Original citation:

Permanent WRAP URL:
http://wrap.warwick.ac.uk/76670

Copyright and reuse:
The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions. Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher's statement:
© 2016, Elsevier. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International
http://creativecommons.org/licenses/by-nc-nd/4.0/

A note on versions:
The version presented here may differ from the published version or, version of record, if you wish to cite this item you are advised to consult the publisher's version. Please see the 'permanent WRAP URL' above for details on accessing the published version and note that access may require a subscription.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk
Graphical Abstract

To create your abstract, type over the instructions in the template box below. Fonts or abstract dimensions should not be changed or altered.

Sodium template synthesis of a 54-membered bis(pyridine) macrocycle

Thibault Troade, Amber L. Thompson and Adrian B. Chaplin
Sodium template synthesis of a 54-membered bis(pyridine) macrocycle

Thibault Troade, Amber L. Thompson and Adrian B. Chaplin

1. Introduction

Since the seminal work by Pedersen in the 1960s, metal templates have been widely employed in macrocyclization reactions, with alkali and alkaline earth metal cations being notable for their use in the preparation of ethylene glycol-based crown ethers. With interesting applications in the construction of molecules with interlocked topologies, methodologies involving transition metal templates and chelating heteroatom ligands have become commonplace in supramolecular chemistry. For these applications nitrogen-based precursors, such as bipyridine-, phenanthroline-, and bis(mimino)pyridine-based ligands, are generally preferred. Mixed nitrogen-oxygen donor ligands, such as 2,6-bis(alkenyl-oxo-methyl)pyridines, are readily accessible and potentially useful building blocks for the construction of large macrocyclic systems via olefin metathesis. Indeed, using elaborate tri- and hexa-nuclear platinum templates together with cross-metathesis, massive tris(pyridine) and hexa(pyridine) cyclic systems have been prepared solely through coordination of the pyridine group. As part of their investigation of transition-metal-based molecular gyroscopes, Gladysz and co-workers have similarly exploited pyridine coordination to a single platinum center to prepare bis(pyridine) macrocycles through olefin cross-metathesis of 2,6-bis(2-propen-1-oxymethyl)pyridine and 2,6-bis(3-buten-1-oxymethyl)pyridine however, the cross-metathesis steps are low yielding (10% and 22%, respectively). Motivated by the potential for tridentate coordination and operational simplicity, we postulated that such bis(pyridine) macrocycles could be alternatively prepared using alkali metal templates and herein report a straightforward and high yielding sodium template-based synthesis of 54-membered bis(pyridine) macrocycle 3 from 2,6-bis(10-undecen-1-oxymethyl)pyridine 1.

2. Results and discussion

The alkene functionalized pyridine 1 was readily obtained from reaction of sodium 10-undecen-1-oxide with commercially available 2,6-bis(bromomethyl)pyridine in 73% isolated yield. Full details are provided in the ESI along with the preparation and solid-state structure of 1-Mel. In anhydrous CD2Cl2, the interaction of 1 with vigorously dried Na[BAr₄] (Ar⁺ = 3,5-C6H4(CF3)2) resulted in dissolution of the otherwise insoluble salt along with a significant downfield shift of the pyCH₂O resonances (ca. 0.16 ppm) and concomitant upfield shift of the 3-pyridyl ¹H resonances (ca. 0.17 ppm). The system was observed to be under fast exchange at 298 K (400 MHz) and a 2:1 coordination stoichiometry, consistent with adoption of an octahedral geometry about the sodium cation, was established through a Job plot analysis (Figure 1). Complexation persisted in the gas-phase, with a signal at m/z +909.727 (37%) observed by ESI-MS for the intact parent cation (calc. 909.742), alongside the 1:1 adduct (m/z 466.357; calc. 466.366; 100%) and protonated ligand (m/z 444.374; calc. 444.384; 17%). Treatment of [Na(I)₂][BAr₄] prepared in situ with Grubbs I (15 mol% I) under a slow stream of argon resulted in complete cross-metathesis of the terminal alkene groups after 20 h. In the absence of a sodium template, metathesis of 1 with Grubbs I principally resulted in ring closing metathesis, although small amounts of 2 were detected by ESI-MS. The sodium template and residual catalyst were removed by addition of HCl, neutralization with triethylammonium and purification by flash column chromatography (silica gel; pentane:Et₂O, 1:1) to afford 54-membered 2 in 51% isolated yield.

* Corresponding author. Tel.: +44 (0) 2476151765; e-mail: a.b.chaplin@warwick.ac.uk; twitter: @chaplinlab.
Analytically pure macrocycle 2 was obtained as mixture of EE/EE/ZZ-isomers that could not be separated on a preparative scale, despite repeated efforts. A small number of single crystals of (primarily) EE-2 were obtained by recrystallization from CH3CN/Et2O which enabled the collection of X-ray crystallographic data.8 The solid-structure of EE-2 exhibits a peculiar rectangle-shaped conformation, with the short edge comprised of the internal alkenes and the pyridine groups adopting an offset head-to-head orientation (Figure 1, bottom right). To reaffirm the purity, macrocycle 2 was hydrogenated to give the corresponding saturated alkyl macrocycle 3 as the sole product (verified by high field 1H and 13C NMR spectroscopy) in quantitative yield.

Recently sodium-ion-based template strategies have begun to be successfully employed in the capture of interlocked systems.7 In the absence of additional directing interactions, such as π-stacking,8 the hydrocarbon pyridine arms in [Na(1)][BArF4] are, however, unlikely to be held in the correct orientation for the formation of two interlocked macrocycles. Selective ESI-MS/MS fragmentation of the signal [3-2H]8 in the ion trap of the spectrometer leads to peaks for [C28H28NaO6] (m/z 418.369; calc. 418.369; 100%) and [C27H24NaO5] (m/z 416.355; calc. 416.353; 50%) as the major ions. The significant presence of the higher molecular weight fragments with two pyridine groups ([C31H22N2O6] m/z 557.435; calc. 557.431; 8%) and two alkyl chain arms ([C30H22NaO6] (m/z 714.677; calc. 741.676; 13%) reaffirms the formulation of 3 (and 2) as a 54-membered macrocycle rather than a [2]catenane alternative.

Acknowledgments

We gratefully acknowledge the Leverhulme Trust (RPG-2012-718, T.T.) and Royal Society (A.B.C) for financial support. We thank Diamond Light Source for an award of beamtime on I19 (MT9981), and Dr. Lijiang Song and Dr. Philip Aston for technical assistance with the collection of ESI-MS data.

Supplementary Material

Full experimental details, including the preparation and solid-state structure of 1-[Me]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1062644, 1-[Me]; 1062645, EE-2; 1062646, EE-2 polymorph) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

References and notes


6. X-ray diffraction data were collected at 100 K (Cosier J.; Glazer, A. M. J. Appl. Crystallogr. 1986, 19, 105–107) with synchrotron radiation using I19 (EH1) at Diamond Light Source (λ = 0.6889 Å; Nowell, H.; Barnett, S. A.; Christensen, K. E.; Teat, S. J.; Allan, D. R. J. Synch. Rad. 2012, 19, 435–441). Cell parameters were determined and refined and raw frame data were integrated using CrysAlisPro (Agilent Technologies, 2010). The structure was
solved with SIR92 (Altomare, A.; Cascarano, G.; Giacobazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori G.; Carnalli, M. J. Appl. Cryst. 1994, 27, 435) and refined by full-matrix least squares on \( F^2 \) using CRYSTALS (Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. J. Appl. Cryst. 2003, 36, 1487; Parois, P.; Cooper, R. I.; Thompson, A. L. Chem. Cent., in press). A small amount of EZ-2 (34%) co-crystallized in the sample and resulted in apparent cis/trans-disorder of one of the double bonds, which was modeled with restraints to maintain the sensible geometries. All non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were generally visible in the difference map and treated in the usual manner (Cooper, R. I.; Thompson, A. L.; Watkin, D. J. J. Appl. Cryst. 2010, 43, 1100–1107). A second disorder free polymorph disorder was also observed (EE-2), with half a molecule in the asymmetric unit. The crystal was of particularly poor quality and the resulting data were found to be very noisy, nevertheless, the structure is included for completeness.
