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KOAc-promoted alkynylation of α-C–H bonds of ethers with alkynyl bromides under transition-metal-free conditions†

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A novel KOAc-promoted α-position C–H activation and alkynylation of ethers with alkynyl bromides to 2-alkynyl ethers has been developed under transition-metal-free and simple reaction conditions. In addition, this methodology can also be extended to the vinylation of ethers with vinyl bromides in excellent regio- and stereo-selectivity. A wide range of direct C(sp)–C(sp³) and C(sp³)–C(sp³) bonds has been formed through this protocol, which offers a new and alternative route.

Introduction

The transition-metal catalyzed direct conversion of C–H bonds into C–C bonds has been one of the most attractive subjects in contemporary organic chemistry. In the past decades, significant efforts have been focused on C–H activation and functionalization, and various high efficiency and versatile protocols have been explored.1 Despite remarkable advances achieved in this field, critical issues such as stoichiometric amounts of metal waste and the presence of metal impurities in the final product may restrict their practical applicability. Hence, the green and economical platform for mediating organic transformations is demanded. Recently, Itami, Kwong/Lei, Shi, and Shirakawa/Hayashi have reported the astonishing results on the construction of C–C bond from unactivated aromatic rings by direct C–H activation without the aid of transition metal,2 and these breakthroughs maybe brought a new era of organic synthesis.3 From the viewpoint of green chemistry, the organic reactions carried out under transition-metal-free conditions with avoiding metal contamination in the final products has been paid much attention in modern organic synthesis, especially in the pharmaceutical industry. In the past two years, a variety of protocols for the direct C–H bond activation and functionalization in the absence of transition-metal have been established.4 The representative system is KOBu,tBu,2b,c,4b,4k,4r or NaOtBu4d in the presence of an effective ligand except one example.5

Substituted tetrahydrofurans are not only valuable building blocks in organic synthesis, but also are ubiquitous motifs present in biological, pharmaceuticals and natural products.6 In general, they are usually accessible through the α-C(sp³)–H activation/functionalization of tetrahydrofuran (THF),6 such as Ni-catalyzed arylation of THF,7 Fe(II)-catalyzed CDC reaction of THF with malonates,8 Cu- and Ir-catalyzed carbeneinsertion of ethyl diazoacetate into α-C–H of THF,9 Cr-promoted reaction of alcohols with THF to 2-tetrahydrofuranyl ethers,10 AIBN-mediated alkenylation of THF with vinyl triflones,11 TBHP-promoted reaction of phenylacetylene with THF to allylic ether,12 and BEt₂- and Me₂Zn-mediated addition of THF with aldehydes and aldimes under air, respectively.13 2-Alkynyl cyclic ethers, potential structural motifs of bioactive molecules and materials, have been successfully prepared by region-specific α-position alkynylation of cyclic ethers.14-16 In 1988, Ley converted 2-benzensulphonyl cyclic ethers to 2-alkynyl tetrahydrofuran by treatment with the corresponding organozinc agents (Scheme 1).14 In 1996, Fuchs developed a synthetic strategy of 2-alkynyl cyclic ethers through the alkynylation of α-position C–H bond in cyclic ethers with acetylenic triflones under peroxide or AIBN or UV-irradiation.15 Most recently, Anderson reported an efficient

![Scheme 1 Preparation of 2-alkynyl tetrahydrofurans.](image-url)
Encouraged by the above transformations, and in continuation of our and others interests in transformation of C(sp)–H bond
into C(sp$^3$)–C bond,$^{17}$ we conceived that alkynylation of α-position C–H bond of ethers with alkynyl bromides without the
assistance of transition metal may be possible. Herein, we wish to
report an efficient reaction of alkynyl bromides with cyclic ethers
for direct C(sp)–C(sp$^3$) bond formation through KOAc-promoted
α-position C–H activation and alkynylation of ethers under transition-metal-free and simple reaction conditions (Scheme 1).
Moreover, this methodology can also be extended to the
vinylation of α-C–H bond, providing excellent regio- and stereo-selectivity.

**Results and discussion**

In the initial investigation of the reaction of alkynyl bromides
to ethers, phenylethynyl bromide (1a) and tetrahydrofuran (THF, 2a) were chosen as model substrates. When the model reaction
was carried out in the presence of Na$_2$CO$_3$ at 150 °C in a sealed
pressure tube for 12 h without additional solvent, a direct
alkynylation product (3a) of THF via α-position C–H bond
activation was isolated in 59% yield (Table 1, entry 1).

**Table 1** Effect of base and catalyst on the reaction.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Catalyst</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Na$_2$CO$_3$</td>
<td>–</td>
<td>59</td>
</tr>
<tr>
<td>2</td>
<td>Na$_2$CO$_3$</td>
<td>Pd(OAc)$_2$</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>Na$_2$CO$_3$</td>
<td>Cu</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>Na$_2$CO$_3$</td>
<td>AgBF$_3$</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>KOAc</td>
<td>–</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>NaOAc</td>
<td>–</td>
<td>74</td>
</tr>
<tr>
<td>7</td>
<td>NaHCO$_3$</td>
<td>–</td>
<td>52</td>
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<tr>
<td>8</td>
<td>(NH$_2$)$_2$CO$_3$</td>
<td>–</td>
<td>47</td>
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<tr>
<td>9</td>
<td>K$_2$CO$_3$</td>
<td>–</td>
<td>43</td>
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<td>10</td>
<td>KHCO$_3$</td>
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<td>42</td>
</tr>
<tr>
<td>11</td>
<td>Cs$_2$CO$_3$</td>
<td>–</td>
<td>32</td>
</tr>
<tr>
<td>12</td>
<td>K$_2$PO$_4$</td>
<td>–</td>
<td>21</td>
</tr>
<tr>
<td>13</td>
<td>NaF</td>
<td>–</td>
<td>18</td>
</tr>
<tr>
<td>14</td>
<td>KF</td>
<td>–</td>
<td>13</td>
</tr>
<tr>
<td>15</td>
<td>LiOBF$_4$</td>
<td>–</td>
<td>NR</td>
</tr>
<tr>
<td>16</td>
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<tr>
<td>19</td>
<td>NaOH</td>
<td>–</td>
<td>NR</td>
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<tr>
<td>20</td>
<td>Et$_3$N</td>
<td>–</td>
<td>NR</td>
</tr>
<tr>
<td>21</td>
<td>DBU</td>
<td>–</td>
<td>NR</td>
</tr>
<tr>
<td>22</td>
<td>DABCO</td>
<td>–</td>
<td>NR</td>
</tr>
<tr>
<td>23</td>
<td>–</td>
<td>–</td>
<td>32</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 1a (0.30 mmol), 2a (2.0 mL, excess, as well as solvent), catalyst (5.0 mol%) if needed, base (0.60 mmol), at 150 °C for
12 h. $^b$Isolated yield.

Encouraged by this positive result, further investigation on the
addition of transition metal to the reaction was examined.
Unfortunately, transition metals, such as Pd(OAc)$_2$, Cu, and
AgBF$_3$ completely shut down the reaction (Table 1, entries 2–4). To improve the desired product yield, detailed
investigation about the effect of base on the reaction was
examined. To our delight, KOAc exhibited the highest
reactivity to the reaction among the tested bases, providing
93% yield of 3a (Table 1, entry 5). Other bases, such as
NaOAc, NaHCO$_3$, (NH$_2$)$_2$CO$_3$, K$_2$CO$_3$, KHCO$_3$, Cs$_2$CO$_3$, K$_2$PO$_4$, NaF, and KF were inferior and generated 3a in
13–74% yields (Table 1, entries 6–14). However, when the reaction was performed in the presence of LiOBF$_4$, NaOBF$_4$, KOBF$_4$, KOH, NaOH, Et$_3$N, DBU, or DABCO as base, no 3a was detected and starting materials were unchanged and
recovered (Table 1, entries 15–22). However, only 32% yield
of 3a was generated in the absence of any base, catalyst and
additive (Table 1, entry 23).

To further examine the effect of ligand for the improvement of model reaction, L-proline, N,N,N’,N’-tetramethylthielenediamine (TMEDA), 1,10-phenanthroline (1,10-Phen) and 2,2’-bipyridine (Bipy), 8-hydroxyquinoline (8-HQ), and 1,1’-bis(diphenylphosphino)ferrocene (Dppf)
were added to the KOAc, NaOAc or LiOAc system to promote the reaction, but failed (Table S1, Supplementary Information, entries 1–18).

With respect to the base loading, 2 equiv. of KOAc was found to be optimal. When the model reaction was carried out in the presence of KOAc, a significant reaction temperature
effect was observed. When the reaction was performed at less
than 100 °C, poor yields of 3a were obtained. The optimal
temperature was found to be 150 °C (Table 2, entries 1–7).

**Table 2** Effect of temperature on the model reaction.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Yield (%) $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>22</td>
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<td>3</td>
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<td>5</td>
<td>150</td>
<td>93</td>
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<tr>
<td>6</td>
<td>160</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>170</td>
<td>90</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 1a (0.30 mmol), 2a (2.0 mL, excess), KOAc (0.60 mmol) at the temperature indicated in this table for 12 h. $^b$Isolated yield.

The final investigation revealed that additional solvent,
such as DMF, DMA, NMP, DMSO, CH$_3$CN, HOAc, CH$_3$CH$_2$OH, CH$_3$NO$_2$, DCE (1,2-dichloroethane) or toluene has a great negative effect on the reaction (Table 3, entries 1–10). The optimized reaction conditions for the model
reaction were in the presence of KOAc at 150 °C for 12 h.
Table 3 Effect of solvent on the model reaction.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent/Temp. (°C)</th>
<th>Yield (%)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMF/150</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>DMA/150</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>NMP/150</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>DMSO/150</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>CH\textsubscript{3}CN/100</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>HOAc/100</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>CH\textsubscript{3}CH\textsubscript{2}OH/100</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>CH\textsubscript{3}NO\textsubscript{2}/100</td>
<td>NR</td>
</tr>
<tr>
<td>9</td>
<td>DCE/100</td>
<td>13</td>
</tr>
<tr>
<td>10</td>
<td>Toluene/150</td>
<td>Trace</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: 1a (0.30 mmol), 2a (2.0 mL, excess), KOAc (0.60 mmol), solvent (2.0 mL) at the temperature indicated in this table for 12 h. \textsuperscript{b}Isolated yield.

With the optimized reaction conditions in our hand, a variety of substituted phenylethynyl bromides were selected to couple with tetrahydrofuran for the synthesis of 2-alkynyltetrahydrofurans (Scheme 2). Pleasingly, phenylethynyl bromides with electron-donating groups, such as MeO, Me, Et, \textsuperscript{3}Pr and \textsuperscript{4}Bu, at the para-, meta-, or ortho-positions of phenyl rings, underwent the reaction smoothly with THF (2a), generating the corresponding products 3b–g in good yields (75–86%). Meanwhile, phenylethynyl bromides with electron-withdrawing groups, such as CH\textsubscript{3}CO and F\textsubscript{3}C also proceeded well with THF to afford the desired products 3h and 3i in 74% and 76% yields, respectively. Moreover, substrates with halogen substituents such as F, Cl, and Br could be well transformed into the target products 3j–l in good yields. In addition, ortho-substituents could also be well tolerated in this reaction (3m and 3n).

Considering the importance of direct functionalization of different ethers, other simple ethers were also tested to couple with phenylethynyl bromide derivatives under optimized conditions (Scheme 3). 2-Methyl tetrahydrofuran was firstly tested to couple with different phenylethynyl bromides. We were surprised to find that reaction selectively occurred at methyne group, affording the corresponding products in good yields and excellent regio-selectivity (3o–q). Tetrahydroprpyran and 1,4-dioxane were also found to react smoothly with phenylethynyl bromide or (4-tert-butylphenyl)ethynyl bromide to generate the alkynylation products 3r–t in moderate yields. Moreover, when benzene fused tetrahydrofurans, such as 2,3-dihydrobenzofuran and 1,3-dihydroisobenzofuran were employed, the anticipated products, 3u and 3v were obtained in 55% and 46% yields, respectively. Notably, this methodology could also be extended to chain-like ethers. 1,2-Dimethoxyethane reacted smoothly with 1a to afford the corresponding product 3w in moderate yield, along with excellent regio-selectivity. In addition, the substrate scope of alkyne bromide was extended into aliphatic alkyne bromides, such as 1-(bromoethyl)cyclohexanol and 1-bromohept-l-yne, and the satisfactory results were achieved (Scheme 3, 3x and 3y).

Scheme 2 KOAc-promoted direct alkynylation of tetrahydrofuran under transition-metal free conditions. Reaction conditions: 1 (0.30 mmol), 2a (2.0 mL, excess, as well as solvent), KOAc (0.60 mmol), at 150 °C for 12 h; isolated product yields after chromatography.

Scheme 3 KOAc-promoted direct alkynylation of other simple ethers under transition-metal free conditions. Reaction conditions: 1 (0.30 mmol), 2 (2.0 mL, excess, as well as solvent), KOAc (0.60 mmol), at 150 °C for 12 h; isolated product yields after chromatography.
Additionally, the region-selectivity of direct alkynylation of 1,3-dioxolane with phenylethynyl bromide was investigated under the present reaction conditions. The results showed that 82% total yield of 3x and 3x' was isolated with a ratio of 65:17 (Scheme 4), which indicated that stability of free radicals plays an important role in this reaction.

Later on, the vinylation of α-C–H bonds of ethers with vinyl bromides was also examined, and the results were shown in Scheme 4. When a mixture of cis- and trans-(2-bromovinyl)benzene (1:5) reacted with tetrahydrofuran and 2-methyltetrahydrofuran to generate the corresponding products 5a and 5b in moderate yields respectively with excellent regio- and stereo-selectivity. When prepared (Z)-2-bromovinyl phenyl ethers, 4b and 4c reacted with THF under the optimized reaction conditions, providing the corresponding exclusive (Z)-type products 5c and 5d (Scheme 5) in moderate yields. It also provides an effective and alternative route to vinyl cycloethers with excellent regio- and stereo-selectivity. Moreover, a representative structure of 5d was confirmed by X-ray single crystal analysis.

To investigate the reaction mechanism, the related experiments were performed. When a radical scavenger, 2,2,6,6-tetramethylpiperidyl-1-oxyl (TEMPO, 1.5 equiv) was added to the standard reaction system, the reaction was completely shut down, along with formation of radical-trapping product, detected by GC/MS (See ESI for detail), suggesting that a carbon-centered radical of THF is probably involved in this reaction. In addition, when reaction was carried out under strictly anhydrous and anaerobic conditions, no any product was detected and only starting materials were recovered, and added peroxide (such as H₂O₂) could improved the reaction significantly. Based on the experimental results, a proposed mechanism of KOAc-promoted direct C–H alkynylation of simple ethers was depicted in Scheme 6. Firstly, tetrahydrofuran radical (I) was generated in the presence of small amounts of peroxide in THF (2a). Subsequently, a radical addition of the obtained (I) to phenylethynyl bromide (1a) underwent smoothly to afford a bromovinyl radical (II), which generated a bromine free radical and the final product (3a) through a bromine radical elimination process. Finally, the bromine radical abstracted a hydrogen radical from THF (2a) to generate intermediate (I) with the aid of a suitable base (KOAc).

**Scheme 4** Region-selectivity investigation of direct alkynylation of 1,3-dioxolane with phenylethynyl bromide.

**Scheme 5** Direct vinylation of α-C–H bonds of ethers with vinyl bromides.

**Scheme 6** Proposed reaction mechanism.

**Conclusion**

In conclusion, we have established a novel Csp–Csp³ bond formation through KOAc-promoted direct C–H alkynylation of simple ethers under transition-metal free and simple reaction conditions. Different substituted phenylethynyl bromides and common simple ethers could be cross-coupled smoothly to afford the corresponding products in good to excellent yields. In addition, this methodology can also be extended to the direct C–H vinylation of ethers with excellent regio- and stereo-selectivity. A wide range of direct Csp–Csp³ and Csp²–Csp³ bonds could be constructed through this protocol, offering a brand-new and alternative route for the synthesis of 2-alkynyl- and 2-alkenylethers. Further detailed investigation of reaction mechanism and application of this kind of strategy is underway in our laboratory.

**Experimental Section**

All the bromoalkynes, and bromo alkenes, such as (Z)-2-bromovinyl phenyl ethers, 4b and 4c as starting materials were...
prepared according to the reported procedure in the literature. All the chemicals and solvents were purchased from commercial suppliers and used without further purification. All reactions were carried out under air. 1H NMR and 13C NMR spectra were measured on a Bruker Avance NMR spectrometer (400 MHz or 100 MHz, respectively) in CDCl3 as solvent and recorded in ppm relative to internal tetramethylsilane standard. 1H NMR data are reported as follows: δ, chemical shift; coupling constants (J) are given in Hertz, Hz) and integration.

Abbreviations to denote the multiplicity of a particular signal were s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad singlet). High resolution mass spectroscopic data of the products were collected on a Waters Micromass GCT instrument using EI (70 eV) or an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS using ESI.

Typical procedure for KOAc-promoted alkynylation of α,C–H bonds of ethers with alkanyl bromides

Under air atmosphere, a 10 mL oven-dried sealable reaction vessel equipped with a magnetic stir bar charged with phenylethynyl bromide (1a, 54.3 mg, 0.30 mmol), KOAc (59 mg, 0.36 mmol) and tetrahydrofuran (THF, 2a, 2.0 mL, excess, as well as solvent) were added to the sealed vessel in one portion. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 150 °C for 12 h. After the reaction was completed, it was cooled to room temperature and diluted with ethyl acetate. The resulting solution was directly filtered through a pad of silica gel using a sintered glass funnel, and the residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 10:1 to 25:1, V/V) to obtain the desired pure product, 2-(phenylethynyl)tetrahydrofuran (3a).

2-(Phenylethynyl)tetrahydrofuran (3a): Colorless oil. 1H NMR (400 MHz, CDCl3) δ: 7.45–7.43 (m, 2H), 7.30–7.29 (m, 3H), 4.83–4.80 (m, 1H), 4.05–3.99 (m, 1H), 3.89–3.83 (m, 1H), 2.26–2.19 (m, 1H), 2.13–2.04 (m, 2H), 1.98–1.92 (m, 1H); 13C NMR (100 MHz, CDCl3) δ: 131.70, 128.24, 128.21, 122.83, 124.29, 124.27, 123.87, 89.11, 84.66, 86.60, 67.92, 33.42, 25.50. HRMS (EI) ([M]+) Calcd. For C10H12O: 172.0888, Found: 172.0883.

2-(4-Methoxyphenylethynyl)tetrahydrofuran (3b): Colorless oil. 1H NMR (400 MHz, CDCl3) δ: 7.37 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 4.82–4.79 (m, 1H), 4.04–3.99 (m, 1H), 3.88–3.85 (m, 1H), 3.80 (s, 3H), 2.25–2.19 (m, 1H), 2.13–2.03 (m, 2H), 1.99–1.92 (m, 1H); 13C NMR (100 MHz, CDCl3) δ: 159.55, 133.16, 114.90, 113.82, 87.59, 84.37, 68.69, 67.88, 55.25, 33.45, 25.51. HRMS (EI) ([M]+) Calcd. For C10H12O2: 202.0994, Found: 202.0990.

2-(p-Tolyethynyl)tetrahydrofuran (3c): Colorless oil. 1H NMR (400 MHz, CDCl3) δ: 7.33 (d, J = 0.8 Hz, 2H), 7.11 (d, J = 7.6 Hz, 2H), 4.83–4.80 (m, 1H), 4.05–3.99 (m, 1H), 3.89–3.84 (m, 1H), 2.34 (s, 3H), 2.26–2.20 (m, 1H), 2.13–2.04 (m, 2H), 1.99–1.92 (m, 1H); 13C NMR (100 MHz, CDCl3) δ: 138.33, 131.61, 128.97, 119.71, 88.31, 84.59, 68.66, 67.91, 33.44, 25.51, 21.46. HRMS (ESI) ([M+H]+) Calcd. For C16H18O: 229.1546, Found: 229.1540.
2-((4-Fluorophenyl)ethynyl)tetrahydrofuran (3h):
Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.42–7.39 (m, 2H), 7.00–6.96 (m, 2H), 4.80–4.77 (m, 1H), 4.03–3.97 (m, 1H), 3.88–3.82 (m, 1H), 2.25–2.18 (m, 1H), 2.10–2.05 (m, 2H), 1.98–1.91 (m, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$: 162.46 (d, $J_{CF} = 247.8$ Hz), 133.58 (d, $J_{CF} = 8.3$ Hz), 118.90 (d, $J_{CF} = 3.5$ Hz), 115.45 (d, $J_{CF} = 21.9$ Hz), 88.78, 83.39, 68.51, 67.93, 33.36, 25.49. HRMS (EI) ([M]$^+$) Calcd. For C$_{13}$H$_7$FO: 190.0794, Found: 190.0793.

2-((4-Chlorophenyl)ethynyl)tetrahydrofuran (3i):
Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.41 (d, $J = 8.4$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 4.81–4.78 (m, 1H), 4.03–3.98 (m, 1H), 3.89–3.83 (m, 1H), 2.26–2.20 (m, 1H), 2.12–2.03 (m, 2H), 2.00–1.91 (m, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$: 134.28, 132.93, 128.54, 121.32, 90.10, 83.35, 68.51, 67.99, 33.34, 25.50. HRMS (EI) ([M]$^+$) Calcd. For C$_{13}$H$_7$ClO: 206.0498, Found: 206.0501.

2-((4-Bromophenyl)ethynyl)tetrahydrofuran (3j):
Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.43 (d, $J = 8.4$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 2H), 4.81–4.78 (m, 1H), 4.04–3.98 (m, 1H), 3.89–3.84 (m, 1H), 2.27–2.20 (m, 1H), 2.13–2.05 (m, 2H), 2.00–1.93 (m, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$: 133.15, 131.48, 122.49, 121.79, 90.30, 83.41, 68.52, 68.00, 33.32, 25.50. HRMS (ESI) ([M+H]$^+$) Calcd. For C$_{13}$H$_7$BrO: 251.0072, Found: 251.0072.

2-((4-Acetophenyl)ethynyl)tetrahydrofuran (3k):
Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.88 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.0$ Hz, 2H), 4.83–4.80 (m, 1H), 4.03–3.98 (m, 1H), 3.89–3.83 (m, 1H), 2.58 (s, 3H), 2.28–2.20 (m, 1H), 2.13–2.04 (m, 2H), 1.99–1.91 (m, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$: 197.25, 136.29, 131.80, 128.12, 127.70, 92.55, 83.68, 68.48, 68.06, 33.30, 26.55, 25.51. HRMS (ESI) ([M+H]$^+$) Calcd. For C$_{14}$H$_{12}$O$_2$: 215.1072, Found: 215.1071.

2-((4-Trifluoromethyl)phenyl)ethynyl)tetrahydrofuran (3l):
Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.57–7.55 (m, 2H), 7.54–7.52 (m, 2H), 4.84–4.81 (m, 1H), 4.05–3.99 (m, 1H), 3.90–3.85 (m, 1H), 2.29–2.22 (m, 1H), 2.14–2.05 (m, 2H), 2.01–1.95 (m, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$: 131.92, 129.99 (q, $J_{CF} = 32.4$ Hz), 126.64, 125.14 (q, $J_{CF} = 3.8$ Hz), 123.88 (q, $J_{CF} = 270.4$ Hz), 91.66, 83.12, 68.42, 68.07, 33.29, 25.50. HRMS (EI) ([M]$^+$) Calcd. For C$_{13}$H$_7$FO: 240.0762, Found: 240.0763.
2-((4-Chlorophenyl)ethynyl)-2-methyltetrahydrofuran (3q): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): δ: 7.34 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 4.03–3.94 (m, 2H), 2.31–2.26 (m, 1H), 2.18–2.09 (m, 1H), 2.03–1.97 (m, 1H), 1.90–1.83 (m, 1H), 1.63 (s, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ: 133.96, 132.80, 128.39, 121.39, 93.28, 81.51, 76.23, 67.61, 39.99, 27.56. HRMS (EI) (M$^+$) Calcd. For C$_{14}$H$_{14}$O: 200.1201, Found: 200.1199.

1-(4-((1,3-Dihydroisobenzofuran-1-yl)ethynyl)phenyl)ethanone (3v): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): δ: 7.89 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 8.2$ Hz, 2H), 7.45–7.43 (m, 1H), 7.37–7.35 (m, 2H), 7.29–7.27 (m, 1H), 6.14 (s, 1H), 5.31–5.28 (m, 1H), 5.16–5.13 (m, 1H), 2.59 (s, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ: 197.16, 138.74, 138.60, 136.39, 131.85, 128.24, 128.02, 127.78, 127.22, 121.75, 121.06, 90.39, 85.10, 73.69, 72.91, 26.48. HRMS (EI) (M$^+$) Calcd. For C$_{18}$H$_{14}$O$_2$: 262.0994, Found: 262.0999.

(3,4-Dimethoxybut-1-yn-1-yl)benzene (3w): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): δ: 7.47–7.45 (m, 2H), 7.33–7.32 (m, 3H), 4.45–4.41 (m, 1H), 3.69–3.66 (m, 2H), 3.54 (s, 3H), 3.47 (s, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ: 131.82, 128.56, 128.28, 122.34, 86.85, 84.86, 74.92, 71.07, 59.37, 56.89. HRMS (ESI) (M$^+$+H$^+$) Calcd. For C$_{16}$H$_{14}$O$_2$: 262.0994, Found: 262.0999.

1-((Tetrahydrofuran-2-yl)ethynyl)cyclohexanol (3x): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): δ: 4.63–4.61 (m, 1H), 3.97–3.92 (m, 1H), 3.83–3.80 (m, 1H), 2.74–2.21 (m, 5H), 1.68–1.66 (m, 2H), 1.58–1.50 (m, 4H), 1.24–1.21 (m, 2H); $^1$C NMR (100 MHz, CDCl$_3$): δ: 88.84, 83.90, 68.42, 68.03, 67.64, 39.74, 33.32, 25.21, 25.04, 23.21.

1-(4-((2,3-Dihydrobenzofuran-2-yl)ethynyl)phenyl)ethanone (3u): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): δ: 7.90 (d, $J = 8.4$ Hz, 2H), 7.50 (d, $J = 8.0$ Hz, 2H), 7.41 (d, $J = 7.2$ Hz, 1H), 7.23–7.19 (m, 1H), 6.98–6.95 (m, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 4.87–4.83 (m, 1H), 4.65–4.61 (m, 1H), 4.56–4.52 (m, 1H), 2.60 (s, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ: 191.1072, 138.74, 138.60, 136.39, 131.98, 131.60, 125.27, 119.01, 86.70, 83.59, 70.49, 66.55, 66.38, 65.84, 34.78, 31.13. HRMS (EI) (M$^+$) Calcd. For C$_{15}$H$_{13}$O: 244.1463, Found: 244.1468.
2-(Phenylethynyl)-1,3-dioxolane (3z): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.48–7.46 (m, 2H), 7.36–7.32 (m, 3H), 5.90 (s, 1H), 4.17–4.13 (m, 2H), 4.01–3.98 (m, 2H); 13C NMR (100 MHz, CDCl₃) δ: 131.94, 128.99, 128.31, 121.60, 93.45, 85.21, 84.45, 64.61.

4-(Phenylethynyl)-1,3-dioxolane (3z): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.47–7.45 (m, 2H), 7.34–7.32 (m, 3H), 5.11 (s, 1H), 5.08 (s, 1H), 4.95 (tt, J = 6.0 Hz, 1H), 4.21–4.18 (m, 1H), 3.95–3.92 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ: 131.81, 128.73, 128.29, 122.08, 86.22, 85.65, 70.59, 65.81. HRMS (EI) ([M]+) Calcd. For C₁₁H₁₃O₂: 174.0681, Found: 174.0677.

(E)-2-Styryl-tetrahydrofuran (E-5a): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.41–7.39 (m, 2H), 7.33–7.30 (m, 2H), 7.27–7.22 (m, 1H), 6.61 (d, J = 16.0 Hz, 1H), 6.23 (dd, J = 16.0, 6.0 Hz, 1H), 4.52–4.47 (m, 1H), 4.02–3.97 (m, 1H), 3.89–3.83 (m, 1H), 2.18–2.10 (m, 1H), 2.03–1.94 (m, 2H), 1.77–1.71 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ: 136.76, 130.43, 130.32, 128.40, 127.39, 126.36, 79.56, 68.08, 32.30, 25.82.

(E)-2-Methyl-2-styryl-tetrahydrofuran (E-5b): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.41–7.39 (m, 2H), 7.34–7.30 (m, 2H), 7.25–7.21 (m, 1H), 6.57 (d, J = 16.0 Hz, 1H), 6.26 (d, J = 16.0 Hz, 1H), 3.97–3.94 (m, 2H), 2.03–1.96 (m, 3H), 1.83–1.76 (m, 1H), 1.43 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ: 137.10, 135.43, 128.38, 127.08, 126.69, 126.27, 82.29, 67.54, 37.76, 26.68, 25.63. HRMS (EI) ([M]+) Calcd. For C₁₃H₁₄O: 188.1201, Found: 188.1202.

(Z)-4-((1-Phenyl-2-(tetrahydrofuran-2-yl)vinyl)oxy)benzonitrile (5c): White solid. 1H NMR (400 MHz, CDCl₃) δ: 7.52–7.50 (m, 2H), 7.30–7.27 (m, 3H), 7.25–7.21 (m, 2H), 6.99–6.93 (m, 3H), 5.92 (d, J = 8.0 Hz, 1H), 4.80–4.74 (m, 1H), 3.97–3.92 (m, 1H), 3.80–3.75 (m, 1H), 2.12–2.07 (m, 1H), 2.01–1.87 (m, 2H), 1.72–1.67 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ: 157.11, 149.90, 134.59, 129.41, 128.33, 125.71, 121.59, 118.83, 115.70, 74.04, 67.82, 32.33, 26.04. HRMS (ESI) ([M+H]+) Calcd. For C₁₃H₁₄O₂N: 267.1385, Found: 267.2382.

(Z)-4-((1-Phenyl-2-(tetrahydrofuran-2-yl)vinyl)oxy)benzonitrile (5d): White solid. 1H NMR (400 MHz, CDCl₃) δ: 7.54 (d, J = 8.0 Hz, 2H), 7.46–7.45 (m, 2H), 7.31–7.27 (m, 3H), 7.05 (d, J = 8.0 Hz, 2H), 5.98 (d, J = 8.0 Hz 1H), 4.70–4.65 (m, 1H), 3.96–3.91 (m, 1H), 3.80–3.74 (m, 1H), 2.11–2.05 (m, 1H), 2.02–1.96 (m, 1H), 1.94–1.89 (m, 1H), 1.72–1.63 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ: 160.49, 149.13, 134.03, 133.49, 128.87, 128.62, 125.43, 119.62, 118.70, 116.49, 105.27, 73.67, 67.94, 32.33, 26.03. HRMS (ESI) ([M+H]+) Calcd. For C₁₃H₁₃NO₂: 292.1338, Found: 292.1338.

(Z)-4-(1-Phenyl-2-(tetrahydrofuran-2-yl)vinyl)oxy)benzonitrile (5d): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.45–7.39 (m, 1H), 7.37–7.34 (m, 5H), 7.15 (d, J = 14.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 0.2H), 6.81 (d, J = 14.0 Hz, 1H), 6.48 (d, J = 8.4 Hz, 0.2H).

(Z)-2-Styryltetrahydrofuran (Z-5a): Colorless solid. 1H NMR (400 MHz, CDCl₃) δ: 7.40–7.38 (m, 2.4H), 7.24–7.20 (m, 2H), 6.61 (d, J = 8.4 Hz, 2H), 4.82–4.77 (m, 2H), 4.70–4.65 (m, 2H), 4.51–4.48 (m, 2H), 3.88–3.79 (m, 1H), 2.17–2.12 (m, 1H), 2.03–1.94 (m, 2H), 1.75–1.71 (m, 1H).

(Z)-2-Methyl-2-styryltetrahydrofuran (Z-5b): Colorless oil. 1H NMR (400 MHz, CDCl₃) δ: 7.40–7.38 (m, 2.4H), 7.33–7.29 (m, 2.6H), 7.24–7.21 (m, 1H), 6.61 (d, J = 8.4 Hz, 0.2H), 6.56 (d, J = 16.0 Hz, 1H), 6.61 (d, J = 16.0 Hz, 1H), 6.20 (d, J = 7.2 Hz, 0.2H), 4.26–4.21 (m, 0.2H), 3.97–3.94 (m, 2H), 2.12–2.07 (m, 1H), 2.01–1.87 (m, 2H), 1.72–1.67 (m, 1H).
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Notes and reference


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KOAc (99.96%) was purchased from Aladdin Co. The reaction solution was analysis by ICP-MS, and the determination data indicated that Cu, Pd, Ni, Fe, Co, Ru, and Rh are less than 0.2 ppm (under detection limit).

During revision of this manuscript, a similar work was reported using NaF by Liang, and see: Y. Yang, H. Huang, X. Zhang, W. Zeng and Y. Liang, *Synthesis*, 2013, 3137−3146 for detail.
