


Cobalt(III)-Catalyzed Diastereoselective Three-Component C–H Bond Addition to Butadiene and Activated Ketones

Zican Shen

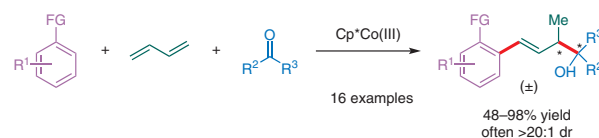
Chen Li

Brandon Q. Mercado

Jonathan A. Ellman* 

Department of Chemistry, Yale University, New Haven, CT 06520, USA
jonathan.ellman@yale.edu

Published as part of the Special Topic
Domino C–H Functionalization Reaction/Cascade Catalysis



Received: 02.10.2019

Accepted after revision: 22.10.2019

Published online: 07.11.2019

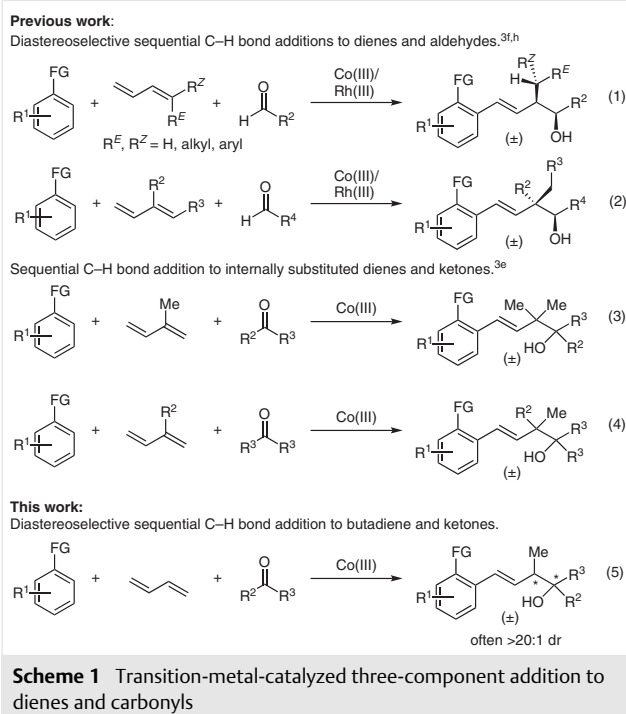
DOI: 10.1055/s-0039-1690741; Art ID: ss-2019-c0566-st

Abstract A highly diastereoselective three-component C–H bond addition across butadiene and activated ketones is described. This transformation provides homoallylic tertiary alcohols through the formation of two C–C σ -bonds and with complete selectivity for an *E*-alkene isomer. The reaction exhibits good scope with respect to activated ketone inputs, including highly strained cyclic and electron-deficient cyclic and acyclic ketones. Additionally, high diastereoselectivities were achieved for alcohols prepared from unsymmetrical ketones.

Key words C–H activation, cobalt, ketones, diastereoselectivity, multicomponent reaction, homogeneous catalysis

Transition-metal-catalyzed C–H bond additions to a large variety of coupling partners provide a robust approach to assemble synthetically useful motifs.¹ While reaction of a C–H bond substrate with two different coupling partners potentially represents a powerful approach to access complex structures, relatively few examples have been reported to date. The Catellani reaction initiated by Pd-catalyzed oxidative addition of an aryl halide has proven to be an effective strategy to accomplish three-component additions.² We and others have recently explored an alternative approach that proceeds by C–H activation followed by sequential coupling with two different coupling partners.³ Relevant to the study described in this article, previous work by our lab^{3e,h} and others^{3f} has demonstrated that Co(III)- and Rh(III)-catalyzed three-component C–H bond additions with butadiene, monosubstituted or 1,2-disubstituted dienes, and aldehydes provide homoallylic alcohols with high diastereoselectivity (Scheme 1, eq. 1, 2).

Ketones are inherently more stable and sterically congested than aldehydes, and consequently, direct C–H bond additions even to activated ketones have only rarely been reported.⁴ Recently, our lab reported the first examples of



Co(III)-catalyzed three-component coupling to internally substituted dienes and activated ketones (eq. 3, 4). However, only those diene and ketone combinations that gave products with a single stereogenic center were investigated. To expand upon these first examples of intermolecular sequential C–H bond additions to dienes and ketones, we sought to evaluate a broader array of ketones, in particular for diastereoselective additions to give products with two stereogenic centers. Herein, we describe a Co(III)-catalyzed three-component C–H bond addition to butadiene and activated ketones to provide homoallylic tertiary alcohols with

the formation of two new C–C σ -bonds (eq. 5). Notably, for the first time, alcohols bearing two stereogenic centers can be obtained with high diastereoselectivity for three-component additions with both cyclic and acyclic unsymmetrical ketones.

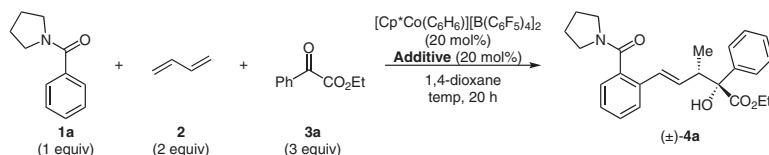
We began by exploring the reaction parameters for the coupling of benzamide **1a** with butadiene (**2**) and ethyl benzoylformate (**3a**), which proved to be one of the more challenging ketone coupling partners (vide infra). Under the optimized reaction conditions that had previously been adopted for the coupling of butadiene and aldehydes (Table 1, entry 1),^{3h} none of the desired three-component product was observed, and only 13% of a product resulting from two-component C–H bond addition to butadiene was obtained. Considering the greater stability and steric encumbrance of ketones relative to aldehydes, a higher reaction temperature was next investigated. At 70 °C, 20% of three-component product **4a** was obtained as a single diastereomer (entry 2). However, at a higher reaction temperature of 90 °C, the yield of **4a** dropped to 12% (entry 3). Substrate concentration was next evaluated, with 1.0 M leading to lower conversion than 0.4 M (entry 4), while 0.2 M provided a modest increase in the yield of **4a** to 25% (entry 5). Finally, additives that have been employed in other Co(III)-catalyzed C–H addition reactions were examined as well.^{3k,5} Although replacing AcOH with LiOAc led to no conversion (entry 6), PivOH was a superior additive for this transformation and provided **4a** in 50% yield (entry 7).

Having optimized the reaction conditions, we next explored the scope for the ketone coupling partner with benzamide **1a** as the C–H bond substrate (Scheme 2). In addition to ethyl benzoylformate (**3a**), highly strained four-membered cyclic ketones also provided homoallylic tertiary alcohols in good to excellent yields. *N*-Carboxybenzyl (Cbz)-

protected 3-azetidinone and 3-oxetanone furnished products **4b** and **4c** in 92% and 83% yield, respectively. Additionally, reaction with less activated cyclobutanone gave alcohol **4d** in 50% yield. Electron-deficient isatin provided homoallylic alcohol **4e** with two contiguous stereogenic centers in high yield and with high diastereoselectivity. Additions with *N*-methylisatin and *N*-benzylisatin afforded products **4f** and **4g** in 66% and 82% yield, respectively, also with high diastereoselectivity. Moreover, more electron-deficient 6-chloroisatin derivatives afforded alcohols **4h** and **4i** in near quantitative yields and with >20:1 dr.

Next, additional C–H bond substrates **1** were investigated for several different ketones **3** (Scheme 3). In addition to tertiary benzamide **1a**, the secondary *N*-methylbenzamide is also an effective C–H bond substrate, coupling with 1-Cbz-3-azetidinone to give product **4j** in 86% yield. The secondary *N*-methylbenzamide also reacted with the acyclic ketone ethyl benzoylformate to furnish product **4k** in 74% yield and with >20:1 dr. An X-ray crystal structure of the major diastereomer of alcohol **4k** rigorously established the relative configuration of the methyl and hydroxyl groups for this ketone coupling partner. *N*-Phenylpyrazole with a methyl substituent at the *meta* position coupled with *N*-methylisatin to provide tertiary alcohol **4l** in 48% yield and with high diastereoselectivity. The relative stereochemistry for **4l** was confirmed by X-ray crystallography, thereby providing the stereochemical relationship for isatin-derived products. Pyrimidine also served as an excellent directing group as demonstrated for three-component addition with ethyl benzoylformate to afford alcohol **4m** in 70% yield and with >20:1 dr. However, a blocking group, such as a methyl group at the *meta* position, is necessary to prevent bis-functionalization. The 2-phenylpyrimidine C–H bond substrate is also effective for coupling with *N*-Cbz-3-azetidinone

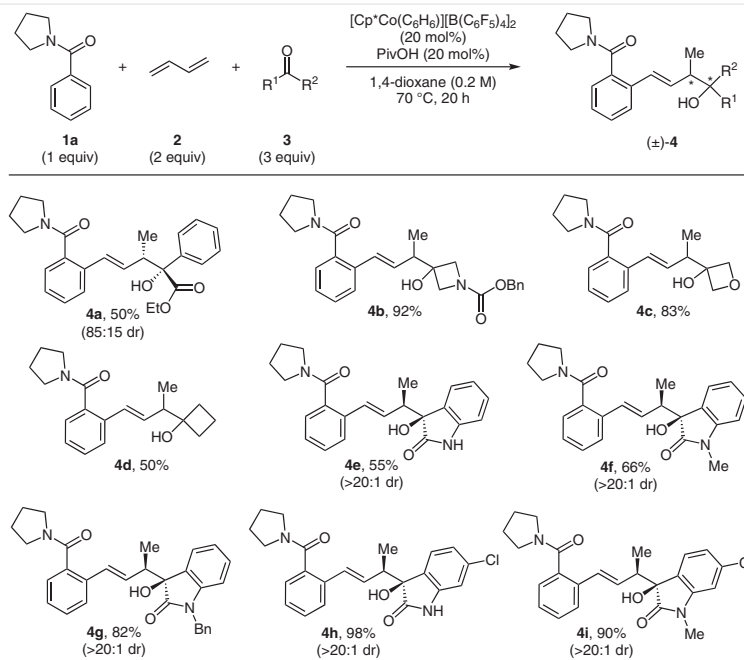
Table 1 Screening of Reaction Conditions^a



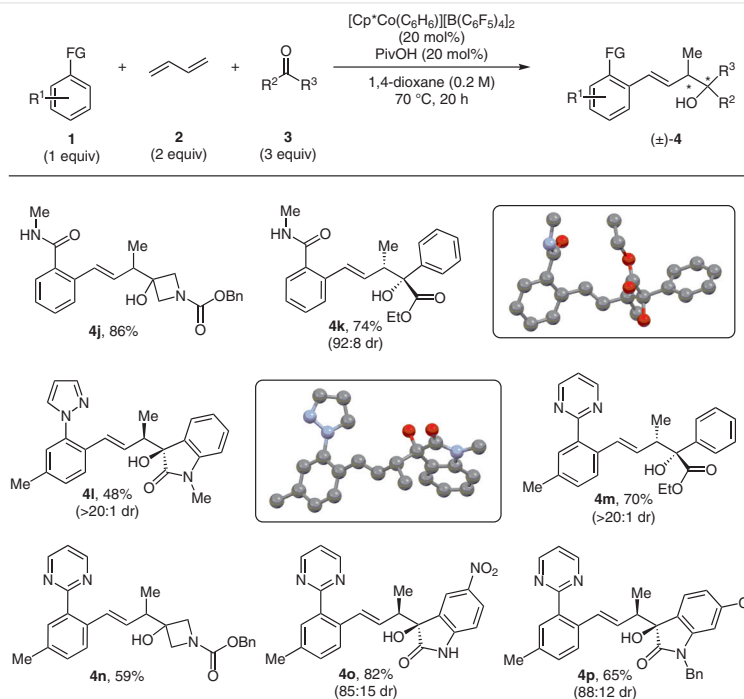
Entry	Additive	Temp (°C)	Concn (M)	Yield ^b (%) of 4a
1	AcOH	50	0.4	0
2	AcOH	70	0.4	20
3	AcOH	90	0.4	12
4	AcOH	70	1.0	15
5	AcOH	70	0.2	25
6	LiOAc	70	0.2	0
7	PivOH	70	0.2	50

^a Reaction conditions: **1a** (0.1 mmol), **2** (0.2 mmol), **3a** (0.3 mmol).

^b Yields determined by ¹H NMR analysis relative to 1,3,5-trimethoxybenzene.



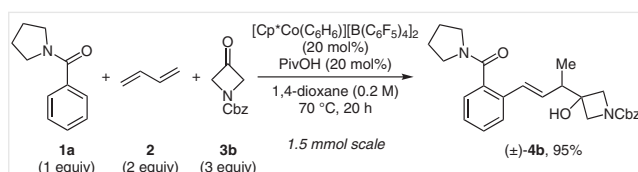
Scheme 2 Three-component coupling of benzamide **1a**, butadiene (**2**), and diverse ketones **3**. Reactions were performed at 0.1 mmol scale; isolated yields of products after purification by chromatography.



Scheme 3 Three-component coupling of C–H bond substrates **1** with butadiene (**2**) and selected ketones **3**. Reactions were performed at 0.1 mmol scale; isolated yields of products after purification by chromatography. For the X-ray crystal structures of **4k** and **4l**, hydrogen atoms are omitted for clarity.

to furnish alcohol **4n**. Isatin derivatives like 5-nitroisatin and *N*-benzyl-6-chloroisatin afforded the corresponding products **4o** and **4p** in 82% and 65% yield, respectively, with good diastereoselectivity.

To evaluate the scalability of the reaction, the three-component product **4b** was prepared at a 15-fold larger scale (Scheme 4). Reaction of benzamide **1a** with butadiene (**2**) and 1-Cbz-3-azetidinone (**3b**) at 1.5 mmol scale provided product **4b** in 95% yield, which is consistent with the yield obtained for the corresponding smaller scale reaction.

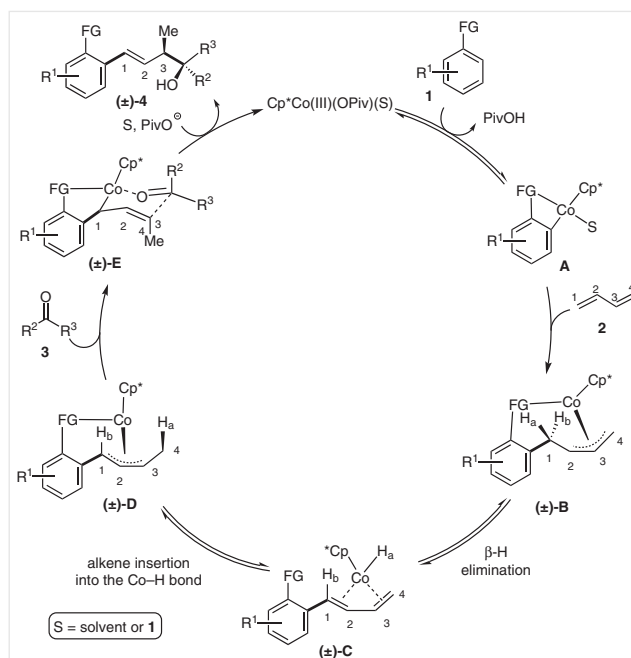


Scheme 4 Three-component coupling of benzamide **1a**, butadiene (**2**), and 1-Cbz-3-azetidinone (**3b**) on 1.5 mmol scale

A catalytic cycle is depicted in Scheme 5, which is based on prior mechanistic studies for three-component additions to dienes and aldehydes.^{3e,h} The Co(III)-catalyzed C–H bond activation of **1** through concerted metalation–deprotonation forms metallacycle **A**. Migratory insertion into butadiene subsequently affords Co–allyl species **B**. To obtain the necessary connectivity observed in the product, β -hydride elimination at C1 then provides Co–diene complex **C**, which undergoes alkene insertion into the Co–H bond to afford Co–allyl species **D**. Diastereoselective addition of intermediate **D** with ketone **3** via a chair-like transition state depicted in **E**, followed by protonolysis to release the catalyst, would then provide product **4**.

In conclusion, we have developed a Co(III)-catalyzed three-component C–H bond addition to butadiene and ketones. Efficient coupling was observed for a number of different activated ketones and C–H bond substrates. Notably, Co(III)-catalyzed diastereoselective additions with unsymmetrical ketones have been demonstrated for the first time. In addition, the relative stereochemistry of the two stereogenic centers in the three-component addition products for isatins and ethyl benzoylformate was rigorously established by X-ray crystallography.

All Co(III)-catalyzed reactions were set up in a N_2 -filled glovebox, using glassware that was oven-dried (150 °C) and evacuated while hot prior to use. Solvents were sparged with argon and purified by elution through a column of activated alumina under argon before use and were stored with 3 Å molecular sieves in a N_2 -filled glovebox (molecular sieves were dried at 200 °C overnight under vacuum). Unless otherwise noted, all reagents were purchased from commercial sources and used without further purification. Microwave vials and caps were purchased from Biotage (part number 351521 and 352298, respectively). Product purification was performed by preparative TLC with plates from Analtech (1 mm silica gel, 20 × 20 cm). ¹H and ¹³C NMR



Scheme 5 Proposed mechanism for the three-component transformation

spectra were recorded on a 400, 500, or 600 MHz instrument. Partial IR spectra are reported. High-resolution mass spectra were obtained using electrospray ionization (ESI) on a time-of-flight mass spectrometer.

Low-temperature X-ray diffraction data (ω -scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Saturn994+ CCD detector with Cu $K\alpha$ radiation ($\lambda = 1.54178 \text{ \AA}$) for the structures of **4k** and **4l**.⁶ The diffraction images were processed and scaled using Rigaku Oxford Diffraction software (CrysAlis^{Pro}). The structures were solved with SHELXT and refined against F^2 on all data by full-matrix least squares with SHELXL.⁷ For the full numbering scheme of compounds **4k** and **4l**, see the full details of the X-ray crystal structure determination (CIF) in the Supporting Information, Section III.

Homoallylic Tertiary Alcohols **4**; General Procedure

In a N_2 -filled glovebox, a 2.0 mL Biotage microwave vial with a triangular stir bar (1 × 0.5 cm) was charged with the indicated C–H bond partner (0.100 mmol, 1.00 equiv) and $[Cp^*Co(C_6H_6)][B(C_6F_5)_4]_2$ (32.6 mg, 0.0200 mmol, 0.200 equiv). Following this, the corresponding ketone (0.300 mmol, 3.00 equiv) was added. A 0.2 M solution of pivalic acid in 1,4-dioxane (100 μ L, 0.0200 mmol, 0.200 equiv) and 1,4-dioxane (350 μ L) were added successively. At last, a commercially available 4 M stock solution of butadiene in THF (50 μ L, 0.200 mmol, 2.00 equiv) was added. The reaction vial was then sealed and taken outside the glovebox. The reaction mixture was stirred in a preheated oil bath at 70 °C for 20 h. The reaction vial was then cooled to room temperature and uncapped. The reaction was quenched with saturated $NaHCO_3$ (10 mL), and the resulting mixture was then extracted with $EtOAc$ (5 × 3 mL). The organic layers were combined and dried over Na_2SO_4 . After filtration of the mixture through a Celite plug using $EtOAc$ as the eluent, the resulting mixture was then concentrated and purified by the indicated chromatographic method to afford the desired product.

Preparation of Homoallylic Tertiary Alcohol 4b on 1.5 mmol Scale

In a N₂-filled glovebox, a 30 mL Biotage microwave vial with a foot-ball-shaped stir bar (2 × 0.5 cm) was charged with phenyl(pyrrolidin-1-yl)methanone (**1a**; 263 mg, 1.50 mmol, 1.00 equiv) and [Cp*Co(C₆H₆)] [B(C₆F₅)₄]₂ (489 mg, 0.300 mmol, 0.200 equiv). Following this, benzyl 3-oxoazetidine-1-carboxylate (923 mg, 4.50 mmol, 3.00 equiv) was added. A 0.2 M solution of pivalic acid in 1,4-dioxane (1500 μL, 0.300 mmol, 0.200 equiv) and 1,4-dioxane (5.25 mL) were added successively. At last, a 4 M stock solution of butadiene in THF (750 μL, 3.00 mmol, 2.00 equiv) was added. The reaction vial was then sealed and taken outside the glovebox. The reaction mixture was stirred in a preheated oil bath at 70 °C for 20 h. The reaction vial was then cooled to room temperature and uncapped. The reaction was quenched with saturated NaHCO₃ (50 mL), and the resulting mixture was then extracted with EtOAc (5 × 15 mL). The organic layers were combined and dried over Na₂SO₄. After filtration of the mixture through a medium fritted funnel using EtOAc as the eluent, the resulting mixture was then concentrated and purified by silica gel chromatography (50% EtOAc in hexane) to provide **4b** (619 mg, 95% yield) as a yellow oil. Both the ¹H NMR and ¹³C NMR spectra are in perfect agreement with the corresponding spectra of **4b** obtained according to the general procedure (see the Supporting Information, Section II).

Ethyl (2R*,3S*,E)-2-Hydroxy-3-methyl-2-phenyl-5-(2-(pyrrolidin-1-ylcarbonyl)phenyl)pent-4-enoate (4a)

The general procedure was followed using phenyl(pyrrolidin-1-yl)methanone (**1a**; 17.5 mg, 0.100 mmol, 1.00 equiv) and ethyl 2-oxo-2-phenylacetate (53.4 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4a** (20.4 mg, 50% yield; 85:15 dr) as a colorless oil.

IR (neat): 3491, 2975, 2876, 1724, 1615, 1449, 1425 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.68 (d, *J* = 7.3 Hz, 1.67 H, major), 7.62 (d, *J* = 7.3 Hz, 0.32 H, minor), 7.49 (d, *J* = 8.2 Hz, 1 H), 7.39–7.32 (m, 2 H), 7.32–7.27 (m, 2 H), 7.23 (m, 2 H), 6.59 (d, *J* = 15.8 Hz, 0.85 H, major), 6.28 (dd, *J* = 15.9, 8.8 Hz, 0.85 H, major), 6.23 (m, 0.15 H, minor), 6.03 (dd, *J* = 15.9, 8.9 Hz, 0.15 H, minor), 4.35–4.08 (m, 2 H), 3.83 (s, 1 H), 3.68 (t, *J* = 7.1 Hz, 1.74 H, major), 3.59 (m, 0.36 H, minor), 3.27 (m, 1 H), 3.14–3.05 (m, 2 H), 1.95 (m, 2 H), 1.87–1.81 (m, 2 H), 1.31 (t, *J* = 7.2 Hz, 0.51 H, minor), 1.23 (t, *J* = 7.1 Hz, 2.71 H, major), 1.15 (d, *J* = 6.8 Hz, 0.44 H, minor), 0.88 (d, *J* = 6.8 Hz, 2.56 H, major).

¹³C NMR (126 MHz, CDCl₃): δ = 174.9, 169.5, 140.2, 136.5, 133.7, 133.3, 132.5, 129.0, 128.8, 128.4, 128.14, 128.06, 127.9, 127.6, 127.44, 127.40, 127.1, 126.2, 126.1, 126.0, 125.9, 125.6, 80.5, 62.7, 60.4, 48.3, 47.8, 45.7, 45.5, 45.3, 26.0, 25.8, 24.6, 24.5, 15.9, 14.4, 14.13, 14.07; peaks for both major and minor isomer are listed.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₅H₃₀NO₄⁺: 408.2169; found: 408.2175.

Benzyl (E)-3-Hydroxy-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)azetidine-1-carboxylate (4b)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and benzyl 3-oxoazetidine-1-carboxylate (61.5 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4b** (40.0 mg, 92% yield) as a yellow oil.

IR (neat): 3390, 2964, 2879, 2362, 1700, 1607, 1462, 1429, 1356 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.40 (d, *J* = 7.7 Hz, 1 H), 7.36–7.27 (m, 5 H), 7.24 (m, 1 H), 7.23–7.15 (m, 2 H), 6.48 (d, *J* = 15.9 Hz, 1 H), 6.06 (dd, *J* = 15.9, 8.2 Hz, 1 H), 5.04 (s, 2 H), 3.92 (m, 2 H), 3.78 (m, 2 H), 3.59 (m, 2 H), 3.06 (m, 2 H), 2.60–2.47 (m, 1 H), 1.98–1.71 (m, 5 H), 1.07 (d, *J* = 6.8 Hz, 3 H).

¹³C NMR (101 MHz, CDCl₃): δ = 169.9, 156.6, 136.4, 135.7, 133.7, 132.7, 129.3, 128.9, 128.5, 128.1, 127.9, 127.5, 126.5, 126.1, 72.6, 66.9, 60.8, 60.5, 48.6, 45.7, 44.4, 25.9, 24.5, 13.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₆H₃₁N₂O₄⁺: 435.2278; found: 435.2284.

(E)-(2-(3-(3-Hydroxyoxetan-3-yl)but-1-en-1-yl)phenyl)(pyrrolidin-1-yl)methanone (4c)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and oxetan-3-one (21.6 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4c** (24.9 mg, 83% yield) as a colorless oil.

IR (neat): 3375, 2962, 2874, 1606, 1452, 1430, 1340 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.45 (d, *J* = 7.7 Hz, 1 H), 7.37–7.26 (m, 1 H), 7.27–7.17 (m, 2 H), 6.52 (d, *J* = 15.9 Hz, 1 H), 6.12 (dd, *J* = 15.9, 8.2 Hz, 1 H), 4.51 (m, 4 H), 3.63 (t, *J* = 7.1 Hz, 2 H), 3.10 (t, *J* = 6.8 Hz, 2 H), 2.77 (m, 1 H), 1.93 (m, 2 H), 1.83 (m, 2 H), 1.11 (d, *J* = 6.8 Hz, 3 H).

¹³C NMR (126 MHz, CDCl₃): δ = 169.7, 136.2, 133.7, 132.8, 129.1, 128.8, 127.4, 126.4, 126.2, 82.4, 82.3, 76.1, 48.4, 45.6, 43.7, 26.0, 24.6, 13.6.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₈H₂₄NO₃⁺: 302.1751; found: 302.1756.

(E)-(2-(3-(1-Hydroxycyclobutyl)but-1-en-1-yl)phenyl)(pyrrolidin-1-yl)methanone (4d)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and cyclobutanone (21.0 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4d** (15.0 mg, 50% yield) as a colorless oil.

IR (neat): 3396, 2971, 2876, 1611, 1452, 1428 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.48 (d, *J* = 7.8 Hz, 1 H), 7.30 (m, 1 H), 7.23 (m, 2 H), 6.50 (d, *J* = 15.9 Hz, 1 H), 6.20 (dd, *J* = 15.9, 8.2 Hz, 1 H), 3.65 (t, *J* = 7.0 Hz, 2 H), 3.10 (t, *J* = 6.8 Hz, 2 H), 2.53–2.44 (m, 1 H), 2.20–2.12 (m, 2 H), 1.98–1.89 (m, 4 H), 1.83 (m, 4 H), 1.09 (d, *J* = 6.9 Hz, 3 H).

¹³C NMR (126 MHz, CDCl₃): δ = 169.8, 136.3, 134.2, 134.0, 129.0, 128.1, 127.2, 126.2, 126.1, 77.4, 48.3, 45.5, 44.9, 34.3, 34.0, 25.9, 24.6, 13.5, 12.1.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₉H₂₆NO₂⁺: 300.1958; found: 300.1964.

(E)-3-Hydroxy-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)indolin-2-one (4e)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and indoline-2,3-dione (44.1 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (70% EtOAc in hexane) provided **4e** (21.0 mg, 55% yield; >20:1 dr) as a yellow oil.

IR (neat): 3271, 2974, 2324, 1712, 1594, 1462, 1433 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 9.28 (s, 1 H), 7.48 (d, *J* = 7.7 Hz, 1 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 7.27–7.24 (m, 1 H), 7.23–7.19 (m, 1 H), 7.13 (m, 2 H), 6.92 (t, *J* = 7.5 Hz, 1 H), 6.70 (d, *J* = 7.7 Hz, 1 H), 6.60 (d, *J* = 15.8 Hz, 1 H), 6.27 (dd, *J* = 15.8, 8.1 Hz, 1 H), 4.99 (s, 1 H), 3.58 (m, 2 H), 3.16 (m, 1 H), 3.11–3.01 (m, 1 H), 2.91 (m, 1 H), 1.79 (m, 4 H), 0.75 (d, *J* = 6.7 Hz, 3 H).

¹³C NMR (101 MHz, CDCl₃): δ = 180.9, 170.0, 141.2, 136.1, 133.8, 131.5, 129.8, 129.5, 129.2, 128.6, 127.5, 126.0, 125.1, 122.7, 110.5, 79.4, 48.5, 45.7, 44.0, 25.8, 24.5, 14.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₃H₂₅N₂O₃⁺: 377.1860; found: 377.1865.

(E)-3-Hydroxy-1-methyl-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)indolin-2-one (4f)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and 1-methylindoline-2,3-dione (48.3 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4f** (25.7 mg, 66% yield; >20:1 dr) as a yellow powder.

IR (neat): 3351, 2972, 2361, 1706, 1612, 1512, 1461 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.46 (d, J = 7.8 Hz, 1 H), 7.30 (m, 2 H), 7.23–7.10 (m, 2 H), 7.04 (d, J = 7.6 Hz, 1 H), 6.99 (t, J = 7.6 Hz, 1 H), 6.77 (d, J = 7.8 Hz, 1 H), 6.47 (d, J = 15.6 Hz, 1 H), 6.19 (dd, J = 15.7, 8.8 Hz, 1 H), 3.38 (m, 2 H), 3.17 (m, 1 H), 3.05 (m, 1 H), 2.99 (s, 3 H), 2.72 (m, 1 H), 1.79 (m, 4 H), 0.64 (d, J = 6.7 Hz, 3 H).

¹³C NMR (101 MHz, CDCl₃): δ = 178.5, 170.0, 143.1, 134.8, 133.8, 131.2, 130.1, 129.9, 129.7, 127.9, 127.6, 126.3, 126.1, 124.7, 123.2, 108.7, 79.1, 49.2, 45.8, 45.0, 26.0, 25.8, 24.3, 14.2.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₄H₂₇N₂O₃⁺: 391.2016; found: 391.2022.

(E)-1-Benzyl-3-hydroxy-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)indolin-2-one (4g)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and 1-benzylindoline-2,3-dione (71.1 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (70% EtOAc in hexane) provided **4g** (38.3 mg, 82% yield; >20:1 dr) as a yellow powder.

IR (neat): 3353, 2974, 1715, 1610, 1465, 1453, 1430, 1359 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.49 (d, J = 7.7 Hz, 1 H), 7.41–7.30 (m, 2 H), 7.30–7.19 (m, 7 H), 7.19–7.13 (m, 1 H), 6.98 (m, 1 H), 6.69 (m, 1 H), 6.55 (d, J = 16.1 Hz, 1 H), 6.38 (dd, J = 15.9, 7.4 Hz, 1 H), 5.03 (d, J = 15.8 Hz, 1 H), 4.69 (d, J = 15.8 Hz, 1 H), 3.58 (m, 2 H), 3.05 (m, 3 H), 1.85 (m, 2 H), 1.76 (m, 2 H), 0.88 (d, J = 6.7 Hz, 3 H).

¹³C NMR (126 MHz, CDCl₃): δ = 177.9, 169.6, 143.0, 136.5, 135.5, 133.7, 131.6, 131.5, 129.7, 129.5, 129.1, 128.8, 127.6, 127.5, 127.3, 127.1, 126.3, 126.0, 124.9, 122.9, 109.3, 78.7, 48.3, 45.6, 44.4, 43.9, 25.9, 24.5, 13.9.

HRMS (ESI): m/z [M + H]⁺ calcd for C₃₀H₃₁N₂O₃⁺: 467.2329; found: 467.2335.

(E)-6-Chloro-3-hydroxy-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)indolin-2-one (4h)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and 6-chloroindoline-2,3-dione (54.5 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4h** (40.3 mg, 98% yield; >20:1 dr) as a red powder.

IR (neat): 3267, 2973, 2361, 1719, 1613, 1455 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 9.70 (s, 1 H), 7.51 (d, J = 7.8 Hz, 1 H), 7.32 (t, J = 7.5 Hz, 1 H), 7.27–7.20 (m, 2 H), 7.12 (d, J = 7.9 Hz, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 6.84 (s, 1 H), 6.61 (d, J = 15.8 Hz, 1 H), 6.28 (dd, J = 15.8, 8.1 Hz, 1 H), 5.28 (s, 1 H), 3.63 (m, 2 H), 3.15 (m, 1 H), 3.09–3.01 (m, 1 H), 3.00–2.89 (m, 1 H), 1.82 (m, 4 H), 0.80 (d, J = 6.7 Hz, 3 H).

¹³C NMR (126 MHz, CDCl₃): δ = 181.0, 169.8, 142.7, 136.3, 135.0, 133.6, 131.2, 130.0, 129.2, 127.5, 127.4, 126.1, 126.0, 125.9, 122.5, 111.2, 79.1, 48.4, 45.7, 43.9, 25.8, 24.5, 14.1.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₃H₂₄ClN₂O₃⁺: 411.1470; found: 411.1476.

(E)-6-Chloro-3-hydroxy-1-methyl-3-(4-(2-(pyrrolidin-1-ylcarbonyl)phenyl)but-3-en-2-yl)indolin-2-one (4i)

The general procedure was followed using **1a** (17.5 mg, 0.100 mmol, 1.00 equiv) and 6-chloro-1-methylindoline-2,3-dione (58.7 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4i** (38.2 mg, 90% yield; >20:1 dr) as a yellow powder.

IR (neat): 3364, 2968, 2877, 2362, 2339, 1733, 1609, 1456 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.49 (d, J = 7.8 Hz, 1 H), 7.34 (m, 1 H), 7.28–7.16 (m, 3 H), 6.98 (d, J = 7.5 Hz, 1 H), 6.80 (s, 1 H), 6.58 (d, J = 15.9 Hz, 1 H), 6.31 (dd, J = 15.9, 7.7 Hz, 1 H), 4.20–3.92 (m, 1 H), 3.59 (m, 2 H), 3.16 (s, 3 H), 3.13–3.03 (m, 2 H), 2.98 (t, J = 7.1 Hz, 1 H), 1.87 (m, 2 H), 1.80 (m, 2 H), 0.75 (d, J = 6.7 Hz, 3 H).

¹³C NMR (126 MHz, CDCl₃): δ = 177.7, 169.5, 145.1, 136.5, 135.4, 133.7, 131.3, 130.2, 129.1, 127.6, 126.7, 126.3, 126.2, 126.0, 122.7, 109.0, 78.6, 48.3, 45.6, 44.1, 26.3, 25.9, 24.5, 13.8.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₄H₂₆ClN₂O₃⁺: 425.1626; found: 425.1632.

Benzyl (E)-3-Hydroxy-3-(4-(2-(methylcarbamoyl)phenyl)but-3-en-2-yl)azetidine-1-carboxylate (4j)

The general procedure was followed using *N*-methylbenzamide (13.5 mg, 0.100 mmol, 1.00 equiv) and benzyl 3-oxoazetidine-1-carboxylate (61.5 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (40% EtOAc in CH₂Cl₂) provided **4j** (33.9 mg, 86% yield) as a colorless oil.

IR (neat): 3317, 2965, 2881, 1689, 1631, 1412, 1357, 1355 cm⁻¹.

¹H NMR (600 MHz, CDCl₃): δ = 7.41–7.38 (m, 1 H), 7.37–7.34 (m, 1 H), 7.33–7.31 (m, 2 H), 7.31–7.30 (m, 1 H), 7.29–7.25 (m, 3 H), 7.24–7.18 (m, 1 H), 6.73 (d, J = 15.9 Hz, 1 H), 6.34–6.11 (m, 1 H), 5.97–5.93 (m, 1 H), 4.98 (s, 2 H), 3.95 (m, 2 H), 3.81 (m, 2 H), 2.91 (d, J = 4.9 Hz, 3 H), 2.58 (m, 1 H), 1.11 (d, J = 6.8 Hz, 3 H).

¹³C NMR (151 MHz, CDCl₃): δ = 170.4, 156.6, 136.4, 135.9, 134.8, 132.2, 130.4, 130.2, 128.5, 128.1, 127.9, 127.3, 127.2, 126.9, 72.8, 66.8, 60.7, 60.0, 43.9, 26.8, 13.3.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₃H₂₇N₂O₄⁺: 395.1965; found: 395.1971.

Ethyl (2*R,3*S**,*E*)-2-Hydroxy-3-methyl-5-(2-(methylcarbamoyl)phenyl)-2-phenylpent-4-enoate (4k)**

The general procedure was followed using *N*-methylbenzamide (13.5 mg, 0.100 mmol, 1.00 equiv) and ethyl 2-oxo-2-phenylacetate (53.4 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (40% EtOAc in hexane) provided **4k** (27.2 mg, 74% yield; 92:8 dr) as a white solid; mp 133–135 °C.

IR (neat): 3529, 3337, 3060, 2939, 2879, 1727, 1630, 1538 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.75 (d, J = 7.2 Hz, minor, 0.26 H), 7.69 (d, J = 7.3 Hz, 1.74 H, major), 7.49 (d, J = 7.9 Hz, 1 H), 7.43 (t, J = 7.8 Hz, 1 H), 7.38–7.35 (m, 3 H), 7.29 (m, 1 H), 7.26–7.23 (m, 1 H), 6.92 (d, J = 15.9 Hz, 0.92 H, major), 6.52 (d, J = 15.9 Hz, 0.08 H, minor), 6.22 (dd, J = 15.9, 8.8 Hz, 1 H), 5.89 (br s, 1 H), 4.24–4.10 (m, 2 H), 3.83 (s, 1 H), 3.35–3.29 (m, 1 H), 3.01 (d, J = 4.7 Hz, 2.77 H, major), 2.91 (d, J = 4.8 Hz, 0.23 H, minor), 1.32 (t, J = 7.1 Hz, 0.23 H, minor), 1.23 (d, J = 7.1 Hz, 2.77 H, major), 1.20–1.19 (m, 0.23 H, minor), 0.91 (d, J = 6.8 Hz, 2.77 H, major).

^{13}C NMR (126 MHz, CDCl_3): δ = 175.0, 170.0, 140.2, 135.6, 135.0, 133.7, 130.2, 129.2, 128.2, 127.6, 127.5, 127.3, 126.7, 126.0, 80.6, 45.6, 26.7, 14.12, 14.06; only peaks for the major isomer are listed.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_4^+$: 368.1862; found: 368.1843.

(E)-3-Hydroxy-1-methyl-3-(4-(4-methyl-2-(1H-pyrazol-1-yl)phenyl)but-3-en-2-yl)indolin-2-one (4l)

The general procedure was followed using 1-(*m*-tolyl)-1H-pyrazole (15.7 mg, 0.100 mmol, 1.00 equiv) and 1-methylindoline-2,3-dione (48.3 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4l** (18.0 mg, 48% yield; >20:1 dr) as a light yellow solid; mp 155–157 °C.

IR (neat): 3341, 2962, 2324, 1699, 1612, 1460, 1373 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ = 7.66 (s, 1 H), 7.56 (m, 1 H), 7.47 (d, J = 7.8 Hz, 1 H), 7.30 (t, J = 7.8 Hz, 1 H), 7.22–7.17 (m, 3 H), 7.02 (t, J = 7.5 Hz, 1 H), 6.80 (d, J = 7.8 Hz, 1 H), 6.40–6.37 (m, 2 H), 6.18 (dd, J = 15.9, 7.9 Hz, 1 H), 3.17 (s, 3 H), 2.96–2.90 (m, 1 H), 2.38 (s, 3 H), 0.76 (d, J = 6.7 Hz, 3 H).

^{13}C NMR (101 MHz, CDCl_3): δ = 177.3, 143.8, 140.8, 138.4, 138.0, 131.1, 130.6, 129.8, 129.5, 129.3, 129.0, 128.5, 127.1, 126.1, 124.7, 122.8, 108.2, 106.5, 79.0, 44.4, 26.1, 21.0, 13.7.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_2^+$: 374.1869; found: 374.1866.

Ethyl (2R*,3S*,E)-2-Hydroxy-3-methyl-5-(4-methyl-2-(pyrimidin-2-yl)phenyl)-2-phenylpent-4-enoate (4m)

The general procedure was followed using 2-(*m*-tolyl)pyrimidine (17.0 mg, 0.100 mmol, 1.00 equiv) and ethyl 2-oxo-2-phenylacetate (53.4 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4m** (28.1 mg, 70% yield; >20:1 dr) as a colorless oil.

IR (neat): 3995, 2974, 2928, 1725, 1568, 1555, 1420 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 8.89 (d, J = 4.9 Hz, 2 H), 7.70 (d, J = 7.7 Hz, 2 H), 7.65 (s, 1 H), 7.48 (d, J = 7.9 Hz, 1 H), 7.36 (m, 2 H), 7.25 (m, 3 H), 7.03 (d, J = 15.9 Hz, 1 H), 6.14 (dd, J = 15.9, 8.2 Hz, 1 H), 4.11–4.04 (m, 2 H), 3.30 (m, 1 H), 2.40 (s, 3 H), 1.10 (t, J = 7.1 Hz, 3 H), 0.88 (d, J = 6.8 Hz, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 174.9, 167.2, 157.0, 140.2, 137.2, 136.3, 134.2, 131.2, 131.1, 130.9, 130.6, 128.0, 127.4, 127.1, 126.1, 118.6, 80.7, 62.3, 45.2, 21.1, 14.0, 13.7.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_3^+$: 403.2016; found: 403.2022.

Benzyl (E)-3-Hydroxy-3-(4-(4-methyl-2-(pyrimidin-2-yl)phenyl)but-3-en-2-yl)azetidine-1-carboxylate (4n)

The general procedure was followed using 2-(*m*-tolyl)pyrimidine (17.0 mg, 0.100 mmol, 1.00 equiv) and benzyl 3-oxoazetidine-1-carboxylate (61.5 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4n** (25.7 mg, 59% yield) as a colorless oil.

IR (neat): 3392, 2961, 2361, 1656, 1569, 1555, 1421, 1355 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ = 8.79 (d, J = 4.9 Hz, 2 H), 7.82 (d, J = 1.9 Hz, 1 H), 7.38–7.25 (m, 7 H), 7.21 (m, 1 H), 6.87 (d, J = 15.9 Hz, 1 H), 5.84 (dd, J = 15.9, 7.6 Hz, 1 H), 5.09 (s, 2 H), 4.04 (m, 2 H), 3.88 (m, 2 H), 2.65 (m, 1 H), 2.40 (s, 3 H), 1.16 (d, J = 6.9 Hz, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 166.2, 157.0, 156.5, 137.6, 136.7, 135.4, 134.8, 134.5, 131.2, 131.1, 129.3, 128.5, 128.0, 127.9, 127.8, 118.7, 73.0, 66.7, 60.4, 59.1, 43.5, 21.1, 13.2.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{28}\text{N}_3\text{O}_3^+$: 430.2125; found: 430.2131.

(E)-3-Hydroxy-3-(4-(4-methyl-2-(pyrimidin-2-yl)phenyl)but-3-en-2-yl)-5-nitroindolin-2-one (4o)

The general procedure was followed using 2-(*m*-tolyl)pyrimidine (17.0 mg, 0.100 mmol, 1.00 equiv) and 5-nitroindoline-2,3-dione (57.6 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in CH_2Cl_2) provided **4o** (34.2 mg, 82% yield; 85:15 dr) as a yellow powder.

IR (neat): 3226, 2361, 1733, 1624, 1523, 1423, 1338 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 8.87–8.85 (d, J = 4.9 Hz, 0.32 H, minor), 8.85–8.81 (d, J = 4.9 Hz, 1.70 H, major), 8.51 (s, 0.82 H, major), 8.20 (s, 0.18 H, minor), 8.19 (m, 1 H), 8.00 (m, 1 H), 7.91 (s, 0.86 H, major), 7.81 (s, 0.18 H, minor), 7.42 (d, J = 7.9 Hz, 0.82 H, major), 7.37 (d, J = 7.9 Hz, 0.18 H, minor), 7.32 (d, J = 7.9 Hz, 0.83 H, major), 7.29 (m, 0.18 H, minor), 7.24 (t, J = 4.9 Hz, 1 H), 7.14 (d, J = 15.7 Hz, 0.88 H, major), 6.98 (d, J = 15.7 Hz, 0.18 H, minor), 6.92 (d, J = 8.6 Hz, 0.89 H, major), 6.87 (d, J = 8.6 Hz, 0.18 H, minor), 6.05 (dd, J = 15.7, 9.2 Hz, 0.15 H, minor), 5.93 (dd, J = 15.7, 9.2 Hz, 0.85 H, major), 3.10–2.93 (m, 1 H), 2.45 (s, 2.67 H, major), 2.42 (s, 0.57 H, minor), 1.25 (s, 0.81 H, major), 1.04 (s, 0.19 H, minor), 0.92 (d, J = 7.0 Hz, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 179.0, 165.9, 157.1, 146.5, 143.6, 138.1, 137.8, 135.3, 134.3, 131.40, 131.35, 131.0, 128.0, 127.4, 126.3, 120.7, 118.7, 109.9, 79.6, 45.0, 21.2, 14.0; only peaks for the major isomer are listed.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{21}\text{N}_4\text{O}_4^+$: 417.1557; found: 417.1563.

(E)-1-Benzyl-6-chloro-3-hydroxy-3-(4-(4-methyl-2-(pyrimidin-2-yl)phenyl)but-3-en-2-yl)indolin-2-one (4p)

The general procedure was followed using 2-(*m*-tolyl)pyrimidine (17.0 mg, 0.100 mmol, 1.00 equiv) and 1-benzyl-6-chloroindoline-2,3-dione (81.5 mg, 0.300 mmol, 3.00 equiv). Purification by silica gel chromatography (50% EtOAc in hexane) provided **4p** (32.2 mg, 65% yield; 88:12 dr) as a yellow powder.

IR (neat): 3371, 3033, 2925, 1723, 1608, 1568, 1555, 1487, 1436, 1422, 1374 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 8.83 (d, J = 5.0 Hz, 2 H), 7.93 (s, 0.81 H, major), 7.92 (s, 0.12 H, minor), 7.43 (d, J = 7.8 Hz, 1 H), 7.37–7.27 (m, 6 H), 7.24–7.15 (m, 2 H), 7.09 (d, J = 8.0 Hz, 1 H), 7.04 (d, J = 7.9 Hz, 0.18 H, minor), 6.90 (d, J = 7.9 Hz, 0.83 H, major), 6.71 (d, J = 1.8 Hz, 0.88 H, major), 6.67 (d, J = 1.8 Hz, 0.12 H, minor), 6.04 (dd, J = 15.8, 9.0 Hz, 0.12 H, minor), 5.94 (dd, J = 15.8, 9.0 Hz, 0.84 H, major), 5.05 (d, J = 15.6 Hz, 0.86 H, major), 4.94 (d, J = 15.6 Hz, 0.15 H, minor), 4.74 (d, J = 15.6 Hz, 0.85 H, major), 4.64 (d, J = 15.6 Hz, 0.15 H, minor), 3.10 (m, 0.88 H, major), 2.90 (m, 0.12 H, minor), 2.45 (s, 2.64 H, major), 2.42 (s, 0.36 H, minor), 0.97 (d, J = 6.8 Hz, 0.36 H, minor), 0.84 (d, J = 6.8 Hz, 2.64 H, major).

^{13}C NMR (126 MHz, CDCl_3): δ = 177.0, 165.9, 157.2, 157.0, 144.3, 137.8, 136.3, 135.4, 135.1, 135.0, 134.8, 131.3, 131.2, 129.1, 128.92, 128.85, 128.0, 127.9, 127.4, 127.3, 125.6, 124.7, 122.9, 122.6, 118.7, 118.6, 109.81, 109.78, 79.2, 46.4, 44.7, 44.1, 43.9, 21.2, 21.1, 14.6, 14.3; peaks for both major and minor isomer are listed.

HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{30}\text{H}_{27}\text{ClN}_3\text{O}_2^+$: 496.1786; found: 496.1792.

Funding Information

This work was supported by the National Institutes of Health (R35GM122473)..

Acknowledgment

The helpful early input provided by Soham Maity is greatly appreciated.

Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0039-1690741>.

References

- Selected relevant reviews on C–H functionalization: (a) Woźniak, Ł.; Cramer, N. *Trends Chem.* **2019**, *1*, 471. (b) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. *Chem. Rev.* **2019**, *119*, 2192. (c) Kim, D.-S.; Park, W.-J.; Jun, C.-H. *Chem. Rev.* **2017**, *117*, 8977. (d) Hummel, J. R.; Boerth, J. A.; Ellman, J. A. *Chem. Rev.* **2017**, *117*, 9163. (e) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900. (f) Yang, L.; Huang, H. *Chem. Rev.* **2015**, *115*, 3468. (g) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369. (h) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; *Angew. Chem.* **2012**, *124*, 9092.
- Selected reviews for three-component Catellani-type reactions: (a) Wang, J.; Dong, G. *Chem. Rev.* **2019**, *119*, 7478. (b) Della Ca', N.; Fontana, M.; Motti, E.; Catellani, M. *Acc. Chem. Res.* **2016**, *49*, 1389. (c) Ye, J.; Lautens, M. *Nat. Chem.* **2015**, *7*, 863. (d) Martins, A.; Mariampillai, B.; Lautens, M. *Top. Curr. Chem.* **2010**, *292*, 1. (e) Catellani, M. *Top. Organomet. Chem.* **2005**, *14*, 21. (f) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119; *Angew. Chem.* **1997**, *109*, 142.
- (a) Pinkert, T.; Wegner, T.; Mondal, S.; Glorius, F. *Angew. Chem. Int. Ed.* **2019**, *58*, 15041; *Angew. Chem.* **2019**, *131*, 15183. (b) Wang, X.-G.; Li, Y.; Liu, H.-C.; Zhang, B.-S.; Gou, X.-Y.; Wang, Q.; Ma, J.-W.; Liang, Y.-M. *J. Am. Chem. Soc.* **2019**, *141*, 13914. (c) Maity, S.; Potter, T. J.; Ellman, J. A. *Nat. Catal.* **2019**, *2*, 756. (d) Yang, J.; Ji, D.-W.; Hu, Y.-C.; Min, X.-T.; Zhou, X.; Chen, Q.-A. *Chem. Sci.* **2019**, *10*, 9560. (e) Dongbang, S.; Shen, Z.; Ellman, J. A. *Angew. Chem. Int. Ed.* **2019**, *58*, 12590; *Angew. Chem.* **2019**, *131*, 12720. (f) Li, R.; Ju, C.-W.; Zhao, D. *Chem. Commun.* **2019**, *55*, 695. (g) Tang, M.; Li, Y.; Han, S.; Liu, L.; Ackermann, L.; Li, J. *Eur. J. Org. Chem.* **2019**, 660. (h) Boerth, J. A.; Maity, S.; Williams, S. K.; Mercado, B. Q.; Ellman, J. A. *Nat. Catal.* **2018**, *1*, 673. (i) Boerth, J. A.; Ellman, J. A. *Angew. Chem. Int. Ed.* **2017**, *56*, 9976; *Angew. Chem.* **2017**, *129*, 10108. (j) Zhang, S.-S.; Xia, J.; Wu, J.-Q.; Liu, X.-G.; Zhou, C.-J.; Lin, E.; Li, Q.; Huang, S.-L.; Wang, H. *Org. Lett.* **2017**, *19*, 5868. (k) Boerth, J. A.; Hummel, J. R.; Ellman, J. A. *Angew. Chem. Int. Ed.* **2016**, *55*, 12650; *Angew. Chem.* **2016**, *128*, 12840. (l) Boerth, J. A.; Ellman, J. A. *Chem. Sci.* **2016**, *7*, 1474.
- Intermolecular addition of unactivated C–H bonds to ketones to give tertiary alcohols has only been reported for a couple of very highly activated ketones: (a) Jo, H.; Park, J.; Choi, M.; Sharma, S.; Jeon, M.; Mishra, N. K.; Jeong, T.; Han, S.; Kim, I. S. *Adv. Synth. Catal.* **2016**, *358*, 2714. (b) Zhang, X. S.; Zhu, Q. L.; Luo, F. X.; Chen, G. H.; Wang, X.; Shi, Z. J. *Eur. J. Org. Chem.* **2013**, 6530.
- Tanaka, R.; Ikemoto, H.; Kanai, M.; Yoshino, T.; Matsunaga, S. *Org. Lett.* **2016**, *18*, 5732.
- CCDC 1956911 (**4k**) and CCDC 1957083 (**4l**) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.
- Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112.