Synthesis of 2-Alkynyltetrahydrofuran Derivatives from Tetrahydrofuran and Alkynyl Bromides

Yuan Yang,[a] Hui Huang,[a] Xiaoyun Zhang,[a] Weilan Zeng,[a] Yun Liang*[a,b]

[a] National & Local Joint Engineering Laboratory for New Petro-chemical Materials and Fine Utilization of Resources, Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research, Ministry of Education, Hunan Normal University, Changsha, Hunan 410081, P. R. of China
Fax +86(731)88872533; E-mail: yliang@hunnu.edu.cn

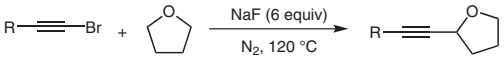
[b] Beijing National Laboratory for Molecular Sciences, Beijing 100871, P. R. of China

Received: 24.06.2013; Accepted after revision: 29.08.2013

Abstract: An efficient and general method for the synthesis of 2-alkynyltetrahydrofuran was developed. The regioselective functionalization of the C(sp^3)–H bond adjacent to an oxygen atom with various alkynyl bromides has been achieved under transition-metal-free reaction conditions. Sodium fluoride was found, for the first time, to promote the efficient functionalization process remarkably. Moreover, 1,2-dibromostyrenes were also found to be effective in this method forming 2-alkenyltetrahydrofurans.

Key words: 2-alkynyltetrahydrofuran, tetrahydrofuran, alkynyl bromides, sodium fluoride, free radical

Alkynes are useful building blocks in organic synthesis.[1] Alkynes are also basic structural units in many natural products and bioactive compounds.[2] For these reasons, much attention has been given to the development of efficient and selective methods for the synthesis of various alkynes.[3–9] Traditionally, alkynes are prepared by the transition-metal-catalyzed Sonogashira reaction starting from terminal alkynes, alkyl halides, or aryl halides.[3,4] However, high catalyst loading is demanded in some transition-metal-catalyzed processes resulting in heavy metal residues in the product, high catalyst cost, and a large workload during purification. Consequently, the development of transition-metal-free methods for the synthesis of alkynes is significant from an atom-economical and environmental point of view. Fuchs and co-workers reported that the reaction of ethers with acetylenic triflones provided facile access to substituted alkynes.[5] The reaction proceeds via radical C–H abstraction by strong electrophilic trifluoromethyl radical and substitution (addition–elimination). In addition to acetylenic triflones as alkynylating agent for radical alkynylation reactions, Russell and co-workers reported radical alkynylation reactions of alkylmercury halides with various alkynes (including alkynyl sulfones, alkynyl sulfides, alkynyl iodides, and alkynyl stannanes) for the first time;[6] Renaud et al. developed the radical-mediated alkynylation of alkynyl sulfones with β-alkylcatecholboranes;[7] Landais et al. extended this method to free-radical three-component carboalkynylation;[8] and Li and co-workers successfully developed a radical-mediated method for C(sp^3)–C(sp) cross-coupling from ethynylbenziodoxolones with aliphatic carboxylic acids.[9] Although these alkynylating agents are useful and interesting, diverse alkynylating agents for the synthesis of alkynes are still in great demand. Herein, we report a sodium fluoride promoted synthesis of substituted alkynes from alkynyl bromides and tetrahydrofuran (Scheme 1). To the best of our knowledge, this is the first example of alkynyl bromides serving as radical acceptors.



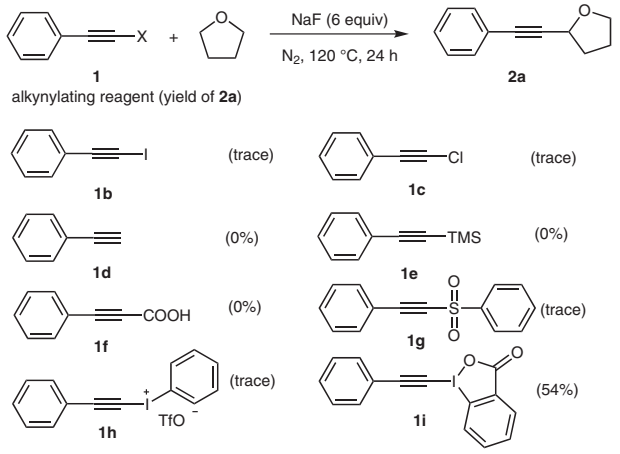
Scheme 1 Synthesis of 2-alkynyltetrahydrofuran derivatives from tetrahydrofuran and alkynyl bromides

As we have a continued interest in the reaction chemistry of 1,2-dibromostyrenes,[10] the reaction of 1,2-dibromostyrene with sulfonamide was tentatively conducted with tetrahydrofuran as solvent. What is interesting is that phenylethynyl bromide and 2-(phenylethynyl)tetrahydrofuran were observed in the final product mixture. Inspired by this result, the reaction of phenylethynyl bromide with tetrahydrofuran was selected for optimization of the reaction conditions, and the results are summarized in Table 1. Firstly, the reaction of phenylethynyl bromide with tetrahydrofuran at 100 °C without an additive was conducted, forming the desired product in 20% isolated yield (entry 1). This result encouraged us to develop an efficient method to synthesize various 2-alkynyltetrahydrofurans. We found that the additive played an important role in this reaction. Thus we screened a variety of additives, such as cesium carbonate, sodium hydroxide, sodium *tert*-butoxide, and cesium fluoride (entries 2–5). Results indicated that cesium fluoride is the best additive for the reaction affording the highest yield.[11] Sequentially, the catalytic efficiency of various fluorides such as lithium fluoride, sodium fluoride, potassium fluoride, and tetrabutylammonium fluoride were tried (entries 6–9), and the highest isolated yield (74%) was obtained with sodium fluoride used as the additive. When the concentration of substrate increased, the yield of product decreased markedly (entry 10). This result displayed the characteristics of a radical reaction mechanism. The trace amount of peroxide contained in the solvent tetrahydrofuran might be the radical

SYNTHESIS 2013, 45, 3137–3146
Advanced online publication: 25.09.2013
DOI: 10.1055/s-0033-1338534; Art ID: SS-2013-H0432-OP

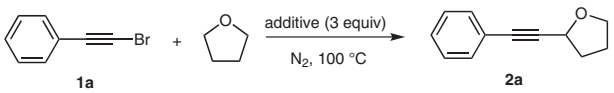
initiator. To test the hypothesis, we used a radical initiator such as 2,2′-azobis(isobutyronitrile) (AIBN) in the presence of sodium fluoride, and the 2-alkynyltetrahydrofuran **2a** was obtained in 80% yield (entry 11). However, when radical initiators such as AIBN and di-*tert*-butyl peroxide (DTBP) were used in the absence of sodium fluoride, the product was obtained in lower yields (entries 12 and 13). These results showed the presence of sodium fluoride could promote the generation of a radical species. When 2,2,6,6-tetramethylpiperidin-1-yloxy (TEMPO, a typical radical scavenger) was added under the same conditions, the desired product was not observed (entry 14). Thus, this radical quenching study also suggested that a radical intermediate is important in this transformation. Finally, the amount of sodium fluoride and the reaction temperature were optimized (entries 15–18). Relatively low yields were found when the reaction was carried out in room temperature or 50 °C, and the highest yield of **2a** was obtained when six equivalents of sodium fluoride was used at the temperature of 120 °C. Thus, the optimal reaction conditions were as follows: **1a** (0.3 mmol), THF (6 mL), and NaF (1.8 mmol), at 120 °C.

Once the optimal reaction conditions between phenylethynyl bromide (**1a**) and tetrahydrofuran were achieved, various alkynylating agents **1b**–**i** were investigated as the starting materials for the synthesis of 2-alkynyltetrahydrofurans, and the results are summarized in Scheme 2. Under the standard reaction conditions, reactions of the alkynylating agents phenylethynyl iodide (**1b**), phenylethynyl chloride (**1c**), phenylacetylene (**1d**), trimethyl(phenylethynyl)silane (**1e**), phenylpropiolic acid (**1f**), [(phenylethynyl)sulfonyl]benzene (**1g**), phenyl(phenylethynyl)iodonium triflate (**1h**), and (phenylethynyl)benziodoxolone (**1i**) were performed in tetrahydrofuran. They either gave none of the expected product **2a** or they gave **2a** in only trace amounts, with the exception of **1i** which afforded **2a** in 54% yield. Compared with phenylethynyl bromide (**1a**), compounds **1b**–**i** were not good alkynylating agents with tetrahydrofuran under the standard reaction conditions.



Scheme 2 Phenylethynylation of tetrahydrofuran

Table 1 Optimization of Reaction Conditions[a]



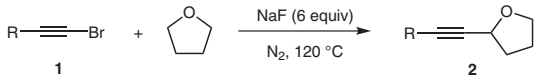
Entry	Additive	Yield[b] (%) of **2a**
1	–	20
2	Cs_2CO_3	26
3	NaOH	25
4	*t*-BuONa	0
5	CsF	57
6	KF	68
7	NaF	74
8	LiF	51
9	TBAF	0
10[c]	NaF	52
11[d]	NaF	80
12	DTBP	68
13	AIBN	53
14[e]	NaF	0
15[f]	NaF	26
16[g]	NaF	77
17[h]	NaF	82
18[i]	NaF	85

[a] Reaction conditions: **1a** (0.3 mmol), additive (3 equiv), THF (6 mL), 100 °C, 24 h.
[b] Isolated yield.
[c] THF (1 mL).
[d] AIBN (20 mol%).
[e] TEMPO (1 equiv).
[f] 50 °C.
[g] 120 °C.
[h] NaF (6 equiv).
[i] NaF (6 equiv), 120 °C.

Under the standard reaction conditions, the coupling reactions of various alkynyl bromides with tetrahydrofuran were then investigated, and the results are summarized in Table 2. The reaction between alkynyl bromides and tetrahydrofuran demonstrated good functional group tolerance for substrates. Arylethynyl bromides bearing electron-withdrawing groups such as F, Cl, Br, CN, COMe, or electron-donating groups such as OMe, Me, Et, Pr, pentyl afforded the corresponding 2-alkynyltetrahydrofuran in good yields. For example, alkynyl bromides bearing 4-fluorophenyl or 4-methoxylphenyl groups afforded the corresponding products **2b** and **2j** in 79% and 80% yields, respectively. Similarly, 4-(bromoethynyl)biphenyl and 1-(bromoethynyl)naphthalene efficiently re-

acted with tetrahydrofuran to afford the corresponding products in **2o** and **2p** in 79% and 70% yields, respectively. Furthermore, heterocyclic 2-(thiophen-2-ylethynyl)tetrahydrofuran (**2q**) was obtained in 67% yield. The results showed that the aryl substituent of ethynyl bromides did not remarkably affect the reaction. Besides arylethynyl bromides, the alk-1-ynyl bromides were also found to be suitable substrates for functionalization of tetrahydrofuran under the standard conditions. When aliphatic alkynes bearing a hydroxy or ester group were employed as substrates, the reaction proceeded in moderate to good yields. In addition, six-membered cyclic ethers such as tetrahydro-2*H*-pyran and 1,4-dioxane gave the desired products **2v**,**w** in moderate yields.

Table 2 Formation of Various 2-Substituted Tetrahydrofurans, a Tetrahydro-2*H*-pyran and a 1,4-Dioxane[a]



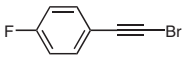
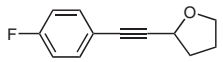
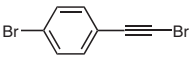
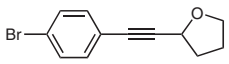
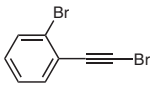
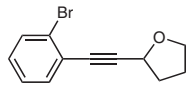
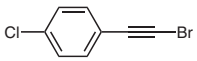
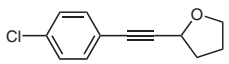
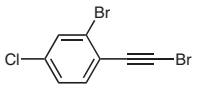
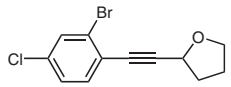
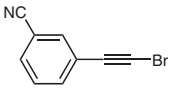
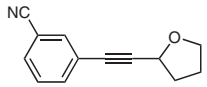
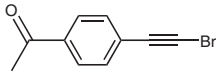
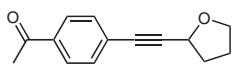
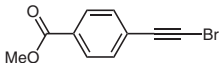
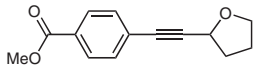
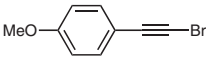
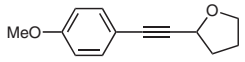
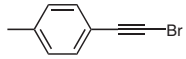
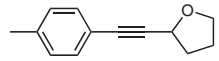
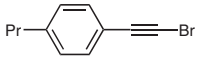
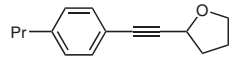
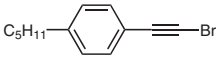
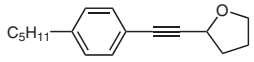
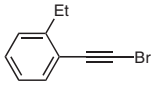
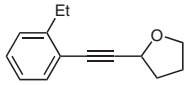
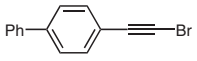
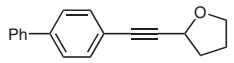
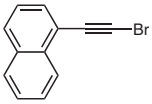
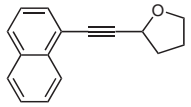
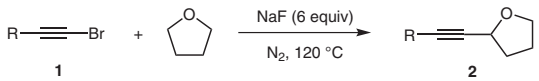
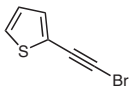
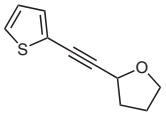
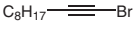
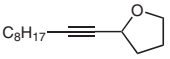
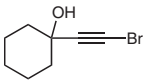
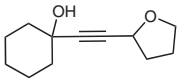
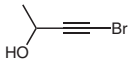
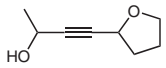
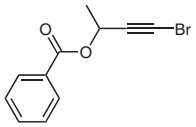
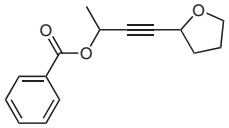
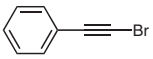
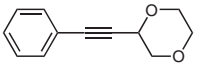
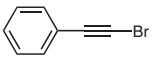
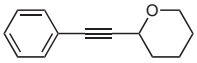
Entry	Substrate **1**	Time (h)	Product **2**	Yield[b] (%)
1		35	**2b** 	79
2		35	**2c** 	90
3		35	**2d** 	74
4		35	**2e** 	80
5		25	**2f** 	68
6		35	**2g** 	77
7		24	**2h** 	75
8		25	**2i** 	75
9		25	**2j** 	80
10		40	**2k** 	80
11		40	**2l** 	76
12		40	**2m** 	85
13		24	**2n** 	71
14		36	**2o** 	79
15		35	**2p** 	70

Table 2 Formation of Various 2-Substituted Tetrahydrofurans, a Tetrahydro-2*H*-pyran and a 1,4-Dioxane[a] (continued)



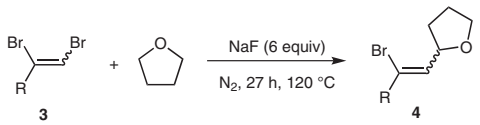
Entry	Substrate **1**	Time (h)	Product **2**	Yield[b] (%)
16		39	**2q** 	67
17		29	**2r** 	62
18		48	**2s** 	58
19		34	**2t** 	42
20		38	**2u** 	51
21		40	**2v**[c] 	32
22		30	**2w**[d] 	58

[a] Compound **1** (0.3 mmol), NaF (1.8 mmol), THF (6 mL), 120 °C, N_2.
[b] Isolated yields.
[c] THF was replaced by 1,4-dioxane.
[d] THF was replaced by tetrahydro-2*H*-pyran.

Importantly, as given in Table 3, the synthetic protocol could be also applied to the reaction of 1,2-dibromostyrenes **3** with tetrahydrofuran. Products **4** could be obtained in good yields under the optimal reaction conditions as given in Table 1. In this case as the product **4** contains two isomers, the investigation of chemoselectivity and stereoselectivity of this reaction is necessary. The selectivity between 1,2-dibromostyrenes and tetrahydrofuran was evaluated with (*Z*)-1,2-dibromostyrene and (*E*)-1,2-dibromostyrene under standard reaction conditions. When (*E*)-1,2-dibromostyrene reacted with tetrahydrofuran, the product 2-(2-bromo-2-phenylvinyl)tetrahydrofuran (**4a**/**4a′** *E*/*Z* 2:1) was obtained in 63% isolated yield. When (*Z*)-1,2-dibromostyrene reacted with tetrahydrofuran, the product 2-(2-bromo-2-phenylvinyl)tetrahydrofuran (**4a**/**4a′** *E*/*Z* 1:10) was obtained in the same yield. These results showed the reaction between 1,2-dibromostyrene and tetrahydrofuran undergoes a radical addition–elimination mechanism. The scope and reactivity of various (*Z*)-1,2-dibromostyrenes were also examined under the optimized conditions. The benzene ring of (*Z*)-1,2-dibromostyrene bearing either electron-withdrawing groups such as Cl, Br or electron-donating groups such as Me or Pr gave the corresponding products in good isolated yields. However, (*Z*)-(2-bromovinyl)benzene was found not to be a suitable substrate and only 18% of (*Z*)-2-styryltetrahydrofuran was obtained.

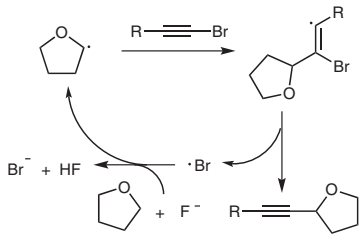
The reaction has the characteristics of a radical process. High purity tetrahydrofuran does not react with alkynyl bromide **1a** when heated under a nitrogen atmosphere. In addition, the addition of TEMPO prevents the reaction from occurring. Based on above experimental observations, a possible mechanism is given in Scheme 3.[12] Firstly, small amounts of peroxide in tetrahydrofuran serve to initiate the process and generate the tetrahydrofuran radicals. Then, a direct radical addition to the alkynyl bromide forms a bromovinyl radical. Subsequent bromine radical elimination occurred and generated the final product. The bromine radical captures the hydrogen atom of tetrahydrofuran with the aid of the fluoro anion and the tetrahydrofuran radical is regenerated. To further understand this radical mechanism, we conducted the competition reaction between tetrahydrofuran (1 mL) and tetrahydrofuran-d_8 (1 mL) in Scheme 4. The observed high K_H/K_D value (4.0) implies that the rate determining step contains C–H bond cleavage. Thus, the elimination of the bromine radical from bromovinyl radical is faster than the abstraction of the hydrogen atom from tetrahydrofuran.

Table 3 Formation of Various 2-Substituted Tetrahydrofurans[a]

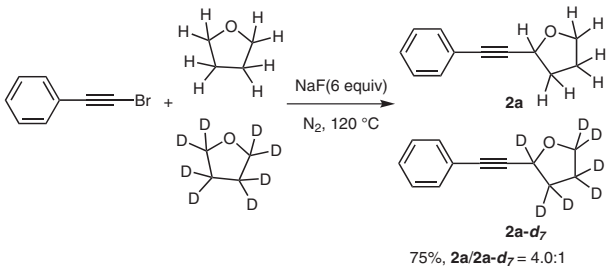


Entry	Substrate **3**	Product **4**		Yield[b] (%)	Ratio
1	**3a′**	**4a**	**4a'**	63	**4a**/**4a′** 2:1
2	**3a**	**4a**	**4a'**	63	**4a**/**4a′** 1:10
3	**3b**	**4b**	**4b'**	65	**4b**/**4b′** 1:8
4	**3c**	**4c**	**4c'**	62	**4c**/**4c′** 1:8
5	**3d**	**4d**	**4d'**	63	**4d**/**4d′** 1:10
6	**3e**	**4e**	**4e'**	62	**4e**/**4e′** 1:8

[a] Compound **3** (0.3 mmol), NaF (1.8 mmol), THF (6 mL), 120 °C, N_2.
[b] Isolated yields.



Scheme 3 Possible mechanism for the reaction



Scheme 4 Competition reaction between tetrahydrofuran and tetrahydrofuran-d_8

In summary, we have developed a novel sodium fluoride promoted alkynylation with various alkynyl bromides. Moreover, this protocol could be extended to construct $C(sp^2)$–$C(sp^3)$ bonds by the reaction between 1,2-dibromostyrenes and tetrahydrofuran. This reaction provides the efficient synthesis of alkynylation or alkenylation products, which represents a novel method for the construction of C(sp)–$C(sp^3)$ and $C(sp^2)$–$C(sp^3)$ bonds. In addition, fluoride was found, remarkably, to promote the efficiency of this activation process; this is the first example of such an activation by fluoride. This method provides an alternative method for the selective activation of the $C(sp^3)$–H bond and their synthetically useful applications can be expected.

^{1}H and ^{13}C NMR spectra were recorded on a standard spectrometer operating at 500 MHz (500 MHz for ^{1}H; 125 MHz for ^{13}C) at r.t., respectively. ^{1}H NMR spectra were recorded in $CDCl_3$ with TMS used as an internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$ and the central peak of the solvent was adjusted to δ = 77.00 and used as a reference. IR spectra were recorded on a Thermo Nicolet Avatar 370 FT-IR spectrophotometer. Mass spectrometry data were collected on an HRMS instrument or a LR-MS instrument using ESI or EI ionization. Melting points were measured uncorrected. Reactions were monitored by TLC or GC-MS analysis. Column chromatography (petroleum ether–EtOAc) was performed on silica gel (200–300 mesh). Unless otherwise noted, all reactions were run under N_2 atmosphere.

Aryl(tetrahydrofuran-2-yl)acetylenes 2; General Procedure

To a Schlenk tube were added alkynyl bromide (0.3 mmol), NaF (1.8 mmol) and THF (6 mL). The tube was charged with N_2 and the mixture was stirred at 120 °C for the appropriate time. When the reaction was complete, the mixture was filtered by a crude column (EtOAc), and evaporated under vacuum. The residue was purified by column chromatography (silica gel, petroleum ether–EtOAc, 40:1) to provide the desired product.

1-Aryl-1-bromo-2-(tetrahydrofuran-2-yl)ethenes 4; General Procedure

To a Schlenk tube were added 1,2-dibromoalk-1-ene (0.3 mmol), NaF (1.8 mmol) and THF (6 mL). The tube was charged with N_2 and the mixture was stirred at 120 °C for the appropriate time. When the reaction was complete, the mixture was filtered by a crude column (EtOAc), and evaporated under vacuum. The residue was purified by column chromatography (silica gel, petroleum ether–EtOAc, 40:1) to provide the desired product.

2-(Phenylethynyl)tetrahydrofuran (2a)[5c]

Pale yellow oil; yield: 44.3 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.42 (m, 2 H), 7.29–7.28 (m, 3 H), 4.82–4.80 (m, 1 H), 4.03–3.99 (m, 1 H), 3.88–3.83 (m, 1 H), 2.25–2.19 (m, 1 H), 2.12–2.05 (m, 2 H), 1.97–1.91 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.6, 128.2, 128.1, 122.7, 89.0, 84.4, 68.5, 67.9, 33.4, 25.4.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{11}O$: 171.0804; found: 171.0802.

2-[(4-Fluorophenyl)ethynyl]tetrahydrofuran (2b)

Pale yellow oil; yield: 45.4 mg (79%).

IR (KBr): 2980, 2947, 2871, 2227, 1599, 1506, 1237, 1157, 1051, 838 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.39 (m, 2 H), 6.99 (t, *J* = 8.8 Hz, 2 H), 4.80–4.78 (m, 1 H), 4.03–3.98 (m, 1 H), 3.88–3.83 (m, 1 H), 2.25–2.20 (m, 1 H), 2.12–2.05 (m, 2 H), 1.98–1.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.4 (d, *J* = 248.0 Hz), 133.6 (d, *J* = 8.25 Hz), 118.8 (d, *J* = 3.5 Hz), 115.4 (d, *J* = 22 Hz), 88.7, 83.4, 68.5, 67.9, 33.3, 25.5.

MS (EI): *m*/*z* = 191 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{10}FO$: 189.0710; found: 189.0706.

2-[(4-Bromophenyl)ethynyl]tetrahydrofuran (2c)

Pale yellow oil; yield: 68.1 mg (90%).

IR (KBr): 2977, 2954, 2924, 2868, 2223, 1483, 1396, 1330, 1260, 1174, 1051, 1008, 818 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 (dd, *J* = 6.5, 1.5 Hz, 2 H), 7.28 (dd, *J* = 6.5, 1.5 Hz, 2 H), 4.80–4.77 (m, 1 H), 4.02–3.98 (m, 1 H), 3.87–3.83 (m, 1 H), 2.25–2.19 (m, 1 H), 2.08–2.04 (m, 2 H), 1.98–1.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.1, 131.4, 122.4, 121.7, 90.2, 83.4, 68.5, 68.0, 33.3. 25.5.

MS (EI): *m*/*z* = 250, 252 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{10}{}^{79}BrO$: 248.9910; found: 248.9906.

2-[(2-Bromophenyl)ethynyl]tetrahydrofuran (2d)

Pale yellow oil; yield: 55.9 mg (74%).

IR (KBr): 3060, 2977, 2951, 2924, 2868, 2227, 1469, 1430, 1333, 1177, 1051, 755 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.45 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.23 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.14 (td, *J* = 7.8, 2.0 Hz, 1 H), 4.88–4.86 (m, 1 H), 4.06–4.01 (m, 1 H), 3.90–3.86 (m, 1 H), 2.27–2.21 (m, 1 H), 2.18–2.12 (m, 2 H), 1.98–1.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.3, 132.3, 129.4, 126.9, 125.6, 124.9, 93.9, 83.0, 68.5, 67.9, 33.3, 25.3.

MS (EI): *m*/*z* = 250 and 252 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{10}{}^{79}BrO$: 248.9910; found: 248.9906.

2-[(4-Chlorophenyl)ethynyl]tetrahydrofuran (2e)

Yellow oil; yield: 49.2 mg (80%).

IR (KBr): 2977, 2954, 2927, 2868, 2223, 1489, 1337, 1091, 1051, 828 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 6.5, 2.0 Hz, 2 H), 7.26 (dd, *J* = 6.5, 2.0 Hz, 2 H), 4.80–4.78 (m, 1 H), 4.02–3.98 (m, 1 H), 3.87–3.83 (m, 1 H), 2.26–2.19 (m, 1 H), 2.11–2.04 (m, 2 H), 1.98–1.91 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 134.2, 132.9, 128.5, 121.2, 90.0, 83.3, 68.4, 67.9, 33.3, 25.5.

MS (EI): *m*/*z* = 206 and 208 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{10}{}^{35}ClO$: 205.0415; found: 205.0411.

2-[(2-Bromo-4-chlorophenyl)ethynyl]tetrahydrofuran (2f)

Pale yellow oil; yield: 58.1 mg (68%).

IR (KBr): 3087, 2977, 2947, 2927, 2868, 2227, 1582, 1466, 1376, 1330, 1101, 1051, 818 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 2.0 Hz, 1 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.22 (dd, *J* = 8.5, 2.5 Hz, 1 H), 4.87–4.85 (m, 1 H), 4.05–4.00 (m, 1 H), 3.90–3.86 (m, 1 H), 2.26–2.21 (m, 1 H), 2.16–2.11 (m, 2 H), 1.98–1.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 134.5, 133.9, 132.1, 127.4, 126.0, 123.5, 94.9, 82.0, 68.5, 67.9, 33.2, 25.3.

MS (EI): *m*/*z* = 284, 286, and 288 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_9{}^{79}Br^{35}ClO$: 282.9520; found: 282.9521.

3-[(Tetrahydrofuran-2-yl)ethynyl]benzonitrile (2g)
Pale yellow oil; yield: 45.6 mg (77%).

IR (KBr): 3070, 2977, 2951, 2871, 2230, 1592, 1476, 1413, 1333, 1180, 1054, 898, 802, 686 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.70 (t, *J* = 1.3 Hz, 1 H), 7.64 (dt, *J* = 8.0, 1.5 Hz, 1 H), 7.58 (dt, *J* = 8.0, 1.5 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 1 H), 4.82–4.80 (m, 1 H), 4.03–3.98 (m, 1 H), 3.89–3.85 (m, 1 H), 2.28–2.23 (m, 1 H), 2.11–2.08 (m, 2 H), 1.98–1.95 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 135.7, 134.9, 131.4, 129.1, 124.3, 117.9, 112.6, 91.7, 82.0, 68.2, 68.0, 33.2, 25.4.

MS (EI): *m*/*z* = 196 $[M - H]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{13}H_{10}NO$: 196.0757; found: 196.0754.

1-{4-[(Tetrahydrofuran-2-yl)ethynyl]phenyl}ethanone (2h)
Pale yellow oil; yield: 48.4 mg (75%).

IR (KBr): 2977, 2951, 2924, 2871, 2220, 1682, 1602, 1406, 1360, 1263, 1177, 1058, 842 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.5 Hz, 2 H), 7.50 (d, *J* = 8.5 Hz, 2 H), 4.84–4.81 (m, 1 H), 4.03–3.99 (m, 1 H), 3.89–3.85 (m, 1 H), 2.58 (s, 3 H), 2.27–2.23 (m, 1 H), 2.13–2.06 (m, 2 H), 1.99–1.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.2, 136.2, 131.7, 128.0, 127.6, 92.5, 83.6, 68.4, 68.0, 33.2, 26.5, 25.4.

MS (EI): *m*/*z* = 214 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{14}H_{13}O_2$: 213.0910; found: 213.0907.

Methyl 4-[(Tetrahydrofuran-2-yl)ethynyl]benzoate (2i)
Pale yellow solid; yield: 52.0 mg (75%); mp 44.7–45.8 °C.

IR (KBr): 2951, 2871, 2227, 1722, 1606, 1436, 1277, 1180, 1107, 1054, 862, 765, 699 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.5 Hz, 2 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 4.84–4.81 (m, 1 H), 4.03–3.99 (m, 1 H), 3.91 (s, 3 H), 3.89–3.85 (m, 1 H), 2.27–2.21 (m, 1 H), 2.12–2.07 (m, 2 H), 1.99–1.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.4, 131.6, 129.5, 129.3, 127.5, 92.2, 83.7, 68.4, 68.0, 52.1, 33.3, 25.5.

MS (EI): *m*/*z* = 230 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{14}H_{13}O_3$: 229.0859; found: 229.0862.

2-[(4-Methoxyphenyl)ethynyl]tetrahydrofuran (2j)
Pale yellow oil; yield: 48.7 mg (80%).

IR (KBr): 2954, 2931, 2871, 2838, 2220, 1606, 1506, 1290, 1250, 1174, 1051, 832 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 9.0 Hz, 2 H), 6.81 (d, *J* = 8.5 Hz, 2 H), 4.80–4.78 (m, 1 H), 4.02–3.98 (m, 1 H), 3.86–3.82 (m, 1 H), 3.78 (s, 3 H), 2.23–2.18 (m, 1 H), 2.11–2.03 (m, 2 H), 1.96–1.91 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 133.1, 114.8, 113.7, 87.5, 84.3, 68.6, 67.8, 55.1, 33.4, 25.4.

MS (EI): *m*/*z* = 202 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{13}H_{13}O_2$: 201.0910; found: 201.0914.

2-(*p*-Tolylethynyl)tetrahydrofuran (2k)
Pale yellow oil; yield: 45.1 mg (80%).

IR (KBr): 3027, 2980, 2924, 2868, 2230, 1509, 1459, 1337, 1058, 818 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 4.81–4.79 (m, 1 H), 4.03–3.99 (m, 1 H), 3.87–3.83 (m, 1 H), 2.33 (s, 3 H), 2.24–2.19 (m, 1 H), 2.10–2.05 (m, 2 H), 1.96–1.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 131.6, 128.9, 119.7, 88.3, 84.6, 68.6, 67.9, 33.4, 25.5, 21.4.

MS (EI): *m*/*z* = 186 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{13}H_{13}O$: 185.0961; found: 185.0956.

2-[(4-Propylphenyl)ethynyl]tetrahydrofuran (2l)
Pale yellow oil; yield: 48.9 mg (76%).

IR (KBr): 3027, 2957, 2927, 2864, 2223, 1506, 1456, 1337, 1174, 1051, 838 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 8.5 Hz, 2 H), 4.81–4.79 (m, 1 H), 4.01–3.98 (m, 1 H), 3.87–3.82 (m, 1 H), 2.56 (t, *J* = 7.8 Hz, 2 H), 2.22–2.19 (m, 1 H), 2.10–2.05 (m, 2 H), 1.94–1.91 (m, 1 H), 1.65–1.59 (m, 2 H), 0.91 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.0, 131.5, 128.3, 119.9, 88.3, 84.6, 68.6, 67.8, 37.8, 33.4, 25.4, 24.2, 13.7.

MS (EI): *m*/*z* = 214 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{15}H_{17}O$: 213.1274; found: 213.1271.

2-[(4-Pentylphenyl)ethynyl]tetrahydrofuran (2m)
Pale yellow oil; yield: 61.7 mg (85%).

IR (KBr): 2957, 2927, 2854, 2220, 1506, 1456, 1340, 1054, 835 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 4.81–4.79 (m, 1 H), 4.02–3.98 (m, 1 H), 3.86–3.82 (m, 1 H), 2.57 (t, *J* = 7.8 Hz, 2 H), 2.24–2.18 (m, 1 H), 2.11–2.04 (m, 2 H), 1.96–1.89 (m, 1 H), 1.61–1.55 (m, 2 H), 1.33–1.28 (m, 4 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.3, 131.5, 128.2, 119.9, 88.3, 84.6, 68.6, 67.8, 35.8, 33.4, 31.4, 30.8, 25.4, 22.4, 13.9.

MS (EI): *m*/*z* = 242 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{17}H_{21}O$: 241.1587; found: 241.1584.

2-[(2-Ethylphenyl)ethynyl]tetrahydrofuran (2n)
Pale yellow oil; yield: 42.9 mg (71%).

IR (KBr): 3060, 2967, 2931, 2871, 2223, 1483, 1453, 1337, 1054, 755 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.23 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.18 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.11 (td, *J* = 7.5, 1.5 Hz, 1 H), 4.87–4.85 (m, 1 H), 4.03–3.99 (m, 1 H), 3.89–3.85 (m, 1 H), 2.81–2.76 (m, 2 H), 2.24–2.19 (m, 1 H), 2.12–2.07 (m, 2 H), 1.96–1.93 (m, 1 H), 1.24 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.2, 132.3, 128.4, 127.8, 125.5, 121.8, 92.5, 83.1, 68.7, 67.7, 33.5, 27.6, 25.3, 14.7.

MS (EI): *m*/*z* = 200 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{14}H_{15}O$: 199.1117; found: 199.1119.

2-(Biphenyl-4-ylethynyl)tetrahydrofuran (2o)
Pale yellow solid; yield: 59.1 mg (79%); mp 50.2–51.4 °C.

IR (KBr): 3057, 3030, 2927, 2871, 2220, 1486, 1333, 1170, 1051, 842, 762, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.0 Hz, 2 H), 7.53–7.48 (m, 4 H), 7.42 (t, *J* = 7.8 Hz, 2 H), 7.34 (t, *J* = 7.3 Hz, 1 H), 4.84–4.82 (m, 1 H), 4.04–4.00 (m, 1 H), 3.88–3.84 (m, 1 H), 2.26–2.20 (m, 1 H), 2.12–2.07 (m, 2 H), 1.98–1.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.9, 140.3, 132.1, 128.8, 127.5, 126.9, 126.8, 121.7, 89.7, 84.3, 68.6, 67.9, 33.4, 25.5.

MS (EI): *m*/*z* = 248 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{18}H_{15}O$: 247.1117; found: 247.1118.

2-(Naphthalen-1-ylethynyl)tetrahydrofuran (2p)
Pale yellow oil; yield: 46.5 mg (70%).

IR (KBr): 3057, 2980, 2947, 2927, 2871, 2223, 1586, 1503, 1459, 1396, 1330, 1180, 1051, 802, 775 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 8.5 Hz, 1 H), 7.82–7.78 (m, 2 H), 7.66 (dd, *J* = 7.0, 0.5 Hz, 1 H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.49 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.40–7.37 (m, 1 H), 4.97–4.95 (m, 1 H), 4.09–4.05 (m, 1 H), 3.92–3.88 (m, 1 H), 2.30–2.27 (m, 1 H), 2.20–2.13 (m, 2 H), 1.97–1.95 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.2, 133.0, 130.4, 128.7, 128.1, 126.6, 126.3, 126.1, 125.1, 120.4, 94.1, 82.5, 68.7, 67.9, 33.6, 25.5.

MS (EI): *m*/*z* = 222 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{16}H_{13}O$: 221.0961; found: 221.0959.

2-(Thiophen-2-ylethynyl)tetrahydrofuran (2q)
Red-brown oil; yield: 35.8 mg (67%).

IR (KBr): 3097, 2977, 2951, 2871, 2220, 1519, 1456, 1423, 1356, 1330, 1194, 1048, 915, 852, 832, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 (dd, *J* = 5.0, 1.0 Hz, 1 H), 7.19 (dd, *J* = 3.5, 1.0 Hz, 1 H), 6.94 (t, *J* = 6.8 Hz, 1 H), 4.83–4.80 (m, 1 H), 4.01–3.97 (m, 1 H), 3.87–3.83 (m, 1 H), 2.24–2.19 (m, 1 H), 2.11–2.06 (m, 2 H), 1.97–1.91 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 132.1, 127.0, 126.8, 122.7, 92.9, 77.7, 68.6, 67.9, 33.2, 25.4.

MS (EI): *m*/*z* = 178 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{10}H_9OS$: 177.0369; found: 177.0364.

2-(Dec-1-ynyl)tetrahydrofuran (2r)
Pale yellow oil; yield: 38.8 mg (62%).

IR (KBr): 2927, 2851, 2230, 1456, 1330, 1184, 1051 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.57–4.54 (m, 1 H), 3.96–3.92 (m, 1 H), 3.80–3.76 (m, 1 H), 2.19 (t, *J* = 7.3 Hz, 2 H), 2.14–2.10 (m, 1 H), 2.04–1.99 (m, 1 H), 1.95–1.87 (m, 2 H), 1.52–1.47 (m, 2 H), 1.39–1.35 (m, 2 H), 1.30–1.26 (m, 8 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 85.2, 79.9, 68.4, 67.6, 33.5, 31.8, 29.1, 29.0, 28.8, 28.6, 25.4, 22.6, 18.7, 14.0.

MS (EI): *m*/*z* = 207 $[M - H]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{14}H_{23}O$: 207.1743; found: 207.1747.

1-[(Tetrahydrofuran-2-yl)ethynyl]cyclohexanol (2s)
Pale yellow oil; yield: 33.7 mg (58%).

IR (KBr): 3372, 2931, 2858, 2233, 1449, 1340, 1184, 1054, 968 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.64–4.62 (m, 1 H), 3.97–3.92 (m, 1 H), 3.83–3.79 (m, 1 H), 2.27 (s, 1 H), 2.18–2.13 (m, 1 H), 2.06–1.87 (m, 5 H), 1.69–1.67 (m, 2 H), 1.59–1.51 (m, 4 H), 1.26–1.23 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 88.2, 83.9, 68.4, 68.1, 67.6, 39.8, 33.4, 25.2, 25.1, 23.3.

MS (EI): *m*/*z* = 194 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{17}O_2$: 193.1223; found: 193.1224.

4-(Tetrahydrofuran-2-yl)but-3-yn-2-ol (2t)
Pale yellow oil; yield: 17.7 mg (42%).

IR (KBr): 3399, 2980, 2927, 2871, 2227, 1456, 1327, 1144, 1054 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.63–4.60 (m, 1 H), 4.58–4.54 (m, 1 H), 3.97–3.92 (m, 1 H), 3.83–3.79 (m, 1 H), 2.28 (s, 1 H), 2.19–2.12 (m, 1 H), 2.06–1.89 (m, 3 H), 1.44 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 86.5, 83.6, 68.0, 67.8, 58.2, 33.2, 25.3, 24.2.

MS (EI): *m*/*z* = 139 $[M - H]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ $[M + Na]^+$ calcd for $C_8H_{12}O_2Na$: 163.0730; found: 163.0729.

4-(Tetrahydrofuran-2-yl)but-3-yn-2-yl Benzoate (2u)
Pale yellow oil; yield: 37.6 mg (51%).

IR (KBr): 3063, 2987, 2934, 2874, 2246, 1718, 1599, 1453, 1313, 1267, 1111, 1048, 712, 686 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07–8.05 (m, 2 H), 7.58–7.54 (m, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 5.76–5.72 (m, 1 H), 4.63–4.61 (m, 1 H), 3.97–3.91 (m, 1 H), 3.82–3.77 (m, 1 H), 2.17–2.11 (m, 1 H), 1.99–1.95 (m, 2 H), 1.91–1.88 (m, 1 H), 1.61 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.3, 133.0, 129.9, 129.7, 128.3, 84.8, 82.8, 67.9, 67.8, 60.9, 33.1, 25.3, 21.4.

MS (EI): *m*/*z* = 244 $[M]^+$.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{15}H_{15}O_3$: 243.1016; found: 243.1018.

2-(Phenylethynyl)-1,4-dioxane (2v)[5c]
Pale yellow oil; yield: 18.1 mg (32%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 2 H), 7.34–7.29 (m, 3 H), 4.58–4.56 (m, 1 H), 3.95–3.92 (m, 2 H), 3.75–3.67 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.8, 128.7, 128.2, 122.0, 86.5, 84.3, 70.4, 66.43, 66.36, 65.8.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{12}H_{11}O_2$: 187.0754; found: 187.0751.

2-(Phenylethynyl)tetrahydro-2*H*-pyran (2w)[5c]
Pale yellow oil; yield: 32.6 mg (58%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.37 (m, 2 H), 7.23–7.21 (m, 3 H), 4.45–4.42 (m, 1 H), 4.00–3.96 (m, 1 H), 3.54–3.49 (m, 1 H), 1.87–1.81 (m, 2 H), 1.75–1.69 (m, 1 H), 1.57–1.49 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.7, 128.24, 128.17, 122.7, 88.1, 85.2, 67.4, 66.6, 32.2, 25.7, 21.8.

HRMS (ESI): *m*/*z* $[M - H]^+$ calcd for $C_{13}H_{13}O$: 185.0961; found: 185.0957.

(*E*)-2-(2-Bromo-2-phenylvinyl)tetrahydrofuran (4a) and (*Z*)-2-(2-Bromo-2-phenylvinyl)tetrahydrofuran (4a′) (2:1)
Pale yellow oil; yield: 48.1 mg (63%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (dd, *J* = 8.5, 2.0 Hz, 1 H), 7.40 (dd, *J* = 8.5, 1.5 Hz, 2 H), 7.36–7.29 (m, 4.5 H), 6.34 (d, *J* = 7.0 Hz, 0.5 H), 6.21 (d, *J* = 9.5 Hz, 1 H), 4.82–4.78 (m, 0.5 H), 4.24–4.19 (m, 1 H), 3.97–3.93 (m, 0.5 H), 3.91–3.87 (m, 1 H), 3.86–3.82 (m, 0.5 H), 3.73–3.69 (m, 1 H), 2.34–2.28 (m, 0.5 H), 2.03–1.93 (m, 3 H), 1.86–1.81 (m, 1 H), 1.72–1.66 (m, 1.5 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.1, 138.1, 134.7, 132.8, 129.0, 128.8, 128.7, 128.2, 128.1, 127.5, 125.4, 124.4, 79.3, 77.2, 68.3, 68.0, 32.3, 31.7, 26.1, 26.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}{}^{79}BrO$: 253.0228; found: 253.0223.

(*E*)-2-(2-Bromo-2-*p*-tolylvinyl)tetrahydrofuran (4b) and (*Z*)-2-(2-Bromo-2-*p*-tolylvinyl)tetrahydrofuran (4b′) (1:8)
Pale yellow oil; yield: 52.1 mg (65%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.0 Hz, 2 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 6.29 (d, *J* = 7.0 Hz, 1 H), 6.18 (d, *J* = 9.5 Hz, 0.12 H) (**4b**), 4.81–4.77 (m, 1 H), 3.97–3.92 (m, 1 H), 3.86–3.81 (m, 1 H), 2.34 (s, 3 H), 2.32–2.27 (m, 1 H), 1.99–1.95 (m, 2 H), 1.71–1.66 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.7, 136.4, 131.9, 128.9, 127.4, 125.6, 79.4, 68.2, 31.7, 26.0, 21.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{16}{}^{79}BrO$: 267.0379; found: 267.0381.

(*E*)-2-[2-Bromo-2-(4-propylphenyl)vinyl]tetrahydrofuran (4c) and (*Z*)-2-[2-Bromo-2-(4-propylphenyl)vinyl]tetrahydrofuran (4c′) (1:8)
Pale yellow oil; yield: 55.1 mg (62%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.0 Hz, 2 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 6.31 (d, *J* = 7.0 Hz, 1 H), 6.18 (d, *J* = 9.5 Hz, 0.12 H) (**4c**), 4.82–4.77 (m, 1 H), 3.97–3.92 (m, 1 H), 3.85–3.81 (m, 1 H), 2.58 (t, *J* = 7.8 Hz, 2 H), 2.33–2.27 (m, 1 H), 1.99–1.95 (m, 2 H), 1.71–1.67 (m, 1 H), 1.65–1.60 (m, 2 H), 0.93 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.5, 136.5, 131.9, 128.3, 127.4, 125.6, 79.4, 68.2, 37.6, 31.7, 26.0, 24.3, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}{}^{79}BrO$: 295.0692; found: 295.0697.

(*E*)-2-[2-Bromo-2-(4-chlorophenyl)vinyl]tetrahydrofuran (4d) and (*Z*)-2-[2-Bromo-2-(4-chlorophenyl)vinyl]tetrahydrofuran (4d′) (1:8)
Pale yellow oil; yield: 54.2 mg (63%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.5 Hz, 2 H), 7.09 (d, *J* = 8.5 Hz, 2 H), 6.33 (d, *J* = 7.0 Hz, 1 H), 6.22 (d, *J* = 9.5 Hz, 0.13 H) (**4d**), 4.80–4.76 (m, 1 H), 3.97–3.93 (m, 1 H), 3.86–3.82 (m, 1 H), 2.34–2.28 (m, 1 H), 2.01–1.96 (m, 2 H), 1.72–1.66 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.6, 134.6, 133.4, 128.7, 128.3, 124.0, 79.3, 68.3, 31.6, 26.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}{}^{79}Br^{35}ClO$: 286.9833; found: 286.9837.

(*E*)-2-[2-Bromo-2-(4-bromophenyl)vinyl]tetrahydrofuran (4e) and (*Z*)-2-[2-Bromo-2-(4-bromophenyl)vinyl]tetrahydrofuran (4e′) (1:10)
Pale yellow oil; yield: 61.9 mg (62%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.5 Hz, 2 H), 7.41 (d, *J* = 8.5 Hz, 2 H), 6.34 (d, *J* = 7.0 Hz, 1 H), 6.22 (d, *J* = 9.5 Hz, 0.1 H) (**4e**), 4.80–4.75 (m, 1 H), 3.97–3.92 (m, 1 H), 3.86–3.82 (m, 1 H), 2.34–2.28 (m, 1 H), 2.00–1.96 (m, 2 H), 1.71–1.66 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 133.4, 131.3, 129.0, 124.0, 122.8, 79.3, 68.3, 31.6, 26.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}{}^{79}Br_2O$: 330.9328; found: 330.9336.

2-(Phenylethynyl)tetrahydrofuran (2a) and 2-(Phenylethynyl)tetrahydrofuran-*d*$_7$ (2a-*d*$_7$)[5c]
Pale yellow oil; yield: 13 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.42 (m, 2 H), 7.30–7.28 (m, 3 H), 4.82–4.80 (m, 0.8 H), 4.04–3.99 (m, 0.8 H), 3.88–3.84 (m, 0.8 H), 2.25–2.20 (m, 0.8 H), 2.12–2.06 (m, 1.6 H), 1.98–1.92 (m, 0.8 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.7, 128.21, 128.18, 122.8, 89.1, 84.4, 68.6, 67.9, 33.4, 25.5.

HRMS (ESI): *m*/*z* [M – H]$^+$ calcd for $C_{12}H_{11}O$ (**2a**): 171.0804; found: 171.0802, *m*/*z* [M + H]$^+$ calcd for $C_{12}H_6D_7O$ (**2a**-*d*$_7$): 180.1400; found: 180.1404.

(*Z*)-2-Styryltetrahydrofuran[12b]
Pale yellow oil; yield: 18 mg (35%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 4 H), 7.25–7.23 (m, 1 H), 6.59 (d, *J* = 11.5 Hz, 1 H), 5.71 (dd, *J* = 12.0, 9.0 Hz, 1 H), 4.69–4.65 (m, 1 H), 3.98–3.93 (m, 1 H), 3.80–3.76 (m, 1 H), 2.14–2.11 (m, 1 H), 2.02–1.91 (m, 2 H), 1.72–1.65 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.7, 132.9, 131.4, 128.8, 128.1, 127.1, 75.0, 68.0, 32.9, 26.4.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{14}O$: 174.1045; found: 174.1037.

(*E*)-2-Styryltetrahydrofuran[12b]
Pale yellow oil; yield: 15 mg (29%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.37 (m, 2 H), 7.30 (t, *J* = 7.5 Hz, 2 H), 7.24–7.21 (m, 1 H), 6.58 (d, *J* = 16.0 Hz, 1 H), 6.21 (dd, *J* = 16.0, 7.0 Hz, 1 H), 4.50–4.45 (m, 1 H), 3.99–3.95 (m, 1 H), 3.86–3.82 (m, 1 H), 2.16–2.10 (m, 1 H), 2.01–1.92 (m, 2 H), 1.75–1.68 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.8, 130.5, 130.4, 128.5, 127.5, 126.4, 79.6, 68.2, 32.4, 25.9.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{14}O$: 174.1045; found: 174.1037.

Acknowledgment

We thank the Natural Science Foundation of China (21072054), New Teachers' Fund for Doctor Stations, Ministry of Education of China (20094306120003), Training Program Foundation for the Young Talents by Hunan Normal University of China (ET21003), Hunan Provincial Natural Science Foundation of China (12JJ2009), Scientific Research Fund of Hunan Provincial Education Department (12A095), and Aid Program for Science and Technology Innovative Research Team in Higher Educational Institutions of Hunan Province for financial support.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) (a) *Acetylene Chemistry: Chemistry, Biology and Material Science*; Diederich, F.; Stang, P. J.; Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, **2005**. (b) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (c) *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**. (d) Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605.

(2) (a) Shi Shun, A. L. K.; Tykwinski, R. R. *Angew. Chem. Int. Ed.* **2006**, *45*, 1034. (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442. (c) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I.; de Meijere, A., Eds.; Wiley-Interscience: New York, **2002**.

(3) For reviews see: (a) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874. (b) Tykwinski, R. R. *Angew. Chem. Int. Ed.* **2003**, *42*, 1566. (c) Negishi, E.-I.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979. (d) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176. (e) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, **2002**, 493–529. (f) Sonogashira, K. In *Metal-Catalyzed Cross-*

Coupling Reactions; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: Weinheim, **1998**, 203–229.

(4) For selected papers on Sonogashira reactions see: (a) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46. (b) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627. (c) Sonogashira, K.; Yatake, T.; Tohda, Y.; Takahashi, S.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1977**, 291. (d) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (e) Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259. (f) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253.

(5) (a) Xiang, J.; Jiang, W.; Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1997**, *119*, 4123. (b) Xiang, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 11986. (c) Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4486.

(6) (a) Russell, G. A.; Ngoviwatchai, P. *Tetrahedron Lett.* **1986**, *27*, 3479. (b) Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530. (c) Russell, G. A.; Ngoviwatchai, P. *J. Org. Chem.* **1989**, *54*, 1836.

(7) Schaffner, A.-P.; Darmency, V.; Renaud, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 5847.

(8) Liautard, V.; Robert, F.; Landais, Y. *Org. Lett.* **2011**, *13*, 2658.

(9) Liu, X.; Wang, Z.; Cheng, X.; Li, C. *J. Am. Chem. Soc.* **2012**, *134*, 14330.

(10) Yang, Y.; Zhang, X.; Liang, Y. *Tetrahedron Lett.* **2012**, *53*, 6557.

(11) Ouyang, K.; Xi, Z. *Acta Chim. Sin.* **2013**, *71*, 13.

(12) (a) Chen, Z.; Zhang, Y.-X.; An, Y.; Song, X.-L.; Wang, Y.-H.; Zhu, L.-L.; Guo, L. *Eur. J. Org. Chem.* **2009**, 5146. (b) Huang, L.; Cheng, K.; Yao, B.; Zhao, J.; Zhang, Y. *Synthesis* **2009**, 3504. (c) Zhang, Y.; Li, C.-J. *Tetrahedron Lett.* **2004**, *45*, 7581. (d) Jang, Y.-J.; Shih, Y.-K.; Liu, J.-Y.; Kuo, W.-Y.; Yao, C.-F. *Chem. Eur. J.* **2003**, *9*, 2123. (e) Liu, Z.-Q.; Sun, L.; Wang, J.-G.; Han, J.; Zhao, Y.-K.; Zhou, B. *Org. Lett.* **2009**, *11*, 1437. (f) Clark, A. J.; Rooke, S.; Sparey, T. J.; Taylor, P. C. *Tetrahedron Lett.* **1996**, *37*, 909.

