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Ligand Influence over the Formation of Dinuclear [2+2] versus Trinuclear [3+3] Cu^{I} Schiff Base Macrocyclic Complexes

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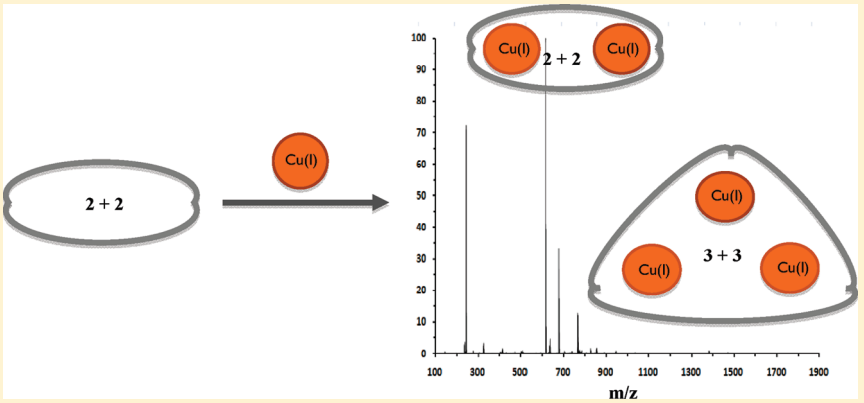
Supporting Information

ABSTRACT:



The preparation and characterization of three new macrocyclic ligands with pendant arms based on the [2+2] condensation of isophthalaldehyde and the corresponding triamine substituted at the central N-atom is reported. None of these new macrocyclic ligands undergo any equilibrium reaction, based on imine hydrolysis to generate [1+1] macrocyclic formation or higher oligomeric compounds, such as [3+3], [4+4], etc., at least within the time scale of days. This indicates the stability of the newly generated imine bond. In sharp contrast, the reaction of the [2+2] macrocyclic Schiff bases with Cu^{I} generates the corresponding dinuclear Cu^{I} complexes $[Cu_2(L^1)]^{2+}$, $\mathbf{1}^{2+}$; $[Cu_2(L^2)(CH_3CN)_2]^{2+}$, $\mathbf{2}^{2+}$; and $[Cu_2(L^3)(CH_3CN)_2]^{2+}$, $\mathbf{3}^{2+}$, together with their trinuclear Cu^{I} homologues $[Cu_3(L^4)]^{3+}$, $\mathbf{4}^{3+}$; $[Cu_3(L^5)(CH_3CN)_3]^{3+}$, $\mathbf{5}^{3+}$; and $[Cu_3(L^6)(CH_3CN)_3]^{3+}$, $\mathbf{6}^{3+}$, where the [2+2] ligand has undergone an expansion to the corresponding [3+3] Schiff base that is denoted as L^4, L^5, or L^6. The conditions under which the dinuclear and trinuclear complexes are formed were analyzed in terms of solvent dependence and synthetic pathways. The new complexes are characterized in solution by NMR, UV−vis, and MS spectroscopy and in the solid state by X-ray diffraction analysis and IR spectroscopy. For the particular case of the L^2 ligand, MS spectroscopy is also used to monitor the metal assisted transformation where the dinuclear complex $\mathbf{2}^{2+}$ is transformed into the trinuclear complex $\mathbf{5}^{3+}$. The Cu^{I} complexes described here, in general, react slowly (within the time scale of days) with molecular oxygen, except for the ones containing the phenolic ligands $\mathbf{2}^{2+}$ and $\mathbf{5}^{3+}$ that react a bit faster.

INTRODUCTION

Schiff bases and their related transition metal complexes have been extensively employed in many fields of science, including biochemistry, material science, catalysis, supramolecular chemistry, transport and separation phenomena, medicine, etc., because of their synthetic versatility.[1−7] A large variety of [1+1] and [2+2] macrocyclic ligands have been synthesized in order to understand the role of the different donor atoms, the influence of their relative position, the number and size of the chelating rings formed, and the flexibility and shape of the coordinating moiety on the selective binding of charged or neutral species.[8−10] In addition, Schiff base macrocyclic ligands can be used as starting materials to generate the corresponding secondary amines that,

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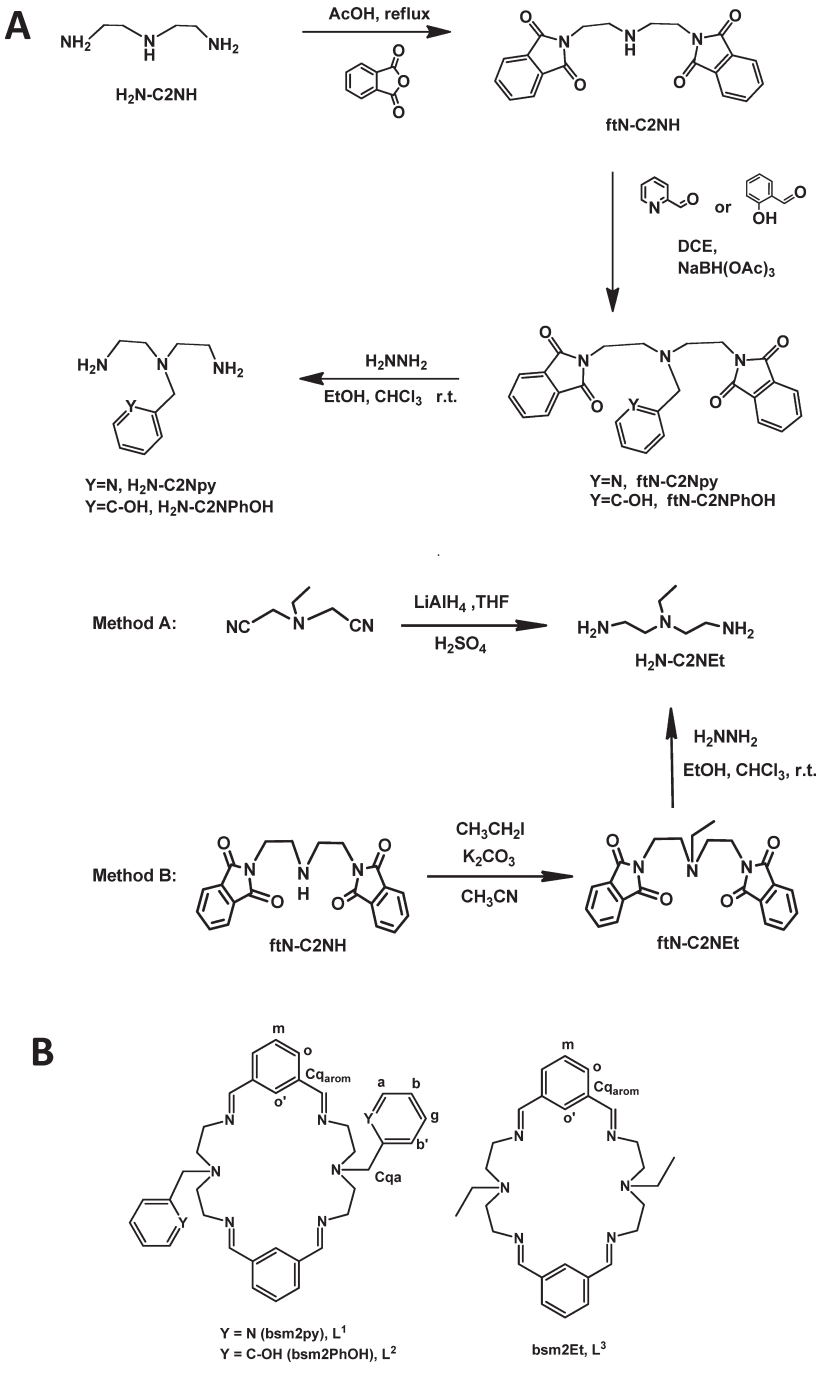
Scheme 1. (A) Synthetic Strategy for the Preparation of Substituted N^2-Triamines: H_2NC_2py, H_2NC_2PhOH, and H_2NC_2Et. (B) Macrocyclic Ligands Obtained from the [2+2] Condensation of N^2-Triamines and Isophthalaldehyde, Including Proton Labeling Used



in turn, can be further functionalized, generating the corresponding tertiary amines.[11] Furthermore, higher condensation products such as [3+3] and [4+4] have also been reported, although they are unusual.[12] The combination of all these macrocycles provides a wide family of ligands, which allows an understanding at a molecular level of phenomena such as anion recognition.[13] Furthermore, these ligands can be coordinated to transition metal ions, and thus, they generate a large family of complexes with subtle differences that enable the understanding of important phenomena related to complex−DNA interactions[14] and the activation of small molecules, such as dioxygen,[15] carbon dioxide, etc.[16] Macrocyclic ligands with peripheral functionalities constitute a specific class within this type of ligand because they have complementary properties that can be used for multirecognition processes, specific separation and transport processes across membranes, or the additional control of small molecule activation and catalysis.[17,18]

The use of a metal ion template is a powerful synthetic tool to direct the Schiff base synthesis to a desired oligomer, controlling

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the size and shape of the resulting macrocycle.[12e,g,i,k] In general, the synthetic routes reported thus far generate single oligomers, although a few exceptions have been described, particularly for the discrimination of [2+2] vs. [4+4].[12a,d,f]

Hereon, we report the synthesis of three new macrocyclic Schiff base ligands with different pendant arms (2-methylpyridyl, 2-methylphenol, and donor-free ethyl) obtained from the [2+2] condensation of isophthalaldehyde and N^2-functionalized triamine. The new ligands are labeled bsm2py (L^1), bsm2PhOH (L^2), and bsm2Et (L^3), where "bs" refers to Schiff base, "m" refers to the meta substitution at the aromatic ring, "2" refers to the number of methylenic units linking the aminic atoms, and, finally, "py", "PhOH," and "Et" refer to 2-methylpyridyl, 2-methylphenol, and ethyl groups, respectively. The latter groups bonded at the central N-atom of triamine become the pendant arms of the macrocyclic ligand. Scheme 1 presents a drawing of these ligands as well as the synthetic strategy used to obtain them. The coordination chemistry of these ligands with Cu^I is also reported, giving the formation of dinuclear [2+2] and trinuclear [3+3] Cu^I complexes. Their interconversion is studied by means of MS spectroscopy. Corresponding [3+3] Schiff bases are denoted as L^4, L^5, and L^6.

EXPERIMENTAL SECTION

Physical Methods. IR spectra of solid samples were taken in a Mattson-Galaxy Satellite FT-IR spectrophotometer using a MKII Golden Gate single reflection ATR system. HRMS analyses were recorded on a Waters LCT Premier liquid chromatograph coupled time-of-flight mass spectrometer (HPLC/MS-TOF) with electrospray ionization (ESI). MS analyses were recorded on an esquire 6000 ESI ion trap LC/MS (Bruker Daltonics) equipped with an electrospray ion source. NMR spectra were measured using a Bruker DPX 200 MHz, a Bruker DXP 300 MHz, or a Bruker DRX 400 MHz instrument. Elemental analysis was performed using a CHNS-O EA-1108 elemental analyzer from Fisons. UV−vis spectra were taken in a Cary 50 Scan spectrophotometer.

Materials and Synthesis. All reagents used in the present work were obtained from Aldrich Chemical Co. and were used without further purification unless otherwise stated. ftN-C2NH, ftN-C2Npy, and H_2N-C2Npy (see Scheme 1 for abbreviations; H_2N-C2Npy is also abbreviated as apme[18]) were synthesized as described in the literature.[19] H_2N-C2NEt was synthesized by the following two methods: (i) Method A as described by Song et al.[20] and (ii) a newly developed Method B (see below). Solvents were purchased from SDS, and they were purified and dried either by passing them through an activated alumina purification system (MBraun SPS-800) or by conventional distillation techniques. Preparation and manipulation of Cu^I complexes were carried out in a drybox (MBraun, N_2, or Ar) with O_2 and H_2O concentrations < 1.0 ppm.

Ligand Synthesis. *bsm2py (L^1).* A solution of isophthalaldehyde (0.228 g, 1.70 mmol) in acetonitrile (40 mL) was slowly added (6.0 mL/h via syringe pump) to a solution of H_2N-C2Npy (0.330 g, 1.70 mmol) in acetonitrile (40 mL) at 0 °C and allowed to react overnight at room temperature. It was then filtered to remove some solid particles, and the filtrate was then concentrated in the rotary evaporator, leading to the separation of an oil. The solvent was decanted, and the oil was dried under a vacuum. Yield: 0.380 g (76%). Anal. Calcd (%) for $C_{36}H_{40}N_8 \cdot 0.6H_2O \cdot 0.4CH_3CN$ (MW = 611.99 g·mol^{-1}): C, 72.22; H, 6.98; N, 19.23. Found: C, 72.24; H, 6.45; N, 19.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.98 (t, J = 4 Hz, 8H, pyN−**CH$_2$**−CH$_2$−N═), 3.72 (t, J = 4 Hz, 8H, pyN−CH$_2$−**CH$_2$**−N═), 3.87 (s, 4H, N−**CH$_2$**−py), 7.04−7.07 (m, 2H, Hβ), 7.16 (s, 2H, $H_{ortho'}$), 7.29−7.33 (m, 2H, H_{meta}), 7.38−7.42 (m, 4H, Hβ' + Hγ), 7.84−7.87 (m, 4H, H_{ortho}), 8.08 (s, 4H, −C**H**═N), 8.49 (d, J = 3.82 Hz, 2H, Hα). ^{13}C NMR ($CDCl_3$, 400 MHz) δ (ppm): 55.22 (pyN−**C**H$_2$−CH$_2$−N═), 59.72 (pyN−CH$_2$−**C**H$_2$−N═), 61.38 (N−**C**H$_2$−py), 121.78 (Cβ), 123.11 (Cβ'), 128.70 (C_{ortho}), 128.90 (Cγ), 129.75 ($C_{ortho'}$), 136.12 (C_{meta}), 136.67 (Cq_{arom}), 148.80 (Cα), 160.15 (Cqα), 161.09 (**C**H═N). FT-IR ν (cm^{-1}): 2838 (C−H), 1644 (C═N), 1588, 1568 (C−C py), 1473, 1433 (C−H), 797 (C−H ar), 756 (C−H py), 692 (C−H ar), 614 (C−H py). HRMS (m/z): [M + Na]$^+$, 607.3279 (100%); calcd mass, 607.3274.

ftN-C2NPhOH. Salicylaldehyde (3.0 mL, 28 mmol) was added to a mixture of ftN-C2NH (10.000 g, 28 mmol) in 1,2-dichloroethane (150 mL). The crude product was stirred for several minutes. Afterward, $NaBH(OAc)_3$ (8.60 g, 0.039 mol) was slowly added, and the mixture was stirred at room temperature for 24 h. The organic layer was extracted after adding 100 mL of water. The aqueous phase was washed with dichloromethane (2 × 100 mL). The organic fractions were dried over $MgSO_4$ and concentrated up to ∼10 mL. Methanol (150 mL) was then added with stirring, producing the white solid precipitated product, which was filtered and dried under vacuum. Yield: 11.21 g (87%). Anal. Calcd (%) for $C_{27}H_{23}N_3O_5 \cdot 0.25H_2O$ (MW = 473.99 g·mol^{-1}): C, 68.42; H, 5.00; N, 8.87. Found: C, 68.33; H, 5.02; N, 9.01. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.95 (t, J = 6 Hz, 4H, ftN−CH$_2$−**CH$_2$**−N), 3.89 (m, 6H, ftN−**CH$_2$**−CH$_2$−N + N−**CH$_2$**−PhOH), 6.24−6.29 (m, 1H, Hα), 6.71−6.78 (m, 1H, Hβ), 6.92−6.98 (m, 1H, Hβ'), 7.01−7.08 (m, 1H, Hγ), 7.70−7.84 (m, 8H, H_{ar}), 9.07 (s, br, PhO**H**). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 34.8 (ftN−**C**H$_2$−CH$_2$−N), 51.5 (ftN−CH$_2$−**C**H$_2$−N), 58.1 (N−**C**H$_2$−PhOH), 116.0 ($C\alpha_{PhOH}$), 119.5 ($C\gamma_{PhOH}$), 121.4 ($Cq\alpha_{PhOH}$), 123.2 (C_{arom}) 129.0, 129.1 ($C\beta_{PhOH}$, $C\beta'_{PhOH}$), 132.2 (Cq_{arom}), 133.8 (C_{arom}), 156.8 (**C**−OH), 168.2 (**C**═O). FT-IR ν (cm^{-1}): 1700 (C═O), 1398 (CO−N), 754 (C−H PhOH), 708 (C−H ar), 532 (C−H ft). HRMS (m/z): [M + Na]$^+$, 492.1526 (100%); calcd mass, 492.1535.

H_2N-C2NPhOH. Hydrazine monohydrate (9.7 mL, 0.2 mol) was added to a solution of ftN-C2NPhOH (8.65 g, 18.42 mmol) in chloroform/ethanol (60:320 mL). The mixture was stirred at room temperature for 24 h, and the obtained white precipitate was filtered off and discarded. The resulting transparent solution was evaporated under reduced pressure. Chloroform (150 mL) was then added to the residue, and the mixture was stirred for another 24 h and filtered again. Evaporation of the chloroform fraction afforded the desired product as oil. Yield: 2.62 g (85%). Anal. Calcd (%) for $C_{11}H_{19}N_3O \cdot 0.14CHCl_3$ (MW = 226.00 g·mol^{-1}): C, 59.20; H, 8.54; N, 18.59. Found: C, 59.39; H, 8.81; N, 18.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.59 (t, J = 6 Hz, 4H, H_2N−CH$_2$−**CH$_2$**−N), 2.86 (t, J = 6 Hz, 4H, H_2N−**CH$_2$**−CH$_2$−N), 3.36 (s, br, −N**H$_2$**), 3.73 (s, 2H, N−**CH$_2$**−PhOH), 6.69−7.22 (m, 4H, H_{PhOH}). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 39.3 (−**C**H$_2$−NH$_2$), 55.7 (−**C**H$_2$−CH$_2$−NH$_2$), 57.9 (−**C**H$_2$−PhOH), 116.4 (Cα), 119.1 (Cγ), 122.7 (Cqα), 128.8 (Cβ), 129.3 (Cβ'), 157.5 (C−OH). FT-IR ν (cm^{-1}): 1587 (C═C), 1472, 1446 (−CH$_2$−), 1269, 1256 (ArC−OH), 753 (C−H ar), 708 (C−H PhOH), 532 (C−H ar). ESI-MS (m/z): [M + H]$^+$, 210.1 (100%).

bsm2PhOH (L^2). A solution of isophthalaldehyde (0.655 g, 4.88 mmol) in MeCN (50 mL) was slowly added (9 mL/h via syringe pump) to a solution of H_2N−C2NPhOH (1.021 g, 4.88 mmol) in MeCN (50 mL) with stirring. After the mixture was stirred for 24 h, a white solid was obtained, filtered, and then dried under a vacuum. Yield: 0.797 g (53%). Crystals for X-ray diffraction were obtained by dissolving 0.015 g of L^2 in 1 mL of chloroform and then diluting the solution with MeOH. Slow evaporation of the solvents afforded white crystals suitable for X-ray diffraction (see the Supporting Information). Anal. Calcd (%) for $C_{38}H_{42}N_6O_2$ (MW = 614.78 g·mol^{-1}): C, 74.24; H, 6.89; N, 13.67. Found: C, 73.88; H, 6.84; N, 13.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.98 (t, J = 6 Hz, 8H, CH═N−CH$_2$−**CH$_2$**−N), 3.72 (t, J = 6 Hz,

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8H, CH=N−**CH$_2$**−CH$_2$−N), 3.90 (s, 4H, N−**CH$_2$**−PhOH), 6.75−6.85 (m, 2H, Hγ_{PhOH}), 6.85−6.90 (m, 2H, Hα_{PhOH}), 7.0−7.1 (m, 2H, Hβ'_{PhOH}), 7.06 (s, 2H, H$_{ortho',arom}$), 7.15−7.25 (m, 2H, Hβ_{PhOH}), 7.35−7.45 (m, 2H, H$_{meta,arom}$), 7.8−7.9 (m, 4H, H$_{ortho,arom}$), 8.04 (s, 4H, C**H**=N), 10.22 (s, br, PhO**H**). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.6 (CH=N−CH$_2$−**C**H$_2$−N), 58.9 (N−**C**H$_2$−PhOH), 59.6 (CH=N−**C**H$_2$−CH$_2$−N), 116.6 (Cα_{PhOH}), 119.1 (Cγ_{PhOH}), 123.0 (Cqα_{PhOH}), 128.6, 128.7, 128.9, 129.0 (C$_{ortho}$, C$_{meta}$, Cβ_{PhOH}, Cβ'_{PhOH}), 130.5 (C$_{ortho'}$), 136.2 (Cq$_{arom}$), 157.8 (C−OH), 161.7 (**C**H=N). FT-IR ν (cm^{-1}): 3185 (OH), 2837, 2805 (C−H), 1642 (C=N), 799 (C−H ar), 746 (C−H PhOH), 691 (C−H ar). HRMS (m/z): [M + H]$^+$, 615.3451 (100%); calcd mass, 615.3448.

EtN(CH$_2$CN)$_2$. In a round-bottom flask containing 70% ethylamine (2 mL, 25 mmol), water (15 mL), and HCl (6 mL), a 4.2 mL sample of 37% formaldehyde (55 mmol) was added, and the mixture was stirred for 30 min. The solution was then cooled to 0 °C, and NaCN (2.94 g, 55 mmol) was added. The mixture was allowed to react at room temperature for 24 h. Then, NaOH (1 g) and dichloromethane (15 mL) were added, the organic phase was extracted, and the aqueous phase was washed with dichloromethane (2 × 15 mL). The combined organic fractions were dried over $MgSO_4$, and the solvent was removed in the rotary evaporator. The oil obtained was then purified via flash chromatography in silica gel, using a hexane/ethyl acetate mixture (2:1) as eluent. Yield: 1.274 g (42%). Anal. Calcd (%) for $C_6H_9N_3\cdot 0.25H_2O$ (MW = 127.66 g·mol^{-1}): C, 56.45; H, 7.50; N, 32.92. Found: C, 56.37; H, 7.42; N, 32.71. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.17 (t, J = 7 Hz, 3H, N−CH$_2$−**CH$_3$**), 2.72 (q, J = 7 Hz, 2H, N−**CH$_2$**−CH$_3$), 3.62 (s, 4H, N−**CH$_2$**−CN). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 12.4 (−**C**H$_3$), 41.7 (−**C**H$_2$−CH$_3$), 48.01 (−**C**H$_2$−CN), 114.35 (−**C**N). FT-IR ν (cm^{-1}): 2978, 2944, 2834 (C−H), 1428 (−CH$_2$−), 1106, 868.

ftN-C2NEt. A mixture of ftNC$_2$H (5.000 g, 13.76 mmol), K_2CO_3 (2.850 g, 20.64 mmol), and iodoethane (2.2 mL, 27.52 mmol) in 150 mL of acetonitrile was refluxed for 18 h. After the reaction mixture was cooled to room temperature, it was filtered, and the solvent was evaporated to dryness. The residue was redissolved in 100 mL of $CHCl_3$ and was washed with 3 N aqueous NaCl solution. The aqueous phase was extracted three times with 3 × 20 mL $CHCl_3$. The combined organic phases were dried over Na_2SO_4. Evaporation of the solvent gave a yellow oil, which turned solid under high vacuum. Yield: 5.10 g (95%). Anal. Calcd (%) for $C_{22}H_{21}N_3O_4$ (MW = 391.42 g·mol^{-1}): C, 67.51; H, 5.41; N, 10.74. Found: C, 67.20; H, 5.42; N, 10.85. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.95 (t, J = 6 Hz, 3H, N−CH$_2$−**CH$_3$**), 2.65 (q, J = 6 Hz, 2H, N−C**H$_2$**−CH$_3$), 2.80 (t, J = 6 Hz, 4H, ftN−CH$_2$−C**H$_2$**−N), 3.75 (t, J = 6 Hz, 4H, ftN−C**H$_2$**−CH$_2$−N), 7.67−7.78 (m, 8H, H$_{ar}$). ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm): 11.91 (N−**C**H$_2$−**C**H$_3$), 35.92 (ftN−**C**H$_2$−CH$_2$−N), 47.24 (N−**C**H$_2$−CH$_3$), 51.21 (ftN−CH$_2$−**C**H$_2$−N), 123.05 (C$_{arom}$), 132.22 (Cq$_{arom}$), 133.68 (C$_{arom}$), 168.26 (**C**=O). HRMS (m/z): [M + Na]$^+$, 414.1436 (100%); calcd mass, 414.1430.

H$_2$N-C2NEt. The compound H$_2$N-C2NEt was synthesized by the following two procedures: Method A and Method B.

Method A. A round-bottom flask, kept under nitrogen, containing $LiAlH_4$ (3.737 g, 95 mmol) and dry THF (110 mL), was cooled to −10 °C. Concentrated H_2SO_4 (5 mL) was carefully added, the mixture was stirred for 30 min at −10 °C, and then, it was allowed to warm to room temperature. EtN(CH$_2$CN)$_2$ (1.274 g, 10.4 mmol) was dissolved in dry THF (10 mL), added carefully to the hydride mixture, and allowed to react overnight. Then, water (7 mL) was added slowly, the mixture was stirred for 24 h, and the solvent was evaporated through a N_2 stream. Afterward, dichloromethane (50 mL) and methanol (50 mL) were added, and the mixture was stirred again for 24 h. The solid obtained was then filtered off and discarded, and the filtrate was evaporated. The product was finally obtained through distillation under reduced pressure. Yield: 0.291 g (21%).

Method B. Hydrazine monohydrate (6.98 mL, 0.14 mol) was added to a solution of ftN-C2NEt (5.000 g, 12.77 mmol) in chloroform/ethanol (50:280 mL). The mixture was stirred at room temperature for 24 h, and then, the obtained white precipitate was filtered off and discarded. The resulting transparent solution was evaporated under reduced pressure. Chloroform (150 mL) was then added to the residue, and the mixture was stirred for another 24 h and filtered again. Evaporation of the chloroform fraction afforded an oil which was purified by distillation at 150 °C in vacuo.Yield: 0.920 g (55%). Anal. Calcd (%) for $C_6H_{17}N_3\cdot 0.15H_2O$ (MW = 133.92 g·mol^{-1}): C, 53.81; H, 13.02; N, 31.38. Found: C, 53.64; H, 13.53; N, 31.59. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.01 (t, J = 7 Hz, 3H, N−CH$_2$−**CH$_3$**), 1.31 (s, br, 4H, N−**CH$_2$**−CH$_2$−N**H$_2$**), 2.40−2.60 (m, 6H, N−**CH$_2$**−CH$_3$ + N−**CH$_2$**−CH$_2$−NH$_2$), 2.75 (t, J = 7 Hz, 4H, N−CH−**CH$_2$**−NH$_2$). ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm): 11.77 (N−H$_2$−**C**H$_3$), 39.86 (N−CH$_2$−**C**H$_2$−NH$_2$), 47.74 (N−**C**H$_2$−CH$_3$), 56.75 (N−**C**H$_2$−CH$_2$−NH$_2$). FT-IR ν (cm^{-1}): 3354, 3289 (NH$_2$), 2962, 2934, 2870, 2804 (C−H), 1460 (−CH$_2$−, CH$_3$), 918, 864 (NH$_2$).

bsm2Et (L^3). The procedure is the same as that for bsm2py, starting with H$_2$N−C2NEt (0.300 g, 2.29 mmol) in MeCN (40 mL) and isophthalaldehyde (0.308 g, 2.29 mmol) in MeCN (40 mL). The product is obtained as a solid. Yield: 0.250 g (48%). Anal. Calcd (%) for $C_{28}H_{38}N_6$ (MW = 458.64 g·mol^{-1}): C, 73.33; H, 8.35; N, 18.32. Found: C, 73.29; H, 8.34; N, 18.24. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.96 (t, J = 7 Hz, 6H, N−CH$_2$−**CH$_3$**), 2.55 (q, J = 7 Hz, 4H, N−**CH$_2$**−CH$_3$), 2.85 (t, J = 6 Hz, 8H, N−**CH$_2$**−CH$_2$−Nbz), 3.66 (t, J = 6 Hz, 8H, N−CH$_2$−**CH$_2$**−Nbz), 7.07 (s, 2H, H$_{ortho',arom}$), 7.43 (t, J = 7 Hz, 2H, H$_{ortho,arom}$), 7.91−7.96 (m, 4H, H$_{meta,arom}$), 8.04 (s, 4H, C**H**=N). ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm): 12.37 (N−**C**H$_2$−**C**H$_3$), 48.57 (N−**C**H$_2$−CH$_3$), 54.35 (N−CH$_2$−**C**H$_2$−N=CH), 60.00 (N−**C**H$_2$−CH$_2$−N=CH), 128.32, 128.88, 129.72 (C$_{ortho'}$, C$_{meta}$, C$_{ortho}$), 136.72 (Cq$_{arom}$), 161.10 (**C**H=N). HRMS (m/z): [M + Na]$^+$, 481.3051 (100%); calcd mass, 481.3056.

Synthesis of Cu^I Complexes. *[Cu$_2$(L^1)](PF$_6$)$_2$,* ***1****(PF$_6$)$_2$.* [Cu(CH$_3$CN)$_4$]PF$_6$ (0.373 g, 1 mmol) was added to a solution of bsm2py (0.292 g, 0.5 mmol) in MeOH (20 mL), and the mixture was stirred for 1 h at room temperature. The resulting yellow-orange precipitate was filtered and washed with Et$_2$O. The solid was then redissolved in CH_2Cl_2 and filtered. The obtained solid was discarded, and the solvent was removed under vacuum to obtain the product. Yield: 0.400 g (0.40 mmol; 80%). The diffusion of a mixture of THF/Et$_2$O (1:1) into the mother solution yielded a dark yellow powder. Anal. Calcd (%) for $C_{36}H_{40}Cu_2F_{12}N_8P_2\cdot 0.5CH_2Cl_2$ (MW = 1044.24 g·mol^{-1}): C, 41.98; H, 3.96; N, 10.73. Found: C, 41.87; H, 3.95; N, 10.77. FD-MS (70 eV, CH$_3$CN): m/z = 857 (71%) [Cu$_2$L^1(PF$_6$)]$^+$, 791 (20%) [CuL^1(PF$_6$)]$^+$, 647 (100%) [CuL^1]$^+$, 356 (17%) [Cu$_2$L^1]$^{2+}$. IR (KBr) ν (cm^{-1}): 2914, 2857 (C−H), 1637 δ(C=N), 1440 δ(C−H$_{aliphatic}$), 842 (P−F), 764/689 δ(C−H$_{arom}$).

[Cu$_3$(L^4)](PF$_6$)$_3$, ***4****(PF$_6$)$_3$.* [Cu(CH$_3$CN)$_4$]PF$_6$ (0.373 g, 1 mmol) was added to a solution of H$_2$NC$_2$py (0.194 g, 1 mmol) and isophthalaldehyde (0.134 g, 1.00 mmol) in MeOH (20 mL), and the mixture was stirred for 2 h at room temperature. The resulting orange precipitate was filtered off, washed with a small amount of MeOH and Et$_2$O, and dried under vacuum. Yield: 0.342 g (0.288 mmol; 68%). Recrystallization of the crude product from CH$_3$CN and diffusion of a mixture of THF/Et$_2$O (1:1) into the mother solution for about 2 weeks yielded red crystals suitable for X-ray diffraction analysis. Anal. Calcd (%) for $C_{54}H_{60}Cu_3N_{12}F_{18}P_3$ (MW = 1502.67 g·mol^{-1}): C, 43.16; H, 4.02; N, 11.19. Found: C, 43.34; H, 4.30; N, 11.06. IR (KBr) ν (cm^{-1}): 2916, 2854 (C−H), 1633 (C=N), 1439 (C−H), 842 (P−F), 763/766 δ(C−H). FD-MS (70 eV, CH$_3$CN): m/z = 939 (95%) [CuL^4]$^+$, 876 (100%) [L^4 + H]$^+$.

[Cu$_3$(L^4)](SbF$_6$)$_3$, ***4****(SbF$_6$)$_3$.* A solution of [Cu(CH$_3$CN)$_4$]SbF$_6$ (0.048 g, 0.10 mmol) in CH$_3$CN (0.5 mL) was added dropwise to a suspension

Table 1. Crystallographic Data for Structures L^2, $4(SbF_6)_3$, $4(PF_6)_3$, $2(CF_3SO_3)_2$, $5(CF_3SO_3)_3$, and $6(CF_3SO_3)_3$

structure	L^2	$4(SbF_6)_3$	$4(PF_6)_3 \cdot 2.5THF \cdot 0.5H_2O \cdot 0.75MeOH$	$2(CF_3SO_3)_2 \cdot MeCN$	$5(CF_3SO_3)_3 \cdot 2\ H_2O$	$6(CF_3SO_3)_3 \cdot 1EtOEt$
empirical formula	$C_{38}H_{42}N_6O_2$	$C_{54}H_{59}Cu_3F_{18}N_{12}Sb_3$	$C_{64.75}H_{84}Cu_3F_{18}N_{12}O_{3.75}P_3$	$C_{48}H_{51}Cu_2N_9O_8F_6S_2$	$C_{66}H_{76}Cu_3F_9N_{12}O_{14}S_3$	$C_{55}H_{76}Cu_3N_{12}F_9O_{10}S_3$
formula weight	614.52	1774.00	1715.97	1163.16	1719.19	1523.08
temperature, K	300(2)	100(2)	100(2)	100(2)	300(2)	373(2)
wavelength, Å	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
crystal system	monoclinic	triclinic	triclinic	monoclinic	triclinic	triclinic
space group	*P*2(1)	$P\bar{1}$	$P\bar{1}$	*P*21/*n*	$P\bar{1}$	$P\bar{1}$
a, Å	13.357(5)	12.008(18)	11.4563(3)	15.203(3)	15.72(2)	11.383(6)
α, deg	90.00	109.82(3)	80.620(2)	90	104.45(3)	84.485(10)
b, Å	35.402(13)	15.72(2)	17.6766(6)	18.211(3)	16.73(2)	14.732(8)
β, deg	101.776(7)	104.97(3)	81.518(2)	99.371(3)	111.79(3)	80.547(9)
c, Å	14.629(6)	20.01(3)	36.255(1)	19.084(3)	18.04(3)	20.652(11)
γ, deg	90.00	97.76(3)	82.902(2)	90	106.39(3)	86.199(10)
vol, Å^3	6772(4)	3328(9)	7127.1(4)	5213.3(16)	3878(10)	3396(3)
Z	8	2	4	4	1	2
ρ (g/cm^3)	1.205	1.770	1.599	1.482	1.462	1.489
R^a [$I > 2\sigma(I)$]	0.0563	0.1057	0.0869	0.0399	0.0818	0.0898
wR^b	0.1371	0.2698	0.1976	0.0617	0.2416	0.2699

$^a R = \Sigma[F_o - F_c]/\Sigma F_o$. $^b wR = [\Sigma(w(F_o^2 - F_c^2)^2)/\Sigma wF_o^4]^{1/2}$.

of L^1 (0.029 g, 0.05 mmol) in CH_3CN (0.5 mL), and the solution was stirred for 1 h. Slow diethyl ether diffusion into the solution for about 2 weeks afforded orange crystals, which have been characterized by X-ray diffraction analysis. Yield: 0.042 g (69%). Anal. Calcd (%) for $C_{54}H_{60}Cu_3N_{12}F_{18}Sb_3$ (MW = 1775.02 g·mol^{-1}): C, 36.54; N, 9.47; H, 3.41. Found: C, 36.86; N, 9.70; H, 3.72. ^{1}H NMR (400 MHz, CD_3COCD_3) δ (ppm): 2.8−3.3 (m, 4H, N−**CH_2**−CH_2−N═), 3.4−4.0 (m, 4H, N−CH_2−**CH_2**−N═), 4.19 (s, 2H, py−**CH_2**−N), 7,2−8.8 (m, 10H, H_{ar} + C**H**═N). FT-IR ν (cm^{-1}): 2916, 2853 (C−H), 1633 (C═N), 1603 (SbF_6), 1440 (def −CH_2−), 764 (def C-H_{ar}), 653 (SbF_6).

[$Cu_2(L^2)(CH_3CN)_2$](CF_3SO_3)$_2$·2MeCN·H_2O, ***2***$(CF_3SO_3)_2$·2MeCN·H_2O. A solution of [$Cu(CH_3CN)_4$][CF_3SO_3] (0.050 g, 0.128 mmol) in MeCN (2 mL) was added to a suspension of L^2 (0.040 g, 0.065 mmol) in MeCN (1 mL). The yellow solution was stirred for 1 h, and then it was filtered. Addition of diethyl ether (50 mL) into the yellow solution generated a yellow powder. Yield: 0.060 g (80%). ESI-MS (*m*/*z*): 615.3 [L^2 + H]$^+$, 637.2 [L^2 + Na]$^+$, 677.2. [L^2 + Cu]$^+$. ^{1}H NMR (200 MHz, CD_3COCD_3) δ (ppm): 2.9−3.3 (m, 4H, ═N−CH_2−**CH_2**−N), 3.9−4.4 (m, 6H, =N−**CH_2**−CH_2−N + N−**CH_2**−PhOH), 6.8−7.4 (mm, 5H, PhOH), 7.8−9.2 (mm, 6H, H_{ar} + C**H**═N). FT-IR ν (cm^{-1}): 3320 (OH), 2916, 2855 (C−H), 1628 (C═N), 1275, 1221, 1025 (CF_3SO_3), 758 (C−H, PhOH), 634 (CF_3SO_3). Anal. Calcd (%) for $C_{60}H_{63}Cu_3N_9F_9O_{12}S_3$·2$CH_3CN$·$H_2O$ (MW = 1660.1 g·mol^{-1}): C, 46.31; N, 9.28; H, 4.31; S, 5.79. Found: C, 46.12; N, 9.31; H, 4.29; S, 5.77.

The compound was also synthesized in MeOH as described initially, and MS analysis indicated the formation of $\mathbf{2}^{2+}$ only. However, the slow diethyl ether diffusion into the acetonitrile solution (first synthesis) of the compound afforded a mixture of yellow and orange crystals after 12−15 days, which were both characterized by X-ray diffraction analysis and show the formation of [$Cu_2(L^2)(CH_3CN)_2$](CF_3SO_3)$_2$, **2**$(CF_3SO_3)_2$ and [$Cu_3(L^5)$](CF_3SO_3)$_3$, **5**$(CF_3SO_3)_3$. MS (*m*/*z*): 615 [L^2 + H]$^+$, 922 [L^5 + H]$^+$.

[$Cu_3(L^6)(CH_3CN)_3$](CF_3SO_3)$_3$, ***6***$(CF_3SO_3)_3$. A solution of [$Cu(CH_3CN)_4$]·CF_3SO_3 (0.025 g, 0.064 mmol) in CH_3CN (2 mL) was added to a suspension of L^3 (0.015 g, 0.032 mmol) in CH_3CN (0.5 mL), and the mixture was stirred for 1 h. Slow diethyl ether diffusion into the solution for about 2 weeks afforded yellow crystals, which have been characterized by X-ray diffraction analysis. Yield: 0.020 g (71%). Anal. Calcd (%) for $C_{45}H_{57}Cu_3N_9F_9O_{12}S_3$·2.25$CH_3CN$·0.75$C_4H_{10}O$ (MW = 1473.66 g·mol^{-1}): C, 42.79; N, 10.69; H, 4.87; S, 6.53. Found: C, 42.86; N, 10.58; H, 4.73; S, 6.38. ^{1}H NMR (400 MHz, CD_3COCD_3) δ (ppm): 1.1−1.3 (m, 3H, N−CH_2−**CH_3**), 2.6−3.1 (m, 6H, N_{ter}−**CH_2**−), 3.6−4.0 (m, 4H, CH═N−**CH_2**−CH_2−N_{ter}), 7.7−8.8 (mm, 6H, H_{ar} + C**H**═N). FT-IR ν (cm^{-1}): 1631 (C═N), 1253, 1223 (CF_3SO_3), 1149 (def −CH_2−), 1027 (CF_3SO_3), 634 (CF_3SO_3).

X-ray Diffraction Studies. The complexes were crystallized as described in the synthetic procedure. Crystals of L^2, **2**$(CF_3SO_3)_2$, **4**$(SbF6)_3$, **5**$(CF_3SO_3)_3$, and **6**$(CF_3SO_3)_3$ were mounted on a nylon loop and used for X-ray structure determination at room temperature. The measurements were carried out on a Bruker Smart Apex CCD diffractometer. Single crystals of **4**$(PF_6)_3$ were coated with polyfluorether oil and mounted on a glass fiber. The data were collected on a Nonius Kappa diffractometer with a CCD array detector at 173(2) K. Mo Kα radiation was used for all measurements (λ = 0.71073 Å). Space groups were determined from systematic absences and subsequent least-squares refinement. The structures were solved by direct methods and refined on F^2 using full-matrix least-squares techniques.[21] The non-hydrogen atoms were refined anisotropically. The H-atoms were placed in a geometrically optimized arrangement and treated with a riding model, except the O−H hydrogen atoms for the **2**$(CF_3SO_3)_3$, which are refined without constraints. For the structure **5**$(CF_3SO_3)_3$ a considerable amount of electron density that is attributable to partially disordered solvent water molecules was removed with the SQUEEZE option of PLATON.[22] Those solvent molecules are, however, included in the reported chemical formula and derived values (e.g., formula weight, *F*(000), etc). Structures **2**$(CF_3SO_3)_3$, **5**$(CF_3SO_3)_3$, and **6**$(CF_3SO_3)_3$ present disorder on one of the $CF_3SO_3^-$ counterions. For the structure **4**$(PF_6)_3$, SAME-restraints where used to refine solvate molecules (THF and MeOH). Further crystallographic experimental details are given in Tables 1 and 2 and in the Supporting Information.

RESULTS AND DISCUSSION

Dinuclear Cu^I complexes containing a macrocyclic ligand obtained from the condensation of isophthalaldehyde and a

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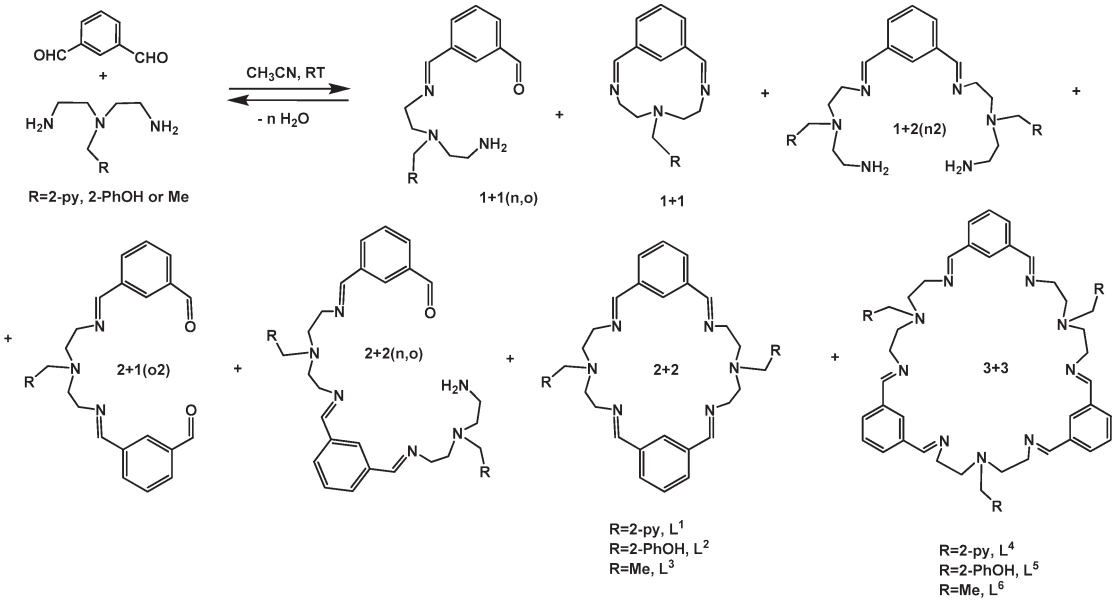
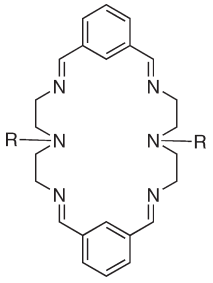
Scheme 2. Potential Condensation Products from Reaction of Isophthalaldehyde and N^2-Substituted Triamine[a]



[a] Labeling note: the numerical values indicate the number of reacted units and, in parentheses, the unreacted groups. For instance [1+1](n,o) means a condensation of one molecule of isophthalaldehyde and one of triamine. In parentheses the (n) indicates an unreacted amine and (o) indicates an unreacted aldehyde.

diethylenetriamine (with R = H in the drawing below, abbreviated as mac from now on) have been described previously.[23]



The derived Cu^I complex was especially interesting because it undergoes an intramolecular ligand hydroxylation reaction when treated with dioxygen.[24] This reaction can be regarded as a model reaction for the enzymatic reaction of tyrosinase, a monooxygenase that is responsible for *o*-hydroxylation of the phenol entity.[25]

To gain more insight into the interesting properties of this macrocyclic ligand type, we now have investigated how the modification of the R group in $[Cu_2(mac)(CH_3CN)_2]^{2+}$ from H to an ethyl group, 2-methylpyridyl, and 2-methylphenol would influence the coordination behavior of these systems.

Synthesis of Macrocycle Components. For the preparation of the substituted triamines, a multistep process, shown in the upper part of Scheme 1, was followed, consisting of the following: (a) the protection of the primary amines with phthalic anhydride to form the corresponding phthalimides; (b) the addition of the pyridyl or phenol aldehyde or iodoethane to the central amine; (c) deprotection of the phthalamides with hydrazine to yield the corresponding primary amines. The ethyl substituted central amine was also prepared by following a different synthetic strategy depicted at the bottom of Scheme 1A. It describes the preparation of the dicyano derivative that is then reduced to the corresponding amine by $LiAlH_4$.

Synthesis of Metal Free [2+2] Macrocyclic Ligands. The direct, metal-free, reaction of a dialdehyde and a diamine can yield a large range of condensation products both macrocyclic and acyclic, as shown in Scheme 2, that can be in equilibrium. The relative amount of each product depends basically on entropic and geometric factors. From an enthalpic viewpoint, it involves the formation and breaking of the same type of bond, and highly strained systems will be enthalpically disfavored. The relative formation of the products shown in Scheme 2 is also influenced by the solvent, reaction temperature, reaction time, and, very importantly, their solubility. This wide range of condensation compounds has been previously described in the literature for related systems (e. g. for the pyridyldialdehyde system).[10b,26]

In our case, the [2+2] macrocyclic ligands were prepared by a condensation of a 1:1 molar ratio of an adequately substituted triamine and isophthalaldehyde that was very slowly added to the respective triamine solution to favor both lower oligomeric compounds as well as macrocyclic type products. The relatively low yields obtained indicate the formation of other products and potentially unreacted starting materials. Once the [2+2] condensation product was formed, it was redisolved in either MeOH or MeCN and was stirred at room temperature (RT) for 24 h. MS analysis of the solution indicates the presence of the [2+2] condensation product only. Thus, once it is formed, and in the absence of a catalyst, there is no equilibration process that could generate a mixture of oligomers, at least on the time scale of days.

Synthesis of Cu^I Complexes. Another factor that strongly influences reactivity is the presence of a metal cation that can act as a templating agent and thus stabilize the formation of a condensation product that possesses a cavity size and shape that is complementary to those of the templating cation.

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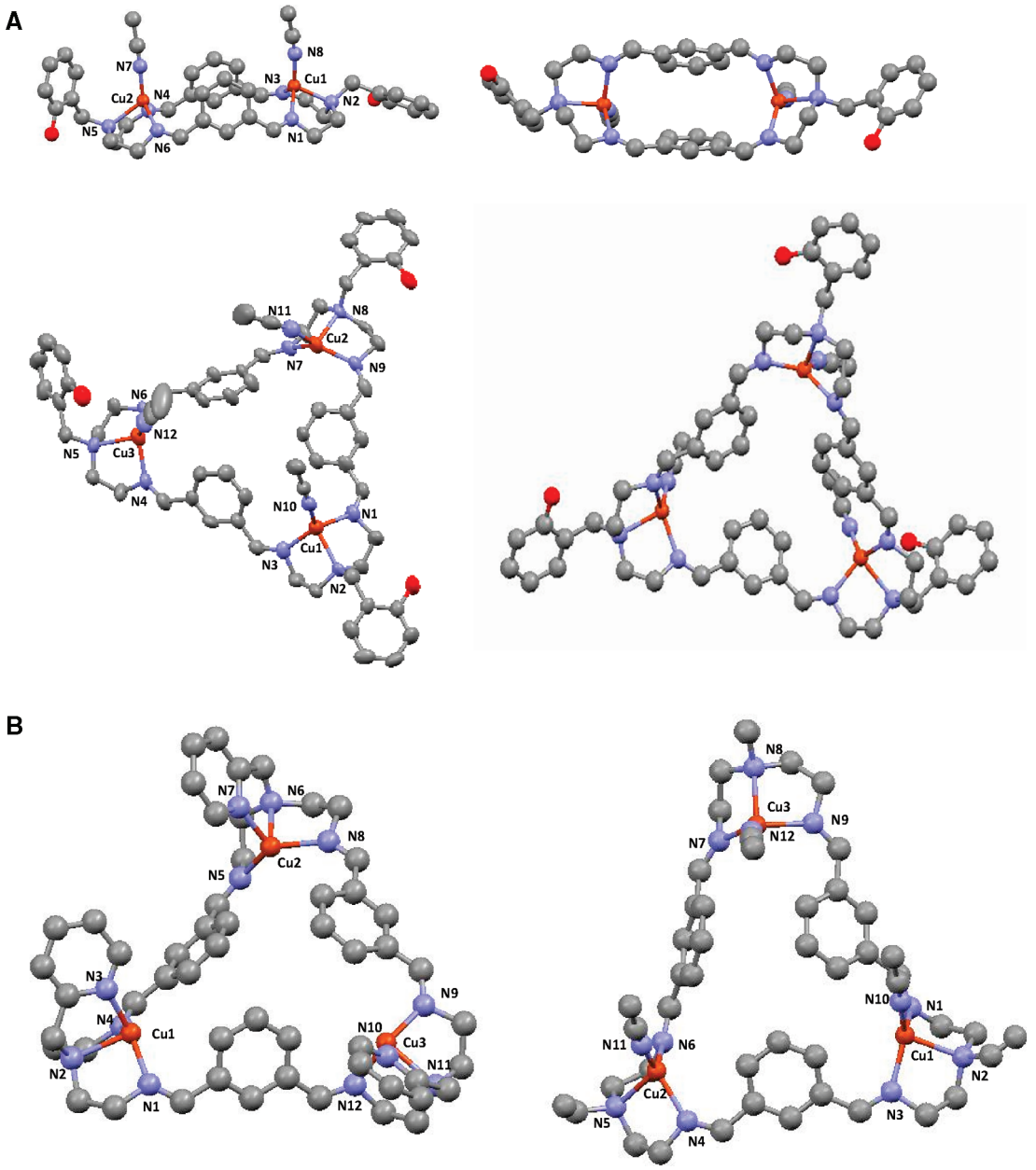

Figure 1. Ball and stick diagrams for the X-ray crystal structure for Cu^{I} complexes: (A) top, two representations of $\mathbf{2}^{2+}$; bottom, two of $\mathbf{5}^{3+}$; (B) left, $\mathbf{4}^{3+}$; right, $\mathbf{6}^{3+}$. Color codes: Cu, orange; N, blue; C, gray; O, red. H atoms are not shown.

The synthesis of the Cu^{I} complexes was carried out either by mixing 2 equivalents of the $[Cu^{I}(MeCN)_4]^+$ salt and one of the [2+2] free ligand or via a template procedure as indicated in the following equations. For the case of the L^1 ligand, the solvent and crystallization time have a strong influence over the complexes obtained. In MeOH, the main product obtained in 80% yield is $\mathbf{1}^{2+}$, as indicated in eq 1.

$$2[Cu^{I}(MeCN)_4]^+ + L^1 \xrightarrow{MeOH,\,RT} \underset{\mathbf{1}^{2+}}{[Cu_2(L^1)]^{2+}} + 8MeCN \quad (1)$$

On the other hand, and in sharp contrast, using MeCN as the solvent generates the analogous trinuclear complex $\mathbf{4}^{3+}$ in 70% yield. Given the fact that the L^1 ligand does not isomerize in solution, it suggests the presence of a metal assisted transformation that generates L^4 out of L^1, which will be discussed later. Further, a one pot synthesis using the triamine and dialdehyde and Cu^{I} as a template metal generates the $\mathbf{4}^{3+}$ complex in 68% yield, as shown in eq 2.

$$3[Cu^{I}(MeCN)_4]^+ + 3[1,3\text{-}Ph(CHO)_2] + 3H_2NC_2py \xrightarrow{MeOH} \underset{\mathbf{4}^{3+}}{[Cu_3(L^4)]^{3+}} \quad (2)$$

For the case of the L^2 ligand, only the dinuclear complex, $\mathbf{2}^{2+}$, is obtained in either MeOH or MeCN in good yields (approximately 80%) after 1 h of mixing the reactants at room temperature. However, if the solution is allowed to stand for

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Table 2. Selected Bond Distances and Angles for the First Coordination Sphere of One of the Cu^I Metal Centers of Complexes $4(PF_6)_3$, $2(CF_3SO_3)_2$, $5(CF_3SO_3)_3$, and $6(CF_3SO_3)_3$

$4(PF_6)_3$		$2(CF_3SO_3)_2$		$5(CF_3SO_3)_3$		$6(CF_3SO_3)_3$	
Cu(1)−N_{py}(10)	2.043(7)	Cu(1)−N_{MeCN}(8)	1.918(2)	Cu(1)−N_{MeCN}(10)	1.97(7)	Cu(1)−N_{MeCN}(10)	1.917(10)
Cu(1)−N_{im}(1)	1.989(7)	Cu(1)−N_{im}(3)	2.0223(19)	Cu(1)−N_{im}(3)	2.04(5)	Cu(1)−N_{im}(1)	2.026(7)
Cu(1)−N_{im}(3)	2.011(7)	Cu(1)−N_{im}(1)	2.0610(18)	Cu(1)−N_{im}(1)	2.05(5)	Cu(1)−N_{im}(3)	2.036(8)
Cu(1)−N_{ter}(2)	2.183(7)	Cu(1)−N_{ter}(2)	2.2078(18)	Cu(1)−N_{ter}(2)	2.19(5)	Cu(1)−N_{ter}(2)	2.209(8)
N_{im}(3)−Cu(1)−N_{im}(1)	130.9(3)	N_{MeCN}(8)−Cu(1)−N_{im}(3)	128.82(8)	N_{MeCN}(10)−Cu(1)−N_{im}(3)	122(2)	N_{MeCN}(10)−Cu(1)−N_{im}(1)	113.7(3)
N_{im}(1)−Cu(1)−N_{py} (10)	115.7(3)	N_{MeCN}(8)−Cu(1)−N_{im}(1)	116.10(8)	N_{MeCN}(10)−Cu(1)−N_{im}(1)	111(2)	N_{MeCN}(10)−Cu(1)−N_{im}(3)	121.0(3)
N_{im}(3)−Cu(1)−N_{py} (10)	110.7(3)	N_{im}(3)−Cu(1)−N_{im}(1)	111.32(8)	N_{im}(3)−Cu(1)−N_{im}(1)	123(2)	N_{im}(1)−Cu(1)−N_{im}(3)	123.7(3)
N_{im}(1)−Cu(1)−N_{ter}(2)	86.2(3)	N_{MeCN}(8)−Cu(1)−N_{ter}(2)	117.68(8)	N_{MeCN}(10)−Cu(1)−N_{ter}(2)	120(2)	N_{MeCN}(10)−Cu(1)−N_{ter}(2)	115.5(3)
N_{im}(3)−Cu(1)−N_{ter}(2)	85.1(3)	N_{im}(3)−Cu(1)−N_{ter}(2)	83.96(7)	N_{im}(3)−Cu(1)−N_{ter}(2)	85(2)	N_{im}(1)−Cu(1)−N_{ter}(2)	83.7(3)
N_{py}(10)−Cu(1)−N_{ter}(2)	81.8(3)	N_{im}(1)−Cu(1)−N_{ter}(2)	84.85(7)	N_{im}(1)−Cu(1)−N_{ter}(2)	85(2)	N_{im}(3)-Cu(1)-N_{ter}(2)	84.4(3)

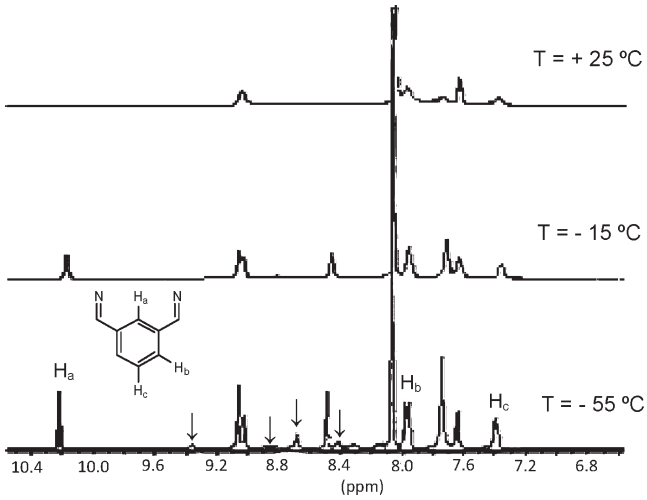

Figure 2. Variable temperature ^{1}H NMR spectra of $\mathbf{1}(PF_6)_2$ in DMF−d_7 at −55, −15, and +25 °C (arrows mark the peaks of the second isomer).

12−15 days, a mixture of dinuclear, $\mathbf{2}^{2+}$, and trinuclear, $\mathbf{5}^{3+}$, complexes is obtained (see eq 3).

$$[Cu^I(MeCN)_4]^+ + L^2 \xrightarrow{MeCN,\ RT} \underset{\mathbf{2}^{2+}}{[Cu_2(L^1)(MeCN)_2]^{2+}} + \underset{\mathbf{5}^{3+}}{[Cu_2(L^5)(MeCN)_3]^{2+}} \quad (3)$$

Finally, for the case of the L^3 macrocyclic ligand, only the trinuclear complex was obtained in 71% yield, indicating the formation of the L^6 ligand, as shown in eq 4.

$$6[Cu^I(MeCN)_4]^+ + 3L^3 \xrightarrow{MeCN,\ RT} 2\underset{\mathbf{6}^{3+}}{[Cu_3(L^6)(MeCN)_3]^{3+}} \quad (4)$$

Solid State Characterization. The crystal structure of the ligand L^2 consists of eight discrete L^2 molecules (see Table 1). The X-ray analysis shows four crystallographically independent but chemically identical L^2 units, which present very slight variations in bond distances and angles. It is interesting to note that, for each molecular structure, the two benzene rings are nearly parallel to one another with an angle of 1.76, 1.84, 6.27, or 6.96° and that the phenol groups are placed in mutually trans position in an inversion center arrangement around the tertiary amine, permitting the establishment of H-bonding with the nearby units. In Figure 1 ball and stick representations of the X-ray structures for the dinuclear complex, $\mathbf{2}^{2+}$, and the trinuclear complexes, $\mathbf{4}^{3+}$, $\mathbf{5}^{3+}$, and $\mathbf{6}^{3+}$, is depicted. For the dinuclear complex, $\mathbf{2}^{2+}$, the metasubstitution of the aromatic ring places the two copper centers at a distance of 7.97 Å; whereas the two benzene rings are nearly parallel to one another with an angle of 29.1°. Each copper center has a distorted tetrahedral arrangement as a result of the constraints imposed by the triaza moiety of the macrocyclic ligand. This generates a long Cu−N (2.208 Å) distance with the central amine group, two medium Cu−N (2.022 Å and 2.061 Å) distances with the imines, and a short distance with the MeCN monodentate ligand Cu−N (1.918 Å). The strain of the macrocyclic ligand also imposes two short N−Cu−N angles of 84.85° and 83.95°, with the rest of the

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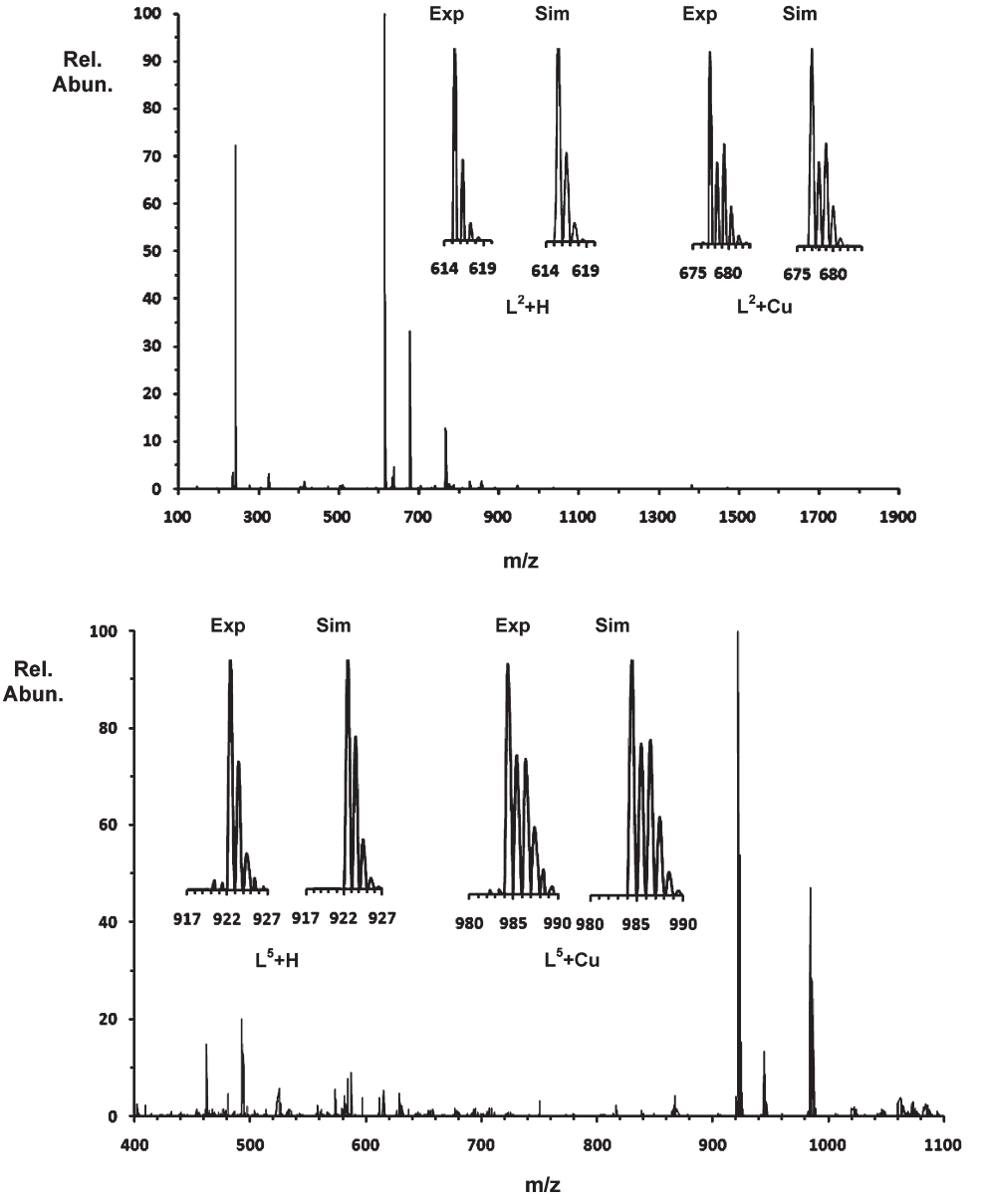

Figure 3. ESI-MS spectra obtained for $\mathbf{2}(CF_3SO_3)_2$ (top) and $\mathbf{5}(CF_3SO_3)_3$ (bottom) in MeCN.

N−Cu−N angles ranging 111−128°. Finally, the dangling phenol group is not coordinating the Cu metal center. The metric parameters described here are also in agreement with related Cu^I complexes that have been previously reported in the literature.[27] Table 2 lists selected bond distances and angles for the first coordination sphere of one of the Cu^I metal centers of complexes **4**, **2**, **5**, and **6**.

For the trinuclear complexes $\mathbf{5}^{3+}$ and $\mathbf{6}^{3+}$, the local Cu^I coordination is comparable to that of the dinuclear $\mathbf{2}^{2+}$ complex. Here, the metal centers are disposed in a triangular arrangement with Cu−Cu distances (ranging from 8.8 to 9.4 Å) that are a bit larger than those for the dinuclear complex, as discussed above, and thus manifest the relative flexibility of this family of [2+2] and [3+3] Schiff base ligands. Comparing the $\mathbf{5}^{3+}$ trinuclear complex and the $\mathbf{2}^{2+}$ dinuclear complex, the major difference is that the latter has slightly shorter $N_{im}-Cu_{(1)}-N_{im}$ angles, 119−123° vs. 108−111.32°, while the Cu bonding distances are practically identical. For the trinuclear complex $\mathbf{4}^{3+}$, the dangling pyridyl group is coordinating the metal center, replacing the MeCN when compared to $\mathbf{5}^{3+}$. For the trinuclear complexes, it is also interesting to see that the three benzene rings altogether adopt a bowl shape arrangement. For the case of $\mathbf{4}^{3+}$, the closest H atoms among the three aromatic rings are situated at 2.52, 2.70, and 2.77 Å, forming an irregular triangle, and the angles between these aromatic rings are 56.7, 69.0, and 83.2°. With regard to the 3D packing of these molecules, it is interesting to realize that those containing the triflate anion have packing that is dominated by H-bonding with triflate oxygen atoms and the macrocycle. A similar situation is found for complex $\mathbf{4}^{3+}$ containing PF_6^- as counteranion that crystallizes with THF, H_2O, and MeOH. Here again, packing interactions are dominated by extensive hydrogen bonding between the solvate oxygen atoms and the macrocycle. However, complex $\mathbf{4}^{3+}$ containing SbF_6^- as counteranion crystallizes with no solvate molecules, and its packing structure is significantly different

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from the rest. In particular, it is interesting to see the presence of dimers of trinuclear units bonded by $\pi-\pi$ and CH$-\pi$ interactions between macrocyclic ligands (see the Supporting Information.).

NMR Spectroscopy. The ^{1}H NMR spectrum of $\mathbf{1}^{2+}$ was recorded in CD_3CN-d_3 or in DMF$-d_7$ and is presented in Figure 2. At room temperature, the spectra show very broad signals that indicate the presence of a dynamic behavior analogous to that previously described for $[Cu_2(mac)(CH_3CN)_2]^{2+}$.[24b] Whereas the aliphatic part is unremarkable, the aromatic part displays sharp resonances at -25 °C and below. Together with these sharp resonances, lower intensity and wider peaks also appear that are presumably the result of another highly symmetric stereoisomer of $\mathbf{1}^{2+}$, given the reduced number of resonances observed. It is also interesting to observe that resonance for H_a in $\mathbf{1}^{2+}$ appears at 10.22 ppm, while for $[Cu_2(mac)(CH_3CN)_2]^{2+}$ it is shifted to 8.74 ppm, manifesting how subtle differences in structure can produce large electronic perturbation at a specific site.

The Cu^I complexes described here, in general, react slowly (within the time scale of days) with molecular oxygen, except for the ones containing the phenolic ligand, $\mathbf{2}^{2+}$ and $\mathbf{5}^{3+}$, which react a bit faster, presumably to form the corresponding bis-μ-hydroxo derivatives Cu($\mu-$OH)$_2$Cu, as has been previously shown for related metasubstituted macrocyclic complexes.[11] Unlike $[Cu_2(mac)(CH_3CN)_2]^{2+}$, no hydroxylation of the ligand occurs with the complexes described in the present work.

MS Spectroscopy and the [2+2] vs. [3+3] Evolution Process. Complexes $\mathbf{2}^{2+}$ and $\mathbf{5}^{3+}$ were analyzed by ESI-MS, and their spectra are presented in Figure 3. In both cases, their molecular peaks could not be identified, but a series of fragments are found. For complex $\mathbf{2}^{2+}$, key monocharged peaks at 615 (L^2 + H, highest intensity), 637 (L^2 + Na), 677 (L^2 + Cu), 739 (L^2 + Cu$_2$ − 1), and 766 m/z (L^2 + Cu$_2$Na − 2) could be identified. For complex $\mathbf{5}^{3+}$, key peaks are found at 922 (L^5 + H, highest intensity), 984 m/z (L^5 + Cu), and their corresponding doubly charged peaks at 461 and 492 m/z, respectively. For both complexes, the relative intensities of their peaks coincide perfectly with the simulated ones. As indicated in the previous section, the reaction of $[Cu^I(MeCN)_4]^+$ in MeCN with the [2+2] condensation macrocyclic ligand L^2 generates a mixture of the dinuclear and trinuclear complexes as indicated in eq 3. Thus, it can be inferred that an equilibrium between the dinuclear and trinuclear complex may exist, as indicated in the following equation:

$$\underset{\mathbf{2}^{2+}}{3[Cu_2(L^2)(MeCN)_2]^{2+}} \overset{MeCN}{\rightleftharpoons} \underset{\mathbf{5}^{3+}}{2[Cu_3(L^5)(MeCN)_3]^{3+}} \quad (5)$$

This reaction was monitored using MS, following the relative intensities of the peaks at 615 m/z for $\mathbf{2}^{2+}$ and 922 m/z for $\mathbf{5}^{3+}$, at room temperature. The initial concentration of complex $\mathbf{2}^{2+}$ was 0.026 M, and no $\mathbf{5}^{3+}$ was observed. As time elapsed, the formation of $\mathbf{5}^{3+}$ was observed, as depicted in Figure 4. After 1.5 months, the system reaches equilibrium with a relative concentration $[\mathbf{5}^{3+}]/[\mathbf{2}^{2+}]$ of 0.65, which implies an equilibrium constant of 0.42 for eq 5. This value indicates that the [2+2] condensation complex $\mathbf{2}^{2+}$ is more energetically favored than the [3+3] complex $\mathbf{5}^{3+}$, probably as a result of entropic factors and also, to a minor extent, of the relative strain of their structures. It is important to bear in mind that these experiments have been carried out under high dilution conditions so that both complexes are completely soluble. Therefore, these results cannot be

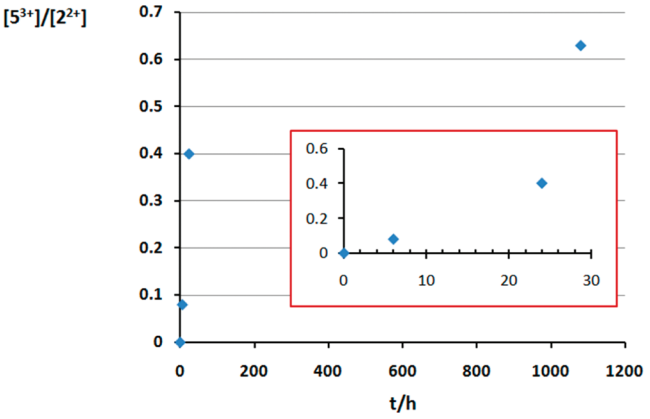

Figure 4. Graph of the $\mathbf{2}^{2+}$ to $\mathbf{5}^{3+}$ oligomerization evolution as a function of time monitored by using MS spectroscopy. The inset shows the first 30 h. Units are the same as in the main graph.

extrapolated at a synthetic level with regard to the relative amount of $\mathbf{2}^{2+}$ and $\mathbf{5}^{3+}$ because in that case we used a mixture of MeCN and ether.

The formation of the trinuclear complex from the dinuclear compound indicates that at least one of the imine C═N of the [2+2] Schiff base ligand has to be broken, and then the fragments have to react again so that the new [3+3] ligand can be formed. This process has not been observed for the free ligand, at least during the time scale of days. Thus, it must be assisted by the Cu^I dinuclear complex. This is in sharp contrast with the cases of other macrocyclic ligands where this process is known to occur very quickly, as is the case for the systems derived from pyridine dialdehyde and diamine.[26] Scheme 2 presents potential condensation products that can be obtained from the reaction of a 1:1 dialdehyde and triamine to illustrate the variety of compounds, including macrocyclic and acyclic compounds. As mentioned earlier, the L^2 does not undergo any reorganization process by itself, but it does so when complexed to Cu^I ions. Thus, potential fragments that can lead to the trinuclear complex are as follows:

$$\{Cu_2[2+1(o2)]\}^{2+} + \{Cu[1+2(n2)]\}^{+} \rightarrow \underset{\mathbf{5}^{3+}}{[Cu_3(L^5)]^{3+}} \quad (6)$$

or

$$\{Cu_2[2+2(n,o)]\}^{2+} + \{Cu[1+1(n,o)]\}^{+} \rightarrow \underset{\mathbf{5}^{3+}}{[Cu_3(L_5)]^{3+}} \quad (7)$$

The ligand nomenclature is described in Scheme 2. For instance, for the case of [2 + 1(o2)], the [2+1] indicates the condensation product of two dialdehydes and one triamine and in the parentheses is indicated the number and nature of unreacted groups, n for a secondary amine and o for aldedyde.

Final Comments and Conclusions. In this paper, we report the synthesis of three new [2+2] macrocyclic ligands, L^1, L^2, and L^3, with pendant arms that consist of the condensation of phthalaldehyde and N^2-substituted triamines with moderate to good yields. We have also shown that once these [2+2] compounds are formed, they do not undergo further rearrangement reactions in solution, and thus, the different compounds shown

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in Scheme 2 are not in equilibrium in our case. Therefore, the formation of the [1+1] condensation product, higher oligomers, such as [3+3], [4+4], etc., and linear polymers represents very minor products, and thus the [2+2] condensation product is the favored one.

In contrast, the reaction of the [2+2] condensation ligands, L^1 and L^2, with Cu^I complexes generates a mixture of dinuclear ($\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$) and trinuclear ($\mathbf{4}^{3+}$ and $\mathbf{5}^{3+}$) complexes that are in equilibrium in solution. The unique reactivity of the present Cu^I complex puts forward the delicate balance between electronic and geometrical factors that allow the making and breaking of imine bonds, and thus observation of the [2+2] and [3+3] equilibrium reaction. Finally, all of the Cu^I complexes described here react only very slowly with molecular oxygen at room temperature and thus manifest the capacity of the Schiff base ligand to stabilize the Cu^I oxidation state in a MeCN solution.

■ ASSOCIATED CONTENT

Supporting Information. Crystallographic information files (CIF) for L^2, $\mathbf{2}(CF_3SO_3)_2$, $\mathbf{4}(SbF_6)_3$, $\mathbf{4}(PF_6)_3$, $\mathbf{5}(CF_3SO_3)_3$, and $\mathbf{6}(CF_3SO_3)_3$ and additional experimental and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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