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# The Synthesis of a New Macrocyclic Dinucleating Ligand,3,6,9,17,20, 23-Hexaaza-29,30-Dihydroxy-13,27- Dimethyl-Tricyclo [23,3,1,1$^{11,15}$]Triaconta -1(28),11,13, 15(30),25,26-Hexaene

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**Abstract:** A new dinucleating 24-membered hexaazadiphenol macrocyclic ligand, 3,6,9,17,20, 23-hexaaza-29,30- dihydroxy-13,27-dimethyl-tricyclo [23, 3, 1, 1$^{11, 15}$] triaconta -1(28), 11,13, 15(30),25, 26-hexaene, BDBPH, was synthesized by the $NaBH_4$ reduction of the Schiff-base obtained from the [2+2] condensation between diethylenetriamine and diformyl -*p*-cresol. The structure was characterized by elemental analysis, $^1$HNMR and FAB-MS. The synthetic method was also discussed.

**Keywords:** Macrocyclic ligand**,** synthesis.

The coordination chemistry of binuclear metal complexes has been a subject of extensive investigation relating to the synthesis of model compounds for the metal-binding sites of metalloproteins that require the presence of two metal centers[1]. During the last decade, a number of synthetic structural models for these proteins with the use of several types of ligands have been reported in literature[2-4]. For ligands with an appropriate disposition of donor atoms, it has been possible to show the presence of hydroxo, imidazolato, azido, and thiocyanato bridges between metal ions[5]. To further the studies in this area, it is necessary to synthesize new macrocyclic ligands with new structural characteristics, and to study the interaction between the macrocycle and the metal, as well as the stabilities of the complexes in solution (especially under physiological conditions). In this paper, we report the synthesis of a new dinucleating 24-membered hexaazadiphenol macrocyclic ligand ---3, 6, 9, 17, 20, 23-hexaaza-29, 30-dihydroxy-13, 27-dimethyl-tricyclo [23,3,1, 1$^{11,15}$] triaconta -1(28),11,13, 15(30), 25,26-hexaene, BDBPH.

## Synthesis

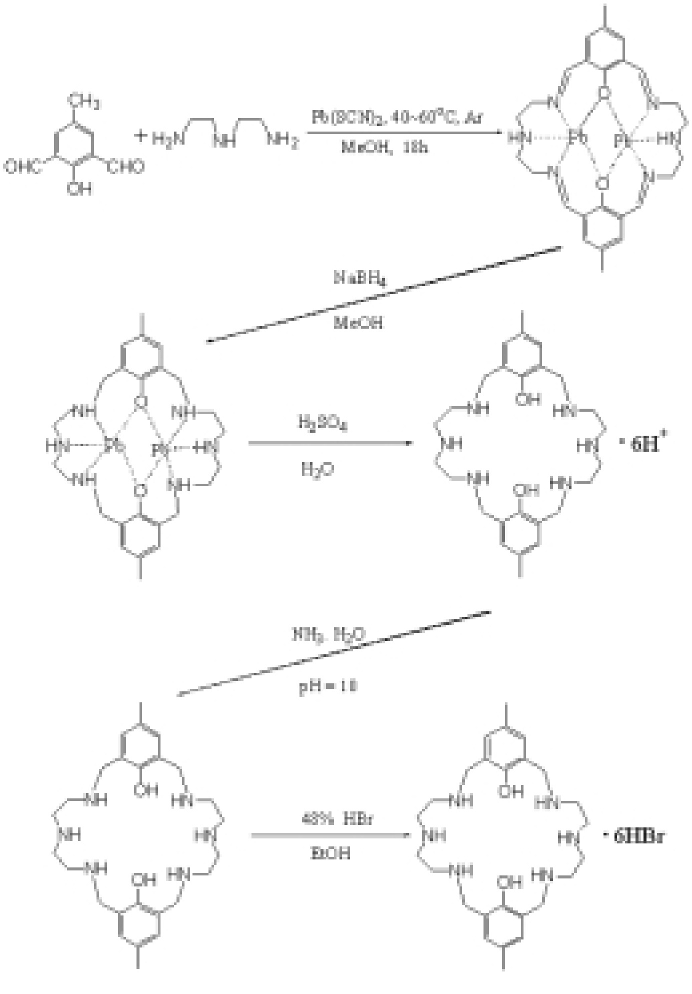
A mixture of 2,6-diformyl-*p*-cresol (1.32 g, 8.0 mmol) and $Pb(SCN)_2$ (2.70 g, 8.34 mmol) in 400 mL methanol was heated at 50~60$^0$ until most of the $Pb(SCN)_2$ was dissolved, and diethylenetriamine (0.83 g, 8.0 mmol) in 80 mL methanol was added dropwise over 4 h. The mixture was stirred for 18 h at 50~60$^0$ under Ar, and then cooled to room temperature. The powdery yellow precipitate was filtered and washed with methanol and chloroform. The precipitate was suspended in 200 mL methanol at room temperature, and 4.0g $NaBH_4$ in 20 mL water was then added in a period of 0.5h. After 2h additional stirring, the black Pb precipitate was filtered off. The filtrate was diluted with 200 mL water and then acidified with cold 8M/L $H_2SO_4$. The $PbSO_4$ precipitate formed was filtered off, and the filtrate was treated with $NH_3H_2O$ in an ice bath until pH = 10. The solution was then extracted with chloroform (2 × 200 mL), the organic phase was dried with anhydrous $Na_2SO_4$ for 24 h. The solution was filtered and then evaporated under reduced pressure to remove all the solvent, and the crude product was obtained. The crude product was dissolved in 50 mL ethanol, and 10 mL 48% HBr in 20 mL ethanol was added slowly until all the precipitate had formed. It was then filtered, and dried at $60^0C$ under vacuum for 3h, giving the flaky light yellow product as the hexahydrobromide salt, BDBPH·6HBr·$4H_2O$ (2.68 g, ~65%). $^1H$ NMR ($D_2O$), δ(ppm): 2.13 (s, -$CH_3$, 6H); 3.35 (q, ethylene, 16H); 4.21 (s, -$CH_2$, 8H); 7.16 (s, Aryl, 4H). FAB-MS, *m/z*: 471 (M+H). Anal. Calcd for $C_{26}H_{56}N_6O_6Br_6$, BDBPH·6HBr·$4H_2O$: C, 30.35; H, 5.44; N, 8.17. Found: C, 30.22; H, 5.46; N, 7.98.

## Discussion

The synthetic route of BDBPH is shown in **Scheme 1**. Chen Dian[6] reported the syntheses of macrocyclic and macrobicyclic Schiff bases in good yields by a dipodal [2+2] and a tripodal [2+3] condensation of a series of dialdehydes with diethylenetriamines and tris(2-aminoethyl)amine. Hydrogenation of the Schiff bases provided the corresponding saturated binucleating polyaza macrocyclic and cryptand ligands. This efficient and facile two-step synthetic method opens up a wide variety of new readily-accessible macrocyclic and cryptand ligands and their metal complexes for investigation. But this kind of method is not always successful; in some cases, it requires a rigid dialdehyde and a flexible polyamine. From the kinetic point of view, metal-free Schiff-base condensation of dialdehyde and diamine, in general, affords polymeric Schiff-base products[7]. Even in the case of metal-template reactions, the Schiff-base condensations sometimes give different macrocycles, *e.g.* the [2+2] tetra-Schiff base[8,9] or [3+3] hexa-Schiff base[10] macrocycles, depending upon the reaction conditions and template conditions. The template method has been used for many types of reactions of starting materials to produce macrocyclic or macrobicyclic ligands, but the most convenient method is the condensation of a polyamine with a dialdehyde to produce, through [2+2] or [2+3] dipodal or tripodal condensation, respectively, the tetra or hexa Schiff bases that may form binuclear complexes[11]. This type of reaction seems to be greatly aided by a central ion acting as an organizer for the Schiff base condensation. Among the metal templates used in the macrocyclization, Pb(II) is one of the most commonly applied, perhaps due to its easy formation of dinuclear Schiff base complexs[12-14].

In this work, the condensation of equimolar amounts of 2,6-diformyl-p-cresol and diethylenetriamine in the presence of $Pb(SCN)_2$ as a template agent leads to a hexaaimine Schiff base macrocyclization forming the dinuclear lead complex in considerable yield. The $Pb^{2+}$ with suitable ionic radius plays an important role in directing the reaction to

**Scheme 1.** The synthesis route of BDBPH



form and stabilize the [2+2] macrocyclization product rather than [1+1] and other forms. Reduction of the [2+2] Schiff base with sodium tretrahydroborate in methanol gave the corresponding saturated macrocycle. During the hydrogenation, some of the $Pb^{2+}$ was also reduced, and the unreduced $Pb^{2+}$ was still coordinated with the saturated macrocycle. After acidification of the solution, the $Pb^{2+}$ is removed in the form of $PbSO_4$ precipitation. The reduced macrocycle is stable in air, no evidence for oxidation of $CH_2$-NH to CH=N was found from either $^1$H NMR or FAB spectra.

## Conclusion

In summary, the results described above provide useful information about the synthesis of macrocyclic ligands with new structural characteristics. On the basis of the research, it would be of interest to study the molecular recognition of biologically important anions, such as organic and inorganic substrates, by the new ligand containing complexed metal ions, or by the protonated ligand, and then to investigate the catalytic behavior. Some of this research is in progress.

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