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An Efficient Synthesis of Versatile Terpyridine Analogues for Cyclometallated Luminescent Cyclodextrins

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Abstract: An efficient synthetic method for preparing functionalised terpyridyl analogues based on Negishi's zinc coupling is developed. These ligands form cyclometallated complexes; attaching them to cyclodextrins allows preparation of luminescent cyclometallated ruthenium cyclodextrins for the assembly of photoactive units *via* non-covalent interactions. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Negishi's cross-coupling, luminescent cyclodextrins, ruthenium complexes.

Photoactive metallo-architectures have attracted a lot of attention for the development of photonic devices and sensors.[1] We have been interested in the development of multimetallic assemblies employing cyclodextrins as receptors to assemble photoactive metal centres *via* non-covalent interactions.[2] Our design involves appending metal centres on the cyclodextrin rim and studying the communication between the appended centre and metalloguests entering the cyclodextrin cavity.

We wish to employ cyclometallated ruthenium complexes based on terpyridine analogues due to their attractive photoluminescent properties.[3] They exhibit room temperature long-lived emission whereas complexes of terpyridine itself do not emit at room temperature unless functionalised on the central ring with appropriate (mainly electron withdrawing) groups, for example -Ph, $-SO_2Me$.[4] To avoid employing phenyl groups that act as "spacers " between the appended unit and the guest we chose for our design cyclometallated complexes that bring the appended luminescent unit in close proximity to the cyclodextrin cavity. Moreover, the reduced charge of the cyclometallated unit with respect to terpyridyl complexes is an advantage for avoiding

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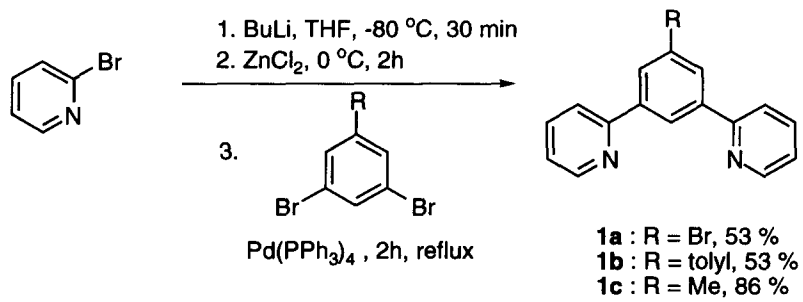
perturbation of the guest binding.[5] In this paper we wish to report an efficient synthesis of a terpyridine analogue which is an important ligand for cyclometallating ruthenium complexes and a useful precursor for the formation of new ruthenium cyclometallated cyclodextrins.

Cyclometallated terpyridine analogues have been prepared by low yielding methods based either on a Stille's cross-coupling reaction which requires isolation of a stannyl derivative,[6] or on a cobalt-catalysed cyclization reaction which requires extreme conditions,[7] or on a Kröhnke synthesis, which restricts the position of the cyclometallated ring in the ligand.[8] To develop versatile derivatives in high yield for cyclodextrin attachment a new preparation method was necessary.

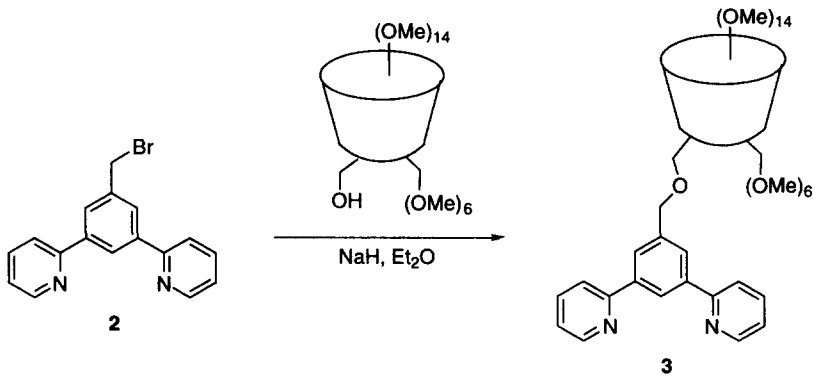
We found a one-pot application of Negishi's zinc chloride cross-coupling method[9] to easily access 5-derivatised 1,3-di-(2'-pyridyl)benzene for preparation of cyclometallated cyclodextrins, avoiding the isolation of an intermediate. Commercially available 2-bromopyridine was converted to 2-lithiopyridine by an exchange reaction with *n*-butyllithium at -78 °C. Addition of $ZnCl_2$ at 0 °C gave the pyridylzinc chloride which was not isolated. Addition of a 1,3-dibromobenzene derivative and the palladium catalyst $Pd(PPh_3)_4$ leads to the formation of the coupling product (**Scheme I**). The 1,3-di-(2'-pyridyl)benzene derivatives are isolated in good yield after alumina column chromatography and fully characterised by NMR spectroscopy and mass spectrometry.

Scheme I



Compound **1c** was brominated (NBS, benzoyl peroxide, CCl_4, reflux) to give **2** in 64 % yield (by NMR). The crude brominated product was used for the attachment to the mono-6-hydroxy permethylated β-cyclodextrin.[10] The advantage of using permethylated derivatives is the higher solubility in organic solvents than the plain cyclodextrin that allows flexibility in the synthetic procedure and easy separation by column chromatography. The coupling to the cyclodextrin was carried under Williamson ether conditions, using an excess of NaH in dried diethyl ether (**Scheme II**). Compound **3** was isolated in 33 % yield after extraction into ethyl acetate and purification by silica gel chromatography (R_f = 0.15; eluent: ethyl acetate/methanol, 9.5:0.5).

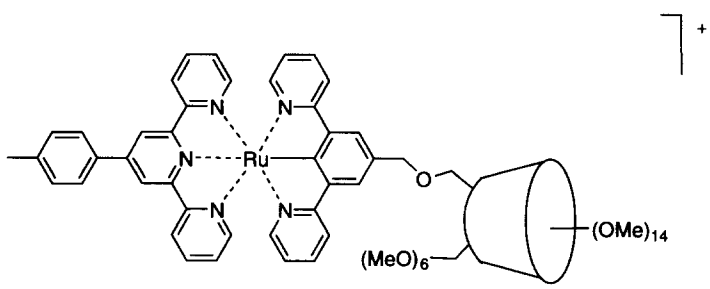
Scheme II



2 3

The compound was fully characterised by detailed NMR studies.[11] A signature of the substitution is the 0.4 ppm upfield shift of the H-6 protons of the derivatised glucose ring as expected for the substitution. The H-6 protons of the glucose ring are diastereotopic with one of them appearing at 4.12 ppm whereas the second is masked in the group of signals in the region of 3.84 – 3.13 ppm corresponding to the rest of the cyclodextrin protons. Its resonance has been identified to be at 3.71 ppm corresponding to a ^{13}C signal at 68.5 ppm by an ^{1}H–^{13}C HMQC experiment. The benzylic protons become diastereotopic due to the chirality of the cyclodextrin with an AB system centred at 4.76 ppm.

The cyclometallated ruthenium cyclodextrin **4** has been prepared by reaction of **3** with [Ru(ttp)Cl_3] (ttp = tolyl-terpyridine) following a procedure developed for cyclometallated ruthenium complexes.[12] The complex [Ru(**3**)(ttp)][PF_6] was isolated in 44 % yield by precipitation after anion exchange with NH_4PF_6.



4

Spin decoupling ^{1}H NMR experiments allowed complete assignment of the aromatic protons.[13] The formation of the carbon-ruthenium bond is confirmed by the disappearance of the

signal corresponding to the H-2' proton of the benzylic ring. The coordination of the ruthenium metal is also confirmed by the 1.7 ppm upfield shift of the H-6 protons of the pyridine rings. In the cyclodextrin region it is interesting to note that one of the anomeric protons is shifted to 5.39 ppm whereas the rest resonate between 5.28 and 5.11 ppm. We attribute this to the H-1 of the substituted glucose ring.

The ruthenium complex exhibits broad MLCT absorption bands with distinct band maxima at 508 nm and 548 nm, characteristic of analogous ruthenium cyclometallated complexes.[7] Excitation at either of the bands leads to room temperature luminescence centred at 790 nm.

This efficient route for preparation of 1,3-di-(2'-pyridyl)benzene derivatives has allowed the development of ruthenium cyclometallated cyclodextrins as photoactive receptor units. Photophysical studies of the effect of metalloguest binding are under investigation.

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11. Selected spectroscopic data for **3**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (d, J = 4.7 Hz, 2H, H-6), 8.55 (s, 1H, H-2'), 8.08 (s, 2H, H-4'), 7.87 (d, J = 7.6 Hz, 2H, H-3), 7.79 (dd, J = 7.6 and 7.1 Hz, 2H, H-4), 7.26 (dd, J = 7.1 and 4.7 Hz, 2H, H-5), 5.16 (d, J = 3.6 Hz, 1H, H-1g), 5.14 (d, J = 3.7 Hz, 1H, H-1g), 5.13-5.08 (m, 5H, H-1g), 4.76 (d, J = 12.1 Hz, 1H, H-b), 4.75 (d, J = 12.1 Hz, 1H, H-b), 4.12 (dd, J = 10.9 and 3.6 Hz, 1H, H-6g), 3.84-3.13 (m, 41H, H-2g, H-3g, H-4g, H-5g, H-6g), 3.64-3.61 (7s, 21H, CH_3O-3g), 3.50-3.48 (7s, 21H, CH_3O-2g), 3.43-3.29 (6s, 18H, CH_3O-6g). (b = benzylic, g = glucose rings). FABMS m/z = 1659 (M^+).
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13. Selected spectroscopic data for **4**:^{1}H NMR (600 MHz, $CDCl_3$): δ 8.92 (s, 2H, H-3'ttp), 8.56 (d, J = 8.0 Hz, 2H, H-3ttp), 8.15 (s, 2H, H-4'), 8.07 (d, J = 7.6 Hz, 2H, H-*o*ttp), 7.98 (d, J = 8.0 Hz, 2H, H-3), 7.68 (dd, J = 8.0 and 7.4 Hz, 2H, H-4ttp), 7.52 (dd, J = 8.0 and 7.6 Hz, 2H, H-4), 7.48 (d, J = 7.6 Hz, 2H, H-*m*ttp), 7.09 (d, J = 5.2 Hz, 2H, H-6ttp), 7.00 (d, J = 5.4 Hz, 2H, H-6), 6.88 (dd, J = 7.4 and 5.2 Hz, 2H, H-5ttp), 6.65 (dd, J = 7.6 and 5.4 Hz, 2H, H-5), 5.39 (d, J = 3.4 Hz, 1H, H-1g), 5.28 (d, J = 3.4 Hz, 1H, H-1g), 5.15-5.14 (m, 3H, H-1g), 5.13 (d, J = 3.7 Hz, 1H, H-1g), 5.11 (d, J = 3.4 Hz, 1H, H-1g), 4.94 (d, J = 10.8 Hz, 1H, H-b), 4.93 (d, J = 10.8 Hz, 1H, H-b), 4.40 (dd, J = 10.8 and 2.9 Hz, 1H, H-6g), 3.99-3.18 (m, 41H, H-2g, H-3g, H-4g, H-5g, H-6g), 3.70-3.64 (7s, 21H, CH_3O-3g), 3.51-3.49 (7s, 21H, CH_3O-2g), 3.41-3.38 (6s, 18H, CH_3O-6g). (ttp = tolyl-terpyridine, *m* = meta, *o* = ortho). FAB-MS m/z = 2083 ([Ru(**3**)(ttp)]$^+$).