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Synthesis of Substituted Phenols by Using the Ring-Closing Metathesis/Isoaromatization Approach

Kazuhiro Yoshida,* Rintaro Narui, and Tsuneo Imamoto*[a]

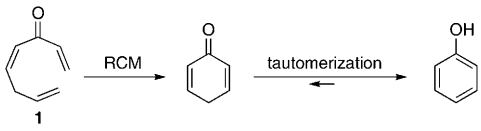
Abstract: Ring-closing olefin metathesis (RCM) of 4-methylene-1,7-octadien-3-ones **2**, followed by isomerization of the carbon–carbon double bond of 6-methylene-2-cyclohexenones **3** from *exo* to *endo*, produced various phenols **4**. As an application of the method, the RCM/Mizoroki–Heck reaction of **2** was proven to be also effective for the synthesis of phenols having an additional substituent at *ortho*-benzylic position.

Keywords: isoaromatization · metathesis · phenols · ring closure · tautomerization

Introduction

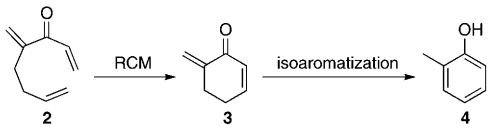
The development of a regiospecific method for the synthesis of substituted aromatic compounds remains a difficult task in organic chemistry.[1] One promising solution is the direct construction of aromatic rings from acyclic precursors.[2] If the acyclic precursors were prepared selectively, exact regiocontrol of substituents on the aromatic rings would be realized with this approach. On the other hand, ruthenium-catalyzed ring-closing olefin metathesis (RCM) has become one of the most important reactions for the construction of cyclic compounds due to its operational simplicity and remarkable functional group tolerance.[3,4] Therefore, the fact that much attention has been recently paid to the synthesis of aromatic compounds using RCM of acyclic precursors is to be expected.[5–7]

In the last few years, we have devoted much of our effort[8] to this field and reported that phenols can be obtained by RCM/tautomerization of 1,4,7-trien-3-ones **1** via cyclohexa-2,5-dienones[8a,c] [Eq. (1)]. Although various phenols could be synthesized without the formation of regioisomers, this approach was limited by the difficulty of preparing **1**. In particular, the construction of the internal *cis* double bond of **1** was the bottleneck in the process.



(1)

Herein we report an efficient method for the synthesis of phenols by using the RCM/isoaromatization[9] approach. The use of new acyclic precursors, 4-methylene-1,7-octadien-3-ones **2**, containing an external carbon–carbon double bond simplifies the overall synthesis of **2**. The combination of RCM of **2** and isomerization of the carbon–carbon double bond of resulting cyclized products **3** from *exo* to *endo*, followed by spontaneous tautomerization, is expected to produce a wide variety of phenols **4** [Eq. (2)].



(2)

Results and Discussion

Our retrosynthetic analysis represented in Scheme 1 suggested that **2** might arise from the oxidation of 4-methylene-1,7-octadien-3-ols **5**. The basic structure of **5** was envisioned to come from two synthetic routes. One involves the vinylation of 2-methylene-5-hexenals **6**, which can be obtained by the Mannich/Hofmann degradation or aldol/dehydration of 5-hexenals **7**. The other involves the coupling of α,β-unsaturated aldehydes with 2-halo-1,5-hexadienes **8**, which can be obtained by the allylation of 2,3-dihalopropenes **9**. In fact, a series of **2** with various substitution patterns could be readily prepared with these routes.[10]

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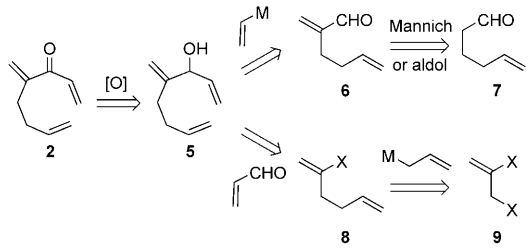
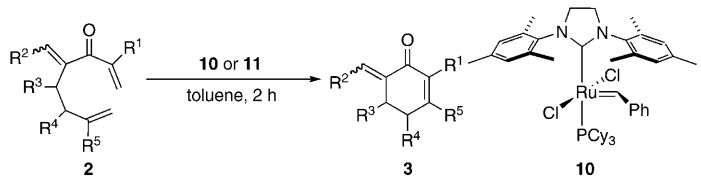


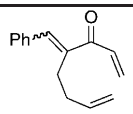
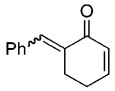
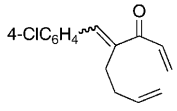
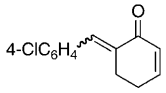
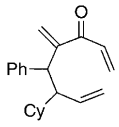
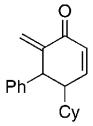
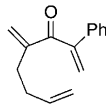
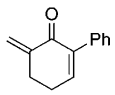
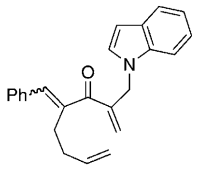
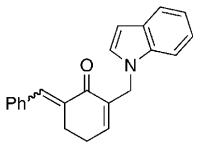
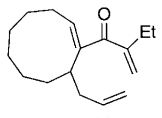
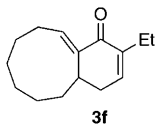
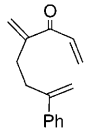
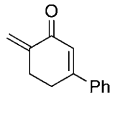
Scheme 1. Retrosynthetic analysis of substrates **2**.

The results of RCM of **2** are summarized in Table 1.[11] When the reaction of **2a** was performed with 1.5 mol% Grubbs' second-generation catalyst **10**[12] at 40°C for 2 h, corresponding cyclized product **3a** was formed in high yield, as expected (Table 1, entry 1). Similarly, **3b** and **3c** were obtained by reacting **2b** and **2c** under the same conditions, respectively (Table 1, entries 2 and 3). The reaction of **2d** that has a phenyl group at R^1 position also proceeded smoothly to give **3d** (Table 1, entry 4). However, decreasing the amount of catalyst from 1.5 to 0.5 mol% for the same reaction lowered the yield of **3d** to half (Table 1, entry 4 vs 5). The RCM of **2e** and **2f**, both of which have another substituent at R^1 position, furnished corresponding **3e** and **f** in good yields, respectively (Table 1, entries 6 and 7). In contrast, introduction of a substituent at R^5 position considerably retarded the reaction. When RCM of **2g** having a phenyl group at the R^5 position was carried out, cyclized product **3g** was obtained in only 31% yield despite the high catalyst load (7.5 mol%) (Table 1, entry 8). However, employing 2.5 mol% Hoveyda–Grubbs catalyst [$(H_2Imes)Cl_2Ru{=}CH(o\text{-}i\text{PrO-}C_6H_4)$] (**11**),[13] which is known to be effective for electron-deficient dienic systems, at elevated temperature improved product yield to 86% (Table 1, entry 9).

As an important part of this study, we next examined the isoaromatization step to phenols and chose **3d** as the model substrate (Table 2). When we tested basic conditions using DBU, which were reported by Kleinman and co-workers,[9d] desired phenol **4d** was obtained in moderate yield (68%) (Table 2, entry 1). Acidic conditions using *p*-toluenesulfonic acid (Table 2, entry 2) and transition-metal-catalyzed isomerization conditions using Pd/C[14] or $RhCl_3$[15] (Table 2, entries 3 and 4) also afforded **4d** in moderate yields (62–79%). After screening numerous reaction conditions, we finally found that **4d** could be successfully obtained in high yield (92%) using $[RhCl(cod)]_2$ (1 mol% Rh) and Cs_2CO_3

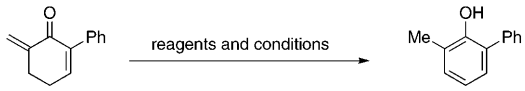
Table 1. Synthesis of 6-methylene-2-cyclohexenones **3** by RCM.[a]



Entry	Substrate	Product	Conditions	Yield [%][b]
1	 **2a**	 **3a**	**10** (1.5 mol%), 40°C	84
2	 **2b**	 **3b**	**10** (1.5 mol%), 40°C	79
3	 **2c**	 **3c**	**10** (1.5 mol%), 40°C	95
4	 **2d**	 **3d**	**10** (1.5 mol%), 40°C	92
5			**10** (0.5 mol%), 40°C	46
6	 **2e**	 **3e**	**10** (1.5 mol%), 40°C	81
7	 **2f**	 **3f**	**10** (1.5 mol%), 40°C	99
8	 **2g**	 **3g**	**10** (7.5 mol%), 40°C	31
9			**11** (2.5 mol%), 100°C	86

[a] The reaction was carried out with **2** and ruthenium catalyst **10** in toluene for 2 h. [b] Isolated yield by silica gel chromatography.

Table 2. Survey of isoaromatization conditions for the synthesis of **4d**.



3d **4d**

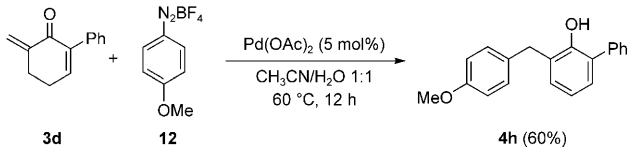
Entry	Reagents	Conditions	Yield [%][a]
1	DBU (1.0 equiv)	toluene, 70 °C, 24 h	68
2	*p*TsOH·H_2O (10 mol %)	toluene, 70 °C, 24 h	79
3	10 mol % Pd/C (10 mol % Pd)	*i*PrOH, 70 °C, 24 h	63
4	$RhCl_3$ (10 mol %)	*i*PrOH/DMF, 100 °C, 24 h	62
5	$[RhCl(cod)]_2$ (1 mol % Rh)/Cs_2CO_3 (1 equiv)	dioxane/H_2O 2:1, 60 °C, 5 h	92
6	$RhCl_3$ (1 mol % Rh)/Cs_2CO_3 (1 equiv)	dioxane/H_2O 2:1, 60 °C, 5 h	0
7	$[RhCl(cod)]_2$ (5 mol % Rh)	dioxane/H_2O 2:1, 70 °C, 3 h	0
8	Cs_2CO_3 (1 equiv)	dioxane/H_2O 2:1, 70 °C, 3 h	0

[a] Isolated yield by silica gel chromatography.

(1 equiv) in dioxane/H_2O (2:1) at 60 °C (Table 2, entry 5). Interestingly, the employment of $RhCl_3$ instead of $[RhCl(cod)]_2$ (Table 2, entry 6) or the lack of either $[RhCl(cod)]_2$ (1 mol % Rh) or Cs_2CO_3 (Table 2, entries 7 and 8) under similar conditions resulted in no reaction.[16]

The results of the isoaromatization of **3** with these conditions to synthesize phenols **4** are summarized in Table 3. The optimal conditions found in Table 2, namely, $[RhCl(cod)]_2$ (1 mol % Rh) and Cs_2CO_3 (1 equiv) in dioxane/H_2O (2:1) at 60 °C, were proved to be effective for most of the isoaromatization reactions of **3**, and various phenols **4** could be obtained in high yields. One exception was the reaction of **3** having a substituent at the R^3 position. The complete absence of products was observed in both reactions of **3c** and **f** (Table 3, entries 3 and 7). Applying the same isomerization conditions to **3c** and **f** but using *p*-toluenesulfonic acid and Pd/C as alternatives, respectively, successfully produced corresponding phenols **4c** and **f**, respectively (Table 3, entries 4 and 8).

Finally, we conducted the Mizoroki–Heck reaction[17] of **3d** with *p*-methoxybenzenediazonium tetrafluoroborate (**12**) in the presence of a catalytic amount of $Pd(OAc)_2$, because introduction of an additional *p*-methoxyphenyl substituent at the *ortho* benzylic position and aromatization to the phenol was expected to occur simultaneously with this approach. As a result, corresponding phenol **4h** was successfully produced (Scheme 2).



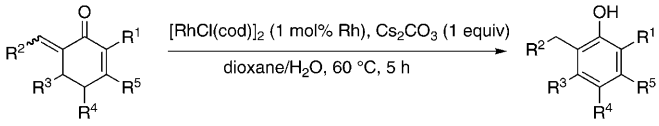
3d **12** **4h** (60%)

Scheme 2. Preparation of **4h** by the Mizoroki–Heck reaction of **3d** with **12**.

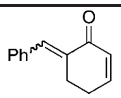
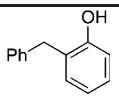
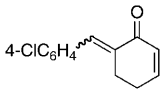
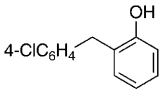
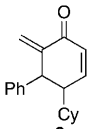
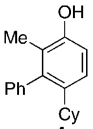
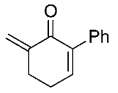
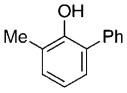
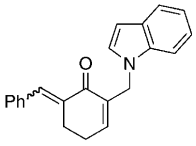
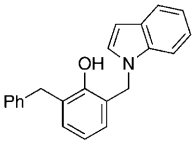
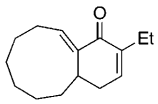
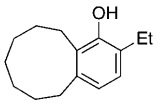
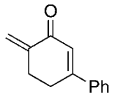
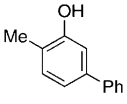
Conclusions

In summary, we have developed an efficient method for the synthesis of substituted phenols by RCM/isoaromatization of **2**, by which the formation of undesirable regioisomers could be completely excluded. The employment of **2** as key acyclic precursor paved the way to smoothly accessing phenols from commercially available compounds. Moreover, the exocyclic carbon–carbon double bond of products **3** could be utilized effectively in the Mizoroki–Heck reaction to introduce

Table 3. Synthesis of phenols **4** by isoaromatization.[a]



3 **4**

Entry	Substrate	Product	Yield [%][b]
1	 **3a**	 **4a**	93
2	 **3b**	 **4b**	75
3	 **3c**	 **4c**	0
4[c]			77
5	 **3d**	 **4d**	92
6	 **3e**	 **4e**	69
7	 **3f**	 **4f**	0
8[d]			86
9	 **3g**	 **4g**	95

[a] The reaction was carried out with **3**, $[RhCl(cod)]_2$ (1 mol % Rh), and Cs_2CO_3 (1 equiv) in dioxane/H_2O at 60 °C for 5 h. [b] Isolated yield by silica gel chromatography. [c] The reaction was carried out with **3c** and *p*TsOH·H_2O (10 mol %) in toluene at 70 °C for 24 h. [d] The reaction was carried out with **3f** and 10 mol % Pd/C (10 mol % Pd) in *i*PrOH at 70 °C for 24 h.

an additional substituent onto the *ortho* benzylic position of the phenols.

Experimental Section

General: All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or glove box techniques under prepurified argon. NMR Spectra were recorded on a JEOL JNM LA-500 spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) and LA-400 spectrometer (400 MHz for ^{1}H and 100 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.

Materials: Dichloromethane and anhydrous *N*,*N*-dimethylformamide were used without further purification. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone-ketyl under nitrogen prior to use. 2-Propanol was distilled from magnesium under nitrogen and stored in a glass flask with a three-way cock under nitrogen. Toluene and dioxane were distilled from sodium benzophenone-ketyl under nitrogen and stored in glass flasks with Teflon stopcocks under nitrogen. Ruthenium complexes, $[(PCy_3)(H_2Imes)Cl_2Ru{=}C(H)Ph]$ (**10**)[12b] and $[(H_2Imes)Cl_2Ru{=}CH(o\text{-}i\text{PrO-}C_6H_4)]$ (**11**)[18] were prepared according to the reported procedures. A rhodium complex, $[RhCl(cod)]_2$ was prepared according to the reported procedure.[19] 2-Methylene-5-hexenals **6** were prepared by Mannich/Hofmann degradation from corresponding 5-hexenals **7** according to the reported procedures.[20] 2-Bromo-5-phenyl-1,5-hexadiene (**8g**) was prepared by allylation of 2,3-dibromo-1-propene with 2-phenylallylmagnesium bromide and copper cyanide analogously to the reported procedure.[21] 2-Bromo-3-indol-1-yl-propene was prepared by alkylation of indole with 2,3-dibromopropene according to the reported procedure.[22] 5-Hexenal,[23] 4-cyclohexyl-3-phenyl-5-hexenol,[24] (*E*)-3-allyl-2-iodocyclononene (**8f**),[25] activated MnO_2,[26] Dess–Martin periodinane,[27] and *p*-methoxybenzenediazonium tetrafluoroborate (**12**)[28] were prepared according to the reported procedures. α-Bromostyrene, 2,3-dibromopropene, indole, *tert*-butyllithium solution, vinylmagnesium chloride solution, DBU, palladium diacetate, rhodium trichloride, and cesium carbonate were used as received.

Procedures for the preparation of 4-methylene-1,7-octadien-3-ols 5

General procedure A (GP A): Vinylmagnesium chloride solution (1.44 mol L^{-1} solution in THF, 3.29 mmol) was added at −78 °C to a solution of 2-methylene-5-hexenal **6** (1.65 mmol) in Et_2O (9.2 mL). The reaction mixture was warmed up to 0 °C. After stirring for 30 min, the reaction mixture was quenched by addition of water and extracted with Et_2O several times. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography or PTLC on silica gel to give **5**.

General procedure B (GP B): *t*BuLi (1.59 mol L^{-1} solution in pentane, 2.60 mmol) was added at −78 °C to a solution of vinylhalide (1.31 mmol) in Et_2O (3.0 mL). After 1 h, **6** (1.19 mmol) in Et_2O (3.0 mL) was added to the mixture and it was stirred for 15 min at the same temperature. Then, the reaction mixture was quenched by addition of water and extracted with Et_2O three times. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography or PTLC on silica gel to give **5**.

General procedure C (GP C): *t*BuLi (1.57 mol L^{-1} solution in pentane, 7.16 mmol) was added at −78 °C to a solution of 2-halo-1,5-hexadiene **8** (3.58 mmol) in Et_2O (25 mL). After 30 min, the mixture was added α,β-unsaturated aldehyde (3.94 mmol) and stirred for 15 min at the same temperature. Then, the reaction mixture was quenched by addition of water and extracted with EtOAc three times. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography or PTLC on silica gel to give **5**.

4-Benzylidene-1,7-octadien-3-ol (5a): The reaction was carried out according to the GP A (see also Scheme S1 in Supporting Information). 2-Benzylidene-5-hexenal (**6a**) (1.65 mmol) and vinylmagnesium chloride (3.29 mmol) were used. The reaction mixture was stirred for 1 h, The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 4:1) and gel permeation chromatography (273 mg, 77 %). ^{1}H NMR ($CDCl_3$): δ = 1.72 (d, J = 3.4 Hz, 1H), 2.22–2.49 (m, 4H), 4.73 (d, J = 4.6 Hz, 1H), 4.96 (ddt, J = 10.1, 1.8, 1.3 Hz, 1H), 5.01 (dq, J = 17.1, 1.6 Hz, 1H), 5.23 (dt, J = 10.1, 1.5 Hz, 1H), 5.38 (dt, J = 17.1, 1.6 Hz, 1H), 5.80 (ddt, J = 16.8, 10.1, 6.4 Hz, 1H), 5.94 (ddd, J = 17.1, 10.4, 6.1 Hz, 1H), 6.63 (s, 1H), 7.22 (tt, J = 7.3, 1.8 Hz, 1H), 7.27 (d, J = 7.0 Hz, 2H), 7.33 ppm (t, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 27.66, 32.84, 76.93, 114.71, 115.75, 126.63, 126.69, 128.22, 128.60, 137.33, 138.13, 139.20, 142.67 ppm; HRMS (FAB): *m*/*z*: calcd for $C_{15}H_{18}O$: 214.1358, found 214.1355 $[M]^+$.

4-(4-Chlorobenzylidene)-1,7-octadien-3-ol (5b): The reaction was carried out according to the GP A (see also Scheme S1 in Supporting Information): 2-(4-Chlorobenzylidene)-5-hexenal (**6b**) (0.691 mmol) and vinylmagnesium chloride (9.36 mmol) were used: The reaction mixture was stirred for 30 min. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (156 mg, 91 %). ^{1}H NMR ($CDCl_3$): δ = 1.77 (d, J = 2.9 Hz, 1H), 2.20–2.46 (m, 4H), 4.71 (ddt, J = 4.9, 2.9, 1.2 Hz, 1H), 4.96 (ddt, J = 10.1, 1.8, 1.3 Hz, 1H), 5.01 (dq, J = 17.1, 1.8 Hz, 1H), 5.24 (dt, J = 10.4, 1.2 Hz, 1H), 5.37 (dt, J = 17.1, 1.6 Hz, 1H), 5.78, (ddt, J = 16.8, 10.4, 6.5 Hz, 1H), 5.92 (ddd, J = 17.4, 10.4, 6.4 Hz, 1H), 6.57 (s, 1H), 7.19 (d, J = 8.3 Hz, 2H), 7.29 ppm (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 27.63, 32.71, 76.75, 114.89, 116.05, 125.39, 128.40, 129.90, 132.35, 135.80, 137.88, 139.04, 143.35 ppm; HRMS (FAB): *m*/*z*: calcd for $C_{15}H_{17}ClO$: 248.0968, found 248.0959 $[M]^+$.

6-Cyclohexyl-4-methylene-5-phenyl-1,7-octadien-3-ol (5c): The reaction was carried out according to the GP A (see also Scheme S1 in Supporting Information): 2-Methylene-4-cyclohexyl-3-phenyl-5-hexenal (**6c**) (5.47 mmol) and vinylmagnesium chloride (6.01 mmol) were used. The reaction mixture was stirred for 1.5 h. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (diastereomeric mixture: 1.47 g, 90 %). One of the diastereomers was separated for the spectral characterization. M.p. 83–86 °C; ^{1}H NMR ($CDCl_3$): δ = 0.81–1.33 (m, 7H), 1.48–1.71 (m, 5H), 2.53 (ddd, J = 11.6, 9.8, 2.5 Hz, 1H), 3.41 (d, J = 11.6 Hz, 1H), 4.34 (dd, J = 5.5, 3.7 Hz, 1H), 4.95 (ddd, J = 17.4, 2.2, 0.4 Hz, 1H), 5.10 (dd, J = 10.4, 2.2 Hz, 1H), 5.11 (ddd, J = 10.4, 1.6, 1.2 Hz, 1H), 5.18 (s, 1H), 5.23 (dt, J = 17.1, 1.5 Hz, 1H), 5.32 (t, J = 0.9 Hz, 1H), 5.52 (dt, J = 16.8, 10.1 Hz, 1H), 5.61 (ddd, J = 17.1, 10.4, 6.7 Hz, 1H), 7.17–7.30 ppm (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 26.51, 26.54, 26.67, 26.70, 32.61, 38.42, 49.59, 52.86, 75.49, 111.75, 116.09, 117.02, 126.46, 128.47, 128.75, 139.11, 139.19, 142.48, 151.82 ppm; HRMS (FAB): *m*/*z*: calcd for $C_{21}H_{27}$: 279.2113, found 279.2109 $[M-OH]^+$.

4-Methylene-2-phenyl-1,7-octadien-3-ol (5d): The reaction was carried out according to the GP B (see also Scheme S1 in Supporting Information). α-Bromostyrene (1.31 mmol), *t*BuLi (2.60 mmol), and 2-methylene-5-hexenal (**6d**) (1.19 mmol) were used. The reaction mixture was stirred for 15 min: The crude mixture was purified by PTLC on silica gel (hexane/EtOAc 4:1) and gel permeation chromatography (125 mg, 49 %). ^{1}H NMR ($CDCl_3$): δ = 1.95 (d, J = 4.1 Hz, 1H), 2.00–2.25 (m, 4H), 4.92–5.02 (m, 3H), 5.07 (d, J = 3.2 Hz, 1H), 5.17, (d, J = 0.8 Hz, 1H), 5.44 (t, J = 1.2 Hz, 1H), 5.46 (dd, J = 1.2, 0.5 Hz, 1H), 5.78 (ddt, J = 17.3, 10.2, 7.1 Hz, 1H), 7.24–7.34 (m, 3H), 7.36–7.43 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 30.98, 31.90, 76.93, 112.19, 114.43, 114.74, 126.85, 127.63, 128.19, 138.21, 139.53, 148.48, 148.90 ppm; HRMS (FAB): *m*/*z*: calcd for $C_{15}H_{17}$: 197.1330, found 197.1326 $[M-OH]^+$.

4-Benzylidene-2-indol-1-ylmethyl-1,7-octadien-3-ol (5e): The reaction was carried out according to the GP B (see also Scheme S1 in Supporting Information). 2-Bromo-3-indol-1-yl-propene (1.38 mmol), *t*BuLi (2.67 mmol), and 2-benzylidene-5-hexenal (**6a**) (1.14 mmol) were used. The reaction mixture was stirred for 1 h: The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (264 mg, 67 %). ^{1}H NMR ($CDCl_3$): δ = 1.85 (d, J = 2.5 Hz, 1H), 2.14–2.50 (m, 4H), 4.67 (s, 1H), 4.71 (d, J = 16.5 Hz, 1H), 4.81 (d, J = 18.0 Hz, 1H), 4.83 (s, 1H), 4.94 (dq, J = 9.2, 1.3 Hz, 1H), 4.97 (dq, J = 15.6, 1.6 Hz, 1H),

5.32 (s, 1H), 5.75 (ddt, J=17.1, 10.4, 6.5 Hz, 1H), 6.52 (dd, J=3.4, 0.7 Hz, 1H), 6.66 (s, 1H), 7.07 (d, J=3.4 Hz, 1H), 7.09 (ddd, J=8.0, 7.0, 0.9 Hz, 1H), 7.17 (ddd, J=8.3, 7.0, 1.2 Hz, 1H), 7.21–7.29 (m, 4H), 7.32–7.38 (m, 2H), 7.62 ppm (dt, J=7.9, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.49, 32.86, 47.76, 76.80, 101.57, 109.64, 113.81, 114.90, 119.43, 120.92, 121.58, 126.55, 126.88, 127.83, 128.33, 128.37, 128.60, 136.24, 136.93, 137.91, 140.99, 145.10 ppm; HRMS (FAB): m/z: calcd for $C_{24}H_{25}NO$: 343.1936, found 343.1951 $[M]^+$.

1-(9-Allyl-1-cyclononenyl)-2-ethyl-2-propen-1-ol (5f): The reaction was carried out according to the GP C (see also Scheme S1 in Supporting Information). 3-Allyl-2-iodocyclononene (**8f**) (0.558 mmol), *t*BuLi (1.12 mmol), and 2-ethylacrolein (1.70 mmol) were used. The reaction mixture was stirred for 30 min: The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 20:3) (diastereomeric mixture: 102 mg, 73%). The following data are for a mixture of two diastereomers (0.5:0.5); ^{1}H NMR ($CDCl_3$): δ = 1.04 (t, J=7.5 Hz, 1.5H), 1.07 (t, J=7.5 Hz, 1.5H), 1.30–2.44 (m, 16H), 2.52 (s, 0.5H), 2.71 (s, 0.5H), 4.46 (d, J=3.4 Hz, 0.5H), 4.48 (d, J=2.4 Hz, 0.5H), 4.93–5.02 (m, 2.5H), 5.05 (ddt, J=17.2, 2.2, 1.4 Hz, 0.5H), 5.16 (t, J=1.2 Hz, 0.5H), 5.23 (t, J=1.2 Hz, 0.5H), 5.64 (t, J=10.1 Hz, 0.5H), 5.66 (t, J=10.1 Hz, 0.5H), 5.74 (ddt, J=16.4, 10.4, 7.2 Hz, 0.5H), 5.84 ppm (ddt, 17.1, 10.1, 6.8 Hz, 0.5H); ^{13}C NMR ($CDCl_3$): δ = 11.98, 12.06, 23.89, 24.61, 24.95, 25.13, 26.16, 26.30, 26.43, 26.56, 26.82, 27.09, 27.18, 31.44, 31.79, 37.97, 38.42, 39.16, 39.63, 77.20, 108.55, 108.67, 115.25, 115.40, 129.54, 129.77, 137.85, 138.43, 141.49, 141.58, 151.83, 151.86 ppm; HRMS (FAB): m/z: calcd for $C_{17}H_{28}OK$: 287.1777, found 287.1780 $[M+K]^+$.

4-Methylene-7-phenyl-1,7-hexadien-3-ol (5g): The reaction was carried out according to the GP C (see also Scheme S1 in Supporting Information). 2-Bromo-5-phenyl-1,5-hexadiene (**8g**) (3.58 mmol), *t*BuLi (7.16 mmol), and acrolein (3.94 mmol) were used: The reaction mixture was stirred for 15 min. The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (513 mg, 67%). ^{1}H NMR ($CDCl_3$): δ = 1.71 (s, 1H), 2.18 (td, J=15.3, 8.3 Hz, 1H), 2.24 (td, J=15.3, 7.9 Hz, 1H), 2.68 (td, J=7.6, 1.1 Hz, 2H), 4.56 (d, J=5.8 Hz, 1H), 4.93 (s, 1H), 5.08 (d, J=1.2 Hz, 1H), 5.14 (d, J=0.9 Hz, 1H), 5.15 (dt, J=10.1, 1.2 Hz, 1H), 5.26 (dt, J=17.4, 1.6 Hz, 1H), 5.29 (d, J=1.1 Hz, 1H), 5.82 (ddd, J=17.1, 10.4, 6.4 Hz, 1H), 7.26 (tt, J=7.6, 1.6 Hz, 1H), 7.32 (td, J=7.9, 1.5 Hz, 2H), 7.40 ppm (d, J=7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 30.61, 33.84, 76.20, 110.40, 112.46, 115.65, 126.06, 127.37, 128.26, 139.08, 141.04, 148.01, 149.81 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{17}$: 197.1330, found 197.1338 $[M-OH]^+$.

Procedures for the preparation of 4-methylene-1,7-octadien-3-ones 2

General procedure D (GP D): Dess–Martin periodinane (0.923 mmol) was added at room temperature to a solution of 4-methylene-1,7-octadien-3-ol (**5**; 0.489 mmol) in CH_2Cl_2 (48 mL). After 4 h, the reaction mixture was quenched by addition of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$, and extracted with EtOAc several times. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography or PTLC on silica gel to give **2**.

4-Benzylidene-1,7-octadien-3-one (2a): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information). 4-Benzylidene-1,7-octadien-3-ol (**5a**) (0.460 mmol) and Dess–Martin periodinane (0.826 mmol) were used. The reaction mixture was stirred for 1.5 h: The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 11:1) (72.3 mg, 74%); ^{1}H NMR ($CDCl_3$): δ = 2.25 (tdt, J=8.0, 6.5, 1.2 Hz, 2H), 2.71 (t, J=7.7 Hz, 2H), 4.97 (ddt, J=10.1, 1.9, 1.2 Hz, 1H), 5.03 (dq, J=17.2, 1.3 Hz, 1H), 5.82 (ddt, J=16.9, 10.8, 6.5 Hz, 1H), 5.82 (dd, J=10.6, 1.9 Hz, 1H), 6.31 (dd, J=17.2, 1.9 Hz, 1H), 6.99 (dd, J=17.1, 10.6 Hz, 1H), 7.32–7.45 (m, 5H), 7.46 ppm (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 26.18, 32.74, 114.98, 128.55, 128.61, 128.72, 129.20, 132.75, 135.46, 137.72, 139.90, 141.91, 193.44 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{17}O$: 213.1279, found 213.1273 $[M+H]^+$.

4-(4-Chlorobenzylidene)-1,7-octadien-3-one (2b): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information). 4-(4-Chlorobenzylidene)-1,7-octadien-3-ol (**5b**) (0.571 mmol) and Dess–Martin periodinane (1.58 mmol) were used: The reaction mixture was stirred for 2 h: The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 10:1) (122 mg, 86%). ^{1}H NMR ($CDCl_3$): δ = 2.22 (tdt, J=7.9, 6.7, 1.6, Hz, 2H), 2.68 (t, J=8.2 Hz, 2H), 4.97 (ddt, J=10.4, 1.9, 1.2 Hz, 1H), 5.02 (dq, J=17.1, 1.9 Hz, 1H), 5.80 (ddt, J=17.1, 10.4, 6.7 Hz, 1H), 5.82 (dd, J=10.7, 1.9 Hz, 1H), 6.31 (dd, J=17.1, 1.9 Hz, 1H), 6.96 (dd, J=17.1, 10.7 Hz, 1H), 7.32 (d, J=8.3 Hz, 2H), 7.37–7.40 ppm (m, 3H); ^{13}C NMR ($CDCl_3$): δ = 26.23, 32.67, 115.19, 128.85, 128.98, 130.47, 132.70, 133.96, 134.58, 137.53, 138.29, 142.49, 193.20 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{16}ClO$: 247.0890, found 247.0887 $[M+H]^+$.

6-Cyclohexyl-4-methylene-5-phenyl-1,7-octadien-3-one (2c): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information). 6-Cyclohexyl-4-methylene-5-phenyl-1,7-octadien-3-ol (**5c**) (0.478 mmol) and Dess–Martin periodinane (0.574 mmol) were used. The reaction mixture was stirred for 1 h, as being warmed from 0°C to room temperature. The crude mixture was purified by PTLC on silica gel (hexane/EtOAc 5:1) (93.6 mg, 67%). The following data are for a mixture of two diastereomers (0.85:0.15). ^{1}H NMR ($CDCl_3$): δ = 0.80–1.80 (m, 11H), 2.55 (ddd, J=11.6, 10.1, 1.5 Hz, 0.85H), 2.59 (td, J=10.1, 3.4 Hz, 0.15H), 4.26, (d, J=10.5 Hz, 0.15H), 4.28 (d, J=11.9 Hz, 0.85H), 4.74 (ddd, J=17.1, 2.2, 0.6 Hz, 0.15H), 4.86 (dd, J=10.4, 2.2 Hz, 0.15H), 4.92 (ddd, J=17.1, 2.2, 0.7 Hz, 0.85H), 5.02 (dd, J=10.4, 2.1 Hz, 0.85H), 5.43 (dt, J=17.1, 10.1 Hz, 0.15H), 5.51 (dt, J=17.1, 10.1 Hz, 0.85H), 5.67 (dd, J=10.4, 1.8 Hz, 0.85H), 5.72 (dd, J=10.4, 1.8 Hz, 0.15H), 5.83 (d, J=0.9 Hz, 0.85H), 5.91 (d, J=0.6 Hz, 0.15H), 6.01 (s, 0.85H), 6.07 (s, 0.15H), 6.13 (dd, J=17.1, 1.8 Hz, 0.85H), 6.18 (dd, J=17.1, 1.9 Hz, 0.15H), 6.72 (dd, J=17.1, 10.7 Hz, 0.85H), 6.78 (dd, J=17.1, 10.7 Hz, 0.15H), 7.09–7.14 (m, 0.15H), 7.15–7.31 ppm (m, 4.85H); ^{13}C NMR ($CDCl_3$): δ = 26.32, 26.40, 26.54, 26.57, 26.61, 26.67, 27.43, 32.38, 32.46, 38.30, 38.80, 46.23, 46.83, 52.67, 53.22, 116.98, 117.27, 124.39, 125.41, 126.05, 126.22, 128.00, 128.33, 128.55, 128.75, 129.06, 129.22, 132.71, 138.10, 138.26, 141.88, 141.95, 150.96, 151.28, 192.51, 192.60 ppm; HRMS (FAB): m/z: calcd for $C_{21}H_{27}O$: 295.2062, found 295.2077 $[M+H]^+$.

4-Methylene-2-phenyl-1,7-octadien-3-one (2d): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information): 4-Methylene-2-phenyl-1,7-hexadien-3-ol (**5d**) (0.489 mmol) and Dess–Martin periodinane (0.923 mmol) were used. The reaction mixture was stirred for 4 h. The crude mixture was purified by PTLC on silica gel (hexane/EtOAc 5:1) (97.3 mg, 94%). ^{1}H NMR ($CDCl_3$): δ = 2.26 (dtt, J=8.2, 7.0, 1.2 Hz, 2H), 2.51 (t, J=6.8 Hz, 2H), 4.99, (ddt, J=10.1, 1.9, 1.2 Hz, 1H), 5.04 (dq, J=17.1, 1.4 Hz, 1H), 5.82 (ddt, J=17.1, 10.4, 6.8 Hz, 1H), 5.86 (td, J=1.4, 0.8 Hz, 1H), 5.55 (d, J=0.5 Hz, 1H), 5.91 (d, J=0.5 Hz, 1H), 5.96 (d, J=0.5 Hz, 1H), 7.27–7.37 ppm (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 30.23, 32.25, 115.23, 119.96, 126.79, 128.27, 128.48, 128.54, 137.12, 137.70, 147.85, 148.16, 199.14 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{17}O$: 213.1279, found 213.1258 $[M+H]^+$.

4-Benzylidene-2-indol-1-ylmethyl-1,7-octadien-3-one (2e): MnO_2 (21.0 mmol) was added to a solution of 4-benzylidene-2-indol-1-ylmethyl-1,7-octadien-3-ol (**5e**) (0.563 mmol) in CH_2Cl_2 (5.6 mL). The resulting mixture was stirred for 2.5 h at room temperature. The mixture was passed through Celite and concentrated under reduced pressure. The residue was purified by column chromatography and PTLC on silica gel (hexane/EtOAc 5:1) to give **2e** (146 mg, 76%); ^{1}H NMR ($CDCl_3$): δ = 2.19 (tdt, J=7.9, 6.7, 1.3 Hz, 2H), 2.69 (t, J=7.9 Hz, 2H), 4.95 (ddt, J=10.1, 1.9, 1.3 Hz, 1H), 4.99 (dq, J=17.1, 1.6 Hz, 1H), 5.08 (t, J=1.6 Hz, 2H), 5.38, (t, J=1.6 Hz, 1H), 5.70 (s, 1H), 5.78 (ddt, J=17.1, 10.4, 6.7 Hz, 1H), 6.51 (dd, J=3.1, 0.9 Hz, 1H), 7.04 (s, 1H), 7.11 (d, J=3.1, 1H), 7.12 (ddd, J=8.0, 7.0, 0.9 Hz, 1H), 7.18, (d, J=7.6 Hz, 1H), 7.22 (dd, J=8.3, 7.0, 1.2 Hz 1H), 7.28 (tt, J=7.3, 1.6 Hz, 1H), 7.31–7.37 (m, 3H), 7.63 ppm (ddd, J=8.0, 1.3, 0.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 26.38, 32.53, 47.79, 101.90, 109.56, 115.29, 119.59, 121.07, 121.77, 124.09, 128.49, 128.56, 128.62, 128.74, 129.14, 135.13, 136.02, 137.54, 141.03, 141.32, 144.31, 198.82 ppm; HRMS (FAB): m/z: calcd for $C_{24}H_{23}NO$: 341.1780, found 341.1775 $[M]^+$.

1-(9-Allyl-1-cyclononenyl)-2-ethylpropenone (2f): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information): 1-(9-Allyl-1-cyclononenyl)-2-ethyl-2-propen-1-ol (**5f**) (0.279 mmol) and Dess–Martin periodinane (0.362 mmol) were used: The reaction mixture was stirred for 30 min at 0°C. The crude mixture was

purified by PTLC on silica gel (hexane/EtOAc 10:1) (55.6 mg, 81%); ^{1}H NMR ($CDCl_3$): δ = 1.04 (t, J=7.6 Hz, 3H), 1.23–1.62 (m, 8H), 1.67–1.77 (m, 1H), 1.94–2.05 (m, 1H), 2.25–2.40 (m, 5H), 2.90–2.99 (m, 1H), 4.90 (dq, J=10.1, 1.2 Hz, 1H), 4.95 (dq, J=17.1, 1.5 Hz, 1H), 5.47 (d, J=0.9 Hz, 1H), 5.52 (q, J=1.5 Hz, 1H), 5.70 (ddt, J=17.4, 10.1, 6.7 Hz, 1H), 6.41 ppm (t, J=8.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 12.31, 24.76, 25.33, 25.91, 26.09, 26.61, 27.18, 32.74, 38.08, 38.41, 115.54, 121.52, 137.81, 143.05, 145.37, 150.80, 201.13 ppm; HRMS (EI): m/z: calcd for $C_{17}H_{26}O$: 246.1984, found 246.1977 $[M]^+$.

4-Methylene-7-phenyl-1,7-octadien-3-one (2g): The reaction was carried out according to the GP D (see also Scheme S1 in Supporting Information): 4-Methylene-7-phenyl-1,7-hexadien-3-ol (**5g**) (2.38 mmol) and Dess–Martin periodinane (2.86 mmol) were used: The reaction mixture was stirred for 30 min: The crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (457 mg, 91%). ^{1}H NMR ($CDCl_3$): δ = 2.48 (t, J=6.8 Hz, 2H), 2.63 (t, J=7.1 Hz, 2H), 4.99 (t, J=1.2 Hz, 1H), 5.24 (d, J=1.2 Hz, 1H), 5.67 (t, J=1.2 Hz, 1H), 5.70 (dd, J=10.5, 1.7 Hz, 1H), 5.90 (s, 1H), 6.21 (dd, J=17.1, 1.7 Hz, 1H), 6.80 (dd, J=17.1, 10.5 Hz, 1H), 7.19 (tt, J=7.3, 1.5 Hz, 1H), 7.26 (t, J=8.3 Hz, 2H), 7.34 ppm (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 30.45, 33.95, 112.91, 125.18, 126.12, 127.39, 128.29, 128.87, 132.10, 140.77, 147.55, 148.19, 192.28 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{17}O$: 213.1279, found 213.1281 $[M+H]^+$.

Procedure for the preparation of 6-methylene-2-cyclohexenones 3

General procedure: A solution of **2** (0.263 mmol) in toluene (26 mL, 0.01 M) was treated with 1.5 mol% catalyst **10** (0.00395 mmol) in one portion under nitrogen and stirred for 2 h at 40°C. The reaction mixture was concentrated under reduced pressure and purified by PTLC on silica gel or silica gel column chromatography to give **3**.

6-Benzylidene-2-cyclohexen-1-one (3a): Purified by PTLC on silica gel (hexane/EtOAc 8:3) (84%); m.p. 70–74°C; ^{1}H NMR ($CDCl_3$): δ = 2.43 (tdd, J=6.4, 4.3, 2.1 Hz, 2H), 3.03 (td, J=6.4, 1.8 Hz, 2H), 6.25 (dt, J=10.1, 2.1 Hz, 1H), 7.04 (dt, J=10.1, 4.3 Hz, 1H), 7.30–7.43 (m, 5H), 7.61 ppm (t, J=1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 25.42, 26.26, 128.27, 128.34, 129.66, 130.73, 134.88, 135.06, 135.64, 149.20, 188.78 ppm; HRMS (FAB): m/z: calcd for $C_{13}H_{13}O$: 185.0966, found 185.0963 $[M+H]^+$.

6-(4-Chlorobenzylidene)-2-cyclohexen-1-one (3b): Purified by PTLC on silica gel (hexane/EtOAc 5:1) (79%); mp=45–47°C; ^{1}H NMR ($CDCl_3$): δ = 2.43 (tdd, J=6.3, 4.4, 1.9 Hz, 2H), 2.98 (td, J=6.3, 1.9 Hz, 2H), 6.24 (dt, J=10.1, 1.9 Hz, 1H), 7.04 (dt, J=10.1, 4.4 Hz, 1H), 7.30 (d, J=8.7 Hz, 2H), 7.37 (d, J=8.4 Hz, 2H), 7.54 ppm (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 25.35, 26.25, 128.63, 130.71, 130.94, 133.73, 134.08, 134.19, 135.39, 149.29, 188.46 ppm; HRMS (FAB): m/z: calcd for $C_{13}H_{12}ClO$: 219.0577, found 219.0561 $[M+H]^+$.

4-Cyclohexyl-6-methylene-5-phenyl-2-cyclohexen-1-one (3c): Purified by PTLC on silica gel (hexane/EtOAc 5:1) (diastereomeric mixture: 95%); one of the diastereomers was separated to clarify the spectral characterization; ^{1}H NMR ($CDCl_3$): δ = 0.80–1.47 (m, 6H), 1.60–1.78 (m, 5H), 2.67 (dtd, J=6.3, 4.6, 1.9 Hz, 1H), 4.02, (d, J=6.3 Hz, 1H), 5.02–5.04 (m, 1H), 6.16 (t, J=1.7 Hz, 1H), 6.25 (dd, J=10.4, 1.7 Hz, 1H), 6.99 (dd, J=10.4, 4.1 Hz, 1H), 7.15 (dd, J=7.2, 1.5 Hz, 2H), 7.24 (tt, J=7.0, 1.5 Hz, 1H), 7.32 ppm (t, J=7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 26.21, 26.33, 26.38, 28.72, 31.25, 40.64, 48.26, 49.58, 123.10, 126.76, 128.17, 128.58, 129.94, 141.77, 145.65, 152.14, 188.12 ppm; HRMS (FAB): m/z: calcd for $C_{19}H_{22}KO$: 305.1308, found 305.1307 $[M+K]^+$.

6-Methylene-2-phenyl-2-cyclohexen-1-one (3d): Purified by PTLC on silica gel (hexane/EtOAc 5:1) (92%): The reaction was also carried out with 0.5 mol% **10**; the crude mixture was purified by PTLC on silica gel (hexane/EtOAc 5:1) (46%); mp=63–66°C; ^{1}H NMR ($CDCl_3$): δ = 2.60 (td, J=6.5, 4.6 Hz, 2H), 2.83 (t, J=6.5 Hz, 2H), 5.36 (q, J=1.4 Hz, 1H), 6.07 (d, J=1.5 Hz, 1H), 7.11 (t, J=4.6 Hz, 1H), 7.28–7.38 ppm (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 26.42, 31.09, 120.62, 127.65, 127.97, 128.69, 136.50, 141.02, 143.40, 147.95, 187.28 ppm; HRMS (FAB): m/z: calcd for $C_{13}H_{13}O$: 185.0966, found 185.0962 $[M+H]^+$.

2-Indol-1-ylmethyl-6-benzylidene-2-cyclohexen-1-one (3e): Purified by PTLC on silica gel (hexane/EtOAc 5:1) (81%); m.p. 103–110°C; ^{1}H NMR ($CDCl_3$): δ = 2.26 (tdt, J=6.3, 4.4, 1.9 Hz, 2H), 2.84 (td, J=6.3, 1.9 Hz, 2H), 5.06 (q, J=1.9 Hz, 2H), 6.23 (tt, J=4.4, 1.5 Hz, 1H), 6.53 (dd, J=3.2, 0.7 Hz, 1H), 7.11 (ddd, J=8.0, 7.0, 1.0 Hz, 1H), 7.14 (d, J=3.2 Hz, 1H), 7.19 (ddd, J=8.0, 7.0, 1.4 Hz, 1H), 7.25–7.41 (m, 6H), 7.64 (dt, J=8.0, 0.8 Hz, 1H), 7.68 ppm (t, J=1.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 24.76, 26.13, 45.36, 101.64, 109.58, 119.47, 120.98, 121.69, 128.42, 128.46, 128.59, 128.72, 129.71, 134.61, 135.62, 135.68, 136.08, 136.41, 144.58, 187.88 ppm; HRMS (FAB): m/z: calcd for $C_{22}H_{19}NO$: 313.1467, found 313.1474 $[M]^+$.

2-Ethyl-4,4a,5,6,7,8,9,10-octahydrobenzocyclononen-1-one (3f): Purified by PTLC on silica gel (hexane/EtOAc 10:1) (99%); ^{1}H NMR ($CDCl_3$): δ = 1.03 (t, J=7.3 Hz, 3H), 1.13–1.27 (m, 1H), 1.29–1.50 (m, 6H), 1.59–1.70 (m, 2H), 1.76–1.88 (m, 1H), 2.12–2.36 (m, 5H), 2.62–2.72 (m, 1H), 3.26–3.32 (m, 1H), 6.59 (ddq, J=6.4, 2.4, 1.2 Hz, 1H), 6.93 ppm (dd, J=10.1, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 12.79, 22.68, 22.89, 24.76, 25.48, 26.25, 26.94, 32.12, 33.08, 33.84, 137.84, 138.42, 140.98, 141.13, 187.81 ppm; HRMS (FAB): m/z: calcd for $C_{15}H_{23}O$: 219.1749, found 219.1742 $[M+H]^+$.

6-Methylene-3-phenyl-2-cyclohexen-1-one (3g): The reaction was carried out with 7.5 mol% **10** at 40°C; the crude mixture was purified by silica gel column chromatography (hexane/EtOAc 5:1) (31%): The reaction was also carried out with 2.5 mol% **11** at 100°C; the crude mixture was purified by PTLC on silica gel (hexane/EtOAc 4:1) (86%); m.p. 54–55°C; ^{1}H NMR ($CDCl_3$): δ = 2.86–2.88 (m, 4H), 5.35 (td, J=0.9, 0.7 Hz, 1H), 6.05 (t, J=0.9 Hz, 1H), 6.54 (d, J=0.7 Hz, 1H), 7.39–7.43 (m, 3H), 7.52–7.57 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 28.58, 31.01, 119.76, 126.12, 128.77, 130.08, 138.68, 141.97, 159.68, 188.72 ppm; HRMS (FAB): m/z: calcd for $C_{13}H_{12}O$: 185.0966, found 185.0972 $[M+H]^+$.

Procedures for the preparation of phenols 4

General procedure E (GP E, Table 2, entry 1): To a solution of **3** (0.170 mmol) in toluene (0.68 mL) was added DBU (0.170 mmol) under nitrogen. After stirring at 70°C for 24 h, the reaction mixture was concentrated under reduced pressure. The residue was worked up with 1 N aq HCl and extracted with EtOAc several times. The organic phases were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC on silica gel to give **4**.

General procedure F (GP F): A mixture of **3** (0.170 mmol) and 10 mol% *p*-toluenesulfonic acid monohydrate (0.017 mmol) in toluene (1.7 mL) was stirred at 70°C for 24 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by PTLC on silica gel to give **4**.

General procedure G (GP G): To a solution of **3** (0.170 mmol) in 2-propanol (1.7 mL) was added 10 mol% Pd/C (0.017 mmol Pd). The resulting mixture was stirred for 24 h at 70°C. The mixture was passed through Celite and concentrated under reduced pressure. The residue was purified by PTLC on silica gel to give **4**.

General procedure H (GP H): A mixture of **3** (0.180 mmol) and 10 mol% $RhCl_3$ (0.018 mmol) in 2-propanol (0.6 mL) and DMF (1.2 mL) was stirred at 100°C for 24 h. The reaction mixture was added to Et_2O and washed with water. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC on silica gel to give **4**.

General procedure I (GP I): A solution of $[RhCl(cod)]_2$ (0.00089 mmol) in dioxane (1 mL) was added to a solution of Cs_2CO_3 (0.180 mmol) in H_2O (0.6 mL). To the mixture were added **3** (0.178 mmol) and dioxane (0.2 mL). After stirring at 60°C for 5 h, the reaction mixture was worked up with brine and extracted with EtOAc several times. The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by PTLC on silica gel to give **4**.

2-Benzyl phenol (4a): The reaction was carried out according to the GP I; purified by PTLC on silica gel (hexane/EtOAc 4:1) (93%). The product was characterized by comparison of the spectroscopic data with those reported previously.[29]

2-(4-Chlorobenzyl)phenol (4b): The reaction was carried out according to the GP I; purified by PTLC on silica gel (hexane/EtOAc 5:2) (75%). M.p. 56–60°C; ^{1}H NMR ($CDCl_3$): δ = 3.95 (s, 2H), 4.67 (s, 1H), 6.76 (d, J=7.9 Hz, 1H), 6.89 (td, J=7.4, 1.2 Hz, 1H), 7.09 (d, J=7.3 Hz, 1H), 7.12 (dd, J=7.9, 1.6 Hz, 1H), 7.15 (d, J=8.3 Hz, 2H), 7.24 ppm (d, J=

8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 35.52, 115.57, 121.03, 126.66, 127.92, 128.57, 130.03, 130.89, 131.93, 138.65, 153.46 ppm; HRMS (FAB): *m/z*: calcd for $C_{13}H_{11}ClO$: 218.0498, found 218.0504 $[M]^+$.

4-Cyclohexyl-2-methyl-3-phenylphenol (4c): The reaction was carried out according to the GP F; purified by PTLC on silica gel (hexane/EtOAc 9:1) (77%). M.p. 58–61°C; ^{1}H NMR ($CDCl_3$): δ = 0.96–1.20 (m, 3H), 1.32 (qd, *J* = 12.5, 3.1 Hz, 2H), 1.55–1.68 (m, 5H), 1.88 (s, 3H), 2.15 (tt, *J* = 12.2, 3.1 Hz, 1H), 4.73 (s, 1H), 6.79 (d, *J* = 8.5 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.34 (tt, *J* = 7.6, 1.6 Hz, 1H), 7.40 ppm (t, *J* = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.49, 26.10, 26.83, 34.69, 40.29, 114.07, 121.81, 123.99, 126.58, 128.09, 129.18, 138.57, 140.66, 142.30, 151.33 ppm; HRMS (FAB): *m/z*: calcd for $C_{19}H_{22}O$: 266.1671, found 266.1676 $[M]^+$.

2-Methyl-6-phenylphenol (4d): The reaction was carried out according to the GP I; purified by PTLC on silica gel (hexane/EtOAc 4:1) (92%); This product was characterized by comparison of the spectroscopic data with those reported previously.[30]

2-Indol-1-ylmethyl-6-benzylphenol (4e): The reaction was carried out according to the GP I; purified by PTLC on silica gel (hexane/EtOAc 5:1) (69%). M.p. 72°C; ^{1}H NMR ($CDCl_3$): δ = 3.97 (s, 2H), 4.77 (s, 1H), 5.28 (s, 2H), 6.52 (dd, *J* = 3.2, 0.5 Hz, 1H), 6.73–6.82 (m, 2H), 7.03–7.35 (m, 10H), 7.63 ppm (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 36.89, 45.49, 77.27, 101.70, 109.79, 119.53, 120.98, 121.67, 124.65, 126.46, 127.04, 127.52, 128.30, 128.56, 128.71, 129.11, 130.50, 136.40, 138.61, 151.88 ppm; HRMS (FAB): *m/z*: calcd for $C_{22}H_{19}NO$: 313.1467, found: 313.1476 $[M]^+$.

4-Cyclohexyl-2-methyl-3-phenylphenol (4f): The reaction was carried out according to the GP G. purified by PTLC on silica gel (hexane/EtOAc 10:1) (86%). ^{1}H NMR ($CDCl_3$): δ = 1.23 (t, *J* = 7.5 Hz, 3H), 1.27–1.50 (m, 6H), 1.64–1.79 (m, 4H), 2.59 (q, *J* = 7.5 Hz, 2H), 2.70–2.74 (m, 2H), 2.78–2.84 (m, 2H), 4.65 (s, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 6.93 ppm (d, *J* = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.90, 22.91, 24.09, 24.94, 25.34, 26.62, 27.44, 29.15, 33.27, 121.78, 126.21, 126.39, 126.88, 141.33, 151.02 ppm; HRMS (FAB): *m/z*: calcd for $C_{15}H_{22}O$: 218.1671, found 218.1672 $[M]^+$.

2-Methyl-5-phenylphenol (4g): The reaction was carried out according to the GP I; purified by PTLC on silica gel (hexane/EtOAc 7:3) (95%); This product was characterized by comparison of the spectroscopic data with those reported previously.[31]

2-(4-Methoxybenzyl)-6-phenylphenol (4h) by Mizoroki–Heck reaction: To a mixture of 6-methylene-2-phenyl-2-cyclohexen-1-one (**3d**) (0.180 mmol) and 5 mol% palladium diacetate (9.0 μmol) in H_2O (0.36 mL) were added 4-methoxyphenyldiazonium tetrafluoroborate (**12**) (0.273 mmol) and acetonitrile (0.36 mL). After stirring at 60°C for 12 h, the mixture was added water and extracted with EtOAc several times. The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC on silica gel (hexane/EtOAc 5:1) to give **4h** (31.5 mg, 60%). ^{1}H NMR ($CDCl_3$): δ = 3.78 (s, 3H), 3.99 (s, 2H), 5.27 (s, 1H), 6.84 (dt, *J* = 7.3, 2.3 Hz, 2H), 6.92 (t, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.11 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.43–7.50 ppm (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 35.47, 55.19, 113.86, 120.39, 127.81, 128.12, 128.13, 128.27, 129.16, 129.24, 129.82, 130.10, 132.47, 137.25, 150.32, 157.95 ppm; HRMS (FAB): *m/z*: calcd for $C_{20}H_{18}O_2$: 290.1370, found 290.1303 $[M]^+$.

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