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Note

A novel sodium template approach for preparing tetraimine macrocyles of 2,6-diformyl-4-methylphenol and diamino derivatives

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Abstract

A number of [2+2] tetraimine macrocycles were synthesised, employing sodium 2,6-diformyl-4-methylphenolate as a precursor to undergo Schiff base condensation with a series of diamino compounds. The resulting dinuclear sodium macrocyclic complexes have been spectroscopically characterised by IR, mass and ^{1}H NMR spectra. The sodium ion here plays a unique template role in the formation of macrocycles with different sizes of cavity in comparison to the other common-used templates such as alkaline earth metal, transition metal and rare earth metal ions.

Keywords: Alkali metal complexes; Macrocycle complexes; Imine complexes

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1. Introduction

Macrocyclic ligands and macrocyclic complexes have been the focus of research in recent years with interest in the recognition of particular metal ions [1] and for modelling of metallo-biosites [2]. Based on the bonding strength of the ligating groups and the cavity of the ring, macrocyclic ligands can combine with metal ions optionally. Thus this kind of compound offers a direct and similar way to mimic the biological system, in which biological cycles containing active metal centres are largely involved. In addition, polynuclear macrocyclic complexes have also been widely investigated for their spectroscopic and magnetic properties as well as their potential application in the extraction or recovery of metals [3,4].

For the synthesis of macrocycles, dicarbonyl precursors and a wide range of diamines have been used. Among these precursors 2,6-diformyl-4-methylphenol was the first one applied for the preparation of the macrocyclic Schiff base by Pilkington and Robson [5] in 1970 via a template method. Since then various diamines have been concerned in cyclo-condensation with 2,6-diformyl-4-substituted phenol by the template [6,7] or sometimes non-template [8] method to prepare [1+1] diimine- and [2+2] tetraimine-typed macrocycles. Since the size of the cation used as a template has proved to be of importance in controlling the synthetic pathway in the Schiff base system [9], transition metals are generally used for the smaller rings, and rare earth metals for the larger ones.

Alkali metals as templates have been previously applied in the synthesis of crown ethers since Pedersen's discovery of dibenzo-18-crown-6 [10]. However, they are seldom involved in the formation of a macrocyclic Schiff base. Recently we discovered a new way to have sodium ion function effectively as a template in the generation of the Schiff base by using sodium 2,6-diformyl-4-methylphenolate as a precursor [11]. In our initial synthesis, the disodium complexes of a Robson macrocycle has been used as the 'free ligand' which readily undergoes transmetallation by transition metals to form dinuclear macrocyclic complexes [12]. Further

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experiments show that several types of macrocycles can be obtained by this method. As part of our research, we report here the synthesis of a series of [2+2] tetraimine macrocycles.

2. Experimental

2.1. Starting materials

2,6-Diformyl-4-methylphenol (dmp) was prepared using the procedure described by Taniguchi [13]. Activated MnO_2 was obtained from Aldrich and heated at 130 °C for 5 h before use. Diamino derivatives used in the synthesis of L_A to L_F were of commercial grade used without further purification; polyamines for L_G and L_H were prepared by the literature method [14].

Sodium 2,6-diformyl-4-methylphenolate (sdmp) was obtained by mixing equimolar amounts of dmp and NaOH in ethanol which produced the product as a yellow powder in 80% yield. *Anal.* Calc. for C_9H_7ONa: C, 58.06; H, 3.76. Found: C, 58.23; H, 3.59%. IR (cm^{-1}): ν (C=O) 1690vs. ^1H NMR (d^4-CH_3OH): δ (ppm) 10.31 (s, 2×CHO), 7.56 (s, ArH_2), 2.24 (s, $ArCH_3$).

2.2. Preparation of macrocycles

Na_2L_A. An ethanolic solution (10 ml) of 1,3-diaminopropane (1.1 mmol) was added into a suspension of sdmp (1 mmol) in absolute ethanol (20 ml). The mixture was stirred and heated to reflux. As the reaction progressed, the solution became clear at first and then solids gradually appeared. After 1 h, the reaction was cooled to room temperature, and the precipitating yellow powder was collected and dried in vacuo.

Na_2L_B. A mixture of sdmp (1 mmol) and 1,5-diamino-3-oxapentane (1.1 mmol) in absolute ethanol (20 ml) was stirred at room temperature. At first the solution gradually cleared, but soon solids precipitated. The reaction was kept under stirring for 2 h, then the products were isolated and dried in vacuo.

Na_2L_C. Sdmp (1 mmol) and 3,3′-iminobispropylamine (1.1 mmol) were blended in absolute ethanol (20 ml). The suspension was kept stirring at room temperature, and gradually became clear. After the reaction had continued for 3 h, the resulting yellow solution was filtered to remove insoluble impurities. Then the filtrate was concentrated on a rotary evaporator, and ether was poured in until solids deposited. The product was dried in vacuo and kept in a desiccator over silica gel.

The remaining dinuclear sodium macrocyclic complexes were synthesised using the method described for Na_2L_C.

Yields and microanalytical data are presented in Table 1. Main IR absorptions and principal FAB-MS peaks of all the compounds are listed in Table 2 and 3, respectively. Typical ^1H NMR data (d^4-CH_3OH) are: Na_2L_A: δ (ppm) 8.44 (s, 4×CH=N), 7.43 (s, 2×ArH_2), 3.71 (m, 2×$NCH^*{}_2CH_2CH^*{}_2N$), 2.24 (s, 2×$ArCH_3$), 2.13 (m, 2×$NCH_2CH^*{}_2CH_2N$); Na_2L_B: δ (ppm) 8.39 (s, 4×CH=N), 7.13 (s, 2×ArH_2), 3.73 (m, 2×$NCH_2CH_2OCH_2CH_2N$), 2.11 (s, 2×$ArCH_3$); Na_2L_G: δ (ppm) 8.57 (s, 4×CH=N), 7.37 (s, 2×ArH_2), 3.64 (t, 4×N=CH_2R), 2.58 (m, 12×R_2NCH_2R), 2.21 (s, 2×$ArCH_3$), 1.85 (m, 4×$R_2NCH_2CH^*{}_2CH_2N$=), 1.03 (m, 4×$R_2NCH_2CH^*{}_3$).

2.3. Instrumentation

Carbon, hydrogen and nitrogen were determined with a Perkin-Elmer elemental analyser model 240C. IR spectra were recorded as solid KBr pellets on a 170SX FT-IR instrument. FAB mass spectra were measured on a VG-2AB-HS mass spectrometer and carried out in different matrices (nitrobenzyl alcohol or glycerol) using xenon gas as primary beam. Proton NMR spectra were determined on a Varian FT-80 spectrometer; all peak positions are relative to TMS.

3. Results and discussion

A scheme of the synthetic route is given in Fig. 1. Since all compounds except Na_2L_A are readily hygroscopic in the air, they gained weight in the course of the elemental analysis measurement. The analytical data are only in agreement with the theoretical values when crystalline water was added in.

The IR spectra of all the complexes showed no bands characteristic of the stretching frequency of the carbonyl groups in sodium 2,6-diformyl-4-methylphenolate, nor of the symmetric and unsymmetric stretching frequencies (ν_s 3324–3340, ν_{as} 3380–3398 cm^{-1}) for the primary amine groups. Sodium complexes, however, all possess a very strong IR absorption band in the range 1633–1642 cm^{-1} assigned to the imino stretching mode, supporting the Schiff base linkage. Strong peaks in the range 1518–1527 cm^{-1} are attributable to the phenolic $>$C–O groups acquiring partial double bond character through conjugation with the imine system in the chelate ring [15]. Compounds Na_2L_C–Na_2L_H exhibit broad bands between 3395 and 3421 cm^{-1} indicative of ν(OH) stretching vibrations of water, whereas ν(NH) stretching modes in Na_2L_C–Na_2L_F were weakly observed, almost overlapped by the strong water absorption. In particular, the presence of a strong band at 1225 cm^{-1} ascribed to ν(C–O–C) reveals the ether chain in Na_2L_B.

In order to find out whether the Schiff base is the [1+1] or [2+2] condensation product of sodium 2,6-diformyl-4-methylphenolate and the diamino derivatives, the positive ion FAB mass spectra of all compounds were obtained. To a large extent, the complexes de-

Table 1
Yields and microanalytical data (calculated values in parentheses)

Compound	Yield[a] (%)	C (%)	H (%)	N (%)
Na_2L_A	90	64.04 (64.29)	5.95 (5.80)	12.16 (12.50)
$Na_2L_B+2.5H_2O$	79	56.55 (56.42)	6.49 (6.33)	9.45 (10.13)
$Na_2L_C+12H_2O$	71	45.38 (46.27)	8.44 (8.23)	11.40 (10.80)
$Na_2L_D+5H_2O$	68	52.22 (52.79)	7.82 (7.62)	17.22 (16.42)
$Na_2L_E+10H_2O$	77	48.82 (49.28)	8.58 (8.45)	13.56 (13.53)
$Na_2L_F+6H_2O$	90	53.07 (52.75)	8.24 (7.97)	14.90 (15.38)
$Na_2L_G+6H_2O$	26	58.59 (58.06)	8.21 (8.99)	12.05 (12.90)
$Na_2L_H+4H_2O$	75	65.13 (64.86)	7.17 (7.37)	10.51 (10.32)

[a] Yields were calculated without considering crystalline water, because almost all compounds obtained weight during measurement.

Table 2
Main IR absorptions

Compound	IR ν (cm^{-1})
Na_2L_A	1633vs, 1518s
Na_2L_B	1642vs, 1523s, 1225s
Na_2L_C	3409br, 3297w, 1635vs, 1527s
Na_2L_D	3420br, 3303w, 1637vs, 1523s
Na_2L_E	3421br, 3306w, 1636vs, 1526m
Na_2L_F	3395br, 3297w, 1636vs, 1525s
Na_2L_G	3412br, 1637s, 1526w
Na_2L_H	3412br, 1637s, 1526m

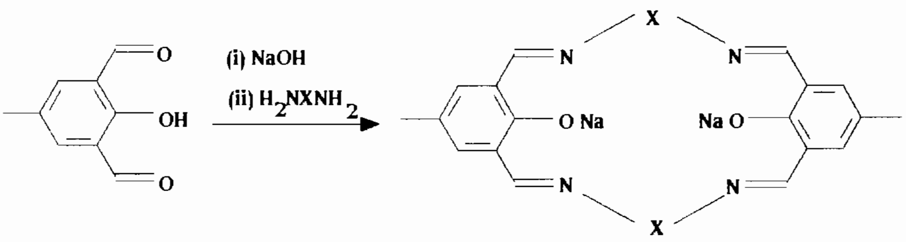
composed and parent molecular ions were not observed, similar to the literatures reports concerning the ligands [15,16]. The only exception was Na_2L_A which gave a parent ion at *m/z* 449 in low abundance corresponding to the $M+1$ peak. However, a conspicuous peak ascribable to the protonated ligand $[H_3L]^+$ among these spectra (exclusive of Na_2L_D) was observed, in which two protons balance two phenolic anions and the third provides the positive charge. In the spectra of homodinuclear macrocyclic lanthanide complexes of L_D [16], definite fragments of the original complexes and/or the protonated ligands were detected. For instance, dinuclear neodymium, europium and erbium complexes gave peaks attributed to the protonated ligand $[H_3L_D]^+$. But neither of these two peaks appeared in Na_2L_D. $[NaH_2L]^+$ species arising from the loss of a sodium cation were also observed in each complex with the exception of Na_2L_F. It is of interest to note that the loss of a sodium cation from the molecular species would generate a proton, unlocalized, to add in, contrary to the splitting mode of other complexes with similar macrocyclic ligands [15–17]. Parent molecular peaks and their fragments of the [1+1] cyclization mode were not discovered in all spectra, demonstrating the formation of [2+2] tetraimine macrocyclic Schiff bases as well.

The ^1H NMR spectra were obtained with CD_3OD as solvent since most of the macrocyclic complexes were hardly soluble either in non-oxidising organic solvents or water. Even in CD_3OD, not all compounds could form a solution with sufficient concentration for measurement, only those of Na_2L_A, Na_2L_B and Na_2L_G could provide significant information. It should be noted that the attaching alkyl groups in Na_2L_G could increase its solubility in organic solvents, which presented a good spectrum for analysis. Among these three spectra, no peaks assigned to CHO groups in sodium 2,6-diformyl-4-methylphenolate were found, again confirming the formation of the 2+2 macrocycle.

Two decades ago, Robson initiated a series of studies concerned with a rational synthetic approach to cluster compounds [5,18], in which L_A was prepared as the macrocyclic ligand. Following research has resulted in many kinds of macrocyclic ligands by a similar method [9]. In Fig. 1, where $X=(CH_2)_n$, $n=2$, 3 or 4 [5,19], the smaller rings, transition metals, are found suitable

Table 3
Principal FAB-MS peaks (*m/z*) with abundances (%) in parentheses

	Na_2L_A	Na_2L_B	Na_2L_C	Na_2L_D	Na_2L_E	Na_2L_F	Na_2L_G	Na_2L_H
MW	448	508	562	592	648	620	760	742
$[Na_2HL]^+$	449 (6)							
$[NaH_2L]^+$	427 (100)	487 (15)	541 (8)	571 (16)	627 (14)		739 (86)	721 (13)
$[H_3L]^+$	405 (6)	465 (31)	519 (15)		605 (21)	577 (17)	717 (10)	699 (66)



Ligand	X
H_2L_A	$(CH_2)_3$
H_2L_B	$(CH_2)_2O(CH_2)_2$
H_2L_C	$(CH_2)_3NH(CH_2)_3$
H_2L_D	$(CH_2)_2NH(CH_2)_2NH(CH_2)_2$
H_2L_E	$(CH_2)_3NH(CH_2)_2NH(CH_2)_3$
H_2L_F	$(CH_2)_2NH(CH_2)_3NH(CH_2)_2$
H_2L_G	$(CH_2CH_2CH_2)_2N(CH_2)_2N(C_2H_5)_2$
H_2L_H	$(CH_2CH_2CH_2)_2NCH_2C_6H_5$

Fig. 1. Scheme of synthetic route.

for the template syntheses; where $X=(CH_2)_2Y(CH_2)_2$ or $(CH_2)_2Y(CH_2)_2Y(CH_2)_2$, Y = NH or O [20], the larger rings, lanthanide cations, could work well as the template. Although different metals could form their macrocyclic complexes with the same ligand, they should be prepared using different metal templates. The shortcoming of the above synthesis is obvious, because transmetallation between related metals does not always occur and the pertinent free ligand is difficult to isolate. Furthermore, not all transition metals or rare earth metals are suitable for use as a template for the macrocyclic synthesis.

Alkaline earth metals usually function as templates when other dicarbonyl precursors are used, e.g. 2,6-diacetylpyridine and 2,5-diformylthiophene, but they seemed infeasible in the [2+2] cyclisation of 2,6-diformyl-4-methylphenol with polyamines [21,22]. In our experiment, sodium cation appeared as a versatile template in this cyclic condensation reaction, and was utilised in the preparation of tetraimine Schiff base macrocycles. Compared with other approaches, this method is quite simple and products are usually obtained with high yields. Moreover evidence has shown that sodium ions in these compounds are easily replaced by transition metals, which turns out to be of great significance in the preparation of related metal complexes. Further studies will be undertaken.

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