An ethylene-linked catechol/8-hydroxyquinoline derivative and its dinuclear gallium(III) complex

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The ethylene-linked catechol/8-hydroxyquinoline derivative 7-H_3 is prepared in a three step procedure by Sonogashira–Hagihara coupling of (2,3-dimethoxyphenyl)acetylene (1) and 7-bromo-8-methoxyquinoline (2), followed by reduction of the alkyne and final ether cleavage. The unsymmetric type II triple-stranded dinuclear helicate $M_3[Ga_2(7)_3]$ (M = Na, K) is obtained with gallium(III) ions in the presence of potassium or sodium carbonate.

Helicates or meso-helicates are metallo-supramolecular coordination compounds, which are formed in self-assembly processes from two or three linear oligo-donor ligands and two or more metal ions.[1,2] If directional or sequential ligands are used, different kinds of complexes can be obtained. Either all ligand strands of the complex are orientated in the same direction (type I) or one of them is orientated in the opposite direction to the other(s) (type II).[3,4]

We have previously reported on alkyl-bridged catechol/aminophenol ligands which are able to selectively form heterodinuclear type I complexes (C_3-symmetry) or homodinuclear type II complexes (C_1-symmetry due to the chiral complex units with an octahedral geometry). In the presence of a 1 : 1 mixture of two different metal ions the type I structure is obtained because of the selective recognition of different metal ions by different ligand units. Homodinuclear complexes adopt the type II structure to minimize charge separation between the metals (similar metal ions prefer to have similar coordination spheres).[4] In this paper we present the preparation of an ethylene-linked catechol/8-hydroxyquinoline ligand and the formation and NMR spectroscopic characterization of its type II gallium(III) complex.

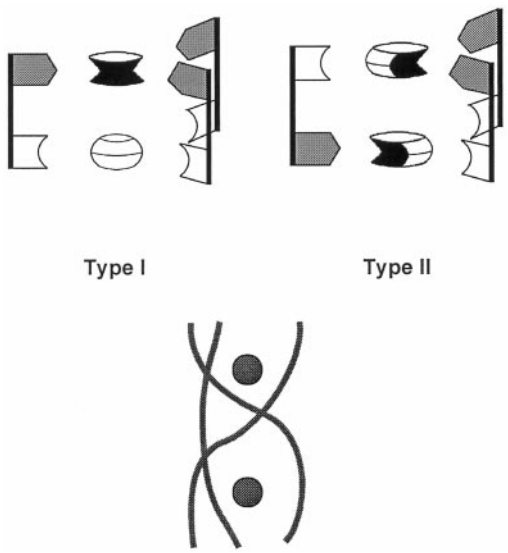


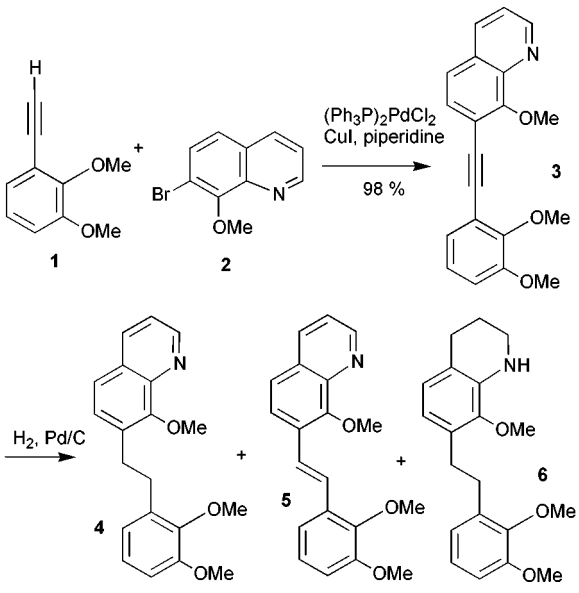
Fig. 1 Schematic representation of the two possible isomers of a triple-stranded helicate formed from two metal ions and three sequential ligand-strands and a schematic representation of the triple-helical structure.

Results and discussion

Synthesis of the ethylene-linked catechol/8-hydroxyquinoline derivative 7-H_3

The ethylene-bridged catechol/8-hydroxyquinoline derivative **7-H_3** is prepared starting from (2,3-dimethoxyphenyl)acetylene **1**, which is obtained from veratrole (1,2-dimethoxybenzene) in a 3 step procedure as was described earlier.[5] The alkyne **1** is coupled with 7-bromo-8-methoxyquinoline (**2**) (prepared in 2 steps from 8-hydroxyquinoline)[6] in a Sonogashira–Hagihara coupling reaction[7] using $(Ph_3P)_2PdCl_2$ and CuI in piperidine as coupling reagent to establish the C_2-linkage between the two aromatic systems of **3** in 98% yield (Scheme 1).

The reduction of the triple bond of **3** to obtain an ethylene-bridged derivative turned out to be the critical step of the reaction sequence. Reaction of **3** with hydrogen in the presence of Pd/C in methanol leads in 15 h to the derivative **6** in quantitative yield. In **6** not only the triple bond but also the heterocyclic portion of the quinoline is reduced and the tetrahydroquinoline skeleton is obtained. Shorter reaction times



Scheme 1

enable the isolation of the desired compound **4**. For example, after 65 min of reaction time **4** is isolated in 9% yield after chromatographic separation. A further fraction is obtained by chromatography which contains the stilbene derivative **5** as the major component (yield: approximately 38%; characteristic doublets at $\delta = 7.15$, 7.28, $J = 12.8$ Hz). This material can be used again in the Pd-catalyzed hydrogenation reaction.

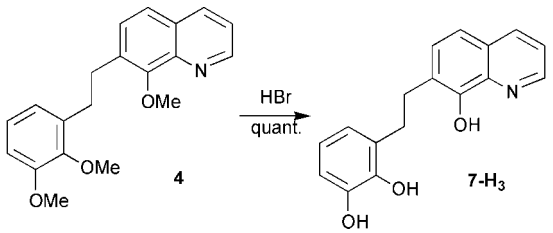
Although the yield of **4** is very poor, we prepared enough material to perform an ether cleavage reaction with HBr and obtained the sequential catechol/8-hydroxyquinoline ligand **7-H$_3$** in quantitative yield as a slightly green solid (Scheme 2). **7-H$_3$** is characterized by ^{1}H, ^{13}C NMR and by mass spectrometry as well as high resolution MS. The ^{1}H NMR spectrum in $CDCl_3$ reveals three characteristic coupling patterns for the aromatic units. At low field three signals are detected at $\delta = 8.79$ (dd, $J = 1.4$, 4.2 Hz), 8.17 (dd, $J = 1.4$, 8.3 Hz), and 7.42 (dd, $J = 4.2$, 8.3 Hz) which correspond to the heterocyclic portion of the quinoline unit. The doublets of the phenolic part of the hydroxyquinoline are observed at $\delta = 7.37$ and 7.34 ($J = 8.4$ Hz each) and the signals of the aromatic catechol protons appear as a multiplet at $\delta = 6.78$–6.72. Two further multiplets at $\delta = 3.09$ and 2.99 are assigned to the spacer protons of **7-H$_3$**.

Preparation and NMR spectroscopic characterization of the homodinuclear type II complex $K_3[Ga_2(7)_3]$

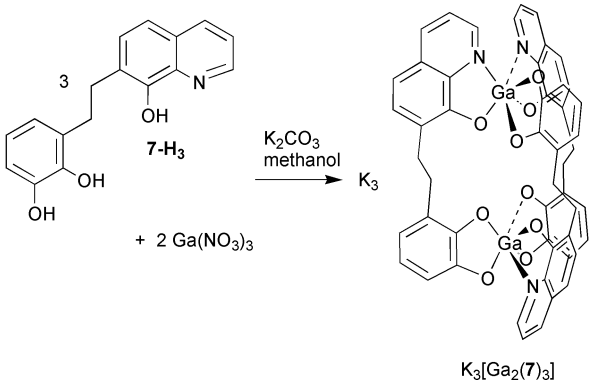
The dinuclear gallium(III) complex $K_3[Ga_2(7)_3]$ is prepared by refluxing **7-H$_3$** (3 eq.), $Ga(NO_3)_3 \cdot H_2O$ (2 eq.), and K_2CO_3 in methanol for 15 h (Scheme 3). The complex is obtained as a mixture with inorganic salts (KNO_3, K_2CO_3) but is characterized by NMR spectroscopy and mass spectrometry.

The positive FAB MS (3-nitrobenzyl alcohol, 3-NBA, as matrix) of the complex $K_3[Ga_2(7)_3]$ shows at high masses peaks at $m/z = 1016$, 1038, 1054, and 1092 which all correspond to the triple-stranded dinuclear coordination compound (Fig. 2). According to our earlier investigations[2,8] we expected one of the potassium cations to be located in the interior of the complex and to act as a template which stabilizes this dinuclear coordination compound.

To show if a type I or II complex (or a mixture of both) is present, NMR spectroscopic studies were performed. In the case of a C_3-symmetric type I complex only one set of signals will appear for the coordinated ligand **7**. Due to the inequivalence of the three ligand strands three sets of signals are



Scheme 2



Scheme 3

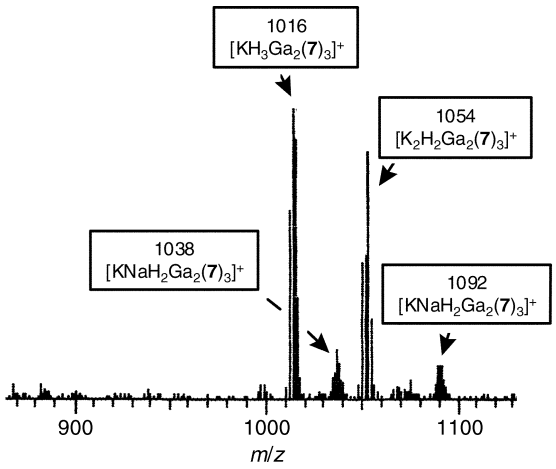


Fig. 2 Positive FAB MS spectrum of $K_3[Ga_2(7)_3]$ in 3-NBA.

expected for **7** if the unsymmetric type II structure is present.[4] NMR spectroscopy cannot be used for the assignment of the relative stereochemistry of the complex units. However, following the concept which we introduced for related non-sequential systems, we expect the two complex units to possess the same configuration.[2,9]

The part of the ^{1}H NMR spectrum of $K_3[Ga_2(7)_3]$ showing the resonances of the protons of the quinoline moieties of **7** is shown in Fig. 3. Many signals can be observed in this region, indicating that either the unsymmetric type II or a mixture of

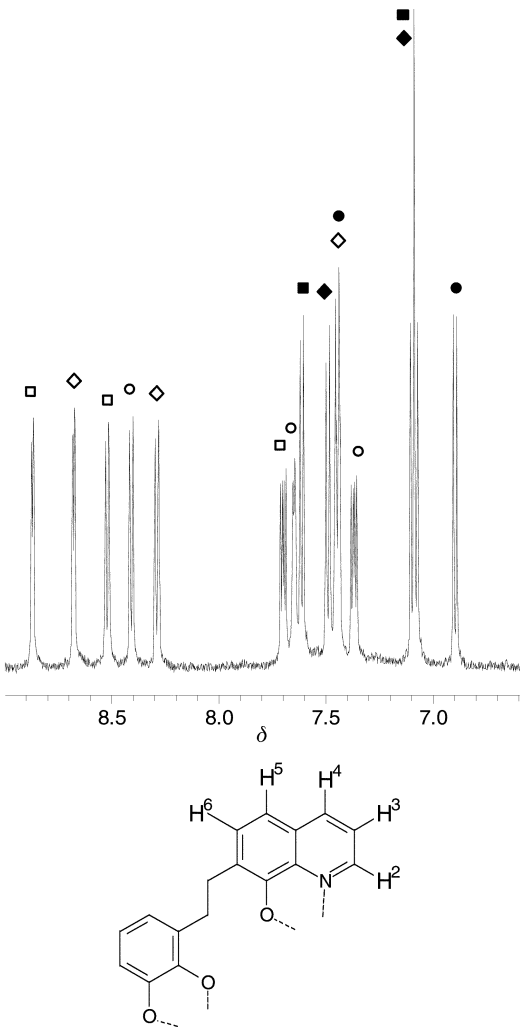


Fig. 3 Part of the ^{1}H NMR spectrum of $K_3[Ga_2(7)_3]$ showing the signals of the protons of the quinoline units and numbering of the quinoline unit.

the type I and type II structures is present. The assignment of the coupling pattern was done by a COSY NMR experiment in dmso-d_6. The protons of the heterocyclic part of the quinoline lead to three sets of signals at $\delta = 8.87$, 8.52, 7.70 (H^2–H^4 of the first ligand **7**, □ in Fig. 3) and 8.68, 8.29, 7.44 (H^2–H^4 of the second ligand **7**, ◇) and 8.41, 7.65, 7.37 (H^2–H^4 of the third ligand **7**, ○) in a ratio 1 : 1 : 1. Consequently, three sets of signals are detected for the phenolic protons of **7** at $\delta = 7.61$, 7.09 (H^5 and H^6, first ligand **7**, ■) and 7.49, 7.09 (H^5 and H^6, second ligand **7**, ◆) and 7.44, 6.89 (H^5 and H^6, third ligand **7**, ●). However, for the catechol moieties only three signals are observed at $\delta = 6.25$–6.22, 6.11–6.08, 6.05–6.00 (m, triple intensity each). The appearance of three sets of signals in the ^{1}H NMR spectrum shows that only the unsymmetric type II complex is formed in the metal directed self-assembly process, leading to three inequivalent ligands in a ratio of 1 : 1 : 1. No signals are observed which correspond to a type I structure.

Due to the C_1-symmetry of $K_3[Ga_2(\mathbf{7})_3]$ all protons of the three spacers are not equivalent and lead to twelve resonances which can be divided into three independent sets of four signals each. Again the COSY NMR experiment shows the presence of three sets of signals at $\delta = 3.22/2.98/2.48$ (hidden under solvent peak)/2.36, 3.13/2.69/2.32/2.20 and 2.94/2.63/2.26/2.13. Similar ^{1}H NMR spectroscopic results are obtained for the corresponding sodium salt $Na_3[Ga_2(\mathbf{7})_3]$.

In the ^{13}C NMR spectrum the C_1-symmetry of $K_3[Ga_2(\mathbf{7})_3]$ leads to the expected 51 nonequivalent carbon atoms. Forty three signals of aromatic carbon atoms (two with double intensity) and five resonances of CH_2 groups (one with double intensity) are detected (see Experimental section).

Our attempts to prepare a heterodinuclear Ti(IV)/Ga(III) complex failed,[4] due to the insolubility of the obtained material.

Conclusions

In this manuscript we have presented the synthesis of the ethylene-bridged catechol/8-hydroxyquinoline derivative **7-H$_3$** which is an interesting sequential ligand for the self-assembly of triple-stranded dinuclear helicates. Although one of the three reaction steps of the preparation of **7-H$_3$** proceeds in only 9% yield we were able to obtain enough material to investigate the formation of the dinuclear gallium(III) complex $K_3[Ga_2(\mathbf{7})_3]$. NMR spectroscopic results show that the unsymmetric type II complex is formed selectively. The type I structure is not observed. The results which are discussed in this article show that the formation of supramolecular and metallo-supramolecular aggregates is influenced by an interaction of steric and electronic factors. In the presented case the high selectivity of the self-assembly process is most probably due to the tendency of similar metal ions to have a coordination sphere as similar as possible. The understanding of the influences which control the self-assembly of supermolecules should help in the design of new molecular building-blocks for the formation of more sophisticated supramolecular structures.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE DRX 500 NMR spectrometer using DEPT techniques for the assignment of the multiplicity of carbon atoms. FT-IR spectra were recorded by diffuse reflection (KBr) on a Bruker IFS spectrometer. Mass spectra (EI, 70 eV, positive FAB in 3-NBA) were measured on a Finnigan MAT 90 mass spectrometer. Elemental analyses were obtained with a Heraeus CHN-O-Rapid analyzer. Solvents were purified by standard methods. Melting points: Büchi 535 (uncorrected).

Synthesis of the ligand

1-(2,3-Dimethoxyphenyl)-2-(8-methoxyquinolin-7-yl)-acetylene (3). 1-(2,3-Dimethoxyphenyl)acetylene[5] (**1**, 200 mg, 1.25 mmol) in 5 ml of piperidine is added to a solution of 7-bromo-8-methoxyquinoline[6] (**2**, 600 mg, 2.52 mmol), CuI (2.4 mg, 0.01 mmol), and $(Ph_3P)_2PdCl_2$ (265 mg, 0.38 mmol) in 50 ml of piperidine. The mixture is heated to 70 °C and after 2, 4, and 20 h additional alkyne **1** (200 mg per 1.25 mmol in 5 ml piperidine each) is added. After 24 h the solvent is removed in vacuum and the residue is purified by column chromatography (silica gel, hexane/ethyl acetate 2 : 1). Yield: 785 mg (98%) of **3** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.94$ (dd, $J = 1.1$, 4.1 Hz, 1 H), 8.07 (dd, $J = 1.1$, 8.3 Hz, 1 H), 7.57 (d, $J = 8.5$ Hz, 1 H), 7.46 (d, $J = 8.5$ Hz, 1 H), 7.37 (dd, $J = 4.1$, 8.3 Hz, 1 H), 7.14 (d, $J = 8.0$ Hz, 1 H), 7.02 (t, $J = 8.0$ Hz, 1 H), 6.89 (d, $J = 8.0$ Hz, 1 H), 4.36 (s, 3 H), 4.04 (s, 3 H), 3.85 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 157.8$ (C), 152.7 (C), 150.3 (C), 150.2 (CH), 142.5 (C), 135.9 (CH), 130.1 (CH), 129.6 (C), 124.8 (CH), 123.9 (CH), 122.5 (CH), 121.7 (CH), 117.8 (C), 115.2 (C), 113.0 (CH), 91.8 (C), 90.0 (C), 62.2 (CH_3), 61.1 (CH_3), 55.9 (CH_3). MS (EI, 70 eV): m/z (%) = 319 (100, $[M]^+$). HRMS calcd. for $C_{20}H_{21}NO_3$: 319.1208, found: 319.1226. IR (KBr, drift): $\tilde{\nu} = 3432$, 2934, 2210, 1573, 1473, 1425, 1361, 1266, 1097, 1078 cm^{-1}.

1-(2,3-Dimethoxyphenyl)-2-(8-methoxyquinolin-7-yl)ethane (4). A mixture of the alkyne **3** (650 mg, 2.04 mmol) and 200 mg of Pd/C in 40 ml of methanol is stirred under an atmosphere of hydrogen for 65 min. The solvent is removed in vacuum and the resulting mixture is separated by column chromatography (silica gel, hexane/ethyl acetate 5 : 1). Yield: 60 mg (9%) of **4** as a white solid. Mp: 65 °C. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.92$ (dd, $J = 1.7$, 4.2 Hz, 1 H), 8.11 (dd, $J = 1.7$, 8.3 Hz, 1 H), 7.50 (d, $J = 8.4$ Hz, 1 H), 7.40 (d, $J = 8.4$ Hz, 1 H), 7.35 (dd, $J = 4.2$, 8.3 Hz, 1 H), 6.98 (t, $J = 7.9$ Hz, 1 H), 6.83–6.78 (m, 2 H), 4.13 (s, 3 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 3.17–3.13 (m, 2 H), 3.02–2.99 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 153.6$ (C), 152.8 (C), 149.4 (CH), 147.3 (C), 143.0 (C), 136.1 (CH), 135.8 (C), 134.6 (C), 129.1 (CH), 128.5 (C), 123.8 (CH), 122.9 (CH), 122.1 (CH), 120.5 (CH), 110.4 (CH), 62.4 (CH_3), 60.7 (CH_3), 55.7 (CH_3), 31.7 (CH_2), 31.4 (CH_2). MS (EI, 70 eV): m/z (%) = 323 (51, $[M]^+$), 172 (100, $[M - C_9H_{11}O_2]^+$). HRMS calcd. for $C_{20}H_{21}NO_3$: 323.1521, found: 323.1511. Elemental analysis calcd. for $C_{20}H_{21}NO_3$: C: 74.28, H: 6.55, N: 4.33; found: C: 73.96, H: 6.68, N: 4.08%. IR (KBr, drift): $\tilde{\nu} = 3405$, 2960, 2933, 1473, 1363, 1221, 1093, 1077, 1009, 836 cm^{-1}.

Longer reaction times do not lead to an improved yield of **4**. After 15 h of reaction time 1-(2,3-dimethoxyphenyl)-2-(8-methoxy-1,2,3,4-tetrahydroquinolin-7-yl)ethane (**6**) is isolated in quantitative yield as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.01$ (t, $J = 7.9$ Hz, 1 H), 6.88 (dd, $J = 1.1$, 7.9 Hz, 1 H), 6.81 (dd, $J = 1.1$, 7.9 Hz, 1 H), 6.73 (d, $J = 7.7$ Hz, 1 H), 6.53 (d, $J = 7.7$ Hz, 1 H), 4.29 (br s, 1 H), 3.89 (s, 3 H), 3.87 (s, 3 H), 3.77 (s, 3 H), 3.34 (t, $J = 5.4$ Hz, 2 H), 2.93 (m, 2 H), 2.87 (m, 2 H), 2.78 (t, $J = 6.4$ Hz, 2 H), 1.96 (q, $J = 5.4$, 6.4 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 152.8$ (C), 147.2 (C), 144.2 (C), 138.2 (C), 136.4 (C), 132.2 (C), 124.8 (CH), 123.9 (CH), 121.9 (CH), 120.4 (C), 116.9 (CH), 110.2 (CH), 60.7 (CH_3), 59.6 (CH_3), 55.7 (CH_3), 41.6 (CH_2), 31.5 (CH_2), 31.0 (CH_2), 26.6 (CH_2), 22.1 (CH_2). MS (EI, 70 eV): m/z (%) = 327 (100, $[M]^+$). HRMS calcd. for $C_{20}H_{25}NO_3$: 327.1834, found: 327.1846. IR (KBr, film): $\tilde{\nu} = 3403$, 2932, 2834, 1584, 1481, 1446, 1430, 1328, 1309, 1274, 1223, 1082, 1012 cm^{-1}.

1-(2,3-Dihydroxyphenyl)-2-(8-hydroxyquinolin-7-yl)ethane (7-H$_3$). 1-(2,3-Dimethoxyphenyl)-2-(8-methoxyquinolin-7-yl) ethane (**4**, 60 mg, 0.19 mmol) in 5 ml of 48% HBr is heated to reflux (2 h). Solvent is removed in vacuum and the residue is

dissolved in dichloromethane, washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and the CH_2Cl_2 is removed again. Yield: 52 mg (100%) **7-H$_3$** as a slightly green solid. Mp: 149–151 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.79 (dd, J = 1.4, 4.2 Hz, 1 H), 8.17 (dd, J = 1.4, 8.3 Hz, 1 H), 7.42 (dd, J = 4.2, 8.3 Hz, 1 H), 7.37 (d, J = 8.4 Hz, 1 H), 7.34 (d, J = 8.4 Hz, 1 H), 6.78–6.72 (m, 3 H), 3.09 (m, 2 H), 2.99 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.7 (C), 148.2 (CH), 144.5 (C), 141.9 (C), 137.8 (C), 136.2 (CH), 129.5 (CH), 127.8 (C), 127.2 (C), 123.8 (C), 121.3 (CH), 121.2 (CH), 120.4 (CH), 118.0 (CH), 113.4 (CH), 31.6 (CH_2), 30.9 (CH_2). MS (EI, 70 eV): m/z (%) = 281 (44, $[M]^+$), 158 (100, $[M - C_7H_7O_2]^+$). HRMS calcd. for $C_{17}H_{15}NO_3$: 281.1052, found: 281.1038. IR (KBr, drift): $\tilde{\nu}$ = 3463, 3051, 2927, 1505, 1478, 1373, 1283, 1238, 1147, 826, 728 cm^{-1}.

Synthesis of homodinuclear type II metal complexes $M_3[Ga_2(7)_3]$

1-(2,3-Dihydroxyphenyl)-2-(8-hydroxyquinolin-7-yl)ethane (**7-H$_3$**, 15 mg, 0.05 mmol), $Ga(NO_3)_3 \cdot H_2O$ and M_2CO_3 (M = Na, K; 0.24 mmol) are refluxed in 10 ml of methanol for 15 h. Solvent is removed in vacuum and the complexes are obtained in a quantitative reaction (by NMR) as a mixture with inorganic salts (M_2CO_3, MNO_3).

K$_3$[Ga$_2$(7)$_3$]. ^{1}H NMR (500 MHz, dmso-d$_6$): δ = 8.87 (d, J = 4.6 Hz, 1 H), 8.68 (d, J = 3.5 Hz, 1 H), 8.52 (d, J = 8.3 Hz, 1 H), 8.41 (d, J = 8.3 Hz, 1 H), 8.29 (d, J = 7.4 Hz, 1 H), 7.70 (dd, J = 4.6, 8.3 Hz, 1 H), 7.65 (d, J = 4.5 Hz, 1 H), 7.61 (d, J = 8.4 Hz, 1 H), 7.49 (d, J = 8.4 Hz, 1 H), 7.44 (d, J = 8.3 Hz, 1 H and dd, J = 3.5, 7.4 Hz, 1 H), 7.37 (dd, J = 4.5, 8.3 Hz, 1 H), 7.09 (t, J = 8.4 Hz, 2 H), 6.89 (d, J = 8.3 Hz, 1 H), 6.25–6.22 (m, 3 H), 6.11–6.08 (m, 3 H), 6.05–6.00 (m, 3 H), 3.22 (m, 1 H), 3.13 (m, 1 H), 2.98 (m, 1 H), 2.94 (m, 1 H), 2.69 (m, 1 H), 2.63 (m, 1 H), 2.36 (m, 1 H), 2.32 (m, 1 H), 2.26 (m, 1 H), 2.20 (m, 1 H), 2.13 (m, 1 H). ^{13}C NMR (126 MHz, dmso-d$_6$): δ = 156.8 (C), 155.4 (C, double intensity), 155.3 (C), 154.9 (C), 154.8 (C), 153.5 (C), 153.0 (C), 152.0 (C), 145.0 (CH), 143.8 (CH), 142.7 (CH), 139.4 (CH), 139.1 (CH), 137.7 (CH), 137.3 (C), 136.9 (C), 136.7 (C), 131.7 (CH), 131.5 (CH), 131.1 (CH), 127.9 (C), 127.8 (C, double intensity), 125.8 (C), 125.3 (C), 124.0 (C), 123.9 (C), 123.1 (C), 122.4 (C), 120.9 (CH), 120.6 (CH), 120.2 (CH), 115.3 (CH), 114.5 (CH), 114.3 (CH), 113.5 (CH), 112.5 (CH), 112.4 (CH), 110.2 (CH), 110.0 (CH), 109.6 (CH), 109.5 (CH), 108.8 (CH), 108.3 (CH), 32.8 (CH_2), 32.6 (CH_2), 32.3 (CH_2), 32.0 (CH_2, double intensity), 31.9 (CH_2). Positive FAB MS: m/z (%) = 1092 (0.1, $[MH]^+$). IR (KBr, drift): $\tilde{\nu}$ = 3364, 3050, 2396, 1883, 1573, 1502, 1460, 1376, 1263, 1111, 826, 734, 678 cm^{-1}.

Na$_3$[Ga$_2$(7)$_3$]. ^{1}H NMR (500 MHz, dmso-d$_6$): δ = 8.71 (d, J = 3.3 Hz, 1 H), 8.59 (dd, J = 1.4, 4.5 Hz, 1 H), 8.53 (dd, J = 1.3, 8.4 Hz, 1 H), 8.39 (d, J = 7.2 Hz, 1 H), 8.27 (dd, J = 1.4, 8.4 Hz, 1 H), 7.66 (dd, J = 4.5, 8.4 Hz, 1 H), 7.57 (d, J = 8.3 Hz, 1 H), 7.46 (d, J = 8.3 Hz, 1 H), 7.41 (d, J = 8.3 Hz, 1 H and dd, J = 4.5, 8.3 Hz, 1 H), 7.29 (dd, J = 4.5, 8.3 Hz, 1 H), 7.12–7.09 (m, 3 H), 6.90 (d, J = 8.2 Hz, 1 H), 6.28–6.16 (m, 4 H), 6.13–6.10 (m, 1 H), 6.06–5.98 (m, 4 H), 6.05–6.00 (m, 3 H), 3.01 (m, 2 H), 2.78 (m, 2 H), 2.43 (m, 1 H), 2.29 (m, 1 H), 2.22 (m, 1 H), 2.15 (m, 1 H), 2.03 (m, 1 H). Positive FAB MS: m/z (%) = 1043 (0.2, $[MH]^+$).

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