HETEROCYCLES, Vol. 99, No. 2, 2019, pp. 1145 - 1153. © 2019 The Japan Institute of Heterocyclic Chemistry
Received, 17th September, 2018, Accepted, 3rd October, 2018, Published online, 28th November, 2018
DOI: 10.3987/COM-18-S(F)85

SYNTHESIS AND PROPERTIES OF A TRICYCLIC HEXAKETONE MONOHYDRATE WITH HEXABUTYL SIDE CHAIN

Mio Ishita,[a] Masanori Ohkoshi,[a] Yoshiyuki Kuwatani,[a,c] Hiroyuki Otani,[b] Tohru Nishinaga,[a] and Masahiko Iyoda[a]*

[a] Department of Chemistry, Graduate School of Science, Tokyo Metropolitan University, Hachioji, Tokyo 192-0397, Japan. [b] Graduate School of Environment and Information Sciences, Yokohama National University, Hodogaya-ku, Yokohama 240-8501, Japan. [c] Present address: Analysts Department, Common Technology Center, Murata Manufacturing Company, Ltd., 2288 Oshinohara, Yasu, Shiga 520-2393, Japan. E-mail: iyoda@tmu.ac.jp

Dedicated to Professor Tohru Fukuyama on the occasion of his 70th birthday

Abstract – A tricyclic hexaketone monohydrate with a hemiacetal structure was synthesized by the ruthenium-catalyzed oxidation of butyl-substituted tribenzotetradehydro[12]annulene-1,2-dione. The oxidation of the annulenedione afforded unique [12]annulene-1,2,5,6,9,10-hexaone, followed by the cyclization to produce corresponding tricyclic hydrate containing two dihydrobenzopyranone rings. The tricyclic hexaketone hydrate weakly interacts with methanol and ethylene glycol to form 1:1 complexes in solution.

INTRODUCTION

A large number of macrocyclic benzo-annulated annulenes have been synthesized to achieve new electronic and optical materials.[1,2] Among them, dehydrobenzoannulenes (fully-conjugated *ortho*-phenylene-ethynylene macrocycles) have been vigorously investigated due to their opto-electronic properties and as substrates of the 2D carbon networks graphyne and graphdiyne.[3,4] Furthermore, C_3-symmetric dehydrobenzo[12]annulenes are a versatile building block, and many groups employed them to create new materials.[5-7] Cyclic polyketones with regularly arranged carbonyl groups have attracted considerable attention because of their unique structures;[8] however, only a limited number of cyclic polyketones have been reported.[9] We already reported the synthesis of **2a** by the oxidation of **1a** with ruthenium catalyst (Figure 1).[10] Interestingly, **1a** easily produced the monohydrate **3** having a

nonsymmetrical structure with two dihydrobenzopyranone units. Since **3** strongly incorporated small molecules in the crystalline lattice using its hydroxy, carbonyl, and ether moieties, we planned to synthesize hexabutyl derivative **4** to compare its association behavior with that of **3**. In this paper, we report on the synthesis and binding properties of the hexabutyl hexaketone monohydrate **4** with alcoholic hydroxyl groups in solution and in the solid state.

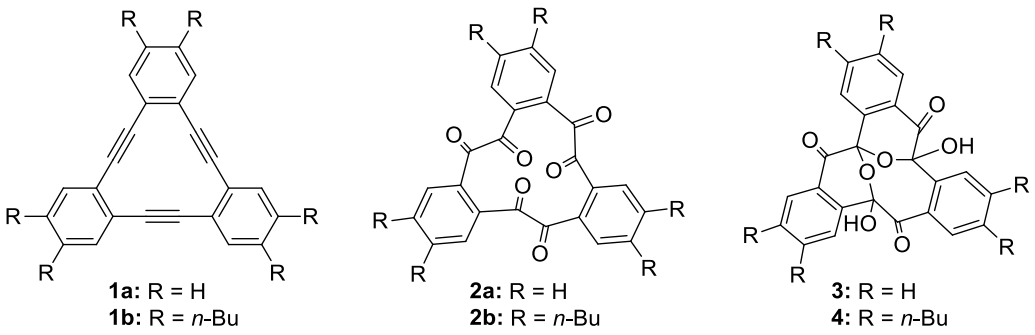
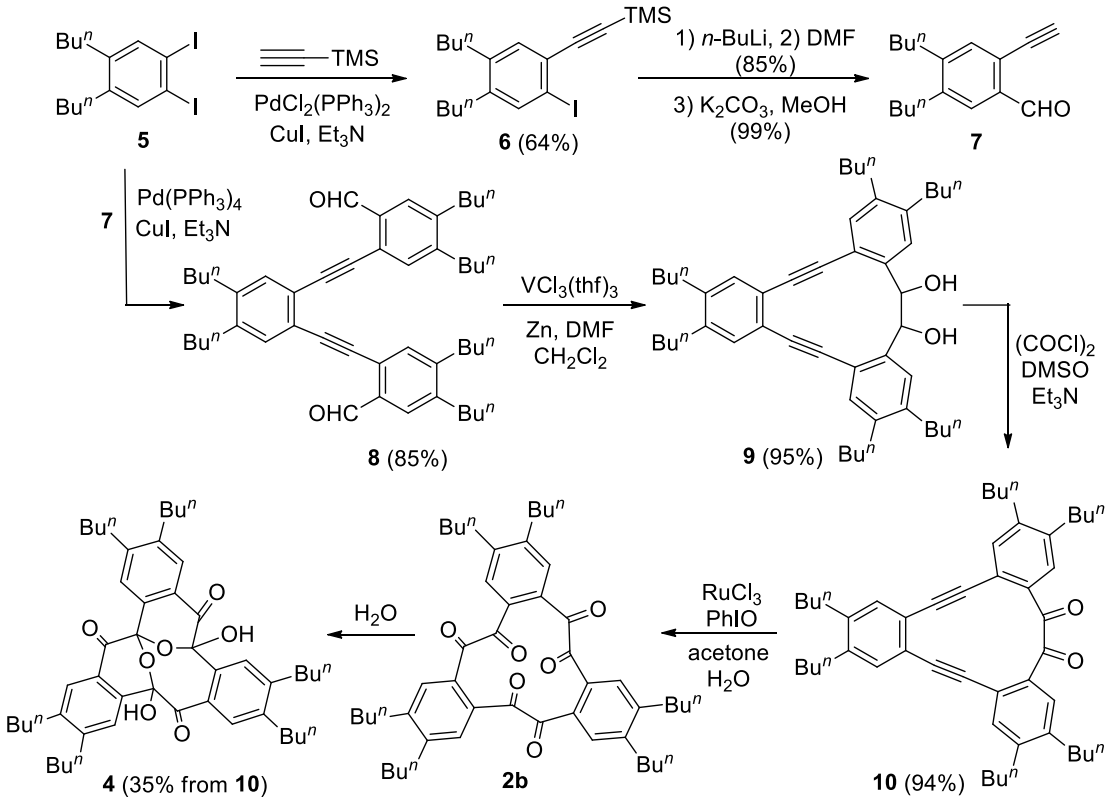


Figure 1. Dehydrobenzo[12]annulene **1**, annulene-1,2,5,6,9,10-hexaone **2**, and hexaone hydrates **3** and **4**

RESULTS AND DISCUSSION

The synthesis of **4** was performed by the oxidation of tribenzotetradehydro[12]annulene-1,2-dione **10** with ruthenium reagent[11] (Scheme 1). Sonogashira coupling of diiodide **5** with 1 equivalent of



Scheme 1. Synthesis of cyclic hexaone hydrate **4**

trimethylsilylacetylene afforded ethynylated iodide **6** in 64% yield. The iodide **6** was converted into ethynyl-aldehyde **7** by formylation, followed by desilylation in total 84% yield. The skeletal chain structure **8** was prepared by using Sonogashira coupling of **5** with **7** in 85% yield. This dialdehyde **8** was cyclized with low valent vanadium complex generated in situ to afford a stereoisomeric mixture of diol **9** in 95% yield. Swern oxidation of **9** produced tribenzotetradehydro[12]annulene-1,2-dione **10** in 94% yield. Ruthenium-catalyzed oxidation of the acetylene units of **10** was carried out with $RuCl_3 \cdot 3H_2O$ and PhIO in aqueous acetone for 10 min at room temperature to produce the desired hexaone hydrate **4** in 35% yield as stable colorless plates. Pristine hexaone hydrate **3** has very low solubility in common organic solvents such as CH_2Cl_2, benzene, and alcohols, but is soluble to some extent in acetone, ethyl acetate, and THF. However, hexabutylhexaone hydrate **4** shows good solubility in common organic solvents.

Although hexaone hydrate **4** was obtained in moderate yield, no hexaone **2b** was detected in the reaction products. Therefore, we calculated the structure and stability of hexaone **2a** as well as its hydrate **3**. As shown in Figure 2, the calculated structure of **2a** exhibits that the three carbonyl groups locate inside the macroring, whereas the other three carbonyl groups locate outside the macroring. Among the inside carbonyl groups, two carbonyls stick up and the other one carbonyl goes downward, and the calculated structure of **3** is similar to the crystal structure obtained from the X-ray analysis (Figure 2b).[12] The bond lengths and angles of **3** containing two dihydrobenzopyranone rings have the normal values. There is no intramolecular hydrogen bond to maintain the unique hemiacetal structure of **3**; however, **3** has a stable, strain-free structure. It is worth noting that the reaction of **2a** with water exothermically produces **3** by 27.4 kcal/mol estimated by B3LYP/6-31G(d) calculations. Furthermore, attempted dehydration of **3** and **4** to **2a** and **3a**, respectively, was unsuccessful due to the stability of **3** and **4** under dehydration conditions.

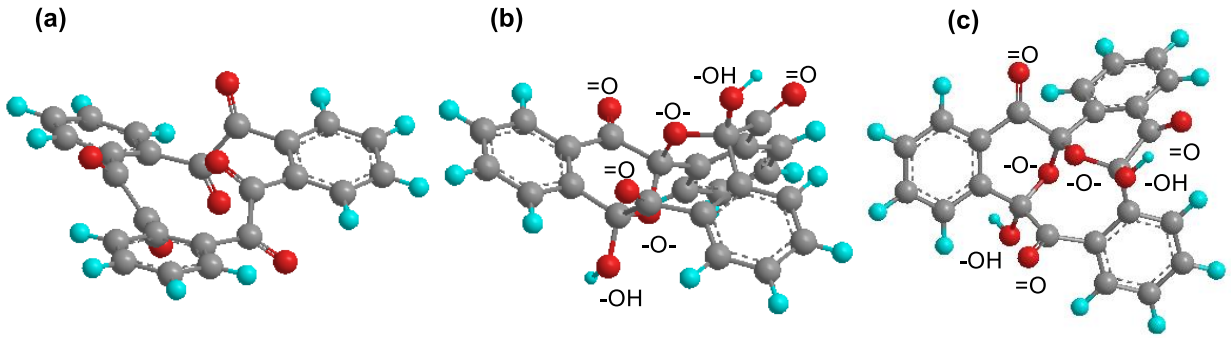


Figure 2. Calculated structures at B3LYP/6-31G(d) level. (a) Side view of **2a**. (b) Side view of **3**. (c) Top view of **3**

Hexabutylhexaone hydrate **4** forms no single crystals with and without solvent of crystallization. It is worth noting that **4** weakly interacts with methanol and ethanol in solution. As shown in Figure 3, a signal of the aromatic proton at δ 6.98 ppm ($CDCl_3$ at 25 °C) shifts downfield by adding methanol,[13] and the binding constant (*Kc*) was determined by using ^{1}H NMR titration. Although the observed *Kc* value, 3.6 M^{-1} (R = 0.99785) is small, the titration curve could be fitted with a theoretical curve of a 1:1 complex formation. In the 1:1 complex **4**·methanol, the alcoholic hydrogen, ethereal oxygen, and carbonyl oxygen of **4** form a bowl-shaped arrangement (Figure 2b), interacting with the oxygen and hydrogen of methanol to produce hydrogen bonds. The ^{13}C NMR spectrum of **4** in $CDCl_3$ at 25 °C exhibited that one carbonyl-carbon shifted downfield by 0.5 ppm by adding methanol, whereas the other carbonyl-carbons remained unchanged.

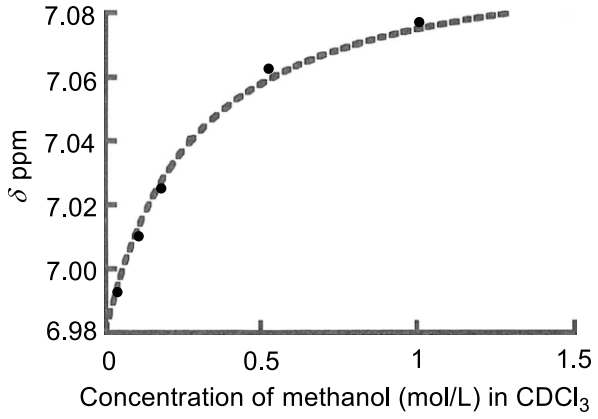


Figure 3. Concentration dependence of the ^{1}H NMR chemical shift of the aromatic proton of **4** (1.3×10^{-2} M/L, $CDCl_3$, 25 °C)

Ethylene glycol interacts with **4** in $CDCl_3$ to form hydrogen bonds. In a solution of **4** (0.013 mmol) and ethylene glycol (0.013 mmol) in $CDCl_3$ (0.5 mL) at 25 °C, the methylene proton of ethylene glycol was observed at δ 3.65 ppm, whereas ethylene glycol showed the methylene proton at δ 3.74 ppm under similar conditions. This upfield shift of the methylene proton is attributable to the shielding effect of aromatic rings on the methylene proton located near aromatic rings of **4**.

In summary, we have successfully synthesized the tricyclic hexabutyl hexaketone monohydrate **4** by using the ruthenium-catalyzed oxidation of butyl-substituted tribenzotetradehydro[12]annulene-1,2-dione **10**. Although hexabutylhexaone hydrate **4** has high solubility in common organic solvents and produces no crystals containing small molecules in the crystalline lattice unlike **3**, **4** forms complexes with methanol and ethylene glycol in solution. Further study on the functional properties of hexaone hydrate system is in progress.

EXPERIMENTAL

4,5-Dibutyl-1,2-diiodobenzene (5). To a solution of 1,2-dibutylbenzene[14] (5.00 g, 26.3 mmol) in acetic acid (75 mL) were added iodine (7.34 g, 28.9 mmol), $NaIO_3$ (2.60 g, 13.1 mmol), conc. H_2SO_4 (4.5 mL), and water (0.5 mL). The mixture was stirred for 12 h at 120 °C. After cooling, saturated aqueous $NaHCO_3$ and hexane were added to the mixture, and the organic layer was separated. The aqueous layer was extracted with hexane, and the combined organic layer was washed successively with aqueous $Na_2S_2O_3$ solution and brine. The organic layer was dried over $MgSO_4$, and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel with hexane as eluent. The product was recrystallized from EtOH at –20 °C to afford **5** (6.19 g, 53%). Colorless oil, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.60 (2H, s, Ar), 2.48 (4H, t, J = 7.9 Hz, CH_2), 1.51 (4H, m, CH_2), 1.37 (4H, m, CH_2), and 0.94 (6H, t, J = 7.3 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.7, 139.8, 104.0, 33.1, 31.6, 22.7, and 13.9; EI-MS *m/z* 442 (M^+). Anal. Calcd for $C_{14}H_{20}I_2$: C, 38.03%; H, 4.56%. Found: C, 37.99%, H, 4.34%.

4,5-Dibutyl-1-iodo-2-trimethylsilylethynylbenzene (6). To a mixture of **5** (0.957 g, 2.16 mmol), $PdCl_2(PPh_3)_2$ (175 mg, 0.25 mmol), CuI (48 mg, 0.25 mmol), and trimethylsilylacetylene (0.43 mL, 3.0 mmol) was added triethylamine (20 mL). The mixture was stirred for 3 h at room temperature. Et_2O and saturated aqueous NH_4Cl solution were added, and the organic layer was separated. The aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with hexane as eluent to give **6** (0.58 g, 64%). Pale yellow oil, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.58 (1H, s, Ar), 7.25 (1H, s, Ar), 2.51 (4H, m, CH_2), 1.50 (4H, m, CH_2), 1.37 (4H, m, CH_2), 0.93 (6H, t, J = 7.3 Hz, CH_3), and 0.28 (9H, s, $SiMe_3$); EI-MS *m/z* 412 (M^+).

4,5-Dibutyl-2-trimethylsilylethynylbenzaldehyde. To a solution of **6** (3.10 g, 7.42 mmol) in Et_2O (20 mL) was added butyllithium (7.1 ml of 1.6 M hexane solution, 11.4 mmol) under argon atmosphere at –78 °C. The solution was stirred for 30 min at –78 °C, and then warmed to –30 °C. To the solution, DMF (14.5 mL, 185 mmol) was added. The solution was stirred for 1 h at –30 °C, and warmed to room temperature. Saturated aqueous NH_4Cl solution and CH_2Cl_2 were added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was successively washed with saturated aqueous NH_4Cl solution and brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with hexane-benzene as eluent to give 4,5-dibutyl-2-trimethylsilylethynylbenzaldehyde (1.99 g, 85%). Yellow oil, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.47 (1H, s, CHO), 7.69 (1H, s, Ar), 7.35 (1H, s, Ar), 2.63 (4H, m, CH_2), 1.56 (4H, m, CH_2), 1.40 (4H, m, CH_2), 0.95 (6H, m, CH_3), and 0.27 (9H, s, $SiMe_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.1, 147.8, 142.4, 134.2, 134.1, 127.5, 124/3, 101.0, 100.8, 33.0, 32.6, 32.3, 22.9, 22.8, and 14.1; EI-MS *m/z* 314 (M^+).

4,5-Dibutyl-2-ethynylbenzaldehyde (7). A mixture of 4,5-dibutyl-2-trimethylsilylethynylbenzaldehyde (120 mg, 0.38 mmol) and K_2CO_3 (48 mg, 0.35 mmol) in MeOH (5 mL) was stirred for 1 h at room temperature. Ether and saturated aqueous NH_4Cl solution were added, and the organic layer was separated. The aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on alumina with hexane-benzene as eluent to give **7** (90 mg, 99%). Yellow oil, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.45 (1H, s, CHO), 7.71 (1H, s, Ar), 7.39 (1H, s, Ar), 3.37 (1H, s, C≡CH), 2.64 (4H, m, CH_2), 1.56 (4H, m, CH_2), 1.40 (4H, m, CH_2), and 0.95 (6H, m, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.4, 147.7, 142.6, 134.41, 134.38, 127.8, 122.8, 82.9, 79.6, 32.9, 32.8, 32.4, 32.2, 22.7, and 13.9; EI-MS *m/z* 242 (M^+).

1,2-Bis(2-(4,5-dibutyl-1-formyl))ethynyl-4,5-dibutylbenzene (8). To a mixture of **7** (260 mg, 1.05 mmol), **5** (230 mg, 0.52 mmol), $Pd(PPh_3)_4$ (18 mg, 0.015 mmol), and CuI (7 mg, 0.03 mmol) was added triethylamine (5 mL). The mixture was stirred for 1 h at 110 °C. After cooling, CH_2Cl_2 and saturated aqueous NH_4Cl solution were added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was successively washed with saturated aqueous NH_4Cl solution and brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with hexane-benzene as eluent to give **8** (300 mg, 85%). Pale yellow needles, mp 78.5–79 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.66 (2H, s, CHO), 7.73 (2H, s, Ar), 7.43 (2H, s, Ar), 7.39 (2H, s, Ar), 2.64 (12H, m, CH_2), 1.58 (12H, m, CH_2), 1.41 (12H, m, CH_2), and 0.95 (18H, m, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.8, 147.9, 142.1, 142.0, 133.8, 127.5, 133.7, 127.6, 124.2, 91.1, 88.5, 33.1, 32.9, 32.8, 32.5, 32.2, 22.8, 22.7, 14.0, and 13.9; TOF-MS *m/z* 670 (M^+).

3,4:7,8:11,12-Tris(4,5-dibutylbenzo)cyclododeca-3,7,11-triene-5,9-diyne-1,2-diol (9). To $VCl_3(thf)_3$ (1.98 g, 5.29 mmol) were added activated zinc (350 mg, 5.29 mmol) and CH_2Cl_2 (30 mL), and the mixture was stirred for 30 min at room temperature. To the resulting mixture was added DMF (1.05 mL, 13.4 mmol), and the mixture was stirred for additional 30 min at room temperature. To this low valent vanadium reagent was dropwise added a solution of **8** (1.47 g, 2.20 mmol) in CH_2Cl_2 (30 mL), and the mixture was stirred for 1 h at room temperature. Ethyl acetate and 10% aqueous solution of sodium tartrate were added, and the mixture was stirred for 1 h at room temperature. After filtration, saturated aqueous NH_4Cl solution and EtOAc were added, and the organic layer was separated. The aqueous layer was extracted with EtOAc, and the combined organic layer was successively washed with saturated aqueous NH_4Cl solution and brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with benzene as eluent to give a 1:1 diastereomeric mixture of **9** (1.40 g, 95%). Colorless thin plates, mp 106.5–107.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.60 (2H, s, Ar), 7.53 (2H, s, Ar), 7.43 (2H, s, Ar), 7.42 (2H, s, Ar), 7.39 (2H, s, Ar), 7.22 (2H, s, Ar), 5.73

(2H, dd, J = 7.1 and 2.5 Hz, CH), 4.41 (2H, t, J = 9.5 Hz, CH), 3.68 (2H, br s, OH), 2.65 (24H, m, CH_2), 1.68 (2H, br s, OH), 1.62 (24H, m, CH_2), 1.45 (24H, m, CH_2), and 0.97 (36H, m, CH_3); TOF-MS *m/z* 672 (M^+).

3,4:7,8:11,12-Tris(4,5-dibutylbenzo)cyclododeca-3,7,11-triene-5,9-diyne-1,2-dione (10). To a solution of $(COCl)_2$ (0.72 mL, 8.28 mmol) in CH_2Cl_2 (50 mL) was added a solution of DMSO (0.80 mL, 11.2 mmol) in CH_2Cl_2 (10 mL) at –78 °C. A solution of **9** (1.39 g, 2.07 mmol) in CH_2Cl_2 (10 mL) was added at –78 °C, and the mixture was stirred for 30 min at the same temperature. After warming up to –50 °C, Et_3N was added, and the mixture was stirred for 1 h at –50 °C and then for 1 h at room temperature. Water and CH_2Cl_2 were added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was successively washed with saturated aqueous NH_4Cl solution and brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with hexane-benzene as eluent to give **10** (1.31 g, 94%). Yellow prisms, mp 101–101.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 (2H, s, Ar), 7.44 (2H, s, Ar), 7.31 (2H, s, Ar), 2.66 (8H, m, CH_2), 2.60 (4H, t, J = 7.3 Hz, CH_2), 1.59 (12H, m, CH_2), 1.42 (12H, m, CH_2), and 0.97 (18H, m, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.5, 144.5, 141.3, 141.0, 136.1, 133.4, 131.5, 130.2, 123.3, 119.4, 92.9, 91.2, 33.1, 33.0, 32.3, 32.2, 22.8, 22.7, and 14.0; TOF-MS *m/z* 668 (M^+).

3,4:7,8:11,12-Tris(4,5-dibutylbenzo)cyclododeca-3,7,11-triene-1,2,5,6,9,10-hexaone hydrate (4). To a mixture of PhI=O (528 mg, 2.4 mmol) in water (0.2 mL) and acetone (1.8 mL) was added $RuCl_3 \cdot 3H_2O$ (7.3 mg, 0.028 mmol), and the mixture was stirred for 10 min at room temperature. A suspension of **10** (189 mg, 0.28 mmol) in water (0.4 mL) and acetone (3.6 mL) was added, and the mixture was stirred for 10 min at room temperature. After filtration, the filtrate was evaporated in *vacuo*, and the residue was purified by column chromatography on silica gel with hexane-EtOAc as eluent to give **4** (74 mg, 35%). Colorless plates, mp 98–99 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.94 (1H, s, Ar), 7.92 (1H, s, Ar), 7.67 (1H, s, Ar), 7.20 (1H, s, Ar), 6.99 (21H, s, Ar), 6.98 (1H, s, Ar), 4.37 (1H, br s, OH), 3.27 (1H, br s, OH), 2.86–2.52 (12H, m, CH_2), 1.72–1.30 (24H, m, CH_2), and 1.02–0.89 (18H, m, CH_3); ^{1}H NMR (MeOH-d_4, 500 MHz) δ 7.92 (1H, s, Ar), 7.86 (1H, s, Ar), 7.68 (1H, s, Ar), 7.18 (1H, s, Ar), 7.02 (21H, s, Ar), 7.00 (1H, s, Ar), 4.87 (2H, br s, OH), 2.91–2.55 (12H, m, CH_2), 1.76–1.30 (24H, m, CH_2), and 0.94–0.78 (18H, m, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 201.4, 190.7, 185.7, 149.5, 148.8, 143.7, 143.4, 143.1, 142.7, 136.7, 134.9, 133.3, 132.1, 129.1, 128.54, 128.45, 128.0, 127.1, 126.2, 126.0, 125.6, 98.9, 96.8, 96.7, 33.0, 33.0, 32.9, 32.83, 32.78, 32.5, 32.22, 32.17, 32.1, 32.0, 22.8, 22.7, 22.6, 14.0, 13.92, 13.89, and 13.8l; ^{13}C NMR (MeOH-d_4, 125 MHz) δ 204.7, 192.2, 188.3, 150.1, 149.4, 144.6, 143.8, 143.24, 143.21, 130.2, 136.0, 135.0, 131.2, 130.3, 130.0, 128.2, 128.1, 127.9, 127.3, 127.1, 100.5, 98.8, 98.2, 34.4, 34.3, 34.22, 34.20, 34.18, 34.0, 33.9, 33.6, 33.1, 23.8, 23.71, 23.69, 23.66, 23.62, 23.4, 14.4, 14.31, 14.27, and 14.23;

EI-MS *m/z* 732 (M^+-18); HRMS (MALDI-TOF-MS) *m/z* calcd for $C_{48}H_{52}O_7$·Na 73.4388, found 773.4411 $[M+Na]^+$.

ACKNOWLEDGEMENTS

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports and Technology, Japan and partly performed under the Cooperative Research Program of "Network Joint Research Center for Materials and Devices". We thank Prof. Masato Yoshida for helpful discussions.

REFERENCES AND NOTES

1. (a) R. H. Mitchell, *Chem. Rev.*, 2001, **101**, 1301; (b) R. D. Kennedy, D. Lloyd, and H. McNab, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1601.
2. (a) T. Kawase and H. Kurata, *Chem. Rev.*, 2006, **106**, 5250; (b) K. Tahara and Y. Tobe, *Chem. Rev.*, 2006, **106**, 5274; (c) E. L. Spitler, C. A. Johnson, and M. M. Haley, *Chem. Rev.*, 2006, **106**, 5345; (d) M. Iyoda, J. Yamakawa, and M. J. Rahman, *Angew. Chem. Int. Ed.*, 2011, **50**, 10522; (e) T. Nishiuchi and M. Iyoda, *Chem. Rec.*, 2015, **15**, 329.
3. (a) K. Kamada, L. Antonov, S. Yamada, K. Ohta, T. Yoshimura, K. Tahara, A. Inaba, M. Sonoda, and Y. Tobe, *ChemPhysChem*, 2007, **8**, 2671; (b) A. R. Guzman, M. R. Harpham, Ö. Süzer, M. M. Haley, and T. G. Goodson III, *J. Am. Chem. Soc.*, 2010, **132**, 7840.
4. (a) R. H. *Baughman*, H. Eckhardt, and M. Kertesz, *J. Chem. Phys.*, 1987, **87**, 6687; (b) G. Li, Y. Li, H. Liu, Y. Guo, Y. Li, and D. Zhu, *Chem. Commun.*, 2010, **46**, 3256.
5. (a) J. M. Kehoe, J. H. Kiley, J. J. English, C. A. Johnson, R. C. Petersen, and M. M. Haley, *Org. Lett.*, 2000, **2**, 969; (b) M. Iyoda, S. Sirinintasak, Y. Nishiyama, A. Vorasingha, F. Sultana, K. Nakao, Y. Kuwatani, H. Matsuyama, M. Yoshida, and Y. Miyake, *Synthesis*, 2004, 1527; (c) T. Yoshimura, A. Inaba, M. Sonoda, K. Tahara, Y. Tobe, and R. V. Williams, *Org. Lett.*, 2006, **8**, 2933.
6. W. J. Youngs, C. A. Tessier, and J. D. Bradshaw, *Chem. Rev.*, 1999, **99**, 3153.
7. (a) S. H. Seo, J. Y. Chang, and G. N. Tew, *Angew. Chem. Int. Ed.*, 2006, **45**, 7526; (b) I. Hisaki, H. Senga, Y. Sakamoto, S. Tsuzuki, N. Tohnai, and M. Miyata, *Chem. Eur. J.*, 2009, **15**, 13336; (c) K. Tahara, S. Lei, J. Adisoejoso, S. De Feyter, and Y. Tobe, *Chem. Commun.*, 2010, **46**, 8507.
8. (a) M. B. Rubin, *Chem. Rev.*, 1975, **72**, 177; (b) G. Seitz and P. Imming, *Chem. Rev.*, 1992, **92**, 1227; (c) M. B. Rubin and R. Gleiter, *Chem. Rev.*, 2000, **100**, 1121.
9. (a) W. Y. Lee, *Synlett*, 1994, 756; (b) S. W. McElvany, M. M. Ross, N. S. Goroff, and F. Diederich, *Science*, 1993, **259**, 1594; (c) Y. Rubin, T. C. Parker, S. J. Pastor, S. Jalisstgi, C. Boulle, and C. L. Wilkins, *Angew. Chem. Int. Ed.*, 1998, **37**, 1226.

10. M. Ohkoshi, T. Horino, M. Yoshida, and M. Iyoda, *Chem. Commun.*, 2003, 2586.
11. (a) H. Gopal and A. J. Gordon, *Tetrahedron Lett.*, 1971, 2941; (b) P. Müller and J. Godoy, *Helv. Chim. Acta*, 1981, **64**, 2531.
12. Crystallographic data for **3**: CCDC 215698.
13. We thank the reviewer's suggestion for the possible formation of mixed acetal with methanol. However, we concluded that hexabutylhexaone hydrate **4** formed no mixed acetal with methanol in the measurements of ^{1}H NMR spectra because **4** remained unchanged in a methanol solution in the presence of sulfuric acid at room temperature. Upon heating the solution, **4** gradually decomposed to produce a complex mixture of side products. This low reactivity of the hemiacetal moiety in **4** is presumably due to the instability of bridge head carbocation located at α-position of carbonyl group. Therefore, the downfield shift of the aromatic proton attributable to mixed acetal formation can be ruled out.
14. Q. Zhou, P. J. Carroll, and T. M. Swager, *J. Org. Chem.*, 1994, **59**, 1294.