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Nickel-Catalyzed Reductive Cycloisomerization of Enynes with CO_2

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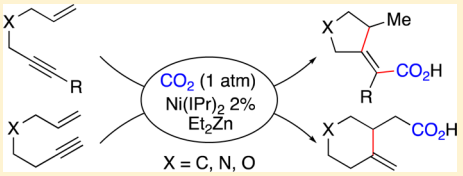
Supporting Information

ABSTRACT: Carboxylate groups are ubiquitous in bioactive molecules. The syntheses of carboxylates from petroleum feedstock require a series of oxidation reactions. CO_2 represents a cheap and sustainable, preoxidized C1 source. Herein, we describe a simple, selective, and mild procedure for the construction of (hetero)cyclic α,β-unsaturated carboxylic acids from 1,6- and 1,7-enyes and CO_2. Terminal 1,7-enynes and sterically hindered alkenes experience a change in regioselectivity and form unconjugated carboxylic acids. Mechanistic studies of the reductive cyclization suggest a hydride insertion pathway, explaining the change in regioselectivity caused by steric effects and distinguishing this work from previous reactions involving CO_2.



INTRODUCTION

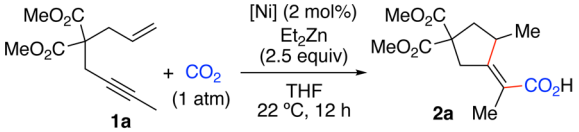
The vast majority of chemicals are derived from petroleum products via a series of oxidation reactions to increase the oxidation state of carbon and install functional groups. Carbon dioxide represents a sustainable, inexpensive, and clean C1 source in which the carbon center is already highly oxidized.[1] The advantages of CO_2 as a chemical feedstock underlie recent efforts to develop catalytic methods of incorporating CO_2 into organic molecules.[2] In particular, functionalization reactions of alkenes and alkynes have provided new synthetic tools for the sustainable construction of molecules.[3]

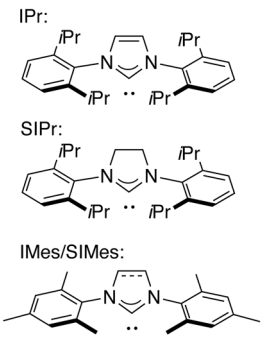
Cyclic molecules with α,β-unsaturated carbonyl functional groups are ubiquitous in bioactive molecules and synthetic intermediates.[4] In light of the recent advances in the field of Ni-catalyzed reductive functionalization of alkenes and alkynes,[5] including work by Martin, Ma, and others, we sought to extend the scope of these reactions to the preparation of α,β-unsaturated cyclic compounds from CO_2. Here, we report a Ni-catalyzed reductive cycloisomerization of enynes[6] that couples CO_2 to form α,β-unsaturated carboxylic acids. The simple and mild conditions provide high yields of a broad scope of cyclic and heterocyclic carboxylic acids. In addition, we conducted mechanistic studies and evaluated possible pathways, including ones invoked in previous CO_2 coupling reactions. Our studies suggest that the reaction proceeds via a classic hydride insertion pathway, which is distinct from previous cyclization reactions to incorporate CO_2.[3]

RESULTS

We initiated our investigation using malonate-derived enyne **1a** as a model substrate and evaluated various conditions for the reductive cycloisomerization with CO_2 (Table 1). Mori and co-workers utilized $Ni(cod)_2$ and PPh_3 to catalyze the cyclization of bis-dienes with CO_2.[3b] This catalyst system exhibits no reactivity in the cyclization of **1a** in the presence of Et_2Zn as the reductant (Table 1, entry 1). Replacing PPh_3 with 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) resulted in the formation of the desired cyclic α,β-unsaturated acid **2a** in 81% yield (entry 2). The incorporation of CO_2 into the alkyne is highly selectively, exclusively forming the *Z*-isomer. The use of $NiCl_2(DME)$ (DME = dimethoxyethane) as the Ni precursor generated **2a** in a lower yield (entry 3). Louie and co-workers discovered that the pregenerated $Ni(IPr)_2$ catalyst outperforms the mixture of $Ni(cod)_2$ and IPr in their [2 + 2 + 2] cycloaddition reactions.[3a] We prepared $Ni(IPr)_2$ via an optimized literature procedure,[7] and indeed, $Ni(IPr)_2$ was superior to the mixture of $Ni(cod)_2$ and IPr, giving **2a** in 99% yield (entry 4). We then continued to investigate the stereo and electronic effects of the NHC ligands. Increasing the electron-donating ability of the carbene and decreasing its steric

Table 1. Development of the Conditions for the Cycloisomerization of Enyne 1a with CO_2[a]





Entry	Catalyst	Yield (%)[b]
1	$Ni(cod)_2/PPh_3$[c]	0
2	$Ni(cod)_2/IPr$[c]	81
3	$NiCl_2(DME)/IPr$[c]	40
4	**$Ni(IPr)_2$**	**99**
5	$Ni(SIPr)_2$	42
6	$Ni(IMes)_2$	11
7	$Ni(SIMes)_2$	10

[a]Conditions: **1a** (0.05 mmol), $Ni(IPr)_2$ (2 mol %), $ZnEt_2$ (0.15 mmol), THF (1 mL), CO_2 (1 atm), 12 h at 23 °C. [b]NMR yields using TMS as the internal standard. [c]4 mol % of ligand.

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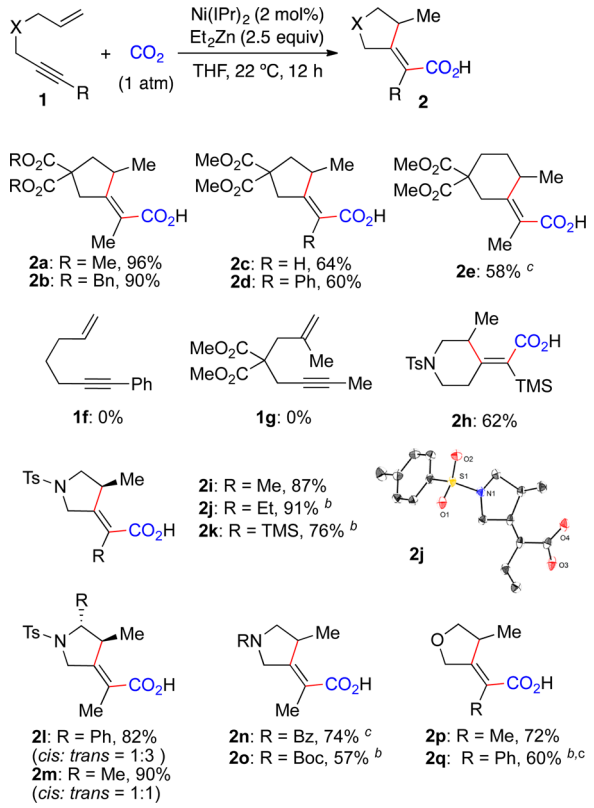
protection led to reduced yields (entries 5−7). We evaluated a variety of reductants as a replacement for Et_2Zn, including EtZnCl, $AlEt_3$, and Et_3SiH, but they failed to produce the product. Ultimately, the optimal conditions for the cyclization were comprised of $Ni(IPr)_2$ as the catalysts and Et_2Zn as the reductant.

We explored the scope of the reductive cycloisomerization with 1 atm of CO_2 (Table 2). Methyl and benzyl malonate

Table 2. Scope of the Reductive Cycloisomerization with CO_2 Incorporated to Alkynes[a]



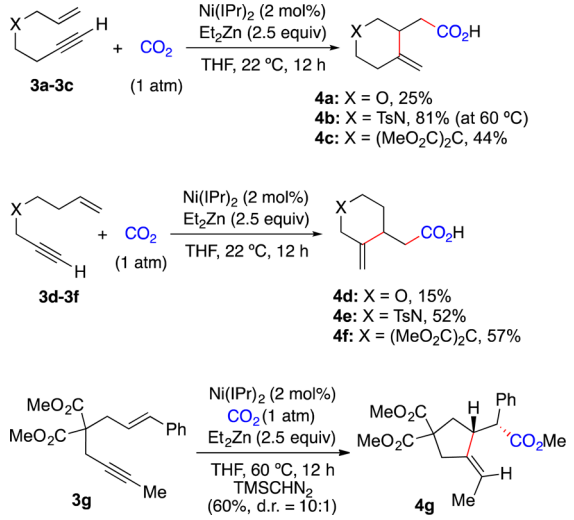
[a]Conditions: enyne = 0.5 mmol. Isolated yields. [b]4% $Ni(IPr)_2$. [c]Crude product treated with $TMSCHN_2$ and isolated as methyl ester.

derived substrates underwent straightforward cyclization to afford the cyclic α,β-unsaturated acids **2a** and **2b** in high yields. Terminal alkyne **1c** proceeded to generate the 5-membered product **2c** in 64% yield. Aromatic alkyne **1d** gave acid **2d** in 60% yield. Cyclization of 1,7-enyne **1e** gave rise to the six-membered product **2e** in 58% yield. Unsubstituted 1,6-enyne **1f** lacked reactivity, suggesting the Thorpe−Ingold effect plays a crucial role in facilitating the cyclization. In addition, sterically hindered olefins, such as geminal disubstituted substrate **1g**, exhibited no reactivity.

The reaction conditions tolerate heteroatoms, giving rise to a variety of piperidine, pyrrolidine, and furan derivatives (**2h−q**). We used single-crystal X-ray diffraction to confirm the structure and the stereochemistry of **2j**. α-Phenyl-substituted tosylamide **2l** was formed as a mixture of *cis*- and *trans*-diastereomers in a 1:3 ratio, while α-methyl-substituted tosylamide **2m** was formed as a 1:1 mixture of diastereomers. We assigned the diastereomers via NOESY experiments. The tosyl-protecting group of the amine substrates could be substituted by benzoyl and Boc groups, giving rise to **2n** and **2o** in 74% and 57% yields, respectively. The use of free amines, however, did not result in any product formation. Allylpropargyl ethers underwent cyclization to generate carboxylic acids **2p** and **2q** in good yields.

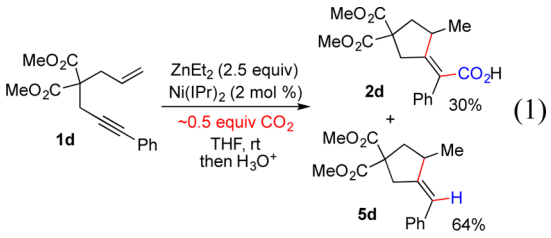
When we evaluated terminal 1,7-enynes, we observed a change in the regioselectivity of the CO_2 incorporation from the alkynes to the alkenes (Scheme 1). Allylhomopropargyl and

Scheme 1. Scope of Reductive Cyclization with CO_2 Incorporated to Alkenes



homoallylpropargyl substrates, **3a−c** and **3d−f**, respectively, underwent cyclization to form carboxylic acids **4a−f**. In contrast with the regioselectivity observed for 1,6-enynes **2a−q**, 1,7-enynes **3a−f**, bearing terminal alkynes, incorporated CO_2 onto the olefin. This reaction tolerated *N*- and *O*-heteroatoms and afforded piperidine and tetrahydropyran derivatives. In addition, introducing a phenyl substituent on the olefin led to the same change in regioselectivity of the CO_2 incorporation to afford saturated carboxylate **4g** as a 10:1 mixture of diastereomers. The addition of the hydride to the alkyne was exclusively *cis* to the newly formed C−C bond in **4g**.

We next directed our focus to probing the mechanism. In the presence of 0.5 equiv of CO_2, relative to the enyne substrate, the cyclization reaction of **1d** proceeded under standard conditions to form the carboxylation product **2d** accompanied by a reductive cycloisomerization product **5d** (eq 1).[8] Cyclization of



(1)

1a with $ZnEt_2$-d_{10} formed carboxylic acid **2a-D** in 85% isolated yield (Scheme 2). ^1H and ^{13}C NMR spectra established that a single deuterium atom was incorporated into the methyl group in 97% efficiency. The use of $ZnEt_2$-d_{10} in the cyclization of **3b** led to >99% deuterium incorporation into the terminal olefin of **4b**. The diastereoselectivity of the deuterium incorporation is high with the deuterium *cis*- to the newly formed C−C bond, and no H/D scrambling observed. We conducted kinetic studies for the carboxylation of **1a** using NMR analysis. The reaction time course fits to a first-order kinetic model (Figure 1A).[9]

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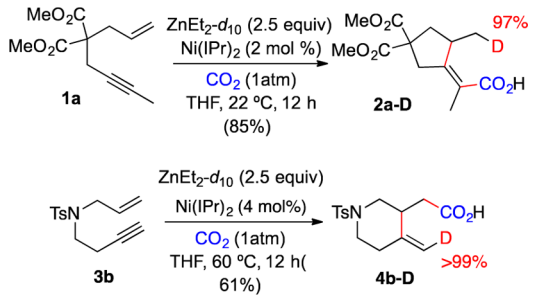
Scheme 2. Cyclization of 1a and 3b with $ZnEt_2$-d_{10}



Comparing the reaction rates with $ZnEt_2$ and $ZnEt_2$-d_{10} revealed a kinetic isotope effect of 0.911 ± 0.1 (Figure 1B).

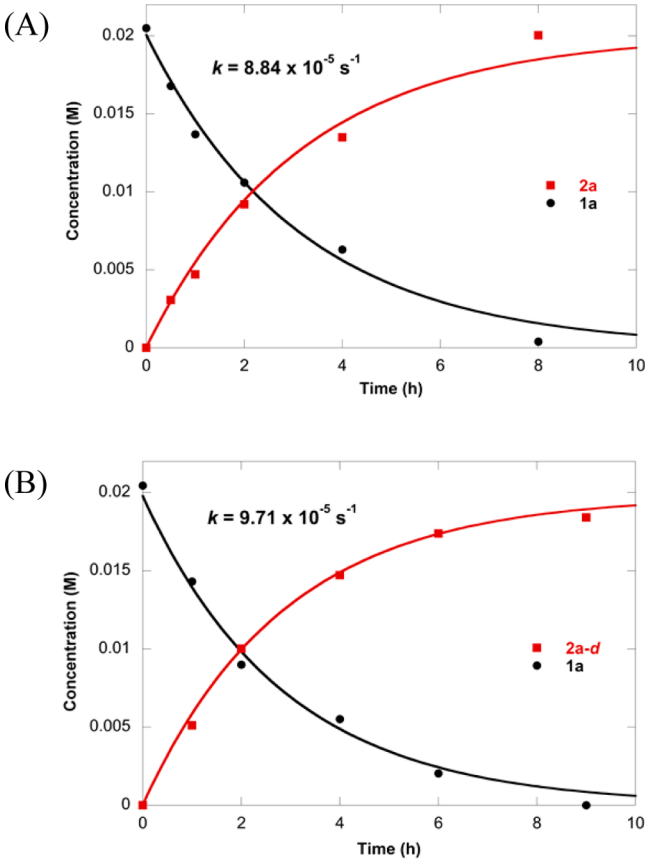


Figure 1. Kinetic profiles of reductive cyclization of **1a** with Et_2Zn (A) and Et_2Zn-d_{10} (B). Conditions: $[\mathbf{1a}]_0$ = 0.021 M, $[Et_2Zn]_0$ = 0.050 mM, CO_2 = 1 atm, solvent = THF, temperature = 22 °C, internal standard = tetramethylsilane.

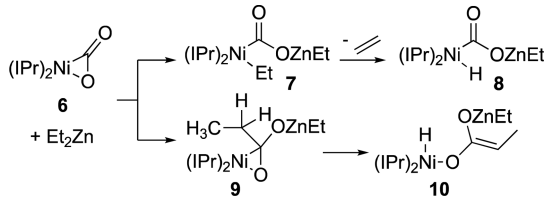
We conducted spectroscopic studies of the catalytic reaction and a series of stoichiometric experiments to elucidate the nature of the Ni catalyst. The EPR spectrum of a reaction mixture of **2a** under standard conditions frozen to 10 K showed no signal. When we monitored the stoichiometric reaction of $Ni(IPr)_2$ with **1a** in the presence of $ZnEt_2$ and CO_2 by in situ ^1H NMR spectroscopy, we observed a diamagnetic Ni species. When CO_2 and/or Et_2Zn were excluded from the reaction, no conversion of **1a** was detected. Mixing stoichiometric $Ni(IPr)_2$ and enyne **1a** resulted in no reaction. When CO_2 was introduced to the dark purple solution of $Ni(IPr)_2$, the color immediately changed to yellow. Upon addition of enyne **1a**, the ^1H NMR spectrum of the mixture exhibits a new Ni species but no conversion of **1a** (Figure S1). Introducing Et_2Zn to the reaction mixture resulted in formation of **2a**.

DISCUSSION

The experiments presented above allow us to evaluate possible pathways for the reductive cyclization. The formation of reductive cycloisomerization product **5d** in the presence of insufficient CO_2 (eq 1) suggests that cyclization occurs prior to the incorporation of CO_2. Deuterium-labeling studies with Et_2Zn-d_{10} (Scheme 2) reveal that the hydrogen atom incorporated into the product originates from Et_2Zn. The lack of H/D scrambling suggests that hydride insertion is irreversible. The negligible KIE with Et_2Zn-d_{10} implies that steps involving the cleavage of the C−H bonds of Et_2Zn and Ni-hydride are fast. Analysis of the reaction mixture by EPR spectroscopy excludes Ni(I) or Ni(III) species as the catalyst resting state. ^1H NMR studies of the catalyst activation provide circumstantial evidence for diamagnetic intermediates involved in catalysis.

Our stoichiometric experiments establish that $Ni(IPr)_2$ alone does not react with the enyne substrate. Both CO_2 and Et_2Zn are crucial to activate the Ni catalyst. The reaction of CO_2 with Ni(0) results in an immediate color change, possibly forming side-on adduct **6**, as is known for Ni(0)−phosphine complexes.[10] The enyne substrate **1a**, however, does not react with **6**, evident from stoichiometric experiments (Figure S1). On the basis of previous studies by Dong and co-workers,[11] $(IPr)_2Ni(0)-CO_2$ adduct **6** can transmetalate with Et_2Zn to form intermediate **7** (Scheme 3). Upon release of ethylene, β-H

Scheme 3. Proposed Activation of the Ni Catalyst by CO_2 and Et_2Zn



elimination gives rise to Ni-H **8**, which enters the catalytic cycle. Alternatively, nucleophilic addition of Et_2Zn to the carbonyl of **6** could form intermediate **9**, followed by β-H elimination to generate Ni(II)-H **10**. Consistent with this proposal, Ni(II) precursors, such as $NiCl_2(DME)$, are active in catalyzing the reductive cyclization reaction (Table 1, entry 3). We attribute the lower yield of $NiCl_2(DME)$ compared with $Ni(IPr)_2$ to catalyst decomposition when the coordination of IPr to $NiCl_2(DME)$ is incomplete.

Oxidative cycloaddition of alkenes and alkynes with Ni(0) has been invoked in Ni-catalyzed reductive coupling reactions[5f] and early reports in Ni-mediated CO_2 functionalization.[12] If the reductive cyclization proceeded through this pathway, CO_2 could undergo nucleophilic attack by the metallocycle intermediate followed by reductive cleavage with Et_2Zn (Scheme 4, path 1). This pathway is consistent with our observation that cyclization precedes the incorporation of CO_2 but is inconsistent with the lack of reactivity between enyne **1a** and $Ni(IPr)_2$ in stoichiometric studies.[13]

Louie and co-workers proposed a cycloaddition between CO_2, Ni(0), and an alkyne.[3a] It is conceivable that a similar reaction could form a metallolactone, which inserts into the

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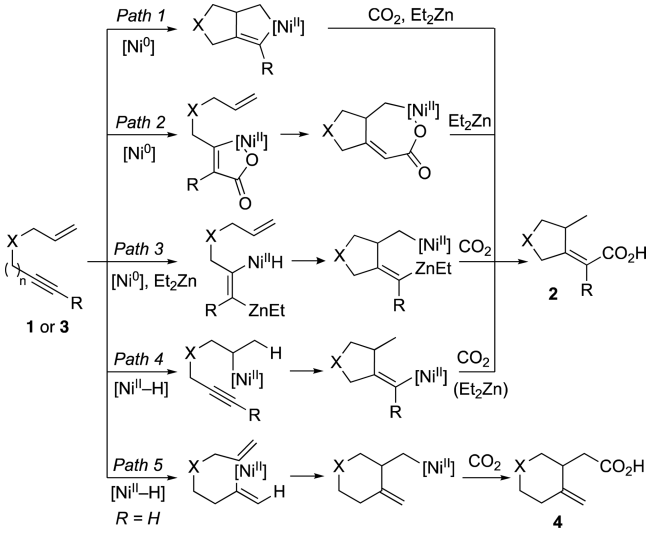
Scheme 4. Possible Pathways of Ni-Catalyzed Reductive Cycloisomerization



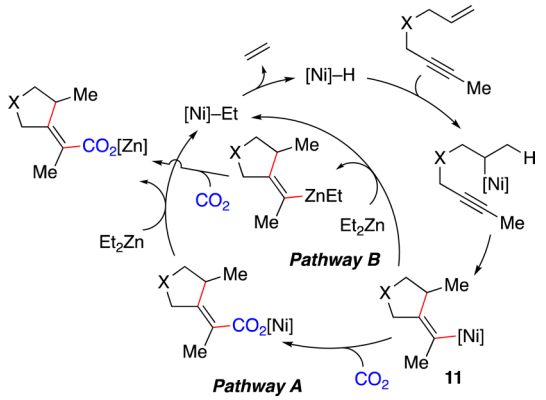
alkene and generate the final product (Scheme 4, path 2). This pathway is inconsistent with cyclization preceding the incorporation of CO_2, evident from the formation of reductive cyclization product **5d**. In addition, the lack of reactivity between $Ni(IPr)_2$, enyne **1a**, and CO_2 in the absence of Et_2Zn contrasts with path 2.

In a Ni-catalyzed reductive cyclization of diynes with CO_2, Ma and co-workers invoked transmetalation between a Ni(0)–alkyne adduct and Et_2Zn to afford a vinylzinc intermediate (Scheme 4, path 3). Further olefin insertion generates the cyclized product.[3g] The vinylzinc intermediate is responsible for the nucleophilic attack on CO_2 to form the carboxylic acid. In the report by Ma, reductive cyclization of the diynes occurs in high yield in the absence of CO_2.[3g] In contrast, our reductive cyclization did not produce any cyclized product in the absence of CO_2. This observation provides circumstantial evidence to rule out Ma's mechanism.

Our mechanistic data are consistent with path 4. The reaction initiates by the insertion of a Ni(II)–H species into the alkene, followed by subsequent insertion of the alkyne and activation of CO_2. When terminal 1,7-enyne **3a–f** and 1,6-enyne **3g**, with steric hindrance on alkene, were used as the substrate, the initial insertion of Ni(II)-H favors the more reactive and sterically more accessible alkyne (path 5).[14] This change of insertion sequence results in the incorporation of CO_2 into the alkene and forms saturated acids **4a–g**. It is noteworthy that the unique change in selectivity with substrates **3a–g** provides further evidence to exclude paths 2 and 3, which cannot account for the observed steric effect on the change of insertion sequence.

Collectively, we propose the catalytic cycle shown in Scheme 5 to account for our experimental observations. Irreversible insertion of Ni-H into the alkene, followed by insertion of the alkyne, gives rise to a vinylnickel intermediate **11**, which may directly react with CO_2 (pathway A).[15] Subsequent transmetalation with Et_2Zn forms a Ni-Et intermediate, which undergoes β-H elimination to regenerate the Ni-H species. Alternatively, the activation of CO_2 could be preceded by transmetalation to Zn, forming a vinylzinc species which ultimately reacts with CO_2 (pathway B).[3c] Our current data do not distinguish between these two pathways, and ongoing

Scheme 5. Proposed Catalytic Cycle



research focuses on elucidating the role of Zn salts in activating CO_2.

CONCLUSION

In conclusion, we have developed a simple, selective, and mild procedure for constructing (hetero)cyclic α,β-unsaturated carboxylic acids from 1,6- and 1,7-enyes and CO_2. Increasing the steric hindrance on alkene or decreasing the steric hindrance on alkyne results in a unique change in the regioselectivity of the carboxylation to afford unconjugated carboxylic acids. Our mechanistic studies suggest a hydride insertion mechanism is operative, which distinguishes this work from previous reactions in incorporating CO_2.

EXPERIMENTAL SECTION

General Considerations. All air- and moisture-sensitive manipulations were carried out in a nitrogen-filled glovebox. Solvents were dried and deoxygenated by passing through alumina in a solvent purification system. $Ni(cod)_2$ was purchased from Strem and used without further purification. Chloroform-*d*, benzene-d_6, and bromoethane-d_5 were purchased from Cambridge Isotope Laboratories. Substrates **1a–g,i–k,o–q** and **3a,d–f** were synthesized according to literature procedures.[16a–n]

^1H and ^{13}C NMR spectra were recorded on Bruker 600, 500, and 400 MHz Avance spectrometers. The chemical shifts (δ) are given in parts per million and referenced to residual solvent peaks or TMS internal standard. The following abbreviations were used to describe multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br = broad. IR spectra were recorded on a Nicolet 6700 FT-IR spectrometer. X-ray crystallographic data were collected on Bruker AXS SMART APEXII single crystal diffractometer. High-resolution mass spectra (HRMS) were collected on an Agilent 6224 TOF LC/MS. Reactions were monitored by thin-layer chromatography (TLC) on Merck TLC silica gel 60 F_{254} plates and compounds were visualized by UV light (254 nm) or $KMnO_4$ staining. Column chromatography was performed on Merck silica gel 60 (0.015–0.040 mm). Carbon dioxide was purchased from Airgas and was passed through 2 Drierite columns before use. Melting points were measured using a Mel-Temp apparatus with open glass capillaries.

Ni(IPr)$_2$. A 20 mL scintillation vial was charged with $Ni(cod)_2$ (100 mg, 0.36 mmol, 1 equiv) and 6 mL of THF. With stirring, IPr[17] (282 mg, 0.73 mmol, 2 equiv) was added in 6 mL of THF. The solution quickly turned dark brown and then black. After the mixture was stirred overnight, solvent was removed under vacuum, the residue was dissolved in 10 mL toluene, and stirring was continued for a further 12 h. After the cycle was repeated two more times, volatiles were removed under vacuum, and the black residue was suspended in pentane (5 mL) and filtered. The solid was washed with pentane twice and dried under vacuum to give 166 mg (0.20 mmol, 56%) of $Ni(IPr)_2$ as a black, microcrystalline solid. The filtrate was stored at −35 °C. After 24 h, the

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supernatant was removed and the solids were dried under vacuum to afford 35 mg (0.04 mmol, 11%) of $Ni(IPr)_2$ (67% overall). The solid was stored at −35 °C. Solutions of $Ni(IPr)_2$ were found to decompose over several days at room temperature. The spectroscopic data is in agreement with the previous reports.[18] ^1H NMR (600 MHz, C_6D_6): δ 7.28 (t, J = 7.7 Hz, 4H), 7.08 (d, J = 7.7 Hz, 8H), 6.11 (s, 4H), 3.06 (sept, J = 6.9 Hz, 8H), 1.25 (d, J = 6.9 Hz, 24H), 1.10 (d, J = 6.9 Hz, 24H). $^{13}C\{^1H\}$ NMR (151 MHz, C_6D_6): δ 193.5, 145.4, 139.3, 123.3, 120.8, 28.3, 24.5, 23.9.

Procedure for Screening Reaction Conditions. An oven-dried 25 mL bomb flask was charged with the nickel catalyst, ligand, and THF (0.8 mL) in a nitrogen-filled glovebox. The flask was sealed and removed from the glovebox. Under a stream of CO_2, enyne **1a** (0.05 mmol, 1 equiv) was added as a solution in 0.1 mL of THF. After addition of the reductant (2.5 equiv), the flask was degassed three times by the freeze−pump−thaw method. The specified amount of CO_2 was then introduced to the flask and the mixture stirred vigorously for 12 h at the specified temperature. The mixture was cooled in an ice bath, diluted with 2 mL of EtOAc, and quenched with 3 mL of 1 M HCl. The aqueous phase was extracted with 2 mL of EtOAc three times. The combined organic phase was dried over Na_2SO_4. Solvent was removed under vacuum. The crude material was dissolved in $CDCl_3$ (0.6 mL) followed by the addition of TMS internal standard (0.02 mmol from a stock solution in $CDCl_3$) and analysis by NMR spectroscopy. All yields were determined by NMR spectroscopy (Table S1).

General Procedure for Cyclization Reactions in Bomb Flasks (General Procedure A). An oven-dried 25 mL bomb flask was charged with $Ni(IPr)_2$ (2−4%) and THF (0.8 mL) in a glovebox. The flask was sealed and removed from the glovebox. Under a stream of CO_2, enyne **1a−q** or **3a−g** (0.05 mmol, 1 equiv) was added as a solution in 0.1 mL of THF. After the addition of $ZnEt_2$ (2.5 equiv) in 0.1 mL of THF the solution became turbid. The flask was degassed three times by the freeze−pump−thaw method. The flask was filled with 1 atm of CO_2. After being vigorously stirred for 12 h, the mixture was cooled in an ice bath, diluted with 2 mL of EtOAc, and quenched with ∼3 mL of 1 M HCl (or satd NH_4Cl for substrate **1o**). The aqueous phase was extracted with 3 × 2 mL EtOAc. The combined organic phase was washed with brine and dried over Na_2SO_4. The crude material was dissolved in $CDCl_3$ (0.6 mL) with TMS (0.02 mmol from a stock solution in $CDCl_3$) added and analyzed by NMR spectroscopy. The crude material was then purified by chromatography on silica with elution by mixtures of $CHCl_3$ and MeOH.

General Procedure for Cyclization Reactions in Round-Bottom Flasks (RBF) (General Procedure B). An oven-dried 50 mL RBF was charged with $Ni(IPr)_2$ (2−4%) and THF (8 mL) in a glovebox. The flask was sealed with a septum and brought out of the glovebox. The flask was purged with a balloon of CO_2 until the solution turned yellow. The balloon was refilled, and enyne **1a−q** or **3a−g** (0.5 mmol, 1 equiv) was added in 1 mL of THF. $ZnEt_2$ (2.5 equiv) was added dropwise in 1 mL of THF, and the solution became turbid. The mixture was stirred vigorously for 12 h. The CO_2 balloon was replaced every 4−8 h due to corrosion of the balloon by $ZnEt_2$. The mixture was cooled in an ice bath, diluted with 10 mL of EtOAc, and quenched with ∼5 mL of 1 M HCl (or satd NH_4Cl for substrate **1o**). The aqueous phase was extracted with EtOAc three times. The combined organic phase was washed twice with brine and dried over Na_2SO_4. Solvent was removed under vacuum to give the crude products, which were purified by recrystallization (carboxylic acids **2i** and **2j**), conversion to the corresponding methyl ester with $TMSCHN_2$ followed by chromatography on silica with hexane/EtOAc (esters **2e**, **2n**, **2q**, and **4g**), or chromatography of the free acids on silica with $CHCl_3$/MeOH (all other carboxylic acids).

General Procedure for Methylation of Carboxylic Acids (General Procedure C). The crude material was dissolved in 3 mL of toluene, and 2 mL of MeOH was added. The solution was cooled in an ice bath, and $TMSCHN_2$ (3 equiv, 2 M in hexane) was added dropwise. The ice bath was removed and the solution stirred at room temperature for 1 h. Acetic acid was added dropwise until the yellow color of $TMSCHN_2$ faded, and then solvent was removed under vacuum. The methyl esters were then purified by column chromatography on silica with elution by hexane and EtOAc.

Procedure for Kinetic Experiments. In parallel, several oven-dried 25 mL bomb flasks were charged with $Ni(IPr)_2$ (0.001 mmol, 0.02 equiv, 0.8 mL THF) from a stock solution in THF, in a glovebox. The flasks were sealed and removed from the glovebox. Under a stream of CO_2, enyne **1a** (0.05 mmol, 1 equiv) was added from a stock solution in THF (0.1 mL). After the addition of $ZnEt_2$ or $ZnEt_2$-d_{10} (2.5 equiv) in 0.1 mL of THF from a stock solution, the flask was degassed three times by the freeze−pump−thaw method. The flask was filled with 1 atm of CO_2. After being stirred vigorously for a specified time, the mixture was cooled in an ice bath, diluted with 2 mL of EtOAc, and quenched with ∼3 mL 1 M HCl. The aqueous phase was extracted 3 × 2 mL of EtOAc. The combined organic phase was washed with brine and dried over Na_2SO_4. The crude material was dissolved in $CDCl_3$ (0.6 mL) with TMS (0.02 mmol from a stock solution in $CDCl_3$) added and analyzed by NMR spectroscopy. Kinetic experiments were repeated twice in order to ensure reproducibility.

Stoichiometric Reaction between $Ni(IPr)_2$, CO_2, and 1a. A J-Young NMR tube was charged with a solution of Ni(IPr)2 (8 mg, 0.009 mmol, 1 equiv) and enyne **1a** (2 mg, 0.009 mmol, 1 equiv) in 0.6 mL C_6D_6. The NMR spectrum of this solution showed no reaction even after 2 days at room temperature. The tube was degassed and refilled with CO_2, causing the solution to turn yellow/orange. The NMR spectrum of this mixture showed $Ni(IPr)_2$ had been consumed and a new Ni species formed. Enyne **1a** was unreactive with this new Ni species (Figure S1).

Reaction with Substoichiometric CO_2. An oven-dried 25 mL bomb flask was charged with $Ni(IPr)_2$ (0.005 mmol, 0.02 equiv) and 4 mL THF in a glovebox. The flask was sealed and removed from the glovebox. Under a stream of CO_2, enyne **1d** (0.25 mmol, 1 equiv) was added in 0.5 mL of THF followed by $ZnEt_2$ (2.5 equiv) in 0.5 mL of THF. The flask was degassed three times by a freeze−pump−thaw method. Using a gas addition bulb and standard Schlenk technique, 0.5 equiv of CO_2 was condensed into the flask. The mixture was stirred overnight, cooled in an ice bath, and quenched with 1 M HCl. The aqueous phase was extracted with EtOAc three times. The combined organic phase was washed twice with brine and dried over Na_2SO_4. Solvent was removed under vacuum to give the crude products (Figure S2), which were purified by chromatography on silica with 100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH to give **2d** (25 mg, 0.075 mmol, 30%) and **5d** (46 mg, 0.16 mmol, 64%) as colorless oils. The spectroscopic data for compound **5d** matches with that reported in the literature.[19]

*(E)-Dimethyl 3-Benzylidene-4-methylcyclopentane-1,1-dicarboxylate (**5d**).* ^1H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 4H), 7.21 (m, 1H), 6.22 (q, J = 2.4 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.39 (d, J = 17.6 Hz, 1H), 3.21 (dd, J = 17.2, 2.8 Hz, 1H), 2.77 (m, 1H), 2.60 (ddd, J = 12.8, 7.2, 1.6 Hz, 1H), 1.77 (dd, J = 12.4, 11.6 Hz, 1H), 1.22 (d, J = 6.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.3, 172.2, 146.0, 137.9, 128.3, 126.2, 121.5, 109.7, 59.0, 52.8, 41.5, 39.1, 39.0, 18.3.

*(Z)-2-(4,4-Bis(methoxycarbonyl)-2-methylcyclopentylidene)-propanoic Acid (**2a**).* Following general procedure B with enyne **1a** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **2a** as a colorless solid in 96% yield (130 mg, 0.48 mmol). Mp 66−68 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 3.75 (s, 3H), 3.71 (s, 3H), 3.59 (m, 1H), 3.28 (d, J = 18.3 Hz, 1H), 2.96 (d, J = 18.3 Hz, 1H), 2.59 (dd, J = 13.5, 8.2 Hz, 1H), 2.17 (dd, J = 13.5, 3.5 Hz, 1H), 1.86 (s, 3H), 1.04 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 173.2, 172.5, 172.2, 162.7, 119.4, 58.1, 53.01, 52.96, 41.8, 40.8, 37.7, 20.5, 16.3. HRMS (ESI-TOF) m/z: $[(M + H) - H_2O]^+$ calcd for $C_{13}H_{17}O_5$ 253.1071, found 253.1070. TLC: R_f = 0.20 (40:1 $CHCl_3$/MeOH).

*(Z)-2-(4,4-Bis((benzyloxy)carbonyl)-2-methylcyclopentylidene)-propanoic Acid (**2b**).* Following general procedure B with enyne **1b** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **2b** as a colorless oil in 90% yield (0.45 mmol, 190 mg). ^1H NMR (600 MHz, $CDCl_3$): δ 7.32 (m, 6H), 7.28−7.26 (m, 2H), 7.23 (m, 2H), 5.18−5.10 (m, 4H), 3.60 (br, 1H), 3.30 (d, J = 18.2 Hz, 1H), 2.99 (d, J = 18.1 Hz, 1H), 2.65 (dd, J = 13.5, 8.3 Hz, 1H), 2.17 (dd, J = 13.5, 3.8 Hz, 1H), 1.83 (s, 3H), 1.03

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(d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.6, 171.6, 171.3, 162.8, 135.3, 135.2, 128.6, 128.6, 128.4, 128.4, 128.2, 128.0, 119.4, 67.6, 67.4, 58.4, 41.8, 40.7, 37.7, 20.7, 16.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{27}O_6$ 423.1808, found 423.1802. TLC: R_f = 0.64 (10:1 $CHCl_3$/MeOH).

*(Z)-2-(4,4-Bis(methoxycarbonyl)-2-methylcyclopentylidene)acetic Acid (**2c**).* Following general procedure B with enyne **1c** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **2c** as a tan oil in 64% yield (0.32 mmol, 82 mg). This compound slowly isomerized to the *E* isomer. ^1H NMR (500 MHz, $CDCl_3$): δ 5.78 (s, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.54 (q, J = 7.0 Hz, 1H), 3.31 (dt, J = 17.2, 2.0 Hz, 1H), 2.95 (d, J = 17.2 Hz, 1H), 2.73 (ddd, J = 13.6, 8.4, 2.0 Hz, 1H), 2.03 (dd, J = 13.6, 8.4 Hz, 1H), 1.16 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.9, 171.6, 170.8, 147.4, 123.8, 58.2, 53.02, 52.99, 42.8, 41.6, 36.3, 20.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{16}O_6Na$ 279.0840, found 279.0858. TLC: R_f = 0.38 (20:1 $CHCl_3$/MeOH).

*(Z)-2-(4,4-Bis(methoxycarbonyl)-2-methylcyclopentylidene)-2-phenylacetic Acid (**2d**).* Following general procedure B with enyne **1d** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2d** as a colorless oil in 60% yield (0.30 mmol, 100 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.39−7.34 (m, 2H), 7.32−7.28 (m, 1H), 7.16 (dd, J = 8.1, 1.3 Hz, 2H), 3.70 (br s, 4H), 3.66 (s, 3H), 3.05 (dd, J = 17.8, 1.9 Hz, 1H), 2.74−2.65 (m, 2H), 2.09 (dd, J = 13.6, 5.2 Hz, 1H), 1.20 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.0, 171.7, 171.3, 165.6, 138.0, 129.2, 128.4, 127.5, 126.5, 58.2, 52.9, 52.9, 41.61, 41.59, 37.1, 20.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}O_6$ 333.1338, found 333.1307. TLC: R_f = 0.48 (10:1 $CHCl_3$/MeOH).

*Dimethyl (Z)-3-(1-Methoxy-1-oxopropan-2-ylidene)-4-methylcyclohexane-1,1-dicarboxylate (**2e**).* Following general procedure B followed by general procedure C with enyne **1e** and purification of the crude material via column chromatography (10:1 hexane/EtOAc) afforded **2e** as a slightly yellow oil in 58% yield (0.29 mmol, 87 mg) (82% brsm). ^1H NMR (500 MHz, $CDCl_3$): δ 3.74 (s, 3H), 3.712 (s, 3H), 3.710 (s, 3H) 3.15 (ddd, J = 14.3, 2.1, 1.1 Hz, 1H), 3.13−3.07 (m, 1H), 2.44 (dd, J = 14.4, 1.4 Hz, 1H), 2.20 (dq, J = 13.7, 3.6 Hz, 1H), 2.03 (td, J = 13.7, 4.2 Hz, 1H), 1.91 (d, J = 1.4 Hz, 3H), 1.68 (tt, J = 13.7, 4.2 Hz, 1H), 1.54 (dq, J = 14.0, 3.6 Hz, 1H), 1.14 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.4, 170.8, 170.7, 144.9, 123.7, 77.4, 56.8, 53.0, 52.6, 51.6, 32.6, 30.0, 26.0, 18.6, 15.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{23}O_6$ 299.1490, found 299.1496. TLC: R_f = 0.20 (10:1 hexane/EtOAc).

*(E)-2-(3-Methyl-1-tosylpiperidin-4-ylidene)-2-(trimethylsilyl)acetic Acid (**2h**).* Following general procedure B with enyne **1h** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2h** as a colorless oil in 62% yield (0.31 mmol, 123 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 3.91 (dq, J = 8.2, 2.6 Hz, 1H), 3.59 (d, J = 11.3 Hz, 1H), 2.76 (d, J = 6.9 Hz, 1H), 2.64 (dd, J = 13.3, 5.3 Hz, 1H), 2.43 (s, 3H), 2.38−2.29 (m, 1H), 2.22−2.13 (m, 1H), 1.30 (d, J = 6.9 Hz, 3H), 1.16 (t, J = 7.6 Hz, 1H), 0.17 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.1, 153.8, 143.7, 133.1, 130.8, 129.7, 127.6, 52.3, 47.2, 36.7, 28.8, 21.5, 18.2, − 0.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{28}NO_4SSi$ 382.1508, found 382.1503. TLC: R_f = 0.33 (10:1 $CHCl_3$/MeOH).

*(E)-2-(4-Methyl-1-tosylpyrrolidin-3-ylidene)propanoic Acid (**2i**).* Following general procedure B with enyne **1i** and purification of the crude material via recrystallization from CH_2Cl_2/hexane afforded **2i** as an off-white solid in 87% yield (0.44 mmol, 136 mg). Mp: 99−101 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.71 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.16 (d, J = 16.6 Hz, 1H), 3.68−3.51 (m, 2H), 3.35 (d, J = 9.1 Hz, 1H), 2.98 (dd, J = 9.1, 6.1 Hz, 1H), 2.43 (s, 3H), 1.75 (s, 3H), 1.18 (d, J = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.0, 157.8, 143.9, 132.1, 129.8, 127.9, 119.2, 55.4, 52.1, 37.8, 21.6, 19.6, 15.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{20}NO_4S$ 310.1108, found 310.1115. TLC: R_f = 0.15 (20:1 $CHCl_3$/MeOH).

*(E)-2-(4-Methyl-1-tosylpyrrolidin-3-ylidene)butanoic Acid (**2j**).* Following general procedure B with enyne **1j** and purification of the crude material via recrystallization from CH_2Cl_2/hexane afforded **2j** as a colorless solid in 91% yield (0.46 mmol, 147 mg). Mp: 83−84 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.71 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 4.20 (d, J = 16.4 Hz, 1H), 3.64 (d, J = 16.4 Hz, 1H), 3.60−3.52 (m, 1H), 3.33 (d, J = 9.1 Hz, 1H), 2.98 (dd, J = 9.1, 6.1 Hz, 1H), 2.43 (s, 3H), 2.17 (dq, J = 14.7, 7.4 Hz, 1H), 2.09 (dq, J = 14.4, 7.4 Hz, 1H), 1.18 (d, J = 7.0 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.5, 157.2, 144.0, 132.0, 129.8, 127.9, 125.7, 55.2, 51.2, 37.7, 23.8, 21.6, 19.7, 12.8. HRMS (ESI, m/z): calcd for $C_{16}H_{21}NO_4S$ $[M + H^+]$ 324.1265, found 324.1264. TLC: R_f = 0.15 (20:1 $CHCl_3$/MeOH).

*(Z)-2-(4-Methyl-1-tosylpyrrolidin-3-ylidene)-2-(trimethylsilyl)-acetic Acid (**2k**).* Following general procedure B with enyne **1k** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **2k** as a tan oil in 76% yield (0.38 mmol, 140 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 4.08 (d, J = 15.4 Hz, 1H), 3.61 (d, J = 15.4 Hz, 1H), 3.27−3.19 (m, 1H), 3.19−3.11 (m, 1H), 2.98 (dd, J = 9.1, 6.1 Hz, 1H), 2.43 (s, 3H), 1.13 (d, J = 7.0 Hz, 3H), 0.15 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 176.0, 160.2, 144.0, 131.9, 129.8, 128.3, 127.8, 54.3, 51.3, 39.0, 21.5, 19.9, − 0.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{26}NO_4SSi$ 368.1347, found 368.1325. TLC: R_f = 0.19 (30:1 $CHCl_3$/MeOH).

*(E)-2-(4-Methyl-5-phenyl-1-tosylpyrrolidin-3-ylidene)propanoic Acid (**2l**).* Following general procedure B with enyne **1l** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2l** as a colorless oil in 82% yield (0.41 mmol, 158 mg, dr = 3:1 *anti*/*syn*). Separation of the diastereomers was not possible, and they were characterized as a mixture. *Anti* isomer: ^1H NMR (600 MHz, $CDCl_3$): δ 7.54 (d, J = 8.2 Hz, 2H), 7.29 (m, J = 8.6 Hz, 2H), 7.23−7.16 (m, 4H), 7.06 (m, 1H), 4.77 (s, 1H), 4.31 (dt, J = 16.9, 1.6 Hz, 1H), 4.21 (dd, J = 16.9, 1.1 Hz, 1H), 3.64 (m, 1H), 2.38 (s, 3H), 1.82 (s, 3H), 1.05 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.7, 157.7, 143.4, 144.7, 129.5, 128.6, 128.4, 127.6, 127.5, 127.2, 126.0, 71.1, 51.7, 47.1, 21.5, 20.4, 16.0. *Syn* isomer: ^1H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, J = 8.2 Hz, 2H), 7.29 (m, 7H), 4.39 (d, J = 17.5 Hz, 1H), 4.25 (d, J = 6.3 Hz, 1H), 4.04 (d, J = 16.4 Hz, 1H), 3.71−3.57 (m, 1H), 2.43 (s, 3H), 1.79 (s, 3H), 0.81 (d, J = 7.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.4, 155.9, 153.9, 144.1, 135.7, 129.6, 128.7, 128.2, 127.8, 120.0, 118.8, 69.0, 53.7, 44.3, 21.6, 20.2, 15.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{24}NO_4S$ 386.1421, found 386.1417. TLC: R_f = 0.43 (10:1 $CHCl_3$/MeOH).

*(E)-2-(4,5-Dimethyl-1-tosylpyrrolidin-3-ylidene)propanoic Acid (**2m**).* Following general procedure B with enyne **1m** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2m** as a colorless oil in 90% yield (0.45 mmol, 146 mg, dr = 1:1 *anti*/*syn*). Separation of the diastereomers was not possible, and they were characterized as a mixture. *Anti* isomer: ^1H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.26 (d, J = 17.2 Hz, 1H), 3.78 (q, J = 6.5 Hz, 1H), 3.66 (dd, J = 17.3, 1.4 Hz, 1H), 3.29 (q, J = 7.0 Hz, 1H), 2.42 (s, 3H), 1.80 (s, 3H), 1.09 (d, J = 7.0 Hz, 3H), 0.78 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.1, 158.1, 143.7, 136.4, 129.9, 127.4, 120.4, 63.9, 50.4, 45.7, 21.8, 19.5, 16.0, 15.5. *Syn* isomer: ^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 4.15−4.07 (m, 1H), 4.03 (dt, J = 16.9, 1.5 Hz, 1H), 3.43 (sept, J = 6.6 Hz, 1H), 3.06 (sept, J = 6.3 Hz, 1H), 2.43 (s, 3H), 1.74 (s, 3H), 1.40 (d, J = 6.4 Hz, 3H), 1.13 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.1, 156.7, 144.1, 132.3, 130.0, 128.1, 118.7, 59.8, 54.4, 43.3, 21.8, 19.5, 16.2, 13.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{22}NO_4S$ 324.1270, found 324.1259. TLC: R_f = 0.23 (30:1 $CHCl_3$/MeOH).

*Methyl (E)-2-(1-Benzoyl-4-methylpyrrolidin-3-ylidene)-propanoate (**2n**).* Following general procedure B followed by general procedure C with enyne **1n** and purification of the crude material via column chromatography (3:1 hexane/EtOAc) afforded **2n** as a colorless oil in 74% yield (0.37 mmol, 96 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.49 (m, 2H), 7.42 (m, 3H), 4.70 (d, J = 19.0 Hz, 1H), 4.17 (d, J = 19.0 Hz, 1H), 3.74 (s, 3H), 3.64 (m, 2H), 3.39 (d, J = 9.9 Hz, 1H), 1.89 (s, 3H), 1.11 (d, J = 6.7 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz,

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$CDCl_3$): δ 170.0, 167.4, 154.8, 136.1, 130.1, 128.4, 127.2, 119.8, 56.7, 51.5, 49.8, 38.0, 19.7, 15.9. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_3Na$ 296.1263, found 296.1247. TLC: R_f = 0.17 (3:1 hexane/EtOAc).

*(E)-2-(1-(tert-Butoxycarbonyl)-4-methylpyrrolidin-3-ylidene)-propanoic Acid (**2o**).* Following general procedure B with enyne **1o** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2o** as a colorless oil in 57% yield (0.29 mmol, 73 mg). Some peaks in the ^1H and ^{13}C NMR spectra appear as broad multiplets due to the Boc group. ^1H NMR (500 MHz, $CDCl_3$): δ 4.25−4.03 (br m, 1H), 4.03−3.84 (br m, 1H), 3.61 (br s, 1H), 3.35 (br m, 2H), 1.76 (br s, 2H), 1.40 (s, 9H), 1.09 (d, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.2, 155.0, 118.5, 79.8, 53.7 (br m), 50.3, 38.0 (br m), 28.5, 20.5, 15.8, 8.9. HRMS (ESI-TOF) *m/z*: $[(M + NH_4) - H_2O]^+$ calcd for $C_{13}H_{23}N_2O_3$ 255.1701, found 255.1703. TLC: R_f = 0.43 (10:1 $CHCl_3$/MeOH).

*(E)-2-(4-Methyldihydrofuran-3(2H)-ylidene)propanoic Acid (**2p**).* Following general procedure B with enyne **1p** and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **2p** as a colorless oil in 72% yield (0.36 mmol, 56 mg). ^1H NMR (600 MHz, $CDCl_3$): δ 4.58 (d, *J* = 16.0 Hz, 1H), 4.31 (d, *J* = 17.3 Hz, 1H), 3.85−3.79 (m, 2H), 3.57 (m, 1H), 1.80 (s, 3H), 1.21 (d, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.9, 162.3, 116.7, 76.2, 71.4, 38.9, 18.9, 15.5. HRMS (ESI-TOF) *m/z*: $[(M + H) - H_2O]^+$ calcd for $C_8H_{11}O_2$ 139.0754, found 139.0754. TLC: R_f = 0.44 (10:1 $CHCl_3$/MeOH).

*Methyl (E)-2-(4-Methyldihydrofuran-3(2H)-ylidene)-2-phenylacetate (**2q**).* Following general procedure B followed by general procedure C with enyne **1q** and purification of the crude material via column chromatography (10:1 hexane/EtOAc) afforded **2q** as a colorless oil in 60% yield (0.3 mmol, 70 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.36 (t, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 2H), 4.31 (d, *J* = 16.1 Hz, 1H), 4.00 (d, *J* = 16.1 Hz, 1H), 3.92 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.78 (d, *J* = 8.5 Hz, 1H), 3.71 (s, 3H), 3.68 (m, 1H), 1.30 (d, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 166.8, 162.1, 137.4, 128.8, 128.6, 127.7, 124.6, 76.1, 71.5, 51.9, 38.7, 18.9. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{17}O_3$ 233.2824, found 233.2831. TLC: R_f = 0.23 (10:1 hexane/EtOAc).

*2-(4-Methylenetetrahydro-2H-pyran-3-yl)acetic Acid (**4a**).* Following general procedure B with enyne **3a** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4a** as a colorless oil in 25% yield (0.13 mmol, 20 mg). ^1H NMR (600 MHz, $CDCl_3$): δ 4.81 (s, 1H), 4.76 (s, 1H), 3.78 (dd, *J* = 11.0, 3.8 Hz, 1H), 3.70 (dqd, *J* = 15.1, 6.7, 3.0 Hz, 2H), 3.49 (dd, *J* = 10.9, 5.3 Hz, 1H), 2.76 (dt, *J* = 11.0, 6.7 Hz, 1H), 2.62 (dd, *J* = 15.9, 6.7 Hz, 1H), 2.52 (dd, *J* = 15.9, 7.7 Hz, 1H), 2.38 (dt, *J* = 12.0, 5.3 Hz, 1H), 2.24 (dt, *J* = 13.8, 5.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 174.7, 146.0, 108.6, 72.8, 69.8, 40.2, 34.2, 34.2. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_8H_{13}O_3$ 157.0859, found 157.0847. TLC: R_f = 0.43 (10:1 $CHCl_3$/MeOH).

*2-(4-Methylene-1-tosylpiperidin-3-yl)acetic Acid (**4b**).* Following general procedure B with enyne **3b** at 60 °C and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4b** as a colorless solid in 81% yield (0.41 mmol, 125 mg). Mp: 160−161 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 4.76 (d, *J* = 13.5 Hz, 2H), 3.25−3.19 (m, 1H), 3.04 (d, *J* = 4.8 Hz, 2H), 2.91 (ddd, *J* = 11.4, 8.5, 4.0 Hz, 1H), 2.84 (m, 1H), 2.61 (d, *J* = 1.4 Hz, 2H), 2.42 (m, 4H), 2.26 (ddd, *J* = 13.5, 6.2, 4.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.5, 145.0, 143.8, 133.5, 129.8, 127.7, 110.4, 51.6, 47.9, 38.8, 35.3, 32.5, 21.7. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{20}NO_4S$ 310.1113, found 310.1104. TLC: R_f = 0.33 (10:1 $CHCl_3$/MeOH).

*2-(5,5-Bis(methoxycarbonyl)-2-methylenecyclohexyl)acetic Acid (**4c**).* Following general procedure B with enyne **3c** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4c** as a colorless solid in 44% yield (0.22 mmol, 59 mg). Mp: 102−104 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 4.78 (s, 1H), 4.60 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 2.66 (m, 2H), 2.51 (dt, *J* = 13.0, 2.8 Hz, 1H), 2.45 (dq, *J* = 13.0, 3.1, 2.8 Hz, 1H), 2.39−2.30 (m, 2H), 2.22 (td, *J* = 13.6, 4.3 Hz, 1H), 1.76 (td, *J* = 13.2, 4.5 Hz, 1H), 1.58 (t, *J* = 12.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.4, 172.4, 171.3, 148.6, 106.5, 55.3, 53.0, 52.9, 38.5, 37.2, 35.7, 33.0, 32.8. HRMS (ESI-TOF) *m/z*: $[(M+H) - H_2O]^+$ calcd for $C_{13}H_{17}O_5$ 253.1071, found 253.1073. TLC: R_f = 0.31 (10:1 $CHCl_3$/MeOH).

*2-(3-Methylenetetrahydro-2H-pyran-4-yl)acetic Acid (**4d**).* Following general procedure B with enyne **3d** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4d** as a colorless oil in 15% yield (0.08 mmol, 12 mg). ^1H NMR (600 MHz, $CDCl_3$) δ 4.92 (s, 1H), 4.77 (s, 1H), 4.17 (d, *J* = 12.2 Hz, 1H), 4.00−3.91 (m, 2H), 3.63 (td, *J* = 11.3, 2.6 Hz, 1H), 2.82−2.69 (m, 2H), 2.40 (dd, *J* = 15.3, 7.2 Hz, 1H), 1.92−1.85 (m, 1H), 1.51 (dtd, *J* = 13.1, 10.7, 4.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 175.9, 145.9, 108.4, 72.9, 67.2, 36.7, 36.6, 34.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_8H_{13}O_3$ 157.0859, found 157.0866. TLC: R_f = 0.33 (10:1 $CHCl_3$/MeOH).

*2-(3-Methylene-1-tosylpiperidin-4-yl)acetic Acid (**4e**).* Following general procedure B with enyne **3e** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4e** as a tan oil in 52% yield (0.26 mmol, 80 mg). ^1H NMR (600 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 5.02 (s, 1H), 4.79 (s, 1H), 4.01 (d, *J* = 12 Hz, 1H), 3.66−3.59 (m, 1H), 3.06 (d, *J* = 12 Hz, 1H), 2.71−2.58 (m, 2H), 2.44 (m, 4H), 2.31 (dd, *J* = 15.9, 7.7 Hz, 1H), 1.89 (dq, *J* = 12.6, 4.2 Hz, 1H), 1.43 (dtd, *J* = 13.1, 10.9, 4.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.5, 143.7, 142.4, 132.9, 129.7, 127.8, 110.7, 52.7, 45.6, 36.9, 36.3, 31.4, 21.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{20}NO_4S$ 310.1113, found 310.1108. TLC: R_f = 0.42 (10:1 $CHCl_3$/MeOH).

*2-(4,4-Bis(methoxycarbonyl)-2-methylenecyclohexyl)acetic Acid (**4f**).* Following general procedure B with enyne **3f** and purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **4f** as a colorless oil in 57% yield (0.29 mmol, 77 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 4.84 (s, 1H), 4.70 (s, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 2.91 (dd, *J* = 13.5, 1.6 Hz, 1H), 2.68−2.53 (m, 3H), 2.35 (dd, *J* = 15.1, 7.3 Hz, 2H), 1.95−1.86 (m, 2H), 1.48−1.37 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.6, 171.9, 171.0, 145.5, 109.8, 57.0, 52.9, 52.7, 40.0, 38.5, 37.0, 30.4, 30.3. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{19}O_6$ 271.1176, found 271.1173. TLC: R_f = 0.36 (10:1 $CHCl_3$/MeOH).

*Dimethyl (E)-3-Ethylidene-4-(2-methoxy-2-oxo-1-phenylethyl)-cyclopentane-1,1-dicarboxylate (**4g**).* Following general procedure B with enyne **3g** at 60 °C followed by general procedure C and purification of the crude material via column chromatography (4:1 hexane/EtOAc) afforded **4g** as a colorless oil in 60% yield (0.30 mmol, 108 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.34−7.24 (m, 5H), 5.30 (m, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.64 (s, 3H), 3.49 (d, *J* = 10.7 Hz, 1H), 3.01 (d, *J* = 16.6 Hz, 1H), 2.90 (d, *J* = 19.9 Hz, 1H), 2.24−2.15 (m, 1H), 1.64−1.59 (m, 3H), 1.58 (s, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 173.9, 172.4, 172.1, 140.7, 137.5, 128.7, 128.6, 127.5, 117.9, 57.9, 56.2, 52.83, 52.77, 52.0, 45.3, 37.8, 36.9, 14.8. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{25}O_6$ 361.1651, found 361.1651. TLC: R_f = 0.43 (3:1 hexane/EtOAc).

EtLi-d_5.[20] An oven-dried 25 mL bomb flask was evacuated and refilled with Ar. Pentane (15 mL) was added to the flask, followed by Li^0 (~400 mg, 57 mmol, 10 equiv) in small chunks. EtBr-d_5 was added (0.43 mL, 5.7 mmol, 1 equiv), and the flask was sealed. The mixture was stirred vigorously at 40 °C for 16 h. In a N_2-filled glovebox, the mixture was filtered through Celite. The filtrate was concentrated under vacuum to give EtLi-d_5 as a colorless, crystalline solid (202 mg, 4.9 mmol, 85%). ^{13}C $\{^1H\}$ NMR (151 MHz, C_6D_6): δ 10.1 (sept), −1.3 (m).

$ZnEt_2$-d_{10}. The deuterated zinc reagent was generated in situ by a modified literature procedure[21] and used without isolation. $ZnCl_2$ (16 mg, 0.12 mmol, 1 equiv) was dissolved in 1 mL of Et_2O in a 4 mL vial. EtLi-d_5 (10 mg, 0.24 mmol, 2 equiv) was added to a 0.5 mL of Et_2O, and the solution became turbid. After the mixture was stirred for 1 h at 23 °C, 0.5 mL pentane was added to precipitate LiCl, and the mixture was filtered. The filtrate was concentrated under vacuum and titrated with I_2 before use.[22]

*(Z)-2-(4,4-Bis(methoxycarbonyl)-2-(methyl-d)cyclopentylidene)-propanoic Acid (**2a-D**).* Following general procedure A with enyne **1a**

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and $ZnEt_2$-d_{10} (2.5 equiv) followed by purification of the crude material via column chromatography (100% $CHCl_3$ → 10:1 $CHCl_3$/MeOH) afforded **2a-D** as a colorless solid in 85% yield (0.043 mmol, 12 mg) with 97% deuterium incorporation. Mp: 65−68 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.77 (s, 3H), 3.73 (s, 3H), 3.60 (m, 1H), 3.30 (d, *J* = 18.3 Hz, 1H), 2.98 (d, *J* = 18.3 Hz, 1H), 2.61 (dd, *J* = 13.5, 8.2 Hz, 1H), 2.19 (dd, *J* = 13.5, 3.5 Hz, 1H), 1.88 (s, 3H), 1.04 (d, *J* = 7.1 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 172.5, 172.3, 172.2, 162.7, 119.2, 58.1, 53.0, 52.9, 41.8, 40.8, 37.7, 20.2 (t), 16.4. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{13}H_{18}DO_6$ 272.1244, found 272.1238. TLC: R_f = 0.20 (40:1 $CHCl_3$/MeOH).

*(Z)-2-(4-(Methylene-d)-1-tosylpiperidin-3-yl)acetic Acid (**4b-D**).* Following general procedure A with enyne **3b** and $ZnEt_2$-d_{10} (2.5 equiv) at 60 °C and purification of the crude material via column chromatography (100% $CHCl_3$ → 100:1 $CHCl_3$/MeOH) afforded **4b-D** as a colorless solid in 61% yield (0.031 mmol, 10 mg) with >99% deuterium incorporation. Mp: 158−160 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.75 (s, 1H), 3.28−3.17 (m, 1H), 3.04 (d, *J* = 4.5 Hz, 2H), 2.91 (ddd, *J* = 11.4, 8.4, 4.0 Hz, 1H), 2.88−2.80 (m, 1H), 2.61 (d, *J* = 7.2 Hz, 2H), 2.45 (m, 1H), 2.42 (s, 3H), 2.30−2.22 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 175.2, 144.8, 143.6, 133.4, 129.7, 127.6, 110.0 (t), 51.4, 47.8, 38.7, 36.0, 32.3, 21.5. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{19}DNO_4S$ 311.1170, found 311.1167. TLC: R_f = 0.33 (10:1 $CHCl_3$/MeOH).

*N-(But-2-yn-1-yl)-4-methyl-N-(1-phenylallyl)benzenesulfonamide (**1l**).* 1-Phenylprop-2-en-1-ol (154 mg, 1.15 mmol, 1 equiv) was dissolved in 10 mL of dry THF under N_2. PPh_3 (477 mg, 1.81 mmol, 1.6 equiv) and TsNHBoc (325 mg, 1.2 mmol, 1.05 equiv) were added, and the solution was cooled to 0 °C. DEAD (0.8 mL of 40% solution in toluene, 1.9 mmol, 1.7 equiv) was added dropwise, and the reaction was stirred for 1 h at 0 °C and then 8 h at room temperature. The solution was diluted with EtOAc and quenched with satd $NH_4Cl_{(aq)}$. The aqueous phase was extracted 2 × 5 mL EtOAc. The combined organic phase was washed with 2 × 10 mL of brine and dried over Na_2SO_4. Solvent was removed, and the yellow residue was dissolved in 5 mL of DCM and treated with 3 mL of TFA. The solution was stirred for 2 h, and solvent was removed to give a yellow oil. Purification was accomplished via column chromatography on silica using 4:1 hexane/EtOAc to give 4-methyl-*N*-(1-phenylallyl)-*p*-toluenesulfonamide as a slightly yellow oil (233 mg, 0.81 mmol, 70%). The spectroscopic data for this compound are in agreement with the published spectra.[23] 4-Methyl-*N*-(1-phenylallyl)-*p*-toluenesulfonamide (66 mg, 0.23 mmol, 1 equiv) was dissolved in 6 mL of dry THF and treated with NaH (60% in mineral oil, 12 mg, 0.28 mmol, 1.2 equiv). The mixture was stirred until the evolution of H_2 ceased (30 min). 1-Bromobut-2-yne (0.03 mL, 0.3 mmol, 1.3 equiv) was added, and the mixture was stirred for 12 h. The reaction was diluted with EtOAc and quenched with satd $NH_4Cl_{(aq)}$. The aqueous phase was extracted with 2 × 5 mL of EtOAc, and the combined organic phase was washed with brine and dried over $MgSO_4$. The product was purified via column chromatography on silica using 10:1 hexane/EtOAc giving a colorless oil (41 mg, 0.12 mmol, 65%). The spectroscopic data for this compound are in agreement with the published spectra.[24] ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 3.3 Hz, 2H), 7.23−7.16 (m, 5H), 6.14 (ddd, *J* = 17.1, 10.3, 7.6 Hz, 1H), 5.56 (d, *J* = 7.6 Hz, 1H), 5.19 (dt, *J* = 10.3, 1.2 Hz, 1H), 5.10 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.01 (dq, *J* = 18.2, 2.4 Hz, 1H), 3.70 (dq, *J* = 18.2, 2.4 Hz, 1H), 2.37 (s, 3H), 1.51 (t, *J* = 2.4 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 143.0, 138.2, 137.9, 134.2, 129.0, 128.4, 128.1, 127.9, 127.8, 119.0, 80.7, 74.5, 63.7, 34.5, 21.6, 3.4.

*N-Allyl-N-(but-2-yn-1-yl)benzamide (**1n**).* A 50 mL RBF was charged with 15 mL of DMF and 60 mg of a 60% dispersion of NaH in mineral oil (1.3 mmol, 1.3 equiv) under N_2. The mixture was cooled in an ice bath, and *N*-allylbenzamide (162 mg, 1 mmol, 1 equiv) was added as a solution in 5 mL of DMF. The mixture was stirred at 0 °C for 20 min, and then 1-bromobut-2-yne (0.11 mL, 1.26 mmol, 1.26 equiv) was added dropwise. The mixture was stirred at room temperature for 12 h, and then the reaction mixture was diluted with EtOAc and quenched with satd $NH_4Cl_{(aq)}$. The aqueous phase was extracted with 4 × 5 mL of EtOAc, and the combined organic phase was washed with 2 × 10 mL of H_2O and 2 × 10 mL brine and dried over $MgSO_4$. Column chromatography on silica with 10:1 hexane/EtOAc gave the product as a slightly yellow oil (203 mg, 0.95 mmol, 95%). The ^{1}H and ^{13}C NMR spectra are broad due to restricted rotation around the benzamide. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60−7.38 (br m, 5H), 5.95−5.69 (br m, 1H), 5.26 (dq, *J* = 10.2, 1.4 Hz, 2H), 4.38−4.19 (br m, 2H), 4.06−3.83 (br m, 2H), 1.86 (s, 3H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 171.4 (br), 135.9, 132.8 (br), 130.0, 128.5, 127.1 (br), 118.1 (br), 80.3 (br) 74.1, 49.0 (br), 36.4 (br), 3.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{14}H_{16}NO$ 214.1226, found 214.1230. TLC: R_f = 0.15 (10:1 hexane/EtOAc).

*N-Allyl-N-(but-3-yn-1-yl)-p-toluenesulfonamide (**3b**).* *N*-(But-3-yn-1-yl)-*p*-toluenesulfonamide[25] (850 mg, 3.8 mmol, 1 equiv) was dissolved in 10 mL of acetone. K_2CO_3 (630 mg, 4.56 mmol, 1.2 equiv) was added, followed by allyl bromide (0.4 mL, 4.56 mmol, 1.2 equiv). The mixture was heated to reflux for 12 h and then filtered, and solvent was removed. Column chromatography on silica with 10:1 hexane/EtOAc gave the product as a colorless oil (590 mg, 2.24 mmol, 59%, 83% brsm) as well as 250 mg (1.12 mmol, 29%) of the alkyne starting material. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74−7.66 (m, 2H), 7.35−7.26 (m, 2H), 5.66 (ddt, *J* = 16.7, 10.1, 6.4 Hz, 1H), 5.23−5.12 (m, 2H), 3.84 (dt, *J* = 6.5, 1.4 Hz, 2H), 3.32−3.23 (m, 2H), 2.49−2.46 (m, 2H), 2.42 (s, 3H), 1.96 (t, *J* = 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 143.6, 137.0, 133.2, 130.0, 127.4, 119.5, 81.2, 70.3, 51.5, 46.2, 21.7, 19.5. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{14}H_{18}NO_2S$ 264.1053, found 264.1055. TLC: R_f = 0.30 (10:1 hexane/EtOAc).

*N-Allyl-4-methyl-N-(4-(trimethylsilyl)but-3-yn-1-yl)-benzenesulfonamide (**1h**).* A RBF was charged with *N*-allyl-*N*-(but-3-yn-1-yl)-*p*-toluenesulfonamide (**3b**) (160 mg, 0.61 mmol, 1 equiv) and 3 mL of dry THF and then cooled to −78 °C under N_2. *n*-BuLi in hexane (1.6 M, 0.46 mL, 0.73 mmol, 1.2 equiv) was added dropwise, and the solution was stirred for 10 min. TMSCl (0.10 mL, 0.67 mmol, 1.1 equiv) was added dropwise. The solution was stirred for 1.5 h at −78 °C and then at room temperature overnight. The reaction was quenched with satd $NH_4Cl_{(aq)}$, and the aqueous layer was extracted with 2 × 5 mL EtOAc. The combined organic phase was washed with 2 × 10 mL brine and dried over $MgSO_4$. Purification via column chromatography on silica with 10:1 hexane/EtOAc gave the product as a colorless oil (185 mg, 0.55 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75−7.69 (m, 2H), 7.34−7.28 (m, 2H), 5.73−5.61 (m, 1H), 5.24−5.14 (m, 2H), 3.86 (d, *J* = 6.4 Hz, 2H), 3.29 (t, *J* = 7.5 Hz, 2H), 2.50 (t, *J* = 5.0 Hz, 2H), 2.43 (s, 3H), 0.14 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 143.5, 137.2, 133.2, 129.9, 127.4, 119.4, 103.8, 86.8, 51.6, 46.3, 21.7, 21.0. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{17}H_{26}NO_2SSi$ 336.1448, found 336.1448. TLC: R_f = 0.33 (10:1 hexane/EtOAc).

*Dimethyl 2-(But-2-yn-1-yl)-2-cinnamylmalonate (**3g**).* A RBF was charged with NaH (54 mg, 2.2 mmol, 1.2 equiv) and cooled to 0 °C under N_2. Ten milliliters of dry DMF were then added to the RBF via syringe. Dimethyl 2-(but-2-yn-1-yl)malonate[26] (345 mg, 1.873 mmol, 1 equiv) was added to the RBF in 1 mL of DMF and stirred for 5 min. Cinnamyl bromide (443 mg, 2.25 mmol, 1.2 equiv) was added to the RBF dropwise. The flask was warmed to room temperature and stirred overnight. The reaction was quenched with satd $NH_4Cl_{(aq)}$ and water. The aqueous layer was extracted 3 × 10 mL diethyl ether. The combined organic layer was washed with 10 mL of brine and then 10 mL of water and dried over $MgSO_4$. Purification via column chromatography on silica with 20:1 hexane/EtOAc gave enyne **3g** as a colorless oil (491 mg, 1.63 mmol, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.27 (m, 4H), 7.23−7.19 (m, 1H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.02 (dt, *J* = 15.7, 7.6 Hz, 1H), 3.74 (s, 6H), 2.94 (dd, *J* = 7.6, 1.2 Hz, 2H), 2.79 (q, *J* = 2.5 Hz, 2H), 1.79 (t, *J* = 2.5 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 170.7, 137.2, 134.5, 128.6, 127.6, 126.4, 123.7, 79.2, 73.4, 57.8, 52.9, 36.1, 23.5, 3.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{18}H_{21}O_4$ 301.1434, found 301.1438. TLC: R_f = 0.40 (4:1 hexane/EtOAc).

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01034.

^{1}H NMR spectra, ^{13}C NMR spectra, IR spectra, reaction optimization table, and crystallographic data for **2j** (PDF)

X-ray crystallographic data for **2j** (CIF)

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Notes

The authors declare no competing financial interest.

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