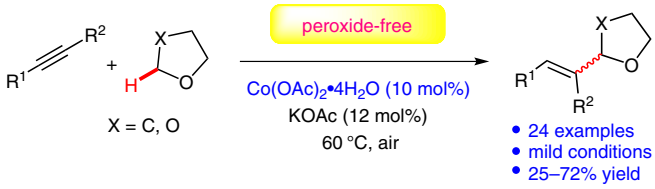
Synthesis M. Zhang et al. Paper

Peroxide-Free $Co(OAc)_2$-Catalyzed Radical Addition of sp^3 C–H Bonds to Alkynes

Min Zhang
Yun Zhao
Wanzhi Chen*

Department of Chemistry, Zhejiang University, Hangzhou 310013, P. R. of China
chenwzz@zju.edu.cn



Received: 29.07.2016
Accepted after revision: 17.10.2016
Published online: 28.11.2016
DOI: 10.1055/s-0036-1588909; Art ID: ss-2016-h0537-op

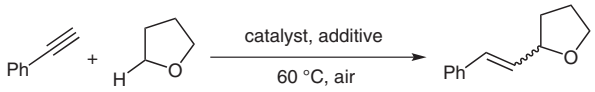
Abstract Cobalt-catalyzed radical addition of C–H bonds adjacent to an oxygen atom towards alkynes is described. The reaction proceeded at 60 °C without using additional radical initiators, and leads to 2-vinyl ether derivatives in good yields.

Key words cobalt catalysis, radical addition, alkyne, tetrahydrofuran

The formation of C–C bonds is the most fundamental transformation in the construction of complex molecules. Traditional strategies include Friedel–Crafts reaction,[1] Aldol condensation,[2] Michael addition reaction,[3] nucleophilic addition, and substitution reaction involving Grignard reagents.[4] In recent decades, palladium-catalyzed cross-coupling reactions were developed as one of the most efficient protocols in modern organic synthetic chemistry.[5] The coupling reactions often rely on prefunctionalized substrates. Transition-metal-catalyzed direct carbon–hydrogen bond functionalization has progressed greatly over the past two decades.[6] Most of these works have focused on directed C–H activation under the influence of a pre-existing donating group. The C–C bond formation through radical coupling and radical addition reactions are also promising,[7] especially reactions that proceed via radicals generated from homolytic fission of a C–H bond. Cyclic ethers such as tetrahydrofuran are good nucleophilic radical precursors that can react with various electrophiles.[8]

2-Vinyl tetrahydrofuran derivatives serving as structural motifs play an important role in biological products and synthetic pharmaceuticals.[9] Synthesis of 2-vinyl tetrahydrofurans through direct radical addition of an sp^3 C–H bond adjacent to the oxygen atom of tetrahydrofuran (THF) with various alkynes has been accomplished. It has been found that copper,[10] cobalt,[11] or rhodium[12] catalysts or visi-

Table 1 Optimization of the Reaction Conditions of Cobalt-Catalyzed Addition of THF with Alkynes[a]



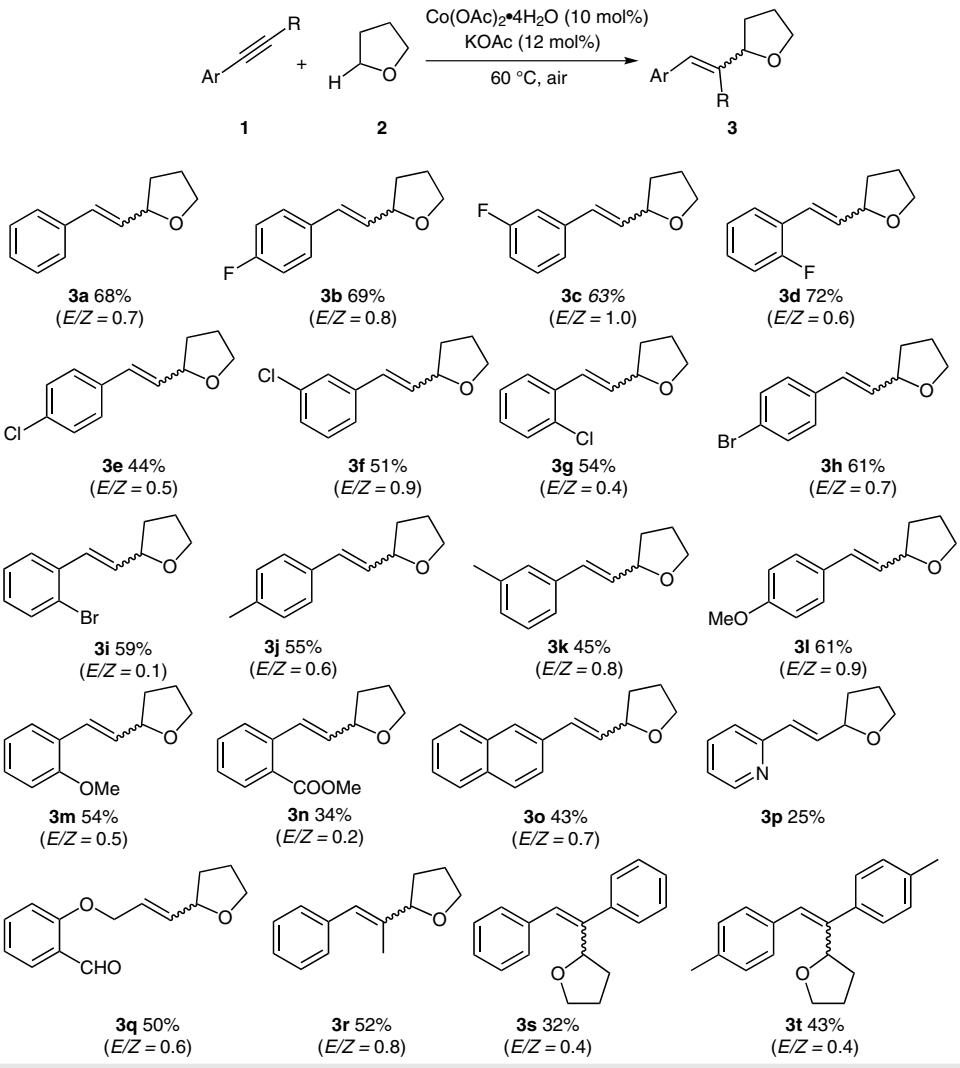
1a 2 3a

Entry	Catalyst (10 mol%)	Additive (12 mol%)	Yield (%)[b]	*E*/*Z*[c]
1	$Co(OAc)_2{\cdot}4H_2O$	NaO^{t}Bu	trace	–
2	$Co(OAc)_2{\cdot}4H_2O$	KO^{t}Bu	trace	–
3	$Co(OAc)_2{\cdot}4H_2O$	NaOH	10	0.8
4	$Co(OAc)_2{\cdot}4H_2O$	K_3PO_4	23	0.6
5	$Co(OAc)_2{\cdot}4H_2O$	KOAc	68	0.7
6	$CoCl_2$	KOAc	34	0.8
7	$CoCO_3$	KOAc	13	0.8
8	$Co(PPh_3)_2Cl_2$	KOAc	18	0.6
9	CuCl	KOAc	trace	–
10	CuBr	KOAc	trace	–
11[d]	$Co(OAc)_2{\cdot}4H_2O$	KOAc	trace	–
12[e]	$Co(OAc)_2{\cdot}4H_2O$	KOAc	trace	–
13	–	–	n.r.	–
14	$Co(OAc)_2{\cdot}4H_2O$	–	n.r.	–
15[f]	$Co(OAc)_2{\cdot}4H_2O$	KOAc	n.r.	–
16[g]	$Co(OAc)_2{\cdot}4H_2O$	KOAc	14	0.8

[a] Unless otherwise mentioned, all reactions were carried out using **1** (0.3 mmol) in THF (1.5 mL) at 60 °C under air for 10 h.
[b] Yield of isolated mixtures of *cis*/*trans* isomers.
[c] *E*/*Z* ratios were determined through ^{1}H NMR analysis of crude reaction mixtures.
[d] The reaction was conducted at room temperature.
[e] The reaction was conducted in a solvent mixture of THF (0.5 mL) and MeCN (1.0 mL).
[f] The reaction was conducted under N_2 atmosphere.
[g] The reaction was conducted under O_2 atmosphere.

ble-light[13] can efficiently catalyze the addition of sp^3 C–H bonds to alkynes. However, organic peroxides such as TBHP are required. Organic peroxides are usually unstable and sensitive to heat and collision. Therefore, it would be a better choice to avoid the use of organic peroxides. Some efforts have been made to improve the reaction. Direct addition of cyclic ethers to alkynes under microwave conditions was reported to require quite high temperature.[14] Allyl and benzyl chlorides could initiate reactions of tetrahydrofuran and alkynes, but the yields were quite low (ca. 20%).[15] Me_2Zn was found to promote the reaction but the scope was limited to internal alkynes.[16] We found that O_2 can initiate the formation of the tetrahydrofuran radical in the presence of $Co(OAc)_2{\cdot}4H_2O$. Herein, we report the preparation of 2-vinyl tetrahydrofurans by using cobalt catalyst under air, without the addition of organic peroxides.

The reaction of phenylacetylene (**1a**; 0.3 mmol) with tetrahydrofuran (**2**; 1.5 mL) was chosen as the model reaction for the optimization study; the results are summarized in Table 1. It was found that at a loading of 10 mol% $Co(OAc)_2{\cdot}4H_2O$ at 60 °C, no desired addition product was observed. In the presence of NaO^{t}Bu or KO^{t}Bu, only 1,4-diphenylbuta-1,3-diyne was isolated resulting from the oxidative dimerization of phenylacetylene. When NaOH and K_3PO_4 were added, the addition product was obtained in 10 and 23% yield, respectively. To our delight, addition of KOAc could efficiently promote the addition reaction, and the yield was sharply increased to 68% (Table 1, entries 1–5). We also examined the effect of different cobalt salts. Under the same conditions, other cobalt catalysts such as $CoCl_2$, $CoCO_3$, and $Co(PPh_3)_2Cl_2$, were less active (entries 6–8). CuBr and CuCl were also examined. Under the same condi-



Scheme 1 Substrate scope of the cobalt-catalyzed addition of THF with alkynes. Isolated yields. *E*/*Z* ratios were determined through ^{1}H NMR analysis of the product.

tions, the desired product was not detected by NMR measurement (entries 9 and 10). When the reaction was conducted at room temperature, no reaction occurred (entry 11). Mixed solvents disfavored the reaction, probably because of the low reactivity of THF (entry 12).[17]

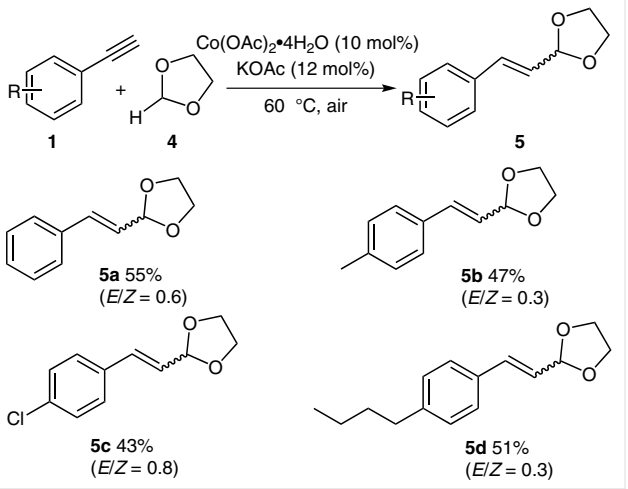
In addition, we failed to obtain the product under N_2 atmosphere, illustrating that O_2 is essential (Table 1, entry 15). Unexpectedly, the yield was also quite low under an O_2 atmosphere, and the major product was diphenylbuta-1,3-diyne (entry 15). In all the reactions, the products were isolated as *cis*/*trans* isomers with the *Z* isomers predominating.

The results presented above showed that $Co(OAc)_2{\cdot}4H_2O$ can catalyze the radical addition of tetrahydrofuran towards triple bonds under the very mild conditions. To examine the generality of the reaction, the reactivity of a number of aromatic alkynes bearing either electron-withdrawing or electron-donating groups was tested. The results are summarized in Scheme 1. By using THF as both the solvent and reactant, unsubstituted phenylacetylene reacted with THF to give 2-styryltetrahydrofuran **3a** in a yield of 68% in the presence of 10 mol% $Co(OAc)_2{\cdot}4H_2O$ and 12 mol% KOAc. Fluorine-containing phenylacetylene showed similar activities to those of phenylacetylene, and *ortho*-, *meta*-, and *para*-fluorophenylacetylene, affording corresponding addition products **3b–d** in 63–72% yields.

Chlorine-containing phenylacetylene also reacted with THF, giving 2-styryltetrahydrofuran derivatives **3e–g** in slightly lower yields. The reactivity of bromine-containing phenylacetylenes were between those of the corresponding chlorophenylacetylene and fluorophenylacetylene, and the target product 2-styryltetrahydrofuran derivatives **3h–i** were obtained in ca. 60% yield. In these reactions, *ortho*-substituents did not show obvious steric effects. Phenylacetylenes bearing electron-donating groups such as methyl and methoxyl were also good reactants, and the target products **3j–m** were obtained in ca. 50% yield at 60 °C. Although 2-ethynylpyridine is also reactive, 2-[2-(tetrahydrofuran-2-yl)vinyl]pyridine (**3p**) was afforded in only 25% yield.

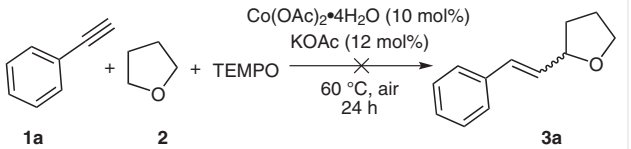
This is probably because the radical intermediate resulting from the electron-deficient alkyne is less stable. Under the same conditions, internal alkynes were applied to give trisubstituted alkenes. Unsymmetric propyn-1-ylbenzene also reacted with THF to give 2-(1-phenylpropen-2-yl)tetrahydrofuran (**3r**), and the regioisomer 2-(1-phenylpropen-1-yl)tetrahydrofuran was not detected by NMR spectroscopy. Similarly, the radical addition of THF towards diphenylacetylene and ditolylacetylene at 60 °C led to the isolation of **3s** and **3t**, respectively.

The addition reactions of alkynes with other cyclic ethers including 1,4-dioxane, 2,5-dimethoxytetrahydrofuran, morpholine, and 2,3-dihydrofuran were also examined under the conditions detailed above. Unfortunately, these reactions gave mixtures containing the desired products in less than 10% yield as determined by gas chromatography. It was found that cobalt(II) could efficiently catalyze the reaction of 1,3-dioxolane with phenylacetylenes; the results are listed in Scheme 2. 1,3-Dioxolane bears two oxygen atoms, and two regioisomers were expected. However, the reaction mainly occurred at the C-2 position of 1,3-dioxolane, and 2-alkenylated 1,3-dioxolanes **5a–d** were afforded in moderate yields.



Scheme 2 Cobalt-catalyzed addition of 1,3-dioxolane with alkynes. Isolated yields. *E*/*Z* ratios were determined through ^{1}H NMR analysis of the product.

Based on the experimental data listed in Table 1, we tentatively propose that the reaction proceeds through a radical mechanism. This is supported by a control experiment that showed that when the reaction was conducted for 24 h in the presence of one equivalent of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) under the standard conditions, no addition product was observed (Scheme 3). The reaction is probably initiated by the reaction of Co(II) with O_2 leading to Co(III)-O-O· radical. Abstraction of a H atom from a THF molecule would generate a THF radical and Co(III)-O-OH. Subsequent radical addition towards the triple bond would form olefinic radicals. Finally, the olefinic radicals would abstract one H atom from THF affording the addition product and regenerate THF radicals.



Scheme 3 A control experiment

In summary, $Co(OAc)_2{\cdot}4H_2O$-catalyzed direct radical addition of a C–H bond adjacent to the oxygen atom of THF and 1,3-dioxolane towards alkynes was described. The reactions afford a number of 2-alkenylated tetrahydrofuran

and 1,3-dioxolane derivatives in good yields under very mild conditions without use of additional radical initiators. This protocol offers an economic and convenient synthetic route to 2-styryltetrahydrofurans.

Unless otherwise noted, all reactions were carried out under air in Schlenk tubes with magnetic stirring. Temperature was maintained by using a thermostat-controlled silicone oil bath. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF was distilled from Na by using benzophenone as the indicator. Purification of the reaction products was carried out by flash column chromatography using 300–400 mesh silica gel. Thin-layer chromatography (TLC) was performed with Huanghai GF254 silica gel coated plates and visualized by exposure to UV light (254 nm). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded with Avance Bruker Spectrometers with $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts are referenced to residual solvent peaks ($CDCl_3$: δ_H = 7.28 ppm; δ_C = 77.0 ppm). Data for ^{1}H NMR spectra are reported as: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet), coupling constant (Hz), and integration. High-resolution mass spectra (HRMS) were recorded with a Bruker Apex IV FTMS mass spectrometer (ESI). IR spectra were recorded with a Perkin–Elmer BXII spectrophotometer.

Cobalt-Catalyzed Addition of THF and 1,3-Dioxolane with Alkynes; General Procedure

$Co(OAc)_2{\cdot}4\,H_2O$ (0.1 equiv) and KOAc (0.12 equiv) were added to either THF or 1,3-dioxolane (1.5 mL) in a Schlenk tube under air. Alkyne (0.3 mmol, 1.0 equiv) was then added and the mixture was stirred and heated at 60 °C for 10 h. The resulting mixture was purified by flash column chromatography (petroleum ether/EtOAc, 50:1) to afford the desired pure product.

2-Styryltetrahydrofuran (3a)[18]

Yield: 35.3 mg (68%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.7; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.22 (m, 8.5 H), 6.61–6.56 (m, 1.7 H), 6.24–6.18 (m, 0.7 H), 5.73–5.68 (m, 1 H), 4.67 (dd, *J* = 15.2, 7.6 Hz, 1 H), 4.48 (dd, *J* = 14.0, 7.2 Hz, 0.7 H), 4.00–3.93 (m, 1.7 H), 3.87–3.76 (m, 1.7 H), 2.18–2.09 (m, 1.7 H), 2.04–1.89 (m, 3.4 H), 1.74–1.70 (m, 1.7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9, 136.7, 132.9, 131.5, 130.5, 130.5, 128.8, 128.5, 128.2, 127.5, 127.1, 126.5, 79.7, 75.1, 68.2, 68.1, 32.9, 32.4, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{14}O$: 175.1045; found: 175.1049.

2-(4-Fluorostyryl)tetrahydrofuran (3b)[18]

Yield: 40.0 mg (69%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.8; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 3.6 H), 7.04–6.96 (m, 3.6 H), 6.56–6.52 (m, 1.8 H), 6.12 (dd, *J* = 16.0, 6.8 Hz, 0.8 H), 5.69 (dd, *J* = 11.6, 8.8 Hz, 0.8 H), 4.63–4.57 (m, 0.8 H), 4.48–4.42 (m, 0.8 H), 3.99–3.93 (m, 1.8 H), 3.86–3.76 (m, 1.8 H), 2.16–2.08 (m, 1.8 H), 2.06–1.88 (m, 3.6 H), 1.75–1.64 (m, 1.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3 (d, J_{C-F} = 245.2 Hz), 162.0 (d, J_{C-F} = 245.1 Hz), 133.0 (d, J_{C-F} = 3.0 Hz), 132.7, 132.7, 130.5 (d, J_{C-F} = 13.9 Hz), 130.5, 130.3 (d, J_{C-F} = 2.3 Hz), 129.3, 128.0 (d, J_{C-F} = 8.0 Hz), 115.4 (d, J_{C-F} = 21.5 Hz), 115.1 (d, J_{C-F} = 21.3 Hz), 79.6, 74.9, 68.2, 68.1, 32.9, 32.4, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}FO$: 192.0950; found: 192.0943.

2-(3-Fluorostyryl)tetrahydrofuran (3c)[18]

Yield: 36.5 mg (63%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 1.0; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–6.83 (m, 8 H), 6.50–6.46 (m, 2 H), 6.14 (dd, *J* = 15.6, 6.4 Hz, 1 H), 5.67 (dd, *J* = 11.6, 8.8 Hz, 1 H), 4.58–4.52 (m, 1 H), 4.43–4.38 (m, 1 H), 3.93–3.86 (m, 2 H), 3.80–3.69 (m, 2 H), 2.11–2.02 (m, 2 H), 1.96–1.84 (m, 4 H), 1.68–1.61 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1 (d, J_{C-F} = 243.3 Hz), 162.6 (d, J_{C-F} = 244.2 Hz), 139.3 (d, J_{C-F} = 7.5 Hz), 138.9 (d, J_{C-F} = 7.5 Hz), 134.0, 132.0, 130.3 (d, J_{C-F} = 1.7 Hz), 129.9 (d, J_{C-F} = 8.7 Hz), 129.6 (d, J_{C-F} = 8.4 Hz), 129.2 (d, J_{C-F} = 2.5 Hz), 124.6 (d, J_{C-F} = 2.7 Hz), 122.4 (d, J_{C-F} = 2.6 Hz), 115.6 (d, J_{C-F} = 21.5 Hz), 114.1 (d, J_{C-F} = 4.7 Hz), 114.1 (d, J_{C-F} = 4.9 Hz), 112.9 (d, J_{C-F} = 21.6 Hz), 79.3, 74.9, 68.3, 68.1, 32.9, 32.4, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}FO$: 192.0950; found: 192.0945.

2-(2-Fluorostyryl)tetrahydrofuran (3d)[18]

Yield: 41.8 mg (72%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.6; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–6.99 (m, 6.4 H), 6.74 (d, *J* = 16.0 Hz, 0.6 H), 6.60 (d, *J* = 8.0 Hz, 1 H), 6.30 (dd, *J* = 16.0, 6.4 Hz, 0.6 H), 5.80 (dd, *J* = 11.6, 8.8 Hz, 1 H), 4.58–4.46 (m, 1.6 H), 4.00–3.92 (m,1.6 H), 3.87–3.75 (m, 1.6 H), 2.18–2.08 (m, 1.6 H), 2.03–1.87 (m, 3.2 H), 1.76–1.64 (m, 1.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3 (d, J_{C-F} = 247.8 Hz), 160.2 (d, J_{C-F} = 245.7 Hz), 134.7, 133.2 (d, J_{C-F} = 4.6 Hz), 130.8 (d, J_{C-F} = 1.7 Hz), 129.0 (d, J_{C-F} = 8.1 Hz), 128.7 (d, J_{C-F} = 8.2 Hz), 127.5 (d, J_{C-F} = 3.9 Hz), 124.6 (d, J_{C-F} =12.3 Hz), 124.4 (d, J_{C-F} = 14.4 Hz), 124.0 (d, J_{C-F} = 3.2 Hz), 123.7 (d, J_{C-F} = 3.6 Hz), 122.8 (d, J_{C-F} = 1.7 Hz), 115.7 (d, J_{C-F} = 22.3 Hz), 115.3 (d, J_{C-F} = 21.7 Hz), 79.8, 75.2, 68.2, 68.1, 32.7, 32.4, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}FO$: 192.0950; found: 192.0943.

2-(4-Chlorostyryl)tetrahydrofuran (3e)[18]

Yield: 27.3 mg (44%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.5; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.15 (m, 6 H), 6.48–6.44 (m, 1.5 H), 6.11 (dd, *J* = 16.0, 6.8 Hz, 0.5 H), 5.64 (dd, *J* = 11.6, 8.8 Hz, 1 H), 4.51 (dd, *J* = 15.6, 8.0 Hz, 1 H), 4.38 (q, *J* = 13.2, 6.4 Hz, 0.5 H), 3.92–3.85 (m, 1.5 H), 3.79–3.68 (m, 1.5 H), 2.09–2.01 (m, 1.5 H), 1.95–1.84 (m, 3.1 H), 1.65–1.59 (m, 1.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.3, 132.5.0, 132.0, 130.2, 129.4, 129.1, 128.1, 127.6, 127.3, 127.0, 126.7, 126.6, 78.4, 73.8, 67.2, 67.1, 31.9, 31.3, 25.4, 24.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}ClO$: 208.0655; found: 208.0651.

2-(3-Chlorostyryl)tetrahydrofuran (3f)[18]

Yield: 31.6 mg (51%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.9; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.10 (m, 7.6 H), 6.47–6.43 (m, 1.9 H), 6.15 (dd, *J* = 15.6, 6.4 Hz, 0.9 H), 5.68 (dd, *J* = 11.6, 9.2 Hz, 0.9 H), 4.56–4.50 (m, 0.9 H), 4.43–4.38 (m, 0.9 H), 3.93–3.86 (m, 1.9 H), 3.80–3.69 (m, 1.9 H), 2.10–2.02 (m, 1.9 H), 1.89–1.83 (m, 3.8 H), 1.68–1.59 (m, 1.9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7, 137.4, 133.4, 133.2, 133.0, 131.1, 129.1, 128.7, 128.4, 127.9, 127.7, 126.4, 126.2, 126.0, 125.3, 123.7, 78.3, 73.8, 67.2, 67.1, 31.9, 31.3, 25.3, 24.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}ClO$: 208.0655; found: 208.0649.

2-(2-Chlorostyryl)tetrahydrofuran (3g)[18]

Yield: 33.5 mg (54%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.4; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.32 (m, 2.8 H), 7.26–7.13 (m, 2.8 H), 6.97 (d, *J* = 16.0 Hz, 0.4 H), 6.69 (d, *J* = 12.0 Hz, 1 H), 6.20 (dd, *J* = 15.6, 6.4 Hz, 0.4 H), 5.81 (dd, *J* = 11.6, 9.2 Hz, 1 H), 4.54–4.45 (m, 1.4 H), 3.99–3.91 (m, 1.4 H), 3.88–3.74 (m, 0.4 H),3.79–3.74 (m, 1 H), 2.19–2.04 (m, 1.4 H), 2.00–1.86 (m, 2.8 H), 1.75–1.65 (m, 1.4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.9, 132.9, 132.6, 132.4, 132.0, 129.8, 128.6, 128.3, 127.7, 127.6, 127.5, 125.9, 125.7, 125.6, 125.3, 78.5, 73.9, 67.2, 67.1, 31.8, 31.3, 28.7, 25.4, 24.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}ClO$: 208.0655; found: 208.0650.

2-(4-Bromostyryl)tetrahydrofuran (3h)[18]

Yield: 46.4 mg (61%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.7; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.34 (m, 3.4 H), 7.19–7.09 (m, 3.4 H), 6.47–6.43 (m, 1.7 H), 6.13 (dd, *J* = 16.0, 6.8 Hz, 0.7 H), 5.66 (dd, *J* = 11.6, 9.2 Hz, 1 H), 4.54–4.48 (m, 0.7 H), 4.41–4.36 (m, 0.7 H), 3.91–3.83 (m, 1.7 H), 3.72–3.67 (m, 1.7 H), 2.09–1.87 (m, 1.7 H), 1.97–1.82 (m, 3.4 H), 1.70–1.56 (m, 1.7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 135.6, 133.6, 131.6, 131.4, 131.3, 130.5, 129.2, 128.0, 121.2, 121.1, 79.5, 74.9, 68.3, 68.1, 32.9, 32.3, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}BrO$: 252.0150; found: 252.0147.

2-(2-Bromostyryl)tetrahydrofuran (3i)[18]

Yield: 44.8 mg (59%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.1; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.48 (m, 1.1 H), 7.32–7.29 (m, 1.1 H), 7.23–7.19 (m, 1.1 H), 7.09–7.02 (m, 1.1 H), 6.85 (d, *J* = 15.6 Hz, 0.1 H), 6.55 (d, *J* = 11.2 Hz, 1 H), 6.08 (dd, *J* = 15.6, 6.4 Hz, 0.1 H), 5.73–5.68 (m, 1 H), 4.41–4.36 (m, 1.1 H), 3.89–3.84 (m, 1.1 H), 3.72–3.67 (m, 1.1 H), 2.04–1.78 (m, 3.3 H), 1.63–1.58 (m, 1.1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.8, 136.7, 133.7, 133.6, 132.9, 132.5, 131.0, 130.9, 129.3, 128.8, 127.5, 127.4, 127.3, 127.1, 127.0, 123.9, 79.5, 75.0, 68.3, 68.2, 32.8, 32.4, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{13}BrO$: 252.0150; found: 252.0148.

2-(4-Methylstyryl)tetrahydrofuran (3j)[18]

Yield: 30.8 mg (55%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.6; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.02 (m, 6.4 H), 6.50–6.46 (m, 1.6 H), 6.11–6.05 (m, 0.6 H), 5.59 (dd, *J* = 11.2, 8.8 Hz, 1 H), 4.60 (q, *J* = 15.2, 7.6 Hz, 1 H), 4.38 (q, *J* = 13.6, 6.8 Hz, 0.6 H), 3.92–3.86 (m, 1.6 H), 3.79–3.68 (m, 1.6 H), 2.27 (s, 3.0 H), 2.25 (s, 1.8 H), 2.10–2.00 (m, 1.8 H), 1.93–1.83 (m, 3.2 H), 1.65–1.60 (m, 1.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.3, 135.9, 133.0, 132.8, 131.1, 130.4, 129.4, 128.4, 128.2, 127.8, 127.7, 125.3, 78.8, 74.1, 67.1, 67.0, 31.9, 31.4, 25.4, 24.9, 20.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{16}O$: 188.1201; found: 188.1198.

2-(3-Methylstyryl)tetrahydrofuran (3k)[18]

Yield: 25.2 mg (45%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.8; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.03 (m, 7.2 H), 6.57–6.53 (m, 1.8 H), 6.19 (dd, *J* = 15.6, 6.4 Hz, 0.8 H), 5.69 (dd, *J* = 11.6, 8.8 Hz, 1 H), 4.69–4.64 (m, 1 H), 4.49–4.44 (m, 0.8 H), 3.99–3.93 (m, 1.8 H), 3.86–3.75 (m, 1.8 H), 2.35 (s, 3.0 H), 2.33 (s, 2.4 H), 2.19–2.08 (m, 1.8 H), 2.02–1.89 (m, 3.6 H), 1.75–1.64 (m, 1.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 137.7, 136.8, 136.7, 132.7, 131.5, 130.6, 130.3, 129.6, 128.4, 128.3, 128.1, 127.9, 127.2, 125.9, 123.6, 79.7, 75.1, 68.2, 68.1, 33.0, 32.4, 26.4, 25.9, 21.5, 21.4.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{16}O$: 188.1201; found: 188.1196.

2-(4-Methoxystyryl)tetrahydrofuran (3l)[18]

Yield: 37.2 mg (61%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.9; R_f = 0.40 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.17 (m, 3.8 H), 6.82–6.76 (m, 3.8 H), 6.47–6.44 (m, 1.8 H), 5.99 (dd, *J* = 15.6, 6.8 Hz, 0.9 H), 5.55 (dd, *J* = 11.6, 8.8 Hz, 1 H), 4.62–4.56 (m, 1 H), 4.40–4.34 (m,0.9 H), 3.92–3.86 (m, 1.9 H), 3.80–3.69 (m, 7.6 H), 2.11–2.00 (m, 1.9 H), 1.94–1.83 (m, 3.8 H), 1.66–1.61 (m, 1.9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 158.8, 131.3, 131.2, 130.2, 130.1, 129.4, 128.9, 128.3, 127.7, 113.9, 113.6, 79.9, 75.2, 68.1, 68.0, 55.3, 55.2, 33.0, 32.5, 26.4, 26.0.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{17}O_2$: 204.1150; found: 204.1148.

2-(2-Methoxystyryl)tetrahydrofuran (3m)[18]

Yield: 32.9 mg (54%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.5; R_f = 0.40 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.43 (m, 0.5 H), 7.33–7.18 (m, 2 H), 6.95–6.84 (m, 4 H), 6.73–6.70 (d, *J* = 11.2 Hz, 1 H), 6.22 (dd, *J* = 16.0, 6.8 Hz, 0.5 H), 5.72 (dd, *J* = 11.6, 9.2 Hz, 1 H), 4.60–4.54 (m, 1 H), 4.47 (q, *J* = 13.6, 6.8, 0.5 H), 3.97–3.74 (m, 7.5 H), 2.11–2.05 (m, 1.5 H), 2.01–1.89 (m, 3 H), 1.72–1.68 (m, 1.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 155.7, 131.4, 130.0, 129.9, 129.4, 127.8, 127.7, 127.5, 126.3, 125.9, 124.8, 124.6, 124.5, 119.5, 119.1, 109.8, 109.2, 79.2, 74.3, 67.1, 67.0, 54.4, 54.3, 31.8, 31.4, 25.4, 25.0.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{17}O_2$: 204.1150; found: 204.1147.

Methyl 2-[2-(Tetrahydrofuran-2-yl)vinyl]benzoate (3n)[18]

Yield: 23.8 mg (34%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.2; R_f = 0.40 (PE/EtOAc, 7:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.95 (m, 1 H), 7.87–7.85 (m, 0.2 H), 7.58–7.32 (m, 3.6 H), 7.07 (d, *J* = 11.6 Hz, 1 H), 6.11 (dd, *J* = 16.0, 6.8 Hz, 0.2 H), 5.73 (dd, *J* = 11.6, 9.6 Hz, 1 H), 4.52 (q, *J* = 13.6, 6.8 Hz, 0.2 H), 4.41–4.35 (m, 1 H), 3.97–3.71 (m, 6 H), 2.03–1.82 (m, 3.6 H), 1.72–1.61 (m, 1.2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.9, 167.5, 138.7, 138.2, 133.4, 132.0, 131.8, 131.6, 131.1, 130.5, 130.4, 129.3, 129.1, 127.5, 127.4, 127.2, 127.1, 79.6, 75.1, 68.2, 68.1, 52.1, 52.0, 32.9, 32.3, 26.4, 25.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{14}H_{16}O_3$: 232.1099; found: 232.1095.

[2-(Naphthalen-2-yl)vinyl]tetrahydrofuran (3o)[18]

Yield: 28.8 mg (43%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.7; R_f = 0.50 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.73 (m, 6.8 H), 7.62–7.59 (m, 0.7 H), 7.48–7.43 (m, 3.4 H), 6.77–6.73 (m, 1.7 H), 6.34 (dd, *J* = 15.6, 6.4 Hz, 0.7 H), 5.79 (dd, *J* = 11.6, 9.2 Hz, 1 H), 4.75 (q, *J* = 15.2, 7.6 Hz, 1 H), 4.53 (q, *J* = 13.6, 6.8 Hz, 0.7 H), 4.02–3.96 (m, 1.7 H), 3.90–3.78 (m, 1.7 H), 2.22–2.14 (m, 1.7 H), 2.05–1.93 (m, 3.4 H), 1.79–1.68 (m, 1.7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.3, 133.2, 132.2, 132.2, 131.9, 131.4, 130.5, 129.9, 129.6, 127.8, 127.1, 127.0, 126.9, 126.7, 126.6, 126.6, 126.0, 125.4, 125.2, 125.1, 124.9, 124.8, 122.6, 78.7, 74.2, 67.2, 67.1, 32.0, 31.4, 25.4, 24.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{16}H_{16}O$: 224.1201; found: 224.1200.

2-[(*E*)-2-(Tetrahydrofuran-2-yl)ethenyl]pyridine (3p)[18]

Yield: 13.0 mg (25%); pale-yellow oil; R_f = 0.30 (PE/EtOAc, 3:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 4.0 Hz, 1 H), 7.62 (dt, *J* = 8.6, 2 Hz, 1 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 7.12 (dd, *J* = 5.2, 1.6 Hz, 1 H), 6.76–6.65 (m, 2 H), 4.60–4.55 (m, 1 H), 3.99 (dd, *J* = 14.4, 7.6 Hz, 1 H), 3.86 (dd, *J* = 14.0, 7.6 Hz, 1 H), 2.19–2.12 (m, 1 H), 2.02–1.91 (m, 2 H), 1.81–1.75 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 149.5, 136.5, 135.3, 129.5, 122.1, 121.8, 79.0, 68.3, 32.2, 25.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{11}H_{13}NO$: 175.0997; found: 175.0998.

2-[3-(Tetrahydrofuran-2-yl)allyloxy]benzaldehyde (3q)

Yield: 31.0 mg (50%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.6; R_f = 0.30 (PE/EtOAc, 5:1).

IR (neat): 2925, 2862, 1725, 1686, 1599, 1482, 1456, 1390, 1286, 1238, 1190, 1161, 1104, 1047, 1011, 969, 841, 810, 757, 650 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.53 (s, 1 H), 10.50 (s, 0.6 H), 7.85–7.51 (m, 6.4 H), 5.95–5.74 (m, 3.2 H), 4.81 (d, *J* = 6.0 Hz, 1.6 H), 4.66 (d, *J* = 4.4 Hz, 1.6 H), 4.31 (t, *J* = 6.8 Hz, 1.6 H), 3.97–3.90 (m, 1.6 H), 3.84–3.78 (m, 1.6 H), 2.10–2.06 (m, 1.6 H), 1.97–1.90 (m, 3.2 H), 1.67–1.63 (m, 1.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.9, 161.0, 160.9, 135.9, 134.9, 130.9, 128.8, 128.4, 126.0, 125.0, 124.9, 120.8, 112.8, 78.7, 75.1, 68.3, 68.2, 65.6, 64.7, 32.7, 32.1, 26.0, 25.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{14}H_{16}O_3$: 232.1099; found: 232.1102.

2-(1-Phenylprop-1-en-2-yl)tetrahydrofuran (3r)[18]

Yield: 29.1 mg (52%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.8; R_f = 0.60 (PE/EtOAc, 7:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.15 (m, 5.4 H), 7.12–7.09 (m, 3.6 H), 6.47–6.38 (m, 1.8 H), 4.68–4.64 (m, 1 H), 4.33–4.29 (m, 0.8 H), 3.95–3.63 (m, 3.6 H), 2.07–1.99 (m, 0.8 H), 1.95–1.83 (m, 4.6 H), 1.80 (d, *J* = 1.6 Hz, 3 H), 1.77 (d, *J* = 1.2 Hz, 2.4 H), 1.75–1.67 (m, 1.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.6, 137.9, 137.5, 129.0, 128.7, 128.3, 128.0, 128.0, 126.4, 126.2, 124.5, 84.0, 68.7, 31.0, 30.5, 26.9, 26.1, 17.9, 14.0.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{16}O$: 188.1201; found: 188.1202.

2-(1,2-Diphenylvinyl)tetrahydrofuran (3s)

Yield: 24.1 mg (32%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.4; R_f = 0.30 (PE/EtOAc, 50:1).

IR (neat): 3055, 3023, 2971, 2866, 1722, 1599, 1492, 1445, 1242, 1178, 1049, 921, 876, 765, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–6.84 (m, 14 H), 6.67 (s, 1 H), 6.61 (s, 0.4 H), 4.90 (dd, *J* = 8.0, 6.8 Hz, 1 H), 4.64–4.60 (m, 0.4 H), 3.81–3.68 (m, 2.8 H), 3.73–3.68 (m, 2.8 H), 1.93–1.57 (m, 5.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.1, 142.4, 141.3, 139.0, 137.0, 136.8, 133.1, 131.6, 129.3, 129.3, 129.1, 128.8, 128.6, 128.4, 128.2, 127.9, 127.8, 127.2, 127.0, 126.5, 125.8, 83.6, 77.0, 68.7, 68.3, 31.1, 30.6, 26.7, 25.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{18}H_{18}O$: 250.1360; found: 250.1358.

2-(1,2-Di-*p*-tolylvinyl)tetrahydrofuran (3t)

Yield: 35.7 mg (43%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.4; R_f = 0.3 (PE/EtOAc, 50:1).

IR (neat): 2960, 2922, 2864, 1698, 1606, 1562, 1511, 1454, 1262, 1048, 965, 886, 817, 730, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–6.83 (m, 11.2 H), 6.70 (s, 1 H), 6.62 (s, 0.4 H), 4.97 (dd, *J* = 8.4, 6.4 Hz, 1 H), 4.67–4.64 (m, 0.4 H), 3.93–3.75 (m, 2.8 H), 2.36 (s, 7.2 H), 2.23 (s, 1.2 H), 1.89–1.76 (m, 4.2 H), 1.71–1.65 (m, 1.4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 141.6, 138.5, 136.7, 136.6, 136.1, 136.1, 134.2, 134.0, 132.8, 131.3, 129.3, 129.1, 129.1, 129.0, 128.7, 128.6, 128.6, 125.5, 83.7, 68.7, 68.3, 31.1, 30.6, 26.7, 25.8, 21.2, 21.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{22}O$: 278.1671; found: 278.1671.

2-Styryl-1,3-dioxolane (5a)[18]

Yield: 29.1 mg (55%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.6; R_f = 0.60 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.27 (m, 8.0 H), 6.84–6.76 (m, 1.6 H), 6.19–6.14 (m, 0.6 H), 5.75–5.70 (m, 1 H), 5.52 (d, *J* = 7.6 Hz, 1 H), 5.43 (d, *J* = 6.0 Hz, 0.6 H), 4.09–4.05 (m, 3.2 H), 3.98–3.91 (m, 3.2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 135.7, 134.9, 129.0, 128.6, 128.4, 128.3, 127.8, 127.7, 127.0, 126.6, 125.1, 103.9, 99.7, 65.2, 65.1.

HRMS: *m*/*z* [M$^+$] calcd for $C_{11}H_{12}O_2$: 176.0837; found: 176.0839.

2-(4-Methylstyryl)-1,3-dioxolane (5b)[18]

Yield: 26.8 mg (47%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.3; R_f = 0.60 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.12 (m, 5.2 H), 6.80–6.71 (m, 1.3 H), 6.11 (dd, *J* = 10.0, 8.4 Hz, 0.3 H), 5.68 (dd, *J* = 11.6, 7.6 Hz, 1 H), 5.53 (d, *J* = 7.2 Hz, 1 H), 5.42 (d, *J* = 6.4 Hz, 0.3 H), 4.08–4.04 (m, 2.6 H), 3.96–3.90 (m, 2.6 H), 2.39 (s, 0.9 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 137.7, 135.7, 134.9, 133.0, 132.9, 129.9, 129.0, 126.9, 126.6, 125.0, 124.0, 104.1, 99.8, 65.2, 65.1, 21.3, 21.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{14}O_2$: 190.0994; found: 190.0997.

2-(4-Chlorostyryl)-1,3-dioxolane (5c)[18]

Yield: 27.1 mg (43%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.8; R_f = 0.60 (PE/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.19 (m, 7.2 H), 6.70–6.64 (m, 1.8 H), 6.07 (dd, *J* = 16.0, 6.0 Hz, 0.8 H), 5.67 (dd, *J* = 11.6, 7.6 Hz, 1 H), 5.39 (d, *J* = 7.6 Hz, 1 H), 5.35 (d, *J* = 6.0 Hz, 0.8 H), 4.00–3.99 (m, 3.6 H), 3.91–3.86 (m, 3.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.4, 134.3, 134.1, 134.1, 133.8, 133.5, 130.3, 128.8, 128.5, 128.4, 128.1, 125.8, 103.6, 99.5, 66.2, 65.1.

HRMS: *m*/*z* [M$^+$] calcd for $C_{11}H_{11}ClO_2$: 210.0448; found: 210.0045.

2-(4-Butylstyryl)-1,3-dioxolane (5d)

Yield: 35.5 mg (51%); pale-yellow oil; mixture of *cis*/*trans* isomers, *E*/*Z* = 0.3; R_f = 0.60 (PE/EtOAc, 10:1).

IR (neat): 2957, 2927, 2869, 1727, 1678, 1610, 1565, 1510, 1461, 1379, 1343, 1115, 1044, 946, 846, 813, 621 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.03 (m, 5.2 H), 6.73–6.65 (m, 1.3 H), 6.07–6.01 (m, 0.3 H), 5.62–5.57 (m, 1 H), 5.47 (d, *J* = 7.6 Hz, 1 H), 5.34 (d, *J* = 6.0 Hz, 0.3 H), 4.01–3.96 (m, 2.6 H), 3.91–3.83 (m, 2.6 H), 2.59–2.50 (m, 2.6 H), 1.52–1.50 (m, 2.6 H), 1.31–1.26 (m, 2.6 H), 0.88–0.83 (m, 3.9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 133.1, 131.6, 129.2, 129.0, 128.6, 128.3, 127.8, 126.8, 126.6, 125.1, 124.0, 104.1, 99.8, 65.3, 65.2, 35.7, 35.4, 33.5, 33.3, 22.4, 22.3, 14.0, 13.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{15}H_{20}O_2$: 232.1463; found: 232.1467.

Acknowledgment

This work was supported by the National Natural Science Foundation of China (Nos. 21572203 and J1210042) and Zhejiang Provincial Natural Science Foundation (LZ16B020001).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588909.

References

(1) Some examples of Friedel–Crafts reaction: (a) Han, Y.-Y.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Tetrahedron Lett.* **2010**, *51*, 2023. (b) Shirakawa, E.; Uchiyama, N.; Hayashi, T. *J. Org. Chem.* **2011**, *76*, 25. (c) Hammer, S. C.; Dominicus, J. M.; Syren, P. O. *Tetrahedron* **2012**, *68*, 7624.

(2) Some examples of Aldol condensation reaction: (a) Heathcock, C. H.; White, C. T. *J. Am. Chem. Soc.* **1979**, *101*, 7076. (b) Mioskowski, C.; Solladie, G. *Tetrahedron* **1980**, *36*, 227. (c) Meyers, A. I.; Reider, P. J. *J. Am. Chem. Soc.* **1979**, *101*, 2501. (d) Masamune, S.; Ali, Sk. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, 557.

(3) Reviews of Michael addition reaction: (a) Li, Z.; Hou, H. L.; Ying, A.; Xu, S. *Chin. J. Org. Chem.* **2014**, *34*, 1074. (b) Ying, A. G.; Wu, C. L.; Fu, Y. Q.; Ren, S. B.; Liang, H. D. *Chin. J. Org. Chem.* **2012**, *32*, 1587. (c) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877.

(4) Nucleophilic addition and substitution reactions involving Grignard reagents: (a) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, **1986**, 820–822. (b) Walborsky, H. M. *Acc. Chem. Res.* **1990**, *23*, 286.

(5) Reviews of palladium-catalyzed cross-coupling reactions: (a) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(6) Reviews of transition-metal-catalyzed direct carbon–hydrogen bond functionalization: (a) Miao, J. M.; Ge, H. B. *Eur. J. Org. Chem.* **2015**, 7859. (b) Huang, Z. X.; Lim, H. N.; Mo, F. Y.; Young, M. C.; Dong, G. B. *Chem. Soc. Rev.* **2015**, *44*, 7764. (c) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879.

(7) C–C bond formation through radical coupling and radical addition reactions: (a) Qian, Q.; Zang, Z. H.; Chen, Y.; Tong, W. Q.; Gong, H. G. *Mini-Rev. Med. Chem.* **2013**, *13*, 802. (b) Ueda, M. *Chem. Pharm. Bull.* **2014**, *62*, 845.

(8) Reactions of cyclic ethers as nucleophilic radical precursors: (a) Jin, J.; MacMillan, D. W. C. *Angew. Chem. Int. Ed.* **2015**, *54*, 1565. (b) Okugawa, N.; Moriyama, K.; Togo, H. *Eur. J. Org. Chem.* **2015**, 4973. (c) Sun, K.; Wang, X.; Li, G.; Zhu, Z. H.; Jiang, Y. Q.; Xiao, B. B. *Chem. Commun.* **2014**, *50*, 12880. (d) Li, X.; Wang, H.-Y.; Shi, Z.-J. *New J. Chem.* **2013**, *37*, 1704. (e) Hasegawa, M.; Ishii, H.; Cao, Y.; Fuchigami, T. *J. Electrochem. Soc.* **2006**, *153*, D162. (f) Minisci, F. *Synthesis* **1973**, 1.

(9) The applications of THF derivatives: (a) Harmange, J. C.; Figadere, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711. (b) Kondo, S.; Yasui, K.; Katayama, M.; Marumo, S.; Kondo, T.; Hattori, H. *Tetrahedron Lett.* **1987**, *28*, 5861. (c) Alali, F. Q.; Liu, X. X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504. (d) Chakraborty, T. K.; Das, S. *Curr. Med. Chem.: Anti-Cancer Agents* **2001**, *1*, 131. (e) Bermejo, A.; Figadere, B.; ZafraPolo, M. C.; Barrachina, I.; Estornell, E.; Cortes, D. *Nat. Prod. Rep.* **2005**, *22*, 269. (f) Vilotijevic, I.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2009**, *48*, 5250. (g) Wan, M.; Meng, Z. L.; Lou, H. X.; Liu, L. *Angew. Chem. Int. Ed.* **2014**, *53*, 13845.

(10) Huang, L.; Cheng, K.; Yao, B.; Zhao, J.; Zhang, Y. *Synthesis* **2009**, 3504.

(11) Chen, L.; Yang, J. J.; Li, L.; Weng, Z. Q.; Kang, Q. *Tetrahedron Lett.* **2014**, *55*, 6096.

(12) Tusun, X.; Lu, C. D. *Synlett* **2013**, *24*, 1693.

(13) Li, J.; Zhang, J.; Tan, H. B.; Wang, Z. G. D. *Org. Lett.* **2015**, *17*, 2522.

(14) Zhang, Y.; Li, C. J. *Tetrahedron Lett.* **2004**, *45*, 7581.

(15) Luigino, T.; Catia, G.; Ludovico, R.; Francesca, R.; Valeria, V. *Tetrahedron Lett.* **2010**, *51*, 5980.

(16) Chen, Z. L.; Zhang, Y. X.; An, Y.; Song, X. L.; Wang, Y. H.; Zhu, L. L.; Guo, L. *Eur. J. Org. Chem.* **2009**, 5146.

(17) Some examples of reactions of THF: (a) Xiang, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 11986. (b) Clark, A. J.; Rooke, S.; Sparey, T. J.; Taylor, P. C. *Tetrahedron Lett.* **1996**, *37*, 909. (c) Dimitrios, T.; Christopher, K.; Paul, K. *Tetrahedron Lett.* **1999**, *40*, 6193. (d) Davies, H. M. L.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063. (e) Díaz-Requejo, M. M.; Belderraín, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 896. (f) Yamada, K.; Yamamoto, Y.; Tomioka, K. *Org. Lett.* **2003**, *5*, 1797. (g) Cao, K.; Jiang, Y. J.; Zhang, S. Y.; Fan, C. A.; Tu, Y. Q.; Pan, Y. J. *Tetrahedron Lett.* **2008**, *49*, 4652. (h) Tortoreto, C.; Achard, T.; Zeghida, W.; Austeri, M.; Gune, L.; Lacour, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 5847.

(18) Analytic data for known compounds: (a) Huang, L.; Cheng, K.; Yao, B.; Zhao, J.; Zhang, Y. *Synthesis* **2009**, 3504. (b) Chen, L.; Yang, J. J.; Li, L.; Weng, Z. Q.; Kang, Q. *Tetrahedron Lett.* **2014**, *55*, 6096. (c) Jang, Y. Y.; Shih, Y. K.; Liu, J. Y.; Kuo, W. Y.; Yao, C. F. *Chem. Eur. J.* **2003**, *9*, 2123.