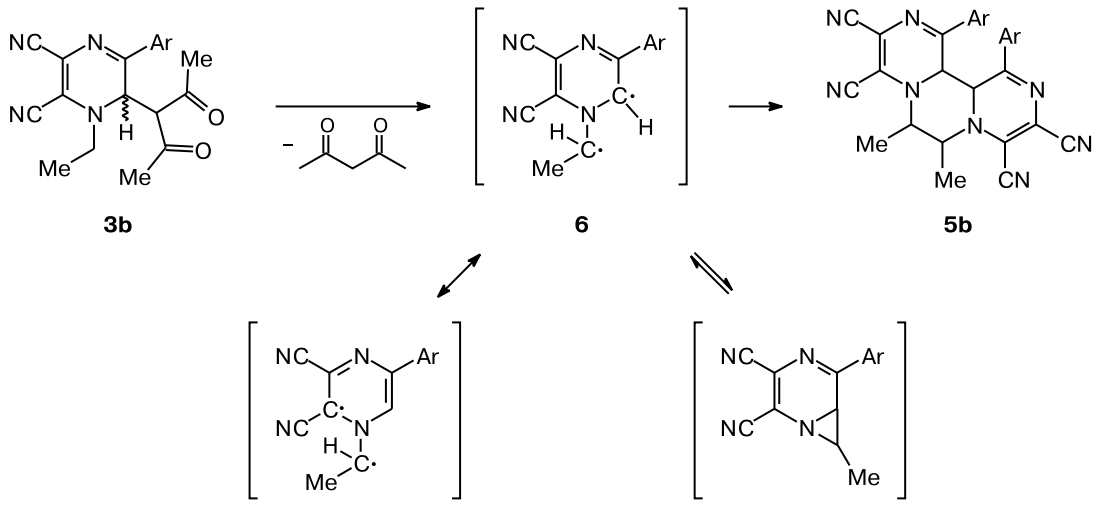


Fig. 3. Fragment of the molecular packing of compound **5a** (the hydrogen atoms are omitted).

Scheme 3



of the solvent and the protons of the carbon framework of tetraazaphenanthrene (O...H, 2.35—2.70 Å). The packing shows no significant π—π-contacts.

Since dimerization processes[9,10] usually involve paramagnetic species, we tried to detect them in the reaction mixtures using the ESR technique. We found that heating of adduct **3b** in *o*-xylene yields relatively stable biradicals capable for recombination into dimer **5b** (Scheme 3).

When a solution of compound **3b** in *o*-xylene is heated at 363 K and above, the EPR spectrum shows an intense signal consisting of nine lines. The maximum amplitude and best resolution were attained at $T = 400$ K. Figure 4 displays the corresponding spectrum and its antiderivative.

The intensity ratio of the hyperfine structure (HFS) components is 1 : 3 : 4 : 5 : 5 : 5 : 4 : 3 : 1. The hyperfine coupling (HFC) constants are $a^1 \approx a^2 = 1.8$ G, $a^3 \approx a^4 = 2.4$ G, and $a^5 \approx a^6 = 2.8$ G. The exact values of the HFC constants and the resonant field strengths of the hyperfine components for an optimum theoretical spectrum are given in Table 2.

When a sample of **3b** is rapidly cooled to 300 K (and further down to 200 K), its spectrum persists for several days. However, the HFS disappears completely, being replaced by a wide unresolved line with $\Delta B = 24$ G and $g = 2.004$ (Fig. 5). On reheating to 400 K, the HFS is restored.

The character of the chemical reaction, the products obtained, and the parameters of the ESR spectra provide evidence for thermoactivated formation of triplet-state biradicals of the type **6**. Apparently, the ESR pattern is mainly contributed by the isotropic component of the HFC. The anisotropic contribution and the dipole-dipole interactions are zero-averaged.

Thus, using ESR spectroscopy, we detected biradicals **6** in the dimerization reactions, studied the dynamics of their formation and recombination, measured the HFC constants ($a^H = 2.2$ G, $a^N = 1.8$ G in the dimerization

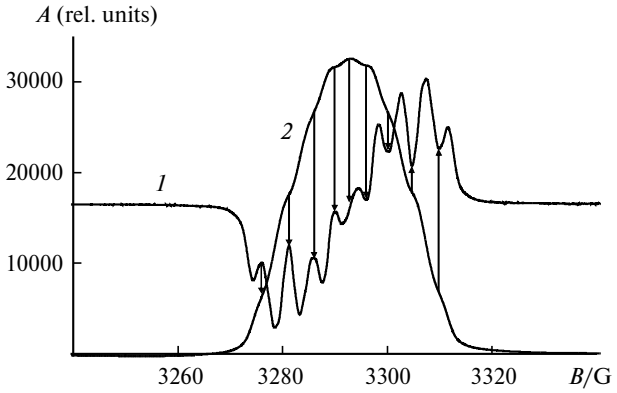


Fig. 4. Resolved ESR spectrum of the reaction mixture in the dimerization of compound **3b** at 400 K (*1*) and its antiderivative (*2*); *A* is the amplitude.

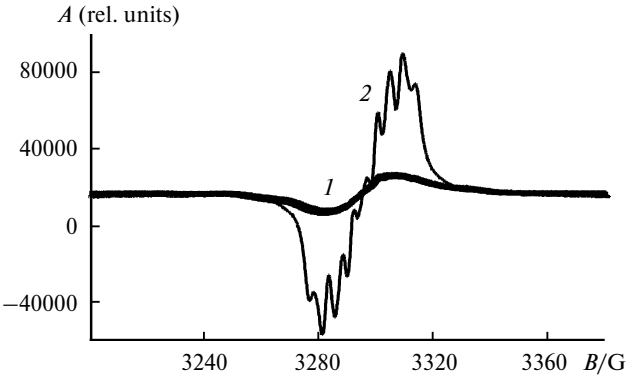


Fig. 5. Changes in the ESR spectrum of the reaction mixture during the dimerization of compound **3b** at 300 (*1*) and 363 K (*2*).

Table 2. Exact values of the HFC constants *a* and the resonant field strengths B_r for the optimum ESR spectrum of the reaction mixture in the dimerization of compound **3b** in *o*-xylene at 400 K

No. of line	B_r	*a*
	G	
1	3279.67	—
2	3284.14	4.47
3	3288.54	4.40
4	3292.90	4.36
5	3295.69	2.79
6	3297.22	1.53
7	3299.90	2.68
8	3304.25	4.35
9	3308.82	4.57
10	3312.78	3.96

reaction), and estimated the exchange parameter $J/a \geq 2$. We also demonstrated that σ^H-adducts of nucleophiles and 5-(het)aryl-2,3-dicyano-1-ethylpyrazinium salts can serve as latent biradicals for the synthesis of tetraazaphenanthrene derivatives.

Experimental

Solvents and reactants were dried and purified as described earlier.[12] The starting compounds **3a,b** and **4** were prepared according to a known procedure.[4]

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 instrument (400 and 100 MHz, respectively) with Me_4Si as the internal standard. Mass spectra were measured on a Shimadzu LCMS-2010 quadrupole liquid GC-MS spectrometer in MeCN (scan rate 0.25 mL min^{-1}, Supelco LC-18 column (4.6×250 mm), positive or negative ion mode, APCI or ESI, working voltage 4.5 kV, nitrogen as a carrier gas, flow rate 2.5 L min^{-1}). Elemental analysis was carried out on a Perkin—Elmer PE-2400 automatic analyzer. Melting points were determined on Boetius combined hot stages and are given uncorrected. Flash chromatography was carried out on Lancaster silica gel (0.040—0.063 mm, 230—400 mesh).

The course of the reaction was monitored and the purity of the products was checked by TLC on Sorbfil plates; spots were visualized under UV light or with the iodine vapor.

X-band ESR spectra (~9.4 GHz) were recorded at ~20 °C on an ERS-231 standard homodyne spectrometer in a rectangular TE_{102} resonator. The experimental conditions were as follows: the central field B_0 = 3300 G, scan range δB_{sr} = 150 G ($\delta B_{sr} > 5\Delta B$, where ΔB is the width of the peak—peak line), microwave power P = 2 mW, modulation amplitude b = 0.5—2 G. The *g*-factor was calibrated against wood pitch pyrolysate.

For ESR studies, weighed samples (5 mg) of compound **3b** were placed in quartz tubes 2 mm in diameter and then *o*-xylene (5 mL) was added. Chemical reactions were watched *in situ* in the TE_{102} resonator of the spectrometer.

Single crystals of compound **5a** were obtained by crystallization from DMF. X-ray diffraction analysis was performed for a red single crystal (0.13×0.08×0.04 mm) on an Xcalibur-3 X-ray diffractometer fitted with a CCD detector (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω scan mode, scan step 1°, 295 K). The crystal is triclinic, space group *P*-1, a = 8.3494(10) Å, b = 10.4577(9) Å, c = 19.445(3) Å, α = 94.214(10)°, β = 94.646(12)°, γ = 104.243(9)°, V = 1632.6(4) Å; $C_{34}H_{34}N_{10}O_2$, Z = 2, d_{calc} = = 1.250 g cm^{-3}, μ = 0.082 mm^{-1}. The structure was solved and refined by using the reflections collected for 2.64° < θ < 28.28°. The number of measured reflections was 20 449, the number of independent reflections was 7931 (R_{int} = 0.0334), and the number of reflections with $I > 2\sigma(I)$ was 3355. The completeness was 98.0 (θ < 28.28°) and 98.9% (θ < 26.0°).

Structure **5a** was solved by the direct method with the SHELXS-97 program and refined with the SHELXL-97 program.[13] The coordinates and thermal parameters of the non-hydrogen atoms were refined isotropically and then anisotropically by the full-matrix least-squares method. The H atoms were located from the electron density maxima and refined using a riding model. The final residuals are R_1 = 0.0445 and wR_2 = 0.1087 for reflections with $I > 2\sigma(I)$ and R_1 = 0.1237 and wR_2 = 0.1247 for all reflections (S = 1.009). The maximum and minimum residual electron densities are 0.454 and –0.193 e Å^{-3}, respectively. The X-ray diffraction data for compound **5a** have been deposited with the Cambridge Crystallographic Data Center (CCDC No. 816 723) and are available from www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of 4,5-di(het)aryl-9,10-dimethyl-4a,4b,9,10-tetrahydro-3,6,8a,10a-tetraazaphenanthrene-1,2,7,8-tetracarbonitriles 5a,b (general procedure). A solution of compound **3a**, **3b**, or **4** (1 mmol) in *o*-xylene (7 mL) was refluxed for 2 h. The precipitate that formed was filtered off and washed with MeCN (~20—30 mL).

9,10-Dimethyl-4,5-diphenyl-4a,4b,9,10-tetrahydro-3,6,8a,10a-tetraazaphenanthrene-1,2,7,8-tetracarbonitrile (5a), dark red powder, m.p. 253—255 °C (decomp.). Found (%): C, 71.62; H, 4.41; N, 23.95. $C_{28}H_{20}N_8$. Calculated (%): C, 71.78; H, 4.30; N, 23.92. Major isomer. ^{1}H NMR (DMF-d_7), δ: 1.95 (d, 6 H, 2 Me, J = 6.9 Hz); 4.33 (q, 2 H, H(9), H(10), J = 6.9 Hz); 6.45 (s, 2 H, H(4a), H(4b)); 7.19 (dd, 4 H, H_m, J = 8.5 Hz, J = 7.3 Hz); 7.39 (tt, 2 H, H_p, J = 7.3 Hz, J = 1.2 Hz); 7.72 (dd, 4 H, H_o, J = 8.5 Hz, J = 1.2 Hz). ^{13}C NMR (DMF-d_7), δ: 15.45 (2 Me); 48.95 (C(4a), C(4b)); 62.27 (C(9), C(10)); 108.86, 112.42 (2 CN); 117.72 (C(2), C(7)); 124.40 (C(1), C(8)); 127.77 (C_o); 128.86 (C_m); 132.46 (C_p); 135.72 (C_{ipso}); 150.13 (C(4), C(5)). Minor isomer. ^{1}H NMR (DMF-d_7), δ: 1.81 (d, 3 H, Me, J = 7.5 Hz); 1.87 (d, 3 H, Me, J = 6.9 Hz); 4.44 (qd, 1 H, H(10) (H(9)), J = 6.9 Hz, J = 3.2 Hz); 4.83 (qd, 3 H, H(9) (H(10)), J = 7.5 Hz, J = 3.2 Hz); 6.29, 6.55 (both d, 1 H each, H(4a), H(4b), J = 8.6 Hz); 7.22—7.27 (m, 4 H, H_m); 7.42—7.46 (m, 2 H, H_p); 7.60 (dd, 2 H, H_o, J = 8.6 Hz, J = 1.2 Hz)*. ^{13}C NMR (DMF-d_7), δ: 10.25 (Me); 16.14 (Me); 47.94, 56.15 (C(4a), C(4b)); 63.11, 63.61 (C(9), C(10)); 109.40, 112.03, 113.04, 113.98 (4 CN); 117.49, 117.58 (C(2), C(7)); 120.97, 124.75 (C(1), C(8)); 127.69, 128.03 (C_o); 128.92, 129.05 (C_m); 132.66, 132.78 (C_p); 135.45, 135.58 (C_{ipso}); 150.50, 151.55 (C(4), C(5)). LC-MS (ESI), m/z (I (%)): 467 $[M - H]^+$ (100), 467 $[M]^+$ (32).

9,10-Dimethyl-4,5-di(3-thienyl)-4a,4b,9,10-tetrahydro-3,6,8a,10a-tetraazaphenanthrene-1,2,7,8-tetracarbonitrile (5b),

* The signals for the H_o protons are masked by the signals for the major isomer.

dark red powder, decomp. at 274—276 °C. Found (%): C, 59.88; H, 3.51; N, 23.15. $C_{24}H_{16}N_8S_2$. Calculated (%): C, 59.98; H, 3.36; N, 23.32. Major isomer. ^{1}H NMR (DMF-d_7), δ: 1.90 (d, 6 H, 2 Me, J = 6.9 Hz); 4.26 (q, 2 H, H(9), H(10), J = 6.9 Hz); 6.16 (s, 2 H, H(4a), H(4b)); 7.04 (dd, 2 H, H(4), 3-thienyl, J = 5.2 Hz, J = 1.3 Hz); 7.37 (dd, 2 H, H(5), 3-thienyl, J = 5.2 Hz, J = 2.7 Hz); 8.65 (dd, 2 H, H(2), 3-thienyl, J = 2.7 Hz, J = 1.3 Hz). ^{13}C NMR (DMF-d_7), δ: 15.47 (Me); 50.26 (C(4a), C(4b)); 61.59 (C(9), C(10)); 109.39, 112.54 (CN); 117.78 (C(2), C(7)); 123.84 (C(1), C(8)); 126.53 (C(4), 3-thienyl); 127.63 (C(5), 3-thienyl); 130.68 (C(2), 3-thienyl); 140.16 (C(3), 3-thienyl); 146.56 (C(4), C(5)). Minor isomer: ^{1}H NMR (DMF-d_7), δ: 1.77 (d, 3 H, Me, J = 7.5 Hz); 1.82 (d, 3 H, Me, J = 6.9 Hz); 4.35 (qd, 1 H, H(10) (H(9)), J = 6.9 Hz, J = 3.2 Hz); 4.66 (qd, 3 H, H(9) (H(10)), J = 7.5 Hz, J = 3.2 Hz); 6.16, 6.42 (both d, 1 H each, H(4a), H(4b), J = 8.8 Hz); 7.06 (dd, 1 H, H(2) (H(2′)), 3-thienyl, J = 2.8 Hz, J = 1.3 Hz); 7.40 (dd, 1 H, H(5) (H(5′)), 3-thienyl, J = 5.1 Hz, J = 2.8 Hz); 7.44 (dd, 1 H, H(5) H((5′)), 3-thienyl, J = 5.1 Hz, J = 2.8 Hz); 8.24 (dd, 1 H, H(2) (H(2′)), 3-thienyl, J = 2.8 Hz, J = 1.3 Hz)*. ^{13}C NMR (DMF-d_7), δ: 10.28 (Me); 16.17 (Me); 49.42, 57.60 (C(4a), C(4b)); 62.39, 63.21 (C(9), C(10)); 110.06, 112.13, 113.60, 114.13 (CN); 117.54, 117.67 (C(2), C(7)); 120.29, 124.11 (C(1), C(8)); 126.34, 127.72, 128.03, 130.08, 130.33, 131.32 (C(2), C(2′), C(4), C(4′), C(5), C(5′), 3-thienyl); 139.87, 139.89 (C(3), C(3′), 3-thienyl); 146.78, 147.90 (C(4), C(5)). LC-MS (ESI), m/z (I (%)): 479 $[M - H]^+$ (100), 480 $[M]^+$ (33), 481 $[M + H]^+$ (11).

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* The signals for the H(4) and H(4′) protons of 3-thienyl are masked by the signals for the major isomer.

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