Copper(II) Bromide Catalyzed Novel Preparation of Propargylic Ethers and Sulfides by S_N1-Type Substitution between Propargylic Alcohols and Alcohols or Thiols

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Abstract: A general and efficient copper(II) bromide catalyzed substitution reaction of propargylic alcohols with carbon and heteroatom-centered nucleophiles, such as alcohols and thiols, leading to the construction of C–O and C–S bonds has been developed. High product yields were obtained with excellent regioselectivity.

Key words: propargylic ethers, alcohols, thiols, etherification, nucleophilic substitution

Propargylic ethers play a vital role in organic chemistry.[1] The Nicholas reaction was considered a powerful tool for propargylic substitution reactions, however, it requires a stoichiometric amount of octacarbonyldicobalt and several steps are necessary to obtain the propargylic product from propargylic alcohols via cationic propargylic complexes $[Co_2(CO)_6(propargyl)]^+$.[2,3] On the other hand, several transition metal and Lewis acid catalyzed propargylic substitution reaction have been reported.[4] Among them, a ruthenium-catalyzed process is a versatile and direct method.[5] A wide variety of nucleophiles such as alcohols, amines, amides, and thiols are available for this reaction. Toste and co-workers[6] and Campagne and co-workers[7] have developed efficient nucleophilic substitution reactions of propargylic alcohols in the presence of catalytic amounts of rhenium $[ReCl_3O(dppm)]$ and/or gold $[NaAuCl_4{\cdot}2H_2O]$ catalysts. However, the high cost of such catalysts is a barrier to their industrial use. More recently, Zhuang-Ping Zhan and co-workers[8] have investigated the bismuth(III) chloride, iron(III) chloride, and copper(II) triflate catalyzed coupling reactions of various propargylic alcohols with nucleophiles, but the catalysts loading was relatively high (10 mol% $BiCl_3$)[8a] and the hydroxy group of the propargylic alcohol needs to be protected,[8c] or the catalysts are more expensive.[8a,d]

In the past, the solvent for transition-metal-catalyzed propargylic substitution reactions was generally acetonitrile,[6b,8] acetone,[5b] or 1,2-dichloroethane.[5c,g,i] Due to their low boiling points, they are easily inhaled and can cause injury to the human body, hence we used nitromethane, which was obtained commercially and used without further purification, as the solvent in our research; this gave better results. When iron(III) chloride was used as the catalyst in this reaction, the solvent must be further purified.[8b] Copper salts are very general catalysts and have received attention in organic synthesis due to their low toxicity and low cost. Catalyst screening was performed for the model reaction of 2-methyl-4-phenylbut-3-yn-2-ol and ethanol to give 3-ethoxy-3-methyl-1-phenylbut-1-yne (**3a**) as the target product. In this study the performance of different copper salts was compared using nitromethane as the solvent at room temperature. Best results for the model coupling reaction were observed in the presence of copper(II) bromide catalyst (Table 1).

Initially we examined the copper(II) bromide catalyzed substitution reactions of propargylic alcohols with nucleophiles; the reactions were performed at room temperature in nitromethane (Scheme 1). The effect of temperature was also studied in our work and we found that when the reaction temperature exceeded 70 °C an unidentified byproduct was generated.

We investigated the copper(II) bromide catalyzed coupling reactions of five propargylic alcohols **1a–e** with several nucleophiles **2**, typical results are shown in Table 2. The reaction proceeded smoothly without exclusion of moisture or air from the reaction mixture. A series of alcohols were utilized as the nucleophile and these were firstly treated with various propargylic alcohols **1a–e** to give the corresponding propargylic ethers in moderate to good yields with complete regioselectivity (confirmed by ^1H NMR). In the case of the reaction of 2-methyl-4-phenylbut-3-yn-2-ol (**1a**) with ethanol, the corresponding ether **3a** was obtained in 84% after ten hours (Table 2, entry 1). By comparison, in the bismuth(III) chloride and iron(III) chloride catalyzed reactions, the desired product **3a** was obtained with lower yield (75% and 82% yields, respectively) and with longer reaction times (15 and 12 h, respectively).[8a,b] We also obtained a new compound **3b** in excellent yield (Table 2, entry 2) . Functional groups, such as acetate, in the propargylic alcohols scarcely affect the course of the C–O bond-forming reaction (Table 2, entry 11). Nucleophiles containing other functional groups such as alkenyl, phenyl, and chloro substituents were also readily reacted (Table 2, entries 2, 4, 5 and 12, 13), allowing the subsequent elaboration of the products after propargylic etherification. Notably, the use of ethanol as the nucleophile did not lead to the formation of the rearranged enone, which was obtained as the main product in the process catalyzed by gold(III) (Table 2, entries 1, 11, 14, and

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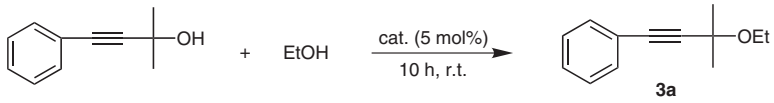
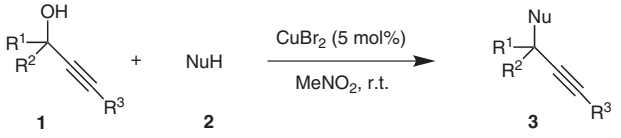
Table 1 Reaction of 2-Methyl-4-phenylbut-3-yn-2-ol (**1a**) with Ethanol



Entry	Catalyst[a]	Yield[b] (%)
1	$CuBr_2$	84
2	$CuCl_2$	23
3	$Cu(OAc)_2$	n.r.
4	$CuNO_3(PPh_3)_2$	n.r.
5	$CuSO_4 \cdot 5H_2O$	n.r.

[a] Reaction conditions: **1a** (0.5 mmol), EtOH (1.5 mmol), $MeNO_2$ (2 mL).
[b] Isolated yield; n.r. = no reaction.

15).[7] The reaction is not limited to alkyl substrates. For example, aromatic secondary alcohol **1d** and aromatic tertiary alcohols **1c** and **1e** readily undergo propargylic etherification to give the corresponding ethers (Table 2, entries 12–15). Gratifyingly, 1-phenylprop-2-yn-ol (**1d**) bearing a terminal alkyne group was successfully propargylated in 74% isolated yield at room temperature (Table 2, entry 14). The primary aliphatic alcohol 3-phenylprop-2-yn-1-ol ($R^1 = R^2 = H$) and aliphatic propargylic alcohols such as 3-butyn-2-ol and 2-methylbut-3-yn-2-ol failed to give propargylated products.



Scheme 1

The steric effect of the nucleophiles was also studied. The use of ethanol and propan-2-ol as nucleophiles led to the products **3a** and **3c** in 84% and 71% isolated yields, respectively (Table 2, entries 1 and 3). However, when we

Table 2 Copper(II) Bromide Catalyzed Substitution of Various Propargylic Alcohols **1** with Various Nucleophiles **2**

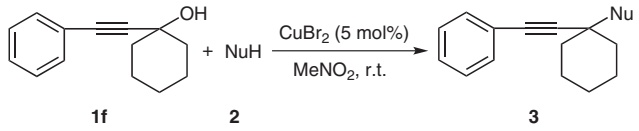
Entry	Substrate	R^1	R^2	R^3	NuH[a]	Time (h)	Product	Yield[b] (%)
1	**1a**	Me	Me	Ph	EtOH	10	**3a**	84
2	**1a**	Me	Me	Ph	BnOH	5	**3b**	98
3	**1a**	Me	Me	Ph	*i*-PrOH	6	**3c**	71
4	**1a**	Me	Me	Ph	$Cl(CH_2)_2OH$	2	**3d**	91
5	**1a**	Me	Me	Ph	$H_2C{=}CHCH_2OH$	8	**3e**[13a]	57
6	**1a**	Me	Me	Ph	*t*-BuOH	12	**3f**	n.r.
7	**1a**	Me	Me	Ph	(oxiran-2-yl)CH_2OH	10	**3g**	n.r.
8	**1a**	Me	Me	Ph	EtSH	4	**3h**	96
9	**1a**	Me	Me	Ph	CySH	6	**3i**	78
10	**1a**	Me	Me	Ph	$HS(CH_2)_2OH$	12	**3j**	85
11	**1b**	Me	Me	2-$AcOC_6H_4$	EtOH	11	**3k**	86
12	**1c**	Ph	Ph	Ph	$Cl(CH_2)_2OH$	5	**3l**	54
13	**1c**	Ph	Ph	Ph	BnOH	6	**3m**	42
14	**1d**	H	Ph	H	EtOH	5	**3n**[8b,c]	74
15	**1e**	Ph	Ph	H	EtOH	3	**3o**[13b]	38

[a] Reaction conditions: **1** (0. 5 mmol), **2** (1. 5 mmol), $CuBr_2$ (0.025 mmol), $MeNO_2$ (2 mL), r.t.
[b] Isolated yield of **3**; n.r. = no reaction.

used *tert*-butyl alcohol and oxiran-2-ylmethanol as nucleophiles, no reaction took place (Table 2, entries 6 and 7).

Transition-metal-catalyzed substitution of propargylic alcohols with thiols has been considered difficult to achieve, probably due to the fact that sulfur-containing compounds are catalyst poisons because of their strong coordinating properties.[5i,9] Fortunately, by employing 5 mol% of copper(II) bromide as the catalyst, the construction of sp^3-C–S bonds was achieved by the nucleophilic substitution of propargylic alcohols with thiols. Owing to the stronger nucleophilicity of ethanethiol compared to ethanol (Table 2, entry 10), we obtained a higher yield of **3h** (96%) than of **3a** (84%) when ethanethiol was used as a nucleophile (Table 2, entries 1 and 8). When used ethanethiol, 2-sulfanylethanol, and cyclohexanethiol were used as nucleophiles, the corresponding propargylic sulfides **3h–j** were obtained in 96%, 85%, and 78% yields as a result of steric effects (Table 2, entries 8–10).

Metal-catalyzed addition of thiols to alkynes sometimes takes place via oxidative addition of the thiol to a palladium complex followed by thiopalladation or hydropalladation,[10] or via the coordination-assisted activation of the triple bond,[11] whereas this side reaction is significantly suppressed in our reaction. We assumed that the reaction mechanism goes through the formation of a propargylic cation intermediate in the present reaction. The results indicated that the reaction proceeded via an S_N1-type substitution step.



Scheme 2

Table 3 Copper(II) Bromide Catalyzed Substitution of 1-(2-Phenylethynyl)cyclohexanol (**1f**) with Various Nucleophiles **2**

Entry	NuH[a]	Time (h)	Product	Yield[b] (%)
1	EtOH	10	**3p**	57
2	$Cl(CH_2)_2OH$	3	**3q**	82
3	BnOH	6	**3r**	75
4	*i*-PrOH	13	**3s**	53
5	EtSH	6	**3t**	86
6	CySH	15	**3u**	38

[a] Reaction conditions: **1f** (0.5 mmol), **2** (1.5 mmol), $CuBr_2$ (0.025 mmol), $MeNO_2$ (2 mL), r.t.
[b] Isolated yield of **3**.

Similarly, reactions of 1-(2-phenylethynyl)cyclohexanol (**1f**)[12] with various nucleophiles were also investigated and we obtained a series of new compounds. All reactions proceeded in the presence of 5 mol% of copper(II) bromide in nitromethane at room temperature (Scheme 2); typical results are shown in Table 3. The corresponding products **3p–u** were obtained in good yields with complete regioselectivity. Ethanol as well as propan-2-ol participated in the reaction without noticeable differences (Table 3, entries 1 and 4), and the steric effect scarcely affected the yields of the products. However, the steric effect played an important role in the reactions when ethanethiol and cyclohexanethiol were used as nucleophiles (Table 3, entries 5 and 6). Due to the stronger nucleophilicity of the thiol, 1-(2-phenylethynyl)cyclohexanol (**1f**) reacted smoothly with ethanethiol affording **3t** in high yield as compared with the formation of **3p** with ethanol (Table 3, entries 5 and 1). 2-Chloroethanol and benzyl alcohol also reacted smoothly with **1f** to give the corresponding C–O coupling products **3q** and **3r** in good yields (Table 3, entries 2 and 3). The results indicated the reaction proceeded via an S_N1-type substitution between propargylic alcohols and alcohols or thiols.

In summary, we have developed a novel etherification reaction of propargylic alcohols and alcohols or thiols in the presence of copper(II) bromide. Propargylic alcohols bearing a terminal alkyne group or an internal alkyne are readily available.[4] In comparison with cobalt, rhenium, ruthenium, gold, bismuth, and iron, our reported catalyst copper(II) bromide offers several advantages in terms of its simple operation, mild reaction conditions, efficiency, and easily availability and it is environmentally friendly. Further developments using this methodology are currently underway in our laboratory.

NMR spectroscopy was performed on a Mercury 4N-PEG-300 (^{1}H: 300 MHz; ^{13}C: 75 MHz) spectrometer, using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. IR spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer as KBr pellets or KBr film. Mass spectra were recorded on an HP 5998 mass spectrometer applying the EI method. Elemental analyses were performed on an Elementar Vario EL analyzer. Commercially available reagents and solvents were used without further purification.

3-Ethoxy-3-methyl-1-phenylbut-1-yne (3a); Typical Procedure

2-Methyl-4-phenylbut-3-yn-2-ol (**1a**, 80 mg, 0.5 mmol), EtOH (69 mg, 1.5 mmol), $MeNO_2$ (2 mL), and anhyd $CuBr_2$ (5.6 mg, 0.025 mmol) were successively added to a 5-mL flask, and then the mixture was stirred magnetically at r.t. for 10 h. The soln was concentrated under reduced pressure by an aspirator and then the residue was purified by column chromatography (silica gel) to afford **3a** (78.7 mg, 84%) as a colorless oil.

IR (KBr): 3080, 3058, 2981, 2932, 2874, 2232, 1598, 1489, 1160 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3 H), 1.55 (s, 6 H), 3.69 (q, *J* = 7.1 Hz, 2 H), 7.25–7.44 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.8, 28.9, 59.4, 70.2, 83.7, 91.7, 122.9, 128.1, 128.2, 131.6.

EI-MS: *m/z* = 173 [$M^+ - CH_3$], 145, 115, 112, 77.

Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.87; H, 8.69.

3-(Benzyloxy)-3-methyl-1-phenylbut-1-yne (3b)
White solid; yield: 98%.

IR (KBr): 3062, 3031, 2984, 2931, 2862, 2732, 2234, 1491, 1277, 1154 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ =1.63 (s, 6 H), 4.71 (s, 2 H), 7.25–7.44 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.0, 66.6, 71.1, 84.4, 91.4, 122.8, 127.3, 127.7, 128.1, 128.2, 128.3, 131.6, 139.1.

EI-MS: *m*/*z* = 251 [M^+ + 1], 235, 143, 129, 127, 91, 77.

Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.27; H, 7.34.

(3-Isopropoxy-3-methylbut-1-yn-1-yl)benzene (3c)
Yellow oil; yield: 71%.

IR (KBr): 3421, 3080, 3059, 2978, 2929, 2859, 1975, 1711, 1594, 1527 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 6.6 Hz, 6 H), 1.53 (s, 6 H), 4.08–4.14 (m, 1 H), 7.28–7.42 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.5, 29.8, 67.0, 70.2, 82.9, 92.6, 123.0, 128.0, 128.2, 131.5.

EI-MS: *m*/*z* = 202 [M^+], 187, 159, 145, 129, 115, 102, 91, 77.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.09; H, 8.95.

[3-(2-Chloroethoxy)-3-methylbut-1-yn-1-yl]benzene (3d)
Yellow oil; yield: 91%.

IR (KBr): 3395, 3509, 2985, 2933, 2863, 2736, 2230, 1598, 1490, 1280, 1152 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.57 (s, 6 H), 3.65 (t, *J* = 6.0 Hz, 2 H), 3.89 (t, *J* = 6.0 Hz, 2 H), 7.30–7.44 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.8, 43.3, 64.6, 71.0, 84.4, 90.8, 122.6, 128.2, 128.3, 131.6.

EI-MS: *m*/*z* = 222 [M^+], 171, 143, 129, 115, 91, 77, 63.

Anal. Calcd for $C_{13}H_{15}ClO$: C, 70.11; H, 6.79. Found: C, 70.14; H, 6.81.

3-(Ethylsulfanyl)-3-methyl-1-phenylbut-1-yne (3h)
Yellow oil; yield: 96%.

IR (KBr): 3080, 3058, 2965, 2926, 2859, 2237, 2207, 1449, 1127 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.6 Hz, 3 H), 1.69 (s, 6 H), 2.85 (q, *J* = 7.6 Hz, 2 H), 7.27–7.42 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 24.7, 30.9, 38.8, 82.1, 93.6, 123.2, 127.9, 128.2, 131.6.

EI-MS: *m*/*z* = 206, 204 [M^+], 189, 175, 143, 128, 77.

Anal. Calcd for $C_{13}H_{16}S$: C, 76.41; H, 7.89. Found: C, 76.53; H, 7.76.

3-(Cyclohexylsulfanyl)-3-methyl-1-phenylbut-1-yne (3i)
Pale yellow oil; yield: 78%.

IR (KBr): 3458, 2928, 2852, 2693, 1363, 1446, 752 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.33–1.75 (m, 12 H), 2.08–2.13 (m, 4 H), 2.13–3.03 (m, 1 H), 7.27–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 26.2, 31.6, 35.3, 39.0, 43.9, 81.8, 94.1, 123.3, 127.8, 128.1, 131.4.

EI-MS: *m*/*z* = 258 [M^+], 243, 230, 175, 161, 143, 128, 115, 77.

Anal. Calcd for $C_{17}H_{22}S$: C, 79.01; H, 8.58. Found: C, 79.12; H, 8.45.

3-Methyl-1-phenyl-3-(2-sulfanylethoxy)but-1-yne (3j)
Pale yellow oil; yield: 85%

IR (KBr): 3448, 2927, 2364, 2140, 1652, 1462, 1424, 1290 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.56 (s, 6 H), 2.83 (t, *J* = 6.8 Hz, 2 H), 3.61 (q, *J* = 6.8, 6.0 Hz, 2 H), 4.86 (t, *J* = 6.0 Hz, 1 H), 7.32–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.0, 34.0, 38.8, 61.1, 82.3, 93.3, 122.7, 128.0, 128.1, 131.4.

EI-MS: *m*/*z* = 220 [M^+], 205, 175, 161, 143, 128, 115, 103, 77.

Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 70.76; H, 7.39.

1-(2-Acetoxyphenyl)-3-ethoxy-3-methylbut-1-yne (3k)
Yellow oil; yield: 86%.

IR (KBr): 3460, 2982, 2933, 2091, 1769, 1636, 1185, 755 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.25 (t, *J* = 6.9 Hz, 3 H), 1.54 (s, 6 H), 2.32 (s, 3 H), 3.65 (q, *J* = 6.9 Hz, 2 H), 7.06–7.48 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.7, 20.7, 28.8, 59.5, 70.2, 78.7, 96.7, 116.9, 122.1, 125.8, 129.3, 133.0, 151.5, 168.6.

EI-MS: *m*/*z* = 246 [M^+], 230, 215, 175, 161, 143, 128, 115, 103, 91, 77.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 83.28; H, 7.23.

1-(2-Chloroethoxy)-1,1,3-triphenylprop-1-yne (3l)
Pale yellow oil; yield: 54%.

IR (KBr): 3060, 3028, 2960, 2928, 2865, 2741, 2223, 1598, 1490, 1448 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.73 (t, *J* = 6.0 Hz, 2 H), 3.84 (t, *J* = 6.0 Hz, 2 H), 7.08–7.66 (m, 15 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.2, 65.0, 80.8, 88.4, 89.8, 122.2, 126.6, 127.8, 128.2, 128.4, 128.8, 131.8, 143.2.

EI-MS: *m*/*z* = 346 [M^+], 283, 267, 189, 165, 129, 105, 77.

Anal. Calcd for $C_{23}H_{19}ClO$: C, 79.64; H, 5.52. Found: C, 79.74; H, 5.45.

3-(Benzyloxy)-1,3,3-triphenylprop-1-yne (3m)
Yellow oil; yield: 42%.

IR (KBr): 3419, 3061, 3030, 2924, 2861, 2222, 1956, 1720, 1491, 1449, 1270, 1053 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.65 (s, 2 H), 7.22–7.71 (m, 20 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.9, 80.9, 88.9, 89.7, 122.5, 126.7, 127.3, 127.6, 127.7, 128.2, 128.3, 128.6, 129.7, 131.8, 138.8, 143.7.

EI-MS: *m*/*z* = 283 [M^+ – Bn], 268, 212, 189, 178, 167, 152, 129, 115, 105, 91, 77.

Anal. Calcd for $C_{28}H_{22}O$: C, 89.81; H, 5.92. Found: C, 89.86; H, 5.95.

1-(1-Ethoxycyclohexyl)-2-phenylethyne (3p)
Brown oil; yield: 57%.

IR (KBr): 3080, 3058, 2937, 2935, 2858, 2733, 2667, 2616, 2220, 1598, 1489 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.2 Hz, 3 H), 1.53–2.03 (m, 10 H), 3.71 (q, *J* = 7.2 Hz, 2 H), 7.27–7.45 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 23.0, 25.5, 37.4, 58.4, 73.8, 85.7, 91.0, 123.1, 128.0, 128.2, 131.6.

EI-MS: *m*/*z* = 228 [M^+], 213, 185, 157, 141, 129, 115, 102, 91, 77.

Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.21; H, 8.97.

1-[1-(2-Chloroethoxy)cyclohexyl]-2-phenylethyne (3q)
Pale yellow oil; yield: 82%.

IR (KBr): 3080, 3058, 3028, 2936, 2858, 2741, 2669, 2221, 1590, 1449 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.58–2.04 (m, 10 H), 3.68 (t, *J* = 6.2 Hz, 2 H), 3.92 (t, *J* = 6.2 Hz, 2 H), 7.28–7.46 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8, 25.4, 37.2, 43.4, 63.8, 74.4, 86.2, 90.1, 122.8, 128.2, 128.2, 131.6.

EI-MS: *m*/*z* = 262 [M^+], 219, 182, 157, 141, 129, 115, 102, 91, 77.

Anal. Calcd for $C_{16}H_{19}ClO$: C, 73.13; H, 7.29. Found: C, 73.21; H, 7.46.

1-[1-(Benzyloxy)cyclohexyl]-2-phenylethyne (3r)
Brown oil; yield: 75%.

IR (KBr): 3084, 3062, 3031, 2935, 2857, 2736, 2668, 2607, 2220, 1722, 1599, 1491, 1448 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.54–2.07 (m, 10 H), 4.73 (s, 2 H), 7.22–7.45 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.9, 25.5, 37.4, 65.6, 74.5, 86.2, 90.8, 123.0, 127.2, 127.7, 128.1, 128.2, 128.2, 131.7, 139.4.

EI-MS: *m*/*z* = 290 [M^+], 247, 233, 205, 192, 141, 129, 91, 77.

Anal. Calcd for $C_{21}H_{22}O$: C, 86.85; H, 7.64. Found: C, 86.97; H, 7.55.

1-(1-Isopropoxycyclohexyl)-2-phenylethyne (3s)
Pale yellow oil; yield: 53%.

IR (KBr): 3080, 3059, 3028, 2970, 2934, 2857, 2711, 2668, 2615, 2203, 1727, 1598, 1490, 1446 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (d, *J* = 6.6 Hz, 6 H), 1.55–2.03 (m, 10 H), 4.19 (m, 1 H), 7.28–7.44 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.2, 24.6, 25.5, 38.4, 66.3, 74.1, 85.2, 91.7, 123.3, 127.9, 128.2, 131.5.

EI-MS: *m*/*z* = 242 [M^+], 227, 199, 184, 171, 157, 129, 115, 102, 91, 77.

Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.47; H, 9.23.

1-[1-(Ethylsulfanyl)cyclohexyl)-2-phenylethyne (3t)
Pale yellow oil; yield: 86%.

IR (KBr): 3078, 3056, 3027, 2931, 2854, 2666, 2219, 1597, 1490, 1445 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.5 Hz, 3 H), 1.60–2.13 (m, 10 H), 2.81 (q, *J* = 7.5 Hz, 2 H), 2.27–7.44 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 23.0, 25.5, 37.4, 58.4, 73.8, 85.7, 91.0, 123.1, 128.0, 128.2, 131.6.

EI-MS: *m*/*z* = 245 [$M^+ + 1$], 244 [M^+], 215, 183, 155, 141, 115, 105, 91, 77.

Anal. Calcd for $C_{16}H_{20}S$: C, 78.63; H, 8.25. Found: C, 78.76; H, 8.19.

1-[1-(Cyclohexylsulfanyl)cyclohexyl]-2-phenylethyne (3u)
Pale yellow oil; yield: 38%.

IR (KBr): 3459, 2930, 2852, 2224, 1637, 1490, 1445, 912 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.25–2.16 (m, 20 H), 3.05–3.12 (m, 1 H), 7.25–7.43 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 25.6, 26.1, 26.3, 35.7, 39.9, 42.8, 44.8, 84.2, 92.4, 123.6, 127.8, 128.2, 131.5.

EI-MS: *m*/*z* = 298 [M^+], 230, 215, 183, 155, 141, 128, 115, 91, 77.

Anal. Calcd for $C_{20}H_{26}S$: C, 80.48; H, 8.78. Found: C, 80.56; H, 8.69.

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