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Visible-Light-Induced Direct $S_0 \rightarrow T_n$ Transition of Benzophenone Promotes C(sp^3)–H Alkynylation of Ethers and Amides

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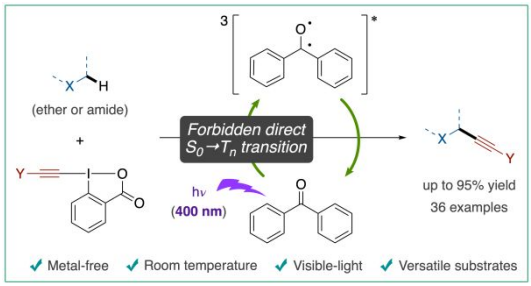
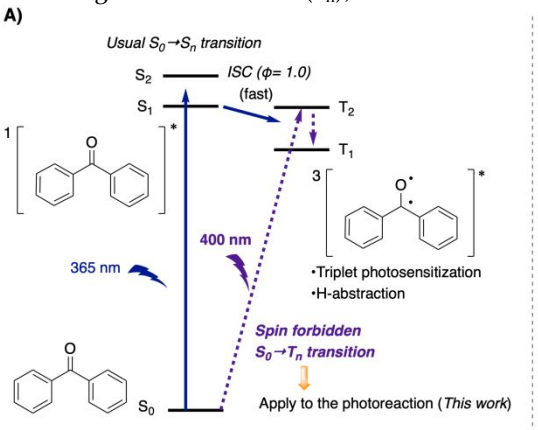
Supporting Information Placeholder



ABSTRACT: Benzophenone has an $S_0 \rightarrow S_1$ absorption band at 365 nm. However, the rarely reported $S_0 \rightarrow T_n$ transition occurs upon irradiation at longer wavelengths. Herein, we employed benzophenone as a catalyst and exploited its $S_0 \rightarrow T_n$ transition in C(sp^3)–H alkynylations with hypervalent iodine reagents. The selective benzophenone excitation prevented alkynylating reagent decomposition, enabling the reaction to proceed under mild conditions. The reaction mechanism was investigated by spectroscopic and computational studies.

INTRODUCTION

The efficient generation of the triplet excited state is imperative in organic photoreactions because such high energy intermediates initiate various photochemical events. The direct electronic transition from the ground state (S_0) to the triplet excited state (T_n) is regarded as a rarely occurring, forbidden transition. Therefore, the triplet excited state is generally accessed by intersystem crossing via a singlet excited state (S_n), such as in the $S_0 \rightarrow S_n \rightarrow S_1 \rightarrow T_1$ transition. We recently reported photoreactions of heavy-atom-containing molecules proceeding via the direct $S_0 \rightarrow T_n$ transition, as the forbidden nature of this transition can be relaxed by the internal heavy-atom effect.[1] Since the T_n energy level is lower than the corresponding S_n one, the $S_0 \rightarrow T_n$ absorption band is associated with longer wavelengths, enabling the mild and selective photoactivation of heavy-atom-containing molecules



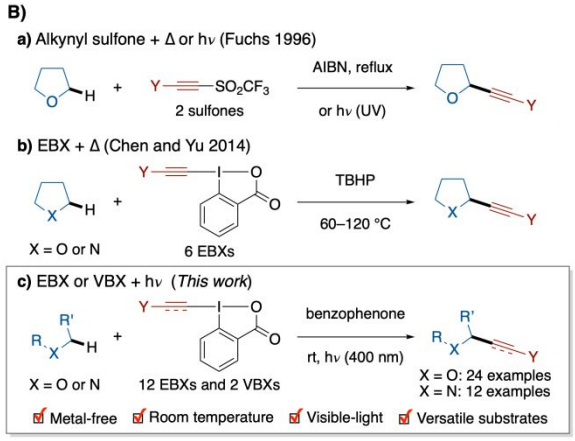


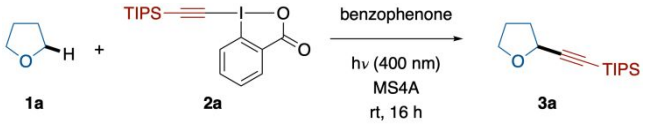
Figure 1. (A) Simplified Jablonski diagram of benzophenone and the envisioned application of the $S_0 \rightarrow T_n$ transition. (B) Reported C(sp^3)–H alkynylations. EBX = Ethynylbenziodoxolone. VBX = Vinyl benziodoxolone.

Benzophenone is an archetypal organic triplet-sensitizer. Generally, irradiation at 365 nm triggers its $S_0 \rightarrow S_1$ transition (n-π*).[2] Subsequently, a $S_1 \rightarrow T_1$ transition occurs via a highly efficient intersystem crossing (ISC, ϕ = 1), enabling benzophenone to promote photochemical reactions such as triplet-sensitization or hydrogen atom abstraction (**Figure 1A**). The $S_0 \rightarrow T_n$ absorption band (400 nm) of benzophenone was reported by Kearns et al. in 1966.[3] Although the use of compact fluorescent lamps in reactions involving benzophenones has been reported,[4] the mechanism of the $S_0 \rightarrow T_n$ transition remains elusive.

Alkynes are attractive building blocks in organic synthesis because of their stability and versatility.[5] The alkyne subunit is featured in pharmaceuticals and undergoes click reactions.[6,7] The biological and medicinal relevance of this functional group has driven the development of alkynylation methods.[8] Among those, cost- and atom-economic C(sp^3)–H alkynylations have attracted much attention.[9] Since the first report in 1996 (**Figure 1Ba**), diverse thermal and photochemical methods have been developed using alkynyl sulfones[9a,b] and bromides.[9c,d,h]. However, the cumbersome preparation[10] and limited applicability of such alkynylating reagents are important drawbacks.

Recently, ethynylbenziodoxolones (EBXs) have emerged as useful, bench-stable radical alkynylating reagents[11] that can be accessed via established synthetic methodologies.[12] In 2014, Chen and Yu developed C(sp^3)–H alkynylations using EBXs (**Figure 1Bb**).[9e] However, the substrate scope of EBXs and product yields are limited. Therefore, we considered whether the $S_0 \rightarrow T_n$ transition of benzophenone could enable mild and efficient alkynylations using EBXs (**Figure 1Bc**). As the $S_0 \rightarrow T_n$ absorption band of EBXs is expected up to 385 nm, the selective excitation of benzophenone is feasible at 400 nm. Herein, we report the C(sp^3)–H alkynylation of ethers and amides using EBX reagents by exploiting the direct $S_0 \rightarrow T_n$ transition of benzophenone.

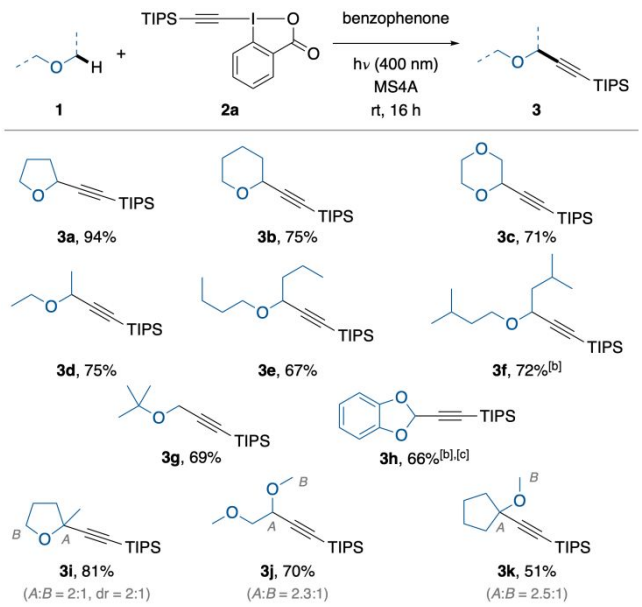
Table 1. Optimized conditions and control experiments.[a]



entry	variation from the standard conditions	yield of **3a** (%)[b]
1	none	96 (94)
2	no hν (400 nm)	0
3	no benzophenone	0
4	no MS4A	29–90
5	hν (365 nm)	66
6	hν (365 nm), no benzophenone	0

[a]Reaction conditions: **1a** (1.0 mL), **2a** (0.05 mmol, 1.0 equiv.), benzophenone (20 mol%), hν (400 nm), MS4A (5.0 mg), rt, 16 h. [b]Calculated by ^{1}H NMR with an internal standard. Yield in parenthesis represents isolated yield on the 0.20 mmol scale of **2a**.

Scheme 1. Substrate scope of ethers.[a]



[a]Reaction conditions: **1** (4.0 mL), **2a** (0.20 mmol, 1.0 equiv.), benzophenone (20 mol%), hν (400 nm), MS4A (20 mg), rt, 16 h. Isolated yields. [b]**1** (10.0 equiv.), benzophenone (50 mol%), MeCN (2.0 mL) were employed. [c]32 h.

RESULTS AND DISCUSSION

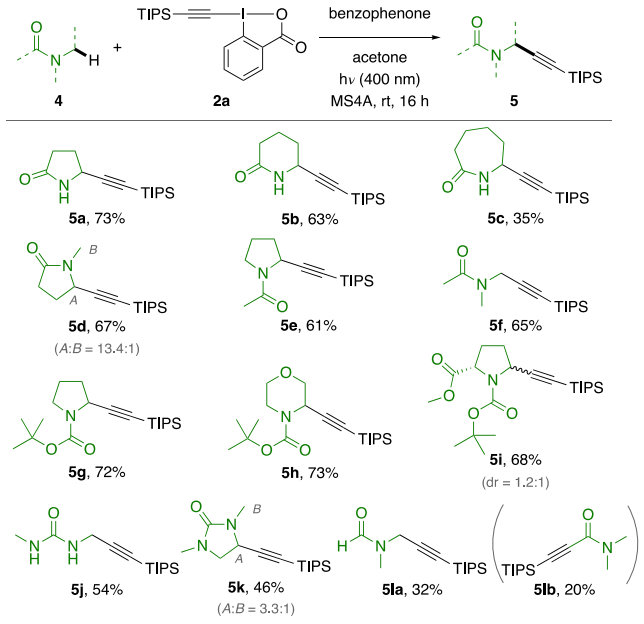
We first investigated the alkynylation of THF **1a** using TIPS-EBX **2a** in the presence of catalytic amounts of benzophenone under irradiation at 400 nm. Upon optimization of the reaction conditions, the desired alkynylated product **3a** was obtained in 96% yield (**Table 1**, entry 1). In the absence of irradiation or benzophenone (entries 2 and 3, respectively), **3a** was not obtained, indicating that the benzophenone excitation is essential to reactivity. The use of MS4A ensured result reproducibility to suppress the formation of side products of iodotriisopropylsilylacetylene and benzoic acid, presumably derived from the reduction of TIPS-EBX **2a** (entry 4). As expected, irradiation at 365 nm led to a decrease in the yield of **3a** to 66% in the presence of benzophenone, and no product was formed in its absence (entries 5 and 6, respectively) because of the direct $S_0 \rightarrow T_n$ transition and subsequent decomposition of **2a**. Hence, the direct $S_0 \rightarrow T_n$ transition of benzophenone induced by light at 400 nm is crucial to the high yield of the product.

Next, we investigated the generality of the reaction regarding different ethers (**Scheme 1**). Alkynylation of

cyclic (**3b**,**c**) and acyclic (**3d–f**) ethers proceeded in good yields. A primary ether (**3g**) and benzodioxole (**3h**) were also competent substrates. Ethers bearing distinct reaction sites afforded product mixtures (**3i–k**). The moderate selectivity correlates with the relative stabilities of the carbon-centered radical intermediates.

Moreover, amides were suitable substrates in this transformation (**Scheme 2**). Using acetone as the solvent, 5-, 6- and 7-membered lactams were alkynylated (**5a–d**). Additionally, various amides (**5e**,**f**), carbamates (**5g–i**), and ureas (**5j**,**k**) were efficiently alkynylated. Analogously to the ether substrates, secondary C(sp^3)–H bonds were more reactive than primary ones (**5d**,**k**). Alkynylated dimethylformamide **5la** was obtained in 32% yield along with 20% of **5lb** resulting from formyl alkynylation. Although excess amounts of the amides were required, up to 94% of the unreacted substrates were recovered.

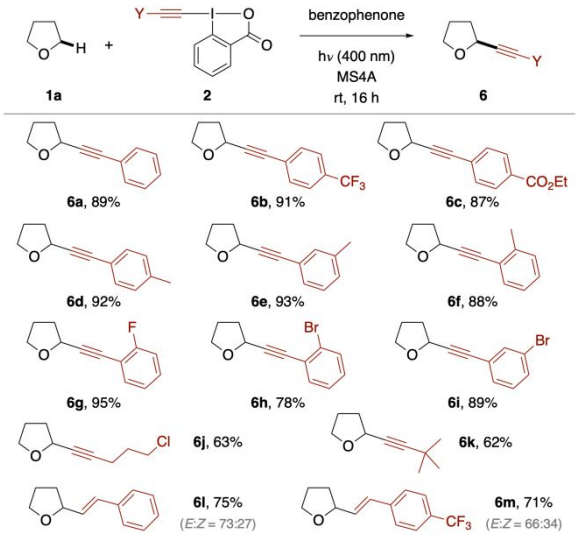
Scheme 2. Substrate scope of amides.[a]



[a]Reaction conditions: **4** (20.0 equiv.), **2a** (0.20 mmol, 1.0 equiv.), benzophenone (50 mol%), acetone (0.50 mL), hν (400 nm), MS4A (20 mg), rt, 16 h. Isolated yields.

Furthermore, diverse EBX reagents were employed, demonstrating the advantages of this methodology (**Scheme 3**). Phenyl-EBX delivered the alkynylated product in high yield (**6a**). The presence of trifluoromethyl (**6b**), ester (**6c**), and methyl groups (**6d–f**) or halides (**6g–i**) at any position of the phenyl ring did not affect the reactivity. In particular, brominated products **6h**,**i** were obtained in good yields despite the photolabile character of the C(sp^2)–Br bonds. Alkyl-substituted EBX reagents afforded the desired alkyne-containing **6j**,**k**, and notably, this protocol can be applied to aryl vinyl benziodoxolone (Ar-VBX)[13] to afford the corresponding styrene derivatives (**6l**,**m**).

Scheme 3. Scope of EBX reagents.[a]



[a]Reaction conditions: **1a** (4.0 mL), **2** (0.20 mmol, 1.0 equiv.), benzophenone (20 mol%), hν (400 nm), MS4A (20 mg), rt, 16 h. Isolated yields are given.

Next, spectroscopic and computational studies were performed to investigate the reaction mechanism. The absorption of a 2.0 mM THF solution of TIPS-EBX was observed up to 340 nm using a 1-cm cell, and up to 370 nm when a 10-cm cell was used (**Figure 2A**). The very weak absorption between 340–370 nm indicates a direct $S_o \rightarrow T_n$ transition of TIPS-EBX[1], this explaining the decrease in the yield of **3a** when a 365 nm source was used (**Table 1**, entries 4–5). In contrast, the well-known $S_o \rightarrow S_1$ absorption (n- π^* transition) of benzophenone occurred until 385 nm, and the very weak absorption observed between 390–420 nm corresponds to the $S_o \rightarrow T_n$ transition (**Figure 2B**). We next measured the absorption of a similar sample under experimental conditions (**Figure 2B**, purple line). In the presence of TIPS-EBX **2a**, no significant change was observed in the absorption, indicating that TIPS-EBX **2a** and benzophenone did not form a complex, and there would be no effective external heavy atom effect by the coordination of TIPS-EBX **2a** with benzophenone.[14] The absorption coefficient of benzophenone at 400 nm was 0.0442 $M^{-1}cm^{-1}$. Although this value was much smaller than that of heavy-atom-containing molecules, it suffices for the selective excitation of benzophenone. We then measured the phosphorescence excitation to show that the $S_o \rightarrow T_n$ absorption band occurs in the 390-420 nm region (**Figure 2C**). Using a degassed 2:1:1 mixed solution of diethyl ether, ethanol, and toluene (EET) as a glassing solvent system, phosphorescence was measured by cooling the sample to 77 K with liquid nitrogen. As a result, phosphorescence with maxima at 413, 421, 476, and 516 nm was observed through $S_o \rightarrow S_1 \rightarrow T_1$ transitions when excited with 350 nm light (green line). A phosphorescence excitation band was observed between 390 and 420 nm, with a small maximum at 405 nm (orange broken line). Furthermore, phosphorescence with the same waveform as the 350 nm excitation was observed for the 405-nm excitation (red line). The 405-nm excitation band and the 413-nm phosphorescence band overlap, indicating that

they are the 0-0 $S_0 \rightarrow T_1$ and $T_1 \rightarrow S_0$ bands. Based on these results, we conclude that the observed small absorption at 390-420 nm corresponds to the $S_0 \rightarrow T_1$ absorption band.

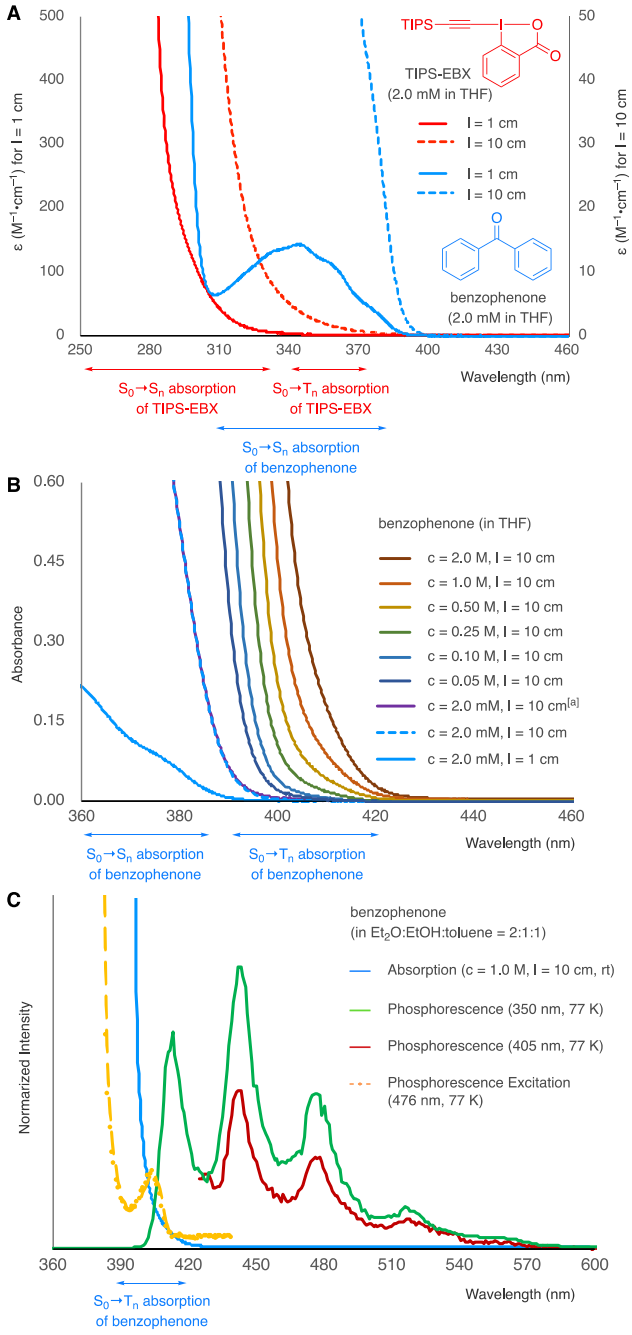


Figure 2. (**A**) Absorption spectra of TIPS-EBX **2a** and benzophenone. (**B**) Absorption spectra of benzophenone at various concentrations. [a]1:1 mixture of TIPS-EBX **2a** and benzophenone. (**C**) Absorption and emission properties of benzophenone; the vertical axis is normalized.

Further DFT calculations were performed using the Gaussian 16 package (**Figure 3**). Based on our benchmark study,[15] the MN15[16] functional with LanL2DZ[17] (for I) and cc-pVDZ[18] (for the other atoms) basis sets were used with the SMD solvation model[19] in THF. According to the calculations, the reaction would start with the benzophenone triplet state excitation upon irradiation at 400 nm. The energy of the triplet state (**INT1**) was 66.0 kcal/mol higher than that of the ground state (**SM**). Next, electrophilic oxy radical **INT1** would abstract the electron-rich hydrogen atom adjacent to the ether functional group of **1a** to afford the THF and ketyl radicals (**INT2a** and **b**, respectively, **Figure 3** inset) via the **TS1** with an activation energy of 9.2 kcal/mol. The subsequent addition of the generated THF radical to TIPS-EBX (**2a**) can occur at different positions.[20] The radical addition to the α-carbon is associated with an activation energy of 11.2 kcal/mol and directly delivers the alkynylated product **3a** (red line). The frequently proposed vinyl radical intermediate was not found as a local minimum, indicating that the α-addition mechanism would proceed in a quasi-concerted manner. Alternatively, the β-addition would require 15.2 kcal/mol activation energy (blue line) and lead to a vinyl radical intermediate (**INT3**), delivering **3a** upon migration of the silyl group. These results indicate that the α-addition is kinetically favored to the β-addition, consistently with the ^{13}C-isotopic experiments reported by Chen et al.[21] Finally, λ^2-iodanyl radical **INT4a** reacts with ketyl radical **INT2a** to give iodobenzoic acid and close the catalytic cycle by regenerating the benzophenone catalyst (ground state).

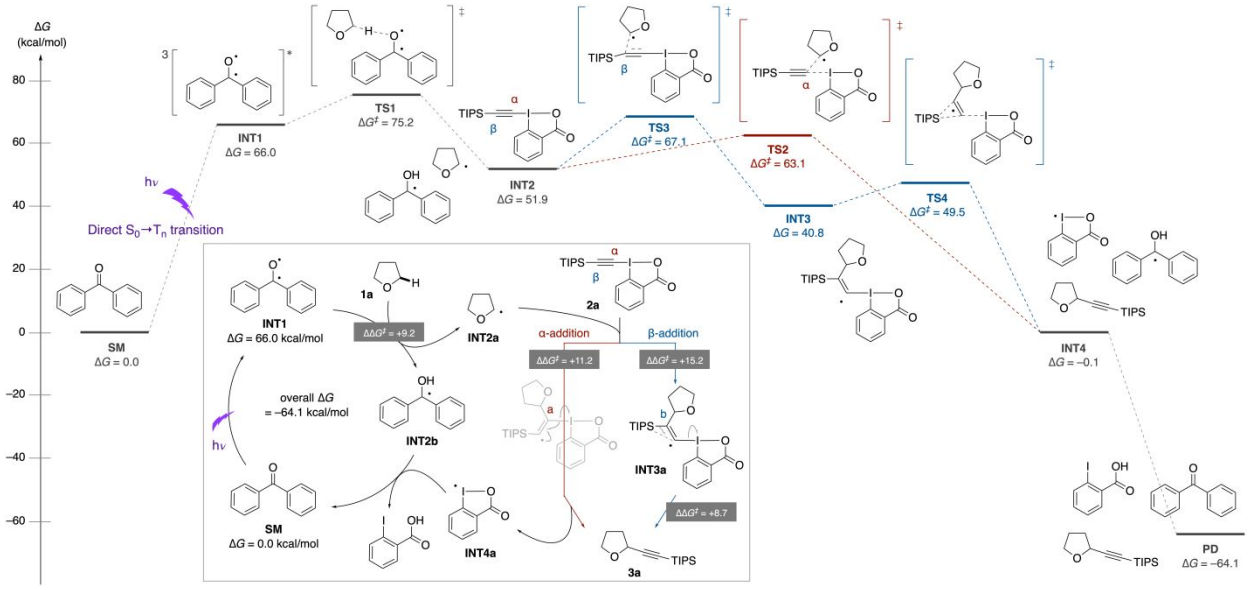


Figure 3. Energy diagram of the reaction according to DFT calculations and proposed reaction mechanism (inset).

Finally, the potential side reaction and the effect of MS4A were investigated. We hypothesized that the observed side products **7** and **8** were generated by the single-electron-transfer (SET) to TIPS-EBX **2a** and the following spontaneous decomposition of radical anion. To elucidate our hypothesis, we performed further DFT calculations (**Figure 4**). The energy barrier ($\Delta\Delta G^{\ddagger}$) of the SET process was estimated using Marcus theory.[22] As a result of calculations, SET proceeds from THF carbon-centered radical **INT2a** and the benzophenone ketyl radical **INT2b** by 21.0 and 25.2 kcal/mol respectively.[23] On the other hand, the coordination of H_2O to TIPS-EBX **2a** gave a lower energy barrier in SET process (18.7 kcal/mol), indicating that the presence of moisture facilitated the SET-induced side reaction. This result is consistent with the experimental result that the addition of MS4A improved the reproducibility and chemical yield (**Table 1**, entry 4). Regarding the decomposition of the TIPS-EBX radical anion **INT6**, the I-Ph bond was most likely to be cleaved, which would lead the observed side products **7** and **8**.[24]

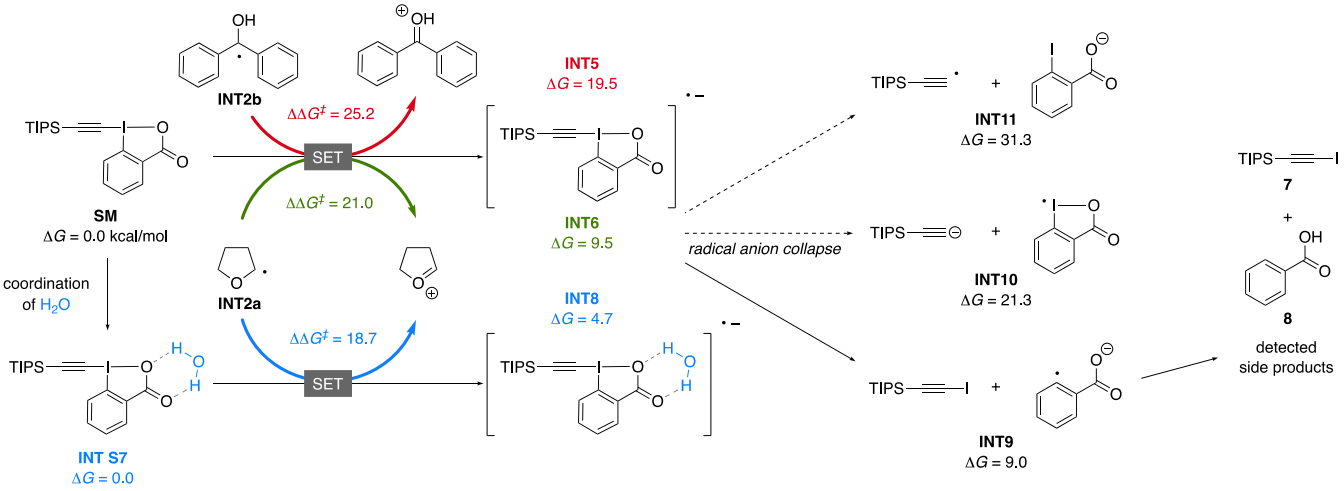


Figure 4. Calculated energy profiles for the SET-induced side reaction.

CONCLUSIONS

In conclusion, the direct $S_0 \rightarrow T_n$ transition of heavy-atom-free benzophenone rendered it a suitable catalyst in C(sp^3)–H alkynylations and alkenylations. Irradiation at 400 nm enabled the selective activation of benzophenone, resulting in efficient reaction of various substrates under mild conditions. Additionally, the proposed reaction mechanism was supported by spectroscopic and computational investigations. As the present protocol allows metal-free, atom-economic, and operationally simple alkynylations, we expect that it will find applications in the synthesis of valuable molecules or industrial use.

EXPERIMENTAL SECTION

General Information. All reactions were performed with dry solvents under argon atmosphere and the reagents were purified by the usual methods. The solvents were degassed by freeze-pump-thaw cycles using argon. Analytical thin layer chromatography was performed on Kieselgel 60F254, 0.25 mm thickness plates. Column chromatographic purification was performed with silica gel 60 N (spherical, neutral 63-210 mesh). Nuclear magnetic resonance (NMR) spectra were recorded on spectrometers of JEOL-JMN-ECS400, ECZ400, and ECZ600 operating at 400 or 600 MHz for ^{1}H NMR, 100 or 150 MHz for ^{13}C{^{1}H} NMR, and 376 MHz for ^{19}F NMR with calibration using residual undeuterated solvent as an internal reference. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), coupling constant (Hz), and integration. Data for ^{13}C{^{1}H} and ^{19}F NMR are reported in terms of chemical shift (δ ppm). Infrared spectra were recorded on JASCO FT/IR-4700. High-resolution mass spectra were measured on JEOL AccuTOF LC-plus JMS-T100LP (Ionization method: ESI or APCI). Melting points were measured with SIBATA NEL-270 melting point apparatus. Absorption spectra were recorded with JASCO V-730 spectrometer at room temperature under aerobic atmosphere.

General Procedure A: Alkynylation of Ether. The reaction vessel was charged with MS4A (20.0 mg) and flame dried under vaccum. After being cooled to room temperature and filled with argon, the reaction vessel was added TIPS-EBX **2a** (85.7 mg, 0.20 mmol, 1.0 equiv.), benzophenone (7.3 mg, 0.040 mmol, 20 mol%), and ether substrate **1** (4.0 mL). The resulting solution was stirred at room temperature for 16 h under the light-irradiation with a 400 nm LED. After removal of solvent in *vacuo*, the crude residue was purified by flash column chromatography to afford the alkynylated product **3**.

General Procedure B: Alkynylation of Ether (1f and 1h). The reaction vessel was charged with MS4A (20.0 mg) and flame dried under vaccum. After being cooled to room temperature and filled with argon, the reaction vessel was added TIPS-EBX **2a** (85.7 mg, 0.20 mmol, 1.0 equiv.), benzophenone (18.2 mg, 0.10 mmol, 50 mol%), ether substrate **1f** or **1h** (2.0 mmol, 10.0 equiv.), and MeCN (2.0 mL). The resulting solution was stirred at room temperature for 16 or 32 h under the light-irradiation with a 400 nm LED. After removal of solvent in *vacuo*, the crude residue was purified by flash column chromatography to afford the alkynylated product **3**.

General Procedure C: Alkynylation of Amide. The reaction vessel was charged with MS4A (20.0 mg) and flame dried under vaccum. After being cooled to room temperature and filled with argon, the reaction vessel was added TIPS-EBX **2a** (85.7 mg, 0.20 mmol, 1.0 equiv.), benzophenone (18.2 mg, 0.10 mmol, 50 mol%), amide substrate **4** (4.0 mmol, 20.0 equiv.), and acetone (0.50 mL). The resulting solution was stirred at room temperature for 16 h under the light-irradiation with a 400 nm LED. After removal of solvent in *vacuo*, the crude residue was purified by flash column chromatography to afford the alkynylated product **5**.

General Procedure D: Various Alkynylation and Alkenylation. The reaction vessel was charged with MS4A (20.0 mg) and flame dried under vaccum. After being cooled to room temperature and filled with argon, the reaction vessel was added EBX or VBX reagent **2** (0.20 mmol, 1.0 equiv.), benzophenone (7.3 mg, 0.040 mmol, 20 mol%), and THF **1a** (4.0 mL). The resulting solution was stirred at room temperature for 16 h under the light-irradiation with a 400 nm LED. After removal of solvent in *vacuo*, the crude residue was purified by flash column chromatography to afford the alkynylated product **6**.

Larger Scale Experiment. The reaction vessel was charged with MS4A (100.0 mg) and flame dried under vaccum. After being cooled to room temperature and filled with argon, the reaction vessel was added TIPS-EBX **2a** (428.4 mg, 1.0 mmol, 1.0 equiv.), benzophenone (36.4 mg, 0.20 mmol, 20 mol%), and THF **1a** (20.0 mL). The resulting solution was stirred at room temperature for 16 h under the light-irradiation with a 400 nm LED. After removal of solvent in *vacuo*, the crude residue was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford the alkynylated product **3a** (231.5 mg, 0.92 mmol) in 92% yield as a colorless oil.

Triisopropyl((tetrahydrofuran-2-yl)ethynyl)silane (**3a**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3a** (47.4 mg, 0.188 mmol) in 94% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.62 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.99–3.93 (m, 1H), 3.85–3.80 (m, 1H), 2.18–1.85 (m, 4H), 1.10–0.98 (m, 21H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 107.7, 85.0, 68.5, 67.6, 33.7, 25.1, 18.6, 11.1; IR (ATR) ν: 2942, 2865, 2168, 1462, 1328, 1173, 1053, 995, 919, 881 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{15}H_{29}OSi$ $[M+H]^+$ 253.1988, found 253.1993.

Triisopropyl((tetrahydropyran-2-yl)ethynyl)silane (**3b**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3b** (39.8 mg, 0.149 mmol) in 75% yield as a colorless oil. ^{1}H NMR (400 MHz, CDCl3) δ: 4.41 (dd, *J* = 6.4, 3.2 Hz, 1H), 4.04–3.99 (m, 1H), 3.59–3.54 (m, 1H), 1.90–1.83 (m, 2H), 1.75–1.66 (m, 1H), 1.62–1.53 (m, 3H), 1.11–0.96 (m, 21H); ^{13}C{1H} NMR (100 MHz, CDCl3) δ: 106.4, 86.2, 67.0, 65.6, 32.1, 25.7, 21.1, 18.6, 11.1; IR (ATR) ν: 2941, 2864, 2168, 1463, 1357, 1333, 1196, 1085, 1039, 882 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{16}H_{31}OSi$ $[M+H]^+$ 267.2144, found 267.2142.

((1,4-Dioxan-2-yl)ethynyl)triisopropylsilane (**3c**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3c** (38.1 mg, 0.142 mmol) in 71% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.38 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.94–3.88 (m, 1H), 3.85 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.71–3.64 (m, 3H), 3.60 (dd, *J* = 11.6, 8.4 Hz, 1H), 1.11–0.96 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 102.5, 87.9, 70.5, 66.5, 66.3, 65.6, 18.5, 11.0; IR (ATR) ν: 2943, 2865, 2176, 1463, 1335, 1257, 1119, 1099, 980, 874 cm^{-1};

HRMS (APCI) *m/z*: calcd for $C_{15}H_{28}NaO_2Si$ $[M+H]^+$ 291.1756, found 291.1755.

(3-Ethoxybut-1-yn-1-yl)triisopropylsilane (**3d**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3d** (38.0 mg, 0.149 mmol) in 75% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.19 (q, *J* = 6.4 Hz, 1H), 3.86–3.79 (m, 1H), 3.49–3.41 (m, 1H), 1.44 (d, *J* = 6.4 Hz, 3H), 1.23 (dd, *J* = 6.8, 6,8 Hz, 3H), 1.10–0.97 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 108.0, 85.0, 65.4, 63.9, 22.4, 18.6, 15.2, 11.1; IR (ATR) ν: 2943, 2866, 2166, 1463, 1367, 1226, 1151, 1111, 882 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{15}H_{31}OSi$ $[M+H]^+$ 255.2144, found 255.2146.

(3-Butoxyhex-1-yn-1-yl)triisopropylsilane (**3e**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3e** (41.6 mg, 0.134 mmol) in 67% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.03 (t, *J* = 6.8 Hz, 1H), 3.79–3.74 (m, 1H), 3.41–3.36 (m, 1H), 1.75–1.64 (m, 2H), 1.61–1.46 (m, 4H), 1.43–1.33 (m, 2H), 1.10–0.98 (m, 21H), 0.93 (t, *J* = 7.6 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}NMRNMR (100 MHz, $CDCl_3$) δ: 107.4, 85.6, 69.8, 68.4, 38.0, 31.7, 19.4, 18.7, 18.6, 13.9, 13.8, 11.1; IR (ATR) ν: 2941, 2866, 2166, 1463, 1382, 1330, 1092, 996, 882 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{19}H_{39}OSi$ $[M+H]^+$ 311.2770, found 311.2764.

(3-(Isopentyloxy)-5-methylhex-1-yn-1-yl)triisopropylsilane (**3f**). Following the general procedure B, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3f** (48.4 mg, 0.143 mmol) in 72% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.07 (t, *J* = 7.2 Hz, 1H), 3.81 (dt, *J* = 9.2, 6.8 Hz, 1H), 3.39 (dt, *J* = 9.2, 6.8 Hz, 1H), 1.93–1.83 (m, 1H), 1.76–1.62 (m, 2H), 1.58–1.45 (m, 3H), 1.10–0.98 (m, 21H), 0.93–0.89 (m, 12H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 107.5, 85.7, 68.6, 67.0, 44.8, 38.5 25.1, 24.8, 22.61, 22.57, 22.5, 18.6, 11.2 (One carbon was not fully resolved.); IR (ATR) ν: 2955, 2866, 2165, 1464, 1385, 1366, 1092, 882 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{21}H_{43}OSi$ $[M+H]^+$ 339.3083, found 339.3086.

(3-(tert-Butoxy)prop-1-yn-1-yl)triisopropylsilane (**3g**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3g** (37.1 mg, 0.138 mmol) in 69% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.15 (s, 2H), 1.25 (s, 9H), 1.09–1.01 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 106.2, 85.3, 74.6, 51.2, 27.8, 18.6, 11.2; IR (ATR) ν: 2942, 2866, 2172, 1463, 1365, 1245, 1191, 1066, 882 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{16}H_{33}OSi$ $[M+H]^+$ 269.2301, found 269.2306.

(Benzo[d][1,3]dioxol-2-ylethynyl)triisopropylsilane (**3h**). Following the general procedure B, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3h** (39.9 mg, 0.132 mmol) in 66% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.85 (s, 4H), 6.58 (s, 1H), 1.12–1.02 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 146.7, 121.8, 108.9, 99.6, 98.1, 90.8, 18.4, 10.9; IR (ATR) ν: 2944, 2866, 2174, 1481, 1385, 1340, 1226, 1063, 881, 734 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{18}H_{27}O_2Si$ $[M+H]^+$ 303.1780, found 303.1782.

Triisopropyl((2-methyltetrahydrofuran-2-yl)ethynyl)silane (**3ia**), *trans-Triisopropyl((5-methyltetrahydrofuran-2-yl)ethynyl)silane* (**3ib**), *cis-Triisopropyl((5-methyltetrahydrofuran-2-yl)ethynyl)silane* (**3ic**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford inseparable mixture of **3ia**, **3ib**, and **3ic** (43.2 mg, 0.162 mmol) in 81% yield as a colorless oil.; inseparable mixture (**3ia**:**3ib**:**3ic** = 6:2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.72 (dd, *J* = 7.2, 4.4 Hz, 0.22H [**3ib**, 1H]), 4.57 (dd, *J* = 7.6, 4.4 Hz, 0.11H [**3ic**, 1H]), 4.28–4.20 (m, 0.22H [**3ib**, 1H]), 4.07–4.01 (m, 0.11H [**3ic**, 1H]), 4.00–3.91 (m, 1.34H [**3ia**, 2H]), 2.24–1.90 (m, 3H), 1.79–1.72 (m, 0.67H [**3ia**, 1H]), 1.58 (s, 2.01H [**3ia**, 3H]), 1.48–1.40 (m, 0.33H [**3ib**, 1H]+[**3ic**, 1H]), 1.32 (d, *J* = 6.0 Hz, 0.33H [**3ic**, 3H]), 1.32 (d, *J* = 6.4 Hz, 0.66H [**3ib**, 3H]), 1.06–1.00 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 111.0, 108.7, 108.3, 84.7, 84.6, 82.7, 76.33, 76.26, 74.7, 68.42, 68.39, 67.3, 40.3, 34.3, 34.0, 32.9, 32.6, 27.3, 25.4, 21.8, 20.9, 18.6, 11.1 (Four carbons were not fully resolved.); IR (ATR) ν: 2942, 2865, 2168, 1463, 1383, 1368, 1244, 1074, 996, 882 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{16}H_{31}OSi$ $[M+H]^+$ 267.2144, found 267.2135.

(3,4-Dimethoxybut-1-yn-1-yl)triisopropylsilane (**3ja**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3ja** (26.5 mg, 0.098 mmol) in 49% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.23 (dd, *J* = 8.0, 3.6 Hz, 1H), 3.62–3.54 (m, 2H), 3.48 (s, 3H), 3.42 (s, 3H), 1.08–0.99 (m, 21H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ: 103.0, 88.1, 75.0, 71.0, 59.2, 56.5, 18.5, 11.1; IR (ATR) ν: 2942, 2866, 2171, 1463, 1200, 1105, 997, 883 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{15}H_{30}NaO_2Si$ $[M+Na]^+$ 293.1913, found 293.1915.

Triisopropyl(3-(2-methoxyethoxy)prop-1-yn-1-yl)silane (**3jb**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **3jb** (11.5 mg, 0.043 mmol) in 21% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.26 (s, 2H), 3.73–3.71 (m, 2H), 3.60–3.57 (m, 2H), 3.40 (s, 3H), 1.09–0.98 (m, 21H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ: 103.1, 87.7, 71.7, 68.5, 59.2, 59.0, 18.5, 11.1; IR (ATR) ν: 2926, 2866, 2170, 1463, 1382, 1272, 1105, 883 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{15}H_{30}NaOSi$ $[M+Na]^+$ 293.1913, found 293.1911.

Triisopropyl((1-methoxycyclopentyl)ethynyl)silane (**3ka**), *(3-(Cyclopentyloxy)prop-1-yn-1-yl)triisopropylsilane* (**3kb**). Following the general procedure A, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 80/1) to afford inseparable mixture of **3ka** and **3kb** (28.4 mg, 0.101 mmol) in 51% yield as a colorless oil.; inseparable mixture (**3ka**:**3kb** = 2.5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.23–4.18 (m, 0.28H [**3kb**, 1H]), 4.16 (s, 0.56H [**3kb**, 2H]), 3.36 (s, 2.16H [**3ka**, 3H]), 2.01–1.88 (m, 3H), 1.78–1.65 (m, 5H), 1.11–0.99 (m, 21H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 109.1, 104.2, 86.6, 85.3, 81.1, 80.3, 56.7, 52.2,

39.4, 32.1, 23.5, 23.3, 18.6, 11.6 (Six carbons were not fully resolved.); IR (ATR) ν: 2942, 2865, 2162, 2463, 1383, 1073, 995, 881, 758 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{17}H_{32}NaOSi$ $[M+Na]^+$ 303.2120, found 303.2120.

5-((Triisopropylsilyl)ethynyl)pyrrolidin-2-one (**5a**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 2/1) to afford **5a** (38.5 mg, 0.145 mmol) in 73% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 5.71 (brs, 1H), 4.40 (dd, *J* = 7.6, 4.8 Hz, 1H), 2.52–2.44 (m, 2H), 2.37–2.27 (m, 1H), 2.24–2.16 (m, 1H), 1.10–0.97 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 177.6, 106.4, 85.0, 45.4, 29.5, 29.4, 18.5, 11.0; IR (ATR) ν: 3251, 2942, 2865, 2170, 1796, 1462, 1328, 1235, 996, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{15}H_{27}NNaOSi$ $[M+Na]^+$ 288.1760, found 288.1761.

6-((Triisopropylsilyl)ethynyl)piperidin-2-one (**5b**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 1/1) to afford **5b** (35.0 mg, 0.125 mmol) in 63% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 6.01 (brs, 1H), 4.32–4.29 (m, 1H), 2.45–2.31 (m, 2H), 2.10–2.00 (m, 2H), 1.94–1.73 (m, 2H), 1.09–0.97 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, CDCl3) δ: 171.2, 106.3, 84.6, 45.2, 31.1, 29.3, 19.0, 18.5, 11.0; IR (ATR) ν: 3210, 2942, 2865, 2172, 1667, 1463, 1384, 1329, 1077, 996, 882 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{30}NOSi$ $[M+H]^+$ 280.2097, found 280.2096.

7-((Triisopropylsilyl)ethynyl)azepan-2-one (**5c**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 3/1) to afford **5a** (20.6 mg, 0.070 mmol) in 35% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 6.04 (brs, 1H), 4.28–4.24 (m, 1H), 2.73–2.67 (m, 1H), 2.47–2.40 (m, 1H), 2.11–2.05 (m, 1H), 1.99–1.85 (m, 2H), 1.78–1.66 (m, 3H), 1.10–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 177.6, 105.2, 85.9, 45.7, 36.8, 36.2, 27.7, 22.9, 18.5, 11.0; IR (ATR) ν: 3223, 2941, 2865, 2167, 1660, 1463, 1384, 1202, 997, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{17}H_{32}NOSi$ $[M+H]^+$ 294.2253, found 294.2248.

1-Methyl-5-((triisopropylsilyl)ethynyl)pyrrolidin-2-one (**5da**), *1-(3-(Triisopropylsilyl)prop-2-yn-1-yl)pyrrolidin-2-one* (**5db**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 1/1) to afford inseparable mixture of **5da** and **5db** (37.3 mg, 0.133 mmol) in 67% yield as a colorless oil.; inseparable mixture (**5da**:**5db** = 13.4:1). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.28 (dd, *J* = 7.6, 5.2 Hz, 0.93H [**5da**, 1H]), 4.16 (s, 0.14H [**5db**, 2H]), 3.51 (t, *J* = 7.2 Hz, 0.14H [**5db**, 2H]), 2.89 (s, 2.79H [**5da**, 3H]), 2.55–2.45 (m, 1H), 2.41–2.32 (m, 2H), 2.13–2.03 (m, 1H), 1.10–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 174.3, 104.8, 86.4, 51.8, 29.7, 27.8, 26.4, 18.5, 11.0 (Carbons of **5db** were not resolved.); IR (ATR) ν: 2943, 2865, 2173, 1676, 1462, 1385, 1264, 1118, 996, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{30}NOSi$ $[M+H]^+$ 280.2097, found 280.2101.

1-(2-((Triisopropylsilyl)ethynyl)pyrrolidin-1-yl)ethan-1-one (**5e**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 2/1) to afford **5e** (35.9 mg, 0.122 mmol) in 61% yield as a colorless oil.; 4.6:1 mixture of rotamers; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.81 (dd, *J* = 8.0, 2.0 Hz, 0.18H), 4.47 (dd, *J* = 6.8, 2.8 Hz, 0.82H), 3.66–3.56 (m, 1H), 3.44–3.35 (m, 1H), 2.27–1.91 (m, 7H), 1.08–0.96 (m, 21H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ: 169.6, 168.4, 107.6, 106.6, 84.5, 82.1, 49.9, 48.0, 46.7, 45.5, 34.7, 32.9, 29.7, 24.7, 23.3, 22.4, 18.6, 18.5, 11.1, 11.0; IR (ATR) ν: 2942, 2865, 2168, 1652, 1408, 1353, 996, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{17}H_{32}NOSi$ $[M+H]^+$ 294.2253, found 294.2251.

N-Methyl-N-(3-(triisopropylsilyl)prop-2-yn-1-yl)acetamide (**5f**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 4/1) to afford **5f** (34.9 mg, 0.130 mmol) in 65% yield as a colorless oil.; 1.3:1 mixture of rotamers; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.30 (s, 1.13H), 4.07 (s, 0.87H), 3.09 (s, 1.7H), 3.00 (s, 1.3H), 2.17 (s, 1.3H), 2.11 (s, 1.7H), 1.08–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, CDCl3) δ: 170.5, 170.1, 102.2, 101.2, 86.0, 85.0, 41.3, 36.7, 34.7, 33.1, 21.7, 21.4, 18.52, 18.49, 11.1, 11.0; IR (ATR) ν: 2942, 2865, 2173, 1654, 1463, 1396, 1240, 1024, 882 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{15}H_{29}NNaOSi$ $[M+Na]^+$ 290.1916, found 290.1925.

tert-Butyl 2-((triisopropylsilyl)ethynyl)pyrrolidine-1-carboxylate (**5g**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 8/1) to afford **5g** (50.4 mg, 0.143 mmol) in 72% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 4.46 (brs, 1H), 3.49–3.44 (m, 1H), 3.34–3.28 (m, 1H), 2.12–1.97 (m, 3H), 1.92–1.84 (m, 1H), 1.47 (s, 9H), 1.09–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ: 154.0, 108.7, 81.7, 79.5, 48.9, 45.4, 34.2, 28.5, 23.7, 18.6, 11.3; IR (ATR) ν: 2942, 2866, 2166, 1703, 1463, 1390, 1365, 1169, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{20}H_{37}NNaO_2Si$ $[M+Na]^+$ 374.2491, found 374.2497.

tert-Butyl 3-((triisopropylsilyl)ethynyl)morpholine-4-carboxylate (**5h**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 20/1) to afford **5h** (54.0 mg, 0.147 mmol) in 73% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 4.69 (brs, 1H), 3.92–3.89 (m, 2H), 3.69–3.66 (brd, 1H), 3.59 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.45 (ddd, *J* = 12.0, 11.6, 2.4 Hz, 1H), 3.32–3.26 (brdd, 1H), 1.47 (s, 9H), 1.10–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 154.7, 104.3, 84.4, 80.5, 69.9, 66.7, 45.4, 40.2, 28.2, 18.6, 11.1; IR (ATR) ν: 2942, 2864, 2170, 1704, 1461, 1381, 1365, 1168, 1125, 883 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{20}H_{37}NNaO_3Si$ $[M+Na]^+$ 390.2440, found 390.2434.

1-(tert-Butyl) 2-methyl (2S)-5-((triisopropylsilyl)ethynyl)pyrrolidine-1,2-dicarboxylate (**5i**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 20/1) to afford **5i** (56.0 mg, 0.137 mmol) in 68% yield as a colorless oil.; 1.2:1 mixture of diastereomers, 2:1 mixture of rotamers for the major diastereomer, 1.2:1 mixture of rotamers for the minor diastereomer; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.71 (d, *J* = 7.6 Hz, 0.18H), 4.64–4.62 (m, 0.36+0.21H), 4.54–4.52 (m,

0.25H), 4.40 (d, *J* = 8.4 Hz, 0.36H), 4.32–4.27 (m, 0.25+0.18H), 4.21–4.17 (m, 0.21H), 3.75–3.72 (m, 3H), 2.54–1.94 (m, 4H), 1.48 (s, 5.59H), 1.40 (s, 3.41H), 1.07–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 173.3, 173.0, 153.7, 107.9, 82.0, 80.4, 80.1, 59.9, 59.6, 58.5, 58.3, 52.2, 52.0, 49.5, 49.4, 33.4, 32.6, 32.4, 31.4, 29.9, 29.6, 28.9, 28.6, 28.3, 28.1, 28.0, 18.6, 18.5, 11.12, 11.08 (Some carbons were not fully resolved.); IR (ATR) ν: 2943, 2893, 2169, 1747, 1702, 1462, 1385, 1365, 1160, 882 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{22}H_{39}NNaO_4Si$ $[M+Na]^+$ 432.2546, found 432.2551.

1-Methyl-3-(3-(triisopropylsilyl)prop-2-yn-1-yl)urea (**5j**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 2/1) to afford **5j** (28.8 mg, 0.107 mmol) in 54% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 4.49 (brs, 2H), 4.02 (d, *J* = 5.2 Hz, 2H), 2.80 (d, *J* = 5.2 Hz, 3H), 1.10–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 158.6, 104.0, 84.2, 31.3, 27.1, 18.5, 11.1; IR (ATR) ν: 3330, 2942, 2865, 2175, 1634, 1574, 1463, 1254, 986, 882 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{14}H_{28}N_2NaOSi$ $[M+Na]^+$ 291.1869, found 291.1869.

1,3-Dimethyl-4-((triisopropylsilyl)ethynyl)imidazolidin-2-one (**5ka**), *1-Methyl-3-(3-(triisopropylsilyl)prop-2-yn-1-yl)imidazolidin-2-one* (**5kb**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 6/1) to afford inseparable mixture of **5ka** and **5kb** (27.0 mg, 0.092 mmol) in 46% yield as a colorless oil.; inseparable mixture (**5ka**:**5kb** = 3.3:1); ^1H NMR (400 MHz, $CDCl_3$) δ: 4.19 (dd, *J* = 8.8, 7.2 Hz, 0.77H [**5ka**, 1H]), 4.06 (s, 0.46H [**5kb**, 2H]), 3.54 (dd, *J* = 8.8, 8.4 Hz, 0.77H [**5ka**, 1H]), 3.42–3.38 (m, 0.46H [**5kb**, 2H]), 3.34–3.29 (m, 0.46H [**5kb**, 2H]), 3.25 (dd, *J* = 8.4, 7.2 Hz, 0.77H [**5ka**, 1H]), 2.84 (s, 2.31H [**5ka**, 3H]), 2.81 (s, 0.69H [**5kb**, 3H]), 2.80 (s, 2.31H [**5ka**, 3H]), 1.11–0.97 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 160.9, 160.6, 103.8, 101.8, 86.5, 85.1, 51.7, 47.7, 44.9, 41.9, 35.2, 31.3, 31.2, 29.3, 18.5, 11.1, 11.0 (One carbon was not fully resolved.); IR (ATR) ν: 2942, 2865, 2173, 1708, 1496, 1439, 1395, 1072, 996, 881 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{30}N_2NaOSi$ $[M+Na]^+$ 317.2025, found 317.2025.

N-Methyl-N-(3-(triisopropylsilyl)prop-2-yn-1-yl)formamide (**5la**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 8/1) to afford **5la** (16.2 mg, 0.064 mmol) in 32% yield as a colorless oil.; 1.2:1 mixture of rotamers; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.11 (s, 0.55H), 8.02 (s, 0.45H), 4.23 (s, 0.9H), 4.06 (s, 1.1H), 3.04 (s, 1.35H), 2.96 (s, 1.65H), 1.11–0.98 (m, 21H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 162.1, 161.9, 100.7, 100.3, 87.2, 85.7, 40.1, 34.0, 33.5, 29.3, 18.52, 18.50, 11.1, 11.0; IR (ATR) ν: 2942, 2865, 2175, 1676, 1463, 1384, 1248, 1068, 1011, 882 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{14}H_{28}NOSi$ $[M+H]^+$ 254.1940, found 254.1936.

N,N-Dimethyl-3-(triisopropylsilyl)propiolamide (**5lb**). Following the general procedure C, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1 to 8/1) to afford **5lb** (10.0 mg, 0.039 mmol) in 20% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.23 (s, 3H), 2.98 (s, 3H), 1.16–1.05 (m, 21H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ: 154.0, 98.2, 94.0, 38.3, 34.1, 18.5, 11.0; IR (ATR) ν: 2943, 2866, 2160, 1635, 1461, 1390, 1267, 1150, 881, 786 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{14}H_{28}NOSi$ $[M+H]^+$ 254.1940, found 254.1935.

2-(Phenylethynyl)tetrahydrofuran (**6a**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 50/1) to afford **6a** (30.6 mg, 0.178 mmol) in 89% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.41 (m, 2H), 7.31–7.28 (m, 3H), 4.81 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.04–3.99 (m, 1H), 3.89–3.83 (m, 1H), 2.29–2.19 (m, 1H), 2.15–2.04 (m, 2H), 1.99–1.90 (m, 1H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 131.7, 128.21, 128.17, 122.7, 89.0, 84.4, 68.6, 67.9, 33.4, 25.5; IR (ATR) ν: 2953, 2883, 2200, 1667, 1490, 1281, 1105, 1050, 920, 757 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{12}H_{13}O$ $[M+H]+$ 173.0966, found 173.0968.

2-((4-(Trifluoromethyl)phenyl)ethynyl)tetrahydrofuran (**6b**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 40/1) to afford **6b** (43.7 mg, 0.182 mmol) in 91% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.57–7.51 (m, 4H), 4.82 (dd, *J* = 7.2, 4.8 Hz, 1H), 4.04–3.99 (m, 1H), 3.90–3.85 (m, 1H), 2.29–2.23 (m, 1H), 2.14–2.05 (m, 2H), 2.01–1.93 (m, 1H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ: 131.9, 130.0 (q, *J* = 33.0 Hz), 126.6, 125.1 (q, *J* = 4.4 Hz), 123.9 (q, *J* = 270.0 Hz), 91.6, 83.1, 68.4, 68.1, 33.3, 25.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –62.8; IR (ATR) ν: 2953, 2874, 2232, 1714, 1614, 1319, 1122, 1051, 1016, 841 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{13}H_{12}F_3O$ $[M+H]^+$ 241.0840, found 241.0832.

Ethyl 4-((tetrahydrofuran-2-yl)ethynyl)benzoate (**6c**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 50/1 to 10/1) to afford **6c** (42.7 mg, 0.175 mmol) in 87% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 4.83 (dd, *J* = 7.6, 4.8 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.05–3.99 (m, 1H), 3.90–3.85 (m, 1H), 2.29–2.22 (m, 1H), 2.16–2.06 (m, 2H), 2.01–1.91 (m, 1H), 1.39 (t, *J* = 7.2 Hz, 3H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 166.0, 131.5, 129.9, 129.3, 127.4, 92.1, 83.8, 68.5, 68.0, 61.1, 33.3, 25.5, 14.3; IR (ATR) ν: 2981, 2874, 2224, 1712, 1605, 1363, 1269, 1105, 1050, 858, 768 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{15}H_{17}O_3$ $[M+H]^+$ 245.1178, found 245.1182.

2-(p-Tolylethynyl)tetrahydrofuran (**6d**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 50/1) to afford **6d** (34.1 mg, 0.183 mmol) in 92% yield as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.32 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.80 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.04–3.98 (m, 1H), 3.88–3.82 (m, 1H), 2.33 (s, 3H), 2.25–2.18 (m, 1H), 2.14–2.03 (m, 2H), 1.98–1.89 (m, 1H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ: 138.3, 131.6, 128.9, 119.7, 88.3, 84.5, 68.6, 67.9, 33.4, 25.5, 21.4; IR (ATR) ν: 2924, 2879, 2197, 1916, 1665, 1508, 1283, 1048, 920, 816 cm^{-1}; HRMS (APCI) *m/z*: calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1123, found 187.1128.

2-(m-Tolylethynyl)tetrahydrofuran (**6e**). Following the general procedure D, the crude product was purified by

flash column chromatography (*n*-hexane/EtOAc = 60/1) to afford **6e** (34.8 mg, 0.187 mmol) in 93% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.26 (s, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 4.80 (dd, *J* = 7.2, 4.8 Hz, 1H), 4.04–3.98 (m, 1H), 3.88–3.83 (m, 1H), 2.31 (s, 3H), 2.25–2.18 (m, 1H), 2.14–2.03 (m, 2H), 1.98–1.89 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 137.8, 132.3, 129.1, 128.7, 128.0, 122.5, 88.6, 84.6, 68.6, 67.9, 33.4, 25.4, 21.2; IR (ATR) ν: 2952, 2883, 2189, 1666, 1210, 1041, 913, 784, 688 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1123, found 187.1130.

2-(o-Tolylethynyl)tetrahydrofuran (**6f**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 50/1) to afford **6f** (32.6 mg, 0.175 mmol) in 88% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, *J* = 7.2 Hz, 1H), 7.22–7.17 (m, 2H), 7.11 (ddd, *J* = 8.0, 7.6, 2.0 Hz, 1H), 4.87 (dd, *J* = 6.8, 4.8 Hz, 1H), 4.05–4.00 (m, 1H), 3.90–3.85 (m, 1H), 2.42 (s, 3H), 2.30–2.18 (m, 1H), 2.15–2.05 (m, 2H), 2.00–1.91 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 140.2, 132.0, 129.3, 128.2, 125.4, 122.5, 93.0, 83.3, 68.7, 67.8, 33.6, 25.4, 20.6; IR (ATR) ν: 2952, 2881, 2196, 1667, 1485, 1121, 1052, 921, 759 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1123, found 187.1128.

2-((2-Fluorophenyl)ethynyl)tetrahydrofuran (**6g**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 80/1) to afford **6g** (36.0 mg, 0.189 mmol) in 95% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (ddd, *J* = 8.0, 7.2, 2.0 Hz, 1H), 7.31–7.26 (m, 1H), 7.10–7.03 (m, 2H), 4.85 (dd, *J* = 7.2, 4.8 Hz, 1H), 4.05–4.00 (m, 1H), 3.90–3.85 (m, 1H), 2.29–2.20 (m, 1H), 2.17–2.07 (m, 2H), 2.00–1.91 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 162.7 (d, *J* = 250.8 Hz), 133.6, 130.0 (d, *J* = 8.6 Hz), 123.8 (d, *J* = 2.9 Hz), 115.4 (d, *J* = 21.0 Hz), 111.3 (d, *J* = 15.3 Hz), 94.3 (d, *J* = 3.8 Hz), 77.8, 68.6, 68.0, 33.3, 25.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –110.0; IR (ATR) ν: 2955, 2890, 2206, 1670, 1491, 1449, 1262, 1050, 755 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{12}H_{12}FO$ $[M+H]^+$ 191.0872, found 191.0874.

2-((2-Bromophenyl)ethynyl)tetrahydrofuran (**6h**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 80/1) to afford **6h** (39.2 mg, 0.156 mmol) in 78% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.26–7.23 (m, 1H), 7.16 (ddd, *J* = 8.0, 7.6, 1.6 Hz, 1H), 4.88 (dd, *J* = 6.8, 5.2 Hz, 1H), 4.07–4.02 (m, 1H), 3.92–3.87 (m, 1H), 2.29–2.10 (m, 3H), 2.01–1.91 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 133.4, 132.3, 129.4, 126.9, 125.6, 124.9, 93.9, 83.0, 68.6, 67.9, 33.3, 25.3; IR (ATR) ν: 2954, 28889, 2204, 1711, 1670, 1469, 1319, 1046, 755 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{12}H_{12}{}^{79}BrO$ $[M+H]^+$ 251.0072, found 251.0078.

2-((3-Bromophenyl)ethynyl)tetrahydrofuran (**6i**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 60/1) to afford **6i** (44.9 mg, 0.179 mmol) in 89% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (dd, *J* = 2.0, 1.2 Hz, 1H), 7.44 (dd, *J* = 8.0, 2.0, 1.2 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.2, 1.2 Hz, 1H), 7.16 (dd, *J* = 8.0, 8.0 Hz, 1H), 4.80 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.03–3.98 (m, 1H), 3.90–3.84 (m, 1H), 2.29¬–2.18 (m, 1H), 2.15–2.03 (m, 2H), 2.00–1.91 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 134.4, 131.4, 130.2, 129.6, 124.7, 122.0, 90.5, 82.9, 68.4, 68.0, 33.3, 25.5; IR (ATR) ν: 2954, 2880, 2205, 1710, 1671, 1557, 1472, 1049, 878, 782 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{12}H_{12}{}^{79}BrO$ $[M+H]^+$ 251.0072, found 251.0077.

2-((4-(3-Chloropropyl)phenyl)ethynyl)tetrahydrofuran (**6j**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **6j** (21.6 mg, 0.125 mmol) in 63% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.56 (ddt, *J* = 7.2, 5.2, 1.6 Hz, 1H), 3.97–3.91 (m, 1H), 3.82–3.76 (m, 1H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.41 (td, *J* = 6.8, 1.6 Hz, 2H), 2.17–2.08 (m, 1H), 2.06–1.83 (m, 5H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 83.0, 81.0, 68.3, 67.7, 43.6, 33.5, 31.3, 25.4, 16.2; IR (ATR) ν: 2956, 2871, 2236, 1727, 1442, 1290, 1183, 1048, 908, 653 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_9H_{13}{}^{35}ClNaO$ $[M+Na]^+$ 195.0553, found 195.0554.

2-((4-(tert-Butyl)phenyl)ethynyl)tetrahydrofuran (**6k**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **6k** (18.9 mg, 0.124 mmol) in 62% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.54 (dd, *J* = 7.2, 6.0 Hz, 1H), 3.97–3.92 (m, 1H), 3.79–3.74 (m, 1H), 2.16–2.06 (m, 1H), 2.05–1.95 (m, 1H), 1.93–1.81 (m, 2H), 1.21 (s, 9H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 93.4, 78.1, 68.4, 67.5, 33.6, 31.0, 27.3, 25.3; IR (ATR) ν: 2968, 2868, 2237, 1457, 1362, 1264, 1204, 1050, 911 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{10}H_{16}NaO$ $[M+Na]^+$ 175.1099, found 175.1099.

2-Styryltetrahydrofuran (**6l**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **6l** (26.1 mg, 0.149 mmol) in 75% yield as a colorless oil.; isomeric mixture (*E*:*Z* = 73:27); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, *J* = 7.6 Hz, 1.46H [*E*, 2H]), 7.34–7.20 (m, 3.54H), 6.61–6.57 (m, 1H), 6.21 (dd, *J* = 15.6, 6.8 Hz, 0.73H [*E*, 1H]), 5.71 (dd, *J* = 11.6, 8.8 Hz, 0.27H [*Z*, 1H]), 4.66 (ddd, *J* = 8.8, 6.8, 6.8 Hz, 0.27H [*Z*, 1H]), 4.47 (ddd, *J* = 6.8, 6.4, 6.4 Hz, 0.73H [*E*, 1H]), 4.00–3.94 (m, 1H), 3.87–3.76 (m, 1H), 2.18–2.09 (m, 1H), 2.06–1.88 (m, 2H), 1.76–1.65 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 136.8, 136.7, 132.8, 131.5, 130.5, 130.4, 128.8, 128.5, 128.1, 127.5, 127.1, 126.4, 79.6, 75.0, 68.1, 68.0, 32.9, 32.4, 26.4, 25.9; IR (ATR) ν: 2947, 2874, 1688, 1608, 1449, 1173, 1047, 976, 690 cm^{-1}; HRMS (APCI) *m*/*z*: calcd for $C_{12}H_{15}O$ $[M+H]^+$ 175.1123, found 175.1117.

(E)-2-(4-(Trifluoromethyl)styryl)tetrahydrofuran (**6ma**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **6ma** (22.9 mg, 0.095 mmol) in 47% yield as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 6.62 (d, *J* = 15.6 Hz, 1H), 6.31 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.58 (ddd, *J* = 7.2, 6.8, 6.4 Hz, 1H), 4.01–3.96 (m, 1H), 3.89–3.83 (m, 1H), 2.20–2.12 (m, 1H), 2.05–1.93 (m, 2H), 1.77–1.68 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 140.3, 133.3, 129.4, 129.1, 128.8, 126.6, 125.5 (q, *J* = 3.8 Hz), 79.2, 68.3, 32.2, 25.9;

^{19}F NMR (376 MHz, $CDCl_3$) δ: –62.4; IR (ATR) ν: 2929, 2872, 1615, 1415, 1324, 1164, 1122, 1066, 859 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{14}F_3O$ $[M+H]^+$ 243.0997, found 243.0996.

(Z)-2-(4-(Trifluoromethyl)styryl)tetrahydrofuran (**6mb**). Following the general procedure D, the crude product was purified by flash column chromatography (*n*-hexane/EtOAc = 100/1) to afford **6mb** (11.6 mg, 0.048 mmol) in 24% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 6.61 (d, *J* = 11.6 Hz, 1H), 6.31 (dd, *J* = 11.6, 9.2 Hz, 1H), 4.58 (ddd, *J* = 9.2, 8.0, 8.0 Hz, 1H), 4.00–3.94 (m, 1H), 3.83–3.77 (m, 1H), 2.18–2.10 (m, 1H), 2.08–1.91 (m, 2H), 1.75–1.66 (m, 1H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ: 140.2, 134.8, 130.2, 129.2, 129.0, 125.1, 123.3, 74.8, 68.2, 32.9, 26.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –62.4; IR (ATR) ν: 2928, 2873, 1617, 1325, 1164, 1124, 1065, 855 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{14}F_3O$ $[M+H]^+$ 243.0997, found 243.0997.

ASSOCIATED CONTENT

Supporting Information

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

Experimental details, computational details, and spectral data (PDF)

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