The first Janus [2]rotaxane

Tatsuhiko Fujimoto, Yoshiteru Sakata and Takahiro Kaneda*

The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Osaka 567-0047, Japan.
E-mail: kaneda@sanken.osaka-u.ac.jp

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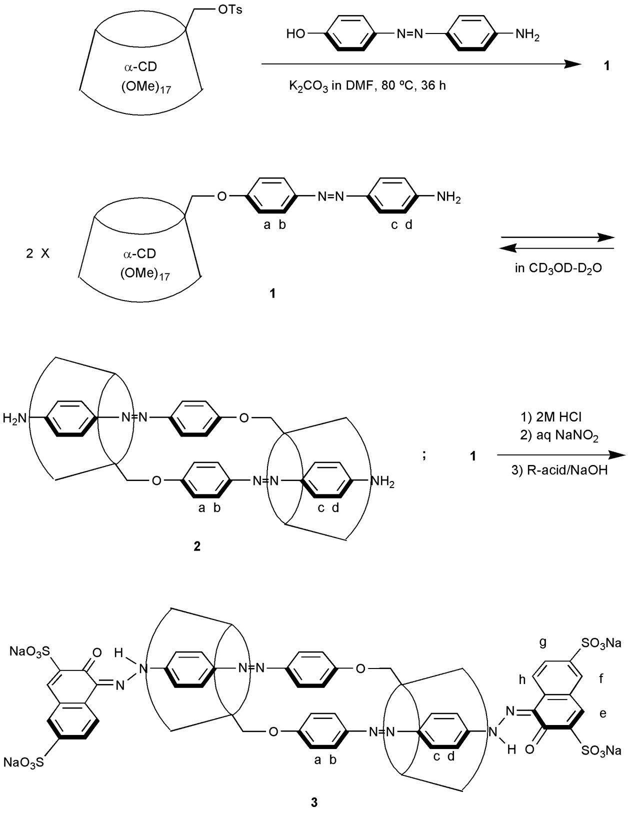
The first Janus [2]rotaxane 3 has been synthesized by bis-azo coupling of 2-naphthol-3,6-disulfonic acid with a Janus [2]pseudorotaxane 2 prepared by dimerization of 6-*O*-[(4-aminophenylazo)phenyl]-permethylated α-cyclodextrin 1 and characterized by MALDI-TOF-MS and ^1H NMR methods.

Mechanically interlocked compounds such as rotaxanes and catenanes have become of interest since the first creative development of molecular machines associated with a so-called mechanical bond characteristic of such compounds.[1] Recently, we have reported the rare lipophilic [2]supercyclodextrins with a 'doubly pseudorotaxaned' superstructure, corresponding to the cyclic homo-dimers of azophenol-branched permethylated α-cyclodextrins (CDs).[2] Although such double-[2]pseudorotaxanes[3] have a tendency to exist only under limited conditions of the temperature, concentration, and medium, they must be regarded as fascinating precursors for so far unknown double-rotaxanes. To fix the dissociable structures of the precursors by capping with bulky stoppers on the terminal groups, azo coupling reactions provide a promising approach because of their practical feasibility in aqueous solutions at low temperatures, with low activation energies. In fact, Anderson *et al.* have succeeded in preparing azo dye [2]- and [3]-rotaxanes in this manner.[4] Here, we describe the synthesis of the first 'Janus [2]rotaxane'[5] **3**[6] from a lipophilic α-CD monomer **1** bearing a diazotizable 4-aminoazobenzene *via* dimerization to a [2]pseudodoublerotaxane **2**.

Competitive substitution reaction of 6-*O*-monotosyl permethylated α-CD[2] with an excess of 4-amino-4′-hydroxyazobenzene as a bifunctional nucleophile gave a mixture of 6-*O*-[(4-aminophenylazo)phenyl]- and 6-deoxy-6-[(4-hydroxyphyenylazo)phenylamino]-permethylated α-CDs (Scheme 1). The former desired compound **1** could be separated from the latter by extraction with toluene from the alkaline aqueous phase, and obtained in 38% yield after purification by preparative GPC column chromatography.[7]

The self-association of monomer **1** has been examined by solvent-, temperature- and concentration-dependent ^1H NMR methods. A spectrum observed at ambient temperature from a solution of **1** in $CD_3OD–D_2O$ (6 : 1) is understood in terms of an equilibrium mixture of two species, **1** and its complex **2** [Fig. 1(b)]. The complexed species disappeared completely at 55 °C to result in the uncomplexed species alone, the spectrum of which [Fig. 1(a)] is similar to that of **1** obtained in $CDCl_3$. By contrast, the association complex **2** was found to exist exclusively in $CD_3OD–D_2O$ (1 : 1) at 23 °C [Fig. 1(c)]. The superstructure of the Janus [2]pseudorotaxane **2** is confirmed by both the determination of the value $n = 2.0$[8] of the degree of association according to the method[2b] reported previously and the appearance of the four sets of doublets due to the aromatic protons. The spectral features mentioned above indicate that the dimerization equilibrium in Scheme 1, for which the association constant K_a was evaluated to be 430 M^{-1},[8] occurred in hydrophilic media at room temp. and that its exchange rate was slow but the free rotations of the guest azobenzene-rods were fast on the NMR timescale. Similar phenomena have been described in other lipophilic α-CD–azobenzene dyads.[2]



Scheme 1

The aromatic protons of **2**[9] were assigned by difference NOE and decoupling experiments in $CD_3OD–D_2O$ (6 : 1) and (1 : 1), respectively. The observations of two correlations due to $H_a–H_b$ and $H_c–H_d$ and of the chemical exchange involving H_c and H_d are compatible with the assignment shown in Fig. 1(c). The up-

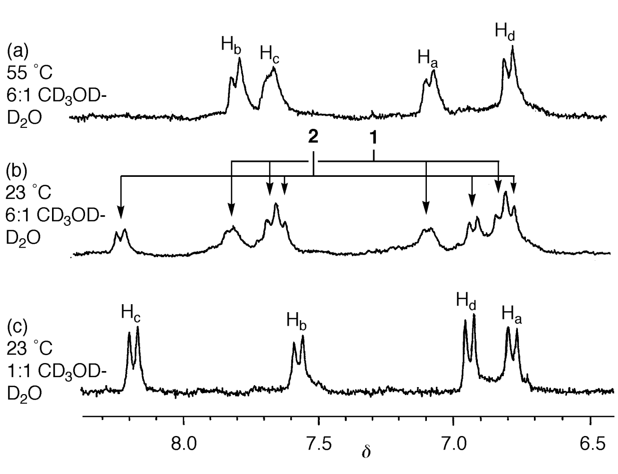


Fig. 1 270 MHz ^1H NMR spectra of solutions of **1**.

and down-field shifts of H_a (−0.27), H_b (−0.19), H_c (+0.56) and H_d (+0.12 ppm) after the dimerization resemble those observed previously with the other [2]supercyclodextrins[2] and therefore, these shifts also support the Janus [2]pseudorotaxane **2** for which a cyclophane-like π–π stacking between the two phenol residues and the binding of the terminal aniline residues with the CD cavities are characteristic.

Bis-azo coupling experiments to introduce two bulky naphthols as stoppers were carried out as follows. To prepare the bisdiazonium salt of **2**, a cold aqueous solution of sodium nitrite was added in portions to a cold solution of the aniline derivative **1** in 2 M HCl. The reaction mixture was treated with an alkaline solution of 2-naphthol-3,6-disulfonic acid (R-acid) at room temperature for 3 h. After neutralization followed by purification by reverse phase column chromatography, the desired Janus [2]rotaxane **3**[10] was isolated in 84% yield as red–purple solid. The symmetrical and dimeric structure of **3** has been confirmed by the observations of a 1 : 1 ratio of the naphthol to the azobenzene moiety in its ^1H NMR spectrum and of a peak at *m/z* 3549 corresponding to $[M+Na]^+$ in its MALDI-TOF-MS spectrum. It is interesting that the possible coupling product of **1** with the R-acid could not be detected. Thus, it is unlikely that the bis-aniline **2**, its dihydrochloride and the corresponding bisdiazonium salt dissociate into the monomeric species during the coupling processes.

The ^1H NMR spectral features of **3** reflect its Janus [2]rotaxane skeleton. It was anticipated that the stoppers introduced at the terminal ends have substantial substituent effects on the aromatic protons H_d situated at the *ortho* positions while this is not so for H_a and H_b which lie further away. Indeed, the following reasonable differences in their chemical shifts were found: $\Delta\delta = \delta(\mathbf{3}) - \delta(\mathbf{2})$, −0.04 for H_a, −0.04 (H_b), +0.17 (H_c), and +1.21 ppm (H_d). Further, no difference between the spectra of **3** recorded at 24 and 90 °C in D_2O was observed, supporting the fixed superstructure. At present, there is no evidence for a potential oscillation, like the stretching vibration of the covalent bond for a diatomic molecule, with respect to the mechanical bond between the two components of **3**.

In conclusion, we have demonstrated that a [2]supercyclodextrin prepared by self-assembly of an α-cyclodextrin–azobenzene dyad serves as a precursor for a very rare Janus [2]rotaxane. Synthesis of other Janus [2]rotaxanes are currently in progress in our laboratory.

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Notes and references

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5 This term is used for a unique face-to-face dimeric structure of **3** according to a referee's suggestion.

6 Although there is no information about the isomeric structure for the naphthol-azo units at present, they are represented here as the hydrazo tautomer rather than as the azo tautomer according to its solid state geometry [see ref. 4(*b*)].

7 **1**: yellow solid. Anal. Found: C, 55.46; H, 7.47; N, 2.80%. Calc. for $C_{65}H_{103}O_{30}N_3$: C, 55.51; H, 7.38; N, 2.99%. MALDI-TOF-MS: *m/z* 1434 $[M+Na]^+$. δ_H(270 MHz, $CDCl_3$, 23 °C): 7.83 (d, *J* 8.9 Hz, 2H, H_b), 7.74 (d, *J* 8.6 Hz, 2H, H_c), 7.03 (d, *J* 8.9 Hz, 2H, H_a), 6.73 (d, *J* 8.6 Hz, H_d), 5.2–4.9 (m, 6H, CD-H_1), 4.5–3.0 (m, CD-H).

8 The following three sets of the parameters (C_0/mM, I_x, I_y) in Scheme 1 of ref. 2(*b*) were used for the determination of the association number *n* and constant K_a: (1.97, 41, 38), (0.99, 56, 30) and (0.66, 54, 22) in CD_3OD–D_2O (5 : 1) at 23 °C.

9 **2**: Selected ^1H NMR data: δ_H(270 MHz, CD_3OD–D_2O (6 : 1), 23 °C): 6.79 (d, *J* 8.9 Hz, H_a), 7.64 (d, *J* 8.9 Hz, H_b), 8.23 (d, *J* 8.9 Hz, H_c), 6.93 (d, *J* 8.9 Hz, H_d).

10 **3**: MALDI-TOF-MS: *m/z* 3555 $(M+Na)^+$ for $C_{150}H_{212}O_{74}N_8S_4Na_5$. Selected ^1H NMR data: δ_H (270 MHz, D_2O, 23 °C): 8.40 (d, *J* 8.9 Hz, 4H, H_c), 8.39 (s, 2H, H_e), 8.18 (d, *J* 8.9 Hz, 2H, H_h), 8.14 (d, *J* 8.9 Hz, 4H, H_d), 8.08 (s, 2H, H_f), 7.82 (d, *J* 8.9 Hz, 2H, H_g), 7.60 (d, *J* 8.4 Hz, 4H, H_b), 6.75 (d, *J* 8.4 Hz, 4H, H_a).