

Synthesis of Terpyridine Derivatives Containing β -Cyclodextrin

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Abstract: A novel β -cyclodextrin-based terpyridine derivatives has been prepared by the coupling of 4'-(4''-bromomethyl phenyl)- 2, 2':6', 2''-terpyridine with mono-6-hydroxy permethylated β -cyclodextrin. The cyclodextrin dimer appending a 4'-phenyl-2,2':6',2''- terpyridine spacer on the primary faces was synthesized by reaction of 4'-phenyl-2,2':6',2''-terpyridine-6,6'-dicyanitrile with an excess of 6-deoxy-6-*O*-tosyl- β -cyclodextrin.

Keywords: Cyclodextrin, terpyridine, synthesis.

The design of luminescent cyclodextrin sensor systems which are able to detect neutral organic compounds, *e.g.* steroids by a change in emission properties is an area which has attracted much interest over the last decade¹. Photoactive metallo-architectures have attracted a lot of attention for the development of photonic devices and sensor². We have been interested in the development of multimetallic assemblies employing cyclodextrins as receptors to assemble photoactive metal centers *via* non-covalent interactions³. Our design involves appending metal centers on the cyclodextrin rim and studying the communication between the appended center and metalloguests entering the cyclodextrin cavity. Cyclodextrins are extremely attractive components of artificial enzymes and other biomimetic materials. Much interest has been aroused in cyclodextrin dimers in recent years because of their ability to ditopic guests effectively and selectively⁴. Although the double recognition that has resulted from the cooperation of two cyclodextrin cavities is very attractive, it would be more interesting to achieve triple recognition by introducing the linker as another binding site. Therefore, we have designed and synthesized a novel cyclodextrin dimer linked by a 4'-phenyl-2,2':6',2''-terpyridine.

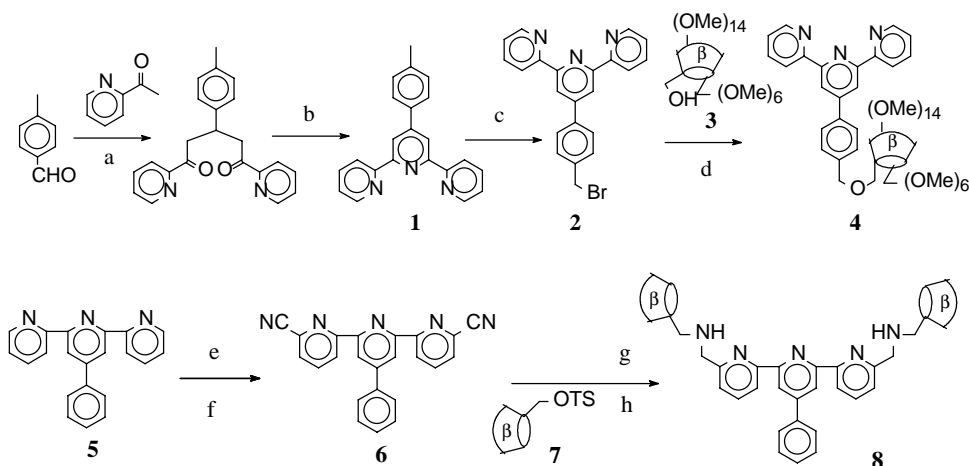
In this paper we wish to report synthesis of a terpyridine analogue binding a cyclodextrin, and a novel cyclodextrin dimer linked by a 4'-phenyl-2,2': 6',2''-terpyridine. The synthetic route is outlined in **Scheme 1**.

Experimental

The C, H, N data were determined using a Varian EL elemental analyzer. ¹H NMR

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Scheme 1



Reagents and conditions: (a) NaOH, EtOH, RT, 1 h, 38 %. (b) NH_4OAc , AcOH, reflux 2 h, 75 %. (c) NBS, C_6H_6 , $(\text{PhCOO})_2$, reflux 18 h, 80 %. (d) Compound **3**, NaH, Et_2O , 24 h, 30 %. (e) MCPBA, CH_2Cl_2 , RT, 12 h, 60 %. (f) Me_3SiCN , CH_2Cl_2 , PhCOCl , RT, 12 h, 82 %. (g) Dry THF, $\text{N}_2\cdot\text{BH}_3\cdot\text{THF}$, RT, 12 h. (h) NEt_3 , DMF, 70–80°C, 48 h, 20 %.

spectra were recorded on a Varian Unity 400 NMR spectrometer. Mass spectra were obtained on a ZAB VG ANALY Mass spectrometer. Compound **1**, **2**, **3**, **5**, **6**, **7** were synthesized respectively referring to literature^{5–10}.

Synthesis of Compound 4

The coupling to the cyclodextrin was carried under Williamson ether condition using an excess of NaH in dried Et_2O . Compound **4** was isolated in 30 % yield after extraction into AcOEt and purification by silica gel (AcOEt:MeOH = 9:1). ^1H NMR (400 MHz, CDCl_3): δ 8.76 (d, 2 H), 7.92 (dd, 2 H), 7.39 (dd, 2 H), 8.70 (d, 2 H), 8.77 (s, 2 H), 7.95 (d, 2 H), 7.58 (d, 2 H), 5.23 (s, 7 H, H_1), 3.89 ~ 3.58 (m, 26 H, $\text{H}_{3,5,6}$), 3.59 ~ 3.43 (m, 14 H, $\text{H}_{2,4}$), 5.13 (s, 2 H, CH_2O), 4.76 (d, 2 H, OCH_2), 3.65 (7s, 21 H, CH_3O), 3.50 (7s, 21 H, CH_3O), 3.38 (6s, 18 H, CH_3O). m/z (FAB): 1736 (M^+). Anal. Calc. For $\text{C}_{84}\text{H}_{125}\text{N}_3\text{O}_{35}$: C 58.09, H 7.25, N 2.42. Found: C 58.14, H 7.36, N 2.58.

Synthesis of Cyclodextrin Dimer 8

A suspension of 4'-phenyl-2,2':6',2''-terpyridine-6,6'-dicyanitrile **6** (0.68 g, 1.9 mmol) and dry THF (15 mL) was deaerated with $\text{N}_2\cdot\text{BH}_3\cdot\text{THF}$ (1 mol/L; 25 mL, 25.0 mmol) within 10 min. After stirring for 12 h, excess BH_3 was destroyed by addition of MeOH, the mixture evaporated, and the residue dissolved in MeOH saturated with dry HCl (30 mL). After stirring for 1 h, the cooled mixture was filtered and solid material washed with cold MeOH. A mixture of this material (0.9 mmol), 6-deoxy-6-O-tosyl- β -cyclodextrin **7** (2.9 g, 2.2 mmol), dry NEt_3 (0.2 mL), and dry DMF (15 mL) was stirred at 70 ~ 80°C under N_2 for 48 h. After being cooled, the mixture was poured into

acetone (200 mL) with vigorous stirring. The solid precipitated was collected by filtration, dried *in vacuo* and dissolved in distilled water (20 mL). The solution was charged onto an ion-exchange column (NKD 113 resin, H⁺ form), which was eluted with distilled water (800 mL), followed by aq. ammonia (0.1 ~ 0.2 mol/L, 1500 mL). The basic fractions were combined and evaporated below 55°C to give dimer **8**. Yield 0.98 g, (20 %). ¹H NMR (400 MHz, D₂O): δ 7.50 (t, 1 H), 7.56 (t, 2 H), 7.75 (dd, 2 H), 7.88 (d, 2 H), 8.00 (t, 2 H), 8.80 (s, 2 H), 8.84 (dd, 2 H), 5.20 (s, 14 H, H₁), 3.88 ~ 3.60 (m, 52 H, H_{3,5,6}), 3.60 ~ 3.46 (m, 28 H, H_{2,4}), 2.85 ~ 2.60 (m, 8 H, NCH₂). *m/z* (FAB): 2604 (M+3). Anal. Calcd. For C₁₀₇H₁₅₇N₅O₆₈: C 49.40, H 6.08, N 2.69. found: C 49.37, H 6.12, N 3.72.

Acknowledgments

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