Tetrahedron Letters 51 (2010) 3112–3115

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis and structure of a bowl-like molecule by threefold metathesis reactions

Jing Cao, Zhi-Ping Song, Xiao-Zhang Zhu, Chuan-Feng Chen *

Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

ARTICLE INFO

Article history:
Received 12 March 2010
Revised 3 April 2010
Accepted 9 April 2010
Available online 13 April 2010

Keywords:
Bowl-like molecule
Threefold metathesis reactions
Synthesis
Structure

ABSTRACT

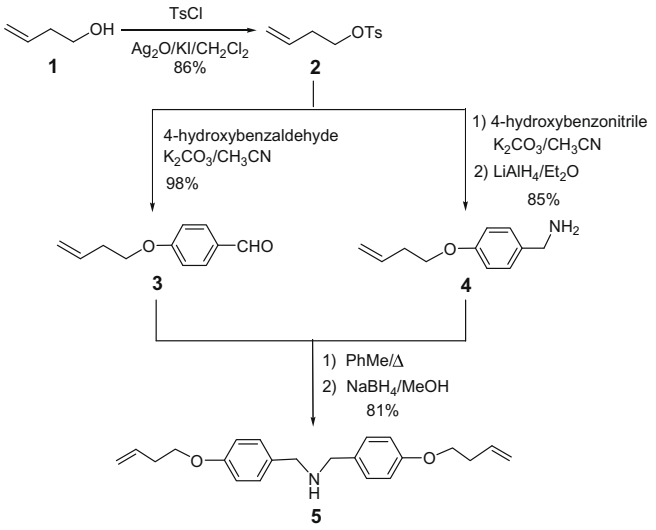
A bowl-like molecule was designed and efficiently synthesized by threefold metathesis reactions, and its structure was determined by NMR, MALDI-TOF MS spectrum, and X-ray crystallographic analysis.

Conformationally rigid, bowl-shaped molecules are an important class of receptors in supramolecular chemistry[1] due to their abilities to encapsulate and stabilize guest molecules, and to catalyze chemical transformations within their 'microreactor' cage.[2] However, most of the interests were focused on the construction of calixarene and resorcin[4]arene cavitands with enforced cavities large enough to complex with complementary organic compounds or ions,[3] and on the synthesis of aromatic molecular-bowl hydrocarbons and their derivatives.[4] So far, the synthesis of a new type of structure connected by covalent bonds with the shape of bowl is still a challenge in this field for chemists.

During the past 20 years, the ring-closing metathesis (RCM) reaction has been rapidly established as an efficient approach toward macrocyclic systems via intramolecular formation of carbon–carbon double bonds.[5] Consequently, it has found wide applications in the synthesis of novel macrocyclic hosts[6] and also in the construction of supramolecular assemblies with specific structures.[7] However, the examples of multifold metathesis reactions are still limited for their synthetic challenges.[5–7]

Recently, we[8a] reported a highly efficient approach to the synthesis of a new kind of [4]pseudocatenane by threefold metathesis reactions. According to the similar approach, we have also synthesized a series of chiral [4]pseudorotaxane, and further obtained a novel ship's wheel-like supramolecular structure.[8b] Inspired by the work reported previously, we here describe the synthesis and structure of a novel bowl-like molecule by threefold metathesis reactions.

Synthesis of dibenzylamine **5** is outlined in Scheme 1. Compound **2** was prepared in 86% yield by the esterification of 3-buten-1-ol **1** employing 4-methylbenzene-1-sulfonyl chloride in the presence of Ag_2O and KI. Compound **3** was synthesized by reaction



Scheme 1. Synthesis of the dibenzylamine **5**.

* Corresponding author. Tel.: +86 10 62588936; fax: +86 10 62554449.
E-mail address: cchen@iccas.ac.cn (C.-F. Chen).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.04.031

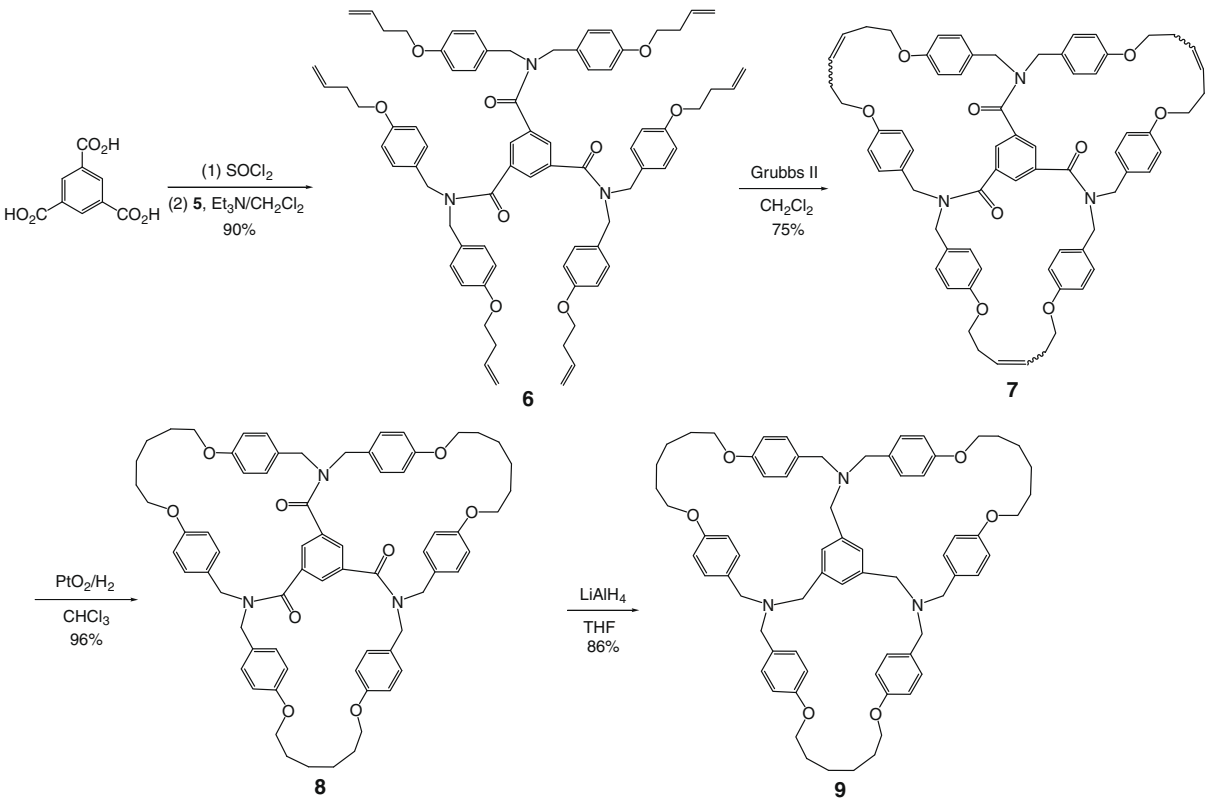
of **2** and 4-hydroxybenzaldehyde in the presence of K_2CO_3. Reaction of **2** with 4-hydroxybenzonitrile, followed by reduction with $LiAlH_4$, gave compound **4** in 85% yield for the two steps from the respective precursor. Finally, by the reaction of **3** and **4** in toluene, and then by reduction with $NaBH_4$, compound **5** was obtained in 81% yield for the two steps.

Synthesis of compound **8**[9] is outlined in Scheme 2. Reaction of 1,3,5-benzenetricarboxylic acid with thionyl chloride gave benzene-1,3,5-tricarboyl trichloride, which then reacted with **5** in the presence of triethylamine to afford compound **6** in 90% yield for the two steps. With the framework in hand, we further performed the threefold metathesis reactions. When a solution of **6** in CH_2Cl_2 (2 mM) was treated with the second-generation Grubbs' catalyst (5 mmol %), it was found that the reaction went along smoothly and gave product **7** in 75% yield. As **7** existed as cis/trans isomers, we further hydrogenated it by Adam's catalyst to afford compound **8**. Moreover, we also reduced compound **8** by $LiAlH_4$, which gave compound **9** in 86% yield. All new compounds were confirmed by the ^1H NMR, ^{13}C NMR, MALDI-TOF MS spectra, and elementary analyses.[9]

In order to determine the structure of molecule **8**, we further compared the ^1H NMR spectrum of **8** with that of compounds **6** and **9**. As shown in Figure 1, the chemical shifts of the inner aromatic protons in **6** were in the downfield compared with those of **9** for the influence of the neighboring C=O, while the outer aromatic protons showed three broadened signals, which implied that the structure of **6** is not with C_3 symmetry as imagined because of the steric hindrance although it has a free end. Compared with **6**, the ^1H NMR spectrum of **8** showed that signals of terminal vinyl protons at 5.0–6.0 ppm disappeared instead of new broadened ones at 2.79–2.83 ppm. Moreover, due to the influence of the closely packed atoms and the C=O groups, the aromatic proton signals of **8** became more complex and indecipherable, which suggested that **8** has a very rigid structure. However, when the C=O group in **8** was reduced to methylene group, the molecular symmetry of the product **9** was enhanced obviously. The outer aromatic protons split into two groups, while the inner aromatic protons move to the upfield. Moreover, the aliphatic proton signals are also sharp and differentiable. These observations suggested the unsymmetric structure of **8** was mainly caused by the carbonyl groups.

The MALDI-TOF mass spectrum of **8** displayed a strong peak at *m/z* 1085.1 for $[M+H]^+$. The structure of **8** was further determined by its X-ray single crystal analysis. The single crystal of **8**[10] suitable for X-ray diffraction was obtained by slow evaporation of ethyl ether to the $CHCl_3$ solution of **8**. As shown in Figure 2, the crystal structure confirmed it as a complete macrocycle as we learned from its ^1H NMR spectrum, and it showed a bowl-like structure with a depth of nearly 5.0 Å in the solid state. In the structure, the adjacent phenyl rings were connected covalently through an ethenylenedioxy bridge. As the molecule **8** was twisted by the closely arrayed atoms, the middle atomic ring lay at the bottom of the bowl, while the ethenylenedioxy bridge was at the rim of the bowl. Moreover, it was found that two molecules of **8** could form a up-face to up-face dimer by a couple of C–H···π interactions ($d_{C-H\cdots\pi}$ = 2.90 Å for a), a couple of C–H···O ($d_{C-H\cdots O}$ = 2.71 Å for b) hydrogen bonding interactions, and one π···π interaction ($d_{\pi\cdots\pi}$ = 3.23 Å for c) between the two molecules (Fig. 2c). The dimers then self-assembled into a liner structure, which could further stack into a 3D microporous architecture view along the *a*-axis (Fig. 2d).

In conclusion, a bowl-like molecule has been efficiently synthesized by threefold metathesis reactions, and its structure was determined by ^1H NMR, ^{13}C NMR, MALDI-TOF MS spectrum, and X-ray analysis. The work described here could provide a new



Scheme 2. Synthesis and reduction of the bowl-like molecule **8**.

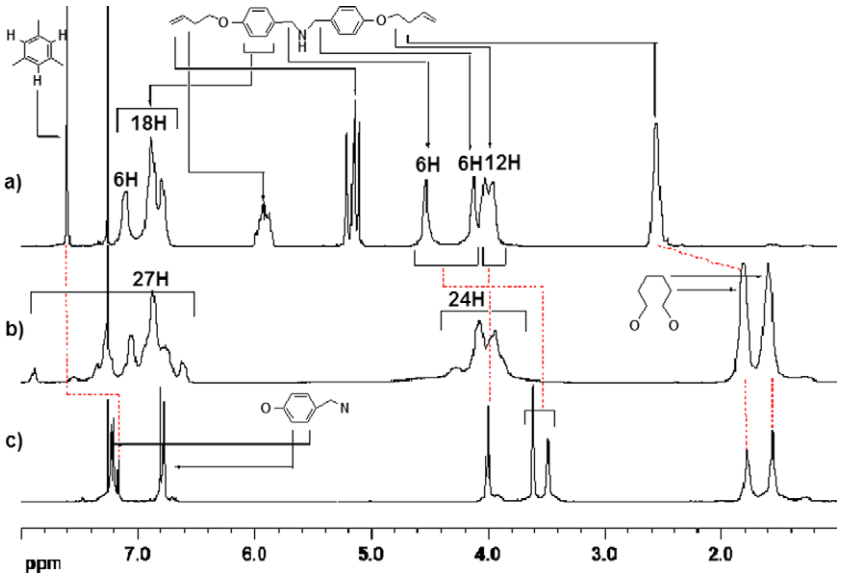


Figure 1. ^{1}H NMR spectra of (a) **6**, (b) **8** and (c) **9** (300 MHz, $CDCl_3$).

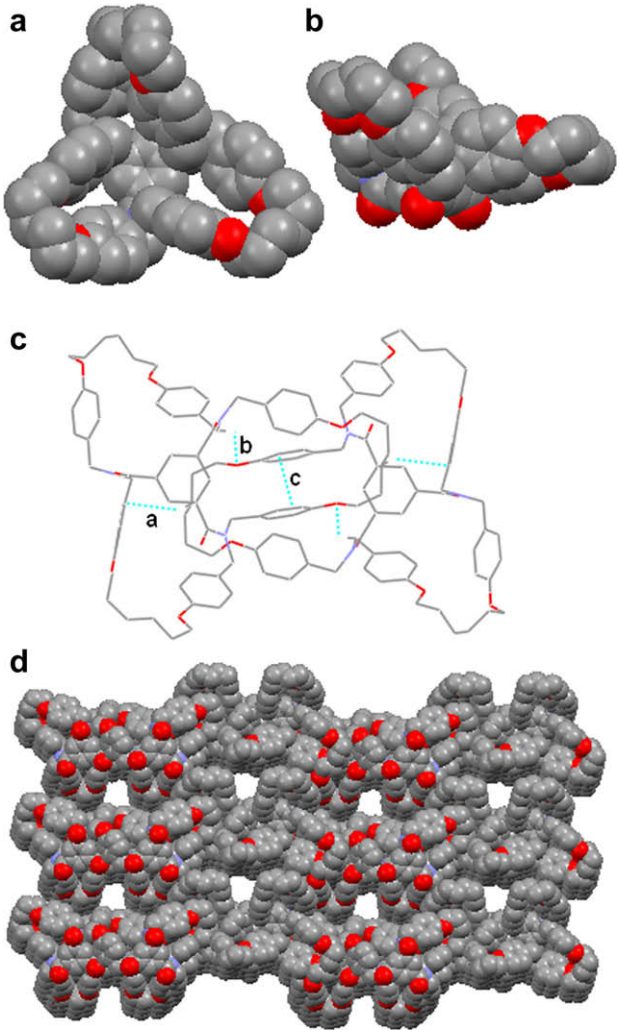


Figure 2. (a) Top view and (b) side view of crystal structure of **8**. (c) View of a dimer, blue lines denote the noncovalent interactions. (d) Packing of **8** viewed along the *a*-axis. Hydrogen atoms not involved in the interactions are omitted for clarity.

approach to the design and synthesis of molecules with specific structures through threefold or multifold metathesis reactions.

Acknowledgments

We thank the National Natural Science Foundation of China (20625206), the Chinese Academy of Sciences and National Basic Research Program of China (2009ZX09501-018) for the financial support.

References and notes

1. (a) Cram, D. J.; Choi, H. J.; Bryant, J. A.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7748–7765; (b) Schramm, M. P.; Hooley, R. J.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2007**, *129*, 9773–9779; (c) Hooley, R. J.; Van Anda, H. J.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2007**, *129*, 13464–13473; (d) Choi, H. J.; Nguyen, Q. T.; Park, Y. S.; Choi, C. H.; Paek, K.; Kim, E. H. *Chem. Commun.* **2009**, 4971–4973; (e) Crisóstomo, F. R. P.; Lledó, A.; Shenoy, S. R.; Iwasawa, T.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2009**, *131*, 7402–7410.
2. (a) Hogberg, G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6046–6050; (b) Purse, B. W.; Rebek, J. *Proc. Natl. Acad. Sci.* **2005**, *102*, 10776–10777; (c) Fox, O. D.; Cookson, J.; Wilkinson, E. J. S.; Drew, M. G. B.; MacLean, E. J.; Teat, S. J.; Beer, P. D. *J. Am. Chem. Soc.* **2006**, *128*, 6990–7002; (d) Kawase, T.; Kurata, H. *Chem. Rev.* **2006**, *106*, 5250–5273; (e) Park, S. J.; Kwon, O. H.; Lee, K. S.; Yamaguchi, K.; Jang, D. J.; Hong, J. I. *Chem. Eur. J.* **2008**, *14*, 5353–5359.
3. Some recent examples, see: (a) Roberta, P.; Suman, M.; Dalcanale, E. *Eur. J. Org. Chem.* **2004**, 451–462; (b) Ihm, C.; In, Y.; Park, Y.; Paek, K. *Org. Lett.* **2004**, *6*, 369–372; (c) Xiao, S. X.; Ajami, D.; Rebek, J., Jr. *Org. Lett.* **2009**, *11*, 3163–3165.
4. Some recent examples, see: (a) Wu, Y. T.; Siegel, J. S. *Chem. Rev.* **2006**, *106*, 4843–4867; (b) Qin, B.; Chen, X. Y.; Fang, X.; Shu, Y. Y.; Yip, Y. K.; Yan, Y.; Pan, S. Y.; Ong, W. Q.; Ren, C. L.; Su, H. B.; Zeng, H. Q. *Org. Lett.* **2008**, *10*, 5127–5130; (c) Nishida, S.; Morita, Y.; Ueda, A.; Kobayashi, T.; Fukui, K.; Ogasawara, K.; Sato, K.; Takui, T.; Nakasuji, K. *J. Am. Chem. Soc.* **2008**, *130*, 14954–14955; (d) Wang, K. K.; Wang, Y. H.; Yang, H.; Akhmedov, N. G.; Petersen, J. L. *Org. Lett.* **2009**, *11*, 2527–2530.
5. (a) Chuchuryukin, A. V.; Dijkstra, H. P.; Suijkerbuijk, B. M. J. M.; Gebbink, R. J. M.; van Klink, G. P. M.; Mills, A. M.; Spek, A. L.; van Koten, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 228–230; (b) Chuchuryukin, A. V.; Chase, P. A.; Dijkstra, H. P.; Suijkerbuijk, B. M. J. M.; Mills, A. M.; Spek, A. L.; van Klink, G. P. M.; van Koten, G. *Adv. Synth. Catal.* **2005**, *347*, 447–462; (c) Song, K. H.; Kang, S. O.; Ko, J. *Chem. Eur. J.* **2007**, *13*, 5129–5134; (d) Constable, E. C.; Housecroft, C. E.; Neuburger, M.; Rösel, P. J.; Schaffner, S.; Zampese, J. A. *Chem. Eur. J.* **2009**, *15*, 11746–11757.
6. (a) Kerckhoffs, J. M. C. A.; ten Cate, M. G. J.; Mateos-Timoneda, M. A.; van Leeuwen, F. W. B.; Snellink-Ruël, B.; Spek, A. L.; Kooijman, H.; Crego-Calama, M.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2005**, *127*, 12697–12708; (b) Parulekar, S. N.; Muppalla, K.; Fronczek, F. R.; Bisht, K. S. *Chem. Commun.* **2007**, 4901–4903; (c) Rudzevich, Y.; Cao, Y. D.; Rudzevich, V.; Böhmer, V. *Chem. Eur. J.* **2008**, *14*, 3346–3354; (d) Bogdan, A.; Bolte, M.; Böhmer, V. *Chem. Eur. J.* **2008**, *14*, 8514–8520.
7. Some recent examples, see: (a) Badjic, J. D.; cantrill, S. J.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2004**, *43*, 3273–3278; (b) Molokanova, O.; Vysotsky, M. O.; Cao,

Y. D.; Thondorf, I.; Böhmer, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 8051–8055; (c) Hiraoka, S.; Yamauchi, Y.; Arakane, R.; Shionoya, M. *J. Am. Chem. Soc.* **2009**, *131*, 11646–11647.

8. (a) Zhu, X.-Z.; Chen, C.-F. *J. Am. Chem. Soc.* **2005**, *127*, 13158–13159; (b) Zhu, X.-Z.; Chen, C.-F. *Chem. Eur. J.* **2006**, *12*, 5603–5609.
9. *Compound* **6**. The solution of 1,3,5-benzenetricarboxylic acid (105 mg, 0.5 mmol) in thionyl chloride (10 mL) was refluxed for 4 h to afford a colorless solution, which was concentrated under reduced pressure, and the residue was dried in vacuo to yield benzene-1,3,5-tricarboyl trichloride. To the trichloride in dry dichloromethane (30 mL) was then added **5** (506 mg, 1.5 mmol) and triethylamine (0.84 mL, 606 mg, 6 mmol). After the mixture was stirred in room temperature for an hour, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography over silica gel (eluent: CH_2Cl_2/methanol = 80:1) to afford **6** (520 mg) in 90% yield as a white solid. Mp: 113–115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.56 (br s, 12H), 3.87–4.03 (m, 12H), 4.13 (s, 6H), 4.53 (s, 6H), 5.11–5.22 (m, 12H), 5.85–5.99 (m, 6H), 6.79 (br s, 6H), 6.88 (br s, 12H), 7.17 (br s, 6H), 7.60 ppm (s, 3H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 33.7, 46.3, 50.8, 67.3, 76.7, 77.1, 77.3, 77.6, 114.9, 117.1, 126.2, 127.6, 128.3, 128.5, 129.8, 134.4, 137.2, 158.5, 170.1. MALDI-TOF MS: *m*/*z* 1169.0 $[M+H]^+$, 1191.0 $[M+Na]^+$, 1206.9 $[M+K]^+$. IR: ν 1632 cm^{-1} (C═O). Anal. Calcd for $C_{75}H_{81}N_3O_9 \cdot 1/2H_2O$: C, 76.50; H, 7.02; N, 3.57. Found: C, 76.43; H, 7.00; N, 3.73. *Compound* **7**. A solution of **6** (117 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (50 mL) was stirred under Ar for a few minutes, Grubbs' II catalyst (4 mg, 0.005 mmol) was then added. After the solution was purged with Ar for 10 min, it was further refluxed for a day under Ar. The solvent was evaporated off under reduced pressure and the crude product was subjected to column chromatography over silica gel with CH_2Cl_2/CH_3OH (60:1) as the eluent to yield 81 mg **7** (75%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (br s, 12H), 4.01 (brm, 24H), 5.66 (s, 6H), 6.60–7.88 (brm, 27H). MALDI-TOF MS: *m*/*z* 1085.1 $[M+H]^+$, 1107.1 $[M+Na]^+$, 1123.1 $[M+K]^+$. IR: ν 2929 (C–H), 1643 cm^{-1} (C═O). *Compound* **8**. A mixture of **7** (54 mg, 0.05 mmol) and PtO_2 (5 mg) in chloroform (20 mL) was stirred under H_2 atmosphere for 3 h. After the mixture was filtrated and the filtrate was then concentrated, 52 mg (96%) of **8** was obtained as a white solid. Mp: 138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59 (br s, 12H), 1.81 (br s, 12H), 3.94–4.29 (brm, 24H), 6.60–7.88 (br s, 27H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 24.5, 25.2, 27.4, 28.4, 29.7, 45.7, 47.6, 51.1, 51.6, 67.7, 67.9, 115.0, 115.2, 115.5, 123.4, 125.8, 126.7, 127.6, 127.9, 128.4, 128.8, 129.3, 130.0, 137.0, 137.5, 138.5, 158.3, 158.9, 169.8, 170.1. MALDI-TOF MS: *m*/*z* 1090.5 $[M+H]^+$, 1112.5 $[M+Na]^+$, 1128.4 $[M+K]^+$. IR: ν 2927 (C–H), 1644 (C═O) cm^{-1}. Anal. Calcd for $C_{69}H_{75}N_3O_9 \cdot H_2O$: C, 74.77; H, 7.00; N 3.79. Found: C, 74.89; H, 7.00; N, 3.60. *Compound* **9**. To a solution of **8** (76 mg, 0.07 mmol) in anhydrous THF (20 mL) was added $LiAlH_4$ (0.14 g, 3.7 mmol) in small portions. After being refluxed for 6 h, the reaction mixture was quenched with water and then extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate. The solvent was evaporated off to afford **9** (63 mg) in 86% yield as a white solid. Mp: 78–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43–1.56 (m, 12H), 1.76–1.80 (m, 12H), 3.48 (s, 9H), 3.61 (s, 9H), 4.00 (t, 12H), 6.79 (d, 9H), 7.17 (s, 3H), 7.21 (d, 9H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 24.6, 28.1, 56.1, 56.5, 67.8, 114.7, 128.5, 130.3, 131.0, 139.2, 158.0. MALDI-TOF MS: *m*/*z* 1048.8 $[M+H]^+$. IR: ν 2935 (C–H) cm^{-1}. Anal. Calcd for $C_{69}H_{81}N_3O_6 \cdot H_2O$: C, 77.71; H, 7.84; N, 3.94. Found: C, 77.65; H, 7.82; N, 3.92.
10. *Crystal data for* **8**: $C_{69}H_{75}N_3O_9$, M_w = 1090.32, crystal size: 0.34 × 0.32 × 0.24 mm^3, crystal system: monoclinic, space group: *P 1 21/a 1*, *a* = 10.810(5) Å, *b* = 39.197(17) Å, *c* = 15.994(7) Å, β = 92.382(4)°, *U* = 6771(5) $Å^3$, *Z* = 4, *T* = 113(2) K, 11911 reflections measured, 9130 unique (R_{int} = 0.0649), R_1 = 0.0733, wR_2 = 0.1716. CCDC 767880 contains the supplementary crystallographic data for **8**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk.