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Article

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

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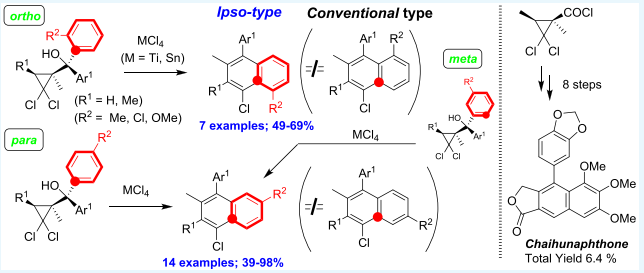
ABSTRACT: A distinctive method for synthesizing a variety of multisubstituted α-arylnaphthalenes utilizing novel regiocontrolled *ipso*-type [4 + 2] benzannulation is presented. *Ortho*- and *para*-substituted 1-Ar^1-1-Ar^2-2,2-dichlorocyclopropylmethanols (AACM) were transformed to the corresponding *ipso*-type α-arylnaphthalenes. (i) The reaction of *ortho*-AACM using $TiCl_4$ or $SnCl_4$ (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.[1] Regiocontrolled benzannulation strategies provide distinctive constructions for elaborated α-arylnaphthalenes.[2] 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[3] and α-diazoketone-mediated Danheiser benzannulation[4] are two pioneering [4 + 2] annulation methods (Scheme 1). Since the development of these innovative studies, several [4 + 2] approaches starting from monofunctionalized benzenes have been reported to date. Five representative benzannulations involve the appropriate alkyne segments for the construction of multisubstituted naphthalenes: (i) $GaCl_3$-catalyzed aldehyde−alkyne condensation,[5] (ii) $TiCl_4$-promoted aldehyde−alkyne condensation,[6] (iii) iron-catalyzed Grignard coupling with two symmetrical alkynes,[7] (iv) Tf_2NH-catalyzed aldehyde−arylated alkyne condensation,[8] and (v) $FeCl_3$-promoted condensation of alkynyl alcohols concomitant with selenylation.[9]

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.[10] Consistent with our longstanding synthetic studies of regio- and stereoselective *gem*-dihalocyclopropane transformations,[11] related drug discovery and process studies of chiral cyclopropane pyrethroid insecticides,[12] and recent total syntheses of all six chiral natural pyrethrins,[13] we previously reported a couple of benzannulation methods (Scheme 2).

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 benzan-

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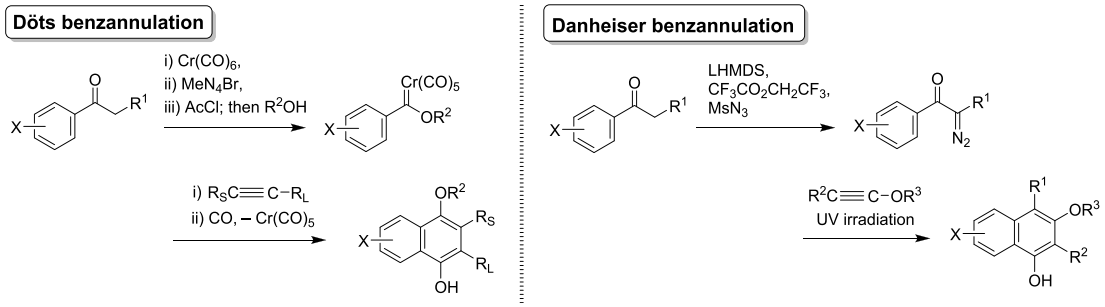
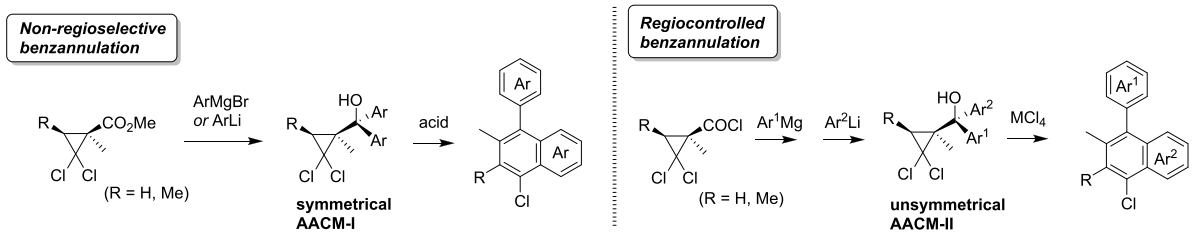
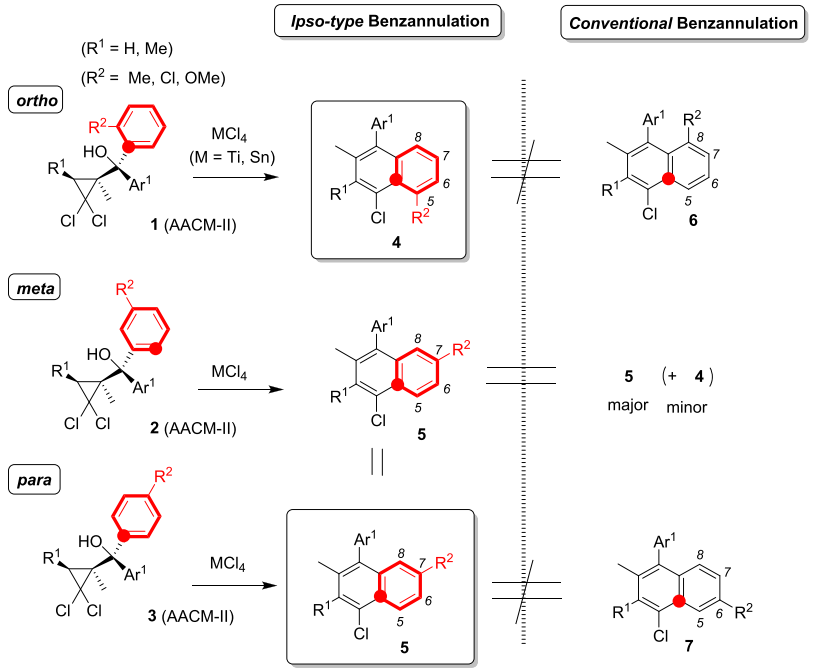
Scheme 1. [4 + 2]-Type Döts and Danheiser Benzannulations



Scheme 2. Two [4 + 2] Types of Benzannulations Using Stereodefined AACM-I and AACM-II



Scheme 3. General Mode of *Ipso*-Type Benzannulations Starting from Three Stereodefined AACM-II 1−3



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 (Ar^1)(Ar^2)(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-

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Scheme 4. Preparation of Stereodefined AACM-II 1−3

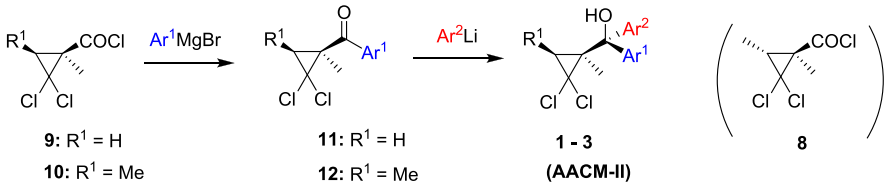
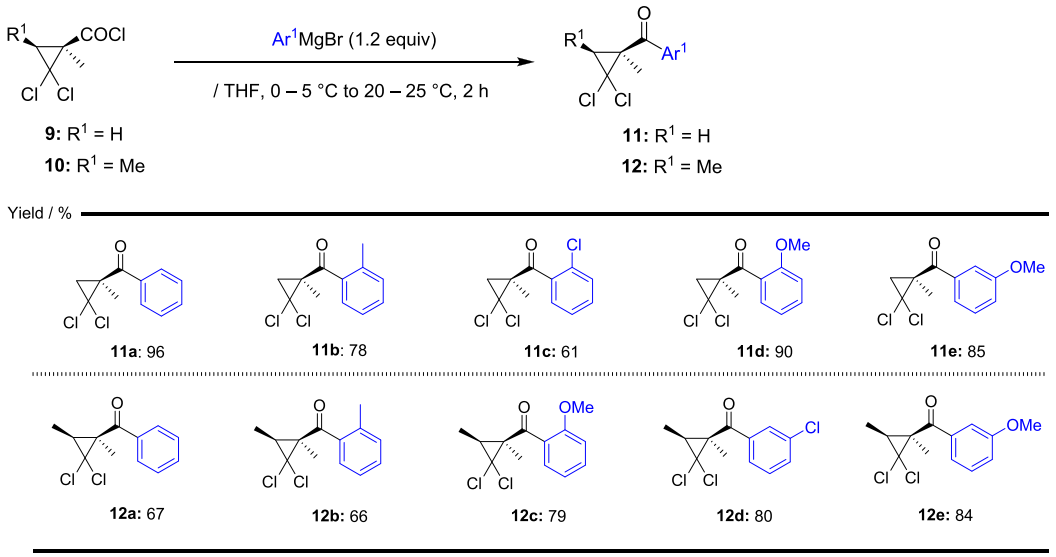


Table 1. Preparation of Ketones 11 and 12



stituted 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 and **1** (*ortho*-form), **2** (*meta*-form), and **3** (*para*-form) were readily prepared through sequential introductions of Ar^1 and Ar^2 groups by basically following the reported method[11d,e] (Scheme 4). The reaction of accessible cyclopropanecarbonyl chlorides **9** (derived from the commercially available acid) and **10** (derived from methyl angelate) with Ar^1MgBr afforded the corresponding Ar^1-substituted ketones **11** and **12**, respectively, in good yield (Table 1).

Subsequent addition to ketones **11** and **12** using Ar^2Li 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 rule[11d,e] (Table 2). The addition reaction using ketones **11** afforded a wide variety of AACM-II **1** and **3** in moderate to high yields. However, ketones **12** smoothly underwent the addition reaction using *para*-substituted Ar^2Li, resulting in a good yield, but *ortho*-substituted Ar^2Li resisted the desired addition (no reaction), probably because of the high stereocongestion.

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 $TiCl_4$ (1.0 equiv) or $SnCl_4$ (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 Ar^1 or Ar^2 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).

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 $AlCl_3$-catalyzed Friedel−Crafts acylation and LAH

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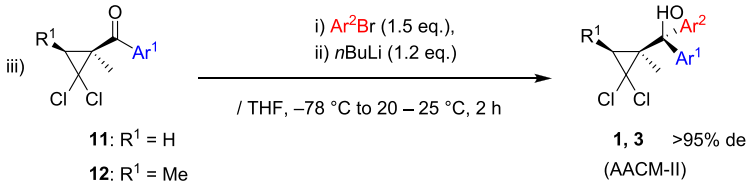
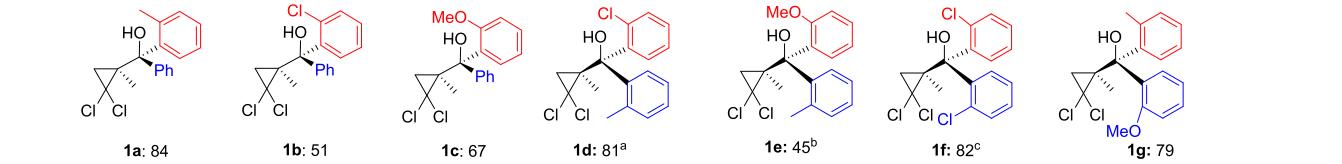
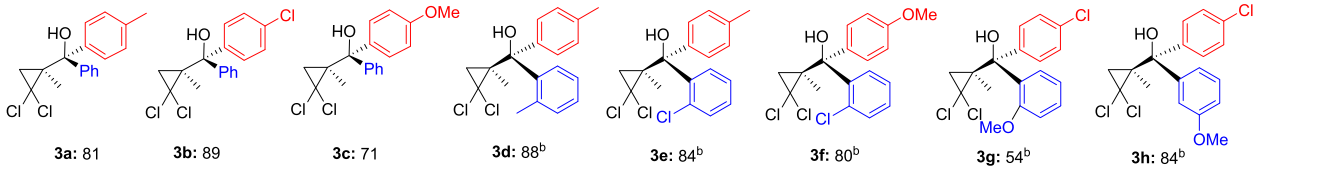
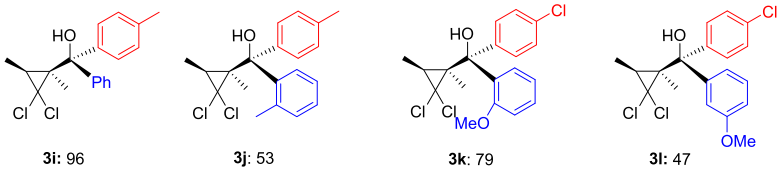
Table 2. Preparation of Stereodefined AACM-II 1 and 3



Yield / %

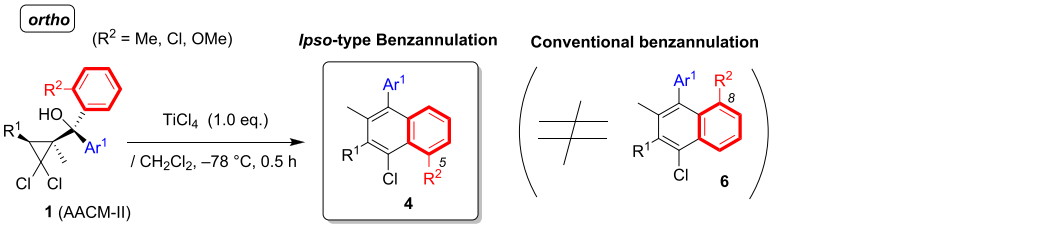




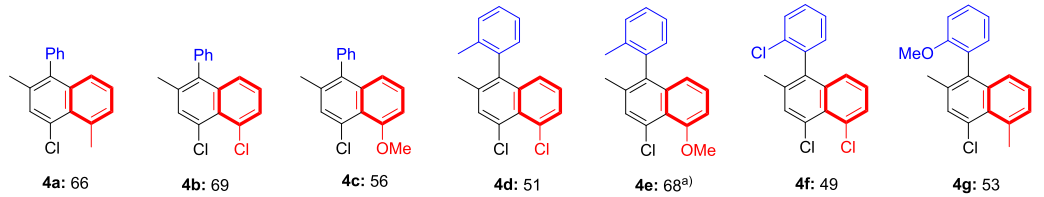


[a]2.2 Equiv of Ar^2Li was used. [b]2-Me THF solvent was used instead of THF. [c]Prepared by an alternative reported method as described in the experimental section.

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



Yield / %



[a]$SnCl_4$ was used instead of $TiCl_4$.

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 $SnCl_4$ affords dichloromethylinium 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 R^2 position are indicated. In contrast to the conventional benzannulations, *ortho*- or *para*-orientation of the R^2 substituents contributes to this 1,5-cyclization. Cation **B** reversibly converts to relatively stable tricyclic carbenium

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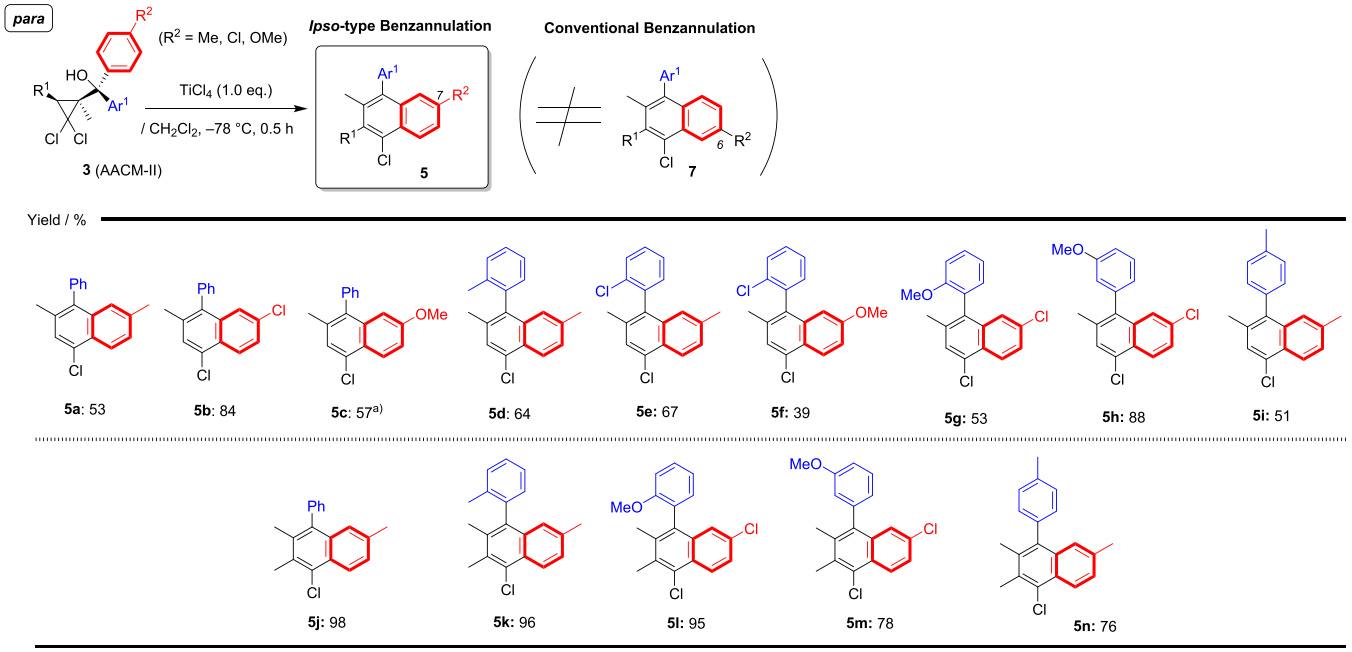
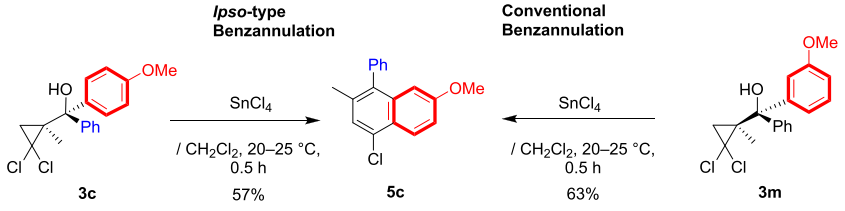
Table 4. *Ipso*-Type Regiocontrolled Benzannulations Using AACM-II 3 (*para*-Form)

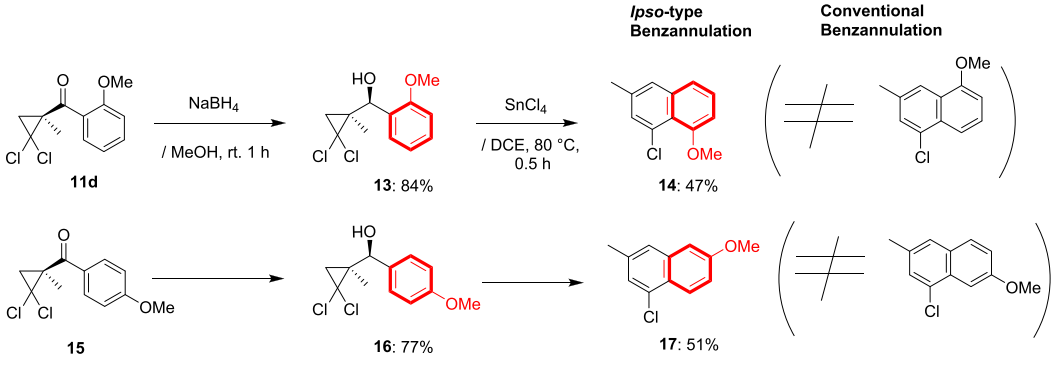


[a]$SnCl_4$ was used instead of $TiCl_4$ in high dilution conditions.

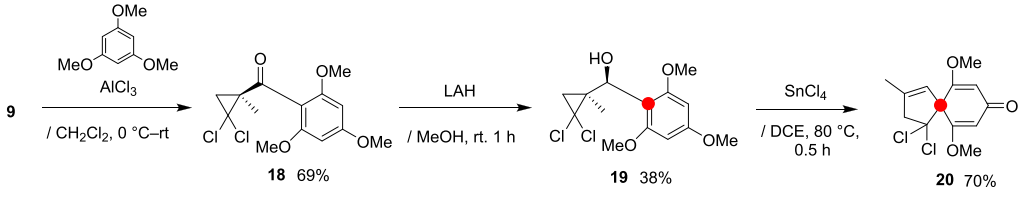
Scheme 5. Two Separate and Independent Reactions for *Ipso*-Type and Conventional Benzannulation



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



Scheme 7. *Ipso*-Type Reaction Using (2,4,6-Trimethoxyphenyl)methanol Substrate



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.

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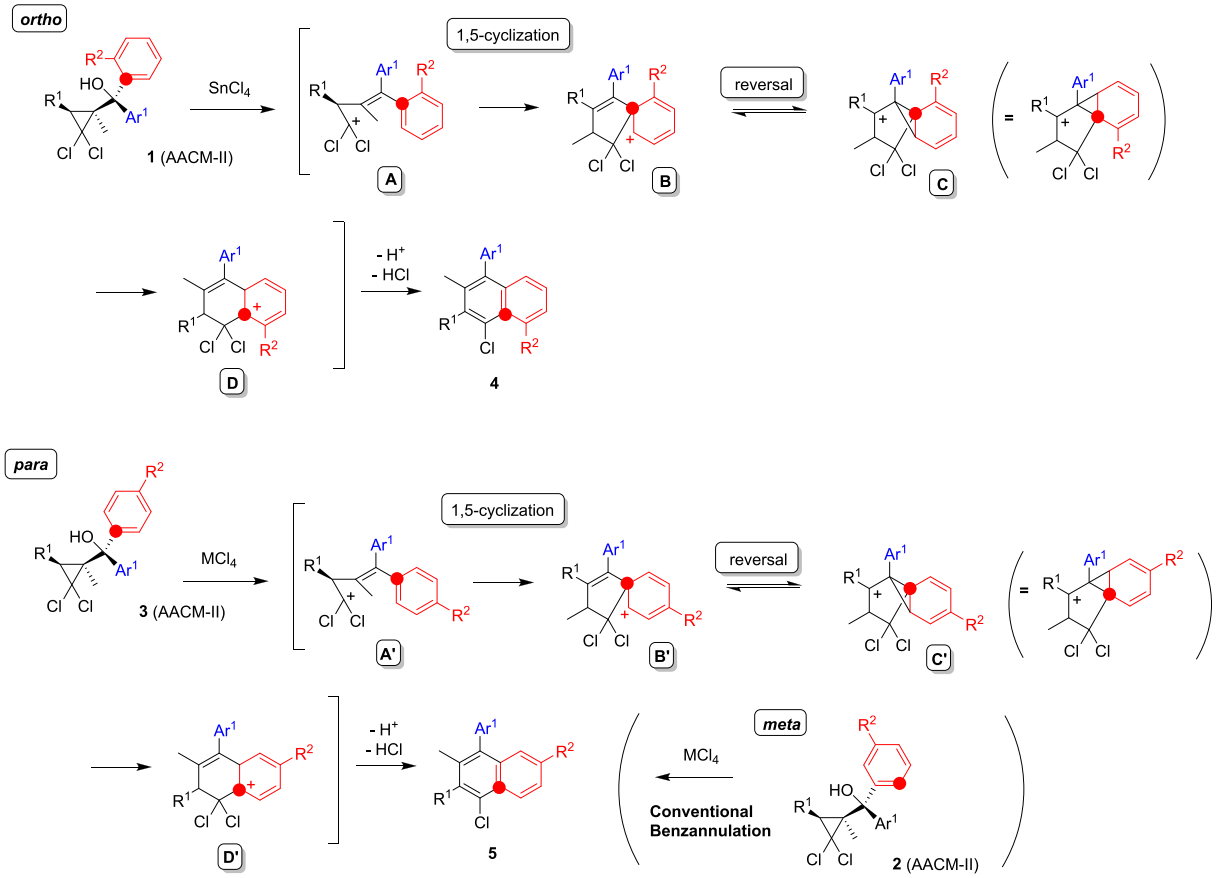
Scheme 8. Reaction Mechanism for *Ipso*-Type Benzannulations Using *ortho*-Form AACM-II 1 and *para*-Form AACM-II 3



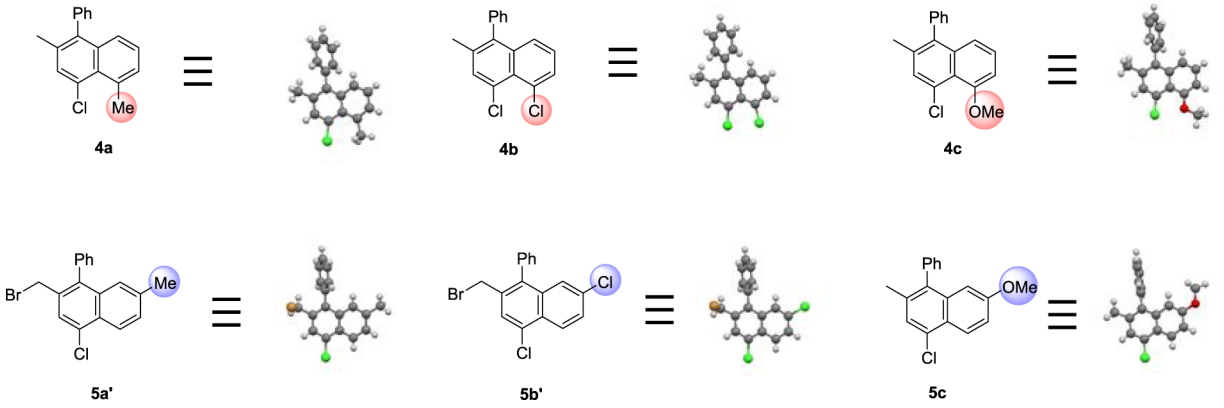


Figure 1. X-ray structures of six key α-arylnaphthalenes.

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).

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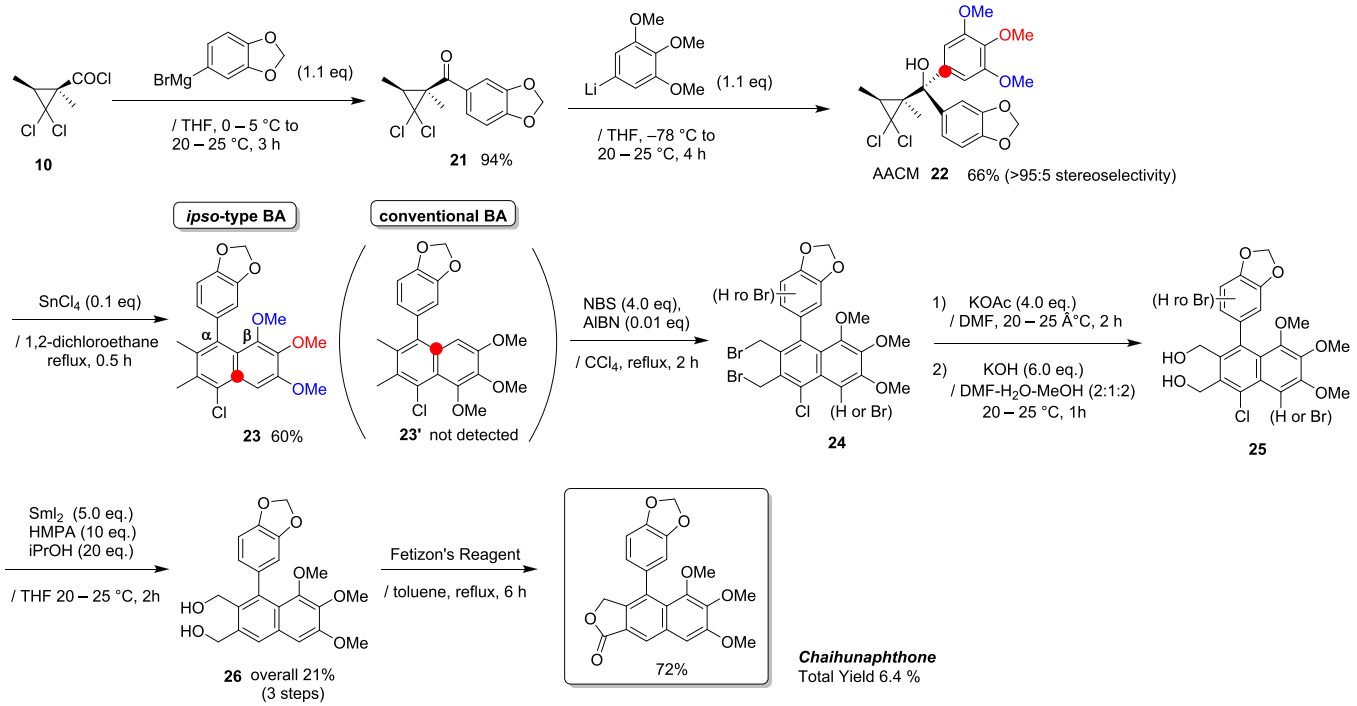
Scheme 9. Total Synthesis of Chaihunaphthone



Chaihunaphthone, isolated from the root of *Bupleurum scorzonerifolium* (Nan-Chai-Hu), exhibits immunosuppressive effects and a uniquely (highly congested) substituted α-arylnaphthalene structure.[15] 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 $SnCl_4$ to produce the desired α-arylnaphthalene **23** in 60% yield with excellent regioselectivity.[16] 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 **23**[11] 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 SmI_2-mediated debromination[17] of the mixture **25** furnished precursor **26** in a pure form with 21% yield from **22** in three steps.

Final oxidation by Fetizon's reagent[18] produced chaihunaphthone in 72% yield (total 6.4% yield from **10**). The melting point and spectroscopic data (^{1}H NMR, ^{13}C 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-trimehoxy-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

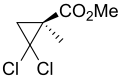
We achieved a regiocontrolled *ipso*-type benzannulation to produce a variety of unique and multisubstituted α-arylnaphthalenes. The reaction mode apparently differs from the reported conventional benzannulation mode; *ortho*- and *para*-substituted 1,1-diaryl-2,2-dichlorocyclopropylmethanols (AACM) 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; ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 18.1, 30.8, 35.3, 52.6, 62.5, 169.5.

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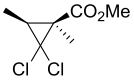
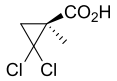
Methyl (1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropane-1-carboxylate.**[10b,13]



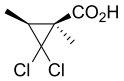
A 16.5 g scale practical preparation: ref 13. Colorless oil; bp 65−66 °C/7.5 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (d, J = 6.9 Hz, 3H), 1.55 (q, J = 6.9 Hz, 1H), 1.57 (s, 3H), 3.74 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 10.8, 21.1, 36.0, 36.8, 52.1, 67.6, 168.9.

(*S)-2,2-Dichloro-1-methylcyclopropane-1-carboxylic acid.**[10b]



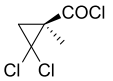
Colorless crystals; mp 65−66 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.47 (d, J = 7.3 Hz, 1H), 1.62 (s, 3H), 2.29 (d, J = 7.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.0, 31.2, 35.1, 62.6, 175.3.

(1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropane-1-carboxylic acid.**[11c]



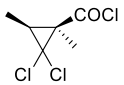
Colorless crystals; mp 95−96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.9 Hz, 3H), 1.61 (q, J = 6.9 Hz, 1H), 1.62 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 10.7, 21.1, 36.59, 36.62, 67.9, 175.2.

(*S)-2,2-Dichloro-1-methylcyclopropane-1-carbonyl chloride (9).**[11e]



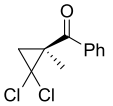
Colorless oil; bp 56−57 °C/10.5 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.62 (d, J = 7.5 Hz, 1H), 1.75 (s, 3H), 2.37 (d, J = 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.3, 32.4, 43.7, 61.8, 171.3.

(*S)-2,2-Dichloro-1-methylcyclopropane-1-carbonyl chloride (10).**[11e]



Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.9 Hz, 3H), 1.74 (q, J = 6.9 Hz, 1H), 1.75 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.2, 21.3, 37.9, 45.3, 66.7, 168.9.

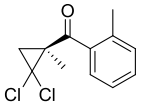
(*S)-2,2-Dichloro-1-methylcyclopropyl(phenyl)-methanone (11a).**[11b]



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. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **11a** (2.19 g, 96%).

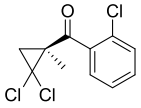
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.49 (d, J = 7.5 Hz, 1H), 1.65 (s, 3H), 2.30 (d, J = 7.5 Hz, 1H), 7.52−7.57 (m, 2H), 7.60−7.64 (m, 1H), 7.94−7.98 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 20.7, 29.5, 39.7, 62.4, 128.7 (2C), 129.6 (2C), 133.4, 134.4, 195.4.

(*S)-2,2-Dichloro-1-methylcyclopropyl(*o*-tolyl)-methanone (11b).**[11d]



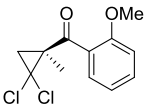
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.45 (d, J = 7.5 Hz, 1H), 1.54 (s, 3H), 2.43 (d, J = 7.5 Hz, 1H), 2.52 (s, 3H), 7.29−7.31 (m, 1H), 7.34−7.38 (m, 1H), 7.41−7.44 (m, 1H), 7.68−7.70 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 20.4, 20.9, 29.4, 40.7, 63.3, 125.8, 129.8, 131.7, 132.0, 134.6, 139.6, 197.4.

(*S)-2,2-Dichloro-1-methylcyclopropyl(2-chlorophenyl)methanone (11c).**[11d]



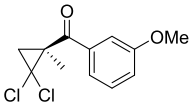
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51 (d, J = 7.45 Hz, 1H), 1.57 (s, 3H), 2.49 (d, J = 7.45 Hz, 1H), 7.38−7.44(m, 2H), 7.45−7.48 (m, 1H), 7.55−7.57 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.3, 30.4, 40.6, 64.1, 127.0, 130.0, 130.7, 132.0, 132.1, 136.4, 196.2.

(*S)-2,2-Dichloro-1-methylcyclopropyl(2-methoxyphenyl)methanone (11d).**[11d]



Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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.

(*S)-2,2-Dichloro-1-methylcyclopropyl(3-methoxyphenyl)methanone (11e).**



Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3005, 2938, 1686, 1597, 1584, 1427, 1317, 1269, 1242, 1045, 866, 773 cm^{-1}; HRMS (DART): m/z calcd for $C_{12}H_{12}Cl_2O_2$ $[M + H]^+$ 259.0293; found: 259.0293.

https://doi.org/10.1021/acsomega.1c02000
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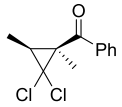
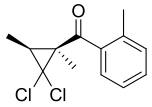
(*S)-2,2-Dichloro-1,3-dimethylcyclopropyl(phenyl)-methanone (12a).**[11e]



Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.9 Hz, 3H), 1.66 (s, 3H), 1.68 (q, J = 6.9 Hz, 1H), 7.48−7.54 (m, 2H), 7.59−7.62 (m, 1H), 7.95−8.00 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.7, 23.2, 35.3, 39.6, 68.1, 128.7 (2C), 129.7 (2C), 133.5, 134.4, 194.9.

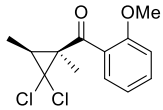
(1*S, 3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl(*o*-tolyl)methanone (12b).**



Following a similar procedure for the preparation of ketone **11a**, the reaction using acid 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 SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **12b** (1.02 g, 66%).

Paled yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (d, J = 6.9 Hz, 3H), 1.64 (s, 3H), 1.66 (q, J = 6.9 Hz, 3H), 2.56 (s, 3H), 7.27−7.28 (m, 1H), 7.35−7.38 (m, 1H), 7.41−7.45 (m, 1H), 7.83−7.84 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 2970, 2931, 1682, 1456, 1306, 1231, 1299, 976, 835, 737 cm^{-1}; HRMS (DART): m/z calcd for $C_{13}H_{14}Cl_1O_1$ $[M - Cl]^+$ 221.0733; found: 221.0745.

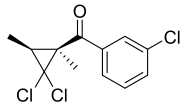
(1*S, 3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl(2-methoxyphenyl)methanone (12c).**



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 *p*-bromoanisole (1.12 g, 6.0 mmol) in THF (10 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **12c** (1.09 g, 79%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 2984, 2954, 1667, 1612, 1503, 1335, 1267, 1043, 851, 772 cm^{-1}; HRMS (DART): m/z calcd for $C_{13}H_{15}Cl_2O_2$ $[M + H]^+$ 273.0449; found: 273.0453.

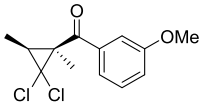
(1*S, 3*S**)-(3-Chlorophenyl)-2,2-dichloro-1,3-dimethylcyclopropyl)methanone (12d).**



Following a similar procedure for the preparation of ketone **11a**, the reaction using acid 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 SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **12d** (1.78 g, 80%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3069, 2972, 2932, 1686, 1572, 1452, 1420, 1304, 1229, 1182, 907, 837, 800, 733 cm^{-1}; HRMS (DART): m/z calcd for $C_{13}H_{15}Cl_2O_2$ $[M + H]^+$ 241.0187; found: 241.0188.

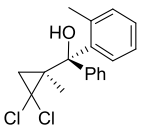
(1*S, 3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl(3-methoxyphenyl)methanone (12e).**



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 SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **12e** (1.15 g, 84%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 2933, 1682, 1597, 1306, 1260, 1043, 1001, 839 cm^{-1}; HRMS (DART): m/z calcd for $C_{13}H_{15}Cl_2O_2$ $[M + H]^+$ 273.0449; found: 273.0443.

(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](*o*-tolyl)(phenyl)methanol (1a).**



*n*BuLi (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, and then warmed up to 20−25 °C for 1 h. Sat. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude solid was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **1a** (1.10 g, 84%).

Colorless crystals; mp 116−118 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3566, 3059, 2940, 1485, 1321, 1217, 1086,

https://doi.org/10.1021/acsomega.1c02000
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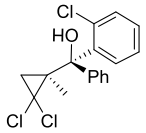
1024, 758, 748, 702 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{18}Cl_2O$ $[M - OH]^+$ 303.0707; found: 303.0698.

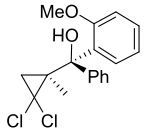
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](2-chlorophenyl)(phenyl)methanol (1b).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (1.00 g, 4.36 mmol), *n*BuLi (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 SiO_2-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, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3566, 3063, 3001, 1472, 1431, 1339, 1163, 1084, 754, 731, 702 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{17}H_{15}Cl_3O$ $[M - OH]^+$ 323.0161; found: 323.0160.

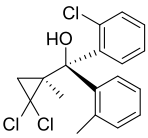
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](2-methoxyphenyl)(phenyl)methanol (1c).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (687 mg, 3.0 mmol), *n*BuLi (1.55 M in hexane, 2.9 mL, 4.5 mmol), and 2-bromoanisole (842 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 **1c** (674 mg, 67%).

Colorless crystals; mp 135−140 °C; ^1H NMR (500 MHz, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3509, 3005, 2941, 1487, 1464, 1234, 1026, 754, 702 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{18}Cl_2O_2$ $[M - OH]^+$ 319.06565; found: 319.0631.

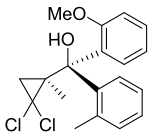
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](2-chlorophenyl)(*o*-tolyl)methanol (1d).**[11d]



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11b** (486 mg, 2.0 mmol), *n*BuLi (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 SiO_2-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, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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.

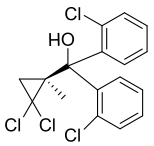
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](2-methoxyphenyl)(*o*-tolyl)methanol (1e).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11b** (486 mg, 2.0 mmol), *n*BuLi (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 SiO_2-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, $CDCl_3$): 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, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3503, 3065, 2941, 1487, 1456, 1385, 1287, 1233, 1028, 754, 733 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{20}Cl_2O_2$ $[M - OH]^+$ 333.0813; found: 333.0814.

(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](2-chlorophenyl)(2-chlorophenyl)methanol (1f).**[11d]



*n*BuLi (1.57 M in hexane, 8.4 mL, 13.2 mmol) was added to a stirred solution of 2-bromo-1-chlorobenzene (276 mg, 14.4 mmol) in THF (13 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Acid chloride **9** (562 mg, 3.0 mmol) in THF (6.5 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. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude solid was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **1f** (931 mg, 82%).

Colorless crystals; mp 102−108 °C; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 3H × 1/3), 1.23 (d, *J* = 7.5 Hz, 1H × 2/3), 1.43 (s, 3H × 2/3), 1.52 (d, *J* = 7.5 Hz, 1H × 1/3), 2.55 (d, *J* = 7.5 Hz, 1H × 2/3), 2.81 (d, *J* = 7.5 Hz, 1H × 1/3), 3.24 (s, 1H × 2/3), 3.75 (s, 1H × 1/3), 6.57−6.59 (m, 1H ×

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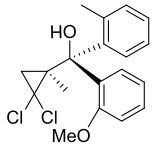
1/3), 7.21−7.23 (m, 1H), 7.35−7.49 (m, 5H), 7.74−7.76 (m, 1H), 7.90−7.91 (m, 1H × 2/3); these two atropisomers were settled to one isomer at high temperature. ^{1}H NMR (500 MHz, DMSO-d_6, 150 °C): δ = 1.36 (s, 3H), 1.47 (br s, 1H), 2.66 (br s, 1H), 4.52 (br s, 1H), 7.30−7.51 (m, 7H), 7.75−7.78 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.7, 24.1, 27.9, 31.3, 36.0, 39.1, 67.1, 68.0, 78.9, 82.4, 126.1, 126.7, 127.0, 127.5, 128.9, 129.0, 129.2, 129.6, 129.7, 131.1, 130.4, 130.9, 131.2, 131.5, 132.5, 131.6.

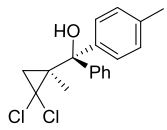
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](*o*-tolyl)(2-methoxyphenyl)methanol (1g).**[11d]



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11d** (518 mg, 2.0 mmol), *n*BuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 2-bromotoluene (513 mg, 3.0 mmol) in THF (4.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **1g** (556 mg, 79%).

Colorless crystals; mp 116−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 3H), 1.40 (d, J = 7.5 Hz, 1H), 2.65 (d, J = 7.5 Hz, 1H), 2.65 (s, 3H), 3.59 (s, 3H), 4.98 (s, 1H), 6.39−6.41 (m, 1H), 6.83−6.87 (m, 1H), 6.97−7.00 (m, 1H), 7.07−7.10 (m, 2H), 7.13−7.18 (m, 1H), 7.37−7.41 (m, 1H), 7.59−7.61 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 22.8, 24.4, 30.9, 35.8, 55.6, 67.1, 81.6, 112.5, 120.9, 124.7, 127.0, 128.5, 128.7, 128.8, 132.5, 132.9, 137.2, 144.8, 157.2.

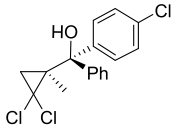
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](*p*-tolyl)(phenyl)methanol (3a).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (301 mg, 1.31 mmol), *n*BuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 4-bromotoluene (471 mg, 3.0 mmol) in THF (2.6 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **3a** (342 mg, 81%).

Paled yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 (s, 3H), 1.27 (d, J = 7.5 Hz, 1H), 2.33 (s, 3H), 2.51 (d, J = 7.5 Hz, 1H), 2.78 (s, 1H), 7.04−7.09 (m, 4H), 7.36−7.45 (m, 3H), 7.51−7.55 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.0 23.4, 27.7, 37.3, 67.7, 80.1, 127.5 (2C), 127.9, 128.10 (2C), 128.13 (2C), 129.1 (2C), 136.8, 143.1, 143.6; IR (neat): ν_{max} = 3564, 3001, 2943, 1607, 1508, 1329, 1302, 1250, 1180, 1165, 1034, 704 cm^{-1}; HRMS (DART): m/z calcd for $C_{18}H_{18}Cl_2O$ $[M - OH]^+$ 303.0707; found: 303.0695.

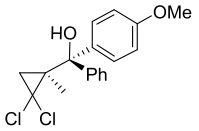
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](4-chlorophenyl)(phenyl)methanol (3b).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (687 mg, 3.0 mmol), *n*BuLi (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, $CDCl_3$): δ = 1.19 (s, 3H), 1.28 (d, J = 7.5 Hz, 1H), 2.49 (d, J = 7.5 Hz, 1H), 2.82 (s, 1H), 7.09−7.13 (m, 2H), 7.24−7.25 (m, 1H), 7.38−7.46 (m, 4H), 7.50−7.52 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ =23.3, 27.7, 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): ν_{max} = 3572, 3458, 2999, 2940, 2837, 1489, 1464, 1240, 1032, 754 cm^{-1}; HRMS (DART): m/z calcd for $C_{17}H_{15}Cl_3O$ $[M - OH]^+$ 323.0161; found: 323.0185.

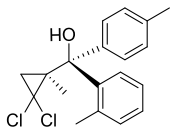
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](4-methoxyphenyl)(phenyl)methanol (3c).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (687 mg, 3.0 mmol), *n*BuLi (1.55 M in hexane, 2.9 mL, 4.5 mmol) and *p*-bromoanisole (842 mg, 4.5 mmol) in THF (6 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, $CDCl_3$): δ = 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, $CDCl_3$): δ = 23.4, 27.8, 37.5, 55.2, 67.7, 80.1, 112.8 (2C), 128.0, 128.2 (2C), 128.8 (2C), 129.1 (2C), 138.9, 143.2, 158.7; IR (neat): ν_{max} = 3570, 3026, 2943, 1329, 1219, 1163, 1026, 762, 704 cm^{-1}; HRMS (DART): m/z calcd for $C_{18}H_{18}Cl_2O_2$ $[M - OH]^+$ 319.0657; found: 319.0654.

(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](*p*-tolyl)(*o*-tolyl)methanol (3d).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11b** (486 mg, 2.0 mmol), *n*BuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 2-bromoanisole (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, $CDCl_3$): δ = 1.15 (s, 3H), 1.20 (d, J = 7.5 Hz, 1H), 1.99 (s, 3H), 2.34 (s, 3H), 2.55 (d, J = 7.5 Hz, 1H), 2.69 (s, 1H), 6.51−6.53 (m, 1H), 6.92−6.95 (m, 1H), 7.21−7.23 (m, 2H), 7.30−7.33 (m, 2H), 7.57−7.62 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.0, 22.0, 23.5, 38.4, 68.7, 80.5, 125.1, 125.6, 127.6 (2C), 128.1, 126.7, 129.2, 133.1, 136.7, 139.5, 139.7, 142.2; IR (neat): ν_{max} = 3551, 3022, 2978, 2940, 1487, 1456, 1036, 910, 760, 735

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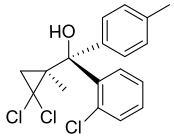
cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{20}Cl_2O$ [*M* − OH]$^+$ 317.0864; found: 317.0858.

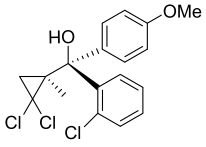
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](*p*-tolyl)(2-chlorophenyl)methanol (3e).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11c** (527 mg, 2.0 mmol), *n*BuLi (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 SiO_2-column chromatography (hexane/AcOEt = 50:1) to give the desired product **3e** (597 mg, 84%).

Paled yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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), 6.49 (br s, 1H), 6.95 (br s, 1H), 7.19−7.26 (m, 1H), 7.33−7.37 (m, 1H), 7.42−7.39 (m, 2H), 7.58 (br s, 1H), 7.71−7.73 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.0, 23.5, 37.9, 67.7, 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): ν_{max} = 3570, 3003, 2943, 1339, 1042, 908, 756, 737 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{17}Cl_3O$ [*M* − OH]$^+$ 337.0318; found: 337.0327.

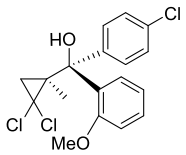
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](4-methoxyphenyl)(2-chlorophenyl)methanol (3f).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11c** (527 mg, 2.0 mmol), *n*BuLi (1.57 M in hexane, 1.6 mL, 2.4 mmol), and 4-bromoanisole (561 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 **3f** (613 mg, 83%).

Colorless crystals; mp 106−109 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 3H), 1.23 (d, *J* = 7.5 Hz, 1H), 2.60 (d, *J* = 7.5 Hz, 1H), 3.41 (s, 1H), 3.80 (s, 3H), 6.52−6.68 (m, 2H), 6.91−7.03 (m, 1H), 7.33−7.37 (m, 1H), 7.42−7.45 (m, 1H), 7.53−7.66 (m, 1H), 7.71−7.73 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 23.6, 27.5, 38.0, 55.2, 67.7, 79.7, 112.3, 114.1, 126.5, 126.8, 128.3, 129.4, 130.6, 132.2, 134.9, 137.6, 138.7, 158.8; IR (neat): ν_{max} = 3566, 3003, 2945, 1606, 1508, 1300, 1250, 1028, 908, 756, 735 cm^{-1}; HRMS (DART): *m/z* calcd for. $C_{18}H_{17}Cl_3O_2$ [*M* − OH]$^+$ 353.0267; found: 353.0263.

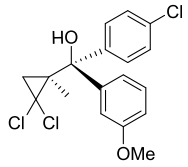
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](4-chlorophenyl)(2-methoxyphenyl)methanol (3g).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11d** (478 mg, 1.84 mmol), *n*BuLi (1.57 M in hexane, 1.4 mL, 2.20 mmol), and 4-bromo-1-chlorobenzene (528 mg, 2.76 mmol) in 2-MeTHF (3.8 mL) gave the crude solid, which was purified by recrystallization (hexane/2-propanol = 1:1) to give the desired product **3g** (444 mg, 65%).

Colorless crystals; mp 154−155 °C; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ = 1.10 (s, 3H), 1.27 (d, *J* = 6.9 Hz, 1H), 2.59 (d, *J* = 6.9 Hz, 1H), 3.60 (s, 3H), 4.76 (s, 1H), 6.68−7.82 (m, 8H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 23.6, 27.4, 36.8, 55.4, 67.0, 78.1, 112.3, 120.9, 127.7 (4C), 129.1, 129.4, 129.9, 132.7, 146.9, 157.4; IR (neat): ν_{max} = 3528, 2974, 2943, 1601, 1437, 1362, 1290, 1234, 1028, 756, 735 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{17}Cl_3O_2$ [*M* − OH]$^+$ 353.0267; found: 353.0252.

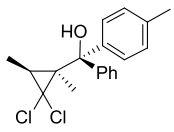
(*S)-[(1*S**)-2,2-Dichloro-1-methylcyclopropyl](*o*-tolyl)(3-methoxyphenyl)methanol (3h).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11e** (518 mg, 2.0 mmol), *n*BuLi (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 recrystallization (hexane/2-propanol = 1:1) to give the desired product **3h** (558 mg, 75%).

Colorless crystals; mp 155−158 °C; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): 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, 2 H), 7.32−7.38 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3561, 3001, 2940, 1703, 1487, 1254, 1028, 781 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{17}Cl_3O_2$ [*M* − OH]$^+$ 353.0267; found: 353.0253.

(*R)-[(1*S**)-(2,2-Dichloro-1,3-dimethylcyclopropyl)](*p*-tolyl)(phenyl)methanol (3i).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **12a** (729 mg, 3.0 mmol), *n*BuLi (1.57 M in hexane, 2.4 mL, 3.6 mmol), and 4-bromotoluene (770 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 **3j** (971 mg, 96%).

Paled yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 3H), 1.51 (q, *J* = 6.9 Hz, 1H), 1.76 (d, *J* = 6.9 Hz, 3H), 2.34 (s, 3H), 7.09−7.12 (m, 4H), 7.34−7.37 (m, 1H), 7.40−7.43 (m, 2H), 7.48−7.53 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.0, 21.0, 27.1, 36.2, 38.0, 73.9, 83.7, 127.7, 128.1 (2C), 128.12 (2C), 128.13 (2C), 128.8 (2C), 136.7, 143.6, 144.8; IR (neat): ν_{max} =3780, 3059, 3024, 2878, 1331, 1030, 970, 812, 760, 704 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{20}Cl_2O$ [*M* − OH]$^+$ 317.0864; found: 317.0866.

https://doi.org/10.1021/acsomega.1c02000
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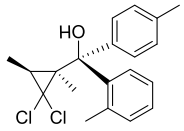
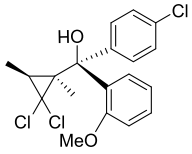
(*S)-[(1*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](*p*-tolyl)(*o*-tolyl)methanol (3j).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **12b** (514 mg, 2.0 mmol), *n*BuLi (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 SiO_2-column chromatography (hexane/AcOEt = 200:1) to give the desired product **3j** (372 mg, 53%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ =1.13 (s, 3H), 1.46 (q, J = 6.9 Hz, 1H), 1.79 (d, J = 6.9 Hz, 3H), 1.93 (s, 3H), 2.34 (s, 3H), 2.72 (s, 1H), 6.51−6.53 (m, 1H), 6.19−6.93 (m, 1H), 7.18−7.25 (m, 2H), 7.28−7.34 (m, 2H), 7.63−7.65 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.2, 21.0, 22.0, 36.2, 39.3, 74.9, 84.3, 125.1, 126.0, 127.6, 128.0, 128.1, 128.5, 129.2, 133.2, 136.5, 139.4, 141.0, 142.5; IR (neat): ν_{max} = 3059, 2928, 2878, 1684, 1456, 1379, 1032, 968, 903, 812, 760, 733 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{20}H_{22}Cl_2O$ $[M - OH]^+$ 331.1020; found: 331.1018.

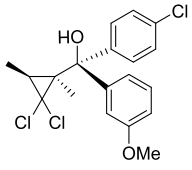
(*S)-[(1*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](4-chlorophenyl)(2-methoxyphenyl)methanol (3k).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **12c** (819 mg, 3.0 mmol), *n*BuLi (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 solid, which was purified by SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **3k** (912 mg, 79%).

Colorless crystals; mp 124−128 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3526, 3001, 2943, 1489, 1329, 1094, 1026, 764, 704 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{19}Cl_2$ $[M - OH]^+$ 367.0423; found: 367.0448.

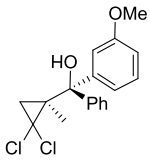
(*S)-[(1*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](4-chlorophenyl)(3-methoxyphenyl)methanol (3l).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **12c** (826 mg, 3.0 mmol), *n*BuLi (1.57 M in hexane, 2.9 mL, 4.5 mmol), and 4-bromochlorobenzene (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 **3l** (366 mg, 47%).

Colorless oil; ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ = 1.18 (s, 3H), 1.64 (q, J = 6.9 Hz, 1H), 1.74 (d, J = 6.9 Hz, 3H), 3.82 (s, 3H), 4.08 (s, 1H), 6.93−6.96 (m, 1H), 7.02−7.04 (m, 1H), 7.11−7.12 (m, 1H), 7.27−7.29 (m, 2H), 7.33−7.38 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.0, 27.0, 36.3, 38.0, 55.4, 73.8, 83.5, 114.0, 114.2, 121.1, 127.6, 129.3, 129.7, 133.1, 144.9, 145.8, 159.4; IR (neat): ν_{max} = 3566, 3375, 2934, 1701, 1599, 1489, 1456, 1254, 1034, 814 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{19}Cl_2O_2$ $[M - OH]^+$ 367.0423; found: 367.0441.

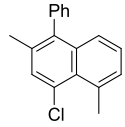
(*R)-[(1*S**)-(2,2-Dichloro-1-methylcyclopropyl)](3-methoxyphenyl)(phenyl)methanol (3m).**



Following a similar procedure for the preparation of AACM **1a**, the reaction using ketone **11a** (687 mg, 3.0 mmol), *n*BuLi (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 SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **3m** (834 mg, 83%).

Colorless crystals; mp 90−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 3H), 1.29 (d, J = 7.5 Hz, 1H), 2.51 (d, J = 7.5 Hz, 1H), 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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, 159.0; IR (neat): ν_{max} = 3566, 3001, 2941, 1582, 1485, 1433, 1317, 1250, 1026, 910, 779, 762, 737, 704 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{18}Cl_2O_2$ $[M - OH]^+$ 319.0657; found: 319.0644.

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



Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1a** (1.07 g, 3.33 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 3.3 mL, 3.3 mmol) in CH_2Cl_2 (6.7 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4a** (259 mg, 66%).

Colorless crystals; mp 74−76 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3024, 2972, 2934, 1385, 903, 760, 704 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{15}Cl$ $[M + H]^+$ 267.0941; found: 267.0940.

https://doi.org/10.1021/acsomega.1c02000
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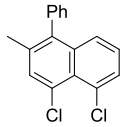
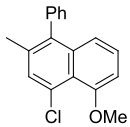
4,5-Dichloro-2-dimethyl-1-phenylnaphthalene (4b).



Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1b** (779 mg, 2.28 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 2.28 mL, 2.28 mmol) in CH_2Cl_2 (4.56 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4b** (449 mg, 69%).

Colorless crystals; mp 94−96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3024, 2920, 1375, 1024, 908, 766, 752, 702 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{17}H_{12}Cl_2$ $[M + H]^+$ 287.0394; found: 287.0381.

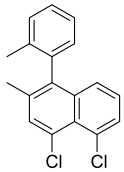
4-Chloro-5-methoxy-2-methyl-1-phenylnaphthalene (4c).



$TiCl_4$ (1.0 M in CH_2Cl_2, 1.4 mL, 1.4 mmol) was added to a stirred solution of AACM **1c** (452 mg, 1.34 mmol) in CH_2Cl_2 (1.4 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 (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product **4c** (211 mg, 56%).

Colorless crystals; mp 153−154 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3001, 2961, 1587, 1570, 1373, 1260, 1086, 770, 746 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{15}ClO$ $[M + H]^+$ 283.0890; found: 283.0885.

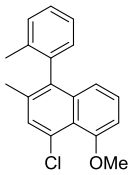
4,5-Dichloro-2-methyl-1-(*o*-tolyl)naphthalene (4d).



Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1d** (356 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4d** (153 mg, 51%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88 (s, 3H), 2.09 (s, 3H), 7.04−7.05 (m, 1H), 7.15−7.19 (m, 2H), 7.29−7.33 (m, 1H), 7.34−7.41 (m, 2H), 7.53−7.56 (m, 1H), 7.60−7.61 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 19.4, 19.8, 125.99, 126.05, 126.1, 126.2, 127.9, 129.1, 129.7, 130.2, 130.5, 133.2, 134.4, 136.3, 136.5, 137.8, 138.4.; IR (neat): ν_{max} = 3059, 3017, 2918, 1585, 1437, 1373, 910, 812, 764, 752, 733 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{14}Cl_2$ $[M]^+$ 300.0473; found: 300.0478.

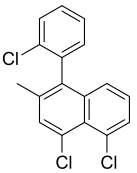
4-Chloro-5-methoxy-2-methyl-1-(*o*-tolyl)naphthalene (4e).



Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1e** (175 mg, 0.5 mmol) and $SnCl_4$ (1.0 M in CH_2Cl_2, 0.5 mL, 0.5 mmol) in CH_2Cl_2 (1.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4e** (96 mg, 68%).

Paled yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.89 (s, 3H), 2.07 (s, 3H), 3.98 (s, 3H), 6.81−6.85 (m, 2H), 7.05−7.06 (m, 1H), 7.19−7.23 (m, 1H), 7.28−7.35 (m, 3H), 7.47−7.48 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 19.4, 19.8, 55.9, 106.2, 119.1, 121.3, 126.0, 126.5, 127.5, 128.3, 129.8, 130.0, 131.1, 133.9, 136.1, 136.6, 136.7, 138.9, 156.4; IR (neat): ν_{max} = 3017, 2934, 2837, 1574, 1462, 1373, 1261, 1082, 910, 764, 750 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{17}ClO$ $[M + H]^+$ 297.1046; found: 297.1045.

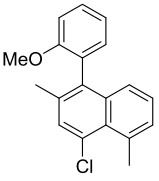
4,5-Dichloro-2-methyl-1-(2-chlorophenyl)-naphthalene (4f).



Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1f** (376 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4f** (159 mg, 49%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 19.8, 125.8, 126.0, 126.2, 127.2, 129.4, 129.8, 129.9, 130.7, 131.6, 133.1, 134.2, 135.0, 136.1, 137.7; IR (neat): ν_{max} = 3059, 2918, 1717, 1585, 1558, 1437, 1360, 1138, 1061, 1036, 910, 808, 750, 736 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{17}H_{11}Cl_3$ $[M + H]^+$ 321.0005; found: 320.9996.

4-Chloro-2,5-dimethyl-1-(2-methoxyphenyl)-naphthalene (4g).



https://doi.org/10.1021/acsomega.1c02000
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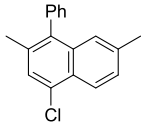
Following a similar procedure for the preparation of naphthalene **4c**, the reaction using AACM **1g** (351 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **4g** (158 mg, 53%).

Colorless crystals; mp 105−107 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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, 1435, 1256. 1246, 1026, 907, 754, 737 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{17}ClO$ $[M + H]^+$ 297.1046; found: 297.1041.

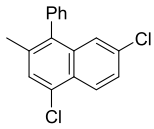
4-Chloro-2,7-dimethyl-1-phenylnaphthalene (5a).



A solution of AACM **3a** (577 mg, 1.8 mmol) in CH_2Cl_2 (1.8 mL) was added to a stirred solution $TiCl_4$ (1.0 M in CH_2Cl_2, 1.8 mL, 1.8 mmol) in CH_2Cl_2 (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 (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product **5a** (361 mg, 75%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.17 (s, 3H), 2.36 (s, 3H), 7.14−7.15 (m, 1H), 7.22−7.15 (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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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 $C_{18}H_{16}Cl$ $[M + H]^+$ 267.0941; found: 267.0937.

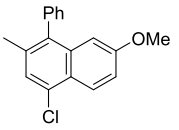
4,7-Dichloro-2-methyl-1-phenylnaphthalene (5b).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3b** (226 mg, 0.66 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 0.7 mL, 0.7 mmol) in CH_2Cl_2 (1.4 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5b** (160 mg, 84%).

Colorless crystals; mp 58−60 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.20 (s, 3H), 7.20−7.22 (m, 2H), 7.37−7.38 (m, 1H), 7.44−7.48 (m, 2H), 7.50−7.53 (m, 3H), 8.20−8.21 (m, 1H), 7.14−7.15 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.6, 125.4, 126.0, 126.6, 127.5, 127.6, 128.7 (2C), 128.8, 130.0 (2C), 130.8, 132.8, 134.8, 135.0, 136.9, 138.1; IR (neat): ν_{max} = 3075, 2938, 1609, 1597, 1406, 1346, 1088, 945, 907, 874, 815, 702 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{17}H_{12}Cl_2$ $[M]^+$ 286.0316; found: 286.0339.

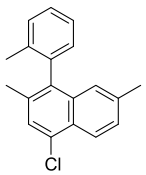
4-Chloro-7-methoxy-2-methyl-1-phenylnaphthalene (5c).



A solution of AACM **3c** (337 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added to a stirred solution $SnCl_4$ (1.0 M in CH_2Cl_2, 1 mL, 1.0 mmol) in CH_2Cl_2 (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 (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product **5c** (163 mg, 57%).

Colorless crystals; mp 83−84 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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, 135.5, 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 $C_{18}H_{16}ClO$ $[M + H]^+$ 283.0890; found: 283.0866.

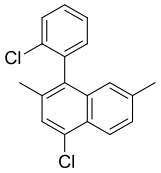
4-Chloro-2,7-dimethyl-1-(*o*-tolyl)naphthalene (5d).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3d** (335 mg, 2.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5d** (335 mg, 64%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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 $C_{19}H_{17}Cl$ $[M + H]^+$ 281.1097; found: 281.1100.

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



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3e** (356 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by

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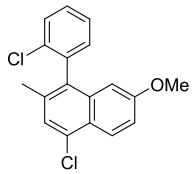
SiO_2-column chromatography (hexane) to give the desired product **5e** (201 mg, 67%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3H), 2.38 (s, 3H), 6.97−6.98 (m, 1H), 7.20−7.22 (m, 1H), 7.35−7.37 (m, 1H), 7.40−7.45 (m, 2H), 7.47−7.48 (m, 1H), 7.57−7.58 (m, 1H), 8.16−8.18 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.1, 21.8, 124.3, 124.7, 127.0, 127.5, 127.6, 128.2, 129.1, 129.7, 131.4, 131.9, 133.6, 134.2, 134.4, 136.8, 137.8; IR (neat): ν_{max} = 3053, 2920, 2856, 1622, 1506, 1356, 1063, 1036, 868, 814, 756 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{14}Cl_2$ $[M + H]^+$ 301.0551; found: 301.0536.

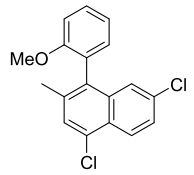
4-Chloro-7-methoxy-2-methyl-1-(2-chlorophenyl)-naphthalene (5f).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3f** (169 mg, 0.45 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 0.45 mL, 0.45 mmol) in CH_2Cl_2 (0.9 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5f** (56 mg, 39%).

Colorless crystals; mp 164−165 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3H). 3.68 (s, 3H), 6.50−6.51 (m, 1H), 7.12−7.23 (m, 2H), 7.38−7.43 (m, 3H), 7.56−7.59 (m, 1H), 8.18−8.20 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.2, 55.1, 104.8, 117.9, 124.6, 126.15, 126.21, 127.1, 129.1, 129.8, 131.4, 131.8, 133.5, 134.3, 134.8, 134.9, 137.8, 158.3; IR (neat): ν_{max} = 3069, 2951, 2363, 1620, 1506, 1437, 1227, 910, 756, 737 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{14}Cl_2O$ $[M + H]^+$ 317.0500; found: 317.0472.

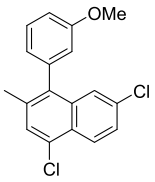
4,7-Dichloro-2-methyl-1-(2-methoxyphenyl)-naphthalene (5g).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3g** (372 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5g** (133 mg, 42%).

Colorless crystals; mp 87−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.17 (s, 3H), 3.69 (s, 3H), 7.05−7.12 (m, 3H), 7.33−7.34 (m, 1H), 7.42−7.48 (m, 2H), 7.51−7.53 (m, 1H), 8.18−8.20 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.3, 55.5, 111.2, 120.9, 125.2, 126.1, 126.5, 126.6, 127.6, 128.8, 129.5, 131.6, 132.6, 135.9, 157.1; IR (neat): ν_{max} = 3069, 3001, 2833, 1611, 1578, 1489, 1458, 1433, 1260, 1246, 1026, 947, 908, 876, 816, 754, 743 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{14}Cl_2O$ $[M + H]^+$ 317.0500; found: 317.0481.

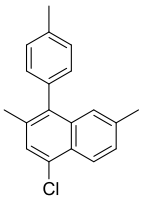
4,7-Dichloro-2-methyl-1-(3-methoxyphenyl)-naphthalene (5h).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3h** (372 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5h** (280 mg, 88%).

Colorless crystals; mp 87−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.21 (s, 3H), 3.85 (s, 3H), 6.74−6.76 (m, 1H), 6.78−6.81 (m, 1H), 6.98−7.02 (m, 1H), 7.40−7.46 (m, 3H), 7.51−7.52 (m, 1H), 8.19−8.21 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.6, 55.3, 113.0, 115.6, 122.4, 125.4, 126.0, 126.7, 127.5, 128.8, 129.8, 130.8, 132.8, 134.7, 136.8, 139.6, 159.8; IR (neat): ν_{max} = 3001, 2920, 1607, 1578, 1495, 1431, 1285, 1047, 924, 874, 816, 735 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{14}Cl_2O$ $[M + H]^+$ 317.0500; found: 317.0480.

4-Chloro-2,7-dimethyl-1-(*p*-tolyl)naphthalene (5i).



*n*BuLi (1.57 M in hexane, 2.8 mL, 4.4 mmol) was added to a stirred solution of 4-bromotoluene (855 mg, 5.0 mmol) in THF (2.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Methyl (*S**)-2,2-dichloro-1-methylcyclopropane-1-carboxylate[10b] (366 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. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude oil in CH_2Cl_2 (2.0 mL) was added to stirred solution of $TiCl_4$ (1.0 M in CH_2Cl_2, 2.0 mL, 2.0 mmol) in CH_2Cl_2 (2.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane) to give the desired product **5i** (287 mg, 51%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.18 (s, 3H), 2.37 (s, 3H), 2.47 (s, 3H), 7.10−7.12 (m, 2H), 7.18−7.19 (m, 1H), 7.30−7.34 (m, 3H), 7.44−7.45 (m, 1H), 8.14−8.16 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.6, 21.3, 21.8, 124.1, 125.6, 127.5, 127.6, 128.0, 129.2 (2C), 130.0 (2C), 133.7, 134.4, 136.1, 136.2, 136.7, 137.0; IR (neat): ν_{max} = 3021, 2918, 1624, 1514, 1429, 1356, 1204, 1043, 908, 868, 812, 735 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{19}H_{17}Cl$ $[M + H]^+$ 281.1097; found: 281.1103.

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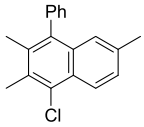
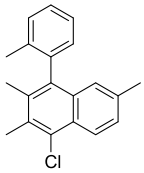
4-Chloro-2,3,7-trimethyl-1-phenylnaphthalene (5j).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3i** (335 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5j** (275 mg, 98%).

Colorless crystals; mp 119−121 °C; ^1H NMR (500 MHz, $CDCl_3$): δ = 2.14 (s, 3H). 2.34 (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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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, 132.1, 132.6, 133.7, 135.2, 136.8, 140.2; IR (neat): ν_{max} = 3057, 2920, 1441, 907, 814, 737, 704 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{18}H_{16}Cl$ $[M + H]^+$ 281.1083; found: 281.1097.

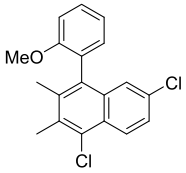
4-Dichloro-2,3,7-trimethyl-1-(*o*-tolyl)naphthalene (5k).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3j** (331 mg, 0.95 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 0.95 mL, 0.95 mmol) in CH_2Cl_2 (2.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5k** (270 mg, 96%).

Colorless crystals; mp 110−115 °C; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.90 (s, 3H), 2.08 (s, 3H), 2.33 (s, 3H), 2.59 (s, 3H), 6.91 (m, 1H), 7.06−7.07 (m, 1H), 7.29−7.38 (m, 4H), 8.20−8.22 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 17.9, 18.3, 19.6, 21.6, 124.4, 126.0, 127.4 127.9, 128.1, 130.0, 130.2, 130.3, 132.1, 133.7, 135.4, 136.0, 136.9, 139.5; IR (neat): ν_{max} = 3019, 2920, 2862, 1497, 1452, 1317, 1042, 910, 814, 758, 731 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{20}H_{19}Cl$ $[M + H]^+$ 295.1254; found: 295.1231.

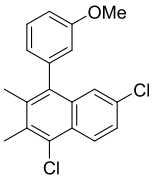
4,7-Dichloro-2,3-dimethyl-1-(2-methoxypheny)-naphthalene (5l).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3k** (386 mg, 1.0 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5l** (313 mg, 95%).

Colorless crystals; mp 129−132 °C; ^1H NMR (500 MHz, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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 $C_{19}H_{16}Cl_2O$ $[M + H]^+$ 331.0657; found: 331.0637.

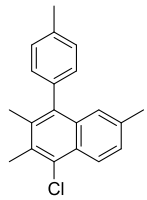
4,7-Dichloro-2,3-dimethyl-1-(3-methoxyphenyl)-naphthalene (5m).



Following a similar procedure for the preparation of naphthalene **5a**, the reaction using AACM **3l** (193 mg, 0.5 mmol) and $TiCl_4$ (1.0 M in CH_2Cl_2, 0.5 mL, 0.5 mmol) in CH_2Cl_2 (1.0 mL) gave the crude solid, which was purified by SiO_2-column chromatography (hexane) to give the desired product **5m** (129 mg, 78%).

Colorless crystals; mp 119−123 °C; ^1H NMR (500 MHz, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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 $C_{12}H_{14}Cl_2O_2$ $[M - OH]^+$ 331.0657; found: 311.0634.

4-Chloro-2,3,7-trimethyl-1-(*p*-tolyl)naphthalene (3n).



*n*BuLi (1.57 M in hexane, 2.8 mL, 4.4 mmol) was added to a stirred solution of 4-bromotoluene (855 mg, 5.0 mmol) in THF (2.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Methyl (1*S**,3*S**)-2,2-dichloro-1,3-dimethylcyclopropane-1-carboxylate[10b] (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. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude oil in CH_2Cl_2 (2.0 mL) was added to stirred solution of $TiCl_4$ (1.0 M in CH_2Cl_2, 2.0 mL, 2.0 mmol) in CH_2Cl_2 (2.0 mL) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried ($NaSO_4$) and concentrated. The obtained crude oil was purified by SiO_2-column chromatography (hexane) to give the desired product **3n** (447 mg, 76%).

https://doi.org/10.1021/acsomega.1c02000
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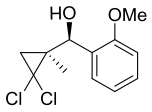
Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3H), 2.34 (s, 3H), 2.47 (s, 3H), 2.58 (s, 3H), 7.07−7.11 (m, 3H), 7.29−7.33 (m, 3H), 8.19−8.21 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 17.9, 19.0, 21.3, 21.6, 124.3, 125.7, 127.7, 128.0, 129.1 (2C), 130.1 (2C), 130.3, 132.1, 132.7, 133.9, 135.1, 136.6, 136.9, 137.1; IR (neat): ν_{max} = 3021, 2918, 2864, 1514, 1494, 1454, 1317, 1043, 1022, 908, 812, 735 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{20}H_{19}Cl$ [*M* + H]$^+$ 331.0657; found: 311.0634.

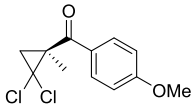
(*S)-((1*S**)-2,2-dichloro-1-methylcyclopropyl)(2-methoxyphenyl)methanol (13).**



$NaBH_4$ (125 mg, 3.3 mmol) was added to a stirred solution ketone **11d** (777 mg, 3.0 mmol) in MeOH (3.0 mL) at room temperature under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Water was added to the mixture, which was extracted twice with ether. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 20:1) to give the desired product **13** (654 mg, 84%).

Colorless crystals; mp 57−59 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 7.5 Hz, 1H), 1.25 (s, 3H), 1.93 (d, *J* = 7.5 Hz, 1H), 2.42 (br s, 1H), 3.80 (s, 3H), 5.13 (s, 1H), 6.87−6.89 (m, 1H), 7.00−7.04 (m, 1H), 7.25−7.29 (m, 1H), 7.56−7.38 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 15.0, 31.7, 35.1, 55.2, 67.4, 71.8, 110.3, 120.6, 128.0, 128.5, 129.0, 155.9; IR (neat): ν_{max} = 3532, 2940, 2878, 2839, 1487, 1462, 1234, 1092, 1028, 916, 814, 756, 735 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{12}H_{14}Cl_2O_2$ [*M* − OH]$^+$ 243.0344; found: 243.0326.

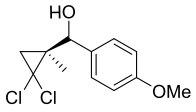
(*S)-(2,2-Dichloro-1-methylcyclopropyl)(4-methoxyphenyl)methanone (15).**



Following a similar procedure for the preparation of ketone **11a**, the reaction using acid chloride **9** (937 mg, 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 SiO_2-column chromatography (hexane/AcOEt = 30:1) to give the desired product **15** (1.26 g, 97%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 7.5 Hz, 1H), 1.65 (s, 3H), 2.24 (d, *J* = 7.5 Hz, 1H), 3.90 (s, 3H), 7.00−7.03 (m, 2H), 7.93−7.96 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.0, 29.6, 39.6, 55.5, 62.5, 114.0 (2C), 127.3, 132.0 (2C),163.8, 193.9; IR (neat): ν_{max} = 3005, 2936, 1678, 1601, 1456, 1317, 1258, 1167, 1032, 984, 777, 503 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{12}H_{12}Cl_2O$ [*M* + H]$^+$ 259.0293; found: 259.0278.

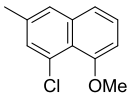
(*S)-((1*S**)-2,2-Dichloro-1-methylcyclopropyl)(4-methoxyphenyl)methanol (16).**



Following a similar procedure for the preparation of alcohol **13**, the reaction using ketone **15** (777 mg, 3.0 mmol) and $NaBH_4$ (125 mg, 3.3 mmol) in MeOH (3.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane/AcOEt = 20:1) to give the desired product **16** (605 mg, 77%).

Colorless crystals; mp 68−71 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3566, 3466, 2938, 1611, 1512, 1385, 1302, 1072, 1034, 959, 831, 770, 752 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{12}H_{12}Cl_2O$ [*M* − OH]$^+$ 243.0344; found: 243.0363.

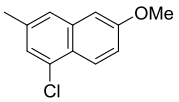
1-Chloro-8-methoxy-3-methylnaphthalene (14).



$SnCl_4$ (1.0 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) was added to a stirred solution of alcohol **13** (261 mg, 1.0 mmol) and MS4A (1.0 g) 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. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product **14** (97 mg, 47%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3063, 3001, 2962, 1587, 1570, 1389, 1373, 1260, 1086, 770, 706 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{12}H_{11}ClO$ [*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** (131 mg, 0.5 mmol), MS4A (0.5 g), and $SnCl_4$ (1.0 M in CH_2Cl_2, 0.5 mL, 0.5 mmol) in 1,2-dichloroethane (5.0 mL) gave the crude oil, which was purified by SiO_2-column chromatography (hexane) to give the desired product **17** (53 mg, 51%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.4, 55.3, 105.5, 118.6, 124.4, 125.1, 125.8, 125.9, 131.5, 136.0, 136.4, 158.2; IR (neat): ν_{max} = 2920, 1628, 1504, 1441, 1265, 1238, 1036, 858, 820 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{12}H_{11}ClO$ [*M* − OH]$^+$ 207.0577; found: 207.0554.

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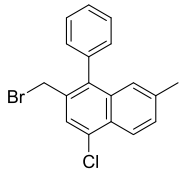
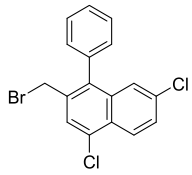
2-(Bromomethyl)-4-chloro-7-methyl-1-phenylnaphthalene (5a′).



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 (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product **5a′** (49 mg, 45%).

Colorless crystals; mp 123−124 °C, ^{1}H NMR (400 MHz, $CDCl_3$): 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).

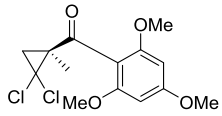
2-(Bromomethyl)-4,7-dichloro-1-phenylnaphthalene (5b′).



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 SiO_2-column chromatography (hexane) to give the desired product **5b′** (176 mg, 69%).

Colorless crystals; mp 139−140 °C, ^{1}H NMR (500 MHz, $CDCl_3$): 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).

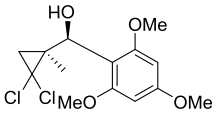
(*S)-2,2-Dichloro-1-methylcyclopropyl(2,4,6-trimethoxyphenyl)methanone (18).**



$AlCl_3$ (480 mg, 3.6 mmol) and acid chloride **9** (187 mg, 1.0 mmol) was added to a stirred solution 1,3,5-trimethoxybenzene (505 mg, 3.0 mmol) in CH_2Cl_2 (2.0 mL) at 0−5 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 2 h, and then warmed up to 20−25 °C for 1 h. 10% NaOH aqueous solution was added to the mixture, which was extracted three times with CH_2Cl_2. The combined organic phase was washed with brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 5:1) to give the desired product **18** (221 mg, 69%)

Colorless crystals; mp 85−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (d, *J* = 7.3 Hz, 1H), 1.49 (s, 3H), 2.50 (d, *J* = 7.3 Hz, 1H), 3.85 (s, 9H), 6.12 (s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 19.4, 30.6, 41.2, 55.4, 55.9 (2C), 66.0, 90.6 (2C), 110.1, 159.9 (2C), 163.4, 195.5; IR (neat): ν_{max} = 3003, 2941, 1684, 1605, 1585, 1456, 1416, 1229, 1207, 1157, 1132, 974, 756 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{14}H_{16}Cl_2O_4$ $[M + H]^+$ 319.0504; found: 319.0503.

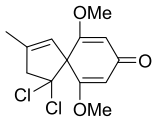
(*S)-((*S**)-2,2-Dichloro-1-methylcyclopropyl)(2,4,6-trimethoxyphenyl)methanol (19).**



Ketone **18** (848 mg, 2.65 mmol) in THF (5.3 mL) was added to a stirred solution $LiAlH_4$ (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 (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 10:1−5:1) to give the desired product **19** (322 mg, 38%)

Colorless crystals; mp 134−137 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3501, 2943, 1609, 1591, 1418, 1217, 1150, 1121, 1032, 754 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{14}H_{18}Cl_2O_4$ $[M - OH]^+$ 303.0555; found: 303.0560.

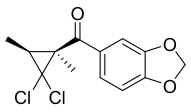
4,4-Dichloro-6,10-dimethoxy-2-methylspiro[4.5]-deca-1,6,9-trien-8-one (20).



$SnCl_4$ (1.0 M in CH_2Cl_2, 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. $NaHCO_3$ aqueous solution was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane/AcOEt = 2:1) to give the desired product **20** (81 mg, 70%).

Colorless crystals; mp 182−184 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 3065, 2978, 2938, 2918, 1668, 1651, 1622, 1591, 1360, 1238, 1211, 1098, 864, 847, 743 cm^{-1}; HRMS (DART): *m/z* calcd for $C_{13}H_{14}Cl_2O_3$ $[M + H]^+$ 289.0398; found: 289.0413.

(1*S,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl(3,4-methylenedioxyphenyl)methanone (21).**[11e]



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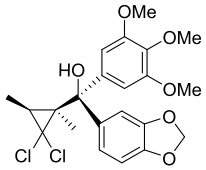
A solution of acid chloride **10** (2.01 g, 10.0 mmol) in THF (10 mL) was added to a stirred solution of Grignard reagent generated from Mg (267 mg, 11.0 mmol) and 4-bromo-1,2-methylenedioxybenzene (2.21 g, 11.0 mmol) in THF (10 mL) at 0−5 °C, and the mixture was stirred at 20−25 °C for 3 h. Sat. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude 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, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 1672, 1602, 1487, 1438, 1300, 1247, 1097 cm^{-1}.

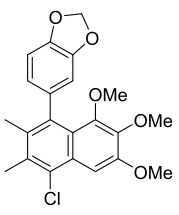
(*R)-[(1*S**,3*S**)-2,2-Dichloro-1,3-dimethylcyclopropyl](3,4-methylenedioxyphenyl)(3,4,5-trimethoxyphenyl)methanol (22).**



*n*BuLi (1.63 M in hexane, 8.2 mL, 13.4 mmol) was added to a stirred solution of 5-bromo-1,2,3-trimethoxybenzene (3.21 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 mixture at −78 °C and warmed up to 20−25 °C during about 4 h. Sat. NH_4Cl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude 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, $CDCl_3$): 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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 2936, 1589, 1504, 1454, 1414, 1335, 1232, 1124 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{24}Cl_2O_6$ $[M + Na]^+$ 477.0848; found: 477.0878.

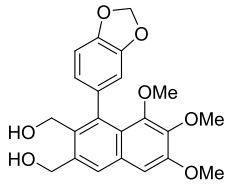
5-(4-Chloro-6,7,8-trimethoxy-2,3-dimethylnaphthalen-1-yl)benzo[d][1,3]dioxole (23).



A solution of alcohol **22** (1.37 g, 3.0 mmol) in CH_2Cl_2 (10 mL) was added to a stirred solution of $SnCl_4$ (1.0 M in CH_2Cl_2, 3 mL, 3.0 mmol) in CH_2Cl_2 (50 mL) at 20−25 °C, and the mixture was stirred at the same temperature for 30 min. $NaHCO_3$ aqueous solution was added to the mixture, which was extracted twice with $CHCl_3$. The combined organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by 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, $CDCl_3$): δ = 2.04 (s, 3H), 2.56 (s, 3H), 3.32 (s, 3H), 3.85 (s, 3H), 4.02 (s, 3H), 6.01 (d, J = 1.7 Hz, 1H), 6.02 (d, J = 1.7 Hz, 1H), 6.58 (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); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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): ν_{max} = 2937, 1611, 1487, 1433, 1337, 1223, 1138, 1040 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{21}ClO_5$ $[M + Na]^+$ 423.0975; found: 423.0989.

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



A mixture of α-arylnaphthalene **23** (361 mg, 0.90 mmol), *N*-bromosuccinimide (641 mg, 3.60 mmol), and AIBN (15 mg, 0.09 mmol) in CCl_4 (9 mL) was refluxed for 2 h. After cooling down, water was added to the mixture, which was extracted twice with $CHCl_3$. The combined organic phase was washed with 1 M HCl aqueous solution, water, 3% $Na_2S_2O_3$ aqueous solution, and brine, dried (Na_2SO_4) 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 Et_2O. The combined organic phase was washed three times with water and brine, dried (Na_2SO_4) 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 SmI_2 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, and the mixture was stirred at the same temperature for 1 h. 1 M HCl aqueous solution was added to the mixture, which was extracted twice with Et_2O. The combined organic phase was washed with water, 3% $Na_2S_2O_3$ aqueous solution, and brine, dried (Na_2SO_4) 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%).

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Colorless crystals; mp 184−187 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.36 (s, 1H), 3.14 (s, 1H), 3.34 (s, 3H), 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 = 7.5 Hz, 1H), 6.98 (s, 1H), 7.72 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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, 146.1, 146.8, 150.2, 153.4; IR (neat): ν_{max} = 3343, 2937, 1607, 1562, 1487, 1379, 1227, 1138 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{22}O_7$ $[M + Na]^+$ 421.1263; found: 421.1263.

Chaihunaphthone[15] **[4-(Benzo[d][1,3]dioxol-5-yl)-5,6,7-trimethoxynaphtho[2,3-c]furan-1(3*H*)-one].** A suspension of diol **25** (22 mg, 0.06 mmol) and Fetizon's reagent (Ag_2CO_3 on Celite) (684 mg) in toluene (18 mL) was stirred under reflux for 5 h using Dean−Stark apparatus with continual removal of water. After cooling down, the mixture was filtrated through Celite with $CHCl_3$ and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 3:1) to give the desired chaihunaphthone (16 mg, 72%).

Colorless crystals; mp 189−191 °C [lit.[15] mp 164−166 °C]; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.39 (s, 3H), 3.94 (s, 3H), 4.03 (s, 3H), 5.05 (d, J = 14.9 Hz, 1H), 5.12 (d, J = 14.9 Hz, 1H), 6.04 (d, J = 1.7 Hz, 1H), 6.06 (d, J = 1.7 Hz, 1H), 6.74 (dd, J = 1.7, 8.0 Hz, 1H), 6.77 (d, J = 1.7 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 7.16 (s, 1H), 8.31 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 55.9, 60.9, 61.1, 69.8, 101.1, 104.5, 107.8, 108.9, 120.7, 122.4, 124.9, 126.2, 131.7, 132.0, 133.2, 139.1, 145.0, 146.6, 147.2, 149.6, 153.4, 171.3.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c02000.

Characterization of all new products for ^{1}H NMR (500 MHz, $CDCl_3$) spectra, ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound **9**, ^{1}H NMR (500 MHz, $CDCl_3$) spectra (PDF)

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Notes

The authors declare no competing financial interest.

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