Intermolecular Pauson–Khand-Type Reaction of Vinyl Iodides with Alkynes and a CO Surrogate

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Supporting Information Placeholder

ABSTRACT: A strategy for the palladium-catalyzed intermolecular synthesis of polysubstituted cyclopentenones is reported. The three-component reaction utilizes vinyl iodides and internal alkynes to form the carbon framework of the cyclopentenone with $Cr(CO)_6$ serving as an easy to handle, solid CO surrogate, and a hydrosilane as a hydride source. We demonstrate the scope of the reaction which includes a wide range of functional groups. The reaction is regioselective, with the use of linear or branched vinyl iodides resulting in the α- or β-substituted cyclopentenones, respectively. Further, we show that a two-step sequence from commercially available alkynes can be used to generate cyclopentenone products via formation of the vinyl iodide and subsequent Pauson–Khand-type reaction.

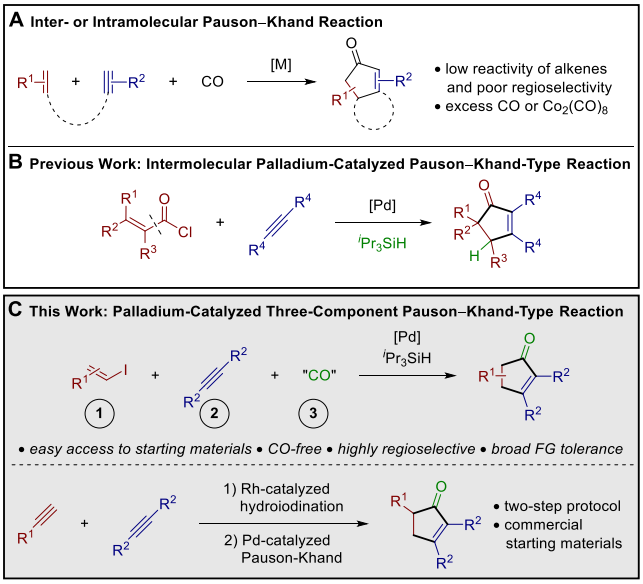
INTRODUCTION

In recent years, considerable effort has been focused on streamlining organic synthesis to access elaborate molecular scaffolds, thus reducing step count, as well as mitigating the generation of waste, resulting in more sustainable synthesis.[1–4] A key step towards this is the formation of multiple carbon–carbon bonds in a single reaction step to generate complex molecular scaffolds. The perennial interest in carbon–carbon bond forming reactions has inspired the development of a plethora of methods, including cycloaddition reactions and cascade reactions mediated by transition metals.[5–16]

A prominent example among these transformations is the Pauson–Khand reaction, a formal [2+2+1] cycloaddition between an alkene, an alkyne (or allene), and carbon monoxide (Scheme 1, A).[17–25] This reaction enables rapid access to highly functionalized cyclopentenone scaffolds, a prevalent motif encountered in natural products and synthetic intermediates.[26–38] Traditionally, the Pauson–Khand reaction uses stoichiometric amounts of cobalt carbonyl ($Co_2(CO)_8$) both as a carbon monoxide source and as a mediator to form three new C–C bonds from an alkyne and an alkene to generate cyclopentenone products.[19–20]

Despite its inherent attractiveness, the Pauson–Khand reaction exhibits several limitations, including the low reactivity of alkenes, issues with regioselectivity, as well as the requirement for hazardous reagents (e.g., stoichiometric cobalt carbonyl or toxic carbon monoxide gas). Attempts to alleviate these limitations have resulted in the deployment of some creative approaches including the installation of cleavable directing groups,[39–44] the use of carbon monoxide surrogates,[45–51] as well as less toxic catalysts and reagents.[52–61] Issues of regio- and enantioselectivity have also been partially address with Rh-based catalyst systems.[24]

Scheme 1. Context of the Research.



Other transition-metal-catalyzed approaches which form these important cyclopentenones take mechanistically distinct pathways.[62,63] Examples of this include the transition metal catalyzed cyclization of α,β-unsaturated carbonyls with alkynes by Ogoshi,[64] Montgomery,[65,66] Barluenga,[67,68] and others.[69–73] Previously, our group has also reported a distinct entry into this class of compounds. We used palladium catalysis to engage α,β-unsaturated acid chlorides and internal alkynes in the presence of a hydrosilane, as a hydride source, to form cyclopentenones through a molecular shuffling approach (Scheme 1, B).[74] The reaction proceeded with a wide variety of acid chlorides and alkynes, and the corresponding densely functionalized cyclopentenones, which can be difficult to access using other

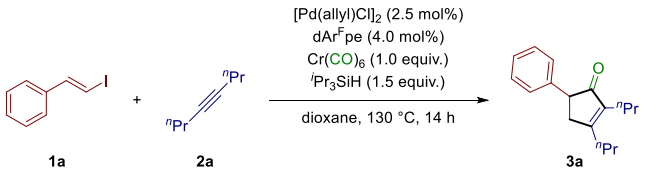
methods, were isolated in good yields. This report also contained one example of a vinyl iodide, which was coupled with an alkyne in the presence of a carbon monoxide source using a palladium catalyst to form cyclopentenones, albeit in low yield.

In a separate line of research, we recently reported the rhodium-catalyzed anti-Markovnikov hydroiodination of terminal alkynes, allowing for rapid access to vinyl iodides.[75] We considered using the hydroiodination methodology to access vinyl iodides in the development of a 4-component synthesis of cyclopentenones (Scheme 1, C). This would provide a modular synthesis of these scaffolds through a two-step synthetic sequence starting from feedstock alkyne starting materials.

RESULTS AND DISCUSSION

In the first step, we aimed to develop the reaction between vinyl iodides and alkynes to access cyclopentenones. Initial conditions focused on employing (*E*)-(2-iodovinyl)benzene (**1a**) and 4-octyne (**2a**) under various catalytic systems depicted in Table 1, to give cyclopentenone **3a**.

Table 1. Reaction Optimization



1a 0.25 mmol 1.0 equiv. + **2a** 1.5 equiv. → **3a**

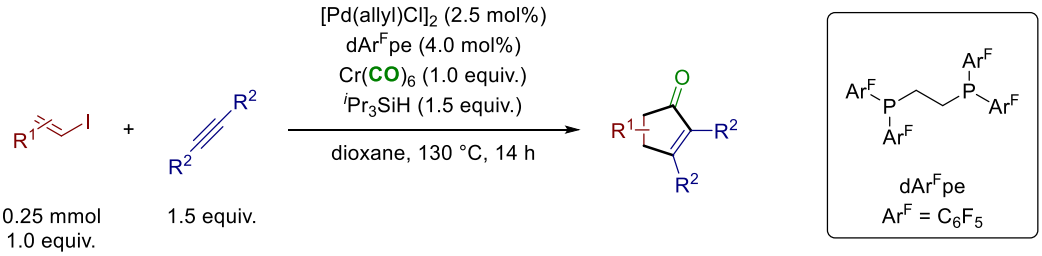
entry	variations from above conditions	**3a** (%)[a]
1	**none**	**74**
2	3,5-CF_3-PPh_3 instead of dAr^Fpe	65
3	dppe instead of dArFpe	64
4	Phenylacetyl chloride instead of $Cr(CO)_6$	36
5	$Mo(CO)_6$ instead of $Cr(CO)_6$	41
6	$Pd(OAc)_2$ instead of $[Pd(allyl)Cl]_2$	55
7	**1a**/**2a**/^{i}Pr$_3$SiH equivalent ratio 1.0/2.0/2.0	68
8	**1a**/**2a**/^{i}Pr$_3$SiH equivalent ratio 1.0/1.0/1.0	43
9	0.167 equiv. instead of 1.0 equiv. $Cr(CO)_6$	50
10	toluene instead of dioxane	35
11	no Pd, no ligand	n.d.

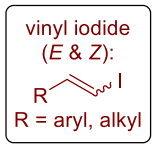
[a]Product yields were determined by GC analysis with *n*-dodecane as internal standard.

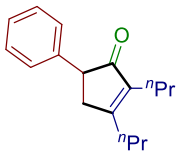
During our investigation, we found that different phosphine ligands performed similarly, with phosphines containing electron-poor substituents (e.g., pentafluorophenyl or 3,5-CF_3-phenyl groups) giving slightly higher yields, and 1,2-bis[bis(pentafluorophenyl)phosphino]ethane (dAr^Fpe) proving optimal (Table 1, entries 1–3).[74,76–78] Phenylacetyl chloride could be used as a CO surrogate in the presence of a hydrosilane to form CO and toluene, to form the cyclopentenone product in poor yield (Table 1, entry 4).[74] Evaluating other common CO surrogates, we found that chromium hexacarbonyl ($Cr(CO)_6$), an easy to handle solid, is a superior CO surrogate. Descending in group 6 to molybdenum hexacarbonyl ($Mo(CO)_6$) resulted in reduced yields (Table 1, entry 5). Alternative CO surrogates, such as paraformaldehyde, failed to deliver the product (see SI for details). Further optimization revealed that the stoichiometry of the two starting materials **1a** and **2a**, as well as the equivalents of hydrosilane affected the yield of **3a**. A ratio of both the alkyne and the hydrosilane of 1.5 equivalents relative to the vinyl iodide gave a maximum yield of 74% (Table 1, entry 1). Increasing or reducing the equivalents of alkyne and hydrosilane (Table 1, entries 7 and 8), and of the CO surrogate (Table 1, entry 9) had a detrimental effect on the yield of the product. Less polar solvents, such as toluene, resulted in a decreased yield (Table 1, entry 10). Control experiments demonstrated that the palladium catalyst was necessary for the reaction to occur, ruling out the possibility of chromium mediating the transformation (Table 1, entry 11).[79]

After optimizing the reaction conditions, the substrate scope was examined (Table 2). A broad variety of substituted vinyl iodides were converted to the corresponding cyclopentenones. Vinyl iodide **1a** afforded the corresponding product **3a** in 71% isolated yield (74% GC yield). Conducting the same reaction at a larger scale (1 mmol) provided **3a** in a comparable yield (69%). Other alkyl- and aryl-substituted vinyl iodides **1b–d** and π-extended vinyl iodide **1e** worked well, with the cyclopentenones **3b–e** being isolated in good yields (57–83%) as single regioisomers. Ethers, including *para*-methoxy- and *para*-benzyloxy-substituents, were well tolerated and the cyclopentenone products **3f** and **3g** were isolated in 61% and 65% yields, respectively. Similarly, vinyl iodides with electron-withdrawing substituents on the aryl ring, including an ester, a methyl ketone and a nitrile, were efficiently converted into their corresponding cyclopentenones **3h**, **3i** and **3j** in 55, 82 and 72% yield, respectively. Vinyl iodides with halide substituents were also successful in this three-component Pauson–Khand-type reaction. For example, a *para*-chloro-substituted vinyl iodide gave the corresponding cyclopentenone **3k** in 88% yield, and a *para*-bromo-substituted vinyl iodide afforded **3l** in 71% yield. Notably, no reactivity of the C(sp^2)–Br bond was observed, showcasing the chemoselectivity of this method. Trifluoromethyl-substituted cyclopentenone **3m** was isolated in 66% yield. β-Diarylsubstituted vinyl iodides worked well in this reaction and product **3n**, featuring a quaternary carbon center, was obtained in 63% yield. Alkyl vinyl iodides were also tested, including (*E*)-1-iodooct-1-ene (**1o**) which formed cyclopentenone **3o** in 64% yield. To our delight, (*Z*)-vinyl iodides also worked successfully in this transformation and products **3p** and **3q** were obtained as single regioisomers in 72% and 47% yields, respectively. While aliphatic α-vinyl iodides were not reactive in this Pauson–Khand-type reaction (see SI for substrate limitations), aromatic α-vinyl iodides featuring *para*-substituted methyl sulfide and trimethylsilyl showed moderate to good reactivity, giving the products **3r** in 51% and **3s** in 61% yield, respectively. It is noteworthy that the substituent is now in the β-position relative to the carbonyl of the cyclopentenone, as confirmed by 2D NMR analysis, showcasing a switch in regioselectivity. Several symmetric internal alkynes were also tested in the three-component reaction. Cyclopentenone **3t**, stemming from the reaction of **1a** with 5-decyne (**2b**), was isolated in 41% yield. A cyclic alkyne was efficiently converted to product **3u** in 80% yield, and product **3v** could be obtained in 67% yield. Lastly, an unsymmetrical alkyl-alkyl alkyne gave **3w** in 63% yield, with a slight preference for the alkenyl insertion at the sterically less crowded position.

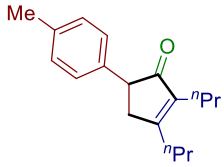
Table 2. Scope of Vinyl Iodides and Alkynes.[a]



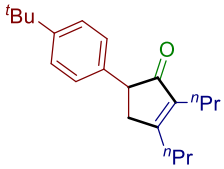




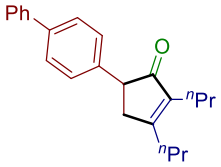
3a 71% (74%)[b]
1 mmol scale: 69%



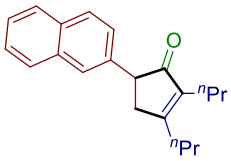
3b 70%



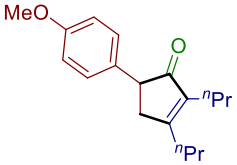
3c 83%



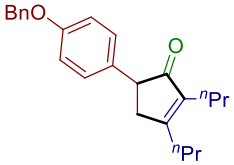
3d 68%



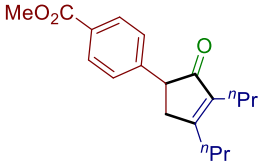
3e 57%



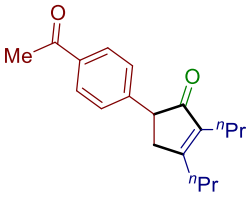
3f 61%



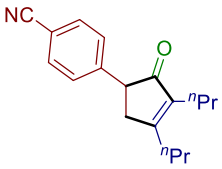
3g 65%



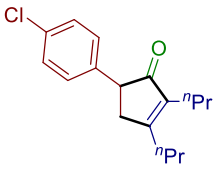
3h 55%



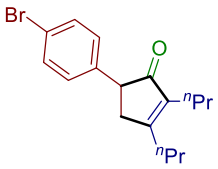
3i 82%



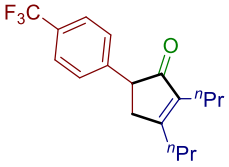
3j 72%



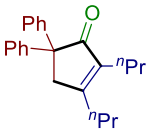
3k 88%



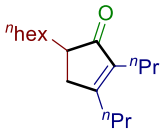
3l 71%



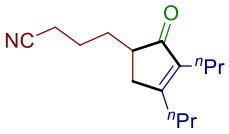
3m 66%



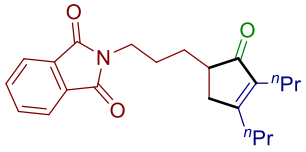
3n 63%



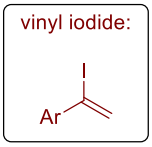
3o 64%

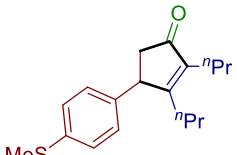


3p 72%[c]

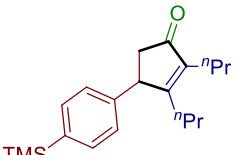


3q 47%[c]

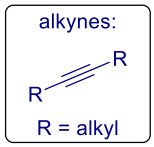


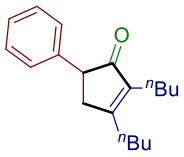


3r 51%

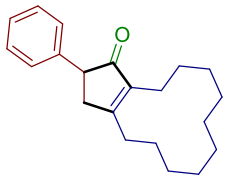


3s 61%

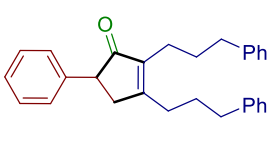




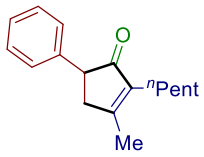
3t 41%



3u 80%



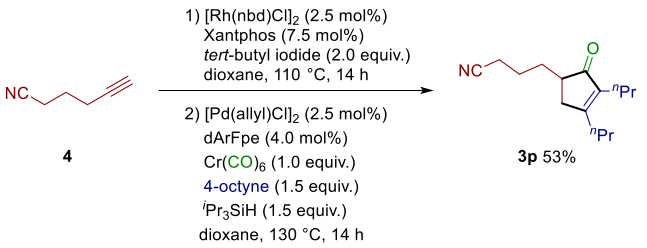
3v 67%



3w 63%
(*rr* = 57:43)

[a]All reported yields are isolated yields of single regioisomers. [b]GC yield is given in brackets. [c]Starting from the corresponding (*Z*)-vinyl iodide.

Scheme 2. Two-Step Protocol for the Iodination/Pauson–Khand-type Reaction of Terminal Alkyne 4.



With a procedure identified to efficiently transform vinyl iodides into cyclopentenones in a three-component palladium-catalyzed Pauson–Khand-type reaction, we considered that a consecutive hydroiodination-Pauson–Khand-type reaction sequence would enable fast and straightforward access to highly decorated cyclopentenones from widely available and inexpensive starting materials, an internal and a terminal alkyne. This was achieved by performing the rhodium-catalyzed hydroiodination reaction of terminal alkyne **4**, affording (*Z*)-vinyl iodide intermediate (**1p**), a reaction that was recently discovered in our group.[75] The crude reaction mixture was then filtered and concentrated, before subjecting it to the conditions for the palladium-catalyzed Pauson–Khand-type reaction (Scheme 2). The desired product **3p** could be isolated in a moderate yield of 53% over two steps, showcasing the potential of this reaction to quickly access cyclopentenones from simple starting materials. This two-step sequence without intermediate purification highlights the synthetic utility of this new synthetic transformation.

CONCLUSIONS

In summary, an operationally simple palladium-catalyzed three-component Pauson–Khand-type reaction between vinyl iodides and internal alkynes is reported. Commercially available and easy to handle chromium hexacarbonyl serves as a CO surrogate and triisopropylsilane as an inexpensive hydride source. A variety of functional groups were compatible, including an ester, a ketone, a nitrile, halides, a sulfide, a protected amine, etc. Importantly, both α- and β-substituted cyclopentenones can be accessed using linear or branched vinyl iodides, respectively. Finally, a two-step protocol allows for the construction of densely functionalized cyclopentenones from widely available terminal and internal alkynes via a hydroiodination/Pauson–Khand-type reaction sequence.

EXPERIMENTAL SECTION

General Information. For the purification of the products, either column chromatography using silica gel 60 (particle size 40–63 μm, Silicycle) or preparative thin-layer chromatography using glass-backed silica gel plates (Merck, 0.25 mm, silica gel, Si 60, F_{254}) was performed, using either *n*-pentane (or *n*-hexane) and ethyl acetate or toluene and ethyl acetate as eluent. ^{1}H, ^{13}C{^{1}H} and ^{19}F{^{1}H} NMR spectra were recorded on commercial instruments (Bruker Avance III 400 MHz, Bruker Neo 400 MHz and Bruker Avance III 500 MHz, all equipped with a BBFO probe). The proton signal of the residual non-deuterated solvent (δ 7.26 ppm for $CDCl_3$, δ 5.32 ppm for CD_2Cl_2) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C{^{1}H} NMR spectra, chemical shifts are reported relative to the δ 77.16 ppm resonance of $CDCl_3$ or the δ 54.00 resonance for CD_2Cl_2. Structural assignments were made by comparison with identical literature spectra or via analogy. High-resolution mass spectra were measured on a Bruker *maXis* – ESI Qq-TOF-MS instrument by the mass spectrometry service facility in the Laboratories of Organic Chemistry at ETH Zürich. The molecular ion [M]+ and [M+H]$^+$ are given in m/z units. The substrates were either purchased from commercial suppliers or synthesized (see SI for details). All other reagents and solvents were purchased from commercial suppliers and used directly without further purification.

General Procedure for the Palladium-Catalyzed Intermolecular Pauson–Khand Reaction between Vinyl Iodides and Internal Alkynes. Inside a glovebox filled with argon, a 4-mL vial equipped with a Teflon-coated stir bar was charged with $[Pd(allyl)Cl]_2$ (2.3 mg, 6.25 μmol, 2.5 mol%), dAr^{F}pe (7.6 mg, 10.0 μmol, 4.0 mol%), $Cr(CO)_6$ (55.0 mg, 0.25 mmol, 1.0 equiv.), dioxane (1.0 mL, 0.25 M), the respective alkyne **2a–d** (0.375 mmol, 1.5 equiv.), triisopropylsilane (76.8 μL, 59.3 mg, 0.375 mmol, 1.5 equiv.), and the respective vinyl iodide **1a–s** (0.25 mmol, 1.0 equiv.). The vial was tightly closed with a screw cap. It was then removed from the glovebox and stirred at 130 °C for 14 hours in a pre-heated heating block. The reaction mixture was allowed to cool to room temperature, filtered over a short plug of Celite, and the solvent was removed under reduced pressure. The residue was purified by either column chromatography over silica or by preparative thin-layer chromatography to afford the corresponding cyclopentenone products **3a–v**.

*5-phenyl-2,3-dipropylcyclopent-2-en-1-one (**3a**).* Compound **3a** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 43.3 mg, 0.179 mmol, 71% yield. Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.27 (m, 2H), 7.25–7.18 (m, 1H), 7.14–7.08 (m, 2H), 3.54 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.04 (ddt, *J* = 18.5, 7.3, 1.2 Hz, 1H), 2.59 (ddt, *J* = 18.4, 2.6, 1.2 Hz, 1H), 2.54–2.43 (m, 2H), 2.29–2.13 (m, 2H), 1.68–1.56 (m, 2H), 1.51–1.40 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.94–0.89 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 208.8, 173.0, 140.7, 139.8, 128.8, 127.6, 126.8, 51.1, 39.2, 33.2, 25.4, 21.9, 21.0, 14.3, 14.2. The spectroscopic data matched those reported in the literature.[74]

*2,3-dipropyl-5-(p-tolyl)cyclopent-2-en-1-one (**3b**).* Compound **3b** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 44.7 mg, 0.174 mmol, 70% yield. Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.14–7.08 (m, 2H), 7.03–6.97 (m, 2H), 3.50 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.08–2.97 (m, 1H), 2.57 (ddt, *J* = 18.5, 2.5, 1.1 Hz, 1H), 2.53–2.40 (m, 2H), 2.31 (s, 3H), 2.26–2.17 (m, 2H), 1.63 (dt, *J* = 7.8, 7.3 Hz, 2H), 1.45 (h, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 209.0, 172.9, 139.8, 137.6, 136.3, 129.5, 127.4, 50.7, 39.2, 33.2, 25.4, 21.9, 21.1, 21.0, 14.3, 14.2. The spectroscopic data matched those reported in the literature.[74]

*5-(4-(tert-butyl)phenyl)-2,3-dipropylcyclopent-2-en-1-one (**3c**).* Compound **3c** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (17:3, v/v) as the eluent: 62.1 mg, 0.208 mmol, 83% yield. Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.29 (m, 2H), 7.07–7.02 (m, 2H), 3.52 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.02 (dddd, *J* = 18.4, 7.2, 2.1, 1.1 Hz, 1H), 2.60 (ddt, *J* = 18.4, 2.4, 1.1 Hz, 1H), 2.53–2.43 (m, 2H), 2.26–2.17 (m, 2H), 1.68–1.56 (m, 2H), 1.45 (q, *J* = 7.5 Hz, 2H), 1.30 (s, 9H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H).^{13}C{^{1}H} NMR (101 MHz,

$CDCl_3$) δ 209.1, 173.0, 149.5, 139.8, 137.5, 127.2, 125.8, 50.6, 39.2, 34.5, 33.2, 31.5, 25.4, 22.0, 21.0, 14.4, 14.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{31}O$, 299.2369; found, 299.2369.

*5-([1,1'-biphenyl]-4-yl)-2,3-dipropylcyclopent-2-en-1-one **(3d)**.* Compound **3d** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 54.1 mg, 0.170 mmol, 68% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.59–7.49 (m, 4H), 7.46–7.38 (m, 2H), 7.36–7.30 (m, 1H), 7.22–7.16 (m, 2H), 3.59 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.08 (ddt, *J* = 18.5, 7.3, 1.2 Hz, 1H), 2.64 (ddt, *J* = 18.4, 2.6, 1.1 Hz, 1H), 2.50 (hept, *J* = 6.8 Hz, 2H), 2.32–2.16 (m, 2H), 1.72–1.58 (m, 2H), 1.47 (h, *J* = 7.4 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.9, 173.1, 141.1, 139.9, 139.8, 139.7, 128.9, 128.0, 127.7, 127.3, 127.2, 50.8, 39.2, 33.3, 25.5, 22.0, 21.0, 14.4, 14.2. The spectroscopic data matched those reported in the literature.[74]

*5-(naphthalen-2-yl)-2,3-dipropylcyclopent-2-en-1-one **(3e)**.* Compound **3e** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 41.8 mg, 0.143 mmol, 57% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84–7.73 (m, 3H), 7.62 (dt, *J* = 1.9, 0.7 Hz, 1H), 7.49–7.38 (m, 2H), 7.18 (dd, *J* = 8.5, 1.8 Hz, 1H), 3.72 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.18–3.04 (m, 1H), 2.69 (ddt, *J* = 18.5, 2.5, 1.1 Hz, 1H), 2.59–2.44 (m, 2H), 2.33–2.18 (m, 2H), 1.66 (h, *J* = 7.5 Hz, 2H), 1.48 (h, *J* = 7.4 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.8, 173.1, 140.1, 138.0, 133.7, 132.5, 128.7, 127.8, 127.7, 126.7, 126.2, 125.7, 125.5, 51.2, 39.2, 33.3, 25.5, 22.0, 21.0, 14.4, 14.3. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{25}O$, 293.1900; found, 293.1898.

*5-(4-methoxyphenyl)-2,3-dipropylcyclopent-2-en-1-one **(3f)**.* Compound **3f** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 41.3 mg, 0.152 mmol, 61% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.06–7.00 (m, 2H), 6.87–6.81 (m, 2H), 3.77 (s, 3H), 3.48 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.02 (ddt, *J* = 18.4, 7.2, 1.1 Hz, 1H), 2.59–2.51 (m, 1H), 2.51–2.40 (m, 2H), 2.26–2.16 (m, 2H), 1.68–1.54 (m, 2H), 1.44 (h, *J* = 7.5 Hz, 2H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 209.1, 172.7, 158.4, 139.7, 132.6, 128.4, 114.2, 55.3, 50.1, 39.2, 33.1, 25.3, 21.8, 20.9, 14.2, 14.1. The spectroscopic data matched those reported in the literature.[74]

*5-(4-(benzyloxy)phenyl)-2,3-dipropylcyclopent-2-en-1-one **(3g)**.* Compound **3g** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 56.6 mg, 0.162 mmol, 65% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.35 (m, 4H), 7.34–7.29 (m, 1H), 7.06–7.00 (m, 2H), 6.95–6.89 (m, 2H), 5.04 (s, 2H), 3.49 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.02 (ddt, *J* = 18.4, 7.2, 1.1 Hz, 1H), 2.62–2.38 (m, 3H), 2.27–2.15 (m, 2H), 1.62 (h, *J* = 7.5 Hz, 2H), 1.45 (h, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 209.2, 172.9, 157.8, 139.8, 137.2, 133.0, 128.7, 128.6, 128.0, 127.6, 115.3, 70.2, 50.3, 39.3, 33.2, 25.4, 22.0, 21.0, 14.4, 14.2. The spectroscopic data matched those reported in the literature.[74]

*methyl 4-(2-oxo-3,4-dipropylcyclopent-3-en-1-yl)benzoate **(3h)**.* Compound **3h** was synthesized according to the general procedure and purified by column chromatography on silica using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 41.2 mg, 0.137 mmol, 55% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.00–7.93 (m, 2H), 7.21–7.15 (m, 2H), 3.89 (s, 3H), 3.60 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.0(ddt, *J* = 18.5, 7.3, 1.1 Hz, 1H), 2.59 (ddt, *J* = 18.5, 2.6, 1.1 Hz, 1H), 2.49 (td, *J* = 7.5, 5.3 Hz, 2H), 2.26–2.16 (m, 2H), 1.63 (h, *J* = 7.5 Hz, 2H), 1.44 (h, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.0, 173.2, 167.1, 145.9, 139.9, 130.2, 128.7, 127.7, 52.2, 51.1, 38.9, 33.2, 25.4, 21.9, 21.0, 14.4, 14.2. The spectroscopic data matched those reported in the literature.[74]

*5-(4-acetylphenyl)-2,3-dipropylcyclopent-2-en-1-one **(3i)**.* Compound **3i** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (7:3, v/v) as the eluent: 58.0 mg, 0.204 mmol, 82% yield. Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.92–7.86 (m, 2H), 7.22–7.17 (m, 2H), 3.61 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.06 (dddd, *J* = 19.6, 8.3, 2.1, 1.0 Hz, 1H), 2.63–2.55 (m, 4H), 2.49 (td, *J* = 7.5, 5.9 Hz, 2H), 2.21 (tdt, *J* = 7.8, 2.3, 1.1 Hz, 2H), 1.63 (h, *J* = 7.5 Hz, 2H), 1.44 (h, *J* = 7.6 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 207.9, 197.8, 173.2, 146.1, 139.9, 135.8, 129.0, 127.9, 51.0, 38.8, 33.2, 26.7, 25.4, 21.9, 21.0, 14.3, 14.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{25}O_2$, 285.1849; found, 285.1850.

*4-(2-oxo-3,4-dipropylcyclopent-3-en-1-yl)benzonitrile **(3j)**.* Compound **3j** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 48.3 mg, 0.181 mmol, 72% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.62–7.55 (m, 2H), 7.25–7.19 (m, 2H), 3.60 (dd, *J* = 7.2, 2.7 Hz, 1H), 3.07 (ddq, *J* = 18.5, 7.3, 1.1 Hz, 1H), 2.62–2.53 (m, 1H), 2.49 (td, *J* = 7.5, 4.2 Hz, 2H), 2.20 (ddt, *J* = 9.0, 6.4, 1.3 Hz, 2H), 1.62 (h, *J* = 7.5 Hz, 2H), 1.48–1.37 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 207.3, 173.3, 145.9, 139.9, 132.6, 128.5, 118.9, 110.7, 51.0, 38.6, 33.2, 25.4, 21.9, 21.0, 14.3, 14.2. The spectroscopic data matched those reported in the literature.[74]

*5-(4-chlorophenyl)-2,3-dipropylcyclopent-2-en-1-one **(3k)**.* Compound **3k** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 60.8 mg, 0.220 mmol, 88% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.29–7.24 (m, 2H), 7.06–7.02 (m, 2H), 3.51 (dd, *J* = 7.2, 2.7 Hz, 1H), 3.04 (dddd, *J* = 18.4, 7.4, 2.1, 1.1 Hz, 1H), 2.54 (ddt, *J* = 18.5, 2.5, 1.1 Hz, 1H), 2.52–2.43 (m, 2H), 2.24–2.17 (m, 2H), 1.67–1.57 (m, 2H), 1.49–1.37 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.3, 173.0, 139.9, 139.0, 132.6, 129.00, 128.98, 50.4, 39.0, 33.2, 25.4, 21.9, 21.0, 14.4, 14.2. The spectroscopic data matched those reported in the literature.[74]

*5-(4-bromophenyl)-2,3-dipropylcyclopent-2-en-1-one **(3l)**.* Compound **3l** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 56.7 mg, 0.176 mmol, 71% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.47–7.41 (m, 2H), 7.05–6.96 (m, 2H), 3.52 (dd, *J* = 7.2, 2.7 Hz, 1H), 3.11–2.99 (m, 1H), 2.62–2.44 (m, 3H), 2.23 (dddd, *J* = 8.8, 7.9, 2.4, 1.1 Hz, 2H), 1.70–1.58 (m, 2H), 1.46 (h, *J* = 7.5 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.2, 173.0, 139.9, 139.6, 131.9, 129.4, 120.7, 50.5, 39.0, 33.2, 25.4, 21.9, 21.0, 14.4, 14.2. The spectroscopic data matched those reported in the literature.[74]

*2,3-dipropyl-5-(4-(trifluoromethyl)phenyl)cyclopent-2-en-1-one **(3m)**.* Compound **3m** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 51.5 mg, 0.166 mmol, 66% yield. Colorless oil. ^1H NMR ($CDCl_3$,

400 MHz): δ 7.59–7.52 (m, 2H), 7.25–7.20 (m, 2H), 3.61 (dd, *J* = 7.2, 2.7 Hz, 1H), 3.07 (dddd, *J* = 19.5, 8.3, 2.1, 1.0 Hz, 1H), 2.59 (ddt, *J* = 18.5, 2.6, 1.1 Hz, 1H), 2.49 (td, *J* = 7.6, 5.8 Hz, 2H), 2.22 (tdt, *J* = 7.8, 2.1, 1.1 Hz, 2H), 1.64 (dt, *J* = 15.0, 7.5 Hz, 2H), 1.44 (h, *J* = 7.5 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 207.9, 173.2, 144.6 (q, *J* = 1.4 Hz), 140.0, 129.2 (q, *J* = 32.6 Hz), 128.0, 125.8 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.9 Hz), 50.8, 38.9, 33.2, 25.4, 21.9, 21.0, 14.4, 14.2. $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$) δ -62.51. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{22}F_3O$, 311.1617; found, 311.1612.

*5,5-diphenyl-2,3-dipropylcyclopent-2-en-1-one (**3n**).* Compound **3n** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 50.3 mg, 0.158 mmol, 63% yield. Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.25 (m, 4H), 7.24–7.18 (m, 6H), 3.32–3.29 (m, 2H), 2.50 (dd, *J* = 8.6, 6.9 Hz, 2H), 2.24 (ddd, *J* = 8.8, 6.8, 1.1 Hz, 2H), 1.71–1.60 (m, 2H), 1.51–1.38 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.1, 171.2, 144.3, 139.0, 128.4, 128.1, 126.6, 60.1, 48.3, 33.1, 25.5, 21.9, 21.1, 14.4, 14.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{27}O$, 319.2056; found, 319.2055.

*5-hexyl-2,3-dipropylcyclopent-2-en-1-one (**3o**).* Compound **3o** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (19:1, v/v) as the eluent: 40.3 mg, 0.161 mmol, 64% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.65 (ddt, *J* = 18.2, 6.7, 1.0 Hz, 1H), 2.41–2.33 (m, 2H), 2.28 (dddd, *J* = 8.8, 6.5, 4.2, 2.1 Hz, 1H), 2.19–2.08 (m, 3H), 1.84–1.72 (m, 1H), 1.62–1.50 (m, 2H), 1.45–1.19 (m, 11H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 212.2, 172.3, 139.9, 45.2, 36.2, 33.2, 31.94, 31.87, 29.5, 27.4, 25.2, 22.8, 22.0, 21.0, 14.3, 14.21, 14.20. The spectroscopic data matched those reported in the literature.[74]

*4-(2-oxo-3,4-dipropylcyclopent-3-en-1-yl)butanenitrile (**3p**).* Compound **3p** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (3:2, v/v) as the eluent: 41.7 mg, 0.179 mmol, 72% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.72 (ddt, *J* = 18.1, 6.9, 1.0 Hz, 1H), 2.45–2.27 (m, 5H), 2.20–2.08 (m, 3H), 1.91–1.66 (m, 3H), 1.63–1.47 (m, 3H), 1.45–1.32 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 210.9, 172.5, 140.0, 119.6, 44.0, 36.1, 33.1, 31.0, 25.2, 23.3, 22.0, 21.0, 17.4, 14.3, 14.2. HRMS(ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{15}H_{23}NNaO$, 256.1672; found, 256.1675.

*2-(3-(2-oxo-3,4-dipropylcyclopent-3-en-1-yl)propyl)isoindoline-1,3-dione (**3q**).* Compound **3q** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (3:2, v/v) as the eluent: 41.4 mg, 0.117 mmol, 47% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.86–7.80 (m, 2H), 7.74–7.66 (m, 2H), 3.76–3.62 (m, 2H), 2.67 (ddt, *J* = 18.2, 7.0, 1.1 Hz, 1H), 2.41–2.33 (m, 2H), 2.32 (dddd, *J* = 9.4, 6.9, 4.5, 2.5 Hz, 1H), 2.18–2.06 (m, 3H), 1.89–1.80 (m, 1H), 1.80–1.70 (m, 2H), 1.60–1.48 (m, 2H), 1.42–1.30 (m, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 211.2, 172.3, 168.5, 139.9, 134.0, 132.3, 123.4, 44.5, 38.0, 36.1, 33.1, 29.0, 26.6, 25.3, 22.0, 21.0, 14.3, 14.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{22}H_{28}NO_3$, 354.2064; found, 354.2064.

*4-(4-(methylthio)phenyl)-2,3-dipropylcyclopent-2-en-1-one (**3r**).* Compound **3r** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (9:1, v/v) as the eluent: 36.8 mg, 0.128 mmol, 51% yield. Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.23–7.17 (m, 2H), 7.03–6.97 (m, 2H), 3.89 (d, *J* = 7.0 Hz, 1H), 2.92–2.79 (m, 1H), 2.47 (s, 3H), 2.38 (ddd, *J* = 13.5, 9.3, 7.0 Hz, 1H), 2.32–2.17 (m, 3H), 1.96 (ddd, *J* = 14.0, 9.3, 5.3 Hz, 1H), 1.56–1.43 (m, 3H), 1.34 (ddt, *J* = 13.3, 9.4, 7.2 Hz, 1H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 209.2, 175.2, 141.6, 139.4, 137.1, 128.0, 127.3, 46.1, 44.9, 31.1, 25.4, 22.1, 20.9, 16.0, 14.33, 14.29. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{25}OS$, 289.1621; found, 289.1620.

*2,3-dipropyl-4-(4-(trimethylsilyl)phenyl)cyclopent-2-en-1-one (**3s**).* Compound **3s** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 48.1 mg, 0.153 mmol, 61% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.47–7.43 (m, 2H), 7.08–7.04 (m, 2H), 3.92 (d, *J* = 7.0 Hz, 1H), 2.86 (ddd, *J* = 18.9, 7.1, 0.7 Hz, 1H), 2.4 3–2.35 (m, 1H), 2.33 (dd, *J* = 18.9, 2.2 Hz, 1H), 2.30–2.17 (m, 2H), 1.97 (ddd, *J* = 13.9, 9.2, 5.3 Hz, 1H), 1.58–1.45 (m, 3H), 1.36 (ddt, *J* = 13.3, 9.2, 7.2 Hz, 1H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.26 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 209.4, 175.5, 143.0, 141.5, 139.1, 134.1, 126.9, 46.5, 44.9, 31.1, 25.4, 22.1, 20.9, 14.30, 14.30, –1.0. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{31}OSi$, 315.2139; found, 315.2144.

*2,3-dibutyl-5-phenylcyclopent-2-en-1-one (**3t**).* Compound **3t** was synthesized according to the general procedure and purified by column chromatography on silica using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 23.0 mg, 0.103 mmol, 41% yield. Colorless oil. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.34–7.31 (m, 2H), 7.26–7.23 (m, 1H), 7.14–7.12 (m, 2H), 3.56 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.09–3.04 (m, 1H), 2.64–2.63 (m, 1H), 2.58–2.47 (m, 2H), 2.30–2.21 (m, 2H), 1.62–1.56 (m, 2H), 1.48–1.32 (m, 6H), 1.00 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 208.8, 173.1, 140.7, 139.9, 128.9, 127.6, 126.8, 51.1, 39.3, 31.0, 30.9, 29.8, 23.2, 23.0, 22.9, 14.0. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{27}O$, 271.2056; found, 271.2056.

*2-phenyl-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-1H-cyclopenta[12]annulen-1-one (**3u**).* Compound **3u** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 59.5 mg, 0.201 mmol, 80% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.28 (m, 2H), 7.25–7.19 (m, 1H), 7.15–7.09 (m, 2H), 3.53 (dd, *J* = 7.3, 2.6 Hz, 1H), 3.03 (dd, *J* = 18.4, 7.3 Hz, 1H), 2.67–2.53 (m, 2H), 2.46 (dt, *J* = 13.9, 7.3 Hz, 1H), 2.31 (td, *J* = 6.6, 1.2 Hz, 2H), 1.73 (dddd, *J* = 11.1, 7.4, 5.4, 2.9 Hz, 2H), 1.62 (ddt, *J* = 11.1, 7.7, 5.8 Hz, 2H), 1.55–1.32 (m, 10H), 1.28–1.13 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 209.2, 173.5, 140.7, 139.4, 128.9, 127.6, 126.8, 51.0, 39.1, 28.0, 25.6, 25.5, 25.3, 25.0, 24.7, 23.8, 22.9, 22.0, 20.9. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{29}O$, 297.2213; found, 297.2220.

*5-phenyl-2,3-bis(3-phenylpropyl)cyclopent-2-en-1-one (**3v**).* Compound **3v** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using toluene and ethyl acetate (4:1, v/v) as the eluent: 61.2 mg, 0.167 mmol, 67% yield. Colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.26 (m, 6H), 7.26–7.16 (m, 7H), 7.13–7.08 (m, 2H), 3.54 (dd, *J* = 7.2, 2.5 Hz, 1H), 3.04 (ddt, *J* = 18.5, 7.3, 1.1 Hz, 1H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.65–2.56 (m, 3H), 2.48 (hept, *J* = 6.6 Hz, 2H), 2.26 (tt, *J* = 10.2, 5.4 Hz, 2H), 1.96–1.84 (m, 2H), 1.80–1.69 (m, 2H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 208.6, 172.7, 142.2, 141.5, 140.4, 139.8, 128.9, 128.6, 128.52, 128.50, 128.4, 127.6, 126.9, 126.3, 125.9, 51.1, 39.3, 36.01, 35.97, 30.8, 30.3, 29.4, 23.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{31}O$, 395.2369; found, 395.2367.

3-methyl-2-pentyl-5-phenylcyclopent-2-en-1-one and 2-methyl-3-pentyl-5-phenylcyclopent-2-en-1-one (**3w**). Compound **3w** was synthesized according to the general procedure and purified by preparative thin-layer chromatography using *n*-pentane and ethyl acetate (9:1, v/v) as the eluent: 38.3 mg, 0.158 mmol, 63% combined yield. The two regioisomers could be separated.

Major isomer: *3-methyl-2-pentyl-5-phenylcyclopent-2-en-1-one* (**3w-1**). Pale yellow oil. 21.8 mg, 0.090 mmol, 36% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.25–7.18 (m, 1H), 7.15–7.08 (m, 2H), 3.54 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.04 (ddq, *J* = 18.5, 7.3, 1.1 Hz, 1H), 2.59 (ddq, *J* = 18.5, 2.4, 1.2 Hz, 1H), 2.23 (td, *J* = 7.3, 3.5 Hz, 2H), 2.12 (td, *J* = 1.1, 0.6 Hz, 3H), 1.47–1.36 (m, 2H), 1.36–1.21 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 208.5, 169.0, 140.6, 140.2, 128.8, 127.7, 126.8, 51.2, 41.7, 31.9, 28.1, 23.3, 22.6, 17.3, 14.2. HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{23}O$, 243.1743; found, 243.1744.

Minor isomer: *2-methyl-3-pentyl-5-phenylcyclopent-2-en-1-one* (**3w-2**). Pale yellow oil. 16.5 mg, 0.068 mmol, 27% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.25–7.19 (m, 1H), 7.14–7.09 (m, 2H), 3.56 (dd, *J* = 7.1, 2.6 Hz, 1H), 3.12–2.96 (m, 1H), 2.61 (dddt, *J* = 18.5, 3.0, 2.0, 1.0 Hz, 1H), 2.49 (h, *J* = 6.2 Hz, 2H), 1.76 (s, 3H), 1.59 (tt, *J* = 7.7, 5.3 Hz, 2H), 1.40–1.31 (m, 4H), 0.96–0.89 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 209.1, 173.2, 140.5, 135.4, 128.9, 127.7, 126.9, 51.1, 39.5, 31.9, 31.3, 27.1, 22.6, 14.1, 8.5. HRMS(ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{22}NaO$, 265.1563; found, 265.1559.

Procedure for the Scale-Up of the Palladium-Catalyzed Intermolecular Pauson–Khand Reaction between Vinyl Iodide 1a and Alkyne 2a. Inside a glovebox filled with argon, a 16-mL vial equipped with a Teflon-coated stir bar was charged with $[Pd(allyl)Cl]_2$ (9.2 mg, 25.0 µmol, 2.5 mol%), dAr^Fpe (30.3 mg, 40.0 µmol, 4.0 mol%), $Cr(CO)_6$ (220 mg, 1.00 mmol, 1.0 equiv.), dioxane (4.0 mL, 0.25 M), 4-octyne (**2a**) (220 µL, 165 mg, 1.50 mmol, 1.5 equiv.), triisopropylsilane (307 µL, 237 mg, 1.50 mmol, 1.5 equiv.), and vinyl iodide **1a** (230 mg, 1.00 mmol, 1.0 equiv.). The vial was tightly closed with a screw cap. It was then removed from the glovebox and stirred at 130 °C for 14 hours in a pre-heated heating block. The reaction mixture was allowed to cool to room temperature, filtered over a short plug of Celite, and the solvent was removed under reduced pressure. The residue was purified by column chromatography over silica using pentane and ethyl acetate (99:1, v/v) to afford product **3a** (168 mg, 0.694 mmol, 69%) as a yellow oil.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its online supplementary material.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Preparation and characterization of starting materials, and NMR (^{1}H, ^{13}C{^{1}H} and ^{19}F{^{1}H}) spectra.

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Notes

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REFERENCES

(1) Corey, E. J.; Cheng, X. M. *The Logic of Chemical Synthesis*; John Wiley & Sons: New York, **1989**.

(2) Anastas, P.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev.* **2010**, *39*, 301–312. https://doi.org/10.1039/b918763b.

(3) Burns, N. Z.; Baran, P. S.; Hoffmann, R. W. Redox Economy in Organic Synthesis. *Angew. Chem. Int. Ed.* **2009**, *48*, 2854–2867. https://doi.org/10.1002/anie.200806086.

(4) Newhouse, T.; Baran, P. S.; Hoffmann, R. W. The Economies of Synthesis. *Chem. Soc. Rev.* **2009**, *38*, 3010–3021. https://doi.org/10.1039/b821200g.

(5) Tietze, L. F. Domino Reactions in Organic Synthesis. *Chem. Rev.* **1996**, *96*, 115–136. https://doi.org/10.1021/cr950027e.

(6) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. Cascade Reactions in Total Synthesis. *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186. https://doi.org/10.1002/anie.200601872.

(7) Nicolaou, K. C.; Chen, J. S. The Art of Total Synthesis through Cascade Reactions. *Chem. Soc. Rev.* **2009**, *38*, 2993–3009. https://doi.org/10.1039/b903290h.

(8) Poulin, J.; Grisé-Bard, C. M.; Barriault, L. Pericyclic Domino Reactions: Concise Approaches to Natural Carbocyclic Frameworks. *Chem. Soc. Rev.* **2009**, *38*, 3092–3101. https://doi.org/10.1039/b819798a.

(9) Juhl, M.; Tanner, D. Recent Applications of Intramolecular Diels–Alder Reactions to Natural Product Synthesis. *Chem. Soc. Rev.* **2009**, *38*, 2983–2992. https://doi.org/10.1039/b816703f.

(10) Ardkhean, R.; Caputo, D. F. J.; Morrow, S. M.; Shi, H.; Xiong, Y.; Anderson, E. A. Cascade Polycyclizations in Natural Product Synthesis. *Chem. Soc. Rev.* **2016**, *45*, 1557–1569. https://doi.org/10.1039/c5cs00105f.

(11) Lautens, M.; Klute, W.; Tam, W. Transition Metal-Mediated Cycloaddition Reactions. *Chem. Rev.* **1996**, *96*, 49–92. https://pubs.acs.org/doi/full/10.1021/cr950016l.

(12) Negishi, E. I.; Copéret, C.; Ma, S.; Liou, S. Y.; Liu, F. Cyclic Carbopalladation. A Versatile Synthetic Methodology for the Construction of Cyclic Organic Compounds. *Chem. Rev.* **1996**, *96*, 365–393. https://doi.org/10.1021/cr950020x.

(13) Trost, B. M.; Krische, M. J. Transition Metal Catalyzed Cycloisomerizations. *Synlett* **1998**, *1998*, 1–16. https://doi.org/10.1055/s-1998-1557.

(14) Gulías, M.; López, F.; Mascareñas, J. L. Development of Transition-Metal-Catalyzed Cycloaddition Reactions Leading to Polycarbocyclic Systems. *Pure Appl. Chem.* **2011**, *83*, 495–506. https://doi.org/10.1351/PAC-CON-10-10-23.

(15) Marchese, A. D.; Larin, E. M.; Mirabi, B.; Lautens, M. Metal-Catalyzed Approaches toward the Oxindole Core. *Acc. Chem. Res.* **2020**, *53*, 1605–1619. https://doi.org/10.1021/acs.accounts.0c00297.

(16) Trost, B. M.; Zuo, Z.; Schultz, J. E. Transition-Metal-Catalyzed Cycloaddition Reactions to Access Seven-Membered Rings. *Chem. Eur. J.* **2020**, *26*, 15354–15377. https://doi.org/10.1002/chem.202002713.

(17) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. A Cobalt Induced Cleavage Reaction and a New Series of Arenecobalt Carbonyl Complexes. *J. Chem. Soc. D.* **1971**, 36a. https://doi.org/10.1039/C2971000036a.

(18) Werner, H. Peter Ludwig Pauson (1925–2013). *Angew. Chemie Int. Ed.* **2014**, *53*, 3309–3309. https://doi.org/10.1002/ANIE.201400432.

(19) Jeong, N. The Pauson-Khand Reaction. In *Comprehensive Organic Synthesis II, 2nd ed.;* Knochel, P.; Molander, G. A.; Eds.; Elsevier: Amsterdam, **2014**; *Vol. 5*, pp 1106–1178. https://doi.org/10.1016/B978-0-08-097742-3.00525-5.

(20) Schore, N. E. The Pauson-Khand Cycloaddition Reaction for Synthesis of Cyclopentenones. *Org. React.* **1991**, *40*, 1–90. https://doi.org/10.1002/0471264180.or040.01.

(21) Lindsay, D. M.; Kerr, W. J. Recent Advances in the Pauson-Khand Reaction. In *Cobalt Catalysis in Organic Synthesis: Methods and Reactions*, 1st ed.; Hapke, M.; Hilt, G., Eds. Wiley-VCH: Weinheim, **2020**; pp 259–285. https://doi.org/10.1002/9783527814855.ch8.

(22) Zhang, S.; Neumann, H.; Beller, M. Synthesis of α,β-Unsaturated Carbonyl Compounds by Carbonylation Reactions. *Chem. Soc. Rev.* **2020**, *49*, 3187–3210. https://doi.org/10.1039/c9cs00615j.

(23) Gibson, S. E.; Mainolfi, N. The Intermolecular Pauson-Khand Reaction. *Angew. Chem. Int. Ed.* **2005**, *44*, 3022–3037. https://doi.org/10.1002/anie.200462235.

(24) Laschat, S.; Becheanu, A.; Bell, T.; Baro, A. Regioselectivity, Stereoselectivity and Catalysis in Intermolecular Pauson-Khand Reactions: Teaching an Old Dog New Tricks. *Synlett* **2005**, *2005*, 2547–2570. https://doi.org/10.1055/S-2005-918922/ID/29.

(25) Zweig, J. E.; Kim, D. E.; Newhouse, T. R. Methods Utilizing First-Row Transition Metals in Natural Product Total Synthesis. *Chem. Rev.* **2017**, *117*, 11680–11752. https://pubs.acs.org/doi/full/10.1021/acs.chemrev.6b00833.

(26) Simeonov, S. P.; Nunes, J. P. M.; Guerra, K.; Kurteva, V. B.; Afonso, C. A. M. Synthesis of Chiral Cyclopentenones. *Chem. Rev.* **2016**, *116*, 5744–5893. https://doi.org/10.1021/cr500504w.

(27) Aitken, D. J.; Eijsberg, H.; Frongia, A.; Ollivier, J.; Piras, P. P. Recent Progress in the Synthetic Assembly of 2-Cyclopentenones. *Synthesis* **2014**, *46*, 1–24. https://doi.org/10.1055/S-0033-1340414.

(28) Nakayama, A.; Kogure, N.; Kitajima, M.; Takayama, H. Asymmetric Total Synthesis of a Pentacyclic Lycopodium Alkaloid: Huperzine-Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 8025–8028. https://doi.org/10.1002/ANIE.201103550.

(29) Jørgensen, L.; McKerrall, S. J.; Kuttruff, C. A.; Ungeheuer, F.; Felding, J.; Baran, P. S. 14-Step Synthesis of (+)-Ingenol from (+)-3-Carene. *Science.* **2013**, *341*, 878–882. https://doi.org/10.1126/science.1241606.

(30) Chuang, K. V.; Xu, C.; Reisman, S. E. A 15-Step Synthesis of (+)-Ryanodol. *Science* **2016**, *353*, 912–915. https://doi.org/10.1126/science.aag1028.

(31) Hu, X.; Musacchio, A. J.; Shen, X.; Tao, Y.; Maimone, T. J. Allylative Approaches to the Synthesis of Complex Guaianolide Sesquiterpenes from Apiaceae and Asteraceae. *J. Am. Chem. Soc.* **2019**, *141*, 14904–14915. https://doi.org/10.1021/jacs.9b08001.

(32) Hugelshofer, C. L.; Palani, V.; Sarpong, R. Calyciphylline B-Type Alkaloids: Total Syntheses of (-)-Daphlongamine H and (-)-Isodaphlongamine H. *J. Am. Chem. Soc.* **2019**, *141*, 8431–8435. https://doi.org/10.1021/jacs.9b03576.

(33) Liang, X. T.; Chen, J. H.; Yang, Z. Asymmetric Total Synthesis of (-)-Spirochensilide A. *J. Am. Chem. Soc.* **2020**, *142*, 8116–8121. https://pubs.acs.org/doi/10.1021/jacs.0c02522.

(34) Qu, Y.; Wang, Z.; Zhang, Z.; Zhang, W.; Huang, J.; Yang, Z. Asymmetric Total Synthesis of (+)-Waihoensene. *J. Am. Chem. Soc.* **2020**, *142*, 6511–6515. https://pubs.acs.org/doi/10.1021/jacs.0c02143.

(35) Cheng, M. J.; Zhong, L. P.; Gu, C. C.; Zhu, X. J.; Chen, B.; Liu, J. S.; Wang, L.; Ye, W. C.; Li, C. C. Asymmetric Total Synthesis of Bufospirostenin A. *J. Am. Chem. Soc.* **2020**, *142*, 12602–12607. https://doi.org/10.1021/jacs.0c05479.

(36) Wang, Y. Q.; Xu, K.; Min, L.; Li, C. C. Asymmetric Total Syntheses of Hypoestin A, Albolic Acid, and Ceroplastol II. *J. Am. Chem. Soc.* **2022**, *144*, 10162–10167. https://doi.org/10.1021/jacs.2c04633.

(37) Ma, T.; Cheng, H.; Pitchakuntla, M.; Ma, W.; Jia, Y. Total Synthesis of (−)-Principinol C. *J. Am. Chem. Soc.* **2022**. https://doi.org/10.1021/JACS.2C08694.

(38) Chen, S.; Jiang, C.; Zheng, N.; Yang, Z.; Shi, L. Evolution of Pauson-Khand Reaction: Strategic Applications in Total Syntheses of Architecturally Complex Natural Products (2016–2020). *Catalysts* **2020**, *10*, 1199. https://doi.org/10.3390/catal10101199.

(39) Krafft, M. E. Regiocontrol in the Intermolecular Cobalt-Catalyzed Olefin-Acetylene Cycloaddition. *J. Am. Chem. Soc.* **1988**, *110*, 968–970. https://doi.org/10.1021/ja00211a048.

(40) Krafft, M. E.; Juliano, C. A.; Scott, I. L.; Wright, C.; McEachin, M. D. The Directed Pauson-Khand Reaction. *J. Am. Chem. Soc.* **1991**, *113*, 1693–1703. https://pubs.acs.org/doi/10.1021/ja00005a038.

(41) Itami, K.; Mitsudo, K.; Yoshida, J. A Pyridylsilyl Group Expands the Scope of Catalytic Intermolecular Pauson–Khand Reactions. *Angew. Chem. Int. Ed.* **2002**, *41*, 3481–3484. https://onlinelibrary.wiley.com/doi/10.1002/1521-3773(20020916)41:18%3C3481::AID-ANIE3481%3E3.0.CO;2-X.

(42) Itami, K.; Mitsudo, K.; Fujita, K.; Ohashi, Y.; Yoshida, J. I. Catalytic Intermolecular Pauson-Khand-Type Reaction: Strong Directing Effect of Pyridylsilyl and Pyrimidylsilyl Groups and Isolation of Ru Complexes Relevant to Catalytic Reaction. *J. Am. Chem. Soc.* **2004**, *126*, 11058–11066. https://doi.org/10.1021/ja047484+.

(43) Rodríguez Rivero, M.; De La Rosa, J. C.; Carretero, J. C. Asymmetric Intermolecular Pauson-Khand Reactions of Unstrained Olefins: The (o-Dimethylamino)Phenylsulfinyl Group as an Efficient Chiral Auxiliary. *J. Am. Chem. Soc.* **2003**, *125*, 14992–14993. https://doi.org/10.1021/ja038491l.

(44) Gallagher, A. G.; Tian, H.; Torres-Herrera, O. A.; Yin, S.; Xie, A.; Lange, D. M.; Wilson, J. K.; Mueller, L. G.; Gau, M. R.; Carroll, P. J.; Martinez-Solorio, D. Access to Highly Functionalized Cyclopentenones via Diastereoselective Pauson-Khand Reaction of Siloxy-Tethered 1,7-Enynes. *Org. Lett.* **2019**, *21*, 8646–8651. https://doi.org/10.1021/acs.orglett.9b03255.

(45) Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. CO-Transfer Carbonylation Reactions. A Catalytic Pauson-Khand-Type Reaction of Enynes with Aldehydes as a Source of Carbon Monoxide. *J. Am. Chem. Soc.* **2002**, *124*, 3806–3807. https://doi.org/10.1021/ja0126881.

(46) Shibata, T.; Toshida, N.; Takagi, K. Catalytic Pauson - Khand-Type Reaction Using Aldehydes as a CO Source. *Org. Lett.* **2002**, *4*, 1619–1621. https://doi.org/10.1021/ol025836g.

(47) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. Aqueous Catalytic Pauson-Khand-Type Reactions of Enynes with Formaldehyde: Transfer Carbonylation Involving an Aqueous Decarbonylation and a Micellar Carbonylation. *Angew. Chem. Int. Ed.* **2003**, *42*, 2409–2411. https://doi.org/10.1002/anie.200351384.

(48) Park, K. H.; Son, S. U.; Chung, Y. K. Immobilized Heterobimetallic Ru/Co Nanoparticle-Catalyzed Pauson–Khand-Type Reactions in the Presence of Pyridylmethyl Formate. *Chem. Commun.* **2003**, *3*, 1898–1899. https://doi.org/10.1039/b304325h.

(49) Park, J. H.; Cho, Y.; Chung, Y. K. Rhodium-Catalyzed Pauson-Khand-Type Reaction Using Alcohol as a Source of Carbon Monoxide. *Angew. Chem. Int. Ed.* **2010**, *49*, 5138–5141. https://doi.org/10.1002/anie.201001246.

(50) For a general review on CO surrogates, see: Morimoto, T.; Kakiuchi, K. Evolution of carbonylation catalysis: No need for carbon monoxide. *Angew. Chem. Int. Ed.* **2004**, *43*, 5580–5588. https://doi.org/10.1002/anie.200301736.

(51) For a review on a two-chamber strategy for carbonylation, see: Friis, S. D.; Lindhardt, A. T.; Skrydstrup, T. The Development and Application of Two-Chamber Reactors and Carbon Monoxide Precursors for Safe Carbonylation Reactions. *Acc. Chem. Res.* **2016**, *49*, 594–605. https://doi.org/10.1021/acs.accounts.5b00471.

(52) Shambayani, S.; Crowe, W. E.; Schreiber, S. L. N-Oxide Promoted Pauson-Khand Cyclizations at Room Temperature. *Tetrahedron Lett.* **1990**, *31*, 5289–5292. https://doi.org/10.1016/S0040-4039(00)98052-3.

(53) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. Catalytic Version of the Intramolecular Pauson-Khand Reaction. *J. Am. Chem. Soc.* **1994**, *116*, 3159–3160. https://doi.org/10.1021/ja00086a070.

(54) Jeong, N.; Lee, S.; Sung, B. K. Rhodium(I)-Catalyzed Intramolecular Pauson-Khand Reaction. *Organometallics* **1998**, *17*, 3642–3644. https://pubs.acs.org/doi/10.1021/om980410k.

(55) Koga, Y.; Kobayashi, T.; Narasaka, K. Rhodium-Catalyzed Intramolecular Pauson-Khand Reaction. *Chem. Lett.* **1998**, *3*, 249–250. https://doi.org/10.1246/cl.1998.249.

(56) Kim, S. W.; Son, S. U.; Lee, S. I.; Hyeon, T.; Chung, Y. K. Cobalt on Mesoporous Silica: The First Heterogeneous Pauson-Khand Catalyst. *J. Am. Chem. Soc.* **2000**, *122*, 1550–1551. https://doi.org/10.1021/ja9939237.

(57) Shibata, T.; Takagi, K. Iridium-Chiral Diphosphine Complex Catalyzed Highly Enantioselective Pauson-Khand-Type Reaction. *J. Am. Chem. Soc.* **2000**, *122*, 9852–9853. https://pubs.acs.org/doi/10.1021/ja000899k.

(58) Grigg, R.; Zhang, L.; Collard, S.; Keep, A. Palladium Catalysed [2 + 2 + 1] Intramolecular Cycloaddition for the Preparation of Bicyclo[3.3.0]Octa-1.5-Dien-3-Ones from 1,6-Diynes. *Chem. Commun.* **2003**, *3*, 1902–1903. https://doi.org/10.1039/b302841k.

(59) Wender, P. A.; Deschamps, N. M.; Williams, T. J. Intermolecular Dienyl Pauson-Khand Reaction. *Angew. Chem. Int. Ed.* **2004**, *43*, 3076–3079. https://doi.org/10.1002/anie.200454117.

(60) Muller, J. L.; Klankermayer, J.; Leitner, W. Poly(Ethylene Glycol) Stabilized Co Nanoparticles as Highly Active and Selective Catalysts for the Pauson-Khand Reaction. *Chem. Commun.* **2007**, 1939–1941. https://doi.org/10.1039/b702330h.

(61) Wang, Y.; Xu, L.; Yu, R.; Chen, J.; Yang, Z. $CoBr_2$-TMTU-Zinc Catalysed-Pauson-Khand Reaction. *Chem. Commun.* **2012**, *48*, 8183–8185. https://doi.org/10.1039/c2cc17971g.

(62) Sakurai, Y.; Ogiwara, Y.; Sakai, N. Palladium-Catalyzed Annulation of Acyl Fluorides with Norbornene via Decarbonylation and CO Reinsertion. *Chem. Eur. J.* **2020**, *26*, 12972–12977. https://doi.org/10.1002/CHEM.202001374.

(63) Hou, L.; Huang, W.; Wu, X.; Qu, J.; Chen, Y. Nickel-Catalyzed Carbonylation of Cyclopropanol with Benzyl Bromide for Multisubstituted Cyclopentenone Synthesis. *Org. Lett.* **2022**, *24*, 2699–2704. https://doi.org/10.1021/acs.orglett.2c00798.

(64) Ohashi, M.; Taniguchi, T.; Ogoshi, S. Nickel-Catalyzed Formation of Cyclopentenone Derivatives via the Unique Cycloaddition of α,β-Unsaturated Phenyl Esters with Alkynes. *J. Am. Chem. Soc.* **2011**, *133*, 14900–14903. https://doi.org/10.1021/ja2059999.

(65) Jenkins, A. D.; Herath, A.; Song, M.; Montgomery, J. Synthesis of Cyclopentenols and Cyclopentenones via Nickel-Catalyzed Reductive Cycloaddition. *J. Am. Chem. Soc.* **2011**, *133*, 14460–14466. https://doi.org/10.1021/ja206722t.

(66) Jenkins, A. D.; Robo, M. T.; Zimmerman, P. M.; Montgomery, J. Nickel-Catalyzed Three-Component Cycloadditions of Enoates, Alkynes, and Aldehydes. *J. Org. Chem.* **2020**, *85*, 2956–2965. https://doi.org/10.1021/acs.joc.9b02446.

(67) Barluenga, J.; Barrio, P.; Riesgo, L.; López, L. A.; Tomás, M. A General and Regioselective Synthesis of Cyclopentenone Derivatives through Nickel(0)-Mediated [3 + 2] Cyclization of Alkenyl Fischer Carbene Complexes and Internal Alkynes. *J. Am. Chem. Soc.* **2007**, *129*, 14422–14426. https://doi.org/10.1021/ja075106+.

(68) Barluenga, J.; Álvarez-Fernández, A.; Suárez-Sobrino, Á. L.; Tomás, M. Regio- and Stereoselective Synthesis of Cyclopentenones: Intermolecular Pseudo-Pauson-Khand Cyclization. *Angew. Chem. Int. Ed.* **2012**, *51*, 183–186. https://doi.org/10.1002/anie.201105362.

(69) Park, K. H.; Jung, I. G.; Chung, Y. K. A Pauson-Khand-Type Reaction between Alkynes and Olefinic Aldehydes Catalyzed by Rhodium/Cobalt Heterobimetallic Nanoparticles: An Olefinic Aldehyde as an Olefin and CO Source. *Org. Lett.* **2004**, *6*, 1183–1186. https://doi.org/10.1021/ol049765s.

(70) Ahlin, J. S. E.; Donets, P. A.; Cramer, N. Nickel(0)-Catalyzed Enantioselective Annulations of Alkynes and Arylenoates Enabled by a Chiral NHC Ligand: Efficient Access to Cyclopentenones. *Angew. Chem. Int. Ed.* **2014**, *53*, 13229–13233. https://doi.org/10.1002/anie.201408364.

(71) Rizzo, C. J.; Dunlap, N. K.; Smith, A. B. A Convenient Preparation of 4- and 5-Substituted Cyclopentenones: A Short Synthesis of Methylenomycin B. *J. Org. Chem.* **1987**, *52*, 5280–5283. https://doi.org/10.1021/jo00232a043.

(72) Yu, S.; Hong, C.; Liu, Z.; Zhang, Y. Synthesis of Cyclopentenones through Rhodium-Catalyzed C-H Annulation of Acrylic Acids with Formaldehyde and Malonates. *Org. Lett.* **2021**, *23*, 5054–5059. https://pubs.acs.org/doi/10.1021/acs.orglett.1c01569.

(73) Tanaka, K.; Fu, G. C. A Versatile New Method for the Synthesis of Cyclopentenones via an Unusual Rhodium-Catalyzed Intramolecular Trans Hydroacylation of an Alkyne. *J. Am. Chem. Soc.* **2001**, *123*, 11492–11493. https://doi.org/10.1021/ja011907f.

(74) Lee, Y. H.; Denton, E. H.; Morandi, B. Modular Cyclopentenone Synthesis through the Catalytic Molecular Shuffling of Unsaturated Acid Chlorides and Alkynes. *J. Am. Chem. Soc.* **2020**, *142*, 20948–20955. https://doi.org/10.1021/jacs.0c10832.

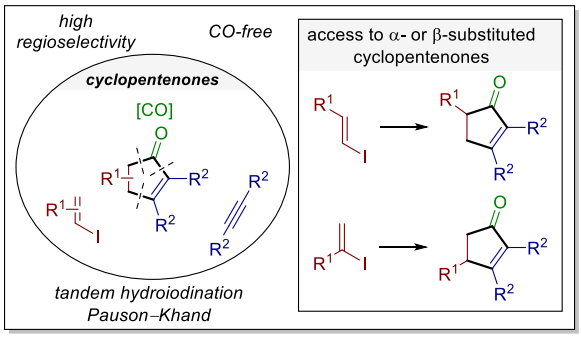
(75) Boehm, P.; Kehl, N.; Morandi, B. Rhodium-Catalyzed Anti-Markovnikov Transfer Hydroiodination of Terminal Alkynes. *ChemRxiv Preprint* **2022**. https://doi.org/10.26434/CHEMRXIV-2022-7DSQD.

(76) Lee, Y. H.; Morandi, B. Palladium-Catalyzed Intermolecular Aryliodination of Internal Alkynes. *Angew. Chem. Int. Ed.* **2019**, *58*, 6444–6448. https://doi.org/10.1002/anie.201812396.

(77) Cook, R. L.; Morse, J. G. 1,2-Bis(Bis(Pentafluorophenyl)Phosphino)Ethane: Synthesis, Characterization, and Some Comparisons to 1,2-Bis(Diphenylphosphino)Ethane. *Inorg. Chem.* **1982**, *21*, 4103–4105. https://pubs.acs.org/doi/abs/10.1021/ic00141a047.

(78) Denton, E. H.; Lee, Y. H.; Roediger, S.; Boehm, P.; Fellert, M.; Morandi, B. Catalytic Carbochlorocarbonylation of Unsaturated Hydrocarbons via C–COCl Bond Cleavage**. *Angew. Chem. Int. Ed.* **2021**, *60*, 23435–23443. https://doi.org/10.1002/anie.202108818.

(79) Jankins, T. C.; Bell, W. C.; Zhang, Y.; Qin, Z. Y.; Chen, J. S.; Gembicky, M.; Liu, P.; Engle, K. M. Low-Valent Tungsten Redox Catalysis Enables Controlled Isomerization and Carbonylative Functionalization of Alkenes. *Nat. Chem.* **2022**, *14*, 632–639. https://doi.org/10.1038/s41557-022-00951-y.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