Metal trflate promoted synthesis of naphthalenes†

Chieh-Kai Chan, Heui-Sin Wang, Yu-Lin Tsai and Meng-Yang Chang

A synthetic route to derive the skeleton of naphthalenes starting with isovanillin is described with modest total yields via the key transformation of metal trflate-mediated intramolecular benzannulation of o-formyl or o-benzoyl allylbenzenes in MeNO₂ at rt.

Introduction

A naphthalene ring system is a key core skeleton for bioactive molecules, natural products and functionalized materials. A considerable number of attempts have been developed to determine the synthetic routes of the bicyclic skeleton. Two major key transformations for the formation of a functionalized naphthalene skeleton include: (1) acids (or Lewis acids) promote intramolecular Friedel–Crafts type annulations, and (2) bases promote intramolecular anionic annulations. Transition metal (e.g., Cr, Mn, Pd, W, Rh, Co, Ru, Ni, Co, Zn, Ti and Au) catalyzed benzannulations provide another approach for preparing the core structure. Therefore, a new synthetic route for diverse naphthalenes via intramolecular annulation of the readily available starting materials is still a continuing need in the synthetic field.

As part of our efforts in the synthetic applications of dialkoxy o-formyl allylbenzenes and the development of metal trflate-promoted robust and efficient reactions, we have now streamlined the facile synthesis of substituted naphthalenes via metal trflate-mediated intramolecular benzannulation of o-carbonyl synthon allylbenzenes, such as o-formyl or o-benzoyl allylbenzenes, in MeNO₂ at rt. To the best of our knowledge, few reports on the metal trflate-mediated intramolecular annulation of o-carbonyl synthon allylbenzenes have been documented. In 2011, Kuninobu and Takai described that metal trflates-catalyzed the dehydrative cycloaromatization of o-benzylbenzaldehyde provided tricyclic anthracene in a 97% yield. Among the metal trflate-mediated syntheses, In(OTf)₃ and Sc(OTf)₃ demonstrated excellent transformation. In 2014, Luo demonstrated that Cu(OTf)₂ provided a tetratalen skeleton via the conjugate addition of 2’-allylchalcone in a higher (90%) yield than the other scanned catalysts. The adopted synthetic routes are described in Scheme 1. Our aim was to find an optimal metal trflate as the catalyst for synthesizing naphthalenes via the intramolecular benzannulation of o-formyl allylbenzene (a hybrid combining the formyl motif of 2 and the allyl group of 3).

Results and discussion

Initially, six metal triflates were chosen as the catalysts for examining the benzannulation of o-formyl allylbenzene 4a. In line with two preliminary studies, 10 mol% catalytic amounts of In(OTf)₃, Sc(OTf)₃, Cu(OTf)₂, Bi(OTf)₃, and AgOTf were first scanned for the formation of 1,2-dimethoxynaphthalene (5a) in MeNO₂ at rt for 8 h, as shown in Table 1 and entries 1–5. However, 5a was isolated in a range of poor to moderate yields (18–72%). When Sn(OTf)₂ or Fe(OTf)₃ was applied to the reaction conditions, yields were increased to 95% or 88% (entries 6 and 7). Under the same conditions, treatment of 4a with Ga(OTf)₃ provided 5a in a 44% yield along with a 38% yield of 6a.

Scheme 1 Metal trflate-catalyzed annulations.
Table 1  Metal triflates mediated reaction conditions*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>5a (%)</th>
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<tr>
<td>1</td>
<td>Bi(OTf)3 (10)</td>
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<td>25</td>
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<td>72</td>
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<td>2</td>
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<td>MeNO2</td>
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<tr>
<td>3</td>
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<td>MeNO2</td>
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<td>18*</td>
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<tr>
<td>6</td>
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<td>MeNO2</td>
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<td>95</td>
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<tr>
<td>7</td>
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<td>88</td>
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<tr>
<td>8</td>
<td>Ga(OTf)3 (10)</td>
<td>MeNO2</td>
<td>25</td>
<td>8</td>
<td>44 (38)*</td>
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<tr>
<td>9</td>
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<td>MeNO2</td>
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<tr>
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<td>Toluene</td>
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<td>15</td>
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<tr>
<td>16</td>
<td>Sn(OTf)2 (10)</td>
<td>MeNO2</td>
<td>25</td>
<td>8</td>
<td>—&lt;c,d&gt;</td>
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<tr>
<td>17</td>
<td>Sn(OTf)2 (10)</td>
<td>MeNO2</td>
<td>25</td>
<td>8</td>
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</table>

* Reactions were run on 4a (0.5 mmol), solvent (5 mL). * Isolated yields. * 4a was recovered (entry 5, 26%; entry 6, 54%; entry 14, 85%; entry 16, 80%). * 6a (25%) was isolated. * Unknown product (35%) was formed. * Proton scavenger (2,6-di-tert-butylpyridine, 10 mol%) was added. * No reaction. * Water (10 mg) was added.

In addition, 6a was generated via Ga(OTf)3-mediated by the addition of 4a with MeNO2. With these results in mind, a series of commercially available lanthanide triflates (Ln(OTf)3) were examined next, including: La(OTf)3, Ce(OTf)3, Pr(OTf)3, Nd(OTf)3, Sm(OTf)3, Eu(OTf)3, Gd(OTf)3, Tb(OTf)3, Dy(OTf)3, Ho(OTf)3, Er(OTf)3, Yb(OTf)3 and Tm(OTf)3. However, no isolation of the desired 5a was observed and only 4a was recovered under Ln(OTf)3-mediated reactions. With the results in hand, we found that Sn(OTf)2 was among the most reactive and used catalyst compared to other metal triflate derivatives. Along this line, we planned to take advantage of the intrinsically high catalytic ability of Sn(OTf)2 to construct the naphthalene system. After decreasing the catalytic amounts (10 → 5 mol%), a poor yield (72%) was observed (entry 9). Furthermore, we studied the factors of solvent and temperature. After changing the solvents (from MeNO2 to CH2Cl2 and toluene), different results were observed (entries 10 and 11). In entry 12, the complex mixture occurred (35%) when elevating the temperature (25 → 101).

Next, Sn(OTf)2 exhibited a low yield (83%) under an elongated reaction time (8 → 20 h), as shown in entry 13. Another type of tin(II) salt (e.g. SnCl2) was examined. In entry 14, 5a was isolated in trace amounts only. By the involvement of 10 mol% TfOH (entry 15), 60% of 5a was generated. The control experiment revealed that the real catalyst was the trace amount of TfOH resulting from the hydrolysis of the metal triflates. In the other hand, proton scavenger (2,6-di-tert-butylpyridine, 10 mol%) was involved in the reaction system (entry 16). The resulting mixture failed to promote dehydrative benzannulation in the presence of 4a due to the proton scavenger could block *in situ* generated TfOH. To examine the stability and reactivity of Sn(OTf)2 in the presence of water, H2O (10 mg) was added to the reaction condition and a 90% yield of 5a was generated (entry 17). According to the results, a 10 mol% of Sn(OTf)2/MeNO2/rt condition would be an optimal combination for yielding 5a.

Aside from the present benzannulation of o-formyl allyl-benzene 4a, Sn(OTf)2 has also been reported as a catalyst for aldol reactions.11a,b Mannish-type reactions,11b,c rearrangements,11d,e (3 + 2) annulations,11f,g and other routes.11h,i For branched, linear and cyclic alkyl substituents of o-formyl allyl-benzenes 4b–d (R = Me, iPr, nBu, and c-C5H9), 5b–d provided good yields (90%, 91% or 88%) under the above-mentioned conditions (Scheme 2).

On the basis of the results, a plausible reaction mechanism is shown in Scheme 3. Mechanistically, two general distinctive activation modes of the o-allylbenzaldehydes can be proposed for intramolecular dehydrative benzannulations. The first one is a purely metallic-based Lewis acid pathway. The sequence initiates the formation of intermediate A by complexation of a carbonyl motif of 3a with Sn(OTf)2. The *in situ* generated triane anion deprotonates the Ha (blue) of A to give B as the result of a tandem intramolecular electrophilic annulation. Following the protonation of B with the TfOH, C is obtained. On the basis of the triane anion-mediated deprotonation of C (for Hb, pink), 5a is provided via the removal of Sn(OH)OTf and TfOH. Subsequently, Sn(OTf)2 is regenerated for the next catalytic cycle by the complexation of Sn(OH)OTf and TfOH. The second
possibility would involve a Brønsted acid catalysis. By Sn(OTf)\textsubscript{2} assisted \textit{in situ} formed TOH, D is generated.\textsuperscript{17} Following the above similar route, 5a is also produced \textit{via} (i) the triflate anion deprotonates the H\textsubscript{4} of D, (ii) protonation of E with the TOH, (iii) triflate anion-mediated deprotonation of F (for H\textsubscript{4}), (iv) the removal of water and the regeneration of TOH. Although metal triflate-mediated transformations have been described proceeding \textit{via} proton transfer, we think that the nature of the catalytic species may be still under debate.\textsuperscript{18} For the overall benzannulation procedure, water is the only by-product. Therefore, it is important to use Sn(OTf)\textsubscript{2} that are stable and show high reactivity even in the presence of water.\textsuperscript{19,21,24} Metal cations (e.g. Bi\textsuperscript{3+}, Al\textsuperscript{3+} or Sn\textsuperscript{2+}) in water exhibit strong acidic properties because of the acidification through coordination of water molecules present in the “inner-sphere” of the cation.\textsuperscript{19} According to Duńach report,\textsuperscript{19a} metal triflates such as Bi(OTf)\textsubscript{3} are generally obtained and used as its hydrate form and therefore presents indubitably a strong induced Brønsted acidity.

Furthermore, Sn(OTf)\textsubscript{2}-mediated conversion of o-aryloxyallylbenzenes 4e-l into aryl-naphthalenes 5e-l was examined, as shown in Scheme 4. The starting materials 4e-l (R = H, allyl; Ar = Ph, 4-FC\textsubscript{6}H\textsubscript{4}, 2-Me\textsubscript{2}C\textsubscript{6}H\textsubscript{4}, 2-MeOC\textsubscript{6}H\textsubscript{4}, 3-MeOC\textsubscript{6}H\textsubscript{4}, 4-MeOC\textsubscript{6}H\textsubscript{4}, 3,4-C\textsubscript{2}H\textsubscript{4}O\textsubscript{2}C\textsubscript{6}H\textsubscript{3}) were prepared by our previous reports.\textsuperscript{19} The substituents of R and Ar on 4e-l did not affect the yield outcome for the benzannulation procedure and no obvious yield changes were observed for the generation of 5e-l. The isolated yields were provided in the range of 88–95%. The structures of 5e and 5f were determined by single-crystal X-ray crystallography.\textsuperscript{14}

As an extension of the benzannulation, the skeleton of aryloxybenzene having two allyl arms (ortho and para positions) was studied (Scheme 5). Treatment of 4m-o (R = H, Me; Ar = 4-MeOC\textsubscript{6}H\textsubscript{4}, 3,4-CH\textsubscript{2}O\textsubscript{2}C\textsubscript{6}H\textsubscript{3}) with Sn(OTf)\textsubscript{2} provided 5m-o in 95%, 90% and 91% yields, respectively. Notably, the p-allyl substituent was unaffected. With the results in hands, 10 mol% of Sn(OTf)\textsubscript{2} was applied to the annulation of two substrates 4j (Ar = 4-MeOC\textsubscript{6}H\textsubscript{4}) or 4l (Ar = 3,4-CH\textsubscript{2}O\textsubscript{2}C\textsubscript{6}H\textsubscript{3}) having two allyl arms: one o-allyl group (blue) and one C-allyl group (red). Under a two-step procedure of Sn(OTf)\textsubscript{2}-mediated reaction and then O-methylation (K\textsubscript{2}CO\textsubscript{3}, MeI), we observed C-allyl isomers 7a or 7b were produced in only 21% and 15% yields, respectively \textit{via} one-pot tandem intramolecular dehydrative benzannulation and Claisen rearrangement (Scheme 6). By increasing the use of Sn(OTf)\textsubscript{2} from catalytic amounts (10 mol%) to stoichiometric amounts (1.0 equivalent),\textsuperscript{19} the yields of 7a or 7b were enhanced to 85% and 80% yields, respectively \textit{via} the two-step route. The non-catalytic amounts (1.0 equivalent) of Sn(OTf)\textsubscript{2} which mediated the tandem intramolecular procedure included: (1) benzannulation of o-allyl and aroyl groups and (2) double Claisen rearrangement of the o-allyl group. In particular, the present double Claisen rearrangement occurred at room temperature. In comparison with the literature reports (150–200 °C),\textsuperscript{19} a few examples were described.

To change the position of the aryl group on the naphthalene skeleton, eight 4p-v (Ar = Ph, 4-FC\textsubscript{6}H\textsubscript{4}, 4-Me\textsubscript{2}C\textsubscript{6}H\textsubscript{4}, 4-MeOC\textsubscript{6}H\textsubscript{4}, 4-C\textsubscript{2}H\textsubscript{4}O\textsubscript{2}C\textsubscript{6}H\textsubscript{3}, 2-MeOC\textsubscript{6}H\textsubscript{4}, 4-PhC\textsubscript{6}H\textsubscript{4}) were investigated next. By this synthetic protocol, 8a-g were synthesized in 74–81% yields, as shown in Scheme 7. By the removal of the m-oxygenated group, 4w-x having the o-allyl side arms (Y = H, MeO) were then examined. When benzannulation of 4w-x was treated with Sn(OTf)\textsubscript{2}, the yields of 9a (61%) and 9b (40%) provide good results (Scheme 8). The structures of 8d, 8g, 9a and 9b were determined by single-crystal X-ray crystallography.\textsuperscript{14} By a one-pot two-step route (Suzuki–Miyaura coupling and our method),\textsuperscript{19} a simple naphthalene 10a could be obtained from o-formyl phenyl boronic acids in a 70% yield \textit{via} the formation of
4w, Y = H
4x, Y = MeO

Scheme 8 Synthesis of 9a-b.

o-allylbenzaldehyde 4y (Scheme 9). Although the isolated yield of 10a was low, it still provided a novel and efficient transformation from o-formyl phenylboronic acid to naphthalene.

Conclusion

In summary, we have successfully presented a synthetic route for the synthesis of substituted naphthalenes in good yields via Sn(OTf)2-mediated benzannulation of o-formyl or o-aryl allylbenzenes. The use of various metal triflates was investigated for the one-pot facile approach and efficient transformation. Further investigations regarding the synthetic application of metal triflates will be conducted and published in due course.

Experimental

General

All reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry air with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. 1H and 13C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (J) are given in Hertz.

A representative procedure of skeleton 5 and compound 6a is as follows

Sn(OTf)2 (42 mg, 0.1 mmol) was added to a solution of 4a-o (1.0 mmol) in MeNO2 (5 mL) at 25 °C. The reaction mixture was stirred for 8 h at 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH2Cl2 (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 100/1–10) afforded 5 and 6a.

1,2-Dimethoxynaphthalene (5a). Yield = 95% (179 mg); colorless oil; HRMS (ESI, M+ + 1) calcd for C12H13O2 189.0916, found 189.0919; 1H NMR (400 MHz, CDCl3): δ 8.15 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.52–7.48 (m, 1H), 7.40–7.36 (m, 1H), 7.31 (d, J = 8.8 Hz, 1H), 4.03 (s, 3H), 4.01 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 148.28, 142.84, 129.63, 128.98, 127.61, 126.05, 124.17, 124.01, 112.23, 115.15, 61.06, 56.83.

1-(2-Allyl-4,4-dimethylphenyl)-2-nitroethanol (6a). For Ga(OTf)3-promoted reaction, 6a was generated in 38% (101 mg); colorless solid; mp = 78–80 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M+ + 1) calcd for C14H15NO4 268.1185, found 268.1188; 1H NMR (400 MHz, CDCl3): δ 7.24 (d, J = 8.4 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.02–5.92 (m, 1H), 5.60 (dd, J = 2.8, 10.0 Hz, 1H), 5.60 (dq, J = 1.6, 10.0 Hz, 1H), 4.93 (dq, J = 1.6, 17.2 Hz, 1H), 4.49 (q, J = 13.2 Hz, 1H), 4.48 (q, J = 13.2 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.53 (s, J = 5.6 Hz, 2H), 2.41 (br s, 1H); 13C NMR (100 MHz, CDCl3): δ 152.87, 147.13, 136.98, 130.59, 129.66, 121.95, 115.74, 110.93, 80.88, 67.28, 60.89, 55.66, 29.86.

1-Isopropoxy-2-methoxynaphthalene (5b). Yield = 90% (194 mg); colorless oil; HRMS (ESI, M+ + 1) calcd for C12H14O3 231.1385, found 231.1388; 1H NMR (400 MHz, CDCl3): δ 8.19 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 9.2 Hz, 1H), 7.49–7.45 (m, 1H), 7.38–7.34 (m, 1H), 7.30 (d, J = 8.8 Hz, 1H), 4.72–4.65 (m, 1H), 3.98 (s, 3H), 1.40 (d, J = 6.0 Hz, 6H); 13C NMR (100 MHz, CDCl3): δ 148.53, 140.93, 130.40, 129.72, 127.43, 125.67, 123.88, 123.67, 122.17, 115.36, 75.30, 56.84, 22.71 (2x).

1-Butoxy-2-methoxynaphthalene (5c). Yield = 91% (209 mg); colorless oil; HRMS (ESI, M+ + 1) calcd for C13H16O3 243.1385, found 243.1388; 1H NMR (400 MHz, CDCl3): δ 8.17 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.50–7.46 (m, 1H), 7.39–7.35 (m, 1H), 7.30 (d, J = 8.8 Hz, 1H), 4.16 (t, J = 6.4 Hz, 2H), 3.99 (s, 3H), 1.94–1.87 (m, 2H), 1.67–1.58 (m, 2H), 1.04 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3): δ 148.36, 142.34, 129.77, 129.45, 127.55, 125.88, 123.98, 123.86, 121.52, 115.53, 73.43, 57.00, 32.50, 19.34, 13.94.

1-Cyclopentyl-2-methoxynaphthalene (5d). Yield = 88% (213 mg); colorless oil; HRMS (ESI, M+ + 1) calcd for C14H18O3 251.1072, found 251.1078; 1H NMR (400 MHz, CDCl3): δ 8.22 (d, J = 8.4 Hz, 1H), 7.56–7.41 (m, 7H), 7.32 (d, J = 6.8 Hz, 1H), 7.19 (d, J = 9.2 Hz, 1H), 6.13 (br s, 1H), 3.98 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 141.02, 139.83, 139.69, 129.98 (2x), 128.90, 128.12 (2x), 127.70, 127.11, 125.33, 124.92, 124.34, 120.72, 117.93, 112.93, 57.00. Single-crystal X-ray diagram: crystal of
compound 5e was grown by slow diffusion of EtOAc into a solution of compound 5e in CH₂Cl₂ to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group *P2₁2₁2₁, a = 13.8853(3) Å, b = 66.3155(18) Å, c = 5.8516(2) Å, V = 4955.62(2) Å³, Z = 16, d_{calcd} = 1.342 g cm⁻³, f(000) = 2112, 2θ range 1.23-26.39°, R indices (all data) R₁ = 0.0428, wR₂ = 0.1154.

5-(4-Fluorophenyl)-2-methoxynaphthalenel-1-ol (5f). Yield = 90% (214 mg); colorless solid; HRMS (ESI, M⁺ + 1) calcd for C₂₁H₂₀FO₂ 321.1491, found 321.1493; 1H NMR (400 MHz, CDCl₃, δ 8.15 (dt, J = 0.8, 8.4 Hz, 1H), 7.66 (dd, J = 0.8, 9.2 Hz, 1H), 7.48 (dd, J = 7.2, 8.8 Hz, 1H), 7.40 (d, J = 8.8 Hz, 2H), 7.27 (dd, J = 0.8, 7.2 Hz, 1H), 7.21 (d, J = 9.2 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.27-6.17 (m, 1H), 5.46 (dq, J = 1.6, 17.2 Hz, 1H), 5.27 (dq, J = 1.6, 10.4 Hz, 1H), 4.68 (dt, J = 1.6, 6.0 Hz, 2H), 3.96 (s, 3H), 3.88 (s, 3H); 13C NMR (100 MHz, CDCl₃, δ 158.90, 148.19, 141.66, 139.76, 134.43, 133.24, 131.03 (2x), 129.93, 128.05, 125.73, 125.18, 122.67, 120.84, 117.49, 114.76, 113.64 (2x), 74.32, 56.79, 55.32.

1-Allyloxy-2-methoxy-5-(4-methoxyphenyl)naphthalene (5j). Yield = 90% (280 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcd for C₂₁H₂₂O₃ 321.1491, found 321.1493; 1H NMR (400 MHz, CDCl₃, δ 8.15 (dt, J = 0.8, 8.4 Hz, 1H), 7.66 (dd, J = 0.8, 9.2 Hz, 1H), 7.48 (dd, J = 7.2, 8.8 Hz, 1H), 7.40 (d, J = 8.8 Hz, 2H), 7.27 (dd, J = 0.8, 7.2 Hz, 1H), 7.21 (d, J = 9.2 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.27-6.17 (m, 1H), 5.46 (dq, J = 1.6, 17.2 Hz, 1H), 5.27 (dq, J = 1.6, 10.4 Hz, 1H), 4.68 (dt, J = 1.6, 6.0 Hz, 2H), 3.96 (s, 3H), 3.88 (s, 3H); 13C NMR (100 MHz, CDCl₃, δ 158.90, 148.19, 141.66, 139.76, 134.43, 133.24, 131.03 (2x), 129.93, 128.05, 125.73, 125.18, 122.67, 120.84, 117.49, 114.76, 113.64 (2x), 74.32, 56.79, 55.32.
5-(6-Allyl-5-methoxynaphthalen-1-yl)benzo[1,3]dioxole (5a). Yield = 91% (289 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcld for C₂₅H₂₃O₃ 335.1647, found 335.1652; ¹H NMR (400 MHz, CDCl₃): δ 8.13 (dt, J = 1.2, 8.4 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.52 (dd, J = 7.2, 8.4 Hz, 1H), 7.37 (dd, J = 1.2, 6.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 6.97 (t, J = 1.6 Hz, 1H), 6.93 (br s, 2H), 6.04 (s, 2H), 6.10–6.00 (m, 1H), 5.14–5.08 (m, 2H), 3.96 (s, 3H), 3.61 (dt, J = 1.6, 6.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 153.50, 147.44, 146.86, 140.04, 137.10, 134.70, 132.21, 128.56, 128.30, 127.86, 126.64, 126.25, 113.47, 112.16, 114.38, 110.58, 108.17, 101.10, 62.18, 33.82.

A representative procedure of skeleton 8 is as follows

Sn(Otf)₂ (42 mg, 0.1 mmol) was added to a solution of 4j or 4l (1.0 mmol) in MeNO₂ (5 mL) at 25 °C. The reaction mixture was stirred for 8 h at 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 100/1–10/1) afforded 8.

1,2-Dimethoxy-4-phenyl naphthalene (8a). Yield = 81% (214 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcld for C₁₉H₁₃O₂ 265.1229, found 265.1230; ¹H NMR (400 MHz, CDCl₃): δ 8.22 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.53–7.43 (m, 6H), 7.34–7.30 (m, 1H), 7.27 (s, 1H), 4.06 (s, 3H), 4.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 147.55, 143.32, 140.49, 136.89, 130.07 (2x), 129.32, 128.26 (2x), 127.74, 127.28, 126.05 (2x), 124.14, 121.54, 116.40, 61.14, 56.91.

4-(4-Fluorophenyl)-1,2-dimethoxynaphthalene (8b). Yield = 74% (209 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcld for C₁₉H₁₃O₂ 279.1385, found 279.1398; ¹H NMR (400 MHz, CDCl₃): δ 8.23–8.20 (m, 1H), 7.85–7.82 (m, 1H), 7.50 (dd, J = 1.2, 6.8, 8.4 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.34–7.29 (m, 3H), 7.25 (s, 1H), 4.06 (s, 3H), 4.02 (s, 3H), 2.48 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 162.28 (d, J = 244.9 Hz), 147.54, 142.51, 136.39 (d, J = 3.1 Hz), 135.75, 131.59 (d, J = 7.6 Hz, 2x), 129.35, 127.83, 126.12, 125.81, 124.31, 121.63, 116.57, 115.21 (d, J = 21.2 Hz, 2x), 61.16, 56.99.

1,2-Dimethoxy-4-p-tolynaphthalene (8c). Yield = 77% (214 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcld for C₁₉H₁₄O₂ 279.1385, found 279.1388; ¹H NMR (400 MHz, CDCl₃): δ 8.23–8.20 (m, 1H), 7.85–7.82 (m, 1H), 7.50 (dd, J = 1.2, 6.8, 8.4 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.34–7.29 (m, 3H), 7.25 (s, 1H), 4.06 (s, 3H), 4.02 (s, 3H), 2.48 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 147.57, 142.17, 137.55, 137.01, 136.91, 129.94 (2x), 129.32, 128.98 (2x), 127.83, 126.13, 125.99, 124.05, 121.51, 116.33, 61.13, 56.88, 21.19.

1,2-Dimethoxy-4-(4-methoxyphenyl)naphthalene (8d). Yield = 76% (223 mg); colorless solid; mp = 118–120 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M⁺ + 1) calcld for C₂₅H₂₂O₄ 395.1334, found 395.1338; ¹H NMR (400 MHz, CDCl₃): δ 8.20 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.51–7.47 (m, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.33–7.29 (m, 1H), 7.23 (s, 1H), 7.14 (d, J = 8.8 Hz, 2H), 4.05 (s, 3H), 4.01 (s, 3H), 3.90 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 159.00, 147.57, 142.10, 136.60, 132.85, 131.11 (2x), 129.34, 127.96, 126.12, 125.99, 124.05, 121.52, 116.36, 113.74 (2x), 61.14, 56.90, 55.36. Single-crystal X-ray diagram: crystal of compound 8d was grown by slow diffusion of EtOAc into a solution of compound 8d in CHCl₃ to yield colorless prisms. The compound crystallizes in the monoclinic crystal space, system group P2₁/a, c = 13.450 (12) Å, b = 15.2538 (14) Å, α = 7.5723 (7) Å, V = 1518.9 (2) Å³, Z = 4, dcalc = 1.287 g cm⁻³, F(000) = 624, 20 range 2.045–26.42¹, R indices (all data) R₁ = 0.1172, wR₂ = 0.1285.

1,2-Dimethoxy-4-(4-trifluoromethylphenyl)naphthalene (8e). Yield = 80% (266 mg); colorless gum; HRMS (ESI, M⁺ + 1) calcld for C₂₅H₂₁F₂O₂ 333.1102, found 333.1108; ¹H NMR (400 MHz, CDCl₃): δ 8.26 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.55–7.51 (m, 1H), 7.37–7.33 (m, 1H), 4.09 (s, 3H), 4.04 (s, 3H), 2.72 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 147.54, 144.19, 142.97, 135.19, 130.41 (2x), 127.54.
129.51 (d, $J = 31.9$ Hz), 129.40, 127.44, 126.26, 125.48, 125.23 (q, $J = 3.8$ Hz, 2x), 124.58, 124.28 (d, $J = 270.6$ Hz), 121.74, 116.60, 61.14, 56.97.

1,2-Dimethoxy-4-(2-methoxyphenyl)naphthalene (8f). Yield = 80% (235 mg); colorless gum; HRMS (ESI, M$^+$ + 1) calcd for C$_{19}$H$_{19}$O$_3$: 295.1334, found 295.1335; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.82 (d, $J = 8.8$ Hz, 1H), 7.76 (d, $J = 8.8$ Hz, 1H), 7.51–7.41 (m, 2H), 7.27 (dd, $J = 1.2$, 6.8 Hz, 1H), 7.21 (d, $J = 2.4$ Hz, 1H), 7.11 (dd, $J = 2.8$, 9.2 Hz, 1H), 7.02–6.96 (m, 2x), 3.98 (s, 3H), 3.97 (s, 3H), 3.90 (s, 3H). Single-crystal X-ray diagram: crystal of compound 9b was grown by slow diffusion of EtOAc into a solution of compound 9b in CH$_2$Cl$_2$ to yield colorless prisms.

Naphthalene (10a). Na$_2$CO$_3$ (106 mg, 1.0 mmol) was added to a solution of allyl bromide (240 mg, 2.0 mmol) in dimethoxyethane (DME, 5 mL) at 25°C. The reaction mixture was stirred at 25°C for 5 min. Then, o-formylphenylboronic acid (150 mg, 1.0 mmol) was added to the reaction mixture at 25°C. The reaction mixture was stirred at 25°C for 5 min. Pd(OAc)$_2$ (11 mg, 0.05 mmol) was added to the reaction mixture at 25°C. The reaction mixture was stirred at 80°C for 5 h. The reaction mixture (in situ formed 4y) was cooled to 25°C and Sn(OTf)$_2$ (42 mg, 0.1 mmol) was added to the reaction mixture. The reaction mixture was stirred for 8 h at 25°C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 100/1–10/1) afforded 10a (51%, 65 mg).

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Notes and references


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