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Synthesis of Naphthaleman Family Utilizing Regiocontrolled Benzannulation: Unique Molecules Composed of Multisubstituted Naphthalenes

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Cite This: *ACS Omega* 2021, 6, 32682−32694

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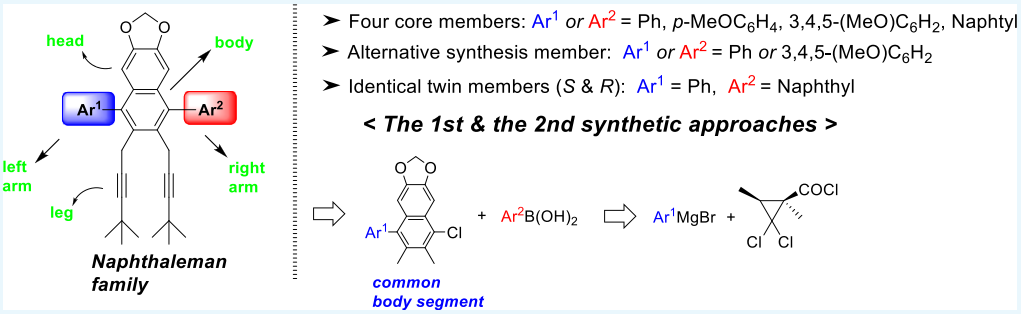

ABSTRACT: The naphthaleman family, a set of uniquely designed visual molecular structures comprising multisubstituted naphthalenes, was synthesized utilizing regiocontrolled benzannulation as a key step. The naphthaleman family possesses a common naphthalene body with a head comprising the 3,4-methylenedioxy group, symmetrical or unsymmetrical right and left arms, and two alkynyl legs. The synthesis involves six C−C bond-forming reaction sequences. (i) *syn*-Stereoselective *gem*-dichlorocyclopropanation of methyl angelate (86%). (ii) Acylation with ArMgBr (three examples, 60−91% yield). (iii) Stereocontrolled introduction of the 3,4-methylenedioxyphenyl group (three examples, 67−92% yield). (iv) Crucial regiocontrolled benzannulation to construct a common body segment (71−73% yield). (v) Two Suzuki−Miyaura cross-couplings to install the right or left arms (first-stage route: four examples, 77−93% and second-stage route: four examples, 42−90% yield). (vi) Double alkynylation to insert two legs (first-stage route: four examples, 61−77% yield and second-stage route: sole example, 83% yield). The four core members were produced through both first-stage and second-stage routes, with the second-stage approach demonstrating superiority over the first-stage approach. One of the members was alternatively synthesized by switching the installation order of the right and left arms, and identical twin members were produced by high-performance liquid chromatography chiral separation. The most stable conformations of two naphthaleman family members were calculated by Spartan software.

INTRODUCTION

Aromatic compounds containing unique visual molecular structures have attracted the attention of many chemists over the past few decades, from not only a scientific but also an educational standpoint. The pioneering synthesis of "nanokid" and his family, introduced by Chanteau and Tour,[1] caused quite sensation for both chemists and students due to their fascinating structures (Figure 1). The subsequent syntheses of nanocar,[2] molecular motor,[3] and penguinone[4] as representative bewitched molecules with distinct aromatic structures have also attracted considerable attention.

Inspired by these unique molecular structures and in close connection with our longstanding studies of the transformation of *gem*-dihalocyclopropanes,[5] we present here the synthesis of a uniquely designed "naphthaleman family" with several charming members that are composed of fully substituted naphthalene structures (Figure 2). They resemble human forms and familiar objects and may evoke images of "a side-throwing pitcher", "a football keeper", "a tennis player", "a flying bird", or "a swimming frog". The family comprises four naphthaleman core members **1a**−**1d**, a clone of **1c** by an alternative synthesis, and identical twins *S*-**1d** and *R*-**1d** by optical resolution.

RESULTS AND DISCUSSION

Retrosyntheses. Regiocontrolled benzannulation strategies provide distinctive constructions for highly substituted and

Received: August 16, 2021
Accepted: November 8, 2021
Published: November 24, 2021

https://doi.org/10.1021/acsomega.1c04413
ACS Omega 2021, 6, 32682−32694

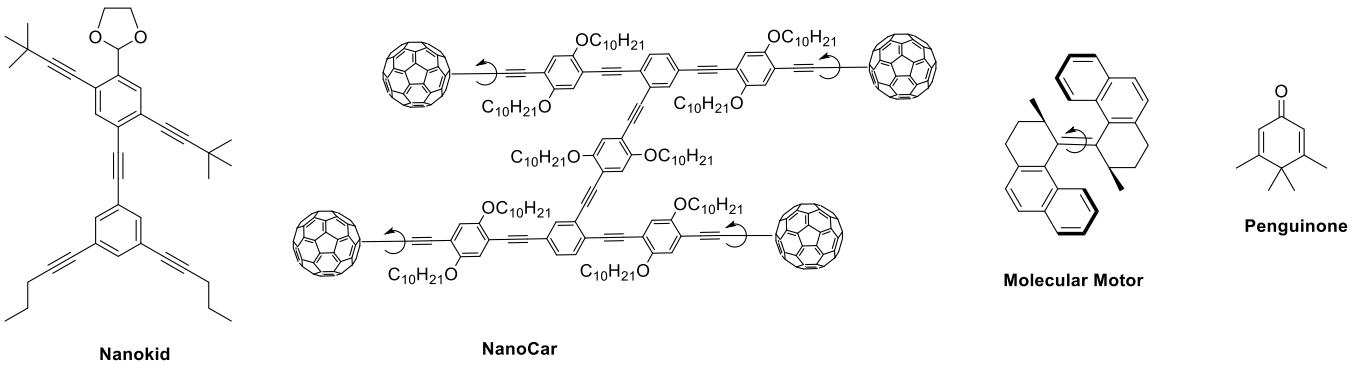

Figure 1. Representative visual compounds: nanokid, nanocar, molecular motor, and penguinone.

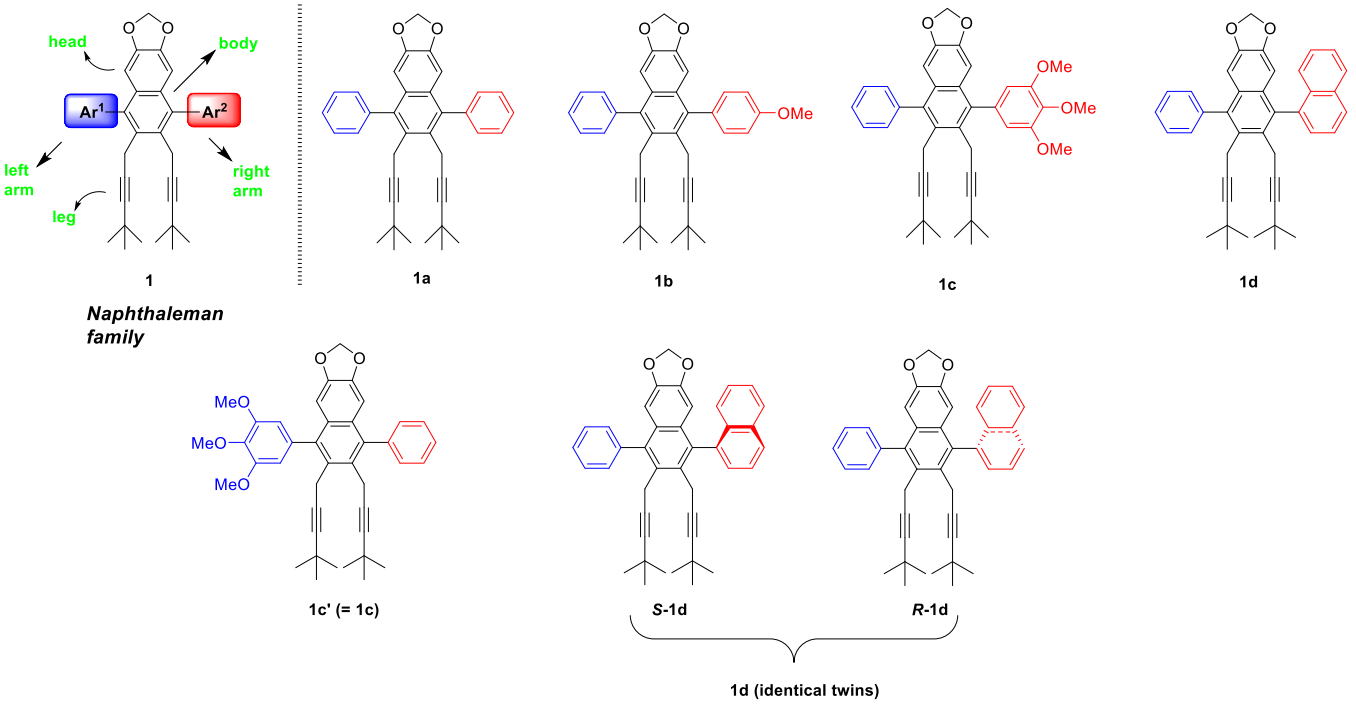

Figure 2. Naphthaleman family members.

elaborated α-arylnaphthalenes, which have useful applications as reagents, catalysts, biologically active natural products, pharmaceuticals, and functionalized materials due to their core structural scaffolds.[6] Our continuing investigations on nonregioselective,[5a,b] regiocontrolled,[5c] chirality exchange,[5d] and large-scale[5e] benzannulations, and the relevant cyclopropane transformations[6] or derivatizations,[7] led us to envision the synthesis of a "naphthaleman family" **1** possessing a common naphthalene body with a head comprising the 3,4-methylenedioxy group, symmetrical or unsymmetrical right and left arms, and two alkynyl legs. Retrosynthetic pathways for the synthesis of **1** are classified as either the first-stage approach or the second-stage approach (Scheme 1).

Common body segment **6** was conveniently prepared following the reported practical procedures.[5e] Three contiguous functional groups in **6** were effectively utilized for the construction of **1**. Two contiguous benzylic positions were transformed to two legs by dibromination and successive ethynylation. On the other hand, the pendant 1-chloro group was coupled with four arms by Suzuki−Miyaura cross-couplings to produce naphthaleman family **1** with uniquely substituted head, hands, and legs.

The first stage approach consists of six C−C bond-forming reactions to construct the naphthaleman family **1**. (i) *Syn*-stereoselective *gem*-dichlorocyclopropanation of methyl angelate leading to the formation of acid chloride **3**. (ii) Acylation of **3** with PhMgBr leading to the formation of phenyl ketone **4**. (iii) Stereocontrolled introduction of 3,4-methylenedioxyphenyl groups to **4** leading to the formation of [*S**-(1*S**,3*S**)]-phenyl(3,4-methylenedioxypheny)-2,2-dichlorocyclopropylmethanol **5**. (iv) Crucial regiocontrolled benzannulation of **5** affording 1-phenyl-4-chloronaphthelene **6** as a common body segment. (v) Suzuki−Miyaura cross-couplings using acceptor **6** leading to the formation of 1-aryl-4-phenyl-2,3-dimethylnaphthalenes **7a−7d**. (vi) Double alkynylation of dibromide **8a−8d** derived from **7a−7d** producing the target naphthaleman family **1a−1d**.

In contrast, the second-stage approach involves another sequence of six C−C bond-forming reactions. The first four steps (i)−(iv) are the same as those for the linear approach. The double alkynylation step of **6** precedes Suzuki−Miyaura cross-

https://doi.org/10.1021/acsomega.1c04413
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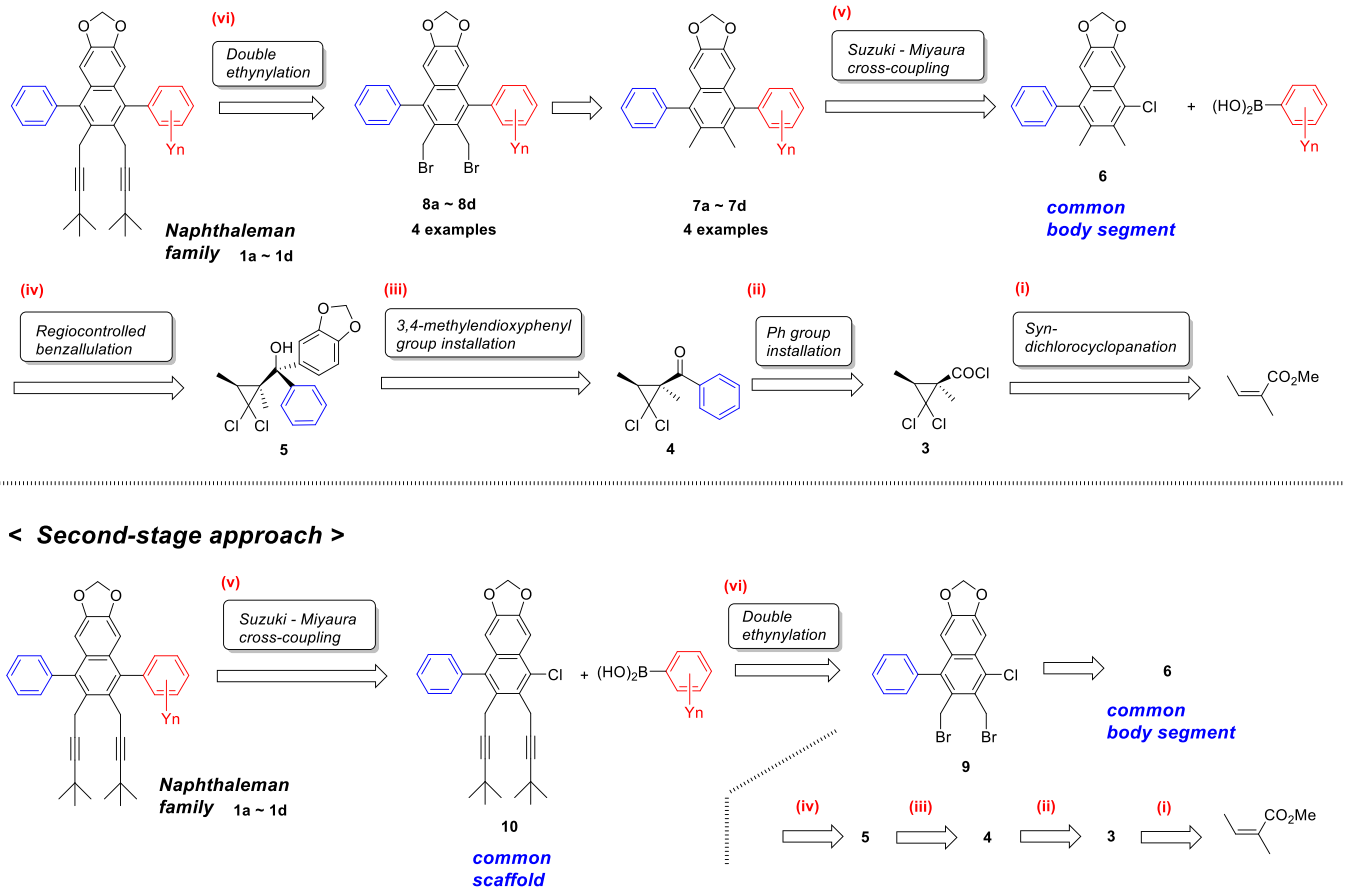
Scheme 1. Two Retrosynthetic Approaches for Naphthaleman Family 1



couplings using common scaffold **10**. The convergent approach is apparently superior to the linear approach from the standpoint of total efficiency to produce family members **1a**−**1d**.

Construction of the Common Body Segment. Scheme 2 shows the construction of the common "body" segment **6** for not only the linear approach but also the convergent approach. Methyl angelate was converted to acid chloride **3** by *syn*-stereoselective *gem*-dichlorocyclopropanation and two conventional transformations (hydrolysis and acid chloride formation) according to the reported method.[5c] Phenylation of **3** with PhMgBr at 0−5 °C afforded 2,2-dichlorocyclopropyl phenyl ketone **4** in 81% yield. Subsequent Cram rule-stereocontrolled 3,4-methylendioxyphenyl group addition to the predominant *s-trans* conformer of **4** proceeded smoothly to afford [*S**-(1*S**,3*S**)]-stereodefined (3,4-methylendioxy)(phenyl)(2,2-dichlorocyclopropyl)methanol **5** in 92% yield.[5b] The key regiocontrolled benzannulation using **5** successfully produced the common body segment **6** in 72% yield with excellent regioselectivity.[5c] The regiocontrolled pathway can be rationalized by the reported chelation mechanism fixing the conformation during the cyclopropane cleavage.

First-Stage Approach for the Synthesis of the Naphthaleman Family. With the body segment **6** in hand, we next examined Suzuki−Miyaura cross-couplings of α-chloronaphthalenes **6** to install four "right arm" parts (Scheme 3). Despite the sterically congested and less reactive α-chloro position in **6**, coupling with $ArB(OH)_2$ (5.0 equiv) proceeded well to afford the desired full-body precursors **7a**−**7d** in 77−93% yield using (1,3-diisopropylimidazol-2-ylidene)(3-chloropyridyl)palladium(II)dichloride (PEPPSI-IPr)[8] (0.20 equiv)-K_2CO_3 (5.0 equiv) catalysis under somewhat harsh conditions (i.e., molar ratio, temperature, and time; optimization of PEPPSI-IPr-K_2CO_3 catalysis using **6**: see the Supporting Information). The two leg parts were introduced by the following sequences: **7a**−**7d** were dibrominated using NBS/cat, AIBN to afford **8a**−**8d** in 75−90% yield, and subsequent double alkynylation with the lithium salt of 3,3-dimethylbut-1-yn provided the four members of the naphthaleman family **1a**−**1d** in 75−86% yield.

Second-Stage Approach for the Synthesis of the Naphthaleman Family. After developing the first-stage approach, we turned our attention to a more straightforward approach. Treatment of body segment **6** with NBS/cat. AIBN under identical conditions afforded dibrominated product **9** in 93% yield (Scheme 4). A similar double ethynylation by the lithium salt of 3,3-dimethylbut-1-yn provided the common α-chloronaphthalene scaffold **10** in 89% yield. Suzuki−Miyaura cross-coupling of **10** with $ArB(OH)_2$ using a similar PEPPSI-IPr catalysis, however, led to the formation of complex mixtures under the conditions described in Scheme 3 because the two alkynyl groups in the legs did not tolerate the identical conditions to give complex mixtures.

Fortuitously, the use of $ArB(OH)_2$ (1.5 equiv) using a more reactive $Pd(OAc)_2$ (0.04 equiv)−SPhos (0.06 equiv)−K_3PO_4 (2.0 equiv) catalysis[9] instead of PEPPSI-IPr catalysis solved the problem with the toleration of the alkynyl moiety to produce the

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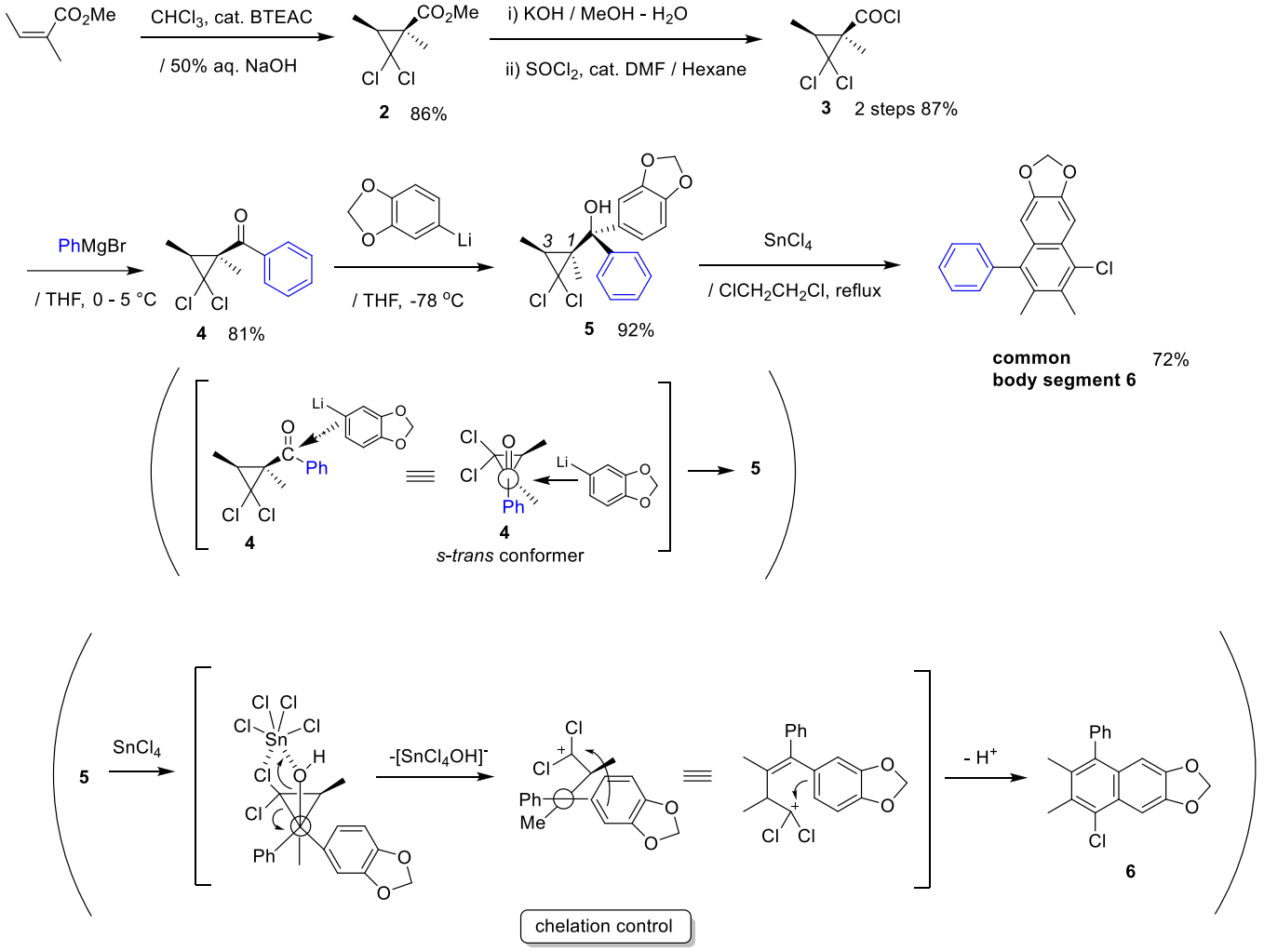
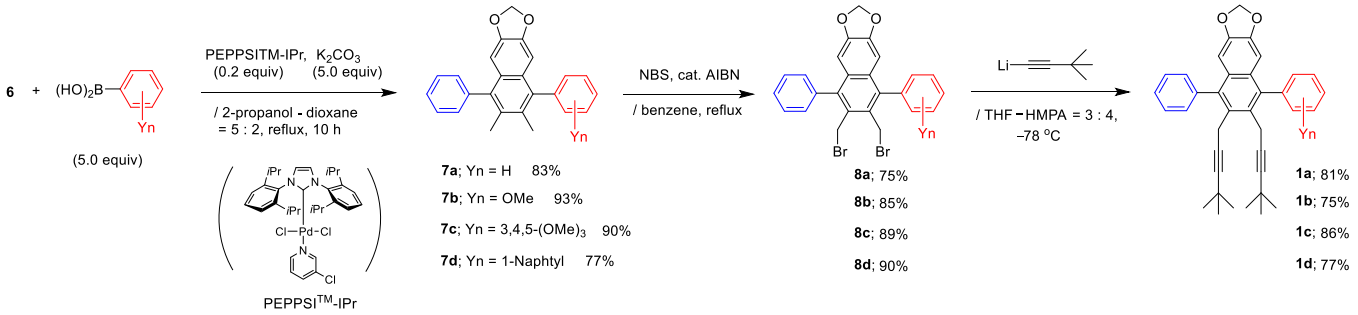
Scheme 2. Construction of Common Body Segment 6



Scheme 3. Syntheses of Naphthaleman Family 1 by the First-Stage Approach



four family members of **1a**−**1d** in 42−90%. Notably, these cross-couplings were implemented under more mild conditions (i.e., better molar ratio, lower catalyst loading, lower temperature, and shorter time).

Alternative Synthesis of Naphthaleman Family 1c by the Switching Route. To expand the scope of this project, we envisaged an alternative synthetic route for synthesizing the naphthaleman family **1c′** (= **1c**) (Scheme 5). The 3,4,5-trimethoxyphenyl "left arm" group was initially installed by acylation with acid chloride **3** to afford ketone **11** in 60% yield. Next, the 3,4-methylenedioxyphenyl "right arm" group was added to **11** to afford alcohol **12** in 86% yield with high stereoselectivity. Alcohol **12** smoothly underwent regiocontrolled benzannulation to produce alternative body segment **13** in 73% yield. Notably, the reaction sequences follow the reported total synthesis of dehydrodesoxypodophyllotoxin, an unsymmetrically substituted lignan lactone.[5c]

Sha's group pointed out that the inherent reactivity order during the Friedel−Crafts-type reaction was 3,4,5-trimethoxyphenyl group >3,4-methylenedioxyphenyl group due to the favorable planar π-electron overlap of the 3,4-dimethoxy group.[8] Nonetheless, the present regiocontrolled benzannulation proceeded smoothly toward the less-reactive 3,4-methylenedioxyphenyl group, probably because the chelation-controlled

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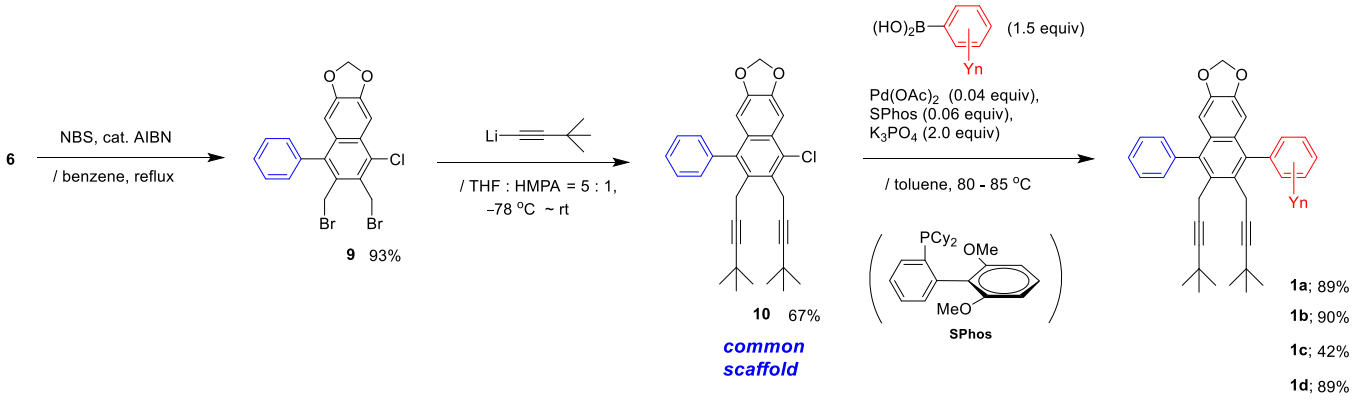
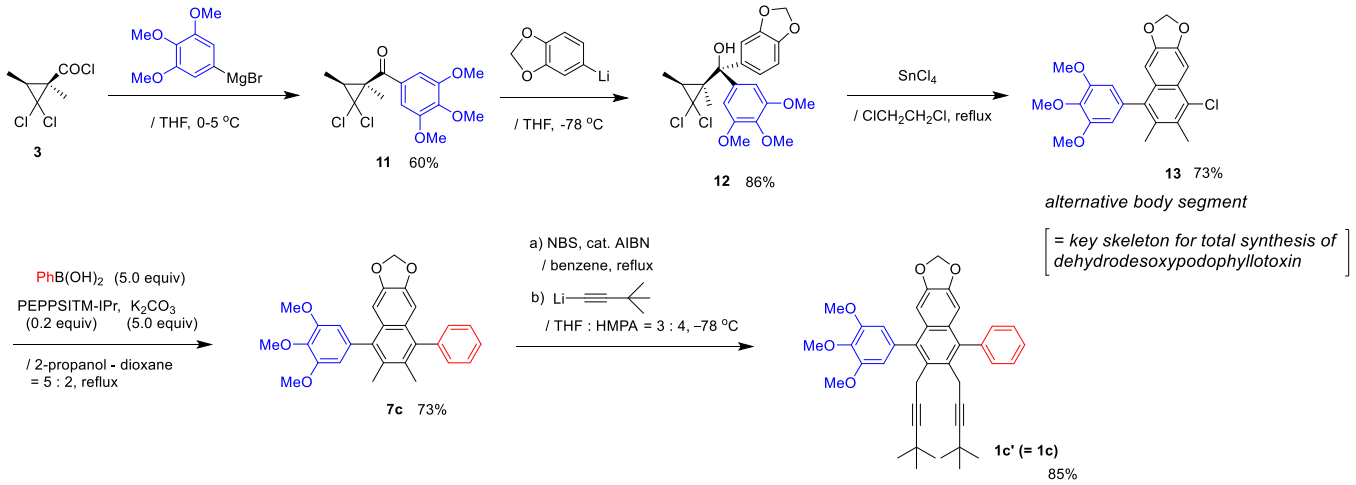
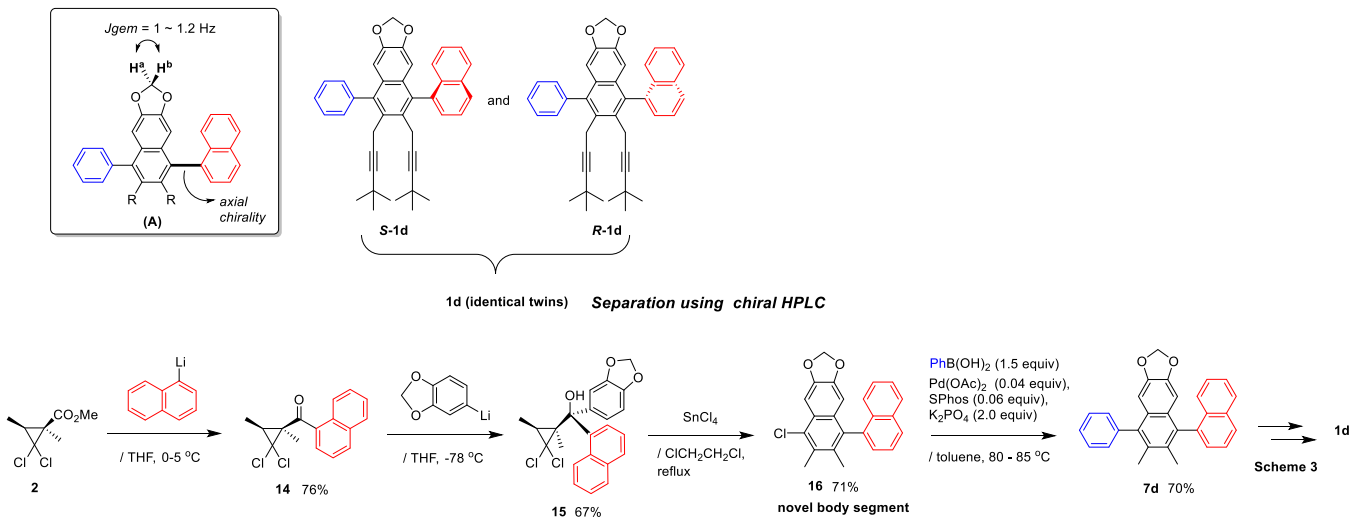
Scheme 4. Syntheses of Naphthaleman Family 1 by the Second-Stage Approach



Scheme 5. Synthesis of the Naphthaleman Family 1c′ (= 1c)



Scheme 6. Synthesis of "Identical Twins" of Naphthaleman 1d via an Alternative Route



mechanism functioned effectively (see Scheme 2). Suzuki–Miyaura cross-coupling of **13** using PEPPSI-IPr-K_2CO_3 catalysis afforded clone precursor **7c** (see Scheme 3). Subsequent dibromination and dialkynylation sequences using **7c** successfully produced the target naphthaleman family **1c′** (= **1c**). Eventually, the introduction order of the right and left arms was switched conversely.

Synthesis of "Identical Twins" by Optical Resolution. Family member **1d** is composed of the body naphthalene connected with the right arm or left arm between the α- and α'-positions, in which axial chirality should emerge (Scheme 6). Actually, chiral high-performance liquid chromatography (HPLC) analysis revealed that **1d** was formed as a racemate (two enantiomeric mixtures) (vide infra).

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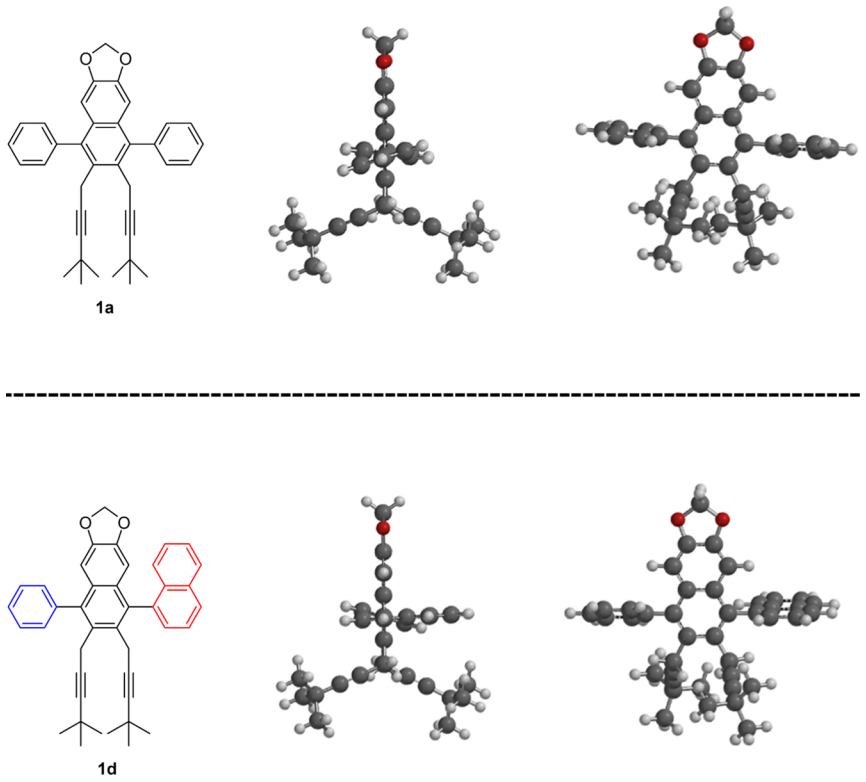

Figure 3. Spartan calculation drawing of naphthaleman **1a** and "identical twin" of naphthaleman **1d**.

With this result in hand, we implemented an alternative shorter synthesis of **1d** than the conventional route, as shown in Scheme 2; parent ester **2** was employed instead of acid chloride **3** for the acylation step (Scheme 6). Ketone **14** was obtained in good yield (67%) by the acylation of **2** with (1-naphthyl)MgBr, in which the use of a stereocongested (1-naphthyl)MgBr nucleophile completely prevented further undesirable addition. The addition of 3,4-methylenedioxyphenyl lithium to **14** also afforded alcohol **15** in better 76% yield, which was subjected to regiocontrolled benzannulation to produce novel body segment **16** in 71% yield. Suzuki−Miyaura cross-coupling of **16** with $PhB(OH)_2$, catalyzed by $Pd(OAc)_2$−SPhos−K_2PO_4, successfully furnished **7d** in 70% yield. As described in the linear approach procedure of the First-Stage Approach for the Synthesis of the Naphthaleman Family, a formal synthesis of the desired family member **1d** was completed. In a series of *α*-naphthyl(naphthalene) compounds (**A**), axial chirality induced *geminal* couplings of ^{1}H NMR between H^a and H^b due to the inequivalency. Chiral HPLC analysis of **1d** resulted in the separation of the identical twins (a couple of enantiomers) ***S*-1d** and ***R*-1d** with high resolution (a chart of the clear separation is addressed in the Supporting Information).

The most stable conformations of naphthaleman family members **1a** and **1d** were calculated by Spartan software (Wavefunction, Inc. ver. '18 1.1.0) (Figure 3). In both compounds, the two legs were located not in parallel but rather spreading at ca. 130° due to the steric repulsion: not standup style but running style. In contrast, the two arms were located perpendicular and parallel to the naphthalene body, the result of which is in good accordance with the reported X-ray structure of the relevant and fundamental 4-chloro-2-methyl-1-phenylnaphthalene.[5b]

CONCLUSIONS

We developed the synthesis of the naphthaleman family, a set of uniquely designed visual molecular structures comprising multisubstituted naphthalenes, utilizing regiocontrolled benzannulation as the key step. The naphthaleman family possesses a common naphthalene body having a head comprising a 3,4-methylenedioxy group, symmetrical or unsymmetrical right and left arms, and two alkynyl legs. The synthetic approaches are classified as either a first-stage approach, catalyzed by PEPPSI-IPr−K_2CO_3 or a superior second-stage approach, catalyzed by $Pd(OAc)_2$−SPhos−K_2PO_4. The four core members were produced through both routes, with the convergent approach demonstrating superiority over the linear approach (i.e., milder conditions, better molar ratio, and lower catalyst loading). One of the members was alternatively synthesized by switching the installation order of the right and left arms, and identical twin members were produced by chiral HPLC separation. The most stable conformations of two naphthaleman family members were calculated by Spartan software; the two legs were spreading and the two arms were located perpendicular and parallel to the naphthalene body.

We are now planning an asymmetric synthesis of twin members by utilizing chirality-transfer benzannulation (a distinctive chiral version) to provide the audience, particularly students, interested in this organic chemistry. The result will be presented in the future.

EXPERIMENTAL SECTION

[(1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl]-phenylmethanone (4).**[5c] Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.40 (d, J = 6.5 Hz, 3H), 1.64 (s, 3H), 1.68 (q, J = 6.5 Hz, 1H), 7.51−7.62 (m, 3H), and 7.98−8.00 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 23.2, 35.3, 39.6,

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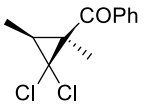
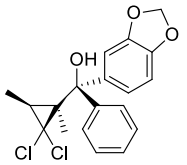
68.1, 128.7, 130.0, 133.5, 134.4, and 194.9; IR (neat) ν_{max}: 2932, 1681, 1597, 1449, 1233, 1318, 1301, 1233, 1175, 984, 836, 792, and 710 cm^{-1}.

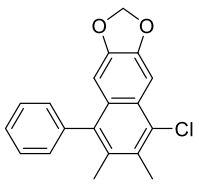


(*S)-[(1*S**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](3,4-methylenedioxyphenyl)-(phenyl)methanol (5).** ^{n}BuLi (1.58 M in hexane, 2.24 mL, 3.53 mmol) was added to a stirred solution of 3,4-methylenedioxy-1-bromobenzene (712 mg, 2.36 mmol) in tetrahydrofuran (THF) (8 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Ketone **4** (574 mg, 2.36 mmol) in THF (5 mL) was added to the mixture at the same temperature, and the mixture was stirred for 2 h. The mixture was poured into ice and maintained. NH_4Cl aqueous solution was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/AcOEt = 100:1 to 50:1) to give the desired product **5** (788 mg, 91%, small amounts of inseparable impurities were contained).



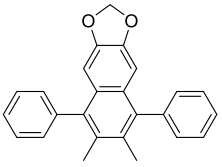
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.19 (s, 3H), 1.53 (q, J = 6.9 Hz, 1H), 1.76 (d, J = 6.9 Hz, 3H), 2.78 (brs, 1H, −OH), 5.96 (s, 2H), 6.57 (dd, J = 1.8 Hz, 8.2 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 6.79 (d, J = 1.8 Hz, 1H), and 7.34−7.52 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.1, 27.2, 36.3, 38.3, 73.8, 83.8, 101.0, 107.0, 108.9, 122.0, 127.9, 128.2, 128.8, 140.8, 144.6, 146.5, and 147.1; IR (neat) ν_{max}: 3570, 2928, 1489, 1444, 1321, 1271, 1240, 1198, 1036, and 934 cm^{-1}.

1-Chloro-2,3-dimethyl-6,7-methylendioxy-4-phenylnaphthalene (6). $SnCl_4$ (261 mg, 1.0 mmol) was added to a stirred solution of alcohol **5** (365 mg, 1.0 mmol) in 1,2-dichloroethane (20 mL, ca. 0.05 M) at 80 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. The mixture was filtered through the Celite with a glass filter, and the filtrate was concentrated under reduced pressure. Sat. $NaHCO_3$ aqueous solution was added to the residue which was extracted by $CHCl_3$, and the separated organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid was purified by recrystallization ($CHCl_3$) to give the desired product **6** (225 mg, 72%).



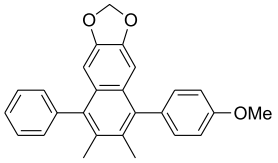
Colorless crystals; mp 160−161 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.11 (s, 3H), 2.56 (s, 3H), 5.98 (s, 2H), 6.58 (s, 1H), 7.15−7.22 (m, 2H), 7.40−7.44 (m, 1H), 7.46−7.50 (m, 2H), and 7.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.0, 18.8, 101.1, 101.3, 103.2, 126.5, 127.1, 128.5 (2C), 129.3, 130.0, 130.1 (2C), 131.5, 132.1, 136.9, 140.3, 147.1, and 147.7; IR (neat) ν_{max}: 2907, 1611, 1501, 1464, 1397, 1310, 1242, 1200, 1041, and 945 cm^{-1}.

2,3-Dimethyl-1,4-diphenyl-6,7-methylenedioxynaphthalene (7a). PEPPSI-IPr (68 mg, 0.1 mmol) and K_2CO_3 (346 mg, 2.5 mmol) were successively added to a stirred solution of $PhB(OH)_2$ (305 mg, 2,5 mmol) in *i*-PrOH (1.3 mL) at 80 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min. A solution of 1-chloronaphthalene **6** (155 mg, 0.5 mmol) in 1,4-dioxane (5 mL) was added to the mixture, which was stirred at the same temperature for 10 h. The mixture was quenched with water, which was filtered through the Celite with a glass filter, and the filtrate was concentrated under reduced pressure. The residue was extracted twice with $CHCl_3$. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane: AcOEt = 1:0 to 50:1) to give the desired product **7a** (146 mg, 83%).



Colorless crystals; mp 277−278 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.13 (s, 6H), 5.88 (s, 2H), 6.64 (s, 2H), 7.28−7.29 (m, 4H), and 7.39−7.55 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.3 (2C), 100.8, 103.0 (2C), 127.0 (2C), 128.4 (2C), 128.6 (4C), 130.3 (4C), 131.5 (2C), 137.5 (2C), 141.2 (2C), and 146.5 (2C); IR (neat) ν_{max}: 3023, 2903, 1497, 1464, 1238, 1038, 1017, 945, 862, and 752 cm^{-1}.

2,3-Dimethyl-4-phenyl-6,7-methylenedioxy-1-(3-methoxyphenyl)naphthalene (7b). Following the procedure for the preparation of **7a**, the reaction using PEPPSI-IPr (27 mg, 0.04 mmol), K_2CO_3 (138 mg, 1.0 mmol), (4-MeO)$C_6H_4B(OH)_2$ (212 mg, 1.0 mmol), and **6** (62 mg, 0.2 mmol) gave the desired product **7b** (83 mg, 93%).



Colorless crystals; mp 265−266 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H), 2.15 (s, 3H) 3.91 (s, 3H), 5.89 (s, 2H), 6.63 (s, 1H), 6.69 (s, 1H), 7.04−7.06 (m, 2H), 7.19−7.21 (m, 2H), 7.27−7.29 (m, 2H), and 7.40−7.52 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4 (2C), 55.3, 100.7, 102.9 (2C), 113.4, 114.1, 126.9, 127.7 (2C), 128.5 (2C), 130.2 (2C), 131.2 (2C), 131.4, 131.9, 133.2, 133.4, 137.1, 137.3, 141.1, 146.4, and 158.5; IR (neat) ν_{max}: 2934, 1578, 1460, 1410, 1238, 1117, 1036, 972, 945, and 860 cm^{-1}.

2,3-Dimethyl-4-phenyl-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene (7c). Following the procedure for the preparation of **7a**, the reaction using PEPPSI-IPr (27 mg, 0.04 mmol), K_2CO_3 (138 mg, 1.0 mmol), 3,4,5-$(MeO)_3C_6H_2B(OH)_2$ (212 mg, 1.0 mmol), and **6** (62 mg, 0.2 mmol) gave the desired product **7c** (80 mg, 90%).

https://doi.org/10.1021/acsomega.1c04413
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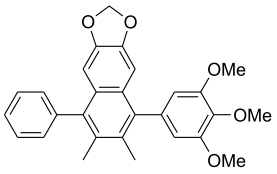
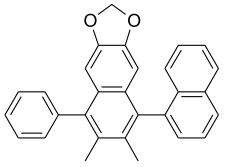


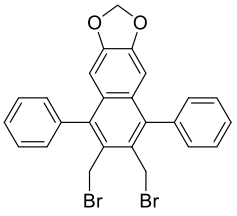
Colorless crystals; mp 274−275 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.18 (s, 3H), 2.18 (s, 3H) 3.85 (s, 6H), 3.97 (s, 3H), 5.91 (s, 2H), 6.51 (s, 2H), 6.64 (s, 1H), 6.74 (s, 1H), 7.27−7.28 (m, 2H), 7.42−7.45 (m, 1H), and 7.49−7.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.3 (2C), 56.1 (2C), 61.1, 100.7, 102.9 (2C), 107.1 (2C), 126.9, 128.2, 128.5 (2C), 130.2 (2C), 131.5 (2C), 136.7, 137.5 (2C), 140.1 (2C), 146.5, and 153.3 (3C); IR (neat) ν_{max}: 2934, 1578, 1460, 1410, 1238, 1117, 1036, 972, 945, and 860 cm^{-1}.

2,3-Dimethyl-4-phenyl-6,7-methylenedioxy-1-naphthylnaphthalene (7d). Following the procedure for the preparation of **7a**, the reaction using PEPPSI-IPr (27 mg, 0.04 mmol), K_2CO_3 (138 mg, 1.0 mmol), naphthalene-1-ylboric acid (103 mg, 0.6 mmol), and a solution of **6** (62 mg, 0.2 mmol) gave the desired product **7d** (68 mg, 77%).



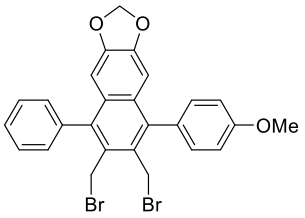
Colorless crystals; mp 203−204 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.00 (s, 3H), 2.16 (s, 3H), 5.81 (d, *Jgem* = 1.0 Hz, 1H), 5.82 (d, *Jgem* = 1.0 Hz, 1H), 6.39 (s, 1H), 6.68 (s, 1H), 7.32−7.63 (m, 10H), and 7.91−8.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.2, 18.3, 100.7, 102.9, 103.0 125.7, 125.9, 126.1, 126.2, 126.9, 127.5, 127.8, 128.2, 128.3, 128.5 (2C), 128.7, 130.3 (2C), 131.4, 132.6, 132.7, 133.8, 135.1, 137.7, 138.7, 141.1 (2C), and 146.4; IR (neat) ν_{max}: 2897, 1615, 1499, 1461, 1234, 1117, 1040, 947, 859, and 779 cm^{-1}.

2,3-Bis(bromomethyl)-1,4-diphenyl-6,7-methylenedioxynaphthalene (8a). NBS (182 mg, 1.0 mmol) and AIBN (4 mg, 0.02 mmol) were successively added to a stirred solution of 2,3-dimethylnaphthalene **7a** (157 mg, 0.45 mmol) in benzene (7.2 mL) at 20−25 °C under an Ar atmosphere, and the mixture was stirred at 80 °C for 1 h. The mixture was quenched with 1 M aqueous HCl, which was extracted twice with $CHCl_3$. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 1:0 to 50:1) to give the desired product **8a** (172 mg, 75%).



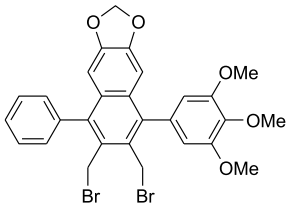
Colorless crystals; mp 261−262 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.67 (s, 4H), 5.93 (s, 2H), 6.63 (s, 2H), 7.38−7.46 (m, 4H), and 7.47−7.61 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.5, 101.3, 103.7, 128.0, 128.6, 129.9, 130.1, 130.4, 138.2, 140.7, and 148.1; IR (neat) ν_{max}: 3058, 2915, 1497, 1472, 1250, 1200, 1071, 1038, 947, and 853 cm^{-1}.

2,3-Bis(bromomethyl)-4-phenyl-6,7-methylenedioxy-1-(3-methoxyphenyl)naphthalene (8b). Following the procedure for the preparation of the reaction of **8a**, the reaction of **7b** (76 mg, 0.2 mmol) using NBS (82 mg, 0.46. mmol) and AIBN (2 mg, 0.01 mmol) gave the desired product **8b** (96 mg, 85%).



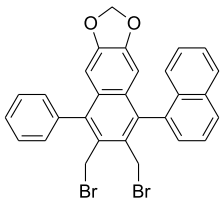
Colorless crystals; mp 266−267 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.92 (s, 3H), 4.66 (s, 2H), 4.70 (s, 2H), 5.92 (s, 2H), 6.62 (s, 1H), 6.68 (s, 1H), 7.03−7.12 (m, 2H), and 7.30−7.60 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.6, 30.7, 55.3, 101.3, 103.7, 103.8, 114.0, 127.9, 128.5, 129.9, 130.1, 130.2, 130.5, 131.0, 138.2, 140.5, 140.6, 148.1, and 159.2; IR (neat) ν_{max}: 2835, 1613, 1497, 1458, 1286, 1234, 1104, 1036, 942, and 865 cm^{-1}.

2,3-Bis(bromomethyl)-4-phenyl-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene (8c). Following the procedure for the preparation of **8a**, the reaction of **7c** (89 mg, 0.2 mmol) using NBS (82 mg, 0.46. mmol) and AIBN (2 mg, 0.01 mmol) gave the desired product **8c** (107 mg, 89%).



Colorless crystals; mp 215−216 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 6H), 3.99 (s, 3H), 4.67 (s, 2H), 4.71 (s, 2H), 5.96 (s, 2H), 6.62 (s, 2H), 6.66 (s, 1H), 6.78 (s, 1H), 7.36−7.44 (m, 2H), and 7.48−7.61 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.1, 30.4, 30.8, 56.2, 61.0, 101.4, 103.7, 106.9, 128.0, 128.6, 129.8, 130.0, 130.1, 130.2, 130.3, 133.4, 137.3, 138.0, 140.5, 140.7, 148.2, and 153.2; IR (neat) 2835, 1610, 1500, 1457, 1285, 1234, 1105, 1036, 942, and 868 cm^{-1}.

2,3-Bis(bromomethyl)-4-phenyl-6,7-methylenedioxy-1-naphthylnaphthalene (8d). Following the procedure for the preparation of the reaction of **8a**, the reaction of **7d** (81 mg, 0.2 mmol) using NBS (82 mg, 0.46. mmol) and AIBN (2 mg, 0.01 mmol) gave the desired product **8d** (107 mg, 90%).



Colorless crystals; mp 186−187 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.34 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 10.0 Hz, 1H), 4.75 (d, J = 10.0 Hz, 1H), 4.79 (d, J = 12.0 Hz, 1H), 5.86 (s, 1H), 5.88 (s, 1H), 6.36 (s, 1H), 6.67 (s, 1H), 7.28−7.76 (m, 10H), and 7.93−8.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.3, 30.5, 101.3, 103.7, 103.8, 125.5, 126.0, 126.2, 126.5, 128.0,

https://doi.org/10.1021/acsomega.1c04413
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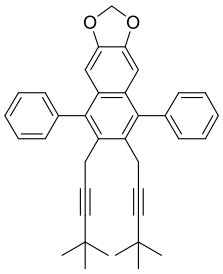
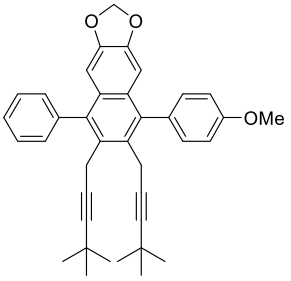
128.1, 128.3, 128.56, 128.61, 129.9, 130.0, 130.3, 130.5, 130.7, 131.1, 132.4, 133.7, 135.4, 138.1, 138.7, 141.0, and 148.2; IR (neat) ν_{max}: 2899, 1615, 1499, 1457, 1343, 1239, 1153, 1038, 945, and 859 cm^{-1}.

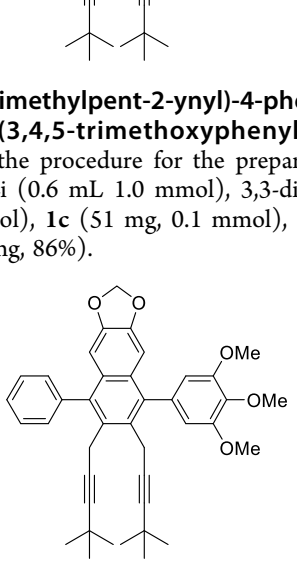
2,3-Bis(4,4-dimethylpent-2-ynyl)-1,4-diphenyl-6,7-methylenedioxynaphthalene (1a). ^{n}BuLi (1.3 mL 2.0 mmol) was added to a stirred solution of 3,3-dimethylbut-1-yne (164 mg, 2.0 mmol) in THF (0.2 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. A solution of **8a** (51 mg, 0.1 mmol) in hexamethylphosphoramide (HMPA) (0.4 mL) and THF (0.3 mL) was added to the mixture, which was stirred at the same temperature for 1 h. The mixture was quenched with aqueous sat. NH_4Cl solution was extracted twice with $CHCl_3$. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 50:1 → 10:1) to give the desired product **1a** (42 mg, 81%).



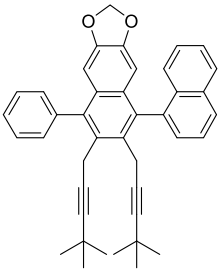
2,3-Bis(4,4-dimethylpent-2-ynyl)-4-phenyl-6,7-methylenedioxy-1-(3-methoxyphenyl)naphthalene (1b). Following the procedure for the preparation of **1a**, the reaction using ^{n}BuLi (1.3 mL, 2.0 mmol) and 3,3-dimethylbut-1-yne (164 mg, 2.0 mmol), **8b** (54 mg, 0.1 mmol), gave the desired product **1b** (41 mg, 75%).



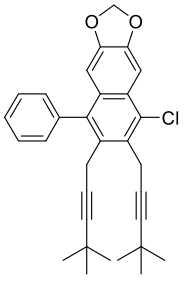
2,3-Bis(4,4-dimethylpent-2-ynyl)-4-phenyl-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene (1c). Following the procedure for the preparation of **1a**, the reaction of ^{n}BuLi (0.6 mL 1.0 mmol), 3,3-dimethylbut-1-yne (82 mg, 1.0 mmol), **1c** (51 mg, 0.1 mmol), gave the desired product **1c** (52 mg, 86%).



2,3-Bis(4,4-dimethylpent-2-ynyl)-4-phenyl-6,7-methylenedioxy-1-naphthylnaphthalene (1d). Following the procedure for the preparation of the reaction of **1a**, the reaction of ^{n}BuLi (0.6 mL, 1.0 mmol) and 3,3-dimethylbut-1-yne (82 mg, 1.0 mmol), **8d** (54 mg, 0.1 mmol), gave the desired product **1d** (44 mg, 77%).



6,7-Bis(bromomethyl)-5-chloro-8-phenylnaphtho-[2,3-*d*][1,3]dioxole (9). Following the procedure for the preparation of the reaction of **8a**, the reaction of **6** (155 mg, 0.5 mmol) using NBS (196 mg, 1.1 mmol) and AIBN (8.2 mg, 0.05 mmol) gave the desired product **9** (218 mg, 93%).



Colorless crystals; mp 162−164 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.53 (s, 2H), 5.11 (s, 2H), 6.04 (s, 2H), 6.58 (s, 1H), 7.33−7.35 (m, 2H), 7.50−7.56 (m, 3H), and 7.70 (s, 1H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 28.7, 29.9, 101.8, 101.9, 104.0, 128.2, 128.4, 128.6 (2C), 129.7 (2C), 130.0, 130.7, 131.3, 132.5, 137.4, 139.7, 148.9, and 149.4; IR (neat) ν_{max}: 3062, 3005, 2906, 1456, 1240, 1199, 1039, and 947 cm^{-1}.

HRMS (DART) m/z: calcd for $C_{19}H_{13}Br_1Cl_1O_2$ $[M]^+$, 386.9787; found, 386.9773.

5-Chloro-6,7-bis(4,4-dimethylpent-2-yn-1-yl)-8-phenylnaphtho[2,3-*d*][1,3]dioxole (10). ^{n}BuLi (42 mL, 66 mmol) was added to a stirred solution of 3,3-dimethylbut-1-yne (5.99 g, 73 mmol) in THF (15 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. A solution of bis(bromomethyl)naphthalene **9** (3.43 g, 7.3 mmol) in HMPA (7.3 mL) and THF (22 mL) was added to the mixture, which was stirred at the same temperature for 1 h, followed by stirring at 20−25 °C for 1 h. The mixture was quenched with water, which was extracted twice with hexane. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid was purified by SiO_2-column chromatography (hexane/AcOEt = 50:1) to give the desired product **10** (2.16 g, 67%).

Paled yellow crystals; mp 159−161 °C; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.14 (s, 9H), 1.16 (s, 9H), 3.41 (s, 2H), 4.03 (s, 2H), 6.00 (s, 2H), 6.63 (s, 1H), 7.32−7.33 (m, 2H), 7.44−7.50 (m, 3H), and 7.70 (s, 1H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 21.0, 21.5, 27.3, 27.4, 31.1 (3C), 31.2 (3C), 75.0, 76.6, 89.3, 89.7, 101.3, 101.5, 103.5, 127.2, 127.5, 128.3 (2C), 130.1, 130.3 (2C),

https://doi.org/10.1021/acsomega.1c04413
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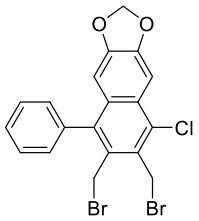
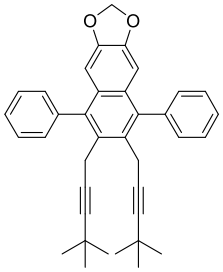


130.4, 131.6, 132.5, 137.5, 139.1, 147.7, and 148.1; IR (neat) ν_{max}: 2966, 2899, 2866, 1483, 1456, 1238, and 758 cm^{-1}.

HRMS (DART) *m*/*z*: calcd for $C_{31}H_{32}ClO_2$ $[M + H]^+$, 471.2091; found, 471.2065.

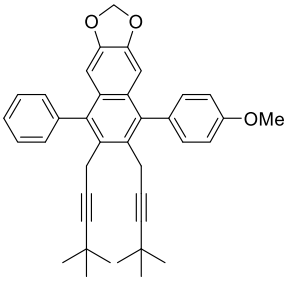
6,7-Bis(4,4-dimethylpent-2-yn-1-yl)-5,8-diphenylnaphtho[2,3-*d*][1,3]dioxole (1a). A mixture of α-chloronaphthalene **10** (221 mg, 0.50 mmol), $PhB(OH)_2$ (91 mg, 0.75 mmol), K_3PO_4 (212 mg, 1.0 mmol), $Pd(OAc)_2$ (3.4 mg, 0.02 mmol), and SPhos (12 mg, 0.03 mmol) in toluene (1.6 mL) was stirred at 80−85 °C for 2 h. After cooling down, water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid was purified by SiO_2-column chromatography (hexane/AcOEt = 50:1) to give desired product **1a** (228 mg, 89%).



Paled yellow crystals; mp 209−210 °C; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.13 (s, 18H), 3.48 (s, 4H), 5.89 (s, 2H), 6.70 (s, 2H), and 7.41−7.52 (m, 10H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 21.1 (2C), 27.4 (2C), 29.7, 31.1 (6C), 89.2 (2C), 100.9 (2C),103.1 (2C), 127.3 (2C), 128.3 (4C), 129.0 (2C), 130.4 (4C), 131.8 (2C), 138.2 (2C), 139.8 (2C), and 146.9 (2C); IR (neat) ν_{max}: 2969, 1541, 1501 1263, 1240, 1044, 955, 858, 754, and 702 cm^{-1}.

HRMS (DART) *m*/*z*: calcd for $C_{37}H_{37}O_2$ $[M + H]^+$, 513.2794; found, 513.2818.

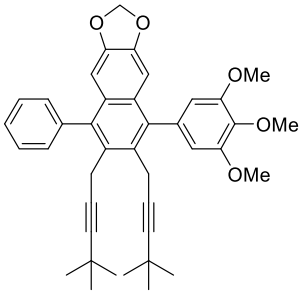
6,7-Bis(4,4-dimethylpent-2-yn-1-yl)-5-(4-methoxyphenyl)-8-phenylnaphtho[2,3-*d*][1,3]dioxole (1b). Following the procedure for the preparation of **1a**, the reaction using α-chloronaphthalene **10** (221 mg, 0.50 mmol), (4-MeO)$C_6H_4B(OH)_2$ (114 mg, 0.75 mmol), K_3PO_4 (212 mg, 1.0 mmol), $Pd(OAc)_2$ (3.4 mg, 0.02 mmol), and SPhos (12 mg, 0.03 mmol) gave the desired product **1b** (244 mg, 90%).



Paled yellow crystals; mp 111−112 °C; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.13 (s, 9H), 1.14 (s, 9H), 3.47 (s, 2H), 3.50 (s, 2H), 3.92 (s, 3H), 5.89 (s, 2H), 6.69 (s, 1H), 6.75 (s, 1H), 7.05 (d, *J* = 8.6 Hz, 2H). 7.34 (d, *J* = 8.6 Hz, 2H), and 7.41−7.52 (m, 5H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 21.1 (2C), 27.4, 31.1 (6C), 55.3, 89.1, 100.9,103.1 (2C), 103.2 (2C), 113.7 (2C), 114.1, 127.3, 127.7, 128.2 (2C), 129.0, 129.3, 130.4 (2C), 131.5 (2C), 131.8, 132.0, 132.2, 137.9, 138.1, 139.8, 146.8, and 158.8; IR (neat) ν_{max}: 2966, 1520 1460, 1287, 1239, 1177, 1039, 947, 864, and 764 cm^{-1}.

HRMS (DART) *m*/*z*: calcd for $C_{38}H_{39}O_3$ $[M + H]^+$, 543.2899; found, 543.2876.

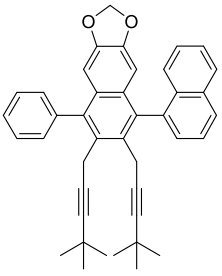
6,7-Bis(4,4-dimethylpent-2-yn-1-yl)-5-phenyl-8-(3,4,5-trimethoxyphenyl)naphtho[2,3-*d*][1,3]dioxole (1c). Following the procedure for the preparation of **1a**, the reaction using α-chloronaphthalene **10** (221 mg, 0.50 mmol), 3,4,5-$(MeO)_3C_6H_2B(OH)_2$ (159 mg, 0.75 mmol), K_3PO_4 (212 mg, 1.0 mmol), $Pd(OAc)_2$ (3.4 mg, 0.02 mmol), and SPhos (12 mg, 0.03 mmol) gave the desired product **1c** (127 mg, 42%).



Paled yellow crystals; mp 83−84 °C; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.13 (s, 9H), 1.14 (s, 9H), 3.53 (s, 2H), 3.55 (s, 2H), 3.88 (s, 6H), 4.00 (s, 3H), 5.92 (s, 2H), 6.65 (s, 2H), 6.69 (s, 1H), 6.83 (s, 1H), 7.39−7.42 (m, 2H), and 7.46−7.52 (m, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 20.9, 21.2, 27.4 (2C), 31.1 (3C), 31.2 (3C), 56.1 (2C), 61.0, 89.0, 89.2, 100.9,103.2 (2C), 103.2 (2C), 107.3 (2C), 127.3, 128.3 (2C), 128.8, 129.0, 130.4 (2C), 131.7 (2C), 132.0, 135.3, 137.0, 137.9, 138.4, 139.6, 146.9, 147.0, and 153.1; IR (neat) ν_{max}: 2969, 2901, 1582, 1501, 1460, 1410, 1360, 1240, 1130, and 947 cm^{-1}.

HRMS (DART) *m*/*z*: calcd for $C_{40}H_{43}O_5$ $[M + H]^+$, 603.3110; found, 603.3100.

6,7-Bis(4,4-dimethylpent-2-yn-1-yl)-5-(naphthalen-1-yl)-8-phenylnaphtho[2,3-*d*][1,3]dioxole (1d). Following the procedure for the preparation of **1a**, the reaction using α-chloronaphthalene **10** (221 mg, 0.50 mmol), naphthalene-1-lyboric acid (129 mg, 0.75 mmol), K_3PO_4 (212 mg, 1.0 mmol), $Pd(OAc)_2$ (3.4 mg, 0.02 mmol), and SPhos (12 mg, 0.03 mmol) gave the desired product **1d** (247 mg, 88%).



Paled yellow crystals; mp 125−126 °C; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.04 (s, 9H), 1.14 (s, 9H), 3.26 (d, 4H), 5.82 (d, *Jgem* = 1.2 Hz, 1H), 5.85 (d, *Jgem* = 1.2 Hz, 1H), 6.36 (s, 1H), 6.73 (s,

https://doi.org/10.1021/acsomega.1c04413
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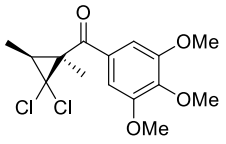
1H) 7.29−7.33 (m, 1H), 7.36−7.38 (m, 1H), 7.44−7.55 (m, 7H), 7.60−7.63 (m, 1H), and 7.95−7.98 (m, 2H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 15.3, 21.0, 21.1, 27.2, 27.4, 31.0 (3C), 31.1 (3C), 65.9, 88.9, 89.4, 100.8, 103.2, 103.2, 125.5, 125.8, 126.1, 126.5, 127.3, 127.9, 128.1, 128.3 (2C), 128.4, 129.0, 129.4, 130.4, 130.5, 132.1, 132.7, 132.8, 133.7, 135.9, 137.4, 138.4, 139.8, and 146.9 (2C); IR (neat) ν_{max}: 2898, 1615, 1459 1341, 1233, 1153, 1040, 947, 906, 858, and 780 cm^{-1}; HRMS (DART) m/z: calcd for $C_{41}H_{39}O_2$ $[M + H]^+$, 563.2950; found, 563.2927.

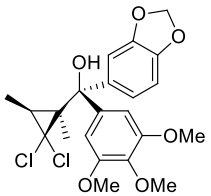
HPLC analysis (Daicel Chiralcel OD-H column, hexane/2-propanol = 100:1, 1.0 mL/min, 254 nm UV detector), t_R = 5.76 min and t_R = 11.85 min.

(1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl]-(3,4,5-trimethoxyphenyl)methanone (11).**[5c] To a stirred solution of (3,4,5-trimethoxyphenyl)magnesium bromide prepared from Mg (48 mg, 2.0 mmol) and 1,2,3-trimethoxy-5-bromobenzene (494 mg, 2.0 mmol) in THF (1.0 mL), acid chloride **3** (201 mg, 1.0 mmol) in THF (1.0 mL) was added at 0−5 °C. The mixture was stirred at the same temperature for 1 h. Sat. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with ether. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/AcOEt = 10:1) to give the desired product **11** (200 mg, 91%).



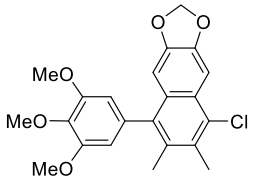
Colorless oil; ^{1}H NMR (400 MHz; $CDCl_3$): δ 1.41 (d, J = 6.6 Hz, 3H), 1.68 (q, J = 6.6 Hz, 1H), 1.68 (s, 3H), 3.87 (s, 3H), 3.95 (s, 6H), and 7.28 (s, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 11.6, 23.6, 35.2, 39.5, 56.2, 61.0, 68.6, 105.2, 107.1, 142.9, 153.0, and 193.8; IR (neat) 3570, 2928, 1489, 1444, 1321, 1271, 1240, 1198, 1036, and 934 cm^{-1}.

(*R)-[(1*S**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](3,4-methylenedioxyphenyl)-(3,4,5-trimethoxyphenyl)methanol (12).**[5c] ^{n}BuLi (1.58 M in hexane, 1.40 mL, 2.21 mmol) was added to a stirred solution of 3,4-methylenedioxy-1-bromobenzene (578 mg, 2.34 mmol) in THF (5 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Ketone **11** (520 mg, 1.56 mmol) in THF (5 mL) was added to the mixture at the same temperature, and the mixture was stirred for 2 h. The mixture was poured into ice and maintained. NH_4Cl aqueous solution was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/AcOEt = 100:1 to 50:1) to give the desired product **12** (610 mg, 86%).



Colorless amorphous solid; ^{1}H NMR (400 MHz; $CDCl_3$): δ 1.19 (s, 3H), 1.56 (q, J = 6.6 Hz, 1H), 1.76 (d, J = 6.6 Hz, 3H), 2.73 (brs, 1H, -OH), 3.86 (s, 6H), 3.92 (s, 3H), 5.96 (d, J = 1.5 Hz, 1H), 5.97 (d, J = 1.5 Hz, 1H), 6.61 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 6.72 (d, J = 8.3 Hz, 1H), 6.77 (s, 2H), and 6.81 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 11.1, 27.1, 36.4, 38.5, 56.3, 60.9, 74.3, 83.9, 101.1, 106.2, 107.1, 108.8, 122.0, 139.9, 140.5, 146.6, 147.2, and 152.7; IR (KBr) ν_{max}: 3569, 1591, 1487, and 1238 cm^{-1}.

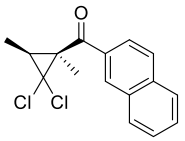
5-Chloro-6,7-dimethyl-8-(3,4,5-trimethoxyphenyl)-naphtho[2,3-*d*][1,3]dioxole (13).[5c] Following the procedure for the preparation of α-chloronaphthalene **6**, the reaction of alcohol **12** (610 mg, 1.34 mmol) and $SnCl_4$ (1 M solution: 1.34 mL, 1.34 mmol) gave the desired product **13** (368 mg, 73%).



Colorless crystals; mp 181−186 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ 2.20 (s, 3H), 2.25 (s, 3H), 3.71 (s, 3H), 3.85 (s, 6H), 5.91 (s, 2H), 6.51 (s, 2H), 6.65 (s, 1H), and 6.75 (s, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 14.4, 16.1, 56.1 (2C), 60.8, 101.2, 103.2, 104.7, 106.3 (2C), 121.9, 125.7, 128.7, 130.8, 132.3, 136.2, 136.4, 138.1, 147.2, 149.5, and 153.1 (2C); IR (KBr) ν_{max}: 1464, 1252, and 1107 cm^{-1}.

Suzuki−Miyaura Cross-Coupling of 13 Affording 7c. Following the procedure for the preparation of α-chloronaphthalene **7b**, the reaction of alcohol **13** (80 mg, 0.20 mmol) gave the desired product **7c** (65 mg, 73%).

((1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl)-(naphthalen-1-yl)methanone (14).** ^{n}BuLi (1.58 M in hexane, 47 mL, 75 mmol) was added to a stirred solution of 1-bromonaphthalene (15.5 g, 75 mmol) in THF (50 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Ester **4** (9.85 g, 50 mmol) in THF (50 mL) was added to the mixture at the same temperature, and the mixture was stirred for 2 h. The mixture was poured into ice and maintained. NH_4Cl aqueous solution was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/AcOEt = 50:1) to give the desired product **14** (11.1 g, 76%).



Colorless oil; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.46 (d, J = 6.9 Hz, 3H), 1.72−1.76 (m, 4H), 7.53−7.56 (m, 1H), 7.60−7.65 (m, 2H), 7.89−7.91 (m, 1H), 8.05−8.07 (m, 1H), 8.10−8.11 (m, 1H), and 8.92−8.94 (m, 1H); ^{13}C NMR (125 MHz, CDCl3): δ 11.9, 24.3, 36.4, 41.3, 69.1, 124.5, 125.8, 126.5, 128.5, 128.6, 131.2, 131.3, 131.5, 134.1, 134.2, and 197.9; IR (neat) ν_{max}: 2899, 1610, 1465, 1240, 1041, 948, 908, 798, 777, and 734 cm^{-1}; HRMS (DART) m/z: calcd for $C_{16}H_{15}Cl_2O_1$ $[M + H]^+$, 293.0500; found, 293.0522.

(*S)-Benzo[*d*][1,3]dioxol-5-yl((1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropyl)(naphthalen-1-yl)methanol (15).** Following the procedure for the preparation of AACM **5**,

https://doi.org/10.1021/acsomega.1c04413
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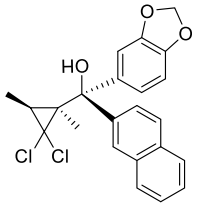
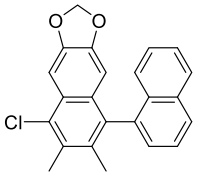
the reaction of ketone **14** (1.47 g, 5.0 mmol), ^{n}BuLi (1.58 M in hexane, 4.7 mL, 7.5 mmol), and 3,4-methylenedioxy-1-bromobenzene (1.51 g, 7.5 mmol) gave the desired product **15** (1.40 g, 67%). Amorphous solid; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.24 (d, J = 12.0 Hz, 3H), 1.57 (q, J = 6.9 Hz 1H), 1.83 (t, J = 8.0 Hz 3H), 5.90−5.94 (m, 1H), 6.00 (d, *Jgem* = 1.2 Hz, 1H), 6.04 (d, *Jgem* = 1.2 Hz, 1H), and 7.16−7.90 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.4, 26.9, 36.5, 39.6, 74.7, 84.7, 101.1, 106.6, 108.3, 119.4, 122.9, 124.5, 125.1, 126.8, 128.7, 129.0, 129.7, 131.5, 135.3, 137.7, 139.9, 146.3, and 148.0; IR (neat) ν_{max}: 3576, 1600, 1002, 966, 908, 810, 794, 781, and 655 cm^{-1}; HRMS (DART) m/z: calcd for $C_{23}H_{19}Cl_2O_2$ $[M - OH]^+$, 397.0762; found, 397.0776.



5-Chloro-6,7-dimethyl-8-(naphthalen-1-yl)naphtho-[2,3-*d*][1,3]dioxole (16). Following the procedure for the preparation of α-chloronaphthalene **6**, the reaction of alcohol **15** (208 mg, 0.5 mmol) and $SnCl_4$ (1 M solution: 500 μL, 0.5 mmol) gave the desired product **16** (128 mg, 71%).



Amorphous solid; ^{1}H NMR (500 MHz; $CDCl_3$): δ 1.99 (s, 3H), 2.60 (s, 3H), 5.91 (d, *Jgem* = 1.2 Hz, 1H), 5.93 (d, *Jgem* = 1.2 Hz, 1H), 6.34 (s, 1H), and 7.27−7.95 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.9, 18.6, 101.1, 101.3, 103.3, 125.6, 125.9, 126.0, 126.2, 126.7, 127.8 (2C), 128.3, 129.8, 130.1, 131.6, 132.5, 133.3, 133.7, 134.6, 137.9, 147.3, and 147.8; IR (neat) ν_{max}: 2985, 2931, 1298, 1228, 1103, 1060, 970, 947, 837, 810, 732, and 619 cm^{-1}; HRMS (DART) m/z: calcd for $C_{23}H_{18}Cl_1O_2$ $[M]^+$, 361.0995; found, 361.1002.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c04413.

Characterization of all new products (^{1}H and ^{13}C NMR spectra), characterization of all new products for ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra (PDF), Chiral HPLC analysis of compound **1d**, and calculation data of **1a** and **1d** using Spartan software (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was partially supported by Grant-in-Aids for Scientific Research on Basic Areas (B) "18350056", Priority Areas (A) "17035087" and "18037068", (C) 15K05508, and Exploratory Research "17655045" from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). We thank Taichi Yoshida and Dr. Yoshinori Nishii in Kwansei Gakuin University for some of their helpful discussions. One of the authors (Y.T.) offers his warmest congratulations to Professor Ben L. Feringa (University of Groningen, The Netherlands) on being awarded the 2016 Nobel Prize in Chemistry. Dedication to the late Professors Teruaki Mukaiyama and Kenji Mori.

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https://doi.org/10.1021/acsomega.1c04413
ACS Omega 2021, 6, 32682−32694