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Facile Isolation of Bisimines Based on 3,3′-Diaminobenzidine: Direct Access to Unsymmetrical Bimetallic Salphen Building Blocks

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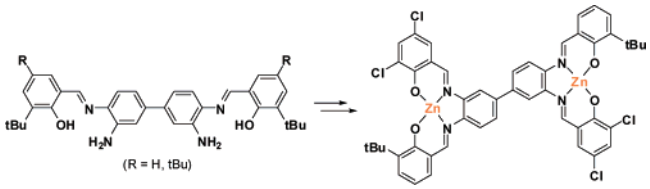

Diimines obtained from 3,3′-diaminobenzidine and *tert*-butyl-substituted salicylaldehydes in MeOH can be readily isolated in 60−90% yield and were obtained as a mixture of geometrical isomers. Two distinct diimine intermediates (**4** and **5**) with a higher molecular symmetry as related to the other isomeric diimine products were both isolated by crystallization of which **5** was subsequently used to demonstrate that nonsymmetrical bis-salphen complexes with different functional groups and metal centers can be assembled via a three-component one-pot procedure.

Salen ligands are among the most powerful ligands in homogeneous catalysis.[1] In most currently known (catalytic) applications, the salen ligand is highly symmetrical and is accessed via a double condensation reaction between a diamine and two equivalents of a salicylaldehyde.[2] The synthesis of nonsymmetrical salens is generally subject to a number of complications.[3] Unsymmetrical versions of this ligand have received, however, increasing attention since the presence of two distinct salicylidene moieties in a complexed form provides a way to tune the catalytic efficiency of the metal center. Also, by preparing unsymmetrical salen derivatives, it is possible to introduce a diverse pallet of functional groups, allowing the introduction of such ligands, for example, onto supports.[4] For instance, Weck et al.[5] have used a monoprotected chiral diamine and two different salicylaldehydes to arrive at unsymmetrical chiral salen ligands with various functional groups. We and others recently reported a direct and convenient method for the preparation of nonsymmetrical metallosalens.[6] The use of a monoimine intermediate derived from *o*-phenylenediamine, which was first reported by Atwood and co-workers,[7] permits the synthesis of nonsymmetric functionalized sal*phen*[8] derivatives when combined with a different salicylaldehyde and a metal salt template in a one-pot two-step procedure.

Cozzi[9] demonstrated that Zn(II)−salens are effective homogeneous catalysts for alkynylation reactions using the significant Lewis acid character of the metal center.[10] The metallosalphen complexes, and in particular the Zn(II)-centered derivatives, have also recently been introduced as versatile supramolecular building blocks. The high Lewis acidic nature of the Zn(II) centers in sal*phen* type complexes[11] results in high binding affinity for pyridine donors,[12] and this feature was utilized to construct box type assemblies and encapsulated homogeneous catalysts.[13] In view of extending the available family of this kind of building block for further development of its supramolecular and catalytic potential, we envisaged that the 3,3′-diaminobenzidine framework (**1**, Scheme 1) would offer a versatile starting point for new bimetallic salphen synthons. Moreover, as reported for the monoimine obtained from 1,2-phenylenediamine, development of procedures for nonsymmetric versions of bis-salphen complexes could contribute to the field of bimetallic catalysis with the option to fine-tune the catalytic properties of the metal chelates upon variation of the second introduced salicylaldehyde. In this note, we present a procedure that allows for the preparation and isolation of such nonsymmetric[14] bis-salphen derivatives by selective introduction of two imine groups in 3,3′-diaminobenzidine (**1**) and a successive reaction with another type of salicylaldehyde and a metal precursor in a selective three-component one-pot procedure.

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(11) The high Lewis acidic nature is also reflected in the microanalyses of all presented Zn complexes. The hygroscopic nature is reflected in the inclusion of water molecules in the prepared samples. This is a common feature for this type of Zn−salens; see also ref 5a.

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(14) With "nonsymmetric", we here try to express the symmetry within each salphen unit.

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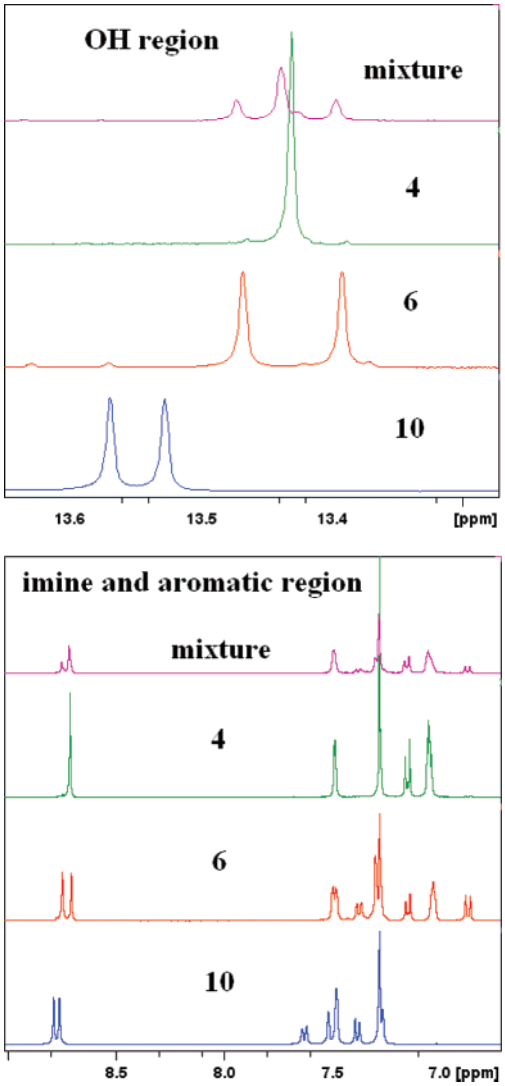


FIGURE 1. Selected and expanded NMR regions for the isolated mixture of diimines based on **1** and **2**, compound **4**, compound **6**, and pure tetraimine **10**.

Initially, we used a standard condensation protocol for the synthesis of the tetraimine of **1** (1 equiv) starting with a slight stoichiometric excess (≥4 equiv) of commercially available 3,5-di-*tert*-butylsalicylaldehyde (**2**) in MeOH at ambient temperature (Scheme 1). In due course, a yellow to orange precipitate was isolated and was analyzed by ^{1}H NMR in $CDCl_3$. To our surprise, the proton spectrum proved to be rather complicated and showed multiple resonances for the respective OH (Figure 1) and imine groups. Rather informative was the presence of a broad singlet located around 4.1 ppm, which was assigned to unreacted NH_2 groups. Mass analysis of this sample also confirmed the presence of incompletely reacted **1**, however, both analyses combined pointed at the almost exclusive formation of diimine species. The presence of multiple resonance patterns was afterward regarded as a consequence of the formation of a mixture of geometrical diimine isomers with different symmetry properties. The reaction of **1** with 2.2 equiv of salicylaldehyde **2** gave a similar mixture of components, and the yield of the diimine mixture amounted in both cases to 80−90%, depending on the amount and type of alcohol solvent used.

Fortunately, when the product was dissolved in hot acetone, needle-shaped crystals separated from solution upon cooling and were analyzed as one of these isomers as a single species with high symmetry (Supporting Information, Figure S1). Although the crystals were of very poor X-ray quality, a provisional crystal structure determination showed this isomer to be compound **4**.[15] In order to determine the identity of the two other (major) components of the crude reaction product (Figure 1), the reaction was also performed at other, though lower concentrations, and this altered experimental procedure gave access to almost exclusive isolation (as was also supported by mass analysis) of one of the other diimine species. The lower symmetry of this particular isomer, as compared to compound **4**, was connected to compound **6** that comprises one *exo*- and one *endo*-orientated imine group (Figure 1, Scheme 1). The third isomer has a similar symmetry as found for **4** and was ascribed to compound **8**.[16]

The poor solubility of the diimine intermediates **4**, **6**, and **8** in alcohol solvents and the isolation of isomer **4** (24%, in quantities up to at least 0.5 g) by a simple crystallization step provides an extremely useful synthetic tool toward nonsymmetrical bis-salphen complexes by combination with another, but different, salicylaldehyde. Furthermore, due to their respective symmetry, all diimine isomers are simply recognized by ^{1}H NMR and are magnetically well-separated from the tri- and tetraimine analogues (cf. tetraimine **10**, Figure 1) using the chemical shifts related to the phenolic hydrogens.

Beside the isolation of pure symmetrical diimine **4**, we also used salicylaldehyde **3** in order to broaden the scope of this selective procedure toward diimine precursors. A similar preparative process using 2.2 equiv of **3** gave an 85% isolated yield of the desired diimine product. Remarkably, in this latter reaction, almost exclusive isolation of one of the possible diimine isomers (with trace amounts of the other isomers) was directly obtained without the need for further purification, and its structure was accredited to compound **5** by comparison with the NMR data for **4**, **6**, and **8**.[17] Fortunately, the molecular structure of diimine **5** was supported by single-crystal X-ray diffraction (as for **4**) and is depicted in Figure S2 (Supporting Information).[18] The tetraimine derived from **1** (Scheme 2) can be isolated upon exhaustive condensation of **1** with a large excess (10 equiv) of aldehyde reagent in a combination of $CHCl_3$ and MeOH (1:1 v/v) as solvent medium.

Due to the biphenyl backbone, compound **10** has a specific symmetry and is characterized by the presence of two separate resonances for both the phenolic OH and imine groups (Figure 1), whereas for the *t*-Bu groups, four distinct resonances were observed. The ^{13}C{^{1}H} NMR spectrum recorded for **10** revealed the presence of two separate sets of peaks for the *t*-Bu groups. When **10** was treated with different metal acetates in a mixture of $CHCl_3$ and MeOH, nonoptimized moderate yields of the bimetallic derivatives **11** (42%) and **12** (43%) were obtained (Scheme 2). Such bimetallic complexes can be considered useful

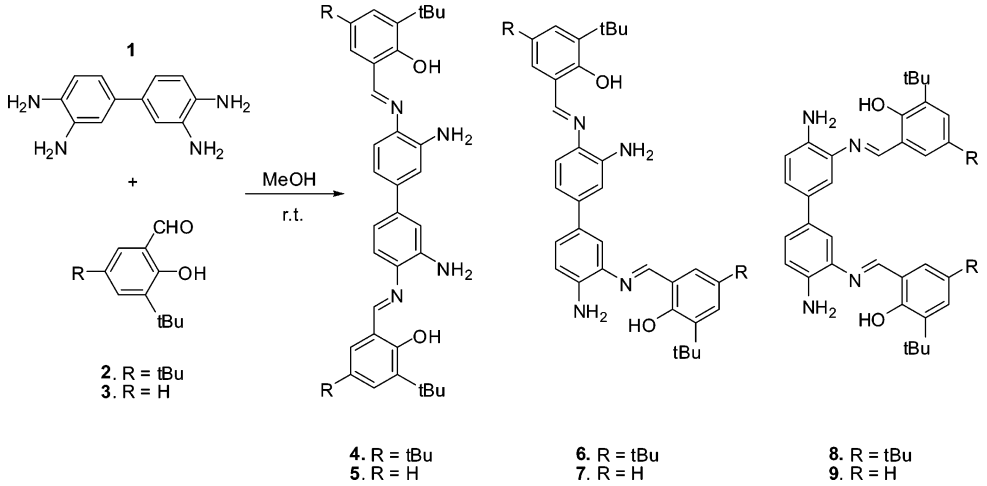
(15) The crystals of isomer **4** were obtained from hot acetone, but the crystal quality was very poor (R = 0.27).

(16) We are aware that a theoretical fourth isomer is possible, namely, with both imine groups residing at the same side of the biphenyl structure. However, the formation of this isomer has a very low probability.

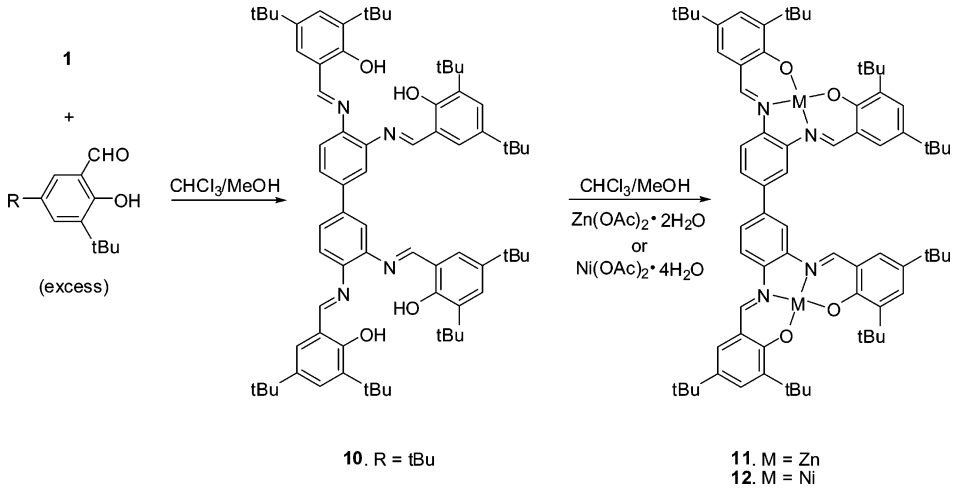
(17) Apparently, the relative crystallization properties of each isomer are different and give rise to exclusive isolation of a single species (i.e., **5**). This will undoubtedly be a function of the concentration of the reactants and the reaction conditions (cf. isolation of compound **6**).

(18) Crystals of **5** suitable for X-ray diffraction were obtained from a concentrated DMSO solution and were of much better quality as compared to **4** (R = 0.0884).

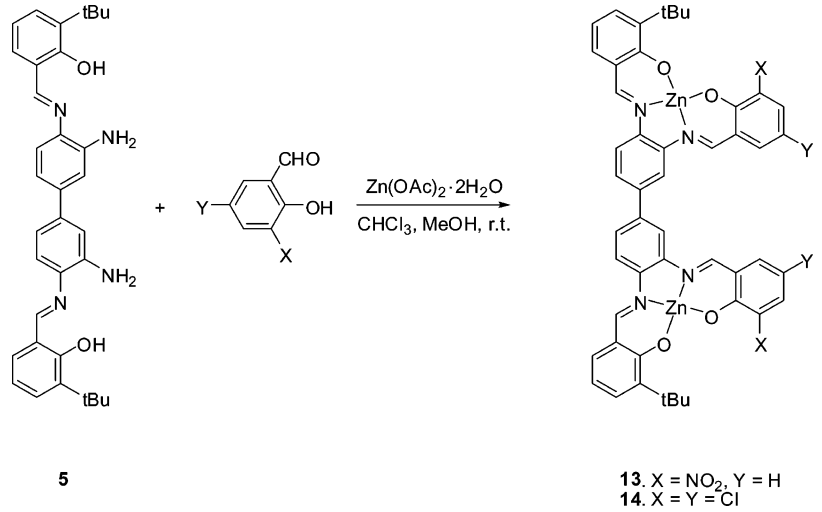
SCHEME 1. Synthesis of Diimine Intermediates 4−9 Derived from 3,3′-Diaminobenzidine 1 and Salicylaldehydes 2 and 3



SCHEME 2. Synthesis of Homobimetallic Symmetrical Complexes 11 and 12 via Tetraimine Intermediate 10



SCHEME 3. Synthesis of the Unsymmetrical Bimetallic Zn−Salphen Complexes 13 and 14



as (precursors for) homogeneous catalysts and supramolecular synthons.[10,13]

Nonsymmetric variations of the homobimetallic Zn complex **11** were obtained using diimine precursor **5** (Scheme 3); the protocol consists of the addition of the second salicylaldehyde and metal acetate reagents dissolved in MeOH to a stirred solution of **5** in $CHCl_3$, resulting in a final 1:1 (v/v) solvent mixture to furnish the bimetallic Zn−salphen complexes **13** (76%) and **14** (83%) in good isolated yields. For both complexes, the NMR data are fully consistent with the presence of a single species that shows a resonance pattern with fully separated and well-resolved peaks. For **13**, two indicative triplets

are found in the aromatic region at 6.48 and 6.65 ppm (signal intensity ratio 1:1), respectively, while for **14**, the presence of two 3,5-dichlorosalicylidene groups in the product is easily recognized by two doublets (^4J = 2.8 Hz) located at 7.60 and 7.56 ppm. Furthermore, for both compounds, two distinct resonances are observed for the imine carbons in the $^{13}C\{^1H\}$ NMR spectrum as for **11** and **12**. Their structures were further supported by mass analysis (see Experimental Section).

In conclusion, we have presented synthetic pathways for both useful di- and tetra-Schiff base precursors based on 3,3′-diaminobenzidine. The tetraimine **10** can be used to prepare symmetrical molecular building blocks with a range of metal ions potentially useful in homogeneous catalysis and supramolecular chemistry applications. Both diimines **4** and **5** represent the first examples of precursors for nonsymmetric bimetallic bis-salphen derivatives in which the electronic properties of the metal center can be regulated by the introduction of different and appropriate salicylaldehydes. This approach will undoubtedly greatly advance the field of bimetallic catalysis based on salen ligands. Selective introduction of a single metal ion in **10** or **5** (after reaction with a second salicylaldehyde) can promote the development of heterobimetallic species that are used in cooperative and/or one-pot multistep processes. Our current activities center on these themes, and results of these studies are expected shortly.

Experimental Section

Diimine Intermediate 4. A mixture of 3,3′-diaminobenzidine **1** (0.59 g, 2.75 mmol) and 3,5-di-*tert*-butylsalicylaldehyde **2** (2.63 g, 11.2 mmol) in MeOH (150 mL) was stirred at rt for 23 h, and the reaction mixture was then filtered to collect the orange solid product (1.78 g, total yield of mixture of diimine isomers 90%). This mixture of isomers was subjected to crystallization from hot acetone, upon which orange needles separated from the solution. The total yield for crystalline **4** amounted to 0.43 g (24%): ^1H NMR (400 MHz, $CDCl_3$) δ 13.43 (s, 2H), 8.71 (s, 2H), 7.49 (d, ^4J = 2.3 Hz, 2H), 7.26 (d, ^4J = 2.3 Hz, 2H), 7.15 (d, ^3J = 8.6 Hz, 2H), 7.06−7.04 (m, 4H), 4.13 (s, 4H), 1.47 (s, 18H), 1.35 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.9, 157.9, 141.0, 140.8, 140.4, 137.0, 134.8, 128.0, 126.8, 118.7, 118.6, 117.6, 114.0, 35.1, 34.2, 31.5, 29.4; MS (APCI) *m*/*z* 648 $(M + H)^+$. Anal. Calcd for $C_{42}H_{54}N_4O_2$: C, 77.98; H, 8.41; N, 8.66. Found: C, 77.97; H, 8.66; N, 8.50.

Diimine Intermediate 5. To a solution of 3,3′-diaminobenzidine **1** (0.91 g, 4.25 mmol) in MeOH (80 mL) was added 3-*tert*-butylsalicylaldehyde **3** (1.58 g, 8.86 mmol) dissolved in MeOH (5 mL). The yellow to orange colored solution was stirred at rt for 24 h during which time a solid precipitated. The product was collected by filtration and dried to give 1.93 g of a yellow to orange solid (3.61 mmol, 85%). Analytically pure **5** was obtained by crystallization from acetone: ^1H NMR (400 MHz, $CDCl_3$) δ 13.62 (s, 2H), 8.72 (s, 2H), 7.42 (d, ^3J = 6.9 Hz, 2H), 7.30 (d, ^3J = 7.4 Hz, 2H), 7.15 (d, ^3J = 6.9 Hz, 2H), 7.06 (m, 4H), 6.93 (t, ^3J = 6.5 Hz, 2H), 4.15 (br s, 4H), 1.50 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, DMF-d_7) δ 162.6, 160.3, 143.6, 140.8, 137.1, 133.8, 131.4, 130.1, 120.2, 119.1, 118.8, 115.9, 113.8, 34.4, 29.2; another carbon resonance of the *t*-Bu group is not visible due to overlap with residual solvent signal(s); MS (MALDI-TOF) *m*/*z* 534.4 (M^+). Anal. Calcd for $C_{34}H_{38}N_4O_2$: C, 76.37; H, 7.16; N, 10.48. Found: C, 76.08; H, 7.32; N, 10.73.

Tetraimine 10. A mixture of 3,3′-diaminobenzidine (0.20 g, 0.93 mmol) and 3,5-di-*tert*-butylsalicylaldehyde **2** (2.19 g, 9.34 mmol) was stirred in MeOH/$CHCl_3$ (1:1, total volume 100 mL) for 24 h at rt. A orange-yellow product (0.69 g, 69%) was isolated by removing the solvents under reduced pressure and crystallization from acetone: ^1H NMR (400 MHz, $CDCl_3$) δ 13.57 (s, 2H), 13.53 (s, 2H), 8.79 (s, 2H), 8.76 (s, 2H), 7.62 (d, ^3J = 8.2 Hz, 2H), 7.52 (s, 2H), 7.48 (m, 4H), 7.38 (d, ^3J = 8.2 Hz, 2H), 7.26 (d, ^4J = 1.8 Hz, 2H), 1.48 (s, 18H), 1.47 (s, 18H), 1.36 (s, 18H), 1.34 (s, 18H); one signal (2H) is missing due to overlap with the residual solvent peak; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.2, 164.5, 158.7, 158.6, 143.4, 141.9, 140.5, 140.4, 139.3, 137.3, 128.41, 128.35, 126.9, 126.8, 125.6, 120.2, 118.5, 118.4, 118.3, 35.1, 34.2, 31.5, 29.4; MS (APCI) *m*/*z* 1080 (M^+). Anal. Calcd for $C_{72}H_{94}N_4O_4 \cdot 1.5H_2O$: C, 78.15; H, 8.84; N, 5.06. Found: C, 78.10; H, 8.77; N, 5.10.

Symmetrical Bimetallic Ni(II)−Salphen Complex 12. A mixture of **10** (102.3 mg, 0.0948 mmol) and $Ni(OAc)_2 \cdot 4H_2O$ (52.3 mg, 0.21 mmol) was stirred in MeOH/$CHCl_3$ (100/40 mL v/v) for 24 h at rt. A dark red solid (47.5 mg, 42%) was isolated by filtration and recrystallized from CH_2Cl_2/MeOH: ^1H NMR (400 MHz, acetone-d_6) δ 8.38 (s, 2H), 8.30 (s, 2H), 7.89 (s, 2H), 7.82 (d, ^3J = 8.7 Hz, 2H), 7.47 (m, 6H), 7.19 (d, ^4J = 2.3 Hz, 2H), 7.16 (d, ^4J = 2.2 Hz, 2H), 1.51 (br s, 36 H), 1.35 (s, 18H), 1.34 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + 10% d_5-C_5D_5N) δ 165.06, 165.02, 154.7, 154.2, 142.7, 141.8, 138.5, 136.8, 136.7, 130.6, 126.7, 126.50, 125.46, 119.8, 119.7, 114.9, 113.4, 35.7, 33.7, 31.0, 29.6; MS (APCI) *m*/*z* 1191 (M^+), 1176 $(M - CH_3)^+$. Anal. Calcd for $C_{72}H_{90}N_4O_4Ni_2$: C, 72.49; H, 7.60; N, 4.70. Found: C, 72.43; H, 7.76; N, 4.69.

Nonsymmetrical Bimetallic Zn−Salphen Complex 13. To a solution of diimine **5** (51.6 mg, 0.0965 mmol) in $CHCl_3$ (20 mL) was first added a solution of 3-nitrosalicylaldehyde (60.8 mg, 0.364 mmol) in MeOH (10 mL). The orange-red solution was stirred, and meanwhile, a solution of $Zn(OAc)_2 \cdot 2H_2O$ (89.9 mg, 0.410 mmol) in MeOH (10 mL) was added. The clear orange reaction mixture was stirred at rt, and after 1 h, a precipitate was noted, which was filtered off after 18 h, washed with MeOH, and dried to yield **13** (70.6 mg, 0.0734 mmol, 76%) as an orange solid: ^1H NMR (400 MHz, DMSO-d_6) δ 9.30 (s, 2H), 9.01 (s, 2H), 8.33 (s, 2H), 8.01 (d, ^3J = 8.6 Hz, 2H), 7.94 (d, ^3J = 8.3 Hz, 2H), 7.86 (d, ^3J = 7.7 Hz, 2H), 7.81 (d, ^3J = 7.8 Hz, 2H), 7.31 (d, ^3J = 7.1 Hz, 2H), 7.25 (d, ^3J = 7.2 Hz, 2H), 6.65 (t, ^3J = 7.7 Hz, 2H), 6.48 (t, ^3J = 7.5 Hz, 2H), 1.46 (s, 18H); $^{13}C\{^1H\}$ (100 MHz, DMSO-d_6) δ 172.7, 164.1, 163.7, 163.4, 143.9, 142.1, 141.4, 140.3, 139.7, 138.3, 135.1, 131.3, 129.8, 127.2, 123.8, 119.9, 117.7, 115.5, 113.0, 111.7, 35.4, 30.0; MS (MALDI-TOF) *m*/*z* 960.5 (M^+), 946.5 $(M - CH_3)^+$. Anal. Calcd for $C_{48}H_{40}N_6O_8Zn_2 \cdot 4H_2O$: C, 55.88; H, 4.69; N, 8.15. Found: C, 55.49; H, 4.34; N, 8.29.

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Supporting Information Available: Figures S1 and S2 (crystal structures for **4** and **5**), crystal data (in cif format) for **5**, copies of ^1H NMR and $^{13}C\{^1H\}$ NMR spectra for all new compounds, and experimental procedures and analytical data for **6**, **11**, and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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