Revue Roumaine de Chimie, **2008**, *53*(1), 15–19

PAPERS

SYNTHESIS OF NEW FUNCTIONALIZED MACROPOLYCYCLIC LIGANDS BASED ON TRIAZACYCLONONANE AND TETRAAZACYCLODODECANE

Gabriela BLĂNIȚĂ, Monica BUCŞA, Maria COROŞ and Mircea VLASSA*

"Babeş-Bolyai" University, Faculty of Chemistry and Engineering Chemistry, Organic Chemistry Department, 11 Arany Janos str., 400028 – Cluj-Napoca, Roumania.

Recived November 23, 2006

The synthesis of new functionalized macropolycyclic ligands using triazacyclononane and tetraazacyclododecane as precursors is presented.

INTRODUCTION

It is well known the ability of complexes with dihydrogen bonds to react in solid state by hydrogen loss, trading the weak H ⋯ H interactions for strong covalent bonds, finally obtaining rational assembly of extended covalent materials with controlled architectures.[1] In order to obtain such new materials, with various practical applications, we have prepared new ligands by linking two macrocycles, namely triazacyclononane and tetraazacyclododecane, with one spacer.[2,3] We have noticed that the cristallinity of extended covalent materials is strongly influenced by the rigidity of the bridge.[4] This was the reason why we have chosen an aromatic moiety as spacer, namely *m*-xylylen , instead of an aliphatic one.

RESULTS AND DISCUSSION

Synthesis of macrocyclic ligands based on tetrazacyclododecane ligand is depicted in Scheme 1.

Tetramide **1,** prepared according to the literature data,[5] was reduced by means of borohydride in THF, and the resulting bis-(macrocycle) **2** was functionalized with two different types of arms, an aliphatic one, hyroxyethylene, which is more flexible and a aromatic one, *o*- hydroxy-benzyl, which is more rigid, obtaining compounds **5** and **6,** respectively. To further rise the rigidity of our bis ligands, the methylantracene moiety was introduced, after removal of protective group (Boc), finally obtaining bis-(macrocyles) **7** and **8.**

The bis-ligands that contain triazacyclononane were obtained according to Scheme 2. Thus by reaction of m-dibromo-xylyene with compound **9,** prepared according to the method of Czarnik and coworkers, [6] compound **10** was obtained, and functionalized with the same arms as above, obtaining compounds **11** and **12**.

The ^{1}H and ^{13}C RMN data support the structure of prepared compounds (see experimental).

EXPERIMENTAL

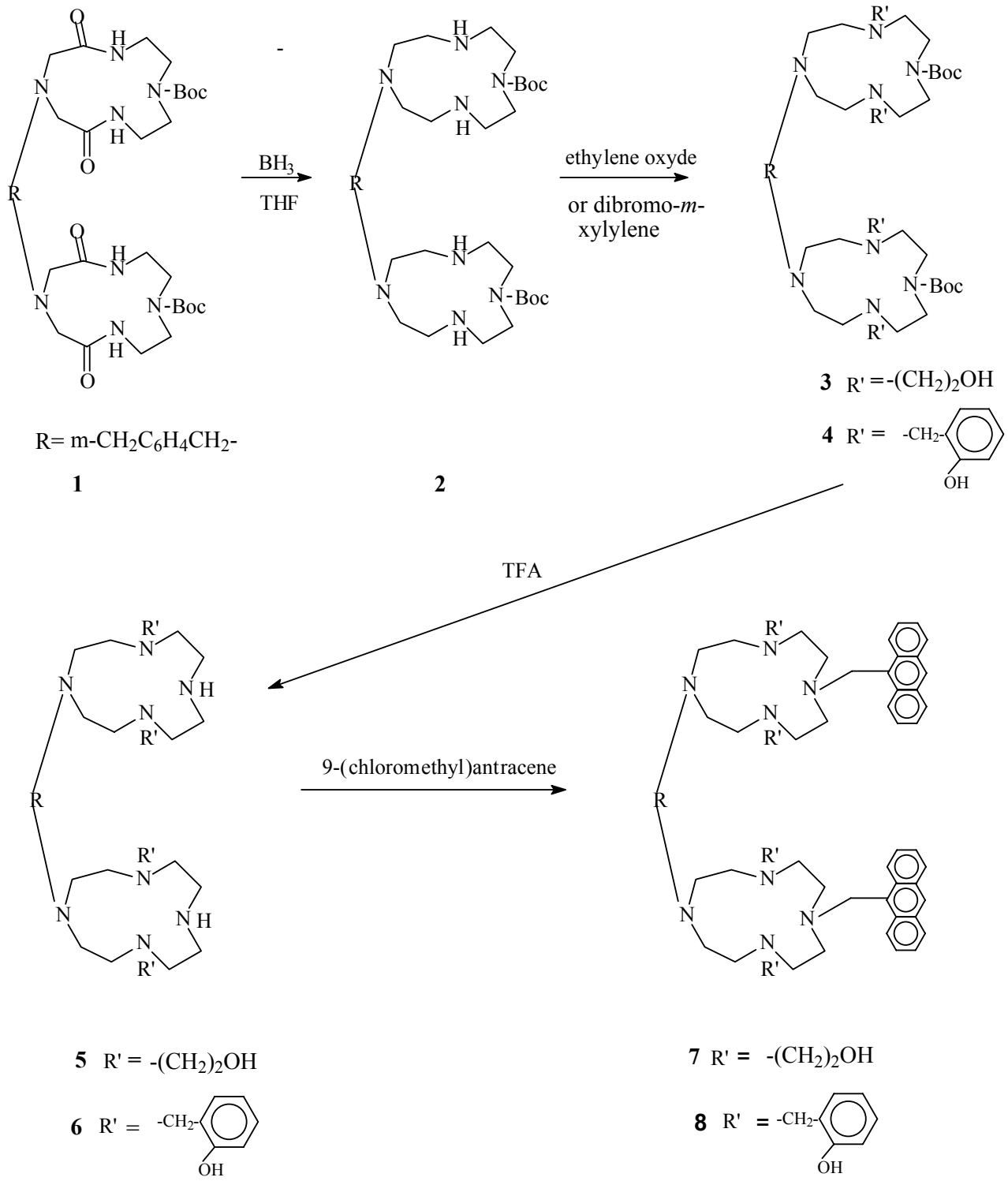
The m.p.'s are uncorrected. The NMR spectra were recorded on a Varian, Gemini 300 spectrometer, in $CDCl_3$ with tetramethylsylane as an internal reference. Elemental analyses were performed on a Perkin-Elmer 2400 instrument. The purity of compounds was checked by TLC on neutral alumina plates using $CHCl_3$ or $CHCl_3$ /MeOH 9:1 v/v as eluents. All chemicals, reagent grades, were commercially available (Aldrich) and used without further purification. Starting materials **1** and **9** were obtained by described procedures.[5,6]

Procedures

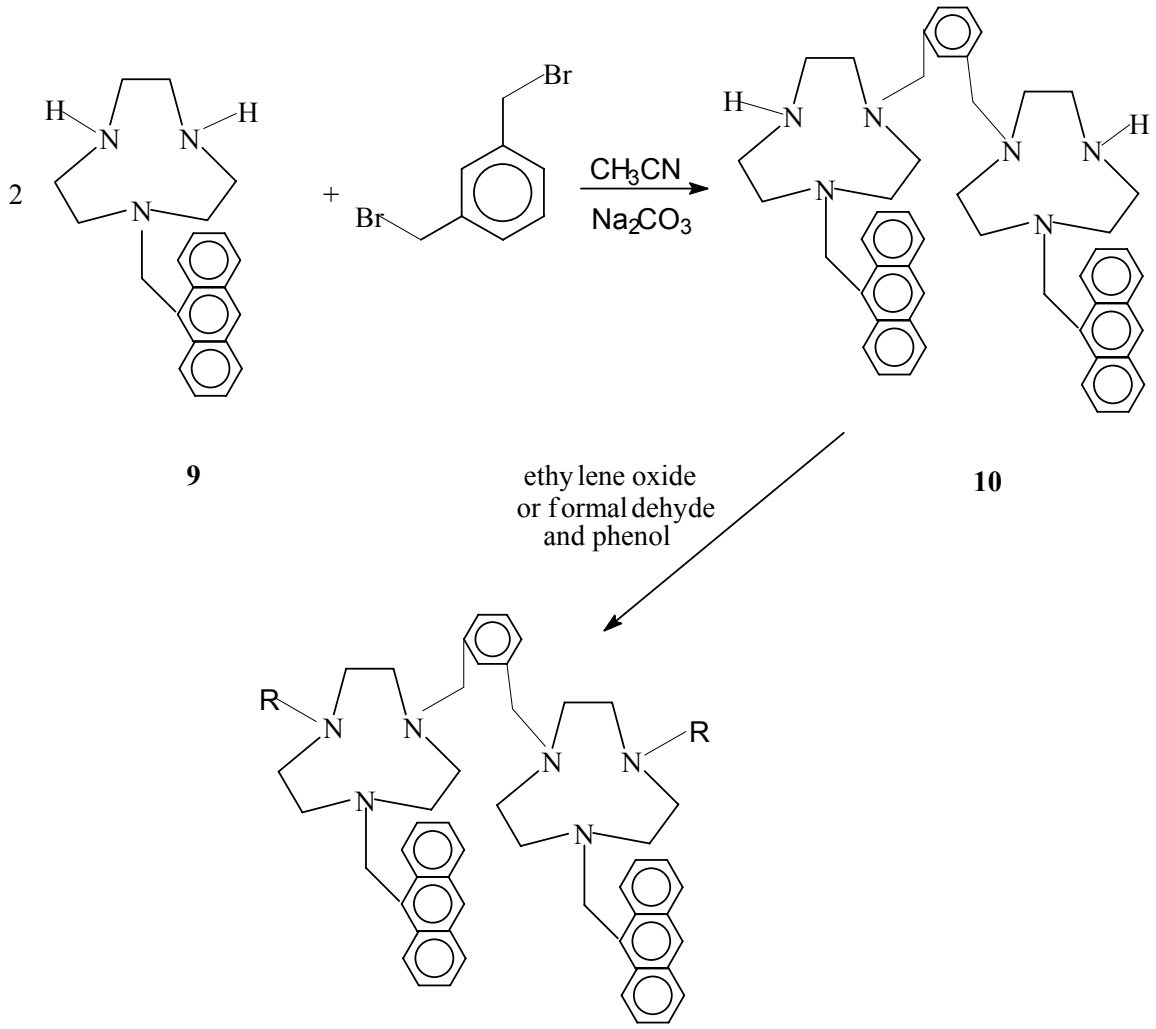
4,4'-*m*-Xylylenebis[10-tert-butoxycarbonyl-1,4,7,10-tetraazacyclododecane] 2 . The bis-(macrocycle) **1** (1.78g, 2.35 mmol) was suspended in 10 mL of THF under argon and 40 mL of 1M borane solution in THF was slowly added at

* Corresponding author: mvlasa@chem.ubbcluj.ro

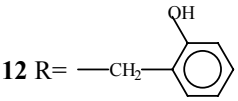
0 ^{0}C. The mixture was stirred at room temperature for 8 h, and then refluxed over night. After cooling, the excess of borane was hydrolyzed with 1:1 mixture of water/MeOH (5 mL) and the solvents were evaporated. The residue was then refluxed in 20 mL of 5 M aqueous HCl solution for 3 h and the mixture was neutralized by the addition of NaOH pellets (pH>11). Extraction of the aqueous solution with chloroform, followed by drying and concentration of organic phase, yielded **2** as a white solid 1.23 g, 84 %, m.p. =120-123 ^{0}C. ^{1}H NMR ($CDCl_3$) δ : 1.40 (s, 18 H, CH_3), 2.48 (t, 8H, CH_2), 2.65 (t, 8H,CH_2), 2.81 (t, 8H, CH_2), 3.08 (t,8H, CH_2), 3.62 (s, 4H, CH_2), 6.86 (s,1H), 6.87(d,2H), 7.02 (m,1H). ^{13}C NMR ($CDCl_3$) δ :28.50, 43.30, 43.93, 50.91, 55.13, 60.42, 79.84, 127.43, 128.22, 130.54, 135.36, 156.10. $C_{34}H_{62}N_8O_4$ (646.9) Calcd. C, 63.12; H, 9.66; N, 17.32; Found. C, 62.90; H, 9.52; N, 17,25.



Scheme 1



11 R= -CH_2CH_2-OH

12 R= 

Scheme 2

4,4'-*m*-Xylylenebis[10-tert-butoxycarbonyl-1,4,7,10-tetraazacyclododecane-1,7-di-hydroxyethyl] 3. Compound **2** (0.7 g, 0.57 mmol) was added in absolute ethanol (3 mL). Water (2 mL) was added, and the solution was cooled to 0 ^{0}C. Ethylene oxide (0.456 g, 10 mmol) was cooled to 0 ^{0}C and was added to the reaction mixture which was stirred at 0 ^{0}C for 3 h, followed by an additional hour of stirring at room temperature. Solvent evaporation under vacuum at 35 ^{0}C yielded an oil which was dissolved in a minimal amount of 2-propanol, and a large excess of Et_2O was added. Upon standing over night, a crystalline solid precipitated, which was filtered and washed with Et_2O to give **3**, 0.5g, 60%, m.p.= 133-135 ^{0}C ^{1}H NMR ($CDCl_3$) δ : 1.45(s,.18 H, CH_3) 2.46 (t, 16 H, CH_2), 2.55(t, 8H, CH2), 2.62(t, 8H, CH_2), 3.06 (t, 8H, CH_2), 3.36 (t, 8H, CH_2), 3.60(s, 4H), 6.82 (s, 1H), 6.88 (d,2H), 7.00 (m, 1H). ^{13}C NMR ($CDCl_3$) δ : 28.35, 48.70, 52.71, 52.91, 53.30, 57.72, 59.43, 60.20, 79.82, 127.00, 128.44, 131.00, 135.56, 156.30. $C_{42}H_{78}N_8O_8$ (823,1) Calcd. C, 61.28; H, 9.55; N. 13.61; Found C, 61.40; H, 9.40; N, 13.75.

4,4'-*m*-Xylylenebis[10-tert-butoxycarbonyl-1,4,7,10-tetraazacyclododecane-1,7-di-*o*-hydroxybenzyl] 4. To a two-necked round bottom flask fitted with a water cooled, nitrogen flushed, condenser, pressure equalized addition funnel, heated by a mantle, stirred magnetically, and containing compound **2** (2.05g, 2.5 mmol) in 25 mL methanol is added formaldehyde as a 37% w/w solution (2.2 mL, 0.41 g, 5 mmol) and the mixture is allowed to stir at 40 ^{0}C for 4 h. Phenol (0.47g, 5 mmol) in 60 mL methanol, is added dropwise to the yellow reaction mixture via the additional funnel. The mixture is stirred at 45 ^{0}C overnight. The reaction is transferred to a single neck round bottom flask, and all volatiles are removed from the reaction mixture by rotary evaporation. The residue is extracted with 6x50 mL Et_2O, and the combined extracts are dried with a small amount of

magnesium sulfate, and concentrated to 15 mL by boiling the solution. The mixture is slowly cooled to room temperature to affect crystallization of the product. Yields 1.03 g, 40%, m.p.= 115-116 ^{0} C. ^{1}H NMR ($CDCl_3$) δ : 1.42 (s, 18H, CH_3), 2.48 (t, 16 H, CH_2), 2.60 (t, 16 H, CH_2), 3.14 (s, 4H, CH_2), 3.62 (s, 8 H, CH_2), 6..61 (d, 4H), 6.70 (m,8H), 6.80 (s, 1H), 6.87(m,2H), 6.90 (m,4H), 7.05 (m,1H). ^{13}C NMR ($CDCl_3$)δ : 28.50, 48.75, 49.92, 52.30, 52.90, 60.45, 79.82, 115.65, 121.12, 122.94, 127.40, 128.22, 128.76, 130.33, 135. 38, 154.12, 156.43. $C_{62}H_{86}N_8O_8$ (1071.4) Calcd. C, 69.50; H, 8.09; N, 10.45; Found C, 69.55; H, 8.10; N, 10.60.

4,4'-*m*-Xylylenebis[1,4,7,10-tetraazacyclododecane-1,7-di-hydroxyethyl] 5. Bis-macrocycle **3** (3.11 g, 5 mmol) was stirred in 35 mL of trifluoroacetic acid for 3 h at room temperature. After evaporation of the solvent, the oily residue was dissolved in 10 mL of water, the pH was adjusted to 10 with triethylamine, and the water was evaporated. The crude product was taken up in a mixture of CH_2Cl_2/pentane/EtOH 40:40:20 and the resulting suspension was filtered to give **5** as a white solid, 1.63 g, 90%, 102-103 ^{0}C. ^{1}H NMR ($CDCl_3$) δ : 2.44 (t, 24 H, CH_2), 2.55 (t, 8H, CH_2), 2.65 (t, 8H, CH_2), 3.60 (s, 4H, CH_2), 3.65 (t, 8H, CH_2), 6.86 (s, 1H), 6.88 (d, 2H), 7.06 (m,1H). ^{13}C NMR ($CDCl_3$)δ : 43.93, 52.90, 53.32, 55.56, 57.75, 59.45, 60.45, 127.44, 128.25, 130.55, 135.40. $C_{32}H_{62}N_8O_4$ (622.9) Calcd. C, 61.70; H, 10.03; N, 18.00; Found C, 61.56; H. 9.89; N, 17, 85.

4,4'-*m*-Xylylenebis[1,4,7,10-tetraazacyclododecane-1,7-di-*o*-hydroxybenzyl)] 6. The title compound was obtained by the same procedure as described above for compound **5** using 4.36 g, 5mmol of compound **4**. Compound **6** precipitated as a white solid, 3.37 g, 95%, m.p.= 116-117 ^{0} C .^{1}H NMR ($CDCl_3$) δ : 2.50 (t, 16 H, CH_2), 2.48 (t, 8H, CH_2), 2.65 (t, 8H, CH_2), 3.62 (s, 12H, CH_2), 6.61(d,4H), 6.64 (d, 4H), 6.72 (m,4H), 6.80(s,1H), 6.87 (d, 2H), 6.89(d, 4H), 7.08 (m,1H). ^{13}C NMR ($CDCl_3$) δ : 43.90, 53.00, 55.10, 60.45, 115.66, 121.25, 122.95, 127.44, 128.20, 128.73, 130.33, 131.54, 135.46, 154.70. $C_{52}H_{70}N_8O_4$ (871,2) Calcd. C, 71.69; H. 8.10; N, 12.86; Found C, 71.58; H. 8.00; N, 12.70.

4,4'-*m*-Xylylenebis[1,4,7,10-tetraazacyclododecane-1,7-di-hydroxyethyl-10-methylantracene] 7. To a solution of bis-(macrocycle) **5 (** 6.23 g, 10 mmol) in toluene (20 mL) was added 9-(chloromethyl)-antracene (4.6 g, 20 mmol) . The resulting solution was heated under reflux for 6 h. After cooling, the precipitated salts were removed by filtration. The resulting clear solution was washed with 5% aqueous NaOH solution (2x20 mL) and with H_2O (4 x 10 mL) and then the organic layer was dried over Na_2SO_4 . After removal of the solvent *in vacuo*, the residue was dissolved in ethanol (20 mL) and concentrated HCl (3 mL) was added. On cooling, the hydrochloride salt precipitated and was collected by filtration and dried *in vacuo* at 80 ^{0} C to afford **7** in 3.9 g, 60%. The free base was obtained as a white solid after selective basic extraction, m.p.= 94-96 ^{0}C. ^{1}H NMR ($CDCl_3$) δ : 2.46 (t, 32 H, CH_2), 2.55(t, 8H, CH_2), 3.55 (t, 4H, CH_2), 3.63 (t, 8H, CH_2), 4.06 (s, 4H, CH_2), 6.83 (s, 1H), 6.88 (d, 2H), 7.10 (m, 1H), 7.30 (m, 4H), 7.40 (m, 4H), 7.51(m, 2H), 7.65 (m, 4H), 7.72 (d, 4H). ^{13}C NMR ($CDCl_3$) δ : 52.90, 53.33, 56.72, 57.00, 59.45, 60.45, 125.53, 126.90, 127.22, 127.41, 127.70, 128.40, 129.56, 130.00, 130.54, 134.00, 135,57, 137.42. $C_{62}H_{82}N_8O_4$ (1003.4) Calcd. C, 74.22; H, 8.24; N,11.17; Found C, 74.00; H, 8.05; N, 11.10.

4,4'-*m*-Xylylenebis[1,4,7,10-tetraazacyclododecane-1,7-di-*o*-hydroxybenzyl-10-methylantracene] 8. The bis-(macrocycle) **6** (8.71 g, 10 mmol) and 9-(chloromethyl)-antracene (4.6g, 20 mmol) were reacted as described for **7** to afford compound **8**, 6.1 g 50%, m.p.=108-110 ^{0}C. ^{1}H NMR ($CDCl_3$) δ : 2.40 (t, 32 H, CH_2), 3.60 (s, 12H, CH_2), 4.10 (s, 4H, CH_2),6.61 (d, 4H) 6.70 (m,4 H), 6.82 (s, 1H), 6.87 (m, 6H, overlapped),6.94 (m, 4H) 7.06 (m, 1H), 7.30 (m, 4H), 7.35 (m, 4H),7.51 (s, 2H), 7.65 (m,4H), 7.72 (m,4H). ^{13}C NMR ($CDCl_3$) δ : 49.90, 52.93, 56.73, 60.43, 115.67, 121.11, 122.95, 125.86, 126.00,126.65, 127.00, 127.45, 127.83, 128.22, 128.81, 129.54, 130.00, 130.34, 134.00, 135.37, 137.40, 156.43.$C_{82}H_{90}N_8O_4$ (1243.6) Calcd. C, 79.20; H, 6.65; N, 9.00; Found C, 79.05; H, 6.50; N, 8.86.

4,4'-*m*-Xylylenebis[1-methylantracene-1,4,7-triazacyclononane] 10. To 1-methylantracene-1,4,7-triazacyclo-nonane (3.69 g, 11.65 mmol) in 100 mL of acetonitrile were added α,α'-dibromo-m-xylene (1.54 g, 5.83 mmol), and anhydrous sodium carbonate (1.5 g). The mixture was refluxed for 20 h and then the hot solution was filtered. The crude product was chromatographed on silica gel ($CHCl_3$ / MeOH 90:10 v/v) to give **10** as a white solid, 6.91 g, 80%, 86-87 ^{0} C. ^{1}H NMR ($CDCl_3$) δ : 2.30 (t,8H, CH_2), 2.46 (t, 8 H, CH_2), 2.65 (t, 8H, CH_2), 3.62 (s, 4H, CH_2), 4.10(s, 4H, CH_2), 6.84 (s,1H), 6.90 (d, 2H), 7.05 (d,1H), 7.30 (m, 8H), 7.50 (s, 2H), 7.65 (m,4H), 7.72 (m, 4H). ^{13}C NMR ($CDCl_3$) δ : 48.93, 53.25, 55.40, 56.74, 60.42, 125.50, 126.00, 126.20, 126.92, 127.20, 127.43, 128.25, 128,40, 129.56, 130.00, 130.58, 134.00, 153.35. $C_{50}H_{56}N_6$ (741.0) Calcd. C, 81.04; H, 7.62; N, 11.34; Found C, 80.94; H, 7.40; N, 11.10.

4,4'-*m*-Xylylenebis[1-methylantracene-7-hydroxyethyl-1,4,7-triazacyclononane] 11. Bis-(macrocycle) **10** (4.22 g, 5.7 mmol) and ethylene oxide (0.64g, 12 mmol) reacted as described for **3** to afford compound **11**, 2.11 g, 45%. M.p.=98-99 ^{0} C.^{1}H NMR ($CDCl_3$) δ : 2.48 (t, 8 H, CH_2), 2.55 (t, 8H, CH_2), 2.60(t,8H,CH_2), 3.50 (s, 4H, CH_2), 3.63 (t, 4H, CH_2)4.06 (s, 4H, CH_2), 6.80 (s, 1H), 6.86 (d, 2H), 7.08 (m, 1H), 7.30 (m, 4H), 7.35 (m, 4H), 7.51 (s, 2H), 7.65 (m,4H), 7.72 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 53.22, 53.68, 56.72, 57.00, 59,43, 60.86, 125.55,126.90, 127.00, 127.20, 127.64, 128.20, 128,66, 129.58, 130.55, 134.00, 135.36, 137.48.$C_{54}H_{64}N_6O_2$ (829.1) Calcd. C, 78.22; H, 7.78; N, 10.13; Found C, 78.00; H, 7.62, N, 10.00.

4,4'-*m*-Xylylenebis[1-methylantracene-7-*o*-hydroxybenzyl-1,4,7-triazacyclononane] 12. Bis-(macrocycle) **10** (18.5 g, 25 mmol) and formaldehyde as a 37% w/w solution (21.8 mL, 4.08 g, 50 mmol) and phenol (4.72 g, 50 mmol) were reacted as described for **4** to afford compound **12**, 13.1 g, 55%, 104-106 ^{0}C. ^{1}H NMR ($CDCl_3$) δ : 2.40 (t, 8 H, CH_2), 2.50 (t, 8H, CH_2), 2.62 (t, 8H, CH_2), 3.62 (s, 8H, CH_2), 4.10. (s, 4H, CH_2), 6.61 (d, 2H), 6.70 (m, 2H), 6.84 (s, 1H), 6.89 (m, 4H), 6.96 (m, 2H), 7.12 (m,1H), 7.30 (m, 4H), 7.35 (m,4H), 7.51(s, 2H), 7.65 (d, 4H,), 7.75 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 121.10, 122.90, 125.64, 126.30, 126.70, 127.00, 127.41, 127.72, 128.24, 128.80, 129.50, 130.00, 130.30, 130.55, 134.00, 135.00, 135.43, 137. 45, 156.00. $C_{64}H_{68}N_6O_2$ (953.3) Calcd. C, 80.63; H, 7.19; N, 8.81; Found C, 80,55; H, 6.95; N, 8.55.

Acknowledgements **:**The authors thank to Roumanian Ministry of Education and Research for the financial support, grant CEEX no. 707/2006.

CONCLUSION

In conclusion we obtained new functionalized bis-macrocyclic ligands. Their complexation with

various borohyrides will allow us to obtain, after hydrogen releasing, the new ordered, extended covalent materials.

REFERENCES

1. a) G. Blăniță and M. Vlassa, *Rev. Chim*.(Bucharest), **2006**, *57*, 167-169; b) R.Custelcean, M. Vlassa and J. E. Jackson, *Angew.Chem*., **2000**, *39*, 3299-3302; c) R. Custelcean and J. E. Jackson, *J.*, *Angew.Chem.Int.Ed*., **1999**, *38*,1661-1663; d) J. W. Hwang, J. P. Cambpell, J. Kozubowski, S. A. Hanson, J. F. Evans and W. L. Gladfelter, *Chem.Mater*., **1995**, *7*, 517-525.
2. J.-M.Lehn, *Pure Appl. Chem.,* **1980**, *52*, 2441-2459.
3. A. Kumr and S. Mageswaran, *Tetdrahedron*, **1986**, *42,* 3291-3302.
4. R. Custelcean, M. Vlassa and J. J. Jackson, *Chem.Eur.,* **2002**, *8*, 302-308.
5. S. Brandes, F. Denat, S.Lacour, F. Barbette, P. Pullumbi and R. Guiard, *Eur. J. Org. Chem*., **1998**, 2349-2360.
6. E. U. Akkaya, M. E. Huston and A. W. Czarnik, *J. Am. Chem. Soc*., **1990**, *112*, 3590-3593.