Linear oligomers composed of a photochromically contractible and extendable Janus [2]rotaxane

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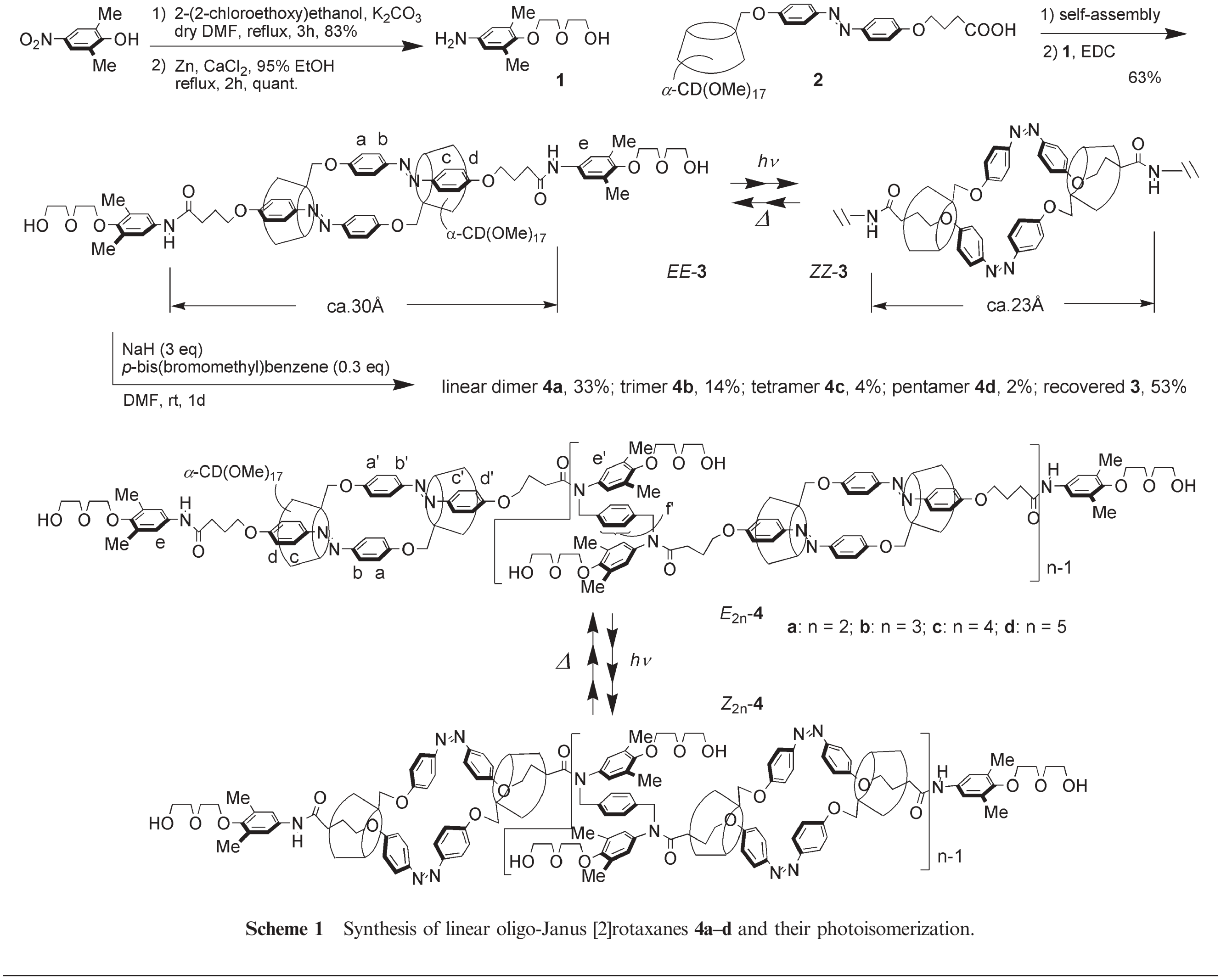
The synthesis and characterization of *N*,*N*′-*p*-xylylene-linked oligo-Janus [2]rotaxanes based on a permethylated α-cyclodextrin and their contractible and extendable nature coupled with photochromism are described.

Among various types of interlocked compounds, molecules that can be contracted and extended by external stimuli are quite rare.[1] Two examples of such molecules are known: a metal ion-[2] and a redox-driven[3] molecular muscle. All real and potential[4] molecular muscles consist of only one contractible and extendable unit. Therefore, it is a challenge to access compounds containing more than two such units. Here, we report on the first synthesis and characterization of the title compounds up to the pentamer and their contractible and extendable nature coupled with photochromism.[5]

We carried out the condensation of a hermaphroditic cyclodextrin (CD), 6-(deoxy-*p*-(*p*-(3-carboxypropoxy)phenylazo)phenoxy)-α-CD permethylate (**2**),[6] and a water-soluble stopper, 3,5-dimethyl-4-(2′-(2″-hydroxyethoxy)ethoxy)aniline (**1**)[6] in 1 : 1 MeOH–H_2O at 0 °C–rt in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) (Scheme 1). The "solubility" of



Scheme 1 Synthesis of linear oligo-Janus [2]rotaxanes **4a–d** and their photoisomerization.

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2 in the medium tended to be higher at 0 °C than at rt, probably due to the self-assembly to a Janus [2]peudorotaxne. A 5 g-scale experiment gave the key intermediate **3**[7] (3.2 g, 56%) as a yellow solid after column chromatography on SiO_2. The Janus rotaxane **3** was treated with NaH in dry DMF at 0 °C and then at rt, and with *p*-bis(bromomethyl)benzene. After recycling preparative GPC, a linear dimer **4a**,[7] trimer **4b**,[7] tetramer **4c**,[7] and pentamer **4d**[7] were obtained as yellow solids in 33, 14, 4, and 2% yields, respectively, accompanied with recovery of **3** (53%). Passing the crude products through the columns three times brought about their base line separation. The MALDI-TOF-MS spectra of **3** and **4a–d** showed $[M + Na]^+$ ion peaks at *m*/*z* 3424, 6929, 10432, 13937, and 17438 corresponding to each oligomer. Unexpectedly, we found the products to be *N*,*N*′-*p*-xylylene-linked oligomers rather than the expected *O*,*O*′-linked isomers as discussed below.

Monomer **3** showed four independent doublets due to the azobenzene protons Ha (6.77), Hb (7.66), Hc (8.43), and Hd (7.23), and two singlets due to He (7.14) and NH (6.95 ppm) (Fig. 1(b)). We could complete this assignment by comparing to that of a previous Janus rotaxane whose assignment has already been established using *d*-labeled derivatives.[8] The proton Hc of **3** is bound in the center of the CD cavity as previously described.[8,9] All the present oligomers **4** belong to point group C_2 and their ^{1}H NMR spectra in the aromatic region are consistent with their symmetry. The two hermaphroditic CDs of a terminal Janus unit are no longer equivalent, whereas the protons of the inner Janus units are expected to be exposed to a similar magnetic environment. Indeed, the protons Ha and Ha′, and Hb and Hb′ appeared as overlapped signals, whereas the protons Hc and Hc′, and Hd and Hd′, appeared as two separated doublets with different intensities, except dimer **4a**. In consideration of the relative intensities, we assigned the signals in the lower and higher fields to the protons Hc and Hd, and Hc′ and Hd′, respectively.

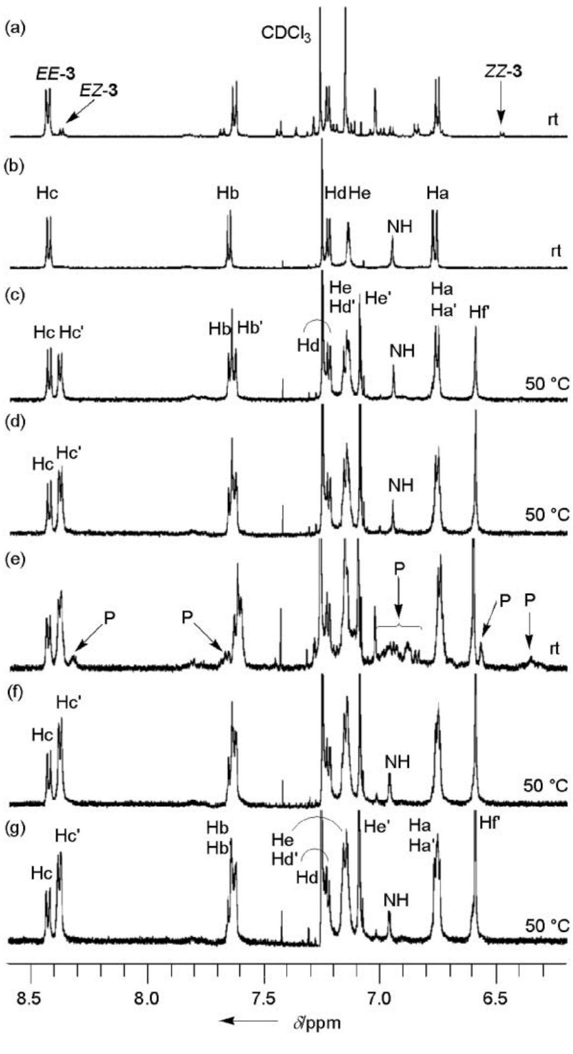

Fig. 1 ^{1}H NMR spectra (600 MHz, $CDCl_3$) of: (a) **3** after irradiation; (b) **3**; (c) **4a**; (d) **4b**; (e) **4b** after irradiation; (f) **4c**; and (g) **4d**. Symbol "P" means signals due to photoisomeric mixtures.

In oligomers **4**, only the new singlets that appeared at *ca.* 7.1 and 6.6 ppm could be reasonably assigned to the inner, stoppered aryl protons He′ and *p*-xylylene ring protons Hf′, respectively. From the following evidence, we identified those oligomers with *N*,*N*′-*p*-xylylene-linked tertiary amides, where the protons Hf′ are located in the shielding areas of two inner stoppered rings: (1) an upfield shift by 0.45 ppm for Hf′ compared to the corresponding chemical shift of *N*,*N*′-*p*-xylylene bis-*p*-methoxyacetanilide[10] as a reference compound; (2) an upfield shift by 0.2 ppm for He′ compared to He; and (3) no detected signals due to the inner amide protons even in $CDCl_3$ at rt and in d_6-DMSO at rt and 100 °C. The steric requirement for the stacking may be attributed to the bulkiness of Janus units as a substituent. A few examples for *N*-benzylation under similar conditions are available.[11]

The irradiation of **3** in $CDCl_3$ gave a mixture of photoisomers, *EE*-, *EZ*-, and *ZZ*-**3**, and the molar ratio was found to be 75 : 20 : 5.[12] We determined the ratio from the relative intensities of the doublets at 8.43, 8.38, and 6.48 ppm whose signals can be assigned to the respective *EE*-, *EZ*-, and *ZZ*-**3** according to their symmetry (Fig. 1(a)). Heating the mixture at 90 °C for a short time or setting it aside at rt for several days completely reproduced the original spectrum. Due to their bulkiness, the *Z*-azobenzene groups of *ZZ*-**3** should be placed outside the CD cavity, and the trimethylene spacers attached to them should occupy the cavity instead. According to molecular simulations,[13] the distances between the two amide-nitrogen atoms of *EE*- and *ZZ*-**3** are estimated as *ca.* 30 and 23 Å, respectively. Therefore, the *ZZ*-isomer is shorter than the *EE*-isomer by 7 Å; **3** is an interlocked compound exhibiting a contractible/extendable nature coupled with the photochromism.

We also observed photochromism with oligomers, *e.g.*, trimer **4b**. There are so many possible photoisomers that the ^{1}H NMR spectrum is complicated (Fig. 1(e)). On the other hand, the absorption spectral features of **4b** are quite similar to those of **3** even after the irradiation[12] (Fig. 2), suggesting that three Janus units in **4b** undergo photoisomerization independently. On the assumption that each Janus unit undergoes photoisomerization with the same probability, the existence probability of the oligomers including at least one *ZZ*-Janus unit, *i.e.*, species having a contractible/extendable nature was as follows: 9.8, 14, 19, and 23% for the di-, tri-, tetra-, and pentamer, respectively. At an extreme, the molecules shorten by 14, 21, 28, and 35 Å with Z_4-, Z_6-, Z_8-, and Z_{10}-**4**, respectively, compared to the corresponding E_{2n}-**4**. However, the theoretical contents of all *Z*-isomers are very small or trace: 0.25, 0.013, 6.3×10^{-4}, and 3.1×10^{-5}% for Z_4-, Z_6-, Z_8-, and Z_{10}-**4**, respectively.

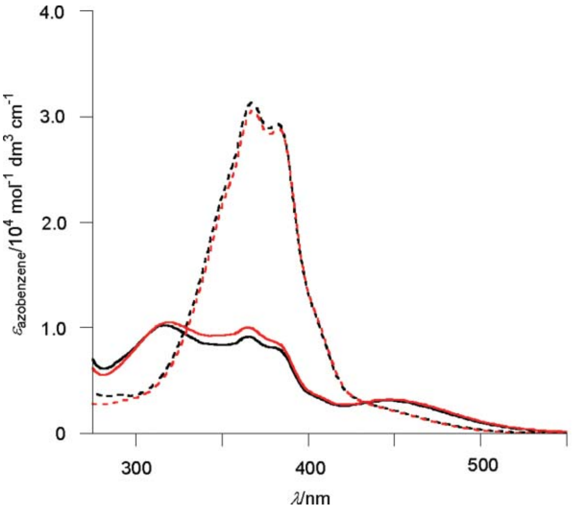

Fig. 2 Absorption spectra ($[c]_{\mathrm{azobenzene}} = 2.9 \times 10^{-5}$ mol l^{-1}, $CHCl_3$, rt) of **3** (black) and **4b** (red) before (dotted line) and after (solid line) irradiation.

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6 The physical properties of the compounds will be reported elsewhere.

7 **3**: mp: >300 °C. Anal. found: C, 55.85; H, 7.21; N, 2.36. Calcd for $C_{162}H_{250}N_6O_{70}\cdot 4H_2O$: C, 56.01; H, 7.49; N, 2.42. **4a**: mp: 200–203 °C. Anal. found: C, 56.40; H, 7.26; N, 2.31. Calcd for $C_{332}H_{506}N_{12}O_{140}\cdot 8H_2O$: C, 56.56; H, 7.46; N, 2.38. **4b**: mp: 198–201 °C. Anal. found: C, 56.74; H, 7.36; N, 2.57. Calcd for $C_{502}H_{762}N_{18}O_{210}\cdot 12H_2O$: C, 56.74; H, 7.46; N, 2.37. **4c**: mp: 203–205 C°. Anal. found: C, 57.06; H, 7.45; N, 2.24. Calcd for $C_{672}H_{1018}N_{24}O_{280}\cdot 16H_2O$: C, 56.83; H, 7.45; N, 2.37. **4d**: mp: 200–203 °C. ^{1}H NMR (270 MHz, $CDCl_3$, 50 °C): δ 8.43 (d, J = 8.8 Hz, 4H), 8.38 (d, J = 8.8 Hz, 16H), 7.66–7.62 (m, 20H), 7.23 (d, J = 8.8 Hz, 4H), 7.16–7.15 (m, 20H), 7.09 (s, 16H), 6.96 (s, 2H), 6.77–6.75 (m, 20H), 6.60 (s, 16H), 5.06–4.85 (m, 60H, CD-H_1), 4.81–4.75 (q, 16H), 4.36–2.87 (m, 970H, CD-H, OMe, OCH_2, OCH_2CH_2O), 2.45–2.01 (m, 110H, $COCH_2$, Me, CH_2, OH) ppm.

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10 The compound was prepared from *p*-methoxyacetanilide and *p*-bis(bromomethyl)benzene under the same conditions as were used for synthesis of compounds **4**. The chemical shift of *p*-xylylene ring protons, 7.07 ppm, was found to be normal.

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12 The irradiation was carried out with a 350 W high-pressure mercury arc lamp equipped with a $CuSO_4$ aqueous solution filter for isolating the light of 366 nm, and required 20 min to reach a photostationary state.

13 *InsightII/Discover*, Applied Biosystems, San Diego, CS, USA.