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One-Pot Enol Silane Formation-Alkylation of Ketones with Propargyl Carboxylates Promoted by Trimethylsilyl Trifluoromethanesulfonate

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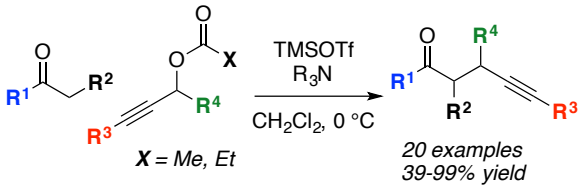
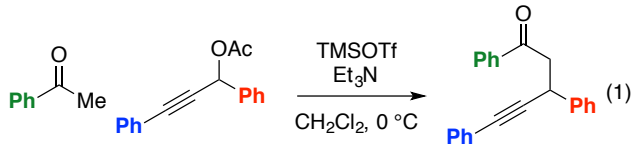
ABSTRACT

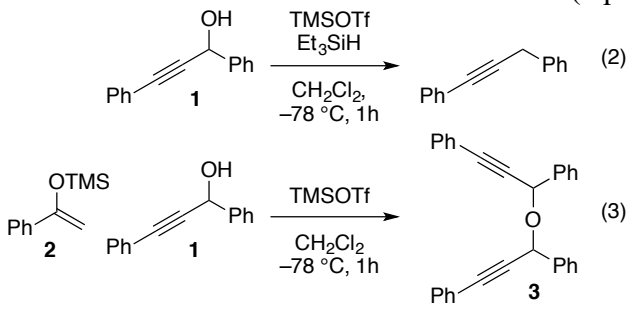
Ketones readily undergo conversion to enol silanes in the presence of trialkylamine base and trimethylsilyl trifluoromethanesulfonate (TMSOTf) and add to propargyl cations to yield β-alkynyl ketones. The propargyl cations are generated in the same reaction flask through the TMSOTf-promoted ionization of propargyl acetates or propargyl propionates. A range of enol silane precursors and propargyl carboxylates reacts efficiently (20 examples, up to 99% yield). Cyclization of a representative product in the presence of TMSOTf provided 61% yield of the trisubstituted furan.



Ketone alkylation is a powerful and established tool for organic synthesis, drawing interest from researchers for decades and continuing to inspire new advances.[1] Although α-alkylation of ketones typically occurs under highly basic conditions, the alkylation of enols and enol silanes also has been shown to proceed under Lewis acidic conditions where the alkylating agent first undergoes ionization to produce a carbocationic intermediate.[2] For example, the ionization of propargyl acetates under metal catalysis allows for reaction with enol silanes to yield β-alkynyl ketones,[3] which have been demonstrated to be useful intermediates in several total syntheses, including (+)-cortistatin,[4] (+)-ryanodol,[5] and morphine.[6] Further synthetic utility for these building blocks derives from their facile conversion to trisubstituted furans.[3b-c,7] Catalysis of a closely related reaction by trimethylsilyl trifluoromethanesulfonate (TMSOTf) provides a route to allenes and enynes when α-substituted enol silanes are employed.[2c] To our knowledge, however, the efficient use of TMSOTf to carry out both the ionization of a propargyl carboxylate[8] *and* the formation of an enol silane nucleophile in a single reaction sequence has not been reported. In the course of our investigation of one-pot enol silane formation-α-substitution reactions,[9] we reported that *para*-methoxybenzyl methyl ether acts as a convenient alkylating agent for aryl methyl ketones in the presence of TMSOTf and a trialkylamine base. We now report that secondary propargyl acetates are readily ionized by TMSOTf and act as efficient alkylation agents for in situ-formed enol silanes to yield β-alkynyl ketones as exemplified by eq 1.

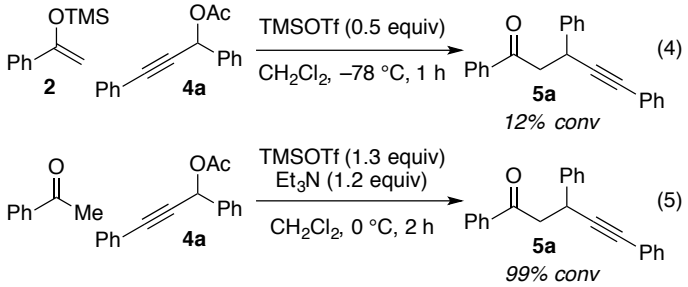


The study began with the attempted activation of propargyl alcohol **1** in the presence of TMSOTf and Et_3SiH. Recovery of the deoxygenated alkyne as the major product demonstrated that TMSOTf-promoted ionization of the propargyl position was viable (eq 2).[10] When the Et_3SiH nucleophile was replaced with enol silane **2**, however, the expected ketone product was not observed. Instead, formation of bispropargyl ether **3** was observed as a mixture of diastereomers (eq 3).[11]



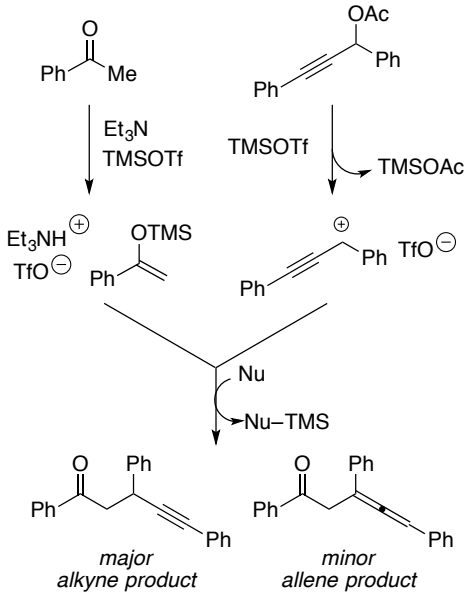
In order to prevent alcohol **1** from acting as a competing nucleophile, it was protected as its acetate ester. When enol silane **2** was reacted with propargyl acetate **4a** in the presence of 0.5 equiv TMSOTf at –78 °C in CH_2Cl_2, 12% conversion to the desired β-alkynyl ketone was observed after 1 h (eq 4), with the remainder of the mixture consisting of unreacted starting materials. Based upon this lead, a survey of reaction

conditions was conducted to determine the optimal conditions for the one-pot enol silane formation-α-alkylation reaction of acetophenone with propargyl acetate **4a**. The optimal conditions are illustrated in eq 5.[12] Several trialkylamine bases promoted the reaction at -78 °C, most notably triethylamine and *N*-methylmorpholine. When the triethylamine reaction was conducted at 0 °C, 95% conversion to the desired product was observed. Further study optimized stoichiometry of the reaction to achieve up to 99% conversion.



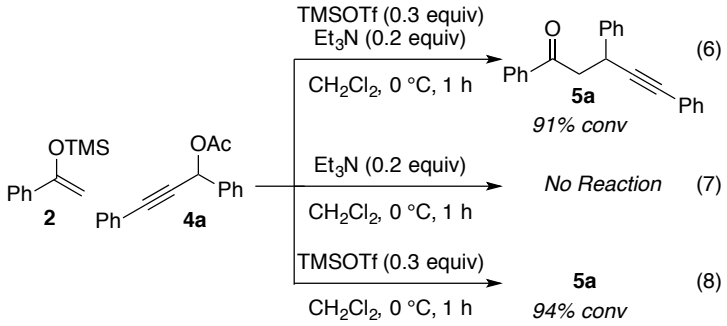
A proposed mechanistic scheme for this reaction is presented in Figure 1. In situ formation of enol silane with Et_3N and TMSOTf provides the active nucleophile and an ammonium salt. Residual TMSOTf activates the propargyl acetate to provide the propargyl cation. Attack of the enol silane on the carbocation forms the new carbon-carbon bond, and desilylation affords a silyl cation capable of activating more of the propargyl acetate. Generation of allenyl products is also possible, either via attack at the γ carbon of the cation or through an SN2' reaction.

Figure 1. Proposed Mechanistic Scheme



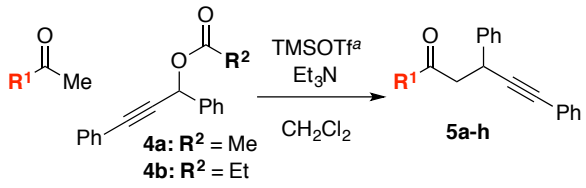
Some experimental evidence supports this mechanism. As described in eq 4 above, it has been observed that enol silane **2** reacts with propargyl acetate **4a** at –78 °C, albeit in lower conversion than under our one-pot reaction conditions. In order to test whether or not the presence of residual Et_3N helps or hinders the carbon-carbon bond-forming reaction, a series of experiments at 0 °C, the optimal reaction temperature, was

conducted. First, enol silane **2** and propargyl acetate **4a** were simply mixed with 0.3 equiv TMSOTf and 0.2 equiv Et_3N, the approximate amounts of these reagents that would be present if 100% conversion of the ketone to the enol silane were to occur. Under these conditions, 91% conversion to the desired product was observed (eq 6). When only Et_3N was present, however, the same attempted reaction provided no product, which demonstrates that TMSOTf must be present to activate the acetate group (eq 7). Finally, when only catalytic TMSOTf was present, enol silane **2** and propargyl acetate **4a** reacted in 94% conversion at 0 °C (eq 8). Together, these results indicate that the presence of Et_3N has no significant impact on the progression of the carbon-carbon bond-forming step, but TMSOTf is catalytically active for the transformation.



Once the optimal reaction conditions were determined, the scope of the one-pot reaction was examined. First, propargyl acetate **4a** was reacted with a series of ketones, as described in Table 1. Most aryl methyl ketones reacted with propargyl acetate **4a** in high yield,[13] as shown in entries 1-3 and 6. The more sterically hindered 1-acetonaphthone and the electron-rich 4-methoxyacetophenone, however, provided relatively disappointing results (typically 70-80% conversion). Preliminary ^1H NMR experiments suggested that enol silane formation was slower for these ketones than for the other aryl methyl ketones examined, which would allow decomposition of the propargyl cation to compete with the desired reaction. Moreover, formation of the trimethylsilyl acetate leaving group appears to be a thermodynamic sink, permanently removing TMSOTf from the reaction mixture and reducing the likelihood of further enol silane formation.

Table 1. Nucleophile scope



entry	R^1	R^2	product	yield (%)[b]
1	Ph	Me	**5a**	86[c]
2	4-FPh	Me	**5b**	83[c]
3	4-BrPh	Me	**5c**	90[c]
4	4-MeOPh	Et	**5d**	74[c]
5	1-naphthyl	Et	**5e**	89[c]
6	2-naphthyl	Me	**5f**	98[d]
7	*t*-Bu	Et	**5g**	94
8	PhS	Et	**5h**	76

[a]Reaction conditions: enol silane precursor (1.0 mmol), propargyl carboxylate (1.1 mmol), TMSOTf (1.3 mmol), Et_3N (1.2 mmol), CH_2Cl_2 (5.0 mL), 0 °C, 2 h. [b]Isolated yield after chromatography. [c]Yield includes trace amount of allene byproduct. [d]Yield includes 4% allene byproduct.

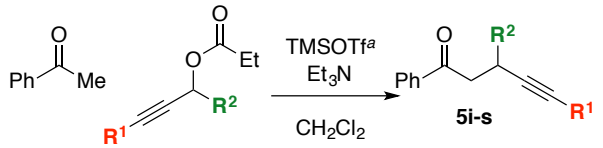
This problem was solved by the replacement of the acetate group with a propionate group, which provides two advantages. *First*, for steric reasons, coordination of the TMSOTf with the carbonyl of the propionate is likely to be slower than coordination to the acetate; ionization of the propionate is consequently slowed but the rate of enol silane formation is not affected. In this situation, the higher concentration of the enol silane would lead to a faster alkylation, which would be competitive with decomposition. *Second*, previous work in our group has shown that trimethylsilyl acetate, which is the byproduct of the ionization of propargyl acetate **4a**, can be readily converted to the highly nucleophilic bis-trimethylsilyl ketene acetal in the presence of TMSOTf and an amine base.[9c] Trimethylsilyl propionate, while still active under those conditions, reacts considerably more slowly and is less likely to compete with our desired nucleophiles.

As shown in entries 4 and 5 of Table 1, propargyl propionate **4b** reacted in good yield when paired with 4-methoxyacetophenone and 1-acetonaphthone. Because of the advantages of the propionate ester described above, all subsequent reactions in this study were examined with propargyl propionates rather than acetates. Indeed, the less active ketone pinacolone was an effective reaction partner when paired with propargyl propionate **4b**, despite its steric hindrance and relatively high pK_a in comparison to aryl methyl ketones (entry 7).[14] A typical thioester also performed well (entry 8), but attempted reactions with amide and ester pronucleophiles resulted only in the decomposition of the electrophile.

With the nucleophile scope firmly established, an investigation into the scope of the propargyl propionate reaction partner commenced. As illustrated in Table 2, a series of propargyl propionates reacted in moderate to high yield when coupled with acetophenone. Entries 1-5 describe substitution at the alkynyl position, demonstrating that a range of aromatic groups as well as an alkyl group are all well tolerated. Only the

triethylsilyl-substituted substrate reacted in poor yield, with the remainder of the reaction mixture consisting of decomposition products. Aryl substitution at the 1-position (R^2) of the propargyl propionate also led to good results (entries 6-11), but some relatively electron-rich substrates did require a modification of the reaction conditions to achieve high yield. Both the 4-methylphenyl substrate (entry 9) and the 4-methoxyphenyl substrate (entry 10) reacted in poor yield when triethylamine was used as the base, but performed well with the somewhat less basic *N*-methylmorpholine. In general, the propargyl propionates represented in Table 2 were less reactive than standard propargyl propionate **4b**, and required additional TMSOTf in order to reach full conversion. The amount of extra TMSOTf necessary varied by substrate, ranging from 0.1-0.55 equiv. For best results, the propargyl propionate and the extra TMSOTf were added sequentially after an incubation period of about 15 min. Not all substrates were entirely successful, however, even under these modified conditions (entries 12-15). Substitution at the 1-position with heteroaromatic groups (2-furyl, 2-thiophenyl) or secondary alkyl groups (cyclohexyl) led only to decomposition of the electrophile, and when the 1-position was occupied by an ethyl group, no ionization was observed even at reflux (40 °C).[15]

Table 2. Electrophile scope

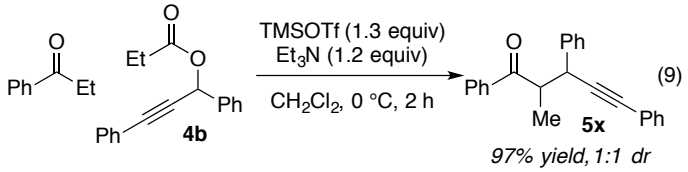


entry	R^1	R^2	product	yield (%)[b]
1	4-ClPh	Ph	**5i**	84
2	4-Me$(CH_2)_4$Ph	Ph	**5j**	92
3	4-(MeO)Ph	Ph	**5k**	60
4	*n*-Bu	Ph	**5l**	94[c]
5	Et_3Si	Ph	**5m**	39[c]
6	Ph	4-(CF_3)Ph	**5n**	71[d]
7	Ph	4-FPh	**5o**	86
8	Ph	4-BrPh	**5p**	75
9	Ph	4-MePh	**5q**	82[e]
10	Ph	4-(MeO)Ph	**5r**	84[e]
11	Ph	2-naphthyl	**5s**	99
12	Ph	2-furyl	**5t**	0
13	Ph	2-thiophenyl	**5u**	0
14	Ph	Cy	**5v**	0
15	Ph	Et	**5w**	0

[a]Reaction conditions: 1. acetophenone (1.0 mmol), propargyl propionate (1.1 mmol), Et_3N (1.2 mmol), TMSOTf (1.3 mmol), CH_2Cl_2 (5.0 mL). 2. TMSOTf (0.1 – 0.55 equiv); see Experimental Section for details. [b]Isolated yield after chromatography. [c]Yield includes 4% allene byproduct. [d]Reaction performed at room temperature. [e]*N*-methylmorpholine used instead of Et_3N.

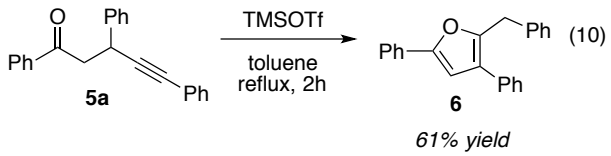
Given the success with methyl ketones, extension to propiophenone was briefly examined. Successful substitution of the propionate group of the electrophile **4b** with propiophenone generated product **5x** as a 1:1 mixture of diastereomers in 97% yield (eq

9). In order to achieve full conversion with this more sterically demanding nucleophile, additional TMSOTf was added after cannula transfer of the in situ-formed enol silane into a solution of the propionate.



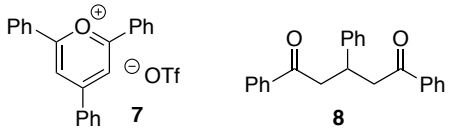
97% yield, 1:1 dr

The cyclization of β-alkynyl ketones analogous to products **5a-t** to yield 2,3,5-trisubstituted furans is well precedented in the literature,[7] and has been achieved under both basic and acidic conditions. Based on these precedents, and because TMSOTf-promoted cyclization would be a convenient addition to our one-pot method, a brief investigation into its feasibility was undertaken. Subjection of β-alkynyl ketone **5a** to TMSOTf in a variety of solvents provided little to no cyclization at room temperature, but significant cyclization was observed in both toluene and cyclopentyl methyl ether when those reactions were heated to reflux. In both cases, however, competing generation of a sparingly soluble yellow byproduct was observed. Analysis of the ^{1}H NMR spectrum of this byproduct showed it to be consistent with previous reports of the 2,4,6-triphenylpyrylium ion (**7**), illustrated in Figure 2.[16] This ion is known to be generated in the presence of trifluoromethanesulfonic acid from dione **8**,[16a] a byproduct resulting from alkyne hydration that was also observed during the cyclization reaction of substrate **5a**. Despite these side reactions, a 61% yield of furan **6** was obtained via TMSOTf-promoted cyclization (eq 10). Attempts to incorporate the cyclization into the one-pot sequence failed, however. When direct cyclization reaction was attempted in one pot starting from acetophenone and propargyl propionate **4b**, addition product **5a** was observed; nonetheless, only trace cyclization occurred even when additional TMSOTf and toluene were added and the reaction mixture was heated to reflux. This lack of reactivity may attributable to the presence of the amine base and its derivatives in the reaction mixture.[17]



61% yield

Figure 2. Byproducts of cyclization reaction



In conclusion, a TMSOTf-promoted one-pot enol silane formation-α-alkylation reaction with propargyl carboxylates has been realized. The TMSOTf plays two distinct roles in the reaction, both in the formation of the enol silane and in the ionization of the propargyl carboxylate. The reaction shows significant reaction scope with regard to the ketone pronucleophile and the substitution pattern on the propargyl carboxylate. Cyclization to yield the trisubstituted furan has been demonstrated.

Experimental Section

General. Reactions were carried out under an atmosphere of nitrogen with a septum cap in oven-dried glassware with magnetic stirring. Methylene chloride and toluene were purified by passage through a bed of activated alumina. [18] Trimethylsilyl trifluoromethanesulfonate (TMSOTf) was stored in a Schlenk flask under inert atmosphere. Triethylamine was distilled from calcium hydride and stored in a Schlenk flask under inert atmosphere. All other chemicals were used as received or prepared according to literature precedent. Purification of reaction products was carried out by flash chromatography using silica gel (230-400 mesh). Analytical thin layer chromatography was performed on silica gel plates. Visualization was accomplished with UV light and phosphomolybdic acid stain, followed by heating. Infrared spectra were recorded on an FT-IR spectrometer. ^{1}H NMR spectra were recorded on a 500 MHz spectrometer or 300 MHz spectrometer, and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.28 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, sx = sextet, sp=septet, m = multiplet, b = broad; coupling constant(s) in Hz; integration). Proton-decoupled ^{13}C NMR spectra were recorded on a 125 MHz spectrometer or 75 MHz spectrometer, and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). High-resolution mass spectra were obtained by electrospray ionization unless otherwise indicated. Melting points were determined using a capillary melting point apparatus.

General Procedure A. *Reactions with 1,3-diphenylprop-2-yn-1-yl acetate*
To an oven-dried flask under N_2 atmosphere was added the 1,3-diphenylprop-2-yn-1yl acetate (1.10 mmol), methylene chloride (10 mL), ketone (1.00 mmol), and Et_3N (167 μL, 121 mg, 1.20 mmol). The reaction mixture was cooled to 0 °C and TMSOTf (235 μL, 289 mg, 1.30 mmol) was added. The reaction mixture was stirred for 2 h. The reaction mixture was passed through a column of silica (2 cm x 1 cm) with diethyl ether. The solvent was removed in vacuo. Column chromatography of the residue (0 – 5% EtOAc/hexanes) provided the product.

General Procedure B. *Reactions with propargyl propionates*
To an oven-dried (flask 1) under N_2 atmosphere was added the propargyl carboxylate (1.10 mmol). To a separate oven-dried flask under N_2 atmosphere was added methylene chloride (2.5 mL), ketone (1.00 mmol), Et_3N (167 μL, 121 mg, 1.20 mmol), and TMSOTf (235 μL, 289 mg, 1.30 mmol). Both flasks were cooled to 0 °C. After 15 min, the contents of flask 2 were transferred via cannula into flask 1. Flask 2 was rinsed with 2.5 mL methylene chloride, then the rinse was transferred via cannula into flask 1. Additional TMSOTf was added, and the reaction mixture was stirred for 2 h. The reaction mixture was passed through a column of silica (2 cm x 1 cm) with diethyl ether. The solvent was removed in vacuo. Column chromatography of the residue (0 – 5% EtOAc/hexanes) provided the product.

1,3,5-Triphenylpent-4-yn-1-one (5a) The title compound[3c] was prepared according to General Procedure A, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl acetate (250 mg, 1.00 mmol). The product was isolated as a white

solid (267 mg, 86% yield): mp: 77-78 °C; IR 3084, 3063, 3029, 2903, 1680, 1488, 1361, 1206, 748, 686 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.63 – 7.56 (m, 3H), 7.53 – 7.46 (m, 2H), 7.45 – 7.38 (m, 4H), 7.34 – 7.29 (m, 4H), 4.72 (dd, J = 7.9, 6.2 Hz, 1H), 3.72 (dd, J = 16.6, 7.9 Hz, 1H), 3.47 (dd, J = 16.6, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 141.3, 136.9, 133.2, 131.7, 128.8, 128.7, 128.3, 128.2, 127.9, 127.7, 127.2, 123.5, 90.8, 83.4, 47.3, 33.8; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{18}ONa$ $[M+Na]^+$, 333.1250; found, 333.1262.

1-(4-Fluorophenyl)-3,5-diphenylpent-4-yn-1-one (5b) The title compound [19] was prepared according to General Procedure A, using 4-fluoroacetophenone (121 μL, 138 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl acetate (275 mg, 1.10 mmol). The product was isolated as a white solid (271 mg, 83% yield): mp: 36-37 °C; IR 3089, 3036, 2933, 1666, 1592, 1506, 1488, 1322, 1258, 1234, 1159, 1026, 831, 756, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 – 7.99 (m, 2H), 7.62 – 7.56 (m, 2H), 7.47 – 7.39 (m, 4H), 7.36 – 7.29 (m, 4H), 7.20 – 7.12 (m, 2H), 4.71 (dd, J = 7.9, 6.2 Hz, 1H), 3.69 (dd, J = 16.6, 7.9 Hz, 1H), 3.43 (dd, J = 16.6, 6.2 Hz, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 195.5, 165.9 (J = 255.0 Hz), 141.2, 133.4 (J = 3.0 Hz), 131.7, 130.9 (J = 9.3 Hz), 128.8, 128.2, 128.0, 127.6, 127.2, 123.4, 115.7 (J = 21.8 Hz), 90.7, 83.5, 47.2, 33.9.; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}OFNa$ $[M+Na]^+$, 351.1156; found, 351.1147.

1-(4-Bromophenyl)-3,5-diphenylpent-4-yn-1-one (5c) The title compound[19] was prepared according to General Procedure A, using 4-bromoacetophenone (200 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl acetate (275 mg, 1.10 mmol). The product was isolated as an off-white solid (351 mg, 90% yield): mp: 95-98 °C; IR 3089, 3060, 3032, 2917, 2897, 2856, 1679, 1584, 1488, 1397, 1202, 1068, 996, 819, 756, 724, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.78 (m, 2H), 7.65 – 7.59 (m, 2H), 7.59 – 7.53 (m, 2H), 7.44 – 7.36 (m, 4H), 7.35 – 7.25 (m, 4H), 4.67 (dd, J = 7.9, 6.2 Hz, 1H), 3.66 (dd, J = 16.6, 7.9 Hz, 1H), 3.41 (dd, J = 16.6, 6.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 141.1, 135.6, 132.0, 131.7, 129.8, 128.8, 128.5, 128.2, 128.0, 127.6, 127.2, 123.3, 90.6, 83.6, 47.2, 33.8; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}OBrNa$ $[M+Na]^+$, 411.0355; found, 411.0345.

1-(4-Methoxyphenyl)-3,5-diphenylpent-4-yn-1-one (5d) The title compound[19] was prepared according to General Procedure B, using 4-methoxyacetophenone (200 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl propionate (290 mg, 1.10 mmol). No additional TMSOTf was added following the transfer via cannula. The product was isolated as a pale yellow solid (252 mg, 74% yield): mp: 62-65 °C; IR 3080, 3055, 3023, 3009, 2963, 2935, 2896, 2840, 1673, 1597, 1486, 1257, 1168, 1024, 978, 827, 759, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 – 7.97 (m, 2H), 7.66 – 7.59 (m, 2H), 7.50 – 7.39 (m, 4H), 7.38 – 7.25 (m, 4H), 7.02 – 6.90 (m, 2H), 4.76 (dd, J = 7.8, 6.2 Hz, 1H), 3.85 (s, 3H), 3.69 (dd, J = 16.4, 7.8 Hz, 1H), 3.43 (dd, J = 16.4, 6.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 163.7, 141.5, 131.7, 130.6, 130.1, 128.8, 128.3, 128.0, 127.7, 127.2, 123.6, 113.9, 91.2, 83.4, 55.5, 47.0, 34.0; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{20}O_2Na$ $[M+Na]^+$, 363.1356; found, 363.1369.

1-(Naphthalen-1-yl)-3,5-diphenylpent-4-yn-1-one (5e) The title compound[19] was prepared according to General Procedure B, using 1-acetonaphthone (152 μL, 200 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl propionate (291 mg, 1.10 mmol). No additional TMSOTf was added following the transfer via cannula. The product was isolated as a yellow oil (320 mg, 89% yield). Yield is corrected for 2 mol% 1-acetonaphthone visible in ^{1}H NMR spectrum: IR 3062, 2978, 2918, 2863, 2244, 1677, 1597, 1490, 1442, 1242, 1103, 911, 802, 755, 690 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 – 8.52 (m, 1H), 8.02 – 7.97 (m, 1H), 7.92 – 7.87 (m, 1H), 7.86 – 7.81 (m, 1H), 7.59 – 7.52 (m, 3H), 7.52 – 7.47 (m, 1H), 7.41 – 7.33 (m, 3H), 7.32 – 7.22 (m, 6H), 4.73 (dd, *J* = 8.4, 6.2 Hz, 1H), 3.72 (dd, *J* = 16.1, 8.4 Hz, 1H), 3.51 (dd, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.5, 141.0, 136.2, 133.9, 132.6, 131.6, 130.1, 128.7, 128.4, 128.1, 127.9, 127.6, 127.4, 127.2, 126.5, 125.8, 124.3, 123.3, 90.5, 83.7, 50.8, 34.5; HRMS (ESI, TOF): Exact mass calcd for $C_{27}H_{20}ONa$ $[M+Na]^+$, 383.1406; found, 383.1392.

1-(Naphthalen-2-yl)-3,5-diphenylpent-4-yn-1-one (5f) The title compound[3e] was prepared according to General Procedure A, using 2-acetonaphthone (171 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl acetate (275 mg, 1.10 mmol). The product was isolated as an off-white solid (352 mg, 98% yield): mp: 99-100 °C; IR 3089, 3056, 3036, 2905, 1676, 1626, 1597, 1490, 1174, 1129, 819, 753, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 – 8.47 (m, 1H), 8.11 – 8.05 (m, 1H), 8.00 – 7.94 (m, 1H), 7.94 – 7.86 (m, 2H), 7.67 – 7.50 (m, 4H), 7.44 – 7.34 (m, 4H), 7.33 – 7.22 (m, 4H), 4.75 (dd, *J* = 7.8, 6.2 Hz, 1H), 3.84 (dd, *J* = 16.5, 7.9 Hz, 1H), 3.58 (dd, *J* = 16.5, 6.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 141.3, 135.7, 134.3, 132.5, 131.7, 130.0, 129.6, 128.7, 128.6, 128.5, 128.1, 127.9, 127.8, 127.7, 127.1, 126.8, 123.9, 123.4, 90.8, 83.4, 47.4, 33.9; HRMS (ESI, TOF): Exact mass calcd for $C_{27}H_{20}ONa$ $[M+Na]^+$, 383.1406; found, 383.1411.

2,2-Dimethyl-5,7-diphenylhept-6-yn-3-one (5g) The title compound[7b] was prepared according to General Procedure B, using pinacolone (125 μL, 100 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl propionate (291 mg, 1.10 mmol). No additional TMSOTf was added following the transfer via cannula. The product was isolated as a pale yellow solid (273 mg, 94% yield): mp: 66-71 °C; IR 3078, 3058, 3030, 2970, 2938, 2907, 2867, 2232, 1704, 1597, 1498, 1362, 1087, 971, 763, 690 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.48 (m, 2H), 7.47 – 7.42 (m, 2H), 7.41 – 7.35 (m, 2H), 7.34 – 7.26 (m, 4H), 4.57 (dd, *J* = 7.8, 6.4 Hz, 1H), 3.22 (dd, *J* = 16.8, 7.9 Hz, 1H), 2.93 (dd, *J* = 16.8, 6.4 Hz, 1H), 1.13 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.2, 141.4, 131.6, 128.6, 128.2, 127.9, 127.6, 127.0, 123.5, 91.0, 82.9, 45.8, 44.1, 33.6, 25.9; HRMS (ESI, TOF): Exact mass calcd for $C_{21}H_{22}ONa$ $[M+Na]^+$, 313.1563; found, 313.1551.

***S*-Phenyl 3,5-diphenylpent-4-ynethioate (5h)** The title compound[19] was prepared according to a variation of General Procedure B, using *S*-phenyl thioacetate (135 μL, 152 mg, 1.00 mmol), 1,3-diphenylprop-2-yn-1yl propionate (291 mg, 1.10 mmol) and a different amount of TMSOTf (272 μL, 333 mg, 1.50 mmol). Additional TMSOTf (10 μL, 12 mg, 0.05 mmol) was added immediately after the contents of the flasks were combined. The product was isolated as a yellow oil (260 mg, 76% yield): IR 3062, 3026, 1701, 1597, 1489, 1441, 1042, 1024, 961, 745, 689 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ

7.53 – 7.45 (m, 4H), 7.45 – 7.36 (m, 7H), 7.35 – 7.29 (m, 4H), 4.49 (dd, *J* = 8.3, 6.7 Hz, 1H), 3.25 (dd, *J* = 14.8, 8.3 Hz, 1H), 3.13 (dd, *J* = 14.8, 6.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.7, 140.0, 134.4, 131.7, 129.5, 129.2, 128.8, 128.2, 128.1, 127.6, 127.5, 127.4, 123.2, 89.3, 84.2, 51.6, 35.2; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{18}OSNa$ $[M+Na]^+$, 365.0971; found, 365.0962.

5-(4-Chlorophenyl)-1,3-diphenylpent-4-yn-1-one (5i) The title compound[19] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol), 3-(4-chlorophenyl)-1-phenylprop-2-yn-1-yl propionate (328 mg, 1.10 mmol) and a different amount of triethylamine (209 μL, 152 mg, 1.50 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added immediately after the contents of the flasks were combined. The product was isolated as a white solid (290 mg, 84% yield): mp: 71-73 °C; IR 3062, 3031, 2911, 2844, 1684, 1600, 1489, 1449, 1088, 1013, 833, 742, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 2H), 7.62 – 7.58 (m, 1H), 7.58 – 7.54 (m, 2H), 7.52 – 7.47 (m, 2H), 7.43 – 7.38 (m, 2H), 7.34 – 7.29 (m, 3H), 7.29 – 7.25 (m, 2H), 4.69 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.71 (dd, *J* = 16.7, 8.1 Hz, 1H), 3.46 (dd, *J* = 16.8, 6.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 141.0, 136.8, 133.9, 133.3, 132.9, 128.8, 128.7, 128.5, 128.2, 127.6, 127.2, 121.9, 91.9, 82.2, 47.2, 33.8; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}OClNa$ $[M+Na]^+$, 367.0860; found, 367.0870.

5-(4-Pentylphenyl)-1,3-diphenylpent-4-yn-1-one (5j) The title compound[3c] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 3-(4-pentylphenyl)-1-phenylprop-2-yn-1-yl propionate (368 mg, 1.10 mmol). Additional TMSOTf (20 μL, 25 mg, 0.11 mmol) was added immediately after the contents of the flasks were combined. The product was isolated as a yellow oil (357 mg, 92% yield): IR 3026, 2958, 2930, 2851, 1685, 1609, 1448, 1354, 1261, 1205, 838, 747, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 – 7.96 (m, 2H), 7.58 (ddt, *J* = 8.0, 6.9, 1.3 Hz, 1H), 7.56 – 7.53 (m, 2H), 7.50 – 7.45 (m, 2H), 7.39 – 7.34 (m, 2H), 7.31 – 7.25 (m, 3H), 7.11 – 7.07 (m, 2H), 4.66 (dd, *J* = 7.8, 6.3 Hz, 1H), 3.68 (dd, *J* = 16.6, 7.8 Hz, 1H), 3.43 (dd, *J* = 16.6, 6.3 Hz, 1H), 2.64 – 2.54 (m, 2H), 1.65 – 1.56 (m, 2H), 1.39 – 1.26 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.1, 143.0, 141.5, 137.0, 133.2, 131.6, 128.7, 128.6, 128.32, 128.26, 127.7, 127.1, 120.6, 90.1, 83.6, 47.4, 35.9, 33.9, 31.5, 31.0, 22.6, 14.1; HRMS (ESI, TOF): Exact mass calcd for $C_{28}H_{28}ONa$ $[M+Na]^+$, 403.2032; found, 403.2035.

5-(4-Methoxyphenyl)-1,3-diphenylpent-4-yn-1-one (5k) The title compound[19] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol), 3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-yl propionate (324 mg, 1.10 mmol) and a different amount of triethylamine (209 μL, 152 mg, 1.50 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added immediately after the contents of the flasks were combined. The product was isolated as an off-white solid (205 mg, 60% yield): mp: 68-71 °C; IR 2967, 2931, 2852, 1682, 1510, 1290, 1249, 1172, 1025, 825, 757, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.63 – 7.56 (m, 3H), 7.54 – 7.46 (m, 2H), 7.44 – 7.38 (m, 2H), 7.38 – 7.34 (m, 2H), 7.34 – 7.29 (m, 1H), 6.88 – 6.80 (m, 2H), 4.70 (dd, *J* = 7.9, 6.2 Hz, 1H), 3.81 (s, 3H), 3.71 (dd, *J* =

16.6, 7.9 Hz, 1H), 3.46 (dd, *J* = 16.7, 6.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 159.3, 141.5, 136.9, 133.3, 133.1, 128.75, 128.67, 128.3, 127.7, 127.1, 115.6, 113.8, 89.3, 83.2, 55.3, 47.4, 33.8; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{20}O_2Na$ $[M+Na]^+$, 363.1356; found, 363.1355.

1,3-Diphenylnon-4-yn-1-one (5l) The title compound[3c] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol), 1-phenylhept-2-yn-1-yl propionate (268 mg, 1.10 mmol). No additional TMSOTf was added after the contents of the flasks were combined. The product was isolated as a yellow oil (273 mg, 94% yield): IR 3072, 2957, 2931, 2867, 1686, 1598, 1494, 1448, 1254, 1206, 1002, 747, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.94 (m, 2H), 7.61 – 7.55 (m, 1H), 7.52 – 7.44 (m, 4H), 7.39 – 7.33 (m, 2H), 7.30 – 7.24 (m, 1H), 4.44 (ddt, *J* = 8.3, 6.0, 2.3 Hz, 1H), 3.57 (dd, *J* = 16.4, 8.2 Hz, 1H), 3.30 (dd, *J* = 16.4, 6.0 Hz, 1H), 2.20 (td, *J* = 7.0, 2.3 Hz, 2H), 1.51 – 1.34 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 142.0, 137.1, 133.1, 128.6, 128.5, 128.2, 127.5, 126.9, 83.6, 81.0, 47.7, 33.4, 31.0, 21.9, 18.5, 13.6; HRMS (ESI, TOF): Exact mass calcd for $C_{21}H_{22}ONa$ $[M+Na]^+$, 313.1563; found, 313.1574.

1,3-Diphenyl-5-(triethylsilyl)pent-4-yn-1-one (5m) The title compound[19] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol), 1-phenyl-3-(triethylsilyl)prop-2-yn-1-yl propionate (333 mg, 1.10 mmol) and, *instead of* triethylamine, diisopropyl(ethyl)amine (261 μL, 194 mg, 1.50 mmol). Additional TMSOTf (20 μL, 25 mg, 0.11 mmol) was added after the contents of the flasks were combined. The product was isolated as a yellow oil (130 mg, 39% yield). Yield is *not* corrected for the presence of significant unknown impurities evident in the NMR spectra, roughly estimated at 25 mol%: IR 2954, 2910, 2874, 2177, 1688, 1494, 1449, 1255, 1017, 724, 689 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 2H), 7.60 – 7.56 (m, 1H), 7.55 – 7.51 (m, 2H), 7.50 – 7.45 (m, 2H), 7.39 – 7.35 (m, 2H), 7.31 – 7.25 (m, 1H), 4.55 (dd, *J* = 7.7, 6.4 Hz, 1H), 3.62 (dd, *J* = 16.4, 7.8 Hz, 1H), 3.34 (dd, *J* = 16.3, 6.4 Hz, 1H), 1.01 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 141.1, 137.1, 133.1, 128.61, 128.57, 128.2, 127.6, 127.0, 108.6, 84.9, 47.6, 34.4, 7.5, 4.5; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{28}OSiNa$ $[M+Na]^+$, 371.1802; found, 371.1796.

1,5-Diphenyl-3-(4-(trifluoromethyl)phenyl)pent-4-yn-1-one (5n) The title compound[19] was prepared according to a variation of General Procedure B *at room temperature*, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 3-phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl propionate (365 mg, 1.10 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added after the contents of the flasks were combined. The product was isolated as a pale yellow solid (268 mg, 71% yield): mp: 82-86 °C; IR 3087, 2908, 2851, 1679, 1328, 1161, 1126, 1108, 1069, 1019, 845, 759, 687 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.94 (m, 2H), 7.72 – 7.57 (m, 5H), 7.53 – 7.45 (m, 2H), 7.43 – 7.37 (m, 2H), 7.33 – 7.26 (m, 3H), 4.75 (ap t, *J* = 6.9 Hz, 1H), 3.71 (dd, *J* = 16.9, 7.1 Hz, 1H), 3.48 (dd, *J* = 16.9, 6.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.4, 145.4, 136.9, 133.2, 131.6, 129.6 (d, *J* = 32.4 Hz), 128.6, 128.15, 128.12, 128.0 (double peak), 125.6 (q, *J* = 3.8 Hz), 123.1, 124.1 (d, *J* = 271.8 Hz), 89.8, 84.0, 46.9,

33.6; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{17}OF_3Na$ $[M+Na]^+$, 401.1124; found, 401.1122.

3-(4-Fluorophenyl)-1,5-diphenylpent-4-yn-1-one (5o) The title compound[19] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol), 1-(4-fluorophenyl)-3-phenylprop-2-yn-1-yl propionate (310 mg, 1.10 mmol), and a different amount of triethylamine (209 μL, 152 mg, 1.50 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added after the contents of the flasks were combined. The product was isolated as a white solid (282 mg, 86% yield): mp: 51-59 °C; IR 3082, 2930, 2905, 1679, 1595, 1508, 1489, 1413, 1228, 1206, 1184, 1001, 838, 758, 687 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.98 (m, 2H), 7.65 – 7.58 (m, 1H), 7.57 – 7.52 (m, 2H), 7.52 – 7.47 (m, 2H), 7.46 – 7.40 (m, 2H), 7.36 – 7.29 (m, 3H), 7.12 – 7.04 (m, 2H), 4.71 (ap t, J = 7.0 Hz, 1H), 3.70 (dd, J = 16.8, 7.4 Hz, 1H), 3.46 (dd, J = 16.7, 6.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 161.9 (d, J = 245.4 Hz), 137.1 (d, J = 3.2 Hz), 136.8, 133.3, 131.7, 129.3 (d, J = 8.0 Hz), 128.7, 128.24, 128.22, 128.1, 123.3, 115.5 (d, J = 21.5 Hz), 90.7, 83.5, 47.3, 33.0; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}OFNa$ $[M+Na]^+$, 351.1156; found, 351.1139.

3-(4-Bromophenyl)-1,5-diphenylpent-4-yn-1-one (5p) The title compound[7a] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 1-(4-bromophenyl)-3-phenylprop-2-yn-1-yl propionate (378 mg, 1.10 mmol), and a different amount of triethylamine (209 μL, 152 mg, 1.50 mmol). Additional TMSOTf (20 μL, 25 mg, 0.22 mmol) was added after the contents of the flasks were combined. The product was isolated as an off-white solid (292 mg, 75% yield): mp: 62-68 °C; IR 3062, 2975, 2927, 2896, 1670, 1489, 1304, 1259, 1010, 828, 752, 688 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 – 7.95 (m, 2H), 7.60 (ddt, J = 8.6, 6.9, 1.3 Hz, 1H), 7.53 – 7.44 (m, 6H), 7.44 – 7.39 (m, 2H), 7.35 – 7.29 (m, 3H), 4.68 (ap t, J = 7.0 Hz, 1H), 3.69 (dd, J = 16.8, 7.3 Hz, 1H), 3.46 (dd, J = 16.8, 6.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.7, 140.4, 136.7, 133.4, 131.8, 131.7, 129.5, 128.7, 128.3, 128.2, 128.1, 123.2, 121.0, 90.3, 83.6, 47.0, 33.2; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}OBrNa$ $[M+Na]^+$, 411.0355; found, 411.0371.

1,5-Diphenyl-3-(*p*-tolyl)pent-4-yn-1-one (5q) The title compound[7a] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 3-phenyl-1-(*p*-tolyl)prop-2-yn-1-yl propionate (334 mg, 1.20 mmol). In the place of triethylamine, dicyclohexyl(methyl)amine was used (138 μL, 127 mg, 1.25 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added after the contents of the flasks were combined. The product was isolated as a pale orange solid (266 mg, 82% yield): mp: 79-83 °C; IR 3087, 3032, 2963, 2908, 2854, 1679, 1329, 1206, 1109, 1069, 760, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.58 (ddt, J = 8.5, 6.9, 1.3 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.45 – 7.40 (m, 2H), 7.40 – 7.34 (m, 2H), 7.29 – 7.25 (m, 3H), 7.21 – 7.15 (m, 2H), 4.63 (dd, J = 7.8, 6.3 Hz, 1H), 3.66 (dd, J = 16.5, 7.8 Hz, 1H), 3.42 (dd, J = 16.5, 6.3 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.1, 158.8, 137.3, 133.4, 132.9, 131.6, 128.5, 128.5, 128.2, 128.0, 127.7, 123.6, 114.2, 91.2, 83.3, 55.3, 47.4, 33.2; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{20}ONa$ $[M+Na]^+$, 347.1406; found, 347.1409.

3-(4-Methoxyphenyl)-1,5-diphenylpent-4-yn-1-one (5r) The title compound[7a] was prepared according to a variation of General Procedure B, using acetophenone (117 μL, 120 mg, 1.00 mmol) and 1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl propionate (353 mg, 1.20 mmol). In the place of triethylamine, dicyclohexyl(methyl)amine was used (138 μL, 127 mg, 1.25 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added after the contents of the flasks were combined. The product was isolated as a white solid (271 mg, 84% yield): mp: 98-100 °C; IR 3087, 3058, 3035, 2949, 2931, 2900, 1679, 1512, 1245, 1205, 1027, 832, 727, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 – 7.96 (m, 2H), 7.61 – 7.55 (m, 1H), 7.50 – 7.42 (m, 4H), 7.39 – 7.35 (m, 2H), 7.30 – 7.25 (m, 3H), 6.94 – 6.88 (m, 2H), 4.62 (dd, *J* = 7.6, 6.6 Hz, 1H), 3.82 (s, 3H), 3.65 (dd, *J* = 16.4, 7.6 Hz, 1H), 3.41 (dd, *J* = 16.5, 6.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.1, 158.8, 137.3, 133.4, 132.9, 131.6, 128.53, 128.51, 128.2, 128.0, 127.7, 123.6, 114.2, 91.2, 83.3, 55.3, 47.4, 33.2; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{20}O_2Na$ $[M+Na]^+$, 363.1356; found, 363.1348.

3-(Naphthalen-2-yl)-1,5-diphenylpent-4-yn-1-one (5s) The title compound[19] was prepared according to a variation of General Procedure B *on a 0.5 mmol scale*, using acetophenone (59 μL, 61 mg, 0.51 mmol), 1-(naphthalen-2-yl)-3-phenylprop-2-yn-1-yl propionate (175 mg, 0.56 mmol), triethylamine (85 μL, 62 mg, 0.61 mmol), TMSOTf (119 μL, 146 mg, 0.66 mmol), and methylene chloride (6 mL). Additional TMSOTf (40 mL, 49 mg, 0.22 mmol) was added after the contents of the flasks were combined. The product was isolated as a white solid (148 mg, 80% yield): mp: 93-98 °C; IR 3057, 3023, 2881, 1681, 1606, 1489, 1262, 1208, 979, 824, 756, 688 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.97 (m 3H), 7.94 – 7.80 (m, 3H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.35 (m, 6H), 7.36 – 7.19 (m, 3H), 4.86 (ap t, *J* = 7.1 Hz, 1H), 3.78 (dd, *J* = 16.7, 7.8 Hz, 1H), 3.55 (dd, *J* = 16.7, 6.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 138.6, 136.9, 133.5, 133.2, 132.6, 131.7, 128.6, 128.5, 128.17, 128.23, 127.93, 127.88, 127.6, 126.3, 126.2, 125.83, 125.80, 123.4, 90.8, 83.6, 47.1, 33.9; HRMS (ESI, TOF): Exact mass calcd for $C_{27}H_{20}ONa$ $[M+Na]^+$, 383.1406; found, 383.1402.

2-Methyl-1,3,5-triphenylpent-4-yn-1-one (5x) The title compound[19] was prepared according to General Procedure B, using propiophenone (133 μL, 134 mg, 1.00 mmol) and 1,3-diphenylprop-2-yn-1yl acetate (291 mg, 1.10 mmol). Additional TMSOTf (100 μL, 123 mg, 0.55 mmol) was added after the contents of the flasks were combined. The product was isolated as a pale yellow oil consisting of a 1:1 mixture of diastereomers, including 5% allene (314 mg, 97% yield): IR 3066, 3027, 2971, 2935, 2876, 1680, 1596, 1447, 1239, 1207, 966, 908, 756, 730, 690 cm^{-1}; HRMS (ESI, TOF): Exact mass calcd for $C_{24}H_{20}ONa$ $[M+Na]^+$, 347.1406; found, 347.1399.

Diastereomer A:

^1H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 2H), 7.65 – 7.59 (m, 1H), 7.55 – 7.50 (m, 2H), 7.50 – 7.44 (m, 3H), 7.43 – 7.37 (m, 2H), 7.36 – 7.30 (m, 1H), 7.24 – 7.15 (m, 2H), 7.14 – 7.10 (m, 2H), 4.17 (d, *J* = 9.6 Hz, 1H), 4.03 – 3.96 (m, 1H), 1.07 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.0, 139.4, 137.2, 133.1, 131.5, 128.66, 128.62, 128.57, 128.51, 127.99, 127.8, 127.4, 123.3, 90.7, 83.8, 47.7, 41.6, 16.1.

Diastereomer B:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 2H), 7.55 – 7.50 (m, 1H), 7.50 – 7.44 (m, 3H), 7.43 – 7.37 (m, 2H), 7.36 – 7.30 (m, 3H), 7.28 – 7.25 (m, 2H), 7.24 – 7.15 (m, 2H), 4.42 (d, *J* = 8.7 Hz, 1H), 3.96 – 3.90 (m, 1H), 1.49 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.3, 140.4, 136.7, 133.0, 131.7, 128.72, 128.59, 128.3, 128.2, 128.1, 128.02, 127.1, 123.5, 89.6, 84.9, 48.0, 41.4, 16.4.

2-Benzyl-3,5-diphenylfuran (6) To an oven-dried flask under N_2 was added compound **5a** (1,3,5-triphenylpent-4-yn-1-one, 311 mg, 1.0 mmol). The substrate was dissolved in toluene (2.5 mL) and TMSOTf (180 μL, 221 mg, 1.0 mmol) was added dropwise. The flask was fitted with a reflux condenser and heated at reflux (110 °C) for 2 h. The reaction mixture was allowed to cool to room temperature, then diluted with Et_2O (150 mL) and washed with saturated $NaHCO_3$ (50 mL). The layers were separated and the organic layer was dried over $MgSO_4$. The solution was filtered and the solvent was removed in vacuo. The title compound[20] was purified by column chromatography on silica gel (0-2% EtOAc/hexanes) to yield a yellow oil contaminated with ~10% of an unidentified impurity (189 mg, 61% yield): IR 3086, 3062, 3031, 1596, 1494, 1453, 1124, 985, 756, 727, 690 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 2H), 7.48 – 7.38 (m, 6H), 7.37 – 7.29 (m, 5H), 7.28 – 7.23 (m, 2H), 6.85 (s, 1H), 4.23 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.5, 149.0, 138.5, 133.8, 130.8, 128.67, 128.65, 128.61, 128.4, 127.7, 127.2, 126.8, 126.4, 124.5, 123.6, 106.6, 33.0.; HRMS (ESI, TOF): Exact mass calcd for $C_{23}H_{17}O$ $[M–H]^+$, 309.1274; found, 309.1288.

SUPPORTING INFORMATION

Table of reaction optimization experiments and ^{1}H and ^{13}C NMR data for products **5a**-**s**, **5x**, and **6**.

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