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Weak bases-Mediated Modified Favorskii Reaction Type Direct Alkynylation/(*E*)-Alkenylation: A Unified Rapid Access to *α*,*β*-Unsaturated Ketones and Propargyl Alcohols

*Mohit K. Tiwari, Lalit Yadav, Bharti Rajesh Kumar Shyamlal and Sandeep Chaudhary**

Abstract: Herein, we report an unprecedented, fast, highly efficient,transition-metal-free, modified Favorskii reaction type direct alkynylation as well as (*E*)-alkenylation protocol towards the synthesis of *α*,*β*-unsaturated ketones **5a-u** and propargyl alcohols **4a-c**, **7a-k** and **9a-j** *via* the identification of the combination of Cs_2CO_3 and Et_3N as weak bases in upto 99% yields. In this reaction, aromatic aldehydes afforded *α*,*β*-unsaturated ketones and aliphatic aldehydes furnished propargyl alcohols, respectively. The operationally simple protocol, large substrate scope, gram-scale synthesis, and practical synthetic applications to bioactive heterocyclic scaffolds **10**-**13** further highlight the practicality of this methodology. The proposed mechanistic pathway illustrates the involvement of weak base-assisted propargylation of carbonyl compounds followed by allenol-enone tautomerism to furnish (*E*)-alkenylated product.

Introduction

Favorskii reaction (discovered by Alexei Y. Favorskii in **1905**) i.e., the nucleophilic addition of alkynes to aldehydes in the presence of strong base such as KOH, has been recognized as an efficient synthetic strategy to afford propargyl alcohols and *α*,*β*-unsaturated ketones.[1] Over the past few decades, particularly with reference to terminal alkyne activation involving C-H bond activation concept, transition-metal-free weak base-mediated direct propargylation/alkenylation involving allenol-enone isomerization sequence still remains a challenging area of interest.

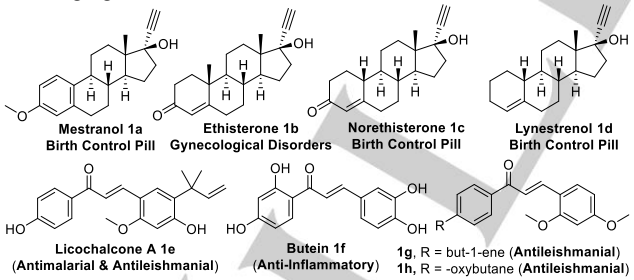

Figure 1. Selected examples of few pharmaceutically important propargyl alcohols and chalcones**1a-h**.

Propargyl alcohols and *α*,*β*-unsaturated ketones/chalcones are important structural motif in a variety of natural products, agrochemicals, organic materials and pharmaceutically bioactive molecules and are also used as reaction intermediates in current organic synthesis (Figure 1).[2-7] Over the years, several efficient synthetic strategies involving transition-metal catalysis,[8-9] organometallic reagent catalysis,[10-13] and/or cross-coupling transformations[14-17] have been used conventionally for direct propargylation/alkenylation to construct pharmaceutically privileged scaffolds (Figure 2). However, transition-metal-free weak base-mediated direct propargylation and/or alkenylation by simply reacting aromatic aldehyde with an unactivated terminal alkyne has yet to be reported.

Previously, strong base such as KO^{t}Bu,[18] $CsOH.H_2O$,[19] quaternary ammonium hydroxide (Triton-B),[20] and Cs_2CO_3 catalyzed decarboxylative coupling (Lee)[21] have been utilized for direct propargylation and alkenylation reactions. In **1999**, Knochel and his co-worker reported that the Cs_2CO_3 is not effective for terminal alkyne activation and can be utilized only as a base for alkylation reactions. Furthermore, aromatic aldehydes and ketones undergoes side-reactions and are not effective for $CsOH.H_2O$-catalyzed alkynylation of aromatic aldehydes and ketones.[19]

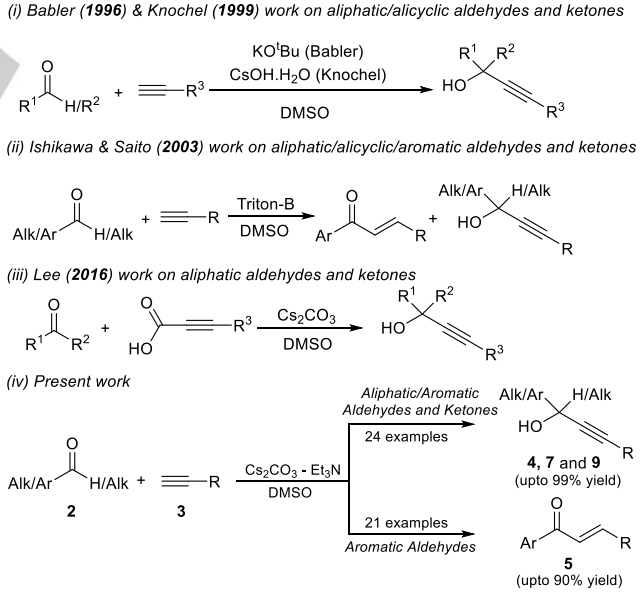

Figure 2. Previous strategies and present work.

In an attempt to develop metal-free direct alkynylation reaction, so far, weak-base mediated propargylation has been reported on aliphatic aldehydes and ketones by pre-functionalized alkynes *via* decarboxylative coupling strategy [Figure 2, (i)-(iii)]. All of these above metal-free approaches have exemplified less selectivity for aromatic carbonyls and distinctive selectivity for aliphatic aldehydes and ketones. However, several drawbacks such as use of strong bases,[18-19] syringe pump technique,[19] lower yields in aromatic substrates,[20] glaser

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formation,[5b] sensitivity towards air and moisture, pre-functionalization of starting materials,[21] decreased selectivity and less substrate scope limits its utility in organic synthesis. Hence, the development of broad-spectrum, operationally simple, and environmentally benign rapid protocol for the synthesis of bioactive motifs i.e., propargyl alcohols and *α,β*-unsaturated ketones, is highly desirable.

Results and Discussion

In our endeavour to develop novel synthetic strategies for bioactive scaffolds,[22] we envisaged based on previous reports[18-21] and proposed a hypothesis that the weak base like Cs_2CO_3, either alone or in combination with an additive or another base can coordinate with both aldehyde and alkyne simultaneously, thereby triggering direct alkynylation which then undergoes allenol-enone tautomerization to furnish **5** with (*E*)-configuration exclusively (Figure 3).

Herein, we disclose an unprecedented, highly efficient, fast, transition-metal-free direct alkynylation as well as (*E*)-alkenylation protocol towards the synthesis of *α,β*-unsaturated ketones and propargyl alcohols *via* the identification of the combination of Cs_2CO_3 and Et_3N as weak bases in upto 99% yields [Figure 2, (iv)]. Because of the low cost and wide availability of starting materials, such an approach would allow direct synthesis of these bioactive scaffolds. The versatility of this strategy is described here by synthesizing an exemplary set of propargyl alcohols (24 examples) and *α,β*-unsaturated ketones/chalcones (21 examples).

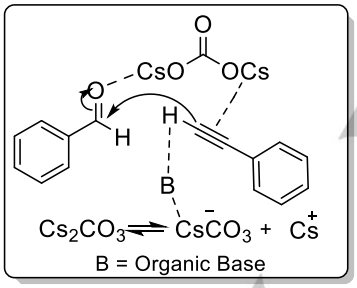


Figure 3. Hypothesis for weak base-mediated dual activation.

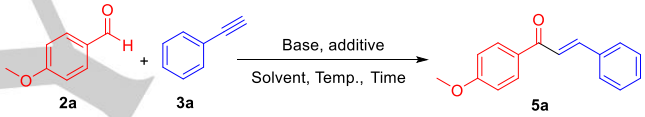
We commenced our investigations by following the reaction of 4-methoxybenzaldehyde (**2a**, 1 equiv.) and phenyl acetylene (**3a,** 1.5 equiv.) in Dry DMF at 60 °C for 24h was chosen as a model system for the optimization studies in the presence of base.

Thus, initial screening of inorganic and organic bases such as KO^{t}Bu, K_2CO_3, Na_2CO_3 K_3PO_4, NaOH, KOH, NaOAc, Cs_2CO_3, Et_3N, pyridine, piperidine, DIPEA, DIPA, DBU, and DABCO etc. were examined. Out of all, keeping all the other reaction parameters same, Cs_2CO_3 provided the best result which furnished **5a** in 30% yield with high (*E*)-selectivity (see Table S1, entry 1-15 in SI as well as Table 1, entry 1).

The non-formation of homocoupling (Glaser) product was the most noticeable feature observed in this reaction. The corresponding propargyl alcohol was either not detected or obtained only in traces. Then, screening of different non-polar/polar solvents such as toluene, xylene, mesitylene, DCE, THF, 1,4-dioxane, ACN, HFIP and *tert*-amyl alcohol were carried out keeping the other parameters same i.e., 4-methoxybenzaldehyde (**2a**,1 equiv.) and phenyl acetylene (**3a,** 1.5 equiv.), Dry solvents (2 mL), 60 °C temperature for 24h. The reaction proceeded well in DMA and DMSO solvents. Out of all, DMSO as solvent gave the best result in which **5a** was obtained in 40% yield in 15 minutes only (see Table S2, entry 1-12 in SI as well as Table 1, entry 2).

Once, the Cs_2CO_3 as base and DMSO as solvent were optimized; we then started screening of various other reaction parameters such as equivalents of base, screening of additives and their equivalents as well as temperature and time. Therefore, the reaction was carried out in double (2.0) equivalents of Cs_2CO_3 dissolved in dry DMSO (2 mL) at 60 °C for 15 min; it furnished **5a** in 60% yield (Table 1, entry 3). Further increase in the equivalents of Cs_2CO_3 have detrimental effect on the yield (Table 1, entry 4). Subsequently, as per our proposed hypothesis, several organic bases such as DMAP, Pyridine, TEA,TBAI, TBAB, etc. were screened along with the Cs_2CO_3 to maximize the yield of **5a** (Table 1, entry 5-20). In increasing the equivalents from 1.0 to 2.2 of Cs_2CO_3 keeping all the other parameters constant; an increase in the yield of the reaction was observed (Table 1, Entry 5-8). However, reducing the equivalents of additive to half keeping other parameters same; 84% yield of **5a** was obtained in 30 minutes (Table 1, Entry 9).

Table 1. Optimization table: Screening of reaction parameters.[a]

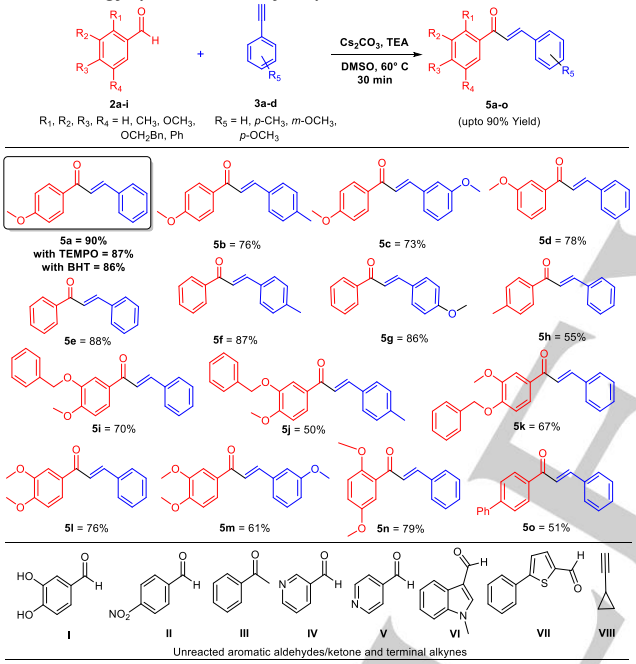


S. No.	Solvent (mL)	Base (Equiv.)	Additive (Equiv.)	Temp. (°C)	Time (min)	Yield (%)[b]
1.	DMF	Cs_2CO_3 (1.0)	-	60	1440	30[c]
2.	DMSO	Cs_2CO_3 (1.0)	-	60	15	40
3.	DMSO	Cs_2CO_3(2.0)	-	60	15	60
4.	DMSO	Cs_2CO_3(3.0)	-	60	15	38
5.	DMSO	Cs_2CO_3(1.0)	DMAP(1.0)	60	15	70
6.	DMSO	Cs_2CO_3(1.5)	DMAP(1.0)	60	15	78
7.	DMSO	Cs_2CO_3(2.0)	DMAP(1.0)	60	15	81
8.	DMSO	Cs_2CO_3(2.2)	DMAP(1.0)	60	15	83
9.	DMSO	Cs_2CO_3(2.4)	DMAP(0.5)	60	30	84
10.	DMSO	Cs_2CO_3(2.4)	DMAP(0.5)	RT	60	45
11.	DMSO	Cs_2CO_3(2.4)	DMAP(0.5)	80	30	70
12.	DMSO	Cs_2CO_3(2.4)	DMAP(0.5)	110	30	17
13.	DMSO	-	DMAP(1.0)	60	120	00
14.	DMSO	Cs_2CO_3(2.4)	DMAP(0.5)	60	30	73[d]
15.	DMSO	Cs_2CO_3(2.4)	C_5H_5N (0.5)	60	30	84
16.	**DMSO**	**Cs_2CO_3 (2.4)**	**TEA (0.5)**	**60**	**30**	**90**
17.	DMSO	Cs_2CO_3(5.0)	TEA (1.0)	60	30	69
18.	DMSO	Cs_2CO_3(2.4)	TEA (1.0)	60	30	62
19.	DMSO	Cs_2CO_3(2.4)	TBAI (0.5)	60	30	69
20.	DMSO	Cs_2CO_3(2.4)	TBAB(0.5)	60	30	72

[a] *Reaction conditions*: **2a** (0.3 mmol), **3a** (0.45 mmol), Cs_2CO_3 and additive were reacted in dry DMSO (2.0 mL) for 15-120 min under inert atmosphere. [b] Isolated Yield. [c] Reaction was carried out for 24 h. [d] Phenylacetylene = 2 equiv.

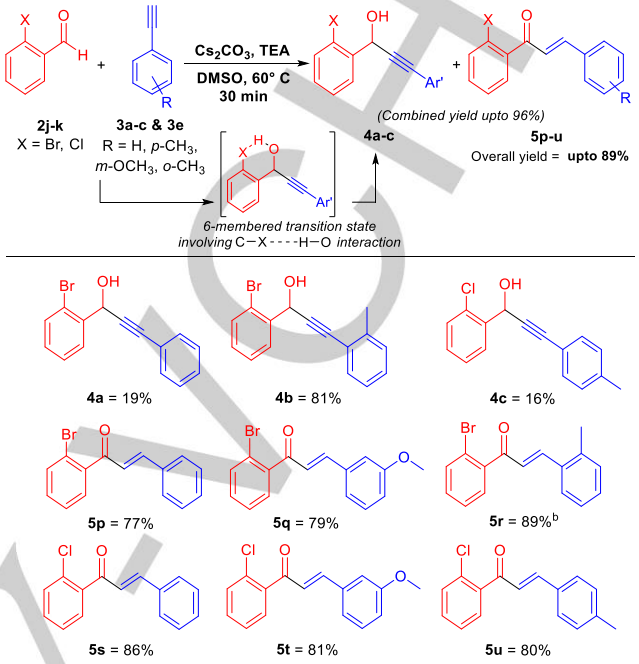
Then, we carried out the screening of temperature and time taking 2.4 equiv. of Cs_2CO_3 and 0.5 equiv. of DMAP in dry DMSO (Table 1, Entry 10-12). Lower yields were obtained either on increasing the temperature or prolonging the reaction time. The importance of Cs_2CO_3 was also practically established where a reaction without Cs_2CO_3 was carried out; it did not furnished the desired product (Table 1, entry 13). Additionally, when the reaction was carried out by increased the amount of **3a** (2.0 equiv.) in comparison to **2a** (1 equiv.) while keeping all the parameters same as in entry no. 7 i.e.,

Cs_2CO_3 (2.4 equiv.) and DMAP (0.5 equiv.) dissolved in dry DMSO (2 mL) at 60 °C for 30 min; it afforded **5a** in comparatively decreased yield (Table 1, Entry 14). Sequentially, screening the other additives such as Pyridine and triethylamine further restore the improved yield while keeping other parameters same (Table 1, Entry 15-16). Infact, the reaction carried out in combination of Cs_2CO_3 (2.4 equiv.) and Et_3N (0.5 equiv.) dissolved in DMSO (2 mL) at 60 °C for 30 min furnished **5a** in 90% yield (Table 1, entry 16). Further attempts to improve the yield of the reaction by taking 5.0 equivalents of Cs_2CO_3 or 1.0 equivalent of triethylamine do not show beneficial effect (Table 1, Entry 17-18). We also attempted other additives such as quaternary ammonium salt TBAI/TBAB (0.5 equiv.) along with Cs_2CO_3 (2.4 equiv.) dissolved in DMSO (2 mL) at 60 °C for 30 minutes; **5a** was obtained in reasonable yields (Table 1, Entry 19-20). Overall, ***2a*** *(1 equiv.),* ***3a*** *(1.5 equiv.), Cs_2CO_3 (2.4 equiv.), Et_3N (0.5 equiv.) dissolved in DMSO (2 mL) at 60 °C for 30 min was found to be the best optimized reaction conditions for our methodology* (Table 1, Entry 16).



Scheme 1. *Reaction Conditions*: **2a-i** (0.3 mmol), **3a-d** (0.45 mmol), Cs_2CO_3 (0.72 mmol) and Et_3N (0.15 mmol) were reacted in dry DMSO (2.0 mL) for 0.5 h under inert atmosphere.

Several substituted aldehydes **2a-i** were reacted with different substituted aromatic alkynes **3a-d** under optimized reaction conditions which furnished substituted (*E*)-chalcones **5a-o** in excellent (upto 90%) yields (Scheme 1). The corresponding propargylic alcohol were either not detected or obtained only in traces. This novel strategy was applicable to a variety of aromatic aldehydes and for the synthesis of pharmaceutically privileged (*E*)-chalcones. The reaction proceeded efficiently with unsubstituted as well as electron-donating groups (EDG) containing aromatic aldehydes with high (*E*)-selectivity. However, electron-withdrawing group (EWG) on aromatic aldehydes was not found suitable for this reaction and undergoes side reactions. Notably, naturally occurring aldehydes such as vanillin, isovanillin etc., and EDG containing benzaldehyde afforded the corresponding products (**5i-k**, **5h** and **5l-n**) in synthetically useful yields with excellent (*E*)-selectivity. Variation of substitution position of EDG do not influence the product yields, as illustrated by 2,5-dimethoxybenzaldehyde (Scheme 1).



Scheme 2. *Reaction Conditions*: **2j-k** (0.3 mmol), **3a-c** and **3e** (0.45 mmol), Cs_2CO_3 (0.72 mmol) and additive (0.15 mmol) were reacted in dry DMSO (2.0 mL) for 0.5 h under inert atmosphere. [b] Obtained in two steps.

Several aromatic/heteroaromatic aldehydes and ketones as well as terminal alkynes **I-VIII** were found unreactive under optimized reaction conditions. It has been anticipated that polar groups on aromatic aldehydes including heteroarenes deactivates the ring due to which dual activation does not occur because of non-formation of nucleophilic centre. The reaction behaves differently with *o*-halo substituted aldehydes **2j-k**, where both propargylic alcohols **4a-c** and chalcones **5p-u** were isolated upto 96% combined yields. The conversion of **4b** to **5r** confirms the involvement of propargyl alcohol as reaction intermediate (Scheme 2). The involvement of six-membered ring transition state C-(Br/Cl)---H–O hydrogen bonding, having low energy, could be the probable reason for the isolation of propargyl alcohols in higher yields.[23]

To understand the mechanistic pathway of the reaction, control experiments were performed under the optimized reaction conditions in TEMPO and BHT (free-radical scavengers), which furnished **5a** upto 87 and 86% yields, respectively. This implies the involvement of ionic mechanism rather than a free-radical mechanism (Scheme 1).

A plausible mechanism involving direct alkynylation/(*E*)-alkenylation *via* allenol-enone isomerization for **5e** has been illustrated in Figure 4. Initially, Cs_2CO_3 activates the carbonyl group of aldehyde and electron-rich terminal alkyne simultaneously.[24] The base (Et_3N) then abstract proton to generate carbanion which attacks on nucleophilic centre and generates intermediate [I]. The proton generated after dissociation of bicarbonate ion forms propargyl alcohol which on reaction with Et_3N forms intermediate [II] which isomerizes

to allenol intermediate [III], which is isomeric to structure [IV]. Then, the allenol intermediate [III] undergoes tautomerization *via* protic transfer to furnish the desired enone **5e** (Figure 4).

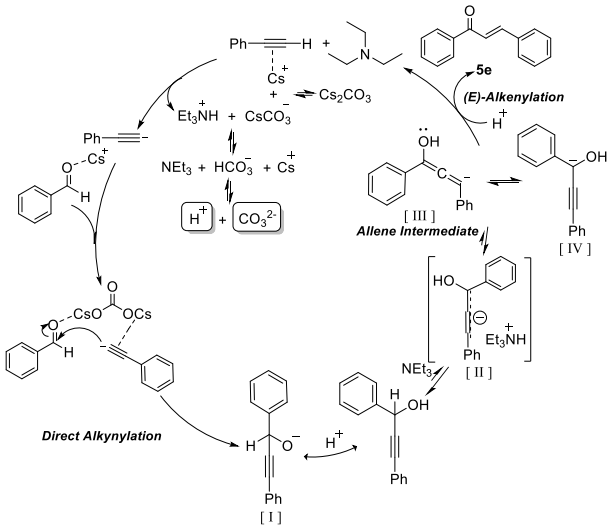
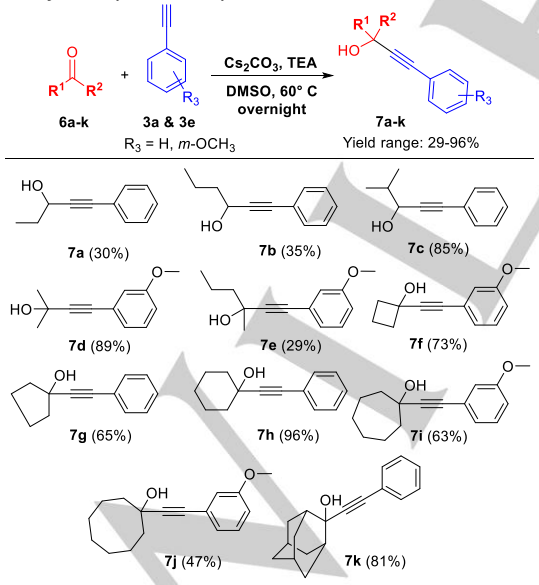


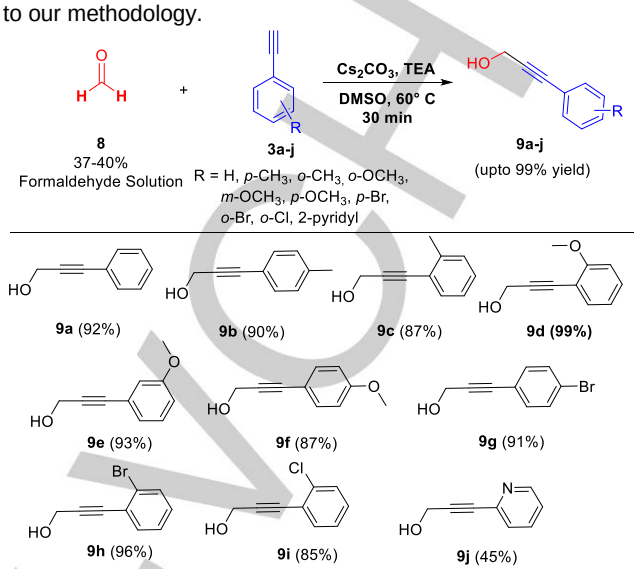
Figure 4. Proposed mechanism.

To show the generality of this reaction, we further expanded the substrate scope to aliphatic aldehydes. Thus, an array of aliphatic aldehydes and ketones **6a-k** were also reacted with substituted terminal alkynes **3a** and **3e** under optimized reaction conditions which afforded secondary/tertiary propargyl alcohols **7a-k** in 29-96% yield range, albeit in more reaction time (Scheme 3). In spite of having high reactivity, the simple aliphatic aldehyde undergoes side reaction and delivered the final product in lower yields. However, branched chain containing aldehydes afforded the desired products in high yields. The cyclic as well as acyclic ketones, though less reactive, undergoes direct propargylation in moderate to excellent yields (Scheme 3).



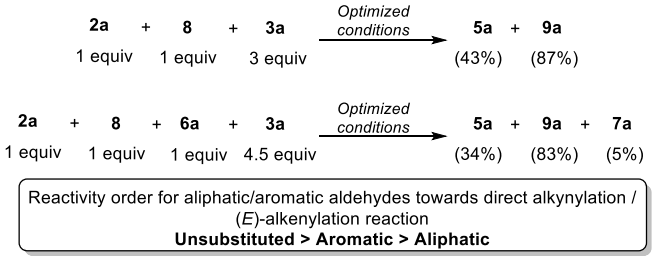
Scheme 3. *Reaction Conditions*: **10a-k** (0.3 mmol), **3a** and **3e** (0.45 mmol), Cs_2CO_3 (0.72 mmol) and Et_3N (0.15 mmol) were reacted overnight in dry DMSO (2.0 mL) under inert atmosphere.

Similarly, to further ascertain the generality of this reaction, we also explored unsubstituted aldehydes. Therefore, the reaction of 37-40% formaldehyde solution **8** with substituted aromatic/heteroaromatic terminal alkynes **3a-j** under the optimized conditions furnished a variety of substituted primary propargyl alcohols **9a-j** exclusively in excellent (upto 99%) yields (Scheme 4). This also illustrates the greener approach to our methodology.



Scheme 4. *Reaction Conditions*: **8** (0.3 mmol), **3a-j** (0.45 mmol), Cs_2CO_3 (0.72 mmol) and Et_3N (0.15 mmol) were reacted in dry DMSO (2.0 mL) for 0.5 h under inert atmosphere.

To examine the reactivity order of aromatic/aliphatic aldehydes towards direct alkynylation/(*E*)-alkenylation reactions, one-pot competition experiments were performed based on our optimized reaction conditions (Scheme 5). **2a** (1 equiv.), **8** (1 equiv.) and **3a** (3 equiv.) were subjected to the optimized conditions of Cs_2CO_3-Et_3N in dry DMSO at 60 °C for 30 min under inert atmosphere, which furnished **5a** and **9a** in 43% and 87% yields, respectively. This inferred that unsubstituted aliphatic aldehydes reacts faster than substituted aromatic aldehydes. In another trial, **2a** (1 equiv.), **8** (1 equiv.), **6a** (1 equiv.) and **3a** (4.5 equiv.) were subjected to the optimized conditions of Cs_2CO_3-Et_3N in dry DMSO at 60 °C for 30 min under inert atmosphere,which furnished **5a, 7a** and **9a** in 34%, 5% and 83% yields, respectively.



Reactivity order for aliphatic/aromatic aldehydes towards direct alkynylation / (*E*)-alkenylation reaction
Unsubstituted > Aromatic > Aliphatic

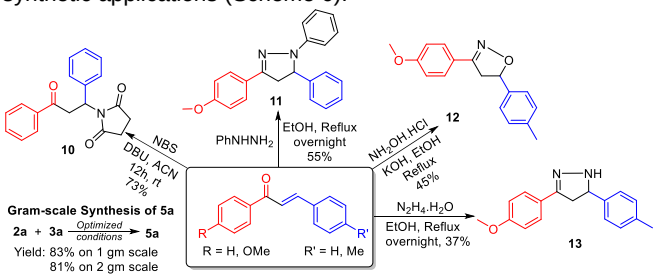
Scheme 5. *Reaction conditions*: Cs_2CO_3 (4 equiv.) and Et_3N (1-1.5 equiv.) were reacted in dry DMSO (5.0 mL) for 0.5 h under inert atmosphere.

Based on the experimental studies, different aldehydes showed the following reactivity order towards direct alkynylation/ (*E*)-alkenylation reactions:

unsubstituted>aromatic>aliphatic

The difference in kinetic acidities, the resonance effect and mesomeric effects could be the most plausible reason for the differences arised in the reactivity order.

The scalability of the method was demonstrated by performing 1 gram scale synthesis of **5a**, in which the optimized reaction conditions gave an 83% yield (Scheme 6). On 2 gram scale reaction, 81% yield of **5a** was obtained. Using literature procedures, further transformations of (*E*)-Chalcones into medicinally important molecules **10**-**13**, having anticancer, antifilarial and antimicrobial activities, exhibits its practical synthetic applications (Scheme 6).[25]



Scheme 6. Practical applications: Synthesis of **10**-**13**.

Conclusion

Our study uncovered an unprecedented, highly efficient, transition-metal-free, Cs_2CO_3-Et_3N-mediated direct alkynylation and (*E*)-alkenylation protocol for the synthesis of propargyl alcohols **4a-c**, **7a-k** and **9a-j** and *α,β*-unsaturated ketones **5a-u**, respectively under mild basic conditions. With the rapid operational simplicity, functional group compatibility, and substrate selectivity; the present protocol demonstrates a fast method for the facile synthesis of bioactive scaffolds in good to excellent yields. The gram-scale synthesis, and its practical applications to the synthesis of bioactive heterocyclic scaffolds **10**-**13** further highlights the practicality of this methodology. The medicinal chemistry and further extension of the present reaction to the synthesis of related heterocyclic motifs and detailed mechanistic studies are ongoing in our laboratory.

Experimental Section

All glass apparatus were oven dried prior to use. Melting points were taken in open capillaries on complab melting point apparatus and are presented uncorrected. All the AR grade chemicals were used as supplied from commercial source (Sigma Aldrich, TCI, Alpha Aesar, Spectrochem etc.) and used without further purification. Drying of DMSO was performed using fractional distillation under reduced pressure and stored under molecular sieves in inert atmosphere. The supplied Cesium carbonate was stored and used under inert atmosphere. Similarly, triethylamine was distilled under reduced pressure, stored in a sealed amber glass bottle, and it was further used under inert atmosphere. The silica gel (100-200 Mesh) used for column chromatography were supplied either from QualigensTM (India) or Rankem (India). UV fluorescence and Iodine vapour served as the visualizing agent for thin layer chromatography (Merck silica gel 60 F_{254} precoated plates (0.25 mm). ^{1}H NMR and ^{13}C NMR spectral data were recorded on a JEOL ECS-400 (2-channel support with an adaptable broadband RF execution) spectrometer working at 400 MHz for ^{1}H and 100 MHz for ^{13}C) utilizing $CDCl_3$ as a solvent. Tetramethylsilane (δ 0.00 ppm) served as an internal standard in ^{1}H NMR and $CDCl_3$ (δ 77.0 ppm) in ^{13}C NMR. Chemical shifts are reported in parts per million. Splitting patterns are described as singlet (s), doublet (d), double doublet (dd), triplet (t), double triplet (dt), multiplet (m), and broad (br). Electron Impact Mass Spectroscopy (HR-EIMS) data were obtained from Xevo G2-S Q-Tof (Waters, USA) compatible with ACQUITY UPLC® and nano ACQUITY UPLC® systems. The BUCHI Rotavapor R-210 was used for drying and concentration of the solvents.

General Procedures for preparation of *α,β*-unsaturated carbonyl compounds/*(E)*-chalcones 5a-u (Preparation of **5a** as representative):

All the reactants, 4-methoxybenzaldehyde (**2a**, 0.3 mmol), phenylacetylene (**3a**, 0.45 mmol), Cs_2CO_3 (0.72 mmol), Et_3N (0.15 mmol) and dry DMSO (2.0 mL) were taken simultaneously and allow to react for 30 minutes at 60 °C in a Fisher brand disposable borosilicate threaded end round bottom glass tube in an inert atmosphere. The progression of the reaction was monitored using TLC. On completion of the reaction, the reaction mixture was allowed to cool at room temperature and quenched using water (5 mL). The organic layer was extracted using ethyl acetate (3×10 mL), washed with water (4 × 10 mL), then with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-hexane as an eluent, which afforded **5a** as a pure white solid product. The use of general chemicals/reagents and no requirement of any special costly chemicals/reagents make our methodology more economic. Moreover, no special instrument i.e., syringe pump was used. In addition, the recovered solvents used for work-up and column chromatography were reused for the next purification.

General procedure for preparation of secondary/tertiary propargyl alcohols (7a-k) (Preparation of **7a** as a representative)**:**

All the reactants, aliphatic aldehydes/ketones (**6a**, 0.3 mmol), phenylacetylene (**3a**, 0.45 mmol), Cs_2CO_3 (0.72 mmol), Et_3N (0.15 mmol) and dry DMSO (2.0 mL) were taken simultaneously and allow to react at 60 °C for 12h in a Fisher brand disposable borosilicate threaded end round bottom glass tube in an inert atmosphere. The progression of the reaction was monitored using TLC. On completion of the reaction, the reaction mixture was allowed to cool at room temperature and quenched using water (5 mL). The organic layer was extracted using ethyl acetate (3×10 mL), washed with water (4 × 10 mL), then with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-hexane as an eluent, which afforded **7a** as a viscous oil.

General procedure for preparation of primary propargyl alcohols (9a-j): Preparation of **9a** as a representative**:**

All the reactants, 37-40% formaldehyde solution (**8**, 0.3 mmol), phenylacetylene (**3a**, 0.45 mmol), Cs_2CO_3 (0.72 mmol), Et_3N (0.15 mmol) and dry DMSO (2.0 mL) were taken simultaneously and allow to react at 60 °C for 30 minutes in a Fisher brand disposable borosilicate threaded end round bottom glass tube in an inert atmosphere. The progression of the reaction was monitored using TLC. On completion of the

reaction, the reaction mixture was allowed to cool at room temperature and quenched using water (5 mL). The organic layer was extracted using ethyl acetate (3 × 10 mL), washed with water (4 × 10 mL), then with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-hexane as an eluent, which afforded **9a** as a viscous oil.

General procedure for the synthesis of chalcones based scaffolds (**10-13**)[25a-c]**:**

Synthesis of **10**:[25b] A bioactive *β*-amino ketone (**10**) was produced when, a magnetically stirred mixture of *E*-chalcone (1 equiv.) and *N*-bromosuccinimide (1.2 equiv.) allowed to react in ACN (2 mL) for 12h at rt in the presence of DBU (1.1 equiv.) as base. The usual work up followed by column chromatography purification afforded pure 1-(3-oxo-1,3-diphenylpropyl)pyrrolidine-2,5-dione **10** (73% yield) as a viscous oil. Synthesized molecule (**10**) is an promising compound having various pharmaceutically important properties like anticancer, antifilarial, antibacterial, and antifungal activities.

Synthesis of **11:** A magnetically stirred mixture of (*E)*-chalcone (1 equiv.) and phenylhydrazine (4 equiv.) was allowed to react in EtOH (10 mL) under refluxing condition for 12 h. The usual work up followed by column chromatography purification afforded pure 3-(4-methoxyphenyl)-1,5-diphenyl-4,5-dihydro-1H-pyrazole **11** (55% yield) as a white solid.Synthesized molecule 3-(4-methoxyphenyl)-1,5-diphenyl-4,5-dihydro-1H-pyrazole (**11**) is an promising compound having various biological activities.

Synthesis of **12:** A magnetically stirred mixture of *E*-chalcone (1 equiv.) and hydroxyl amine (4 equiv.) was allowed to react in EtOH (10 mL) under refluxing condition for 12 h. The usual work up followed by column chromatography purification afforded pure 3-(4-methoxyphenyl)-5-(p-tolyl)-4,5-dihydroisoxazole **12** (45% yield) as a white solid.

Synthesis of **13:** A magnetically stirred mixture of *E*-chalcone (1 equiv.) and hydrazine hydrate (4 equiv.) was allowed to react in EtOH (10 mL) under refluxing condition for 12 h. The usual work up followed by column chromatography purification afforded pure 3-(4-methoxyphenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole **13** (37% yield) as a viscous oil.

Characterization Data of 4a-c, **5a-u**, **7a-k**, **9a-j and 10-13** (Superscript on the name of the Compound indicates the references for the known compound).

Compound 4a: 1-(2-bromophenyl)-3-phenylprop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 19%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J*= 7.6, 1.6 Hz, 1H), 7.58 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.39 – 7.36 (m, 1H),7.33 – 7.30 (m, 2H), 7.23 – 7.18 (m, 2H), 6.01 (s, 1H), 2.63 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.56, 133.17, 131.87, 130.10, 128.79, 128.40, 128.02, 122.91, 122.35, 87.70, 86.90, 64.80; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{15}H_{12}BrO]^+$ 287.0066; Found 287.0065.

Compound 4b: 1-(2-bromophenyl)-3-(o-tolyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 8% ethyl acetate: *n*-Hexane as an eluent. Yield: 81%; Solid; m.p.73–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.59 – 7.57 (m, 1H), 7.43 (d, *J*= 7.6 Hz, 1H) 7.39 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.22 – 7.20 (m, 2H), 7.19 – 7.17 (m, 1H), 7.15 – 7.10 (m, 1H), 6.05 (s, 1H), 2.59 (br, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.54, 139.76, 133.16, 132.21, 130.04, 129.55, 128.78, 128.68, 128.00, 125.62, 122.84, 122.13, 91.58, 85.87, 64.91, 20.85; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}BrO]^+$ 301.0223; Found 301.0226.

Compound 4c: 1-(2-chlorophenyl)-3-(p-tolyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 16%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.39 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H),7.33 – 7.28 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.03 (s, 1H), 2.53 (br, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.96, 138.06, 132.95, 131.77, 129.87, 129.79, 129.15, 128.60, 127.36, 119.24, 86.99, 86.90, 62.61, 21.60.; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}ClO]^+$ 257.0728; Found 257.0726.

Compound 5a: (*E*)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 3% ethyl acetate: *n*-Hexane as an eluent. Yield: 90%; White Solid; m.p. 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$), 8.06 – 8.01 (m, 2H), 7.80 (d, *J* = 15.6 Hz, 1H), 7.66 – 7.61 (m, 2H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.43 – 7.39 (m, 3H), 6.99 – 6.96 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.83, 163.51, 144.07, 135.16, 131.17, 130.91, 130.42, 129.01, 128.45, 121.95, 113.93, 55.60.

Compound 5b: (*E*)-1-(4-methoxyphenyl)-3-(p-tolyl)prop-2-en-1-one[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 76%; White Solid; m.p. 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 15.6 Hz, 1H), 7.54–7.48 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.92, 163.42, 144.16, 140.92, 132.41, 131.31, 130.86, 129.76, 128.48, 120.93, 113.89, 55.59, 21.63.

Compound 5c: (*E*)-3-(3-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one[27]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 8% ethyl acetate: *n*-Hexane as an eluent. Yield: 73%; White Solid; m.p. 101–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.01 (m, 2H), 7.75 (d, *J* = 15.6 Hz, 1H), 7.51 (d, *J* = 15.6 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.15 – 7.14 (m, 1H), 6.99 – 6.93 (m, 3H), 3.88 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.80, 163.53, 159.99, 143.97, 136.54, 131.13, 130.93, 130.00, 122.25, 121.09, 116.14, 113.94, 113.47, 55.59, 55.44.

Compound 5d: (*E*)-1-(3-methoxyphenyl)-3-phenylprop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 78%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 15.6 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.61 – 7.57 (m, 1H), 7.54 – 7.53 (m, 1H),7.52 – 7.49 (d, *J* = 16.0 Hz, 1H), 7.43 – 7.39 (m, 4H), 7.14 – 7.11 (m, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.37, 159.98, 144.97, 139.67, 134.95, 130.66, 129.67, 129.06, 128.56, 122.18,

121.15, 119.43, 112.91, 55.59; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{15}O_2]^+$; 239.1067; Found 239.1068.

Compound 5e: (*E*)-1,3-Diphenylprop-2-en-1-one)[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 88%; White Solid; m.p. 54–56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 8.00 (m, 2H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.65 – 7.62 (m, 2H), 7.61 – 7.56 (m, 1H), 7.55 – 7.48 (m, 3H), 7.45 – 7.39 (m, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.67, 144.96, 138.29, 134.96, 132.89, 130.65, 129.06, 128.73, 128.60, 128.55, 122.16.

Compound 5f: (*E*)-1-phenyl-3-(p-tolyl)prop-2-en-1-one[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 87%; White Solid; m.p. 95–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.99 (m, 2H),7.78 (d, *J* = 15.6 Hz, 1H), 7.59 – 7.46 (m,6H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.78, 145.07, 141.20, 138.44, 132.77, 132.23, 129.80, 128.68, 128.56, 121.18, 21.64.

Compound 5g: (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 86%; Yellow Solid; m.p. 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.98 (m, 2H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.60 – 7.38 (m, 6H), 6.93 – 6.91 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.70, 161.76, 144.80, 138.58, 132.65, 130.33, 128.65, 128.50, 127.69,119.85, 114.50, 55.50.

Compound 5h: (*E*)-3-phenyl-1-(p-tolyl)prop-2-en-1-one[26]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 55%; Solid; m.p.78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.92 (m, 2H), 7.80 (d, *J* = 15.6 Hz, 1H), 7.65 – 7.63 (m, 2H), 7.53 (d, *J* = 15.6 Hz, 1H),7.42 – 7.40 (m, 3H), 7.30 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.13, 144.50, 143.75, 135.70, 135.08, 130.52, 129.43, 129.03, 128.75, 128.50, 122.16, 21.79.

Compound 5i: (*E*)-1-(3-(benzyloxy)-4-methoxyphenyl)-3-phenylprop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 70%; Solid; m.p. 111–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 15.6 Hz, 1H), 7.69 – 7.60 (m, 4H), 7.49 – 7.45 (m, 3H), 7.43 – 7.35 (m, 5H), 7.32–7.31 (m, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 5.22 (s, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.64, 153.94, 148.32, 144.02, 136.69, 135.14, 131.23, 130.44, 129.01, 128.73, 128.45, 128.15, 127.63, 123.42, 121.77, 113.39, 110.54, 71.10, 56.22; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{23}H_{21}O_3]^+$ 345.1485; Found 345.1481.

Compound 5j: (*E*)-1-(3-(benzyloxy)-4-methoxyphenyl)-3-(p-tolyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 50%; Solid; m.p. 117–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 15.6 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.52 – 7.49 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.40 –7.39 (m, 1H), 7.38 – 7.36 (m, 2H), 7.33 – 7.29 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 1H), 5.22 (s, 2H), 3.96 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.73, 153.83, 148.27, 144.11, 140.94, 136.72, 132.39, 131.36, 129.75, 128.72, 128.48, 128.14, 127.63, 123.34, 120.75, 113.40, 110.53, 71.09, 56.21, 21.63; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{24}H_{23}O_3]^+$ 359.1642; Found 359.1641.

Compound 5k: (*E*)-1-(4-(benzyloxy)-3-methoxyphenyl)-3-phenylprop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 67%; Solid; m.p. 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 15.6 Hz, 1H), 7.64 – 7.59 (m, 4H),7.52 (d, *J* = 15.6 Hz, 1H), 7.46 – 7.29 (m, 8H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.25 (s, 2H), 3.97 (s, 3H); ^{13}C (100 MHz, $CDCl_3$) δ 188.72, 152.45, 149.80, 144.07, 136.36, 135.14, 131.61, 130.44, 129.02, 128.79, 128.45, 128.21, 127.29, 122.91, 121.75, 112.18, 111.25, 70.91, 56.23; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{23}H_{21}O_3]^+$ 345.1485; Found 345.1482.

Compound 5l:(*E*)-1-(3,4-dimethoxyphenyl)-3-phenylprop-2-en-1-one[28]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 76%; Solid; m.p. 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 15.6 Hz, 1H), 7.66 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.63 – 7.59 (m, 3H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.39 – 7.37 (m, 3H), 6.90 (d, *J* = 8.4 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.64, 153.34, 149.31, 144.05, 135.13, 131.36, 130.45, 129.01, 128.46, 123.13, 121.70, 110.80, 110.03, 56.17, 56.11.

Compound 5m: (*E*)-1-(3,4-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 15% ethyl acetate: *n*-Hexane as an eluent. Yield: 61%; Solid; m.p.62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 15.6 Hz, 1H), 7.66 (dd, *J* = 8.4 Hz, 2 Hz, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 15.6 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.14 – 7.13 (m, 1H), 6.94 – 6.89 (m, 2H), 3.94 (s, 3H), 3.93 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.65, 159.99, 153.36, 149.32, 143.96, 136.52, 131.33, 130.00, 123.15, 122.03, 121.06, 116.07, 113.57, 110.81, 110.02, 56.17, 56.12, 55.43; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{18}H_{19}O_4]^+$ 299.1278; Found 299.1279.

Compound 5n: (*E*)-1-(2,5-dimethoxyphenyl)-3-phenylprop-2-en-1-one[29]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 79%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 16.0 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.43 – 7.37 (m, 4H), 7.18 (d, *J* = 3.2 Hz, 1H), 7.03 – 7.00 (m, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.57, 153.68, 152.66, 143.39, 135.22, 130.36, 129.71, 128.96, 128.52, 126.96, 119.28, 114.45, 113.45, 56.58, 55.95.

Compound 5o: (*E*)-1-([1,1'-biphenyl]-4-yl)-3-phenylprop-2-en-1-one[30]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 51%; Solid; m.p.172–174 °C; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.09 (m, 2H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.74 – 7.71 (m, 2H), 7.68 – 7.63 (m, 4H), 7.58 (d, *J* = 15.6 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.44 – 7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.06, 145.64, 144.87, 140.03, 136.98, 135.01, 130.66, 129.23, 129.07, 128.58, 128.31, 127.40, 122.08.

Compound 5p: (*E*)-1-(2-bromophenyl)-3-phenylprop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 77%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.46 – 7.29 (m, 7H), 7.09 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.88, 146.79, 141.20, 134.46, 133.53, 131.49, 131.05, 129.27, 129.11, 128.70, 127.46, 126.23, 119.59; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{15}H_{12}BrO]^+$ 287.0066; Found 287.0065.

Compound 5q: (*E*)-1-(2-bromophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 79%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.63 (m, 1H), 7.41 – 7.39 (m, 2H), 7.35 – 7.28 (m, 3H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.10 – 7.03 (m, 2H), 6.95 (ddd, *J* = 8.4, 2.4, 0.8 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.86, 160.03, 146.71, 141.16, 135.81, 133.53, 131.49, 130.09, 129.26, 127.46, 126.49, 121.42, 119.59, 116.99, 113.34, 55.43; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}BrO_2]^+$ 317.0172; Found 317.0173.

Compound 5r: (*E*)-1-(2-bromophenyl)-3-(o-tolyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-Hexane as an eluent. Yield: 89%; Solid; m.p. 61–63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 16.0 Hz, 1H), 7.65 – 7.62(m, 2H), 7.45 – 7.38 (m, 2H), 7.35 – 7.27 (m, 2H), 7.24 – 7.18 (m, 2H), 7.03 (d, *J* = 16.0 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.74, 144.21, 141.37, 138.43, 133.52, 133.42, 131.53, 131.03, 130.74, 129.35, 127.48, 127.02, 126.71, 126.56, 119.59, 19.83; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}BrO]^+$ 301.0223; Found 301.0225.

Compound 5s: (*E*)-1-(2-chlorophenyl)-3-phenylprop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 3% ethyl acetate: *n*-Hexane as an eluent. Yield: 86%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.54 (m, 2H), 7.51 – 7.31 (m, 8H), 7.12 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.01, 146.43, 139.18, 134.49, 131.50, 131.39, 130.99, 130.39, 129.44, 129.09, 128.69, 126.94, 126.38; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{15}H_{12}ClO]^+$ 243.0571; Found 243.0570.

Compound 5t: (*E*)-1-(2-chlorophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 81%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.31(m, 5H), 7.28 (t, *J* = 8Hz, 1H), 7.14 – 7.07 (m, 2H), 7.05 (t, *J* = 2Hz, 1H), 6.95 – 6.92 (m, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.92, 160.03, 146.35, 139.13, 135.82, 131.54, 131.37, 130.40, 130.09, 129.45, 126.97, 126.62, 121.39, 116.93, 113.40, 55.41;HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}ClO_2]^+$ 273.0677; Found 273.0675.

Compound 5u: (*E*)-1-(2-chlorophenyl)-3-(p-tolyl)prop-2-en-1-one

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-Hexane as an eluent. Yield: 80%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.31 (m, 7H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 16.0 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.10, 146.68, 141.66, 139.30, 131.75, 131.39, 131.34, 130.36, 129.86, 129.39, 128.73, 126.91, 125.46, 21.67; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{14}ClO]^+$ 257.0728; Found 257.0726.

Compound 7a: 1-phenylpent-1-yn-3-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 3% ethyl acetate: *n*-hexane as an eluent. Yield: 30%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.40 (m,2H), 7.30 – 7.28 (m, 3H), 4.54 (t, *J* = 6.4 Hz, 1H), 2.05 (br, 1H), 1.87 – 1.76 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.77, 128.45, 128.36, 122.72, 89.98, 85.00, 64.31, 31.05, 9.60.

Compound 7b: 1-phenylhex-1-yn-3-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-hexane as an eluent. Yield: 35%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.40 (m, 2H), 7.31 – 7.28 (m, 3H), 4.62 – 4.58 (m, 1H), 1.99 (d, *J* = 5.2 Hz, 1H), 1.84 – 1.71 (m, 2H), 1.59 – 1.49 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.76, 128.44, 128.36, 122.73, 90.26, 84.89, 62.86, 40.05, 18.60, 13.89.

Compound 7c: 4-methyl-1-phenylpent-1-yn-3-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-hexane as an eluent. Yield: 85%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.43 (m, 2H), 7.31 – 7.27 (m, 3H), 4.41 (d, *J* = 5.6 Hz, 1H), 2.68 (br, 1H), 2.04 – 1.93(m, 1H), 1.07 (dd, *J* = 12.8, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.81, 128.40, 128.38, 122.89, 89.14, 85.63, 68.40, 34.78, 18.39, 17.67.

Compound 7d: 4-(3-methoxyphenyl)-2-methylbut-3-yn-2-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 89%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 1H), 7.00 – 6.97 (m, 1H), 6.93 – 6.92 (m, 1H), 6.85 – 6.82 (m, 1H), 3.75 (s, 3H), 2.75 (br, 1H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.28, 129.41, 124.27, 123.86, 116.48, 114.96, 93.85, 82.06, 65.61, 55.31, 31.54; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{12}H_{15}O_2]^+$ 191.1067; Found 191.1065.

Compound 7e: 1-(3-methoxyphenyl)-3-methylhex-1-yn-3-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 29%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8.0, 1H), 7.01 – 6.97 (m, 1H), 6.93 – 6.92 (m, 1H), 6.85 (ddd, *J* = 8.4, 2.8, 0.8 Hz, 1H), 3.78 (s, 3H), 1.93 (br, 1H), 1.75 – 1.68 (m, 2H), 1.61 – 1.52 (m, 5H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.33, 129.40, 124.27, 123.86, 116.52, 114.91, 92.82, 83.27, 68.71, 55.36, 46.10, 29.93, 18.22, 14.35; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{14}H_{19}O_2]^+$ 219.1380; Found 219.1382.

Compound 7f: 1-((3-methoxyphenyl)ethynyl)cyclobutan-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 73%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 8.0, 1H),7.09 – 6.99 (m, 1H), 6.98 – 6.84 (m, 2H), 3.78 (s, 3H), 2.55 – 2.24 (m, 5H), 1.90 – 1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.33, 129.44, 124.30, 123.79, 116.52, 115.05, 92.42, 83.43, 68.37, 55.36, 38.68, 13.07; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{13}H_{15}O_2]^+$ 203.1067; Found 203.1065.

Compound 7g: 1-(phenylethynyl)cyclopentan-1-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 60%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 7.30 – 7.27 (m, 3H), 2.09 – 1.98 (m, 5H), 1.93 – 1.83 (m, 2H), 1.82 – 1.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.70, 128.33, 128.25, 122.97, 92.99, 83.18, 74.99, 42.61, 23.60.

Compound 7h: 1-(phenylethynyl)cyclohexan-1-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 96%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 7.30 – 7.27 (m, 3H), 2.49 (br, 1H), 2.02 – 1.99 (m, 2H), 1.77 – 1.54 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.76, 128.33, 128.27, 123.01, 92.96, 84.45, 69.22, 40.13, 25.31, 23.53.

Compound 7i: 1-((3-methoxyphenyl)ethynyl)cycloheptan-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 63%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8.0, 1H), 7.02 – 6.99 (m, 1H), 6.93 – 6.83 (m, 2H), 3.78 (s, 3H), 2.16 – 2.07 (m, 3H), 1.93 – 1.87 (m, 2H), 1.74 – 1.58 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.32, 129.40, 124.29, 124.02, 116.54, 114.85, 93.78, 83.56, 72.29, 55.35, 43.26, 28.08, 22.40; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{16}H_{21}O_2]^+$ 245.1536; Found 245.1538.

Compound 7j: 1-((3-methoxyphenyl)ethynyl)cyclooctan-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-hexane as an eluent. Yield: 47%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8.0, 1H), 7.09 – 6.92 (m, 2H), 6.91 – 6.83 (m, 1H), 3.78 (s, 3H), 2.08 – 1.95 (m, 4H), 1.70 – 1.49 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ159.32, 129.38, 124.32, 124.00, 116.56, 114.85, 93.63, 83.30, 71.89, 55.36, 38.40, 28.00, 24.57, 22.26; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{17}H_{23}O_2]^+$ 259.1693; Found 259.1692.

Compound 7k: 2-(phenylethynyl)adamantan-2-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 2% ethyl acetate: *n*-hexane as an eluent. Yield: 81%; Solid, m.p. 104–106 ºC;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 7.30 – 7.27 (m, 3H), 2.21 (d, *J* = 12.0 Hz, 4H), 2.08 – 2.03 (m, 3H), 1.87 – 1.78 (m, 4H), 1.71 (s, 2H), 1.66 – 1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.69, 128.32, 128.19, 123.12, 93.82, 84.92, 73.00, 39.06, 37.69, 35.68, 31.74, 26.99, 26.84; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{18}H_{21}O]^+$ 253.1587; Found 253.1586.

Compound 9a: 3-phenylprop-2-yn-1-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 92%; Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H), 7.33 – 7.28 (m, 3H), 4.49 (s, 2H), 1.91 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.81, 128.57, 128.44, 122.71, 87.52, 85.63, 51.44.

Compound 9b: 3-(p-tolyl)prop-2-yn-1-ol[21]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 90%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 2H), 4.52 (s, 2H), 2.35 (s, 3H), 1.74 (br, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ138.69, 131.69, 129.17, 119.58, 86.73, 85.84, 51.66, 21.56.

Compound 9c: 3-(o-tolyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 87%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.6 Hz, 1H), 7.24 – 7.18 (m, 2H), 7.12 (dt, *J* = 7.2, 2.0 Hz, 1H), 4.53 (s, 2H), 2.42 (s, 3H), 1.78 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.35, 132.16, 129.53, 128.60, 125.63, 122.35, 91.10, 84.68, 51.85, 20.75; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{10}H_{11}O]^+$ 147.0805; Found 147.0802.

Compound 9d: 3-(2-methoxyphenyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 15% ethyl acetate: *n*-Hexane as an eluent. Yield: 99%; Solid; m.p. 69–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 7.6, 16 Hz, 1H), 7.31 – 7.26 (m, 1H),6.91 – 6.85 (m, 2H), 4.53 (s, 2H), 3.87 (s, 3H), 1.81 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.04, 133.89, 130.11, 120.57, 111.65, 110.63, 91.43, 82.03, 55.85, 51.99; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{10}H_{11}O_2]^+$ 163.0754; Found 163.0755.

Compound 9e: 3-(3-methoxyphenyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 15% ethyl acetate: *n*-Hexane as an eluent. Yield: 93%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 8.0, 1H), 7.03 – 7.01 (m, 1H), 6.97 – 6.94 (m, 1H), 6.87 (ddd, *J* = 8.4, 2.8, 0.8 Hz, 1H), 4.48 (s, 2H), 3.78 (s, 3H), 1.94 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.34, 129.50, 124.29, 123.58, 116.61, 115.16, 87.12, 85.68, 55.36, 51.70; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{10}H_{11}O_2]^+$ 163.0754; Found 163.0756.

Compound 9f: 3-(4-methoxyphenyl)prop-2-yn-1-ol[5b]

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 87%; Solid; m.p. 51–53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.34 (m, 2H), 6.83 – 6.81 (m, 2H), 4.47 (s, 2H), 3.79 (s, 3H), 1.80 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.82, 133.27, 114.66, 114.03, 85.92, 85.74, 55.37, 51.81.

Compound 9g: 3-(4-bromophenyl)prop-2-yn-1-ol

The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 91%; Solid; m.p. 81–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H), 7.29 – 7.26 (m, 2H), 4.47 (s, 2H), 1.77 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.20, 131.70, 122.90, 121.54, 88.39, 84.76, 51.71; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_9H_8BrO]^+$ 210.9753; Found 210.9752.

Compound 9h: 3-(2-bromophenyl)prop-2-yn-1-ol
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 96%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.16 (dt, *J* = 8.0, 2.0 Hz,1H), 4.54 (s, 2H), 1.84 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.64, 132.50, 129.78, 127.12, 125.52, 124.72, 91.89, 84.29, 51.79; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_9H_8BrO]^+$ 210.9753; Found 210.9752.

Compound 9i: 3-(2-chlorophenyl)prop-2-yn-1-ol
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 10% ethyl acetate: *n*-Hexane as an eluent. Yield: 85%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.26 – 7.17 (m, 2H), 4.54 (s, 2H), 2.06 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.94, 133.59, 129.64, 129.35, 126.56, 122.52, 92.52, 82.48, 51.73; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_9H_8ClO]^+$ 167.0258; Found 167.0257.

Compound 9j: 3-(pyridin-2-yl)prop-2-yn-1-ol
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 80% ethyl acetate: *n*-Hexane as an eluent. Yield: 45%; Solid, mp 91–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 – 8.52 (m, 1H), 7.65 – 7.61 (m, 1H), 7.42 – 7.40 (m, 1H), 7.24 – 7.22 (m, 1H), 4.53 (s, 2H), 4.00 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.75, 142.81, 136.58, 127.29, 123.19, 88.68, 84.14, 51.08; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_8H_8NO]^+$ 134.0601; Found 134.0605.

1-(3-oxo-1,3-diphenylpropyl)pyrrolidine-2,5-dione (10):[25b]
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 12% ethyl acetate: *n*-hexane as an eluent. Yield: 73%; Viscous oil;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.94 (m, 2H), 7.58 – 7.52 (m, 3H), 7.46 – 7.43 (m, 2H), 7.36 – 7.26 (m, 3H), 5.87 (dd, *J* = 10.0, 4.8 Hz, 1H), 4.58 (dd, *J* = 18.4, 10.0 Hz, 1H), 3.65 (dd, *J* = 18.4, 4.8 Hz, 1H), 2.62 (d, *J* = 1.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.04, 177.42, 138.89, 136.45, 133.56, 128.85, 128.78, 128.33, 128.16, 128.12, 51.28, 39.24, 28.10.

3-(4-methoxyphenyl)-1,5-diphenyl-4,5-dihydro-1H-pyrazole (11):
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 15% ethyl acetate: *n*-hexane as an eluent. Yield: 55%; Solid; m.p. 104–106 ºC;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.69 (m, 2H), 7.39 – 7.31 (m, 3H), 7.24 – 7.14 (m, 4H), 7.07 – 7.05 (m, 2H), 6.86 – 6.74 (m, 3H), 5.24 – 5.19 (m, 1H), 3.84 – 3.76 (m, 1H), 3.76 (s, 3H), 3.11 (dd, *J* = 16.8, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.05, 146.81, 144.97, 134.74, 132.90, 130.16, 128.96, 128.62, 127.14, 125.80, 119.13, 114.56, 113.50, 64.10, 55.35, 43.70.

3-(4-methoxyphenyl)-5-(p-tolyl)-4,5-dihydroisoxazole (12):
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 5% ethyl acetate: *n*-hexane as an eluent. Yield: 45%; Solid; m.p. 118–120 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.66 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.79 (s, 3H), 3.70 (dd, *J* = 16.8, 10.8 Hz, 1H), 3.32 – 3.26 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.66, 156.25, 140.41, 132.99, 129.50, 127.46, 126.74, 114.18, 82.40, 55.41, 43.14, 21.53; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{17}H_{18}NO_2]^+$ 268.1332; Found 268.1333.

3-(4-methoxyphenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole (13):
The crude product was purified by column chromatography over silica gel (100-200 mesh) using 15% ethyl acetate: *n*-hexane as eluent. Yield: 37%; Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.37 – 7.34 (m, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.91 – 6.88 (m, 2H), 5.27 (t, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.32 (d, *J* = 6.1 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.06, 159.18, 144.65, 135.29, 134.24, 129.47, 128.37, 127.12, 114.01, 69.83, 55.39, 47.24, 21.78; HRMS (ESI/QTOF) m/z: $[M+H]^+$ Calcd for $[C_{17}H_{19}N_2O]^+$ 267.1492; Found 267.1491.

ASSOCIATED CONTENT

Supporting Information
Optimization Tables S1 & S2, ^{1}H NMR and ^{13}C NMR spectra of all compounds **4a-c**, **5a-u**, **7a-k**, **9a-j** and **10-13** are presented in the Supporting Information and available free of charge on the journal website.

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Notes
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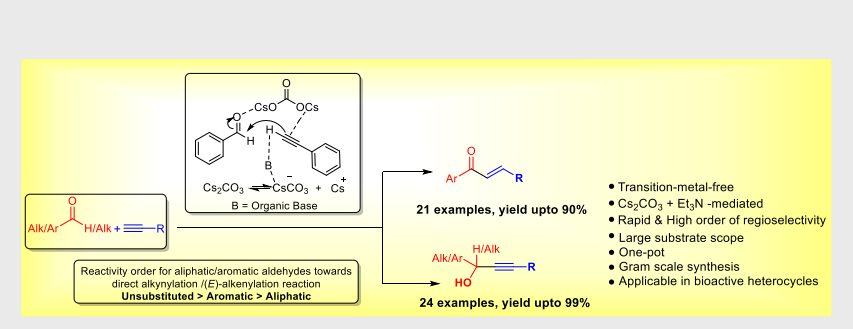

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Weak bases-Mediated Modified Favorskii Reaction Type Direct Alkynylation/(*E*)-Alkenylation: A Unified Rapid Access to *α,β*-Unsaturated Ketones and Propargyl Alcohols

A fast and efficient, transition-metal-free Cs_2CO_3-Et_3N mediated direct alkynylation as well as (*E*)-alkenylation *via* allenol-enone isomerization sequence under mild basic conditions has been developed.