Cyclophanes

DOI: 10.1002/ange.201301180

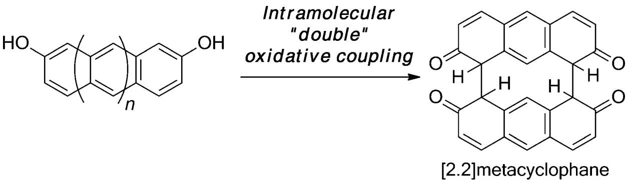
Synthesis of Highly Distorted π-Extended [2.2]Metacyclophanes by Intermolecular Double Oxidative Coupling**

Yutaro Koyama, Satoru Hiroto, and Hiroshi Shinokubo**

π-Conjugated molecules with a distorted structure have attracted increasing interest for the understanding of π-conjugation on a curved surface.[1] Recently, a number of such distorted π-systems have been constructed.[2,3] However, the synthesis of distorted structures often requires forcing reaction conditions to overcome strain energies and high activation barriers. Such high-temperature reactions often result in uncontrollable side processes, leading to the formation of undesired byproducts and decomposition of the desired products.

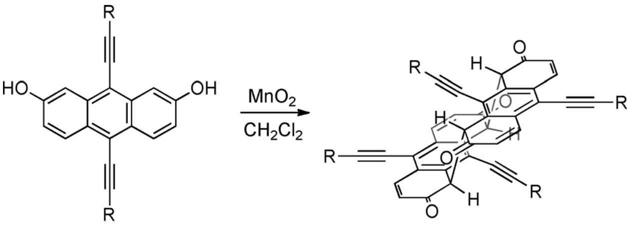
Cyclophanes often consist of curved aromatic ring systems.[4] In particular, cyclophanes have been recognized as promising candidates for a new class of optoelectronic materials, such as optical devices,[5] biosensors,[6] and electron-conducting materials.[7] In particular, [2.2]metacyclophane systems have been useful precursors of polycyclic aromatic hydrocarbons[8] and dihydropyrenes that exhibit thermo- and photochromic behavior.[9] However, there has been few reports on the synthesis of [2.2]metacyclophanes based on large π-conjugated compounds.[10] Only one example of [2.2]anthracenophane was reported in 1984 by Staab and Sauer through construction of thioether bridges followed by desulfuration.[10d] However, the desulfuration often requires heating conditions, which causes decomposition of the substrates.

Herein we present the radical-mediated synthesis of highly distorted [2.2]metacyclophanes from anthracene and pentacene scaffolds under mild conditions at room temperature. Oxidation of phenols and related hydroxyarenes has been investigated as a useful synthetic method for biaryls through radical-mediated carbon–carbon bond formation.[11,12] In particular, oxidation of 2-naphthol derivatives provides binaphthols (BINOLs), which serve as one of the most powerful chiral source for a number of asymmetric processes.[13] However, further studies on oxidation of higher oligoacenes with hydroxy groups have been overshadowed by versatility of BINOL derivatives.[14] We anticipated that oxidation of a dihydroxylated oligoacene would form a face-to-face dimer [2.2]metacyclophane through double oxidative coupling (Scheme 1).[15] This method demonstrates a novel use of oxidative coupling in the synthesis of distorted π-systems.



Scheme 1. Synthesis of π-extended [2.2]metacyclophanes by double oxidative coupling.

We chose 9,10-dialkynyl-2,7-dihydroxyanthracenes as starting materials because of their high solubility and stability. We attempted oxidation of **1a** with various oxidants and eventually found that the use of MnO_2 provided a dimeric product **2a** in 15% yield (Scheme 2). Its parent mass ion peaks was observed at $m/z = 1159.6267$ (calcd for $(C_{72}H_{96}O_4Si_4Na)^+$ 1159.6278). The ^1H NMR spectrum of **2a** displayed one singlet peak at 3.97 ppm and two doublet peaks in the aromatic region. Furthermore, its ^{13}C NMR spectrum indicated the presence of six sp^2 and four sp carbon atoms as well as one carbonyl carbon at 196.6 ppm. These spectral analyses allowed us to assign the product as [2.2]metacyclophane **2a**. A high-quality single crystal was obtained by vapor diffusion of methanol into the chloroform solution. The structure of **2a** was unambiguously elucidated by X-ray diffraction analysis to be a highly distorted face-to-face dimer (Figure 1a).[16] Oxidation of 2,7-dihydroxyanthracenes **1b** and **1c** with *tert*-butylethynyl and 1-octynyl groups also furnished [2.2]metacyclophanes **2b** and **2c**, respectively. The product yields were improved to 27% and 37% for **2b** and **2c**, respectively. These results imply that the bulkiness of alkynyl



1a: R = Si*i*Pr_3
1b: R = *t*Bu
1c: R = C_6H_{13}

2a (15%)
2b (27%)
2c (37%)

Scheme 2. Oxidation of 2,7-dihydroxyanthracenes **1a**, **1b**, and **1c**.

---

[*] Y. Koyama, Dr. S. Hiroto, Prof. Dr. H. Shinokubo
Department of Applied Chemistry, Graduate School of Engineering
Nagoya University, Aichi, 464-8603 (Japan)
E-mail: hiroto@apchem.nagoya-u.ac.jp
hshino@apchem.nagoya-u.ac.jp

[**] This work was supported by Grants-in-Aid for Scientific Research (Nos. 22750036 and 24350023) from MEXT (Japan). H.S. also acknowledges the Toyoaki Scholarship Foundation for financial support.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201301180.

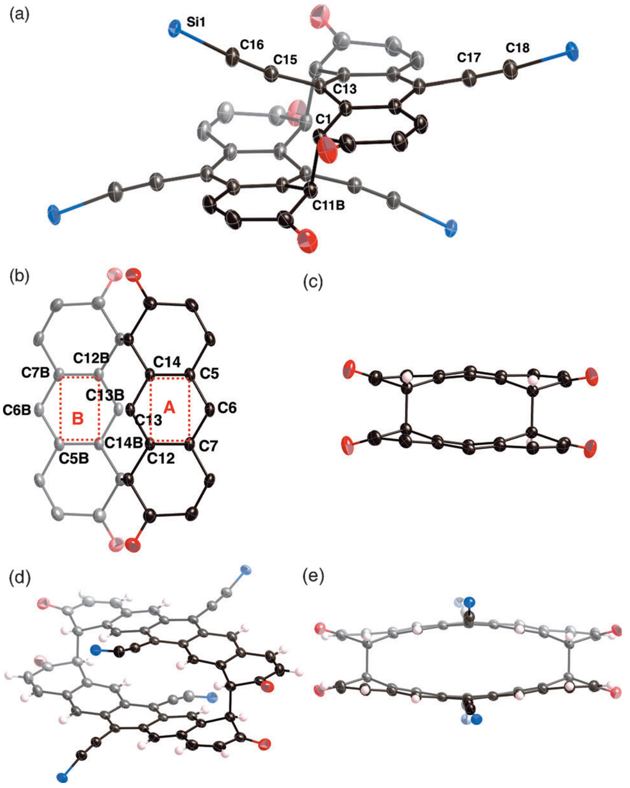
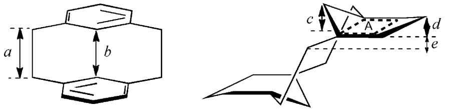


Figure 1. X-ray crystal structures of **2a** and **5**. a) Side view, b) top view, and c) front view of **2a**. d) Top view and e) side view of **5**. Thermal ellipsoids are set to 50% probability. Isopropyl groups in (a)–(e) and alkynyl groups in (b) and (c) were omitted for clarity.

groups influences the efficiency of the coupling process. The structures of **2b** and **2c** were also determined by X-ray diffraction analysis (Supporting Information, Figures S38 and S39).[17,18]

The structural parameters of **2a**, **2b**, **2c**, and the parent [2.2]metacyclophane are summarized in Table 1. In **2a**, the distance *b*, the closest carbon atoms between two benzene rings, is 2.71 Å, which is much shorter than the sum of van der Waals radii of two carbon atoms (3.5 Å). The bond length *a* of C1−C11B is 1.63 Å in **2a**, which is considerably longer than standard C(sp^3)−C(sp^3) single bond (1.53 Å). This elongation is induced by the large coulombic repulsion between two facing aromatic cores. All compounds exhibit similar values for *a* and *b*. Similarly to reported [2.2]metacyclophanes, each benzene unit takes distorted boat-like conformation.[19] The displacements *c* and *d*, the distances of C13 and C6 from the plane A (the plane consisting of C5, C7, C12, and C14), are good indexes of the benzene distortion, which are 0.187 Å and 0.110 Å in **2a**. These values are the largest among [2.2]metacyclophanes reported in literature. The values *c* and *d* becomes larger in the order **2c** < **2b** < **2a**. The distance *e* between the plane A and the adjacent methine carbon reflects the curvature of the cyclophanes. In contrast to *c* and *d*, the largest value of *e* is observed for **2c** (0.391 Å). The alkynyl groups are also significantly bending: The angles C13-C15-C16 and C15-C16-Si1 in **2a** are 170° and 173°, respectively (Figure 1a).

Table 1: Summary of structural parameters [Å] for **2a**, **2b**, and **2c**.



Compound	*a*	*b*	*c*	*d*	*e*[a]
2a	1.63	2.71	0.187	0.110	0.369
2b	1.63	2.71	0.178	0.103	0.359
2c	1.63	2.75	0.163	0.080	0.391
[2.2]MCP	1.57	2.69	0.143	0.042	0.368

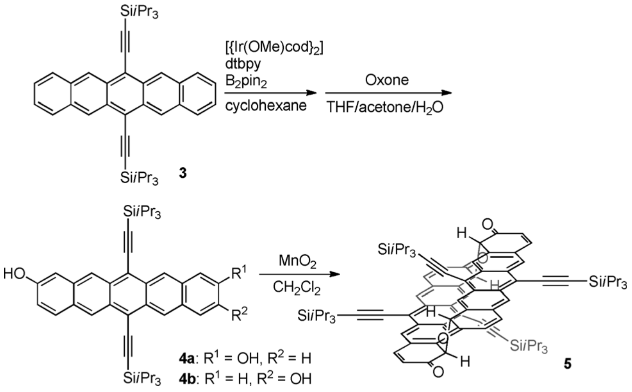
[a] Averaged values.

We calculated strain energies of **2a**, **2b**, and **2c** by DFT calculations at the wB97XD/6-31G(d) level.[20] The strain energies were estimated as a reaction enthalpy on a homodesmotic reaction (Supporting Information, Scheme S1). The values are 30.8 kcal mol^{-1} for **2a**, 4.56 kcal mol^{-1} for **2b**, and 12.1 kcal mol^{-1} for **2c**. The distortion of the benzene rings is mitigated for the dimers with less bulky substituents. The slightly larger value for **2c** over **2b** can be explained by the strain around bridges. The more planar benzene ring in **2** would induce larger coulombic repulsion between two benzene units, resulting in elongation of *a* and *e*.

The large distortion of **2a** induced an unusual reactivity. Treatment of **2a** with silica gel for 24 h afforded **1a** in 45% at room temperature by C−C bond cleavage, while such reactivity was not observed for **2b** and **2c**, suggesting substantial distortion of **2a**.[21] The ability to construct highly distorted molecules at room temperature underscores the powerfulness of this radical-mediated oxidative coupling procedure.

The deformation also influences the aromaticity of the benzene unit, which is evaluated on the basis of the harmonic oscillator model of aromaticity (HOMA) calculations. The HOMA values for the central benzene rings are 0.897, 0.649, and 0.882 for **2a**, **2b**, and **2c**, respectively. These values are meaningfully smaller than that of regular benzene (HOMA value = 0.98), indicating attenuated aromaticity of the curved benzene rings in cyclophanes **2**. The bridgehead protons of **2b** appear at 3.86 ppm, which are shifted upfield in comparison to **2a** (3.97 ppm) and **2c** (3.96 ppm). This chemical shift change is probably due to the weaker aromatic ring current effect of **2b**.

We then applied the present dimerization procedure to pentacene derivatives (Scheme 3). A mixture of 2,9- and 2,10-dihydroxypentacenes **4a** and **4b** was prepared from 6,13-pentacenequinone through iridium-catalyzed direct borylation.[22] As we could not isolate the 2,10-dihydroxy isomer **4a** from the mixture, we subjected the isomeric mixture to oxidation. Oxidation of **4a** and **4b** with MnO$_2$ afforded the corresponding face-to-face pentacene dimer **5** in 6% yield. In this reaction, no other dimeric compounds were obtained. The cyclophane structure of **5** was determined by X-ray diffraction analysis; in this structure the alkynyl groups are also bent (Figure 1d and e).[23] While the anthracene units in **5** take a domed conformation, the individual benzene units are almost planar. The mean plane deviations are calculated to be 0.039 and 0.027 Å, and the distance between two central benzene units is 3.39 Å. These results indicate that the strain



Scheme 3. Synthesis of a face-to-face pentacene dimer **5**.

suppressed in **5** because of dispersion of the distortion over the entire anthracene units.

Figure 2 a shows UV/Vis absorption spectra of **2a**, **2b**, and **2c** measured in CH_2Cl_2. For comparison, we required the absorption spectrum of the corresponding monomer unit of cyclophane **2a**. Consequently, we prepared bissilylethynylbenzene **6** with α,β-enone moieties as the monomer model, the absorption spectrum of which is also shown in Figure 2 a. Each dimer exhibits two large and broad absorption bands around 300 and 350 nm and one weak band around 475 nm. Compared to the monomer **6**, the lowest-energy absorption bands of the dimers **2** are bathochromically shifted, suggesting narrowing of the HOMO–LUMO gap owing to through-space interaction.[24] Interestingly, the red-shifts in the dimers **2c**, **2b**, and **2a** becomes smaller in this order, indicating that the distortion weakens the through-space interaction between two π-systems. The similar feature is also observed for π-extended derivative **5**. As shown in Figure 2 b, the lowest-energy absorption band is red-shifted (495 nm) in comparison to the corresponding monomer **7** (463 nm). Fluorescence was observed for **6** (555 nm in dichloromethane solution) with moderate quantum yield ($\Phi = 0.188$), while no emission was detected for **2** (Supporting Information, Figure S42).

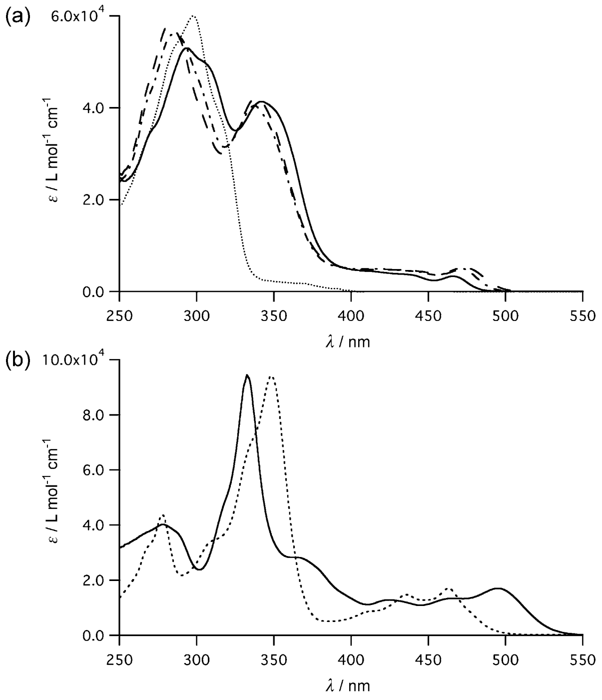


Figure 2. UV/Vis absorption spectra of a) **2a** (——), **2b** (–•–•), **2c** (-----), and monomer **6** (•••••), and b) **5** (——) and monomer **7** (•••••) in CH_2Cl_2.

We further investigated the electrochemical properties of the dimer **5** and the corresponding monomer **7** by cyclic voltammetry (CV). The CV experiments were performed in dichloromethane solution with Bu_4NPF_6 as an electrolyte. In comparison to **7**, the gap between oxidation and reduction potentials (ΔE) of **5** decreased from 2.55 V to 2.35 V, indicating a narrowing of the HOMO–LUMO gap. In particular, the reduction potential of **5** was significantly lowered. This result suggested that the dimerization of anthracene units influenced mainly on the LUMO level. To confirm this situation, we performed DFT calculations at the B3LYP/6-31G(d) level of theory.[25] Figure 3 depicts the frontier orbitals of **5**, which clearly indicate substantial intramolecular overlap between two anthracene moieties in the LUMO but not in the HOMO.[26] This interaction would contribute to the larger stabilization of the LUMO.

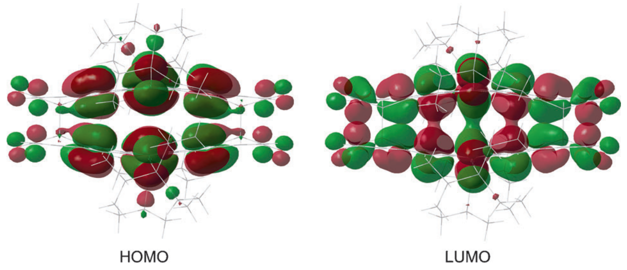


Figure 3. The HOMO and LUMO of **5**.

In conclusion, we have succeeded in the intermolecular oxidative dimerization of dihydroxyacenes to create face-to-face dimers with [2.2]metacyclophane skeletons. The dimers take on highly strained structures owing to steric and electronic repulsion between benzene unit and alkynyl groups. Dimerization induces bathochromic shifts of the lowest-energy absorption bands, indicating the existence of effective electronic interaction between two aromatic units. Electrochemical measurements and DFT calculations indicate that the decrease of the HOMO–LUMO gap is mainly resulted from stabilization of the LUMO. These observations would be applicable for investigations of intermolecular interaction of π-systems in a face-to-face stacking manner. Application of the present method to other π-conjugated molecules is now under investigation.

Received: February 9, 2013

Keywords: anthracene · cyclophanes · dimerization · oxidation · through-space interactions

[1] a) *Fragments of Fullerenes and Carbon Nanotubes: Designed Synthesis Unusual Reactions, and Coordination Chemistry* (Eds.: M. A. Petrukhina, L. T. Scoot), Wiley, Hoboken, **2012**; b) *Fullerenes: Principles and Applications* (Eds.: F. Lanfa, J.-F. Nierengarten), RSC, Cambridge, **2007**; c) *Carbon-Rich Compounds: From Molecules to Materials* (Eds.: M. M. Haley, R. R. Tykwinski), Wiley-VCH, Weinhim, **2006**.

[2] a) H. Omachi, Y. Segawa, K. Itami, *Acc. Chem. Res.* **2012**, *45*, 1378; b) A. Sygula, *Eur. J. Org. Chem.* **2011**, 1611; c) S. Higashibayashi, H. Sakurai, *Chem. Lett.* **2011**, *40*, 122; d) T. Amaya, T. Hirao, *Chem. Commun.* **2011**, *47*, 10524; e) V. M. Tsefrikas, L. T. Scott, *Chem. Rev.* **2006**, *106*, 4868; f) Y.-T. Wu, J. S. Siegel, *Chem. Rev.* **2006**, *106*, 4843.

[3] For recent breakthroughs for the synthesis of distorted π-conjugated compounds, see: a) T.-C. Wu, M.-K. Chen, Y.-W. Lee, M.-Y. Kuo, Y.-T. Wu, *Angew. Chem.* **2013**, *125*, 1327; *Angew. Chem. Int. Ed.* **2013**, *52*, 1289; b) L. T. Scott, E. A. Jackson, Q. Zhang, B. D. Steinberg, M. Bancu, B. Li, *J. Am. Chem. Soc.* **2012**, *134*, 107; c) Y. Segawa, S. Miyamoto, H. Omachi, S. Matsuura, P. Senel, T. Sasamori, N. Tokitoh, K. Itami, *Angew. Chem.* **2011**, *123*, 3302; *Angew. Chem. Int. Ed.* **2011**, *50*, 3244; d) R. Jasti, J. Bhattachrjee, J. B. Neaton, C. R. Bertozzi, *J. Am. Chem. Soc.* **2008**, *130*, 17646; e) S. Yamago, Y. Watanabe, T. Iwamoto, *Angew. Chem.* **2010**, *122*, 769; *Angew. Chem. Int. Ed.* **2010**, *49*, 757; f) B. L. Merner, L. N. Dawe, G. J. Bodwell, *Angew. Chem.* **2009**, *121*, 5595; *Angew. Chem. Int. Ed.* **2009**, *48*, 5487.

[4] a) *Modern Cyclophane Chemistry* (Eds.: R. Gleiter, H. Hopf), Wiley-VCH, Weinheim, **2004**; b) F. Vötle, *Cyclophane Chemistry*, Wiley-VCH, New York, **1993**; c) H. Hopf, *Angew. Chem.* **2008**, *120*, 9954; *Angew. Chem. Int. Ed.* **2008**, *47*, 9808.

[5] a) G. P. Bartholomew, I. Ledoux, S. Mukamel, G. C. Bazan, J. Zyss, *J. Am. Chem. Soc.* **2002**, *124*, 13480; b) W. Nakanishi, S. Hitosugi, A. Piskareva, Y. Shimada, H. Taka, H. Kita, H. Isobe, *Angew. Chem.* **2010**, *122*, 7397; *Angew. Chem. Int. Ed.* **2010**, *49*, 7239; c) S. P. Jagtap, D. M. Collard, *J. Am. Chem. Soc.* **2010**, *132*, 12208; d) Y. Morisaki, Y. Chujo, *Bull. Chem. Soc. Jpn.* **2009**, *82*, 1070.

[6] D. Ramaiah, P. P. Neelakandan, A. K. Nair, R. R. Avirah, *Chem. Soc. Rev.* **2010**, *39*, 4158.

[7] L. Valentini, F. Mengoni, J. M. Kenny, A. Marrocchi, A. Taticchi, *Small* **2007**, *3*, 1200.

[8] a) W. Baker, J. F. W. McOmie, J. M. Norman, *J. Chem. Soc.* **1951**, 1114; b) W. D. Rohrbach, F. Gerson, R. Möckel, V. Boekelheide, *J. Org. Chem.* **1984**, *49*, 4128.

[9] a) K. Ayub, R. Li, C. Bohne, R. V. Williams, R. H. Mitchell, *J. Am. Chem. Soc.* **2011**, *133*, 4040; b) R. V. Williams, W. D. Edwards, R. H. Mitchell, S. G. Robinson, *J. Am. Chem. Soc.* **2005**, *127*, 16207; c) P. A. Liddell, G. Kodis, J. Andréasson, L. Garza, S. Bandyopadhyay, R. H. Mitchell, T. A. Moore, A. L. Moore, D. Gust, *J. Am. Chem. Soc.* **2004**, *126*, 4803; d) Y. Ting, Y.-H. Lai, *J. Am. Chem. Soc.* **2004**, *126*, 909; e) G. J. Bodwell, J. N. Bridson, T. J. Houghton, J. W. J. Kennedy, M. R. Mannion, *Angew. Chem.* **1996**, *108*, 1418; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1320.

[10] a) W. Baker, F. Glockling, J. F. W. McOmie, *J. Chem. Soc.* **1951**, 1118; b) W. Jenny, R. Peter, *Angew. Chem.* **1965**, *77*, 1027; *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 979; c) F. Vötle, H. A. Staab, *Chem. Ber.* **1968**, *101*, 2709; d) M. Sauer, H. A. Staab, *Liebigs Ann. Chem.* **1984**, 615.

[11] H. Musso, *Angew. Chem.* **1963**, *75*, 965; *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 723, and references therein.

[12] For recent examples for the oxidation of phenol, see: a) M. Uyanik, T. Mutsuga, K, Ishihara, *Molecules* **2012**, *17*, 8604; b) A. Kirste, M. Nieger, I. M. Malkowsky, F. Stecker, A. Fischer, S. R. Waldvogel, *Chem. Eur. J.* **2009**, *15*, 2273.

[13] a) H. Egami, K. Matsumoto, T. Oguma, T. Kunisu, T. Katsuki, *J. Am. Chem. Soc.* **2010**, *132*, 13633; b) H. Wang, *Chirality* **2010**, *22*, 827; c) J. M. Brunel, *Chem. Rev.* **2005**, *105*, 857; d) T. Chen, S. Yekta, A. K. Yudin, *Chem. Rev.* **2003**, *103*, 3155.

[14] A few examples of oxidation of hydroxy-substituted anthracenes have been reported; see: H. Laatsch, *Liebigs Ann. Chem.* **1986**, 839.

[15] S. Hiroto, I. Hisaki, H. Shinokubo, A. Osuka, *J. Am. Chem. Soc.* **2008**, *130*, 16172.

[16] Crystallographic data for **2a**: $C_{74}H_{98}O_4Cl_6Si_4$, $M_r = 1376.58$, tetragonal, space group $P4_32_12$, $a = b = 19.4656(10)$, $c = 19.711(2)$ Å, $V = 7468.8(9)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.224\ \text{g cm}^{-3}$, $R = 0.0416$ ($I > 2.0\sigma(I)$), $R_w = 0.1117$ (all data), GOF = 1.095.[27]

[17] Crystallographic data for **2b**: $C_{53}H_{48}O_4Cl_3$, $M_r = 855.26$, monoclinic, space group C_2/c, $a = 16.127(5)$, $b = 14.313(5)$, $c = 20.389(7)$ Å, $\beta = 109.146(7)°$, $V = 4466(3)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.278\ \text{g cm}^{-}{}_{3}$, $R = 0.0876$ ($I > 2.0\sigma(I)$), $R_w = 0.2509$ (all data), GOF = 1.065.[27]

[18] Crystallographic data for **2c**: $C_{60}H_{64}O_4$, $M_r = 849.11$, triclinic, space group $P\bar{1}$, $a = 8.936(4)$, $b = 10.057(4)$, $c = 14.039(5)$ Å, $\alpha = 71.113(6)$, $\beta = 78.297(7)$, $\gamma = 84.127(6)°$, $V = 1168.1(8)$ Å^3, $Z = 1$, $\rho_{\text{calcd}} = 1.207\ \text{g cm}^{-}{}_{3}$, $R = 0.0495$ ($I > 2.0\sigma(I)$), $R_w = 0.1477$ (all data), GOF = 1.041.[27]

[19] F. Vögtle, P. Neumann, *Angew. Chem.* **1972**, *84*, 75; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 73.

[20] Geometry optimization with a wB97XD functional resulted in better agreement with the X-ray crystal structures than other DFT methods, such as B3LYP; a) S. M. Bachrach, *J. Phys. Chem. A* **2011**, *115*, 2396; b) G. F. Caramori, S. E. Galembeck, *J. Phys. Chem. A* **2008**, *112*, 11784.

[21] H. J. Reich, D. J. Cram, *J. Am. Chem. Soc.* **1969**, *91*, 3517.

[22] a) T. Kimoto, K. Tanaka, Y. Sakai, A. Ohno, K. Yoza, K. Kobayashi, *Org. Lett.* **2009**, *11*, 3658; b) R. Ozawa, K. Yoza, K. Kobayashi, *Chem. Lett.* **2011**, *40*, 941.

[23] Crystallographic data for **5**: $C_{90}H_{106}O_4Cl_6Si_4$, $M_r = 1576.81$, monoclinic, space group $P2_1/c$, $a = 12.285(2)$, $b = 13.464(3)$, $c = 26.580(5)$ Å, $\beta = 101.257(4)°$, $V = 4312.0(14)$ Å^3, $Z = 2$, $\rho_{\text{calcd}} = 1.214\ \text{g cm}^{-}{}_{3}$, $R = 0.0448$ ($I > 2.0\sigma(I)$), $R_w = 0.1418$ (all data), GOF = 1.024.[27]

[24] a) S. Mukhopadhyay, S. P. Jagtap, V. Coropceanu, J.-L. Brédas, D. M. Collard, *Angew. Chem.* **2012**, *124*, 11797; *Angew. Chem. Int. Ed.* **2012**, *51*, 11629; b) S. P. Jagtap, S. Mukhopadhyay, V. Coropceanu, G. L. Brizius, J.-L. Brédas, D. M. Collard, *J. Am. Chem. Soc.* **2012**, *134*, 7176.

[25] The calculations with wB97XD/6-31G(d) afforded overestimated energies of the HOMO–LUMO gap for all of the molecules herein.

[26] In contrast to **5**, the HOMO and LUMO of **1a** indicated no through-space overlap between two benzene moieties, suggesting the presence of through-space non-orbital interactions, such as columbic repulsion (Supporting Information, Figure S43).

[27] CCDC 922823 (**2a**), CCDC 922824 (**2b**), 922825 (**2c**), and 922826 (**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.