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Synthesis of new macrocyclic ligands for hetero-multinuclear transition-metal complexes

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Abstract. The [3 + 3] macrocyclic compounds 2a-2c were easily prepared by cyclization of the dialdehyde 8 with the appropriate diamines in refluxing CH₃CN/MeOH (1/1), in the presence of Ba²⁺ as a template ion. These macrocycles contain three salen units and are therefore, in combination with the crown ether interior, potentially tetranucleating. The length of the diamine bridge and the temperature at which the reaction is carried out, appear to influence the size of the macrocycle formed. In this way, the [4 + 4] macrocycle 2d could be formed selectively over the [3 + 3] macrocycles by carrying out the reaction at room temperature.

Introduction

Schiff-base-containing macrocyclic ligands designed for complexing more than one transition metal, are widely used in coordination chemistry¹⁻⁴. The distinctive properties of these multinuclear complexes are related to the close proximity of two or more transition metal cations. This is of theoretical interest because of metal-metal interactions⁵, and also plays an important role when the complexes are used in studies as enzyme mimics or as homogeneous catalysts. The metals can function as multiple coordination sites for substrate binding and/or activation. Complexes containing two different transition metals with a short intermetallic distance, have interesting redox properties⁶. Furthermore, *Floriani* et al.⁷ have shown that an alkaline cation (Lewis acid) can assist in the activation and binding of small substrate molecules, like CO₂, to a Co(I) center (Lewis base) by stabilizing the CO_2^- intermediate. Previously we have reported on hetero-di- and -trinuclear complexes combining transition metal cations and alkali-metal or alkaline-earth-metal cations⁸ (Chart 1).

These macrocyclic ligands contain a salen unit which forms stable transition-metal complexes⁹, and a crownether unit which complexes various alkali- or alkalineearth-metal cations¹⁰. In these hetero-multinuclear complexes it is possible to tune the redox behavior of the transition metals by co-complexation of various 'hard' cations¹¹.

The electrocatalytic properties of the Ni cation in complexes 1a and 1b are influenced by co-complexation of the Ba^{2+} cation. The Ni/Ba complex converts benzyl chloride and acetic anhydride into 1-phenylpropan-2-one (11%), whereas the Ni complex does not show any catalytic activity¹².

In this paper we describe an extension to a tetranucleating macrocycle by combining the 'hard' polyether cavity with three 'soft' salen units. We report the synthesis of a macrocyclic ligand, in which six phenolic OH groups are



Chart 1.

bridged intramolecularly by hydrogen bonds to the imine nitrogens¹³. In this way the oxygens resemble the arrangement in 18-crown-6 with the ethylene bridges replaced by salen units (Chart 2).

Results and discussion

The synthesis of the dialdehyde 8, required for the macrocyclization with an appropiate diamine, is depicted in Scheme 1^{14,15}. Firstly, naphthalene-2,3-diol was diallylated with allyl bromide in acetone, using K_2CO_3 as a base¹⁶. Subsequently a Claisen rearrangement at 170°C of the 2,3-diallyloxynaphthalene gave the 1,4-di(prop-1enyl)naphthalenediol. The product was not isolated but immediately reacted with acetyl chloride, in order to prevent oxidation reactions at the phenolic OH groups in the subsequent steps. Isomerization of the double bonds to the 2-alkenes was carried out using RhCl₃ as catalyst in THF/EtOH at 50°C¹⁷. After this isomerization, ozonolysis was carried out in CH₂Cl₂ at -70°C, followed by reductive work-up with dimethyl sulfide to give the dialde-





hyde 7 in 90% yield. Deprotection of the phenolic OH groups gave 2,3-dihydroxy-1,4-naphthalenedialdehyde. The macrocyclic ligand was prepared by a [3 + 3] macro-

cyclic condensation reaction of dialdehyde 8 and several diamines, using Ba²⁺ as a template cation. The macrocyclization with diamines 9a-9c, in the presence of 0.33 mol% of Ba(CF₃SO₃)₂, gave the highly colored [3 + 3]macrocycles 2a-2c in approximately 70% yield (Scheme 2). Cs(CF₃SO₃) and Pb(ClO₄)₂ did not produce cyclic products, but, when the Ba²⁺ cation was used, a macrocyclic product was formed. The role of the template cation was shown unambiguously by the following control experiment. When the dialdehyde 8 and an appropiate diamine were refluxed in the absence of $Ba(CF_3SO_3)_2$, no cyclic products were obtained according to FAB-MS, and only a high molecular weight residue was formed. When this was redissolved and refluxed again in the presence of the Ba^{2+} salt, a cyclic product was formed, albeit in somewhat lower yields than in the templated reaction of dialdehyde and diamine.

Compounds 2 were characterized by ¹H- and ¹³C-NMR, fast atom bombardment (FAB) MS and Fourier-Transform (FT) IR spectroscopy. The simplicity of the ¹H NMR spectrum of macrocycle 2a is a good indication that a macrocycle is formed. Because of the high symmetry, all phenolic and imine protons are equivalent and give only one singlet each. The ¹H-NMR spectrum of 2b shows two



imine protons at room temperature (δ 9.35 and 9.38 ppm). This means that this macrocycle is not completely planar. When the spectrum is recorded at 75°C, the two signals coalesce at δ 9.36 ppm. In the FT-IR spectra the imine C=N stretch frequency for all macrocyles was present at approximately 1620 cm⁻¹. In addition, FAB-MS shows only peaks corresponding to the molecular ion peak (M⁺) and the subsequent loss of one or two counter-anions ($CF_3SO_3^-$). The largest intensity in the positive FAB-MS spectrum is the $(M-CF_3SO_3)^+$ cation, but in the negative FAB-MS there is a small peak corresponding to M⁻. With propane-1,3-diamine as the diamine, a mixture of [3+3] and [4+4] macrocycles was formed. When the reaction was carried out at room temperature instead of reflux temperature, the [4 + 4] macrocycle formed selec-tively over the [3 + 3] product¹⁸. In the FAB-MS spectrum there were also peaks present that could be attributed to a [2+2] macrocycle. The [4+4] macrocycle 2d was purified by column chromatography. The ¹H-NMR spectrum shows a highly symmetric pattern with two imine protons at δ 9.90 and 9.84 ppm which indicate some deviation from planarity.

Preliminary FAB-MS results indicate that, with transition metals like Cu(II), Ni(II) and Zn(II), tetranuclear complexes are formed. The FT-IR spectra show a shift in the imine C=N stretch to lower wavelengths, indicating complexation of the transition metals in the salen moiety¹⁹. Plasma-desorption (PD) and electrospray-ionisation (EI) MS indicate intermolecular stacking of the macrocyclic complexes.

Conclusions

Macrocyclic ligands are easily formed when dialdehyde 8 is refluxed with various diamines in the presence of Ba^{2+} as a template ion. The macrocycles 2a-2c are made up of three dialdehydes and three diamines. Lowering the temperature and using propane-1,3-diamine resulted in a [4 + 4] instead of a [3 + 3] macrocyclization. Preliminary FAB-MS data show that the corresponding transition metal complexes can be formed.

Experimental

General methods

NMR spectra were recorded on a Bruker AC 250 spectrometer in CDCl₃, unless otherwise stated. The residual protons of the solvents were used as internal standard. Mass spectra were obtained with a Finnigan MAT 90 spectrometer. FAB-MS spectra were obtained with 3-nitrobenzyl alcohol as a matrix. IR spectra were recorded with a Biorad Digilab FTS 60 IR-spectrometer. Melting points were determined using a Reichert melting point apparatus and are uncorrected. Elemental analyses were carried out with a Model 1106 Carlo Erba Strumentazione elemental analyzer. CH_2Cl_2 was distilled over CaCl₂ before use. CH_3CN (p.a., Merck) was stored over molecular sieves (4 Å) prior to use. THF was distilled from sodium/benzophenone. Other chemicals were of reagent grade and used without further purification. All reactions were carried out under an argon atmosphere.

1,4-Bis(prop-2-enyl)-2,3-diacetoxynaphthalene (5)

2,3-Bis(prop-2-enyloxy)naphthalene (100.0 g, 0.417 mol) was heated neat at 170°C for 1 h. When the rearrangement was complete on NMR, the temperature was lowered to room temperature and 500 ml of CH₂Cl₂ and 100 ml of Et₃N were added. At 0°C, acetyl chloride (76.5 g, 1.0 mol) was added over a period of 1 h. After stirring overnight, the reaction mixture was washed twice with H₂O and dried over MgSO₄. Removal of the solvent and trituration with MeOH yielded 95.1 g (71%) of pure 5; m.p. 128–129°C. ¹H-NMR: δ 8.15, dd, 2H, J 3.2 Hz, H6 and H7; 7.05, dd, 2H, J 3.2 Hz, H5 and H8; 6.1–5.9, m, 2H, =CH; 5.1–5.0, m, 4H, =CH₂; 3.73, d, 4H, J 5.9 Hz, ArCH₂; 2.35, s, 6H, CH₃. ¹³C-NMR: δ 168.5, C=O; 139.5, ArO; 135.2, =CH₂; 131.1, 127.0, Ar; 126.0, 125.0, Ar; 30.7, ArCH₂. IR (KBr): 1770, C=O, cm⁻¹. MS (EI): m/z 324.1, M⁺, calcd. 324.1. Anal. calcd. for C₂₀H₂₀O₄: C 74.06, H 6.21; found C 73.98, H 6.21%.

1,4-Bis(prop-2-enyl)-2,3-diacetoxynaphthalene (6)

1,4-Bis(prop-1-enyl)-2,3-diacetoxynaphthalene (78.0 g, 0.24 mol) was dissolved in a mixture of 100 ml of EtOH and 100 ml of THF. RhCl₃ (0.5 g) was added and the reaction mixture was stirred at 50°C, until conversion was complete by NMR (48 h); the multiplet at δ 5.1–5.0 disappeared and was replaced by a double doublet at δ 1.96. After filtration over silica gel to remove the catalyst, removal of the solvent and subsequent recrystallization from MeOH yielded 42.9 g (55%) of **6**; m.p. 144–145°C. ¹H-NMR: δ 8.07, dd, 2H, J 3.0 Hz, H6 and H7; 7.46, dd, 2H, J 3.0 Hz, H-5,8; 6.56, dd, 2H, J 16 Hz, 1.4 Hz, ArCH; 6.1–5.9, m, 2H, =CH; 2.75, s, 6H, OAc; 1.96, dd, 6H, J 6.2 Hz, 1.4 Hz, CHCH₃. ¹³C-NMR: δ 168.9, C=O; 138.4, Ar; 133.7, ArCH=; 130.7, 128.1, Ar; 126.0, =CH; 125.6, 124.6, 122.6, Ar; 20.5, C(O)CH₃; 9.2, CHCH₃. IR (KBr): 1769, C=O, cm⁻¹. MS (EI): m/z 324.1, M⁺, calcd. 324.0. Anal calcd. for C₂₀H₂₀O₄: C 74.06, H 6.21; found C 74.12, H 6.32%.

2,3-Diacetoxy-1,4-naphthalenedialdehyde (7)

Compound 6 (5.0 g, 0.015 mol) was dissolved in 100 ml dry CH_2Cl_2 and cooled to $-70^{\circ}C$. Ozone was passed through the solution until the color changed to slightly greenish-blue. The excess of ozone was removed by leading N₂ through the solution. Subsequently 20 ml dimethyl sulfide (DMS) was added and the mixture was allowed to warm and stand for 48 h. DMS and solvent were evaporated and the crude product was triturated with propan-2-ol to give 4.2 g (90%) of 7; m.p. 194–195°C. ¹H-NMR: δ 10.64, s, 2H, CHO; 8.87, dd, 2H, J 3.3 Hz, H6 and H7); 7.61, dd, 2H, J 3.3 Hz, H5 and H8; 2.42, s, 6H, CH₃. ¹³C-NMR (DMSO-*d*₆): δ 174.0, CH=O; 168.9, C=O; 144.8, ArO; 133.5, Ar; 129.5, 124.8, Ar; 20.3, CH=3, IR (KBr): 1774, COO; 1698, CH=O, cm⁻¹. MS (EI): *m*/*z* 300.063, M⁺, calcd. 300.063. Anal. calcd. for C₁₆H₁₂O₆·0.3H₂O: C 62.87, H 4.15; found: C 62.80, H 4.13%.

2,3-Dihydroxy-1,4-naphthalenedialdehyde (8)

To a degassed solution of NaOH (1 g, 25 mmol) in 55 ml of MeOH was added 3.74 g (12.5 mmol) of 2,3-diacetoxy-1,4-naphthalenedialdehyde and 20 ml of THF was added to give a homogeneous dark-green solution. After 30 min, the solvent was evaporated and THF (90 ml) and H₂O (60 ml) were added. 4-Toluenesulfonic acid was added until the pH was 3 and the reaction mixture was stirred overnight. Compound **8** (1.97 g, 73%) precipitated as yellow crystals and was collected by filtration and dried in air; m.p. 158– 159°C. ¹H-NMR: δ 13.0, bs, 2H, OH; 10.87, s. 2H, CH=O; 8.38, dd, 2H, J 3.3 Hz, H6 and H7; 7.54, dd, 2H, J 3.3 Hz, H5 and H8. ¹³C-NMR (DMSO- d_6): δ 194.1, CH=O; 154.2, ArOH; 126.3, 125.4, 122.3, 117.1, Ar. IR (KBr): 1671, CH=O, cm⁻¹. MS (E1): m/z 216.0, M⁺ calcd. 216.0. Anal. calcd. for C₁₂H₈O₄·0.75H₂O: C 62.75, H 3.84; found: C 62.75, H 3.76%.

General procedure for the synthesis of macrocycles 2a-2c

Dialdehyde 8 (0.20 g, 0.926 mmol) and $Ba(CF_3SO_3)_2$ (0.134 g, 0.309 mmol) were refluxed in a mixture of 50 ml CH₃CN and 50 ml MeOH for 15 min. To the slightly yellow solution, 0.926 mmol of diamine was added in one portion, resulting in an immediate color change from yellow to (orange)red. After 1 h reflux the solution was cooled to room temperature and 50 ml diisopropyl ether were added to induce precipitation of the macrocyclic complex, in typical yields of 70% and pure by ¹H-NMR, FAB-MS and elemental analysis.

Barium(2 +), (5,42:14,19:28,33-triethenohexabenzo[b,g,l,q,v,a₁] [1,4,11,14,21,24]hexaazacyclotriacontine-43,44,45,46,47,48-hexol- O, O',O",O",O"',O"'',O"''')-, (OC-6-11)-, salt with trifluoromethanesulfonic acid (1:2) (2a) Dark red solid; m.p. > 300°C. ¹H-NMR (DMSO- d_6 , 60°C): δ 14.4, bs, 6H, OH; 8.75, s, 6H, CH=N; 7.58, bs, 6H, PhenH; 7.40, bs, 6H, PhenH; 7.20, m, 6H, ArH; 7.09, m, 6H, ArH. IR (KBr): 1616, C=N, cm⁻¹. FAB-MS (+VE): m/z 1151.1 (M-CF₃SO₃)⁺; 1002.1 (M-2CF₃SO₃)⁺. Anal. calcd. for C₅₆H₃₆BaF₆N₆O₁₂S₂: C 51.72, N 6.46, H 2.79; found: C 51.84, N 6.29, H 2.94%.

Barium(2 +), (8.9,20,21,32,33-hexahydro-5,36 : 12,17 : 24,29-triethenotribenzo $[g,q,a_1]$ [1,4,11,14,21,24]hexaazacyclotriacontine37,38,39,40,41,42-hexol-O,O',O",O"",O"",O"",O,O''',O''',O''',O'''',O'',O''

Barium(2 +), (7a,8,9,10,11,11a,21a,22,23,24,25,25a,35a,36,37,38,39, 39a-octadecahydro-5,42:14,19:28,33-triethenohexabenzo[b,g,l,q,v,a_1] [1,4,11,14,21,24]hexaazacyclotriacontine-43,44,45,46,47,48-hexol-O,O',O'',O''',O'''',O'''')-, (OC-6-11)-, salt with trifluoromethanesulfonic acid (1:2) (2c) Orange solid; m.p. > 300°C. ¹H-NMR (DMSO-d₆, 75°C): δ 15.09, bs, 6H, OH; 9.30, s, 6H, CH=N; 8.01, m, 6H, ArH; 7.39, m, 6H, ArH; 4.38, m, 6H, NCH; 1.95, m, 6H, CH₂; 1.61, m, 18H, CH₂. ¹³C-NMR (DMSO-d₆): δ 174.1, C=N; 160.8, ArOH; 128.0, 125.4, 124.0, 119.5, ArH; 107.2, NCH; 59.2, 26.9, CH₂. IR (KBr): 1623, C=N, cm⁻¹. FAB-MS (-VE): m/z 1317 (M⁻); (+VE): 1169.1 (M-CF₃SO₃)⁺; 1019.2 (M-2CF₃SO₃)⁺. Anal. calcd. for C₅₆H₅₄BaF₆N₆O₁₂S₂: C 51.01, N 6.37, H 4.13; found: C 51.25, N 6.93, H 4.53%.

Barium (2 +), (8,9,10,21,22,23,34,35,36,47,48,49-dodecahydro- $5,52:13,18:26,31:39,44-tetraethenotetrabenzo[h,s,d_1,o_1][1,5,12,16,$ 23,27,34,38]octaazacyclotetratetracontine-53,54,55,56,57,58,

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