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Hydrogen-Mediated C−C Bond Formation: Catalytic Regio- and Stereoselective Reductive Condensation of α-Keto Aldehydes and 1,3-Enynes

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Abstract: Hydrogenation of 1,3-enynes in the presence of α-keto aldehydes using cationic Rh(I) catalysts enables regio- and stereoselective reductive coupling to the acetylenic terminus of the enyne to afford (*E*)-2-hydroxy-3,5-dien-1-one products. Reductive condensation of 1-phenyl but-3-en-1-yne **1a** with phenyl glyoxal **2a** performed under an atmosphere of D_2 provides the product of mono-deuteration, (*E*)-2-hydroxy-3-deuterio-3,5-dien-1-one *deuterio*-**3a**, in 85% yield. Competition experiments involving catalytic hydrogenation of phenyl glyoxal in the presence of equimolar quantities of 1,4-diphenylbutadiene and 1,4-diphenylbut-3-en-1-yne **10a**, as well as 1,4-diphenylbut-3-en-1-yne **10a** and 1,4-diphenylbutadiyne, are chemoselective for coupling to the more highly unsaturated partner, suggesting a preequilibrium involving precoordination and exchange of the π-unsaturated pronucleophiles with the catalyst prior to C−C bond formation, as well as a preference for coordination of the most π-acidic reacting partner, as explained by the Dewar−Chatt−Duncanson model for alkyne coordination.

Introduction

With the goal of developing a broad new class of hydrogen-mediated C−C bond formations, the electrophilic trapping of organometallic intermediates obtained in the course of catalytic hydrogenation has become the focus of intensive investigation in our laboratory.[1] Through implementation of cationic Rh-based catalyst systems, the hydrogen-mediated reductive coupling of enones,[1a,b] dienes,[1c] and diynes[1d] to carbonyl partners has been achieved, including a highly enantioselective variant of the latter transformation. In all cases, π-unsaturated products are formed under hydrogenation conditions without over-reduction. These new catalytic hydrogen-mediated C−C bond formations complement selectivities observed in related catalytic reductive couplings involving condensation of alkenes,[2] alkynes,[3] enones,[4,6] and dienes[5,6] to carbonyl partners. Moreover, as exemplified by alkene hydroformylation and related Fischer−Tropsch type processes,[7,8] prior to our studies, the trapping of hydrogenation intermediates through C−C bond formation hitherto has only been achieved through migratory insertion of carbon monoxide.

A unifying feature of these transformations appears to involve the formal heterolytic activation of elemental hydrogen by cationic rhodium catalysts ($H_2 + Rh^+X^- \rightarrow Rh{-}H + HX$).[9,10]

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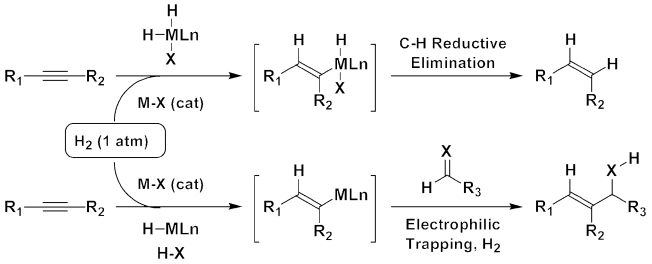
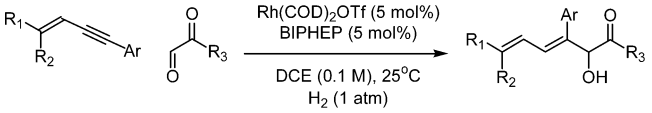
10.1021/ja0316566 CCC: $27.50

Scheme 1. Heterolytic Activation of Elemental Hydrogen Facilitates Electrophilic Trapping of Hydrogenation Intermediates



Heterolytic activation of elemental hydrogen is facilitated by cationic rhodium catalysts, due to the enhanced acidity of the dihydrides derived upon oxidative addition of hydrogen.[11] Deprotonation, or base-assisted reductive elimination, of cationic Rh(III)−dihydrides affords neutral Rh(I)−hydrides, which, in turn, enable mono-hydride-based catalytic cycles. In contrast to related dihydride-based catalytic cycles, mono-hydride-based catalytic cycles appear to attenuate ordinary "non-C−C bond forming" hydrogenation pathways, as direct alkyl-hydrogen reductive elimination manifolds are disabled (Scheme 1).[5,6]

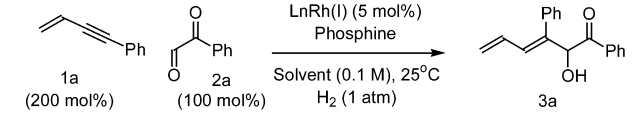
To further expand the scope of this uncommon reaction type, pronucleophile−electrophile combinations amenable to catalytic reductive coupling under hydrogenation conditions were sought. Here, we report that exposure of 1,3-enynes to α-keto aldehydes under the conditions of hydrogenation at ambient temperature and pressure results in regio- and stereoselective reductive coupling to afford (*E*)-2-hydroxy-3,5-dien-1-one products. The unsaturated products are formed under hydrogenation conditions without over-reduction.



Results

The development of efficient conditions for the reductive condensation of dienes and diynes to α-keto aldehydes under hydrogenation conditions supports the feasibility of related enyne-α-keto aldehyde couplings. To explore this prospect, 1-phenyl but-3-en-1-yne **1** was exposed to phenyl glyoxal under an atmosphere of hydrogen in the presence of various Rh(I) complexes. Applying conditions optimized for related diyne−glyoxal couplings,[1d] which involves use of $Rh(COD)_2OTf$ (5 mol %) and Ph_3P (10 mol %) in DCE (0.1 M) at ambient temperature and pressure, the enyne−glyoxal condensation product **3a** is obtained in only 3% yield (Table 1, entry 1). Under otherwise identical conditions, use of bidentate ligands such as *rac*-BINAP and BIPHEP provide diene **2a** in 85% and 86% yields, respectively (Table 1, entries 2 and 3). Reactions performed in THF and benzene provide comparable yields of reductive coupling product **3a** (Table 1, entries 4 and 5). Using $Rh(COD)_2BF_4$ as precatalyst, **3a** was obtaining in 87% yield (Table 1, entry 6). As anticipated on the basis of prior studies conducted in our lab,[1c,d] reductive coupling fails upon use of neutral Rh(I) sources, such as Wilkinson's catalyst and $[Rh(COD)Cl]_2$ (Table 1, entries 7 and 8). Notably, in all cases, the highly unsaturated diene-containing product **3a** is obtained without over-reduction and as a single regio- and stereoisomer. The structural assignment of diene **3a** is supported by single-crystal X-ray diffraction analysis of the corresponding *p*-nitrophenyl derivate **3h** (vide supra).

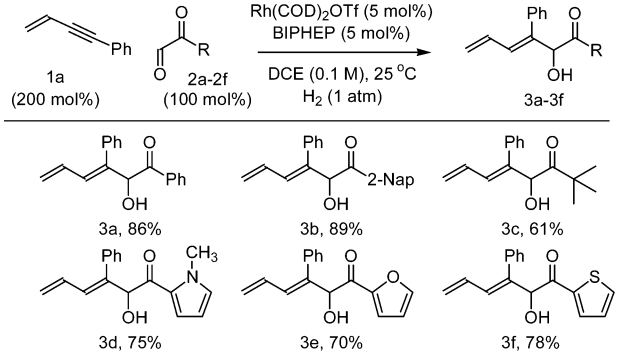
Table 1. Reductive Condensation of Enyne **1a** with Phenyl Glyoxal[a]



entry	rhodium source	ligand (mol %)	solvent	yield[b]
1	$Rh(COD)_2OTf$	Ph_3P (10%)	DCE	3%
2	$Rh(COD)_2OTf$	*rac*-BINAP (5%)	DCE	85%
3	$Rh(COD)_2OTf$	BIPHEP (5%)	DCE	86%
4	$Rh(COD)_2OTf$	BIPHEP (5%)	THF	85%
5	$Rh(COD)_2OTf$	BIPHEP (5%)	benzene	71%
6	$Rh(COD)_2BF_4$	BIPHEP (5%)	DCE	87%
7	$Rh(PPh_3)_3Cl$		DCE	–
8	$[Rh(COD)Cl]_2$	BIPHEP (5%)	DCE	–

[a] See Experimental Section for detailed procedures. [b] Isolated yields after purification by silica gel chromatography.

Table 2. Reductive Condensation of Enyne **1a** with Assorted Glyoxals[a,b]



[a] See Experimental Section for detailed procedures. [b] Isolated yields after purification by silica gel chromatography.

Under conditions optimized for the condensation of **1a** and phenyl glyoxal **2a** (Table 1, entry 3), the catalytic reductive coupling of **1a** to diverse glyoxal partners was explored. As demonstrated by the formation of dienes **3a**−**3c**, both aromatic and aliphatic glyoxals provide good yields of reductive coupling products. Heteroaromatic glyoxal partners also participate in the reaction, as evidenced by the formation of dienes **3d**−**3f**. Attempted condensation of enyne **1a** with simple aldehydes under these conditions does not provide reductive coupling products (Table 2).

Tolerance with respect to variation of the 1,3-enyne was investigated using phenyl glyoxal **2a** as the electrophilic partner. As demonstrated by the formation of dienes **3g**−**3j**, aromatic and heteroaromatic substitution is tolerated at the acetylenic terminus of the 1,3-enyne. As demonstrated by the formation of dienes **3k** and **3l**, aliphatic substitution is tolerated at the alkene terminus of the 1,3-enyne, independent of alkene geometry (Table 3).

Catalytic reductive condensation of enyne **1a** with phenyl glyoxal **2a** conducted under 1 atm of elemental deuterium provides the mono-deuterated product *deuterio*-**3a** in 85% yield. This result excludes pathways involving tandem alkyne hy-

(11) For a review of the acidity of metal hydrides, see: Norton, J. R. In *Transition Metal Hydrides*; Dedieu, A., Ed.; VCH Pub.: New York, 1992; Chapter 9.

Scheme 2. Catalytic Reductive Condensation of **1a** and **2a** Conducted under an Atmosphere of Elemental Deuterium: (Left) Proposed Catalytic Mechanism Based on Alkyne Hydrometalation; (Right) Proposed Catalytic Mechanism Based on Carbonyl Insertion

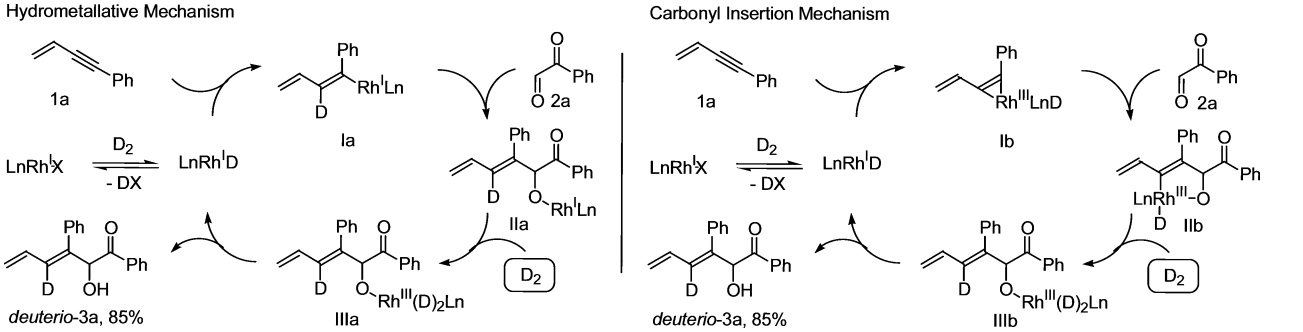
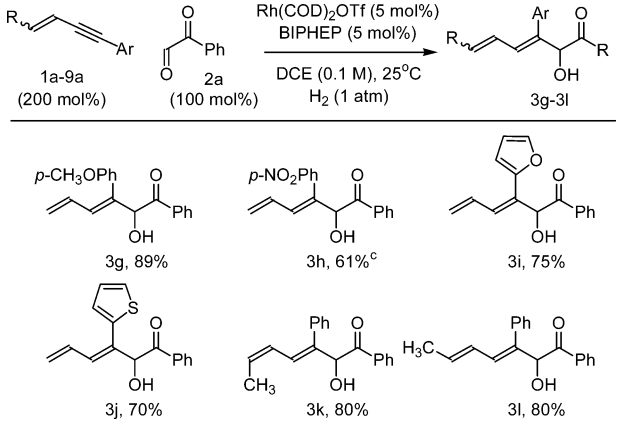
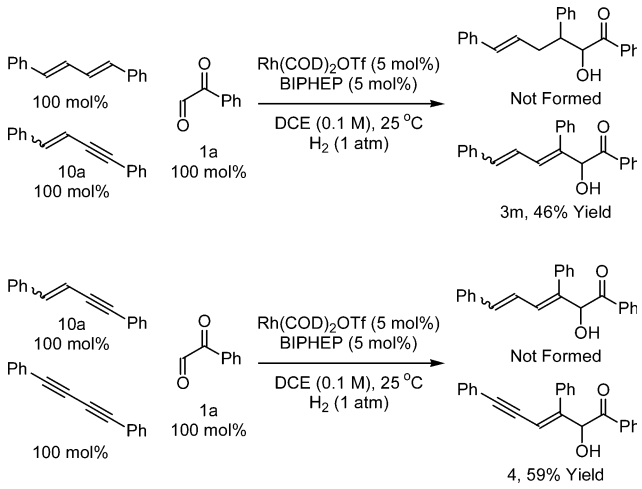


Table 3. Reductive Condensation of Assorted Enynes **1a**−**9a** with Phenyl Glyoxal **2a**[a,b]



[a] See Experimental Section for detailed procedures. [b] Isolated yields after purification by silica gel chromatography. [c] The structural assignment of **3h** is supported by single-crystal X-ray diffraction analysis.

Scheme 3. Competition Experiments



droacylation−carbonyl reduction.[12] A mechanism consistent with the results of the deuterium labeling experiment entails *deuterio*-metalation of alkyne to afford vinyl rhodium intermediate **Ia**. Carbonyl addition then affords alkoxy-rhodium intermediate **IIa**, which upon D_2-oxidative addition and oxygen−deuterium reductive elimination provides *deuterio*-**3a** along with LnRh(I)D to complete the catalytic cycle (Scheme 2, left). An alternative mechanism involves nucleophilic activation of the alkyne through coordination of low-valent rhodium. The resulting complex, which may be viewed as metallocyclopropene **Ib**, may insert phenyl glyoxal **2a** to afford the Rh(III)−oxametallocyclopentene **IIb**. Carbon−deuterium reductive elimination, followed by D_2-oxidative addition, gives complex **IIIb**, which upon oxygen−deuterium reductive elimination provides *deuterio*-**3a** along with LnRh(I)D to complete the catalytic cycle (Scheme 2, right).

The fact that products of over-reduction and over-addition are not observed under standard reaction conditions suggests a preequilibrium involving precoordination and exchange of the π-unsaturated precursors present in solution with the catalyst prior to C−C bond formation. To test this hypothesis, competition experiments were performed involving catalytic hydrogenation of phenyl glyoxal in the presence of equimolar quantities of 1,4-diphenylbutadiene and 1,4-diphenylbut-3-en-1-yne **10a**, as well as 1,4-diphenylbut-3-en-1-yne **10a** and 1,4-diphenylbutadiyne. In the former case, catalytic hydrogenation results in a 46% yield of the enyne reductive coupling product **3m**. Condensation products derived from 1,4-diphenylbutadiene were not formed. In the latter case, catalytic hydrogenation provides a 59% yield of the diyne reductive coupling product **4**. Condensation products derived from enyne **10a** were not formed (Scheme 3).

These results are consistent with the observation that low-valent late transition metals prefer to coordinate electron-deficient alkenes rather than electron-rich alkenes,[13] and the general notion that low-valent transition metals prefer ligands that are strong π-acids, as explained by the Dewar−Chatt−Duncanson model for alkyne coordination.[14,15] Thus, the chemo- and regioselectivity of C−C bond formation under hydrogenation conditions likely stems from the preference of low-valent rhodium to coordinate the reacting partner that is the strongest π-acid at the position that embodies the largest LUMO coefficient.

Conclusion

Since the discovery of catalytic hydrogenation over a century ago,[16,17] the interception of hydrogenation intermediates has only been achieved through migratory insertion of carbon monoxide.

(12) For a selected review on Rh-catalyzed alkene hydroacylation, see: Bosnich, B. *Acc. Chem. Res.* **1998**, *31*, 667.

(13) Stahl, S. S.; Thorman, J. L.; de Silva, N.; Guzei, I. A.; Clark, R. W. *J. Am. Chem. Soc.* **2003**, *125*, 12.

(14) (a) Dewar, M. J. S. *Bull. Soc. Chim. Fr.* **1951**, *18*, C71. (b) Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939.

(15) For a recent review, see: Frenking, G. *Mod. Coord. Chem.* **2002**, 111 and references therein.

(16) For the first example of catalytic homogeneous hydrogenation, see: Calvin, M. *Trans. Faraday Soc.* **1938**, *34*, 1181.

The present results, along with earlier studies from our lab, represent the first examples of the electrophilic trapping of hydrogenation intermediates. Future studies will be devoted to expanding the scope of this new reaction type through the development of improved second generation catalyst systems with the goal of achieving the catalytic coupling of unactivated alkenes and alkynes to simple carbonyl partners.

Experimental Section

General. All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Dichloroethane was distilled from calcium hydride. Substrates **1a**−**10a**,[18] **2a**−**2f**,[19] and **4**[1d] were prepared according to the previously reported procedures. Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Krieselgel 60 F_{254}). Preparative column chromatography employing silica gel was performed according to the method of Still.[20] Solvents for chromatography are listed as volume/volume ratios. Infrared spectra were recorded on a Perkin-Elmer 1420 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as *m*/*z* (relative intensity). Accurate masses are reported for the molecular ion (M + 1) or a suitable fragment ion. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Mercury (400 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Mercury 400 (100 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadbrand decoupling.

Representative Procedure for the Reductive Coupling of Enynes and Glyoxals. To a solution of phenyl glyoxal monohydrate (152 mg, 1 mmol, 100 mol %) and enyne **1a** (256 mg, 2 mmol, 200 mol %) in DCE (0.1 M) at ambient temperature were added $Rh(COD)_2OTf$ (23.4 mg, 0.05 mmol, 5 mol %) and BIPHEP (26 mg, 0.05 mmol, 5 mol %). The system was purged with hydrogen gas, and the reaction was allowed to stir until the glyoxal was complete consumed, at which point the reaction mixture was evaporated onto silica gel. Purification by silica gel chromatography using an eluant composed of ethyl acetate−hexane affords the product of reductive condensation.

2-Hydroxy-1,3-diphenyl-hexa-3,5-dien-1-one (3a). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84 (m, 2H), 7.56 (m, 1H), 7.40 (m, 2H), 7.25 (m, 3H), 7.04 (m, 2H), 6.46 (d, J = 11.2 Hz, 1H), 6.21 (m, 1H), 5.67 (d, J = 6.4 Hz, 1H), 5.37 (ddd, J = 16.8, 1.6, 0.4 Hz, 1H), 5.12 (ddd, J = 0.4, 1.6, 10.0 Hz, 1H), 4.32 (d, J = 6.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 140.6, 136.7, 133.9, 133.8, 133.4, 133.2, 129.2, 128.8, 128.5, 128.1, 127.7, 120.3, 78.6. IR (NaCl): 3428, 1678, 1642, 1448, 1262, 1089, 1001, 972, 917 cm^{-1}. HRMS: calcd for $C_{18}H_{16}O_2$ [M] 264.1150, found 264.1140.

***deuterio*-2-Hydroxy-1,3-diphenyl-hexa-3,5-dien-1-one (*deuterio*-3a).** ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (m, 2H), 7.53 (m, 1H), 7.37 (m, 2H), 7.24 (m, 3H), 7.04 (m, 2H), 6.21 (dd, J = 10.0, 16.8 Hz, 1H), 5.68 (s, 1H), 5.33 (dd, J = 2.0, 17.2 Hz, 1H), 5.10 (dd, J = 2.0, 10.0 Hz, 1H), 4.38 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 140.5, 136.6, 133.8, 133.7, 133.3, 129.1, 128.7, 128.5, 128.0, 127.6, 120.2, 78.5. IR (NaCl): 3431, 1673, 1643, 1259, 1088, 964 cm^{-1}. HRMS: calcd for $C_{18}H_{15}D_1O_2$ [M + 1] 266.1291, found 266.1283.

2-Hydroxy-1-naphthalen-2-yl-3-phenyl-hexa-3,5-dien-1-one (3b). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28 (s, 1H), 7.91 (dd, J = 1.6, 8.4 Hz, 1H), 7.83 (m, 2H), 7.77 (dd, J = 0.8, 8.4 Hz, 1H), 7.59 (m, 1H), 7.51 (m, 1H), 7.25 (m, 3H), 7.09 (m, 2H), 6.52 (d, J = 10.8 Hz, 1H), 6.23 (m, 1H), 5.82 (d, J = 5.6 Hz, 1H), 5.34 (ddd, J = 0.4, 1.6, 16.8 Hz, 1H), 5.06 (ddd, J = 0.8, 2.0, 9.6 Hz, 1H), 4.67 (d, J = 6.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.2, 140.8, 136.9, 135.8, 133.4, 133.0, 132.1, 131.2, 130.9, 129.7, 129.2, 128.9, 128.4, 128.2, 127.7, 127.70, 126.9, 124.0, 120.4, 78.6. IR (NaCl): 3430, 1674, 1628, 1352, 1281, 1086 cm^{-1}. HRMS calcd for $C_{22}H_{18}O_2$ [M + 1] 315.1385, found 315.1385.

4-Hydroxy-2,2-dimethyl-5-phenyl-octa-5,7-dien-3-one (3c). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (m, 5H), 6.36 (m, 1H), 6.20 (d, J = 10.9 Hz, 1H), 3.24 (dd, J = 1.7, 16.8 Hz, 1H), 5.18 (dd, J = 2.1, 10.3 Hz, 1H), 5.15 (d, J = 7.5 Hz, 1H), 3.90 (d, J = 7.9 Hz, 1H), 1.14 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 215.2, 140.1, 137.8, 133.7, 132.6, 129.3, 128.5, 128.0, 120.9, 77.7, 43.4, 27.4, 27.4. IR (NaCl): 3358, 2931, 2859, 1464, 1378, 1341, 1303, 1161, 1130, 953, 871, 725 cm^{-1}. HRMS calcd for $C_{16}H_{21}O_2$ [M + 1] 245.1542, found 245.1535.

2-Hydroxy-1-(1-methyl-1*H*-pyrrol-2-yl)-3-phenyl-hexa-3,5-dien-1-one (3d). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27 (m, 3H), 7.08 (m, 2H), 6.89 (dd, J = 1.7, 4.1 Hz, 1H), 6.83 (t, J = 1.7 Hz, 1H), 6.49 (d, J = 10.9 Hz, 1H), 6.22 (m, 1H), 6.08 (dd, J = 2.4, 4.1 Hz, 1H), 5.40 (d, J = 6.2 Hz, 1H), 5.35 (dd, J = 1.7, 17.1 Hz, 1H), 5.10 (dd, J = 1.7, 10.1 Hz, 1H), 4.37 (d, J = 6.5 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.7, 142.6, 137.1, 134.0, 132.6, 132.2, 129.6, 128.2, 128.0, 127.7, 121.1, 119.9, 109.0, 78.3, 37.8. IR (NaCl): 3053, 2958, 2926, 2871, 2305, 1645, 1527, 1408, 1265, 1061, 946, 896, 740 cm^{-1}. HRMS calcd for $C_{17}H_{17}NO_2$ [M + 1] 268.1338, found 268.1340.

1-Furan-2-yl-2-hydroxy-3-phenyl-hexa-3,5-dien-1-one (3e). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56 (m, 1H), 7.28 (m, 3H), 7.16 (m, 1H), 7.10 (m, 3H), 6.51 (m, 2H), 6.24 (m, 1H), 5.47 (d, J = 6.4 Hz, 1H), 5.36 (ddd, J = 16.8, 1.6, 0.4 Hz, 1H), 5.12 (ddd, J = 0.4, 2.0, 10.0 Hz, 1H), 4.08 (d, J = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 186.6, 150.0, 147.3, 140.2, 136.4, 133.4, 132.8, 129.2, 128.0, 127.6, 120.2, 119.6, 112.4, 78.4. IR (NaCl): 3401, 1658, 1465, 1384, 1291, 1080, 1025, 957 cm^{-1}. HRMS calcd for $C_{16}H_{14}O_3$ [M + 1] 255.1021, found 255.1011.

2-Hydroxy-3-phenyl-1-thiophen-2-yl-hexa-3,5-dien-1-one (3f). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66 (m, 2H), 7.27 (m, 3H), 7.09 (m, 3H), 6.55 (d, J = 10.8 Hz, 1H), 6.25 (m, 1H), 5.50 (d, J = 5.2 Hz, 1H), 5.39 (ddd, J = 17.2, 2.0, 0.8 Hz, 1H), 5.15 (ddd, J = 0.8, 1.6, 10.4 Hz, 1H), 4.20 (d, J = 5.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.8, 140.8, 139.6, 136.6, 134.9, 133.8, 133.4, 133.38, 129.3, 128.2, 128.1, 127.7, 120.5, 79.5. IR (NaCl): 3413, 2097, 1657, 1515, 1413, 1353, 1265, 1092, 1058, 997 cm^{-1}. HRMS calcd for $C_{16}H_{14}O_2S_1$ [M + 1] 271.0793, found 271.0802.

2-Hydroxy-3-(4-methoxy-phenyl)-1-phenyl-hexa-3,5-dien-1-one (3g). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (m, 2H), 7.52 (m, 1H), 7.37 (m, 2H), 6.96 (m, 2H), 6.76 (m, 2H), 6.41 (d, J = 11.2 Hz, 1H), 6.23 (m, 1H), 5.63 (d, J = 5.6 Hz, 1H), 5.31 (dd, J = 1.6, 16.8 Hz, 1H), 5.08 (dd, J = 1.6, 10.0 Hz, 1H), 4.33 (d, J = 6.4 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.5, 159.0, 140.3, 133.79, 133.76, 133.5, 133.0, 130.3, 128.9, 128.8, 128.5, 119.9, 113.5, 78.8, 55.1. IR (NaCl): 3444, 1678, 1640, 1608, 1510, 1462, 1449, 1288, 1249, 1178, 1089 cm^{-1}. HRMS calcd for $C_{19}H_{18}O_3$ [M] 294.1256, found 294.1268.

2-Hydroxy-3-(4-nitro-phenyl)-1-phenyl-hexa-3,5-dien-1-one (3h). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06 (dt, J = 2.1, 8.9 Hz, 2H), 7.82 (m, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 10.9 Hz, 1H), 6.06 (m, 1H), 5.70 (d, J = 5.5 Hz, 1H), 5.42 (dd, J = 1.0, 16.8 Hz, 1H), 5.19 (dd, J = 1.0, 10.3 Hz, 1H), 4.37 (d, J = 5.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.3, 147.5, 143.7, 138.6, 135.3, 134.6, 133.8, 132.6, 130.5, 129.1, 129.0, 123.5, 122.7, 78.6. IR (NaCl): 3055, 2985, 2305, 1681, 1599,

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1520, 1347, 1265, 1107, 737 cm^{-1}. HRMS calcd for $C_{18}H_{16}NO_4$ [M + 1] 310.1079, found 310.1073.

3-Furan-2-yl-2-hydroxy-1-phenyl-hexa-3,5-dien-1-one (3i). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.89 (m, 2H), 7.52 (m, 1H), 7. 40 (m, 3H), 7.01 (m, 1H), 6.42 (m, 2H), 6.23 (d, J = 10.9 Hz, 1H), 5.72 (d, J = 5.8 Hz, 1H), 5.38 (m, 1H), 5.28 (m, 1H), 4.42 (d, J = 5.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1, 151.3, 142.8, 134.2, 133.9, 132.4, 129.0, 128.9, 128.9, 122.3, 111.6, 111.3, 76.8. IR (NaCl): 3053, 2959, 2928, 2361, 2338, 2306, 1717, 1265, 947, 740 cm^{-1}. HRMS calcd for $C_{16}H_{15}O_3$ [M + 1] 255.1021, found 255.1014.

2-Hydroxy-1-phenyl-3-thiophen-2-yl-hexa-3,5-dien-1-one (3j). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.87 (dd, J = 1.4, 8.2 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.9 Hz, 2H), 7.26 (dd, J = 1.0, 5.1 Hz, 1H), 6.92 (dd, J = 3.4, 5.1 Hz, 1H), 6.78 (dd, J = 1.0, 3.4 Hz, 1H), 6.56 (m, 2H), 5.66 (d, J = 5.8, 1H), 5.42 (m, 1H), 5.22 (m, 1H), 4.48 (d, J = 5.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 136.9, 135.4, 134.2, 133.9, 133.7, 133.6, 129.1, 128.9, 128.3, 127.0, 126.7, 121.8, 79.2. IR (NaCl): 3054, 2959, 2928, 2305, 1681, 1460, 1422, 1379, 1265, 739 cm^{-1}. HRMS calcd for $C_{16}H_{15}O_2S$ [M + 1] 271.0793, found 271.0786.

2-Hydroxy-1,3-diphenyl-*cis*-hepta-3,5-dien-1-one (3k). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84 (m, 2H), 7.53 (m, 1H), 7.37 (m, 2H), 7.23 (m, 3H), 7.03 (m, 2H), 6.77 (d, J = 11.2 Hz, 1H), 5.87 (tq, J = 1.8, 11.2 Hz, 1H), 5.72 (s, 1H), 5.52 (m, 1H), 4.38 (s, 1H), 1.79 (dd, J = 1.6, 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 139.4, 136.8, 133.9, 133.7, 129.6, 129.2, 128.8, 128.4, 128.0, 127.4, 125.7, 78.9, 13.5. IR (NaCl): 3451, 3058, 3031, 2991, 2929, 1681, 1598, 1448, 1381, 1260, 1088, 967 cm^{-1}. HRMS calcd for $C_{19}H_{18}O_2$ [M] 278.1307, found 278.1310.

2-Hydroxy-1,3-diphenyl-*trans*-hepta-3,5-dien-1-one (3l). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84 (m, 2H), 7.50 (m, 1H), 7.35 (m, 2H), 7.23 (m, 3H), 7.06 (m, 2H), 6.41 (d, J = 10.4 Hz, 1H), 5.94 (m, 1H), 5.82 (m, 1H), 5.65 (d, J = 6.0 Hz, 1H), 4.35 (d, J = 6.0 Hz, 1H), 1.63 (dd, J = 1.2, 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 137.3, 137.0, 133.8, 133.6, 133.2, 132.9, 129.1, 128.7, 128.4, 127.9, 127.3, 78.7, 18.2. IR (NaCl): 3473, 3058, 3028, 2931, 2912, 1681, 1648, 1598, 1578, 1492, 1447, 1380, 1259, 1098, 1075, 971 cm^{-1}. HRMS calcd for $C_{19}H_{18}O_2$ [M] 278.1307, found 278.1305.

2-Hydroxy-1,3,6-triphenyl-hexa-3,5-dien-1-one (3m). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.83 (m, 2H), 7.56 (m, 1H), 7.41 (m, 2H), 7.31 (m, 4H), 7.17 (m, 6H), 6.79 (dd, J = 0.8, 11.2 Hz, 0.34 × 1H), 6.63 (m, 0.66 × 3H), 6.44 (d, J = 11.6, 0.34 × 1H), 6.09 (m, 0.34 × 1H), 5.71 (m, 1H), 4.40 (d, J = 6.4 Hz, 0.66 × 1H), 4.30 (d, J = 6.0 Hz, 0.34 × 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 198.37, 142.0, 140.3, 137.0, 136.9, 136.86, 136.77, 135.5, 133.9, 133.89, 133.83, 133.80, 132.83, 132.7, 129.3, 129.2, 129.0, 128.97, 128.8, 128.6, 128.5, 128.49, 128.2, 128.19, 128.13, 127.9, 127.7, 127.4, 126.6, 126.4, 125.3, 78.8, 78.6. IR (NaCl): 3029, 1681, 1597, 1448, 1261, 1087, 968, 752, 699 cm^{-1}. HRMS calcd for $C_{24}H_{20}O_2$ [M + 1] 341.1542, found 341.1539.

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Supporting Information Available: Spectral data for all new compounds (^1H NMR, ^{13}C NMR, IR, HRMS) (PDF). X-ray crystallographic data for compound **3h** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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