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Disaggregation Reaction of [2]Pseudorotaxanes Composed of Dibenzo[24]crown-8 and Dialkylammonium Having Isopropyl End Groups

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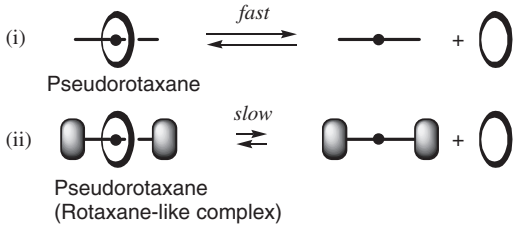
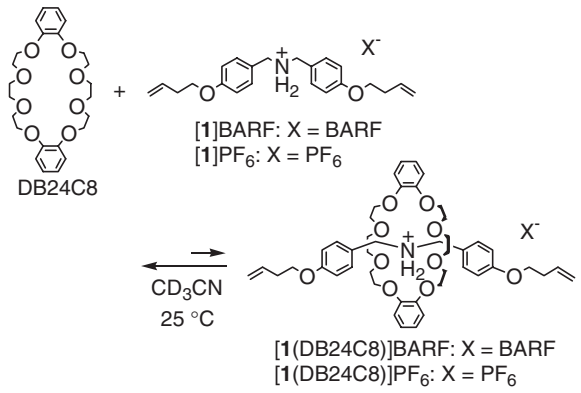
[2]Pseudorotaxanes composed of dibenzo[24]crown-8 (DB24C8) and dialkylammonium having isopropyl end groups are converted into the component molecules in C_6D_6 solution containing PF_6^- anion.

Rotaxanes are defined as supramolecules composed of interlocked macrocyclic molecules and axle molecules with two bulky end groups.[1,2] Pseudorotaxanes with less bulky end groups of the axle component undergo disaggregation to the component molecules rapidly because the end groups are smaller than the cavity of the macrocycle.[3–5] The reaction is intrinsically reversible, and relative stability of the pseudorotaxanes and the component molecules governs the ratio of the components in the equilibrated mixture (Scheme 1(i)). Disaggregation of pseudorotaxanes having more bulky end groups of the axle component proceeds more slowly ($t_{1/2}$ = 4–143 h)[6a] (Scheme 1(ii)).[6–9] Stoddart named these pseudorotaxanes rotaxane-like complex,[7,8] and disaggregation has been applied to a drug delivery system.[10] Raising temperature, use of polar solvents, and change of pH have been reported to enhance the disaggregation of the rotaxane-like complexes.[8–11] Elimination of BMP25C8 (BMP25C8 = benzometaphenylene[25]crown-8) with a larger cavity than common macrocyclic components from the rotaxane-like complex [(*t*-BuC_6H_4-4-$CH_2NH_2CH_2C_6H_4$-4-CH_2PPh_3)(BMP25C8)]$(PF_6)_2$ proceeds smoothly in polar solvent or by additional base.[8] The rotaxane-like complex of a macrocyclic octaoxa[22]ferrocenophane with dialkylammonium [An$CH_2NH_2CH_2C_6H_4$-4-OCH_2CH_2CH=$CHCOOC_6H_3$-3,5-Me_2]BARF (An = 9-anthryl, BARF = B{C_6H_3-3,5-$(CF_3)_2$}$_4$) undergoes disaggregation in CD_3CN and DMSO-d_6, while similar reaction was not observed in less polar $CDCl_3$.[9] In this paper, we report synthesis of cationic rotaxane-like complexes, composed of dibenzo[24]crown-8 (DB24C8) and dialkylammonium with isopropyl groups, and its disaggregation enhanced by PF_6^- anion.

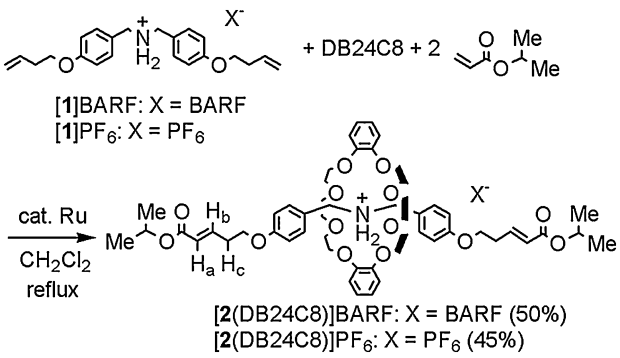
Scheme 2 shows preparation of [2]pseudorotaxane, which is employed as precursors of rotaxane-like complexes. Dissolution of DB24C8 and [$NH_2(CH_2C_6H_4$-4-OCH_2CH_2CH=$CH_2)_2$]BARF ([**1**]BARF) in CD_3CN at 25 °C (10 mM for each compound)



Scheme 1. Dethreading reactions of [2]pseudorotaxane.



Scheme 2. Formation of [2]pseudorotaxane [**1**(DB24C8)]X (X = BARF and PF_6) in CD_3CN.



Scheme 3. Synthesis of [**2**(DB24C8)]X (X = BARF and PF_6).

gave an equilibrated mixture with [2]pseudorotaxane [**1**(DB24C8)]BARF within 10 min. ^{1}H NMR spectroscopy of the mixture shows a signal at δ 4.58 assigned to NCH_2 hydrogen of [**1**(DB24C8)]BARF where the molar ratio between [**1**(DB24C8)]BARF and [**1**]BARF was 26/74. A similar reaction of DB24C8 with [**1**]PF_6 yielded the mixture with [**1**(DB24C8)]PF_6 ([[**1**(DB24C8)]PF_6]/[[**1**]PF_6] = 7/93). These results indicate that formation of the [2]pseudorotaxane from [**1**]BARF with DB24C8 is more favorable than that of [**1**]PF_6.[12]

Scheme 3 depicts synthesis of the rotaxane-like complexes. Cross-metathesis reaction of [**1**]BARF with CH_2=$CHCOOi$-Pr catalyzed by (H_2IMes)(PCy_3)Cl_2RuCHPh (H_2IMes = *N*,*N*-bis-(mesityl)-4,5-dihydroimidazol-2-ylidene) for 13 h,[13] in the presence of DB24C8 yielded [$NH_2(CH_2C_6H_4$-4-OCH_2CH_2CH=$CHCOOi$-Pr)$_2$(DB24C8)]BARF ([**2**(DB24C8)]BARF) in 50% isolated yield.[5,14–16] The ESI-MS spectrum of [**2**(DB24C8)]BARF showed a peak at m/z 958 assigned to the cationic rotaxane-like complex, [**2**(DB24C8)]$^+$.[17] ^{1}H NMR spectrum of [**2**(DB24C8)]BARF in $CDCl_3$ contains signals at δ

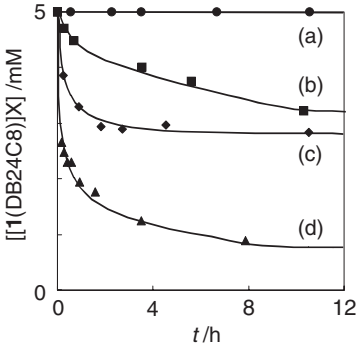
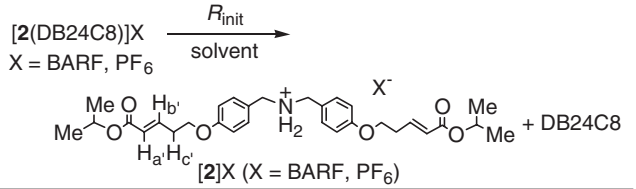


Figure 1. Profile of disaggregation of [**1**(DB24C8)]X ($[[\mathbf{1}(DB24C8)]X]_0 = 5.0$ mM) in C_6D_6. (a) X = BARF at 50 °C. (b) X = BARF with added $[NH_2(CH_2Ph)_2]PF_6$ (5.0 mM). (c) X = BARF at 50 °C with added *n*-Bu_4NPF_6 (25.0 mM). (d) X = PF_6 at 25 °C.

7.35 and 4.46, which are assigned to NH_2 and NCH_2 hydrogens of the axle component, respectively. The peak positions are at lower magnetic fields than those of uncomplexed dialkylammonium, [**1**]BARF (δ 6.83 (NH_2) and 4.02 (NCH_2)). These ^{1}H NMR results indicate that DB24C8 is complexed with the ammonium group of the axle component by the N–H···O hydrogen bonds between oxygens of DB24C8 and NH_2 group.[18] Rotaxane-like complex with PF_6^- counter anion, [**2**(DB24C8)]PF_6, was obtained by a similar reaction for 12 h in 45% as a mixture with uncomplexed DB24C8. The molar ratio of [**2**(DB24C8)]PF_6 to DB24C8 did not change in $CDCl_3$ at room temperature for 17 days.

Heating a C_6D_6 solution of [**2**(DB24C8)]BARF at 50 °C did not change its NMR spectrum for 4 days (Figure 1a, Table 1 (Run 1)). Addition of $[NH_2(CH_2Ph)_2]PF_6$ to the solution (5.0 mM) at 50 °C caused degradation of the rotaxane-like complex to form a mixture of $[NH_2(CH_2Ph)_2]^+$, DB24C8, $\mathbf{2}^+$, $[\{NH_2(CH_2Ph)_2\}(DB24C8)]^+$, and [**2**(DB24C8)]$^+$, as revealed by ^{1}H NMR and ESI-MS spectrometry (Figure 1b, Run 2). The ^{1}H NMR spectrum of the C_6D_6 solution after 47 h exhibits peaks at δ 5.88 ($H_{a'}$), 5.11 ($H_{b'}$), 2.06 ($H_{c'}$) assigned to the signals of $\mathbf{2}^+$ as well as the corresponding signals of [**2**(DB24C8)]$^+$ (δ 5.93 (H_a), 5.10 (H_b), 2.16 (H_c)) (Figure 2). The positions of the signal H_a, H_b, and H_c in Figure 2b were shifted from the spectrum obtained after 17 min (δ 5.92 (H_a), 5.08 (H_b), 2.17 (H_c)) (Figure 2a). The observed initial rate of the disaggregation, R_{init}, was determined to be 1.9×10^{-2} mmol min^{-1}. Addition of *n*-Bu_4NPF_6 to [**2**(DB24C8)]BARF ($[n\text{-}Bu_4NPF_6]_0 = 25.0$ mM, $[[\mathbf{2}(DB24C8)]BARF]_0 = 5.0$ mM) at 50 °C converted 43% of [**2**(DB24C8)]BARF to a mixture with DB24C8 and [**2**]BARF after 10.5 h ($R_{init} = 7.6 \times 10^{-2}$ mmol min^{-1}) (Figure 1c, Run 3). Disaggregation of [**2**(DB24C8)]PF_6 in C_6D_6 occurs smoothly without the additives ($R_{init} = 2.1 \times 10^{-1}$ mmol min^{-1}) (Figure 1d, Run 7) and attains an equilibrium after 8 h at 25 °C ($[[\mathbf{2}(DB24C8)]PF_6]/[[\mathbf{2}]PF_6] = 14{:}86$). Thus, the presence of PF_6^- in the solution induces the disaggregation of the pseudorotaxanes. The disaggregation reactions of [**2**(DB24C8)]X were enhanced also by addition of Et_3N (Runs 4 and 8) or in polar solvent such as CD_3CN and DMSO-d_6 (Runs 5, 6, 9, and 11). Addition of HCl to the CD_3CN solution of [**2**(DB24C8)]PF_6 affects the dethreading reaction to a limited extent (Run 10).

Table 1. Disaggregation reaction of [**2**(DB24C8)]X (X = BARF and PF_6)[a]



Run	X	Solvent	Conversion[b] /%	R_{init} /mmol min^{-1}
1	BARF	C_6D_6[c]	0	—[d]
2		$C_6D_6 + [NH_2(CH_2Ph)_2]PF_6$[c,e]	59	1.9×10^{-2}
3		$C_6D_6 + n\text{-}Bu_4NPF_6$[c,f]	43	7.6×10^{-2}
4		$C_6D_6 + Et_3N$[g]	28	1.3×10^{-1}
5		CD_3CN	59	4.2×10^{-1}
6		DMSO-d_6	100	—[h]
7	PF_6[i]	C_6D_6	86	2.1×10^{-1}
8		$C_6D_6 + Et_3N$[g]	100	—[h]
9		CD_3CN	86	4.7×10^{-1}
10		$CD_3CN + HCl$[j]	78	5.3×10^{-1}
11		DMSO-d_6	100	—[h]

[a] $[[\mathbf{2}(DB24C8)]X]_0 = 5.0$ mM at 25 °C. [b] $100\{([[\mathbf{2}(DB24C8)]X]_0 - [[\mathbf{2}(DB24C8)]X]_\infty)/[[\mathbf{2}(DB24C8)]X]_0\}$. [c] At 50 °C. [d] Disaggregation was not observed for 4 days. [e] $[[NH_2(CH_2Ph)_2]PF_6]_0 = 5.0$ mM (partially undissolved). [f] $[n\text{-}Bu_4NPF_6]_0 = 25.0$ mM (partially undissolved). [g] $[Et_3N]_0 = 10.0$ mM. [h] The reaction was finished within 8 min. [i] [**2**(DB24C8)]PF_6 used as a mixture with DB24C8 ([**2**(DB24C8)]PF_6:DB24C8 = 38/62). [j] $[HCl]_0 = 10.0$ mM.

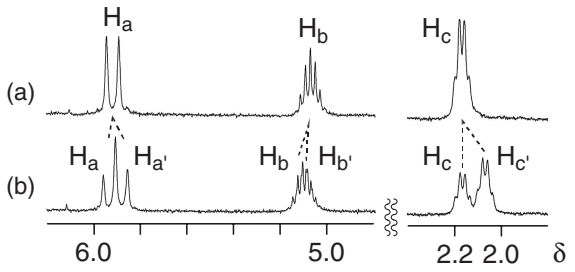


Figure 2. ^{1}H NMR spectra of [**2**(DB24C8)]BARF with addition of $[NH_2(CH_2Ph)_2]PF_6$ ($[[\mathbf{2}(DB24C8)]BARF]_0 = 5.0$ mM, $[[NH_2(CH_2Ph)_2]PF_6]_0 = 5.0$ mM, in C_6D_6, 25 °C). a) 17 min, b) 47 h after addition. See Scheme 3 and Table 1 for the assignment of the signals.

The above results indicate that the disaggregation of [**2**(DB24C8)] involves activation of the N–H···O hydrogen bonds. Chart 1 depicts plausible intermediates of the reaction. Formation of an ion-pair of the ammonium and PF_6^- counter anion in intermediate **A** assists the activation of the N–H···O hydrogen bonds even in nonpolar C_6D_6.[19,20] Polar P–F bonds form a stable hydrogen bond with the ammonium group. The reaction of [**2**(DB24C8)]BARF with *n*-Bu_4NPF_6 or $[NH_2(CH_2Ph)_2]PF_6$ causes partial counter ion exchange forming [**2**(DB24C8)]PF_6 and its facile disaggregation. Activation of N–H···O hydrogen bonds by interaction of the ammonium group with solvent molecules forms intermediate **B** and contributes to the disaggregation reaction. Intermediate **B** is favorable in the polar solvents such as DMSO-d_6 and CD_3CN. The similar N–H···PF_6 and N–H···L (L = solvent) interactions also affect the thermal stability of [**2**]X and [**2**(DB24C8)]X in solution which

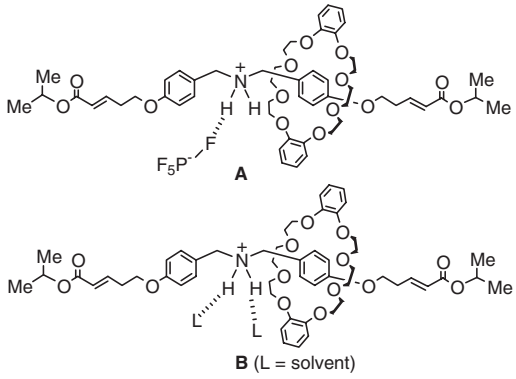


Chart 1. Plausible intermediates for the disaggregation.

controls the equilibrium position to reach in disaggregation reactions.[21,22] The N–H···O hydrogen bonds were activated also with Et_3N via neutralization of the ammonium group to form the corresponding amine.[9–11]

In summary, we succeeded in synthesis of a rotaxane-like complex [**2**(DB24C8)]BARF whose interlocked structure is stable in C_6D_6. The counter ion exchange of BARF with PF_6 induces disaggregation of the rotaxane-like complex to form a mixture of the uncomplexed component molecules. Effect of the added anion to the reaction rate is more significant than that expected from difference in thermodynamic stability of analogous [2]pseudorotaxane depending on the counter anion. The PF_6^- activates the N–H···O hydrogen bond between the component molecules, similarly to Et_3N and polar solvents. This approach using the controlled release of component molecule from a supramolecular system may provide a new means to design artificial transportation of molecules.

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16 Data of [**2**(DB24C8)]BARF. ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 1.26 (d, 12H, CH_3, $J = 7$ Hz), 2.65 (dt, 4H, OCH_2CH_2, $J = 6$, 6 Hz), 3.32 (s, 8H, CH_2-DB24C8), 3.69 (m, 8H, CH_2-DB24C8), 3.97 (t, 4H, CH_2-Axle, $J = 7$ Hz), 4.09 (m, 8H, CH_2-Axle), 4.46 (4H, NCH_2), 5.07 (sept, 2H, $CH(CH_3)_2$, $J = 7$ Hz), 5.93 (dt, 2H, CH_2CH=C*H*, $J = 16$, 2 Hz), 6.70 (d, 4H, C_6H_4-Axle, $J = 9$ Hz), 6.79 (m, 4H, C_6H_4-DB24C8), 6.91 (m, 4H, C_6H_4-DB24C8), 7.00 (dt, 2H, CH_2CH=CH, $J = 16$, 7 Hz), 7.12 (d, 4H, C_6H_4-Axle, $J = 9$ Hz), 7.35 (brs, 2H, NH_2), 7.52 (s, 4H, *p*-$C_6H_3(CF_3)_2$), 7.70 (m, 8H, *o*-$C_6H_3(CF_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 21.8 (CH_3), 31.8 (OCH_2CH_2), 52.1 (NCH_2), 65.9 (OCH_2-Axle), 67.8 ($OCH(CH_3)_2$), 68.2 (CH_2-DB24C8), 70.2 (CH_2-DB24C8), 70.6 (CH_2-DB24C8), 112.8 (C_6H_4-DB24C8), 114.4 (C_6H_4-Axle), 117.4 (*p*-$C_6H_3(CF_3)_2$), 121.9 (C_6H_4-DB24C8), 123.8, 124.0 (CH_2CH=*C*H), 124.5 (q, CF_3, J(CF) = 271 Hz), 128.8 (q, *C*CF_3, J(CF) = 31 Hz), 130.5 (C_6H_4-Axle), 134.7 (*o*-$C_6H_3(CF_3)_2$), 143.8 (CH_2CH=CH), 147.3, 159.2, 161.6 (q, BC, J(BC) = 50 Hz), 165.7 (C=O). Anal. Calcd for $C_{86}H_{84}BF_{24}NO_{14}$: C, 56.68; H, 4.65; N, 0.77%. Found: C, 56.28; H, 4.54; N, 0.88%. ESI-MS (MeCN) m/z; [**2**(DB24C8)]$^+$ calcd for $C_{54}H_{72}NO_{14}$, 958; found, 958.
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