The Hiratani–Double-Claisen Rearrangement as a Key Step in the Preparation of Sequential Bis(8-hydroxyquinoline) Ligands

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Abstract: Symmetric and sequential isobutenylidene-bridged bis-(8-hydroxyquinoline)s are prepared by application of the Hiratani– double-Claisen rearrangement as a key step in the reaction sequence. The formation of a dinuclear helicate-type zinc(II) complex is also described.

Keywords: 8-hydroxyquinoline, complexes, Claisen rearrangement, self-assembly, supramolecular chemistry

8-Hydroxyquinoline derivatives **1** are well-established metal binding units. Initially they were mainly used for analytical purposes,¹ however, more recently they have been exploited due to the extraordinary emission properties of their metal complexes.²

We became interested in bis(8-hydroxyquinoline)s in the context of helicate self-assembly. We prepared a series of alkyl-bridged derivatives.³ Our approach employed the method described by Hiratani:⁴ a double-Claisen rearrangement resulting in the formation of two carbon–carbon bonds in one reaction step.⁵ Thus, we were able to obtain triple-stranded dinuclear helicate-type complexes (Figure 1) in a template-directed self-assembly process.⁶



appropriate templates M'+.5

Figure 1 Triple-stranded helicate-type complexes, which are formed from a simple bis(8-hydroxyquinoline) in the presence of

SYNLETT 2006, No. 6, pp 0924–0926 Advanced online publication: 14.03.2006 DOI: 10.1055/s-2006-933140; Art ID: G00206ST © Georg Thieme Verlag Stuttgart · New York In order to extend this chemistry and to prepare more sophisticated homo- or heterodinuclear complexes we applied the Hiratani–double-Claisen rearrangement to the preparation of functionalized and sequential bis(8-hy-droxyquinoline)s.⁷ Therefore, we prepared 2-cyano-8-hy-droxyquinoline **2** starting from 8-hydroxyquinoline **1** by a known three-step procedure.⁸ In the last step the desired compound **2** was obtained in 60% yield together with 15% of the corresponding amide **3** (Scheme 1), which also represents an interesting building block.



Scheme 1 Preparation of the building blocks 2 and 3 following a literature procedure.

Williamson ether formation of **2** with an excess of 3,3'-dichloroisobutene **4** in the presence of potassium carbonate afforded the bis-ether **5** in 32% together with the mono-ether **6** in 35% yield (Scheme 2).

For the Hiratani–double-Claisen rearrangement, **5** was heated in a vacuum for five hours at 175 °C to obtain the rearranged product **7** in 95% yield. Hydrolysis of the nitrile **7** afforded the bis-carboxylic acid **8**.⁹ However, due to the low solubility of this diacid **8** and its metal complexes we were not able to obtain defined coordination compounds.

In order to prepare a sequential ligand, Williamson ether synthesis of the mono-ether **6** and 8-hydroxyquinoline **1** was performed (Scheme 3). The resulting compound **9** (90–95%) underwent rearrangement at 175 °C to give the isobutenylidene-bridged dihydroxyquinoline **10** in 95% yield (crude product). Hydrolysis of the nitrile **10** yielded the carboxylic acid **11**-H₃ in 70%, which was characterized by standard analytical methods.¹⁰



Scheme 2 Preparation of the dicarboxylic acid derivative 8.



Scheme 3 Preparation of the sequential bis(8-hydroxyquinoline) derivative 11-H₃.

Preliminary coordination studies of ligand 11-H₃ were performed with zinc(II) acetate in the presence of potassium carbonate as base (Figure 2); a solid yellow material was obtained in quantitative yield, which exhibited a single set of signals by ¹H NMR spectroscopy.¹¹

X-ray quality crystals were obtained for the rubidium salt $Rb_2[(11)_2Zn_2]$. The molecular structure of the dianion $[(11)_2Zn_2]^{2-}$ is represented in Figure 2.¹² Two ligands 11 are bridging the two zinc(II) ions in an anti-parallel fashion resulting in the coordination of a bidentate quinolinate



Figure 2 Formation of the dinuclear zinc(II) complex $M_2[(11)_2Zn_2]$ and two representations of the molecular structure of the dianion as found in the crystal of $Rb_2[(11)_2Zn_2]$ and intertwined packing of the dimer (blue: Zn, yellow: Rb).

as well as a tridentate quinolinate-2-carboxylate unit to each of the metal centers.¹³ Thus the zinc(II) ions adopt a distorted trigonal bipyramidal geometry. Due to a bent arrangement of the dinuclear complex it forms a dimeric structure in the solid phase (Figure 2).

Herein we presented the preparation of bis(8-hydroxyquinoline) derivatives with at least one tridentate ligand moiety using the Hiratani–double-Claisen rearrangement as a key step of the reaction sequence. In addition we described the formation of a dinuclear helicate-type zinc(II) complex with an anti-parallel orientation of the two sequential ligand strands. Further studies are required to obtain hetero-dinuclear d-d or d-f complexes.¹⁴

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- (9) Characterization of **5**: ¹H NMR (300 MHz, CDCl₃): $\delta = 8.22$ (d, J = 8.2 Hz, 2 H), 7.69 (t, J = 8.2 Hz, 2 H), 7.67 (d, J = 8.2 Hz, 2 H), 7.44 (d, J = 8.2 Hz, 2 H), 7.40 (br d, J = 7.7 Hz, 2 H), 5.59 (s, 2 H), 5.09 (s, 4 H). MS (EI): $m/z = 392 [M + H]^+$. Characterization of 6: ¹H NMR (300 MHz, CDCl₃): $\delta = 8.28$ (d, J = 8.4 Hz, 1 H), 7.62 (t, J = 8.2 Hz, 1 H), 7.48 (d, J = 8.2 Hz, 1 H), 7.40 (d, J = 8.4 Hz, 1 H), 7.23 (br d, J = 7.4 Hz, 1 H), 5.49 (s, 1 H), 5.48 (s, 1 H), 4.97 (s, 2 H), 4.33 (s, 2 H). MS (EI): $m/z = 223 [M + H]^+$. Characterization of 7: ¹H NMR $(300 \text{ MHz}, \text{CDCl}_3)$: $\delta = 10.07 \text{ (s, 2 H)}, 8.50 \text{ (d, } J = 8.5 \text{ Hz}, 2$ H), 7.92 (d, J = 8.2 Hz, 2 H), 7.51 (d, J = 8.2 Hz, 2 H), 7.44 (d, J = 8.5 Hz, 2 H), 4.66 (s, 2 H), 3.53 (s, 4 H). Characterization of 8: ¹H NMR (300 MHz, DMSO-*d*₆): $\delta = 8.39$ (d, J = 8.7 Hz, 2 H), 8.14 (d, J = 8.4 Hz, 2 H), 7.51 (d, J = 8.24, 2 H), 7.44 (d, J = 8.5 Hz, 2 H), 4.66 (s, 2 H), 3.53 (s, 4 H). MS (EI): $m/z = 427.3 [M + H]^+$.
- (10) Characterization of **9**: ¹H NMR (300 MHz, CDCl₃): $\delta = 8.92$ (dd, J = 8.4, 1.8 Hz, 1 H), 8.22 (d, J = 8.5 Hz, 1 H), 8.12 (dd, J = 8.2, 1.8 Hz, 1 H), 7.69 (d, J = 8.3 Hz, 1 H), 7.40 (m, 7 H), 5.58 (s, 2 H), 5.11 (s, 2 H), 5.05 (s, 2 H). Characterization of **10**: ¹H NMR (300 MHz, CDCl₃): $\delta = 8.75$ (dd, J = 4.4, 1.6 Hz, 1 H), 8.24 (d, J = 8.3 Hz, 1 H), 8.10 (dd, J = 8.2, 1.4 Hz, 1 H), 7.94 (br s, 1 H), 7.65 (d, J = 8.6 Hz, 1 H), 7.57 (d, J = 8.6 Hz, 1 H), 7.30 (m, 4 H), 4.91 (s, 1 H), 4.86 (s, 1 H), 3.67 (s, 2 H), 3.65 (s, 2 H). Characterization of **11**-H₃: Mp 136 °C. ¹H NMR (300 MHz, DMSO- d_6): $\delta = 8.81$ (dd, J = 4.2, 1.7 Hz, 1 H), 8.48 (d, J = 8.4 Hz, 1 H), 8.27 (dd, J = 8.4, 1.5 Hz, 1 H), 8.08 (d, J = 8.2 Hz, 1 H), 7.48 (m, 3 H), 7.35 (s, 2 H), 4.70 (s, 2 H), 3.58 (s, 2 H), 3.55 (s, 2 H). MS

(ESI+): $m/z = 387 [M + H]^+$. Anal. Calcd for C₂₃H₁₈O₄N₂·0.66H₂O: C, 69.34; H, 4.89; N, 7.03. Found: C, 69.21; H, 4.76; N, 6.92.

- (11) Characterization of $K_2[(11)_2Zn_2]$: ¹H NMR (300 MHz, DMSO- d_6): $\delta = 8.45$ (d, J = 8.2 Hz, 1 H), 8.34 (m, 1 H), 7.96 (m, 2 H), 7.53 (d, J = 8.2 Hz, 1 H), 7.36 (m, 2 H), 6.92 (m, 2 H), 4.81 (s, 1 H). 4.18 (s, 1 H); the signals of the benzylic protons are hidden under the solvent and water peaks. MS (ESI+): $m/z = 899 [M + H]^+$. Anal. Calcd for $C_{46}H_{30}O_8N_4Zn_2K_2 \cdot 5H_2O$: C, 51.84; H, 3.78; N, 5.26. Found: C, 51.82; H, 3.37; N, 4.95.
- (12) (a) $Rb_2[(11)_2Zn_2]$: ¹H NMR (300 MHz, DMSO- d_6): $\delta = 8.31$ (m, 3 H), 7.92 (d, J = 8.2 Hz, 1 H), 7.54 (dd, J = 8.2, 4.7 Hz, 1 H), 7.35 (m, 2 H), 6.85 (m, 2 H), 4.43 (m, 2 H). 3.78 (d, J = 15.3 Hz, 1 H), 3.36 (d, J = 8.7 Hz, 1 H); two further signals are hidden under the water peak. (b) X-ray crystal structure analysis: formula Rb₂(CH₃OH)₃(H₂O) $[(C_{23}H_{15}N_{2}O_{4})_{2}Zn_{2}]$ ·CH₃OH, M = 1214.60, yellow-orange crystal $0.30 \times 0.30 \times 0.05$ mm, a = 12.944 (1), b = 13.320(1), c = 15.608 (1) Å, $\alpha = 101.26$ (1), $\beta = 107.06$ (1), $\gamma = 99.84 (1)^{\circ}, V = 2447.2 (3) \text{ Å}^3, \rho_{\text{calcd}} = 1.648 \text{ gcm}^{-3},$ $\mu = 0.303 \text{ mm}^{-1}$, empirical absorption correction ($0.464 \le T$ \leq 0.863), Z = 2, triclinic, space group P1bar (No. 2), $\lambda = 0.71073$ Å, T = 198 K, ω and φ scans, 25862 reflections collected $(\pm h, \pm k, \pm l)$, $[(\sin\theta)/\lambda] = 0.67 \text{ Å}^{-1}$, 11911 independent ($R_{int} = 0.051$) and 8202 observed reflections $[I \ge 2 \sigma(I)]$, 656 refined parameters, R = 0.047, $wR^2 = 0.100$, max. residual electron density 0.72 (-0.57) eÅ-3, hydrogen atoms are calculated and refined. (c) Data set was collected with a Nonius Kappa CCD diffractometer, equipped with a rotating anode generator, COLLECT (Nonius B.V., 1998). (d) Data reduction, Denzo-SMN: Otwinowski, Z.; Minor, W. Methods Enzymol. 1997, 276, 307. (e) Absorption correction, Denzo: Otwinowski, Z.; Borek, D.; Majewski, W.; Minor, W. Acta Crystallogr., Sect. A 2003, 59, 228. (f) Structure solution, SHELXS-97: Sheldrick, G. M. Acta Crystallogr., Sect. A 1990, 46, 467. (g) Structure refinement: Sheldrick, G. M. SHELXL-97; Universität Göttingen: Germany, 1997. (h) Graphics: Keller, E. SCHAKAL; Universität Freiburg: Germany, 1997. (i) CCDC 294394 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/ retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (1223)336033; E-mail: deposit@ccdc.cam.ac.uk]. (13) Piguet, C.; Hopfgartner, G.; Williams, A. F.; Bünzli, J.-C. G.
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