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Pyriporphyrin – A Porphyrin Homologue Containing A Built-in Pyridine Moiety

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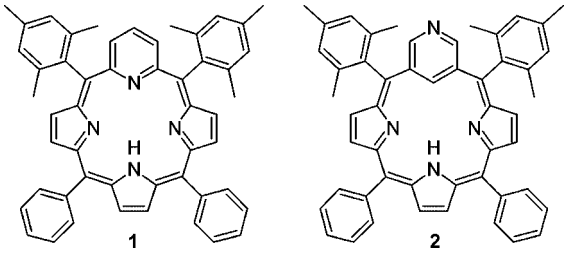
Pyriporphyrin **1** (6,11,16,21-tetraaryl-22-aza-*m*-benziporphyrin), the simplest homologue of 5,10,15,20-tetraarylporphyrin can be constructed by replacement of one of the pyrrole rings of 5,10,15,20-tetraarylporphyrin with a pyridine moiety, linked to the macrocycle through α,α′-carbon atoms.

In spite of the extensive effort aimed to control porphyrin properties involving core modifications,[1] a synthesis of true pyriporphyrin **1** has remained a continuing challenge. Recently reported carbaporphyrinoid 6,11,16,21-tetraaryl-3-aza-*m*-benziporphyrin (*N*-confused pyriporphyrin) **2** was the very first pyriporphyrin containing an unperturbed pyridine ring, though in the *N*-confused macrocyclic frame.[2] Previously, the significant effort was devoted to synthesize porphyrin-related macrocyles containing pyridine instead of pyrrole yielding, eventually, phlorin- or chlorin-like derivatives.[3] Correspondingly, the incorporation of 3-hydroxypyridine into the porphyrinic framework led to 2-oxypyriporphyrin containing a pyridone moiety.[4] Contrary to regular pyriporphyrin **1** the contracted {subpyriporphyrin – a [14]triphyrin(1.1.1) homologue with an embedded pyridine moiety}[5] and expanded [12-hydroxypyrisapphyrin,[6a] dipyrihexaphyrin(1.0.0.1.0.0),[6b,6c] torand – tetrapyrioctaphyrin(0.0.0.0.0.0.0.0)[6d]] counterparts containing pyridine were already reported. The relevant case of a phthalocyanine modification can be exemplified by hemiporphyrazines, non-aromatic cross-conjugated macrocycles, containing two pyridine and two pyrrole units bound through aza bridges.[7] At a porphyrinogen oxidation state the homologation of pyrrole to pyridine within the *meso*-octaethylcalix[4](pyridine)$_n$(pyrrole)$_{4-n}$ skeleton was achieved.[8]

Here we report on the synthesis and characterization of pyriporphyrin **1** (Scheme 1). The molecule reveals one of the simplest imaginable frames for a modified porphyrin, which involves one pyrrole ring expansion to give a pyridine ring embedded into the tetraarylporphyrin structure.



Scheme 1. Pyriporphyrin **1** and *N*-confused pyriporphyrin **2**.

The synthetic strategy (Scheme 2) applies some features used for the synthesis of 3-azabenziporphyrin[2] and subpyriporphyrin.[5] In particular, introduction of bulky substituents at the *ortho* positions of the *meso*-aryl groups at **4**, adjacent to the incorporated pyridine ring, increased the stability of 2,6-bis[(2-pyrrolyl)(mesityl)methyl]pyridine toward acidolysis during the condensation which eliminates a scrambling effect. Dibenzoylation of **4** yielded **5**. Subsequently, **5** was reduced to the dialcohol derivative, which was used in the [3 + 1] condensation. After oxidation and chromatographic workup, the green pyriporphyrin **1** was obtained in 5.5% yield.

The electronic spectrum of **1** (Figure 1) resembles those of non-aromatic benziporphyrin[9] or 3-azabenziporphyrin.[2] The ^{1}H NMR spectrum of **1** presents the resonances at positions consistent with its non-aromatic structure (Figure 2, trace B).

Thus, the macrocyclic aromatic ring current is practically absent for **1**, as clearly illustrated by positions of pyrrole and pyridine resonances, assigned by 2D experiments {[D_2]-dichloromethane, 203 K: δ = 7.56 (3-H), 7.28 (2/4-H), 7.04 (13/14-H), 7.00 (8/19-H), 6.62 (9/18-H) ppm}. Scalar coupling, detected between pyrrole hydrogen atoms N-24-H ([D_2]dichloromethane, 203 K: δ = 9.22 ppm) and 13/14-H, is consistent with the prevalence of the symmetrical tautomer **1** (N-22,N-23,N-24-*H*,N-25) (Scheme 3).

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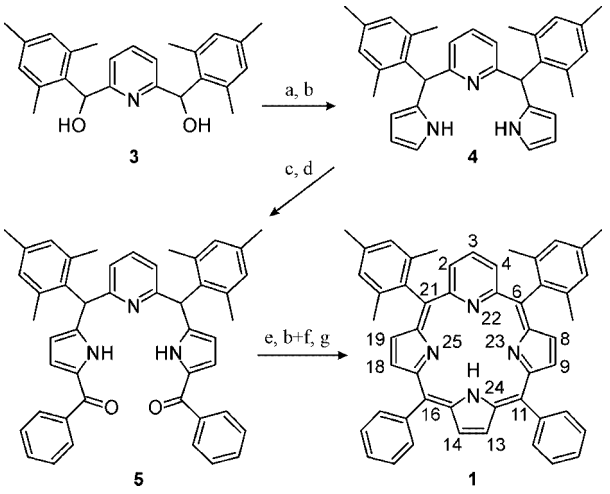


Scheme 2. Synthesis of pyriporphyrin **1**: a) MsCl/TEA, b) pyrrole, c) EtMgBr, d) PhCOCl, e) $NaBH_4$, f) TFA/MeCN, g) TEA, DDQ.

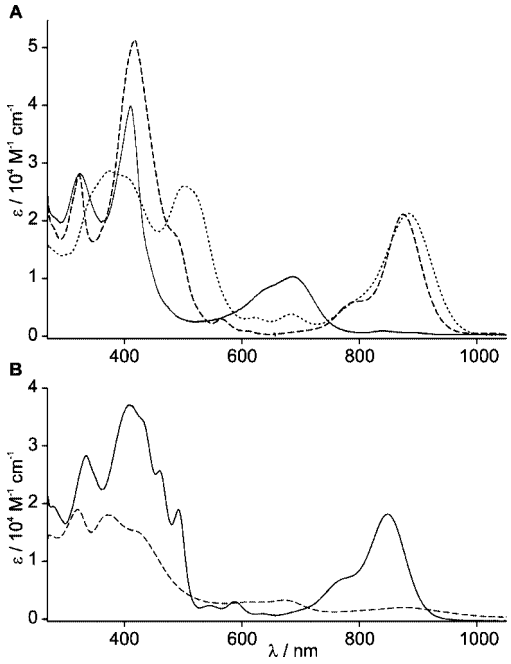


Figure 1. Electronic spectra: trace A: **1** – solid black line, **1**-H – black dashed line, **1**-H_2 – black dotted line; trace B: spectra of **6** – solid line, **7**-Cl_2 – dashed line.

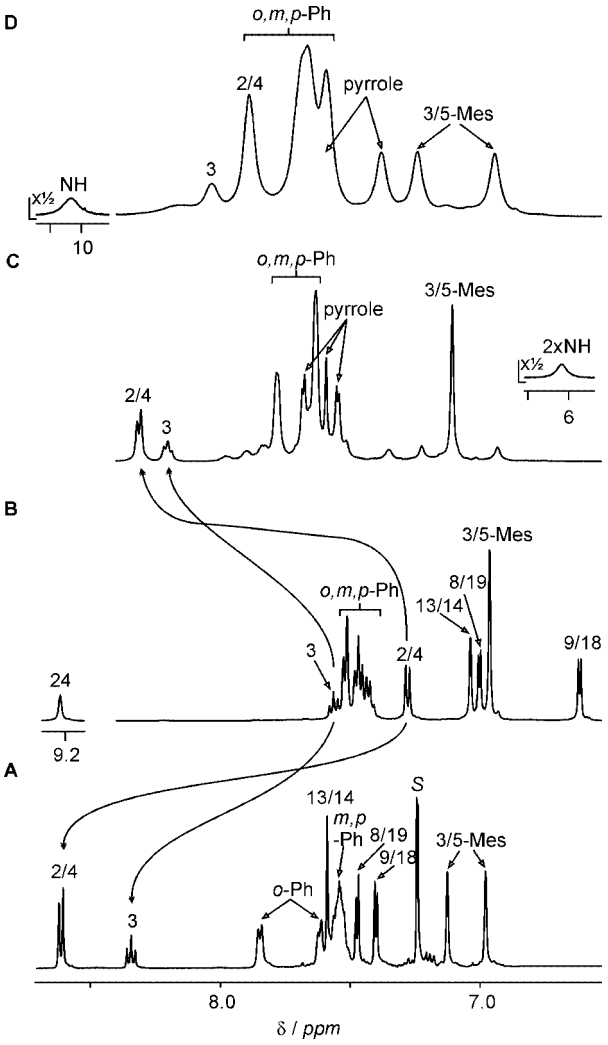
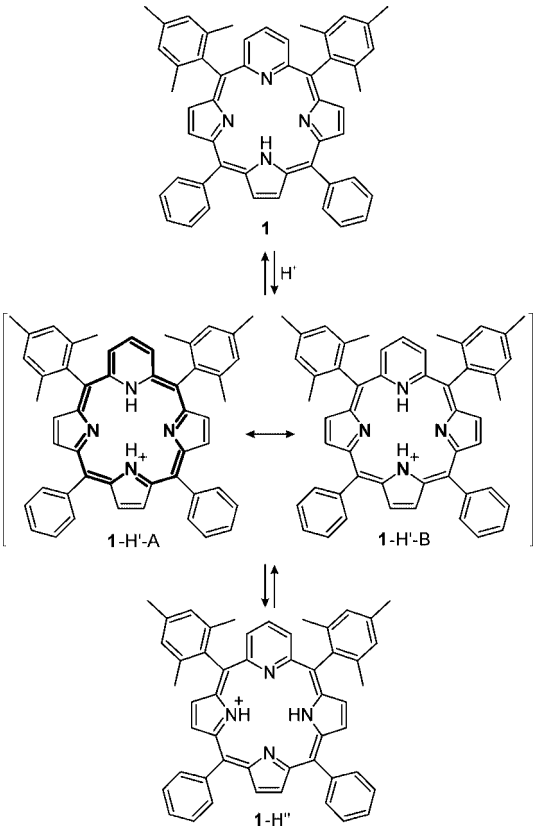


Figure 2. ^{1}H NMR spectra (downfield regions presented) of **6** (A), **1** (B), **1**-H (C), and **1**-H_2 (D). Assignments follow the numbering given in Scheme 2. The remarkable relocation of pyridine resonances of **1** due to protonation (**1**-H) or complexation (**6**) marked with curved arrows.

Two stages of protonation of **1** have been demonstrated by ^{1}H NMR and electronic spectroscopy (Figure 2, Scheme 3). The addition of the first proton resulted in formation of two symmetrical *trans* tautomers (N-22-*H*,N-23,N-24-*H*,N-25) **1**-H′ and (N-22,N-23-*H*,N-24,N-25-*H*) **1**-H′′, which remain in fast exchange even at 203 K ([D_2]-dichloromethane). To account for spectroscopic characteristics of **1**-H′, it is necessary to include the canonical form **1**-H′-A in the description of **1**-H (Scheme 3). It defines a single 18e-macrocyclic π-delocalization pathway (**1**-H′-A), which may coexist with the [6]annulene aromaticity of the pyridine ring (**1**-H′-B). Thus, the marked upfield relocation of **1**-H macrocyclic resonances with respect to **1** [δ = 8.31 (2/4-H), 8.20 (3-H) ppm; pyrrole: δ = 7.68, 7.59, 7.55; 6.10 (2 × NH)] reflects the macrocyclic aromaticity related to **1**-H′-A (Figure 2, trace C). The further titration produces the different tautomeric species of **1**-H_2. The introduction of the second proton causes a severe distortion of the macrocycle from planarity as demonstrated by differentiation of originally equivalent mesityl resonances in the ^{1}H NMR spectrum of **1**-H_2.

The density functional theory (DFT) has been applied to model the molecular and electronic structure of three pyriporphyrin tautomers: **1** (N-22,N-23,N-24-*H*,N-25), **1**′ (N-22,N-23-*H*,N-24,N-25), **1**′′ (N-22-*H*,N-23,N-24,N-25). The total energies, calculated using the B3LYP/6-31G** approach [0 (**1**), 2.5 (**1**′), 17.9 (**1**′′) kcal/mol] demonstrate some preference for the central pyrrole protonation. The total energies calculated for (N-22-*H*,N-23,N-24-*H*,N-25) **1**-H′ and (N-22,N-23-*H*,N-24,N-25-*H*) **1**-H′′ reveal an energy



Scheme 3. The first protonation step of **1**.

difference of 5.4 kcal/mol pointing to the larger stability of **1**-H′′. Contrary to **1** the protonation of the pyridine nitrogen atom seems to be acceptable for the monocationic form.

Compound **1** reacts smoothly with $ZnCl_2$ in dichloromethane to yield chloro(6,21-dimesityl-11,16-diphenylpyriporphyrin)zinc(II) (**6**), wherein the macrocycle acts as a monoanionic ligand. The coordination is confirmed by the substantial changes detected in the UV/Vis and ^{1}H NMR spectra (Figures 1 and 2). The molecular structure of **6** has been determined by X-ray investigations (Figure 3). The coordinating environment of the zinc(II) ion resembles a distorted square pyramid with the nitrogen atoms occupying equatorial positions and the chloro ligand lying at the unique apex. The zinc(II) ion is displaced by 0.512 Å from the N_4 plane (Figure 3), resembling the structure of a chloro(*N*-methylated porphyrin)zinc(II) complex.[11] The unique Zn–N(22) distance equals 2.353(3) Å and is significantly longer than the other three Zn–N distances [Zn–N(23) 2.053(4), Zn–N(24) 2.108(4), Zn–N25, 2.049(4) Å]. Actually, the Zn–N(22) bond is longer than any of the Zn–N bonds determined for axially coordinated pyridine in (porphyrin)zinc(II) complexes which are typically found in the 2.1–2.2 Å range[12] and the Zn–N bond lengths of the equatorial pyridine rings of (tetrahydroxyhemiporphyrazine)-zinc(II) [2.265(1) and 2.276(1) Å].[13] All Zn–N(pyrrolic) bond lengths are comparable to the Zn–N distances in (porphyrin)zinc(II) complexes.[12]

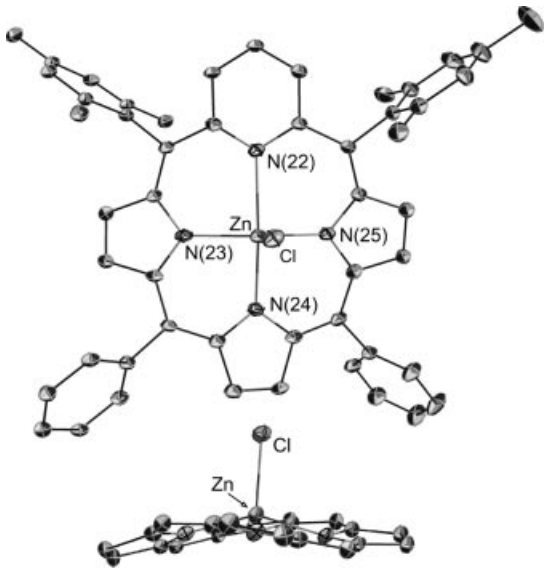
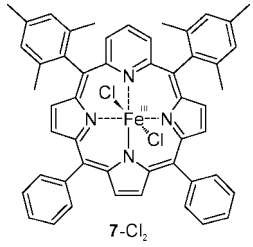


Figure 3. Molecular structure of **6** (top: perspective view, bottom: side view with phenyl groups omitted for clarity). The thermal ellipsoids represent 30% probability.[10]

Insertion of iron into **1** has been achieved by the addition of iron(II) chloride hydrate to a chloroform/acetonitrile solution of the ligand in the presence of air. The reaction yields a six-coordinate complex **7**-Cl_2 which is stable as a solid and in solution (Scheme 4). The UV/Vis spectrum of **7** markedly differs from that of **6** (Figure 1).



Scheme 4. (Pyriporphyrin)iron(III) complex **7**-Cl_2.

^{1}H NMR spectroscopy was shown to be a definitive method for detecting and characterizing (porphyrin)iron complexes[14] at different coordination/oxidation states. Here, the ^{1}H NMR spectroscopic data for **7**-X_2 (X = Cl, CN) have been analyzed. Compound **7**-X_2 appears to have effective C_{2v} geometry in solution, consistent with six-coordinate iron(III) with one of the mirror planes passing through the iron ion, the chloro ligand, and the pyridine nitrogen atom. The three pyrrole resonances of **7**-Cl_2 are in the δ = 90–60 ppm region (298 K) which is typical for high-spin (tetraarylporphyrin)iron(III) complexes (Figure 4, trace A).[14a,14c,14d] The single resonance detected for the *meta* positions is diagnostic of six-coordination.[14c] Addition of potassium cyanide in [D_4]MeOH to a [D_8]toluene solution of **7**-Cl_2 resulted in its conversion to the neutral six-coordinate complex **7**-$(CN)_2$ (Figure 4, trace B), which presents the patterns of pyrrole and *meso*-aryl resonances assigned to the $(d_{xz}d_{yz})^4(d_{xy})^1$ less-common low-spin electronic ground state.[14a,14e]

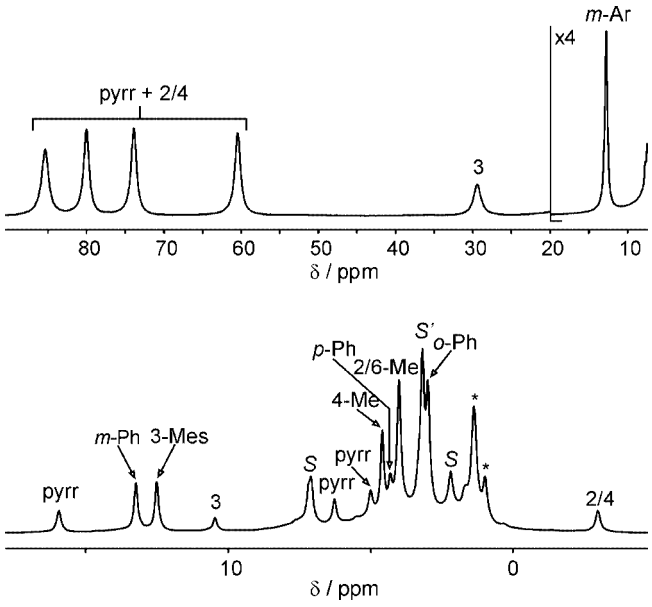


Figure 4. ^{1}H NMR spectra (298 K, [D$_8$]toluene) of (A) **7**-Cl$_2$, (B) **7**-CN$_2$. The pyrrole and *meta* resonances of **7**-Cl$_2$ are labeled pyrr and *m*, respectively. Other assignments follow the systematic labeling.

In conclusion, the long awaited pyriporphyrin, the simplest homologue of porphyrin with a supplementary carbon atom located in a pyrrolic β–β bond, has been synthesized. In light of the extensive search for suitable porphyrins and metalloporphyrins to act as biomimetic models and catalysts, pyriporphyrin **1** provides a remarkable potential. Pyriporphyrin creates nearly a porphyrin-like coordinating environment easily matching the ionic radii of a large variety of metal ions with a feasible coordination to four trigonally hybridized nitrogen atoms albeit – importantly – in the monoanionic core instead of a dianionic one.

Experimental Section

Synthesis of 1 and 6: The [3 + 1] condensation of reduced **5** (0.3 mmol) and pyrrole (1 equiv.), catalyzed by TFA (28 equiv.) in CD_3CN, was performed under nitrogen overnight. After alkalization (TEA) and oxidation (DDQ, 5 equiv.), the solvent was removed and the oily residue was dissolved in dichloromethane and chromatographed (grade-II basic alumina, 100 g). *n*-Heptane (50 mL) was added and the solvent was evaporated. Compound **1** was extracted from the solid using *n*-hexane. The solvent was evaporated and the residue was dissolved in dichloromethane. Subsequently, $ZnCl_2{\cdot}(H_2O)_6$ and K_2CO_3 were added in excess. The mixture was stirred vigorously (30 min), washed with water, dried and filtered. The product was chromatographed (silica gel). The yellow fraction (eluted with 1–2% acetone in dichloromethane) was collected. Recrystallization (dichloromethane/*n*-hexane) yielded 13.3 mg of **6** (5.5%). Next, **6** was quantitatively demetallated to **1** by using concentrated HCl. The procedure involved washing of the dichloromethane solution of **6** with concentrated HCl (3×), water (2×), diluted K_2CO_3 and finally drying with Na_2SO_4.

1: ^{1}H NMR ($CDCl_3$, 298 K): δ = 9.38 (v. br. s, 1 H, 24-H), 7.54, 7.33 [AB$_2$, ^3J(H,H) = 7.79 Hz, 1- + 2-H, 3- + 2/4-H], 7.51–7.39 (A$_2$M$_2$X, 10 H, Ph), 7.03 [*A*B, ^3J(H,H) = 4.77 Hz, 2 H, 8/19-H], 6.96 (s, 4 H, *m*-Mes), 6.94 (s, 2 H, 13/14-H), 6.66 [A*B*, ^3J(H,H) = 4.77 Hz, 2 H, 9/18-H], 2.37 (s, 6 H, 4-Me), 2.05 (s, 12 H, 2/6-Me) ppm. ^{13}C NMR ($CDCl_3$, 298 K): δ = 171.6, 157.8, 155.5, 148.9, 139.8, 139.5, 138.8, 138.5, 137.9, 137.6, 134.9, 131.6, 130.3, 128.3, 127.9, 127.5, 124.8, 115.3, 21.3, 21.2 ppm. UV/Vis (CH_2Cl_2): λ_{max} (logε) = 324 (4.46), 411 (4.61), 685 (4.00) nm. HRMS (ESI): calcd. for $[C_{51}H_{42}N_4+H]^+$ 711.34822; found 711.35166.

6: ^{1}H NMR ($CDCl_3$, 213 K): δ = 8.61, 8.34 [AB$_2$, ^3J(H,H) = 7.88 Hz, 2 + 1 H, 2/4- + 3-H], 7.85, 7.61, 7.56–7.52 (AA′M$_2$X, 10 H, Ph), 7.47, 7.40 [AB, ^3J(H,H) = 5.05 Hz, 2 + 2 H, 8/19- + 9/18-H], 7.12/6.98 [s, 2 + 2 H, *m*-Mes], 2.44 (s, 6 H, 4-Me), 2.20/1.49 (s, 6 + 6 H, 2/6-Me) ppm. ^{13}C NMR ($CDCl_3$, 213 K): δ = 165.7, 161.5, 154.0, 150.0, 139.8, 138.9, 138.8, 138.3, 138.2, 137.4, 135.9, 135.3, 133.7, 133.4, 131.2, 129.9, 129.1, 128.3, 127.8, 127.7, 127.6, 127.4, 118.6, 22.0, 21.5, 20.9 ppm. UV/Vis (CH_2Cl_2): λ_{max} (logε) = 278 (4.30), 335 (4.46), 409 (4.57), 460 (4.41), 492 (4.28), 545 (3,42), 587 (3.52), 638 (3.09), 848 (4.27) nm. HRMS (ESI): calcd. for $[C_{51}H_{41}N_4Zn]^+$ 773.2623; found 773.2932.

7-Cl$_2$: A solution of **1** and $Fe^{II}Cl_2{\cdot}6H_2O$ (excess) in dichloromethane/acetonitrile was stirred in the presence of air. After 15 min, the insertion was complete as determined by electron spectroscopy. The mixture was concentrated to dryness, the residue dissolved in dichloromethane and the mixture filtered. After crystallization from dichloromethane/*n*-hexane, **7** was obtained.

7-Cl$_2$: UV/Vis (CH_2Cl_2): λ_{max} (logε) = 321 (4.28), 372 (4.26), 673 (3.52), 877 (3.31) nm. MS (ESI): calcd. for $[C_{51}H_{41}N_4FeCl]^+$ 801.2; found 801.0.

Supporting Information (see footnote on the first page of this article): Synthetic protocols and computational details.

Acknowledgments

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[10] Data collection: the measurement was performed with an Xcalibur PX κ-geometry diffractometer using Cu-K_α radiation (λ = 1.5418 Å), T = 100 K. **6**·CH_2Cl_2: crystals were prepared by slow concentration of a solution of **6** in dichloromethane/*n*-hexane yielding a green plate crystal of $C_{51}H_{41}ClN_4Zn{\cdot}CH_2Cl_2$, size 0.02×0.15×0.15 mm, triclinic, space group $P\bar{1}$, a = 11.161(5), b = 12.762(6), c = 17.186(9) Å, α = 73.12(4), β = 77.94(4), γ = 69.41(4)°, V = 2177.2(2) Å^3, Z = 2, total no. of reflections collected: 20939; no. of independent reflections: 8220 [of which 4556 > 2σ(I)] were included in the refinement of 558 parameters; an absorption correction was not applied. The structure was solved by using direct methods with SHELXS-97 and refined against |F^2| using SHELXL-97 (G. M. Sheldrick, University of Göttingen, Germany, **1997**), final $R1$/$wR2$ indices [for I > 2σ(I)]: 0.078/0.189; max./min. residual electron density: +1.02/–1.00 e·Å^{-3}; H atoms were fixed in idealized positions using the riding model constraints. Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-602185. Copies of the data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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