Synthesis of tetrafunctionalized pentiptycenequinones for construction of cyclic dimers with a cylindrical shape by boronate ester formation

Shigehisa Akine, Daisuke Kusama, Yuri Takatsuki, Tatsuya Nabeshima

PII: S0040-4039(15)01089-8
DOI: http://dx.doi.org/10.1016/j.tetlet.2015.06.070
Reference: TETL 46462

To appear in: *Tetrahedron Letters*

Received Date: 1 April 2015
Revised Date: 13 June 2015
Accepted Date: 24 June 2015

Please cite this article as: Akine, S., Kusama, D., Takatsuki, Y., Nabeshima, T., Synthesis of tetrafunctionalized pentiptycenequinones for construction of cyclic dimers with a cylindrical shape by boronate ester formation, *Tetrahedron Letters* (2015), doi: http://dx.doi.org/10.1016/j.tetlet.2015.06.070

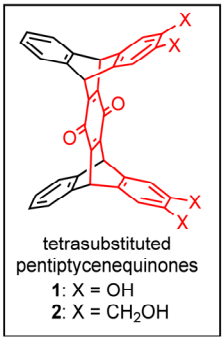
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

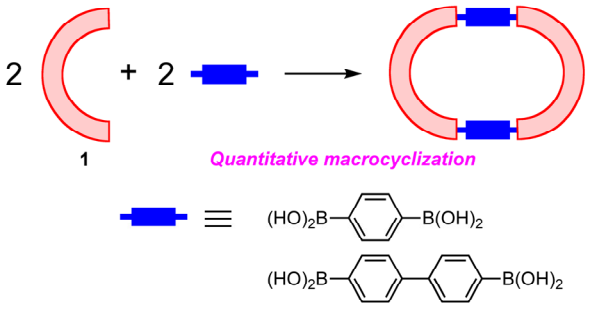
Synthesis of tetrafunctionalized pentiptycenequinones for construction of cyclic dimers with a cylindrical shape by boronate ester formation

Leave this area blank for abstract info.

Shigehisa Akine, Daisuke Kusama, Yuri Takatsuki and Tatsuya Nabeshima



tetrasubstituted pentiptycenequinones
1: X = OH
2: X = CH_2OH



Tetrahedron Letters
journal homepage: www.elsevier.com

Synthesis of tetrafunctionalized pentiptycenequinones for construction of cyclic dimers with a cylindrical shape by boronate ester formation

Shigehisa Akine[a],* Daisuke Kusama[b], Yuri Takatsuki[a,b] and Tatsuya Nabeshima[b]*

[a] Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan
[b] Faculty of Pure and Applied Sciences, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8571, Japan

ARTICLE INFO

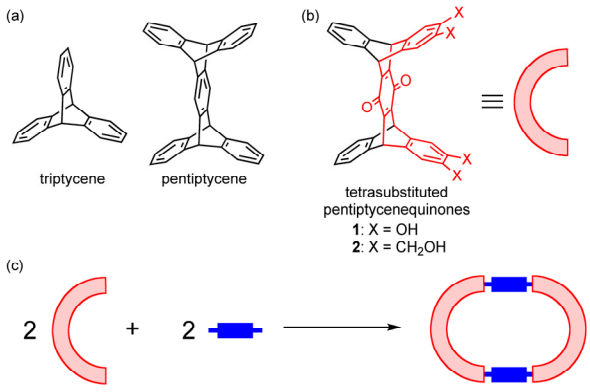
Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Iptycene
Boronate
Macrocycle
Belt-like structure
Quinone

ABSTRACT

New tetrasubstituted pentiptycenequinone derivatives **1** and **2** having two sets of diol moieties in a syn orientation were synthesized from the corresponding 2,3-disubstituted anthracene derivatives. The semicircular scaffold of these molecules is expected to be useful to create a belt-like structure having an aromatic π-wall. Indeed, the reaction with **1** with 1,4-phenylenediboronic acid or 4,4'-biphenyldiboronic acid quantitatively gave a 2:2 macrocyclic product via boronate ester formation. The efficient formation of these cyclic structures can be explained by favorable intramolecular cyclization at the final step.

Triptycene is a paddle-wheel-like molecule that has three fused benzene rings around [2.2.2]bicyclooctatriene framework. The very rigid molecular framework is useful for constructing various kinds of functional molecules[1] such as molecular gears,[2] non-stacking emissive polymers,[3] porous materials,[4] etc. The triptycene and its homologues are known as iptycenes. Representative members of the iptycene families are pentiptycene (Scheme 1a) with five benzene rings and heptiptycene with seven benzene rings, in which the benzene rings are connected by two and three bicyclic cores, respectively. One of the most important structural motifs of the iptycene derivatives is the non-coplanar arrangement of the benzene rings strictly fixed at an angle of about 120 deg by the rigid framework. This arrangement of the benzene rings is suitable for making a bent π-wall, and the resulting concave surface could nicely emulate the partial structure of an aromatic π-belt.[5,6] Indeed, there have been a number of reports on macrocyclic molecules in which two or more triptycene units are connected by suitable linkers.[7,8] If larger-sized iptycenes such as pentiptycene and heptiptycene are used, we would obtain a more rigid belt-like cylindrical structure that has a well-defined and shape-persistent cavity. For example, cyclododeciptycenequinone is a macrocyclic compound that is completely composed of iptycene scaffold.[9] The rigid framework of this molecule could particularly be useful to make a well-defined belt-like structure[10] in which flipping motions of the aromatic rings are completely suppressed. In this context, development of versatile precursors for a wide variety of such belt-like structures is important to create a new type of molecular receptors, porous materials, organic–inorganic hybrid nanotubes, etc.



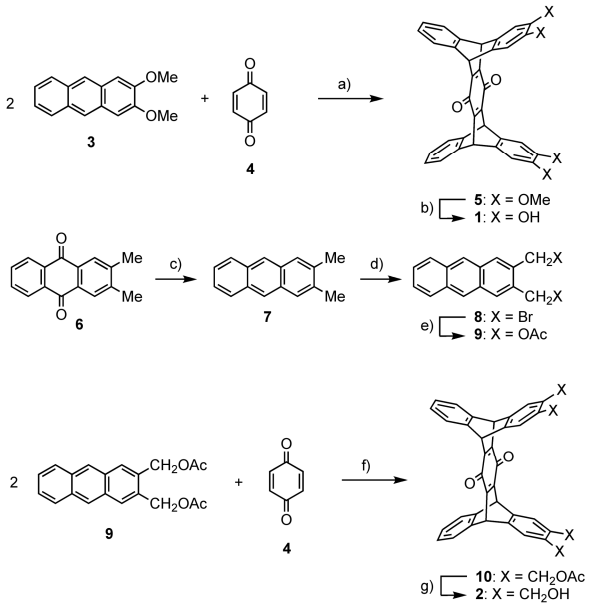
Scheme 1. (a) Triptycene and pentiptycene. (b) Tetrasubstituted pentiptycenequinones **1** and **2**. (c) Formation of a macrocyclic structure from semicircular molecules and bifunctional molecules.

Thus, we focused on tetrasubstituted pentiptycene derivatives (Scheme 1b) as one-half of a macrocyclic structure, which are expected to give a series of belt-like structures by the reaction with other suitable bifunctional building blocks (Scheme 1c).

* Corresponding authors. Tel.: +81 76 264 5701; fax: +81 76 264 5742 (S.A.); tel./fax: +81 29 853 4507 (T.N.). E-mail addresses: akine@se.kanazawa-u.ac.jp (S. Akine), nabesima@chem.tsukuba.ac.jp (T. Nabeshima).

Among the reported synthetic protocols to suitably functionalized pentiptycene derivatives,[11] the reaction of 1,4-benzoquinone with 2 equiv of anthracene in the presence of chloranil is advantageous.[12] Various functionalized pentiptycenequinones can be obtained from simple precursors via facile one-pot procedure based on this protocol. In order to obtain tetrasubstituted pentiptycene derivatives that could be used as a building block of a belt-like structure, two pairs of substituents have to be introduced in a syn orientation. We chose hydroxy and hydroxymethyl groups as the substituents so that the two diol moieties can be utilized to link the two semicircular units together by the reaction with a suitable bifunctional unit. Herein, we report the synthesis of tetrahydroxy pentiptycenequinone derivatives **1** and **2**. We found that the reactions of the tetrahydroxy derivative **1** with some diboronic acids quantitatively gave a macrocyclic compound.

The tetrahydroxy derivative **1** was synthesized from tetramethoxypentiptycenequinone (**5**),[13] which was prepared from 2,3-dimethoxyanthracene (**3**)[14] and 1,4-benzoquinone (**4**) (Scheme 2). The pentiptycenequinone **5** was obtained as a mixture of syn and anti isomers, which were separated by silica gel chromatography according to literature to yield the anti isomer with the higher Rf value and the syn isomer with the lower Rf value. The demethylation of the syn isomer of **5** with boron tribromide afforded tetrahydroxy derivative **1**. For the synthesis of the hydroxymethyl derivative **2**, we used 2,3-bis(acetoxymethyl)anthracene (**9**) as a precursor. 2,3-Bis(bromomethyl)anthracene (**8**) was synthesized by the reduction of 2,3-dimethylanthraquinone (**6**)[15] with sodium borohydride followed by bromination with *N*-bromosuccinimide. This dibromide **8** was converted to the diacetate **9** by the reaction with potassium acetate. The tetraacetoxypentiptycenequinone (**10**) was synthesized by the reaction of this diacetate **9** with 1,4-benzoquionone (**4**) in acetic acid in the presence of chloranil. The syn and anti isomers of this pentiptycenequinone derivative **10** were separated by silica gel chromatography in a manner similar to that for the methoxy derivative **5**, and the anti isomer (the higher Rf value) and the syn isomer (the lower Rf value) were isolated. The complete separation was confirmed by the ^{1}H NMR spectra in benzene-d_6, while the two isomers were observed at very similar chemical shifts in other solvents. The stereoconfiguration of the anti isomer of **10** was confirmed by X-ray crystallographic analysis[16] and the other was unambiguously assigned to the syn isomer. This syn isomer of the tetraester **10** was hydrolyzed using potassium carbonate in aqueous methanol/THF mixed solvent to yield tetrahydroxy derivative **2**.



Scheme 2. Synthesis of tetrasubstituted pentiptycenequinones. Reagents and conditions, a) chloranil, AcOH, yield 33% (anti isomer 24%); b) BBr_3, dichloromethane, yield 61%; c) $NaBH_4$, LiCl, 2-propanol, yield 83%; d) NBS, AIBN, CCl_4, yield 67%; e) KOAc, DMF, yield 92%; f) chloranil, AcOH, yield 31% (anti isomer 45%); g) K_2CO_3, H_2O/methanol/THF, yield 100%.

In recent years, there are a number of reports on macrocyclization utilizing boronate ester formation.[17] Since the tetrahydroxy compounds **1** and **2** have two sets of diol moieties fixed in a syn orientation, these compounds are expected to form a macrocycle with an appropriate diboronic acid. We investigated the macrocyclization of **1** with diboronic acid **A** in $CDCl_3$. At the initial stage, no signal of diboronic acid **A** was observed due to its low solubility in $CDCl_3$. After 2 days,

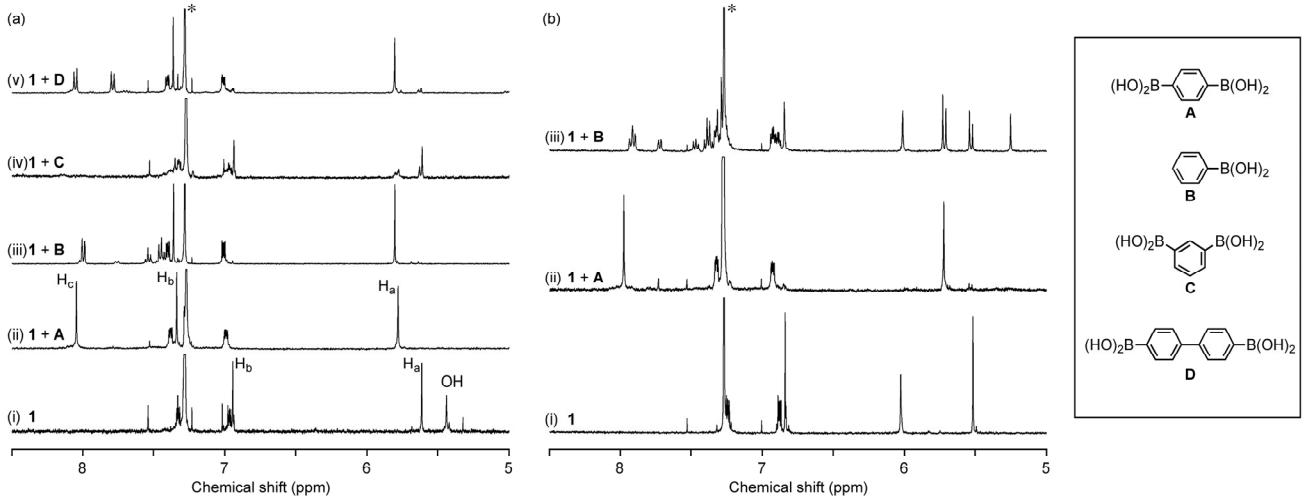
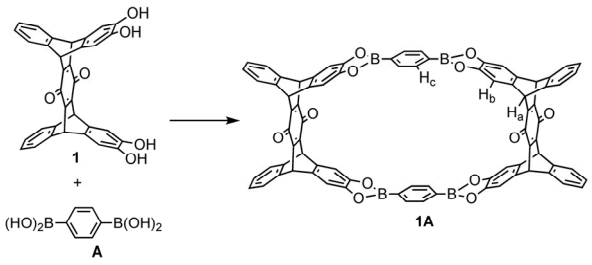


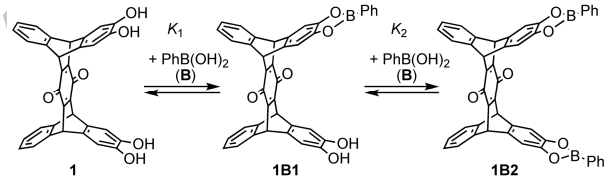
Figure 1. ^{1}H NMR spectra of **1** (400 MHz, 1.0 mM) before and after the reaction with boronic acids **A**–**D**. (a) In $CDCl_3$ and (b) in $CDCl_3$/CD_3CN (9:1). Asterisks denote the solvent signal.

however, a yellow clear solution was obtained. In the ^{1}H NMR spectrum, the protons of bridgehead methyne (H_a) and catechol (H_b) were observed at 5.77 and 7.33 ppm respectively, which appeared at lower field than the corresponding protons of the hydroxy derivative **1** (Figure 1a, i and ii). The signal of 1,4-phenylenediboronate moiety (H_c) was observed at 8.04 ppm. Since each of these signals was observed as one singlet, formation of a macrocyclic compound having an *n*:*n* stoichiometry was suggested. The mass spectrum (MALDI-TOF MS; anthracene matrix with silver triflate as an additive) showed a peak at m/z = 1344.3 for $[M + Ag]^+$, attributed to the 2:2 macrocycle. Thus, the reaction of pentiptycenequinone **1** and diboronic acid **A** afforded a macrocyclic compound formulated as **1A** (Scheme 3). The macrocycle **1A** readily dissociated into its constituents in polar solvents such as $CDCl_3/CD_3OD$ (9:1), $CDCl_3$/DMSO-d_6 (9:1), and $CDCl_3$/DMF-d_7 (9:1), while it remained intact in $CDCl_3/CD_3CN$ (9:1) (Figure 1b, ii) and $CDCl_3$/acetone-d_6 (9:1).



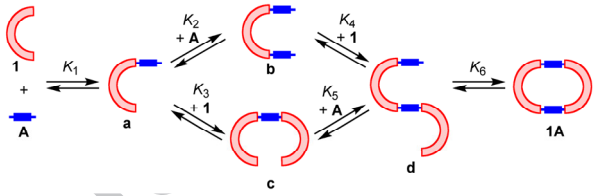
Scheme 3. Formation of macrocyclic boronate **1A** from pentiptycenequinone **1** and diboronic acid **A**.

The corresponding non-cyclic compound **1B2** was also prepared quantitatively by the condensation of tetrahydroxy derivative **1** with 2 equiv of phenylboronic acid (**B**) in $CDCl_3$ (Figure 1a, iii). However, compared to the macrocycle **1A**, this non-cyclic compound **1B2** was found to be less stable in $CDCl_3/CD_3CN$ (9:1) and $CDCl_3$/acetone-d_6 (9:1). The diboronate ester **1B2** was readily hydrolyzed to give a mixture containing monoboronate ester **1B1** and the tetrahydroxy derivative **1** in these solvents. The equilibrium constants for the boronate ester formation in $CDCl_3/CD_3CN$ (9:1) (Figure 1b, iii) were determined to be $K_1 = 3.5\times10^3$ M^{-1} and $K_2 = 7.4\times10^2$ M^{-1} (Scheme 4). The K_2/K_1 ratio was approximately 0.25, which nicely agrees with the ideal independent binding model of a two-site receptor.[18] This indicates that the boronate ester formation at one catechol moiety does not affect the boronate formation at the other side. From the values of K_1 and K_2, we estimated the equilibrium constants for the condensation of one catechol moiety and one boronic acid moiety as $K' = 1.6\times10^3$ M^{-1} (~ $1/2K_1$ ~ $2K_2$).



Scheme 4. Equilibria for the formation of diboronate ester **1B2**.

In contrast to the non-cyclic derivative **1B2**, the formation of **1A** from two molecules of **1** and two molecules of **A** involves more complicated equilibria. The macrocyclization proceeds via at least six equilibrium steps involving four intermediates **a–d** (Scheme 5). To simplify the analysis, we assumed that all the boronate ester formation steps have the same equilibrium constant (= K') except for the final intramolecular cyclization step (K_6). Based on this assumption, the five equilibrium constants K_1–K_5 satisfy the conditions $K_1 = 4K'$, $K_2 = K_3 = K'$, and $K_4 = K_5 = 2K'$, given the statistical correlation. We determined these equilibrium constants as K' ~ 1×10^4 M^{-1} and K_6 ~ 50 (dimensionless) by ^{1}H NMR spectroscopy. This large equilibrium constant at the final step (K_6 ~ 50), which is defined as [**1A**]/[**d**], means that the macrocycle **1A** is about 50 times more favorable than the acyclic species **d**. On the basis of this estimation, we can conclude that this favorable cyclization at the final step significantly contributes to the efficient macrocycle formation of **1A**, compared to the formation of the non-cyclic analog **1B2**. Thus, the stability of **1A** can be explained by favorable intramolecular cyclization at the final step.



Scheme 5. Proposed equilibria for the formation of macrocyclic boronate ester **1A**. Excess water is assumed to be present in the solution.

We also investigated the macrocyclization using diboronic acids with different structures. The ^{1}H NMR spectrum of the reaction mixture of **1** with 1,3-phenylenediboronic acid (**C**) showed several signals assignable to the bridgehead methyne protons and broad aromatic signals (Figure 1a, iv). This indicates that several oligomers with different chain lengths were formed instead of a macrocyclic compound with a discrete structure. On the other hand, the reaction of **1** with 4,4'-biphenyldiboronic acid (**D**) yielded a single macrocyclic compound, which showed a simple ^{1}H NMR signal pattern similar to that of **1A** (Figure 1a, v). The chemical shifts of the bridgehead methyne proton H_a and catechol proton H_b were similar to those of **1A**, indicating that a similar high symmetrical macrocycle **1D** was quantitatively formed. The 2:2 macrocyclic structure was confirmed by MALDI-MS measurement (m/z = 1496.5 for $[M + Ag]^+$). It is interesting to note that the reaction of hydroxymethyl analog **2** with 1,4-phenylenediboronic acid **A** did not form a single macrocyclic product. This inefficient macrocyclization can be explained by the seven-membered ring formation, which should be less advantageous than the formation of a five-membered ring with a more planar structure.

In conclusion, we have newly synthesized pentiptycenequinone derivatives **1** and **2** that have two diol groups in a syn arrangement. The reaction of **1** with diboronic acids such as 1,4-phenylenediboronic acid (**A**) and 4,4'-biphenyldiboronic acid (**D**) gave a 2:2 macrocyclic compound in a quantitative yield. In this macrocyclization, the linear arrangement of the two boronic acid moieties in the diboronic acids is crucial for the efficient macrocyclization. Thus, tetrahydroxypentiptycenequinone **1** was a useful building block for belt-like macrocyclic boronate compounds. The rigid macrocycles based on a pentiptycene skeleton generally have a shape-persistent cavity, which would be useful as porous materials for adsorption of larger organic molecules.

Investigation on the synthesis of porous materials using this class of pentiptycene derivatives is now in progress.

Acknowledgments

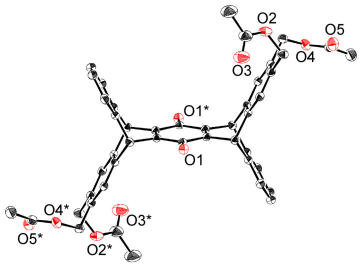
We thank Dr. Takashi Nirasawa (Bruker Daltonics K.K.) for the MALDI-TOF MS measurement of compound **1D**. This work was supported in part by Grant for Basic Science Research Projects from The Sumitomo Foundation (S.A.), Kanazawa University CHOZEN project, and Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Sciences and Technology, Japan.

Supplementary Material

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tetlet.####.

References and notes

1. Jiang, Y.; Chen, C.-F. *Eur. J. Org. Chem.* **2011**, 6377–6403.
2. Yamamoto G. *Pure Appl. Chem.* **1990**, *62*, 569–574. (b) Oki, M. *Acc. Chem. Res.* **1990**, *23*, 351–356.
3. Swager, T. M. *Acc. Chem. Res.* **2008**, *41*, 1181–1189.
4. Chong, J. H.; MacLachlan, M. J. *Chem. Soc. Rev.* **2009**, *38*, 3301–3315.
5. (a) Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 892–894. (b) Ashton, P. R.; Brown, G. R.; Isaacs, N. S.; Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Slawin, A. M. Z.; Smith, D. R.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 6330–6353. (c) Cory, R. M.; McPhail, C. L.; Dikmans, A. J.; Vittal, J. J. *Tetrahedron Lett.* **1996**, *37*, 1983–1986.
6. For reviews, see: (a) Tahara, K.; Tobe, Y. *Chem. Rev.* **2006**, *106*, 5274–5290. (b) Esser, B.; Bandyopadhyay, A.; Rominger, F.; Gleiter, R. *Chem. Eur. J.* **2009**, *15*, 3368–3379. (c) Eisenberg, D.; Shenhar, R.; Rabinovitz, M. *Chem. Soc. Rev.* **2010**, *39*, 2879–2890.
7. (a) Han, Y.; Meng, Z.; Ma, Y.-X.; Chen, C.-F. *Acc. Chem. Res.* **2014**, *47*, 2026− 2040. (b) Chen, C.-F. *Chem. Commun.* **2011**, *47*, 1674–1688. (c) Ma, Y.-X.; Han, Y.; Chen, C.-F. *J. Incl. Phenom. Macrocycl. Chem.* **2014**, *79*, 261–281.
8. (a) Zong, Q.-S.; Chen, C.-F. *Org. Lett.*, **2006**, *8*, 211–214. (b) Han, T.; Zong, Q.-S.; Chen, C.-F. *J. Org. Chem.*, **2007**, *72*, 3108–3111. (c) Han, T.; Chen, C.-F. *J. Org. Chem.*, **2008**, *73*, 7735–7742. (d) Tian, X.-H.; Chen, C.-F. *Org. Lett.*, **2010**, *12*, 524–527. (e) Tian, X.-H.; Hao, X.; Liang, T.-L.; Chen, C.-F. *Chem. Commun.*, **2009**, 6771–6773. (f) Tian, X.-H.; Chen, C.-F. *Chem. Eur. J.*, **2010**, *16*, 8072–8079. (g) Zhang, C.; Chen, C.-F. *J. Org. Chem.* **2007**, *72*, 3880–3888. (h) Hu, S.-Z.; Chen, C.-F. *Chem. Commun.*, **2010**, *46*, 4199–4201. (i) Xue, M.; Su, Y.-S.; Chen, C.-F. *Chem. Eur. J.* **2010**, *16*, 8537–8544. (j) Xue, M.; Chen, C.-F. *Chem. Commun.*, **2011**, *47*, 2318–2320.
9. Lou, K.; Prior, A. M.; Wiredu, B.; Desper, J.; Hua, D. H. *J. Am. Chem. Soc.* **2010**, *132*, 17635–17641.
10. (a) Kawase, T.; Darabi, H. R.; Oda, M. *Angew. Chem. Int. Ed.* **1996**, *35*, 2664–2666. (b) Takaba, H.; Omachi, H.; Yamamoto, Y.; Bouffard, J.; Itami, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 6112–6116. (c) Yamago, S.; Watanabe, Y.; Iwamoto, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 757–759.
11. (a) Yang, J.-S.; Yan, J.-L. *Chem. Commun.* **2008**, 1501–1512. (b) Zhao, L.; Li, Z.; Wirth, T. *Chem. Lett.* **2010**, *39*, 658–667. (c) Ma, Y.-X.; Meng, Z.; Chen, C.-F. *Synlett* **2015**, *26*, 6–30. (d) Hart, H. *Pure Appl. Chem.* **1993**, *65*, 27–34.
12. Zhu, X.-Z.; Chen, C.-F. *J. Org. Chem.* **2005**, *70*, 917–924.
13. Cao, J.; Lu, H.-Y.; Chen, C-F. *Tetrahedron* **2009**, *65*, 8104–8112.
14. (a) Miao, Q.; Nguyen, T.-Q.; Someya, T.; Blanchet, G. B.; Nuckolls, C. *J. Am. Chem. Soc.* **2003**, *125*, 10284–10287. (b) Pozzo, J.-L.; Clavier, G. M.; Colomes, M.; Bouas-Laurent, H. *Tetrahedron* **1997**, *53*, 6377–6390.
15. Allen, C. F. H.; Bell, A. *Org. Synth. Coll. Vol.* **1955**, *3*, 310–312.
16. X-ray crystallographic analysis of the anti isomer of **10**•$2CH_2Cl_2$ ($C_{48}H_{40}Cl_4O_{10}$ = 918.60): triclinic $P\bar{1}$, a = 8.7047(8), b = 11.5288(11), c = 11.6509(11) Å, α = 96.427(3), β = 110.015(3), γ = 96.690(3) deg, V = 1076.59(18) Å^3, Z = 1, T = 140 K, $R1$ = 0.0628 ($I > 2\sigma(I)$), $wR2$ = 0.1694 (all data). The ORTEP drawing (50% probability) is shown below.



Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no CCDC 1057177. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).
17. (a) Fujita, N.; Shinkai, S.; James, T. D. *Chem. Asian J.* **2008**, *3*, 1076–1091. (b) Nishiyabu, R.; Kubo, Y.; James, T. D. Fossey, J. S. *Chem. Commun.* **2011**, *47*, 1124–1150.
18. (a) Rebek, J., Jr.; Costello, T.; Marshall, L.; Wattley, R.; Gadwood, R. C.; Onan, K. *J. Am. Chem. Soc.* **1985**, *107*, 7481–7487. (b) Hunter, C. A.; Anderson, H. L. *Angew. Chem. Int. Ed.* **2009**, *48*, 7488–7499.