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Regio-defined syntheses of tetra-brominated dibenzo[*g*,*p*]chrysene scaffolds with high solubility

Yoshino Fujii, Tomoyuki Maruyama, Ryuhei Akasaka, Kazuki Sakao, Shugo Tokai, Yuta Taguchi, Yasuhiro Matsumoto, Shinsuke Kamiguchi, Naoki Yoshida, Tetsuo Iwasawa *

Department of Materials Chemistry, Ryukoku University, Seta, Otsu 520-2194, Japan

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ABSTRACT

Regio-defined syntheses of tetra-brominated dibenzo[*g*,*p*]chrysene (DBC) derivatives are described, with a description of different patterns of the four-bromine-positions. These derivatives were designed with two features: one is installation of butyl groups for being processable in solution-phase, and the other is attachment of bromine atoms for being variable. Thus, these brominated devices would enable us to achieve diversity-oriented preparation of solution-processable DBC derivatives.

Multiply functional dibenzo[*g*,*p*]chrysene (DBC, Fig. 1) rings are attractive, appealing, and inviting to chemists in organic materials science [1–3a,b], because they allow manipulation of the photophysical and electronic properties such as good hole mobilities [4a,b], high quantum yields, and long excited state lifetime [5]. Fine tunings in structure or composition of DBC derivatives can greatly alter their properties as electronic organic devices [6a,b]. Thus, expectation of appearance of DBC derivatives increases, and organic chemists are trying to develop synthetic platforms and methodologies for flexible installation of multi-functional groups into a DBC core [7]. Among such molecular platforms, a multi-brominated derivative can be one of the most valuable scaffolds, because the bromine atoms are readily changeable in a lithium–halogen exchange protocol and a transition metal-catalyzed cross-coupling strategy: indeed, Fan group excellently synthesized 3,6,11,14-tetrabromo-DBC as a molecular scaffold, but it was *practically insoluble* [8]. Even if the steric congestion lead by peripheral hydrogen atoms at 4, 5, 12, 13-positions makes the core twisted with somewhat of a solubility, the DBC sparingly dissolves in organic solvents. The low solubility prevents us to functionalize its four bromine sites freely and precisely, which precludes flexible, diverse, and adaptable preparation of DBC derivatives. This type of problem is often seen in other fused-PAHs (polycyclic aromatic hydrocarbons) [9a–e,10]. To overcome the intrinsic drawback, any solubilizing substructures have to be anchored on the multi-brominated DBC cores, and will likely allow the DBCs to be functionalized with high precision, and to be eventually utilized as real functional organic materials.

Herein we report regio-defined syntheses of multi-brominated DBCs **1**, **2**, **3, 4** and **5** those are solution-processable (Fig. 1). These compounds were designed with two features in our mind: First, the butyl groups would be included to provide high solubility in organic solvents for being processable in solution-phase. Second, the bromine substituents can be flexibly changeable tags in metal-mediated homogeneous transformations to achieve creating new derivatives. We anticipated that solution-processable DBCs with electron-donating groups undergo smooth bromination substitutions in regio-selective manners.

We started to synthesize **1**: to a suspension of 2,7,10,15-tetrabromo-DBC in THF at −78 °C was added *n*-BuLi, which was subjected to 1-bromobutane in high-yielding transformation into **6** of 83% (Scheme 1) [11]. To our surprise, **6** dissolved in hexane, toluene, ethyl acetate, and THF, or rather **6** was not solid but viscous (colorless) material at ambient temperature [12]. Upon addition of Br_2 into **6** in CH_2Cl_2, regio-selective tetra-bromination reaction occurred cleanly at optimized low temperature of −20 °C, and followed by recrystallization from toluene/EtOAc to give **1** in 75% yield as white solid substrates. The solubility of **1** is spectacularly improved; for example, 100 mg of **1** is soluble in 22 mL of toluene at ambient temperature [13] although 3,6,11,14-tetrabromo-DBC are practically insoluble in toluene [8].

* Corresponding author.
E-mail address: iwasawa@rins.ryukoku.ac.jp (T. Iwasawa).

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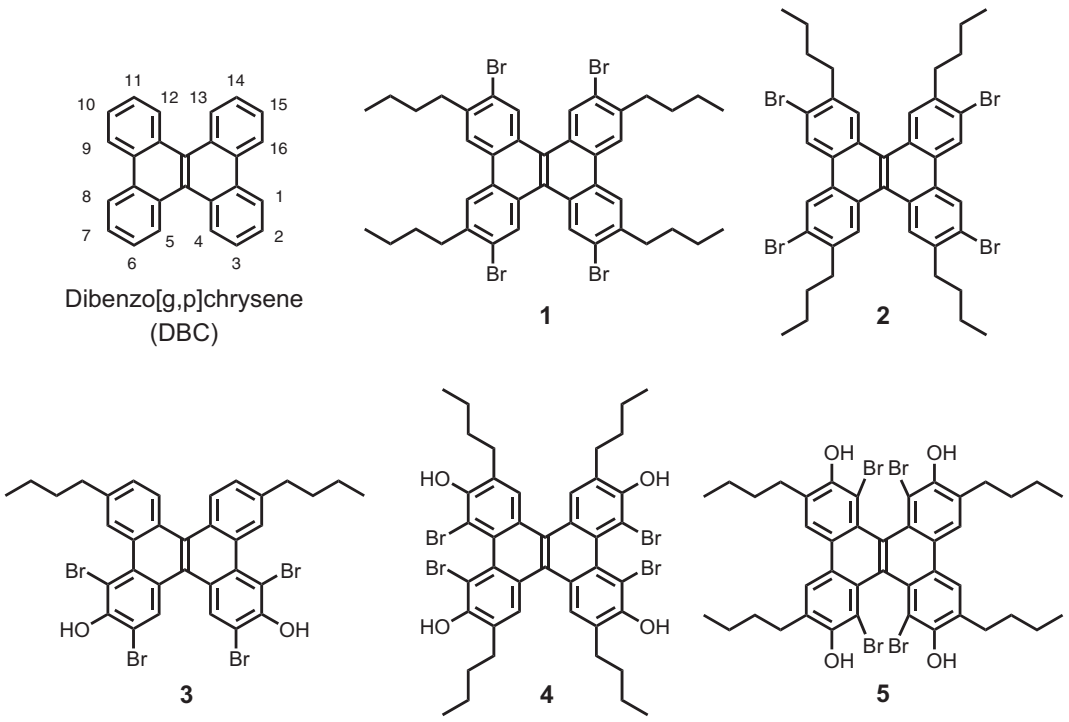
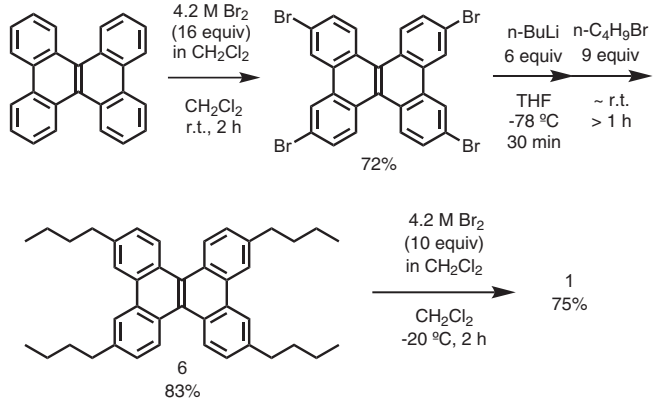
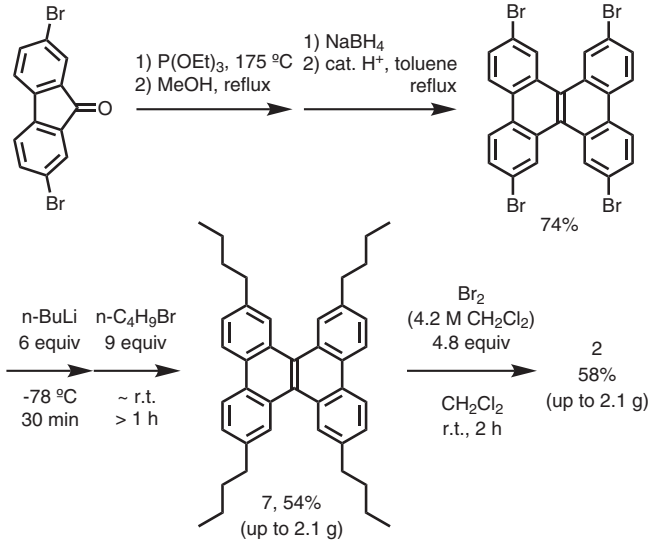


Fig. 1. Dibenzo[*g*,*p*]chrysene (DBC), and tetra-brominated DBC molecules **1**, **2**, **3**, **4**, and **5**.



Scheme 1. Synthesis of **1** *via* colorless viscous material **6**.

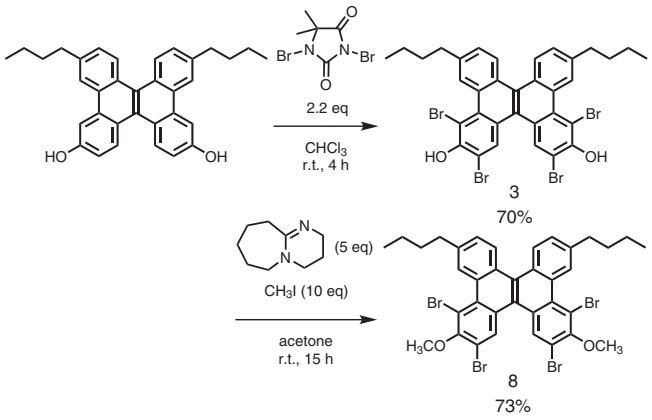


Scheme 2. Synthesis of **2** *via* **7**.

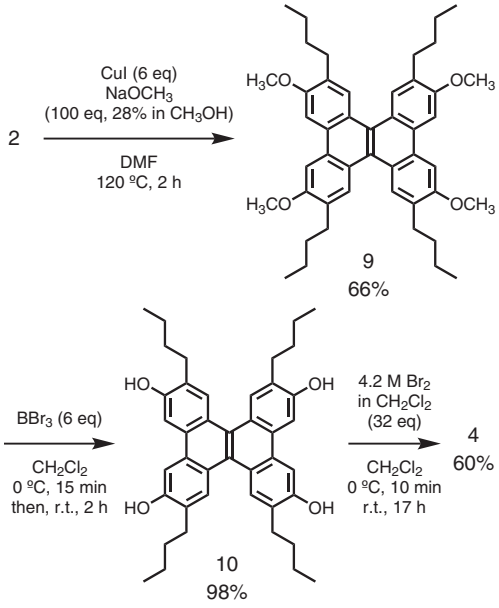
Next, we performed to synthesize **2**, which started from homo-dimerization of commercially available 2,7-dibromo-9-fluorenone (Scheme 2). We already reported this type of dimerization in previous paper that described synthesis of DBC *via* homo-dimerization of 9-fluorenone; here, the method was applicable to preparation of 3,6,11,14-tetrabromo-DBC [14]. Indeed, the tetra-bromide was practically insoluble as Fan stated [8], but, to our delight, it was amenable to the lithiation at −78 °C and the following alkylation to give well-soluble **7** in 54% yield as white solid materials [15], Regio-specific 4-fold bromination of **7** achieved definite transformation into **2** with 58%, and **2** gained much higher solubility in organic solvents as compared to 2,7,10,15-tetrabromo-DBC lacking four butyl groups [16], The solubility of **2** was improved; for example, 100 mg of **2** at ambient temperature was soluble in 0.4 mL of toluene, 4 mL of hexane, 1.3 mL of CH_2Cl_2, 0.3 mL of $CHCl_3$, and 0.3 mL of THF, although 2,7,10,15-tetrabromo-DBC are scarcely dissolved in these solvents.

Then, we turned our attention to the starting tetra-substituted DBC that has two hydroxyl groups at 2, 7-positions and two butyl moieties at 10, 15-positions (Scheme 3). This starting molecule was already synthesized in our previous report [17]. Preliminary research after several tests for regio-defined brominations of the starting diol reached use of 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) [18]: tetra-brominations at 1, 3, 6, 8-positions cleanly occurred to give **3** in 70% yield although the dihydroxy-**3** has proved to be weak against heat [19]. The molecular structure of **3** was crystallographically ascertained by preparing its dimethoxy derivative **8** (Figure 2), which clearly disclosed the arrangement of four bromines with the torsion angle of 44.59° [20]. The *ortho*-positions of phenolic hydroxy groups tethered DBC seemed to be reactive in regio-selective bromination reactions.

Do the sterically congested 1- and/or 4-positions of DBC core undertake direct multiple bromination reactions? For the



Scheme 3. Synthesis of tetra-bromide **3** and its derivative dimethoxy-**8**.



Scheme 4. Synthesis of **4** from **2** *via* **9** and **10**.

experimental bromination at 1-, 8-, 9-, and 16-positions of bay-area regions, we put **9** and **10** to use (Scheme 4): because we anticipated that electron-donating methoxy moieties and/or hydroxy groups intensively assist the direct bromination of their *ortho*-positions. **9** was readily prepared in 66% yield with up to 1.2 g through the copper-mediated cross-coupling between **2** and sodium methoxide, and the following demethylation of **9** smoothly gave **10** in 98% [21]. Upon addition of bromine to a solution of **9** in CH_2Cl_2, the reaction stopped within 1 h and resultant products formed complicated mixtures those gave multi-spots in TLC monitoring and messy ^{1}H NMR spectrum of its crude state. On the other hand, the reaction of the hydroxy-**10** with bromine in CH_2Cl_2 was slow but effective to converge in one spot on TLC plates: purification by silica-gel column chromatography yielded **4** in 60% as pure form. The molecular structure of **4** was successfully ensured by crystallographic analysis (Fig. 3), which disclosed that four bromine atoms undoubtedly reside in bay-area regions with the torsion angle of 55.89°. Actually, this large value of 55.89° was totally unexpected, because the value was much larger than the maximum value of 37.3° reported by pioneering Nakamura group.[7a] Indeed, judging from the illustrations of part (c) and (d) in Fig. 3 [22], the pi-conjugated **4** obviously and actively bent due to the bay-area environments congested with two sets of two bromines. These congested environments are also indicated by IR spectroscopic analysis. IR measurement of **4** displayed one very sharp peak of OH groups at 3470 cm^{-1}, which would mean OH groups don't make definite aggregation with other molecules owing to the sterically crowded parts.

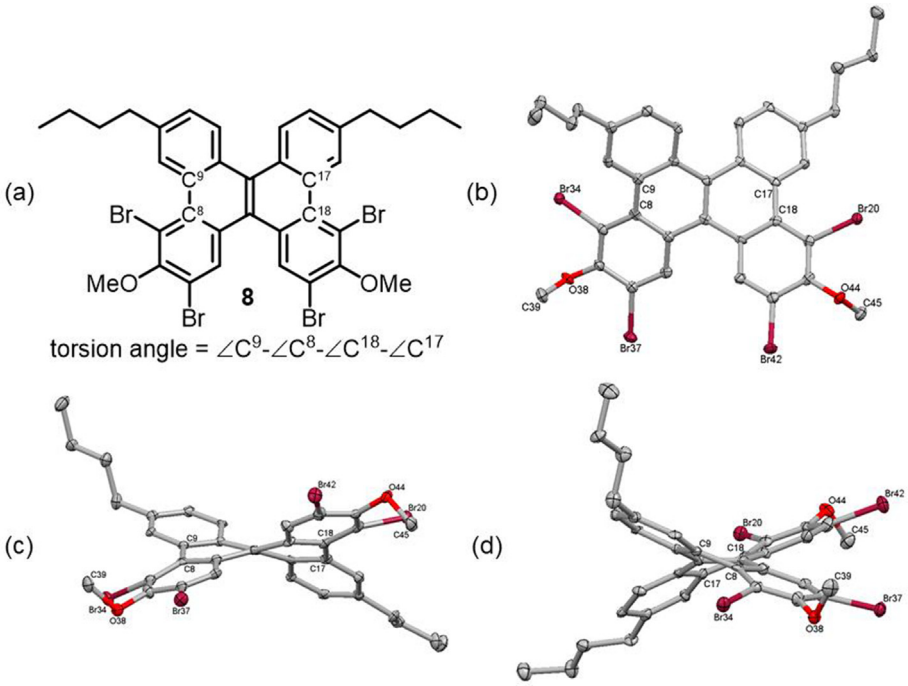


Fig. 2. Molecular structures with ORTEP drawing of **8** with thermal ellipsoids at the 50% probability level; (a) torsion angles determined by the four carbon atoms of C^8, C^9, C^{17} and C^{18}; (b) top view; (c) side view from a fjord region with a description of the torsion angle 44.59°; (d) side view from a bay-area region. The hydrogen atoms are omitted for clarity.

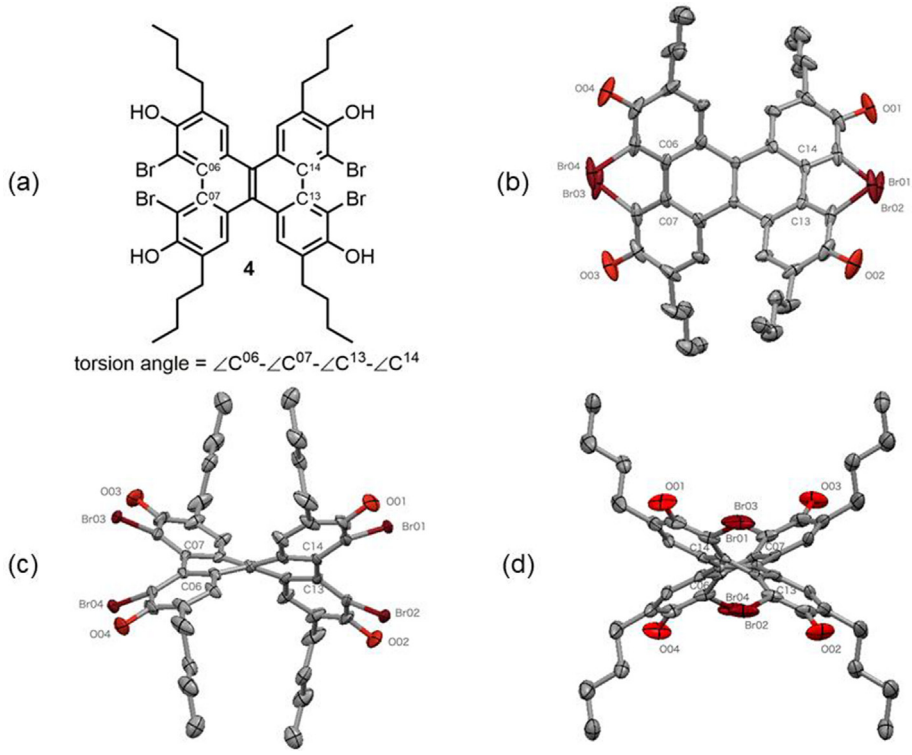
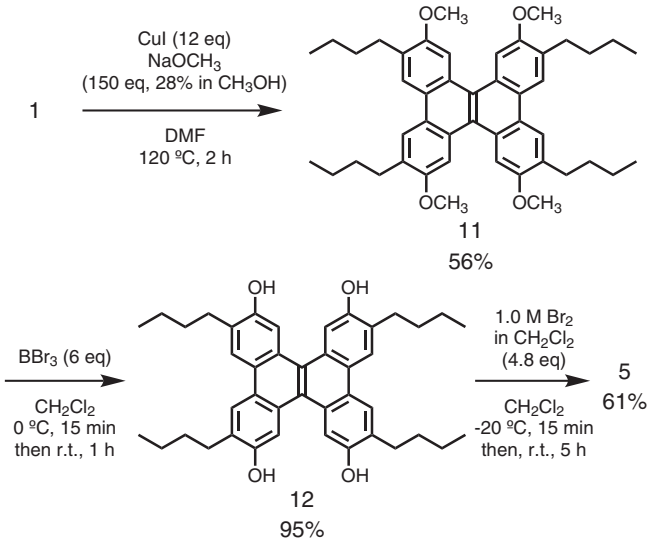


Fig. 3. Molecular structures with ORTEP drawing of **4** with thermal ellipsoids at the 50% probability level; (a) torsion angles determined by the four carbon atoms of C^{06}, C^{07}, C^{13}, and C^{14}; (b) top view; (c) side view from a fjord region with a description of the torsion angle 55.89°; (d) side view from a bay-area region. The hydrogen atoms are omitted for clarity.

Next, we attempted a synthetically demanding tetra-bromination at fjord region 4-, 5-, 12-, and 13-positions of **11** and **12** (Scheme 5) [23]. Upon addition of bromine to a solution of the methoxy-**11** in CH_2Cl_2, the reaction was sluggish and the ^1H NMR spectrum of its crude state was in such a mess that we didn't understand what kinds of bromide molecules were formed. In contrast, to our delight, the hydroxy-**12** undertook the smooth and clean brominations: the addition of Br_2 at low −20 °C found complete consumption of the starting **12** and definite production of **5** in 61% yield. The molecular structure of **5** was determined by crystallographic analysis (Fig. 4) [24], which disclosed that four bromine atoms were surely bonded to the fjord regions. The torsion angle in **5** was 53.97° that is comparable to the 55.89° in **4**: thus, two bromines at the fjord region as well as bay-area region force the DBC to be distorted in around 55°.



Scheme 5. Synthesis of **5** from **1** *via* **11** and **12**.

Encouraged by these results, we expected that different and unique patterned-bromination of the DBC core would be possible: we intensively tried to make tetra-bromination of DBC **13** and/or its corresponding octol (Scheme 6), and wondered which positions the brominations occur in. The octa-methoxy **13** was prepared in one step through the copper-mediated etherification of the tetra-bromine precursor [25]. Actually, we demonstrated demethylation of **13** with aid of BBr_3 and successfully prepared the corresponding octol that has low solubility in organic solvents. While the octol in bromination reactions didn't give any products specifically, the octa-methoxy **13** materialized definite production. Indeed, the bromination using Br_2 was slow, but the TLC analysis displayed complete consumption of the starting **13** and one certain spot along with a tedious stretched mark of messy mixtures of side-products. The unambiguous spot was isolated in 28% yield: its ^1H NMR spectrum showed two singlet peaks at 8.95 and 7.36 ppm those correspond to aromatic protons, and four singlet peaks at 4.15, 3.98, 3.94, and 3.93 ppm those correspond to four different types of OCH_3 moieties. Its ^{13}C NMR spectrum also exhibited four peaks of methoxy groups at 61.1, 61.0, 56.7, and 56.4 ppm and thirteen peaks of aromatic carbons. These results present five possible isomeric products of 1,5,9,13- (**14**), and 1,5,12,16-, and 1,4,13,16-, and 1,8,12,13-, and 1,4,9,12-tetrabrominated DBCs: Among these isomers, 1,5,9,13-DBC, namely **14**, would be rationally inferred because the only 1,5,9,13-positined one satisfies the most uncrowded and the most symmetrical quadrant [26]. The bromination pattern in **14** uniquely differs from compounds **1**–**5**.

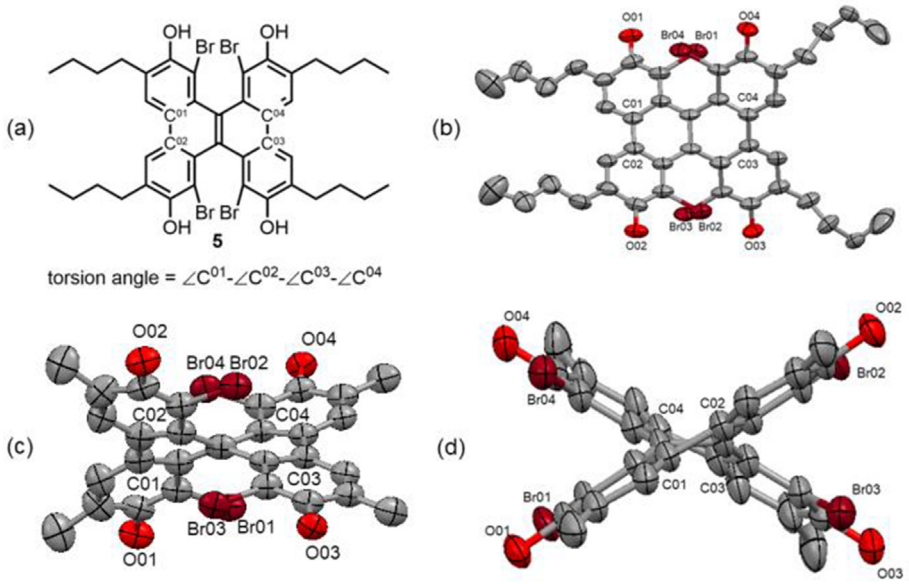
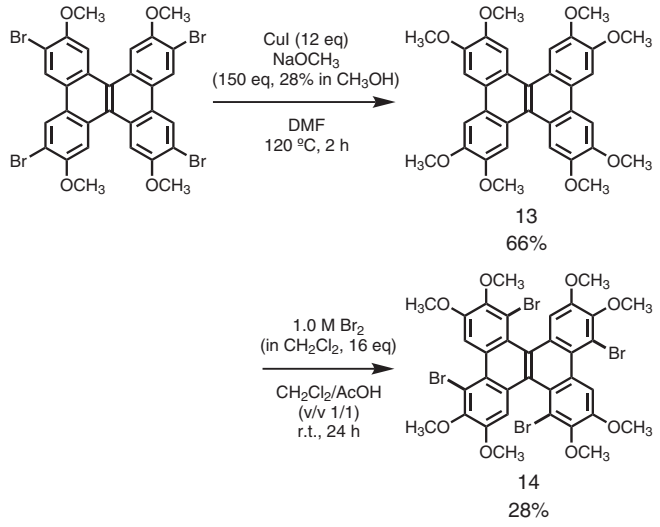


Fig. 4. Molecular structures with ORTEP drawing of **5** with thermal ellipsoids at the 50% probability level; (a) torsion angles determined by the four carbon atoms of C^{01}, C^{02}, C^{03}, and C^{04}; (b) top view; (c) side view from a fjord region with a description of the torsion angle 53.97°; four butyl groups are removed for ease of viewing. (d) side view from a bay-area region; four butyl groups are removed for ease of viewing. The hydrogen atoms are omitted for clarity.



Scheme 6. Bromination of **13** to synthesize **14** that is structurally inferred among five possible isomers.

In summary, highly soluble tetra-brominated DBC scaffolds were successfully synthesized through simple and straightforward protocols. This research outcome suggests providing the following three salient features: One, DBC cores tend to readily undertake regio-specific tetra-bromination reactions: six patterns of regio-defined 4-fold bromination of DBC cores were achieved (**1**–**5** and **13**). Those aryl molecules **1**–**5** potentially play important roles as scaffolds to produce diverse DBC derivatives because the platforms are relevant to the "programmed synthesis for PAHs" suggested by Itami and Yamaguchi [27]. Noteworthy is that sterically demanding bromination at fjord and bay-area regions proceeded to successfully form **4** and **5** with the aid of *ortho*-hydroxyl groups. Two, the resultant DBCs of **1**–**5** have *n*-butyl groups those work as good solubilizing agents, which enables us to handle them advantageously in homogeneous conditions. Three, the crystallographic analyses reveal that the sterically demanding bromine atoms at fjord and bay-area regions strongly bend the pi-conjugation with large torsion angles: tetra-brominated **4** and **5** distorted with around 55°. These features will constitute a diversity-oriented approach for a variety of DBC derivatives those have outstanding properties in materials chemistry. In fact, we don't yet find the effective conditions for smooth substitution reactions in four bromines in **4** and **5** presumably due to the formidable crowded areas. Further synthetic endeavor for clean chemical transformation of those bromine atoms from the viewpoint of creation of highly-distorted non-planar pi-conjugation is ongoing and will be reported in due course.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data (The ^{1}H and ^{13}C NMR spectra of all new compounds) to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.152758.

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[12] The picture of **6** is printed in Supporting Information.
[13] 100 mg of **1** was dissolved in 35 mL of CH_2Cl_2, 9 mL of $CHCl_3$, and 9 mL of THF.
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[18] Br_2 didn't work: Complicated mixtures including unreacted starting diols were produced.
[19] When the crystals 3 in pure form was dried up at 100 °C for 30 min, 3 decomposed with multi-spots in TLC analysis. The compound 8 had good resistance to heat.
[20] The single crystal of **8** was prepared by slow evaporation of CH2Cl2/MeCN (2.5 mL/2.5 mL) solution of the sample (5 mg); CCDC-2031652 (for **8**) contains 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. Monoclinic, space group p 1 21/c 1, colorless, a = 20.7708(3) Å, b = 18.9068(3) Å, c = 8.0337(1) Å, α = 90°, β = 96.963°, γ = 90°, V = 3131.64(8) Å^3, Z = 4, T = 93 K, $d_{calcd.}$ = 1.731 g cm^{-3}, μ(Mo-$K\alpha$) = 6.523 mm^{-1}, R_1 = 0.0798, wR_2 = 0.2127, GOF = 1.127.
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[22] The single crystal of **4** was prepared by slow evaporation of Hexane (4 mL) solution of the sample (4 mg); CCDC-2031645 (for **4**) contains 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. Tetragonal, space group P -4 b 2, colorless, a = 12.0219(1) Å, b = 12.0219(1) Å, c = 13.7594(2) Å, α = 90°, β = 90°, γ = 90°, V = 1988.59(4) Å^3, Z = 2, T = 93 K, $d_{calcd.}$ = 1.557 g cm^{-3}, μ(Mo-$K\alpha$) = 5.252 mm^{-1}, R_1 = 0.0332, wR_2 = 0.0781, GOF = 1.070.
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[24] The single crystal of **5** was prepared by slow evaporation of CH_3CN (7 mL) solution of the sample (5 mg); CCDC-2032239 (for **5**) contains 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. Monoclinic, space group c 1 2/c 1, colorless, a = 15.2175(8) Å, b = 11.9914(6) Å, c = 21.0696(10) Å, α = 90°, β = 105.619°, γ = 90°, V = 3702.8(3) Å^3, Z = 4, T = 293 K, $d_{calcd.}$ = 1.673 g cm^{-3}, μ(Mo-$K\alpha$) = 5.641 mm^{-1}, R_1= 0.0863, wR_2= 0.2633, GOF = 1.091.
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[26] **13** is sparingly dissolved in CH_2Cl_2 and $CHCl_3$. Actually, the reactions in Scheme 6 were demonstrated in suspension state. On the other hand, **14** dissolved in CH_2Cl_2 and $CHCl_3$ without any problem.
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