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SYNTHESIS AND CRYSTAL STRUCTURE OF 4^5,8^5-DI-*tert*-BUTYL-1,3,5,7(2,5)-TETRAOXADIAZOLA-2,6(2,6)-DIPYRIDINA-4,8(1,3)-DIBENZENACYCLOOCTAPHANE

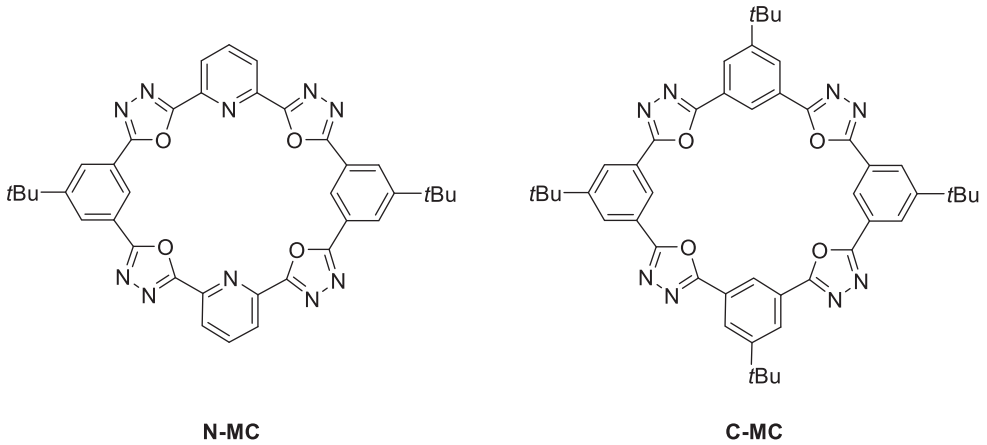
Katsuhiko Ono,* Satoshi Karasuda, and Masaaki Tomura[†]

Department of Life Science and Applied Chemistry, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

[†] Institute for Molecular Science, Myodaiji, Okazaki 444-8585, Japan

Abstract – The title compound (**N-MC**) was synthesized as a nitrogen analog of 2^5,4^5,6^5,8^5-tetra-*tert*-butyl-1,3,5,7(2,5)-tetraoxadiazola-2,4,6,8(1,3)-tetrabenzena-cyclooctaphane (**C-MC**). The crystal structure of **N-MC** was investigated by an X-ray crystallographic analysis, and the crystal was characterized by a step-like columnar structure, which is different from the supramolecular nanotube structure of **C-MC**. The molecular framework and the number of *tert*-butyl groups affected the molecular arrangement in the crystal.

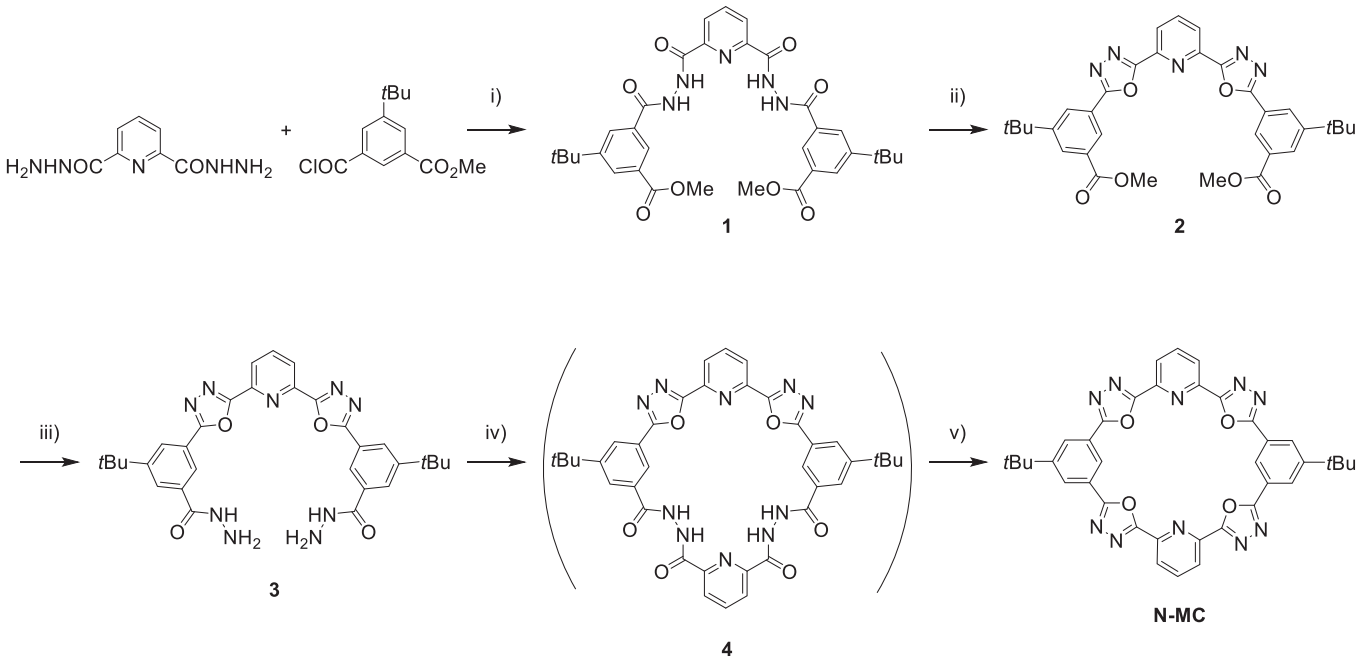
Macrocyclic compounds have attracted considerable attention as functional frameworks in materials science because these are unique molecules having a cavity inside. When these molecules are one-dimensionally arranged, the assembly forms a supramolecular nanotube giving transporting functions such as ion transporter.[1] When these molecules contain other molecules or ions selectively, they are



Scheme 1. Structure of **N-MC** and **C-MC**

used as building blocks having recognition functions such as molecular or ion receptor.[2–7] In our previous study, a macrocyclic tetramer of 2-(3-*tert*-butylphenyl)-1,3,4-oxadiazole (**C-MC**) was synthesized (Scheme 1).[8] Its self-assembly was investigated by an X-ray crystallographic analysis, and it was found that the macrocycles were stacked to form a supramolecular nanotube containing a unique one-dimensional water arrangement in the solid state. This organic and water hybrid is a promising candidate for future applications in nanomaterials. For the purpose of functionalization of **C-MC**, we synthesized the title compound (**N-MC**). Its X-ray crystallographic analysis showed a molecular arrangement different from that of **C-MC**. We report herein the synthesis and crystal structure of **N-MC**.

The synthesis of **N-MC** is illustrated in Scheme 2. The reaction of pyridine-2,6-dicarbohydrazide and methyl 3-*tert*-butyl-5-(chlorocarbonyl)benzoate afforded compound **1** in 48% yield. Compound **2** was obtained in 71% yield via the cyclization and dehydration reactions of **1**. Hydrazide **3** was prepared in 70% yield by the reaction of **2** and hydrazine monohydrate. **N-MC** was synthesized in 25% yield via the reaction of **3** and pyridine-2,6-dicarbonyl dichloride and the subsequent cyclization and dehydration reactions in phosphoryl chloride. **N-MC** was obtained as colorless crystals (mp > 300 °C) after recrystallization from a chloroform/methanol solution. The structures of **N-MC** and the related compounds were determined based on their spectral data and on elemental analyses.[9]



Scheme 2. Synthesis of **N-MC**. Reagents and conditions: i) 1,4-dioxane, reflux; yield 48%; ii) phosphoryl chloride, reflux; yield 71%; iii) hydrazine monohydrate, $CHCl_3$/MeOH, reflux; yield 70%; iv) pyridine-2,6-dicarbonyl dichloride, DMF/1,4-dioxane, reflux; v) phosphoryl chloride, reflux; yield 25% as a two-step process of iv and v

Single crystals suitable for X-ray crystallographic analysis were obtained by slow evaporation from a chloroform/methanol solution.[10] Reflection data were collected by using a Rigaku/MSC Mercury CCD diffractometer equipped with a graphite monochromator with Mo *K*α radiation (λ = 0.71073 Å) at 173(1) K. No absorption correction was applied. The structure was solved by direct method using SIR2004.[11] All non-hydrogen atoms were refined anisotropically by full-matrix least-squares technique on F^2 by using SHELXL2016.[12] A mixing model of two configurations was applied to one of *tert*-butyl groups (0.57:0.43) and one of chloroform molecules (0.55:0.45) for the refinement. All hydrogen atoms were positioned geometrically and refined by using a riding model. The final values of R_1 = 0.044, GOF = 1.08, and max/min residual electron density 0.28/−0.39 e Å^{-3} were obtained for 7975 unique reflections [$I > 2\sigma(I)$].

The molecular structure of **N-MC** is shown in Figure 1. The molecular framework is not a flat surface but nearly a saddle-type structure unlike the structure of **C-MC**, suggesting that **N-MC** has a more flexible skeleton than **C-MC**. The maximum torsion angle between neighboring aromatic rings is 33.66(1)°, and the value was found at a single bond between pyridine and 1,3,4-oxadiazole rings. One of *tert*-butyl groups is disordered over two sites (C36A–C38A and C36B–C38B) with an occupancy ratio of 0.57:0.43.

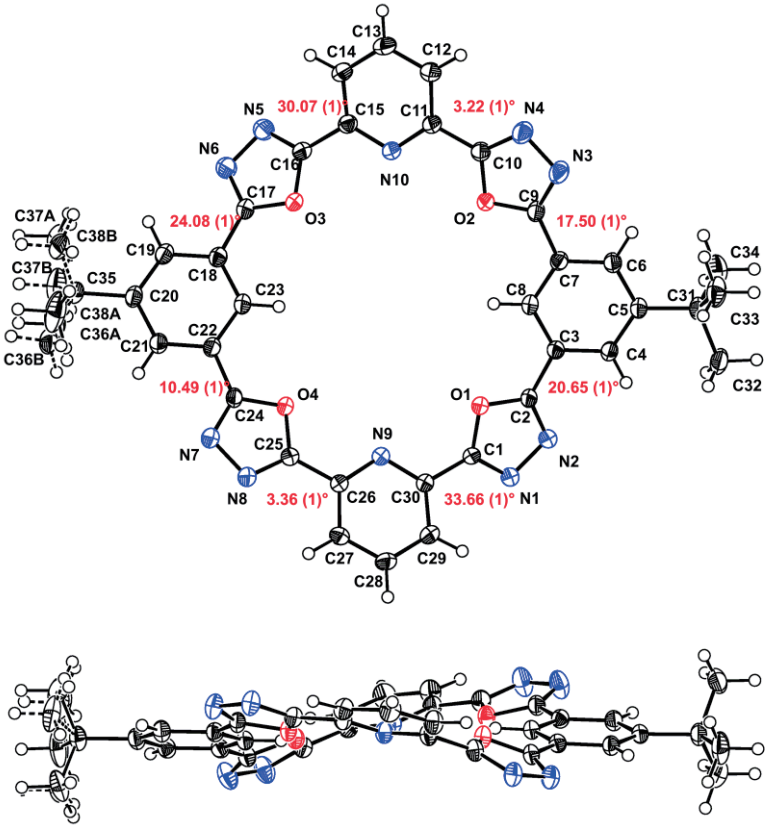


Figure 1. Top and side views of **N-MC**, in which the molecule is shown as ellipsoids at the 50% probability level for non-H atoms and as small spheres of arbitrary radius for H atoms

In the crystal, the molecules form a stack, and the disordered *tert*-butyl group fits into the adjacent macrocyclic cavity (Figure 2a). In addition, the other *tert*-butyl group fits into the cavity of another adjacent macrocycle. Therefore, the crystal structure is characterized by a step-like columnar structure, as shown in Figure 2b. In the crystal, two molecules of chloroform (not water) are included for one molecule of **N-MC** and adhere to the surface of the step-like columnar structure. These structures are in contact with each other via hydrogen bonds [N5···H14^{i} 2.59 Å and N6···H14^{i} 2.73 Å; symmetry code: (i) $-x+1$, $-y$, $-z+1$] (Figure 2c).

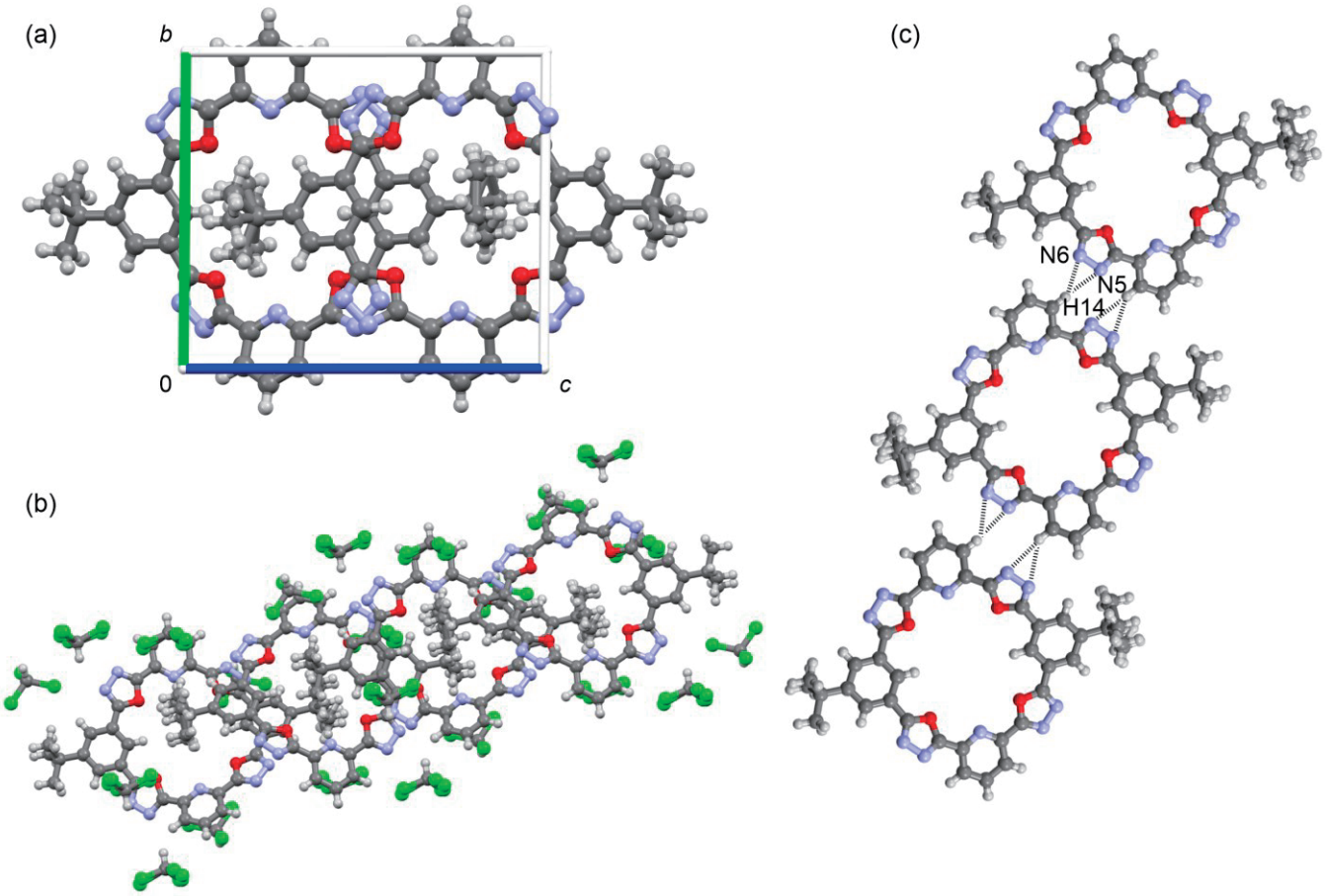


Figure 2. Molecular packing of **N-MC**: (a) overlap mode viewed down the *a* axis, (b) step-like columnar structure attaching chloroform molecules on the surface, (c) ribbon-like structure via hydrogen bonds across the step-like columnar structure

Modification of molecular structures changed intermolecular interactions, resulting in a morphological change to the step-like columnar structure of **N-MC** from the nanotube structure of **C-MC**. We concluded that the pyridine rings contributed to increasing the flexibility of macrocyclic framework and that the number of *tert*-butyl groups affected the supramolecular arrangement.

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9. Compound **1**: colorless crystals. mp 162–163 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.38 (s, 18H), 3.92 (s, 6H), 8.19 (t, J = 1.7 Hz, 2H), 8.27 (t, J = 1.7 Hz, 2H), 8.30–8.37 (m, 3H), 8.40 (t, J = 1.7 Hz, 2H), 10.97 (br s, 2H), 11.34 ppm (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 30.91, 34.86, 52.49, 125.38, 125.88, 129.04, 129.04, 130.07, 132.92, 140.19, 147.81, 152.09, 162.38, 165.38, 165.94 ppm; IR (KBr): $\tilde{\nu}$ = 3287, 2964, 1730, 1668, 1515, 1249 cm^{-1}; MS (EI): *m/z* (%): 631 (3)

[M]$^+$, 219 (100), 149 (61), 104 (45); HR-MS (EI) calcd for $C_{33}H_{37}N_5O_8$: 631.2642, found: 631.2641.

Compound **2**: colorless crystals. mp 284–285 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 18H), 3.98 (s, 6H), 8.17 (t, J = 8.0 Hz, 1H), 8.31 (t, J = 1.7 Hz, 2H), 8.48 (t, J = 1.7 Hz, 2H), 8.53 (d, J = 8.0 Hz, 2H), 8.72 ppm (t, J = 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.32, 35.31, 52.54, 123.81, 125.57, 125.98, 128.72, 130.51, 131.29, 138.79, 144.44, 153.18, 163.54, 165.85, 166.44 ppm; IR (KBr): $\tilde{\nu}$ = 2954, 1721, 1544, 1466, 1312, 1256, 739 cm^{-1}; MS (EI): m/z (%): 595 (67) [M]$^+$, 580 (100), 548 (75), 516 (38), 119 (32). Anal. Calcd for $C_{33}H_{33}N_5O_6$: C, 66.54; H, 5.58; N, 11.76. Found: C, 66.14; H, 5.55; N, 11.60.

Compound **3**: colorless crystals. mp > 300 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.42 (s, 18H), 4.62 (br s, 4H), 8.17 (t, J = 1.7 Hz, 2H), 8.25 (t, J = 1.7 Hz, 2H), 8.39 (dd, J = 7.9, 7.5 Hz, 1H), 8.45 (t, J = 1.7 Hz, 2H), 8.56 (d, J = 7.9 Hz, 1H), 8.56 (d, J = 7.5 Hz, 1H), 10.14 ppm (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 30.89, 34.93, 123.22, 123.32, 125.59, 125.64, 127.69, 134.41, 139.82, 143.48, 152.47, 163.07, 164.79, 164.86 ppm; IR (KBr): $\tilde{\nu}$ = 3456, 3343, 3310, 3208, 2964, 1644, 1541, 1466, 1276, 1109, 968, 738, 698 cm^{-1}; MS (EI): m/z (%): 595 (71) [M]$^+$, 564 (100), 546 (39). Anal. Calcd for $C_{31}H_{33}N_9O_4 \cdot H_2O$: C, 60.67; H, 5.75; N, 20.54. Found: C, 60.57; H, 5.67; N, 20.53.

N-MC: colorless crystals. mp > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (s, 18H), 8.17 (t, J = 7.9 Hz, 2H), 8.57 (t, J = 1.5 Hz, 2H), 8.67 (d, J = 7.9 Hz, 4H), 8.68 (d, J = 1.5 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.23, 35.46, 121.66, 124.65, 126.96, 129.80, 138.71, 144.74, 153.96, 164.34, 166.43 ppm; IR (KBr): $\tilde{\nu}$ = 2964, 1587, 1518, 1460, 1254, 1084, 964, 782, 737 cm^{-1}; MS (EI): m/z (%): 690 (39) [M]$^+$, 675 (100); HR-MS (EI) calcd for $C_{38}H_{30}N_{10}O_4$: 690.2451, found: 690.2463.

10. X-Ray crystallographic data for **N-MC**. Crystal data: 0.33 × 0.23 × 0.15 mm; $C_{38}H_{30}N_{10}O_4 \cdot 2(CHCl_3)$; M_r = 929.45; colorless block; triclinic; space group $P\bar{1}$; a = 12.1313(18), b = 12.9179(19), c = 14.003(2) Å; α = 88.690(5)º, β = 87.166(5)º, γ = 72.253(3)º; V = 2087.4(5) Å^3; Z = 2; D_x = 1.479 g cm^{-3}; μ = 0.47 mm^{-1}; F(000) = 952. The final values of R_1 = 0.044, GOF = 1.08, and max/min residual electron density 0.28/−0.39 e Å^{-3} were obtained for 7975 unique reflections [I > 2σ(I)]. CCDC-1570959.
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