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Synthesis of Substituted Styrenes and 3-Vinylphenols Using Ruthenium-Catalyzed Ring-Closing Enyne Metathesis

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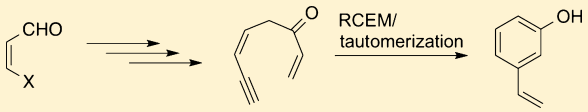
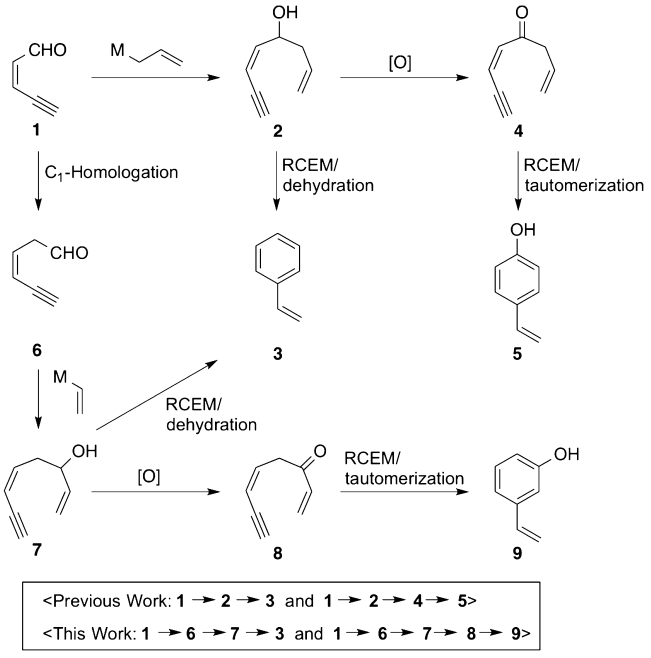
Supporting Information

ABSTRACT: The synthesis of substituted styrenes **3** and 3-vinylphenols **9** was achieved by ring-closing enyne metathesis (RCEM)/dehydration of **7** and RCEM/tautomerization of **8**, respectively. Those methods provide selective access to unique aromatic compounds and solve the problem of regioisomer formation.



As the demand for substituted aromatic compounds continues to increase, the development of new synthetic methods for such compounds remains an important subject in organic synthesis. Recently, much attention is being devoted to aromatic ring construction using ruthenium-catalyzed ring-closing metathesis (RCM),[1,2] a new method that selectively produces unique aromatic compounds.[3,4] As our contribution to this field,[5] in 2009, we developed the ring-closing enyne metathesis (RCEM)/dehydration of **2** to produce styrenes **3** and the RCEM/tautomerization of **4** to generate 4-vinylphenols **5** (Scheme 1).[5j] Those methods have great generality because acyclic precursors **2** and **4** can be readily prepared from well-known building blocks **1** using only highly reliable transformations. In fact, a wide variety of aromatic compounds can be synthesized by those methods.

Scheme 1. Strategy for Synthesizing Styrenes 3, 4-Vinylphenols 5, and 3-Vinylphenols 9



The purpose of this study was to extend the application of the previous methods from two points of view. First, we expected to increase the variety of obtainable styrenes **3** by the RCEM/dehydration of new enyne substrates **7**, which were anticipated to be prepared through the C_1-homologation of **1** followed by vinyl addition to resulting aldehydes **6** (Scheme 1). Second, we expected to synthesize 3-vinylphenols **9**, which are new target molecules and the regioisomers of **5**, by the RCEM/tautomerization of **8**, which were expected to be prepared from **7**. We report herein the results in detail.

The acyclic precursors for the ring-closing process are enynes **7** and **8**. To show how these compounds were prepared, a typical example is presented in Scheme 2 where **7a** and **8a** were synthesized. Ynal **1a** was prepared from commercially available 2-bromobenzaldehyde[6] and phenylacetylene by means of the Sonogashira coupling. Our choice of reaction for the subsequent C_1-homologation from **1a** to **6a** was the Wittig olefination with (methoxymethyl)triphenylphosphonium chloride and hydrolysis sequence. Resulting aldehyde **6a** was reacted

Scheme 2. Representative Example of the Preparation of 7 and 8

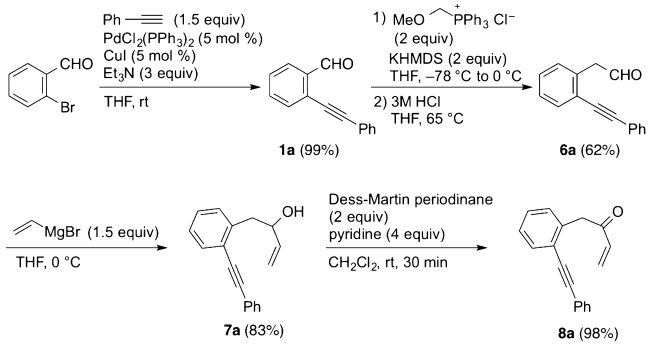


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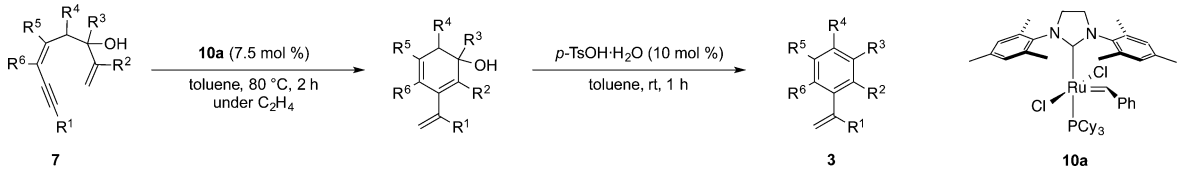
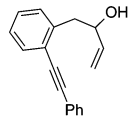
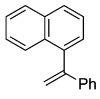
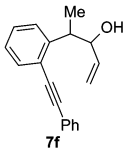
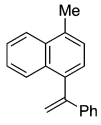
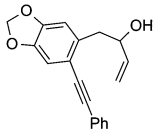
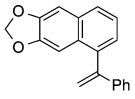
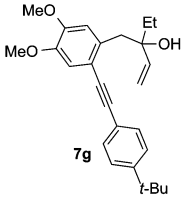
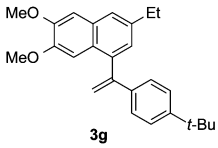
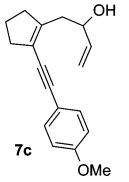
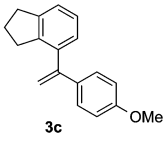
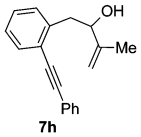
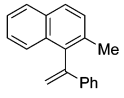
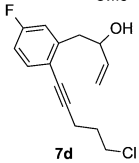
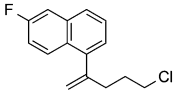
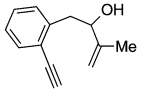
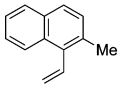
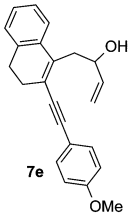
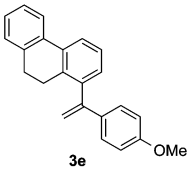
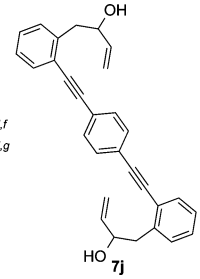
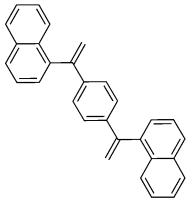
Table 1. Synthesis of Substituted Styrenes 3 by RCEM/Dehydration of 7[a]



entry	substrate	product	yield (%)[b]	entry	substrate	product	yield (%)[b]
1[c,d]	 **7a**	 **3a**	58	7[d]	 **7f**	 **3f**	84
2[d]			99				
3	 **7b**	 **3b**	93	8	 **7g**	 **3g**	77
4[d]	 **7c**	 **3c**	77	9	 **7h**	 **3h**	0
				10[e]			0
5[d]	 **7d**	 **3d**	89	11[d]	 **7i**	 **3i**	92
6[d]	 **7e**	 **3e**	>99	12[d,f]	 **7j**	 **3j**	48
				13[d,g]			60

[a]Ring-closing enyne metathesis was carried out with **7** and ruthenium catalyst (**10a**, 7.5 mol %) in toluene under ethylene atmosphere (1 atm) at 80 °C for 2 h. The reaction mixture was treated with *p*-toluenesulfonic acid (10 mol %) at rt for 1 h. [b]Isolated yield by silica gel chromatography. [c]The reaction was performed under nitrogen atmosphere. [d]Dehydration with *p*-toluenesulfonic acid was accomplished at 50 °C. [e]RCEM was conducted with 15 mol % of **10a** at 100 °C for 24 h. [f]RCEM was executed with 15 mol % of **10a**. [g]RCEM was realized with 30 mol % of **10a**.

with vinyl Grignard reagent to produce desired enyne **7a**. Finally, we converted **7a** into the other desired enyne substrate **8a** by simple oxidation with Dess–Martin periodinane.[7]

The results of the synthesis of substituted styrenes **3** from various enynes **7** are shown in Table 1. When RCEM of **7a** with Grubbs second-generation catalyst **10a**[8] at 80 °C under nitrogen atmosphere followed by dehydration with a catalytic amount of *p*-toluenesulfonic acid was carried out, desired styrene **3a** was obtained in 58% yield (entry 1). As we have experienced in the past that ethylene gas accelerated the RCEM process,[5j] we next conducted the reaction under ethylene atmosphere. As a result, the product was obtained in an almost quantitative yield (entry 2). Using those conditions, we obtained several styrenes **3b–e** having various substituents from **7b–e** in good yields (entries 3–6). Substrates **7f** and **7g**, which have a methyl group at R^4 position and an ethyl group at R^3 position, respectively, were also converted into corresponding products **3f** and **3g**, respectively (entries 7 and 8). However, the conversion of **7h** having a methyl group at R^2 position into **3h** met with failure (entries 9 and 10).[9] On the other hand, regardless of the presence of a methyl group at R^2 position, the reaction of **7i** having a terminal alkyne part proceeded to give **3i** in 92% yield (entry 11). Finally, the construction of two rings simultaneously gave **3j** in moderate yield from **7j** (entries 12 and 13).

Table 2 shows the results of the RCEM/tautomerization of **8**[10] to produce 3-vinylphenols **9**. From these, it is proved that this procedure can provide unique aromatic compounds. Analogously to the case of **7**, the reaction of **8** under ethylene atmosphere proceeded more smoothly than that under nitrogen

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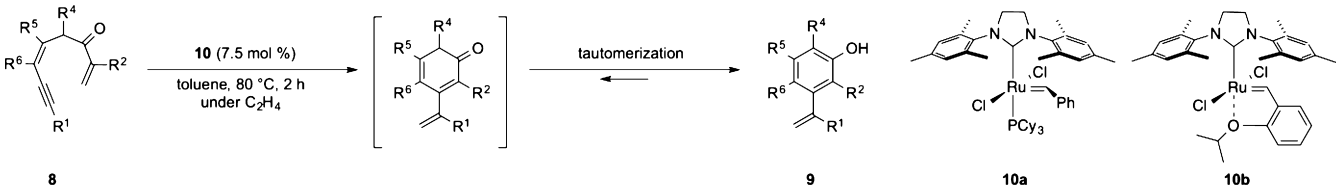
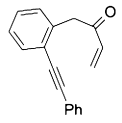
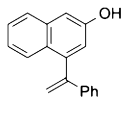
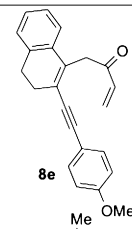
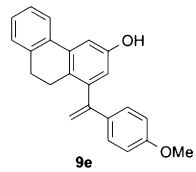
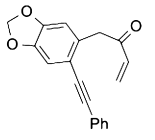
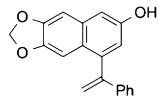
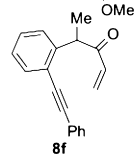
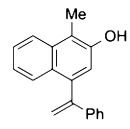
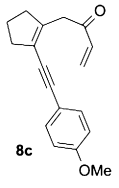
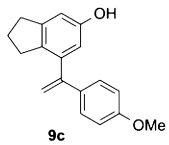
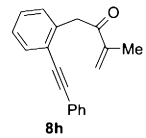
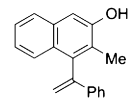
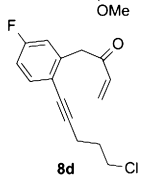
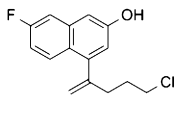
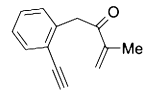
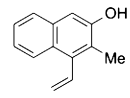
Table 2. Synthesis of Substituted 3-Vinylphenols 9 by RCEM/Tautomerization of 8[a]



entry	substrate	product	yield (%)[b]	entry	substrate	product	yield (%)[b]
1[c]	 **8a**	 **9a**	46	9	 **8e**	 **9e**	35
2			92	10[d]			55
3	 **8b**	 **9b**	84	11	 **8f**	 **9f**	67
4	 **8c**	 **9c**	57	12	 **8h**	 **9h**	0
5[d]			68	13[f]			0
6[e]			87				
7	 **8d**	 **9d**	42	14	 **8i**	 **9i**	86
8[d]			61				

[a]Ring-closing enyne metathesis was carried out with **8** and ruthenium catalyst (**10a**, 7.5 mol %) in toluene under ethylene atmosphere (1 atm) at 80 °C for 2 h. [b]Isolated yield by silica gel chromatography. [c]The reaction was performed under nitrogen atmosphere. [d]The reaction was conducted with 7.5 mol % of **10b**. [e]The reaction was executed with 10 mol % of **10b** for 12 h. [f]The reaction was accomplished with 15 mol % of **10a** at 100 °C for 24 h.

atmosphere. In fact, the reaction of **8a** under ethylene atmosphere doubled the isolated yield of **9a** (entry 1 vs 2). The reactivity of **8** was lower than that of **7** in general, but use of Hoveyda–Grubbs second-generation catalyst **10b**[11] improved the reactivity to a certain extent (entries 4 vs 5, 7 vs 8, and 9 vs 10). Once again, the reaction of the substrate having a methyl group at R^2 position failed (entries 12 and 13), but the reaction of **8i** having a terminal alkyne part proceeded well to give the corresponding product in good yield (entry 14).

In conclusion, on the basis of our previous work, we have developed new synthetic methods for styrenes **3** and 3-vinylphenols **9**. Easy access to the products and no formation of undesirable regioisomers are proof of the generality of the methods for producing unique aromatic compounds.

EXPERIMENTAL SECTION

All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or glovebox techniques under prepurified argon. NMR spectra were recorded at 400 or 500 MHz for ^{1}H and 100 or 125 MHz for ^{13}C. Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^{1}H NMR and chloroform-*d* (δ 77.0) for ^{13}C NMR. High-resolution mass spectra were recorded on Orbitrap mass spectrometers. Tetrahydrofuran was distilled from sodium benzophenone-ketyl under nitrogen prior to use. Triethylamine and dichloromethane were distilled from CaH_2 under nitrogen and stored in a glass flask with a Teflon stopcock under nitrogen. Toluene was distilled from sodium benzophenone-ketyl under nitrogen and stored in a glass flask with a Teflon stopcock under nitrogen. Grubbs second-generation catalyst **10a**[11a,12] and Hoveyda–Grubbs second-generation catalyst **10b**[11b] were prepared according to the reported procedures. *β*-Bromo-*α*,*β*-unsaturated aldehydes **11c** and **11e** were prepared according to the reported procedures.[13] Dess–Martin periodinane was prepared according to the reported procedure.[14] MnO_2 was prepared according to the reported procedure.[15] *β*-Bromo-*α*,*β*-unsaturated ketone **11f** was prepared from the corresponding alcohol by oxidation with Dess–Martin periodinane. Isopropenylmagnesium bromide solution (**16c**) was prepared by a general method from propenyl bromide and magnesium in THF. Aromatic aldehydes **11a**, **11b**, **11d**, and **11g**, dichlorobis(triphenylphosphine)palladium, copper iodide, all terminal acetylenes **15a–f**, (methoxymethyl)triphenylphosphonium chloride, potassium hexamethyldisilazide, hydrochloric acid, vinylmagnesium bromide solution (**16a**), pyridine, methyltriphenylphosphonium bromide, potassium *tert*-butoxide, *n*-butyllithium solution, 9-borabicyclo[3.3.1]nonane (9-BBN) solution, sodium peroxoborate tetrahydrate, palladium acetate, triphenylphosphine, ethylmagnesium bromide solution (**16b**), potassium carbonate, and *p*-toluenesulfonic acid monohydrate were used as received.

Preparation of Acyclic Precursors 7 and 8. General Procedure A: Sonogashira Coupling. To a mixture of dichlorobis(triphenylphosphine)palladium (5 mol %) and bromoarene or bromoalkene (1 equiv) in THF (0.13–0.15 M) was added triethyl

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amine (3 equiv). After being stirred for 10 min at room temperature, terminal acetylene (1.5 equiv) and copper iodide (5 mol %) were added to the mixture. The resulting mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with saturated aq. NH_4Cl, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The crude mixture was purified by silica-gel column chromatography.

General Procedure B: C_1-Homologation by Wittig Reaction/Hydrolysis. To a suspension of (methoxymethyl)triphenylphosphonium chloride (2 equiv) in anhydrous THF was added 0.5 M solution of KHMDS in toluene (2 equiv) at −78 °C. The mixture was stirred at the same temperature for 1 h, and then a solution of aldehyde or ketone (1 equiv) in anhydrous THF (0.13 M) was added to the mixture. The resulting mixture was allowed to warm up to 0 °C over 3 h and then diluted with hexane and passed through Celite. The residual solid was washed with hexane thoroughly. The filtrate was concentrated under reduced pressure. The crude mixture was taken up in THF (0.69 M) and treated with 3 M HCl (0.46 M). The mixture was stirred at a refluxing temperature (65 °C) overnight. Then, the reaction mixture was quenched with saturated aq. Na_2CO_3, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The crude mixture was purified by silica-gel column chromatography.

General Procedure C: Grignard Reaction. To a stirred solution of aldehyde **6** or enone **8g** (1 equiv) in THF (0.18 M) was added Grignard reagent **16** (1.0 M solution in THF, 2 equiv) at 0 °C. The mixture was stirred at the same temperature for 30 min and then quenched by addition of saturated aq. NH_4Cl, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The crude mixture was purified by silica-gel column chromatography to afford **7**.

General Procedure D: Oxidation with Dess−Martin Periodinane. To a stirred suspension of Dess−Martin periodinane (2 equiv) and pyridine (4 equiv) in CH_2Cl_2 (0.15 M) was added a solution of alcohol **7** or **14** (1 equiv) at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 30 min. The mixture was then diluted with Et_2O and passed through Celite. The residual solid was washed with Et_2O thoroughly. The filtrate was concentrated under reduced pressure and purified by silica-gel column chromatography.

General Procedure E: Wittig Reaction. A suspension of *t*-BuOK (0.96 M suspension in THF, 1.5 equiv) or a solution of *n*-BuLi (1.6 M solution in THF, 1.5 equiv) was added to a suspension of methyltriphenylphosphonium bromide (1.5 equiv) in anhydrous THF (0.34 M) at 0 °C. The mixture was stirred at the same temperature for 30 min, and then a solution of aldehyde **11** (1 equiv) in anhydrous THF (2.56 M) was added to the mixture. After being stirred at 0 °C for 2 h, the reaction mixture was diluted with saturated aqueous NH_4Cl, extracted with Et_2O, washed with brine, dried over $MgSO_4$, and evaporated. The crude mixture was purified by silica-gel column chromatography or vacuum distillation to afford **12**.

General Procedure F: Hydroboration/Oxidation. A solution of 9-BBN (0.5 M solution in THF, 3 equiv) was added to **12** (1 equiv) at room temperature, and the mixture was stirred at refluxing temperature for 24 h. After H_2O (0.30 M) and $NaBO_3{\cdot}4H_2O$ (15 equiv) were added at room temperature, the reaction mixture was stirred for 70 min. Then, the reaction mixture was diluted with saturated aqueous NH_4Cl, extracted with Et_2O, washed with brine, dried over Na_2SO_4, and evaporated. The crude mixture was purified by silica-gel column chromatography to afford **13**.

General Procedure G: Oxidation with MnO_2. MnO_2 (20 equiv) was added to a solution of **7** (1 equiv) in CH_2Cl_2 (0.02 M). After being stirred at a refluxing temperature overnight (ca. 17 h), the reaction mixture was passed through Celite. The residual solid was washed with CH_2Cl_2 thoroughly. The filtrate was concentrated under reduced pressure and purified by silica-gel column chromatography to afford **8**.

*2-(Phenylethynyl)benzaldehyde (**1a**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (3.53 g, 99% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[16]

*2-(2-(Phenylethynyl)phenyl)acetaldehyde (**6a**).* Following the General Procedure B; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (1.66 g, 62% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[17]

*1-(2-(Phenylethynyl)phenyl)but-3-en-2-ol (**7a**).* Following the General Procedure C; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (388.3 mg, 83% yield, white solid): mp 35−40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50−1.90 (br s, 1H), 2.98−3.03 (m, 1H), 3.20 (dd, J = 13.5, 5.0 Hz, 1H), 4.54−4.59 (m, 1H), 5.14 (dt, J = 10.5, 1.2 Hz, 1H), 5.26 (dt, J = 17.4, 1.4 Hz, 1H), 5.97−6.05 (m, 1H), 7.22−7.39 (m, 6H), 7.50−7.56 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.6, 73.1, 88.0, 93.5, 114.84, 114.89, 123.2, 126.6, 128.35, 128.40, 130.3, 131.5, 132.3, 139.9, 140.3, 140.4; HRMS (ESI) calcd for $C_{18}H_{16}OK$ (M^+ + K) 287.0833, found 287.0824.

*1-(2-(Phenylethynyl)phenyl)but-3-en-2-one (**8a**).* Following the General Procedure D; The reaction was carried out at room temperature for 1 h. Pyridine was not used; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (77.7 mg, 98% yield, white solid): mp 55−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (s, 2H), 5.82 (dd, J = 10.3, 1.4 Hz, 1H), 6.37 (dd, J = 17.8, 1.4 Hz, 1H), 6.48 (dd, J = 17.9, 10.3 Hz, 1H), 7.25−7.36 (m, 6H), 7.47−7.52 (m, 2H), 7.55−7.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.9, 87.7, 93.8, 123.0, 123.5, 127.1, 128.4, 128.5, 128.7, 128.9, 130.0, 131.5, 132.3, 135.7, 136.4, 197.4; HRMS (ESI) calcd for $C_{18}H_{15}O$ (M^+ + H) 247.1117, found 247.1117.

*6-(Phenylethynyl)benzo[d][1,3]dioxole-5-carbaldehyde (**1b**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (2.66 g, >99% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[16]

*2-(6-(Phenylethynyl)benzo[d][1,3]dioxol-5-yl)acetaldehyde (**6b**).* Following the General Procedure B; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (1.14 g, 54% yield, yellow solid): mp 74−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (d, J = 2.0 Hz, 2H), 6.01 (s, 2H), 6.73 (s, 1H), 7.03 (s, 1H), 7.31−7.37 (m, 3H), 7.46−7.50 (m, 2H), 9.76−9.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.2, 87.5, 92.9, 101.6, 110.4, 111.7, 116.8, 122.9, 128.4, 129.0, 131.3, 147.0, 148.4, 199.3; HRMS (APCI) calcd for $C_{17}H_{13}O_3$ (M^+ + H) 265.0859, found 265.0855.

*1-(6-(Phenylethynyl)benzo[d][1,3]dioxol-5-yl)but-3-en-2-ol (**7b**).* Following the General Procedure C; purified by silica-gel column chromatography (hexane/EtOAc = 8/1) (650.1 mg, 98% yield, yellow solid): mp 68−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65−1.80 (br s, 1H), 2.93 (dd, J = 13.8, 8.2 Hz, 1H), 3.12 (dd, J = 13.5, 4.8 Hz, 1H), 4.48−4.52 (m, 1H), 5.14 (dt, J = 10.5, 1.4 Hz, 1H), 5.26 (dt, J = 17.2, 1.4 Hz, 1H), 5.95−6.03 (m, 3H), 6.77 (s, 1H), 6.98 (s, 1H), 7.32−7.37 (m, 3H), 7.48−7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.5, 73.3, 88.2, 92.2, 101.4, 110.6, 111.6, 114.9, 116.0, 123.3, 128.1, 128.4, 131.3, 135.0, 140.3, 146.2, 148.0; HRMS (ESI) calcd for $C_{19}H_{16}O_3Na$ (M^+ + Na) 315.0992, found 315.0981.

*1-(6-(Phenylethynyl)benzo[d][1,3]dioxol-5-yl)but-3-en-2-one (**8b**).* Following the General Procedure D; The reaction was carried out at room temperature for 1 h. Pyridine was not used; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (57.2 mg, 98% yield, yellow solid): mp 60−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (s, 2H), 5.82 (dd, J = 10.4, 1.5 Hz, 1H), 5.99 (s, 2H), 6.38 (dd, J = 17.8, 1.5 Hz, 1H), 6.47 (dd, J = 17.5, 10.3 Hz, 1H), 6.73 (s, 1H), 6.99 (s, 1H), 7.29−7.36 (m, 3H), 7.44−7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.6, 87.8, 92.4, 101.5, 110.2, 111.6, 116.3, 123.1, 128.2, 128.4, 129.0, 131.1, 131.3, 135.6, 146.6, 148.2, 197.4; HRMS (ESI) calcd for $C_{19}H_{15}O_3$ (M^+ + H) 291.1016, found 291.1013.

*2-(2-((4-Methoxyphenyl)ethynyl)cyclopent-1-en-1-yl)ethanol (**14c**).* Following the General Procedure E−F−A; General Procedure E/*n*-BuLi was used. The crude mixture was purified by vacuum distillation; General Procedure A/After stirring a mixture of $Pd(OAc)_2$

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(10 mol %) and PPh_3 (40 mol %) in NEt_3 at room temperature for 10 min, alcohol **13c** was added to the mixture. 1-Ethynyl-4-methoxybenzene (**15b**) (3 equiv) and CuI (10 mol %) were used. The reaction was carried out at 90 °C for 24 h; purified by recycling gel permeation chromatography ($CHCl_3$) (652.9 mg, 5% yield for 3 steps, colorless oil): Because of the difficulty of separation of intermediates from impurities, the yield was calculated through 3 steps; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61−1.75 (br s, 1H), 1.91 (quint, J = 7.8 Hz, 2H), 2.42−2.49 (m, 2H), 2.54−2.62 (m, 2H), 2.60−2.66 (m, 2H), 3.78 (s, 3H), 3.78−3.83 (m, 2H), 6.81−6.86 (m, 2H), 7.35−7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5, 34.0, 35.9, 36.8, 55.2, 60.9, 84.7, 93.1, 113.9, 115.7, 120.3, 132.8, 147.4, 159.3; HRMS (ESI) calcd for $C_{16}H_{19}O_2$ (M^+ + H) 243.1380, found 243.1378.

*1-(2-((4-Methoxyphenyl)ethynyl)cyclopent-1-en-1-yl)but-3-en-2-ol (**7c**).* Following the General Procedure D−C; General Procedure D/Pyridine was not used. The reaction mixture was stirred for 1 h; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (25.6 mg, 41% yield for 2 steps, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 (br d, J = 3.9 Hz, 1H), 1.91 (quint, J = 7.6 Hz, 2H), 2.40−2.70 (m, 6H), 3.81 (s, 3H), 4.37 (unresolved q, J = 4.1 Hz, 1H), 5.12 (dt, J = 10.5, 1.4 Hz, 1H), 5.39 (dt, J = 17.4, 1.4 Hz, 1H), 5.94 (ddd, J = 16.5, 10.5, 6.0 Hz, 1H), 6.82−6.86 (m, 2H), 7.35−7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 36.4, 36.7, 38.5, 55.3, 71.6, 84.7, 93.5, 113.9, 114.7, 115.7, 121.1, 132.8, 140.7, 147.0, 159.4; HRMS (ESI) calcd for $C_{18}H_{21}O_2$ (M^+ + H) 269.1536, found 269.1534.

*1-(2-((4-Methoxyphenyl)ethynyl)cyclopent-1-en-1-yl)but-3-en-2-one (**8c**).* Following the General Procedure D; Pyridine was not used. The reaction mixture was stirred for 1 h; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (63.7 mg, 61% yield, cream yellow solid): mp 38−44 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 (quint, J = 7.8 Hz, 2H), 2.39−2.46 (m, 2H), 2.56−2.64 (m, 2H), 3.62 (s, 2H), 3.82 (s, 3H), 5.93−5.87 (m, 1H), 6.36−6.47 (m, 2H), 6.83−6.88 (m, 2H), 7.36−7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 35.8, 36.7, 42.6, 55.4, 84.5, 94.3, 114.1, 115.6, 122.4, 129.2, 132.9, 135.9, 143.2, 159.6, 197.7; HRMS (ESI) calcd for $C_{18}H_{19}O_2$ (M^+ + H) 267.1380, found 267.1380.

*2-(5-Chloropent-1-yn-1-yl)-5-fluorobenzaldehyde (**1d**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (1.85 g, 82% yield, red orange oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (quint, J = 6.4 Hz, 2H), 2.70 (t, J = 6.8 Hz, 2H), 3.72 (t, J = 6.4 Hz, 2H), 7.22−7.29 (m, 1H), 7.51 (dd, J = 8.7, 5.3 Hz, 1H), 7.56 (dd, J = 8.7, 3.0 Hz, 1H), 10.46 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 31.0, 43.5, 76.2, 95.4, 113.5 (d, J = 23.0 Hz), 121.2 (d, J = 23.0 Hz), 123.3 (d, J = 2.9 Hz), 135.3 (d, J = 7.7 Hz), 137.8 (d, J = 6.7 Hz) 162.0 (d, J = 253.9 Hz), 190.5; HRMS (APCI) calcd for $C_{12}H_{11}ClFO$ (M^+ + H) 225.0477, found 225.0479.

*2-(2-(5-Chloropent-1-yn-1-yl)-5-fluorophenyl)acetaldehyde (**6d**).* Following the General Procedure B; The crude mixture was taken up in THF (2.76 M) and then treated with 3 M HCl (1.84 M); purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (156.7 mg, 53% yield, yellow oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (quint, J = 6.4 Hz, 2H), 2.62 (t, J = 7.1 Hz, 2H), 3.69 (t, J = 6.4 Hz, 2H), 3.83 (d, J = 2.0 Hz, 2H), 6.91−6.96 (m, 2H), 7.44 (dd, J = 8.5, 5.7 Hz, 1H), 9.73 (t, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8, 31.1, 43.6, 49.1, 78.7, 92.9, 114.7 (d, J = 21.9 Hz), 117.2 (d, J = 22.9 Hz), 120.1, 134.1 (d, J = 8.6 Hz), 136.6 (d, J = 7.6 Hz), 162.0 (d, J = 253.7 Hz), 198.4; HRMS (ESI) calcd for $C_{13}H_{11}ClFO$ (M^- − H) 237.0488, found 237.0496.

*1-(2-(5-Chloropent-1-yn-1-yl)-5-fluorophenyl)but-3-en-2-ol (**7d**).* Following the General Procedure C; purified by recycling gel permeation chromatography ($CHCl_3$) (165.8 mg, 62% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57−1.82 (br s, 1H), 2.06 (quint, J = 6.5 Hz, 2H), 2.64 (t, J = 6.8 Hz, 2H), 2.92 (dd, J = 13.5, 8.0 Hz, 1H), 3.03 (dd, J = 13.8, 5.3 Hz, 1H), 3.72 (t, J = 6.4 Hz, 2H), 4.42−4.48 (m, 1H), 5.14 (dt, J = 10.6, 1.4 Hz, 1H), 5.25 (dt, J = 17.4, 1.4 Hz, 1H), 5.94 (ddd, J = 17.4, 10.8, 6.2 Hz, 1H), 6.88 (td, J = 8.5, 2.8 Hz, 1H), 6.96 (dd, J = 9.6, 2.8 Hz, 1H), 7.37 (dd, J = 8.7, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 31.3, 42.3, 43.7, 72.9, 79.3, 91.8, 113.7 (d, J = 22.0 Hz), 115.1, 117.1 (d, J = 22.0 Hz), 119.5, 134.0 (d, J = 8.6 Hz), 140.1, 142.4 (d, J = 7.7 Hz), 161.9 (d, J = 250.0 Hz); HRMS (ESI) calcd for $C_{15}H_{17}ClFO$ (M^+ + H) 267.0946, found 267.0949.

*1-(2-(5-Chloropent-1-yn-1-yl)-5-fluorophenyl)but-3-en-2-one (**8d**).* Following the General Procedure G; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (95.6 mg, 37% yield, yellow oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.02 (quint, J = 6.4 Hz, 2H), 2.60 (t, J = 7.1 Hz, 2H), 3.67 (t, J = 6.4 Hz, 2H), 4.03 (s, 2H), 5.87 (dd, J = 10.3, 1.8 Hz, 1H), 6.36 (dd, J = 17.9, 1.6 Hz, 1H), 6.44 (dd, J = 17.9, 10.1 Hz, 1H), 6.90−6.95 (m, 2H), 7.37−7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8, 31.2, 43.6, 45.5, 79.0, 92.3, 114.3 (d, J = 22.9 Hz), 117.1 (d, J = 21.9 Hz), 119.9, 129.1, 133.9 (d, J = 8.6 Hz), 135.6, 138.7 (d, J = 8.6 Hz), 162.0 (d, J = 252.7 Hz), 196.6; HRMS (ESI) calcd for $C_{15}H_{15}ClFO$ (M^+ + H) 265.0790, found 265.0789.

*2-(2-((4-Methoxyphenyl)ethynyl)-3,4-dihydronaphthalen-1-yl)-ethanol (**14e**).* Following the General Procedure E−F−A; General Procedure E/*t*-BuOK was used. The crude mixture was purified by silica-gel column chromatography (hexane only); General Procedure A/After stirring a mixture of $Pd(OAc)_2$ (10 mol %) and PPh_3 (40 mol %) in NEt_3 was stirred at room temperature for 10 min, alcohol **13e** was added to the mixture. 1-Ethynyl-4-methoxybenzene (**15b**) (3 equiv) and CuI (10 mol %) were used. The reaction was carried out at 90 °C for 24 h; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (994.9 mg, 13% yield for 3 steps, orange gum): Because of the difficulty of separation of intermediates from impurities, the yield was calculated through 3 steps; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64−1.75 (br s, 1H), 2.52 (t, J = 8.0 Hz, 2H), 2.80 (t, J = 8.0 Hz, 2H), 3.16 (t, J = 6.8 Hz, 2H), 3.61−3.92 (m, 2H), 3.81 (s, 3H), 6.83−6.90 (m, 2H), 7.12−7.27 (m, 3H), 7.35 (d, J = 7.8 Hz, 1H), 7.39−7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 28.5, 34.3, 55.3, 62.0, 88.8, 96.0, 114.0, 115.6, 120.1, 123.4, 126.6, 127.3, 127.7, 132.8, 134.3, 136.3, 137.7, 159.6; HRMS (ESI) calcd for $C_{21}H_{21}O_2$ (M^+ + H) 305.1536, found 305.1535.

*2-(2-((4-Methoxyphenyl)ethynyl)-3,4-dihydronaphthalen-1-yl)-acetaldehyde (**6e**).* Following the General Procedure D; The reaction mixture was stirred for 1 h; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (24.4 mg, 62% yield, yellow oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (t, J = 8.5 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 3.83 (s, 3H), 3.90 (s, 2H), 6.84−6.91 (m, 2H), 7.14−7.26 (m, 4H), 7.38−7.44 (m, 2H), 9.69 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9, 28.5, 46.3, 55.3, 88.2, 97.6, 114.1, 115.1, 122.6, 123.4, 126.9, 127.7, 127.8, 132.2, 132.9, 134.3, 135.9, 159.9, 200.2; HRMS (ESI) calcd for $C_{21}H_{17}O_2$ (M^- − H) 301.1234, found 301.1245.

*1-(2-((4-Methoxyphenyl)ethynyl)-3,4-dihydronaphthalen-1-yl)-but-3-en-2-ol (**7e**).* Following the General Procedure C; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (266.8 mg, 62% yield, yellow oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.83−1.89 (br s, 1H), 2.53 (t, J = 8.4 Hz, 2H), 2.78−2.84 (m, 2H), 3.10 (dd, J = 14.0, 6.0 Hz, 1H), 3.16 (dd, J = 14.0, 7.8 Hz, 1H), 3.82 (s, 3H), 4.45 (unresolved q, J = 6.2 Hz, 1H), 5.11 (dt, J = 10.3, 1.4 Hz, 1H), 5.26 (dt, J = 17.0, 1.4 Hz, 1H), 6.03 (ddd, J = 19.7, 15.3, 9.2 Hz, 1H), 6.84−6.89 (m, 2H), 7.14−7.25 (m, 3H), 7.38−7.43 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.2, 28.5, 38.6, 55.3, 72.7, 89.1, 96.4, 114.0, 114.5, 115.6, 120.5, 123.7, 126.6, 127.3, 127.7, 132.8, 134.4, 136.4, 137.8, 140.7, 159.6; HRMS (ESI) calcd for $C_{23}H_{23}O_2$ (M^+ + H) 331.1693, found 331.1690.

*1-(2-((4-Methoxyphenyl)ethynyl)-3,4-dihydronaphthalen-1-yl)-but-3-en-2-one (**8e**).* Following the General Procedure G; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (21.1 mg, 89% yield, brown gum): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (t, J = 8.5 Hz, 2H), 2.86 (t, J = 7.6 Hz, 2H), 3.83 (s, 3H), 4.09 (s, 2H), 5.75 (dd, J = 10.5, 1.4 Hz, 1H), 6.38 (dd, J = 17.6, 1.4 Hz, 1H), 5.68 (dd, J = 17.6, 10.5 Hz, 1H), 6.84−6.90 (m, 2H), 7.13−7.22 (m, 4H), 7.37−7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 28.5, 44.4, 55.3, 88.6, 97.2, 114.1, 115.3, 121.7, 123.9, 126.8, 127.5, 127.6, 128.6, 132.9, 134.3, 134.7, 134.8, 135.9, 159.8, 197.9; HRMS (ESI) calcd for $C_{23}H_{21}O_2$ (M^+ + H) 329.1536, found 329.1534.

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*1-(2-(Phenylethynyl)phenyl)ethanone (**1f**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (1.45 g, 91% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[18]

*2-(2-(Phenylethynyl)phenyl)propanal (**6f**).* Following the General Procedure B; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (647.0 mg, 51% yield, brown oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 4.19 (q, J = 7.2 Hz, 1H), 7.18 (d, J = 7.7 Hz, 1H), 7.30 (td, J = 7.5, 1.5 Hz, 1H), 7.34−7.38 (m, 4H), 7.50−7.54 (m, 2H), 7.61 (dd, J = 7.5, 1.6 Hz, 1H), 9.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 51.2, 87.2, 94.1, 122.8, 123.4, 127.4, 127.9, 128.4, 128.6, 129.0, 131.4, 132.8, 140.0, 201.2; HRMS (ESI) calcd for $C_{18}H_{18}NaO_2$ (M^+ + Na+MeOH) 289.1199, found 289.1186.

*4-(2-(Phenylethynyl)phenyl)pent-1-en-3-ol (**7f**).* Following the General Procedure C; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (28.0 mg, 75% yield, yellow oil): The following data are for a mixture of two diastereomers (0.84/0.16); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, J = 7.1 Hz, 0.48H), 1.36 (d, J = 7.1 Hz, 2.52H), 1.55−1.75 (br s, 1H), 3.58−3.65 (m, 1H), 4.40 (t, J = 6.8 Hz, 0.16H), 4.44 (tt, J = 5.7, 4.1 Hz, 0.84H), 5.12 (dt, J = 10.5, 1.6 Hz, 0.84H), 5.18 (dt, J = 10.5, 1.4 Hz, 0.16H), 5.24 (dt, J = 17.4, 1.4 Hz, 0.84H), 5.26 (dt, J = 17.4, 1.4 Hz, 0.16H), 5.88−5.97 (m, 1H), 7.19−7.24 (m, 1H), 7.32−7.38 (m, 5H), 7.50−7.55 (m, 3H); The following data are for a major diastereomer; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 42.6, 76.2, 88.1, 93.7, 115.3, 122.8, 123.2, 126.2, 127.1, 128.3, 128.4, 128.5, 131.4, 132.5, 139.4, 145.5; HRMS (ESI) calcd for $C_{19}H_{18}NaO$ (M^+ + Na) 285.1250, found 285.1245.

*4-(2-(Phenylethynyl)phenyl)pent-1-en-3-one (**8f**).* Following the General Procedure D; The crude mixture was purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (46.3 mg, 78% yield, yellow solid): mp 30−34 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (d, J = 6.8 Hz, 3H), 4.66 (q, J = 6.8 Hz, 1H), 5.65 (dd, J = 9.4, 2.5 Hz, 1H), 6.32 (dd, J = 17.6, 2.5 Hz, 1H), 6.34 (dd, J = 17.4, 9.4 Hz, 1H), 7.16 (dd, J = 7.8, 1.4 Hz, 1H), 7.24 (td, J = 7.6, 1.4 Hz, 1H), 7.30 (td, J = 7.6, 1.6 Hz, 1H), 7.34−7.40 (m, 3H), 7.52−7.59 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0, 48.3, 87.5, 93.9, 122.8, 122.9, 127.0, 127.3, 128.4, 128.4, 128.6, 129.0, 131.5, 132.7, 135.1, 142.3, 199.8; HRMS (ESI) calcd for $C_{19}H_{16}NaO$ (M^+ + Na) 283.1093, found 283.1090.

*2-((4-tert-Butylphenyl)ethynyl)-4,5-dimethoxybenzaldehyde (**1g**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 7/1) (2.56 g, 97% yield, beige solid): mp 120−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.96 (s, 3H), 4.00 (s, 3H), 7.06 (s, 1H), 7.39−7.43 (m, 3H), 7.48−7.50 (m, 2H), 10.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 34.9, 56.1, 56.3, 84.2, 95.2, 108.1, 114.2, 119.4, 121.9, 125.5, 130.0, 131.3, 149.6, 152.3, 153.6, 190.6; HRMS (ESI) calcd for $C_{21}H_{22}NaO_3$ (M^+ + Na) 345.1461, found 345.1461.

*2-(2-((4-tert-Butylphenyl)ethynyl)-4,5-dimethoxyphenyl)-acetaldehyde (**6g**).* Following the General Procedure B; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (1.08 g, 48% yield, yellow solid): mp 79−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 9H), 3.86 (d, J = 2.0 Hz, 2H), 3.90 (s, 3H), 3.92 (s, 3H), 6.72 (s, 1H), 7.08 (s, 1H), 7.35−7.39 (m, 2H), 7.42−7.45 (m, 2H), 9.78 (t, J = 2.3 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 34.8, 49.0, 55.96, 56.01, 86.9, 92.9, 112.8, 114.5, 115.9, 119.9, 125.4, 127.3, 131.1, 148.1, 149.5, 151.7, 199.6; HRMS (ESI) calcd for $C_{22}H_{25}O_3$ (M^+ + H) 337.1798, found 337.1796.

*1-(2-((4-tert-Butylphenyl)ethynyl)-4,5-dimethoxyphenyl)butan-2-ol (**17**).* Following the General Procedure C; Ethyl Grignard reagent (**16b**) (1.0 M solution in THF) was used; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (599.2 mg, 82% yield, yellow gum): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, J = 7.5 Hz, 3H), 1.33 (s, 9H), 1.52−1.60 (br s, 1H), 1.56−1.69 (m, 2H), 2.78 (dd, J = 13.5, 8.5 Hz, 1H), 3.13 (dd, J = 13.7, 4.1 Hz, 1H), 3.90 (s, 3H), 3.90 (s, 3H), 3.87−3.96 (m, 1H), 6.78 (s, 1H), 7.03 (s, 1H), 7.36−7.39 (m, 2H), 7.42−7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.1, 30.0, 31.2, 34.8, 42.0, 55.9, 56.0, 73.7, 87.6, 92.0, 113.0, 114.6, 115.0, 120.4, 125.4, 131.0, 134.1, 147.2, 149.1, 151.4; HRMS (ESI) calcd for $C_{24}H_{31}O_3$ (M^+ + H) 367.2268, found 367.2262.

*1-(2-((4-tert-Butylphenyl)ethynyl)-4,5-dimethoxyphenyl)butan-2-one (**18**).* Following the General Procedure D; Dess−Martin periodinane (2.5 equiv) was used; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (331.0 mg, 93% yield, white solid): mp 72−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (t, J = 7.3 Hz, 3H), 1.33 (s, 9H), 2.53 (q, J = 7.6 Hz, 2H), 3.89 (s, 2H), 3.89 (s, 3H), 3.90 (s, 3H), 6.74 (s, 1H), 7.03 (s, 1H), 7.36−7.39 (m, 2H), 7.43−7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 31.1, 34.7, 35.2, 48.0, 55.9, 55.9, 87.2, 92.3, 112.6, 114.3, 115.4, 120.1, 125.3, 130.0, 131.0, 147.7, 149.3, 151.5, 209.0; HRMS (ESI) calcd for $C_{24}H_{28}NaO_3$ (M^+ + Na) 387.1931, found 387.1920.

*3-(2-((4-tert-Butylphenyl)ethynyl)-4,5-dimethoxybenzyl)pent-1-en-3-ol (**7g**).* Following the General Procedure C; purified by silica-gel column chromatography (hexane/EtOAc = 3/1) (138.6 mg, 90% yield, white solid): mp 93−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 7.3 Hz, 3H), 1.33 (s, 9H), 1.67 (q, J = 7.6 Hz, 2H), 1.75−1.84 (br s, 1H), 3.09 (s, 2H), 3.88 (s, 3H), 3.88 (s, 3H), 5.09 (dd, J = 11.0, 1.4 Hz, 1H), 5.13 (dd, J = 17.4, 1.4 Hz, 1H), 5.99 (dd, J = 17.4, 10.7 Hz, 1H), 6.81 (s, 1H), 7.01 (s, 1H), 7.37−7.39 (m, 2H), 7.43−7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.9, 31.1, 33.2, 34.7, 44.8, 55.9, 88.6, 91.6, 112.9, 113.8, 114.3, 116.1, 120.4, 125.4, 131.0, 132.4, 143.2, 147.3, 148.7, 151.3; HRMS (ESI) calcd for $C_{26}H_{33}O_3$ (M^+ + H) 393.2424, found 393.2412.

*3-Methyl-1-(2-(phenylethynyl)phenyl)but-3-en-2-ol (**7h**).* Following the General Procedure C; Isopropenyl Grignard reagent (**16c**) (0.51 M solution in THF) and THF (0.08 M) were used; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (151.9 mg, 73% yield, yellow solid): mp 54−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68 (d, J = 3.4 Hz, 1H), 1.86 (s, 3H), 2.93 (dd, J = 13.8, 9.4 Hz, 1H), 3.28 (dd, J = 13.7, 4.1 Hz, 1H), 4.49 (dt, J = 8.2, 3.6 Hz, 1H), 4.87 (t, J = 1.4 Hz, 1H), 5.00 (t, J = 0.9 Hz, 1H), 7.22−7.28 (m, 1H), 7.28−7.32 (m, 2H), 7.33−7.39 (m, 3H), 7.50−7.57 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 41.3, 75.7, 88.1, 93.5, 111.0, 123.0, 123.2, 126.6, 128.3, 128.4, 130.2, 131.5, 132.4, 140.5, 147.1; HRMS (ESI) calcd for $C_{19}H_{18}NaO$ (M^+ + Na) 285.1250, found 285.1248.

*3-Methyl-1-(2-(phenylethynyl)phenyl)but-3-en-2-one (**8h**).* Following the General Procedure D; purified by silica-gel column chromatography (hexane/EtOAc =7/1) (24.3 mg, 84% yield, yellow solid): mp 64−69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (dd, J = 1.6, 0.9 Hz, 3H), 4.29 (s, 2H), 5.83−5.85 (m, 1H), 6.19 (s, 1H), 7.22−7.38 (m, 6H), 7.44−7.50 (m, 2H), 7.53−7.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 43.3, 87.9, 93.5, 123.1, 123.2, 125.3, 126.9, 128.4, 128.5, 129.8, 131.4, 132.3, 137.4, 144.4, 199.0; HRMS (ESI) calcd for $C_{19}H_{16}ONa$ (M^+ + Na) 283.1093, found 283.1083.

*2-((Trimethylsilyl)ethynyl)benzaldehyde (**1i**).* Following the General Procedure A; purified by silica-gel column chromatography (hexane/EtOAc = 9/1) (4.41 g, >99% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[16]

*2-(2-Ethynylphenyl)acetaldehyde (**6i**).* Following the General Procedure B; After the Wittig reaction, the crude mixture was taken up in MeOH (0.44 M) and treated with K_2CO_3 (0.1 equiv). The mixture was stirred at room temperature for 2 h, and then quenched by addition of saturated aq. NH_4Cl, extracted with EtOAc three times, and washed with brine. The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure after filtration. Then, the crude mixture was used for hydrolysis; purified by silica-gel column chromatography (hexane/EtOAc = 20/1) (1.32 g, 46% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[19]

*1-(2-Ethynylphenyl)-3-methylbut-3-en-2-ol (**7i**).* Following the General Procedure C; Isopropenyl Grignard reagent (**16c**) (0.51 M solution in THF) was used; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (178.2 mg, 49% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58−1.72 (br s, 1H), 1.84 (t, J = 1.2 Hz, 3H), 2.87 (dd, J = 13.7, 9.2 Hz, 1H), 3.19 (dd, J = 13.8, 4.1 Hz, 1H), 3.29 (s, 1H), 4.39−4.43 (m, 1H), 4.84−4.88 (m, 1H), 4.98−4.99 (m, 1H), 7.21 (td, J = 7.6, 1.8 Hz, 1H), 7.28−7.33 (m,

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2H), 7.51 (dd, J = 7.6, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 40.9, 75.6, 81.2, 82.4, 110.9, 121.9, 126.4, 128.9, 130.1, 133.0, 141.1, 147.1; HRMS (ESI) calcd for $C_{13}H_{14}NaO$ (M^+ + Na) 209.0937, found 209.0937.

*1-(2-Ethynylphenyl)-3-methylbut-3-en-2-one (**8i**).* Following the General Procedure D; The crude mixture was purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (47.2 mg, >99% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (t, J = 0.9 Hz, 3H), 3.23 (s, 1H), 4.23 (s, 2H), 5.82−5.86 (m, 1H), 6.15 (s, 1H), 7.18−7.26 (m, 2H), 7.31 (td, J = 7.6, 1.4 Hz, 1H), 7.51 (dd, J = 7.8, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7, 42.9, 81.2, 82.1, 122.1, 125.4, 126.8, 129.0, 129.8, 132.9, 137.8, 144.2, 198.8; HRMS (ESI) calcd for $C_{13}H_{12}NaO$ (M^+ + Na) 207.0780, found 207.0776.

*2,2′-(1,4-Phenylenebis(ethyne-2,1-diyl))dibenzaldehyde (**1j**).* Following the General Procedure A; The crude mixture was purified by silica-gel column chromatography (2.56 g, 97% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[20]

*2,2′-((1,4-Phenylenebis(ethyne-2,1-diyl))bis(2,1-phenylene))diacetaldehyde (**6j**).* Following the General Procedure B; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (842.7 mg, 38% yield, yellowish solid): mp 119−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (d, J = 2.1 Hz, 4H), 7.23−7.38 (m, 6H), 7.49 (s, 4H), 7.58−7.62 (m, 2H), 9.80 (t, J = 2.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.3, 89.3, 93.8, 122.9, 123.4, 127.6, 129.1, 130.2, 131.4, 132.4, 134.3, 199.2; HRMS (APCI) calcd for $C_{26}H_{19}O_2$ (M^+ + H) 363.1380, found 363.1376.

*1,1′-((1,4-Phenylenebis(ethyne-2,1-diyl))bis(2,1-phenylene))bis(but-3-en-2-ol) (**7j**).* Following the General Procedure C; purified by silica-gel column chromatography (CH_2Cl_2/EtOAc = 4/1) (71.0 mg, 67% yield, white solid): The following data are for a mixture of two diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69−1.76 (br s, 2H), 3.01 (dd, J = 13.5, 8.2 Hz, 2H), 3,19 (dd, J = 13.5, 5.0 Hz, 2H), 4.55 (q, J = 6.2 Hz, 2H), 5.14 (dt, J = 10.5, 1.2 Hz, 2H), 5.26 (dt, J = 17.4, 1.4 Hz, 2H), 6.00 (ddd, J = 21.7, 10.5, 6.2 Hz, 2H), 7.22−7.34 (m, 6H), 7.49 (s, 4H), 7.55 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.6, 73.2, 90.0, 93.2, 114.9, 122.9, 123.1, 126.7, 128.6, 130.4, 131.4, 132.4, 140.0, 140.3; HRMS (APCI) calcd for $C_{30}H_{27}O_2$ (M^+ + H) 419.2006, found 419.1999.

Synthesis of Substituted Styrenes 3 by RCEM/Dehydration of 7. General Procedure H: RCEM/Dehydration. To a solution of 1,5-octadiene-7-yn-3-ols **7** (1 equiv) in toluene (0.01 M) was added catalyst **10a** (7.5 mol %) under nitrogen, and then the system was evacuated carefully and filled with ethylene gas (1 atm) in three cycles. The reaction mixture was heated to 80 °C and stirred for 2 h. After cooling to room temperature, the reaction mixture was treated with *p*-toluenesulfonic acid monohydrate (10 mol %) and stirred for 1 h at room temperature. The mixture was concentrated under reduced pressure and purified by silica-gel column chromatography to afford **3**.

*1-(1-Phenylvinyl)naphthalene (**3a**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C overnight; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (30 mg, 99% yield). This product was characterized by comparison of the spectroscopic data with those reported previously.[21]

*5-(1-Phenylvinyl)naphtho[2,3-d][1,3]dioxole (**3b**).* Following the General Procedure H; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (31.9 mg, 93% yield, white solid): mp 79−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (d, J = 1.4 Hz, 1H), 5.94 (d, J = 1.6 Hz, 1H), 5.96 (s, 2H), 7.05 (s, 1H), 7.13 (s, 1H), 7.23−7.37 (m, 7H), 7.66 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.9, 102.8, 104.0, 116.0, 124.0, 125.9, 126.5, 126.9, 127.7, 128.4, 128.8, 130.8, 139.0, 140.8, 147.3, 147.5, 148.5; HRMS (APCI) calcd for $C_{19}H_{15}O_2$ (M^+ + H) 275.1067, found 275.1061.

*4-(1-(4-Methoxyphenyl)vinyl)-2,3-dihydro-1H-indene (**3c**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C overnight; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (19.3 mg, 77% yield, yellow oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (quint, J = 7.6 Hz, 2H), 2.52 (t, J = 7.6 Hz, 2H), 2.90 (t, J = 7.6 Hz, 2H), 3.80 (s, 3H), 5.15 (d, J = 1.6 Hz, 1H), 5.55 (d, J = 1.6 Hz, 1H), 6.80−6.85 (m, 2H), 7.08 (d, J = 7.3 Hz, 1H), 7.15 (t, J = 7.3 Hz, 1H), 7.19−7.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 32.4, 33.0, 55.2, 113.2, 113.5, 123.6, 126.1, 127.0, 128.3, 133.6, 138.5, 142.6, 144.4, 148.8, 159.1; HRMS (ESI) calcd for $C_{18}H_{19}O$ (M^+ + H) 251.1430, found 251.1432.

*1-(5-Chloropent-1-en-2-yl)-6-fluoronaphthalene (**3d**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at room temperature for 1 h, then stirred at 50 °C for 1 h; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (30.5 mg, 89% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84−1.92 (m, 2H), 2.67 (t, J = 5.7 Hz, 2H), 3.55 (t, J = 5.3 Hz, 2H), 5.12−5.16 (m, 1H), 5.45 (q, J = 1.4 Hz, 1H), 7.20−7.25 (m, 1H), 7.23−7.28 (m, 1H), 7.43−7.48 (m, 2H), 7.70 (d, J = 6.6 Hz, 1H), 8.01 (dd, J = 7.6, 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 35.6, 44.4, 111.2 (d, J = 16.2 Hz), 116.1 (d, J = 20.0 Hz) 116.6, 124.3, 126.4, 126.7, 126.7, 128.2 (d, J = 6.7 Hz), 134.6 (d, J = 6.7 Hz), 140.8, 146.9, 160.5 (d, J = 196.5 Hz); HRMS (APCI) calcd for $C_{15}H_{15}ClF$ (M^+ + H) 249.0841, found 249.0840.

*1-(1-(4-Methoxyphenyl)vinyl)-9,10-dihydrophenanthrene (**3e**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C overnight; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (31.3 mg, >99% yield, cream yellow solid): mp 80−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54−2.60 (m, 2H), 2.66−2.72 (m, 2H), 3.79 (s, 3H), 5.15 (d, J = 1.4 Hz, 1H), 5.73 (d, J = 1.4 Hz, 1H), 6.78−6.83 (m, 2H), 7.15−7.35 (m, 7H), 7.75−7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 28.9, 55.2, 113.0, 113.7, 123.3, 124.0, 126.4, 126.9, 127.3, 127.6, 127.8, 129.3, 133.2, 134.73, 134.79, 135.7, 137.4, 141.0, 148.3, 159.2; HRMS (ESI) calcd for $C_{23}H_{21}O$ (M^+ + H) 313.1587, found 313.1587.

*1-Methyl-4-(1-phenylvinyl)naphthalene (**3f**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C overnight; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (28.8 mg, 84% yield, white solid): mp 46−51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.73 (s, 3H), 5.37 (d, J = 1.4 Hz, 1H), 5.96 (d, J = 1.4 Hz, 1H), 7.22−7.28 (m, 3H), 7.28−7.37 (m, 5H), 7.47 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.78 (m, 1H), 8.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 116.1, 124.3, 125.5, 126.2, 126.6, 126.9, 127.1, 127.6, 128.3, 131.9, 132.7, 134.2, 138.1, 141.2, 148.4; HRMS (APCI) calcd for $C_{19}H_{17}$ (M^+ + H) 245.1325, found 245.1327.

*1-(1-(4-tert-Butylphenyl)vinyl)-3-ethyl-6,7-dimethoxynaphthalene (**3g**).* Following the General Procedure H; purified by silica-gel column chromatography (hexane/EtOAc = 3/1) (15.4 mg, 77% yield, colorless gum): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 9H), 1.33 (t, J = 7.8 Hz, 3H), 2.79 (q, J = 7.8 Hz, 2H), 3.62 (s, 3H), 3.97 (s, 3H), 5.38 (d, J = 1.4 Hz, 1H), 5.88 (d, J = 1.4 Hz, 1H), 6.95 (s, 1H), 7.08 (s, 1H), 7.20 (d, J = 1.6 Hz, 1H), 7.24−7.29 (m, 4H), 7.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 28.8, 31.3, 34.5, 55.4, 55.7, 105.5, 106.1, 115.2, 124.2, 125.2, 125.7, 126.5, 126.6, 129.8, 138.5, 139.7, 148.3, 148.7, 149.1, 150.6; HRMS (ESI) calcd for $C_{26}H_{31}O_2$ (M^+ + H) 375.2319, found 375.2311.

*2-Methyl-1-vinylnaphthalene (**3i**).* Following the General Procedure H; The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C overnight; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (33.8 mg, 92% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3H), 5.43 (dd, J = 18.1, 2.0 Hz, 1H), 5.76 (dd, J = 11.7, 2.0 Hz, 1H), 7.03 (dd, J = 18.1, 11.4 Hz, 1H), 7.33 (d, J = 8.5 Hz, 1H), 7.38−7.47 (m, 2H), 7.67 (d, J = 8.5 Hz, 1H), 7.78−7.80 (m, 1H), 8.11 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 121.0, 124.7, 125.2, 125.8, 126.9, 128.0, 128.8, 131.8, 132.1, 132.6, 134.2, 134.5; HRMS (ESI) calcd for $C_{13}H_{13}$ (M^+ + H) 169.1012, found 169.1013.

*1-(1-(4-(1-(3-Methyl-2-vinylphenyl)vinyl)phenyl)vinyl)naphthalene (**3j**).* Following the General Procedure H; **10a** (30 mol %) was used. The reaction mixture was treated with *p*-toluenesulfonic acid monohydrate at 50 °C for 4 h; purified by silica-gel column chromatography (hexane/EtOAc = 10/1) (23.5 mg, 60% yield, colorless gum): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 2H), 5.95 (s,

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2H), 7.16−7.22 (m, 4H), 7.28−7.36 (m, 2H), 7.34−7.54 (m, 6H), 7.74 (d, J = 8.7 Hz, 2H), 7.82 (t, J = 7.3 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.1, 125.4, 125.7, 125.8, 126.4, 126.6, 127.1, 127.9, 128.1, 131.8, 133.6, 139.6, 140.2, 147,7; HRMS (APCI) calcd for $C_{30}H_{23}$ (M^+ + H) 383.1794, found 383.1789.

Synthesis of Substituted 3-Vinylphenols 9 by RCEM/Tautometization of 8. General Procedure I: RCEM/Tautomerization. To a solution of 1,5-octadiene-7-yn-3-ones **8** (1 equiv) in toluene (0.01 M) was added catalyst **10a** (7.5 mol %) under nitrogen, and then the system was evacuated carefully and filled with ethylene gas (1 atm) in three cycles. The reaction mixture was heated to 80 °C and stirred for 2 h. After cooling to room temperature, the mixture was concentrated under reduced pressure and purified by silica-gel column chromatography to afford **9**.

*4-(1-Phenylvinyl)naphthalen-2-ol (**9a**).* Following the General Procedure I; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (6.60 mg, 92% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00−5.03 (br m, 1H), 5.39 (d, J = 1.2 Hz, 1H), 5.97 (d, J = 1.2 Hz, 1H), 7.07 (d, J = 2.6 Hz, 1H), 7.15−7.19 (m, 2H), 7.25−7.34 (m, 5H), 7.38 (ddd, J = 8.3, 6.9, 1.4 Hz, 1H), 7.68 (dd, J = 14.1, 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.4, 116.4, 119.0, 123.6, 126.4, 126.6, 126.7, 127.4, 127.8, 128.4, 135.0, 140.6, 142.0, 147.6, 152.7; HRMS (ESI) calcd for $C_{18}H_{13}O$ (M^- − H) 245.0972, found 245.0974.

*8-(1-Phenylvinyl)naphtho[2,3-d][1,3]dioxol-6-ol (**9b**).* Following the General Procedure I; purified by silica-gel column chromatography (hexane/EtOAc = 5/1) (11.3 mg, 84% yield, brown solid): mp 107−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93−4.99 (br m, 1H) 5.34 (d, J = 1.4 Hz, 1H), 5.92 (s, 2H), 5.92 (d, J = 1.4 Hz, 1H), 6.90 (d, J = 2.5 Hz, 1H), 6.97 (m, 2H), 7.03 (d, J = 2.8 Hz, 1H), 7.22−7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.9, 102.9, 109.7, 116.1, 116.9, 123.8, 126.5, 127.8, 128.4, 132.1, 140.4, 140.8, 146.0, 147.9, 151.9; HRMS (ESI) calcd for $C_{19}H_{13}O_3$ (M^- − H) 289.0870, found 289.0875.

*7-(1-(4-Methoxyphenyl)vinyl)-2,3-dihydro-1H-inden-5-ol (**9c**).* Following the General Procedure I; **10b** (10 mol %) was used and the reaction mixture was stirred for 12 h; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (16.2 mg, 87% yield, cream yellow solid): mp 84−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (quint, J = 7.6 Hz, 2H), 2.43 (t, J = 7.6 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 3.81 (s, 3H), 4.60 (s, 1H), 5.15 (d, J = 1.4 Hz, 1H), 5.53 (d, J = 1.6 Hz, 1H), 6.57 (d, J = 2.5 Hz, 1H), 6.70 (d, J = 2.3 Hz, 1H), 6.81−6.85 (m, 2H), 7.20−7.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 31.6, 33.1, 55.3, 110.6, 113.3, 113.6, 114.0, 128.3, 133.4, 134.9, 139.2, 146.3, 148.5, 154.2, 159.2; HRMS (APCI) calcd for $C_{18}H_{19}O_2$ (M^+ + H) 267.1380, found 267.1383.

*4-(5-Chloropent-1-en-2-yl)-7-fluoronaphthalen-2-ol (**9d**).* Following the General Procedure I; **10b** (7.5 mol %) was used; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (11.3 mg, 61% yield, brown solid): mp 107−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.83−1.92 (m, 2H), 2.65 (t, J = 8.2 Hz, 2H), 3.55 (t, J = 6.6 Hz, 2H), 5.02−5.05 (br s, 1H), 5.13 (d, J = 1.6 Hz, 1H), 5.45 (q, J = 1.4 Hz, 1H), 6.85 (d, J = 2.5 Hz, 1H), 7.02 (d, J = 2.5 Hz, 1H), 7.08 (ddd, J = 9.4, 8.5, 2.8 Hz, 1H), 7.28 (dd, J = 10.1, 2.5 Hz, 1H), 7.89 (dd, J = 9.4, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 35.4, 44.4, 108.4 (d, J = 4.8 Hz), 109.9 (d, J = 21.1 Hz), 113.7 (d, J = 24.9 Hz), 116.1, 116.8, 123.8, 128.1 (d, J = 9.6 Hz), 136.2 (d, J = 9.6 Hz), 143.1, 146.3, 153.6, 161.2 (d, J = 247.2 Hz); HRMS (ESI) calcd for $C_{15}H_{13}ClFO$ (M^- − H) 263.0644, found 263.0652.

*1-(1-(4-Methoxyphenyl)vinyl)-9,10-dihydrophenanthren-3-ol (**9e**).* Following the General Procedure I; **10b** (7.5 mol %) was used; purified by silica-gel column chromatography (hexane/EtOAc = 2/1) (5.4 mg, 55% yield, brown gum): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43−2.51 (m, 2H), 2.62−2.70 (m, 2H), 3.79 (s, 3H), 4.67−4.76 (br s, 1H), 5.15 (d, J = 1.4 Hz, 1H), 5.71 (d, J = 1.4 Hz, 1H), 6.70 (d, J = 2.5 Hz, 1H), 6.79−6.84 (m, 2H), 7.15−7.33 (m, 6H), 7.70 (d, J = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.4, 29.1, 55.3, 110.1, 113.0, 113.7, 116.2, 123.9, 126.8, 127.5, 127.6, 127.9, 128.2, 132.9, 134.4, 136.2, 137.67, 142.3, 148.0, 153.9, 159.3; HRMS (APCI) calcd for $C_{23}H_{21}O_2$ (M^+ + H) 329.1536, found 329.1534.

*1-Methyl-4-(1-phenylvinyl)naphthalen-2-ol (**9f**).* Following the General Procedure I; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (16.5 mg, 67% yield, colorless oil): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (s, 3H), 4.94 (s, 1H), 5.37 (d, J = 1.4 Hz, 1H), 5.96 (d, J = 1.4 Hz, 1H), 7.04 (s, 1H), 7.20 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.22−7.34 (m, 5H), 7.45 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 115.1, 116.3, 118.9, 123.1, 123.3, 126.2, 126.6, 126.9, 127.6, 127.7, 128.4, 134.1, 139.3, 140.8, 147.7, 149.8; HRMS (ESI) calcd for $C_{19}H_{15}O$ (M^- − H) 259.1128, found 259.1131.

*3-Methyl-4-vinylnaphthalen-2-ol (**9i**).* Following the General Procedure I; purified by silica-gel column chromatography (hexane/EtOAc = 4/1) (13.5 mg, 86% yield, white solid): mp 56−59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 5.03 (d, J = 2.1 Hz, 1H), 5.40 (dd, J = 18.1, 2.1 Hz, 1H), 5.79 (dd, J = 11.7, 2.1 Hz, 1H), 7.01 (dd, J = 18.3, 11.7 Hz, 1H), 7.05 (s, 1H), 7.30 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.37 (ddd, J = 8.2, 7.1, 1.4 Hz, 1H), 7.60−7.65 (m, 1H), 7.96−8.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 108.3, 121.5, 123.4, 123.7, 125.4, 125.5, 126.2, 127.5, 133.0, 134.1, 136.9, 152.2; HRMS (ESI) calcd for $C_{13}H_{11}O$ (M^- − H) 183.0815, found 183.0808.

■ ASSOCIATED CONTENT

Supporting Information

Summary of synthetic schemes for all compounds and ^{1}H NMR and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For a comprehensive review, see: (a) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, 2003. For recent reviews, see:. (b) Hoveyda, A. H.; Zhugralin, A. R. *Nature* **2007**, *450*, 243−251. (c) Samojłowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708−3742. (d) Prunet, J. *Eur. J. Org. Chem.* **2011**, 3634−3647. (e) Kress, S.; Blechert, S. *Chem. Soc. Rev.* **2012**, *41*, 4389−4408. (f) Paek, S.-M. *Molecules* **2012**, *17*, 3348−3358.

(2) For a review on the pharmaceutical application of ring-closing metathesis on an industrial scale, see: Briel, O.; Cazin, C. S. J. *N*-Heterocyclic Carbene Complexes in Industrial Processes. In *N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*; Cazin, C. S. J., Ed.; Springer: New York, 2011; pp 315−324.

(3) For reviews, see: (a) Donohoe, T. J.; Orr, A. J.; Bingham, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2664−2670. (b) van Otterlo, W. A. L.; de Koning, C. B. *Chem. Rev.* **2009**, *109*, 3743−3782. (c) Yoshida, K. Metathesis Reactions. In *Transition-Metal-Mediated Aromatic Ring Construction*; Tanaka, K., Ed.; Wiley: Hoboken, NJ, 2013; pp 721−742.

(4) For recent examples, see: (a) Ziffle, V. E.; Cheng, P.; Clive, D. L. J. *J. Org. Chem.* **2010**, *75*, 8024−8038. (b) Donohoe, T. J.; Jones, C. R.; Barbosa, L. C. A. *J. Am. Chem. Soc.* **2011**, *133*, 16418−16421. (c) Schmidt, B.; Krehl, S.; Jablowski, E. *Org. Biomol. Chem.* **2012**, *10*,

5119−5130. (d) Chen, W.; Wang, J. *Organometallics* **2013**, *32*, 1958−1963. (e) Vermeulen, N. A.; Karagiaridi, O.; Sarjeant, A. A.; Stern, C. L.; Hupp, J. T.; Farha, O. K.; Stoddart, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 14916−14919.

(5) (a) Yoshida, K.; Imamoto, T. *J. Am. Chem. Soc.* **2005**, *127*, 10470−10471. (b) Yoshida, K.; Kawagoe, F.; Iwadate, N.; Takahashi, H.; Imamoto, T. *Chem.—Asian J.* **2006**, *1*, 611−613. (c) Yoshida, K.; Horiuchi, S.; Iwadate, N.; Kawagoe, F.; Imamoto, T. *Synlett* **2007**, 1561−1564. (d) Yoshida, K.; Toyoshima, T.; Imamoto, T. *Chem. Commun.* **2007**, 3774−3776. (e) Yoshida, K.; Takahashi, H.; Imamoto, T. *Chem.—Eur. J.* **2008**, *14*, 8246−8261. (f) Yoshida, K.; Shishikura, Y.; Takahashi, H.; Imamoto, T. *Org. Lett.* **2008**, *10*, 2777−2780. (g) Yoshida, K.; Narui, R.; Imamoto, T. *Chem.—Eur. J.* **2008**, *14*, 9706−9713. (h) Yoshida, K.; Toyoshima, T.; Imamoto, T. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1512−1517. (i) Yoshida, K.; Kawagoe, F.; Hayashi, K.; Horiuchi, S.; Imamoto, T.; Yanagisawa, A. *Org. Lett.* **2009**, *11*, 515−518. (j) Takahashi, H.; Yoshida, K.; Yanagisawa, A. *J. Org. Chem.* **2009**, *74*, 3632−3640. (k) Yoshida, K.; Shida, H.; Takahashi, H.; Yanagisawa, A. *Chem.—Eur. J.* **2011**, *17*, 344−349. (l) Yoshida, K.; Hayashi, K.; Yanagisawa, A. *Org. Lett.* **2011**, *13*, 4762−4765. (m) Hayashi, K.; Yoshida, K.; Yanagisawa, A. *J. Org. Chem.* **2013**, *78*, 3464−3469.

(6) For a review on halovinyl aldehydes, see: Brahma, S.; Ray, J. K. *Tetrahedron* **2008**, *64*, 2883−2896.

(7) See the Experimental Section and Supporting Information for experimental details. It should be noted that substrates **7c** (**8c**) and **7e** (**8e**) were prepared through another synthetic route. Since the C_1-homologation by the Wittig olefination and hydrolysis sequence failed, a longer synthetic route was required to prepare these RCEM substrates. Preparation of more challenging substrates for single ring styrenes has not been attempted.

(8) (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956. (b) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746−1787.

(9) This result is compatible with our previous experiment. No reaction was observed in RCEM with a substrate having a methyl group at a similar position (see ref 5j).

(10) The oxidation of **7j** to **8j** failed.

(11) (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179. (b) Bujok, R.; Bieniek, M.; Masnyk, M.; Michrowska, A.; Sarosiek, A.; Stepowska, H.; Arlt, D.; Grela, K. *J. Org. Chem.* **2004**, *69*, 6894−6896.

(12) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546−2558.

(13) Salem, B.; Delort, E.; Klotz, P.; Suffert, J. *Org. Lett.* **2003**, *5*, 2307−2310.

(14) (a) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899. (b) Boeckman, R. K., Jr.; Shao, P.; Mullins, J. J. *Org. Synth.* **2000**, *77*, 141−152. (c) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537−4538.

(15) Attenburrow, J.; Cameron, A. F. B.; Chapman, J. H.; Evans, R. M.; Hems, B. A.; Jansen, A. B. A.; Walker, T. *J. Chem. Soc.* **1952**, 1094−1111.

(16) Park, J. H.; Bhilare, S. V.; Youn, S. W. *Org. Lett.* **2011**, *13*, 2228−2231.

(17) Zhang, S.-W.; Sugioka, T.; Takahashi, S. *J. Mol. Catal. A: Chem.* **1999**, *143*, 211−228.

(18) Chernyak, N.; Gorelsky, S. I.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2011**, *50*, 2342−2345.

(19) Tsukamoto, H.; Ueno, T.; Kondo, Y. *J. Am. Chem. Soc.* **2006**, *128*, 1406−1407.

(20) Rustagi, V.; Tiwari, R.; Verma, A. K. *Eur. J. Org. Chem.* **2012**, *2012*, 4590−4602.

(21) Sun, C.-L.; Wang, Y.; Zhou, X.; Wu, Z.-H.; Li, B.-J.; Guan, B.-T.; Shi, Z.-J. *Chem.—Eur. J.* **2010**, *16*, 5844−5847.