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THE SYNTHESIS OF NEW BINUCLEATING POLYAZA MACROCYCLIC AND MACROBICYCLIC LIGANDS: DIOXYGEN AFFINITIES OF THE COBALT COMPLEXES

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Abstract Six macrocyclic and five macrobicyclic Schiff bases have been synthesized by condensation of rigid dialdehydes with diethylenetriamine or tris(aminoethyl)amine, and have been reduced to the corresponding saturated hexaaza macrocyclic complexes or octaaza macrobicyclic complexes Six of the dicobalt complexes of these new ligands were found to be oxygen carriers

Introduction

Recently Lehn, Nelson and coworkers[1,2] reported the synthesis of macrocyclic and macrobicyclic Schiff bases in good yield by a dipodal(2 + 2) and a tripodal (2 + 3) condensation of a series of dialdehydes with diethylenetriamine and tris(2-aminoethyl)amine Hydrogenation of the Schiff bases provides 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

Results and Discussion

Synthetic Methods All the macrocyclic and macrobicyclic ligands listed in Table I were obtained in good yield (35-70%), by a one step dipodal (2 + 2) or tripodal (3 + 2) amine and aldehyde condensation to produce the macrocyclic or macrobicyclic Schiff bases, which were readily hydrogenated to the macrocyclic or macrobicyclic polyamines Of the eighteen macrocyclic and macrobicyclic ligands in Table I, eleven **2**, **4**, **6**, **8**, **9**, **10**, **14**, **15**, **16**, **17**, and **18** are new compounds The Schiff bases **1** and **13** seemed pure, but the NMR spectra obtained showed them to be complex, and probably consisted of mixtures of the desired macrocycle with an isomer formed by the addition of the NH groups to the imine double bonds, as has been reported recently for the macrocycle formed by the condensation of isophthaldehyde with DIEN [5]

Of the remaining Schiff bases, which were not characterized as new compounds, **3** and **7** were previously reported by MacDowell and Nelson,[6] **5** was prepared by Kol'chinskii and Yatsimirskii,[7] and **11** was synthesized by Drew et al [2]

Our investigations show that this kind of reaction is not always successful Glutaric dialdehyde with tris(2-aminoethyl)amine always forms polymers, although several solvents were employed This result may be due in part to the more flexible nature of the aldehyde

Table I Macrocyclic and Macrobicyclic Ligands Synthesized

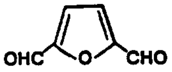
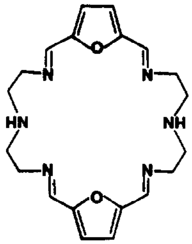
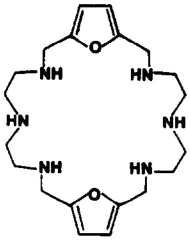
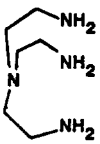
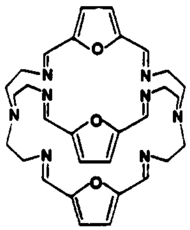
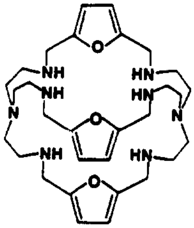
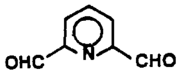
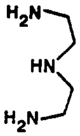
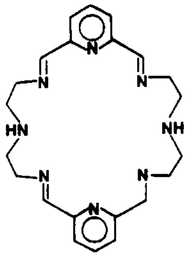
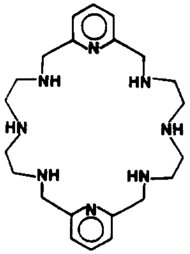
Aldehyde	Polyamine	Product	Product ($NaBH_4$ reduce)	Yield %
		 1 BisfuranBISDIEN Schiff base	 2 BisfuranBISDIEN	45
		 3 TrisfuranBISTREN Schiff base	 4 trisfuranBISTREN	38
		 5 BispyridineBISDIEN Schiff base	 6 BispyridineBISDIEN	70

Table I (continued)

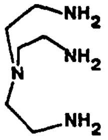
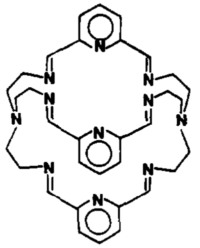
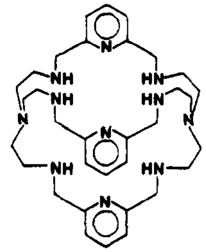
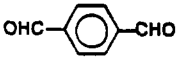
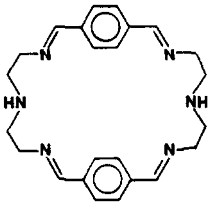
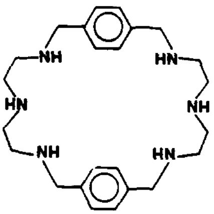
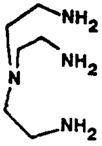
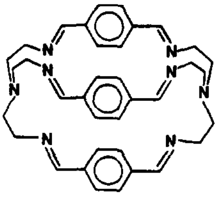
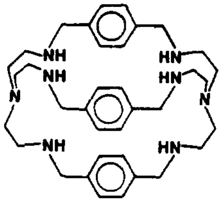
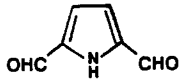
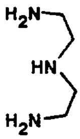
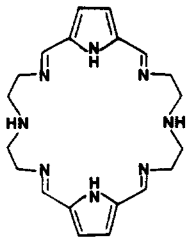
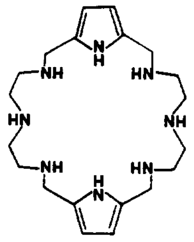
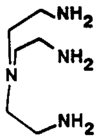
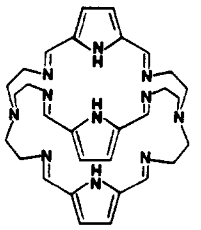
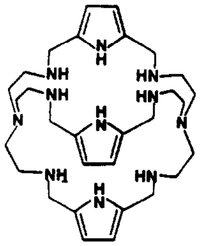
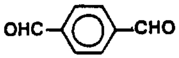
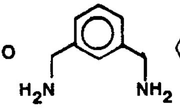
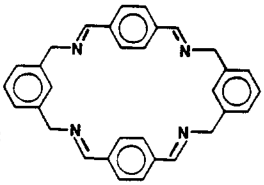
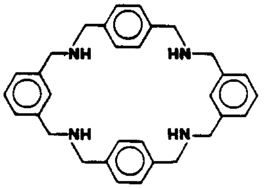
Aldehyde	Polyamine	Product	Product ($NaBH_4$ reduce)	Yield %
		 **7** TrispyridineBISTREN Schiff base	 **8** TrispyridineBISTREN	40
		 **9** Bis p-xylylBISDIEN Schiff base	 **10** Bis p xylylBISDIEN	56
		 **11** Tris-p-xylylBISTREN Schiff base	 **12** Tris p xylylBISTREN	40

Table I (continued)

Aldehyde	Polyamine	Product	Product ($NaBH_4$ reduce)	Yield %
		 **13** BispyrroleBISDIEN Schiff base	 **14** BispyrroleBISDIEN	40
		 **15** TrispyrroleBISTREN Schiff base	 **16** TrispyrroleBISTREN	34
		 **17** Bis-p-xylylbis-m-xylyldiamine Schiff base	 **18** Bis-p-xylylbis m-xylyldiamine	36

Although furan-2,5-dicarboxaldehyde is rigid, it does not form the (2 + 2) macrocyclic Schiff base when it reacts with the 2,6-bis(aminomethyl)pyridine The reason for this failure is unknown, and it is possible that the synthesis would be successful with a solvent other than those employed The fact that the solvent is very important, is indicated by the synthesis of trispyrroleBISTREN (16) When CH_3CN was used as solvent, a polymer always formed, but with MeOH as solvent a good yield of the macrobicyclic cryptand was obtained On the basis of the results described in this report, it seems that successful synthesis of macrocyclic and macrobicyclic Schiff bases by dipodal (2 + 2) or tripodal (3 + 2) condensation of a dialdehyde with a bis or tris primary amine requires a suitable solvent and a rigid dialdehyde with the carbonyl groups extended in the bridging positions Other combinations which did not yield macrocyclic or macrobicyclic condensation products are furan-2,5-dicarboxaldehyde with 2,6-bis(aminomethyl)pyridine, glutaric dialdehyde with TREN, and phthalic dialdehyde with DIEN and TREN In these cases it is possible that a change in solvent would promote the desired condensation (only CH_3CN and MeOH were employed in this study) It should also be possible to promote cyclic condensation with an appropriate metal ion as template Several examples of this type of template synthesis are summarized in a recent publication [8]

Oxygenation of the Binuclear Cobalt(II) Macrocyclic and Cryptate Complexes All of the hexaaza macrocyclic and octaaza macrobicyclic ligands synthesized (**2**, **4**, **6**, **8**, **10**, **12**, **14**, **16**, **18**) were converted to their dinuclear cobalt complexes and their dioxygen affinities were determined by the method described in the Experimental Of these only the dicobalt(II)-trisfuran-BISTREN, dicobalt(II)-tris-*p*-xylylBISTREN, and dicobalt(II)-bis-*p*-xylyl-bis-*m*-xylyldiamine were found not to react with dioxygen The remaining six cobalt(II) complexes all absorb dioxygen slowly at 25°C from air at pH ~10 The color of the solutions changed from the beginning green or yellow of the dinuclear complex to red brown of the dioxygen adduct, and then to the red color typical of inert Co(III) complexes After the oxygenation had been carried our for more than 24 hours, all six of the cobalt(II) complexes had absorbed more than 100% of the dioxygen needed for formation of a peroxo-bridged dinuclear cobalt dioxygen complex The uv-visible spectra of the final solutions did not have an absorption band characteristic of dioxygen complexes, indicating that degradation to inert species was complete

It is noted that all of the dinuclear Co(II) complexes absorb dioxygen rapidly at first, and then more slowly as degradation begins to take place as a secondary reaction The fact that more than the theoretical amount of dioxygen is absorbed indicates that the degradation products initially formed may also have affinity for dioxygen and thus, at least initially, begin a secondary cycle of oxygenation and degradation This type of successive oxygenation and degradation has been observed for other cobalt polyamine oxygen carrying complexes [9]

If one makes the reasonable assumption that formation of 50 per cent of the theoretical amount of dioxygen complexes takes place without a predominant amount of degradation having occurred, it would be possible to use the times of 50% uptake indicated in Table II as rough measures of the rates of dioxygen complex formation On this basis rates of uptake of dioxygen by the dinuclear cobalt(II) complexes of the various binucleating ligands studied vary in the order **16** < **2**, **8** < **6** < **10**, **14** In general it seems that the macrocyclic complexes take up dioxygen more rapidly than do the cryptands This difference in rate, plus the fact that two of the cryptands do not bind oxygen at all, indicates that steric factors probably play an important role in determining the rate of oxygenation

Table II Uv-visible Spectra and Dioxygen Uptake for Dicobalt Dioxygen Complexes

Dioxygen Complex	Peak, nm	Time of 50% Dioxygenation (min)
Co(II)-bispyrroleBISDIEN	340	24
Co(II)-trispyrroleBISTREN	345	60
Co(II)-bis-*p*-xylylBISDIEN	360	20
Co(II)-bispyridineBISDIEN	460	29
Co(II)-trispyridineBISTREN	370	34
Co(II)-bisufuranBISDIEN	360	40

Uv-Visible Absorbance Spectra Because of rapid degradation of the dioxygen complexes, their absorbances must be measured within the first thirty minutes of dioxygen exposure in order to see the absorbance peaks As in the case of the cobalt trispyrroleBISTREN dioxygen complex, when air is bubbled through the solution for more than 30 minutes, the uv-visible spectra shows a strong peak at about 310 nm, which increases with further exposure to dioxygen This peak cannot be assigned to the dioxygen complex, because when HCl solution was added to the reaction mixture to reduce the pH to 2 0, the 310 nm peak did not disappear This peak is assigned to the inert dicobalt(III) complex formed by the irreversible degradation reaction, indicated by reaction (2)

$$\text{Oxygenation} \quad Co(II)_2L^{4+} + O_2 \longrightarrow Co\text{-}O\text{-}O\text{-}CoL^{4+} \quad (1)$$

$$\text{Degradation} \quad Co\text{-}O\text{-}O\text{-}CoL^{4+} + 2H^+ \longrightarrow H_2O_2 + Co_2L^{6+} \quad (2)$$

The presence of H_2O_2 in the reaction mixture was confirmed by standard iodometric titration The overlapping of reactions (1) and (2) prevents more than qualitative measurement of the absorbance maxima (some of which are visible only as shoulders) for the six dioxygen complexes listed in Table II

Experimental

Materials The following compounds were all reagent grade and were used without further purification cobalt acetate ($CoAc_2$ $4H_2O$), Fisher Scientific Company, terephthaldicarboxaldehyde, diethylenetriamine (DIEN), tris(2-aminoethyl)amine (TREN), 2,6-pyridinedicarboxaldehyde, and 2,5-furandimethanol (Aldrich Chemical Company)

Pyrrole-2,5-dicarboxaldehyde was prepared by the method of Miller and Olsson [3] Furan-2,5-dicarboxaldehyde was prepared by the method of Alenik and Noviskii [4]

General synthesis of macrocyclic and macrobicyclic ligands A solution of 0 0090 mol of aldehyde in 150 ml of CH_3CN was added dropwise to 0 0090 mol of diethylenetriamine or 0 0060 mol tris(2-

aminoethyl)amine in 280 ml CH_3CN over 1 5 hr at room temperature with stirring (MeOH was employed as solvent for the condensation of pyrrole with TREN) After the mixture was stirred for 24 hr the precipitate which formed was filtered out and washed with ether The Schiff base was recrystallized from EtOH and the product was then dissolved in 300 ml MeOH The solution was heated to 45°C, and 2 5 g of $NaBH_4$ was added to the solution with stirring After the addition of the $NaBH_4$ was complete, the reaction solution was stirred an additional hour, and then cooled The reaction mixture was evaporated to dryness, 10 ml H_2O and 100 ml of CH_2Cl_2 were added to the mixture to extract the product The organic phase was filtered and the filtrate was evaporated to dryness The residue was mixed with 10 ml of 48% HBr and 100 ml of EtOH The precipitate was filtered off and washed in EtOH and ether The product was recrystallized from EtOH The compounds were characterized by ^1H NMR, ^{13}C NMR, M S , and elemental analysis

BisfuranBISDIEN (2) ^1H NMR (D_2O) 3 5 (s, 16H, -CH_2), 4 4 (s, 8H, furan-CH_2), 6 6 (s, 4H, furan) Anal Calcd for $C_{20}H_{34}N_6O_2$ 6HBr C, 27 43, H, 4 60, N, 9 59 Found C, 27 44, H, 5 01, N, 9 34

TrisfuranBISTREN (4) ^1H NMR (D_2O) 2 7 (m, 12H, N-CH_2), 3 2 (m, 12H, CH_2-NH), 4 2 (s, 12H, furan-CH_2), 6 6 (s, 6H, furan) Anal Calcd for $C_{30}H_{48}N_8O_3$ 6HBr 2 5H_2O C, 32 78, H, 5 41, N, 10 19 Found C, 32 79, H, 5 55, N, 10 11

BispyridineBISDIEN (6) ^1H NMR (D_2O) 3 6 (m, 16H, -CH_2), 4 4 (s, 8H, pyridine-CH_2), 7 4 (d, 4H, pyridine), 7 8 (t, 2H, pyridine) Anal Calcd for $C_{22}H_{36}N_8$ 6HBr H_2O C, 28 85, H, 4 84, N, 12 23 Found C, 28 98, H, 4 91, N, 12 46

TrispyridineBISTREN (8) ^1H NMR (D_2O) 3 1 (m, 12H, -CH_2), 3 2 (m, 12H, -CH_2), 4 4 (s, 12H, py-CH_2), 7 3 (d, 6H, pyridine), 7 8 (t, 3H, pyridine) ^{13}C NMR (D_2O) 44 0 ppm (-N-CH_2), 50 6 ppm (NH-CH_2), 52 1 ppm (pyridine-CH_2), 124 4, 140, 151 ppm (pyridine) Anal Calcd for $C_{33}H_{51}N_{11}$ 6HCl 5H_2O C, 43 52, H, 7 42, N, 16 92 Found C, 43 71, H, 7 43, N, 16 58

Bis-p-xylylBISDIEN Schiff Base (9) ^1H NMR ($CDCl_3$-4MeSi) 3 0 (m, 8H, NH-CH_2), 3 8 (M, 8H, =N-CH_2), 7 6 (s, 8H, benzene), 8 3 (s, 4H, -CH=N) The molecular weight measured from the mass spectra is 380 Anal Calcd for $C_{24}H_{30}N_6$ C, 71 61, H, 7 51, N, 20 88 Found C, 71 57, H, 7 51, N, 20 80

Bis-p-xylylBISDIEN (10) ^1H NMR (D_2O) 3 2 (m, 8H, NH-CH_2), 3 3 (m, 8H, NH-CH_2), 4 3 (s, 8H, benzene-CH_2), 7 5 (s, 8H, benzene) Anal Calcd for $C_{24}H_{38}N_6$ 6HBr C, 32 17, H, 4 95, N, 9 37 Found C, 32 65, H, 5 10, N, 9 17

Tris-p-xylylBISTREN (12) ^1H NMR (D_2O) 2 7 (m, 12H, N-CH_2), 3 2 (m, 12H, NH-CH_2), 4 1 (s, 12H, benzene-CH_2), 7 3 (s, 12H, benzene) Anal Calcd for $C_{36}H_{54}N_8$ 6HBr 4 5H_2O C, 37 11, H, 5 97, N, 9 62 Found C, 37 15, H, 6 13, N, 9 51

BispyrroleBISDIEN (14) ^1H NMR (D_2O) 3 3 (M, 8H, NH-CH_2), 3 4 (M, 8H, NH-CH_2), 4 3 (s, 8H, pyrrole-CH_2), 6,3 (s, 4H, pyrrole) Anal Calcd for $C_{20}H_{36}N_8$ 6HBr 0 5H_2O C, 27 20, H, 4 91, N, 12 69 Found C, 27 18, H, 5 08, N, 12 45

TrispyrroleBISTREN Schiff Base (15) ^1H NMR ($CDCl_3$-4MeSi) 2 7 (m, 12H, N-CH_2), 3 5 (m, 12H, C=N-CH_2), 6 8 (s, 6H, pyrrole), 7 8 (s, 6H, N=CH) Anal Calcd for $C_{30}H_{39}N_{11}$ 1 25H_2O C, 62 53, H, 7 26, N, 26 74 Found C, 62 39, H, 7 44, N, 26 94

TrispyrroleBISTREN (16) ^{1}H NMR (D_2O) 2 7 (m, 12H, N-CH_2), 3 2 (m, 12H, N-CH_2), 4 1 (s, 12H, pyrrole-CH_2), 6 3 (s, 6H, pyrrole) Anal Calcd for $C_{30}H_{51}N_{11}$ 6HBr $5H_2O$ C, 31 57, H, 5 92, N, 13 50 Found C, 31 50, H, 6 13, N, 13 35

Bis-p-xylyl-bis-m-xylyldiamine Schiff Base (17) ^{1}H NMR ($CDCl_3$-4MeSi) 4 9 (s, 8H, benzene-CH_2), 7 2-7 5 (m, 8H, benzene), 7 7 (s, 8H, benzene), 8 4 (s, 4H, N=CH-) Anal Calcd for $C_{32}H_{28}N_4$ C, 82 02, H, 6 02, N, 11 96 Found C, 81 74, H, 6 24, N, 11 90

Bis-p-xylyl-bis-m-xylyldiamine (18) ^{1}H NMR (D_2O) 4 1 (s, 8H, NH-CH_2), 4 2 (s, 8H, NH-CH_2), 7 2 (s, 2H, benzene), 7 4 (s, 8H, benzene), 7 5 (s, 6H, benzene) Anal Calcd for $C_{32}H_{36}N_4$ 4HBr C, 48 03, H, 5 04, N, 7 00 Found C, 48 07, H, 5 06, N, 6 96

Spectroscopic Measurements The proton and carbon-13 NMR spectra were recorded with a Varian XL-200 NMR spectrometer operating at 200 M Hz, and the chemical shifts are reported in ppm on the scale relative to tetramethylsilane, with $CDCL_3$ as solvent

The mass spectra were obtained with a VG analytical 70S high resolution double focusing magnetic sector spectrometer with attached analytical 11/250J data system, operated by the Department of Chemistry Mass Spectrometry Facility Elemental C, H, and N analyses were performed by Galbraith Laboratories, Inc , Knoxville, Tennessee

Oxygen Uptake Measurements The oxygen absorption of the dicobalt complexes were measured by determining the volume of gaseous dioxygen taken up by the complexes in aqueous solution with the apparatus and procedure described previously [10]

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