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Synthesis of two asymmetric half-*salen* imine-type ligands as precursors of polynuclear metal complexes†

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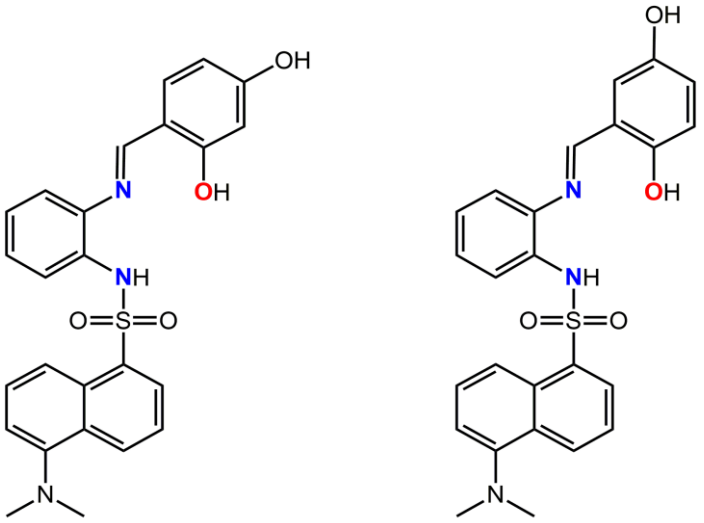
Abstract: Herein we report the synthesis and characterization of two asymmetric [NNO] tridentate imine ligands (H_2L^1 and H_2L^2) functionalized with two hydroxyl groups and a bulky dansyl moieity. The existence of two hydroxyl substituents able to form bridges between metal ions make both molecules suitable as precursors of metallosupramolecular polynuclear species.

Keywords: Imine-type ligands, dansyl fluorophore, polynuclear complexes

1. Introduction

Polydentate [N,O] ligands are considered as good candidates for the formation of polynuclear metal complexes with novel metal cores [1]. For example, N,N′-*bis*(salicylidene)ethylenediamine (*salen*) derived imine-type ligands have been employed for the assembly of polynuclear compounds [2]. In particular, *salen*-derived metal complexes have attracted an increasing interest due to their potential as models for mimicking the active sites in metalloenzymes [3] and their application in catalysis [4].

Our research group has employed *salen* or half-*salen* imine-type ligands to assemble polynuclear complexes that could be involved in catalytic processes [5] or mimic the activity of the Photosystem II [6] and the peroxidase or catalase enzymes [7]. Herein we have designed and synthesized two tridentate [NNO] half-*salen*-type ligands H_2L^1 and H_2L^2 (Scheme 1) in which we have incorporated a further hydroxyl group as potential binding site. We have functionalized these ligands with a fluorophore dansyl group that might be useful for the spectroscopic detection of conformational changes upon binding to a metal ion [5b] These asymmetric molecules bearing two hydroxyl substituents are suitable precursors for the formation of polynuclear supramolecular complexes.



Scheme 1. Half-*salen* imine-type tridentate ligands H_2L^1 (left) and H_2L^2 (right).

2. Materials and Methods

H_2L^1: 2,4-dihydroxybenzaldehyde (0.45 g, 3.2 mmol) was added to a solution of *N*-(2-aminophenyl)-5-(dimethylamino)-1-naphthalenesulfonamide (1.11 g, 3.2 mmol) in chloroform (120 mL). The synthesis of *N*-(2-aminophenyl)-5-(dimethylamino)-1-naphthalenesulfonamide was previously described by us [5a]. The reaction was carried out for 7 h under reflux conditions using a Dean-Stark trap. The solvent was reduced to a small volume (ca. 20 mL), the suspended solid particles were filtered off and the solution was concentrated to dryness. The thick brown oil formed was dried under vacuum thus affording a solid product. The yellow solid was characterized with the usual techniques. Yield 1.10 g (75%). M.p. 96-98 °C. Elemental analysis, Calc. for $C_{25}H_{23}N_3O_4S$: C, 65.0; H, 5.0; N, 8.9; S, 6.7. Found: C, 64.6; H, 5.2; N, 9.1; S, 6.9 %. ESI$^+$ MS (m/z): 462.3 ([H_2L+H]$^+$); IR (KBr, cm^{-1}): ν(O-H/N-H) 3409/3284, ν(C=N+C-N) 1629, $\nu(SO_2)_{as}$ 1327, $\nu(SO_2)_s$ 1163. ^{1}H NMR (300 MHz, DMSO-d_6, ppm), δ (m, nH): 12.05 (s, H_1, 1H), 10.22 (s, H_2, 1H), 10.01 (s, H_3, 1H), 8.32 (d, H_4, 1H, J = 8.6 Hz), 8.21 (d, H_5, 1H, J = 8.6 Hz), 7.97 (dd, H_6, 1H, J_1 = 7.5 Hz, J_2 = 1.1 Hz), 7.95 (s, H_7, 1H), 7.45 (dd, H_8, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.35 (dd, H_9, 1H, J_1 = 8.1 Hz, J_2 = 7.8 Hz), 7.23-7.07 (m, H_{10}+H_{11}+H_{12}+H_{13}, 4H), 7.03 (d, H_{14}, 1H, J = 7.5 Hz), 6.98 (d, H_{15}, 1H, J = 7.5 Hz), 6.32 (dd, H_{16}, 1H, J_1 = 8.4 Hz, J_2 = 2.2 Hz), 6.23 (d, H_{17}, 1H, J = 2.2 Hz), 2.75 (s, H_{18}, 6H). ^{13}C NMR (75 MHz, CD_3CN, ppm): δ165.36 (C=N), 163.62 (C_{ar}), 163.05 (C_{ar}), 152.53 (C_{ar}), 144.62 (C_{ar}), 135.94 (CH_{ar}), 135.54 (C_{ar}), 131.54 (CH_{ar}), 130.64 (CH_{ar}), 130.26 (C_{ar}), 130.23 (C_{ar}), 129.37 (CH_{ar}), 127.82 (CH_{ar}), 127.37 (CH_{ar}), 125.20 (CH_{ar}), 123.70 (CH_{ar}), 120.54 (CH_{ar}), 118.98 (CH_{ar}), 118.22 (C_{ar}), 115.73 (CH_{ar}), 113.65 (C_{ar}), 108.51 (CH_{ar}), 103.28 (CH_{ar}), 45.51 (CH_3).

H_2L^2: This ligand was obtained through the condensation reaction of 2,5-dihydroxybenzaldehyde (0.45 g, 3.2 mmol) with *N*-(2-aminophenyl)-5-(dimethylamino)-1-naphthalenesulfonamide (1.11 g, 3.2 mmol) in chloroform (120 mL) by following the same procedure described above for H_2L^1. The orange solid was isolated and characterized with the usual techniques. Yield 1.19 g (79%). M.p. 90-92 °C. Elemental analysis, Calc. for $C_{25}H_{23}N_3O_4S$: C, 65.0; H, 5.0; N, 8.9; S, 6.7. Found: C, 64.5; H, 5.1; N, 8.7; S, 6.6 %. ESI$^-$ MS (m/z): 460.2 ([H_2L-H]$^-$); IR (KBr, cm^{-1}): ν(O-H/N-H) 3431/3283, ν(C=N+C-N)

1616, $\nu(SO_2)_{as}$ 1331, $\nu(SO_2)_s$ 1161. ^{1}H NMR (300 MHz, DMSO-d_6, ppm), δ (m, nH): 11.01 (s, H_1, 1H), 10.00 (s, H_2, 1H), 9.01 (s, H_3, 1H), 8.33 (d, H_4, 1H, J = 8.5 Hz), 8.22 (d, H_5, 1H, J = 8.5 Hz), 8.04 (s, H_6, 1H), 8.01 (d, H_7, 1H, J = 7.3 Hz), 7.45 (t, H_8, 1H, J = 7.8 Hz), 7.34 (t, H_9, 1H, J = 7.9 Hz), 7.27-7.09 (m, H_{10}+H_{11}+H_{12}, 3H), 7.08-6.96 (m, H_{13}+H_{14}, 2H), 6.85 (dd, H_{15}, 1H, J_1 = 8.2 Hz, J_2 = 2.1 Hz), 6.80-6.68 (m, H_{16}+H_{17}, 2H), 2.75 (s, H_{18}, 6H). ^{13}C NMR (75 MHz, CD_3CN, ppm): δ 165.95 (C=N), 154.69 (C_{ar}), 152.53 (C_{ar}), 149.95 (C_{ar}), 144.54 (C_{ar}), 135.44 (C_{ar}), 131.59 (CH_{ar}), 130.77 (C_{ar}), 130.65 (CH_{ar}), 130.21 (C_{ar}), 129.41 (CH_{ar}), 127.93 (CH_{ar}), 127.86 (CH_{ar}), 125.39 (CH_{ar}), 123.65 (CH_{ar}), 122.40 (CH_{ar}), 120.50 (CH_{ar}), 119.79 (C_{ar}), 118.86 (CH_{ar}), 118.71 (CH_{ar}), 118.29 (CH_{ar}), 118.21 (CH_{ar}), 115.69 (CH_{ar}), 45.50 (CH_3).

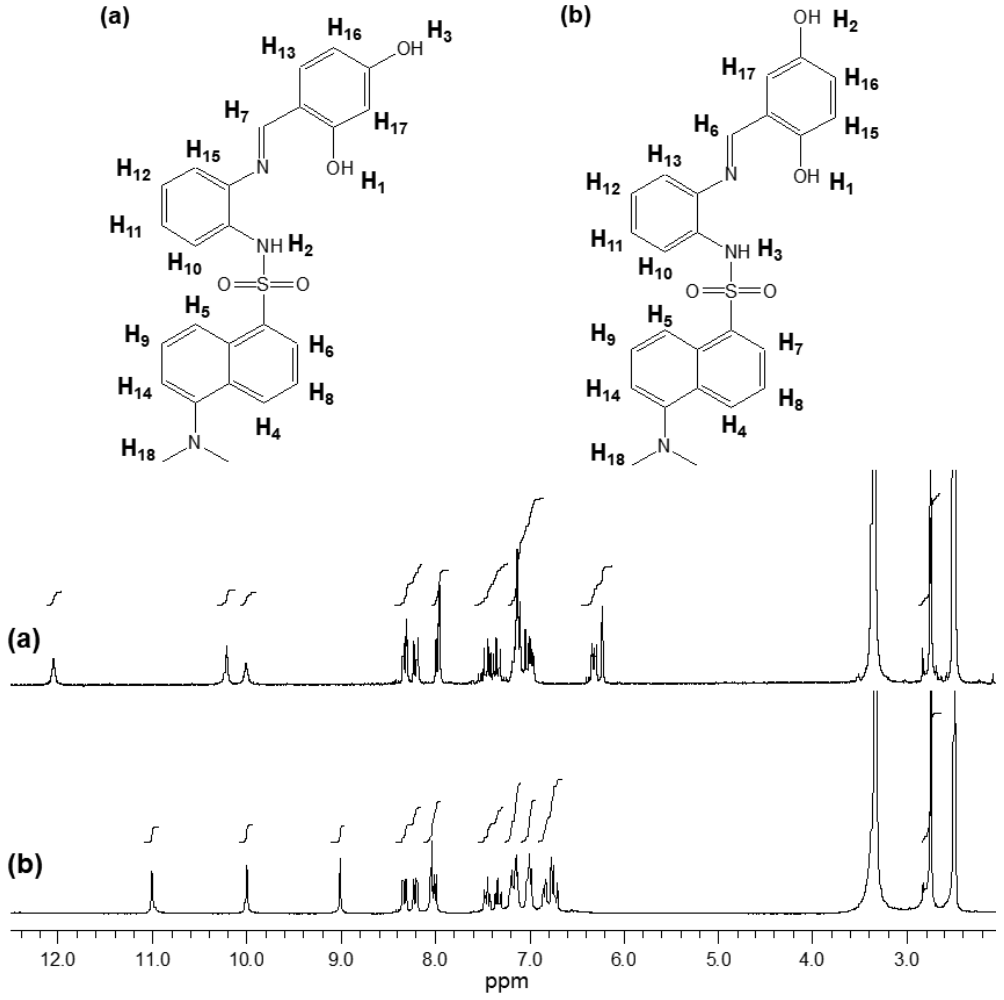


Figure 1. Overlapped ^{1}H NMR spectra of H_2L^1 **(a)** and H_2L^2 **(b)** recorded in DMSO-d_6.

3. Results and discussion

H_2L^1 and H_2L^2 have been succesfully obtained by a condensation reaction between a primary dansylamine and the corresponding dihydroxy-functionalized aldehyde. Both organic molecules have been obtained with high yield and purity as confirmed by several analytical and spectroscopic techniques. The ligand H_2L^2 with two hydroxyl groups in *para*- position relative to each other has a lower melting point (ca. 90 °C) compared to that observed for H_2L^1 with the two

OH substituents in *meta*- position to each other (ca. 96 °C). These potentially [NNO] tridentate ligands exhibit high solubility in most organic solvents.

A comparison of the ^{1}H NMR spectra of H_2L^1 and H_2L^2 is shown in Figure 1. The formation of the imine-type ligands was confirmed by the appearance of a singlet at ca. 8 ppm (H_7 and H_6, respectively) assigned to the imine proton in both spectra. The signals assigned to the two phenolic OH and the sulfonamide NH groups are observed in the range 12.0-9.0 ppm. In general, the dansyl aromatic protons are deshielded in comparison with the other aromatic protons. Moreover the change in the position of a hydroxyl substituent in the ligand has an effect on the shielding of the salicylic OH group (H_1), as its signal is significantly shifted upfield when changing from the *meta*-substituted ligand H_2L^1 (ca. 12 ppm) to the *para*-substituted ligand H_2L^2 (ca. 11 ppm). A similar effect is observed for the sulfonamide NH signal.

The formation of polynuclear complexes with these tridentate ligands would be feasible due to their low denticity and the possibility of establishing hydroxido bridges between two or more metal centers. The different positions in which the hydroxyl substituents are located might give rise to diverse metallosupramolecular structures depending on the nature of the metal ion and steric effects.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. a) Constable, E. C. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., Lehn, J.-M., MacNicol, D. D., Vögtle, F., Eds.; Pergamon, Oxford, 1996; Volume 9, pp. 213-252; b) Vigato, P. E.; Tamburini, S. *Coord. Chem. Rev.* **2008**, *252*, 1871-1995.
2. a) Yu, T.; Zhang, K.; Zhao, Y.; Yang, C.; Zhang, H.; Fan, D.; Dong, W. *Inorg. Chem. Commun.* **2007**, *10*, 401-403; b) Kleij, A. W.; Kuil, M.; Tooke, D. M.; Spek, A. L.; Reek, J. N. H. *Inorg. Chem.* **2007**, *46*, 5829-5831.
3. a) Kramer, R.; Gajda, T. *Perspect. Bioinorg. Chem.* **1999**, *4*, 209-240; b) Carlsson, H.; Haukka, M.; Nordlander, E. *Inorg. Chem.* **2004**, *43*, 5681-5687; c) Chen, J.; Wang, X.; Zhu, Y.; Lin, J.; Yang, X.; Li, Y.; Lu, Y.; Guo, Z. *Inorg. Chem.* **2005**, *44*, 3422-3430; d) Jarenmark, M.; Kappen, S.; Haukka, M.; Nordlander, E. *Dalton Trans.* **2008**, 993-996.
4. a) Matsumoto, K.; Katsuki, T. In *Asymmetric Synthesis–The Essentials*, 2nd ed.; Christmann, M., Bräse, S., Eds.; Wiley-VCH, Weinheim, Germany, 2008, pp. 123-127; b) Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, *299*, 1691-1693; c) Venkataramanan, N. S.; Kuppuraj, G.; Rajagopal, S. *Coord. Chem. Rev.* **2005**, *249*, 1249-1268; d) Cozzi, P. G. *Chem. Soc. Rev.* **2004**, *33*, 410-421; e) Baleizão, C.; García, H. *Chem. Rev.* **2006**, *106*, 3987-4043.
5. a) Romero, M. J.; Pedrido, R.; González-Noya, A. M.; Martínez-Calvo, M.; Zaragoza, G.; Bermejo, M. R. *Chem. Commun.* **2010**, *46*, 5115-5117; b) Romero, M. J.; Pedrido, R.; González-Noya, A. M.; Maneiro, M.; Fernández-García, M. I.; Zaragoza, G.; Bermejo, M. R. *Dalton Trans.* **2012**, *41*, 10832-10844.
6. a) Aurangzeb, N.; Hulme, C. E.; McAuliffe, C. A.; Pritchard, R. G.; Watkinson, M.; Bermejo, M. R.; García-Deibe, A.; Sanmartín, J.; Sousa, A. *J. Chem. Soc., Chem. Commun.* **1994**, *9*, 1153-1155; b) González-Riopedre, G.; Fernández-García, M. I.; González-Noya, A. M.; Vázquez-Fernández, M. A.; Bermejo, M. R.; Maneiro, M. *Phys. Chem. Chem. Phys.* **2011**, *13*, 18069-18077.
7. a) Vázquez-Fernández, M. A.; Bermejo, M. R.; Fernández-García, M. I.; González-Riopedre, G.; Rodríguez-Doutón, M. J.; Maneiro, M. *J. Inorg. Biochem.* **2011**, *105*, 1538-1547; b) González-Riopedre, G.;

Bermejo, M. R.; Fernández-García, M. I.; González-Noya, A. M.; Pedrido, R.; Rodríguez-Doutón, M. J.; Maneiro, M. *Inorg. Chem.* **2015**, *54*, 2512-2521.