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Crown ether–*tert*-ammonium salt complex fixed as rotaxane and its derivation to nonionic rotaxane

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Abstract

First rotaxane having *tert*-ammonium axle was prepared from *tert*-ammonium salt axle and dibenzo-24-crown-8-ether (DB24C8) wheel, suggesting that *tert*-ammonium salt axle forms the corresponding threaded complex with a crown ether. Same rotaxane was obtained quantitatively by N-methylation of *sec*-ammonium-type rotaxane. The *tert*-ammonium-type rotaxane was neutralized with amine base to *tert*-amine-type rotaxane in 100% yield, indicating the first isolation of 'nonionic' amine-type rotaxane. The reversible protonation and deprotonation of *tert*-amine-type rotaxane were achieved.

Components such as *sec*-ammonium salt and crown ether combine particularly well to yield a stable pseudorotaxane as a precursor of rotaxane.[1,2] This type of rotaxane can be readily obtained by a variety of synthetic methods, among which the end-capping approach often results in a high yield synthesis over 90%.[3] Ammonium–crown ether rotaxanes, therefore, have been used in various systems, that is, molecular devices,[4] polymeric materials,[5] and so on.[6] The most reliable combination of *sec*-ammonium salt and 24-crown-8-ether (DB24C8) is based on the particularly efficient formation of a threaded complex, which is extremely favorable for rotaxane synthesis.[2] However, *tert*-ammonium-type rotaxane has never been synthesized, as opposed to *sec*-ammonium-type rotaxane. This is probably due to the fact that it is not generally believed that the threaded complex formation between *tert*-ammonium salt and crown ether leads to the formation of a stable pseudorotaxane, and therefore, no complex formation has hitherto been reported, as far as we know. We have recently succeeded in synthesizing rotaxane from *tert*-ammonium salt and crown ether. This is the first clear evidence of complexation between these two components. Furthermore, it has been found that *tert*-ammonium rotaxane is neutralized to stable 'nonionic' and 'free' amine-type rotaxane. This paper discloses the synthesis and characterization of *tert*-ammonium-type and *tert*-amine-type rotaxanes, shedding a new light on ammonium-type rotaxanes.

When a mixture of *tert*-ammonium salt **1** and DB24C8 was treated with 3,5-dimethylbenzoic anhydride in the presence of a catalytic amount of tributylphosphane for 48 h in chloroform at room temperature, rotaxane **2**·$\mathbf{PF_6}$ was isolated as a white solid in 3.0% yield by preparative HPLC (Scheme 1).[7]

The structure of **2**·$\mathbf{PF_6}$ was examined by NMR and IR. The ^{1}H NMR spectrum of **2**·$\mathbf{PF_6}$ is shown in Figure 1c, along with that of *sec*-ammonium-type rotaxane **3**·$\mathbf{PF_6}$[3a] (Fig. 1d), which was prepared independently for comparison. The most evident spectral characteristic is the presence of two kinds of split benzylic protons (d and e), which were identified as diastereotopic protons generated from the *tert*-ammonium structure. The appearance of the methyl signal at around 2.9 ppm is also suggestive of a *tert*-ammonium structure. These benzyl and methyl proton signals (d and e) of **2**·$\mathbf{PF_6}$ clearly shifted to downfield in comparison

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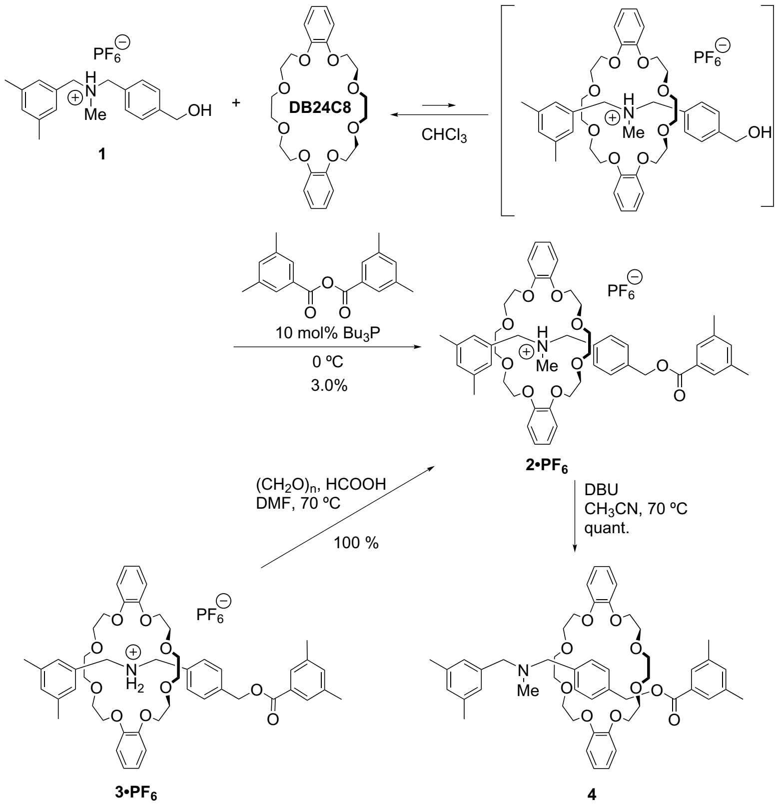

Scheme 1. Synthesis of rotaxane **2**·**PF**$_6$ having *tert*-ammonium axle and nonionic *tert*-amine rotaxane **4**.

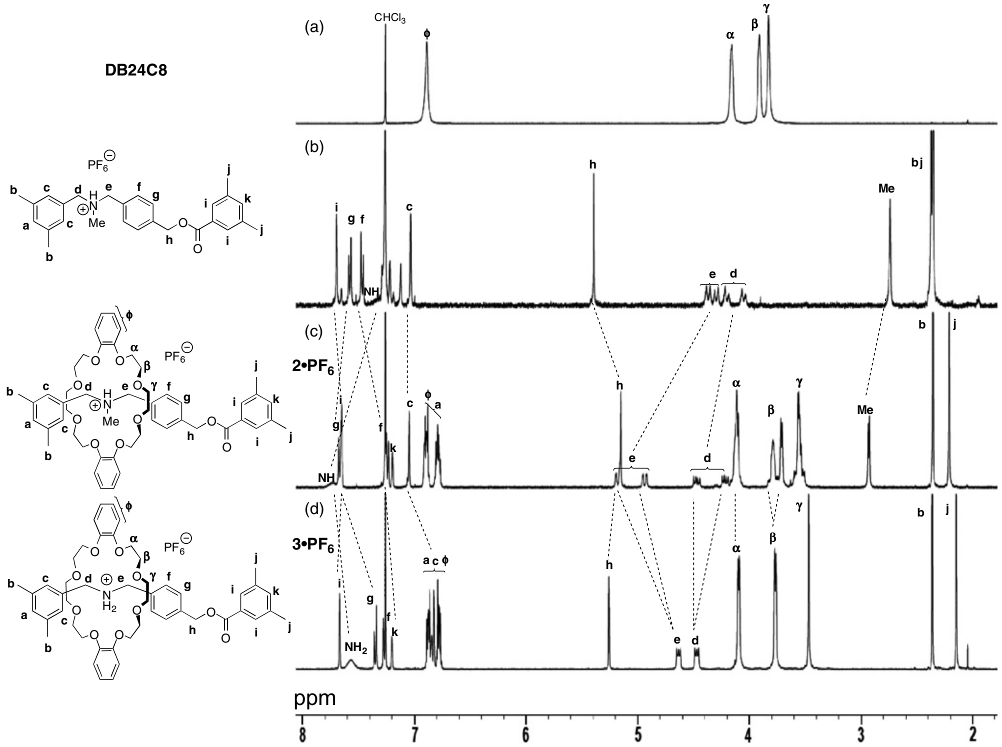

Fig. 1. ^{1}H NMR spectra (400 MHz, CDCl$_3$, 298 K) of (a) DB24C8, (b) axle of *tert*-ammonium rotaxane **2**·**PF**$_6$, (c) *tert*-ammonium rotaxane **2**·**PF**$_6$, and (d) *sec*-ammonium rotaxane **3**·**PF**$_6$.

with those of the axle component (Fig. 1b). This is attributed to the effect of DB24C8 which surrounds the *tert*-ammonium group. Thus, the wheel still lays around the *tert*-ammonium nitrogen atom even in solution state, despite the fact that $\mathbf{2}{\cdot}\mathbf{PF_6}$ has only one hydrogen atom at the nitrogen atom capable of participating in hydrogen bonding with the crown ether wheel. The typical absorption of PF_6 anion (856 cm^{-1}) as well as the ester carbonyl absorption (1718 cm^{-1}) was consistent with the proposed structure.

Additional evidence to the isolation of $\mathbf{2}{\cdot}\mathbf{PF_6}$ from **1** was obtained by the direct N-methylation of *sec*-ammonium-type rotaxane $\mathbf{3}{\cdot}\mathbf{PF_6}$ by the *Eschweiler–Clarke* reaction. A mixture of rotaxane $\mathbf{3}{\cdot}\mathbf{PF_6}$, paraformaldehyde, and formic acid in DMF was heated at 70 °C for 24 h (Scheme 1). From the resulting mixture, a white solid product assigned as *tert*-ammonium rotaxane $\mathbf{2}{\cdot}\mathbf{PF_6}$ was collected in a quantitative yield.[8]

The spectroscopic data of the product obtained from $\mathbf{3}{\cdot}\mathbf{PF_6}$ were completely consistent with that of rotaxane $\mathbf{2}{\cdot}\mathbf{PF_6}$ obtained from *tert*-ammonium salt **1**. Thus, the formation of $\mathbf{2}{\cdot}\mathbf{PF_6}$ from **1** was also confirmed by the derivation of $\mathbf{3}{\cdot}\mathbf{PF_6}$ to $\mathbf{2}{\cdot}\mathbf{PF_6}$. The preparation of rotaxane $\mathbf{2}{\cdot}\mathbf{PF_6}$ from *tert*-ammonium salt **1** has quite an important significance, even though the yield was low (3.0%),[9] because the actual isolation of $\mathbf{2}{\cdot}\mathbf{PF_6}$ demonstrates that the threaded complex is formed from *tert*-ammonium salt and crown ether. Thus, the rotaxane system can be regarded as a stabilizing system for labile species, since the unidentified complex is fixed in a rotaxane form, as shown in the present study (Fig. 1).

Meanwhile, neutralization of *sec*-ammonium-type rotaxane to 'nonionic' or 'free' amine-type rotaxane has never been attained so far,[2,10] although a few dual and multi cationic station-containing rotaxanes could be neutralized. Namely it has been well known that rotaxane having single *sec*-ammonium station cannot be neutralized. We examined the neutralization of *tert*-ammonium-type rotaxane $\mathbf{2}{\cdot}\mathbf{PF_6}$, since the attractive interaction between the wheel and axle components of $\mathbf{2}{\cdot}\mathbf{PF_6}$ seemed to be considerably weaker than that of $\mathbf{3}{\cdot}\mathbf{PF_6}$.

An acetonitrile solution of $\mathbf{2}{\cdot}\mathbf{PF_6}$ was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at 70 °C to yield a new product. This product was eventually determined to be *tert*-amine-type rotaxane **4** whose yield was quantitative.[11] The structure of **4** was confirmed by ^{1}H NMR spectral analysis (Fig. 2b).

The spectral pattern of **4** shows significant differences from that of $\mathbf{2}{\cdot}\mathbf{PF_6}$, while it has marked similarities to that of N-acetylated nonionic rotaxane **5**,[3] suggesting close structural resemblance between **4** and **5**. It has been reported that the crown ether wheel of $\mathbf{3}{\cdot}\mathbf{PF_6}$ moves from

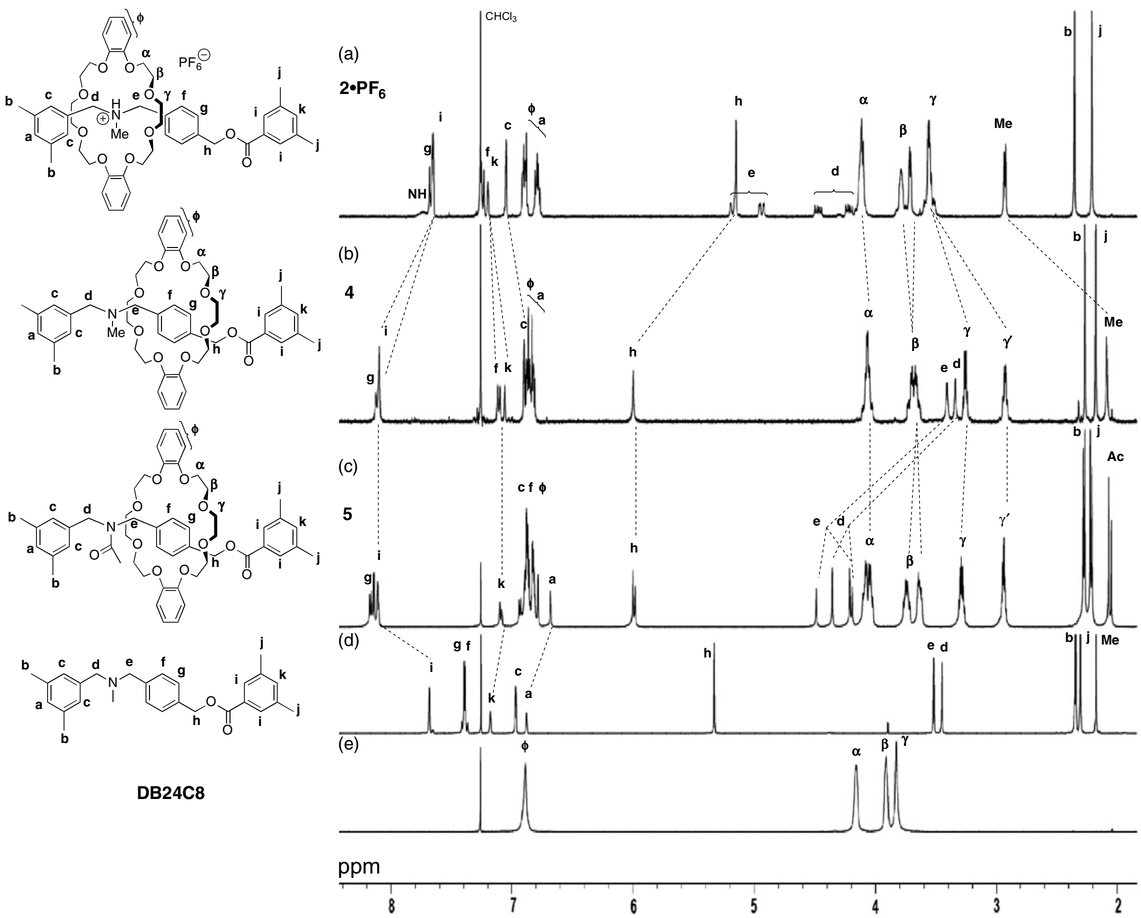

Fig. 2. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of (a) *tert*-ammonium rotaxane $\mathbf{2}{\cdot}\mathbf{PF_6}$, (b) *tert*-amine rotaxane **4**, (c) N-acetylated rotaxane **5**, (d) axle of *tert*-amine rotaxane **4**, and (e) DB24C8.

the *N* atom to the ester methylene by N-acetylation in both solid and solution states.[3] Thus, the present ^{1}H NMR spectral characteristics are fully consistent with the structure of **4** which lost its ionic character.

The structure of **4** was finally determined by X-ray crystal structure analysis.[12] The whole structure of **4**, which is very similar to that of **5**,[3] is confirmed by Figures 3 and 4. One of the important structural features of **4** is the position of the crown ether wheel on the axle. The wheel stays around the benzyl ester group in each rotaxane. This coincides well with the ^{1}H NMR spectral characteristics, that is, the structure in solution state (Fig. 2). A typical signal common to both **4** and **5** is the benzylic proton signal (h) appearing around 6 ppm, which is largely down field shifted by the deshielding effect resulting from the wheel translation caused by the neutralization of $\mathbf{2{\cdot}PF_6}$.

As stated above, the 'neutralization' which does not occur in *sec*-ammonium-type rotaxane becomes possible in *tert*-amine-type rotaxane. As a result, the neutralization made possible the isolation of the first 'free (neutral)' or 'nonionic' rotaxane. Since the quantitative transformation of *sec*-ammonium-type rotaxane to *tert*-amine-type rotaxane via *tert*-ammonium-type rotaxane has been shown in this study, the present conversion protocol is expected to widely expand the potential utility of *sec*-ammonium-type rotaxanes, which are most easily accessible.

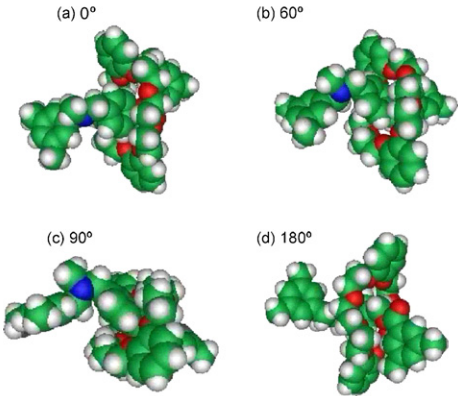

Fig. 3. Molecular structures (a)–(d) (rotated along the axle) of *tert*-amine rotaxane **4** obtained by the X-ray crystal structure analysis.[12]

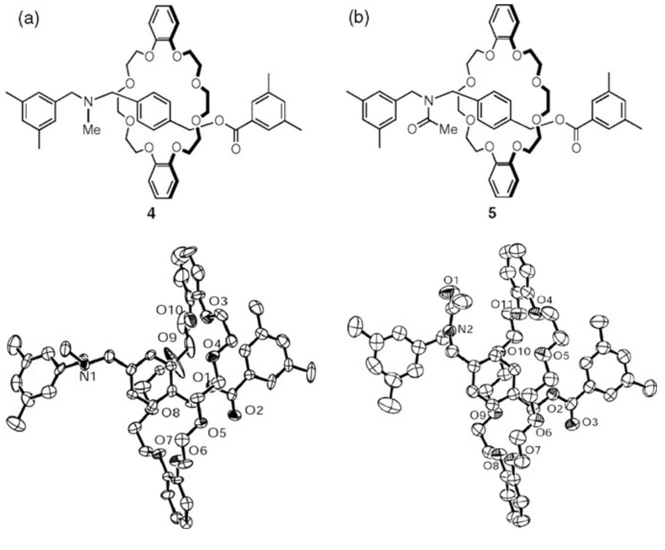

Fig. 4. ORTEP views of (a) *tert*-amine rotaxane **4**[12] and (b) N-acetylated rotaxane **5**.[3]

In this study, we have shown novel aspects of ammonium–crown ether-type rotaxane: (1) rotaxane is prepared from *tert*-ammonium salt axle and DB24C8 wheel, clarifying for the first time that the combination of *tert*-ammonium salt and crown ether forms the corresponding threaded complex;[2] (2) N-methylation of *sec*-ammonium-type rotaxane proceeds to give *tert*-ammonium-type rotaxane in 100% yield; (3) *tert*-ammonium-type rotaxane is neutralized quantitatively with amine base to *tert*-amine-type rotaxane, indicating the isolation of the first 'nonionic' amine-type rotaxane;[2,10] (4) reversible protonation and deprotonation of *tert*-amine-type rotaxane are achieved. Thus, the results obtained here can markedly enhance the potential utility of *sec*- and *tert*-ammonium rotaxanes.

Acknowledgments

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7. *Preparation of tert-ammonium-type rotaxane* **2·PF$_6$** *from* **1**: A mixture of *tert*-ammonium salt **1** (125 mg, 0.300 mmol) and DB24C8 (202 mg, 0.450 mmol) in chloroform (0.6 mL) was stirred at 0 °C for 10 min. To the mixture were added 3,5-dimethylbenzoic anhydride (106 mg, 0.380 mmol) and tributylphosphane (7.4 µL, 0.03 mmol) and the mixture was stirred at 0 °C for 48 h. Diluted sodium hydrogen carbonate solution was added and organic layer was separated. The organic layer was washed with 2 M HCl and brine. The resulting organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporated. The residue was subjected to preparative HPLC using chloroform as an eluent to give colorless solid (**2**·**PF**$_6$, 9.3 mg, 3.0%). Mp 99–100 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.73 (br, 1H), 7.68–7.65 (m, 4H), 7.29–7.23 (m, 2H), 7.20 (s, 1H), 7.05 (s, 2H), 6.90–6.87 (m, 5H), 6.81–6.77 (m, 4H), 5.20–5.15 (m, 3H), 4.94 (dd, $J = 2.3$ Hz, $J = 13.1$ Hz, 1H), 4.50–4.44 (m, 1H), 4.24–4.19 (m, 1H), 4.11–4.10 (m, 8H), 3.79–3.70 (m, 8H), 3.60–3.50 (m, 8H), 2.94–2.92 (m, 3H), 2.36 (s, 6H), 2.21 (s, 6H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.2, 147.1, 138.3, 138.1, 137.5, 134.8, 132.1, 130.4, 129.9, 129.8, 129.2, 127.8, 127.3, 121.5, 121.3, 111.9, 111.7, 77.2, 76.6, 71.7, 71.5, 70.4, 70.3, 68.1, 68.0, 65.8, 60.9, 60.4, 39.3, 29.7, 21.1 ppm. IR (KBr) 1718, 1578, 1444, 1375, 1196, 856, 670 cm^{-1}. MALDI-TOF MS (matrix DHBA) [**2**·**PF**$_6$–PF$_6$] calcd for $C_{51}H_{64}NO_{10}^{+}$ 850.4530, found 850.2540.
8. *N-Methylation of sec-ammonium-type rotaxane* **3**·**PF**$_6$: To a solution of rotaxane **3**·**PF**$_6$[3] (98 mg, 0.10 mmol) in DMF (1 mL) were added formic acid (98 mg, 2.0 mmol) and paraformaldehyde (60 mg, 2.0 mmol). The mixture was stirred at 70 °C for 24 h, cooled to room temperature, and poured into water (50 mL) and stirred for 1 h at rt. The precipitate formed was collected by filtration to afford *tert*-ammonium rotaxane **2**·**PF**$_6$ as a colorless solid in 100% yield (100 mg).
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10. It is possible to deprotonate *sec*-ammonium to *sec*-amine group of crown ether-containing rotaxane by *i*-Pr$_2$NEt or electrochemical reduction, when the rotaxane has another suitable cationic sites for the crown ether wheel such as 4,4′-bipyridinium group on the axle component: (a) Martínez-Díaz, M.-V.; Spencer, N.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **1997**, *36*, 1904–1907; (b) Ashton, P. R.; Ballardini, R.; Balzani, V.; Baxter, I.; Credi, A.; Fyfe, M. C. T.; Gandlfi, M. T.; López, M. G.; Díaz, M. V. M.; Piersanti, A.; Spencer, N.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 11932–11942; (c) Lin, C. F.; Lai, C. C.; Liu, Y. H.; Peng, S. M.; Chiu, S. H. *Chem. Eur. J.* **2007**, *13*, 4350–4355; (d) Chen, N. C.; Huang, P. Y.; Lai, C. C.; Liu, Y. H.; Wang, Y.; Peng, S. H.; Chiu, S. H. *Chem. Commun.* **2007**, 4122–4224.
11. *Preparation of* **4**: To a solution of rotaxane **2**·**PF**$_6$ (25 mg, 0.025 mmol) in CH$_3$CN was added DBU (37 µL, 0.25 mmol). The colorless suspension was heated to 70 °C to stir for 24 h. The mixture was poured into water (30 mL) and stirred for 30 min. The precipitate formed was collected by filtration and washed with water. The solid material was dried under reduced pressure. Colorless powder (21 mg, 100% yield). Mp 158 °C, ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.13–8.10 (m, 4H), 7.11 (d, $J = 8.0$ Hz, 2H), 7.06 (s, 2H), 6.90–6.81 (m, 10H), 6.00 (s, 2H), 4.11–4.03 (m, 8H), 3.73–3.64 (m, 8H), 3.41 (s, 2H), 3.34 (s, 2H), 3.28–3.24 (m, 4H), 2.27 (s, 6H), 2.18 (s, 6H), 2.09 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.2, 148.6, 139.5, 137.5, 136.5, 136.2, 134.0, 130.9, 128.6, 128.4, 128.2, 128.2, 126.8, 120.4, 111.5, 77.2, 69.5, 69.3, 67.9, 67.0, 62.0, 61.3, 42.1, 21.3, 20.8 ppm. IR (KBr) 2917, 1720, 1505, 1455, 1321, 1251, 1218, 1127, 1037, 739 cm^{-1}. MALDI-TOF MS (matrix DHBA) [**4**+H] calcd for $C_{51}H_{64}NO_{10}$ 850.4530, found 850.5493.
12. The refinement of the structure failed to be completed due to the efflorescent nature of the crystal and poor reflection data. Still, the atom-connecting scheme and relative arrangement of the molecules have been confirmed. Crystal data for **4**·2(*i*-PrOH) obtained by recrystallization from chloroform–*i*-PrOH–ethyl acetate: orthorhombic, $Pna2_1$, $a = 15.365(5)$, $b = 29.691(9)$, $c = 12.193(4)$ Å, $V = 5562.6(29)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.158$ g cm^{-3}, $F_{000} = 2096$, $\mu = 0.80$ cm^{-1}, reflection measured 47,401, independent reflections 12,390, $R_1 = 0.106$ [$I > 2\sigma(I)$], $wR_2 = 0.260$ (all data).