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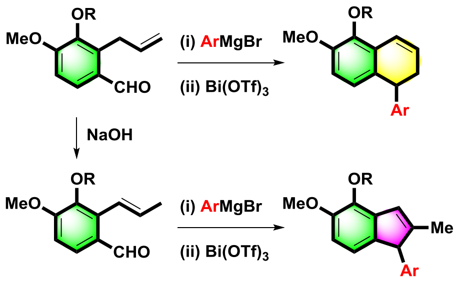
Bi(OTf)$_3$-mediated Intramolecular Olefinic Cyclization: Synthesis of Substituted Aryl-Dihydronaphthalenes and Indenes

Chieh-Kai Chan, Nai-Chen Hsueh, Yu-Lin Tsai and Meng-Yang Chang*

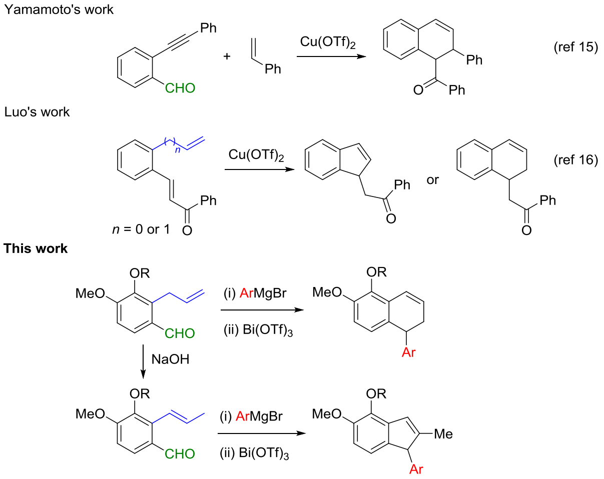
Department of Medicinal and Applied Chemistry, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung 807, Taiwan



ABSTRACT: In this article, a facile two-step and one-pot synthetic route for the preparation of substituted aryl dihydronaphthalenes starting from 2-allylbenzaldehydes via Grignard 1,2-addition and Bi(OTf)$_3$-catalyzed intramolecular olefinic cyclization has been developed. A five-membered ring indene skeleton is also prepared via olefin isomerization, 1,2-addition followed by cyclization. Some key structures are determined using single-crystal X-ray crystallography. A possible mechanism is presented herein.

The preparation of carbocycles, regarded as a crucial structural motif in many compounds with meaningful utilization in pharmaceutical and industry fields, plays an important role and acts as an useful synthetic tool in organic synthesis.[1] In particular, five- and six-membered carbocycles have been recognized as important framework in medicinal chemistry and bioactive natural products with privileged characteristics.[2] Among them, the six-membered dihydronaphthalene derivatives have attracted considerable attention due to existing bioactive natural products such as cyclogalgravin, magnoshinin, trilobatin A and B, a wide range of biological activities[3] and useful synthetic intermediates.[4] Nevertheless, a five-membered indene core is also found in some natural products, such as cyanosporaside A, taiwaniaquinol D, and trikentramine[5] and serves as significant precursors for organometallic catalysts[6] and bioactive molecules.[7] With these advantages and the importance of dihydronaphthalene and indene compounds, many methods have been developed to construct the skeletons. The existing methodologies include transition metal-catalyzed C-H bond activation[8], photocatalytic annulation[9], ring-expansion of cyclopropanes[10] or cyclopropenes[11], organometallic nucleophilic addition[12], and Lewis[13] or Brønsted[14] acid-catalyzed Friedel-Crafts cyclization.

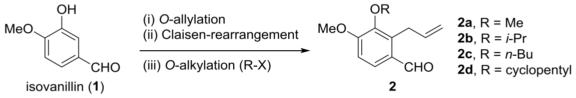
Scheme 1. Synthesis of dihydronaphthalenes and indenes



In 2003, Yamamoto and colleagues described a Cu(OTf)$_2$-catalyzed [4+2] cycloaddition reaction of alkynylbenzaldehydes with alkenes to form dihydronaphthalene derivatives.[15] Recently, Luo's group reported a Cu(OTf)$_2$-catalyzed intramolecular conjugated addition of alkenes to α,β-unsaturated carbonyls to construct dihydronaphthalene and indene skeletons.[16] Our study attempts to develop the versatilities of 2-allylbenzaldehyde[17] and the utilizations of Bi(OTf)$_3$[18] in organic methodologies, and to show a comparison of these metal triflate-mediated synthetic works for the synthesis of dihydronaphthalenes or indenes. However, substituted 2-allylbenzaldhydes including olefin and aldehyde groups were selected as the starting materials to develop the synthetic route. The preparation of substituted dihydronaphthalenes and indenes from 2-allylbenzaldehydes using $Bi(OTf)_3$ as a catalyst have not been developed. Herein, a $Bi(OTf)_3$-mediated intramolecular cyclization of aryl-substituted benzylic alcohol for the preparation of substituted aryl-dihydronaphthalenes and indenes starting from versatile 2-allylbenzaldehydes is reported (Scheme 1).

Initially, a series of substituted 2-allylbenzaldehyde **2** was prepared from isovanillin (**1**) in a three-step process with excellent yields overall (Scheme 2).[17] On the basis of our experience, we believe that the 1,2-addition of 2-allylbenzaldehyde **2** with a Grignard reagent could be conducted smoothly and provide corresponding alcohol in high yields.[17a] Unfortunately, the benzyl alcohols **3** were unstable, only representative **3a-3d** were provided (Scheme 3).

Scheme 2. Three-step synthesis of 2-allylbenzaldehyde **2**



Scheme 3. Synthesis of benzyl alcohol **3**

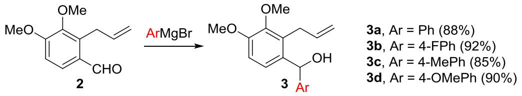
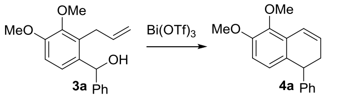


Table 1. Conditions for the construction of **4a**[a]



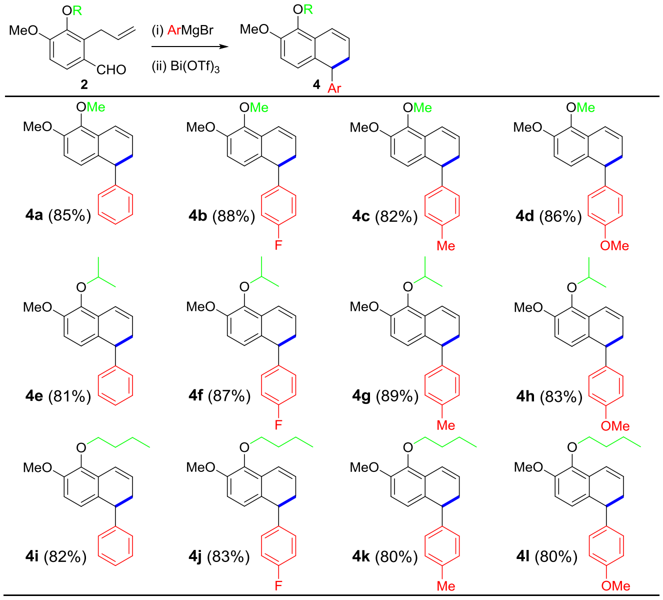
entry	catalyst (mol %), solvent (mL), temp (°C)	**4a** (%)[b]
1	AgOTf (2), CH_2Cl_2 (20), 25	15[c]
2	$Mg(OTf)_2$ (2), CH_2Cl_2 (20), 25	—
3	$Zn(OTf)_2$ (2), CH_2Cl_2 (20), 25	—
4	$Cu(OTf)_2$ (2), CH_2Cl_2 (20), 25	—
5	$Ni(OTf)_2$ (2), CH_2Cl_2 (20), 25	—
6	$Sc(OTf)_3$ (2), CH_2Cl_2 (20), 25	—
7	$Ga(OTf)_3$ (2), CH_2Cl_2 (20), 25	—
8	$Fe(OTf)_3$ (2), CH_2Cl_2 (20), 25	58
9	$In(OTf)_3$ (2), CH_2Cl_2 (20), 25	62
10	$Hg(OTf)_2$ (2), CH_2Cl_2 (20), 25	65
11	$Sn(OTf)_2$ (2), CH_2Cl_2 (20), 25	81
12	$Bi(OTf)_3$ (2), CH_2Cl_2 (20), 25	85
13	$Bi(OTf)_3$ (5), CH_2Cl_2 (20), 25	85
14	$Bi(OTf)_3$ (2), CH_2Cl_2 (30), 25	81
15	$Bi(OTf)_3$ (2), CH_2Cl_2 (20), 100	75
16	$Bi(OTf)_3$ (2), $MeNO_2$ (20), 25	82
17	$Bi(OTf)_3$ (2), MeCN (20), 25	80
18	$Bi(OTf)_3$ (2), $(CH_2Cl)_2$ (20), 25	81
19	$Bi(OTf)_3$ (2), benzene (20), 25	78
20	$Bi(OTf)_3$ (2), dioxane (20), 25	72
21	TfOH (2), CH_2Cl_2 (20), 25	25[d]

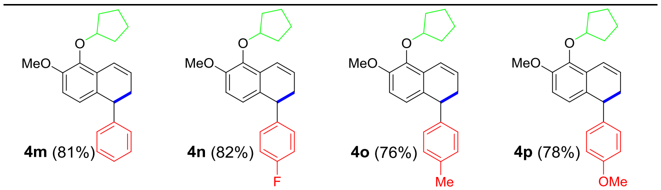
[a]Reaction was run on a 0.5 mmol scale with **3a**, 2h. [b]Isolated yield. [c]74% of **3a** was recovered. [d]Unknown products were isolated.

Next, benzyl alcohol **3a** was selected as the model substrate to screen the metal triflate-mediated intramolecular cyclization of reaction conditions. As shown in Table 1, the involvement of various metal triflates as catalyst was tested for the construction of dihydronaphthalene **4a**. Catalytic amounts of Ag(OTf), $Mg(OTf)_2$, $Zn(OTf)_2$, $Cu(OTf)_2$, $Ni(OTf)_2$, $Hg(OTf)_2$, $Sn(OTf)_2$, $Sc(OTf)_3$, $Ga(OTf)_3$, $Fe(OTf)_3$, $In(OTf)_3$ and $Bi(OTf)_3$ provided different results in CH_2Cl_2 at 25 °C for 2 h. In entry 1, Ag(OTf) only provided **4a** in 15% with recovered **3a** in a yield of 74% . Using $Mg(OTf)_2$, $Zn(OTf)_2$, $Cu(OTf)_2$, $Ni(OTf)_2$, $Sc(OTf)_3$ or $Ga(OTf)_3$ as catalyst, the reaction was unworkable and no isolation of desired product **4a** was observed (entries 2-7). Other metal triflates such as $Fe(OTf)_3$, $In(OTf)_3$ and $Hg(OTf)_2$ promoted the reaction to proceed, and the isolated yields of **4a** was ranged from 58% to 65% (entries 8-10). Notably, $Sn(OTf)_3$ and $Bi(OTf)_3$ increased the desired product **4a** in higher 81% and 85% yields, respectively (entries 11-12). No obvious yields changes occurred when increasing the amounts of $Bi(OTf)_3$, the volume of CH_2Cl_2 or the reaction temperature (entries 13-15). Further examined other solvent, including $MeNO_2$, MeCN, $C_2H_4Cl_2$, benzene and dioxane, but the yields of **4a** was declined (entries 16-20). By the use of TfOH, only 25% **4a** was obtained with complex mixture (entry 21).

As shown in Table 2, the 1,2-addition of **2** with a Grignard reagent, including the electron-neutral PhMgBr, the electron-withdrawing group $4\text{-}FC_6H_4MgBr$, and the electron-donating $4\text{-}MeC_6H_4MgBr$ and $4\text{-}OMeC_6H_4MgBr$ reacted in a high yield. Owing to unstable benzyl alcohol, the crude product was used without further purification, and a $Bi(OTf)_3$ catalyst was added to the solvent of *in-situ* benzyl alcohol in CH_2Cl_2 at 25 °C. The desired dihydronaphthalenes **4a-4p** were obtained in modest to good yields between 76% and 88%. The structure of **4a** was confirmed by single-crystal X-ray diffraction.[19]

Table 2. Synthesis of **4**[a,b]





[a]Conditions: for 1,2-addition, **2** (1.0 mmol), ArMgBr (1.0 M, 1.5 mL, 1.5 mmol), dry THF (10 mL), 0 °C, 3h; for cyclization, Bi(OTf)$_3$ (13 mg, 2.0 mol%), CH$_2$Cl$_2$ (20 mL), 25 °C, 2h. [b]Isolated yields.

To our delight, changing the double bond position met our goal. Therefore, using a NaOH/MeOH system to transfer the terminal double bond on **2** to the internal double bond on **5** is completely migrated (Scheme 4).[17c,d,20] Based on the results in Table 1, we believe that the internal double bond benzaldehyde **5** is also suitable for this one-pot two-step preparation of substituted indenes. As shown in Table 3, the reaction of vinylbenzaldehyde **5** with a Grignard reagent is smooth. Bi(OTf)$_3$-catalyzed synthesis of the desired indenes **6a**-**6p** in the yields ranged from 78% to 94%. The structure of **6a**, **6d**, **6f** and **6h** were confirmed by single-crystal X-ray diffraction.[19]

Scheme 4. Synthesis of **5**

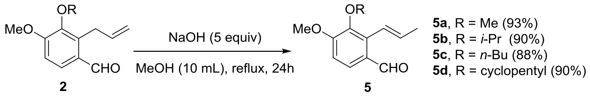
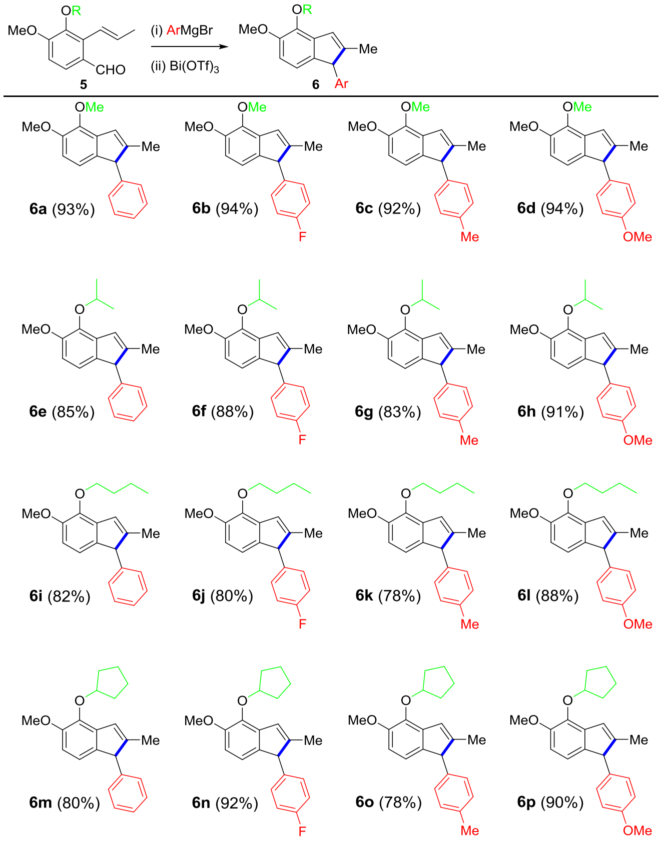
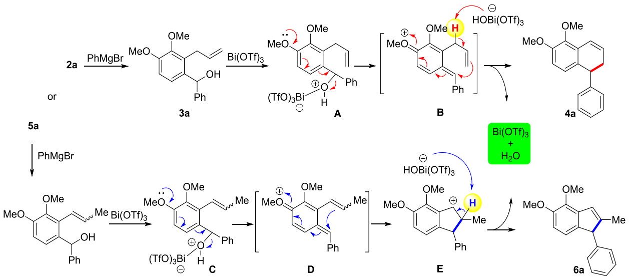


Table 3. Synthesis of **6**[a,b]



[a]Conditions: for 1,2-addition, **5** (1.0 mmol), ArMgBr (1.0 M, 1.5 mL, 1.5 mmol), dry THF (10 mL), 0 °C, 3h; for cyclization, Bi(OTf)$_3$ (13 mg, 2.0 mol%), CH$_2$Cl$_2$ (20 mL), 25 °C, 2h. [b]Isolated yields.

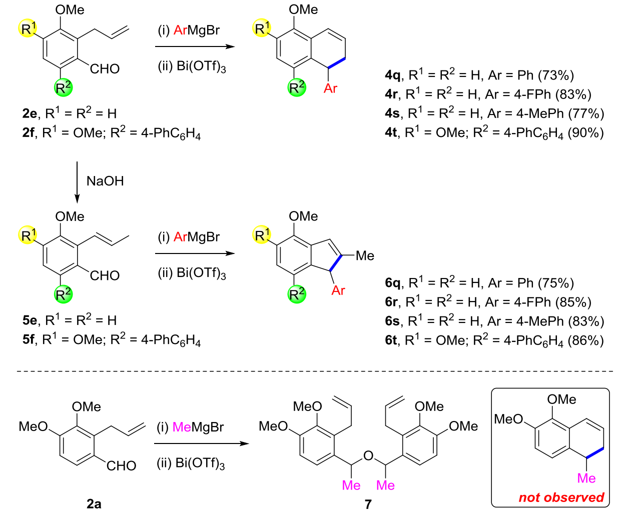
Scheme 5. Possible mechanism



Based on the results in Tables 1-3, a mechanism for the preparation of dihydronaphthalene **4a** and indene **6a** were proposed, as shown in Scheme 5.[18] First, 1,2-addition of terminal olefin **2a** or internal olefin **5a** with a Grignard reagent (PhMgBr) gave corresponding benzylic alcohol. For **4a**, the formation of **A** was by alcohol moiety chelated with Bi(OTf)$_3$. A tandem intramolecular cyclization was formed by an ene-reaction to form **B**. After the methoxy group promoted debismuthation, the *in-situ* generated HOBi(OTf)$_3$ anion deprotonated the H (red) of **B** to afford **4a**. For **6a**, Bi(OTf)$_3$ chelated with hydroxyl group to give intermediate **C**. Then an intramolecular ene reaction was achieved to obtain **D**. Following the above pathway of **4a**, the *in situ* generated HOBi(OTf)$_3$ anion deprotonated the H (blue) of **E** to construct **6a**.

Other prepared 2-allylbenzaldehydes were also investigated in this two-step procedure.[17] As shown in Scheme 6, mono-methoxy substituted benzaldehyde **2e** and aryl-substituted benzaldehyde **2f** were suitable for the synthesis of aryl-substituted dihydronaphthalenes **4q-4t** in good yields. Similarly, through the NaOH-mediated olefin migration to construct **5e-5f**, the corresponding indenes **6q-6t** were isolated in high yields. Furthermore, after changing ArMgBr to MeMgBr for the addition with **2a** in this two-step procedure, no desired product was observed, instead of dimer **7** that was expected. Therefore, we believe that dibenzylic alcohol is more powerful than mono-benzylic alcohol in this annulation. The structure of **4t** was confirmed by single-crystal X-ray diffraction.[19]

Scheme 6. Reaction scope



In summary, a Bi(OTf)$_3$-mediated intramolecular cyclization for synthesis substituted aryl-dihydronaphthalenes has been developed. Further investigation was made into changing the terminal olefin to an internal olefin in the optimal condition, and the corresponding substituted aryl-indenes were also prepared in high yields. The structures of some products were confirmed by X-ray single-crystal diffraction analysis.

EXPERIMENT SECTION

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 nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Purity was determined by NMR and melting point. Melting points were determined with a SMP3 melting apparatus. ^1H and ^{13}C NMR spectra were recorded on a Varian 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. High resolution mass spectra (HRMS) were measured with a mass spectrometer microTOF-Q by ESI using a hybrid ion-trap. X-ray crystal structures were obtained with a diffractometer (CAD4, Kappa CCD).

General synthetic route for the synthesis of 3a-3d. A solution of a Grignard reagent (1.0 M in THF, 1.5 mL, 1.5 mmol) was added to a stirred solution of **2** (1.0 mmol) in THF (10 mL) at ice bath. The reaction mixture was stirred at 25 °C for 3 h. Water (5 mL) was added to the reaction mixture and the mixture was filtered through a short plug of Celite. The filtrate was concentrated under reduced pressure. The residue was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 6/1~3/1) afforded **3a-3d**.

*2-Allyl-3,4-dimethoxyphenyl(phenyl)methanol (**3a**).* Yield = 88% (250 mg); Colorless oil; HRMS (ESI, M^++Na) calcd for $C_{18}H_{20}O_3Na$ 307.1310, found 307.1312; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.24 (m, 5H), 7.04 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 6.03-5.94 (m, 1H), 6.00 (s, 1H), 5.03 (dq, J = 1.6, 10.0 Hz, 1H), 4.94 (dq, J = 1.6, 17.2 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.66-3.57 (m, 2H), 3.45-3.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 147.2, 143.4, 137.5, 135.0, 131.5, 128.2 (2x), 127.2, 126.7 (2x), 123.2, 115.1, 110.3, 72.3, 60.8, 55.5, 29.9.

*2-Allyl-3,4-dimethoxyphenyl(4-fluorophenyl)methanol (**3b**).* Yield = 92% (278 mg); Colorless oil; HRMS (ESI, M^++Na) calcd for $C_{18}H_{19}FO_3Na$ 325.1216, found 325.1213; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31-7.27 (m, 2H), 7.01 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.01-5.92 (m, 1H), 5.96 (s, 1H), 5.02 (dq, J = 1.6, 10.0 Hz, 1H), 4.91 (dq, J = 1.6, 17.2 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.58 (ddt, J = 1.6, 6.0, 16.0 Hz, 1H), 3.39 (ddt, J = 1.6, 6.0, 16.0 Hz, 1H), 2.21 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0 (d, J = 243.3 Hz), 152.2, 147.3, 139.2, 137.5, 134.9, 131.4, 128.4 (d, J = 7.5 Hz, 2x), 123.1, 115.2, 115.0 (d, J = 21.3 Hz, 2x), 110.4, 71.7, 60.8, 55.6, 29.9.

*2-Allyl-3,4-dimethoxyphenyl(p-tolyl)methanol (**3c**).* Yield = 85% (253 mg); Colorless oil; HRMS (ESI, M^++Na) calcd for $C_{19}H_{22}O_3Na$ 321.1467, found 321.1465; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, J = 8.4 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.4 Hz, 1H), 6.03-5.94 (m, 1H), 5.97 (br s, 1H), 5.03 (dq, J = 1.6, 10.0 Hz, 1H), 4.79 (dq, J = 1.6, 17.2 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 3.60 (ddt, J = 1.6, 6.0, 16.0 Hz, 1H), 3.38 (ddt, J = 1.6, 6.0, 16.0 Hz, 1H), 2.34 (s, 3H), 1.86 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1 (2x), 147.2, 140.5, 137.5, 137.0, 135.2, 131.4, 129.1, 129.0 (2x), 126.7 (2x), 125.3, 123.0, 115.1, 110.3, 72.2, 60.8, 55.6, 30.0, 21.1.

*2-Allyl-3,4-dimethoxyphenyl(4-methoxyphenyl)methanol (**3d**).* Yield = 90% (283 mg); Colorless oil; HRMS (ESI, M^++Na) calcd for $C_{19}H_{22}O_4Na$ 337.1416, found 337.1415; ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.8 Hz, 1H), 6.85 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 1H), 6.01-5.91 (m, 1H), 5.95 (s, 1H), 5.02 (dq, J = 1.6, 10.0 Hz, 1H), 4.92 (dq, J = 1.6, 17.2 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.61-3.55 (m, 1H), 3.35 (ddt, J = 1.6, 6.4, 15.6 Hz, 1H), 2.18 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 152.0, 147.2, 137.5, 135.6, 135.2, 131.3, 128.1 (2x), 122.8, 115.1, 113.7 (2x), 110.3, 72.0, 60.8, 55.6, 55.2, 29.9.

General synthetic route for the synthesis of 4a-4t, 6a-6t and 7. A solution of a Grignard reagent (1.0 M in THF, 1.5 mL, 1.5 mmol) was added to a stirred solution of skeletons **2** and **5** (1.0 mmol) in THF (10 mL) at ice bath. The reaction mixture was stirred at 25 °C for 3 h. Water (5 mL) was added to the reaction mixture and the mixture was filtered through a short plug of Celite. The filtrate was concentrated under reduced pressure. The residue was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Without further purification, a solution of the resulting secondary alcohol in DCM (10 mL) was added to a mixture of $Bi(OTf)_3$ (13 mg, 2.0 mol%) in DCM (20 mL). After being stirred at 25 °C for 2 h, the mixture was filtered through a short silica gel column. The filtrate was dried, filtered, and evaporated to yield crude compound. Purification on silica gel (hexanes/EtOAc = 10/1~6/1) afforded **4a-4t**, **6a-6t** and **7**.

*5,6-Dimethoxy-1-phenyl-1,2-dihydronaphthalene (**4a**).* Yield = 85% (226 mg); Colorless solid; mp = 97-98 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{18}H_{18}O_2Na$ 289.1205, found 289.1197; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34-7.30 (m, 2H), 7.27-7.22 (m, 3H), 6.93 (dt, J = 1.6, 9.6 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 6.07 (dt, J = 4.4, 9.6 Hz, 1H), 4.09-4.05 (m, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 2.65-2.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 144.6, 131.2, 128.4 (3x), 128.3 (2x), 127.9, 127.7, 126.4, 123.2, 122.0, 110.4, 61.1, 55.7, 43.4, 31.9. Single-crystal X-ray diagram: crystal of **4a** was grown by slow diffusion of EtOAc into a solution of **4a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Orthorhombic crystal system, space group P b c n, a = 20.772(2) Å, b = 7.4286(8) Å, c = 18.5851(17) Å, V = 2867.8(5) $Å^3$, Z = 8, d_{calcd} = 1.234 g/cm^3, $F(000)$ = 1136, 2θ range 1.96-26.47°, R indices (all data) $R1$ = 0.1256, $wR2$ = 0.3111.

*1-(4-Fluorophenyl)-5,6-dimethoxy-1,2-dihydronaphthalene (**4b**).* Yield = 88% (250 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{18}H_{17}FO_2Na$ 307.1110, found 307.1105; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19-7.14 (m, 2H), 7.01-6.95 (m, 2H), 6.93-6.90 (m, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 6.04 (dt, J = 4.4, 10.0 Hz, 1H), 4.06-4.02 (m, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 2.66-2.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5 (d, J = 243.3 Hz), 151.5, 144.7, 140.2 (d, J = 2.3 Hz), 131.0, 129.7 (d, J = 8.3 Hz, 2x), 127.9, 127.5, 123.1, 122.1, 115.1 (d, J = 21.2 Hz, 2x), 110.5, 61.1, 55.7, 42.6, 32.0.

*5,6-Dimethoxy-1-(p-tolyl)-1,2-dihydronaphthalene (**4c**).* Yield = 82% (230 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for

$C_{19}H_{20}O_2Na$ 303.1361, found 303.1358; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (br s, 4H), 6.90 (dt, J = 1.6, 9.6 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 6.05 (dt, J = 4.4, 9.6 Hz, 1H), 4.05-4.00 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.61-2.56 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 144.5, 141.5, 135.9, 131.5, 129.1 (2x), 128.3 (2x), 128.0, 127.8, 123.2, 122.0, 110.4, 61.1, 55.7, 43.0, 32.0, 21.0.

*5,6-Dimethoxy-1-(4-methoxyphenyl)-1,2-dihydronaphthalene (**4d**).* Yield = 86% (255 mg); Brown gum; HRMS (ESI, M^++Na) calcd for $C_{19}H_{20}O_3Na$ 319.1310, found 319.1305; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, J = 8.8 Hz, 2H), 6.91 (dt, J = 1.6, 10.0 Hz, 1H), 6.85 (d, J = 8.8 Hz, 2H), 6.65 (d, J = 8.4 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 6.05 (dt, J = 4.4, 10.0 Hz, 1H), 4.03-3.98 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 2.60-2.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 151.3, 144.6, 136.6, 131.6, 129.3 (2x), 127.9, 127.8, 123.1, 122.0, 113.7, 110.4, 70.5, 61.1, 55.7, 55.2, 42.6, 32.0.

*5-Isopropoxy-6-methoxy-1-phenyl-1,2-dihydronaphthalene (**4e**).* Yield = 81% (238 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{20}H_{22}O_2Na$ 317.1518, found 317.1512; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.21 (m, 5H), 6.95 (dt, J = 1.6, 10.0 Hz, 1H), 6.65 (d, J = 8.8 Hz, 1H), 6.50 (d, J = 8.0 Hz, 1H), 6.01 (dt, J = 4.4, 9.6 Hz, 1H), 4.48-4.41 (m, 1H), 4.09-4.04 (m, 1H), 3.81 (s, 3H), 2.68-2.53 (m, 2H), 1.34 (t, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 144.8, 142.6, 131.1, 128.9, 128.4 (2x), 128.3 (2x), 126.8, 126.3, 123.1, 122.7, 110.5, 75.3, 55.7, 43.5, 31.9, 22.54, 22.51.

*1-(4-Fluorophenyl)-5-isopropoxy-6-methoxy-1,2-dihydronaphthalene (**4f**).* Yield = 87% (272 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{20}H_{21}FO_2Na$ 335.1423, found 335.1420; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.11 (m, 2H), 7.02 (s, 1H), 6.98 (d, J = 8.4 Hz, 2H), 6.67 (d, J = 8.0 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 6.03-5.98 (m, 1H), 4.51-4.44 (m, 1H), 4.06 (t, J = 8.0 Hz, 1H), 3.82 (s, 3H), 2.68-2.60 (m, 1H), 2.57-2.49 (m, 1H), 1.35 (t, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4 (d, J = 242.5 Hz), 151.7, 142.6, 140.4 (d, J = 3.0 Hz), 130.8, 129.6 (d, J = 7.6 Hz, 2x), 128.8, 126.5, 123.1, 122.6, 115.0 (d, J = 20.5 Hz, 2x), 110.5, 75.3, 55.6, 42.6, 32.0, 22.48, 22.45.

*5-Isopropoxy-6-methoxy-1-(p-tolyl)-1,2-dihydronaphthalene (**4g**).* Yield = 89% (274 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_2Na$ 331.1674, found 331.1669; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (br s, 4H), 6.98 (d, J = 10.0 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 6.03 (dt, J = 4.4, 10.0 Hz, 1H), 4.50-4.44 (m, 1H), 4.08-4.04 (m, 1H), 3.83 (s, 3H), 2.64-2.58 (m, 2H), 2.37 (s, 3H), 1.36 (t, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 142.6, 141.7, 135.7, 131.3, 129.2, 129.0 (2x), 128.2 (2x), 126.9, 123.0, 122.7, 110.4, 75.3, 55.7, 43.0, 32.0, 22.52, 22.49, 21.0.

*5-Isopropoxy-6-methoxy-1-(4-methoxyphenyl)-1,2-dihydronaphthalene (**4h**).* Yield = 83% (269 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_3Na$ 347.1623, found 347.1617; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, J = 8.4 Hz, 2H), 6.93 (dt, J = 1.6, 10.0 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 8.4 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 6.00 (dt, J = 4.4, 10.0 Hz, 1H), 4.46-4.40 (m, 1H), 4.01 (dd, J = 7.2, 9.6 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 2.64-2.48 (m, 2H), 1.32 (t, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 151.6, 142.6, 136.8, 131.5, 129.3 (2x), 128.9, 126.9, 123.1, 122.7, 113.7 (2x), 110.5, 75.3, 55.7, 55.2, 42.6, 32.0, 22.54, 22.51.

*5-Butoxy-6-methoxy-1-phenyl-1,2-dihydronaphthalene (**4i**).* Yield = 82% (253 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_2Na$ 331.1674, found 331.1667; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.21 (m, 5H), 6.94 (dt, J = 1.6, 10.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 6.04 (dt, J = 4.4, 10.0 Hz, 1H), 4.08-4.04 (m, 1H), 4.01-3.95 (m, 2H), 3.82 (s, 3H), 2.64-2.58 (m, 2H), 1.84-1.77 (m, 2H), 1.60-1.50 (m, 2H), 1.01 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 144.7, 144.0, 131.2, 129.1, 128.4 (2x), 128.3 (2x), 127.3, 126.3, 122.9, 122.4, 110.6, 73.5, 55.8, 43.4, 32.3, 31.9, 19.2, 13.9.

*5-Butoxy-1-(4-fluorophenyl)-6-methoxy-1,2-dihydronaphthalene (**4j**).* Yield = 83% (271 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{21}H_{23}FO_2Na$ 349.1580, found 349.1574; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.17 (m, 2H), 7.03-6.98 (m, 3H), 6.68 (d, J = 8.0 Hz, 1H), 6.52 (d, J = 8.0 Hz, 1H), 6.05 (dt, J = 4.4, 9.6 Hz, 1H), 4.09-3.98 (m, 3H), 3.84 (s, 3H), 2.69-2.61 (m, 1H), 2.59-2.51 (m, 1H), 1.88-1.81 (m, 2H), 1.64-1.55 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4 (d, J = 242.6 Hz), 151.5, 143.9, 140.3 (d, J = 3.0 Hz), 130.8, 129.6 (d, J = 7.6 Hz, 2x), 128.0, 127.0, 122.8, 122.4, 114.9 (d, J = 21.3 Hz, 2x), 110.5, 73.4, 55.6, 42.6, 32.3, 32.0, 19.2, 13.8.

*5-Butoxy-6-methoxy-1-(p-tolyl)-1,2-dihydronaphthalene (**4k**).* Yield = 80% (258 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{22}H_{26}O_2Na$ 345.1831, found 345.1827; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (br s, 4H), 6.96 (dt, J = 1.6, 10.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.53 (d, J = 8.4 Hz, 1H), 6.06 (dt, J = 4.4, 10.0 Hz, 1H), 4.05-3.98 (m, 3H), 3.83 (s, 3H), 2.64-2.58 (m, 2H), 2.37 (s, 3H), 1.86-1.79 (m, 2H), 1.62-1.54 (m, 2H), 1.03 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 141.6, 135.8, 131.4, 129.2, 129.0 (2x), 128.2 (2x), 128.0, 127.4, 122.9, 122.3, 110.5, 73.4, 55.8, 43.0, 32.3, 32.0, 21.0, 19.2, 13.9.

*5-Butoxy-6-methoxy-1-(4-methoxyphenyl)-1,2-dihydronaphthalene (**4l**).* Yield = 80% (271 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1777; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 8.4 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 6.05-6.01 (m, 1H), 4.03-3.94 (m, 4H), 3.81 (s, 3H), 3.80 (s, 3H), 2.60-2.53 (m, 2H), 1.83-1.76 (m, 2H), 1.58-1.49 (m, 2H), 1.00 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 151.4, 136.7, 131.6, 129.3 (2x), 129.1, 128.1, 127.5, 122.8, 122.3, 113.7 (2x), 110.5, 73.5, 55.8, 55.2, 42.6, 32.3, 32.0, 19.2, 13.9.

*5-(Cyclopentyloxy)-6-methoxy-1-phenyl-1,2-dihydronaphthalene (**4m**).* Yield = 81% (259 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{22}H_{24}O_2Na$ 343.1674, found 343.1670; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.20 (m, 5H), 6.90 (dt, J = 1.6, 9.6 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.48 (d, J = 8.4 Hz, 1H), 6.00 (dt, J = 4.8, 9.6 Hz, 1H), 4.85-4.81 (m, 1H), 4.07-4.03 (m, 1H), 3.81 (s, 3H), 2.06-1.85 (m, 4H), 1.81-1.65 (m, 4H), 1.63-1.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 144.8, 142.8, 131.2, 130.0, 128.4 (2x), 128.3 (2x), 126.9, 126.3, 122.9, 122.7, 110.7, 84.9, 55.8, 43.5, 32.74, 32.69, 31.9, 23.7 (2x).

*5-(Cyclopentyloxy)-1-(4-fluorophenyl)-6-methoxy-1,2-dihydronaphthalene (**4n**).* Yield = 82% (277 mg); Yellow gum; HRMS (ESI, M^++Na) calcd for $C_{22}H_{23}FO_2Na$ 361.1580, found 361.1576; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.16 (m, 2H), 7.03-6.95 (m, 3H), 6.68 (d, J = 8.4 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 6.02 (dt, J = 4.4, 9.6 Hz, 1H), 4.91-4.88 (m, 1H), 4.09-4.05 (m, 1H), 3.84 (s, 3H), 2.69-2.61 (m, 1H), 2.59-2.51 (m, 1H), 2.01-1.93 (m, 4H), 1.83-1.73 (m, 2H), 1.67-1.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4 (d, J = 242.5 Hz), 151.5, 140.3 (d, J = 3.1 Hz), 130.8, 129.6 (d, J = 7.5 Hz, 2x), 129.5, 128.6, 126.6, 122.9, 122.5, 114.9 (d, J = 20.4 Hz, 2x), 110.6, 84.7, 55.6, 42.6, 32.7, 32.6, 31.9, 23.6 (2x).

*5-(Cyclopentyloxy)-6-methoxy-1-(p-tolyl)-1,2-dihydronaphthalene (**4o**).* Yield = 76% (254 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{23}H_{26}O_2Na$ 357.1831, found 357.1822; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (s, 4H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.09-6.05 (m, 1H), 4.93-4.89 (m, 1H), 4.09 (dd, *J* = 7.6, 9.6 Hz, 1H), 3.86 (s, 3H), 2.67-2.61 (m, 2H), 2.40 (s, 3H), 2.37-1.94 (m, 4H), 1.84-1.73 (m, 2H), 1.71-1.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 142.6, 141.6, 135.7, 131.3, 128.9 (2x), 128.7, 128.2 (2x), 126.9, 122.8, 122.6, 110.6, 84.7, 55.7, 43.0, 32.7, 32.6, 31.9, 23.6 (2x), 21.0.

*5-(Cyclopentyloxy)-6-methoxy-1-(4-methoxyphenyl)-1,2-dihydronaphthalene (**4p**).* Yield = 78% (273 mg); Brown gum; HRMS (ESI, M^++Na) calcd for $C_{23}H_{26}O_3Na$ 373.1780, found 373.1772; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (d, *J* = 8.4 Hz, 2H), 6.92 (dt, *J* = 2.0, 10.0 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 6.02 (dt, *J* = 4.4, 10.0 Hz, 1H), 4.88-4.84 (m, 1H), 4.03 (dd, *J* = 7.6, 9.6 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 2.64-2.55 (m, 2H), 2.00-1.88 (m, 4H), 1.79-1.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 151.4, 142.7, 136.7, 131.5, 129.2 (2x), 128.7, 127.0, 122.8, 122.6, 113.6 (2x), 110.6, 84.8, 55.7, 55.1, 42.6, 32.7, 32.7, 32.0, 23.6 (2x).

*5-Methoxy-1-phenyl-1,2-dihydronaphthalene (**4q**).* Yield = 73% (172 mg); yellow gum; HRMS (ESI, M^++Na) calcd for $C_{17}H_{16}ONa$ 259.1099, found 259.1098; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.23 (m, 5H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.97 (dt, *J* = 1.6, 10.0 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 7.6 Hz, 1H), 6.01 (dt, *J* = 4.4, 9.6 Hz, 1H), 4.13-4.09 (m, 1H), 3.88 (s, 3H), 2.71-2.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 144.4, 139.2, 128.4 (2x), 128.3 (2x), 127.6, 126.4, 126.0, 123.3, 121.7, 120.5, 109.0, 55.6, 43.9, 31.5.

*1-(4-Fluorophenyl)-5-methoxy-1,2-dihydronaphthalene (**4r**).* Yield = 83% (211 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{17}H_{15}FONa$ 277.1005, found 277.1008; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.16 (m, 2H), 7.10-7.06 (m, 2H), 7.01-6.94 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 1H), 5.99 (dt, *J* = 4.0, 10.0 Hz, 1H), 4.08 (t, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 2.70-2.62 (m, 1H), 2.59-2.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5 (d, *J* = 242.6 Hz), 154.8, 140.1 (d, *J* = 3.1 Hz), 139.0, 129.7 (d, *J* = 7.5 Hz, 2x), 127.7, 125.7, 123.5, 121.8, 120.3, 115.1 (d, *J* = 21.2 Hz, 2x), 109.1, 55.6, 43.1, 31.6.

*5-Methoxy-1-(p-tolyl)-1,2-dihydronaphthalene (**4s**).* Yield = 77% (193 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{18}H_{18}ONa$ 273.1255, found 273.1256; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (br s, 4H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.02 (dt, *J* = 1.6, 10.0 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 6.05 (dt, *J* = 4.4, 10.0 Hz, 1H), 4.12 (dd, *J* = 8.0, 9.6 Hz, 1H), 3.91 (s, 3H), 2.74-2.59 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 141.3, 139.5, 135.8, 129.0 (2x), 128.2 (2x), 127.6, 126.1, 123.0, 121.7, 120.4, 108.9, 55.5, 43.5, 31.6, 21.0.

*8-([1,1'-Biphenyl]-4-yl)-1-(4-fluorophenyl)-5,6-dimethoxy-1,2-dihydronaphthalene (**4t**).* Yield = 90% (393 mg); Colorless solid; mp = 188-189 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{30}H_{25}FO_2Na$ 459.1736, found 459.1738; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.60 (m, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.48-7.44 (m, 2H), 7.39-7.34 (m, 1H), 7.06-7.01 (m, 3H), 6.89 (s, 3H), 6.87 (s, 1H), 6.76 (s, 1H), 5.88-5.83 (m, 1H), 4.07 (d, *J* = 6.8 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 2.82-2.75 (m, 1H), 2.46-2.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2 (d, *J* = 241.8 Hz), 151.1, 144.2, 140.9 (d, *J* = 3.1 Hz), 140.6, 140.0, 139.7, 136.9, 129.5 (2x), 129.2 (d, *J* = 7.6 Hz, 2x), 128.8 (2x), 128.1, 127.3, 127.0 (2x), 126.9, 126.4 (2x), 126.3, 122.7, 114.7 (d, *J* = 21.3 Hz, 2x), 113.1, 61.3, 55.8, 38.0, 32.3. Single-crystal X-ray diagram: crystal of **4t** was grown by slow diffusion of EtOAc into a solution of **4t** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Triclinic crystal system, space group P -1, *a* = 11.399(2) Å, *b* = 11.510(2) Å, *c* = 19.440(4) Å, *V* = 2240.2(8) Å^3, *Z* = 2, d_{calcd} = 1.294 g/cm^3, *F*(000) = 920, 2θ range 1.09-28.30^o, *R* indices (all data) *R*1 = 0.0781, w*R*2 = 0.1123.

*4,5-Dimethoxy-2-methyl-1-phenyl-1H-indene (**6a**).* Yield = 93% (248 mg); Colorless solid; mp = 117-118 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{18}H_{18}O_2Na$ 289.1205, found 289.1198; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.22 (m, 3H), 7.07-7.04 (m, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.74 (s, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.31 (s, 1H), 3.98 (s, 3H), 3.87 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 150.2, 142.3, 141.4, 139.9, 137.6, 128.6 (2x), 128.0 (2x), 126.6, 123.4, 118.9, 108.6, 61.1, 59.0, 56.0, 15.3. Single-crystal X-ray diagram: crystal of **6a** was grown by slow diffusion of EtOAc into a solution of **6a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Triclinic crystal system, space group P -1, *a* = 7.0295(6) Å, *b* = 9.8296(8) Å, *c* = 11.7070(9) Å, *V* = 725.41(11) Å^3, *Z* = 2, d_{calcd} = 1.219 g/cm^3, *F*(000) = 284, 2θ range 1.88-26.49^o, *R* indices (all data) *R*1 = 0.0935, w*R*2 = 0.1873.

*1-(4-Fluorophenyl)-4,5-dimethoxy-2-methyl-1H-indene (**6b**).* Yield = 94% (267 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{18}H_{17}FO_2Na$ 307.1110, found 307.1105; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01-6.94 (m, 4H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.71 (t, *J* = 1.6 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.26 (s, 1H), 3.96 (s, 3H), 3.86 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, *J* = 242.6 Hz), 151.5, 150.0, 142.1, 141.5, 137.6, 135.6 (d, *J* = 3.0 Hz), 129.5 (d, *J* = 7.6 Hz, 2x), 123.5, 118.8, 115.4 (d, *J* = 21.2 Hz, 2x), 108.6, 61.1, 58.2, 56.1, 15.2.

*4,5-Dimethoxy-2-methyl-1-(p-tolyl)-1H-indene (**6c**).* Yield = 92% (258 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{19}H_{20}O_2Na$ 303.1361, found 303.1360; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.73-6.71 (m, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.27 (s, 1H), 3.97 (s, 3H), 3.86 (s, 3H), 2.34 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 150.4, 142.5, 141.4, 137.6, 136.8, 136.1, 129.3 (2x), 127.9 (2x), 123.3, 118.8, 108.6, 61.1, 58.7, 56.1, 21.0, 15.3.

*4,5-Dimethoxy-1-(4-methoxyphenyl)-2-methyl-1H-indene (**6d**).* Yield = 94% (278 mg); Colorless solid; mp = 92-93 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{20}O_3Na$ 319.1310, found 319.1306; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.24 (s, 1H), 3.96 (s, 3H), 3.85 (s, 3H), 3.79 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 151.3, 150.5, 142.5, 141.4, 137.6, 131.8, 129.0 (2x), 123.1, 118.8, 114.0 (2x), 108.5, 61.1, 58.3, 56.1, 55.1, 15.2. Single-crystal X-ray diagram: crystal of **6d** was grown by slow diffusion of EtOAc into a solution of **6d** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Monoclinic crystal system, space group P 21/n, *a* = 7.6240(7) Å, *b* = 23.566(2) Å, *c* = 8.4581(7) Å, *V* = 1516.8(2) Å^3, *Z* = 4, d_{calcd} = 1.298 g/cm^3, *F*(000) = 632, 2θ range 1.73-26.52^o, *R* indices (all data) *R*1 = 0.0531, w*R*2 = 0.1345.

*4-Isopropoxy-5-methoxy-2-methyl-1-phenyl-1H-indene (**6e**).* Yield = 85% (250 mg); Orange gum; HRMS (ESI, M^++Na) calcd for $C_{20}H_{22}O_2Na$ 317.1518, found 317.1512; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.23 (m, 5H), 7.05-7.02 (m, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.68-6.67 (m, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 4.49-4.43 (m, 1H), 4.30 (s, 1H), 3.83 (s, 3H), 1.92 (s, 1H), 1.38 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 149.8, 142.0, 140.2, 139.4, 128.6 (2x), 128.3, 128.1 (2x), 126.6, 124.1, 118.7, 108.6, 75.2, 59.1, 56.0, 22.7, 22.6, 15.3.

1-(4-Fluorophenyl)-4-isopropoxy-5-methoxy-2-methyl-1H-indene ***(6f)***. Yield = 88% (275 mg); Colorless solid; mp = 82-83 °C (re-crystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{20}H_{21}FO_2Na$ 335.1423, found 335.1416; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99-6.94 (m, 4H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.66-6.63 (m, 1H), 6.61 (d, *J* = 8.0 Hz, 1H), 4.46-4.40 (m, 1H), 4.26 (d, *J* = 0.8 Hz, 1H), 3.82 (s, 3H), 1.88 (d, *J* = 0.8 Hz, 3H), 1.35 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, *J* = 242.6 Hz), 152.2, 149.6, 141.9, 139.3 (d, *J* = 3.8 Hz), 135.9, 135.8, 129.5 (d, *J* = 7.6 Hz, 2x), 124.3, 118.7, 115.4 (d, *J* = 21.2 Hz, 2x), 108.7, 75.3, 58.3, 56.1, 22.7 (2x), 15.2. Single-crystal X-ray diagram: crystal of **6f** was grown by slow diffusion of EtOAc into a solution of **6f** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Orthorhombic crystal system, space group P 21 21 21, a = 8.1071(6) Å, b = 9.3064(7) Å, c = 22.2481(17) Å, V = 1678.6(2) Å^3, Z = 4, d_{calcd} = 1.236 g/cm^3, F(000) = 664, 2θ range 1.83-26.40°, R indices (all data) R1 = 0.0483, wR2 = 0.1287.

4-Isopropoxy-5-methoxy-2-methyl-1-(p-tolyl)-1H-indene ***(6g)***. Yield = 83% (256 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{21}H_{24}O_2Na$ 331.1674, found 331.1670; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, *J* = 7.6 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 4.47-4.41 (m, 1H), 4.26 (s, 1H), 3.82 (s, 3H), 2.32 (s, 3H), 1.90 (s, 3H), 1.35 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 150.0, 142.2, 137.1, 136.1, 129.3 (2x), 129.0, 128.7, 128.0 (2x), 124.0, 118.7, 108.7, 75.2, 58.8, 56.1, 22.69, 22.66, 21.0, 15.3.

4-Isopropoxy-5-methoxy-1-(4-methoxyphenyl)-2-methyl-1H-indene ***(6h)***. Yield = 91% (295 mg); Colorless solid; mp = 73-74 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{21}H_{24}O_3Na$ 347.1623, found 347.1618; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 1.6 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 4.46-4.40 (m, 1H), 4.23 (s, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 1.89 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 152.0, 150.1, 142.3, 139.34, 139.29, 132.1, 129.0 (2x), 123.8, 118.6, 114.1 (2x), 108.7, 75.2, 58.4, 56.1, 55.2, 22.69, 22.66, 15.3. Single-crystal X-ray diagram: crystal of **6h** was grown by slow diffusion of EtOAc into a solution of **6h** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the Monoclinic crystal system, space group P 21, a = 5.4384(9) Å, b = 7.1721(12) Å, c = 22.371(3) Å, V = 869.7(2) Å^3, Z = 2, d_{calcd} = 1.239 g/cm^3, F(000) = 348, 2θ range 0.91-26.58°, R indices (all data) R1 = 0.0554, wR2 = 0.1431.

4-Butoxy-5-methoxy-2-methyl-1-phenyl-1H-indene ***(6i)***. Yield = 82% (253 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{21}H_{24}O_2Na$ 331.1674, found 331.1668; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.19 (m, 4H), 7.03-7.01 (m, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.68-6.65 (m, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 4.27 (s, 1H), 4.10-4.04 (m, 2H), 3.83 (s, 3H), 1.90 (s, 3H), 1.82-1.75 (m, 2H), 1.58-1.52 (m, 2H), 1.00 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 150.0, 142.2, 140.6, 140.1, 138.4, 128.6 (2x), 128.1 (2x), 126.6, 123.7, 118.8, 108.7, 73.5, 59.1, 56.2, 32.4, 19.2, 15.3, 13.9.

4-Butoxy-1-(4-fluorophenyl)-5-methoxy-2-methyl-1H-indene ***(6j)***. Yield = 80% (261 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{21}H_{23}FO_2Na$ 349.1580, found 349.1574; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04-6.96 (m, 4H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.73 (s, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 4.29 (s, 1H), 4.17-4.11 (m, 2H), 3.86 (s, 3H), 1.93 (s, 3H), 1.89-1.81 (m, 2H), 1.66-1.58 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6 (d, *J* = 242.6 Hz), 151.8, 149.6, 141.9, 140.7, 138.2, 135.7 (d, *J* = 3.1 Hz), 129.4 (d, *J* = 7.6 Hz, 2x), 123.7, 118.6, 115.3 (d, *J* = 21.3 Hz, 2x), 108.8, 73.3, 58.2, 56.0, 32.3, 19.1, 15.1, 13.8.

4-Butoxy-5-methoxy-2-methyl-1-(p-tolyl)-1H-indene ***(6k)***. Yield = 78% (251 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{22}H_{26}O_2Na$ 345.1831, found 345.1826; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.69 (s, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.27 (s, 1H), 4.13-4.07 (m, 2H), 3.85 (s, 2H), 2.38-2.32 (m, 1H), 2.34 (s, 3H), 1.93 (s, 3H), 1.88-1.78 (m, 2H), 1.61-1.55 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 150.1, 142.4, 140.6, 138.4, 137.0, 136.1, 129.3 (2x), 128.0 (2x), 123.5, 118.7, 108.8, 73.5, 58.8, 56.2, 32.4, 21.0, 19.2, 15.3, 13.9.

4-Butoxy-5-methoxy-1-(4-methoxyphenyl)-2-methyl-1H-indene ***(6l)***. Yield = 88% (298 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1775; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.71 (s, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.27 (s, 1H), 4.16-4.10 (m, 2H), 3.85 (s, 3H), 3.79 (s, 3H), 1.94 (s, 3H), 1.88-1.81 (m, 2H), 1.63-1.58 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 151.6, 150.1, 142.4, 140.6, 138.2, 131.9, 128.9 (2x), 123.3, 118.6, 114.0 (2x), 108.7, 73.3, 58.3, 56.0, 55.0, 32.3, 19.1, 15.2, 13.8.

4-(Cyclopentyloxy)-5-methoxy-2-methyl-1-phenyl-1H-indene ***(6m)***. Yield = 80% (256 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{22}H_{24}O_2Na$ 343.1674, found 343.1668; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.22 (m, 3H), 7.07-7.04 (m, 2H), 6.49 (d, *J* = 8.0 Hz, 1H), 6.68 (s, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.93-4.89 (m, 1H), 4.31 (s, 1H), 3.85 (s, 3H), 2.03-1.95 (m, 4H), 1.93 (s, 3H), 1.81-1.63 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 149.8, 142.1, 140.2, 139.35, 139.27, 128.6 (2x), 128.3, 128.1 (2x), 126.6, 124.0, 118.6, 108.9, 84.5, 59.1, 56.1, 32.82, 32.78, 23.6, 15.3.

4-(Cyclopentyloxy)-1-(4-fluorophenyl)-5-methoxy-2-methyl-1H-indene ***(6n)***. Yield = 92% (311 mg); Orange gum; HRMS (ESI, M$^+$+Na) calcd for $C_{22}H_{23}FO_2Na$ 361.1580, found 361.1576; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02-6.95 (m, 4H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.67 (t, *J* = 1.6 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.93-4.89 (m, 1H), 4.28 (s, 1H), 3.84 (s, 3H), 2.03-1.93 (m, 4H), 1.91 (s, 3H), 1.81-1.64 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6 (d, *J* = 243.3 Hz), 152.0, 149.5, 141.9, 139.4, 139.1, 135.8 (d, *J* = 3.1 Hz), 129.4 (d, *J* = 7.6 Hz, 2x), 124.1, 118.5, 115.4 (d, *J* = 21.2 Hz, 2x), 108.9, 84.4, 58.3, 56.0, 32.8, 32.7, 23.6 (2x), 15.1.

4-(Cyclopentyloxy)-5-methoxy-2-methyl-1-(p-tolyl)-1H-indene ***(6o)***. Yield = 78% (261 mg); Orange gum; HRMS (ESI, M$^+$+1) calcd for $C_{23}H_{26}O_2$ 334.1933, found 334.1932; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 6.84-6.82 (m, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.09-5.05 (m, 1H), 4.41 (s, 1H), 3.95 (s, 3H), 2.46 (s, 3H), 2.20-2.06 (m, 4H), 2.06 (s, 3H), 1.94-1.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 149.7, 142.1, 139.2, 139.1, 136.9, 135.8, 129.1 (2x), 127.8 (2x), 123.7, 118.4, 108.7, 84.2, 58.7, 55.9, 32.7, 32.6, 23.5 (2x), 20.8, 15.1.

4-(Cyclopentyloxy)-5-methoxy-1-(4-methoxyphenyl)-2-methyl-1H-indene ***(6p)***. Yield = 90% (315 mg); Colorless solid; mp = 82-83 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{23}H_{26}O_3Na$ 373.1780, found 373.1772; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.63-6.61 (m, 2H), 4.90-4.86 (m, 1H), 4.24 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 2.01-1.93 (m, 4H), 1.90 (s, 3H), 1.79-1.61 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 151.9, 150.1, 142.3, 139.18, 139.17, 132.0, 129.0 (2x), 123.7, 118.5, 114.0 (2x), 108.8, 84.5, 58.4, 56.1, 55.1, 32.82, 32.76, 23.6 (2x), 15.3.

4-Methoxy-2-methyl-1-phenyl-1H-indene (***6q***). Yield = 75% (177 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{17}H_{16}ONa$ 259.1099, found 259.1098; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.22 (m, 4H), 7.05-7.01 (m, 3H), 6.78-6.75 (m, 1H), 6.71-6.70 (m, 1H), 4.31 (s, 1H), 3.90 (s, 3H), 1.92 (d, J = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 150.5, 148.2, 139.7, 133.0, 128.7 (2x), 128.2 (2x), 126.7, 125.5, 123.3, 116.8, 109.0, 59.9, 55.5, 15.2.

1-(4-Fluorophenyl)-4-methoxy-2-methyl-1H-indene (***6r***). Yield = 85% (216 mg); Colorless solid; mp = 68-69 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{15}FONa$ 277.1005, found 277.1007; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07-7.03 (m, 1H), 7.00-6.94 (m, 4H), 6.79-6.75 (m, 2H), 6.72-6.71 (m, 1H), 4.29 (s, 1H), 3.90 (s, 3H), 1.91 (d, J = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8 (d, J = 242.6 Hz), 152.1, 150.3, 147.9, 135.3 (d, J = 3.0 Hz), 132.9, 129.6 (d, J = 7.6 Hz, 2x), 125.6, 123.4, 116.6, 115.5 (d, J = 20.5 Hz, 2x), 109.1, 59.0, 55.4, 15.1.

4-Methoxy-2-methyl-1-(p-tolyl)-1H-indene (***6s***). Yield = 83% (208 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{18}H_{18}ONa$ 273.1255, found 273.1253; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, J = 7.6 Hz, 2H), 7.03 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.6 Hz, 2H), 6.79 (s, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.71-6.69 (m, 1H), 4.29 (s, 1H), 3.90 (s, 3H), 2.33 (s, 3H), 1.93 (d, J = 0.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 150.6, 148.3, 136.5, 136.2, 133.0, 129.4 (2x), 128.1 (2x), 125.4, 123.1, 116.7, 108.9, 59.5, 55.4, 21.1, 15.2.

7-([1,1'-Biphenyl]-4-yl)-1-(4-fluorophenyl)-4,5-dimethoxy-2-methyl-1H-indene (***6t***). Yield = 86% (375 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{30}H_{25}FO_2Na$ 459.1736, found 459.1735; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.0 Hz, 2H), 7.49-7.46 (m, 4H), 7.41-7.38 (m, 1H), 7.19 (d, J = 8.0 Hz, 2H), 6.78-6.77 (m, 1H), 6.71-6.66 (m, 2H), 6.64-6.60 (m, 3H), 4.51 (s, 1H), 4.05 (s, 3H), 3.92 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1 (d, J = 242.6 Hz), 151.8, 151.0, 140.8, 140.7, 139.7, 139.7, 139.5, 138.3, 134.4 (d, J = 3.0 Hz), 133.7, 129.4 (d, J = 8.3 Hz, 2x), 128.8 (2x), 128.7 (2x), 127.2, 126.9 (2x), 126.4 (2x), 123.0, 114.6 (d, J = 21.2 Hz, 2x), 109.6, 61.3, 58.0, 56.0, 15.1.

4,4'-(Oxybis(ethane-1,1-diyl))bis(3-allyl-1,2-dimethoxybenzene) (***7***). Yield = 78% (332 mg); Colorless gum; HRMS (ESI, M^++Na) calcd for $C_{26}H_{34}O_5Na$ 449.2304, found 449.2305; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.73-5.63 (m, 2H), 4.81 (dq, J = 1.6, 10.0 Hz, 2H), 4.69 (dq, J = 1.6, 17.2 Hz, 2H), 4.39 (q, J = 6.4 Hz, 2H), 3.88 (s, 6H), 3.79 (s, 6H), 3.30 (dq, J = 1.6, 13.6 Hz, 2H), 3.50 (dq, J = 1.6, 6.4 Hz, 2H), 1.32 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4 (2x), 146.8 (2x), 136.9 (2x), 135.5 (2x), 131.2 (2x), 121.3 (2x), 114.9 (2x), 110.8 (2x), 70.0 (2x), 60.6 (2x), 55.5 (2x), 29.6 (2x), 24.5 (2x).

ASSOCIATED CONTENT

Supporting Information

Scanned spectroscopic data for all compounds and X-ray analysis data of **4a**, **4t**, **6a**, **6d**, **6f** and **6h**. This information is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author *Email: mychang@kmu.edu.tw

Notes The authors declare no competing financial interest.

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