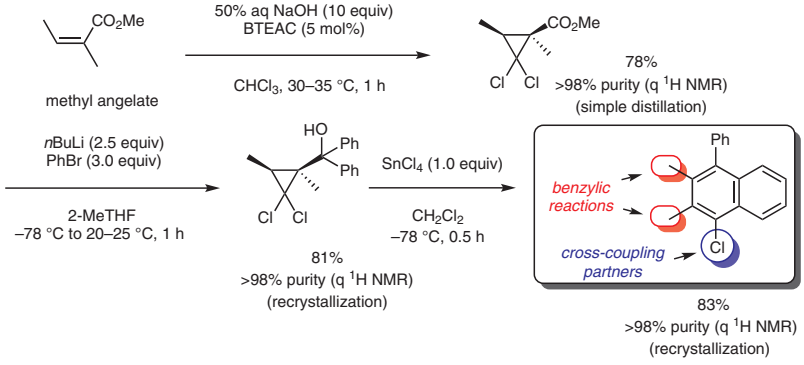
Synthesis K. Moriguchi et al. PSP

Gram-Scale Robust Synthesis of 1-Chloro-2,3-dimethyl-4-phenylnaphthalene: A Promising Scaffold with Three Contiguous Reaction Positions

Kento Moriguchi
Taro Kono
Shinzo Seko
Yoo Tanabe*

Department of Chemistry, School of Science and Technology, Kwansei Gakuin University, 2-1 Gakuen, Sanda, Hyogo, 669-1337, Japan
tanabe@kwansei.ac.jp



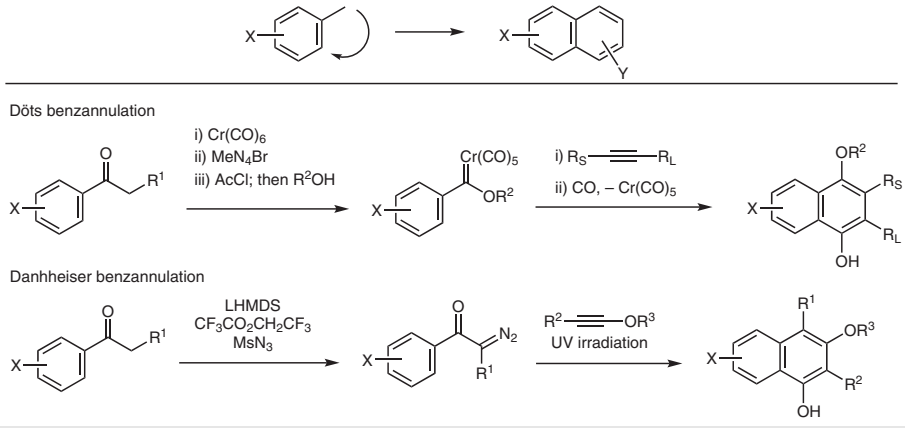
Received: 22.07.2020
Accepted after revision: 14.08.2020
Published online: 30.09.2020
DOI: 10.1055/s-0040-1706471; Art ID: ss-2020-f0394-psp

Abstract A three-step reaction sequence for the gram-scale synthesis of 1-chloro-2,3-dimethyl-4-phenylnaphthalene was developed. (i) Stereoselective dichlorocarbene addition to methyl angelate afforded methyl (1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate (78% yield, >98% purity, distillation). (ii) Addition reaction of two molar amounts of PhLi afforded (1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropyldiphenylmethanol (81% yield, >98% purity, recrystallization). (iii) Key $SnCl_4$-mediated benzannulation produced the desired product (83% yield, >98% purity, recrystallization) with three contiguous reaction sites. Five derivatization examples including benzylic reactions and cross-couplings at the pendant Cl-position are demonstrated. Some relevant distinctive benzannulations are also discussed.

Key words *gem*-dichlorocyclopropane, benzannulation, naphthalene, gram-scale, benzylic, cross-coupling partners

Multi-substituted naphthalenes comprise a wide range of key synthetic building blocks for natural products, pharmaceuticals, agrochemicals, and functionalized materials. Benzannulation strategies provide unique access to regioselective construction of multi-substituted naphthalene derivatives. Among these strategies, the reaction starting from benzenes bearing a mono-functionalized group is superb due to its diverse synthetic scope (Scheme 1). The Döts benzannulation utilizing Fisher carbene complexes[1] and the Danheiser benzannulation utilizing α-diazoketones[2] are two pioneering methods.

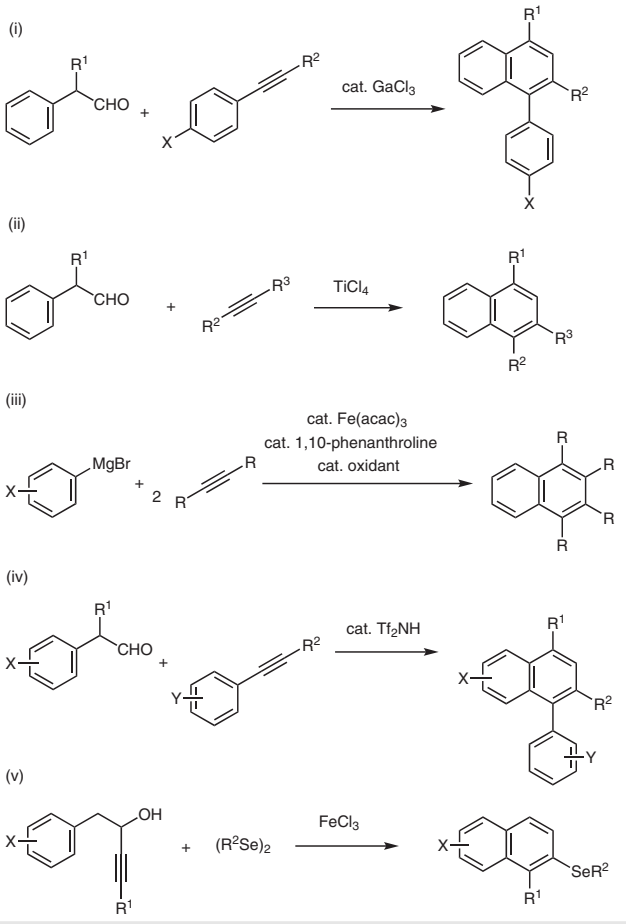
Since the development of these innovative studies, several approaches starting from benzenes bearing a mono-functionalized group have appeared to date and are described in chronologic order (Scheme 2). Five representative benzannulation methods involve the appropriate alkyne partners for the construction of multi-substituted naphthalenes: (i) $GaCl_3$-catalyzed aldehyde–alkyne condensation,[3]



Scheme 1 Two pioneering naphthalene benzannulations

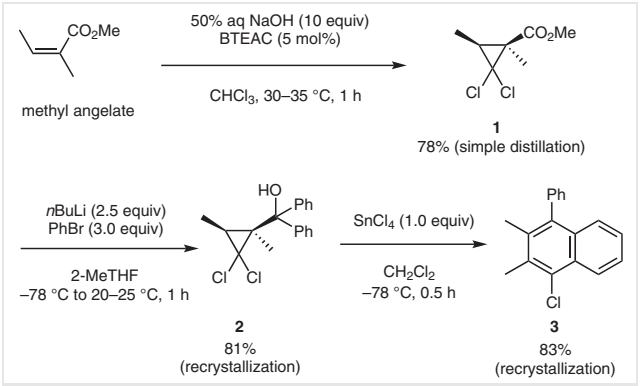
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

(ii) $TiCl_4$-promoted aldehyde–alkyne condensation,[4] (iii) Iron-catalyzed Grignard coupling with two alkynes,[5] (iv) Tf_2NH-catalyzed aldehyde–alkyne condensation,[6] and (v) $FeCl_3$-promoted condensation of alkynyl alcohols concomitant with selenylation.[7]



Scheme 2 Representative naphthalene benzannulations using monofunctionalized arene substrates

The present article describes an accessible synthesis of elaborated tetra-substituted naphthalene **3** from methyl angelate in three steps (Scheme 3). Fedorynski and Anilkumar's group provided a comprehensive review of the synthetic application of 1,1-dihalocyclopropanes.[8] Stereoselective dichlorocarbene addition[9] to methyl angelate afforded methyl (1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate (**1**) in 78% yield with >98% purity [quantitative ^{1}H NMR (q ^{1}H NMR)] by a simple distillation purification. A similar substrate, methyl (1*S**)-2,2-dichloro-1-methylcyclopropane-1-carboxylate, derived from methyl methacrylate is commercially available.[9] An addition reaction of two molar amounts of PhLi with **1** afforded (1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropyldiphenylmethanol (**2**) in 81% isolated yield with >98% purity (q ^{1}H NMR), in which the crude solids of **2** were purified by a recrystallization with hexane/2-propanol (1:1). The reaction using PhMgBr instead of PhLi afforded not **2** (only ca. 10% yield) but mainly (ca. 60–70%) the phenyl ketone intermediate at 0–5 °C to room temperature for 2 hours.



Scheme 3 Present reaction sequences

The key $SnCl_4$-promoted benzannulation of **2** proceeded smoothly to produce 1-chloro-2,3-dimethyl-4-phenylnaphthalene (**3**) in 83% isolated yield with >98% purity (q ^{1}H NMR) by recrystallization with hexane/2-propanol (2:1). Various Lewis or Brønsted acid screenings of the present benzannulation are listed in Table 1 with the ^{1}H NMR yield. The use of $SnCl_4$ or $TiCl_4$ at –78 °C afforded the best results.

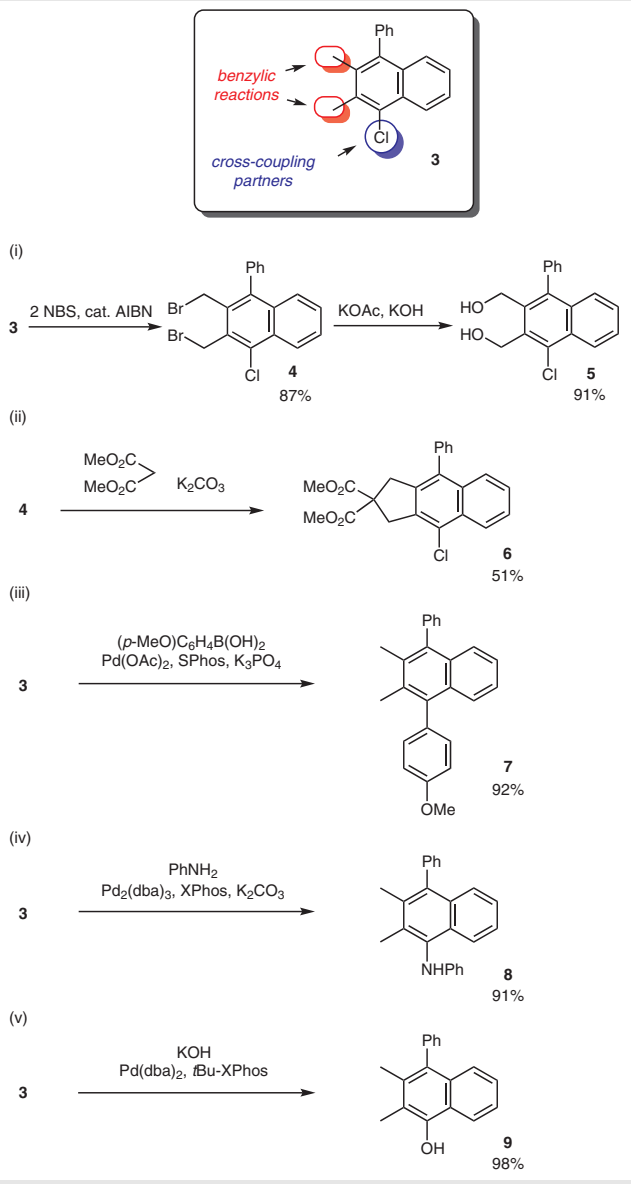
Table 1 Lewis or Brønsted Acid Screening for the Benzannulation

Lewis or Brønsted acid	Temp (°C)	^{1}H NMR yield (%)[a]
$BF_3{\cdot}OEt_2$	0–5	88
	–78	84
$SnCl_4$	0–5	83
	–78	96
TMSOTf	0–5	83
	–78	71
$TiCl_4$	0–5	78
	–78	98
$ZrCl_4$	0–5	37
	–78	80
$AlCl_3$	0–5	59
$ZnCl_2$	0–5	37
$MgCl_2$	0–5	no reaction

[a] Internal standard: ethylene carbonate.

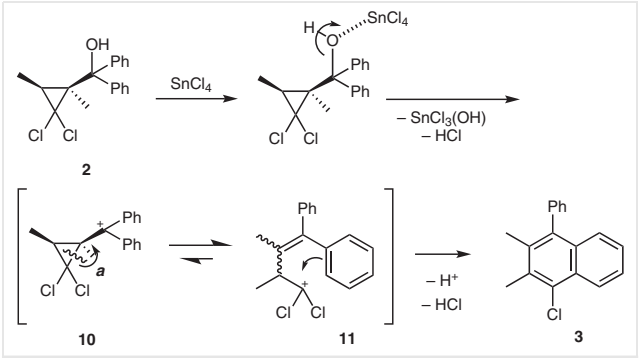
Derivatizations of the obtained naphthalene **3** were presented to demonstrate the utility (Scheme 4), because **3** possesses two promising contiguous benzylic positions and a pendant 1-chloro group. (i) Dibromination of the 2,3-dimethyl group proceeded smoothly using two molar amounts of NBS-cat. AIBN to afford the product **4** in 77% yield. Conversion of **4** using KOAc and KOH afforded diol **5** in 91% yield; this type of reaction was successfully em-

ployed for the total syntheses of natural and unnatural lignan lactones.[10,11] (ii) Cyclopentane formation of **4** with dimethyl malonate proceeded smoothly to afford tricyclic product **6** (51%). (iii) Suzuki–Miyaura cross-coupling successfully proceeded at the 1-chloro group of **3** to produce the desired product **7** in excellent yield (92%), despite of the highly stereocongested position. (iv) Buchwald–Hartwig cross-coupling was implemented to afford aniline derivative **8** in 91% yield. (v) Buchwald hydroxylation cross-coupling[12] of **3** similarly produce the desired 1-naphthol product **9** in excellent yield (98%).



Scheme 4 Various useful derivatizations of naphthalene **3**

A plausible mechanism of the key benzannulation is shown in Scheme 5. The initially formed benzyl cation **10** derived from **2** by the action of $SnCl_4$, in turn, rearranges into the homoallyl cation **11** through regioselective ring-cleavage of bond ***a***.[9] The *Z*-form of **11** undergoes intramolecular Friedel–Crafts reaction to produce the desired 1-chloro-2,3-dimethyl-3-phenylnaphthalene (**3**).

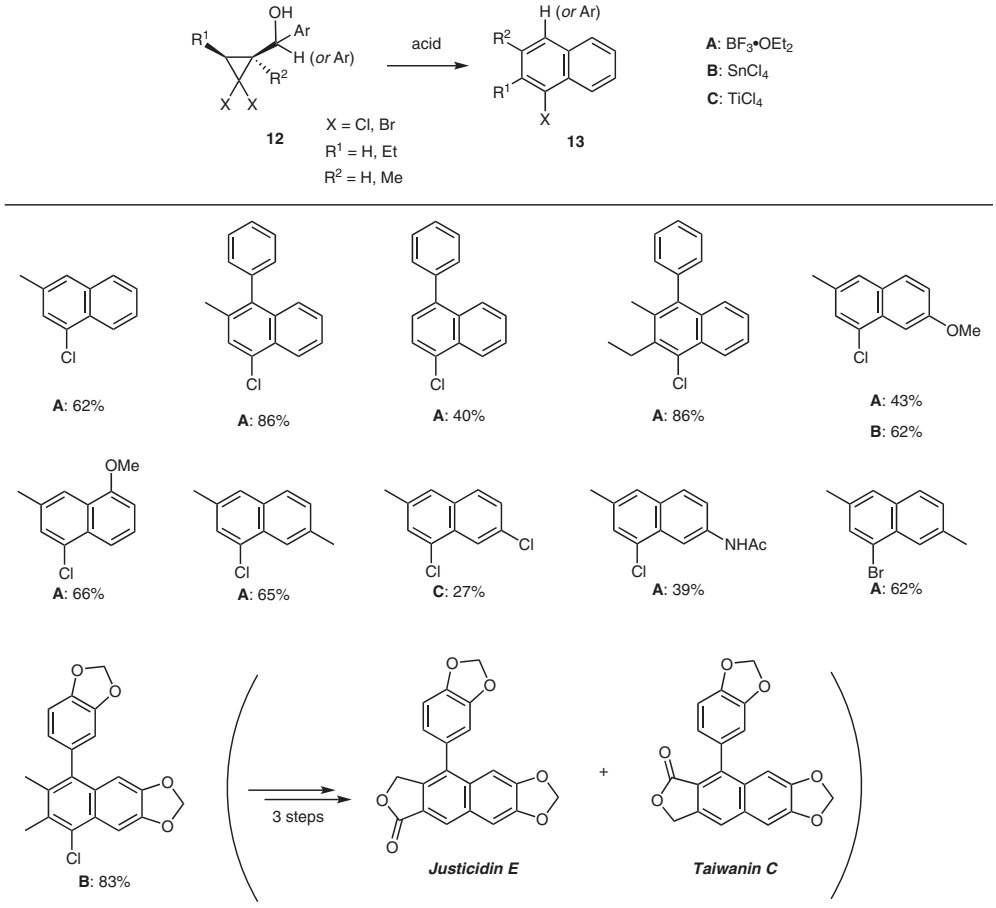


Scheme 5 Plausible mechanism for the benzannulation

The substrate scope for the benzannulation is depicted in Scheme 6. Not only diaryl cyclopropylmethanols but also monoarylcyclopropylmethanols served as the substrate **12** to furnish a variety of 1-chloro and 1-bromonaphthalenes **13**. The introduction of a 1-chloro or 1-bromo group into naphthalenes and the use of a cyclopropane unit for the naphthalene formation are unique but practical strategies.

On the other hand, a related reaction using (1*S**,3*S**)-2,2-dihalo-1-methyl-3-phenylcyclopropylmethanols **14** using CF_3CO_2H reagent proceeded smoothly to produce 2-chloro (or 2-bromo)-3-methyl-1-phenylnaphthalenes **15** through highly regioselective cleavage of bond ***b*** (Scheme 7).[10] Obviously, the formation of benzyl cation intermediate **16** predominates over that of the competitive dilalogenomethylinium cation like **11**. This distinctive switching mode is a notable feature of the present benzannulation.

As an extension of primary non-regioselective benzannulation, we already reported a distinctive regiocontrolled benzannulation[11] (Scheme 8). Stereodefined (aryl^1)(aryl^2)(2,2-dichloro-1-methylcyclopropyl)methanols **18** were prepared by sequential addition of Ar^{1}MgBr and Ar^{2}Li with (1*S**)-2,2-dichlorocyclopropane-1-carbonyl chloride or the (1*S**,3*S**)-analogue **17**. The obtained adducts **18** successfully underwent the desired $SnCl_4$- or $TiCl_4$-mediated regiocontrolled reactions to produce unsymmetrically substituted 1-(aryl^1)-4-chloronaphthalene families **19** bearing a variety of substituents. An application to the total syntheses of unsymmetrically substituted natural lignan lactones, justicidin B,[13] retrojusticidin B,[14] and dehydrodesoxypodophyllotoxin[15] was achieved.[11] In addition, unique chirality-exchange benzannulations from central

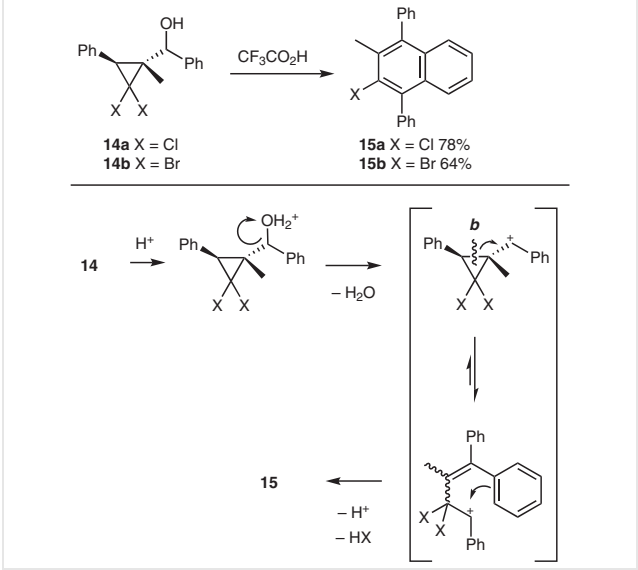


Scheme 6 Substrate scope for the benzannulation

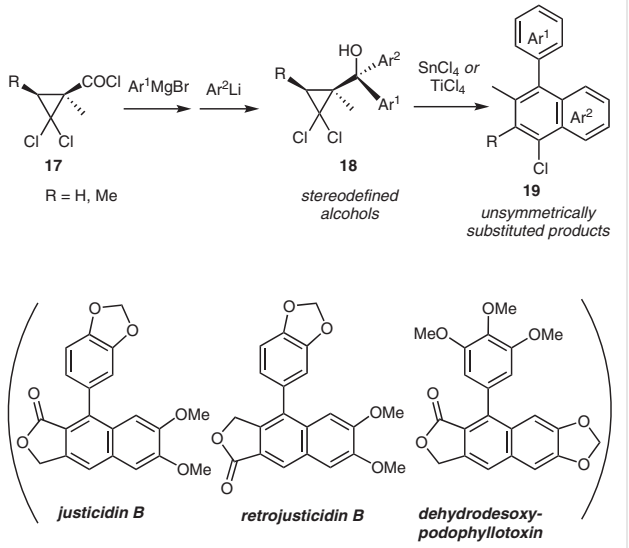
chiral alcohols **20** into axially chiral α-arylnaphthalenes **21** were performed with nearly complete transfer of the chirality (all five examples >98%) (Scheme 9).[16]

As a related work, one of the authors (S.S.) reported the synthesis of 1-phenyldihydronaphthalene **23** from (2,2,3,3-tetramethylcyclopropyl)diphenylmethanol (**22**) (Scheme 10).[17] Following this study, the method was applied to the syntheses of dihydronaphthalene derivatives including several lignan natural products (Scheme 8).[18]

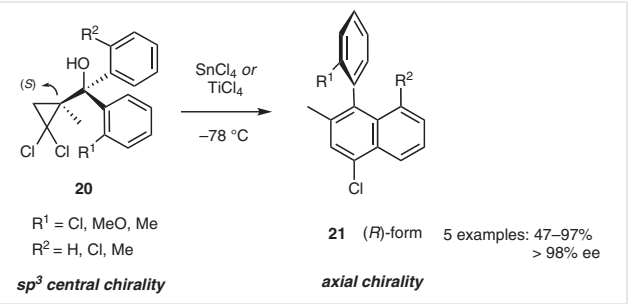
In conclusion, a three-step reaction sequence for the synthesis of 1-chloro-2,3-dimethyl-4-phenylnaphthalene was developed: (i) stereoselective dichlorocarbene addition to methyl angelate, (ii) addition reaction of two molar amounts of PhLi, and (iii) key benzannulation promoted by $SnCl_4$. All procedures are accessible and user-friendly to produce multi-substituted naphthalenes. Extensive studies on the development of a variety of unique and selective benzannulations are discussed. This strategy will contribute to the construction of elaborated and useful naphthalene synthetic blocks.



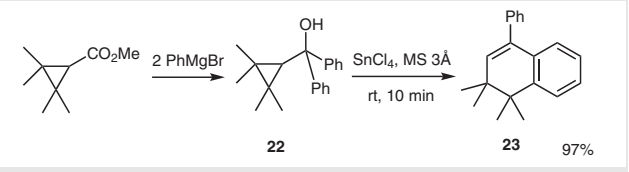
Scheme 7 Relevant regioselective benzannulation of 2,2-dihalo-1-methyl-3-phenylcyclopropylmethanols



Scheme 8 Regiocontrolled benzannulation strategy



Scheme 9 Chirality exchange benzannulation



Scheme 10 Synthesis of dihydronaphthalene **23**

All reactions were carried out in oven-dried glassware under an argon atmosphere. Flash column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). TLC analysis was performed on 0.25 mm silica gel Merck 60 F254 plates. Melting points were determined on a hot stage microscope apparatus (AS ONE, ATM-01) and were uncorrected. NMR spectra were recorded on a JEOL DELTA 300 or JEOLRESONANCE ECX-500 spectrometer, operating at 300 MHz or 500 MHz for ^{1}H NMR and 75 MHz or 125 MHz for ^{13}C NMR. Chemical shifts (δ ppm) in $CDCl_3$ were reported downfield from TMS (= 0) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CDCl_3$ (77.00 ppm) as an internal reference. IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer. Mass spectra were measured on a JEOL JMS-T100LC spectrometer.

Products **2–9** are new compounds.

Methyl (1*S**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropane-1-carboxylate (1)[11]

Caution: The preparation of 50% NaOH viscous aqueous solution required careful procedure: gradual addition of NaOH pellet into H_2O with sufficient stirring and gentle cooling.

Using a 300 mL, four-necked, round-bottomed flask equipped with a 100 mL dropping funnel, a thermometer, a pressure-equalizing argon balloon, aq NaOH (50% w/w, 80 g, 1.00 mol) was added through a 100 mL dropping funnel to a vigorously stirred solution of methyl angelate (11.4 g, 0.10 mol), $CHCl_3$ (29.7 g, 0.50 mol), and benzyltriethylammonium chloride (BTEAC; 1.15 g, 5.0 mmol) over a period of 15 min while maintaining the inner temperature at 30–35 °C [Vigorous stirring was required throughout the phase-transfer reaction using a magnetic stirring bar (for an example, egg-shaped, 50 mm length × 20 mm diameter). When the inner temperature raised over 40 °C, the yield significantly decreased probably due to polymerization of methyl angelate]. The reaction mixture was vigorously stirred for 1 h while maintaining the same temperature, and then diluted with H_2O (50 mL) below 30 °C. The black-colored mixture was filtered through a Celite pad (15 g) on a glass filter (G3, 70 mm diameter), into a 200 mL round-bottomed flask. The filtrate was moved into a 500 mL separatory funnel. The organic phase was separated and the aqueous phase was re-extracted with $CHCl_3$ (2 × 50 mL). The combined organic phases were washed with H_2O (40 mL) and brine (40 mL), dried, and concentrated. The obtained black-colored crude oil was purified by distillation to give the desired colorless product **1** with >98% purity (q ^{1}H NMR); yield: 16.50 g (84%); colorless oil; bp 65–66 °C/7.5 mmHg.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 6.9 Hz, 3 H), 1.55 (q, *J* = 6.9 Hz, 1 H), 1.57 (s, 3 H), 3.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.8, 21.1, 36.0, 36.8, 52.1, 67.6, 168.9.

[(1*S**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl]diphenylmethanol (2)

*n*BuLi (1.57 M in hexane, 49 mL, 77 mmol) was added dropwise through a 100 mL dropping funnel to a stirred solution of bromobenzene (16.5 g, 105 mmol) in 2-methyltetrahydrofuran (55 mL) over a period of 15 min while maintaining the inner temperature at –60 to –75 °C (slightly exothermic) and the mixture was stirred at –60 to –75 °C for 1 h. Then, methyl ester **1** (6.90 g, 35 mmol) in 2-methyltetrahydrofuran (15 mL) was added to the stirred mixture through a 30 mL dropping funnel over 10 min, while maintaining the inner temperature at –60 to –75 °C (slightly exothermic). The mixture was stirred at the same temperature for 1 h, and was gradually warmed up to 20–25 °C. Sat. aq NH_4Cl (70 mL) was added to the mixture below 25 °C over 15 min, and the mixture was moved into a 500 mL separatory funnel. The organic phase was separated and the aqueous phase was re-extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with H_2O (70 mL) and brine (70 mL), dried, and concentrated. The obtained crude solid (12.2 g) was purified by recrystallization from hexane/2-propanol (1:1; 13 mL) to give the desired product **2** with >98% purity (q ^{1}H NMR); yield: 9.02 g (81%); colorless crystals; mp 95–96 °C.

When THF solvent was used instead, the yield decreased slightly (ca. 65%).

IR (neat): 3578, 3059, 3024, 2995, 2932, 2878, 1447, 1028 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 3 H), 1.52 (q, *J* = 6.9 Hz, 1 H), 1.78 (d, *J* = 6.9 Hz, 3 H), 2.80 (s, 1 H), 7.20–7.23 (m, 2 H), 7.27–7.32 (m, 3 H), 7.35–7.39 (m, 1 H), 7.41–7.45 (m, 2 H), 7.52–7.53 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.1, 27.1, 36.3, 38.1, 73.9, 83.8, 127.1, 127.5 (2 C), 127.8, 128.2 (4 C), 128.9 (2 C), 144.6, 146.5.

HRMS (DART): *m*/*z* calcd for $C_{18}H_{18}Cl_2O$ [M + H]$^+$: 320.0735; found: 320.0731.

1-Chloro-2,3-dimethyl-4-phenylnaphthalene (3)

A 300 mL, four-necked, round-bottomed flask equipped with a 100 mL dropping funnel, a thermometer, a pressure-equalizing argon balloon was charged with alcohol **2** (8.03 g, 25 mmol) in CH_2Cl_2 (50 mL). $SnCl_4$ (1 M in CH_2Cl_2, 25 mL, 25 mmol) was added through a 100 mL dropping funnel to the stirred solution at –55 to –75 °C for 30 min [At the initial addition stage of $SnCl_4$ (ca. 5 mL), the reaction was considerably exothermic. Then, it changed over slightly exothermic stage], and the mixture was stirred at –72 to –75 °C for 30 min. After gradual warming up to 20–25 °C, H_2O (50 mL) was added to the mixture, which was moved into a 500 mL separatory funnel. The mixture was extracted with EtOAc (100 mL). The organic phase was separated and the aqueous phase was re-extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with water (50 mL) and brine (50 mL), dried, and concentrated. The obtained crude solid (7.03 g) was purified by recrystallization from hexane/2-propanol (2:1; 27 mL) to give the desired first-crop product **3**; yield: 4.67 g (70%) (q ^{1}H NMR purity: 98%). The mother liquid was concentrated to give crude solid, which was recrystallized with hexane/2-propanol (2:1; 4 mL) to give the desired second-crop of product **3** (q ^{1}H NMR purity: 94%); yield: 0.84 g (13%); colorless crystals; mp 110–111 °C.

Comparable temperature varying experiments were as follows: 78% ^{1}H NMR yield at 0 °C and 89% ^{1}H NMR yield at –20 °C. This result means this reaction is sufficiently robust for temperature change.

IR (neat): 3063, 1584, 1501, 1441, 1379, 1329, 1155 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.18 (s, 3 H), 2.62 (s, 3 H), 7.21–7.24 (m, 2 H), 7.29–7.33 (m, 2 H), 7.42–7.46 (m, 1 H), 7.47–7.52 (m, 3 H), 8.31 (d, *J* = 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.0, 18.9, 124.4, 125.5, 125.9, 126.7, 127.1, 128.4 (2 C), 129.4, 130.2 (2 C), 130.5, 132.4, 133.2, 133.7, 137.4, 140.0.

HRMS (DART): *m*/*z* calcd for $C_{18}H_{15}Cl$ [M + H]$^+$: 267.0941; found: 267.0952.

2,3-Bis(bromomethyl)-1-chloro-4-phenylnaphthalene (4)

A mixture of naphthalene **3** (1.33 g, 5.0 mmol), NBS (1.96 g, 11.0 mmol), and AIBN (82 mg, 0.5 mmol) in CCl_4 (10 mL) was refluxed for 1 h. After cooling down, H_2O was added to the mixture, which was extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with aq 1 M HCl, H_2O and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid was washed with hexane/Et_2O (1:1; 5 mL) to give the desired product **4**; yield: 1.85 g (87%); colorless crystals; mp 150–154 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.59 (s, 2 H), 5.16 (s, 2 H), 7.32–7.47 (m, 4 H), 7.50–7.57 (m, 3 H), 7.59–7.63 (m, 1 H), 8.38–8.40 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.2, 29.5, 125.1, 127.67, 127.71, 128.0, 128.2, 128.5 (2 C), 129.8 (2 C), 130.8, 131.5, 132.1, 133.7, 137.0, 140.7.

(1-Chloro-4-phenylnaphthalene-2,3-diyl)dimethanol (5)

A mixture of naphthalene **4** (1.27 g, 3.0 mmol) and KOAc (1.18 g, 12.0 mmol) in DMF (12 mL) was stirred at rt for 2 h. A solution of KOH (1.01 g, 18.0 mmol) in H_2O (6.0 mL) and MeOH (12 mL) were added to the stirred mixture at 20–25 °C, and the mixture was stirred at the same temperature for 2 h. Aq 1 M HCl was added to the mixture, which was extracted with Et_2O (2 × 50 mL). The combined organic phases were washed with H_2O (3 ×) and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid was washed by hexane to give desired product **5**; yield: 817 mg (91%); colorless crystals; mp 151–153 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.63 (br s, 1 H), 2.95 (br s, 1 H), 4.69 (s, 2 H), 5.28 (s, 2 H), 7.29–7.32 (m, 2 H), 7.39–7.44 (m, 2 H), 7.47–7.53 (m, 3 H), 7.59–7.62 (m, 1 H), 8.42–8.43 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 60.8, 61.1, 125.1, 126.9, 127.3, 127.6, 127.7, 128.3 (2 C), 130.2 (2 C), 130.4, 132.3, 133.5, 134.5, 135.5, 138.0, 139.5.

HRMS: *m*/*z* calcd for $C_{18}H_{15}ClO_2$ [M + H]$^+$: 298.1551; found: 298.1547.

Dimethyl 4-Chloro-9-phenyl-1,3-dihydro-2*H*-cyclopenta[*b*]naphthalene-2,2-dicarboxylate (6)

A mixture of naphthalene **4** (425 mg, 1.00 mmol), dimethyl malonate (132 mg, 1.00 mmol), K_2CO_3 (276 mg, 1.00 mmol) in MeCN (10 mL) was stirred at reflux for 14 h. After cooling down, the mixture was filtered through a Celite pad, and the obtained filtrate was concentrated. The obtained crude oil was purified by silica gel column chromatography (hexane/EtOAc 10:1) to give the desired product **6**; yield: 202 mg (51%); paled yellow crystals; mp 129–131 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.53 (s, 2 H), 3.74 (s, 6 H), 3.89 (s, 2 H), 7.32–7.34 (m, 2 H), 7.36–7.39 (m, 1 H), 7.43–7.47 (m, 1 H), 7.49–7.54 (m, 2 H), 8.26–8.28 (m, 1 H),

^{13}C NMR (125 MHz, $CDCl_3$): δ = 40.5, 40.8, 53.0 (2 C), 59.5, 123.7, 126.0, 126.2 (2 C), 127.6, 128.6 (2 C), 129.8 (2 C), 130.5, 133.3, 134.1, 136.5, 137.5, 137.9, 171.6.

HRMS: *m*/*z* calcd for $C_{23}H_{19}ClO_4$ [M + H]$^+$: 394.1762; found: 394.1766.

1-(4-Methoxyphenyl)-2,3-dimethyl-4-phenylnaphthalene (7)

A mixture of naphthalene **3** (134 mg, 0.50 mmol), *p*-$MeOC_6H_4B(OH)_2$ (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) in toluene (1.0 mL) was stirred at 80–85 °C for 2 h. After cooling down, H_2O was added to the mixture, which was extracted with EtOAc (2 × 20 mL). The combined organic phases were washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The obtained crude solid were purified by silica gel column chromatography (hexane/EtOAc 30:1) to give the desired product **7**; yield: 156 mg (92%); colorless crystals; mp 167–168 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 2.21 (s, 3 H), 3.92 (s, 3 H), 7.05–7.07 (m, 2 H), 7.22–7.44 (m, 4 H), 7.31–7.32 (m, 3 H), 7.38–7.40 (m, 1 H), 7.43–7.47 (m, 1 H), 7.50–7.53 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.48, 18.51, 55.3, 113.8 (2 C), 124.6 (2 C), 126.3, 126.4, 126.9, 128.3 (2 C), 130.3 (2 C), 131.4 (3 C), 131.7, 132.9, 133.0, 133.4, 137.6, 137.8, 140.8, 158.5.

HRMS: *m*/*z* calcd for $C_{25}H_{22}O$ [M + H]$^+$: 338. 2461; found: 338.2457.

2,3-Dimethyl-4-phenyl-1-(*p*-tolyamino)naphthalene (8)

$PhNH_2$ (47 mg, 0.5 mmol), K_2CO_3 (138 mg, 1.0 mmol), $Pd_2(dba)_3$ (9 mg, 0.01 mmol), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos) (16 mg, 0.03 mmol) were successively added to a stirred suspension of naphthalene **3** (133 mg, 0.5 mmol) in *t*BuOH (1.0 mL) at 20–25 °C under argon atmosphere, and the mixture was stirred at 85–90 °C for 14 h. H_2O was added to the mixture, which was extracted with EtOAc (2 × 30 mL). The combined organic phases were washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The

obtained crude solid was purified by silica gel column chromatography (hexane/EtOAc 30:1) to give the desired product **8**; yield: 148 mg (91%); pale yellow crystals; mp 143–145 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 2.40 (s, 3 H), 5.62 (s, 1 H), 6.58–6.59 (m, 2 H), 6.74–6.77 (m, 1 H), 7.15–7.19 (m, 2 H), 7.27–7.30 (m, 3 H), 7.33–7.36 (m, 2 H), 7.43–7.47 (m, 1 H), 7.50–7.53 (m, 2 H), 8.00–8.01 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.6, 18.6, 113.4 (2 C), 117.95, 123.2, 125.1, 125.2, 126.8, 126.9, 128.4 (2 C), 129.3 (2 C), 130.0, 130.3 (2 C), 132.4, 133.4, 133.5, 133.7, 137.1, 140.5, 147.4.

HRMS: *m*/*z* calcd for $C_{24}H_{21}N$ [M + H]$^+$: 323.2464; found: 323.2467.

2,3-Dimethyl-4-phenylnaphthalen-1-ol (9)

A mixture of naphthalene **3** (133 mg, 0.50 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.01 mmol), *t*Bu-XPhos (17 mg, 0.04 mmol), and KOH (140 mg, 2.50 mmol) in 1,4-dioxane (0.50 mL) and H_2O (0.50 mL) was stirred at 95–100 °C for 14 h. After cooling down, aq 1 M HCl was added to the mixture, which was extracted with EtOAc (2 × 20 mL). The combined organic phases were washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The obtained crude crystals were purified by silica gel column chromatography (hexane/EtOAc 5:1) to give the desired product **9**; yield: 121 mg (98%); colorless crystals: mp 93–94 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.16 (s, 3 H), 2.40 (s, 3 H), 5.19 (s, 1 H), 7.23–7.25 (m, 2 H), 7.27–7.30 (m, 2 H), 7.38–7.43 (m, 2 H), 7.46–7.49 (m, 2 H), 8.10–8.12 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.5, 18.3, 116.7, 120.6, 122.7, 124.3, 125.2, 126.3, 126.7, 128.2 (2 C), 130.8 (2 C), 1315, 132.1, 133.4.

HRMS: *m*/*z* calcd for $C_{18}H_{16}O$ [M + H]$^+$: 248.1280; found: 248.1277.

Funding Information

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).

Acknowledgment

One of the author (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.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1706471.

References

(1) (a) Döts, K. H. *Angew. Chem. Int. Ed.* **1975**, *14*, 644. (b) Döts, K. H. *Pure Appl. Chem.* **1983**, *55*, 1689. (c) Timko, J. M.; Yamashita, A. *Org. Synth.* **1993**, *71*, 72.
(2) Danheiser, L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093.
(3) Viswanathan, G. S.; Wang, M.; Li, C-J. *Angew. Chem. Int. Ed.* **2002**, *41*, 2138.
(4) Kabalka, G. W.; Ju, Y.; Wu, Z. *J. Org. Chem.* **2003**, *68*, 7915.
(5) Ilies, L.; Matsumoto, A.; Kobayashi, M.; Yoshikai, N.; Nakamura, E. *Synlett* **2012**, *23*, 2381.
(6) Ponra, S.; Vitale, M. R.; Michelet, V.; Ratovelomanana-Vital, V. *J. Org. Chem.* **2015**, *80*, 3250.
(7) Recchi, A. M. S.; Back, D. F.; Zeni, G. *J. Org. Chem.* **2017**, *82*, 2713.
(8) (a) Fedorynski, M. *Chem. Rev.* **2003**, *103*, 1099. (b) Thankachan, A. P.; Shndhu, K. S.; Krishnan, K. K.; Anilkumar, G. *Org. Biomol. Chem.* **2015**, *13*, 8780.
(9) Sigma-Aldrich Catalogue No. 35934.
(10) (a) Seko, S.; Tanabe, Y.; Suzukamo, G. *Tetrahedron Lett.* **1990**, *31*, 6883. (b) Tanabe, Y.; Seko, S.; Nishii, Y.; Yoshida, T.; Utsumi, N.; Suzukamo, G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2157.
(11) Nishii, Y.; Yoshida, T.; Asano, H.; Wakasugi, K.; Morita, J.; Aso, Y.; Yoshida, E.; Motoyoshiya, J.; Aoyama, H.; Tanabe, Y. *J. Org. Chem.* **2005**, *70*, 2667.
(12) Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 10694.
(13) Wada, K.; Munakata, K. *Tetrahedron Lett.* **1970**, 2017.
(14) Lin, T.-Y.; Lo, T.-B.; Wang, K. T.; Weinstein, B. *Tetrahedron Lett.* **1967**, 849.
(15) (a) Newmann, D. J.; Cragg, G. M. *J. Nat. Prod.* **2007**, *70*, 461. (b) Kumar, K.; Waldmann, H. *Angew. Chem. Int. Ed.* **2009**, *48*, 3224. (c) Zhao, C.; Rakesh, K. P.; Mumtaz, S.; Moku, B.; Asiri, A. M.; Marwani, H. M.; Manukumar, H. M.; Qin, H. *RSC Adv.* **2018**, *8*, 9487.
(16) Nishii, Y.; Wakasugi, K.; Koga, K.; Tanabe, Y. *J. Am. Chem. Soc.* **2004**, *126*, 5358.
(17) Seko, S. *Japan Kokai Tokkyo Koho*. 1994271484, **1994**.
(18) (a) Nishii, Y. *J. Synth. Org. Jpn.* **2015**, *73*, 701. (b) Nishii, Y. *J. Synth. Org. Jpn.* **2018**, *76*, 922.