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A Method for Synthesis of Homoallylic Bromide

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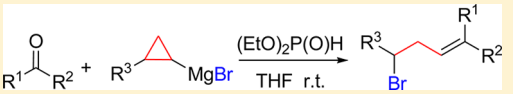
Supporting Information

ABSTRACT: Cyclopropyl Grignard reagents react with carbonyl compounds in the presence of diethyl phosphite to give homoallylic bromides. The reaction is effectively carried out under mild conditions in a one-pot fashion with moderate to good yields.

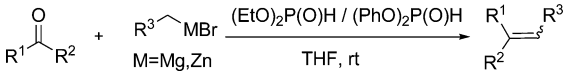


INTRODUCTION

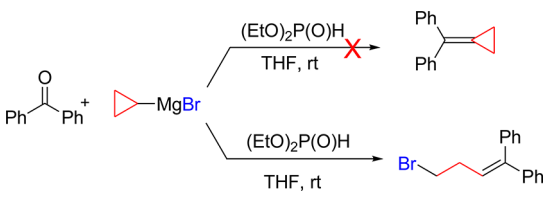
Homoallylic halides have attracted a great deal of interest due to their versatility as building blocks or starting substrates in organic synthesis[1] and in the pharmaceutical/agrochemical industries.[2] However, the synthetic approaches of homoallylic halides are very limited. Previously described methodologies involve treatment of the appropriate cyclopropyl methanol with 48% hydrobromic acid,[3] PBr_3,[4] zinc bromide[4c] or a magnesium halide.[5] Shi et al. used the methylenecyclopropanes (MCPs) to react with various metal chlorides or bromides to give the corresponding homoallylic halides in good yields.[6] However, under the above conditions, the isolation of cyclopropylcarbinols or methylenecyclopropanes is necessary, and a mixture of *E* and *Z* alkenes is always obtained. In 2003, Wong et al. reported a one-pot synthetic pathway for the preparation of homoallylic halides by the in situ generated MgBrCl-promoted ring-opening of cyclopropylcarbinyl acetates.[7] But in this method, a mixture of homoallylic bromide and chloride was obtained.

Recently, our group discovered an olefination reaction of carbonyl compounds using Grignard reagents[8] or organozinc reagents[9] (Scheme 1). A cyclopropylmagnesium bromide was employed; instead of the expected product methylenecyclopropane, it was interesting to notice the formation of homoallylic halide (Scheme 2). In view of the importance of this class of compound and the limitation of previous synthesis methods, we believe it is necessary and meaningful to further investigate and develop this method to afford homoallylic halides. Herein, we report a convenient one-pot protocol for the synthesis of homoallylic halides by the reaction of carbonyl compounds with cyclopropyl Grignard reagents in the presence of diethyl phosphite.

Scheme 1. Olefination of Carbonyl Compounds with Grignard Reagents or Organozinc Reagents



Scheme 2. Reaction of Cyclopropylmagnesium Bromide with Benzophenone in the Presence of Diethyl Phosphite



RESULTS AND DISCUSSION

Initially, ketone **1a** and cyclopropylmagnesium bromide were used as model substrates for the optimization of the reaction conditions. As shown in Table 1, the additives were first examined with THF as the solvent at room temperature. When diethyl phosphite and diphenyl phosphite were employed as additives, the desired product was obtained in good or moderate yield (Table 1, entries 1 and 2). On the contrary, much less product was isolated with diethyl chlorophosphite and triphenylphosphine as additives (Table 1, entries 3 and 4). Subsequently, we focused on the quantity of additive and Grignard reagent (Table 1, entries 5−10). In the presence of 1.2 equiv of diethyl phosphite and 3 equiv of Grignard reagent, a gratifying yield was obtained. In addition, the effect of temperature was examined in a range from 0 to 60 °C (Table 1, entries 11−13). THF turned out to the best solvent for this transformation (Table 1, entries 14−16) after solvent screening.

In order to investigate the generality of this reaction, different carbonyl compounds were employed as substrates. Aryl ketones react with cyclopropylmagnesium bromide under the conditions listed in Table 2 to afford the corresponding homoallylic bromides in 61−74% yield (Table 2, entries 1−5). Aryl aldehydes (Table 2, entries 6−10, 13−17, 19) also can give good to moderate yields in the reaction. When furaldehyde was used as the substrate, a 68% yield was obtained (Table 2, entry 12). The reactions of cinnamaldehyde (Table 2, entry 11) and 2-naphthaldehyde (Table 2, entry 18) proceeded smoothly to give the desired products with 65% and 60% yields, respectively. Additionally, benzaldehydes with electron-donating groups (Table 2, entries 6, 8, 9, 13) afforded better yields than benzaldehydes with electron-withdrawing groups (Table 2,

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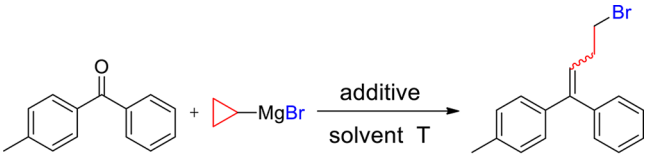
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

entry	additive (equiv)	cyclopropylmagnesium bromide (equiv)	T (°C)	solvent	yield (%)[b]
1	$(EtO)_2P(O)H$ (1.0)	3	rt	THF	70
2	$(PhO)_2P(O)H$ (1.0)	3	rt	THF	64
3	$(EtO)_2P(O)Cl$ (1.0)	3	rt	THF	20
4	Ph_3P (1.0)	3	rt	THF	0
5	$(EtO)_2P(O)H$ (1.2)	3	rt	THF	73
6	$(EtO)_2P(O)H$ (1.4)	3	rt	THF	72
7	$(EtO)_2P(O)H$ (0.8)	3	rt	THF	65
8	$(EtO)_2P(O)H$ (1.2)	2	rt	THF	70
9	$(EtO)_2P(O)H$ (1.2)	4	rt	THF	70
10	$(EtO)_2P(O)H$ (1.2)	2.5	rt	THF	72
11	$(EtO)_2P(O)H$ (1.2)	3	0	THF	69
12	$(EtO)_2P(O)H$ (1.2)	3	40	THF	70
13	$(EtO)_2P(O)H$ (1.2)	3	60	THF	64
14	$(EtO)_2P(O)H$ (1.2)	3	rt	toluene/THF (1:1)	53
15	$(EtO)_2P(O)H$ (1.2)	3	rt	Et_2O/THF (1:1)	60
16	$(EtO)_2P(O)H$ (1.2)	3	rt	dioxane/THF (1:1)	30

[a]Cyclopropylmagnesium bromide (1.5 mmol) in THF was added to a solution of phenyl(*p*-tolyl)methanone (0.5 mmol) in THF (3 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 3 h, and then diethyl phosphite (0.6 mmol) was added to this mixture and stirred at room temperature for 5 h. [b]Isolated yield based on phenyl(*p*-tolyl)methanone after silica gel chromatography.

entries 7, 14, 15, 18). Geometries of alkene products were determined by ^{1}H NMR coupling constants and NOESY analyses. Trisubstituted alkene products were obtained as a mixture of *E* and *Z* isomers; however, (*E*)-alkenes were preferable for disubstituted alkene bromides.

The scope of the Grignard reagents suitable for this reaction was explored with 2-phenyl cyclopropylmagnesium bromide (Table 3, entries 1−4), cyclobutylmagnesium bromide (Table 3, entry 5), and cyclopentylmagnesium bromide (Table 3, entry 6). When aryl aldehydes reacted with 2-phenyl cyclopropylmagnesium bromide, corresponding homoallylic bromides were obtained with low to moderate yields (Table 3, entries 1−4). As shown in Table 3, when cyclobutylmagnesium bromide or cyclopentylmagnesium bromide was employed (Table 3, entries 5 and 6), only ordinary olefins were obtained in 40% and 15% yields, respectively.

To further investigate the role of diethyl phosphite and Grignard reagents in the reaction, studies similar to our previous work[8] were carried out under the optimum reaction conditions (Scheme 3). Cyclopropyl(phenyl)(*p*-tolyl)methanol (**5a**) was employed to react with the diethyl phosphite, magnesium bromide diethoxy(oxo)phosphite (**6**), or magnesium bromide diethylphosphinite individually. The desired product was obtained with moderate yield using **6** as an additive, which was thus considered to be an important intermediate in the reaction. Interestingly, when magnesium chloride diethoxy(oxo)-phosphite (**7**) was used, the corresponding homoallylic chloride was obtained in a good yield.

On the basis of our preliminary results, a plausible mechanism for this transformation is proposed in Scheme 4. First, ketone **4** transforms into intermediate **5** through nucleophilic addition. Then the oxygen atom of intermediate **5** coordinates with the phosphorus atom of **6**, which leads to the transition state **9**. Opening the strained cyclopropane ring with bromide and elimination of phosphite gives homoallylic bromides **10** with **6** and MgO.

In summary, we have established an efficient one-pot synthetic protocol for the preparation of homoallylic halides from carbonyl compounds using cyclopropyl Grignard reagents in the presence of diethyl phosphite. Efforts are in progress to elucidate the mechanistic details of this reaction.

EXPERIMENTAL SECTION

General Information. THF was distilled from sodium benzophenone under nitrogen. All reactions were conducted under a nitrogen atmosphere. Metallic magnesium and all solvents were purchased from a commercial source without further purification before use. The flash column chromatography was carried out on silica gel (300−400 mesh). ^{1}H and ^{13}C NMR spectra (Supporting Information) were recorded on a 400 MHz spectrometer as solutions in $CDCl_3$. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm, δ) downfield from the internal standard Me_4Si (TMS). Chemical shifts in ^{13}C NMR spectra are reported relative to the central line of the chloroform signal (δ = 77.50 ppm). High-resolution mass spectra were obtained with a GCT-TOF instrument.

General Procedure for the Syntheses of Homoallylic Bromides. Grignard reagent (1.5 mmol) in THF was added to a solution of carbonyl compounds (0.5 mmol) in THF (3 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 3 h, and then diethyl phosphite (0.6 mmol) was added to this mixture and stirred at room temperature for 5 h (the reaction was monitored by TLC). Then the mixture was quenched with dilute hydrochloric acid. The resulting mixture was extracted with diethyl ether (3 × 10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure. Purification by column chromatography on silica gel afforded the products (300−400 mesh, petroleum ether and ethyl acetate as eluent).

1-((*E*)-4-Bromo-1-*p*-tolylbut-1-enyl)benzene (3a). Yellow oil. Yield: 109.5 mg, 73%. IR (KBr): 3053, 3017, 1653, 1510, 1491, 1451, 1261 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27−6.96 (m, 9H), 5.95 (t, *J* = 7.2 Hz, 1H), 3.33−3.28 (m, 2H), 2.62−2.54 (m, 2H), 2.22 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.8, 133.6, 126.2, 126.1, 125.4, 124.8, 123.9, 123.8, 123.7, 122.0, 121.3, 29.5, 29.3, 17.6. HRMS (EI$^+$): calcd for $C_{17}H_{17}{}^{81}Br$ (M^+) 302.0493, found 302.0487; calcd for $C_{17}H_{17}{}^{79}Br$ (M^+) 300.0514, found 300.0511.

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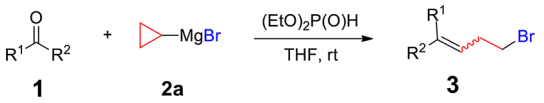
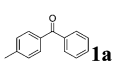
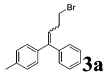
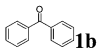
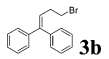
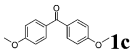
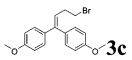
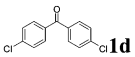
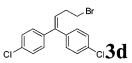
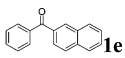
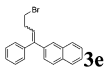
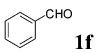
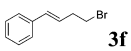
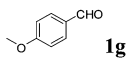
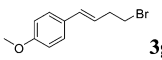
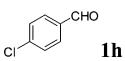
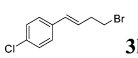
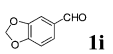
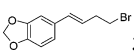
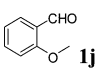
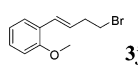
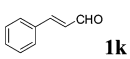
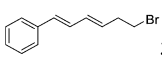
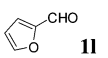
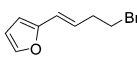
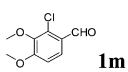
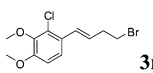
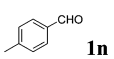
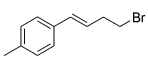
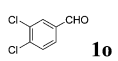
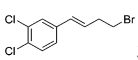
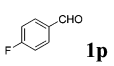
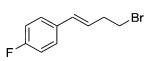
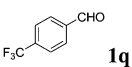
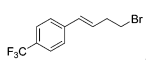
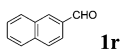
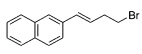
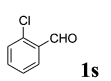
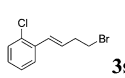
Table 2. Reactions of Carbonyl Compounds with Cyclopropylmagnesium Bromide[a]



1 2a 3

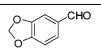
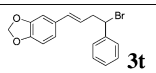
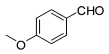
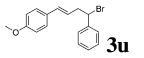
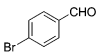
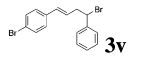
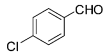
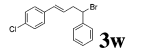
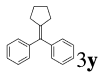
Entry	Substrate	Product	Yield(%)[b]
1	 1a	 3a	73
2	 1b	 3b	74
3	 1c	 3c	68
4	 1d	 3d	61
5	 1e	 3e	69
6	 1f	 3f	73
7	 1g	 3g	71
8	 1h	 3h	62
9	 1i	 3i	70
10	 1j	 3j	72
11	 1k	 3k	65
12	 1l	 3l	68
13	 1m	 3m	74
14	 1n	 3n	71
15	 1o	 3o	40
16	 1p	 3p	49
17	 1q	 3q	45
18	 1r	 3r	60
19	 1s	 3s	40

[a]Grignard reagent (1.5 mmol) in THF was added to a solution of carbonyl compounds (0.5 mmol) in THF (3 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 3 h, and then diethyl phosphite (0.6 mmol) was added to this mixture and stirred at room temperature for 5 h. [b]Isolated yield based on carbonyl compounds after silica gel chromatography.

4-Bromo-1,1-diphenylbut-1-ene (3b). Colorless oil. Yield: 106.2 mg, 74%. IR (KBr): 3056, 3024, 1660, 1510, 1494, 1445, 1266 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.41−7.16 (m, 10H), 6.09 (t, J = 7.3 Hz, 1H), 3.42 (t, J = 6.9 Hz, 2H), 2.68 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 144.7, 142.6, 140.1, 130.2, 128.8, 128.6, 128.0, 127.8, 126.2, 33.4,

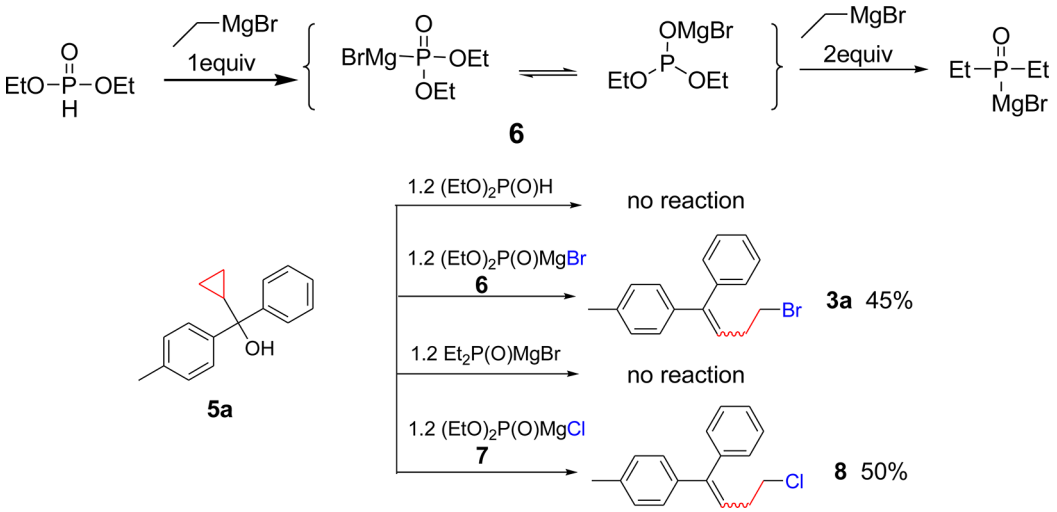
dx.doi.org/10.1021/jo400580n | J. Org. Chem. XXXX, XXX, XXX−XXX

Table 3. Reactions of Carbonyl Compounds with 2-Phenyl Cyclopropylmagnesium Bromide[a]

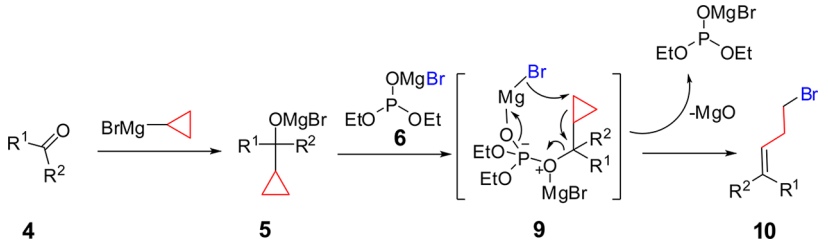
Entry	Substrate	Grignard reagent	Product	Yield(%)[b]
1		 **2b**	 **3t**	38
2		**2b**	 **3u**	28
3		**2b**	 **3v**	50
4		**2b**	 **3w**	38
5		 **2c**	 **3x**	40
6		 **2d**	 **3y**	15

[a]Grignard reagent (1.5 mmol) in THF was added to a solution of carbonyl compounds (0.5 mmol) in THF (3 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 30 min, and then diethyl phosphite (0.6 mmol) was added to this mixture and stirred at room temperature for 5 h. [b]Isolated yield based on carbonyl compounds after silica gel chromatography.

Scheme 3. Reaction of Cyclopropyl(phenyl)(*p*-tolyl)methanol with Diethyl Phosphite, Magnesium Bromide Diethoxy(oxo)phosphite, Magnesium Bromide Diethylphosphinite, or Magnesium Chloride Diethoxy(oxo)phosphite



Scheme 4. Probable Mechanism for Cyclopropyl Grignard Reagents Reacting with Carbonyl Compounds



33.2. HRMS (EI$^+$): calcd for $C_{16}H_{15}{}^{81}Br$ (M^+) 288.0337, found 288.0337; calcd for $C_{16}H_{15}{}^{79}Br$ (M^+) 286.0357, found 286.0358.

4-Bromo-1,1-bis(4-methoxyphenyl)but-1-ene (3c). Colorless oil. Yield: 117.6 mg, 68%. IR (KBr): 2923, 2831, 1604, 1510, 1462, 1244, 1175, 1109, 1035 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.16 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 5.94 (t, J = 7.2 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.41 (t, J = 7.0 Hz, 2H), 2.68 (q, J = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 159.2, 143.8, 135.7, 132.6, 131.3, 128.9, 124.2, 114.1, 113.9, 55.7, 33.5, 33.4. HRMS (EI$^+$): calcd for $C_{18}H_{19}{}^{81}BrO_2$ (M^+) 348.0548, found 348.0527; calcd for $C_{18}H_{19}{}^{79}BrO_2$ (M^+) 346.0568, found 346.0568.

4,4′-(4-Bromobut-1-ene-1,1-diyl)bis(chlorobenzene) (3d). Colorless oil. Yield: 108.6 mg, 61%. IR (KBr): 3030, 2963, 1661, 1590, 1491, 1268, 1091 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 6.07 (t, J = 7.2 Hz,

dx.doi.org/10.1021/jo400580n | J. Org. Chem. XXXX, XXX, XXX–XXX

1H), 3.43 (t, J = 6.7 Hz, 2H), 2.67 (q, J = 6.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.53, 140.59, 137.95, 133.92, 133.85, 131.50, 129.20, 128.99, 128.85, 127.30, 33.21, 32.87. HRMS (EI$^+$): calcd for $C_{16}H_{13}{}^{35}Cl_2{}^{79}Br$ (M^+) 353.9578, found 353.9579; calcd for $C_{16}H_{13}{}^{35}Cl^{37}Cl^{79}Br$ (M^+) 355.9548, found 355.9548; calcd for $C_{16}H_{13}{}^{35}Cl_2{}^{81}Br$ (M^+) 355.9557, found 355.9557; calcd for $C_{16}H_{13}{}^{37}Cl_2{}^{79}Br$ (M^+) 357.9519, found 357.9503.

(*E*)-2-(4-Bromo-1-phenylbut-1-enyl)naphthalene (3e). White solid. Yield: 115.9 mg, 69%. Compound purity: 98.21%. IR (KBr): 3050, 3017, 1656, 1589, 1497, 1444, 1256 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90−7.74 (m, 3H), 7.62−7.26 (m, 9H), 6.27 (t, J = 7.3 Hz, 1H), 3.50 (t, J = 7.0 Hz, 2H), 2.78 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.65, 144.61, 142.44, 139.98, 139.86, 137.50, 133.70, 133.12, 132.99, 130.25, 128.98, 128.87, 128.76, 128.66, 128.44, 128.37, 128.15, 127.95, 127.86, 127.83, 127.41, 127.03, 126.71, 126.58, 126.52, 126.34, 125.66, 33.47, 33.37, 33.22, 33.18. HRMS (EI$^+$): calcd for $C_{20}H_{17}{}^{81}Br$ (M^+) 338.0493, found 338.0468; calcd for $C_{20}H_{17}{}^{79}Br$ (M^+) 336.0514, found 336.0514.

(*E*)-(4-Bromobut-1-enyl)benzene (3f). Colorless oil. Yield: 77.0 mg, 73%. IR (KBr): 3057, 3021, 2943, 1601, 1500, 1447, 1275, 961 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.40 (d, J = 7.4 Hz, 2H), 7.34 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.2 Hz, 1H), 6.51 (d, J = 15.9 Hz, 1H), 6.21 (td, J = 6.9 Hz, J = 15.7 Hz, 1H), 3.50 (t, J = 7.1 Hz, 2H), 2.80 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.4, 133.1, 129.0, 127.9, 127.1, 126.6, 36.7, 32.8. HRMS (EI$^+$): calcd for $C_{10}H_{11}{}^{81}Br$ (M^+) 212.0024, found 212.0012; calcd for $C_{10}H_{11}{}^{79}Br$ (M^+) 210.0044, found 210.0045.

(*E*)-1-(4-Bromobut-1-enyl)-4-methoxybenzene (3g). Colorless oil. Yield: 85.6 mg, 71%. Compound purity: 98.77%. IR (KBr): 3000, 2952, 1610, 1487, 1415, 1098, 964, 813 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.29 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.42 (d, J = 15.8 Hz, 1H), 6.03 (td, J = 6.9 Hz, J = 15.7 Hz, 1H), 3.79 (s, 3H), 3.45 (t, J = 7.1 Hz, 2H), 2.74 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 132.5, 130.3, 127.8, 124.8, 114.4, 55.7, 36.8, 33.0. HRMS (EI$^+$): calcd for $C_{11}H_{13}{}^{81}BrO$ (M^+) 242.0129, found 242.0118; calcd for $C_{11}H_{13}{}^{79}BrO$ (M^+) 240.0150, found 240.0151.

(*E*)-1-(4-Bromobut-1-enyl)-4-chlorobenzene (3h). Colorless oil. Yield: 75.3 mg, 62%. Compound purity: 99.10%. IR (KBr): 3041, 2975, 1634, 1502, 1417, 1093, 973, 820 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32−7.26 (m, 4H), 6.44 (d, J = 15.8 Hz, 1H), 6.17 (td, J = 6.9 Hz, J = 15.6 Hz, 1H), 3.48 (t, J = 6.9 Hz, 2H), 2.77 (q, J = 6.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.9, 133.4, 131.9, 130.8, 129.1, 127.8, 36.6, 32.6. HRMS (EI$^+$): calcd for $C_{10}H_{10}{}^{35}Cl^{79}Br$ (M^+) 243.9654, found 243.9655; calcd for $C_{10}H_{10}{}^{35}Cl^{81}Br$ (M^+) 245.9634, found 245.9637; calcd for $C_{10}H_{10}{}^{37}Cl^{79}Br$ (M^+) 245.9625, found 245.9637.

(*E*)-5-(4-Bromobut-1-enyl)benzo[*d*][1,3]dioxole (3i). Colorless oil. Yield: 88.5 mg, 70%. Compound purity: 96.21%. IR (KBr): 3032, 2947, 1611, 1507, 1441, 1231, 957 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.91 (s, 1H), 6.76 (q, J = 8.0 Hz, 2H), 6.39 (d, J = 15.8 Hz, 1H), 6.05−5.98 (m, 1H), 5.94 (s, 2H), 3.45 (t, J = 7.1 Hz, 2H), 2.73 (q, J = 6.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.5, 147.5, 132.7, 132.0, 125.3, 121.2, 108.7, 106.0, 101.5, 36.7, 32.8. HRMS (EI$^+$): calcd for $C_{11}H_{11}{}^{81}BrO_2$ (M^+) 255.9922, found 255.9924; calcd for $C_{11}H_{11}{}^{79}BrO_2$ (M^+) 253.9942, found 253.9942.

(*E*)-1-(4-Bromobut-1-enyl)-2-methoxybenzene (3j). Colorless oil. Yield: 86.4 mg, 72%. Compound purity: 99.01%. IR (KBr): 3012, 2980, 1613, 1500, 1423, 1108, 971, 733 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45 (d, J = 7.6 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.88 (t, J = 8.3 Hz, 1H), 6.84 (d, J = 16.0 Hz, 1H), 6.21 (td, J = 6.9 Hz, J = 14.3 Hz, 1H), 3.86 (s, 3H), 3.49 (t, J = 7.2 Hz, 2H), 2.81 (q, J = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.9, 129.0, 127.8, 127.7, 127.1, 126.4, 121.1, 111.2, 55.9, 37.2, 33.0. HRMS (EI$^+$): calcd for $C_{11}H_{13}{}^{81}BrO$ (M^+) 242.0129, found 242.0118; calcd for $C_{11}H_{13}{}^{79}BrO$ (M^+) 240.0150, found 240.0151.

((1*E*,3*E*)-6-Bromohexa-1,3-dienyl)benzene (3k). Colorless oil. Yield: 76.7 mg, 65%. Compound purity: 98.35%. IR (KBr): 3038, 2998, 1621, 1502, 1408, 955, 762, 691 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.3 Hz, 1H), 6.78 (dd, J = 10.4 Hz, J = 15.7 Hz, 1H), 6.53 (d, J = 15.7 Hz, 1H), 6.31 (dd, J = 10.4 Hz, J = 15.1 Hz, 1H), 5.83−5.76 (m, 1H), 3.45 (t, J = 7.1 Hz, 2H), 2.73 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.7, 133.7, 132.3, 131.3, 129.1, 129.0, 127.9, 126.7, 36.5, 32.7. HRMS (EI$^+$): calcd for $C_{12}H_{13}{}^{81}Br$ (M^+) 238.0180, found 238.0178; calcd for $C_{12}H_{13}{}^{79}Br$ (M^+) 236.0201, found 236.0201.

(*E*)-2-(4-Bromobut-1-enyl)furan (3l). Colorless oil. Yield: 67.6 mg, 68%. Compound purity: 99.01%. IR (KBr): 3076, 1645, 1511, 1418, 978 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (s, 1H), 6.37−6.36 (m, 1H), 6.31 (d, J = 15.8 Hz, 1H), 6.22−6.21 (m, 1H), 6.16−6.10 (m, 1H), 3.45 (t, J = 7.1 Hz, 2H), 2.75 (q, J = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9, 142.2, 125.8, 121.6, 111.7, 107.8, 36.5, 32.5. HRMS (EI$^+$); calcd for $C_8H_9{}^{81}BrO$ (M^+) 201.9816, found 201.9823; calcd for $C_8H_9{}^{79}BrO$ (M^+) 199.9837, found 199.9838.

(*E*)-1-(4-Bromobut-1-enyl)-2-chloro-3,4-dimethoxybenzene (3m). Colorless oil. Yield: 99.9 mg, 74%. Compound purity: 99.51%. IR (KBr): 3042, 2981, 1616, 1502, 1415, 961 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (d, J = 8.9 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.81 (d, J = 16.1 Hz, 1H), 6.08 (td, J = 7.0 Hz, J = 15.7 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.50 (t, J = 7.0 Hz, 2H), 2.81 (q, J = 7.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 145.7, 129.2, 129.1, 128.3, 127.9, 122.0, 111.1, 61.0, 56.5, 36.7, 32.8. HRMS (EI$^+$): calcd for $C_{12}H_{14}O_2{}^{35}Cl^{79}Br$ (M^+) 303.9866, found 303.9867; calcd for $C_{12}H_{14}O_2{}^{35}Cl^{81}Br$ (M^+) 305.9845, found 305.9845; calcd for $C_{12}H_{14}O_2{}^{37}Cl^{81}Br$ (M^+) 307.9816, found 307.9829.

1-((*E*)-4-Bromobut-1-enyl)-4-methylbenzene (3n). Colorless oil. Yield: 79.5 mg, 71%. Compound purity: 99.32%. IR (KBr): 3055, 2980, 1671, 1592, 1455, 1384, 1283, 1038, 850 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.25 (d, J = 7.6 Hz, 2H), 7.11 (d, J = 7.3 Hz, 2H), 6.45 (d, J = 15.8 Hz, 1H), 6.12 (td, J = 6.7 Hz, J = 14.3 Hz, 1H), 3.45 (t, J = 6.9 Hz, 2H), 2.75 (d, J = 6.6 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.5, 134.4, 132.8, 129.5, 126.3, 125.8, 36.6, 32.6, 21.4. HRMS (EI$^+$): calcd for $C_{11}H_{13}Br$ (M^+) 224.0201, found 224.0199.

4-((*E*)-4-Bromobut-1-enyl)-1,2-dichlorobenzene (3o). Colorless oil. Yield: 55.7 mg, 40%. Compound purity: 99.03%. IR (KBr): 3051, 2963, 2831, 1500, 1403, 1167, 970, 833 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.44 (d, J = 1.6 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.20−7.16 (m, 1H), 6.39 (d, J = 15.9 Hz, 1H), 6.20 (td, J = 6.8 Hz, J = 15.8 Hz, 1H), 3.48 (t, J = 6.8 Hz, 2H), 2.82−2.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 132.6, 131.0, 130.4, 130.1, 128.8, 127.9, 125.4, 36.0, 31.9. HRMS (EI$^+$): calcd for $C_{10}H_9Cl_2Br$ (M^+) 277.9265, found 277.9265.

1-((*E*)-4-Bromobut-1-enyl)-4-fluorobenzene (3p). Colorless oil. Yield: 56.0 mg, 49%. Compound purity: 98.97%. IR (KBr): 3029, 2960, 1633, 1500, 1297, 1005, 810 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.31 (d, J = 3.2 Hz, 2H), 6.99 (d, J = 4.5 Hz, 2H), 6.44 (d, J = 15.7 Hz, 1H), 6.09 (td, J = 6.5 Hz, J = 14.6

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Hz, 1H), 3.46 (dd, J = 4.1 Hz, J = 9.0 Hz, 2H), 2.77−2.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 161.2, 133.4, 133.4, 131.7, 127.9, 127.8, 126.6, 115.7, 115.6, 36.4, 32.5. HRMS (EI^+): calcd for $C_{10}H_{10}FBr$ (M^+) 227.9947, found 227.9950.

1-((*E*)-4-Bromobut-1-enyl)-4-(trifluoromethyl)benzene (3q). Colorless oil. Yield: 62.3 mg, 45%. Compound purity: 98.74%. IR (KBr): 3062, 2871, 1659, 1491, 1375, 990, 810 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.57 (d, J = 5.9 Hz, 2H), 7.47 (d, J = 5.8 Hz, 2H), 6.53 (dd, J = 4.3 Hz, J = 15.6 Hz), 6.31 (td, J = 6.1 Hz, J = 21.1 Hz, 1H), 3.54−3.49 (m, 2H), 2.83−2.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.7, 118.7, 115.9, 114.9, 114.8, 113.3, 112.7, 110.9, 110.6, 110.5, 108.7, 21.4, 17.2. HRMS (EI^+): calcd for $C_{11}H_{10}F_3Br$ (M^+) 277.9919, found 277.9918.

2-((*E*)-4-Bromobut-1-enyl)naphthalene (3r). Colorless oil. Yield: 78.3 mg, 60%. Compound purity: 99.50%. IR (KBr): 3064, 2959, 2925, 1609, 1509, 1457, 913, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.10 (d, J = 6.6 Hz, 1H), 7.84−7.75 (m, 2H), 7.55−7.40 (m, 4H), 7.22 (d, J = 15.5 Hz, 1H), 7.20−6.14 (m, 1H), 3.56−3.51 (m, 2H), 2.89−2.86 (m, 2H). HRMS (EI^+): calcd for $C_{14}H_{13}Br$ (M^+) 260.0200, found 260.0201.

1-((*E*)-4-Bromobut-1-enyl)-2-chlorobenzene (3s). Colorless Oil. Yield: 52.2 mg, 40%. Compound purity: 99.26%. IR (KBr): 3042, 2980, 1587, 1413, 1264, 1123, 990, 751 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.52 (d, J = 5.9 Hz, 1H), 7.34 (d, J = 6.3 Hz, 1H), 7.21−7.17 (m, 2H), 6.88 (d, J = 15.5 Hz, 1H), 6.21−6.14 (m, 1H), 3.50−3.48 (m, 2H), 2.83 (d, J = 5.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.1, 132.8, 129.6, 129.6, 128.9, 128.5, 126.8, 126.7, 36.3, 32.1. HRMS (EI^+): calcd for $C_{10}H_{10}ClBr$ (M^+) 243.9654, found 243.9658.

5-((*E*)-4-Bromo-3-phenylbut-1-enyl)benzo[*d*][1,3]-dioxole (3t). White solid. Yield: 62.9 mg, 38%. Compound purity: 99.07%. IR (KBr): 3063, 3030, 2960, 1594, 1491, 1454, 1091, 1012 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41 (d, J = 7.2 Hz, 2H), 7.36−7.28 (m, 3H), 6.84 (s, 1H), 6.72 (s, 2H), 6.37 (d, J = 15.8 Hz, 1H), 5.95−5.91 (m, 3H), 4.99 (t, J = 7.4 Hz, 1H), 3.14−3.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 145.1, 139.6, 130.8, 129.5, 126.8, 126.5, 125.4, 122.5, 118.9, 106.3, 103.6, 99.1, 52.6, 41.3. HRMS (EI^+): calcd for $C_{17}H_{15}BrO_2$ (M^+) 330.0255, found 330.0245.

1-((*E*)-1-Bromo-4-(4-methoxyphenyl)but-3-enyl)-benzene (3u). Colorless oil. Yield: 44.3 mg, 28%. Compound purity: 99.11%. IR (KBr): 3032, 1645, 1630, 1445, 912, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, J = 7.3 Hz, 2H), 7.37−7.23 (m, 5H), 6.82 (d, J = 8.4 Hz, 2H), 6.41 (d, J = 15.8 Hz, 1H), 6.01−5.93 (m, 1H), 5.00 (t, J = 7.4 Hz, 1H), 3.78 (s, 3H), 3.18−3.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 141.9, 132.8, 130.0, 128.9, 128.6, 127.6, 127.6, 124.2, 114.1, 55.5, 54.9, 43.6. HRMS (EI^+): calcd for $C_{17}H_{17}BrO$ (M^+) 316.0463, found 316.0466.

1-((*E*)-1-Bromo-4-(4-bromophenyl)but-3-enyl)-benzene (3v). White solid. Yield: 91 mg, 50%. Compound purity: 96.30%. IR (KBr): 3033, 2988, 1595, 1490, 1440, 1029, 771, 701 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44−7.14 (m, 9H), 6.38 (d, J = 15.8 Hz, 1H), 6.14−6.07 (m, 1H), 4.99 (t, J = 7.4 Hz, 1H), 3.17−3.01 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 134.0, 130.1, 129.7, 126.8, 126.6, 125.8, 125.4, 125.1, 119.2, 52.3, 41.3. HRMS (EI^+): calcd for $C_{16}H_{14}Br_2$ (M^+) 363.9462, found 363.9450.

1-((*E*)-1-Bromo-4-(4-chlorophenyl)but-3-enyl)benzene (3w). White solid. Yield: 61.0 mg, 38%. Compound purity: 98.41%. IR (KBr): 3064, 2959, 2925, 1609, 1509, 1457, 913, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.43−7.23 (m, 9H), 6.42 (d, J = 15.8 Hz, 1H), 6.14−6.06 (m, 1H), 5.00 (t, J = 7.4 Hz, 2H), 3.19−3.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 135.7, 133.3, 132.2, 129.0, 128.9, 128.8, 127.7, 127.6, 127.2, 54.5, 43.5. HRMS (EI^+): calcd for $C_{16}H_{14}ClBr$ (M^+) 319.9967, found 319.9958.

5-((*E*)-4-*p*-Tolylbut-1-enyl)benzo[*d*][1,3]dioxole (3x). White solid. Yield: 44 mg, 40%. Compound purity: 98.94%. IR (KBr): 3026, 2925, 1637, 1498, 1456, 840, 816 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.29−7.16 (m, 10H), 2.93 (t, J = 7.9 Hz, 4H), 2.95−2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 138.7, 126.9, 126.3, 126.1, 124.3, 30.3, 15.4. HRMS (EI^+): calcd for $C_{17}H_{16}$ (M^+) 220.1252, found 220.1250.

1-((*E*)-4-(4-Chlorophenyl)but-3-enyl)-4-methylbenzene (3y). White solid. Yield: 17.6 mg, 15%. Compound purity: 98.29%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30−7.18 (m, 10H), 2.42−2.38 (m, 4H), 1.70−1.66 (m, 4H). HRMS (EI^+): calcd for $C_{18}H_{18}$ (M^+) 234.1409, found 234.1411.

Cyclopropyl(phenyl)(*p*-tolyl)methanol (5a). Cyclopropylmagnesium bromide (4.5 mL, 4.5 mmol, 1 M in THF) was added dropwise to a solution of phenyl(*p*-tolyl)methanone (0.784 g, 4 mmol) in 40 mL of THF under a nitrogen atmosphere at room temperature. Then the mixture was stirred at 40 °C for 2 h. The reaction was quenched with water, and the mixture was extracted with diethyl ether (3 × 20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure. Purification by column chromatography on silica gel afforded the products (300−400 mesh, petroleum ether and ethyl acetate as eluent). Colorless oil. Yield: 762 mg yield: 80%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.00 (m, 9H), 2.2 (s, 3H), 1.82 (s, 1H), 1.51−1.48 (m, 1H), 0.507−0.42 (m, 2H), 0.395−0.366 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 144.6, 136.9, 128.9, 128.2, 127.2, 127.1, 77.7, 21.9.1, 21.4, 2.1, 2.0.

1-(4-Chloro-1-*p*-tolylbut-1-enyl)benzene (8). Isopropylmagnesium chloride (0.6 mL, 1.2 mmol, 2 M in THF) was added to a solution of diethyl phosphite (1.2 mmol) in THF (6 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 1 h, and then cyclopropyl(phenyl)(*p*-tolyl)-methanol (**5a**) (0.238 g, 1.0 mmol) was added to the mixture. After 5 h, the reaction was quenched with water, and the mixture was extracted with diethyl ether (3 × 10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure. Purification by column chromatography on silica gel afforded the products (300−400 mesh, petroleum ether and ethyl acetate as eluent). Colorless oil. Yield: 128 mg, 50%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.10 (m, 9H), 6.10 (t, J = 7.2 Hz), 3.60−3.57 (m, 2H), 2.65−2.57 (m, 2H), 2.41 (s, 1H), 2.35 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 139.8, 139.3, 137.1, 136.9, 129.6, 129.0, 128.9, 128.3, 128.1, 127.3, 127.2, 124.6, 123.9, 44.4, 33.0, 32.9, 29.7, 21.1. HRMS (EI^+): calcd for $C_{17}H_{17}Cl$ (M^+) 256.1019, found 256.1022.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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