Ipso-Type Regiocontrolled Benzannulation for the Synthesis of Uniquely Substituted α-Arylnaphthalenes: Application to the First Total Synthesis of Chaihunaphthone

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ABSTRACT: A distinctive method for synthesizing a variety of multisubstituted α-arylnaphthalenes utilizing novel regiocontrolled ipso-type [4 + 2] benzannulation is presented. Ortho- and para-substituted 1-Ar1−1-Ar2−2,2-dichlorocyclopropylmethanols (AACM) were transformed to the corresponding ipso-type α-arylnaphthalenes. (i) The reaction of ortho-AACM using TiCl4 or SnCl4 (1.0 equiv) proceeded smoothly to afford ipso-type α-arylnaphthalenes (seven examples; 49–69% yield) exclusively, without producing conventional benzannulation isomers. (ii) Para-AACM also underwent the reaction successfully to afford the desired ipso-type α-arylnaphthalenes (14 examples; 39–98% yield) without producing conventional benzannulation isomers. (iii) In contrast, meta-AACM underwent the previously reported conventional benzannulation. (iv) The present method exhibited sufficient substrate generality for application to ortho- and para-substituted AACM substrates bearing Me-, Cl-, and MeO- groups. (v) The six key structures were unambiguously confirmed by X-ray structure analyses. (vi) A plausible reaction mechanism for the present ipso-type reaction is proposed and supported by three careful cross-over and comparable experiments. To demonstrate the utility of the present reaction, we achieved the first total synthesis of chaihunaphthone, a uniquely (highly congested) substituted and less accessible natural lignan lactone with three contiguous trimethoxy substituents (total eight steps, overall 6.4% yield).

INTRODUCTION

Highly substituted α-arylnaphthalenes have useful applications as reagents, catalysts, biologically active natural products, pharmaceuticals, and functionalized materials because of their core structural scaffolds. Regiocontrolled benzannulation strategies provide distinctive constructions for elaborated α-arylnaphthalenes. Among these strategies, regioselective reactions starting from accessible monofunctionalized benzene substrates have a diverse synthetic scope for multisubstituted naphthalene derivatives.

Fischer carbene complex-mediated Döts benzannulation and α-diazoketone-mediated Danheiser benzannulation are two pioneering [4 + 2] annulation methods. Since the development of these innovative studies, several [4 + 2] approaches starting from multifunctionalized benzenes have been reported to date. Five representative benzannulations involve the appropriate alkyne segments for the construction of multisubstituted naphthalenes: (i) GaCl4-catalyzed aldehyde−alkyne condensation, (ii) TiCl4-promoted aldehyde−alkyne condensation, (iii) iron-catalyzed Grignard coupling with two symmetrical alkynes, (iv) Tf2NH-catalyzed aldehyde−arylated alkyne condensation, and (v) FeCl3-promoted condensation of alkynyl alcohols concomitant with selenylation.

The present article discloses distinctive ipso-type benzannulations for the syntheses of a variety of uniquely substituted and much less accessible α-arylnaphthalenes. Fedorynski and Anilkumar’s group provided impressive and comprehensive reviews of the synthetic application of gem-dihalocyclopropanes. Consistent with our longstanding synthetic studies of regio- and stereoselective gem-dihalocyclopropane transformations, related drug discovery and process studies of chiral cyclopropane pyrethroid insecticides, and recent total syntheses of all six chiral natural pyrethrins, we previously reported a couple of benzannulation methods.

The first-stage non-regiocontrolled [4 + 2] benzannulation using (Ar)(Ar)(2,2-dichlorocyclopropyl)methanols (AACM-I) produced symmetrically substituted α-arylnaphthalenes, including natural lignan lactones, such as justicidin E and taiwanin C. One representative non-regiocontrolled benzannulation...
nulation method using an AACM-I was the subject of a practical Gram-scale synthetic procedure.14 The second-stage regiocontrolled [4 + 2] benzannulation strategy using (Ar1)(Ar2)(2,2-dichlorocyclopropyl)methanols (AACM-II) produced various unsymmetrically substituted α-arylnaphthalenes. This strategy was successfully applied for total syntheses of unsymmetrically substituted natural lignan lactones, such as justicidin B, retrojusticidin B, and dehydrodesoxypodophyllotoxin.11e In addition, chirality exchange [4 + 2] benzannulation using optically active AACM-II was achieved to produce axially chiral α-arylnaphthalenes with a nearly complete transfer of chirality.11d

During the course of our investigations, we recently encountered a unique and unusual mode of benzannulation, in which ortho- and para-substituted (Cl-, Me-, and MeO-) and stereodefined AACM-II 1 and 3 consistently underwent ipso-type reactions to furnish a variety of isomeric α-arylnaphthalenes 4 and 5, respectively, which were not produced by hitherto-reported conventional reactions even under the same reaction conditions, as illustrated in Scheme 3. The ortho-form AACM-II 1 produced 4-chloro-5-substituted 1-phenylnaphthalene 4 instead of 4-chloro-8-substituted 1-arylnaphthalene 6 via the expected conventional benzannulation. However, benzannulation using the meta-form AACM-II 2 proceeded in the usual manner to afford 4-chloro-7-substituted 1-arylnaphthalene 5. The para-form AACM-II 3 underwent ipso-type benzannulation to produce 4-chloro-7-substituted 1-arylnaphthalene 5 instead of 4-chloro-6-sub-
sttuted 1-arylnaphthalene 7 via the expected conventional reaction pathway.

The present eventful mode involves wide substrate generality as described in the Results and Discussion section.

Application of the present ipso-type benzannulation to the first total synthesis of chaihunaphthone, an unsymmetrically substituted lignan lactone, is demonstrated.

## RESULTS AND DISCUSSION

### 1. Basic Investigation of Ipso-Type Regiocontrolled Benzannulations

Stereodefined AACM-II 1 and 1 (ortho-form), 2 (meta-form), and 3 (para-form) were readily prepared through sequential introductions of Ar1 and Ar2 groups by basically following the reported method11d,e (Scheme 4). The reaction of accessible cyclopropanecarbonyl chlorides 9 (derived from the commercially available acid) and 10 (derived from methyl angelate) with Ar1MgBr afforded the corresponding Ar1-substituted ketones 11 and 12, respectively, in good yield (Table 1). Subsequent addition to ketones 11 and 12 using Ar2Li reagents furnished a variety of stereodefined AACM-II 1 and 3 in an acceptable yield with excellent diastereoselectivity (>95:5) by way of Cram’s rule11d,e (Table 2). The addition reaction using ketones 11 afforded a wide variety of Ar1-AACM-II 1 and 3 in moderate to high yields. However, ketones 12 smoothly underwent the addition reaction using para-substituted Ar2Li, resulting in a good yield, but ortho-substituted Ar2Li resisted the desired addition (no reaction), probably because of the high stereocongestion.

[Scheme 4. Preparation of Stereodefined AACM-II 1-3]

Key regiocontrolled and ipso-type regiocontrolled benzannulations using AACM-II 1 (ortho-form) and AACM-II 3 (para-form) were successfully performed (Tables 3 and 4) with the following salient features. (i) The reaction of AACM-II 1 using TiCl4 (1.0 equiv) or SnCl4 (1.0 equiv) proceeded smoothly to produce ipso-type products 4 with nearly exclusive regioselectivity (seven examples; 49−69% yield) (Table 3); compounds 6 were not detected following the conventional benzannulation. (ii) AACM-II 3 also underwent the reaction successfully to produce the desired compounds 5 (14 examples; 39−98% yield) (Table 4); compounds 7 were not detected following the conventional benzannulation. (iii) The present method was consistently applied to 1 and 3 bearing Me−, Cl−, and MeO− groups. No specific correlation of either the reactivity or the yield between EDG (Me− and MeO−) or EWG (Cl−) groups in Ar1 or Ar2 was observed, consistent with the reported the conventional benzannulation reactions. However, 3,4-dimethoxyphenyl substrate requires high dilution technique probably because of the high reactivity (vide infra).

Two separate and independent reactions for ipso-type and conventional benzannulations using AACM-II 3c and 3m support and justify our proposed hypothesis and aforementioned results, in which the same product 5c was obtained with high regioselectivity (Scheme 5).

[Table 1. Preparation of Ketones 11 and 12]

Notably, even (Ar)(2,2-dichlorocyclopropyl)methanols 13 and 16 smoothly underwent a similar ipso-type benzannulation to furnish naphthalenes 14 and 17, respectively, with excellent ipso-regioselectivity (Scheme 6).

To support the ipso-type benzannulation pathway (vide infra, Plausible Reaction Mechanism for Ipso-Type and Regiocontrolled Benzannulations section), a controlled reaction was examined using (2,2-dichlorocyclopropyl)(2,4,6-trimethoxyphenyl)methanol 19, which was readily prepared from 9 by AlCl3-catalyzed Friedel–Crafts acylation and LAH...
reduction sequence (Scheme 7). The reaction of 19 under identical conditions produced the expected spiro compound 20 successfully in 70% yield.

2. Plausible Reaction Mechanism for *Ipso*-Type and Regiocontrolled Benzannulations. Similarly to the reported conventional benzannulations,11b11e the treatment of ortho-form AACM-II 1 with SnCl₄ affords dichloromethinium cation A, which in turn forms key benzenonium cationic intermediate B by the *ipso*-type mode through 1,5-cyclization (Scheme 8). Reactive dotted carbons adjacent to the R₂ position are indicated. In contrast to the conventional benzannulations, *ortho* - or *para*-orientation of the R₂ substituents contributes to this 1,5-cyclization. Cation B reversibly converts to relatively stable tricyclic carbenium.

Table 2. Preparation of Stereodefined AACM-II 1 and 3

|   | Yield / % |
|---|-----------|
| 11: R₁ = H | 84        |
| 12: R₁ = Me| 51        |
| 13: R₂ = Me| 67        |
| 1d: R₂ = Me| 81        |
| 1e: R₂ = Me| 45        |
| 1f: R₂ = Me| 82        |
| 1g: R₂ = Me| 79        |
| 3a: R₂ = Me| 81        |
| 3b: R₂ = Me| 71        |
| 3c: R₂ = Me| 69        |
| 3d: R₂ = Me| 89        |
| 3e: R₂ = Me| 64        |
| 3f: R₂ = Me| 80        |
| 3g: R₂ = Me| 54        |
| 3h: R₂ = Me| 84        |
| 3i: R₂ = Me| 96        |
| 3j: R₂ = Me| 53        |
| 3k: R₂ = Me| 79        |
| 3l: R₂ = Me| 47        |

“2.2 Equiv of Ar²Li was used. *b*2-Me THF solvent was used instead of THF. *c*Prepared by an alternative reported method as described in the experimental section.

Table 3. *Ipso*-Type Regiocontrolled Benzannulations Using AACM-II 1 (*ortho*-Form)

|   | Yield / % |
|---|-----------|
| 4a: R₂ = Me | 66        |
| 4b: R₂ = Me | 69        |
| 4c: R₂ = Me | 56        |
| 4d: R₂ = Me | 51        |
| 4e: R₂ = Me | 68        |
| 4f: R₂ = Me | 49        |
| 4g: R₂ = Me | 53        |

“SnCl₄ was used instead of TiCl₄.
intermediate C, which immediately rearranges into more stable cation D by ring fission in a cyclopropane moiety. Finally, α-arylnaphthalenes 4 are produced by aromatization with the elimination of HCl.

Table 4. Ipso-Type Regiocontrolled Benzannulations Using AACM-II 3 (para-Form)

| R1 | R2 | Ipso-type Benzannulation | Conventional Benzannulation |
|----|----|--------------------------|-----------------------------|
| Ph | Cl | ![Reaction Diagram](image1) | ![Reaction Diagram](image2) |
| ![Product Image](image3) | 5a: 53 |
| ![Product Image](image4) | 5b: 64 |
| ![Product Image](image5) | 5c: 57% |
| ![Product Image](image6) | 5d: 64 |
| ![Product Image](image7) | 5e: 61% |
| ![Product Image](image8) | 5f: 39 |
| ![Product Image](image9) | 5g: 53 |
| ![Product Image](image10) | 5h: 88 |
| ![Product Image](image11) | 5i: 51 |
| ![Product Image](image12) | 5j: 98 |
| ![Product Image](image13) | 5k: 96 |
| ![Product Image](image14) | 5l: 95 |
| ![Product Image](image15) | 5m: 78 |
| ![Product Image](image16) | 5n: 76 |

“SnCl₄ was used instead of TiCl₄ in high dilution conditions.

Scheme 5. Two Separate and Independent Reactions for Ipso-Type and Conventional Benzannulation

Scheme 6. Ipso-Type Benzannulations Using (Ar)(2,2-Dichlorocyclopropyl)methanols

Scheme 7. Ipso-Type Reaction Using (2,4,6-Trimethoxyphenyl)methanol Substrate
A similar transformation mechanism for para-form AACM-II 3 is depicted involving the sequence of cationic intermediates A′, B′, C′, and D′ for the production of α-arylnaphthalenes 5. Notably, α-arylnaphthalenes 5 were the very same products derived from meta-form AACM-II 2 through conventional benzannulation.

3. X-ray Determination of the Structure of Six Representative α-Arylnaphthalenes. X-ray structure analyses of six key α-arylnaphthalenes bearing ortho-Me, MeO, and Cl groups, and para-Me, MeO, and Cl groups were performed to unambiguously confirm the structure. Figure 1 shows the resultant structures of α-arylnaphthalenes 4a, 4b, 4c, 5a′ (brominated compound derived from 5a), 5b′ (brominated compound derived from 5b), and 5c. Conformations around the axial moiety are in good accordance with that of the X-ray structure of the reported compound.11b

4. First Total Synthesis of Chaihunaphthone, an Unsymmetrically Substituted Lignan Lactone. Natural arylnaphthalene lactones and their analogues have attracted considerable attention because of their characteristic structures and biologic activities.2 The total synthesis of unsymmetrically substituted compounds of β-alkoxy-substituted arylnaphthalene lignan lactones, such as symmetrically substituted helioxanthin and diphiline, is quite limited because of their structural complexity. With this background, we next focused our attention on the total synthesis of chaihunaphthone, a natural lignan lactone, as a distinctive application for the present ipso-type benzannulation (Scheme 9).

Figure 1. X-ray structures of six key α-arylnaphthalenes.
Chaihunaphthone, isolated from the root of *Bupleurum scorzonerifolium* (Nan-Chai-Hu), exhibits immunosuppressive effects and a uniquely (highly congested) substituted α-arylnaphthalene structure. Following a reaction similar to that shown in Scheme 4, 3,4-methylenedioxyphenylmagnesium bromide was coupled with acid chloride 10 to afford aryl cyclopropyl ketone 21 in 94% yield. An addition reaction of 3,4,5-trimethoxyphenyllithium to 21 led to AACM-II 22 in 66% yield with excellent stereoselectivity. The key ipso-type benzannulation using 22 was successfully implemented using SnCl₄ to produce the desired α-arylnaphthalene 23 in 60% yield with excellent regioselectivity. Notably, undesirable regioisomer 23’ was not detected following the conventional benzannulation; the orientation effect of the mono para-MeO group toward the ipso-type benzannulation absolutely predominated over that of the two reactive meta-MeO groups toward the conventional benzannulation. Traditional dibromination using 23¹¹ yielded the desired product 24, including small amounts of poly brominated byproducts because of highly reactive aromatic rings. Without any purification, the crude mixture of 24 was treated successively with KOAc and KOH to yield the diol mixture 25. Mild but powerful SmI₂-mediated debromination¹⁷ of the mixture 25 furnished precursor 26 in a pure form with 21% yield from 22 in three steps.

Final oxidation by Fetizon’s reagent¹⁸ produced chaihunaphthone in 72% yield (total 6.4% yield from 10). The melting point and spectroscopic data (¹H NMR, ¹³C NMR, and HRMS) of this synthetic specimen reasonably matched with those of the reported natural product.¹⁵ To the best of our knowledge, this is the first example of the total synthesis of a stereocongested and less accessible 6,7,8-trimethoxy-substituted natural lignan lactone. We speculate that the previously reported methodologies are not capable of concise and straightforward synthesis of β-alkoxy-type lignan lactones.

**CONCLUSIONS**

We achieved a regiocontrolled ipso-type benzannulation to produce a variety of unique and multisubstituted α-arylnaphthalenes. The reaction mode apparently differs from the reported conventional benzannulation mode; ortho- and para-substituted 1,1-diaryl-2,2-dichlorocyclopropylmethanols (AACM) were transformed to the corresponding ipso-type α-arylnaphthalenes, whereas the meta-substituted AACM underwent the reaction in the expected conventional manner. The structure of six multisubstituted representative α-arylnaphthalenes derived from three ortho-substituted AACM and three para-substituted AACM was unambiguously established by X-ray analyses.

We present a plausible mechanism supported by three careful cross-over experiments using AACM and monosubstituted substrates. To demonstrate the utility of the present reaction, we achieved the first total synthesis of chaihunaphthone, a stereocongested and less accessible natural lignan lactone with three contiguous trimethoxy substituents.

The present methodology provides diverse syntheses for multisubstituted and less accessible arylnaphthalenes. Further investigation of the asymmetric versions of benzannulation using chiral AACM is currently in progress.

**EXPERIMENTAL SECTION**

Methyl (S*)-2,2-Dichloro-1-methylcyclopropane-1-carboxylate.¹⁰b

Commercially available. Colorless oil; bp 63–65 °C/10.5 mmHg; ¹H NMR (500 MHz, CDCl₃): δ = 1.43 (d, J = 7.5 Hz, 1H), 1.59 (s, 3H), 2.28 (d, J = 7.5 Hz, 1H), 3.78 (s, 3H). ¹³C (¹H) NMR (125 MHz, CDCl₃): δ = 18.1, 30.8, 35.3, 52.6, 62.5, 169.5.
Methyl (15S,35S)-2,2-Dichloro-1,3-dimethylcyclopropane-1-carboxylate. 10b, 13

A 16.5 g scale practical preparation: ref 13. Colorless oil; bp 65–66 °C/7.5 mmHg. 1H NMR (500 MHz, CDCl3): δ = 1.41 (d, J = 6.9 Hz, 3H), 1.55 (q, J = 6.9 Hz, 1H), 1.57 (s, 3H), 3.74 (s, 3H). 13C{1H} NMR (125 MHz, CDCl3): δ = 10.8, 21.1, 36.0, 36.8, 52.1, 67.6, 168.9.

(5S)-2,2-Dichloro-1-methylcyclopropane-1-carboxylic acid. 11b

Colorless crystals; mp 65–66 °C. 1H NMR (500 MHz, CDCl3): δ = 1.47 (d, J = 7.3 Hz, 1H), 1.62 (s, 3H), 2.29 (d, J = 7.3 Hz, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 10.7, 31.2, 35.1, 62.6, 175.3.

(15S,35S)-2,2-Dichloro-1,3-dimethylcyclopropane-1-carboxylic acid. 11c

Colorless crystals; mp 95–96 °C. 1H NMR (500 MHz, CDCl3): δ = 1.43 (d, J = 6.9 Hz, 3H), 1.61 (q, J = 6.9 Hz, 1H), 1.62 (s, 3H). 13C{1H} NMR (125 MHz, CDCl3): δ = 10.7, 21.1, 36.0, 36.8, 67.9, 175.2.

(5S)-2,2-Dichloro-1-methylcyclopropane-1-carboxyl chloride (9). 11b

Colorless oil; bp 56–57 °C/10.5 mmHg. 1H NMR (500 MHz, CDCl3): δ = 1.62 (d, J = 7.6 Hz, 1H), 1.75 (s, 3H), 2.37 (d, J = 7.6 Hz, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 19.3, 32.4, 43.7, 61.8, 171.3.

(5S)-2,2-Dichloro-1-methylcyclopropane-1-carboxyl chloride (10). 11e

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.43 (d, J = 6.9 Hz, 3H), 1.74 (q, J = 6.9 Hz, 1H), 1.75 (s, 3H). 13C{1H} NMR (125 MHz, CDCl3): δ = 11.2, 21.3, 33.7, 45.3, 66.7, 168.9.

(5S)-2,2-Dichloro-1-methylcyclopropyl(phenyl)methane (11a). 11b

An improved procedure for the reported method (73%). 10e A solution of acid chloride 9 (1.87 g, 10 mmol) in THF (10 mL) was added to a stirred solution of PhMgBr generated from Mg (292 mg, 12.0 mmol) and bromobenzene (1.88 g, 12.0 mmol) in THF (10 mL) at 0–5 °C, and the mixture was stirred at the same temperature for 1 h and then warmed up to 20–25 °C for ca. 30 min. Sat. NH4Cl aqueous solution was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude oil was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 11a (2.19 g, 96%).

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.49 (d, J = 7.5 Hz, 1H), 1.65 (s, 3H), 2.30 (d, J = 7.5 Hz, 1H), 7.52–7.57 (m, 2H), 7.60–7.64 (m, 1H), 7.94–7.98 (m, 2H). 13C{1H} NMR (125 MHz, CDCl3): δ = 20.7, 29.5, 39.7, 62.4, 128.7 (2C), 129.6 (2C), 133.4, 134.4, 195.4.

(5S)-2,2-Dichloro-1-methylcyclopropyl(o-tolyl)methane (11b). 11d

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.45 (d, J = 7.5 Hz, 1H), 1.54 (s, 3H), 2.43 (d, J = 7.5 Hz, 1H), 2.52 (s, 3H), 7.29–7.31 (m, 1H), 7.34–7.38 (m, 1H), 7.41–7.44 (m, 1H), 7.68–7.70 (m, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 20.4, 20.9, 29.4, 40.7, 63.3, 125.8, 129.8, 131.7, 132.0, 134.6, 139.6, 197.4.

(5S)-2,2-Dichloro-1-methylcyclopropyl(2-chlorophenyl)methane (11c). 11d

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.51 (d, J = 7.45 Hz, 1H), 1.57 (s, 3H), 2.49 (d, J = 7.45 Hz, 1H). 7.38–7.44 (m, 2H). 7.45–7.48 (m, 1H), 7.55–7.57 (m, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 19.3, 30.4, 40.6, 64.1, 72.7, 130.0, 130.7, 132.0, 132.1, 136.4, 196.2.

(5S)-2,2-Dichloro-1-methylcyclopropyl(2-methoxyphenyl)methane (11d). 11d

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.38 (d, J = 7.5 Hz, 1H), 1.56 (s, 3H), 2.43 (d, J = 7.5 Hz, 1H), 4.01 (s, 3H), 7.00–7.07 (m, 2H), 7.51–7.55 (m, 1H), 7.72–7.74 (m, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 18.9, 30.0, 41.7, 55.7, 64.8, 111.5, 120.7, 125.9, 131.4, 134.2, 158.4, 195.8.

(5S)-2,2-Dichloro-1-methylcyclopropyl(3-methoxyphenyl)methane (11e). 11e

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.49 (d, J = 7.5 Hz, 1H), 1.65 (s, 3H), 2.29 (d, J = 7.5 Hz, 1H), 3.89 (s, 3H), 7.15–7.18 (m, 1H), 7.44–7.48 (m, 2H), 7.54–7.55 (m, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ = 20.8, 29.6, 39.8, 55.4, 62.5, 113.7, 120.1, 122.3, 129.7, 135.8, 159.9, 195.3; IR ( neat): νmax = 3005, 2938, 1686, 1597, 1584, 1427, 1317, 1269, 1242, 1045, 866, 773 cm−1; HRMS (DART): m/z calcd for C12H13Cl2O2 [M + H]+ 259.0293; found: 259.0293.
Following a similar procedure for the preparation of ketone 11a, the reaction using acic chloride 10 (1.23 g, 6.0 mmol), Mg (175 mg, 7.2 mmol), and 2-bromotoluene (1.23 g, 7.2 mmol) in THF (12 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 12b (1.02 g, 66%).

Paled yellow oil; 1H NMR (500 MHz, CDCl3); δ = 1.41 (d, J = 6.9 Hz, 3H), 1.64 (s, 3H), 1.66 (q, J = 6.9 Hz, 1H), 2.56 (s, 3H), 7.45–7.66 (m, 1H), 7.72–7.92 (m, 1H), 1.41–1.47 (m, 1H), 7.83–7.84 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3); δ = 11.7, 22.0, 23.7, 36.0, 40.6, 68.8, 125.8, 131.0, 132.1, 132.4, 134.0, 140.8, 197.4; IR (neat): νmax = 2970, 2931, 1682, 1456, 1306, 1231, 1299, 976, 835, 737 cm⁻¹; HRMS (DART): m/z calcd for C13H15Cl2O2 [M–Cl]⁺ 221.0733; found: 221.0745.

(15*, 35*)-2,2-Dichloro-1,3-dimethylcyclopropyl(o-toly)methanone (12b).

Following a similar procedure for the preparation of ketone 11a, the reaction using acic chloride 10 (1.01 g, 5.0 mmol), Mg (146 mg, 6.0 mmol), and p-bromoanisole (1.12 g, 6.0 mmol) in THF (10 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 12c (1.09 g, 79%).

Colorless oil; 1H NMR (500 MHz, CDCl3); δ = 1.30 (d, J = 6.9 Hz, 3H), 1.59 (q, J = 6.9 Hz, 1H), 1.63 (s, 3H), 4.02 (s, 3H), 6.99–7.03 (m, 2H), 7.50–7.55 (m, 1H), 7.83–7.85 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3); δ = 12.0, 21.6, 36.5, 42.5, 55.8, 70.0, 111.5, 120.6, 126.1, 131.5, 134.7, 159.2, 194.9; IR (neat): νmax = 2984, 2954, 1667, 1612, 1503, 1335, 1267, 1043, 851, 772 cm⁻¹; HRMS (DART): m/z calcd for C13H14Cl2O2 [M + H]⁺ 273.0449; found: 273.0453.

(15*, 35*)-(3-Chlorophenyl)-2,2-dichloro-1,3-dimethylcyclopropylm ethanone (12d).

Following a similar procedure for the preparation of ketone 11a, the reaction using acic chloride 10 (1.61 g, 8.0 mmol), Mg (233 mg, 9.6 mmol), and m-bromochlorobenzene (1.84 g, 9.6 mmol) in THF (16 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 12d (1.78 g, 80%).

Colorless oil; 1H NMR (500 MHz, CDCl3); δ = 1.39 (d, J = 6.9 Hz, 3H), 1.65 (s, 3H), 1.69 (q, J = 6.9 Hz, 1H), 7.46–7.49 (m, 1H), 7.57–7.59 (m, 1H), 7.84–7.86 (m, 1H), 7.94–7.95 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3); δ = 11.6, 22.9, 35.3, 39.5, 67.8, 127.9, 129.4, 130.0, 133.4, 135.0, 136.0, 193.6; IR (neat): νmax = 3069, 2972, 2932, 1686, 1572, 1452, 1420, 1304, 1229, 907, 837, 800, 733 cm⁻¹; HRMS (DART): m/z calcd for C13H13Cl2O [M + H]⁺ 241.0187; found: 241.0188.

(15*, 35*)-2,2-Dichloro-1,3-dimethylcyclopropyl(3-methoxyphenyl)methanone (12e).

Following a similar procedure for the preparation of ketone 11a, the reaction using acid chloride 10 (1.01 g, 5.0 mmol), Mg (146 mg, 6.0 mmol), and m-bromoanisole (1.12 g, 6.0 mmol) in THF (10 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 12e (1.15 g, 84%).

Colorless oil; 1H NMR (500 MHz, CDCl3); δ = 1.40 (d, J = 6.9 Hz, 3H), 1.666 (s, 3H), 1.67 (q, J = 6.9 Hz, 1H), 3.88 (s, 3H), 7.14–7.82 (m, 1H), 7.42–7.45 (m, 1H), 7.51–7.52 (m, 1H), 7.57–7.60 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3); δ = 11.7, 23.3, 35.4, 39.8, 55.4, 68.3, 113.5, 120.4, 122.5, 129.7, 135.8, 159.9, 194.7; IR (neat): νmax = 2933, 1682, 1597, 1306, 1260, 1043, 1001, 839 cm⁻¹; HRMS (DART): m/z calcd for C13H13Cl2O [M + H]⁺ 273.0449; found: 273.0443.

(R*)-{(15*)-2,2-Dichloro-1-methylcyclopropyl[3](o-toly)[phenyl]methylene} (1a).

νBuLi (1.55 M in hexane, 3.94 mL, 6.1 mmol) was added to a stirred solution of 2-bromotoluene (104 mg, 6.10 mmol) in THF (4 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 30 min. A solution of ketone 11a (932 mg, 4.1 mmol) in THF (4 mL) was added to the mixture at −78 °C, followed by stirring at the same temperature for 1 h, then warmed up to 20–25 °C for 1 h. Sat. NH4Cl aqueous solution was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude solid was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 1a (1.10 g, 84%).

Colorless crystals; mp 116–118 °C; 1H NMR (500 MHz, CDCl3); δ = 1.26 (s, 3H), 1.46 (d, J = 7.5 Hz, 1H), 2.40 (s, 3H), 2.51 (d, J = 7.5 Hz, 1H), 2.65 (s, 1H), 6.59–6.70 (m, 1H), 6.92–7.00 (m, 1H), 7.08–7.15 (m, 2H), 7.36–7.45 (m, 3H), 7.50–7.64 (m, 2H); 13C{1H} NMR (125 MHz, CDCl3); δ = 22.9, 24.1, 30.9, 37.0, 67.2, 82.3, 124.9, 127.4 (2C), 127.8 (2C), 128.5 (2C), 130.3, 132.3, 137.0, 144.0, 145.9; IR (neat): νmax = 3566, 3059, 2940, 1485, 1321, 1217, 1086, 722 cm⁻¹; HRMS (DART): m/z calcd for C13H13Cl2O [M + H]⁺ 273.0449; found: 273.0443.
Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11a (1.00 g, 4.36 mmol), nBuLi (1.55 M in hexane, 4.22 mL, 6.54 mmol), and 2-bromo-1-chlorobenzene (1.25 g, 6.54 mmol) in THF (8.72 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 1b (779 mg, 51%).

Colorless crystals; mp 122–124 °C; 1H NMR (500 MHz, CDCl3): δ = 1.32 (s, 3H), 1.49 (d, J = 8.0 Hz, 1H), 2.58 (d, J = 8.0 Hz, 1H), 3.07 (s, 1H), 6.75–7.00 (br s, 1H), 7.08–7.11 (m, 1H), 7.17–7.20 (m, 1H), 7.37–7.41 (m, 2H), 7.43–7.46 (m, 2H), 7.57–7.59 (m, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 23.7, 31.2, 36.8, 67.2, 81.4, 126.2, 128.0 (2C), 128.4 (3C), 128.9, 131.6 (2C), 132.8, 143.0, 144.1; IR (neat): νmax = 3566, 3063, 3001, 1472, 1431, 1339, 1163, 1084, 754, 731, 702 cm⁻¹; HRMS (DART): m/z calcd for C17H16Cl2O [M – OH]⁺: 293.0552; found: 293.0560.

(R*)-[(1S*)-(2,2-Dichloro-1-methylcyclopropyl)](2-methoxyphenyl)(phenyl)methanol (1c).

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11a (687 mg, 3.0 mmol), nBuLi (1.55 M in hexane, 2.45 mmol), and 2-bromoanisole (842 mg, 4.5 mmol) in THF (6.0 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 1c (674 mg, 67%).

Colorless crystals; mp 135–140 °C; 1H NMR (500 MHz, CDCl3): δ = 1.23 (br s, 3H), 1.38 (d, J = 7.5 Hz, 1H), 2.27 (br s, 1H), 3.88 (br s, 3H), 4.82 (br s, 1H), 6.40–6.48 (m, 1H), 6.74–6.82 (m, 1H), 6.94–6.96 (m, 1H), 7.20–7.25 (m, 1H), 7.34–7.42 (m, 3H), 7.53–7.67 (m, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 24.5, 30.1, 36.8, 55.5, 66.7, 81.1, 111.1, 120.6, 127.4 (2C), 128.0 (2C), 128.9 (2C), 130.6, 134.9, 143.7, 156.7; IR (neat): νmax = 3509, 3050, 2941, 1487, 1464, 1234, 1026, 754, 702 cm⁻¹; HRMS (DART): m/z calcd for C16H13Cl2O2 [M – OH]⁺: 319.0665; found: 319.0631.

(S*)-[(1S*)-2,2-Dichloro-1-methylcyclopropyl] [(2-chlorophenyl)(o-toly)]methanol (1d).

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11b (486 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 2.8 mL, 4.4 mmol), and 2-bromo-1-chlorobenzene (957 mg, 5.0 mmol) in THF (2.0 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 1d (573 mg, 81%).

Paled yellow crystals; mp 95–100 °C; 1H NMR (500 MHz, CDCl3): δ = 1.15 (s, 3H), 1.21 (d, J = 7.5 Hz, 1H), 1.97 (s, 3H), 2.52 (d, J = 7.5 Hz, 1H), 2.73 (s, 1H), 6.57–6.59 (m, 1H), 7.11–7.12 (m, 1H), 7.21–7.23 (m, 1H), 7.31–7.33 (m, 2H), 7.37–7.41 (m, 1H), 7.59–7.61 (m, 1H), 7.65–7.67 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 21.1, 21.8, 22.5, 24.1, 27.8, 31.3, 36.5, 39.5, 67.5, 68.6, 79.4, 83.3, 125.6, 127.3, 128.1, 128.3, 128.7, 128.7, 130.8, 132.2, 132.4, 133.4, 139.0, 139.1, 139.2, 140.8, 141.8.

(S*)-[(1S*)-2,2-Dichloro-1-methylcyclopropyl](2-methoxyphenyl)(o-toly)methanol (1e).

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11b (486 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 2-bromoanisole (449 mg, 2.4 mmol) in 2-MeTHF (4.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 1e (314 mg, 45%).

Colorless crystals; mp 122–125 °C; 1H NMR (500 MHz, CDCl3): δ = 1.13 (s, 3H), 1.35 (d, J = 7.5 Hz, 1H), 2.11 (s, 3H), 2.29 (d, J = 7.5 Hz, 1H), 4.00 (s, 3H), 5.12 (s, 1H), 6.47–6.49 (m, 1H), 6.75–6.78 (m, 1H), 6.98–7.00 (m, 1H), 7.21–7.25 (m, 2H), 7.29–7.31 (m, 2H), 7.61–7.63 (m, 3H); 13C{1H} NMR (125 MHz, CDCl3): δ = 22.6, 24.5, 29.5, 36.8, 55.7, 67.0, 82.8, 111.6, 120.8, 124.9, 127.7, 128.5, 128.7, 130.3, 132.7, 132.9, 139.5, 139.7, 156.8; IR (neat): νmax = 3503, 3065, 2941, 1487, 1456, 1385, 1287, 1233, 1028, 754, 733 cm⁻¹; HRMS (DART): m/z calcd for C19H19Cl2O2 [M – OH]⁺: 333.0813; found: 333.0814.

(S*)-[(1S*)-2,2-Dichloro-1-methylcyclopropyl] [(2-chlorophenyl)(o-toly)]methanol (1f).
Following a similar procedure for the preparation of AACC 1a, the reaction using ketone 11a (687 mg, 3.0 mmol), nBuLi (1.55 M in hexane, 2.9 mL, 4.5 mmol), and 4-bromo-1-chlorobenzene (862 mg, 4.5 mmol) in THF (6.0 mL) gave the crude solid, which was purified by SiO$_2$-column chromatography (hexane/AcOEt = 30:1) to give the desired product 3b (906 mg, 89%).

Colorless crystals; mp 105–106 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 1.19$ (s, 3H), 1.28 (d, $J = 7.5$ Hz, 1H), 2.50 (d, $J = 7.5$ Hz, 1H), 2.79 (s, 1H), 3.80 (s, 3H), 6.79–6.82 (m, 2H), 7.07–7.10 (m, 1H), 7.36–7.40 (m, 1H), 7.42–7.45 (m, 2H), 7.52–7.55 (m, 2H); $^{13}$C($^1$H) NMR (125 MHz, CDCl$_3$): $\delta = 23.3, 27.4, 37.2, 67.5, 80.0, 127.7 (2C), 128.3, 128.4 (2C), 129.1 (2C), 129.2 (2C), 133.3, 142.5, 145.0; IR (neat): $\nu_{\text{max}}$ = 3572, 3458, 2999, 2940, 2837, 1489, 1464, 1203, 754 cm$^{-1}$; HRMS (DART): m/z calcld for C$_{17}$H$_{15}$Cl$_3$O, [M − OH]$^+$ 323.0161; found: 323.0164.

$^{(R^*)}$$^{-}$$^{(15^*)}$$^{-}$$^{(2,2-Dichloro-1-methylcyclopropyl)}$$^{(4}$-methoxyphenyl)$^{(phenyl)}$methanol (3c).

Following a similar procedure for the preparation of AACC 1a, the reaction using ketone 11a (687 mg, 3.0 mmol), nBuLi (1.55 M in hexane, 2.9 mL, 4.5 mmol), and p-bromoanisole (842 mg, 4.5 mmol) in THF (6.0 mL) gave the crude oil, which was purified by SiO$_2$-column chromatography (hexane/AcOEt = 30:1) to give the desired product 3c (721 mg, 71%).

Colorless crystals; mp 145–147 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 1.19$ (s, 3H), 1.28 (d, $J = 7.5$ Hz, 1H), 2.50 (d, $J = 7.5$ Hz, 1H), 2.79 (s, 1H), 3.80 (s, 3H), 6.79–6.82 (m, 2H), 7.07–7.10 (m, 2H), 7.36–7.40 (m, 1H), 7.42–7.45 (m, 2H), 7.52–7.55 (m, 2H); $^{13}$C($^1$H) NMR (125 MHz, CDCl$_3$): $\delta = 23.3, 27.4, 37.2, 67.5, 80.1, 128.2 (2C), 128.0 (2C), 128.8 (2C), 129.1 (2C), 138.9, 143.2, 158.7; IR (neat): $\nu_{\text{max}}$ = 3570, 3026, 2943, 1329, 1219, 1163, 1026, 762, 704 cm$^{-1}$; HRMS (DART): m/z calcld for C$_{17}$H$_{15}$Cl$_3$O$_2$, [M − OH]$^+$ 319.0657; found: 319.0654.

$^{(S^*)}$$^{-}$$^{(15^*)}$$^{-}$$^{(2,2-Dichloro-1-methylcyclopropyl)}$$^{(p}$-tolyl)$^{(phenyl)}$methanol (3d).

Following a similar procedure for the preparation of AACC 1a, the reaction using ketone 11a (486 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 2-bromotoluene (471 mg, 3.0 mmol) in 2-MeTHF (4.0 mL) gave the crude oil, which was purified by SiO$_2$-column chromatography (hexane/AcOEt = 50:1) to give the desired product 3d (589 mg, 88%).

Paled yellow oil; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 1.19$ (s, 3H), 1.28 (d, $J = 7.5$ Hz, 1H), 2.50 (d, $J = 7.5$ Hz, 1H), 2.79 (s, 1H), 3.80 (s, 3H), 6.79–6.82 (m, 2H), 7.07–7.10 (m, 2H), 7.36–7.40 (m, 1H), 7.42–7.45 (m, 2H), 7.52–7.55 (m, 2H); $^{13}$C($^1$H) NMR (125 MHz, CDCl$_3$): $\delta = 23.3, 27.4, 37.2, 67.5, 80.1, 128.2 (2C), 128.0 (2C), 128.8 (2C), 129.1 (2C), 138.9, 143.2, 158.7; IR (neat): $\nu_{\text{max}}$ = 3570, 3026, 2943, 1329, 1219, 1163, 1026, 762, 704 cm$^{-1}$; HRMS (DART): m/z calcld for C$_{16}$H$_{13}$Cl$_2$O$_2$, [M − OH]$^+$ 319.0657; found: 319.0654.

$^{(S^*)}$$^{-}$$^{(15^*)}$$^{-}$$^{(2,2-Dichloro-1-methylcyclopropyl)}$$^{(p}$-tolyl)$^{(o}$-tolyl)$^{(methanol (3e).}
Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11c (527 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 4-bromotoluene (513 mg, 3.0 mmol) in 2-MeTHF (4.0 mL) gave the crude oil, which was purified by SiO₂-column chromatography (hexane/AcOEt = 50:1) to give the desired product 3e (597 mg, 84%).

Paled yellow oil; 1H NMR (500 MHz, CDCl₃): δ = 1.12 (s, 3H), 1.22 (d, J = 7.5 Hz, 1H), 2.34 (s, 3H), 2.61 (d, J = 7.5 Hz, 1H), 3.41 (s, 1H), 4.69 (br s, 1H), 6.95 (br s, 1H), 7.19–7.26 (m, 1H), 7.33–7.37 (m, 1H), J = 7.5 Hz, 1H), 7.42–7.39 (m, 2H), 7.58 (br s, 1H), 7.71–7.73 (m, 1H); 13C{1H} NMR (125 MHz, CDCl₃): δ = 21.0, 23.5, 37.9, 54.7, 77.7, 79.8, 125.4, 126.4, 127.1, 127.7, 129.3, 129.5, 130.5, 132.1, 134.8, 136.9, 138.7, 142.3; IR (neat): νmax = 3570, 3003, 2943, 1339, 1042, 908, 756, 737 cm⁻¹; HRMS (DART): m/z calcd for C₁₁H₁₂Cl₂O [M − OH]⁺ 353.0267, found: 353.0252.

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 11e (518 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 1.9 mL, 3.0 mmol), and 4-bromochlorobenzene (574 mg, 3.0 mmol) in 2-MeTHF (4.0 mL) gave the crude solid, which was purified by hexane/propanol (2/1) to give the desired product 3h (558 mg, 75%).

Colorless crystals; mp 155–155 °C; 1H NMR (500 MHz, (CD₃)₂CO): δ = 1.20 (s, 3H), 1.37 (d, J = 7.5 Hz, 1H), 2.52 (d, J = 7.5 Hz, 1H), 3.81 (s, 3H), 4.17 (s, 1H), 6.95–6.97 (m, 1H), 7.08–7.11 (m, 2H), 7.22–7.24 (m, 2H), 7.32–7.38 (m, 3H); 13C{1H} NMR (125 MHz, CDCl₃): δ = 23.4, 27.9, 37.3, 55.3, 67.5, 80.0, 114.1, 114.6, 121.3, 127.7 (2C), 129.1 (2C), 129.3, 133.3, 144.2, 144.9, 159.5; IR (neat): νmax = 3561, 3001, 2940, 1703, 1487, 1254, 1028, 781 cm⁻¹; HRMS (DART): m/z calcd for C₁₈H₁₇Cl₂O₂ [M − OH]⁺ 353.0267, found: 353.0253.

(R*)-{(15S*)-(2,2-Dichloro-1-methylcyclopropyl)(phenyl-1,3-dimethylcyclopropyl)(p-tolyl)(phenyl-1,3-dimethylcyclopropyl)(p-tolyl)(phenyl-1,3-dimethylcyclopropyl)(phenyl-1,3-dimethylcyclopropyl)(p-tolyl) methanol (3i).
Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 12b (514 mg, 2.0 mmol), nBuLi (1.57 M in hexane, 2.8 mL, 4.4 mmol), and 4-bromotoluene (855 mg, 5.0 mmol) in THF (4.0 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane/AcOEt = 200:1) to give the desired product 3j (372 mg, 53%).

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 1.08 (s, 3H), 1.59 (q, J = 6.9 Hz, 1H), 1.66 (d, J = 6.9 Hz, 3H), 3.66 (s, 3H), 4.65 (s, 1H), 6.95–7.65 (m, 8H); 13C{1H} NMR (125 MHz, CDCl3): δ = 11.7, 27.5, 36.6, 37.4, 55.3, 73.5, 82.7, 112.0 (2C), 120.8 (2C), 129.2 (2C), 129.3 (2C), 131.6, 132.6, 146.5, 157.1; IR (neat): νmax = 3526, 2928, 2878, 1684, 1456, 1379, 1032, 968, 903, 812, 760, 733 cm⁻¹; HRMS (DART): m/z calcd for C20H22Cl2O2 [M + OH]⁺ 331.1020; found: 331.1018.

(S*)-(1S*),(1'R*)-2,2-Dichloro-1,3-dimethylcyclopropyl][p-toly] (p-toly)methanol (3j).

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 12c (819 mg, 3.0 mmol), nBuLi (1.55 M in hexane, 2.4 mL, 3.6 mmol), and 4-bromochlorobenzene (862 mg, 4.5 mmol) in THF (6.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 3k (912 mg, 79%).

Colorless crystals; mp 124–128 °C; 1H NMR (500 MHz, CDCl3): δ = 1.08 (s, 3H), 1.59 (q, J = 6.9 Hz, 1H), 1.66 (d, J = 6.9 Hz, 3H), 3.66 (s, 3H), 4.65 (s, 1H), 6.95–7.65 (m, 8H); 13C{1H} NMR (125 MHz, CDCl3): δ = 11.7, 27.5, 36.6, 37.4, 55.3, 73.5, 82.7, 112.0 (2C), 120.8 (2C), 129.2 (2C), 129.3 (2C), 131.6, 132.6, 146.5, 157.1; IR (neat): νmax = 3526, 3001, 2943, 1485, 1385, 1317, 1250, 1026, 910, 779, 762, 737, 704 cm⁻¹; HRMS (DART): m/z calcd for C19H19Cl2O2 [M – OH]⁺ 319.0657; found: 319.0644.

(S*)-(1S*),(1'R*)-2,2-Dichloro-1,3-dimethylcyclopropyl][4-chlorophenyl][2-methoxyphenyl] methanol (3k).

Following a similar procedure for the preparation of AACM 1a, the reaction using ketone 12a (687 mg, 3.0 mmol), nBuLi (1.55 M in hexane, 2.9 mL, 3.6 mmol), and 3-bromoanisole (842 mg, 4.5 mmol) in THF (6.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 3l (834 mg, 83%).

Colorless crystals; mp 90–91 °C; 1H NMR (500 MHz, CDCl3): δ = 1.21 (s, 3H), 1.29 (d, J = 7.5 Hz, 1H), 2.51 (d, J = 7.5 Hz, 3H), 2.79 (s, 1H), 3.76 (s, 3H), 6.70–6.71 (m, 1H), 6.79–6.82 (m, 2H), 7.17–7.20 (m, 1H), 7.36–7.39 (m, 1H), 7.41–7.45 (m, 2H), 7.52–7.55 (m, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 23.4, 27.9, 37.4, 55.4, 67.7, 80.3, 112.2, 114.1, 120.5, 128.1, 128.2 (2C), 128.4, 129.1 (2C), 142.9, 148.1, 150.9; IR (neat): νmax = 3566, 3001, 2943, 1485, 1433, 1317, 1250, 1026, 4910, 779, 762, 737, 704 cm⁻¹; HRMS (DART): m/z calcd for C19H16Cl2O2 [M – OH]⁺ 319.0657; found: 319.0644.

4-Chloro-2,5-dimethyl-1-phenylnapthalene (4a).

Following a similar procedure for the preparation of napthalene 4c, the reaction using AACM 1a (1.07 g, 3.33 mmol) and TiCl4 (1.0 M in CH2Cl2, 3.3 mL, 3.3 mmol) in CH2Cl2 (6.7 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane) to give the desired product 4a (259 mg, 66%).

Colorless crystals; mp 74–76 °C; 1H NMR (500 MHz, CDCl3): δ = 2.13 (s, 3H), 3.09 (s, 3H), 7.15–7.21 (m, 3H), 7.23–7.26 (m, 2H), 7.41–7.44 (m, 1H), 7.47–7.53 (m, 3H); 13C{1H} NMR (125 MHz, CDCl3): δ = 20.2, 26.1, 125.8, 125.9, 127.2, 128.5 (2C), 128.7, 129.6, 130.0 (2C), 130.6, 131.3, 133.2, 134.8, 135.9, 138.4, 139.8; IR (neat): νmax = 3024, 2972, 2934, 1385, 903, 760, 704 cm⁻¹; HRMS (DART): m/z calcd for C18H14Cl [M + H]⁺ 267.0941; found: 267.0940.
4,5-Dichloro-2-dimethyl-1-phenynaphthalene (4b).

Following a similar procedure for the preparation of naphthalene 4c, the reaction using AACM 1b (779 mg, 2.28 mmol) and TiCl4 (1.0 M in CH2Cl2, 2.28 mL, 2.28 mmol) in CH2Cl2 (4.56 mL) gave the crude solid, which was purified by SiO2-column chromatography (hexane) to give the desired product 4b (449 mg, 69%).

Colorless crystals; mp 94–96 °C; 1H NMR (500 MHz, CDCl3): δ = 2.15 (s, 3H), 7.16–7.21 (m, 3H), 7.32–7.34 (m, 1H), 7.43–7.47 (m, 1H), 7.49–7.52 (m, 2H), 7.53–7.55 (m, 1H), 7.59–7.60 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 20.3, 125.7, 126.0, 126.8, 127.5, 128.7 (2C), 129.1, 129.6, 129.9 (2C), 130.4, 133.1, 134.4, 136.8, 138.5, 139.1; IR (neat): νmax = 3059, 2920, 1375, 1024, 908, 766, 752, 733 cm⁻¹; HRMS (DART): m/z calcd for C17H12Cl2 [M+H]+ 283.0890; found: 283.0885.

4-Chloro-5-methoxy-2-methyl-1-phenynaphthalene (4c).

TiCl4 (1.0 M in CH2Cl2, 1.4 mL, 1.4 mmol) was added to a stirred solution of AACM 1c (452 mg, 1.34 mmol) in CH2Cl2 (4.56 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 30 min. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by SiO2-column chromatography (hexane) to give the desired product 4c (211 mg, 56%).

Colorless crystals; mp 153–154 °C; 1H NMR (500 MHz, CDCl3): δ = 2.14 (s, 3H), 3.97 (s, 3H), 6.84–6.85 (m, 1H), 6.95–6.97 (m, 1H), 7.19–7.23 (m, 3H), 7.40–7.44 (m, 1H), 7.46–7.50 (m, 3H); 13C{1H} NMR (125 MHz, CDCl3): δ = 20.3, 56.1, 106.3, 119.7, 121.3, 126.2, 127.2, 128.4, 128.5 (2C), 130.0 (2C), 131.1, 134.0, 136.6, 137.4, 139.7, 156.3; IR (neat): νmax = 3001, 2934, 2837, 1574, 1462, 1373, 910, 812, 764, 750 cm⁻¹; HRMS (DART): m/z calcd for C17H14ClO [M+H]+ 297.1046; found: 297.1045.

4-Chloro-5-methoxy-2-dimethyl-1-phenynaphthalene (4d).

Following a similar procedure for the preparation of naphthalene 4c, the reaction using AACM 1f (376 mg, 1.0 mmol) and TiCl4 (1.0 M in CH2Cl2, 1.0 mL, 1.0 mmol) in CH2Cl2 (2.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane) to give the desired product 4d (159 mg, 49%).

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 2.13 (s, 3H), 7.16–7.21 (m, 3H), 7.38–7.44 (m, 2H), 7.55–7.58 (m, 2H), 7.61–7.62 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 19.8, 125.8, 126.0, 126.2, 127.2, 129.4, 129.8, 130.9, 131.6, 133.1, 134.2, 135.0, 136.1, 137.7; IR (neat): νmax = 3059, 2918, 1717, 1585, 1558, 1437, 1360, 1138, 1061, 1036, 910, 808, 750, 736 cm⁻¹; HRMS (DART): m/z calcd for C18H14ClO [M+H]+ 321.0005; found: 320.9996.

4-Chloro-5-methoxy-2-(2-methoxyphenyl)naphthalene (4f).

Following a similar procedure for the preparation of naphthalene 4c, the reaction using AACM 1e (175 mg, 0.5 mmol) and SnCl4 (1.0 M in CH2Cl2, 0.5 mL, 0.5 mmol) in CH2Cl2 (1.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane) to give the desired product 4e (96 mg, 68%).
Following a similar procedure for the preparation of naphthalene 4c, the reaction using AACM 1g (351 mg, 1.0 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) gave the crude solid, which was purified by SiO₂-column chromatography (hexane) to give the desired product 4g (158 mg, 53%).

Colorless crystals; mp 105–107 °C; ¹H NMR (500 MHz, CDCl₃): δ = 2.11 (s, 3H), 3.08 (s, 3H), 3.67 (s, 3H), 7.04–7.09 (m, 3H), 7.14–7.17 (m, 1H), 7.21–7.24 (m, 2H), 7.41–7.45 (m, 1H), 7.51–7.52 (m, 1H); ¹³C¹H NMR (125 MHz, CDCl₃): δ = 19.9, 26.1, 55.5, 111.1, 120.8, 125.6, 125.7, 128.3, 128.7, 129.0, 129.5, 131.3, 131.6, 133.9, 134.9, 135.8, 157.2; IR (neat): ν max = 2934, 1506, 1489, 1458, 1345, 1256. 1H NMR (500 MHz, CDCl₃) for C₁₉H₁₇ClO [M + H]^+ 297.1046; found: 297.1041.

4-Chloro-2,7-dimethyl-1-phenynaphthalene (5a).

A solution of AACM 3a (577 mg, 1.8 mmol) in CH₂Cl₂ (1.8 mL) was added to a stirred solution TiCl₄ (1.0 M in CH₂Cl₂, 1.8 mL, 1.8 mmol) in CH₂Cl₂ (1.8 mL) at −78 °C, and the mixture was stirred at the same temperature for 30 min. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na₂SO₄) and concentrated. The obtained crude product was purified by SiO₂-column chromatography (hexane) to give the desired product 5a (361 mg, 75%).

Colorless oil; ¹H NMR (500 MHz, CDCl₃): δ = 2.17 (s, 3H), 2.36 (s, 3H), 7.14–7.15 (m, 1H), 7.22–7.25 (m, 2H), 7.33–7.36 (m, 1H), 7.42–7.46 (m, 2H), 8.15–8.17 (m, 2H), 7.14–7.15 (m, 1H); ¹³C¹H NMR (125 MHz, CDCl₃): δ = 20.6, 21.8, 124.1, 125.5, 127.2, 127.4, 127.6, 128.0 (2C), 130.1 (2C), 130.7, 133.6, 134.3, 136.3, 136.9, 139.2; IR (neat): ν max = 3055, 2920, 2859, 1030, 907, 868, 814, 758, 702 cm⁻¹; HRMS (DART): m/z calcd for C₁₉H₁₆Cl [M + H]^+ 267.0941; found: 267.0937.

4-Chloro-7-methoxy-2-methyl-1-phenynaphthalene (5c).

A solution of AACM 3c (337 mg, 1.0 mmol) in CH₂Cl₂ (5 mL) was added to a stirred solution SnCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (15 mL; Caution: this high dilution was necessary) at 20–25 °C, and the mixture was stirred at the same temperature for 30 min. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na₂SO₄) and concentrated. The obtained crude product was purified by SiO₂-column chromatography (hexane) to give the desired product 5c (163 mg, 57%).

Colorless crystals; mp 83–84 °C; ¹H NMR (500 MHz, CDCl₃): δ = 2.18 (s, 3H), 3.66 (s, 3H), 6.68–6.69 (m, 1H), 7.16–7.18 (m, 1H), 7.23–7.25 (m, 2H), 7.37–7.39 (m, 1H), 7.41–7.45 (m, 1H), 7.48–7.52 (m, 2H), 8.17–8.18 (m, 1H); ¹³C¹H NMR (125 MHz, CDCl₃): δ = 20.7, 55.1, 105.5, 117.8, 124.6, 125.9, 126.3, 127.3, 128.6 (2C), 130.0 (2C), 130.7, 134.2, 133.5, 136.5, 139.2, 158.0; IR (neat) ν max = 3001, 2934, 1620, 1506, 1416, 1227, 1115, 1028, 908, 822, 758, 702 cm⁻¹; HRMS (DART): m/z calcd for C₁₈H₁₅ClO [M + H]^+ 283.0890; found: 283.0866.

4-Chloro-2,7-dimethyl-1-(o-toly)napthalene (5d).

Following a similar procedure for the preparation of napthalene 5a, the reaction using AACM 3d (335 mg, 2.0 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) gave the crude solid, which was purified by SiO₂-column chromatography (hexane) to give the desired product 5d (335 mg, 64%).

Colorless oil; ¹H NMR (500 MHz, CDCl₃): δ = 1.91 (s, 3H), 2.10 (s, 3H), 2.36 (s, 3H), 6.98–7.00 (m, 1H), 7.07–7.08 (m, 1H), 7.29–7.37 (m, 4H), 7.46–7.47 (m, 1H), 8.15–8.17 (m, 1H); ¹³C¹H NMR (125 MHz, CDCl₃): δ = 19.5, 20.1, 21.8, 124.2, 125.0, 126.0, 127.52, 127.57, 127.65, 128.1, 130.0, 130.1, 130.6, 133.6, 133.8, 136.2, 136.5, 136.7, 138.5; IR (neat): ν max = 3019, 2918, 2859, 868, 814, 756 cm⁻¹; HRMS (DART): m/z calcd for C₁₉H₁₄Cl [M + H]^+ 281.1097; found: 281.1100.

4-Chloro-2,7-methyl-1-(2-chlorophenyl)napthalene (5e).

Following a similar procedure for the preparation of napthalene 5a, the reaction using AACM 3e (356 mg, 1.0 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) gave the crude oil, which was purified by
Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3f (169 mg, 0.45 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 0.45 mL, 0.45 mmol) in CH₂Cl₂ (0.9 mL) gave the crude solid, which was purified by SiO₂-column chromatography (hexane) to give the desired product 5f (56 mg, 39%).

Authors: [Names]

Institute: [Institution]

Article: [Title of the article]

Publisher: [Publisher]

Abstract: [Summary of the research findings]

Keywords: [Keywords related to the research]

Introduction: [Historical context or problem statement]

Results: [Detailed description of the experimental results]

Discussion: [Interpretation of the results and comparison with previous work]

Conclusion: [Summary of the main findings and implications]

References: [List of cited sources]

Supporting Information: [Additional data or methods]

Acknowledgments: [Gratitude to funding agencies, contributors, etc.]

Appendix: [Additional material for detailed methods or data]

Corresponding Author: [Name, contact information]

Conflict of Interest: [Declaration of any conflicts of interest]

Data Availability: [Information on availability of the data used in the study]
Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3i (335 mg, 0.95 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) gave the crude oil, which was purified by SiO₂-column chromatography (hexane) to give the desired product 5j (275 mg, 98%).

Colorless crystals; mp 119–121 °C; ¹H NMR (500 MHz, CDCl₃): δ = 2.14 (s, 3H), 2.59 (s, 3H), 7.03–7.05 (m, 1H), 7.19–7.22 (m, 2H), 7.31–7.32 (m, 1H), 7.42–7.45 (m, 1H), 7.48–7.51 (m, 2H), 8.20–8.22 (m, 1H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 17.9, 18.9, 21.6, 124.3, 125.7, 127.0, 127.7, 128.1, 128.4 (2C), 130.2 (2C), 130.4, 131.2, 132.6, 133.7, 135.2, 136.8, 140.2; IR (neat): ν_max = 3057, 2952, 2920, 1458, 1366, 1246, 1026, 953, 910, 814, 754 cm⁻¹; HRMS (DART): m/z calcd for C₁₉H₁₆Cl₂O [M + H]⁺ 331.0657; found: 331.0634.

Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3j (335 mg, 0.95 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) at 20 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Sat. NH₄Cl aqueous solution was added to the mixture, which was stirred at the same temperature for 0.5 h. Methyl (15⁰,35⁰)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate 5k (394 mg, 2.0 mmol) in THF (2.0 mL) was added to the mixture, which was stirred at the same temperature for 1 h and then warmed up to 25 °C during 1 h. Sat. NH₄Cl aqueous solution was added to the mixture, which was extracted twice with Et₂O. The combined organic phase was washed with water and brine, dried (Na₂SO₄) and concentrated. The obtained crude oil was purified by SiO₂-column chromatography (hexane) to give the desired product 5k (270 mg, 96%).

Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3j (335 mg, 0.95 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 0.95 mL, 0.95 mmol) in CH₂Cl₂ (2.0 mL) at 20 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Sat. NH₄Cl aqueous solution was added to the mixture, which was stirred at the same temperature for 0.5 h. Methyl (15⁰,35⁰)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate 5k (394 mg, 2.0 mmol) in THF (2.0 mL) was added to the mixture, which was stirred at the same temperature for 1 h and then warmed up to 20–25 °C during 1 h. Sat. NH₄Cl aqueous solution was added to the mixture, which was extracted twice with Et₂O. The combined organic phase was washed with water and brine, dried (Na₂SO₄) and concentrated. The obtained crude oil was purified by SiO₂-column chromatography (hexane) to give the desired product 5k (275 mg, 98%).

Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3k (386 mg, 1.0 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) gave the crude solid, which was purified by SiO₂-column chromatography (hexane) to give the desired product 5l (313 mg, 95%).

Colorless crystals; mp 129–132 °C; ¹H NMR (500 MHz, CDCl₃): δ = 2.14 (s, 3H), 2.60 (s, 3H), 3.69 (s, 3H), 7.05–7.10 (m, 3H), 7.246–7.249 (m, 1H), 7.39–7.41 (m, 1H), 7.44–7.48 (m, 1H), 8.24–8.25 (m, 1H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 18.1, 18.7, 55.5, 111.1, 120.8, 125.1, 126.4, 126.5, 127.5, 129.3, 131.6, 131.7, 133.1, 133.6, 135.9, 157.2; IR (neat): ν_max = 3001, 2934, 2835, 1601, 1580, 1495, 1481, 1458, 1366, 1246, 1026, 953, 910, 814, 754 cm⁻¹; HRMS (DART): m/z calcd for C₁₉H₁₆ClO [M + H]⁺ 331.0657; found: 331.0634.

Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3i (193 mg, 0.5 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 0.5 mL, 0.5 mmol) in CH₂Cl₂ (1.0 mL) gave the crude solid, which was purified by SiO₂-column chromatography (hexane) to give the desired product 5m (129 mg, 78%).

Colorless crystals; mp 119–123 °C; ¹H NMR (500 MHz, CDCl₃): δ = 2.18 (s, 3H), 2.59 (s, 3H), 3.84 (s, 3H), 6.73–6.74 (m, 1H), 6.78–6.79 (m, 1H), 6.99–7.01 (m, 1H), 7.298–7.303 (m, 1H), 7.41–7.44 (m, 2H), 8.24–8.26 (m, 1H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 18.0, 19.0, 52.3, 112.9, 115.7, 122.5, 125.4, 126.3, 126.7, 127.8, 129.7, 130.5, 131.7, 133.0, 133.6, 135.1, 136.6, 140.6, 159.7; IR (neat): ν_max = 2999, 2937, 1607, 1578, 1314, 1246, 1049, 930, 910, 814, 735 cm⁻¹; HRMS (DART): m/z calcd for C₁₂H₁₄ClO₂ [M – OH]⁺ 311.0657; found: 311.0634.

Following a similar procedure for the preparation of naphthalene 5a, the reaction using AACM 3l (193 mg, 0.5 mmol) and TiCl₄ (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) in CH₂Cl₂ (2.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Methyl (15⁰,35⁰)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate 5n (394 mg, 2.0 mmol) in THF (2.0 mL) was added to the mixture, which was stirred at the same temperature for 1 h and then warmed up to 20–25 °C during 1 h. Sat. NH₄Cl aqueous solution was added to the mixture, which was extracted twice with Et₂O. The combined organic phase was washed with water and brine, dried (Na₂SO₄) and concentrated. The obtained crude oil was purified by SiO₂-column chromatography (hexane) to give the desired product 5n (447 mg, 76%).
Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 2.15 (s, 3H), 2.34 (s, 3H), 2.47 (s, 3H), 2.58 (s, 3H), 7.07−7.11 (m, 3H), 7.29−7.33 (m, 3H), 8.19−8.21 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 17.9, 19.0, 21.3, 21.6, 124.3, 125.7, 127.7, 128.0, 129.1 (2C), 130.1 (2C), 130.3, 132.1, 132.7, 133.9, 135.1, 136.6, 136.9, 137.1; IR (neat): νmax = 3021, 2918, 2864, 1514, 1454, 1437, 1042, 922, 808, 712 cm−1; HRMS (DART): m/z calcd for C13H13Cl[Me + H]+ 331.0657; found: 311.0634.

Following a similar procedure for the preparation of alcohol 13, the reaction using ketone 15 (777 mg, 3.0 mmol) and NaBH4 (125 mg, 3.3 mmol) in MeOH (3.0 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 20:1) to give the desired product 16 (605 mg, 77%).

Colorless crystals; mp 58−71 °C; 1H NMR (500 MHz, CDCl3): δ = 1.22 (s, 3H), 1.31 (d, J = 7.5 Hz, 1H), 1.70 (d, J = 7.5 Hz, 1H), 2.24 (br s, 1H), 3.82 (s, 3H), 4.73 (s, 1H), 6.89−6.92 (m, 2H), 7.30−7.96 (m, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 14.5, 31.7, 36.2, 55.2, 66.7, 76.8, 113.6 (2C), 127.1 (2C), 132.8, 159.0; IR (neat): νmax = 3566, 3466, 2938, 1611, 1512, 1385, 1302, 1072, 1034, 959, 831, 770, 752 cm−1; HRMS (DART): m/z calcd for C13H15ClO [M + OH]+ 243.0344; found: 243.0363.

1-Chloro-6-methoxy-3-methylnaphthalene (14). SnCl4 (1.0 M in CH2Cl2 1.0 mL, 1.0 mmol) was added to a stirred solution of alcohol 13 (261 mg, 1.0 mmol) and MS4A (0.5 g) in THF (10 mL) at 80 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 30 min. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by SiO2-column chromatography (hexane/AcOEt = 20:1) to give the desired product 14 (97 mg, 47%).

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 2.43 (s, 3H), 3.95 (s, 3H), 6.82−6.84 (m, 1H), 7.33−7.35 (m, 2H), 7.44−7.46 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 20.9, 55.9, 106.3, 120.7, 121.0, 126.4, 126.6, 129.2, 130.8, 135.8, 137.2, 156.3; IR (neat): νmax = 3063, 3001, 2962, 1587, 1570, 1389, 1373, 1260, 1086, 770, 706 cm−1; HRMS (DART): m/z calcd for C13H10ClO [M + H]+ 207.0577; found: 207.0552.

1-Chloro-6-methoxy-3-methylnaphthalene (17). Following a similar procedure for the preparation of naphthalene 14, the reaction using alcohol 16 (53 mg, 0.5 mmol) and p-bromoanisole (1.12 g, 6.0 mmol) in THF (10 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane/AcOEt = 30:1) to give the desired product 17 (53 mg, 51%).

Colorless oil; 1H NMR (500 MHz, CDCl3): δ = 2.46 (s, 3H), 3.92 (s, 3H), 7.05−7.06 (m, 1H), 7.15−7.18 (m, 1H), 7.26−7.28 (m, 1H), 7.41−7.43 (m, 1H), 8.09−8.10 (m, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 21.4, 55.3, 105.5, 118.6, 124.5, 125.5, 125.9, 131.5, 136.0, 136.4, 158.2; IR (neat): νmax = 2920, 1628, 1504, 1441, 1265, 1238, 1036, 858, 820 cm−1; HRMS (DART): m/z calcd for C14H16ClO[M + OH]+ 207.0577; found: 207.0554.
2-(Bromomethyl)-4-chloro-7-methyl-1-phenynaphthalene (5a').

A mixture of naphthalene 5a (84 mg, 0.3 mmol), N-bromosuccinimide (53 mg, 0.3 mmol), and AIBN (1 mg, 0.015 mmol) in benzene (0.6 mL) was refluxed 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 (Na2SO4) and concentrated. The obtained crude product was purified by SiO2-column chromatography (hexane) to give the desired product 5a' (49 mg, 45%).

Colorless crystals; mp 123–124 °C; 1H NMR (400 MHz, CDCl3): δ = 2.38 (s, 3H), 4.34 (s, 2H), 7.16–7.17 (m, 1H), 7.34–7.36 (m, 2H), 7.42–7.43 (m, 1H), 7.50–7.54 (m, 2H), 7.635–7.642 (m, 1H), 8.18–8.20 (m, 1H).

2-(Bromomethyl)-4,7-dichloro-1-phenynaphthalene (5b').

Following a similar procedure for the preparation of naphthalene 5a', the reaction using naphthalene 5b (229 mg, 0.8 mmol), N-bromosuccinimide (142 mg, 0.8 mmol), and AIBN (7 mg, 0.04 mmol) in benzene (0.6 mL) gave the crude oil, which was purified by SiO2-column chromatography (hexane) to give the desired product 5b' (176 mg, 69%).

Colorless crystals; mp 139–140 °C; 1H NMR (500 MHz, CDCl3): δ = 4.33 (s, 2H), 7.33–7.34 (m, 2H), 7.386–7.391 (m, 1H), 7.50–7.57 (m, 4H), 7.70–7.72 (m, 1H), 8.23–8.25 (m, 1H).

(S*)-2,2-Dichloro-1-methylcyclopropyl(2,4,6-trimethoxyphenyl)methanone (18).

(5b')-(S*)-2,2-Dichloro-1-methylcyclopropyl(2,4,6-trimethoxyphenyl)methanol (19).

Ketone 18 (848 mg, 2.65 mmol) in THF (5.3 mL) was added to a stirred solution LiAlH4 (101 mg, 3.0 mmol) in THF (5.3 mL) at 0–5 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. 15% NaOH aqueous solution was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by SiO2-column chromatography (hexane/AcOEt = 10:1:5) to give the desired product 19 (322 mg, 38%).

Colorless crystals; mp 134–137 °C; 1H NMR (500 MHz, CDCl3): δ = 1.05 (d, J = 7.3 Hz, 1H), 1.36 (s, 3H), 1.81 (d, J = 7.3 Hz, 1H), 3.82 (s, 3H), 3.83 (s, 6H), 4.85 (d, J = 11.0 Hz, 1H), 5.20 (d, J = 11.0 Hz, 1H), 6.12 (s, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 15.9, 30.8, 36.1, 55.3, 55.6 (2C), 67.9, 71.5, 91.1 (2C), 109.0, 158.5 (2C), 160.5; IR (neat): νmax = 3501, 2943, 1609, 1591, 1418, 1217, 1150, 1121, 1032, 754 cm−1; HRMS (DART): m/z calcld for C14H18Cl2O4 [M – OH]+ 303.0555; found: 303.0560.

4,4-Dichloro-6,10-dimethoxy-2-methylspiro(4.5)-deca-1,6,9-trien-8-one (20).

SnCl4 (1.0 M in CH2Cl2, 1.0 mL, 1.0 mmol) was added to a stirred solution of alcohol 19 (127 mg, 10.4 mmol) in 1,2-dichloroethane (10 mL) at 80 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 30 min. Sat. NaHCO3 aqueous solution was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by SiO2-column chromatography (hexane/AcOEt = 2:1) to give the desired product 20 (81 mg, 70%).

Colorless crystals; mp 182–184 °C; 1H NMR (500 MHz, CDCl3): δ = 1.89 (d, J = 1.4 Hz, 3H), 3.35 (s, 2H), 3.69 (s, 6H), 5.24 (q, J = 1.4 Hz, 1H), 5.56 (s, 2H); 13C{1H} NMR (125 MHz, CDCl3): δ = 16.9, 55.9(2C), 60.0, 69.5, 95.1, 103.2 (2C), 122.2, 143.0, 169.8 (2C), 187.9; IR (neat): νmax = 3065, 2978, 2938, 2918, 1668, 1651, 1622, 1591, 1360, 1238, 1211, 1098, 864, 847, 743 cm−1; HRMS (DART): m/z calcld for C15H16Cl2O5 [M + H]+ 289.0398; found: 289.0413.

(15*S,35*)-2,2-Dichloro-1,3-dimethylcyclopropyl(3,4-methylenedioxyphenyl)methanone (21)."
A solution of acid chloride 10 (2.01 g, 10.0 mmol) in THF (10 mL) was added to a stirred solution of Grignard reagent generated from Mg (267 mg, 11.0 mmol) and 4-bromo-1,2-methylenedioxynaphthalene (2.21 g, 11.0 mmol) in THF (10 mL) at 0−5 °C, and the mixture was stirred at 20−25 °C for 3 h. Sat. NH4Cl aqueous solution was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:AcOEt = 25:1−20:1) to give the desired product 21 (2.70 g, 94%).

Pale yellow oil; 1H NMR (500 MHz, CDCl3): δ = 1.37 (d, J = 6.9 Hz, 3H), 1.63 (q, J = 6.9 Hz, 1H), 1.63 (s, 3H), 6.055 (d, J = 1.2 Hz, 1H), 6.063 (d, J = 1.2 Hz, 1H), 6.91 (d, J = 8.6 Hz, 1H), 7.41 (d, J = 1.7 Hz, 1H), 7.57 (dd, J = 1.7, 8.6 Hz, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 11.7; 23.4, 35.3, 39.6, 68.3, 101.9, 108.1, 109.0, 126.5, 129.3, 148.1, 152.1, 193.0; IR (neat): νmax = 1672, 1602, 1487, 1438, 1300, 1247, 1097 cm−1. (R*)-[15*,35*]-2,2-Dichloro-1,3-dimethylcyclopropyl][3,4-methylenedioxyphenyl](3,4,5-trimethoxyphenyl)methanol (22).

nBuLi (1.63 M in hexane, 8.2 mL, 13.4 mmol) was added to a stirred solution of 5-bromo-1,2,3-trimethylenobenzene (2.21 g, 13.4 mmol) in THF (15 mL) at −78 °C, and the mixture was stirred at the same temperature for 1 h. A solution of ketone 21 (2.49 g, 8.67 mmol) in THF (7.5 mL) was added to the stirred solution of nBuLi at −78 °C and warmed up to 20−25 °C during about 4 h. Sat. NH4Cl aqueous solution was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:AcOEt = 4:1) to give the desired product 22 (2.60 g, 66%).

Colorless crystals; mp 150–152 °C; 1H NMR (500 MHz, CDCl3): δ = 1.19 (s, 3H), 1.52 (q, J = 6.87 Hz, 1H), 1.77 (d, J = 6.87 Hz, 3H), 2.74 (s, 1H), 3.78 (s, 6H), 3.86 (s, 3H), 6.01 (d, J = 1.15 Hz, 1H), 6.02 (d, J = 1.15 Hz, 1H), 6.47 (s, 2H), 6.87 (d, J = 8.02 Hz, 1H), 6.96 (d, J = 1.72 Hz, 1H), 7.05 (dd, J = 1.72, 8.02 Hz, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 11.1, 27.0, 36.2, 38.3, 56.1 (2C), 60.8, 73.7, 83.8, 101.2, 106.0 (2C), 107.5, 109.7, 122.3, 137.1, 138.1, 141.9, 147.1, 147.4, 152.2 (2C); IR (neat): νmax = 2936, 1589, 1504, 1454, 1414, 1335, 1232, 1124 cm−1; HRMS (ESI): m/z calcd for C26H26Cl2O2 [M + Na]+ 477.0848; found: 477.0878.

5-(4-Chloro-6,7,8-trimethoxy-2,9-dimethylphenyl)benzo[d][1,3]dioxole (23).

A solution of alcohol 22 (1.37 g, 3.0 mmol) in CH2Cl2 (10 mL) was added to a stirred solution of SnCl4 (1.0 M in CH2Cl2, 3 mL, 3.0 mmol) in CH2Cl2 (50 mL) at 20−25 °C, and the mixture was stirred at the same temperature for 30 min. NaHCO3 aqueous solution was added to the mixture, which was extracted twice with CHCl3. The combined organic phase was washed with water and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:AcOEt = 15:1) to give the desired product 23 (722 mg, 60%).

Colorless crystals; mp 147−149 °C; 1H NMR (500 MHz, CDCl3): δ = 2.04 (s, 3H), 2.56 (s, 3H), 3.32 (s, 3H), 3.85 (3H), 4.02 (s, 3H), 6.01 (d, J = 1.7 Hz, 1H), 6.02 (d, J = 1.7 Hz, 1H), 6.38 (dd, J = 1.7, 8.0 Hz, 1H), 6.68 (d, J = 1.7 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 7.50 (s, 1H); 13C{1H} NMR (125 MHz, CDCl3): δ = 18.3, 18.5, 55.7, 60.7, 60.8, 100.0, 100.7, 107.4, 109.6, 121.4, 123.0, 127.2, 129.7, 132.8, 133.4, 134.4, 137.6, 142.3, 145.5, 146.8, 149.5, 152.7; IR (neat): νmax = 2937, 1611, 1487, 1433, 1337, 1223, 1138, 1040 cm−1; HRMS (ESI): m/z calcd for C22H24Cl2O6 [M + Na]+ 423.0975; found: 423.0989.

1-(3,4-Methylenedioxyphenyl)-6,7,8-trimethoxynaphthalene-2,3-diyldimethanol (26).

A solution of α-arylnaphthalene 23 (361 mg, 0.90 mmol), N-bromosuccinimide (641 mg, 3.60 mmol), and AIBN (15 mg, 0.09 mmol) in CCl4 (9 mL) was refluxed for 2 h. After cooling down, water was added to the mixture, which was extracted twice with CHCl3. The combined organic phase was washed with 1 M HCl aqueous solution, water, 3% Na2S2O3 aqueous solution, and brine, dried (Na2SO4) and concentrated. The obtained crude product 25 was used in the next step without any purification. A suspension of the obtained crude product 25 (672 mg) and KOAc (353 mg, 3.60 mmol) in DMF (3.6 mL) was stirred at room temperature for 2 h. KOH (303 mg, 5.40 mmol) in water (1.8 mL) and MeOH (3.4 mL) was added to the stirred mixture at 20−25 °C, and the mixture was stirred at the same temperature for 2 h. 1 M HCl aqueous solution was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed three times with water and brine, dried (Na2SO4) and concentrated. The obtained crude product 25 was used in the next step without any purification. HMPA (1.53 mL, 8.80 mmol) was added to a solution of SmI2 in THF (ca. 0.1 M, 22 mL), which was stirred at 20−25 °C for 15 min. To the resultant solution, a solution of the crude solid 26 (238 mg) in THF (1.0 mL) and the mixture was stirred for 15 min. Then, 2-propanol (0.34 mL, 4.40 mmol) was added to the mixture, which was extracted twice with Et2O. The combined organic phase was washed with water, 3% Na2S2O3 aqueous solution, and brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:AcOEt = 1:2) to give the desired product 26 (75 mg, 21%).
Colorless crystals; mp 184–187 °C; 1H NMR (500 MHz, CDCl3): δ = 2.36 (s, 1H), 3.14 (s, 1H), 3.34 (s, 1H), 3.86 (s, 3H), 3.98 (s, 3H), 4.52 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.88 (d, J = 12.6 Hz, 1H), 4.92 (d, J = 12.6 Hz, 1H), 6.02 (d, J = 1.7 Hz, 1H), 6.04 (d, J = 1.7 Hz, 1H), 6.70 (dd, J = 1.7, 7.5 Hz, 1H), 6.78 (d, J = 1.7 Hz, 1H), 6.86 (d, J = 1.7 Hz, 1H), 6.98 (s, 1H), 7.72 (s, 1H); 13C(1H) NMR (125 MHz, CDCl3): δ = 55.9, 60.0, 60.8, 61.0, 65.2, 101.0, 103.1, 107.3, 109.9, 121.7, 123.2, 128.2, 131.2, 134.3, 135.9, 137.1, 137.7, 143.1, 146.8, 150.2, 153.4; IR ( neat): νmax = 3343, 2937, 1607, 1562, 1487, 1379, 1227, 1138 cm⁻¹; HRMS (ESI): m/z calc for C12H12O4 [M + Na]+ 421.1263; found: 421.1263.

Chaihnaphthone 15 [4-(Benzo[d][1,3]dioxol-5-yl)-5,6,7-trimethoxynaphtho[2,3-c]furan-1(3H)]-one. A suspension of diol 25 (22 mg, 0.06 mmol) and Fetizon chloride (Ag2CO3 on Celite) (684 mg) in toluene (18 mL) was stirred for 5 h using Dean–Stark apparatus with continual removal of water. After cooling down, the mixture was filtrated through Celite with CHCl3 and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 3:1) to give the desired chaihnaphthone (16 mg, 72%).

Notes
The authors declare no competing financial interest.

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