Inorg. Chem. **2004**, *43*, 411–420

Syntheses and Thermal Reactivities of Tetradentate Metalloenediynes of Cu(II) and Zn(II)

Tilak Chandra,[†] Russell A. Allred,[‡] Brian J. Kraft,[†] Lisa M. Berreau,*[,‡] and Jeffrey M. Zaleski*[,†]

[†]*Department of Chemistry, Indiana University, Bloomington, Indiana 47405, and Department of Chemistry and Biochemistry, Utah State University, Logan, Utah 84322-0300*

Received July 7, 2003

The syntheses and Bergman cyclization temperatures of disubstituted tetradentate enediyne ligands based on a dibenzylethylenediamine backbone are reported relative to the corresponding Cu(II) and Zn(II) analogues. For these compounds, the R-groups dimethylamine (dma), pyridine (py), quinoline (quin), and 3-oxypyridine (pyO) have been symmetrically and asymmetrically incorporated at the alkyne termini positions directly (0:0) or via a methylene spacer (1:0, 0:1, 1:1). Electron paramagnetic resonance (EPR) reveals that all Cu(II) complexes are monomeric with near axial symmetry and *g*-values ($g_x \approx 2.04$, $g_y \approx 2.09$ $g_z \approx 2.25$) representative of tetragonal Cu(II) geometries. The hyperfine splitting parameter A_z values are $\sim 170 \times 10^{-4}$ cm^{-1}, which is consistent with distorted 4-coordinate, or weakly 6-coordinate, structures. In contrast, solution conductivity measurements show that Zn(II) complexes with rigid py or quin ligands (e.g., py-py 0:0, py-quin 0:0) behave as 1:4 electrolytes indicative of dimeric, bridging enediyne structures. Consequently, these Zn(II) complexes have very high Bergman cyclization temperatures (>290 °C), while their less rigid, 1:1 analogues (<185 °C) and monomeric Cu(II) counterparts (110–136 °C) have markedly lower cyclization temperatures. The results underscore the important consequences metal center structure plays in influencing Bergman cyclization temperatures of metalloenediynes.

Introduction

The use of metals to influence the temperatures at which enediynes cyclize[1−15] to generate the potent 1,4-phenyl diradical intermediate is an emerging extension of the reactivities of the their natural product analogues.[16] Within this theme, direct chelation[1−8,10−13,15] or π-complexation[9,14] of metals to enediynes has been shown to have a pronounced influence on their Bergman cyclization temperatures. Metals can inhibit[6,7,9,11,13] or activate[1,2,6,9−12,14,15] diradical formation by simple complexation or variation in metal center geometry. In some cases, the flexibility of the ligand framework for a given metal center geometry can also modulate the Bergman cyclization temperatures, but to a lesser extent.[10,11]

Due to the potential fluxionality of simple chelates and π-complexes, the reactivities of tetradentate enediynes are of interest for the preparation of stable structures in solution. One of the potential advantages of such structures is that metal exchange could be used to activate the molecule for Bergman cyclization. Unfortunately, there are only limited reports describing the reactivities of such complexes.[4,5,10] In earlier work on macrocyclic enediynes, we showed that Cu-

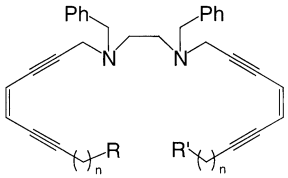
* To whom correspondence should be addressed. E-mail: zaleski@indiana.edu.
[†] Indiana University.
[‡] Utah State University.

(1) Warner, B. P.; Millar, S. P.; Broene, R. D.; Buchwald, S. L. *Science* **1995**, *269*, 814−816.
(2) Konig, B.; Pitsch, W.; Thondorf, I. *J. Org. Chem.* **1996**, *61*, 4258−4261.
(3) Basak, A.; Shain, J. *Tetrahedron Lett.* **1998**, *39*, 1623−1624.
(4) Basak, A.; Shain, J. C. *Tetrahedron Lett.* **1998**, *39*, 3029−3030.
(5) Basak, A.; Shain, J. C.; Khamrai, U. K.; Rudra, K. R.; Basak, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1955−1964.
(6) Benites, P. J.; Rawat, D. S.; Zaleski, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 7208−7217.
(7) Coalter, N.; Concolino, T. E.; Streib, W. E.; Hughes, C. G.; Rheingold, A. L.; Zaleski, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 3112−3117.
(8) Konig, B. *Eur. J. Org. Chem.* **2000**, 381−385.
(9) O'Connor, J. M.; Lee, L. I.; Gantzel, P.; Rheingold, A. L.; Lam, K.-C. *J. Am. Chem. Soc.* **2000**, *122*, 12057−12058.
(10) Chandra, T.; Pink, M.; Zaleski, J. M. *Inorg. Chem.* **2001**, *40*, 5878−5885.
(11) Rawat, D. S.; Benites, P. J.; Incarvito, C. D.; Rheingold, A. L.; Zaleski, J. M. *Inorg. Chem.* **2001**, *40*, 1846−1857.
(12) Rawat, D. S.; Zaleski, J. M. *J. Am. Chem. Soc.* **2001**, *123*, 9675−9676.
(13) Schmitt, E. W.; Huffman, J. C.; Zaleski, J. M. *Chem. Commun.* **2001**, 167−168.
(14) O'Connor, J. M.; Friese, S. J.; Tichenor, M. *J. Am. Chem. Soc.* **2002**, *124*, 3506−3507.
(15) Bhattacharyya, S.; Clark, A. E.; Pink, M.; Zaleski, J. M. *Chem. Commun.* **2003**, 1156−1157.
(16) Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103−2117.

10.1021/ic030218x CCC: $27.50
Published on Web 11/20/2003

(II) and Zn(II) complexation lowers the Bergman cyclization temperature of the enediyne unit.[10] More subtly, the preference of the d^9 electron configuration of the Cu(II) center for tetragonal symmetry relative to the tetrahedral geometry of the d^{10} configuration of Zn(II), combined with enhanced ring size and flexibility, can lead to systematic variations in Bergman cyclization temperatures over a modest range (~50 °C).

By the nature of a macrocycle, the structure at the metal center is restricted, and variation of coordinating R-group cannot be readily explored. Since it is clear that these features play a prominent role in influencing Bergman cyclization temperatures of tetradentate complexes, we were interested in the effect on reactivity of opening the macrocycle on one side and varying the flexibility and steric bulk of the R-group at those ligand termini. Toward these goals, we have prepared a series of tetradentate enediyne ligands built on a dibenzylethylenediamine scaffold, where dimethylamine (dma), pyridine (py), quinoline (quin), and 3-oxypyridine (pyO) have been symmetrically and asymmetrically incorporated as the third and fourth metal ligands directly (0:0), or via a methylene spacer (1:0, 0:1, 1:1).



n = 0 or 1
R, R' = dma, py, quin, pyO

As a result, the structures and reactivities of these ligands in the presence of Cu(II) and Zn(II) are markedly different, and distinct from their macrocyclic precursors.

Experimental Section

Materials and Methods. All chemicals and solvents used were of the highest purity available from Aldrich and Fluka. Reactions were carried out under nitrogen using Schlenk and drybox techniques. Benzene and methylene chloride were dried and degassed according to literature methods.[17] Acetonitrile used for conductance measurements was dried over calcium hydride, distilled, and then collected by vacuum distillation prior to use. Similarly, *n*-butylamine was dried and distilled from calcium hydride. The organic enediynes were purified by flash chromatography using silica gel (200−440 mesh).

Physical Measurements. Electron paramagnetic resonance spectra were recorded on a Bruker ESP 300 spectrometer under the following conditions: microwave frequency, ~ 9.5 GHz; microwave power, 10 mW; modulation amplitude, 3.16 G; modulation frequency, 100 kHz; receiver gain, 2.0×10^4. ^{1}H NMR and ^{13}C NMR were recorded on a VXR 400 NMR spectrometer using the residual proton resonance of the solvent as an internal reference. The multiplicities of the ^{13}C NMR signals were determined by the DEPT technique. Infrared spectra (KBr) were recorded on a Nicolet 510P FT IR spectrometer. Elemental analyses on all samples were obtained from Robertson Microlit Laboratories Inc. ESI and FAB mass data were obtained at University of Illinois with a Micromass Quattro-I mass spectrometer. Differential scanning calorimetry (DSC) traces were recorded on a V4.1 Dupont 910 DSC differential scanning calorimeter coupled to DuPont thermal analyst 2100 at a heating rate of 10 °C min^{-1}.

Conductance measurements were made at 22(1) °C using a YSI model 31A conductivity bridge with a cell having a cell constant of 1.0 cm^{-1} and using Me_4NClO_4 as a standard.[18] Using a measured amount of material, typically 40−50 mg, solutions ranging from approximately 3 to 0.2 mM were prepared by serial dilution. To reduce electrolyte contamination, all glassware was rigorously cleaned, rinsed with distilled water, and subsequently oven-dried.

The data derived from conductance measurements of all solutions were used to calculate respective equivalent conductances (Λ_e), which were plotted as a function of the square root of the equivalent concentration ($c^{1/2}$) for each complex.[19,20] The data of the linear portion (found between anomalous behavior at either end of the concentration range) was extrapolated to give a limiting equivalent conductance (Λ_0) at infinite dilution as the *y*-intercept. Onsager plots were constructed by plotting the difference between Λ_0 and Λ_e, versus $c^{1/2}$. For complexes wherein the solution behavior could conceivably be either a 1:2 or 1:4 electrolyte, the Onsager slopes were calculated for both cases. The electrolyte type was then determined by eliminating the slope inconsistent with either possibility.

Syntheses. *N*,*N*′-Dibenzyl-*N*,*N*′-bis[8-(*N*,*N*′-dimethylamino)-oct-4-ene-2,6-diynyl]-ethane-1,2-diamine (dma:dma 1:1) (2). A solution of *N*,*N*′-Dibenzyl-*N*,*N*′-bis((*Z*)-5-chloropent-4-ene-2-ynyl)-ethane-1,2-diamine[10] (**1**) (1.0 g, 2.2 mmol) in benzene (20 mL) was added to a mixture of $Pd(Ph_3P)_4$ (0.160 g, 0.13 mmol), CuI (0.086 g, 0.45 mmol), and *n*-butylamine (0.83 g, 11 mmol) under nitrogen. The mixture was stirred for 10 min at 40 °C, and a solution of 1-(dimethylamino)-2-propyne (0.41 g, 5 mmol) in benzene (30 mL) was added via cannula directly at 60 °C over 30 min. The reaction mixture was stirred for 2 h and monitored by NMR and TLC. After completion of the reaction, the crude mixture was cooled and filtered through Celite and washed with methylene chloride (50 mL). The filtrate was concentrated under reduced pressure, and the residue was extracted with methylene chloride (100 mL). After washing with water (50 mL), the organic layer was concentrated and subsequently passed through a silica gel column eluted with methanol/methylene chloride (5:95) to give the desired product in 67% yield as a brown viscous oil. R_f. 0.2. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.28 (s, 12H, $4NCH_3$), 2.76 (s, 4H, $2CH_2$), 3.43 (s, 4H, $2CH_2$), 3.56 (s, 4H, $2CH_2$), 3.68 (s, 4H, $2CH_2$), 5.85 (s, 4H, 4CH), 7.23−7.35 (m, 10H, Ar). ^{13}C NMR ($CDCl_3$): 42.61(CH_2), 43.97 (CH_3), 48.62 (CH_2), 51.23 (CH_2), 58.01 (CH_2), 82.82 (Cquat), 83.03 (Cquat), 92.27 (Cquat), 92.34 (Cquat), 119.00 (CH), 119.16 (CH), 126.97 (CH), 128.13 (CH), 129.01 (CH), 138.63 (Cquat). MS (EI) *m*/*z*: 531 ($M^+ + 1$), 486, 439, 265. HRMS *m*/*z*: 531.3487; (calcd for $C_{36}H_{42}N_4$; 531.3487) (M + H). IR (neat, cm^{-1}): 3027, 2970, 2939, 2822, 2774, 2199, 1681, 1575, 1494, 1453, 1393, 1355, 1322, 1261, 1177, 1098, 970, 837, 699.

***N*,*N*′-Dibenzyl-*N*,*N*′-bis[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl]-ethane-1,2-diamine (pyO:pyO 1:1) (3).** To a stirring mixture of $Pd(Ph_3P)_4$ (0.158 g, 0.14 mmol), CuI (0.086 g, 0.45 mmol**),** and *n*-butylamine (0.83 g, 11 mmol), was added **1** (1.0 g, 2.2 mmol) in benzene (25 mL) under nitrogen, and this mixture was stirred for

(17) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518−1520.
(18) Coetzee, J. F.; Cunningham, G. P. *J. Am. Chem. Soc.* **1965**, *87*, 2529−2534.
(19) Feltham, R. D.; Hayter, R. G. *J. Chem. Soc.* **1964**, 4587−4591.
(20) Geary, W. J. *Coord. Chem. Rev.* **1971**, *7*, 81−122.

10 min. A solution of 3-(2-propynyloxy)pyridine[21] (0.73 g, 5.4 mmol) in benzene (50 mL) was added dropwise to the above solution over 4 h at 30 °C. The reaction mixture was further stirred for an additional 6 h at 30 °C. Completion of the reaction was monitored by TLC and ^{1}H NMR. The resulting solid was filtered and washed with ether (3 × 50 mL), and the combined layers were concentrated under reduced pressure. The residue was extracted with methylene chloride (2 × 100 mL) and washed with (3 × 100 mL) of water. The organic layer, after drying over anhydrous sodium sulfate, was concentrated under reduced pressure. The viscous oil was purified on a silica gel column initially eluted with methylene chloride, and subsequently with methanol/methylene chloride (5:95) to give **3** in 50% yield as a viscous yellow oil. R_f 0.5. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.75 (s, 4H, $2CH_2$), 3.54 (d, J = 1.6 Hz, 4H, $2CH_2$), 3.67 (s, 4H, $2CH_2$), 4.86 (d, J = 2 Hz, 4H, $2CH_2$), 5.81−5.84 (m, 2H, 2CH), 5.90 (d, 2H, 2CH), 7.14−7.36 (m, 14H, Ar), 8.22 (bs, 2H, Ar), 8.35 (bs, 2H, Ar). ^{13}C NMR ($CDCl_3$): 42.52 (CH_2), 51.21 (CH_2), 56.72 (CH_2), 58.00 (CH_2), 82.66 (Cquat), 85.24 (Cquat), 89.89 (Cquat), 93.51 (Cquat), 117.76 (CH), 121.06 (CH), 121.42 (CH), 127.00 (CH), 128.12 (CH), 128.39 (CH), 128.96 (CH), 138.14 (Cquat), 138.47 (CH), 142.61 (CH), 153.72 (Cquat). MS (FAB) *m*/*z*: 631 (M + H), 538, 492, 448, 436, 307, 155, 119. HRMS: *m*/*z* 631.3071 (calcd for $C_{42}H_{38}N_4O_2$; 631.3071) (M + H). IR (neat, cm^{-1}): 3028, 2917, 2829, 2210, 1574, 1475, 1453, 1426, 1369, 1323, 1275, 1217, 1188, 1151, 1102, 1047, 999, 796, 741.

***N,N′*-Dibenzyl-*N,N′*-bis(7-pyridin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (py:py 0:0) (4).** Compound **4** was prepared by reacting **1** with 3-ethynylpyridine[22] at 40 °C (analogous to **2**). Yield: 70%. Viscous yellow oil. R_f 0.6. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.80 (s, 4H, $2CH_2$), 3.61 (d, J = 1.6 Hz, 4H, $2CH_2$), 3.70 (s, 4H, $2CH_2$), 5.98 (dt, J = 2, 10.8 Hz, 2H, 2CH), 6.05 (d, J = 11.2 Hz, 2H, 2CH), 7.17−7.33 (m, 12H, Ar), 7.70 (dt, J = 2, 8 Hz, 2H, Ar), 8.51 (dd, J = 1.6, 3.2 Hz, 2H, Ar), 8.71 (d, 2H, Ar). ^{13}C NMR ($CDCl_3$): 42.65 (CH_2), 51.32 (CH_2), 58.14 (CH_2), 82.99 (Cquat), 90.19 (Cquat), 92.85 (Cquat), 93.97 (Cquat), 118.27 (CH), 120.13 (Cquat), 120.65 (CH), 122.94 (CH), 127.04 (CH), 128.19 (CH), 129.04 (CH), 138.34 (CH), 138.49 (Cquat), 148.74 (CH), 152.19 (CH); MS (FAB) *m*/*z*: 571 (M + H), 479, 285. HRMS: *m*/*z*: 571.2861 (calcd for $C_{40}H_{34}N_4$; 571.2861) (M + H). IR (neat, cm^{-1}): 3027, 2917, 2828, 2185, 1683, 1585, 1559, 1494, 1475, 1407, 1359, 1323, 1274, 1186, 1108, 1022, 976, 803, 741, 700.

***N,N*-Dibenzyl-*N,N′*-bis(7-quinolin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (quin:quin 0:0) (5).** Compound **5** was prepared by reacting **1** with 3-ethynylquinoline.[22] Yield: 70%. Viscous yellow oil. R_f. 0.6. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.87 (s, 4H, $2CH_2$), 3.67 (d, 4H, $2CH_2$), 3.76 (s, 4H, $2CH_2$), 5.99 (dt, J = 1.6, 10.8 Hz, 2H, 2CH), 6.09 (d, J = 11.2 Hz, 2H, 2CH), 7.19−7.25 (m, 6H, Ar), 7.32−7.35 (m, 4H, Ar), 7.51−7.55 (m, 2H, Ar), 7.65−7.74 (m, 4H, Ar), 8.09 (d, 2H, Ar), 8.19 (d, J = 2 Hz, 2H, Ar), 8.96 (d, J = 2 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$): 42.65 (CH_2), 51.24 (CH_2), 58.18 (CH_2), 83.11 (Cquat), 90.20 (Cquat), 93.54 (Cquat), 94.01 (Cquat), 117.03 (Cquat), 118.28 (CH), 120.57 (CH), 126.98 (CH), 127.17 (CH), 127.55 (CH), 128.13 (CH), 129.00 (CH), 129.27 (CH), 130.09 (CH), 138.23 (CH), 138.37 (Cquat), 146.78 (Cquat), 151.84 (CH). MS (FAB) *m*/*z*: 671 (M + H), 579, 489, 335, 216. HRMS: *m*/*z*: 671.3174 (calcd for $C_{48}H_{38}N_4$; 671.3173) (M + H). IR (neat, cm^{-1}): 3060, 3027, 2828, 2184, 2018, 1734, 1487, 1453, 907, 745, 698.

(21) Rawat, D. S.; Zaleski, J. M. *Synth. Commun.* **2002**, *32*, 1489−1494.
(22) Sakamoto, T.; Shiraiwa, M.; Kondo, Y.; Yamanaka, H. *Synthesis* **1983**, 312−314.

[Cu(dma:dma 1:1)](BF$_4$)$_2$ (6). A solution of $Cu(BF_4)_2 \cdot xH_2O$ (0.111 g, 0.47 mmol) in acetonitrile (10 mL) was charged to a Schlenk flask under nitrogen. The solution was heated at 30 °C while a solution of **2** (0.25 g, 0.47 mmol) in methylene chloride (10 mL) and acetonitrile (10 mL) was added dropwise over 30 min. The reaction mixture was stirred at 30−40 °C for 4 h, and solvent was removed under reduced pressure. The crude product obtained was dissolved in acetonitrile (5 mL) and precipitated with dry ether (20 mL) and stirred for 3 h. The solid was filtered and washed with ether (2 × 5 mL) and vacuum-dried. The solid was further stirred in ether (25 mL) for 2 h, filtered, and finally dried under vacuum at 40 °C. Yield (0.30 g, 83%); brown solid. Mp: 105−112 °C (dec). MS (ESI) *m*/*z*: 595, 593. ^{63,65}Cu (M$^+$ calcd for $C_{36}H_{42}N_4Cu$; 593, 595), 531, 532. IR (KBr, cm^{-1}): 3029, 2933, 2190, 1630, 1454, 1401, 1205, 1083, 745, 702, 533. Anal. Calcd for $C_{36}H_{42}N_4Cu \cdot 2BF_4$: C, 56.30; H, 5.51; N, 7.29. Found: C, 56.90; H, 5.83; N, 7.05.

[Cu(pyO:pyO 1:1)](BF$_4$)$_2$ (7). Yield: 85%; brown solid. Mp: 118−125 °C (dec). MS (ESI) *m*/*z*: 693, 695, ^{63,65}Cu (M$^+$ calcd for $C_{42}H_{38}N_4O_2Cu$; 693, 695), 632, 631. IR (KBr, cm^{-1}): 3063, 2927, 2220, 1577, 1494, 1437, 1282, 1235, 1062, 996, 806, 742, 698, 649. Anal. Calcd for $C_{42}H_{38}N_4O_2Cu \cdot 2BF_4$: C, 58.10; H, 4.41; N, 6.45. Found: C, 58.33; H, 4.85; N, 6.26.

[Cu(py:py 0:0)](BF$_4$)$_2$ (8). Yield: 85%; light brown solid. Mp: 131−134 °C (dec). MS (ESI) *m*/*z*: 721, 723, ^{63,65}Cu (M$^+$ calcd for $C_{40}H_{34}N_4Cu \cdot BF_4$; 721, 723), 633, 635, ^{63,65}Cu (M$^+$ calcd for $C_{40}H_{34}N_4Cu$; 633, 635), 571, 573. IR (KBr, cm^{-1}): 3062, 2198, 1697, 1576, 1415, 1481, 1083, 812, 744, 698, 657. Anal. Calcd for $C_{40}H_{34}N_4Cu \cdot 2BF_4 \cdot 1/2H_2O$: C, 58.81; H, 4.32; N, 6.86. Found: C, 58.82; H, 4.49; N, 6.85.

[Cu(quin:quin 0:0)](BF$_4$)$_2$ (9). Yield: 82%; brown solid. Mp: 120−125 °C (dec). MS (ESI) *m*/*z*: 733, 735, ^{63,65}Cu (M$^+$ calcd for $C_{48}H_{38}N_4Cu$; 733, 735), 671, 673. IR (KBr, cm^{-1}): 3059, 2192, 1616, 1495, 1365, 1336, 1285, 1208, 1061, 915, 782, 748, 702, 637, 520. Anal. Calcd for $C_{48}H_{38}N_4Cu \cdot 2BF_4 \cdot 2H_2O$: C, 61.05; H, 4.48; N, 5.93. Found: C, 61.28; H, 4.36; N, 6.03.

[Zn(dma-dma 1:1)](ClO$_4$)$_2$ (10). A Schlenk flask was charged with $Zn(ClO_4)_2 \cdot 6H_2O$ (0.070 g, 0.18 mmol) and acetonitrile (10 mL) under nitrogen. The mixture was stirred for 10 min at 40 °C. A solution of **2** (0.10 g, 2.0 mmol) in methylene chloride (5 mL) and acetonitrile (20 mL) was then added over 30 min. The reaction mixture was stirred overnight at 40 °C. The solvent was subsequently removed and the residue stirred in ether (50 mL). After filtration and washing with ether (2 × 10 mL), the solid was dried under vacuum to give **10** in 80%. ^{1}H NMR (CD_3CN) δ (ppm): 2.80 (s, 12H, $4NCH_3$), 2.84 (s, 4H, $2CH_2$), 3.60 (s, 4H, $2CH_2$), 3.75 (s, 4H, $2CH_2$), 4.04 (s, 4H, $2CH_2$), 5.99 (d, J = 11.2 Hz, 2H, 2CH), 6.10 (d, J = 11.2 Hz, 2H, 2CH), 7.29−7.36 (m, 10H, Ar). ^{13}C NMR (CD_3OD): 43.39 (CH_3), 43.58 (CH_2), 49.62 (CH_2), 51.79 (CH_2), 59.23 (CH_2), 84.53 (Cquat), 87.03 (Cquat), 87.77 (Cquat), 93.59 (Cquat), 119.14 (CH), 122.34 (CH), 128.67 (CH), 129.51 (CH), 130.57 (CH), 138.80 (Cquat). MS (ESI) *m*/*z*: 593, 595; ^{64,66}Zn ((M − H)$^+$ calcd for $C_{36}H_{42}N_4Zn$; 593, 595), 531, 532. Anal. Calcd for $C_{36}H_{42}N_4Zn \cdot 2ClO_4 \cdot 1.5H_2O$; C, 52.60; H, 5.51; N, 6.81. Found: C, 52.72; H, 5.54; N, 6.74.

[Zn(pyO:pyO 1:1)](ClO$_4$)$_2$ (11). Yield: 89%. ^{1}H NMR (CD_3CN) δ (ppm): 3.12 (s, 4H, $2CH_2$), 3.60 (s, 4H, $2CH_2$), 3.98 (s, 4H, $2CH_2$), 4.99 (s, 4H, $2CH_2$), 6.02 (s, 4H, 4CH), 7.35−7.38 (m, 10H, Ar), 7.46−7.49 (m, 2H, Ar), 7.58−7.61 (m, 2H, Ar), 8.14 (d, 2H, Ar), 8.19 (bs, 2H, Ar). ^{13}C NMR (CD_3CN): 43.36 (CH_2), 49.72 (CH_2), 58.41 (CH_2), 86.12 (Cquat), 86.34 (Cquat), 89.45 (Cquat), 91.47 (Cquat), 120.89 (CH), 121.35 (CH), 127.33 (CH), 129.89 (CH), 131.31 (CH), 137.83 (Cquat), 143.05 (CH), 156.04

(Cquat). MS (ESI) *m*/*z*: 693, 695; ^{64,66}Zn ((M − H)$^+$ calcd for $C_{42}H_{38}N_4O_2Zn$; 693, 695), 631, 633. IR (KBr, cm^{-1}): 3060, 2927, 2200, 1576, 1485, 1437, 1281, 1097, 995, 743, 689, 622. Anal. Calcd for $C_{42}H_{38}N_4O_2Zn\cdot 2ClO_4\cdot H_2O$: C, 55.08; H, 4.40; N, 6.12. Found: C, 54.77; H, 4.31; N, 5.97.

[Zn(py:py 0:0)](ClO$_4$)$_2$ (12). Yield: 83%. ^{1}H NMR (CD_3CN) δ (ppm): 3.00 (s, 4H, $2CH_2$), 3.68 (s, 4H, $2CH_2$), 3.89 (s, 4H, $2CH_2$), 6.12 (d, J = 10.4 Hz, 2H, 2CH), 6.22 (d, J = 10.4 Hz, 2H, CH), 7.33 (bs, 10H, Ar), 7.51 (d, 2H, Ar), 8.01 (d, 2H, Ar), 8.48 (d, 4H, Ar). ^{13}C NMR (CD_3OD): 43.36 (CH_2), 51.69 (CH_2), 59.19 (CH_2), 84.51 (Cquat), 91.87 (Cquat), 92.78 (Cquat), 94.17 (Cquat), 119.40 (Cquat), 122.03 (CH), 125.30 (CH), 128.36 (CH), 129.26 (CH), 130.31 (CH), 138.89 (Cquat), 140.88 (CH), 149.28 (CH), 152.11 (CH). MS (ESI) *m*/*z*: 733, 735,^{64,66}Zn (M$^+$ calcd for $C_{40}H_{34}N_4Zn\cdot ClO_4$; 733, 735), 633, 635, ^{64,66}Zn ((M − H)$^+$ calcd for $C_{40}H_{34}N_4Zn$; 633, 635), 571, 572, 573. IR (KBr, cm^{-1}): 3061, 2844, 2200, 1603, 1483, 1419, 1331, 1281, 1198, 1102, 928, 812, 744, 698, 623, 556. Anal. Calcd for $C_{40}H_{34}N_4Zn\cdot 2ClO_4\cdot 3H_2O$: C, 54.06; H, 4.53; N, 6.30. Found: C, 53.85; H, 4.40; N, 6.10.

[Zn(quin:quin 0:0)](ClO$_4$)$_2$ (13). Yield: 86%. ^{1}H NMR (CD_3CN) δ (ppm): 3.11 (s, 4H, $2CH_2$), 3.76 (s, 4H, $2CH_2$), 3.98 (s, 4H, $2CH_2$), 6.06 (d, J = 10.8 Hz, 2H, 2CH), 6.27 (d, J = 10.8 Hz, 2H, CH), 7.26−7.33 (m, 10H, Ar), 7.61 (t, 2H, Ar), 7.75−7.82 (m, 4H, Ar), 8.01 (d, J = 8.8 Hz, 2H, Ar), 8.30 (s, 2H, Ar), 8.83 (d, J = 1.6 Hz, 2H, Ar). ^{13}C NMR (CD_3OD): 43.69 (CH_2), 50.32 (CH_2), 59.01 (CH_2), 84.58 (Cquat), 91.25 (Cquat), 94.31 (Cquat), 94.98 (Cquat), 118.26 (Cquat), 121.04 (CH), 128.67 (CH), 129.00 (CH), 129.25 (CH), 129.29 (CH), 129.51 (CH), 129.75 (CH), 131.09 (CH), 132.11 (CH), 140.41 (CH), 147.56 (Cquat), 152.47 (CH). MS (ESI) *m*/*z*: 733, 735, ^{64,66}Zn ((M − H)$^+$ calcd for $C_{48}H_{38}N_4Zn$; 733, 735), 671, 673. IR (KBr, cm^{-1}): 3054, 2844, 2193, 1499, 1457, 1108, 918, 781, 747, 700, 623. Anal. Calcd for $C_{48}H_{38}N_4Zn\cdot 2ClO_4\cdot 5H_2O$: C, 56.23; H, 4.71; N, 5.45. Found: C, 56.21; H, 4.35; N, 5.26.

***N*,*N*′-Dibenzyl-*N*-(*Z*)-5-chloropent-4-ene-2-ynyl-*N*′-[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl-ethane]-1,2-diamine (14).** A solution of **1** (2.2 g, 5.0 mmol) in benzene (10 mL) was added to $Pd(Ph_3P)_4$ (0.35 g, 0.30 mmol), CuI (0.20 g, 1.0 mmol), and *n*-butylamine (1.8 g, 25 mmol) under nitrogen at room temperature. The mixture was vigorously stirred at 25 °C for 10 min. A solution of 3-(2-propynyloxy)pyridine (0.73 g, 5.4 mmol) in dry degassed benzene (50 mL) was then added dropwise under nitrogen over 2 h at 25 °C. The reaction mixture was stirred for 6 h, and completion was determined by TLC and ^{1}H NMR. The reaction mixture was concentrated under reduced pressure and the residue extracted with methylene chloride (200 mL) and washed with water (2 × 100 mL). Upon concentration, the organic layer yields a viscous oil. Purification on silica gel with methylene chloride initially, and then ethyl acetate/hexane (1:1) yields the desired product **14** (1.0 g, 37%). Viscous oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.83 (s, 4H, $2CH_2$), 3.60 (d, J = 1.6 Hz, 4H, $2CH_2$), 3.73 (d, J = 4 Hz, 4H, $2CH_2$), 4.90 (d, J = 2 Hz, 2H, CH_2), 5.84−5.97 (m, 3H, 3CH), 6.39 (d, J = 8 Hz, 1H, CH), 7.19−7.42 (m, 12H, Ar), 8.25 (dd, J = 1.6, 3.2 Hz, 1H, Ar), 8.39 (d, J = 2.8 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.43 (CH_2), 42.55 (CH_2), 51.23 (CH_2), 56.73 (CH_2), 58.01 (CH_2), 58.07 (CH_2), 79.47 (Cquat), 82.66 (Cquat), 85.28 (Cquat), 89.87 (Cquat), 93.33 (Cquat), 93.58 (Cquat), 111.94 (CH), 117.74 (CH), 121.15 (CH), 121.43 (CH), 123.60 (CH), 127.01 (CH), 127.85 (CH), 128.15 (CH), 129.02 (CH), 129.04 (CH), 138.24 (CH), 138.53 (Cquat), 138.55 (Cquat), 142.66 (CH), 153.69 (Cquat). MS (EI) *m*/*z*: 534 (M + H), 442, 347, 345, 337, 315, 218, 91. HRMS: *m*/*z*: 534.22937 (calcd for $C_{34}H_{32}ClN_3O$; 534.2311) (M + H). IR (neat, cm^{-1}): 3028, 2917, 2830, 2208, 1574, 1426, 1393, 1367, 1324, 1218, 1108, 1046, 1000, 739, 700.

***N*,*N*′-Dibenzyl-*N*-[8-(*N*,*N*′-dimethylamino)-oct-4-ene-2,6-diynyl]-*N*′-[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl]-ethane-1,2-diamine (dma-pyO 1:1) (15).** To a stirring mixture of $Pd(Ph_3P)_4$ (0.10 g, 0.86 mmol), CuI (0.05 g, 0.26 mmol), *n*-butylamine (0.41 g, 5.6 mmol), and benzene (10 mL) was added a solution of **14** (0.6 g, 1.1 mmol) in benzene (20 mL) and the composite stirred for 10 min under nitrogen. A solution of 1-(dimethylamino)-2-propyne (0.23 g, 2.8 mmol) in benzene (30 mL) was then added dropwise to the above solution over 1 h at 40−50 °C. The reaction mixture was stirred for 2 h, and completion was determined by ^{1}H NMR. The reaction mixture was concentrated under reduced pressure, and the residue was extracted with methylene chloride (100 mL) and washed with water (2 × 50 mL). Upon drying over sodium sulfate and concentration under reduced pressure, the organic layer affords a viscous residue. Purification of the viscous material on silica gel in methanol/methylene chloride (1:9) yields **15** (0.4 g, 62%) as a viscous colorless oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.29 (s, 6H, $2CH_3$), 2.78 (s, 4H, $2CH_2$), 3.44 (s, 2H, CH_2), 3.56−3.58 (m, 4H, $2CH_2$), 3.69 (d, J = 4 Hz, 4H, $2CH_2$), 4.88 (d, J = 2 Hz, 2H, CH_2), 5.82 (dd, J = 10.8, 13.2 Hz, 2H, 2CH), 5.92 (d, J = 12.2 Hz, 2H, 2CH), 7.15−7.38 (m, 12H, Ar), 8.22 (dd, J = 1.2, 3.6 Hz, 1H, Ar), 8.35 (d, J = 2.8 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.62 (CH_2), 42.70 (CH_2), 44.05 (CH_3), 48.70 (CH_2), 51.30 (CH_2), 51.36 (CH_2), 56.81 (CH_2), 58.10 (CH_2), 82.72 (Cquat), 82.87 (Cquat), 83.11 (Cquat), 85.33 (Cquat), 89.94 (Cquat), 92.39 (Cquat), 93.62 (Cquat), 117.82 (CH), 119.11 (CH), 119.21 (CH), 121.17 (CH), 121.52 (CH), 123.67 (CH), 127.06 (CH), 127.09 (CH), 128.23 (CH), 129.08 (CH), 138.32 (CH), 138.62 (Cquat), 138.68 (Cquat), 142.75 (CH), 153.77 (Cquat). MS (FAB) *m*/*z*: 581 (M + H), 489, 437, 384, 315, 286. HRMS: *m*/*z* 581.3280 (calcd for $C_{39}H_{40}N_4$; 581.3279) (M + H). IR (neat, cm^{-1}): 3027, 2939, 2823, 2776, 2206, 1574, 1493, 1474, 1452, 1426, 1393, 1356, 1322, 1274, 1227, 1187, 1151, 1100, 1075, 1046, 999, 837, 796, 740, 700.

***N*,*N*′-Dibenzyl-*N*-[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl]-*N*′-7-(Pyridin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (pyO:py 1:0) (16).** Compound **16** was prepared in the same manner as **15**. Yield: 55%. Viscous oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.75−2.84 (m, 4H, $2CH_2$), 3.55 (d, J = 4 Hz, 2H, CH_2), 3.63 (d, J = 1.6 Hz, 2H, CH_2), 3.68 (s, 2H, CH_2), 3.73 (s, 2H, CH_2), 4.88 (d, J = 2 Hz, 2H, CH_2), 5.83 (dt, 1H, CH), 5.92 (d, 1H, CH), 5.98 (dt, J = 1.6, 10.8 Hz, 1H, CH), 6.05 (d, 1H, CH), 7.15−7.38 (m, 13H, Ar), 7.71 (dt, J = 2, 8.0 Hz, 1H, Ar), 8.23 (dd, J = 1.6, 3.2 Hz, 1H, Ar), 8.36 (d, J = 2.8 Hz, 1H, Ar), 8.51 (dd, J = 1.6, 3.2 Hz, 1H, Ar), 8.71−8.72 (m, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.58 (CH_2), 51.21 (CH_2), 51.34 (CH_2), 56.75 (CH_2), 58.03 (CH_2), 58.12 (CH_2), 82.66 (Cquat), 82.99 (Cquat), 85.28 (Cquat), 89.89 (Cquat), 90.15 (Cquat), 92.84 (Cquat), 93.56 (Cquat), 93.92 (Cquat), 117.74 (CH), 118.28 (CH), 120.06 (Cquat), 120.57 (CH), 121.14 (CH), 121.46 (CH), 122.90 (CH), 123.61 (CH), 127.03 (CH), 128.16 (CH), 129.01 (CH), 138.29 (CH), 138.45 (Cquat), 138.55 (Cquat), 142.68 (CH), 148.70 (CH), 152.12 (CH), 153.71 (Cquat). MS (FAB) *m*/*z*: 601 (M + H). HRMS: *m*/*z*: 601.2967 (calcd for $C_{41}H_{36}N_4O$; 601.2967) (M + H). IR (neat, cm^{-1}): 3028, 2917, 2829, 2206, 1574, 1493, 1475, 1452, 1394, 1367, 1275, 1187, 1108, 1022, 922, 803, 741, 701.

***N*,*N*′-Dibenzyl-*N*-[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl]-*N*′-(7-qunolin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (pyO:quin 1:0) (17).** Yield: 67%. Viscous oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.83−2.90 (m 4H, $2CH_2$), 3.59 (d, 2H, CH_2), 3.70−3.72 (m, 4H, $2CH_2$), 3.80 (s, 2H, CH_2), 4.88 (d, J = 1.6 Hz, 2H, CH_2), 5.82 (dt, J = 2, 10.8 Hz, 1H, CH), 5.91 (d, 1H, CH), 6.05 (dt, J =

1.6, 10.8 Hz, 1H, CH), 6.14 (d, J = 11.2 Hz, 1H, CH), 7.16−7.39 (m, 12H, Ar), 7.53−7.57 (m, 1H, Ar), 7.67 (d, 1H, Ar), 7.71−7.76 (m, 1H, Ar), 8.12 (d, J = 8.4 Hz, 1H, Ar), 8.22 (d, J = 2 Hz, 1H, Ar), 8.28 (d, J = 3.6 Hz, 1H, Ar), 8.42 (s, 1H, Ar), 8.99 (d, J = 2 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.49 (CH_2), 42.61 (CH_2), 51.15 (CH_2), 51.21 (CH_2), 56.67 (CH_2), 57.94 (CH_2), 58.14 (CH_2), 82.63 (Cquat), 83.09 (Cquat), 85.24 (Cquat), 89.81 (Cquat), 90.17 (Cquat), 93.50 (Cquart), 93.98 (Cquat), 116.95 (Cquat), 117.67 (CH), 118.31 (CH), 120.53 (CH), 121.04 (CH), 121.43 (CH), 123.60 (CH), 126.93 (CH), 127.13 (CH), 127.48 (CH), 128.07 (CH), 128.09 (CH), 128.92 (CH), 128.95 (CH), 129.21(CH), 130.05 (CH), 138.17 (CH), 138.24 (CH), 138.33 (Cquat), 138.43 (Cquat), 142.66 (CH), 146.71 (Cquat), 151.78 (CH), 153.67 (Cquat). MS (FAB); 651 (M + H). HRMS: m/z: 651.3123 (calcd for $C_{45}H_{38}N_4O$; 651.3123) (M + H); IR (Neat, cm^{-1}): 3027, 2917, 2828, 2200, 1573, 1486, 1452, 1426, 1368, 1322, 1275, 1188, 1103, 1047, 1000, 908, 784, 699.

[Cu(dma:pyO 1:1)](BF$_4$)$_2$ (18). Yield: 78%; brown solid. Mp: 125−134 °C (dec). MS (ESI): 643, 645, ^{63,65}Cu (M$^+$ calcd for $C_{39}H_{40}N_4OCu$; 643, 645), 581, 582. IR (KBr, cm^{-1}): 3065, 2190, 1577, 1496, 1435, 1283, 1061, 806, 749, 703, 521. Anal. Calcd for $C_{39}H_{40}N_4OCu\cdot 2BF_4\cdot 4H_2O$: C, 52.64; H, 5.43; N, 6.29. Found: C, 52.64; H, 5.25; N, 5.89.

[Cu(pyO:py 1:0)](BF$_4$)$_2$ (19). Yield: 90%; brown solid. Mp: 120−124 °C (dec). MS (ESI): 663, 665, ^{63,65}Cu (M$^+$ calcd for $C_{41}H_{36}N_4OCu$; 663, 665), 601, 603. IR (KBr, cm^{-1}): 3064, 2210, 1694, 1576, 1494, 1455, 1437, 1282, 1236, 1197, 1061, 809, 746, 699. Anal. Calcd for $C_{41}H_{36}N_4OCu\cdot 2BF_4\cdot 3H_2O$: C, 55.19; H, 4.74; N, 6.28; Found: C, 54.99; H, 4.57; N, 6.33.

[Cu(pyO:quin 1:0)](BF$_4$)$_2$ (20). Yield: 85%; brown solid. Mp: 115−120 °C (dec). MS (ESI) m/z: 801, 803; ^{63,65}Cu (M$^+$ calcd for $C_{45}H_{38}N_4OCu\cdot BF_4$; 801, 803), 713, 715, ^{63,65}Cu (M$^+$ calcd for $C_{45}H_{38}N_4OCu$; 713, 715), 651, 653. IR (KBr, cm^{-1}): 3063, 2362, 1694, 1618, 1576, 1495, 1455, 1436, 1365, 1336, 1282, 1237, 1061, 783. Anal. Calcd for $C_{45}H_{38}N_4OCu\cdot 2BF_4\cdot 1.5\ H_2O$: C, 59.08; H, 4.52; N, 6.12. Found: C, 59.05; H, 4.95; N, 5.84.

[Zn(dma:pyO 1:1)](ClO$_4$)$_2$ (21). Yield: 88%. ^{1}H NMR (CD_3CN) δ (ppm): 2.88 (s, 6H, $2CH_3$), 2.98 (d, 4H, $2CH_2$), 3.65 (d, 4H, $2CH_2$), 3.85 (d, 4H, $2CH_2$), 4.12 (s, 2H, CH_2), 4.98 (bs, 2H, CH_2), 6.00 (d, 2H, 2CH), 6.10 (d, 2H, 2CH), 7.36 (bs, 10H, Ar), 7.46 (bs, 2H, Ar), 8.15 (s, 1H, Ar), 8.27(S, 1H, Ar). ^{13}C NMR (CD_3CN): 43.46 (CH_3), 48.88 (CH_2), 50.13 (CH_2), 50.45 (CH_2), 57.95 (CH_2), 58.47 (CH_2), 58.57 (CH_2), 85.11 (Cquat), 85.23 (Cquat), 85.82 (Cquat), 85.93 (Cquat), 88.17 (Cquat), 90.40 (Cquat), 91.79 (Cquat), 92.03 (Cquat), 119.32 (CH), 120.62 (CH), 121.50 (CH), 122.80 (CH), 124.91 (CH), 126.14 (CH), 129.26 (CH), 129.60 (CH), 129.68 (CH), 129.77 (CH), 130.80 (CH), 131.10 (CH), 135.17 (Cquat), 136.43 (Cquat), 138.44 (CH), 143.17 (CH), 155.31 (Cquat). MS (ESI) m/z: 643, 645, ^{64,66}Zn ((M − H)$^+$ calcd for $C_{39}H_{40}N_4OZn$; 643, 645), 581, 582. IR (KBr, cm^{-1}): 3058, 2927, 2849, 2210, 1576, 1455, 1369, 1281, 1234, 1093, 995, 804, 742, 700, 623. Anal. Calcd for $C_{39}H_{40}N_4OZn\cdot 2ClO_4\cdot 4H_2O$: C, 51.08; H, 5.27; N, 6.10. Found: C, 51.36; H, 4.96; N, 5.74.

[Zn(pyO:py 1:0)](ClO$_4$)$_2$ (22). Yield: 85%. ^{1}H NMR (CD_3CN) δ (ppm): 3.12 (s, 4H, $2CH_2$), 3.70 (s, 2H, CH_2), 4.00 (s, 4H, $2CH_2$), 4.99 (s, 2H, CH_2), 6.03 (s, 2H, 2CH), 6.12 (d, 1H, CH), 6.24 (d, 1H, CH), 7.37 (bs, 10H, Ar), 7.54 (s, 2H, Ar), 7.62 (s, 2H, Ar), 7.62 (s, 2H, Ar), 8.03 (s, 1H, Ar), 8.14 (d, 2H, Ar), 8.48 (d, 1H, Ar). ^{13}C NMR (CD_3CN): 43.34 (CH_2), 43.60 (CH_2), 49.53 (CH_2), 58.41 (CH_2), 86.03 (Cquat), 86.50 (Cquat), 89.01 (Cquat), 90.02 (Cquat), 91.52 (Cquat), 92.03 (Cquat), 92.64 (Cquat), 120.94 (CH), 121.07 (CH), 121.22 (CH), 121.59 (CH), 122.35 (Cquat), 126.45 (CH), 127.45 (CH), 129.90 (CH), 131.28 (CH), 137.60 (CH), 143.01 (Cquat), 143.24 (Cquat), 149.43 (CH), 151.77 (CH), 156.08 (Cquat). MS (ESI) m/z: 663, 665, ^{64,66}Zn ((M − H)$^+$ calcd for $C_{41}H_{36}N_4OZn$; 663, 665), 600, 603. IR (KBr, cm^{-1}): 3061, 2190, 1604, 1577, 1484, 1331, 1282, 1198, 1106, 995, 928, 809, 742, 698, 623. Anal. Calcd for $C_{41}H_{36}N_4OZn\cdot 2ClO_4\cdot 5H_2O$: C, 51.56; H, 4.86; N, 5.87. Found: C, 51.98; H, 4.43; N, 5.59.

[Zn(pyO:quin 1:0)](ClO$_4$)$_2$ (23). Yield: 89%. ^{1}H NMR (CD_3CN) δ (ppm): 3.11 (s, 2H, CH_2), 3.19 (s, 2H, CH_2), 3.67 (s, 2H, CH_2), 3.84 (s, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.05 (s, 2H, CH_2), 4.99 (s, 2H, CH_2), 5.97 (s, 2H, 2CH), 6.13 (d, 1H, CH), 6.30 (d, 1H, CH), 7.29−7.36 (m, 10H, Ar), 7.56−7.63 (m, 3H, Ar), 7.75 (t, J = 7.2 Hz, 1H, Ar), 7.84 (d, J = 7.6 Hz, 1H, Ar), 8.01 (d, J = 8 Hz, 1H, Ar), 8.20 (d, 2H, Ar), 8.40 (s, 1H, Ar), 8.85 (s, 1H, Ar). ^{13}C NMR (CD_3CN): 43.35 (CH_2), 43.78 (CH_2), 49.38 (CH_2), 49.47 (CH_2), 55.28 (CH_2), 58.43 (CH_2), 86.04 (Cquat), 86.45 (Cquat), 86.95 (Cquat), 88.95 (Cquat), 89.35 (Cquat), 90.97 (Cquat), 91.38 (Cquat), 94.43 (Cquat), 117.69 (Cquat), 120.84 (CH), 120.91 (CH), 121.14 (CH), 121.63 (CH), 127.51 (CH), 127.71 (CH), 128.35 (CH), 128.84 (CH), 129.12 (CH), 129.35 (CH), 129.88 (CH), 129.98 (CH), 130.04 (CH), 131.31 (CH), 131.36 (CH), 132.53 (CH), 133.50 (CH), 133.79 (CH), 137.45 (CH), 141.25 (Cquat), 142.43 (CH), 146.66 (Cquat), 152.97 (CH), 156.14 (Cquat). MS (ESI) m/z: 713, 715, ^{64,66}Zn ((M − H)$^+$ calcd for $C_{45}H_{38}N_4OZn$; 713, 715), 651, 653. IR (KBr, cm^{-1}): 3057, 2205, 1605, 1496, 1456, 1437, 1367, 1283, 1238, 1101, 922, 746, 699, 623. Anal. Calcd for $C_{45}H_{38}N_4OZn\cdot 2ClO_4\cdot 5.5H_2O$: C, 53.30; H, 4.86; N, 5.52. Found: C, 53.20; H, 4.55; N, 5.44.

***N,N′*-dibenzyl-*N*-(*Z*)-5-chloropent-4-ene-2-ynyl-*N′*-[7-quinolin-3-yl-hept-4-ene-2,6-diynyl-ethane]-1,2-diamine (24).** Compound **24** was prepared in the same manner as **14**. Yield: 40%; yellow viscous oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.78−2.87 (m, 4H, $2CH_2$), 3.55 (d, J = 1.6 Hz, 2H, CH_2), 3.68 (s, 4H, $2CH_2$), 3.76 (s, 2H, CH_2), 5.87 (dt, J = 1.6, 7.2 Hz, 1H, CH), 6.02 (dt, J = 2, 10.8 Hz, 1H, CH), 6.11 (d, J = 10.8 Hz, 1H, CH), 6.35 (d, J = 7.2 Hz, 1H, CH), 7.21−7.36 (m, 10H, Ar), 7.52−7.56 (m, 1H, Ar), 7.66 (d, J = 8 Hz, 1H, Ar), 7.71−7.75 (m, 1H, Ar), 8.08 (d, J = 8 Hz, 1H, Ar), 8.21 (d, J = 1.6 Hz, 1H, Ar), 8.95 (d, J = 2 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.52 (CH_2), 42.76 (CH_2), 51.30 (CH_2), 51.36 (CH_2), 58.14 (CH_2), 58.27 (CH_2), 79.51 (Cquat), 83.16 (Cquat), 90.25 (Cquat), 93.40 (Cquat), 93.60 (Cquat), 94.14 (Cquat), 112.02 (CH), 117.17 (Cquat), 118.37 (CH), 120.70 (CH), 127.04 (CH), 127.08 (CH), 127.28 (CH), 127.65 (CH), 127.87 (CH), 128.19 (CH), 128.23 (CH), 129.13 (CH), 129.38 (CH), 130.19 (CH), 138.34 (CH), 138.54 (Cquat), 138.60 (Cquat), 146.89 (Cquat), 151.95 (CH). MS (EI) m/z: 554 (M$^+$ + 1), 518, 454, 426, 335, 304, 218, 131, 91. HRMS m/z: 554.2265 (calcd for $C_{37}H_{32}ClN_3$; 554.2362) (M + H). IR (neat, cm^{-1}): 3029, 2917, 2825, 2185, 2019, 1875, 1735, 1675, 1580, 1565, 1480, 1455, 1357, 1277, 1119, 1045, 990, 865, 785, 760.

***N,N′*-Dibenzyl-*N*-(7-pyridin-3-yl-hept-4-ene-2,6-diynyl)-*N′*-(7-quinolin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (py:quin 0:0) (25).** Yield: 72%. ^{1}H NMR ($CDCl_3$) δ (ppm): 2.85 (t, J = 3.2 Hz, 4H, $2CH_2$), 3.63 (d, J = 1.6 Hz, 2H, CH_2), 3.68 (d, J = 1.2 Hz, 2H, CH_2), 3.72 (s, 2H, CH_2), 3.77 (s, 2H, CH_2), 5.96 (dt, J = 1.6, 10.8 Hz, 1H, CH), 6.03−6.06 (m, 2H, 2CH), 6.12 (d, J = 10.8 Hz, 1H, CH), 7.17−7.37 (m, 11H, Ar), 7.52−7.56 (m, 1H, Ar), 7.66−7.75 (m, 3H, Ar), 8.10 (d, J = 8.4 Hz, 1H, Ar) 8.21 (d, J = 2 Hz, 1H, Ar), 8.52 (dd, J = 2, 5.2 Hz, 1H, Ar), 8.73−8.73 (m, 1H, Ar), 8.97 (d, J = 2 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$): 42.60 (CH_2), 42.69 (CH_2), 51.24 (CH_2), 51.31 (CH_2), 58.11 (CH_2), 58.21 (CH_2), 82.98 (Cquat), 83.12 (Cquat), 90.17 (Cquat), 90.22 (Cquat), 92.81 (Cquat), 93.58 (Cquat), 93.93 (Cquat), 94.05 (Cquat), 117.08 (Cquat), 118.22 (CH), 118.34 (CH), 120.09 (Cquat), 120.60 (CH),

120.63 (CH), 122.90 (CH), 122.99 (Cquat), 127.03 (CH), 127.22 (CH), 127.58 (CH), 128.14 (CH), 128.16 (CH), 128.99 (CH), 129.04 (CH), 129.32 (CH), 130.14 (CH), 138.27 (CH), 138.30 (CH), 138.43 (Cquat), 146.83 (Cquat), 148.69 (CH), 151.87 (CH), 152.14 (CH). MS (FAB) *m*/*z*: 621 (M + H). HRMS: *m*/*z*: 621.3018 (calcd for $C_{44}H_{36}N_4$; 621.3017) (M + H). IR (neat, cm^{-1}): 3027, 2918, 2828, 2184, 1872, 1678, 1599, 1566, 1488, 1475, 1427, 1357, 1280, 1204, 1107, 1045, 1022, 953, 862, 784, 742.

[Cu(py:quin 0:0)](BF$_4$)$_2$ (26). Yield: 90%; brown solid. Mp: 130−138 °C (dec). MS (ESI) *m*/*z*: 683, 685, ^{63,65}Cu (M^+ calcd for $C_{44}H_{36}N_4Cu$; 683, 685), 621, 623. IR (KBr, cm^{-1}): 3033, 2930, 2190, 1630, 1454, 1401, 1200, 1080, 740, 700, 533. Anal. Calcd for $C_{44}H_{36}N_4Cu\cdot 2BF_4\cdot 2.5H_2O$: C, 58.69; H, 4.30; N, 6.22. Found: C, 58.49; H, 4.35; N, 6.22.

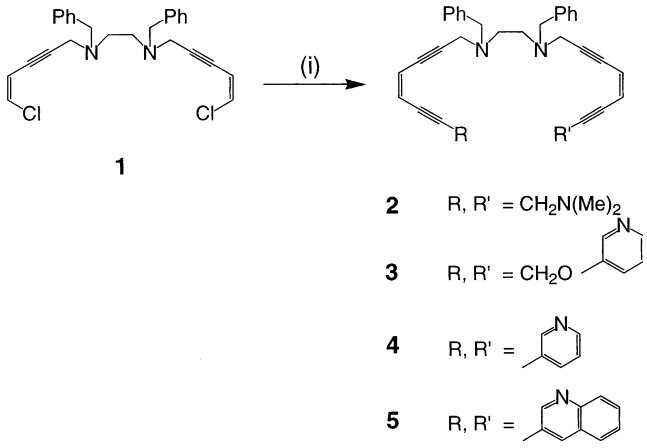
[Zn(py:quin 0:0)](ClO$_4$)$_2$ (27). Yield: 81%. ^{1}H NMR (CD_3CN) δ (ppm): 3.06 (d, 2H, CH_2), 3.11 (d, 2H, CH_2), 3.69 (s, 2H, CH_2), 3.79 (d, 2H, CH_2), 3.93 (s, 2H, CH_2), 4.02 (s, 2H, CH_2), 6.06 (d, J = 11.2 Hz, 1H, CH), 6.12 (d, J = 11.2 Hz, 1H, CH), 6.20 (d, J = 10.8 Hz, 1H, CH), 6.31 (d, J = 10.8 Hz, 1H, CH), 7.30−7.38 (m, 10H, Ar), 7.45−7.48 (m, 1H, Ar), 7.60−7.64 (m, 1H, Ar), 7.75−7.79 (m, 1H, Ar), 7.82 (d, 1H, Ar), 7.89 (d, 1H, Ar), 8.02 (d, 1H, Ar), 8.35 (d, 1H, Ar), 8.52−8.54 (m, 1H, Ar), 8.58 (d, 1H, Ar), 8.84 (d, 1H, Ar). ^{13}C NMR (CD_3CN): 43.39 (CH_2), 43.68 (CH_2), 49.24 (CH_2), 49.43 (CH_2), 58.34 (CH_2), 86.41 (Cquat), 86.97 (Cquat), 89.12 (Cquat), 89.86 (Cquat), 90.88 (Cquat), 91.91 (Cquat), 92.55 (Cquat), 94.51 (Cquat), 117.61 (Cquat), 120.91 (CH), 121.48 (CH), 121.70 (CH), 122.18 (Cquat), 126.30 (CH), 128.28 (CH), 129.06 (CH), 129.29 (CH), 129.88 (CH), 130.04 (CH), 131.21 (CH), 131.35 (CH), 132.43 (CH), 133.33 (CH), 133.91 (CH), 141.01 (CH), 143.27 (Cquat), 146.81 (Cquat), 149.24 (CH), 151.63 (CH), 152.90 (CH). MS (ESI) *m*/*z*: 683, 685. ^{64,66}Zn ($(M - H)^+$ calcd for $C_{44}H_{36}N_4Zn$; 683, 685), 621, 623. IR (KBr, cm^{-1}): 3058, 2850, 2190, 1618, 1575, 1494, 1457, 1418, 1337, 1266, 1197, 1106, 922, 810, 784, 743, 699, 623. Anal. Calcd for $C_{44}H_{36}N_4Zn\cdot 2ClO_4\cdot 2H_2O$: C, 57.37; H, 4.37; N. 6.08. Found: C, 57.55; H, 4.20; N, 6.32.

Results and Discussion

Syntheses of Enediyne Ligands and Metalloenediyne Complexes. Metalloenediynes were prepared from the tetradentate enediyne ligands **2**−**5**, **15**−**17**, and **25** which were synthesized in good yields (50−72%) from the chloro-enyne precursor *N*,*N*′-dibenzyl-*N*,*N*′-bis-((*Z*)-5-chloropent-4-en-2-ynyl)-ethane-1,2-diamine[10] (**1**) by Pd(0)-catalyzed Sonogashira coupling[23] with the corresponding amino- or imino-alkyne in the presence of *n*-BuNH_2 and CuI (Schemes 1−4). The ^{1}H NMR of **2**[24] exhibits a sharp singlet (12H) at δ 2.28 ppm for 4NCH_3 units and a four proton singlet at δ 2.76 ppm for the protons of the ethylenediamine framework. Two sharp, four proton singlets are also observed at δ 3.43 and 3.56 ppm for the methylene centers, while the benzylic protons are easily detected at δ 3.68 ppm as a sharp singlet. The vinyl protons are present at δ 5.85 ppm as a sharp singlet while the aromatic protons are clustered at δ 7.23−7.35 ppm and appear as a multiplet. The ^{13}C NMR spectrum reveals resonances at δ 42.61 and 43.97 ppm for the methylene and $-NCH_3$ carbons of the dimethylamine functionalities, respectively, while the benzylic carbons are detected at δ 58.01 ppm. The alkyne carbons are all inequivalent and appear at δ 82.82, 83.03, 92.27, and 92.34 ppm. The vinyl carbons are also inequivalent by substitution, resulting in two resonances at δ 119.00 and 119.16 ppm, each corresponding to two of the four vinyl carbons.

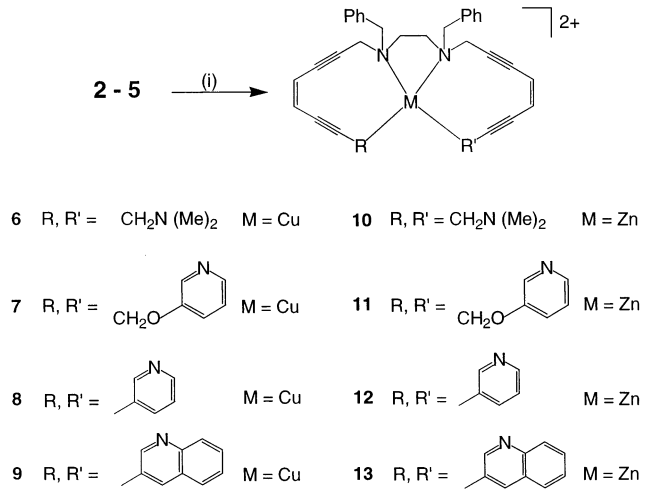
Compound **3** was prepared in 50% yield by reaction of excess 3-(2-propynyloxy)pyridine[21] with **1** at room temperature (Scheme 1). During the formation of **3**, the monochloro derivative (**14**, vide infra) is also isolated in 5−10% yield. The structure of **3** was confirmed by ^{1}H NMR and ^{13}C NMR as well as mass spectrometry. In the ^{1}H NMR spectrum, a sharp singlet is present at δ 2.75 ppm corresponding to two $-NCH_2-$ functionalities (ethylenediamine), and a doublet deriving from four protons of the two $-CH_2-$ units is observed at δ 3.54 ppm. The methylene protons of the 3-(2-propynyloxy)pyridine fragment also appear at δ 4.86 ppm

Scheme 1. Synthesis of Tetradentate Enediyne Ligands[a]



[a] (i) 1-Dimethylamino-2-propyne; 3-(propynyloxy)pyridine; 3-ethynylpyridine; 3-ethynylquinoline, Pd(0), CuI, *n*-BuNH_2.

Scheme 2. Synthesis of Cu(II) and Zn(II) Complexes of **2**−**5**[a]

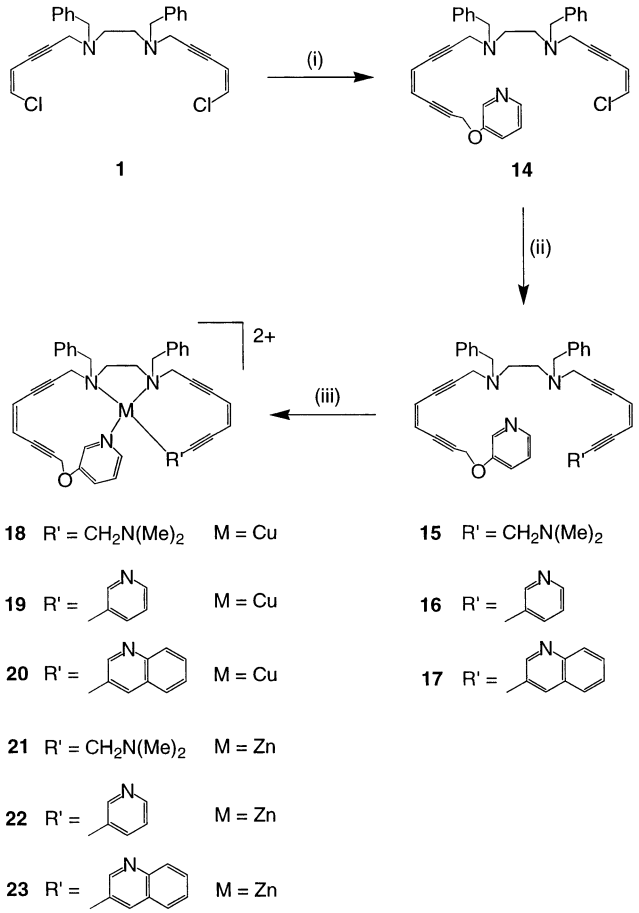


[a] (i) Cu(BF$_4$)$_2$, CH_3CN/Zn(ClO$_4$)$_2$.

(23) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470.

(24) In general, in these and related compounds, the ^{1}H NMR resonances from the ethylenediamine unit occur between δ 2.4 and 3.1 ppm, while those of the methylene units are typically observed in the δ 3.4−4.4 ppm range, with the benzylic protons frequently lying furthest downfield (δ 3.6−4.6 ppm). The assignments of these NCH_2 protons can typically be made straightforwardly based on multiplicity. In the preparation of the narrative section of ref 10, these resonances were inadvertently mislabeled.

Scheme 3. Synthesis of Asymmetric Enediyne Ligands and Their Cu(II) and Zn(II) Complexes[a]



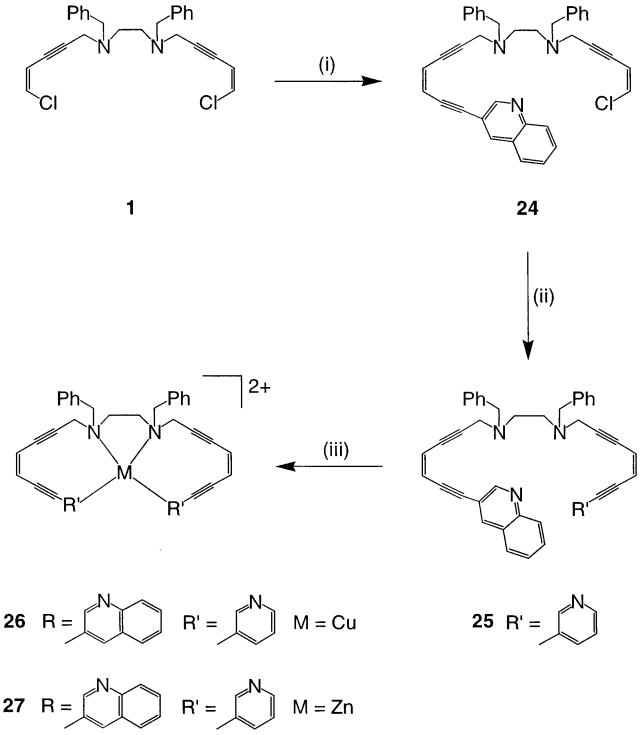
[a] (i) 3-(2-Propynyloxy)pyridine, Pd(0), CuI, *n*-$BuNH_2$, benzene, 40−50 °C; (ii) dimethylaminopropyne/3-ethynylpyridine/3-ethynylquinoline, Pd(0), CuI, *n*-$BuNH_2$, benzene, 40 °C; (iii) $Cu(BF_4)_2$, $CH_3CN/Zn(ClO_4)_2$.

as a doublet. The vinyl protons are inequivalent, generating a multiplet at δ 5.81−5.84 ppm (for two CH) and a doublet at δ 5.90. The ^{13}C NMR spectrum reveals four resonances for each of the alkyne carbons at δ 82.66, 85.24, 89.89, and 93.51 ppm. The NMR spectra of the bis(pyridyl) and bis(quinoline) enediyne ligands **4**−**5** are analogous and can be similarly assigned.

Reaction of a 1:1 molar ratio of tetradentate enediyne ligands **2**−**5** with either $Cu(BF_4)_2 \cdot xH_2O$ or $Zn(ClO_4)_2 \cdot 6H_2O$ in acetonitrile at 30−40 °C yields the corresponding Cu(II) (**6**−**9**) and Zn(II) (**10**−**13**) complexes in ≥80% yield (Scheme 2). The metal complexes were characterized by elemental analyses and mass spectrometry, as well as ^1H, ^{13}C NMR (Zn(II)), and EPR (Cu(II)), where appropriate.

The asymmetrically substituted ligands (**15**−**17**, Scheme 3) are prepared by reacting **1** with 1.08 equiv of 3-(2-propynyloxy)pyridine at 25 °C to generate *N*,*N*′-dibenzyl-*N*-(*Z*)-5-chloropent-4-ene-2-ynyl-*N*′-[8-(pyridin-3-yloxy)-oct-4-ene-2,6-diynyl-ethane]-1,2-diamine (**14**) in 37% yield. Traces of symmetric ligand **3** contribute to the overall mass balance. Purification on silica gel with methylene chloride initially, and then ethyl acetate/hexane (1:1), yields the desired product **14**. Reaction of the mono-chloro-enyne with 1-dimenthylamino-2-propyne, 3-ethynylpyridine, or 3-ethynylquinoline at 40−50 °C produces the desired asymmetric ligands (**15**−**17**). The ligands were fully characterized by ^1H and ^{13}C NMR, as well as high-resolution mass spectrometry. Copper (**18**−**20**) and zinc (**21**−**23**) complexes of these ligands were prepared analogously to **6** and **10**, respectively.

Scheme 4. Synthesis of **24**−**27**[a]



[a] (i) 3-Ethynylquinoline, Pd(0), CuI, *n*-$BuNH_2$, benzene, 40−50 °C; (ii) 3-ethynylpyridine, Pd(0), CuI, *n*-$BuNH_2$; (iii) $Cu(BF_4)_2/(Zn(ClO_4)_2$.

N,*N*′-Dibenzyl-*N*-(7-pyridin-3-yl-hept-4-ene-2,6-diynyl)-*N*′-(7-quinolin-3-yl-hept-4-ene-2,6-diynyl)-ethane-1,2-diamine (**25**, Scheme 4) was prepared in two sequential Pd(0)-catalyzed Sonogashira coupling reactions using first 1 equiv of 3-ethynylquinoline to give precursor **24**, and subsequently 1 equiv of 3-ethynylpyridine to produce **25** in 72% yield. The low structural symmetry produces 5 resonances from the $-NCH_2-$ protons at δ 2.85 ppm (triplet, ethylenediamine), δ 3.63 ppm (doublet, methylene), δ 3.68 ppm (doublet, methylene), δ 3.72 ppm (singlet, benzyl), and 3.77 ppm (singlet, benzyl). Two of the four vinyl protons are observed as a double triplet at δ 5.96 ppm, and as a doublet at δ 6.12 ppm. The other two resonances form a complex multiplet between δ 6.03 and 6.06 ppm. In the ^{13}C NMR, the alkyne carbons are all inequivalent, with resonances at δ 82.98, 83.12, 90.17, 90.22, 92.81, 93.58, 93.93, and 94.05 ppm. Gentle heating (30−40 °C) of **25** in the presence of $Cu(BF_4)_2 \cdot xH_2O$ or $Zn(ClO_4)_2 \cdot 6H_2O$ yields the desired divalent complexes in high yields (**26**, 90%; **27**, 81%).

Thermal Bergman Cyclization Reactivity. Solid-state differential scanning calorimetry (DSC) traces reflecting the thermal Bergman cyclization reactivity of tetradentate enediyne ligands **2**−**5**, **15**−**17**, and **25** are shown in Figure 1, with peak maxima given in Table 1. In general, the cyclization temperatures for these compounds are very closely clustered between 168 and 187 °C, which is typical

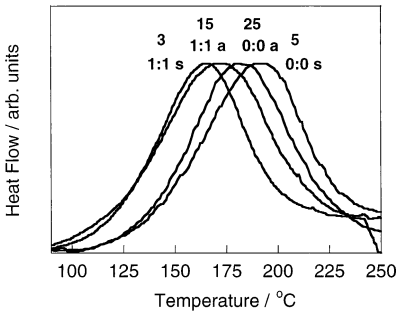


Figure 1. Differential scanning calorimetry traces for the thermal cyclization of enediynes **3**, **5**, **15**, and **25**. The letters a and s designate symmetric and asymmetric R-group substitution, respectively.

Table 1. Bergman Cyclization Temperatures of Tetradentate Enediyne Ligands (**2**−**17**) Determined by Differential Scanning Calorimetry (DSC)

ligand	DSC temp/°C	R-group
dma:dma 1:1 (**2**)	188	dimethylamine
quin-quin 0:0 (**5**)	187	quinoline
py-py 0:0 (**4**)	184	pyridine
py-quin 0:0 (**25**)	182	pyridine-quinoline
pyO-py 1:0 (**16**)	178	3-oxypyridine-pyridine
dma-pyO 1:1 (**15**)	174	3-oxypyridine-dimethylamine
pyO-pyO 1:1 (**3**)	170	3-oxypyridine-3-oxypyridine
pyO-quin 1:0 (**17**)	168	3-oxypyridine-quinoline

of acyclic, nonbenzannulated enediyne frameworks.[6,11] There is no strong correlation with molecular structure as R-group orientation is not restricted. The systematic increase in peak maxima along the series **3**, **15**, **25**, and **5** suggests that if bulky R-groups are rigidly fixed by reduced ligand flexibility, sterically modulated increases in the Bergman cyclization temperatures may be expected.

In contrast to the relative insensitivity of the Bergman cyclization temperatures of the ligands to the structural flexibility and R-group bulk, the corresponding Cu(II) and Zn(II) metalloenediynes show marked differences in their DSC traces (Figure 2) and Bergman cyclization temperatures (Table 2). The Cu(II) complexes all possess very modest Bergman cyclization temperatures between 110 and 136 °C (Table 2, Figure 2), which are typical for Cu(II) metalloenediyne complexes. Low metalloenediyne cyclization temperatures such as these have been shown to derive from a pseudo-square planar or tetragonal geometry about the divalent metal center that effectively draws the alkyne termini into close proximity and reduces the activation barrier to Bergman product.[6,10,11,15] Within the Cu(II) series, it is apparent that the more rigid and bulky aromatic R-group structures (e.g., **4**, py-py 0:0; **25**, py-quin 0:0) lie at the higher end of this range (**8**, 134 °C; **26**, 136 °C), while the more flexible constructs (e.g., **2**, dma-dma 1:1; **3**, pyO-pyO 1:1) exhibit lower cyclization temperatures (**6**, 110 °C; **7**, 125 °C). This is consistent with the propensity of the bulky substituents to induce minor steric crowding at the Cu(II) center and thus small deviations in structure.

The Zn(II) complexes of these tetradentate enediyne ligands are not as well behaved. In an earlier work, it was shown that macrocyclic enediyne complexes similar to these ligands assume a slightly different structure in the presence of Cu(II) (tetragonal geometry) and Zn(II) (tetragonal to

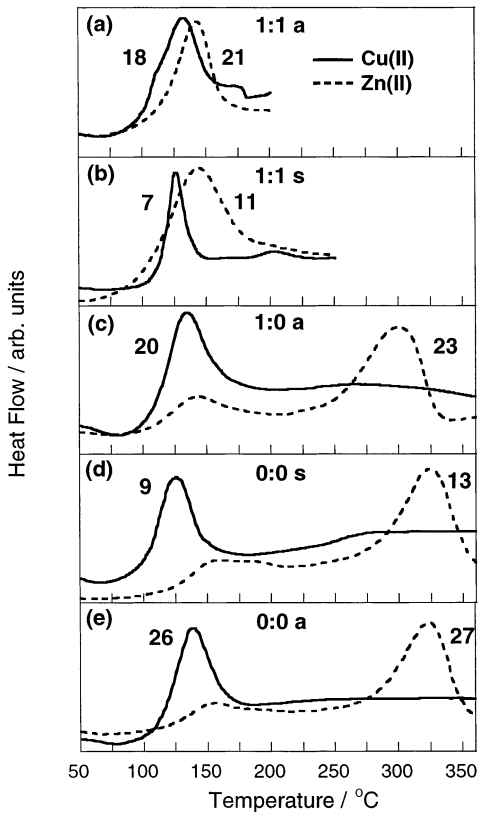


Figure 2. DSC traces for thermal the cyclization of tetradentate metalloenediynes: (a) **18**, **21**; (b) **7**, **11**; (c) **20**, **23**; (d) **9**, **13**; (e) **26**, **27**. The letters a and s designate symmetric and asymmetric R-group substitution, respectively.

Table 2. Bergman Cyclization Temperatures of Tetradentate Metalloenediynes by DSC

ligand	Cu(II)/°C	Zn(II)/°C
py-quin 0:0 (**25**)	136 (**26**)	325 (**27**)
py-py 0:0 (**4**)	134 (**8**)	324 (**12**)
pyO-quin 1:0 (**17**)	132 (**20**)	292 (**23**)
dma-pyO 1:1 (**15**)	131 (**18**)	141 (**21**)
quin-quin 0:0 (**5**)	125 (**9**)	326 (**13**)
pyO-pyO 1:1 (**3**)	125 (**7**)	147 (**11**)
pyO-py 1:0 (**16**)	124 (**19**)	321 (**22**)
dma-dma 1:1 (**2**)	110 (**6**)	183 (**10**)

distorted tetrahedral geometry) as a function of the macrocycle ring size, ultimately leading to Zn(II) complex cyclization temperatures as high as 163 °C.[10] This is consistent with the preference of d^{10} metals for tetrahedral geometry within conformationally flexible ligands. For the open structures in this study, once again the Zn(II) complexes exhibit significant variability in their enediyne complex structures as a function of ligand flexibility (number of methylene carbons) and steric bulk of the R-group (Figure 2, Table 2). For example, Zn(II) complex **21** of the flexible dma-pyO 1:1 ligand exhibits a Bergman cyclization temperature of 141 °C, which is only 10 °C higher than the Cu(II) analogue (Figure 2a). The same trend is observed for pyO-pyO 1:1 ligand with ∼22 °C between Cu(II) and Zn(II) derivatives (Figure 2b). The correlation breaks down, however, when the more strained pyO-quin 1:0 complexes are considered. Here, the cyclization temperature of the Cu(II) complex **20** (132 °C) appears invariant to the change in

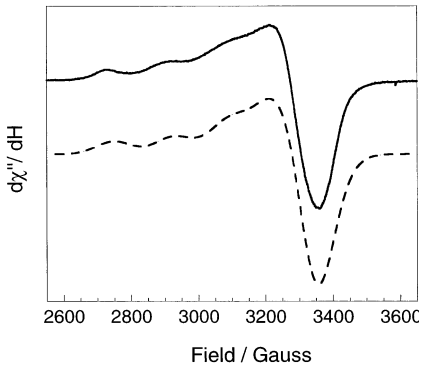


Figure 3. Powder EPR spectrum (—) and spin Hamiltonian simulation (- - -) of **8** collected at 77 K in KBr.

Table 3. Powder EPR Spin Hamiltonian Parameters for Cu(II) Metalloenediynes

ligand (complex)	g_x	g_y	g_z	A_z[a]
py-quin 0:0 (**26**)	2.052	2.071	2.266	173
py-py 0:0 (**8**)	2.048	2.091	2.258	171
pyO-quin 1:0 (**20**)	2.044	2.087	2.248	168
dma-pyO 1:1 (**18**)	2.017	2.104	2.244	166
quin-quin 0:0 (**9**)	2.058	2.101	2.268	171
pyO-pyO 1:1 (**7**)	2.019	2.106	2.253	172
pyO-py 1:0 (**19**)	2.049	2.094	2.257	174
dma-dma 1:1 (**6**)	2.042	2.094	2.236	177

[a] A_z values are $\times 10^{-4}$ cm^{-1}.

ligand structure, while that of the Zn(II) complex (**23**) soars to 292 °C (Figure 2c). The same trend is also observed between the Cu(II) and Zn(II) complexes **9** (125 °C) and **13** (326 °C), as well as **26** (136 °C) and **27** (325 °C) of the quin:quin 0:0 and py:py 0:0 ligands (Figure 2c,d, Table 2). It is clear from previous work in metal-modulated Bergman cyclization studies that this behavior could not solely be due to variation in metal site geometry. Moreover, closer inspection of the DSC traces reveals a bimodal peak distribution that is not observed in the Cu(II) traces, or for these types of cyclization reactions in general. Such deviations could only derive from variations in structure; however, the high temperatures for the cyclization reactions suggest structural consequences beyond simple variation between tetragonal and tetrahedral geometry as previously observed.

EPR Analysis of Copper Metalloenediyne Structure. The tetradentate Cu(II) metalloenediynes are all EPR active and exhibit near axial ($g_x \sim g_y < g_z$) powder pattern spectra characteristic of mononuclear metal/ligand stoichiometry (Figure 3). Spectral simulation[25] reveals spin Hamiltonian parameters of $g_x \approx 2.04$, $g_y \approx 2.09$, $g_z \approx 2.25$ representative of tetragonal Cu(II) geometries (Table 3). The hyperfine splitting parameter A_z values are $\sim 170 \times 10^{-4}$ cm^{-1} which are consistent with distorted 4-coordinate, or weakly 6-coordinate, structures.[6,11,26,27] Due to the steric bulk of the ligands, especially the 0:0 derivatives, it seems likely that the four coordinating nitrogens do not lie in the same plane and that water fills two of the equatorial positions *trans* to

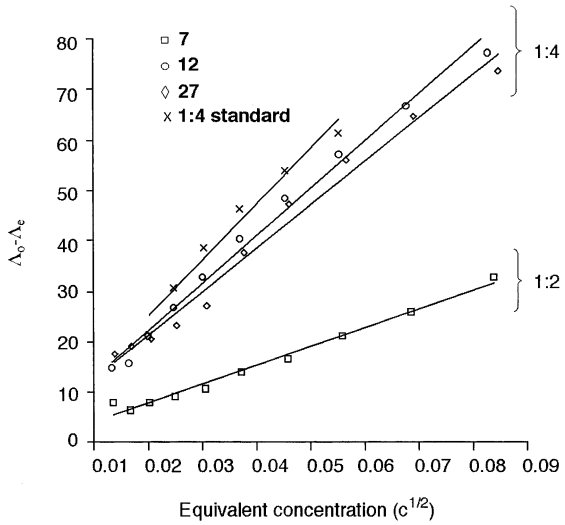


Figure 4. Onsagar plot for metalloenediynes **7** (□), **12** (○), and **27** (◇) and 1:4 electrolyte $[Cu_2(tmpdtne)](ClO_4)_4$ (×).

the ethylenediamine framework. Such a structure would allow the bulky R-groups to be weak ligands and have sufficient orientational freedom. This may explain how the Cu(quin-quin 0:0) complex **9** has such a modest cyclization temperature (~125 °C) despite the apparent steric bulk and rigidity of the R-groups. Irrespective of the exact ligand orientation, the EPR analysis confirms the formation of simple mononuclear Cu(II) metalloenediynes, with no significant dependence of metal center geometry on ligand flexibility or steric hindrance of the R-groups.

Conductance Measurements. The straightforward correlation of the Cu(II) metalloenediyne Bergman cyclization temperatures with simple mononuclear coordination and weak, tetragonal or distorted 4-coordinate geometries[6,11,15] contrasts sharply with the highly variable Bergman cyclization temperatures for the Zn(II) analogues. To confirm mononuclear Cu(II) complexation and to gain insight into the Zn(II) metal/ligand stoichiometry, Onsager plots from solution conductivity measurements of select Cu(II) (**7**) and Zn(II) (**12**, **27**) metalloenediynes were compared to the control compound, $[Cu_2(tmpdtne)](ClO_4)_4 \cdot 2H_2O$ (tmpdtne = 1,2-bis[*N*,*N*′-bis(2-pyridylmethyl)-1,4,7-triazacyclononyl]-ethane), which has been shown to exist in solution as a 1:4 electrolyte (Figure 4).[28,29] The slopes of the Onsager plots for **12** and **27** are nearly identical to that obtained for $[Cu_2(tmpdtne)](ClO_4)_4 \cdot 2H_2O$ and on the order of twice that of **7**, indicating that these compounds exist as bimetallic structures (Figure 4). Since mass spectral analyses of these complexes exhibit *m*/*z* values consistent with 1:1 metal/ligand stoichiometry, **12** and **27** must be dimeric complexes. One possible structure for a bimetallic complex could involve coordination of three of the four N-ligands to a given Zn(II) from the ethylenediamine backbone and one of the two R-groups, while the remaining R-group bridges to/from a second metal/ligand framework. This has the consequence of creating two

(25) Neese, F. *Quantum Chemistry Program Exchange* **1995**, *Bull. 15*, 5.
(26) Peisach, J.; Blumberg, W. E. *Arch. Biochem. Biophys.* **1974**, *165*, 691−708.
(27) Peisach, J. In *Bioinorganic Chemistry of Copper*; Karlin, K., Tyeklar, Z., Eds.; Chapman and Hall: New York, 1993; pp 21−33.
(28) Brudenell, S. J.; Spiccia, L.; Tiekink, E. R. T. *Inorg. Chem.* **1996**, *35*, 1974−1979.
(29) Wieghardt, K.; Tolksdorf, I.; Herrmann, W. *Inorg. Chem.* **1985**, *24*, 1230−1235.

distinct enediyne units around Zn(II), one that derives from chelation, and a second that bridges the two Zn(II) ions. The chelated enediyne functionality would then have a lower Bergman cyclization temperature (<160 °C), while the bridging enediyne would cyclize only at very high temperatures (>300 °C). This could explain the origin of the bimodal behavior of the DSC traces for compounds **12**−**13**, **23**, and **27** (Figure 2), all of which have more steric bulk and are conformationally somewhat rigid. However, due to the disparate intensities of the two DSC features for these Zn(II) complexes, the coexistence of two distinct monomeric and dimeric solid-state structures, one where both enediynes are chelated (∼20%), and one containing only bridging enediyne units (∼80%), may be a more appropriate interpretation of the cumulative data.

The existence of a dimeric structure is not case for Zn(II) complexes **10**, **11**, and **21**, which all have Bergman cyclization temperatures below 185 °C and no additional maxima at higher temperatures. Consistent with the emerging model, these complexes are structurally more flexible as they each have one additional methylene carbon adjacent to each R-group (i.e., 1:1 ligands). These latter complexes each behave more analogously to their Cu(II) counterparts (e.g., **7** and **11**, Table 2), which, on the basis of the EPR data and conductance analysis of **7** in Figure 4 (1:2 electrolyte), are tetradentate, mononuclear structures. Thus, the high DSC temperatures derive from reaction of a bridging enediyne motif, while those below 185 °C indicate cyclization of a chelated enediyne unit. These results are congruous with trends in the Bergman cyclization temperatures of other metalloenediyne constructs and show that metal−ligand structure plays a prominent role in the activation barrier to enediyne reactivity.

Conclusion

The Bergman cyclization temperatures of a series of tetradentate Cu(II) and Zn(II) metalloenediynes are very sensitive to three factors: (i) the flexibility of the ligand (e.g., number of methylene carbons); (ii) the steric bulk of the chelating R-groups; and (iii) the metal complex structure (monomeric vs dimeric). The Cu(II) analogues are all monomeric and exhibit thermal cyclization temperatures between 110 and 136 °C, the lower temperatures corresponding to increased ligand flexibility and decreased steric bulk. In contrast, the Zn(II) complexes formed can be either mono- or bimetallic, once again as a function of ligand flexibility and steric bulk. As a consequence, the thermal cyclization temperatures of the set vary widely (141−326 °C), with the Zn(II) monomers mirroring the low cyclization temperatures of their Cu(II) counterparts, while bridging enediynes give the Zn(II) dimers high cyclization temperatures. Overall, the study underscores the important consequences metal center structure plays in influencing Bergman cyclization temperatures of metalloenediynes.

Acknowledgment. We acknowledge the generous support of the National Institutes of Health (Grant R01 GM62541-01A1 to J.M.Z.) and the National Science Foundation (CAREER Award CHE-0094066 to L.M.B.).

Note Added after ASAP: This paper was posted ASAP on November 20, 2003, with errors in the Figure 4 caption. The version posted on January 5, 2004, contains the correct figure caption.

IC030218X