COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Unprecedented detection of inherent chirality in uranyl–salophen complexes

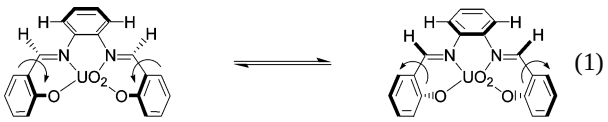
Antonella Dalla Cort, Luigi Mandolini,* Giovanni Palmieri, Chiara Pasquini and Luca Schiaffino
IMC-CNR and Dipartimento di Chimica, Università La Sapienza, Box 34-ROMA 62, 00185 Roma, Italy

Received (in Cambridge, UK) 9th June 2003, Accepted 10th July 2003
First published as an Advance Article on the web 24th July 2003

In complexes with the uranyl dication salophen ligands are highly puckered. This implies that non-symmetrically substituted uranyl–salophen derivatives exist in principle as a pair of enantiomers. However, due to easy disrotations about the bonds connecting the phenoxide units to the imine carbons, the rate of interconversion between enantiomeric forms of simple, sterically unhindered compounds is extremely fast. Bulky substituents in appropriate positions decrease the interconversion rate and make this novel type of inherent chirality detectable by ^{1}H and ^{13}C NMR.

† Salophen ligands are diimino tetradentate dianionic ligands that form very strong complexes with the uranyl dication UO_2^{2+}.[1] A fifth coordination site is available in the equatorial plane of the uranyl dication for complexation with an additional monodentate ligand. Hence uranyl–salophen complexes behave as electrically neutral, hard Lewis acids which have found applications in the molecular recognition of anions[2] and neutral molecules,[3] and also in catalysis of ester cleavage[4] and of 1,4-thiol addition to enones.[5]

Because of the large ionic radius of the uranium in the uranyl cation, the ligand cannot assume a planar geometry, but is highly puckered, as shown by the computer calculated structure of the uranyl–salophen unit (Fig. 1), which is consistent with available X-ray crystallographic data.[3b,6] In non-symmetrically substituted uranyl–salophen derivatives (*e.g.* **1**), the non-planar geometry results in the absence of any symmetry element and, consequently, makes these compounds inherently chiral. It should be considered, however, that more or less concerted disrotations about the bonds connecting the imine carbons to the phenoxide rings could possibly invert the curvature of the salophen ligand through a flipping of the salicylaldehyde units [eqn. (1)] and lead to interconversion of enantiomeric forms.



(1)

No information of any kind is available on the inherent chirality of non-symmetrically substituted uranyl–salophen complexes. To the best of our knowledge the mere existence of the flipping motion has never been documented. Here we show that in simple uranyl–salophen compounds enantiomers are rapidly interconverted, and describe the synthesis of derivatives in which the stiffness of the molecular framework is increased through steric congestion to such an extent that the chirality is maintained and easily detected by NMR spectroscopy.

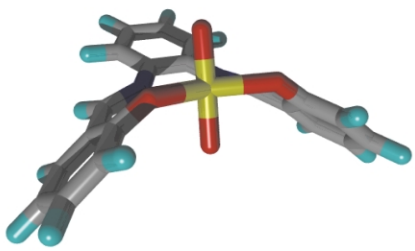


Fig. 1 Computer calculated structure of the uranyl–salophen unit.

The substrate chosen for initial study is the simple derivative **1**, in which the function of the isopropyl is to act as a diastereotopic NMR probe because the two methyls become inequivalent in a chiral environment. Complex **1** was prepared by reacting a 1 : 1 : 1 mixture of salicylaldehyde, 3-isopropylsalicylaldehyde, and 1,2-diaminobenzene with 1 mol equiv. of $UO_2(OAc)_2{\cdot}2H_2O$ in MeOH at room temperature, followed by chromatographic treatment of the statistical mixture of products. The ^{1}H NMR spectrum of this compound shows that the doublet corresponding to the methyl protons is not split even at −40 °C (Fig. 2a). A single sharp line is also obtained for the methyl carbon resonance in the ^{13}C NMR spectrum (Fig. 3, spectrum a). An obvious interpretation of the above observations is that interconversion between enantiomeric forms is fast on the NMR time scale, but the possibility that chemical shift differences are too small to measure cannot be ruled out.

Inspection of molecular models shows that the flipping motion is resisted by van der Waals interactions between the hydrogens shown in the formulae of eqn. (1), because these hydrogens are required to move past each other. Thus, the presence of one or more bulky substituents in place of the hydrogens is expected to hinder the interconversion process to a significant extent. To test this idea, compound **2** was synthesized according to the stepwise procedure outlined in Scheme 1. The variable temperature ^{1}H NMR spectra in CD_3OD (Fig. 2b) indeed show two well resolved doublets at

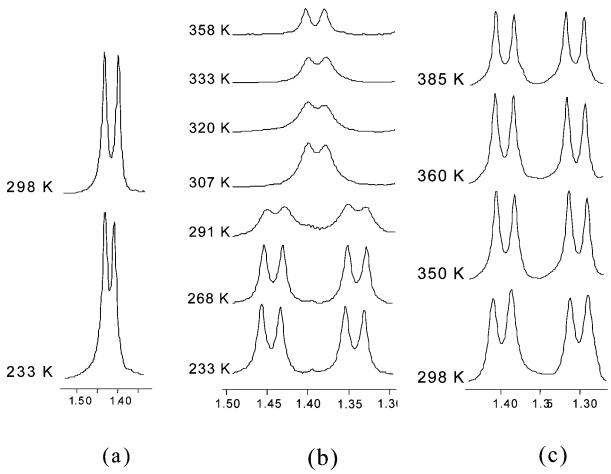


Fig. 2 (a) Portion of the ^{1}H NMR spectral region of **1** (300 MHz in CD_3OD) displaying the sharp doublet of the methyl protons at 298 K and at 233 K. (b) Temperature dependent ^{1}H NMR spectra of the methyl group signals of **2** (300 MHz in CD_3OD). (c) Temperature dependence of the methyl groups signals of **3** (300 MHz in $(CD_3)_2SO$) showing that the two doublets do not coalesce even at 112 °C.

† Electronic Supplementary Information (ESI) available: experimental details describing the synthesis and characterization of compounds **1–3**, and computational details for the calculation of the structure in Fig. 1. See http://www.rsc.org/suppdata/cc/b3/b306478f/

DOI: 10.1039/b306478f

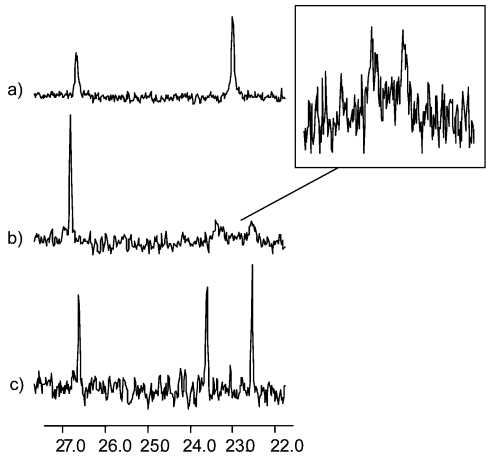
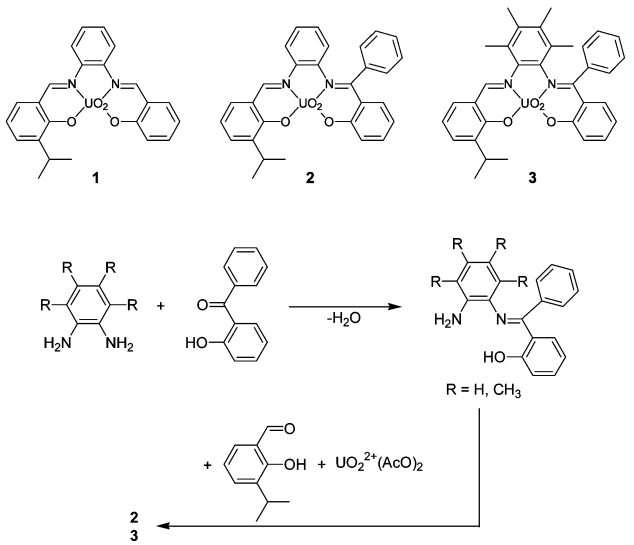


Fig. 3 Portion of the ^{13}C NMR spectral regions of **1** (a), **2** (b), and **3** (c) in CD_3COCD_3 at 75 MHz displaying the resonances of the methyl group signal at 298 K.



Scheme 1 Syntheses of complexes **2** and **3**.

lower temperatures, and a single doublet at higher temperatures. Computer line shape simulation of the spectrum at 291 K (Fig. 2, trace b) yields a rate constant of 10 s^{-1}, corresponding to an activation energy of 15.7 kcal mol^{-1}. This result is further confirmed by the line shape simulation of the ^{13}C NMR spectrum at 298 K (Fig. 3, trace b) which yields a rate constant of 20 s^{-1}, thus again a $\Delta G^{\neq}$ of 15.7 kcal mol^{-1}. These observations clearly show that the bulky phenyl substituent indeed hinders the flipping motion, and demonstrate that in compound **1** this motion is fast on the NMR time scale.

A further step towards an increase in the height of the barrier for enantiomerization was made with compound **3**, which was synthesized as above starting from the 3,4,5,6-tetramethyl derivative of 1,2-diaminobenzene in place of its parent compound. Fig. 2c shows that the room temperature ^1H NMR spectrum in $(CD_3)_2SO$,[7] consisting in two well resolved doublets, is unchanged upon heating up to 112 °C, which corresponds to a free energy barrier $\Delta G^{\neq} \geq 21$ kcal mol^{-1}. Consistently, the ^{13}C NMR spectrum of **3** at room temperature shows two sharp singlets for the resonances of methyl carbons (Fig. 3, spectrum c).

It should be emphasized that the chirality in **2** and **3** arises from complexation of the uranyl dication with achiral salophen ligands, and bears no direct relationship to the well known chiral salophen- or salen-complexes widely used in asymmetric syntheses (*e.g.* Jacobsen's catalysts)[8] which are prepared from chiral diamine[9] and/or aldehyde[10] precursors.

To sum up, the bird-like uranyl–salophen unit, whose bent shape is imposed by the bulky uranium, flaps its wings frenziedly due to easy disrotations about the bonds connecting the phenoxide units to the imine carbons. As a consequence, an unsymmetrically substituted derivative like **1** exists in principle as a pair of enantiomers, but the rate of interconversion is fast on the NMR time scale even at −40 °C. Strategically placed bulky substituents slow down the flipping motion and make the chirality detectable by NMR spectroscopy. Interconversion of enantiomeric forms of **3** is slow on the NMR time scale even at +112 °C.

We are presently pursuing the resolution of racemic **3**, which represents a prototype structure for a family of novel inherently chiral hosts whose structure can be modulated within wide limits using suitably substituted aldehydes and/or ketones as starting materials. These hosts are expected to have potential in the selective recognition of chiral neutral molecules and chiral anions. Furthermore, upon reaction with hard anions such as F^- and Cl^-,[6c] highly structured inherently chiral anions can be obtained, for use in the recognition of chiral organic cations.

We gratefully acknowledge financial contributions from MIUR, progetto Dispositivi Supramolecolari.

Notes and references

1 (*a*) P. Pfeiffer, T. Hesse, H. Pfitzner, W. Scholl and H. J. Thielert, *Prakt. Chem.*, 1937, 217; (*b*) G. Bandoli, D. A. Clemente, U. Croatto, M. Vidali and P. A. Vigato, *J. Chem. Soc., Chem. Commun.*, 1971, 1330.

2 D. M. Rudkevich, W. T. S. Huck, F. C. J. M. van Veggel and D. N. Reinhoudt, Metallomacrocycles and -clefts: receptors for neutral molecules and anions, in *Transition Metals in Supramolecular Chemistry*, eds L. Fabbrizzi and A. Poggi, NATO ASI Series (No. 448), Series C: Mathematical and Physical Science, Kluwer, Dordrecht 1994 329.

3 (*a*) A. R. Van Doorn, W. Verboom and D. N. Reinhoudt, Molecular recognition of neutral molecules by synthetic receptors, in *Advances in Supramolecular Chemistry*, ed. G. W. Gokel, **vol 3**, JAI Press, Greenwich ,1993, 159; (*b*) A. R. van Doorn, R. Schaafstra, M. Bos, S. Harkema, J. van Eerden, W. Verboom and D. N. Reinhoudt, *J. Org. Chem.*, 1991, **56**, 6083; (*c*) V. van Axel Castelli, A. Dalla Cort, L. Mandolini, V. Pinto, D. N. Reinhoudt, F. Ribaudo, C. Sanna, L. Schiaffino and B. H. M. Snellink-Ruël, *Supramol. Chem.*, 2002, **14**, 211.

4 V. van Axel Castelli, R. Cacciapaglia, G. Chiosis, F. C. J. M. van Veggel, L. Mandolini and D. N. Reinhoudt, *Inorg. Chim. Acta*, 1996, **246**, 181.

5 V. van Axel Castelli, A. Dalla Cort, L. Mandolini, D. N. Reinhoudt and L. Schiaffino, *Eur. J. Org. Chem.*, 2003, 627 and references cited therein.

6 (*a*) C. J. van Staveren, D. E. Fenton, D. N. Reinhoudt, J. van Eerden and S. Harkema, *J. Am. Chem. Soc.*, 1987, **109**, 3456; (*b*) A. R. van Doorn, W. Verboom, S. Harkema and D. N. Reinhoudt, *Synthesis*, 1992, 119; (*c*) D. M. Rudkevich, W. P. R. V. Stauthamer, W. Verboom, J. F. J. Engbersen, S. Harkema and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1992, **114**, 9671; (*d*) C. J. van Staveren, J. van Eerden, F. C. J. M. van Veggel, S. Harkema and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1988, **110**, 4994; (*e*) D. N. Reinhoudt and H. J. den Hertog Jr., *Bull. Soc. Chim. Belg.*, 1988, **97**, 645.

7 A control experiment showed only one doublet for the methyl groups of **2** in $(CD_3)_2SO$ at 112 °C. However, the low solubility of **2** in $(CD_3)_2SO$ at lower temperatures did not permit the coalescence temperature to be determined in this solvent.

8 E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker and L. Deng, *J. Am. Chem. Soc.*, 1991, **113**, 7063.

9 (*a*) A. Berkessel, D. Menche, C. A. Sklorz, M. Schröder and I. Paterson, *Angew. Chem., Int. Ed.*, 2003, **42**, 1032; (*b*) W. Sun, H. Wang, C. Xia, J. Li and P. Zhao, *Angew. Chem., Int. Ed.*, 2003, **42**, 1042; (*c*) M. Bandini, P. G. Cozzi, P. Melchiorre and A. Umani-Ronchi, *Angew. Chem., Int. Ed.*, 1999, **38**, 3357; (*d*) M. Bandini, P. G. Cozzi and A. Umani-Ronchi, *Angew. Chem., Int. Ed.*, 2000, **39**, 2327; (*e*) M. Bandini, P. G. Cozzi and A. Umani-Ronchi, *Chem. Commun.*, 2002, 919 and references cited therein (*f*) W. T. S. Huck, F. C. J. M. van Veggel and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas*, 1995, **114**, 273.

10 (*a*) E. F. DiMauro and M. C. Kozlowski, *Org. Lett.*, 2001, **3**, 1641; (*b*) E. F. DiMauro and M. C. Kozlowski, *Organometallics*, 2002, **21**, 1454; (*c*) H. Brunner and H. Schiessling, *Bull. Soc. Chim. Belg.*, 1994, **103**, 119; (*d*) A. R. van Doorn, D. J. Rushton, M. Bos, W. Verboom and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 415.