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Note

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Regioselective Synthesis of Enones via a Titanium Promoted Coupling of Unsymmetrical Alkynes with Weinreb Amides

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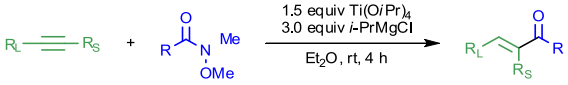


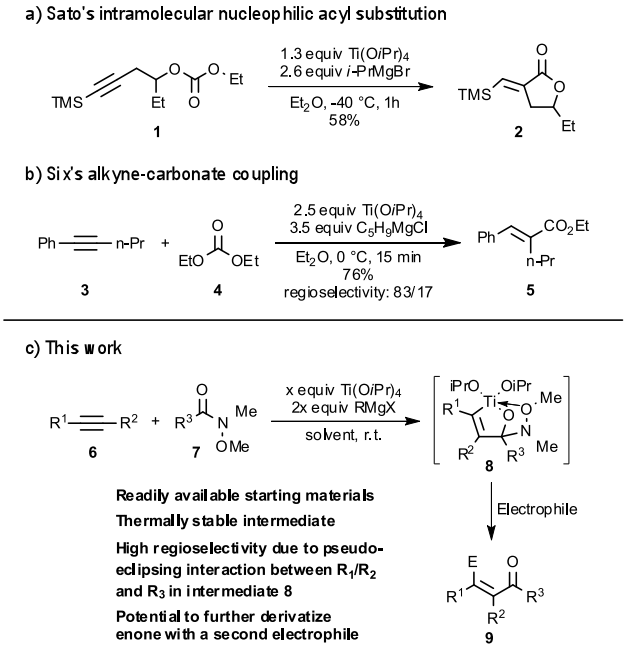
ABSTRACT: A modular titanium promoted coupling of unsymmetrical internal alkynes with Weinreb amides is described. The coupling reaction takes place at room temperature affording (*E*)-trisubstituted enones in moderate to good yields with high levels of regioselectivity. The system showed moderate chemoselectivity.

α,β-Unsaturated ketones (enones) are an important building block that have found widespread use in the synthesis of natural products[1] and biologically active small molecules.[2] The utility of enones is in the diverse array of structures that can be accessed from this motif. As such, numerous methods have been developed for the preparation of enones[3] such as, dehydrative Aldol's,[4] oxidations,[5] olefination reactions with α-ketophosphonates,[6] palladium dehydrogenation,[7] transition metal catalyzed isomerization of propargylic alcohols,[8] hydroacylation of alkynes,[9] and acylation of organometallic reagents.[10] While all of these methods complement each other there is still a need for a method that can prepare tri- and tetra-substituted enones in a modular manner from readily available and easily modifiable substrates.

As part of our endeavors in developing methodology for applications in natural product mimic libraries, we speculated that a titanium promoted coupling[11] of an alkyne and an acyl electrophile could afford enones in a modular manner with high selectivity. Stemming from the seminal work of Kulinkovich on the cyclopropanation of esters,[12] Sato demonstrated that diisopropoxytitanacyclopropenes undergo intramolecular nucleophilic acyl substitution with carbonates (Scheme 1a).[13] This work was expanded upon by Six for the formation of α,β-unsaturated carboxylic acids and esters via an intermolecular titanium reductive coupling of alkynes with carbon dioxide[14] and carbonates (Scheme 1b).[15] Complementarily, zirconocene mediated couplings of alkynes with chloroformates[16] and carbon dioxide[17] have also been reported. The use of group IV metallacycles to form enones from alkynes, surpris-

ingly, has not been reported. For applications in library preparation a vast pool of readily available acyl electrophiles are needed to facilitate diversification of the library. Based on this requirement, we chose to investigate Weinreb amides, which are bench stable reactive acyl electrophiles that can easily and efficiently be prepared from ubiquitous carboxylic acids.[18] Weinreb amides have been utilized in enone synthesis with vinyl lithium[19] and Grignard[20] reagents, but not with titana- or zircona-cyclopropenes.

Scheme 1. Titanium mediated synthesis of conjugated carbonyls from alkynes

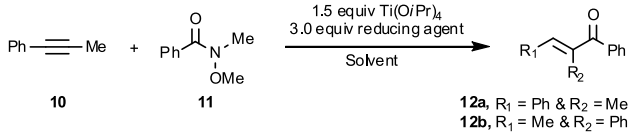


Evaluation of the titanacycle literature indicated the optimal starting point was generation of the titanacyclopropene via Sato's methods, where Ti(O*i*Pr)$_4$ is reduced with *i*-PrMgCl followed by ligand exchange with an alkyne.[21] A limitation of this method for application in small molecule library synthesis is that diisopropoxytitanacyclopropenes are thermally unstable and typically cannot be warmed above -30 °C. It was speculated that the rate of reaction of the titanacyclopropene with a Weinreb amide would be faster than the decomposition pathways and side reactions at room temperature, in addition the coupling would generate a stabilized intermediate that would be thermally stable through coordination of the methoxy group to the titanium.

While the ultimate goal was development of a simple mix and stir procedure that would operate at room temperature, the reaction was first investigated under cryogenic reaction conditions. A room temperature procedure would require the titanacyclopropene to be generated in the presence of the Weinreb amide and it was not clear if the Grignard reagent would preferentially react with the Ti(O*i*Pr)$_4$ over the Weinreb amide. Thus, for the initial optimization reactions the titanacyclopropene of alkyne **10** was generated under prototypical cryogenic conditions (-78 to -40 °C for 3 hours) followed by addition of the Weinreb amide (**11**) at -78 °C and warming to room temperature. Under these conditions the desired enone was formed (Table 1, entry 1), establishing that a titanacyclopropene can undergo coupling with a Weinreb amide and with high regioselectivity, favoring enone **12a**. Increasing the concentration of Weinreb amide **11** to 2 equivalents increased the yield of the enone (entry 2) but further increases had no effect (entry

3).[22] Attempts to further increase the yield through adjustment of the solvent (entries 4-6) established Et_2O as the optimal choice. The choice of reducing agent was critical as a negative effect was seen with EtMgBr (entry 7) and cyclopentylmagnesium chloride (entry 8). It has been demonstrated that the use of *n*-BuLi produces thermally stable titanacycles.[23] Surprisingly, under this reaction manifold the use of *n*-BuLi to generate the titanacyclopropene afforded the enone in moderate yield but with a complete reversal in regioselectivity, favoring enone **12b** (entry 9). Simplification of the procedure by generating the titanacyclopropene in the presence of the Weinreb amide was explored next. It was found that addition of *n*-BuLi to the reaction mixture last did not result in titanacycle formation, instead the *n*-BuLi selectively reacted with only the Weinreb amide affording 1-phenylpentanone (entry 10). Conversely, addition of *i*-PrMgCl to the reaction mixture last (entry 11) at -78 °C followed by warming to room temperature afforded the desired enone in the same yield and regioselectivity as the stepwise process (entry 2). The yield was increased further to 67% by running this sequential addition of reagents at room temperature (entry 12).

Table 1. Optimization of Titanium Coupling Conditions[a]



10 **11** **12a**, R_1 = Ph & R_2 = Me; **12b**, R_1 = Me & R_2 = Ph

entry	solvent	equiv **12**	reducing agent	%yield[b] (**13a**/**13b**)[c]
1	Et_2O	1	*i*-PrMgCl	32 (>99/1)
2	Et_2O	2	*i*-PrMgCl	59 (97/3)
3	Et_2O	5	*i*-PrMgCl	52 (97/3)
4	THF	2	*i*-PrMgCl	34
5	MTBE	2	*i*-PrMgCl	0
6	Toluene	2	*i*-PrMgCl	0
7	Et_2O	2	EtMgBr	0
8	Et_2O	1	*c*-C_5H_9MgCl	20
9[d]	THF	2	*n*BuLi	37 (14/86)
10[e,f]	THF	2	*n*BuLi	0
11[g]	Et_2O	2	*i*-PrMgCl	58 (97/3)
12[h]	**Et_2O**	**2**	***i*-PrMgCl**	**67 (97/3)**

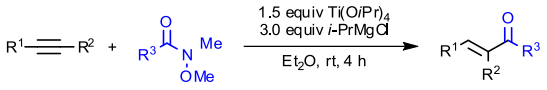
[a]Conditions: alkyne **10** (1 mmol), $Ti(OiPr)_4$ (1.5 mmol), reducing agent (3 mmol), and Et_2O (10 mL) at -78 °C, warmed to -40 °C for 3 hours, cooled to -78 °C then addition of Weinreb amide **11**, and warm to room temperature. [b]isolated yield after flash chromatography. [c]ratio of regioisomers determined by GCMS of the crude reaction mixture. [d]*n*BuLi added at -78 °C, warm to room temperature then addition of Weinreb amide **11**. [e]*n*BuLi added last at room temperature. [f]1-phenylpentanone was isolated in 84%. [g]*i*-PrMgCl added last at -78 °C then warm to room temperature. [h]*i*-PrMgCl added last at room temperature

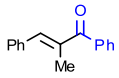
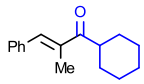
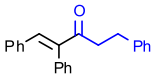
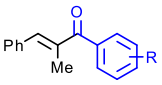
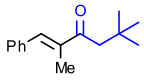
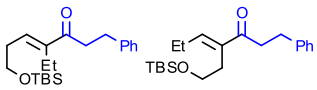
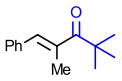
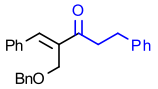
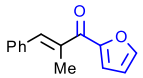
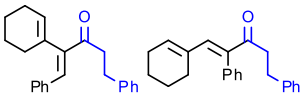
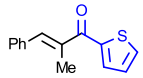
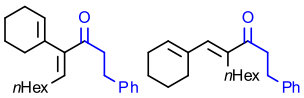
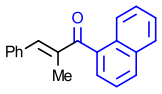
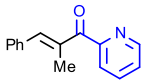
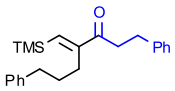
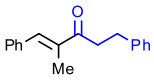
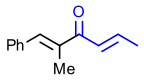
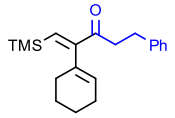
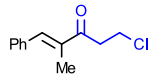
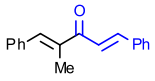
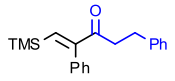
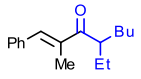
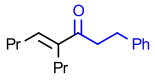
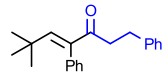
Having established the optimal conditions to be the operationally simple procedure of combining all of the reagents and adding the *i*-PrMgCl last at room temperature followed by stirring for 4 hours, substrate screening was initiated to determine the scope of this coupling reaction (Table 2). Initial efforts focused on varying the Weinreb amide while keeping the alkyne static with the unsymmetrical alkyne 1-phenyl-1-propyne (**10**). In all of the cases examined (entries 1-22) the regioselectivity of the coupling reaction was greater than 97/3. Formation of the carbon-carbon bond favored the alkyne carbon that contained the sterically smaller substituent, regardless of the Weinreb amide employed. Aliphatic Weinreb amides (entries 12-16) were higher yielding than the

aromatic Weinreb amides (entries 1-11), except for the sterically large *N*-methoxy-*N*-methylpivalamide which afforded the enone in moderate yield (entry 17) comparable to its aromatic counterparts. The system tolerated aromatic and aliphatic halogens (entries 2-6 and 13), of note is that an aromatic bromide did not undergo magnesium halogen exchange with the Grignard reagent.[24] The system tolerated *meta* and *para* substituted aromatic Weinreb amides, whereas *ortho*[25] substituted aromatics (I, OMe, Me) would not react with the in situ formed titanacycle (entries 7 and 10), with the exception of a naphthalene (entry 11). Methoxy groups (entry 8) inhibited coupling, presumably due to coordination with the titanium complex. To establish that coordination was the issue and not deactivation of the Weinreb amide carbonyl from electron donation, a Weinreb amide with a TBS protected phenol was prepared, which reacted without incident (entry 9). Additional functional groups on the aromatic Weinreb amide that were found to be incompatible with the system were a $–NO_2$, –CN, –OAc, and $–C(O)CH_3$. Furan (entry 18) and thiophene (entry 19) heteroaromatics were tolerated, but a pyridine (entry 20) inhibited coupling.[26] Conjugated Weinreb amides underwent coupling producing the 1,4-dien-3-one's (entries 21 and 22) in modest yield. These products have the potential to undergo a Nazarov cyclization,[27] but under these reaction conditions less than 3% of the Nazarov product was observed.

A near quantitative yield was obtained with 4-octyne (entry 23) whereas the sterically more congested diphenylacetylene (entry 24) afforded the enone in moderate yield. As already demonstrated with 1-phenyl-1-propyne, an alkyne with a clear steric difference between the groups attached to the alkyne, undergoes coupling with high regioselectivity. To test the limits of the regioselectivity unsymmetrical alkynes of varying steric bulk were examined. The coupling reaction afforded a near one to one mixture of regioisomers when the steric differentiating group was distal to the alkyne (entry 25) or when the two groups were similarly sized (entry 27). A single isomer was obtained with 3-benzyloxy-1-propynylbenzene (entry 26), albeit in low yield, presumably due to formation of a dimeric titanacycle that inhibited reaction with the Weinreb amide. High regioselectivity was seen with silyl protected terminal alkynes (entries 29-31). The sterically congested phenyl-*tert*-butylacetylene participated in the coupling affording the enone in moderate yield but with high selectivity (entry 32). Increasing the sterics further with *tert*-butyltrimethylsilylacetylene completely inhibited the reaction.[28]

Table 2. Substrate Screening of Titanium Mediated Coupling of Alkynes and Weinreb Amides[a,b]



entry	product	%yield[c]	entry	product	%yield[c]	entry	product(s)	%yield[c]
1		67	15		95	24		48
			16		92	25		75 (53/47)
2	R = 4-F	60						
3	R = 4-Cl	57	17		52	26		13
4	R = 3-Br	57						
5	R = 4-CF_3	55						
6	R = 3-CF_3	56	18		53	27		60 (50/50)
7	R = 2-CF_3	0						
8	R = 4-OMe	0						
9	R = 4-OTBS	53	19		52	28		64 (23/77)
10	R = 2,6-Me	trace						
11		20	20		0	29		51 (91/9)
12		87	21		31[d]	30		46 (86/14)
13		74	22		27[e]	31		53 (86/14)
14		80	23		95	32		35

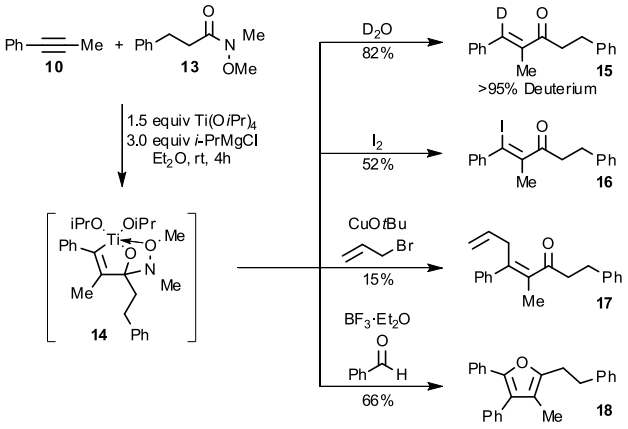
[a]Conditions: alkyne (1 mmol), Weinreb amide (2 mmol), Ti(O*i*Pr)$_4$ (1.5 mmol), Et_2O (10 mL), added last *i*-PrMgCl (3 mmol), room temperature, 4 hours. [b]Unless otherwise stated ratio of regioisomers was ≥ 97/3 as determined by GCMS of the crude reaction mixture, major isomer shown. [c]Isolated yield by flash chromatography. [d]41% alkyne recovered. [e]52% alkyne recovered.

Our earlier findings demonstrated when *n*-BuLi was used as the reducing agent (Table 1, entry 9) the enone was formed favoring the opposite regioisomer. Based on this result, we became interested in the possibility to selectively access either regioisomer by simply changing the reducing agent. Unfortunately, when *n*-BuLi was employed in the coupling reaction the yields were considerably lower and with a number of the substrates screened there was no reaction. Control reactions were run to help determine which element was causing the reversal in regioselectivity. First, we explored the possibility of a solvent effect. Since the solution of *i*-PrMgCl used was in ether and the *n*-BuLi was in hexanes we ran the coupling reaction with the Grignard reagent in the presence of added hexanes. This only resulted in a lower yield of enone with no erosion in the selectivity, consistent with the solvent screening data where the reaction did not take place in toluene (Table 1, entry 6). Next we examined the role of the metal cations. To examine if the lithium cation was interacting with the titanium complex and thereby affecting the regiocontrol, 10 equivalents of

LiCl was added to the reaction with *i*-PrMgCl, which was found to have no effect. In theory, reduction of the $Ti(OiPr)_4$ with the reducing agent produces two equivalents of a metal alkoxide, which could be affecting the aggregate structure of the titanacycle and/or coordinating to the titanium and forming an ate complex. Thus, we ran the coupling reaction using *i*-PrMgCl with 2 equivalents of lithium *tert*-butoxide added, which lowered the yield of the enone to 66% from 92% and slightly eroded the regiocontrol to 96/4. The root cause of the regioselectivity difference with *n*-BuLi and *i*-PrMgCl remains unclear.

Titanacycles are carbanion reagents, as such, we examined subsequent reactions of the stabilized titanacycle intermediate. As shown in Scheme 2, the in situ formed titanacycle **14** could be quenched with deuterium oxide to afford the deuterated enone in 82% yield with greater than 95% deuterium incorporation, and titanium halogen exchange of **14** with iodine afforded the conjugated vinyl iodide in moderate yield. Attempts to transmetallate the chelated and stabilized titanium-carbon bond in titanacycle **14** with copper(I) salts would only occur with CuO*t*Bu, albeit in low yield, but could be used to couple with allyl bromide to form the skipped diene-one **17**. Reaction of titanacycle **14** with benzaldehyde did not occur due to the decreased reactivity of the stabilized titanacycle, however, precomplexation of the aldehyde with BF_3•OEt_2 facilitated addition and a subsequent cyclization to yield the tetrasubstituted furan **18** in 66% yield.[29] A more detailed examination of this approach to furan and heterocycle synthesis is underway and will be reported in due course.

Scheme 2. Subsequent Reactions of Stabilized Intermediate Titanacycle 14



In summary, this report describes a titanium mediated coupling of internal alkynes with Weinreb amides to yield (*E*)-trisubstituted enones in moderate to good yields. The regioselectivity of the reaction is due to the steric difference between the groups attached to the alkyne, with levels as high >99/1 being obtained. Additionally, this is the first demonstration that organotitanium reagents react with Weinreb amides, thereby expanding the arsenal of nucleophiles that can react with this important acyl electrophile.

EXPERIMENTAL SECTION

Methods: All reactions were carried out in oven dried or flame dried glassware under an atmosphere of argon, with magnetic stirring. Reactions were monitored either by thin-layer chromatography with 0.25mm precoated silica gel plates, or Gas Chroma-

tography. Visualization of all TLCs were performed by UV and/or staining with phosphomolybdic acid, $KMnO_4$, or Seebach's stain. Purifications were performed by flash chromatography with silica gel (60 Å, 230-400 mesh) packed in glass columns and eluted with hexanes/Et_2O, unless otherwise noted.

Materials: Diethyl ether, dichloromethane, chloroform, and tetrahydrofuran were purified and dried using a solvent-purification system that contained activated alumina. 1,2-Dichloroethane and pyridine were freshly distilled from calcium hydride under argon. All Weinreb amides were prepared following literature procedures[30] from purchased carboxylic acids.

Instrumentation: ^{1}H NMR and ^{13}C NMR spectra were obtained on a 400 MHz NMR Spectrometer (400 MHz for ^{1}H and 101 MHz for ^{13}C) with chemical shifts reported relative to residual chloroform solvent peaks (δ = 7.26ppm for ^{1}H and δ = 77.0ppm for ^{13}C). Data for ^{1}H NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, sept = septet, m = multiplet or unresolved), coupling constant(s) in Hz, integration. Melting points reported are uncorrected. Low Resolution Mass Spectra was performed by GC-MS and High Resolution Mass Spectra (HRMS) were determined using an Orbitrap operated in FT mode to provide a nominal resolution of 100,000.

General procedure: A round bottom flask was sealed with a septa followed by placing the system under an atmosphere of argon by performing a vacuum-purge cycle three times, then attaching a balloon of argon. The round bottom flask was charged with the alkyne (1 mmol), Weinreb amide (2 mmol), dry diethyl ether (10 mL), and titanium isopropoxide (1.5 mmol, 0.44 mL). To this stirring mixture was injected a solution of isopropyl magnesium chloride (2M in ether, 3 mmol, 1.5 mL) dropwise over 5 minutes. The reaction was stirred at room temperature for 4 hours, followed by opening the system to the air and quenching with 1 mL of water. The mixture was dried over magnesium sulfate, filtered, and concentrated. The crude material was subjected to flash chromatography eluting with hexanes/EtOAc (98/2), unless otherwise noted. **Note 1:** any solid reagents were added to the flask prior to the vacuum-purge cycle. **Note 2:** a small aliquot of the quenched reaction mixture was used to determine the regioisomer ratio by GCMS.

(*E*)-2-Methyl-1,3-diphynylprop-2-en-1-one (**Table 2, entry 1**): subjection of 1-phenyl-1-propyne (1 mmol, 0.125 mL) and N-methoxy-N-methylbenzamide (2.0 mmol, 0.304 mL) to the general procedure afforded 0.149 g (67%) of the enone as a yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 3H), 7.59 – 7.52 (m, 1H), 7.51 – 7.32 (m, 7H), 7.21 (q, J = 1.2 Hz, 1H), 2.30 (d, J = 1.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 142.1, 138.4, 136.7, 135.6, 131.5, 129.6, 129.4, 128.5, 128.4, 128.1, 14.3. Physical and spectral data were consistent with those reported in literature.[31]

(*E*)-2-Methyl-3-phenyl-1-(4-fluoro-phenyl)prop-2-en-1-one (**Table 2, entry 2**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 4-fluoro-N-methoxy-N-methyl benzamide (2.0 mmol, 0.311 mL) to the general procedure afforded 0.145 g (60%) of the enone as yellowish liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 8.6, 5.5 Hz, 2H), 7.42 (m, 5H), 7.14 (m, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 164. 9, 163.6, 141.7, 136.6, 135.5, 134.4, 132.0, 131.9, 129.6, 128.6, 128.4, 115.4, 115.3, 14.5; IR (neat) 3055, 2923, 1644, 1594, 1258, 1225, 1154, 1010, 691. 637 cm^{-1}. HRMS (ESI) *m/*z: $[M+H]^+$ Calcd for $C_{16}H_{13}FO$: 241.1024, Found 241.1020.

(*E*)-1-(4-Chlorophenyl)-2-methyl-3-phenylprop-2-en-1-one (**Table 2, entry 3**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 4-Chloro-N-methoxy-N-methyl benzamide (2.0 mmol, 0.326 mL) to the general procedure afforded 0.145 g (57%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (m, 2H), 7.42 (m, 7H), 7.14 (m, 1H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 142.2, 137.9, 136.7, 136.5, 135.4, 130.8, 129.6, 128.7, 128.4, 128.4, 14.4; Physical and spectral data were consistent with those reported in literature.[32]

(*E*)-1-(3-Bromophenyl)-2-methyl-3-phenylprop-2-en-1-one (**Table 2, entry 4**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 3-Bromo-*N*-methoxy-*N*-methyl benzamide (2.0 mmol, 0.334 mL) to the general procedure afforded 0.171 g (57%) of the enone as a brownish liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.45 – 7.30 (m, 6H), 7.18 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 142.9, 140.4, 136.4, 135.3, 134.4, 132.1, 129.7, 128.8, 128.4, 128.2, 127.8, 122.4, 14.2; IR (neat): 3058, 2923, 1645, 1562, 1248, 1018, 728, 695 cm^{-1}. HRMS (ESI) *m/*z: $[M+H]^+$ Calcd for $C_{16}H_{13}BrO$: 301.0223, Found 301.0221.

(*E*)-2-Methyl-3-phenyl-1-(4-(trifluoromethyl)phenyl) prop-2-en-1-one (**Table 2, entry 5**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 4-trifluoromethyl-*N*-methoxy-*N*-methylbenzamide (2.0 mmol, 0.369 mL) to the general procedure afforded 0.159 g (55%) of the enone as a yellow liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.42 (m, 5H), 7.17 (s, 1H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 143.7, 141.9, 136.5, 135.3, 133.1, 132.7, 129.8, 129.5, 128.9, 128.5, 125.2, 125.2, 125.2, 125.1, 14.0; IR (neat) 3055, 2962, 1649, 1616, 1321, 1107, 1064, 1022, 693 cm^{-1}. HRMS (ESI) *m/*z: $[M+H]^+$ Calcd for $C_{17}H_{13}F_3O$: 291.0992, Found 291.0992.

(*E*)-2-Methyl-3-phenyl-1-(3-trifluoromethyl)phenyl) prop-2-en-1-one (**Table 2, entry 6**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 3-trifluoromethyl-*N*-methoxy-*N*-methylbenzamide (2.0 mmol, 0.369 mL) to the general procedure afforded 0.161 g (56%) of the enone as a yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.43 (m, 5H), 7.17 (s,1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 143.2, 139.2, 136.5, 135.3, 132.5, 130.9, 130.6, 129.7, 128.9, 128.8, 128.5, 128.07, 128.03, 128.00, 127.9, 126.17, 126.13, 126.09, 126.05, 14.2; IR (neat) 2926, 1647, 1611, 1575, 1331, 1244, 1093, 1071, 695 cm^{-1}. HRMS (ESI) *m/*z: $[M+H]^+$ Calcd for $C_{17}H_{13}F_3O$: 291.0992, Found 291.0994.

(*E*)-1-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-2-methyl-3-phenylprop-2-en-1-one (**Table 2, entry 9**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and TBS protected-4 hydroxy-*N*-methoxy-*N*-methylbenzamide (2.0 mmol, 0.529 mL) to the general procedure afforded 0.189 g (54%) of the enone as a yellowish oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.8 Hz, 2H), 7.42 (m, 5H), 7.14 (s, 1H), 6.91 (d, J = 8.8 Hz, 2H), 2.27 (s, 3H), 1.02 (s, 9H), 0.27 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 159.3, 140.0, 136.8, 135.8, 131.8, 131.2, 129.5, 128.2, 119.5, 29.8, 25.5, 18.1, 14.8, -4.4; IR (neat): 2955, 2928, 2857, 1643, 1595, 1505, 1253, 906, 837, 805, 736, 691 cm^{-1}. HRMS (ESI) *m/*z: $[M+H]^+$ Calcd for $C_{22}H_{28}O_2Si$: 353.1932, Found 353.1936.

(*E*)-2-Methyl-1-(naphthalen-1-yl)-3-phenylprop-2-en-1-one (**Table 2, entry 11**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methyl-1-naphthamide (2.0 mmol, 0.430 g) to the general procedure afforded 0.055 g (20%) of the enone as a yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1 H), 7.93 m, 1H), 7.53(m, 4H), 7.40 – 7.29 (m, 5H), 7.22 (s,1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 144.9, 138.5, 137.4, 135.6, 133.6, 131.0, 130.2, 129.8, 128.8, 128.4, 128.3, 126.9, 126.4, 126.3, 125.6, 124.4, 13.4; IR (neat): 3054, 2922, 1643, 1574, 1245, 1197, 777, 692 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{16}O$: 273.1274, Found 273.1270.

(*E*)-2-Methyl-1,5-diphenylpent-1-en-3-one (**Table 2, entry 12**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.217 g (87%) of the enone as yellow oil after flash chromatography;. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.44 – 7.19 (m, 10H), 3.15 (t, *J* = 8.0 Hz, 2H), 3.02 (t, *J* = 8.0 Hz, 2H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 141.5, 138.7, 137.2, 135.8, 129.7, 128.47, 128.42, 128.40, 126.1, 39.6, 30.8, 13.2. Physical and spectral data were consistent with those reported in literature.[33]

(*E*)-5-Chloro-2-methyl-1-phenylpent-1-en-3-one (**Table 2, entry 13**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 3-chloro-*N*-methoxy-*N*-methylpropanamide (2.0 mmol, 0.266 mL) to the general procedure afforded 0.153 g, (74%) of the enone as a yellow oil after flash chromatography (r.r. = 97:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.43 (m, 5H), 3.87 (t, *J* = 6.4 Hz, 2H), 3.31 (t, *J* = 6.9, 2H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 139.4, 136.9, 135.4, 129.6, 128.7, 128.4, 40.2, 39.2, 12.9; IR (neat): 2962, 2919, 1661, 1575, 1195, 1065, 727, 694, 657 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{13}ClO$: 209.0728, Found 209.0729.

(*E*)-4-Ethyl-2-methyl-1-phenyloct-1-en-3-one (**Table 2, entry 14**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and 2-ethyl-*N*-methoxy-*N*-methylhexanamide (2.0 mmol, 0.410 mL) to the general procedure afforded 0.196 g (80%) of the enone as a yellow liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.43 (m, 4H), 7.33 (m, 1H), 3.26 (quin, *J* = 6.8 Hz, 1H), 2.08 (s, 3H), 1.70 (m, 2H), 1.58 – 1.41 (m, 2H), 1.35 – 1.18 (m, 4H), 0.88 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.9, 138.5, 137.9, 136.1, 129.6, 128.3, 128.3, 46.5, 32.4, 29.8, 26.0, 22.9, 13.9, 13.4, 12.0; IR (neat): 2958, 2928, 2858, 1658, 1047, 694 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}O$: 245.1900, Found 245.1900.

(*E*)-1-Cyclohexyl-2-methyl-3-phenylprop-2-en-1-one (**Table 2, entry 15**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methyl-1-cyclohexanamide (2.0 mmol, 0.335 mL) to the general procedure afforded 0.217 g (95%) of the enone as a yellow liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.40 (m, 5H), 3.16 (t, *J* = 11.7 Hz, 1H), 2.04 (s, 3H), 1.82 (d, *J* = 10.8 Hz, 4H), 1.53 – 1.19 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8, 137.6, 136.4, 136.0, 129.5, 128.2, 128.2, 44.5, 29.8, 25.83, 25.80, 13.4; IR (neat): 2927, 2852, 1658, 1448, 1590, 1005, 753, 696 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{20}O$: 229.1587, Found 229.1587.

(*E*)-2,5,5-Trimethyl-1-phenylhex-1-en-3-one(**Table 2, entry 16**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*,3,3-trimethylbutanamide (2.0 mmol, 0.340 mL) to the general procedure afforded 0.198 g (92%) of the enone as a yellow liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.37 (m, 5H), 2.71 (s, 2H), 2.04 (s, 3H), 1.06 (s,

9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 139.0, 138.6, 136.1, 129.57, 128.4, 128.3, 49.2, 31.4, 30.1, 13.2; IR (neat): 2953, 2866, 1655, 1362, 764, 698 cm^{-1}; HRMS (ESI) Calculated for $C_{15}H_{20}O$ $[M+H]^+$: 217.1587, observed: 217.1585.

(*E*)-2,4,4-Trimethyl-1-phenylpent-1-en-3-one (**Table 2, entry 17**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methylpivalamide (2.0 mmol, 0.310 mL) to the general procedure afforded 0.106 g (52%) of the enone as a yellowish liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 5H), 6.93 (s, 1H), 2.09 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 137.6, 135.9, 131.8, 129.1, 128.2, 127.5, 44.1, 27.9, 16.0; IR (neat): 2966, 2869, 1683, 1659, 1477, 1047, 765, 694 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}O$: 203.1431, Found 203.1429.

(*E*)-1-(Furan-2-yl)-2-methyl-3-phenylprop-2-en-1-one (**Table 2, entry 18**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methylfuran-2-carboxamide (2.0 mmol, 0.268 mL) to the general procedure afforded 0.111g (53%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.50 (s,1H), 7.46 – 7.30 (m, 5H), 7.17 (d, J = 3.2 Hz, 1H), 6.55 (d, J = 3.6 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.1, 151.8, 146.7, 139.3, 136.3, 135.7, 129.6, 128.4, 128.3, 119.5, 111.7, 14.5; IR (neat): 2916, 2848, 1630, 1575, 1558, 1463, 1389, 1273, 1024, 1011, 889, 761, 706, 692 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{12}O_2$: 213.0911, Found 213.0910.

(*E*)-2-Methyl-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-one (**Table 2, entry 19**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methylthiophene-2-carboxamide (2.0 mmol, 0.281 mL) to the general procedure afforded 0.117 g (52%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 3.6 Hz, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.48 – 7.32 (m, 6H), 7.14 (t, J = 4.4 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.5, 143.4, 139.0, 136.9, 135.6, 133.5, 133.4, 129.5, 128.4, 128.3, 127.6, 14.8; IR (neat): 2917, 1618, 1512, 1411, 1263, 1002, 847, 723, 693 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{12}OS$: 229.0682, Found 229.0679.

(*E*,*E*)-2-Methyl-1-phenylhexa-1,4-dien-3-one (**Table 2, entry 21**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and (*E*)-*N*-methoxy-*N*-methylbut-2-enamide (2.0 mmol, 0.264 mL) to the general procedure afforded 0.056 mg (31%) of the enone as yellowish liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 1H), 7.44 – 7.30 (m, 5H), 6.95 (dq, J = 15.2, 6.8 Hz, 1H), 6.79 (dq, J = 15.2, 1.49 Hz, 1H), 2.11 (s, 3H), 1.95 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 143.0, 138.4, 137.9, 135.9, 129.6, 128.3, 128.2, 126.9, 18.3, 13.5; IR (neat): 3024, 2913, 1659, 1612, 1575, 1491, 1441, 1287, 1206, 1063, 964, 915, 753, 694 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{14}O$: 187.1118, Found 187.1116.

(*E*,*E*)-2-Methyl-1,5-diphenylpenta-1,4-dien-3-one (**Table 2, entry 22**): subjection of 1-phenyl-1-propyne (1.0 mmol, 0.125 mL) and *N*-methoxy-*N*-methylcinnamamide (2.0 mmol, 0. 382 g) to the general procedure afforded 0.066 g (27%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 15.6 Hz, 1H), 7.62 (m, 3H), 7.50 – 7.33 (m, 9H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 143.4, 138.6, 138.5, 135.9, 135.1, 130.1, 129.7, 128.8, 128.5, 128.4, 128.2, 121.9, 13.8; IR (neat): 3025, 2920, 1650, 1593, 1494, 1448, 1328, 1200, 1061, 762, 698 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{16}O$: 249.1274, Found 249.1272.

(*E*)-1-Phenyl-4-propyloct-4-en-3-one (**Table 2, entry 23**): subjection of 4-octyne (1.0 mmol, 0.147 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.232 g (95%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.21 (m, 3H), 6.57 (t, *J* = 7.3 Hz, 1H), 2.97 (m, 4H), 2.27 (m, 2H), 2.21 (q, *J* = 7.4 Hz, 2H), 1.47 (sex, *J* = 7.2 Hz, 2H), 1.33 (sex, *J* = 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.7, 142.8, 141.8, 141.6, 128.39, 128.38, 125.9, 39.2, 30.9, 30.8, 27.7, 22.5, 22.2, 14.2, 13.9. Physical and spectral data were consistent with those reported in literature.[34]

(*E*)-1,2,5-Triphenylpent-1-en-3-one (**Table 2, entry 24**): subjection of diphenyl acetylene (1.0 mmol, 0.178 g) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.149 g (48%) of the enone as colorless solid after flash chromatography; m.p. = 88 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.44 (m, 3H), 7.36 – 7.13 (m, 10H), 7.06 (m, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 141.3, 140.4, 138.2, 136.8, 134.6, 130.8, 129.5, 129.1, 129.0, 128.39, 128.38, 128.2, 127.9, 125.9, 41.8, 30.4; IR (neat): 3027, 2922, 1676, 1568, 1353, 1281, 1190, 738, 696 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{20}O$: 313.1587, Found 313.1584.

(*E*)-7-((*tert*-Butyldimethylsilyl)oxy)-4-ethyl-1-phenylhept-4-en-3-one (**Table 2, entry 25**): subjection of *tert*-butyl(hex-3-yn-1-yloxy)dimethylsilane (1.0 mmol, 0.252 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.259 g (75%) of the enone as colorless liquid after flash chromatography that was an inseparable mixture of regioisomers (r.r. = 53:47); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 2H), 7.13 (m, 3H), 6.59 (t, *J* = 7.2 Hz, 1H, measured 0.43H), 3.51 (t, *J* = 6.8 Hz, 2H, measured 0.89H), 2.89 (m, 4H), 2.49 (t, *J* = 6.8 Hz, 2H, measured 0.87H), 2.27 (m, 2H), 0.99 (t, *J* = 7.6 Hz, 3H, measured 1.37H), 0.82 (s, 9H, measured 3.64H), -0.03 (s, 6H, measured 2.40H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 146.4, 141.54, 137.6, 128.38, 128.33, 125.94, 62.2, 39.13, 32.3, 30.6, 29.4, 25.9, 18.3, 13.4, -5.4; (E)-4-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-1-phenylhept-4-en-3-one: ^{1}H NMR (400 MHz, CDCl3) δ 7.21 (m, 2H), 7.13 (m, 3H), 6.54 (t, *J* = 7.2 Hz, 1H, measured 0.49H), 3.65 (t, *J* = 6.4 Hz, 2H, measured 1.04H), 2.89 (m, 4H), 2.40 (q, *J* = 6.8 Hz, 2H, measured 1.09H), 2.24 (m, 2H), 0.88 (t, *J* = 7.6 Hz, 3H, measured 1.96H), 0.83 (s, 9H, measured 5.04H), 0.00 (s, 6H, measured 3.29H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 144.4, 141.49, 138.7, 128.35, 128.32, 125.91, 61.8, 39.10, 30.7, 25.8, 22.4, 19.0, 18.2, 13.8, -5.4; IR (neat): 2955, 2928, 2856, 1668, 1496, 1471, 1251, 1094, 833, 774, 697 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{34}O_2Si$: 347.2401, Found 347.2391.

(*E*)-2-((Benzyloxy)methyl)-1,5-diphenylpent-1-en-3-one (**Table 2, entry 26**): subjection of (3-(benzyloxy)prop-1-yn-1-yl)benzene (1.0 mmol, 0.206 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.045 g (13%) of the enone as yellow oil after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.48 (m, 2H), 7.39 – 7.19 (m, 13H), 4.59 (s, 2H), 4.35 (s, 2H), 3.12 (t, *J* = 8.0 Hz, 2H), 3.01 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.2, 143.4, 141.4, 137.9, 136.8, 134.7, 129.8, 129.4, 128.5, 128.48, 128.43, 128.3, 128.2, 127.7, 126.1, 73.1, 63.6, 40.0, 30.4; IR (neat): 3026, 2924, 1668, 1494, 1452, 1069, 1027, 733 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{24}O_2$: 357.1850, Found 357.1837.

(*E*)-2-(Cyclohex-1-en-1-yl)-1,5-diphenylpent-1-en-3-one (**Table 2, entry 27**): subjection of (cyclohex-1-en-1-ylethynyl)benzene (1.0 mmol, 0.189 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.191 g (60%) of the enone as yellow oil after flash chromatography that was an inseparable mixture of regioisomers (r.r. = 50:50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 2H), 7.42 – 7.15 (m, 9H), 5.66 (m, 1H), 3.05 (m, 4H), 2.19 (m, 2H), 1.75 (m, 4H), 1.51 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.10, 142.40, 141.48, 137.6, 136.3, 135.7, 135.2, 130.2, 128.6, 128.3, 128.2, 127.8, 125.9, 40.6, 30.6, 28.3, 25.4, 22.3, 21.7; (*E*)-1-(cyclohex-1-en-1-yl)-2,5-diphenylpent-1-en-3-one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.15 (m, 11H), 6.22 (m, 1H), 2.92 (m, 2H), 2.84 (m, 2H), 2.11 (m, 4H), 1.65 (q, *J* = 7.6 Hz, 2H), 1.41 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.6, 142.8, 141.5, 140.8, 136.6, 134.1, 130.1, 129.0, 128.5, 128.4, 128.3, 127.4, 125.8, 41.6, 30.5, 27.2, 26.8, 22.5, 21.5; IR: 3025, 2929, 1668, 1571, 1494, 1446, 1179, 1071, 908, 729 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}O$: 317.1900, Found 317.1890.

(*E*)-4-(Cyclohex-1-en-1-ylmethylene)-1-phenyldecan-3-one (**Table 2, entry 28**): Subjection of 1-(oct-1-yn-1-yl)cyclohex-1-ene (1.0 mmol, 0.219 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.208 g (64%) of the enone as yellowish liquid after flash chromatography that was an inseparable mixture of regioisomers (r.r. = 77:23); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.05 (m, 5H), 6.75 (s, 1H, measured 0.58H), 5.85 (m, 1H, measured 0.56H), 2.89 (m, 4H), 2.35 (t, *J* = 7.2 Hz, 2H, measured 1.74H), 2.10 (m, 4H, measured 3.69H), 1.57 (m, 4H), 1.21 (m, 8H), 0.81 (t, *J* = 6.8 Hz, 3H); (*E*)-4-(cyclohex-1-en-1-yl)-1-phenylundec-4-en-3-one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.05 (m, 5H), 6.57 (t, *J* = 7.6 Hz, 1H, measured 0.19H), 6.53 (s, 1H, measured 0.22H), 2.83 (m, 2H), 2.69 (m, 2H, measured 0.41H), 2.35 (m, 2H, measured 1.74H), 1.86 (m, 4H, measure 0.75H), 1.57 (m, 4H), 1.21 (m, 8H), 0.81 (t, *J* = 6.8 Hz, 3H).; combined ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.5, 141.9, 141.6, 139.3, 135.0, 133.6, 128.3, 127.1, 125.9, 39.5, 31.5, 30.9, 30.2, 29.5, 28.2, 26.6, 26.1, 22.6, 22.5, 21.7, 14.0; IR (neat): 3026, 2924, 2855, 1663, 1495, 1452, 1105, 921, 747, 697 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{32}O$: 325.2526, Found 325.2517.

(*E*)-1,7-Diphenyl-4-((trimethylsilyl)methylene)heptan-3-one (**Table 2, entry 29**): subjection of trimethyl(5-phenylpent-1-yn-1-yl)silane (1.0 mmol, 0.240 mL) and *N*-methoxy-*N*-methyl-3-phenyl propanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.180 g (51%) of the enone as yellowish liquid after flash chromatography; (r.r. = 91:9, only a single isomer was isolated); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (m, 4H), 7.07 (m, 6H), 6.42 (s, 1H), 2.88 (t, *J* = 8.0 Hz, 2H), 2.80 (t, *J* = 7.6 Hz, 2H), 2.52 (t, *J* = 7.6 Hz, 2H), 2.28 (t, *J* = 8.0 Hz,2H), 1.52 (quin, *J* = 7.6 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 156.1, 142.0, 141.4, 139.9, 128.4, 128.39, 128.37, 128.2, 126.0, 125.7, 39.4, 36.3, 31.9, 31.0, 30.6, -0.4; IR (neat): 3025, 2951, 1672, 1602, 1495, 1452, 1248, 836, 745, 696 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{30}OSi$: 351.2139, Found 351.2137.

(*E*)-2-(Cyclohex-1-en-1-yl)-5-phenyl-1-(trimethylsilyl) pent-1-en-3-one (**Table 2, entry 30**): subjection of (cyclohex-1-en-1-ylethynyl)trimethylsilane (1.0 mmol, 0.207 mL) and *N*-methoxy-*N*-methyl-3-phenyl propanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.143 g (46%) of the enone as yellow oil after flash chromatography that was an inseparable mixture of regioisomers (r.r. = 86:14); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.24 (m, 3H), 6.57 (bs, 1H, measured 0.02H), 6.52 (bs, 1H,

measured 0.75H), 5.62 (m, 1H, measured 0.18H), 5.53 (tt, J = 3.6, 1.7 Hz, 1H, measured 0.77H), 2.97 (m, 4H), 2.15 (m, 2H), 2.03 (m, 2H), 1.69 (m, 4H), 0.12 (s, 9H, measured 7.69H), -0.04 (s, 9H, measured 1.29H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.4, 158.8, 141.5, 139.5, 137.4, 128.4, 127.4, 126.0, 40.4, 30.5, 29.0, 25.1, 22.4, 21.7, -0.2; IR (neat): 3027, 2928, 1674, 1496, 1245, 836, 748, 697 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{28}OSi$: 313.1983, Found 313.1978.

(*E*)-2,5-Diphenyl-1-(trimethylsilyl)pent-1-en-3-one (**Table 2, entry 31**): subjection of 1-phenyl-2-trimethylsilylacetylene (1.0 mmol, 0.197 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.149 g (53%) as yellow liquid after flash chromatography that was an inseparable mixture of regioisomers; (r.r. = 86:14); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.15 (m, 10H), 7.11 (m, 1H, measured 0.92H), 3.04 (m, 4H, measured 3.18H), 3.00 – 2.75 (m, 4H, measured 0.89H), 0.00 (bs, 9H, measured 6.96H), -0.37 (bs, 9H, measured 1.37H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 155.4, 142.3, 141.3, 138.7, 129.3, 128.4, 128.4, 127.9, 127.7, 125.9, 41.1, 30.4, -0.7; IR (neat): 3027, 2952, 1679, 1578, 1247, 1099, 856, 834, 747, 697 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{24}OSi$: 309.1670, Found 309.1667.

(*E*)-6,6-Dimethyl-1,4-diphenylhept-4-en-3-one (**Table 2, entry 32**): Subjection of (3,3-dimethylbut-1-yn-1-yl)benzene (1.0 mmol, 0.180 mL) and *N*-methoxy-*N*-methyl-3-phenylpropanamide (2.0 mmol, 0.365 mL) to the general procedure afforded 0.104 g (35%) of the enone as colorless liquid after flash chromatography; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 3H), 7.30 – 7.18 (m, 4H), 7.13 (m, 3H), 6.89 (s, 1H), 2.89 (t, J = 8.0 Hz, 2H), 2.75 (t, J = 8.0 Hz, 2H), 0.94 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 151.1, 141.4, 139.5, 137.0, 130.0, 128.3, 128.2, 127.8, 127.3, 125.8, 44.8, 41.5, 34.1, 30.4; IR (neat): 3026, 2959, 1688, 1593, 1495, 1475, 1359, 1215, 1111, 1072, 1030, 747 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}O$: 293.1900, Found 293.1890.

ASSOCIATED CONTENT

Notes

The authors declare no competing financial interest

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Supporting Information

^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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