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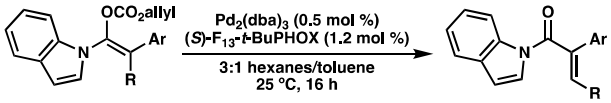
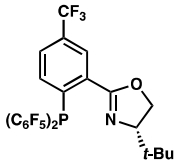


9 examples
up to >99% yield
and up to >20:1 E/Z



(S)-F$_{13}$-t-BuPHOX
newly developed electron deficientPHOX ligand

Palladium-catalyzed α,β-dehydrogenation of acyclic ester equivalents promoted by a novel electron deficient phosphinooxazoline ligand

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Abstract

A unique example of Pd-catalyzed decarboxylative dehydrogenation of fully substituted *N*-acyl allyl enol carbonates is enabled by a new electron deficient phosphinooxazoline (PHOX) ligand. The reaction proceeds from the *Z*-enol carbonate to provide dehydrogenation products exclusively in high *E*/*Z* selectivity, while the *E*-enol carbonate provides the α-allylation product with only minor dehydrogenation. The reaction proceeds with a broad scope of (*Z*)-enol carbonates derived from *N*-acyl indoles to furnish acyclic formal α,β-unsaturated ester equivalents.

Dedicated to Professor John F. Hartwig on his receipt of the Tetrahedron Prize.

Keywords:
Dehydrogenation;
Palladium
PHOX ligand

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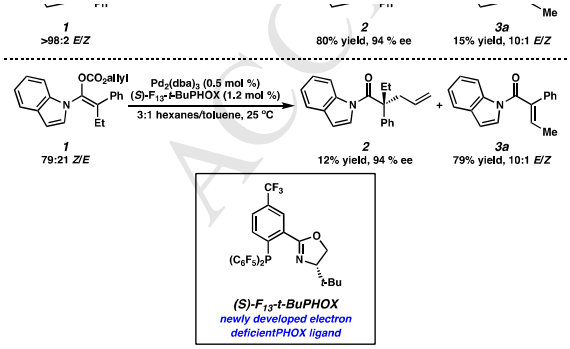
Introduction

Our lab has recently become interested in developing palladium-catalyzed asymmetric allylic alkylation reactions of acyclic stereodefined fully substituted enol carbonates to generate acyclic quaternary stereogenic centers. In our initial efforts, we reported the application of a highly *E*-selective enolization[1] of acylic α-aryl ketones to generate stereodefined fully substituted acyclic ketone enol carbonates which we employed in a highly enantioselective Pd-catalyzed allylic alkylation to generate all carbon quaternary centers.[2] More recently, we became intrigued by the possibility of extending this reactivity toward acyclic ester enolate equivalents to generate α-quaternary carboxylic acid derivatives. In our initial optimization of this transformation, we investigated new electron deficient phosphinooxazoline (PHOX) ligands with *N*-acyl hetereocycle derived enol carbonates as ester enolate equivalents. To our delight, we found that the combination of *N*-acyl indole derived enol carbonate **1** and fluorinated ligand *(S)-F_{13}-t-BuPHOX* afforded allylation product **2** in an excellent 94% ee and promising 80% yield (Scheme 1). Further investigation of this reaction revealed that despite excellent conversion of **1**, allylation product **2** was isolated in only 80% yield with a 15% yield of α,β-unsaturation product **3a**. Surprisingly, when a 79:21 *Z*/*E* mixture of enol carbonate **1** was utilized, α,β-unsaturation product **3a** predominated, suggesting a preference for the *Z*-enol carbonate to undergo α,β-dehydrogenation rather than a standard α-alkylation. Control experiments revealed that the reaction does not proceed in the absence of *(S)-F_{13}-t-BuPHOX* ligand with either enol carbonate mixture, instead providing >95% recovery of the starting material with unaffected *E*/*Z* enol carbonate ratios. The high synthetic value of α,β-unsaturated carboxylic acids and their derivatives coupled with the limited synthetic methods which enable access to this motif prompted further investigation of this unusual reactivity with our newly synthesized fluorinated PHOX ligand.

Numerous distinct strategies have been developed to access α,β-unsaturated moieties from carbonyl and carboxylic acid motifs including selenium,[3] sulfur,[4] hypervalent iodine,[5] and quinone[6] based transformations, as well as palladium catalyzed dehydrogenations.[7] One-step allyl-palladium catalyzed dehydrogenations have recently been developed by Newhouse, with pioneering studies from Tsuji,[8] as an effective method to generate α,β-unsaturated carbonyls,[9] carboxylic acids,[10] and carboxylic acid derivatives,[11] however, there are limited examples regarding acyclic systems bearing α-substitution, especially in high *E*/*Z* selectivity. Moreover, to the best of our knowledge, this is the first example of an electron deficient PHOX ligand promoting dehydrogenation reactivity with an allyl-palladium species. This new reactivity complements the available methodology for the generation of α,β-unsaturated compounds and could serve as a new avenue for methodology development in the α,β-unsaturation of carbonyl compounds.

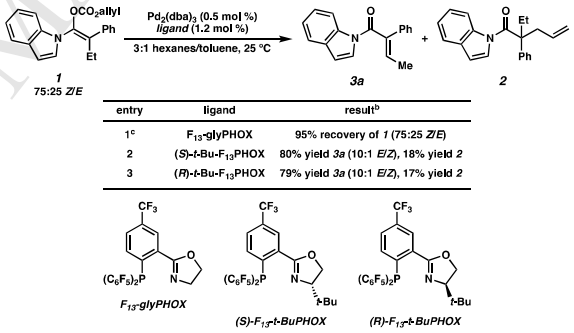
Scheme 1. Initial reaction discovery.



2. Results and discussion

We began our investigation with an examination of the ligand system (Table 1). To our surprise, when analogous achiral *F_{13}-glyPHOX* ligand was employed, no reaction occurred even with elevated reaction temperatures of up to 60 °C (Table 1, entry 1). Though the *t*-Bu group was

Table 1. Investigation of the ligand.[a]

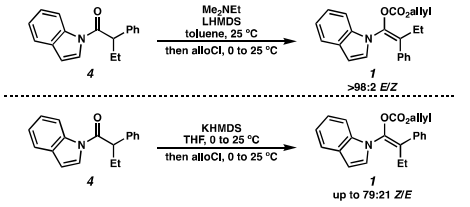


entry	ligand	result[b]
1[c]	F_{13}-glyPHOX	95% recovery of *1* (75:25 *Z*/*E*)
2	(*S*)-*t*-Bu-F_{13}PHOX	80% yield *3a* (10:1 *E*/*Z*), 18% yield *2*
3	(*R*)-*t*-Bu-F_{13}PHOX	79% yield *3a* (10:1 *E*/*Z*), 17% yield *2*

Conditions: [a] 0.2 mmol substrate, 0.5 mol % $Pd_2(dba)_3$, 1.2 mol % ligand, 2.0 mL solvent, 25 °C. [b] Yields of isolated products. *E*/*Z* ratios measured by ^{1}H NMR integration.

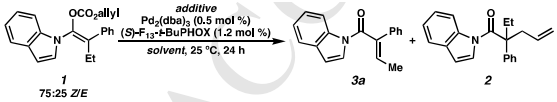
required on the ligand scaffold, both enantiomeric series of the *F_{13}-t-BuPHOX* provided α,β-dehydrogenation product **3a** in essentially identical yield and *E*/*Z* selectivity (entries 2 and 3). These results demonstrate that this unique resolution of the enol carbonate geometries is likely the result of the electron withdrawing nature of the *F_{13}-t-BuPHOX* ligand in combination with the preference for dehydrogenation of the *Z*-enol carbonate. While the *E*-enol carbonate can be obtained with excellent selectivity (generally >98:2) utilizing previously reported selective enolization conditions[1a], selective formation of the *Z*-enol carbonate is more challenging with modest selectivity of 79:21 *Z*/*E* obtained in THF with KHMDS as the base (Scheme 2).

Scheme 2. *E*- and *Z*-selective enol carbonate formation.



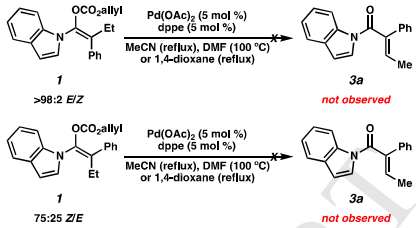
Subsequent optimization of the reaction aimed to identify conditions which favored dehydrogenation for both enol carbonate geometries. Other solvents common for dehydrogenation reactions were examined, but provided no improvement over the 3:1 hexanes/toluene solvent system (Table 2, entries 1–6). With either toluene or MTBE as a solvent full conversion of **1** is observed, albeit with lower selectivity for dehydrogenation product **3a** over alkylation product **2** compared with 3:1 hexanes/toluene (entries 2 and 3). In THF, the reaction becomes sluggish and 65% of the enol carbonate mixture is recovered after 24 h with no change in the ratio of enol carbonates (entry 4). Polar, aprotic solvents such as DMF and MeCN utilized in allyl-palladium catalyzed dehydrogenation by Tsuji[8] provide no reaction (entries 5 and 6). Newhouse and co-workers have previously demonstrated the application of zinc salts to disfavor allylation via a postulated transmetalation to afford a less nucleophilic zinc enolate in allyl-palladium catalyzed dehydrogenations.[9–11] To our disappointment, the incorporation of $ZnCl_2$ in our reaction conditions as a stoichiometric additive stymies both allylation and dehydrogenation pathways (entry 7). Heating the reaction with a 75:25 *Z*/*E* mixture of **1** to 60 ºC also fails to promote any measurable level of conversion. Notably, when $ZnCl_2$ is used with a >98:2 *E*/*Z* mixture of enol carbonates, trace conversion to the allylation product is observed after prolonged heating (>24 h) at 60 ºC, further exemplifying the importance of enolate geometry in this transformation. In addition, we found *N*-acyl indole derived enol carbonate **1** was incompatible with Tsuji's classic decarboxylative dehydrogenation conditions,[8a] instead providing complex mixtures of decarboxylative allylation and protonation with recovered enol carbonate (Scheme 3).

Table 2. Optimization of the Pd-catalyzed dehydrogenation.



entry	solvent	additive	result[b]
1	3:1 hexanes/toluene	none	80% yield *3a* (10:1 *E*/*Z*), 18% yield *2*
2	toluene	none	70% yield *3a* (10:1 *E*/*Z*), 26% yield *2*
3[c]	MTBE	none	71% yield *3a* (10:1 *E*/*Z*), 28% yield *2*
4	THF	none	65% recovery of *1* (75:25 *Z*/*E*)
5	DMF	none	94% recovery of *1* (75:25 *Z*/*E*)
6	MeCN	none	92% recovery of *1* (75:25 *Z*/*E*)
7	3:1 hexanes/toluene	$ZnCl_2$ (6.0 equiv)	92% recovery of *1* (75:25 *Z*/*E*)
8[d]	3:1 hexanes/toluene	$ZnCl_2$ (6.0 equiv)	94% recovery of *1* (75:25 *Z*/*E*)

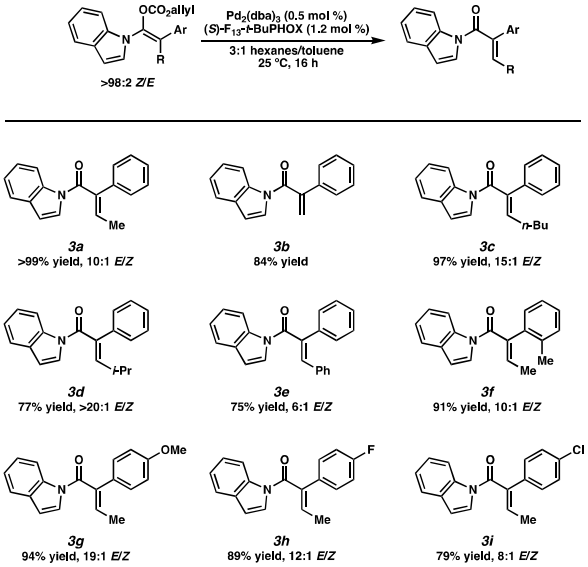
Conditions: [a] 0.2 mmol substrate, 0.5 mol % $Pd_2(dba)_3$, 1.2 mol % ligand, 2.0 mL solvent, 25 °C, 24 h reaction time. [b] Yields of isolated products. *E*/*Z* ratios measured by ^1H NMR integration. [c] Incomplete conversion. [d] Reaction performed at 40 ºC. [e] Reaction performed at 60 ºC.



Bereft of reaction conditions favoring dehydogenation for both enolate geometries, we examined the reaction scope with pure *Z*-enol carbonates to simplify reaction analysis and product purification. A variety of *N*-acyl indoles were enolized using *Z*-selective conditions (vide supra) and trapped as the corresponding allyl enol carbonates. The geometrically pure *Z*-enol carbonates were then isolated by preparative chromatography and subjected to our standard reaction conditions (Table 3). Pleasingly, a broad range of alkyl and aryl group substitutions were well tolerated under the reaction conditions and α,β-unsaturated products were obtained in high yield and excellent *E*-selectivity. With pure *Z*-enol carbonate **1**, product **3a** was obtained in >99% yield and in 10:1 *E*/*Z* selectivity. Unsubstituted compound **3b** was obtained in 84% yield despite elevated potential to undergo intermolecular conjugate addition during the course of the reaction. Longer alkyl chains were well tolerated with *n*-butyl product **3c** isolated in 97% yield and 15:1 *E*/*Z* selectivity. Sterically encumbered *i*-propyl product **3d** was also well tolerated with >98:2 *E* selectivity, albeit in a diminished 77% yield. Product **3e** bearing 1,2- diphenyl substitution could be obtained in 75% yield and 6:1 *E*/*Z* selectivity. A variety of aryl groups were also compatible with the dehydrogenation reaction. Notably, *ortho*-substituted product **3f** was obtained in an excellent 91% yield and 10:1 *E*/*Z* selectivity. Electron rich *p*-OMe-C_6H_4 aryl compound **3g** was isolated in an excellent 94% yield and 18:1 *E*/*Z* selectivity. Finally, products with electron poor aryl groups *p*-F-C_6H_4 (**3h**) and *p*-Cl-C_6H_4 (**3i**) were also obtained in high yields (89% and 79% yield, respectively) and excellent *E*-selectivity (12:1 and 8:1 *E*/*Z*, respectively).

While we were pleased with the scope of α,β-unsaturated *N*-acyl indoles afforded by the Pd-catalyzed decarboxylative dehydrogenation, we ultimately desired to extend this methodology toward a general manifold of carbonyl compounds. In these initial efforts, we deternubed this reaction was unsuccessful with other substrates commonly utilized in Pd-catalyzed asymmetric decarboxylative allylic alkylation in our laboratory (Figure 1). Cyclic allyl enol carbonate **4** and β-ketoesters **5**–**7** failed to convert to either allylation or dehydrogenation products with these reaction conditions. Even with the

Table 3. Substrate scope of the Pd-catalyzed decarboxylative dehydrogenation.[a]



analogous acyclic phenyl ketone derived allyl enol carbonate **8** (75:25 *Z*/*E*) no conversion was observed. Future efforts will be directed toward investigation of the

[a] Conditions: 0.2 mmol substrate, 0.5 mol % $Pd_2(dba)_3$, 1.2 mol % ligand, 2.0 mL solvent, 25 °C, 16 h reaction time. Yields of isolated product. Product *E*/*Z* ratios were measured by ^1H NMR integration.

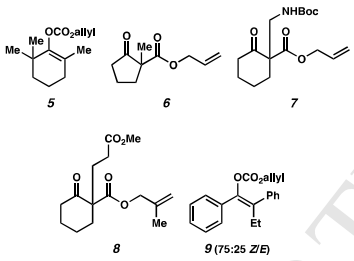


Figure 1. Unsuccessful substrates for the Pd-catalyzed decarboxylative dehydrogenation.

dehydrogenation reaction with substrate classes unsuccessful in this unique system toward a more general transformation and understanding the nature of the ligand promoted dehydrogenation.

We posit a plausible catalytic cycle for this transformation can proceed as shown in Figure 2 where the allyl group of the enol carbonate ultimately serves as a hydride acceptor. A ligated Pd^0 species can undergo oxidative addition to allyl enol carbonate **1**, generating palladium carboxylate **9**. Subsequent decarboxylation produces allyl palladium complex **10** and enolate **11** which can form carbon-bound palladium enolate **12**. At this stage, β-hydride elimination can occur to furnish product **3a** and palladium hydride **13**. Finally, reductive elimination of **13** regenerates the Pd^0 species and generates propene as a by-product.

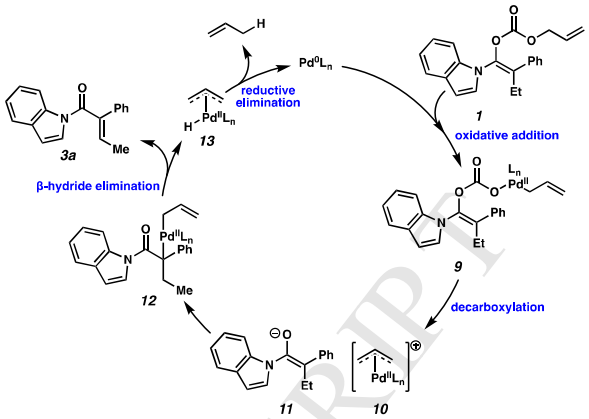


Figure 2. Plausible catalytic cycle.

3. Conclusion and outlook

In summary, we have developed the first example of an allyl-palladium catalyzed decarboxylative dehydrogenation reaction of fully substituted *N*-acyl indole derived allyl enol carbonates promoted by a newly developed electron deficient PHOX ligand. The reaction was quite general with respect to *N*-acyl indole derived allyl enol carbonates and occurs only with F_{13}-*t-BuPHOX* ligand. Other substrate classes typically utilized in decarboxylative allylic alkylation in our laboratory proved unreactive. Future efforts will aim to probe the nature of this unusual resolution of enolate geometries and expand this methodology into a more general transformation for α,β-dehydrogenation. Ultimately, this methodology provides new precedent for ligand controlled selectivity of dehydrogenation over allylic alkylation with allyl-palladium catalysis.

4. Selected experimentals

4.1 General

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. The *Z*-enol carbonates were purified by

preparative LC on a Teledyne Isco ACCQPrep HP125; column: C–18, 100 Å, 5 μm, ID 20 mm. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell. High resolution mass spectra (HRMS) were obtained from Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+). Reagents were purchased from commercial sources and used as received unless otherwise stated.

4.2 General procedure for dehydrogenation

A representative procedure for the decarboxylative dehydrogenation of *N*-acyl indole derived enol carbonates:

In a nitrogen-filled glovebox, a solution of $Pd_2(dba)_3$ (1.8 mg/mL) and (*S*)-F_{13}-*t*-BuPHOX (2.8 mg/mL) in toluene was stirred for 30 min at 25 °C, then 0.5 mL of the resulting catalyst solution was added to a one dram vial containing the allyl enol carbonate substrate (0.2 mmol) dissolved in hexanes (1.5 mL). The vial was sealed with a Teflon-lined cap, removed from the glovebox, and stirred at 25 °C for 16 h unless noted otherwise. The crude reaction mixture was concentrated then purified by silica gel flash chromatography to provide the desired dehydrogenation product.

4.2.1 (*E*)-1-(1*H*-indol-1-yl)-2-phenylbut-2-en-1-one (3a)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (52.1 mg, 0.199 mmol, >99% yield, 10:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.54 (dq, *J* = 7.6, 0.8 Hz, 1H), 7.43–7.27 (m, 8H), 6.50 (dd, *J* = 3.8, 0.7 Hz, 1H), 6.46 (q, *J* = 7.2 Hz, 1H), 1.99 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 138.0, 136.0, 134.9, 134.6, 130.8, 129.1, 128.8, 128.2, 127.2, 125.6, 125.0, 123.9, 120.9, 116.7, 108.5, 15.3; IR (Neat Film, NaCl) 3054, 2918, 2854, 1682, 1585, 1535, 1495, 1472, 1451, 1385, 1359, 1331, 1240, 1204, 1158, 1144, 1079, 1016, 946, 881, 815, 752, 703 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{16}NO$ $[M+H]^+$: 262.1226, found 262.1222.

4.2.2 1-(1*H*-indol-1-yl)-2-phenylprop-2-en-1-one (3b)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (41.4 mg, 0.167 mmol, 84% yield);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57–8.54 (m, 1H), 7.57 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.51–7.45 (m, 2H), 7.43–7.28 (m, 6H), 6.54 (d, *J* = 3.7 Hz, 1H), 6.08 (s, 1H), 5.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 144.5, 135.7, 135.4, 131.0, 129.2, 129.2, 127.1, 126.2, 125.3, 124.3, 121.0, 118.6, 116.8, 109.3; IR (Neat Film, NaCl) 3055, 2926, 1692, 1535, 1496, 1471, 1450, 1378, 1348, 1293, 1205, 1156, 1072, 1016, 931, 880, 752, 696 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{14}NO$ $[M+H]^+$: 248.1070, found 248.1063.

4.2.3 (*E*)-1-(1*H*-indol-1-yl)-2-phenylhept-2-en-1-one (3c)

Purified by column chromatography (3% Et_2O in hexanes) to provide a colorless oil (58.9 mg, 0.194 mmol, 97% yield, 14:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.42 – 7.26 (m, 7H), 6.57–6.48 (m, 2H), 6.33 (t, *J* = 7.5 Hz, 1H), 2.36 (q, *J* = 7.5 Hz, 2H), 1.50 (tt, *J* = 8.2, 6.9 Hz, 2H), 1.37 (dq, *J* = 14.4, 7.2 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 140.2, 136.8, 136.0, 135.2, 130.8, 129.0, 128.8, 128.2, 127.2, 125.0, 123.9, 120.9, 116.7, 108.5, 31.5, 28.9, 22.6, 14.0; IR (Neat Film, NaCl) 3053, 2957, 2928, 2858, 1688, 1636, 1600, 1585, 1534, 1494, 1472, 1450, 1379, 1333, 1205, 1157, 1143, 1113, 1078, 1016, 938, 882, 816, 769, 752, 702 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{21}H_{22}NO$ $[M+H]^+$: 304.1696, found 304.1688.

4.2.4 (*E*)-1-(1*H*-indol-1-yl)-4-methyl-2-phenylpent-2-en-1-one (3d)

Purified by column chromatography (3% Et_2O in hexanes) to provide a colorless oil (44.3 mg, 0.153 mmol, 77% yield, >20:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.55 (ddd, *J* = 7.7, 1.3, 0.7 Hz, 1H), 7.42–7.27 (m, 8H), 6.54 (d, *J* = 3.8 Hz, 1H), 6.10 (d, *J* = 10.5 Hz, 1H), 2.80 (dhept, *J* = 10.5, 6.6 Hz, 1H), 1.11 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 146.6, 136.0, 135.3, 134.5, 130.9, 128.9, 128.8, 128.8, 127.2, 125.0, 123.9, 120.9, 116.7, 108.5, 28.3, 22.7; IR (Neat Film, NaCl) 3054, 2962, 2868, 1687, 1534, 1494, 1450, 1377, 1334, 1238, 1201, 1112, 1078, 1017, 882, 795, 769, 752, 698 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{20}NO$ $[M+H]^+$: 290.1539, found 290.1528.

4.2.5 (*E*)-1-(1*H*-indol-1-yl)-2,3-diphenylprop-2-en-1-one (3e)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (48.3 mg, 0.149 mmol, 75% yield, 6:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.2 Hz, 1H), 7.70 (dd, *J* = 11.3, 7.5 Hz, 2H), 7.65 (d, *J* = 3.8 Hz, 1H),

7.59–7.44 (m, 7H), 7.44–7.30 (m, 5H), 6.71 (d, *J* = 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 136.4, 136.1, 135.3, 134.6, 130.9, 130.0, 129.3, 129.2, 128.9, 128.7, 128.5, 127.1, 126.0, 125.1, 124.1, 121.0, 116.8, 108.9.; IR (Neat Film, NaCl) 3053, 3026, 2923, 1684, 1535, 1492, 1472, 1450, 1381, 1333, 1235, 1206, 1155, 1141, 1112, 1077, 1016, 908, 882, 862, 753, 721, 694 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{23}H_{18}NO$ $[M+H]^+$: 324.1383, found 324.1380.

4.2.6 (*E*)-1-(1*H*-indol-1-yl)-2-(*o*-tolyl)but-2-en-1-one (3f)

Purified by column chromatography (3% Et_2O in hexanes) to provide a colorless oil (50.1 mg, 0.182 mmol, 91% yield, 12:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.2 Hz, 1H), 7.46 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.31–7.26 (m, 1H), 7.25 (d, *J* = 3.8 Hz, 1H), 7.22–7.16 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.42 (d, *J* = 3.8 Hz, 1H), 6.35 (q, *J* = 7.2 Hz, 1H), 2.28 (s, 3H), 1.91 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 138.0, 137.9, 135.9, 134.0, 131.9, 130.8, 129.7, 129.5, 128.9, 127.2, 125.5, 124.9, 123.9, 120.8, 116.7, 108.4, 21.4, 15.3; IR (Neat Film, NaCl) 3027, 2919, 2856, 1688, 1533, 1513, 1472, 1450, 1384, 1329, 1239, 1206, 1157, 1143, 1113, 1080, 1017, 946, 882, 828, 770, 753, 723 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{18}NO$ $[M+H]^+$: 276.1383, found 276.1375.

4.2.7 (*E*)-1-(1*H*-indol-1-yl)-2-(4-methoxyphenyl)but-2-en-1-one (3g)

Purified by column chromatography (8% Et_2O in hexanes) to provide a colorless oil (55.0 mg, 0.189 mmol, 94% yield, 19:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.3 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.41–7.24 (m, 5H), 6.96–6.87 (m, 2H), 6.50 (d, *J* = 3.8 Hz, 1H), 6.40 (q, *J* = 7.1 Hz, 1H), 3.81 (s, 3H), 1.99 (d, *J* = 7.1 Hz, 3H).;^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 159.4, 137.6, 135.9, 133.6, 130.8, 130.3, 127.3, 127.2, 124.9, 123.9, 120.8, 116.7, 114.2, 108.4, 55.4, 15.3; IR (Neat Film, NaCl) 2934, 2361, 1684, 1607, 1511, 1450, 1328, 1292, 1250, 1202, 1178, 1110, 1079, 1032, 948, 881, 838, 815, 770, 753 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{18}NO_2$ $[M+H]^+$: 292.1332, found 292.1340.

4.2.8 (*E*)-2-(4-fluorophenyl)-1-(1*H*-indol-1-yl)but-2-en-1-one (3h)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (49.8 mg, 0.178 mmol, 89% yield, 13:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.2 Hz, 1H), 7.55 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.40–7.32 (m, 4H), 7.32–7.26 (m, 1H), 7.13–7.06 (m, 2H), 6.53 (d, *J* = 3.8 Hz, 1H), 6.45 (q, *J* = 7.1 Hz, 1H), 1.96 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 162.45 (d, J_{C-F} = 248.2 Hz), 136.9, 135.9, 134.9, 130.9, 130.8, 127.0, 125.1, 124.0, 120.9, 116.6, 116.0, 115.7, 108.7, 15.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –113.18 (dtq, *J* = 10.8, 5.3, 2.3 Hz). IR (Neat Film, NaCl) 3051, 2917, 1685, 1602, 1534, 1509, 1472, 1450, 1385, 1331, 1224, 1202, 1160, 1101, 1080, 1016, 948, 881, 842, 786, 770, 754 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{15}FNO$ $[M+H]^+$: 280.1132, found 280.1137.

4.2.9 (*E*)-2-(4-chlorophenyl)-1-(1*H*-indol-1-yl)but-2-en-1-one (3i)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (46.7 mg, 0.158 mmol, 79% yield, 8:1 *E*/*Z*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.1 Hz, 1H), 7.59–7.51 (m, 1H), 7.40–7.26 (m, 7H), 6.53 (d, *J* = 3.7 Hz, 1H), 6.46 (q, *J* = 7.2 Hz, 1H), 1.97 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 136.9, 135.9, 135.3, 134.2, 133.2, 130.4, 129.2, 129.0, 127.0, 125.1, 124.1, 120.9, 116.6, 108.8, 15.3; IR (Neat Film, NaCl) 3051, 2916, 1688, 1534, 1491, 1472, 1451, 1384, 1330, 1204, 1143, 1089, 1016, 947, 881, 838, 802, 770, 754 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{15}ClNO$ $[M+H]^+$: 296.0837, found 296.0835.

Supplementary data

NMR spectra for compounds **3a**–**3i**, as well as experimental and characterization data for substrate and ligand synthesis.

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