Novel One-pot Synthetic Method for Propargyl Alcohol Derivatives from Allyl Alcohol Derivatives

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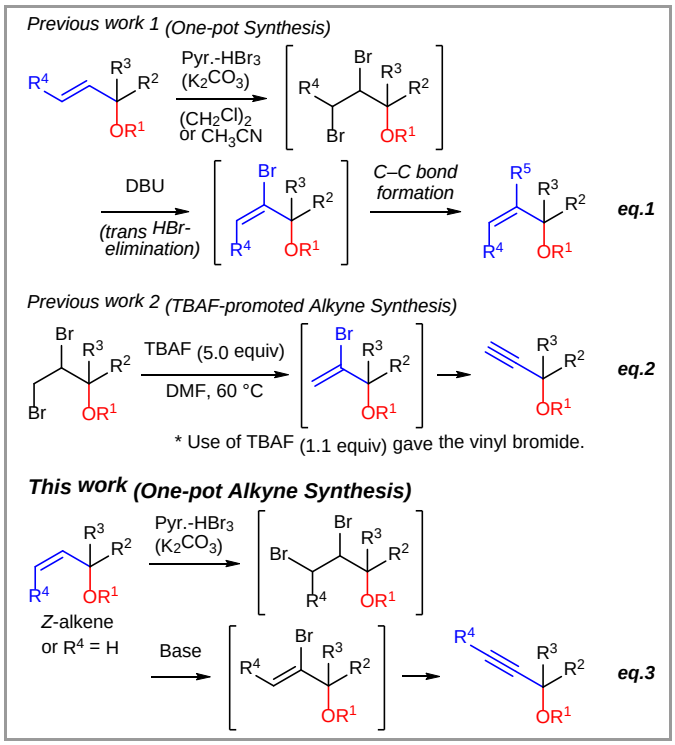
Dedication – The paper is dedicated to Professor Amos B. Smith, III on the occasion of his 70th birthday.

Abstract: An efficient one-pot procedure for the synthesis of propargyl alcohol derivatives from allyl alcohol derivatives has been developed. The key to this transformation from the C–C double bond to the C–C triple bond is the fact that the HBr-elimination of the 1,2-dibromoalkanes having a neighboring O-functional group was promoted by the inductive electron-withdrawing effects of the O-functional group. In the one-pot reaction, TBAOH was the best base, and the addition of molecular sieves 13X was also effective.

Key words: elimination, one-pot synthesis, propargyl alcohol derivative, allyl alcohol derivative, neighboring-group effects.

Propargyl alcohols are key synthetic intermediates for many biologically natural products, their effective analogues, and agricultural and pharmaceutical chemicals because of the transformation versatility of both the C–C triple bond and the O-functional group.[1] The general synthetic method for both chiral and achiral propargyl alcohols is the addition of acetylenes to carbonyl compounds.[2]

We recently reported one-pot synthetic procedures for vinyl bromides and di- or trisubstituted alkenes from terminal or internal disubstituted alkenes having an O-functional group at the adjacent position (Scheme 1, equation 1).[3] The noteworthy point of these methods is that those sequential reactions proceed with high yields and selectivity in the same vessel, and the key factor is DBU-promoted HBr-elimination utilizing the inductive electron-withdrawing effects of the neighboring O-functional group in the second reaction. Aside from the one-pot synthesis, we also reported a novel tetrabutylammonium fluoride (TBAF)-mediated transformation from 1,2-dibromoalkanes having a neighboring O-functional group to alkynes (Scheme 1, equation 2).[4] This elimination made it possible to produce the alkynes or their intermediates, the vinyl bromides under milder conditions than previously reported.[5] Against this research background, that is, unique HBr-elimination effected by the electronegativity of the neighboring oxygen atom, we initiated the development of a novel one-pot transformation from allyl alcohol derivatives to the corresponding propargyl alcohol derivatives (Scheme 1, equation 3). In this paper, we disclose the intriguing results and full details.

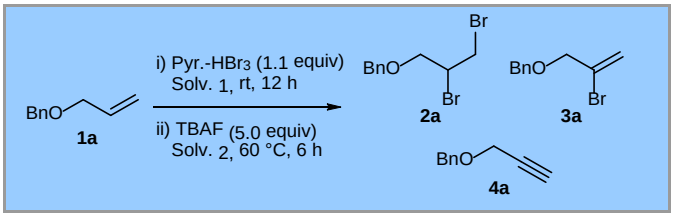


Scheme 1

Based on our previous research results,[3,4] the study started with the benzyl (Bn)-protected allyl alcohol **1a** as a substrate, which was treated with pyridinium bromide perbromide (Pyr.-HBr_3) and the following TBAF (5.0 equiv)-promoted HBr-eliminations in one pot. Screening of the solvents is shown in Table 1. After the bromine addition in 1,2-dichloroethane or acetonitrile at room temperature, 5.0 equiv of TBAF (1.0 M THF sol.) were added to the same pot and then the reaction system was stirred at 60 °C for 6 h (Entries 1 and 2). However, elimination did not provide the desired Bn-protected propargyl alcohol **4a**, and the dibromoalkane **2a** or the vinyl bromide **3a** still remained. On the other hand, when aprotic polar solvent DMF or DMSO was used, the bromine addition was not completed, and thus the subsequent elimination was not carried out (Entries 3 and 4). Therefore, after the bromine addition in acetonitrile, TBAF and DMF or DMSO of seven times the volume of acetonitrile were added (Entries 5 and 6). As a result, the mixed solvent

system (acetonitrile/DMSO = 1/7) was the most effective for the second TBAF-promoted elimination process (Entry 6).

Table 1 Screening of Solvents

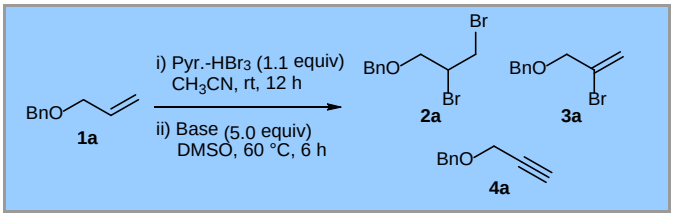


Entry	Solv. 1	Solv. 2[a]	Yield (%)			
			1a	**2a**	**3a**	**4a**
1	$(CH_2Cl)_2$	–	0	12	73	0
2	CH_3CN	–	0	0	98	0
3[b]	DMF	–	11	74	–	–
4[b]	DMSO	–	28	61	–	–
5	CH_3CN	DMF	0	0	80	16
6	CH_3CN	DMSO	0	0	38	50

[a] Before the addition of TBAF, Solv. 2 of seven times the volume of Solv. 1 was added at the second elimination step.
[b] The elimination process was not carried out because the first bromine addition was not finished completely.

Next, we examined a variety of counter anions (chloride, bromide, acetate,[6] and hydroxide) of the quaternary ammonium salt as a base for the HBr-elimination, instead of TBAF (Table 2). However, most of the bases did not give the desired compound **4a** (Entries 2–4). Significantly, a solution of 40% TBAOH in water gave **4a** in 83% yield (Entry 5).

Table 2 Screening of Counter Anions of Quaternary Ammonium Bases

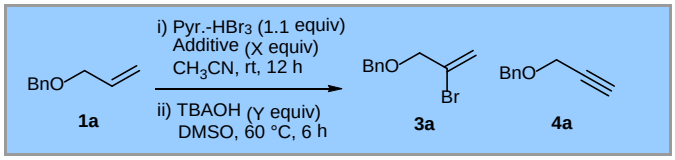


Entry	Base	Yield (%)			
		1a	**2a**	**3a**	**4a**
1	TBAF	0	0	38	50
2	TBAC[a]	0	97	0	0
3	TBAB[b]	0	92	0	0
4	TBAOAc[c]	0	91	0	0
5	TBAOH[d]	0	0	0	83

[a] Tetrabutylammonium chloride
[b] Tetrabutylammonium bromide
[c] Tetrabutylammonium acetate[6]
[d] Tetrabutylammonium hydroxide (40% in water)

To accelerate effectively the reaction under milder conditions, the consecutive bromine addition/TBAOH-promoted HBr-elimination was further examined in the presence of an additive (Table 3). Initially, 4.0 equiv of TBAOH were used without any additive; however, the elimination was not complete and the intermediate, vinyl bromide **3a** still remained (Entry 2). Based on previous studies of one-pot methods,[3] when 1.1 equiv of potassium carbonate was added as a HBr scavenger at the first reaction stage, the elimination successfully proceeded despite 4.0 equiv of TBAOH (Entry 3). A variety of molecular sieves (MS) were also examined instead of potassium carbonate based on reports in which the appropriate molecular sieve can be an effective HBr trapping agent (Entries 4–7).[7] Although the activated molecular sieves 3A and 4A did not affect the efficacy, the 5A and 13X, whose pore diameters are larger, acted in a manner similar to potassium carbonate (Entries 6 and 7). As for the most effective additive, MS 13X, the requisite amounts of TBAOH were successfully reduced to 3.5 equiv (Entry 8, for reference Entries 9 and 10). In addition, use of 1.1 equiv of triethylamine and 3.1 equiv of TBAOH for the HBr-elimination also afforded the desired Bn-protected propargyl alcohol **4a** in quantitative yield (Entry 11).

Table 3 Screening of Additives



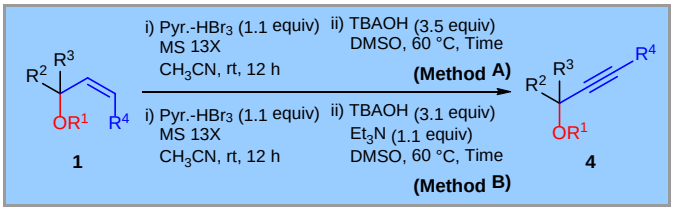
Entry	Additive (X equiv)	Y (equiv)	Yield (%)	
			3a	**4a**
1	–	5.0	0	83
2	–	4.0	16	70
3	K_2CO_3 (1.1)	4.0	0	82
4[a]	MS 3A	4.0	10	72
5[a]	MS 4A	4.0	11	76
6[a]	MS 5A	4.0	0	83
7[a,b]	MS 13X	4.0	0	93
8[a]	**MS 13X**	**3.5**	**0**	**96**
9[c]	–	3.5	50	27
10[a]	MS 13X	3.1	11	75
11[a,b,d]	**MS 13X, Et_3N (1.1)**	**3.1**	**0**	**95**

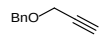
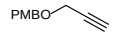
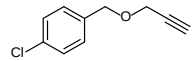
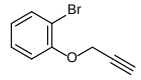
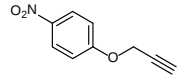
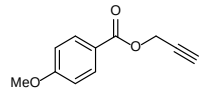
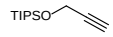
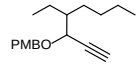
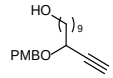
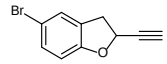
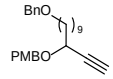
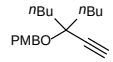
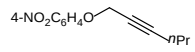
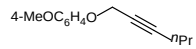
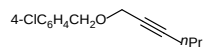
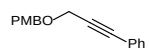
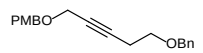
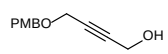
[a] All molecular sieves (MS) were powdered (< 10 μm) and activated. MS of 10 times the amount of **1a** was used.
[b] The second HBr-elimination reaction time was 2 h.
[c] The second HBr-elimination reaction time was 9 h.
[d] Et_3N (1.1 equiv) was added together with DMSO and TBAOH.

To confirm the generality of the one-pot synthesis of propargyl alcohol derivatives **4**, we examined a variety of allyl alcohol derivatives **1** using optimized Method A (Table 3, Entry 8) and/or B (Table 3, Entry 11). Reaction of the allyl alcohols protected with substituted benzyl (**1a**–**c**) and phenyl (**1d**) groups basically afforded the desired propargyl alcohol derivatives **4a**–**d** in good yields using both methods (Table 4, Entries 1–8). However, the reaction of **1e**, having a 4-nitrophenyl group gave **4e** with unsatisfactory yield because overreaction gave the undesired corresponding allenes (Entries 9 and 10).[8] Reaction of the benzoyl-protected **1f** and silyl-protected **1g** also gave **4f** in low yield and **4g** in moderate yield, respectively, because the bromine addition of **1f** was not completed and the TIPS group of **1g** was partly removed (Entries 11 and 12). Next, we examined more complicated substrates. For secondary alcohol derivatives **1h**, **1i**, **1j**, and **1k**, those reaction yields were sufficient (Entries 13–20), although PMB-protected tertiary alcohol **4l** was also produced in low

yield (Entries 21 and 22). In addition, compounds **4m**–**r**, having an internal C–C triple bond were produced in good yields from the corresponding *Z*-allyl alcohol derivatives **1m**–**r** through double *trans*-HBr-eliminations.

Table 4 Synthesis of Propargyl Alcohol Derivatives **4** from Allyl Alcohol Derivatives **1** Using a One-pot Procedure



Entry	Products		Method	Time (h)	Yield (%)
1		(**4a**)	A	2	95
2			B	2	96
3		(**4b**)	A	2	82
4			B	2	91
5		(**4c**)	A	2	67
6			B	2	96
7		(**4d**)	A	3	80
8			B	3	74
9		(**4e**)	A	1	41[a]
10			B	1	42[b]
11		(**4f**)	B	7	12[c]
12		(**4g**)	B[d]	8	49
13		(**4h**)	A	4	74
14			B	4	70
15		(**4i**)	A	6	83
16			B	7	72
17		(**4j**)	A	2	83
18			B	2	87
19		(**4k**)	A	6	74
20			B	6	75
21		(**4l**)	A	4	26[e]
22			B	4	31[f]
23		(**4m**)	A	1	89
24			B	1	87
25		(**4n**)	A	2	77
26			B	3	82
27		(**4o**)	A	4	85
28			B	6	80
29		(**4p**)	A	0.3	82
30			B	0.3	85
31		(**4q**)	A	8	76
32			B	8	79
33		(**4r**)	A[g]	6	72
34			B[h]	6	75

[a] The corresponding allene was obtained (42%).
[b] The corresponding allene was obtained (38%).
[c] The starting material **1f** was recovered (40%).
[d] 10% TBAOH (in MeOH sol.) was used.
[e] The starting material **1l** was recovered (42%).
[f] The starting material **1l** was recovered (43%).
[g] 5.5 equiv of TBAOH (40% in water) were used.
[h] 5.1 equiv of TBAOH (40% in water) were used.

In summary, we have established a novel one-pot synthesis of propargyl alcohol derivatives **4** from allyl alcohol derivatives **1** through TBAOH-promoted, double *trans*-HBr-eliminations. Both the one-pot methods should be applicable to the total synthesis of natural products and for use in modern drug-discovery research. In addition, method B might be more suitable for base-sensitive substrates than method A, because of the small amount of TBAOH. As reported in our previous research,[9] neighboring O-functional-group participation is an important factor in this synthetic procedure.

Infrared spectra were recorded with a Horiba FT-710 model spectrophotometer. ^{1}H and ^{13}C NMR spectral data were obtained with a JEOL JNM-LA 500, or a JEOL JNM-AL 300 instrument. Chemical shifts are quoted in ppm using tetramethylsilane (TMS, δ = 0 ppm) as the reference for ^{1}H NMR spectroscopy, and $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR spectroscopy. Mass spectra were measured with a Bruker Daltonics microTOF or a Hitachi double-focusing M-80B spectrometer. Column chromatography was carried out on silica gel (Kanto Chemical Co. or Merck Co., Ltd). All reactions were performed under an argon atmosphere. Allyl alcohol derivatives **1a**–**g**, **1j**, **1m**, **1n**, and **1r** are known and their analytical data have been reported.[10] Propargyl alcohol derivatives **4a**–**g**, **4j**, **4m**, **4n**, and **4r** are known and their analytical data have been reported.[11]

General Procedure for the One-pot Synthesis of 4 (Method A)

A mixture of allyl alcohol derivative **1** (x g, 1.0 equiv), pyridinium bromide perbromide (1.1 equiv), and MS 13X (ca. 10x g) in CH_3CN (y mL, 0.1 M) was stirred at room temperature for 12–14 h. Then, DMSO (7y mL) and TBAOH (3.5 equiv, 40% in water) were added to the reaction mixture at 0 °C and the system was heated to 60 °C. The reaction was quenched with sat. aq NH_4Cl at 0 °C. After the removal of MS 13X through a cotton filter, the resulting filtrate was extracted with hexane/EtOAc (= 2/1, 30 mL × 3) and dried over $MgSO_4$. The combined extracts were concentrated under reduced pressure, and the residue was purified using silica gel column chromatography to afford the propargyl alcohol derivative **4**.

General Procedure for the One-pot Synthesis of 4 (Method B)

A mixture of allyl alcohol derivative **1** (x g, 1.0 equiv), pyridinium bromide perbromide (1.1 equiv), and MS 13X (ca. 10x g) in CH_3CN (y mL, 0.1 M) was stirred at room temperature for 12–14 h. Then, DMSO (7y mL), TBAOH (3.1 equiv, 40% in water), and Et_3N (1.1

equiv) were added to the reaction mixture at 0 °C and the system was heated to 60 °C. The reaction was quenched with sat. aq NH_4Cl at 0 °C. After the removal of MS13X through a cotton filter, the resulting filtrate was extracted with hexane/EtOAc (= 2/1, 30 mL × 3) and dried over $MgSO_4$. The combined extracts were concentrated under reduced pressure, and the residue was purified using silica gel column chromatography to afford the propargyl alcohol derivative **4**.

1-{[(4-Ethyloct-1-en-3-yl)oxy]methyl}-4-methoxybenzene (1h)

Yield: 1.44 g (54%); colorless oil.[12]
IR (neat): 3074, 2958, 2870 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 0.83–0.87 (m, 6H), 1.12–1.53 (m, 9H), 3.63 (dd, *J* = 13.4, 5.8 Hz, 1H), 3.80 (s, 3H), 4.25 (d, *J* = 10.0 Hz, 1H), 4.52 (d, *J* = 10.0 Hz, 1H), 5.18 (dd, *J* = 18.0, 1.8 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.8 Hz, 1H), 5.73 (ddd, *J* = 18.0, 10.5, 5.8 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 11.1 (CH_3), 14.0 (CH_3), 21.9 (CH_2), 23.0 (CH_2), 28.6 (CH_2), 29.1 (CH_2), 43.9 (CH), 55.0 (CH_3), 69.7 (CH_2), 82.1 (CH), 113.6 (CH×2), 117.4 (CH_2), 129.1 (CH×2), 131.1 (C), 137.7 (CH), 158.9 (C).
Diastereomer: 11.4 (CH_3), 14.0 (CH_3), 22.2 (CH_2), 23.1 (CH_2), 28.7 (CH_2), 29.3 (CH_2), 44.0 (CH), 55.0 (CH_3), 69.7 (CH_2), 82.2 (CH), 113.6 (CH×2), 117.4, (CH_2), 129.1 (CH×2), 131.1 (C), 137.7 (CH), 158.9 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{28}O_2Na$: 299.1982; found: 299.1985.

10-[(4-Methoxybenzyl)oxy]dodec-11-en-1-ol (1i)

Yield: 299 mg (89%); colorless oil.[12]
IR (neat): 3398, 3005 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 1.23–1.66 (m, 17H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.69 (td, *J* = 14.2, 7.0 Hz, 1H), 3.80 (s, 3H), 4.28 (d, *J* = 11.0 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 5.18 (d, *J* = 17.4 Hz, 1H), 5.21 (d, *J* = 10.1 Hz, 1H), 5.72 (ddd, *J* = 17.4, 10.1, 7.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.2 (CH_2), 25.6 (CH_2), 29.3 (CH_2), 29.38 (CH_2×2), 29.41 (CH_2), 32.6 (CH_2), 35.4 (CH_2), 55.1 (CH_3), 62.8 (CH_2), 69.6 (CH_2), 80.2 (CH), 113.6 (CH×2), 116.7 (CH_2), 129.2 (CH×2), 130.8 (C), 139.2 (CH), 158.9 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{32}O_3Na$: 343.2244; found: 343.2246.

1-({[12-(Benzyloxy)dodec-1-en-3-yl]oxy}methyl)-4-methoxybenzene (1k)

Yield: 1.59 g (63%); colorless oil.[12]
IR (neat): 3005, 2931 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 1.21–1.69 (m, 16H), 3.46 (t, *J* = 6.5 Hz, 2H), 3.68 (td, *J* = 14.2, 7.0 Hz, 1H), 3.80 (s, 3H), 4.27 (d, *J* = 11.0 Hz, 1H), 4.50 (s, 2H), 4.52 (d, *J* = 11.0 Hz, 1H), 5.18 (d, *J* = 16.6 Hz, 1H), 5.21 (d, *J* = 10.9 Hz, 1H), 5.72 (ddd, *J* = 16.6, 10.9, 7.0 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 7.24–7.36 (m, 7H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.3 (CH_2), 26.1 (CH_2), 29.4 (CH_2×2), 29.5 (CH_2×2), 29.7 (CH_2), 35.5 (CH_2), 55.1 (CH_3), 69.6 (CH_2), 70.4 (CH_2), 72.8 (CH_2), 80.2 (CH), 113.6 (CH×2), 116.7 (CH_2), 127.4 (CH_2), 127.5 (CH×2), 128.2 (CH×2), 129.2 (CH×2), 130.9 (C), 138.7 (C), 139.3 (CH), 159.0 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{38}O_3Na$: 433.2713; found: 433.2716.

1-Methoxy-4-{[(5-vinylnonan-5-yl)oxy]methyl}benzene (1l)

Yield: 771 mg (69%); colorless oil.[12]
IR (neat): 3086, 2947 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 6H), 1.30 (m, 8H), 1.50–1.65 (m, 4H), 3.79 (s, 3H), 4.25 (s, 2H), 5.17 (dd, *J* = 17.6, 1.5 Hz, 1H), 5.22 (dd, *J* = 11.1, 1.5 Hz, 1H), 5.78 (dd, *J* = 17.6, 11.1 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.1 (CH_3×2), 23.2 (CH_2×2), 25.3 (CH_2×2), 35.0 (CH_2×2), 55.2 (CH_3), 63.3 (CH_2), 79.5 (C), 113.7 (CH×2), 114.9 (CH_2), 128.7 (CH×2), 131.9 (C), 143.0 (CH), 158.8 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{19}H_{30}O_2Na$: 313.2138; found: 313.2136.

(*Z*)-1-Chloro-4-[(hex-2-en-1-yloxy)methyl]benzene (1o)

Yield: 1.00 g (88%); colorless oil.[12]
IR (neat): 3016, 2962, 2861 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.4 Hz, 3H), 1.39 (tq, *J* = 7.4, 7.4 Hz, 2H), 2.02 (td, *J* = 7.4, 7.1 Hz, 2H), 4.07 (d, *J* = 5.4 Hz, 2H), 4.47 (s, 2H), 5.60 (m, 2H), 7.24–7.33 (m, 4H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.7 (CH_3), 22.7 (CH_2), 29.6 (CH_2), 65.8 (CH_2), 71.2 (CH_2), 125.9 (CH), 128.5 (CH×2), 129.0 (CH×2), 133.3 (CH), 133.9 (C), 137.0 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{13}H_{17}ClONa$: 247.0860; found: 247.0855.

(*Z*)-1-Methoxy-4-{[(3-phenylallyl)oxy]methyl}benzene (1p)

Yield: 209 mg (79%); colorless oil.[12]
IR (neat): 3062 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 3.78 (s, 3H), 4.27 (d, *J* = 6.1 Hz, 2H), 4.45 (s, 2H), 5.89 (dt, *J* = 12.1, 6.1 Hz, 1H), 6.61 (d, *J* = 12.1 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 7.7 Hz, 2H), 7.22–7.26 (m, 2H), 7.30–7.33 (m, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 55.2 (CH_3), 66.6 (CH_2), 72.1 (CH_2), 113.7 (CH×2), 127.1 (CH), 128.2 (CH×2), 128.7 (CH×2), 129.0 (CH), 129.5 (CH×2), 130.2 (C), 131.7 (CH), 136.6 (C), 159.2 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{18}O_2Na$: 277.1199; found: 277.1201.

(*Z*)-1-({[5-(Benzyloxy)pent-2-en-1-yl]oxy}methyl)-4-methoxybenzene (1q)

Yield: 123 mg (83%); pale yellow oil.[12]
IR (neat): 3016, 2854, 1095, 818 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 2.38 (td, *J* = 13.4, 7.0 Hz, 2H), 3.49 (t, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 4.06 (d, *J* = 6.3 Hz, 2H), 4.43 (s, 2H), 4.50 (s, 2H), 5.66 (m, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.25–7.35 (m, 7H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.4 (CH_2), 55.3 (CH_3), 65.5 (CH_2), 69.6 (CH_2), 71.8 (CH_2), 72.9 (CH_2), 113.8 (CH×2), 127.5 (CH), 127.6 (CH×2), 128.2 (CH), 128.3 (CH×2), 129.4 (CH×2), 129.5 (CH), 130.4 (C), 138.4 (C), 159.2 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{24}O_3Na$: 335.1618; found: 335.1616.

1-{[(4-Ethyloct-1-yn-3-yl)oxy]methyl}-4-methoxybenzene (4h)

Yield: 36.7 mg (74%); yellow oil (Method A).
IR (neat): 3302, 2962, 2866, 1612 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 0.84–0.89 (m, 6H), 1.21–1.65 (m, 9H), 2.43 (d, *J* = 2.4 Hz, 1H), 3.80 (s, 3H), 4.03–4.05 (m, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 11.4 (CH_3), 14.0 (CH_3), 22.5 (CH_2), 23.0 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 44.2 (CH), 55.3 (CH_3), 70.2 (CH_2), 70.6 (CH), 74.3 (CH), 82.3 (C), 113.7 (CH×2), 129.5 (CH×2), 130.2 (C), 159.2 (C).
Diastereomer: 11.6 (CH_3), 14.1 (CH_3), 22.6 (CH_2), 23.0 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 44.3 (CH), 55.3 (CH_3), 70.3 (CH_2), 70.8 (CH), 74.3 (CH), 82.3 (C), 113.7 (CH×2), 129.5 (CH×2), 130.2 (C), 159.2 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{26}O_2Na$: 297.1825; found: 297.1821.

10-[(4-Methoxybenzyl)oxy]dodec-11-yn-1-ol (4i)

Yield: 40.1 mg (83%); colorless oil (Method A).
IR (neat): 3433, 3290 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 1.25–1.77 (m, 17H), 2.46 (d, *J* = 2.0 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.80 (s, 3H), 4.03 (td, *J* = 6.6, 2.0 Hz, 1H), 4.44 (d, *J* = 11.3 Hz, 1H), 4.73 (d, *J* = 11.3 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.2 (CH_2), 25.7 (CH_2), 29.2 (CH_2), 29.35 (CH_2), 29.38 (CH_2), 29.5 (CH_2), 32.8 (CH_2), 35.6 (CH_2), 55.3 (CH_3), 63.1 (CH_2), 68.0 (CH), 70.1 (CH_2), 73.6 (CH), 83.1 (C), 113.7 (CH×2), 129.7 (CH×2), 129.9 (C), 159.2 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{30}O_3Na$: 341.2087; found: 341.2088.

1-({[12-(Benzyloxy)dodec-1-yn-3-yl]oxy}methyl)-4-methoxybenzene (4k)

Yield: 35.9 mg (74%); pale yellow oil (Method A).
IR (neat): 3294 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 1.21–1.77 (m, 16H), 2.45 (d, *J* = 2.1 Hz, 1H), 3.46 (t, *J* = 6.6 Hz, 2H), 3.80 (s, 3H), 4.03 (td, *J* = 6.3, 2.1 Hz, 1H), 4.44 (d, *J* = 11.0 Hz, 1H), 4.50 (s, 2H), 4.73 (d, *J* = 11.0 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 2H), 7.23–7.37 (m, 7H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.2 (CH_2), 26.2 (CH_2), 29.2 (CH_2), 29.4 (CH_2×2), 29.5 (CH_2), 29.8 (CH_2), 35.6 (CH_2), 55.3 (CH_3), 68.1 (CH), 70.1 (CH_2), 70.5 (CH_2), 72.9 (CH_2), 73.6 (CH), 83.2 (C), 113.8 (CH×2), 127.4 (CH), 127.6 (CH×2), 128.3 (CH×2), 129.6 (CH×2), 131.5 (C), 138.7 (C), 159.3 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{36}O_3Na$: 431.2557; found: 431.2554.

1-{[(5-Ethynylnonan-5-yl)oxy]methyl}-4-methoxybenzene (4l)

Yield: 14.7 mg (26%); pale yellow oil (Method A).
IR (neat): 3302, 2946 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 6H), 1.25–1.76 (m, 12H), 2.49 (s, 1H), 3.80 (s, 3H), 4.53 (s, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.1 (CH_3×2), 22.9 (CH_2×2), 26.0 (CH_2×2), 38.2 (CH_2×2), 55.3 (CH_3), 65.7 (CH_2), 73.9 (C), 76.5 (CH), 79.6 (C), 113.8 (CH×2), 129.1 (CH×2), 131.9 (C), 159.0 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{19}H_{28}O_2Na$: 311.1982; found: 311.1980.

1-Chloro-4-[(hex-2-yn-1-yloxy)methyl]benzene (4o)

Yield: 38.7 mg (85%); colorless oil (Method A).
IR (neat): 2962, 2854, 2283, 2225 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.3 Hz, 3H), 1.51–1.59 (m, 2H), 2.21 (tt, *J* = 7.0, 2.2 Hz, 2H), 4.16 (t, *J* = 2.2 Hz, 2H), 4.55 (s, 2H), 7.16–7.31 (m, 4H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.5 (CH_3), 20.8 (CH_2), 22.1 (CH_2), 57.9 (CH_2), 70.5 (CH_2), 75.7 (C), 87.4 (C), 128.5 (CH×2), 129.3 (CH×2), 133.5 (C), 136.3 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{13}H_{15}ClONa$: 245.0704; found: 245.0705.

1-Methoxy-4-{[(3-phenylprop-2-yn-1-yl)oxy]methyl}benzene (4p)

Yield: 40.6 mg (82%); colorless oil (Method A).
IR (neat): 2839, 2237 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 4.36 (s, 2H), 4.61 (s, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 7.30–7.33 (m, 5H), 7.46 (dd, *J* = 6.6, 2.6 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 55.3 (CH_3), 57.5 (CH_2), 71.3 (CH_2), 85.2 (C), 86.4 (C), 113.9 (CH×2), 122.7 (C), 128.3 (CH×2), 128.4 (CH), 129.6 (C), 129.8 (CH×2), 131.8 (CH×2), 159.4 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{16}O_2Na$: 275.1043; found: 275.1042.

1-({[5-(Benzyloxy)pent-2-yn-1-yl]oxy}methyl)-4-methoxybenzene (4q)

Yield: 32.8 mg (76%); pale yellow oil (Method A).
IR (neat): 3433, 1097 cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$): δ = 2.57 (tt, *J* = 7.3, 2.4 Hz, 2H), 3.61 (t, *J* = 7.3 Hz, 2H), 3.79 (s, 3H), 4.12 (t, *J* = 2.4 Hz, 2H), 4.51 (s, 2H), 4.56 (s, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.24–7.36 (m, 7H).
^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_2), 55.2 (CH_3), 57.3 (CH_2), 68.4 (CH_2), 71.0 (CH_2), 72.9 (CH_2), 77.1 (C), 83.7 (C), 113.8 (CH×2), 127.7 (CH×2), 128.3 (CH), 128.4 (CH×2), 129.6 (C), 129.7 (CH×2), 138.0 (C), 159.3 (C).
HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{22}O_3Na$: 333.1461; found: 333.1461.

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Short title.

One-pot Transformation from Alkenes to Alkynes

Graphical abstract.