New Polyaza Macrobicyclic Cryptands Based on 1,2,4-Triazole Ligands and Their Cu(I), Ag(I), Cu(II) and Ni(II) Complexes

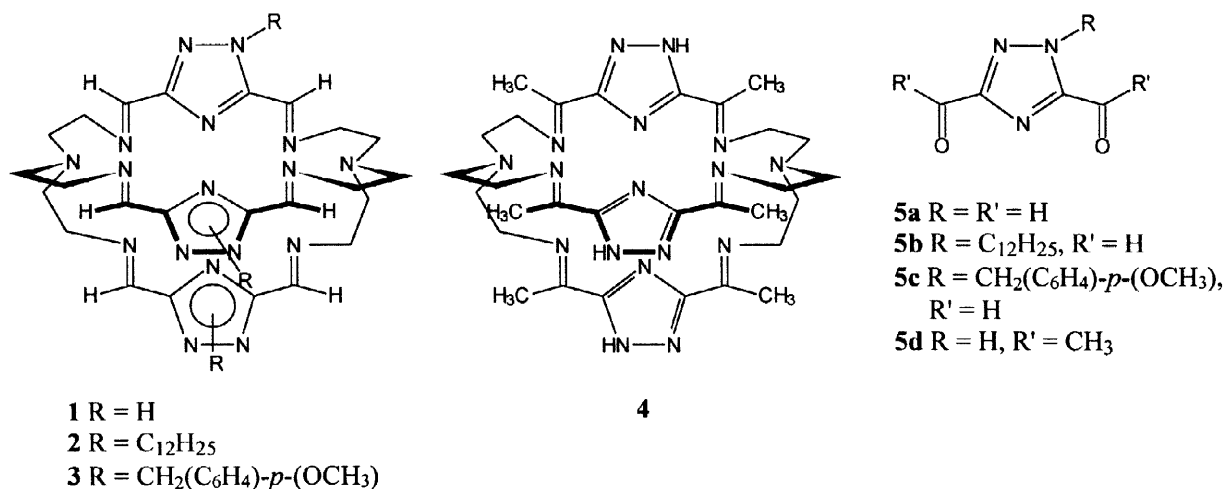## Beatriz Cabezón, María Irurzun, Tomás Torres* and Purificación Vázquez*

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Abstract: New polytopic cryptands 2-4 containing 1,2,4-triazole subunits have been synthesized by [2+3] condensation of the corresponding acyltriazole 5 and tris(2-aminoethyl)amine (Tren) in excellent yield; 2 and 3 gave dinuclear Ag(I) and trinuclear Cu(I) cryptates, and 4 yielded trinuclear Ni(II) and Cu(II) complexes in alkaline media. The nature of the complexes has been established by LSIMS and MALDI-TOF mass spectrometry. © 1998 Elsevier Science Ltd. All rights reserved.

The synthesis of polytopic macrobicyclic ligands containing recognition sites for binding several guests has reached a very high level of sophistication.[1] In addition, the incorporation of proton-ionizable subunits into macrobicyclic receptors to form polynuclear metal complexes may have multiple uses in bioinorganic chemistry, materials science, catalysis, metal/metal interactions, transport and activation of small molecules.[2]

Recently, we have investigated in detail the incorporation of one or more 1,2,4-triazole subunits into macrocyclic assemblies.[3] This moiety provides an excellent way for complexing a variety of transition metal ions[3,4] in both neutral and alkaline media. In the last case the triazole anion generated facilitates considerably the metal co-ordination. The physical properties of 1,2,4-triazole containing macrocycles have been also extensively studied by us.[5] To our knowledge, the 1,2,4-triazole unit has never been incorporated into a macrobicyclic structure, being this is an important goal to pursue in order to increase the co-ordination possibilities of triazole containing systems.

1 R = H
2 R = C₁₂H₂₅
3 R = CH₂(C₆H₄)-p-(OCH₃)

4

5a R = R' = H
5b R = C₁₂H₂₅, R' = H
5c R = CH₂(C₆H₄)-p-(OCH₃), R' = H
5d R = H, R' = CH₃

Thus, we are currently interested in investigating the synthesis and the co-ordination properties of macrobicyclic ligands, such as **1-4**, which contain both 1,2,4-triazole and tris(2-aminoethyl)amine subunits. In the present letter we report on these new macrobyclic cryptand receptors and some of their polyatomic Ag(I), Cu(I), Cu(II) and Ni(II) complexes.

The preparation of macrobicyclic compound **1**, having three proton-ionizable triazole moieties, was attempted without success by direct condensation of 3,5-diformyl-1,2,4-triazole (**5a**)[6] with tris(2-aminoethyl)amine (Tren) in acetonitrile and other polar solvents. Most probably the lack of solubility of the dialdehyde **5a** in all kinds of solvents (other than water) precludes the condensation reaction.

In order to increase the solubility of the starting aldehyde, N-substituted derivatives of it were used. Thus, compounds **2** and **3**, the last having removable protecting groups, were prepared, as regioisomeric mixtures, in excellent yields[7] by reaction of Tren and the corresponding 1-substituted triazoledialdehyde **5b** and **5c**.[8]

Cryptands **2** and **3** form metal complexes with $AgBF_4$ (2 equiv.) or $Cu(CH_3CN)_4PF_6$ (3 equiv.) to give the dinuclear bis-Ag^I and trinuclear tris-Cu^I complexes **2a**, **3a**, **2b** and **3b**, respectively.[11] The new compounds were characterized on the basis of spectroscopic evidence.[12] The ^1H NMR spectra of the metal complexes are markedly different from those of the free ligands. The strongest shielding effect is observed for the iminic proton (in *ca.* $\Delta\delta$ 1.5). The nature of the complexes was established by LSIMS. The mass spectra indicate complexes with the composition $(Ag_22)(BF_4)_2$, $(Ag_23)(BF_4)_2$, $(Cu_32)(PF_6)_3$ and $(Cu_33)(PF_6)_3$ for **2a**, **3a**, **2b** and **3b**, respectively. In the case of the copper complexes **2b** and **3b**, the signals of cations, are observed arised from an initial complex $[(Cu_32)(PF_6)_2]^+$ or $[(Cu_33)(PF_6)_2]^+$ through the successive loss of PF_6^- anions. The binuclear silver complexes **2a** and **3a** show identical initial breakdown patterns; thus, in the case of **2a** the loss of a BF_4^- ion from a neutral parent molecule generates the cationic $[(Ag_22)(BF_4)]^+$ species, which correspond to the principal peak observed in the mass spectrum.

On the other hand, reaction of Tren with 3,5-diacetyl-1,2,4-triazole (**5d**) gave the macrobicyclic ligand **4**.[13] Cryptand **4** has three proton-ionizable subunits and it is expected to form cryptates with transition metals both in neutral and in alkaline media; however all the attempts to prepare complexes of Ag(I) and Cu(I), in a similar way to that described above for compounds **2** and **3**, were unsuccessful. On the contrary, the Cu(II) and Ni(II) complexes, **4a** and **4b** respectively, were synthesized by metallation of **4** with the corresponding metal(II) bromides.[14] Thus, treatment of **4** (LH_3, representing L^{3-} the trianionic framework after deprotonation) with three equivalent each of lithium hydroxide and the corresponding nickel(II) or copper(II) bromide in acetonitrile at reflux temperature afforded high insoluble complexes LM_3Br_3 [**4a**, M=Ni(II); **4b**, Cu(II)] as was pointed out by LSIMS, using acetonitrile/4% TFAA as solvent, and MALDI-TOF-MS, and IR spectroscopy.[15] The use of lower amounts of metal (II) bromide or the absence of base lead to mixtures of metal complexes with different stoichiometry with recovering of starting free macrobicycle (monitoring by MS).

In conclusion, the new family of cryptands here synthesized offer the possibility of producing new polymetallic complexes of interest in bioinorganic chemistry and materials science.

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7.   Preparation of **2** and **3**. *General procedure*: A solution of Tren [tris(2-aminoethyl)amine] (2 equiv.) in 10 mL of dry CH_3CN was stirred at room temperature under argon. To this was added dropwise a solution of the appropriate dialdehyde[8] **5b** or **5c**, (3 equiv.) in 15 mL of dry CH_3CN. The yellow precipitate was filtered and washed with CH_3CN and then with hexane. **2**: 93% yield, m.p. $\geq$ 250 °C (dec.). ^{1}H NMR (200 MHz, CD_3CN) δ 9.95 (s, 6H, CH=N), 4.58 (m, 6H, CH_2N-triazole), 3.09 (m, 12H, CH_2N=), 2.71 (m, 12H, CH_2N<), 1.85 (m, 6H), 1.25 (br. s, 54H), 0.86 (m, 9H); FAB-MS (*m*-NBA) *m/z* 1065 [(M+H)$^+$], 1064 (M$^+$). Anal. Calcd. for $C_{60}H_{105}N_{17}\cdot 3H_2O$: C, 64.42; H, 10.00; N, 21.28. Found: C, 64.46; H, 9.84; N, 21.89%. **3**: 80% yield, m.p. $\geq$ 250 °C (dec.). ^{1}H NMR (200 MHz, CD_3CN) δ 9.97 (s, 3H, CH=N), 9.93 (s, 3H, CH=N), 7.33 and 6.88 (AA'BB' system, 12H, Ar), 5.71 (s, 6H, CH_2N-triazole), 3.75 (s, 9H, OMe), 3.11 (m, 12H, CH_2N=), 2.74 (m, 12H, CH_2N<); FAB-MS (*m*-NBA) *m/z* 943 [(M+Na)$^+$], 921 [(M+H)$^+$].

8.   Dialdehydes **5b** and **5c**, precursors of **2** and **3**, were obtained in yields of up to 95% by Swern oxidation[9] of the corresponding dialcohols.[10] To a stirred solution of 0.09 mL (1.01 mmol) of oxalyl chloride in 2 mL of CH_2Cl_2 at -63 °C (dry ice/CHCl$_3$) was added a solution of 0.09 mL of DMSO in 2 mL of CH_2Cl_2 over 10 min. Immediately, a solution of 0.34 mmol of the corresponding dialcohol in 7 mL of CH_2Cl_2 was added over 10 min. The cloudy solution obtained was stirred for 35 min. Then, 0.034 mL of triethylamine was added. After 35 min. the cooling bath was removed, then 3 mL of 20% saturated $KHSO_4$ and 8 mL of hexane were added, and the resulting mixture was stirred vigorously while warming. The layers were separated and the aqueous phase was extracted with 10 mL of Et_2O. The combined organic layers were washed with saturated $NaHCO_3$, H_2O and saturated NaCl, and then dried over $MgSO_4$, filtered, and evaporated in vacuo at room temperature, giving a yellow oil of **5b** and **5c**. **5b**: 98% yield. ^{1}H NMR (200 MHz, CDCl$_3$) δ 10.06 (s, 2H, CHO), 4.65 (t, *J* = 7.2, 2H, CH_2N-triazole), 1.90 (m, 2H), 1.25 (br. s, 18H), 0.88 (m, 3H); ^{13}C NMR (50,3 MHz, CDCl$_3$) δ 182.9, 180.9 (CHO), 159.5, 150.0 (C=N), 51.8 (CH_2N), 31.9, 29.8, 29.5, 29.4, 29.3, 28.9, 26.2, 22.6 (CH_2), 14.1 (CH$_3$); IR (KBr) ν 1725 (CO), 1490 (C=N) cm^{-1}; EI-MS *m/z* 293 (17) (M$^+$), 264 (100) [(M-CHO)$^+$]. Anal. Calcd. for $C_{16}H_{27}N_3O_2$: C, 65.50; H, 9.28; N, 14.32. Found: C, 65.52; H, 9.13; N,

14.74%. **5c**: 96% yield. ^{1}H NMR (200 MHz, CDCl$_3$) δ10.05 (s, 2H, CHO), 7.37, 6.86 (AA'BB' system, J = 8.6, 4H, Ar), 5.75 (s, 2H, CH$_2$N-triazole), 3.78 (s, 3H, OMe); ^{13}C NMR (50,3 MHz, CDCl$_3$) δ 182.9, 181.0 (CHO), 166.5 (C=N), 160.0 (C-4'), 159.36 (C=N), 130.2 (C-2'), 125.9 (C-1'), 114.3 (C-3'), 55.3 (OMe), 54.5 (CH$_2$N); IR (KBr) ν 1750 (CO), 1510 (C=N) cm^{-1}; EI-MS m/z 245 (60) (M$^+$), 216 (47) [(M-CHO)$^+$], 121 (100) [(CH$_2$C$_6$H$_4$OCH$_3$)$^+$]. Anal. Calcd. for C$_{12}$H$_{11}$N$_3$O$_3$: C, 58.77; H, 4.52; N, 17.13. Found: C, 58.51; H, 4.75; N, 16.79%.

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11. Metal complexes **2a** and **3a**: To a CH$_3$CN suspension of the corresponding ligand **2** or **3**, in the dark, a solution of AgBF$_4$ (2 equiv.) in CH$_3$CN was added. After the ligand was dissolved, the reaction mixture was left for *ca.* 1 week under argon at room temperature; the solution was filtered over celite and the solvent was then removed under vacuo to afford light yellow **2a** (30%) and **3a** (28%) complexes.

    Metal complexes **2b** and **3b**: A solution of Cu(CH$_3$CN)$_4$PF$_6$ (3 equiv.) in CH$_3$CN under argon was added by cannula at room temperature to a degassed solution of **2** and **3** (1 equiv.) in CH$_3$CN. The mixtures turned orange instantaneously. The solvent was then removed under vacuum and the residue was purified by column chromatography on alumina. Elution with CH$_2$Cl$_2$ afforded pure **2b** (40%) and **3b** (35%).

12. Spectroscopic data of the complexes **2a**, **2b**, **3a** and **3b**. **2a**: ^{1}H NMR (200 MHz, CD$_3$CN) δ 8.54 (s, 3H, CH=N), 8.43 (s, 3H, CH=N), 4.43 (m, 6H, CH$_2$N-triazole), 3.67 (m, 12H, CH$_2$N=), 2.86 (m, 12H, CH$_2$N<), 1.86 (m, 6H), 1.25 (br. s, 54H), 0.88 (m, 9H); FAB-MS (*m*-NBA) m/z 1367 [(M-BF$_4$)$^+$], 1173 [(M-BF$_4$-AgBF$_4$)$^+$]. **2b**: ^{1}H NMR (200 MHz, CD$_3$CN) δ 8.33 (m, 6H, CH=N), 4.45 (m, 6H, CH$_2$N-triazole), 3.64 (m, 12H, CH$_2$N=), 2.93 (m, 12H, CH$_2$N<), 1.84 (m, 6H), 1.22 (br. s, 54H), 0.84 (m, 9H); FAB-MS (*m*-NBA) m/z 1544 [(M-PF$_6$)$^+$], 1399 [(M-2PF$_6$)$^+$], 1252 [(M-3PF$_6$)$^+$]. **3a**: ^{1}H NMR (200 MHz, CD$_3$CN) δ 8.45 (m, 6H, CH=N), 7.1 (AA'BB' system, 12H, Ar), 5.55 (m, 6H, CH$_2$N-triazole), 3.70 (s, 9H, OMe), 3.30 (m, 12H, CH$_2$N=), 2.86 (m, 12H, CH$_2$N<); FAB-MS (*m*-NBA) m/z 1223 [(M-BF$_4$)$^+$], 1029 [(M-BF$_4$-AgBF$_4$)$^+$]. **3b**: ^{1}H NMR (200 MHz, CD$_3$CN) δ 8.25 (m, 6H, CH=N), 7.1 (AA'BB' system, 12H, Ar), 5.55 (m, 6H, CH$_2$N-triazole), 3.72 (m, 9H, OMe), 3.10 (m, 12H, CH$_2$N-), 2.50 (m, 12H, CH$_2$N<); FAB-MS (*m*-NBA as matrix) m/z 1400 [(M-PF$_6$)$^+$], 1254 [(M-2PF$_6$)$^+$], 1108 [(M-3PF$_6$)$^+$].

13. The same procedure described in ref. 7 was followed for the preparation of compound **4**: yellow powder (methanol-diethyl ether) m.p. ≥ 250 °C (dec.), 90% yield. ^{1}H NMR (200 MHz, CD$_3$CN) δ 3.05 (m, 12H, CH$_2$N=), 2.65 (m, 12H, CH$_2$N<), 2.59 (s, 18H, Me); ^{13}C NMR (50.3 MHz, CD$_3$CN) δ 160.5 (N=C<), 160.1 (C-triazole), 50.4 (CH$_2$N=), 36.6 (CH$_2$N<), 26.0 (Me); FAB-MS (*m*-NBA) m/z 662 [(M+H+H$_2$O)$^+$], 661 [(M+H$_2$O)$^+$], 644 [(M+H)$^+$]; MALDI-MS m/z 644 [(M+H)$^+$]; Anal. Calcd. for C$_{30}$H$_{45}$N$_{17}$·5H$_2$O: C, 49.08; H, 7.55; N, 32.43. Found: C, 49.38; H, 7.28; N, 32.80%.

14. Cryptates containing divalent cations have been described: a) see ref. 2b. b) see ref. 2d. c) Drew, M.G.B.; Howarth, O. W.; Morgan, G. G.; Nelson, J. *J. Chem. Soc. Dalton Trans.*, **1994**, 3149-3155.

15. Selected spectroscopic data for complexes **4a** and **4b**: MALDI-TOF-MS m/z 1059-1053 [(LNi$_3$Br$_3$+H)$^+$], 977-973 [(LNi$_3$Br$_2$)$^+$] for the nickel compound and 1074-1068 [(LCu$_3$Br$_3$+H)$^+$], 992-988 [(LCu$_3$Br$_2$)$^+$] for the copper compound; IR (KBr) ν 1635 and 1500-1450 (C=N) cm^{-1}.