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Article

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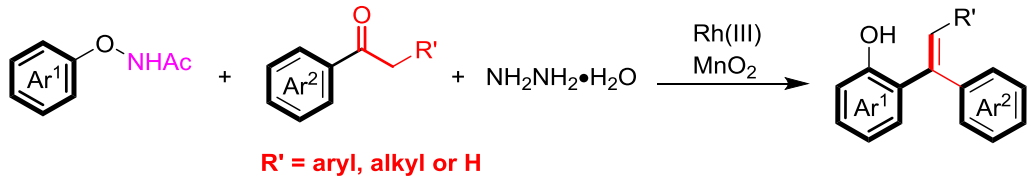
Synthesis of Polyaryl Substituted Olefins via Rh(III)-Catalyzed One-Pot Reaction Using N-phenoxyacetamides, Ketones, and Hydrazines

Yan Zhang,* Yu He, Lisha Li, Mingming Ji, Xiao-Zong Li and Gangguo Zhu

Key Laboratory of the Ministry of Education for Advanced Catalysis Materials, Department of Chemistry, Zhejiang Normal University, Jinhua 321004, China

zhangyan001@zjnu.edu.cn



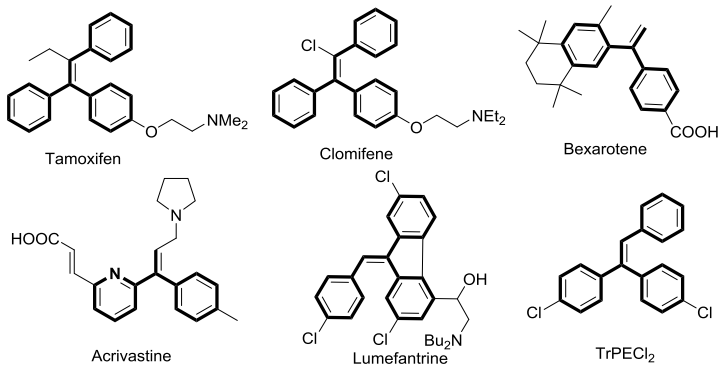
A Rh(III)-catalyzed one-pot reaction of N-phenoxyacetamides, ketones, and hydrazines for facile access to di- and trisubstituted ethylenes is reported. In this method, various ketones are transformed into donor-donor diazo compounds, which engage in insertion with N-phenoxyacetamides, following β-H elimination under Rh(III) catalysis to generate (*E*)-polyaryl substituted olefins. This chemistry features simple starting materials, mild reaction conditions and good functional group tolerance.

INTRODUCTION

Di- and triarylsubstituted ethylenes are privilege scaffolds, which frequently exist in biologically active compounds and aggregation-induced emission (AIE) molecules.[1] Representative examples are depicted in Figure 1. Tamoxifen, a selective estrogen receptor modulator, is used for the treatment of breast cancer;[2] Clomifene has been used for the induction of ovulation in anovulatory women and for the treatment of oligospermia in men;[3] Bexarotene is another anticancer agent which is used as a treatment for cutaneous T cell lymphoma;[4] Acrivastine and Lumefantrine are antiallergic agent and antimalarial drug, respectively;[5] Triphenylethylene derivative ($TrPECl_2$) has been reported as a new

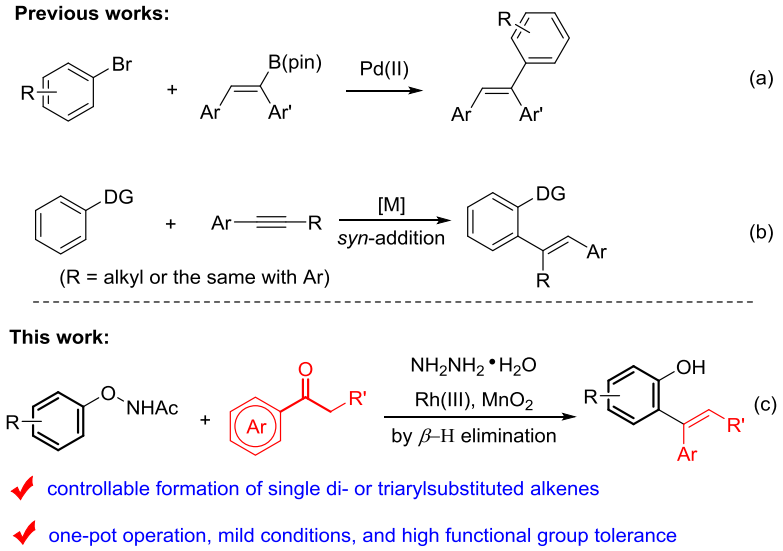
type AIE molecule.[6] Therefore, the reaction to access these types of polyaryl substituted ethylenes from simple materials in mild conditions is highly desired.

Figure 1. Selected examples of drugs and AIE molecules containing di- or triarylsubstituted olefins.



The well established synthetic approaches to form polyarylsubstituted olefins include Horner-Wittig [7] and Suzuki-Miyaura reactions (Scheme 1a),[8] as well as various metal-catalyzed C-H hydroarylations of alkynes.[9] Obviously, direct C-H functionalization protocol is more attractive than others, as prefunctionalized substrates are not necessary (Scheme 1b). However, the stereoselectivity issue constantly exists when using the unsymmetrical diaryl acetylenes for the synthesis of triarylsubstituted ethylenes.

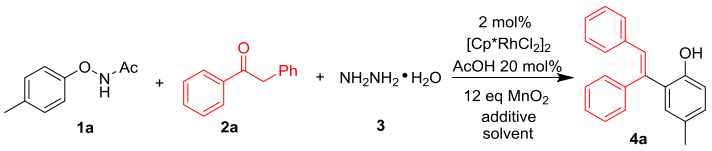
Scheme 1. Methods for the synthesis of polyarylsubstituted ethylenes.



Rh(III)-catalyzed chelation-assisted (especially by oxidizing directing groups[10]) have been well developed by Miura, Fagnou, Glorius, Li, Wang, Rovis, etc. over the past seven years.[11, 12] Among these, [4+n] cyclization was usually observed when a protic X-H (X = N or O) bond is present, and this anionic X atom acts as a sufficient directing group. However, there is seldom report on selective formation of olefins by β-H elimination when facing reductive elimination as the other possible route to form cyclocompounds.[13] Meanwhile, the group of Wang has developed an efficient Rh(III)-catalyzed synthesis of ortho-alkenyl phenols from N-Tosylhydrazones or diazoesters. This transformation needs relatively harsh conditions or must be limited to the stable donor/acceptor diazo compounds.[14] Herein we report a facile synthesis of polyarylsubstituted olefins via a Rh(III)-catalyzed one-pot reaction of N-phenoxyacetamides and ketones using MnO_2 as oxidant.[15] This process demonstrates many advantages: reaction proceeds under mild conditions, starting from simpler materials and products featuring broader substrate scope (Scheme 1c).

RESULTS AND DISCUSSION

Table 1. Optimization of the reaction conditions.[a]

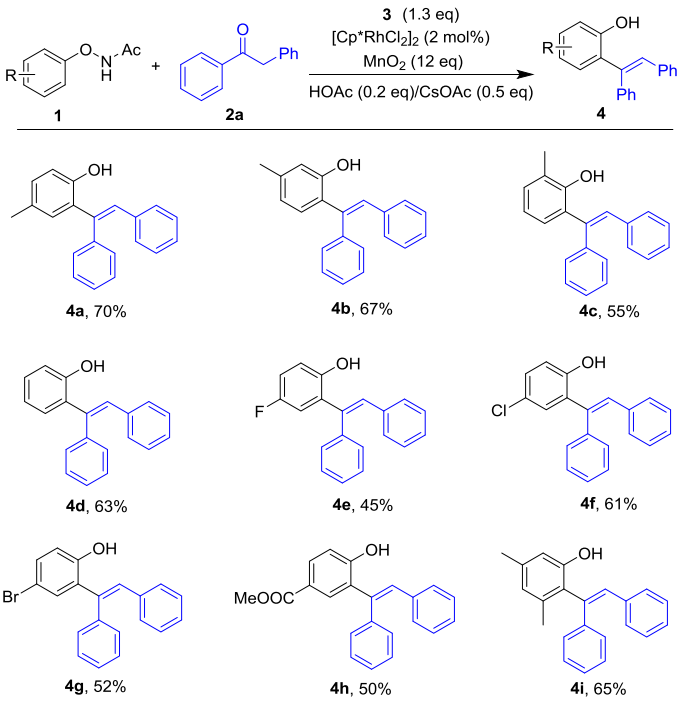


Entry	Additive	Solvent	Yield (%) [b]
1	CsOAc (1 eq)	1,4-dioxane	34
2	CsOAc (1 eq)	MeOH	25
3	CsOAc (1 eq)	DCM	49
4	CsOAc (1 eq)	THF	69
5	KOAc (1 eq)	THF	45
6	NaOAc (1 eq)	THF	60
7	Na_2CO_3 (1 eq)	THF	64
8 [c]	CsOAc (1 eq)	THF	59
9	**CsOAc (0.5 eq)**	**THF**	**70**
10[d]	CsOAc (1 eq)	THF	72

[a] Reaction Conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), solvent (2.0 mL), **3** (0.26 mmol), $[Cp^*RhCl_2]_2$ (2 mol%) and additive, RT, 8 h. [b] Yields of isolated products. [c] 8.0 eq MnO_2. [d] Replacing **2a** and **3** with acetophenone(2-phenyl)hydrazone.

Phenol derivatives are of great importance, thus, we selected a phenol derivatives containing an N-O bond as oxidizing directing group. We commenced our study by investigating the one-pot reaction of N-phenoxyacetamide **1a**, 2-phenylacetophenone **2a**, and hydrazone **3** with catalytic amount of $[Cp^*RhCl_2]_2$ and AcOH (accelerate the formation of the hydrazine intermediate) in 1,4-dioxane at room temprature. To our delight, we found the formation of triarylsubstituted ethylene **4a** in 34% yield (Table 1, entry 1). The next survey of solvents (entries 2-4) showed that THF was optimal to furnish the product in 69% yield (entry 4). Replacement of CsOAc to other additives resulted in a lower yield (entries 5-7). An attempt to lower MnO_2 loading failed as a decreased yield (entry 8), while lower CsOAc loading to 0.5 equiv without loss of the yield (entry 9). Direct use of (1,2-diphenylethylidene)hydrazine would deliver the product in a slightly higher yield (entry 10).

Table 2. Substrate scope of N-phenoxyacetamides[a]

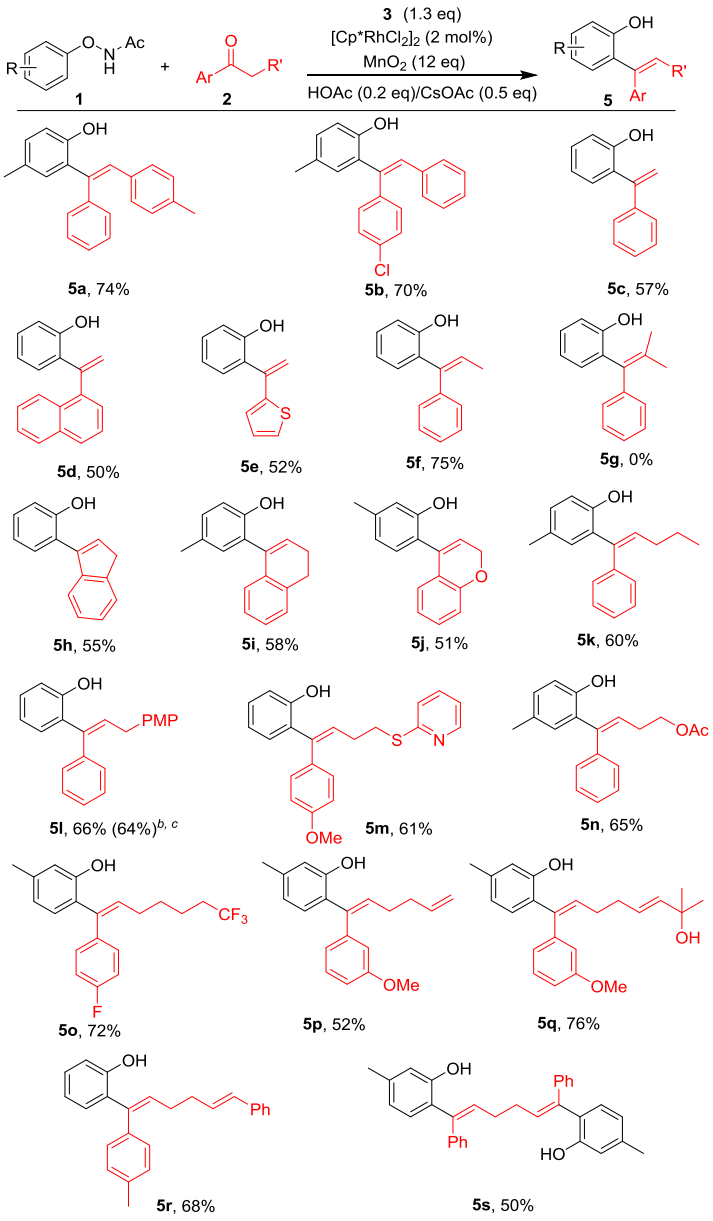


[a] Isolated yields are given. Reaction conditions: **3** (0.26 mmol), **2** (0.24 mmol), HOAc (0.04 mmol), THF (2 mL), 2-3 h, 60 °C; then **1** (0.2 mmol), MnO_2 (12 eq), CsOAc (0.1 mmol), $[Cp^*RhCl_2]_2$ (2 mol%), RT, 5-10 h. Isolated yields.

With the optimized conditions in hand, we evaluated the generality of this reaction. The scope of the N-phenoxyacetamides was first examined. As depicted in Table 2, various N-phenoxyacetamides with *ortho*, *meta* or *para* substituents on the aromatic ring were reacted smoothly with

2-phenylacetophenone **2a**, affording the desired triarylsubstituted ethylenes in good yields (**4a-4d** and **4i**). Additionally, good regioselectivity favouring activation of the less hindered C-H bond was observed in product **4b**. Electron-deficient functional groups like fluoro, chloro, bromo and ester were also tolerated in this one-pot transformation in relatively lower yields (**4e-4h**).

Table 3. Substrate Scope of aromatic ketones.[a]

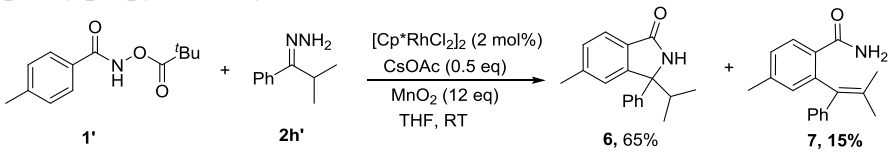


[a] Isolated yields are given. Reaction conditions: **3** (0.26 mmol), **2** (0.24 mmol), HOAc (0.04 mmol), THF (2 mL), 2-3 h, 60 °C; then **1** (0.2 mmol), MnO_2 (12 eq), CsOAc (0.1 mmol), $[Cp^*RhCl_2]_2$ (2 mol%), RT, 5-10 h. Isolated yields [b] The value in parenthese refers to 2 mmol scale. [c] PMP = *para*-methoxyphenyl.

Next, a variety of aryl ketones were utilized to construct diverse polysubstituted olefins (Table 3). Many important functional groups like alcohols, ester (on the alkyl), ether, trifluoromethyl, terminal alkenes and internal alkenes could react smoothly with **1** to afford the corresponding olefins in moderate to good yields (**5l**-**5r**). In addition, ketones bearing naphthalene and heterocyclic groups (**5d**, **5e**, and **5j**) also reacted well. Notably, in the case of all the *meta*-substituted substrates, **5o**-**5q**, and **5j** were isolated as the sole products, which suggesting that good regioselectivity favouring activation of the less hindered C-H bonds. Moreover, using 1,6-diphenyl-1,6-hexanedinone (**2t**) as substrate, the expected symmetrical product **5s** was isolated after reaction with 2 equiv N-phenoxyacetamide **1b**. However, we could not get **5g** when **2h** was used as the starting material. For one thing, it's hard to form of the hydrazine intermediate for the ketones substituted with two alkyls at the α-position of carbonyl in this recation condition; What's more, β-H elimination may also become hard due to the additional alkyl, as we failed by using hydrazine **2h'** as starting material which is prepared from other reaction conditions.

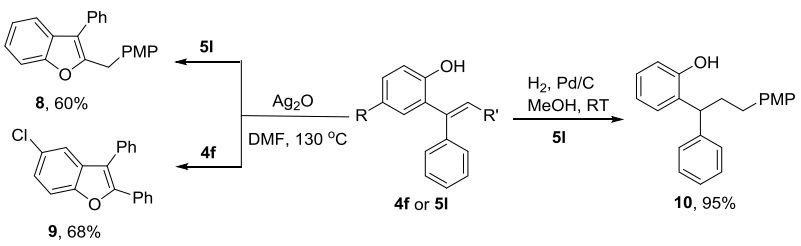
We also have tried to use other oxidizing directing group **1'** to react with this type of hydrazine **2h'** (Scheme 2).[16] Luckily, the expected β-H elimination product **7** was observed, showing that the reaction pathway would be changed by choice of different directing groups.

Scheme 2 Rh(III)-catalyzed C-H activation of N-pivaloyloxy benzamides with (2-methyl-1-phenylpropylidene)hydrazine 2h'.



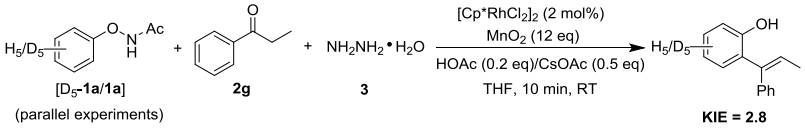
Derivation of the products was also performed (Scheme 3). Since the olefin and the phenol units in these products offer additional synthetic opportunities. For example, either diarylsubstituted olefin **5k** or triarylsubstituted ethylene **4f** could convert to 2, 3-disubstituted benzofurans **8** and **9** at high temperature using Ag_2O as oxidant.[17] Saturated biphenyl molecule **10** could be prepared by reduction in the presence of Pd/C (10%) with excellent yield.

Scheme 3 Derivatization of compound 4f and 5k.

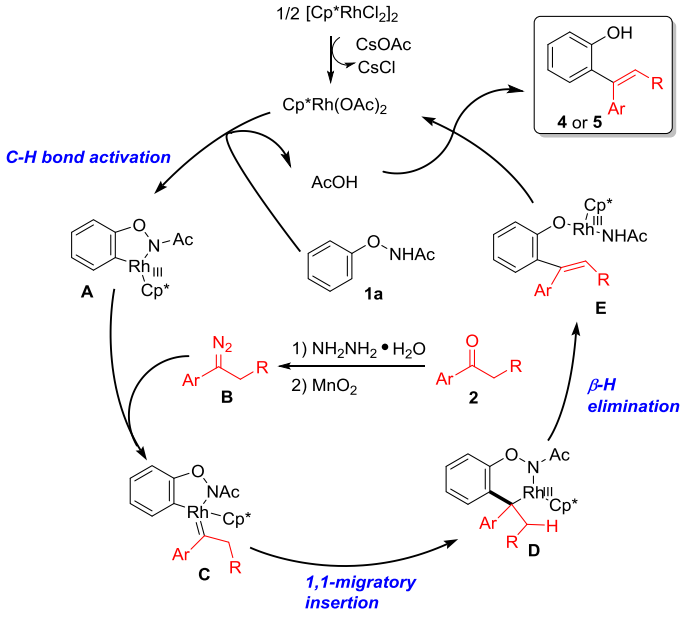


Considering that this conversion process includes a C-H activation step, a kinetic isotope effect (KIE) study was conducted to probe the mechanism. The KIE was determined to be 2.8 under the standand reaction conditions, thus, indicating that C-H bond cleavage occurs during the rate-determining step (Scheme 4).

Scheme 4 The study of the kinetic isotope effects.



Scheme 5 Proposed Catalytic Cycle.



A plausible mechanism for this C-H activation/β-H elimination process is proposed in Scheme 5, which is similar to those reported in the literature.[12i, 14] First, the active catalyst [Cp*Rh(OAc)$_2$] is generated from [Cp*RhCl$_2$]$_2$ and CsOAc through anion exchange, and a carboxylate-assisted C-H activation of N-phenoxyacetamide **1a** occurs via a concerted metalation/deprotonation (CMD) pathway to form rhodacycle **A**. Then a dediazoniation occurs between **A** and **B**, which is generated in situ from the ketones, hydrazine, and MnO_2 to form intermediate **C**. The subsequent 1,1-migratory insertion of **C** generates **D**.[18] β-H elimination and oxidative addition of N-O bond to Rh(I) gives

intermediate **E**. Finally, protonation of **E** to furnish the polysubstituted olefin product **4** or **5** with the regeneration of Rh(III) catalyst.

CONCLUSION

In summary, we have developed a unique Rh(III)-catalyed one-pot reaction of N-phenoxyacetamide, ketones, and hydrazines for efficient synthesis of stereodefined di- and triarylsubstituted olefins. This transformation tolerates a wide variety of ketones and generates the desired polyarylsubstituted olefins in moderate to good yields. A kinetic isotope effect study was conducted and a plausible mechanism is proposed.

EXPERIMENTAL SECTION

General Information

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on 600 or 400 spectrometer using $CDCl_3$ as the solvent. Chemical shifts were referenced relative to residual solvent signal ($CDCl_3$: ^{1}H NMR: δ 7.26 ppm, ^{13}C NMR: δ 77.16 ppm). The following abbreviations are used to describe peak patterns where appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants (*J*) are reported in Hertz (Hz). HRMS were performed on AB Sciex LC 30A-Triple TOF 4600 apparatus (ESI). Melting points were measured with micro melting point apparatus.

General Experimental Procedure for the Synthesis of 4 and 5

Typical procedure for synthesis of di- or triarylsubstituted ethylenes: Ketone **2** (0.24 mmol), hydrazine hydrate **3** (21 μL, 0.26 mmol), THF (2 mL) and HOAc (3 μL, 0.04 mmol) were added to a 5 mL round-bottomed flask and stirred for 2-3 h at 60 ^{o}C (monitored by TLC). Then N-phenoxyacetamides **1** (0.2 mmol), $[Cp^*RhCl_2]_2$ (2 mol%, 2.4 mg), CsOAc (20 mg, 0.5 equiv) were added to this vial and the solution was cooled to 0-5 ^{o}C. Afterwards, activated MnO_2 (210 mg, 12 equiv.) was added in one portion and the solution was kept at RT. After completion (8h - 10 h), it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under vacuum. The purification was performed by flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:10) as eluent to give the product **4** or **5**.

3-methyl-3-phenylisoindolin-1-one (4a): 40 mg, 70% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.40-7.31 (m, 5H), 7.22-7.14 (m, 6H), 7.11 (dd, J_1 = 10.2 Hz, J_2 = 1.8 Hz, 1H), 6.91 (s, 1H), 6.86 (d, J = 8.4 Hz 1H), 4.98 (s, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 150.6, 142.1, 136.7, 136.4, 131.2, 130.5, 130.41, 130.38, 129.1, 128.7, 128.5, 128.2, 128.0, 127.2, 125.8, 115.9, 20.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{19}O$ 287.1431; found 287.1426.

(E)-2-(1,2-diphenylvinyl)-5-methylphenol (4b): 38.3 mg, 67% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.40-7.32 (m, 5H), 7.21-7.16 (m, 6H), 6.98 (d, J = 8.4 Hz, 1H), 6.80-6.79 (m, 2H), 5.06 (s, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 152.8, 142.1, 140.1, 136.7, 136.5, 130.9, 130.4, 129.1, 128.7, 128.5, 128.2, 127.9, 127.3, 123.1, 122.2, 116.7, 21.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{19}O$ 287.1431; found 287.1430.

(E)-2-(1,2-diphenylvinyl)-6-methylphenol (4c): 31.4 mg, 55% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.39-7.31 (m, 5H), 7.20-7.11 (m, 7H), 6.94 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 6.87 (t, J = 7.2 Hz, 1H), 5.14 (s, 1H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 151.1, 141.9, 136.8, 136.4, 131.0, 130.7, 129.1, 128.7, 128.52, 128.49, 128.3, 127.9, 127.2, 125.6, 125.1, 120.8, 16.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{19}O$ 287.1431; found 287.1430.

(E)-2-(1,2-diphenylvinyl)phenol (4d): 34.2 mg, 63% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.39-7.30 (m, 6H), 7.21-7.18 (m, 4H), 7.13 - 7.09 (m, 3H), 6.96 (t, J = 7.2 Hz, 2H), 5.09 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.0, 141.8, 136.5, 136.3, 131.2, 130.7, 129.8, 129.1, 128.8, 128.5, 128.3, 128.0, 127.2, 126.1, 121.3, 116.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{17}O$ 273.1274; found 273.1273.

(E)-2-(1,2-diphenylvinyl)-4-fluorophenol (4e): 26.1 mg, 45% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.38-7.35 (m, 5H), 7.24-7.22 (m, 4H), 7.15(q, J = 3.0 Hz, 2H), 7.03-7.00(m, 1H), 6.91 (q, J = 4.8 Hz, 1H), 6.85 (dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz, 1H), 5.03 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 157.3 (d, J = 239 Hz), 149.10, 149.09, 141.2, 135.9, 135.6, 131.1, 129.1, 128.8, 128.6, 128.5, 128.3, 127.1, 117.2 (d, J = 12 Hz), 117.1 (d, J = 3 Hz), 116.4 (d, J = 22.5 Hz); HRMS (ESI-TOF) m/z: $[M-H]^-$ calcd for $C_{20}H_{14}FO$ 289.1034; found 289.1023.

(E)-4-chloro-2-(1,2-diphenylvinyl)phenol (4f): 37.3 mg, 61% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.38-7.35 (m, 5H), 7.27-7.23 (m, 5H), 7.16-7.12 (m, 3H), 6.90 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 5.18 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 151.6, 141.2, 135.9, 135.3, 131.2, 130.6, 129.7, 129.1, 128.8, 128.7, 128.5, 128.3, 127.7, 127.2, 125.9, 117.5; HRMS (ESI-TOF) m/z: $[M-H]^-$ calcd for $C_{20}H_{14}ClO$ 305.0739; found 305.0729.

(E)-4-bromo-2-(1,2-diphenylvinyl)phenol (4g): 36.4 mg, 70% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.40-7.35 (m, 6H), 7.24-7.21 (m, 5H), 7.15-7.12 (m, 2H), 6.84 (d, J = 9.0 Hz, 1H), 5.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 152.2, 141.3, 135.8, 135.2, 133.4, 132.7, 131.3, 129.1, 128.9, 128.7, 128.6, 128.4, 128.3, 127.2, 118.0, 113; HRMS (ESI-TOF) m/z: $[M-H]^-$ calcd for $C_{20}H_{14}BrO$ 349.0234; found 349.0228.

Methyl (E)-3-(1,2-diphenylvinyl)-4-hydroxybenzoate (4h): 33 mg, 50% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 8.01 (dd, J_1 = 10.8 Hz, J_2 = 2.4 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.37-7.33 (m, 6H), 7.19 (t, J = 3.0 Hz, 3H), 7.12-7.10 (m, 2H), 6.98 (d, J = 9.0 Hz, 1H), 5.90 (s, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 166.9, 157.1, 141.4, 136.0, 135.4, 133.3, 131.7, 131.2, 129.0, 128.8, 128.6, 128.4, 128.2, 127.1, 126.3, 123.2, 116.1, 52.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{19}O_3$ 331.1329; found 331.1325.

(E)-2-(1,2-diphenylvinyl)-3,5-dimethylphenol (4i): 39 mg, 65% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.40-7.39 (m, 2H), 7.35-7.30 (m, 4H), 7.21-7.18 (m, 3H), 7.12 (dd, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 2H), 6.71 (s, 1H), 6.67 (s, 1H), 5.07 (s, 1H), 2.36 (s, 3H), 1.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 152.4, 141.0, 139.3, 137.6, 136.4, 135.2, 131.5, 128.84, 128.76, 128.6, 128.1, 128.0, 126.4, 123.7, 122.7, 113.7, 21.5, 19.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}O$ 301.1587; found 301.1572.

(E)-4-methyl-2-(1-phenyl-2-(p-tolyl)vinyl)phenol (5a): 44.4 mg, 74% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.40-7.31 (m, 5H), 7.17 (s, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.04 (q, J = 8.4 Hz, 4H), 6.92 (s, 1H), 6.88 (d, J = 8.4 Hz, 1H), 5.04 (s, 1H), 2.30 (s, 3H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 150.6, 142.2, 138.0, 135.6, 133.5, 131.2, 130.4, 130.3, 129.3, 129.0, 128.6, 128.0, 127.2, 126.0, 115.8, 21.4, 20.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}O$ 301.1587; found 301.1560.

(E)-2-(1-(4-chlorophenyl)-2-phenylvinyl)-4-methylphenol (5b): 44.8 mg, 70% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.31 (s, 4H), 7.21 (dd, J_1 = 4.8 Hz, J_2 = 2.4 Hz, 3H), 7.16-7.14 (m, 3H), 7.12 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.88 (d, J = 1.8 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.98 (s, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 150.6, 140.6, 136.1, 135.6, 134.0, 131.1, 130.60, 130.59, 130.5, 129.1, 128.8, 128.6, 128.5, 128.2, 125.4, 116.0, 20.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{21}H_{17}ClO$ 343.0860; found 343.0838.

2-(1-phenylvinyl)phenol (5c): 22.3 mg, 57% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.39-7.34 (m, 5H), 7.28-7.25 (m, 1H), 7.15 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.00-6.92 (m, 2H), 5.88 (d, J = 1.2 Hz 1H), 5.43 (d, J = 1.2 Hz 1H), 5.17 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.2, 145.4, 139.5, 130.6, 129.6, 128.9, 128.8, 127.7, 127.2, 120.6, 116.9, 116.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{13}O$ 197.0961; found 197.0960.

2-(1-(naphthalen-1-yl)vinyl)phenol (5d): 24.6 mg, 50% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.92 (q, J = 8.4 Hz, 3H), 7.54-7.53 (m, 3H), 7.42 (dt, J_1 = 6.6 Hz, J_2 = 1.2 Hz, 1H), 7.21 (dt, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 7.15 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 6.94 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 6.86 (dt, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 5.90 (d, J = 1.2 Hz, 1H), 5.73 (d, J = 1.8 Hz, 1H), 5.63 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.0, 145.6, 139.5, 134.1, 131.3, 129.7, 129.5, 129.0, 128.6, 128.5, 127.3, 126.6, 126.2, 125.6, 125.5, 120.8, 120.2, 116.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{14}O$ 247.1118; found 247.1116.

2-(1-(thiophen-2-yl)vinyl)phenol (5e): 21 mg, 52% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ:

7.29-7.26 (m, 2H), 7.21 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 6.98-6.94 (m, 3H), 6.83 (dd, J_1 = 9.6 Hz, J_2 = 0.6 Hz, 1H), 5.87 (s, 1H), 5.27 (s, 1H), 5.25 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.0, 143.7, 138.7, 130.2, 129.9, 127.9, 127.1, 126.9, 126.3, 120.5, 116.0, 115.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{10}OS$ 203.0525; found 203.0525.

(E)-2-(1-phenylprop-1-en-1-yl)phenol (5f): 31.5 mg, 75% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.34-7.27 (m, 6H), 7.08-7.04 (m, 2H), 6.99 (dt, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 6.51 (q, *J =7.2* Hz, 1H), 5.13 (s, 1H), 1.77 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.0, 140.6, 136.8, 130.7, 129.3, 128.6, 127.66, 127.61, 126.6, 125.4, 120.7, 115.4, 15.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{15}H_{14}O$ 211.1118; found 211.1117.

2-(1H-inden-3-yl)phenol (5h): 22.9 mg, 55% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.58 (d, *J* =7.2 Hz, 1H), 7.38-7.29 (m, 5H), 7.06-7.01 (m, 2H), 6.68 (t, *J* = 7.8 Hz, 1H), 5.40 (s, 1H), 3.61 (d, *J* = 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.3, 144.5, 144.0, 140.7, 133.0, 129.7, 129.5, 126.6, 125.7, 124.3, 121.8, 120.8, 120.6, 115.8, 38.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{15}H_{12}O$ 209.0961; found 209.0960.

2-(3,4-dihydronaphthalen-1-yl)-4-methylphenol (5i): 27.4 mg, 58% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.26-7.21 (m, 2H), 7.16 (dt, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.12 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 7.02 (d, *J* = 2.4 Hz, 1H), 6.93-6.91 (m, 2H), 6.20 (t, *J* = 4.2 Hz, 1H), 4.93 (s, 1H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.52 (s, 2H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 151.0, 136.3, 134.9, 133.8, 131.0, 130.6, 129.8, 128.0, 127.9, 126.9, 126.1, 125.1, 115.4, 28.0, 23.5, 20.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{17}H_{17}O$ 237.1274; found 237.1275.

2-(2H-chromen-4-yl)-5-methylphenol (5j): 24.3 mg, 51% yield; White solid; m.p. 84-86 ^{o}C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.18-7.15 (m, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.89-6.80 (m, 5H), 5.86 (d, *J* = 9.6 Hz, 1H), 5.13 (s, 1H), 4.91 (d, *J* = 3.6 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 154.5, 153.0, 140.1, 132.5, 130.3, 130.0, 125.7, 122.8, 122.6, 121.7, 121.6, 121.0, 116.5, 116.4, 65.4, 21.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{14}O_2$ 239.1067; found 239.1048.

(E)-4-methyl-2-(1-phenylpent-1-en-1-yl)phenol (5k): 30.2 mg, 60% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.29-7.24 (m, 5H), 7.07 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 1.8 Hz, 1H), 6.39 (t, *J* = 7.8 Hz, 1H), 4.92 (s, 1H), 2.28 (s, 3H), 2.05 (q, *J* = 7.2 Hz, 2H), 1.49 (q, *J* = 7.2 Hz, 2H), 0.92 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 150.8, 140.8, 135.9, 133.4, 130.9, 129.8, 129.78, 129.75, 127.6, 126.7, 125.5, 115.1, 32.0, 22.8, 20.7, 14.0; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{20}O$ 253.1587; found 253.1574.

(E)-2-(3-(4-methoxyphenyl)-1-phenylprop-1-en-1-yl)phenol (5l): 41.7 mg, 66% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.33 - 7.25 (m, 6H), 7.13 - 7.09 (m, 3H), 7.04 - 6.97 (m, 2H), 6.85 (dd, J_1 = 10.2 Hz, J_2 = 3.0 Hz, 2H), 6.54 (d, *J* = 11.4 Hz, 1H), 5.06 (s, 1H), 3.79 (s, 3H), 3.34 (d, *J* = 10.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 158.2, 153.2, 140.1, 135.9, 132.1, 131.9, 130.9, 129.5, 128.7, 127.9, 126.7, 125.4, 120.9, 115.7, 114.2, 55.4, 35.4; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for

$C_{22}H_{20}O_2$ 339.1356; found 339.1336.

(E)-2-(1-(4-methoxyphenyl)-4-(pyridin-2-ylthio)but-1-en-1-yl)phenol (5m): 44.3 mg, 61% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 8.26 (d, *J* = 8.4 Hz, 1H), 7.45-7.42 (m, 1H), 7.26-7.24 (m, 1H), 7.16-7.14 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.01-6.97 (m, 2H), 6.93-6.89 (m, 2H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.45 (s, 1H), 6.33 (t, *J* = 7.8 Hz, 1H), 3.77 (s, 3H), 3.28 (t, *J* = 7.2 Hz, 2H), 2.45 (q, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 159.3, 158.9, 153.6, 149.3, 137.2, 136.2, 132.9, 130.7, 130.4, 128.5, 127.7, 126.0, 122.6, 120.5, 119.4, 116.1, 113.9, 129.2, 55.4, 30.3, 29.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{21}NO_2S$ 364.1366; found 364.1368.

(E)-4-(2-hydroxy-5-methylphenyl)-4-phenylbut-3-en-1-yl acetate (5n): 38.5 mg, 65% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.28 (s, 5H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 6.6 Hz, 1H), 6.82 (s, 1H), 6.32 (t, *J* = 10.8 Hz, 1H), 5.12 (s, 1H), 4.17 (d, *J* = 9.6 Hz, 2H), 2.42 (q, *J* = 3,6 Hz, 2H), 2.27 (s, 3H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 171.2, 150.6, 140.4, 138.8, 130.9, 130.0, 129.9, 128.7, 127.9, 127.0, 126.7, 125.1, 115.6, 63.7, 29.7, 21.1, 20.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{20}O_3$ 297.1485; found 297.1479.

(E)-5-methyl-2-(7,7,7-trifluoro-1-(4-fluorophenyl)hept-1-en-1-yl)phenol (5o): 50.7 mg, 72% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.28-7.25 (m, 2H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 2H), 6.29 (t, *J* = 7.6 Hz, 1H), 4.97 (s, 1H), 2.39 (s, 3H), 2.01 (m, 4H), 1.57-1.55 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 162.5 (d, *J* = 246 Hz), 152.7, 139.8, 136.7, 135.7, 131.7, 130.3, 128.2 (d, *J* = 7.5 Hz), 127.3 (q, *J* = 274.5 Hz), 122.3, 121.8, 116.1, 115.4(d, *J* = 21 Hz), 33.5 (q, *J* = 28.5 Hz), 29.4, 28.6, 21.5(q, *J* = 3 Hz), 21.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{20}OF_4$ 353.1523; found 353.1532.

(E)-2-(1-(3-methoxyphenyl)hexa-1,5-dien-1-yl)-5-methylphenol (5p): 30.6 mg, 52% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.20 (t, *J* = 8.0 Hz, 1H), 6.92-6.75 (m, 6H), 6.36 (t, *J* = 6.8 Hz, 1H), 5.81-5.72 (m, 1H), 5.05-4.95 (m, 3H), 3.77 (s, 3H), 2.35 (s, 3H), 2.35-2.16 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 159.8, 152.8, 142.3, 139.5, 137.9, 136.1, 132.8, 130.4, 129.6, 122.6, 121.6, 119.3, 116.1, 115.5, 112.7, 55.3, 29.4, 33.6, 29.3, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{22}O_2$ 295.1693; found 295.1692.

2-((1E,5E)-7-hydroxy-1-(3-methoxyphenyl)-7-methylocta-1,5-dien-1-yl)-5-methylphenol (5q): 53.5 mg, 76% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.21 (t, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.87-6.77 (m, 4H), 6.33 (s, 1H), 5.65-5.58 (m, 2H), 5.30 (s, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 2.18 (d, *J* = 6.0 Hz, 4H), 1.30 (s, 6H), 1.19 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 159.7, 152.7, 142.3, 139.3, 138.9, 136.4, 132.5, 130.5, 129.5, 126.2, 122.8, 121.5, 119.2, 116.2, 112.6, 70.7, 55.3, 31.9, 29.8, 21.4; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{28}O_3$ 375.1931; found 375.1927.

2-((1E,5E)-6-phenyl-1-(p-tolyl)hexa-1,5-dien-1-yl)phenol (5r): 46.2 mg, 68% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.34-7.33 (m, 2H), 7.29 (t, *J* = 7.8 Hz, 3H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J*

= 7.8 Hz, 2H), 7.03 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 1H), 7.00 (dd, J_1 = 7.8 Hz, J_2 = 0.6 Hz, 1H), 6.95 (dt, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 6.38 (t, J = 3.0 Hz, 2H), 6.19-6.15 (m, 1H), 5.04 (s, 1H), 2.37-2.33 (m, 6H), 2.23 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 153.0, 137.7, 137.6, 137.5, 136.2, 131.5, 130.8, 130.7, 129.7, 129.4, 129.3, 128.6, 127.1, 126.6, 126.1, 125.8, 120.7, 115.5, 33.0, 29.7, 21.2; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{24}O$ 341.1900; found 341.1914.

6,6'-((1E,5E)-1,6-diphenylhexa-1,5-diene-1,6-diyl)bis(3-methylphenol) (5s): 44.6 mg, 50% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.28 (s, 12H), 6.90-6.78 (m, 6H), 6.33 (s, 2H), 5.03 (s, 2H), 2.40 (s, 6H), 2.24 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 152.8, 140.5, 139.5, 136.7, 131.8, 130.5, 128.6, 127.7, 126.6, 122.6, 121.6, 116.1, 29.8, 21.5; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{30}O_2$ 469.2138; found 469.2122.

3-isopropyl-5-methyl-3-phenylisoindolin-1-one (6): 34 mg, 65% yield; White solid; m.p. 203-205 ^{o}C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.69 (d, J = 7.8 Hz, 2H), 7.61 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 7.8 Hz, 2H), 7.28 (d, J = 6.0 Hz, 1H), 7.20 (t, J = 7.8 Hz, 2H), 2.95 (m, J = 7.2 Hz, 1H), 2.41 (s, 3H), 2.33 (d, J = 6.6 Hz, 3H), 0.69 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 171.8, 151.8, 143.1, 142.3, 129.1, 129.0, 128.1, 127.5, 125.3, 123.8, 122.6, 70.9, 35.2, 22.2, 18.4, 16.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{19}NO$ 266.1540; found 266.1542.

4-methyl-2-(2-methyl-1-phenylprop-1-en-1-yl)benzamide (7): 8 mg, 15% yield; White solid; m.p. 120-122 ^{o}C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.93 (d, J = 7.8 Hz, 1H), 7.35 (t, J = 7.8 Hz, 2H), 7.28 (t, J = 8.4 Hz, 3H), 7.23 (d, J = 7.8 Hz, 1H), 7.07 (s, 1H), 6.65 (s, 1H), 6.15 (s, 1H), 2.45 (s, 3H), 2.03 (s, 3H), 1.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 170.6, 141.5, 140.8, 136.1, 133.9, 131.9, 130.4, 130.1, 129.8, 128.1, 128.0, 126.7, 23.1, 22.3, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{19}NO$ 266.1539; found 266.1540.

2-(4-methoxybenzyl)-3-phenylbenzofuran (8): 37.7 mg, 60% yield; Oil; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.62 (d, J = 1.8 Hz, 1H), 7.56-7.51 (m, 2H), 7.51-7.47 (m, 2H), 7.41 (t, J = 0.8 Hz, 1H), 7.30-7.25 (m, 2H), 7.20 (d, J = 1.2 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 4.18 (s, 2H), 3.81 (s, 3H), 1.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 158.4, 154.4, 153.1, 132.7, 130.1, 129.6, 129.2, 129.0, 128.8, 127.4, 124.0, 122.8, 119.8, 118.1, 114.2, 111.3, 55.4, 32.1; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{18}O_2$ 315.1380; found 315.1371.

5-chloro-2,3-diphenylbenzofuran (9): 41.3 mg, 68% yield; Yelllow solid; m.p. 83-85 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.67-7.64 (m, 2H), 7.48-7.46 (m, 7H), 7.33-7.27 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 152.5, 152.0, 132.3, 131.8, 130.3, 129.8, 129.3, 128.9, 128.7, 128.6, 128.1, 127.2, 125.0, 119.8, 117.2, 112.3.

2-(3-(4-methoxyphenyl)-1-phenylpropyl)phenol (10): 60.4 mg, 95% yield; Oil; ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 7.33-7.29 (m, 5H), 7.23-7.21 (m, 1H), 7.13-7.09 (m, 3H), 6.96 (dt, J_1 = 7.2 Hz, J_2 = 0.6 Hz, 1H), 6.84 (d, J = 2.4 Hz, 2H), 6.74 (dt, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 4.76 (s, 1H), 4.25 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 2.58 (t, J = 7.8 Hz, 2H), 2.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 157.8,

153.5, 144.1, 134.3, 130.9, 129.4, 128.7, 128.2, 128.1, 127.5, 126.5, 121.1, 116.1, 113.9, 55.4, 43.7, 36.8, 33.2; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{22}H_{22}O_2$ 341.1521; found 341.1504.

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Supporting Information. Spectroscopic data of products **4** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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