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Copper (I) Iodide-Catalyzed One-Step Preparation of Functionalized Allenes from Terminal Alkynes: Amine Effect

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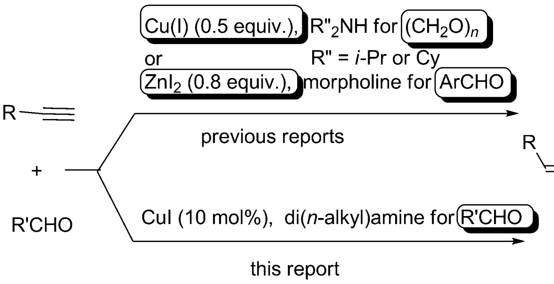
Abstract: An efficient one-step synthesis of functionalized allenes from readily available functionalized terminal alkynes and aldehydes by applying the effect of a dialkylamine has been developed. The protocol is catalyzed by copper(I) iodide and the dialkylamine is believed to play a very important role in the transformation.

Keywords: amine effect; catalysis; copper(I) iodide; synthesis of allenes

Introduction

Due to the recent extensive studies on the chemistry of allenes, this class of compounds is becoming more and more versatile in organic synthesis.[1] Thus, a one-step procedure from the most commonly available chemicals in a synthetic laboratory will surely become one of the hottest research topics in this area.[2] A one-step synthesis of terminal allenes from terminal alkynes with paraformaldehyde has been realized with 0.5 equivalents of a Cu(I) salt.[3,4] In addition, 1,3-disubstituted allenes may be prepared *via* the reaction of terminal alkynes with aldehydes by using 0.8 equivalents of ZnI_2 with very limited success for aliphatic aldehydes.[5] In the meantime, it was reported that microwave may promote such one-step transformations.[6,7] Thus, in terms of atom economy and for large-scale synthesis as well as the generality for aliphatic aldehydes, an efficient catalytic version of such a reaction is of high interest for the future of allene chemistry.[7] In this paper, we wish to report a CuI-catalyzed one-step synthesis of allenes with functional groups ready for further transformation from terminal alkynes and aldehydes, especially aliphatic ones, by using dialkylamines (Scheme 1).



Scheme 1. Synthesis of allenes from 1-alkynes and aldehydes.

Results and Discussion

For the purpose of developing a practical catalytic version of such a reaction with direct inclusion of functional groups, we initiated our study with the reaction of 1-phenyl-2-propyn-1-ol **1a**, instead of a simple non-functionalized terminal alkyne, and *n*-butanal by using 10 mol% CuI as the catalyst to screen the effect of amine: all the amines or cyclic urea shown in Figure 1 failed to affect the reaction shown in Table 1. With the original base used by Crabbé

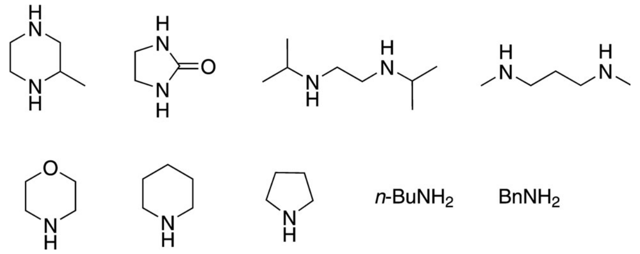
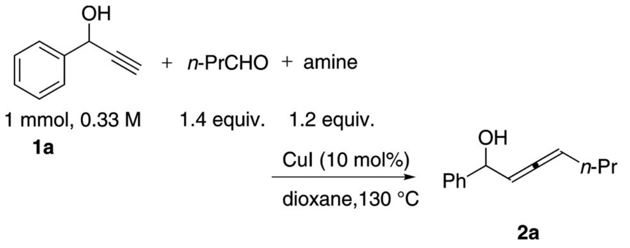


Figure 1. Amines failing to promote the reaction shown in Table 1 within 11 h.

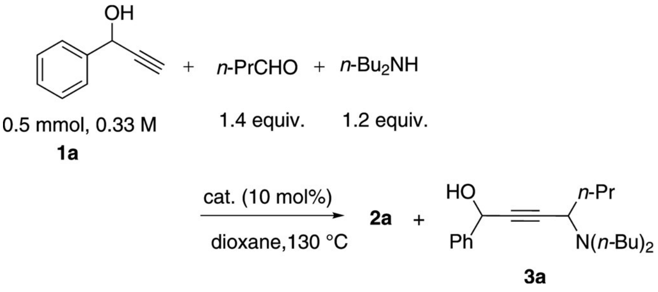
Table 1. Effect of amines.



Entry	Amine	Time [h]	Yield of **2a** [%][a]
1	*i*-Pr_2NH	22	31[b]
2	Cy_2NH	20	27
3	*N*-ethylisopropylamine	20	38
4	2-methylpiperidine	11	20
5	*n*-Pr_2NH	11	56
6	*n*-Bu_2NH	11	70

[a] NMR yield with CH_2Br_2 as the internal standard.
[b] 16% of **1a** was recovered.

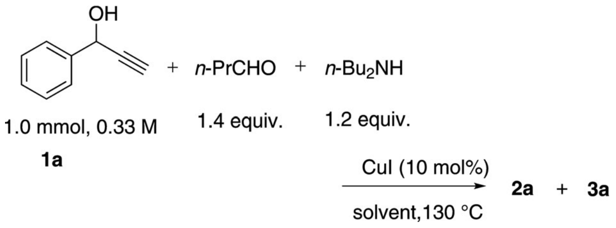
Table 2. The effect of catalyst.



Entry	Catalyst	Time [h]	Yield of **2a** [%][a]	Yield of **3a** [%][a]
1	CuBr	25	58	24
2	CuBr	46	40	17
3	CuCl	25	43	27
4	CuCN	25	–	70
5	$CuBr_2$	25	55	25
6	$CuBr_2$	46	44	10
7	$Cu(OAc)_2$	17	2	50
8	$ZnCl_2$	40	52	42
9	ZnI_2	40	68	18
10	$Cu(OTf)_2$	21	19	32
11[b]	AgI	21	–	68

[a] NMR yield determined by using 1,3,5-trimethylbenzene as the internal standard.
[b] 10 mol% of **1a** was recovered.

Table 3. The effect of solvent.



Entry	Solvent	Time [h]	Yield of **2a** [%][a]	Yield of **3a** [%][a]
1	dioxane	11	70	–
2	DME	22.5	61	14
3	DMSO	13	<2	46
4	THF	17	66	9
5	DCE	12	complicated	–
6	hexane	13	6	79
7	*o*-xylene	16	59	–

[a] NMR yield determined by using 1,3,5-trimethylbenzene as the internal standard.

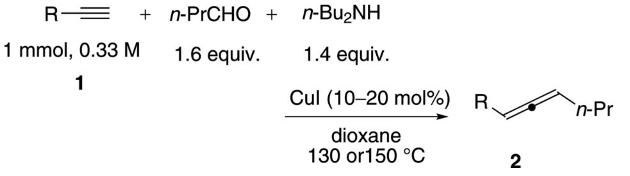
et al., the reaction was slow (entry 1, Table 1); with the amine used in our modified protocol,[4] the reaction was finished within 20 h, however, the yield is still low (entry 2, Table 1); interestingly, the reaction with isopropyl(ethyl)amine was completed within 20 h to afford allenol **2a** in 38% yield, indicating the importance of the replacement of one isopropyl group with the ethyl group (compare entry 1 with entry 3, Table 1); with this notion in mind, such a cyclic amine, 2-methylazacyclohexane, was tried, unfortunately, the yield was even lower. Thus, we decided to replace both secondary alkyl groups with a normal alkyl group, i.e., dipropylamine. To our delight, with this amine the yield was improved to 56%! Quite excitingly, dibutylamine is even better, improving the yield to 70% (entry 6, Table 1).

Then we started to screen different Cu(I), Cu(II) or Zn(II) catalysts with *n*-Bu_2NH as the amine. The results shown in Table 2 clearly indicate that $ZnCl_2$ and ZnI_2[5] are not good enough (entries 8 and 9) and CuI is still the best.

A quick screen on the solvent revealed that dioxane and *o*-xylene are among the best (entries 1 and 7, Table 3).

Optimization on the ratio of each reactant led to a set of optimal conditions for such a catalytic reaction: alkyne, 1.6 equivalents of *n*-PrCHO, and 1.4 equivalents of *n*-Bu_2NH with 10 mol% of CuI in dioxane. Then the scope of this catalytic reaction has been studied with the results shown in Table 4. It should be noted that the reaction is very smooth for the synthesis of functionalized allenes[8,9] with hydroxy (entries 1–13 and 17), amide (entries 14–16), and ether functionalities (entries 18 and 19). Primary, secondary, and tertiary propargylic alcohols may all be applied (entries 1–12) and other non-propargylic ω-alkynols may also afford the corresponding allene products (entry 17). We previously noted that the reaction of terminal alkynes with aliphatic aldehydes using ZnI_2 was not very general: limited substrates have been applied.[5] The current method nicely complements this issue as demonstrated by more examples in Table 4 and Scheme 2.

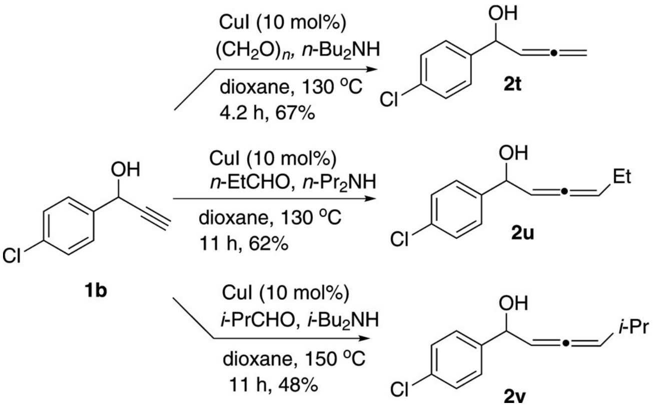
Table 4. CuI-catalyzed one-step synthesis of functionalized allenes from terminal alkynes, *n*-butanal, and dibutylamine.



Entry	R	CuI [mol%]/ T [°C]/t [h]	Isolated yield of **2** [%]
1	PhCH(OH) (**1a**)	10/130/12	73 (**2a**)
2	PhCH(OH) (**1a**)	10/130/13	66[b] (**2a**)
3	4-ClC$_6$H$_4$CH(OH) (**1b**)	10/130/12	77 (**2b**)
4	4-MeOC$_6$H$_4$CH(OH) (**1c**)	10/130/12	68 (**2c**)
5	R[a] (**1d**)	10/130/12	74 (**2d**)
6	n-C$_7$H$_{15}$CH(OH) (**1e**)	10/130/36	60 (**2e**)
7	n-C$_9$H$_{19}$CH(OH) (**1f**)	10/150/18	60 (**2f**)
8	c-CyCH(OH) (**1g**)	10/150/16	64 (**2g**)
9	c-(CH$_2$)$_5$C(OH) (**1h**)	10/150/21.5	73 (**2h**)
10	4-MeC$_6$H$_4$CMe(OH) (**1i**)	10/150/26	72 (**2i**)
11	n-C$_6$H$_{13}$CMe(OH) (**1j**)	10/150/26	65 (**2j**)
12	Ph$_2$C(OH) (**1k**)	20/150/26	59 (**2k**)
13	4-EtC$_6$H$_4$CH(OH)CH$_2$ (**1l**)	10/150/19	62 (**2l**)
14	TsNHCH$_2$ (**1m**)	20/150/46	49 (**2m**)
15	n-C$_5$H$_{11}$CH(NHTs) (**1n**)	20/150/41	58 (**2n**)
16	n-C$_7$H$_{15}$CH(NHTs) (**1o**)	20/150/48	54 (**2o**)
17	HO(CH$_2$)$_9$ (**1p**)	15/150/28	54 (**2p**)
18	BnOCH$_2$ (**1q**)	20/150/28	55 (**2q**)
19	THPOCH$_2$ (**1r**)	20/150/8.5	40 (**2r**)
20	n-C$_8$H$_{17}$ (**1s**)	15/150/43	66 (**2s**)

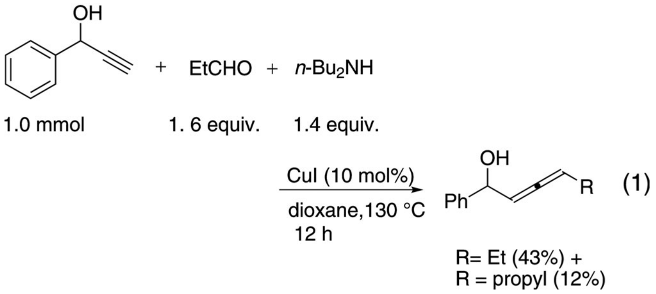
[a] R = c-3,4-OCH$_2$OC$_6$H$_3$CH(OH).

[b] The reaction was carried out in 8.0-mmol scale in 20 mL of dioxane.



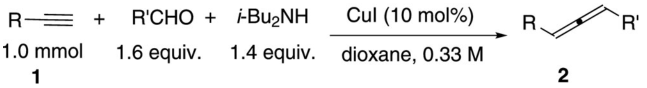
Scheme 2. CuI-catalyzed reaction of **1b** with paraformaldehyde, propanal or isobutanal.

This reaction may also be applied to paraformaldehyde forming terminal allenols (the first reaction in Scheme 2). We also noticed that if the dialkylamine used does not match with the aldehyde, a mixture of allenes was produced [Eq. (1)]. This was caused by the formation of butanal from the hydrolysis of imine **7** *in-situ* generated in the step of intramolecular hydride-transfer (see Scheme 3),[3,10,11] thus, each aldehyde required a specific dialkylamine (e.g., dipropylamine for propanal; i-Bu$_2$NH for *iso*-butanal), which is not so convenient for practical use. Further screening on the amine led to the observation that i-Bu$_2$NH may be used as a common amine without contamination of the allenol derived from i-Bu$_2$NH, although



(1)

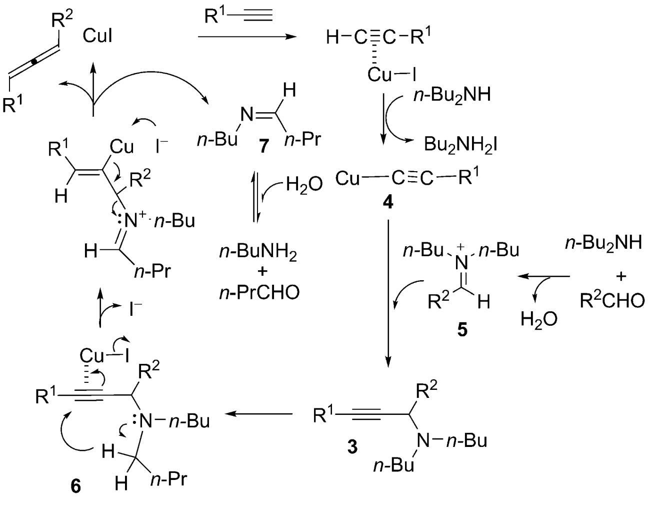
Table 5. CuI-catalyzed one-step synthesis of functionalized allenes from terminal alkynes, aldehydes, and diisobutylamine.[a]



Entry	**1**	R′	T [°C]/ t [h]	Isolated yield [%]
1	**1a**	Et	130/18	49 (**2w**)
2	**1a**	Cy	130/18	39 (**2x**)
3	**1a**	n-C$_5$H$_{11}$	140/12	55 (**2y**)
4	**1a**	i-PrCH$_2$	140/12	45 (**2z**)
5[b]	prop-2-yn-1-ol (**1t**)	n-C$_7$H$_{15}$	130/8	41 (**2aa**)

[a] The allene derived from alkyne and isobutyral is less than 5% in the allene product, if there is any.

[b] 20 mol% of CuI were used.



Scheme 3. Proposed mechanism.

the yields are not as high as those shown in Table 4 (Table 5).

A rationale for this transformation is proposed (Scheme 3): the interaction of the terminal alkyne with CuI in the presence of a base would form the 1-alkynyl copper intermediate **4**, which would react with the *in-situ* generated iminonium intermediate **5** to yield propargylic amine **3**. Intramolecular hydride transfer would yield the allene product with the regeneration of CuI to finish the catalytic cycle. The *in-situ* generated butanal would lead to the formation of the by-product shown in Eq. (1).

Conclusions

In conclusion, we have developed an efficient catalytic one-step synthesis of functionalized allenes from readily available functionalized terminal alkynes and aldehydes by applying the effect of the amine, which may be explained by the intermediacy of an iminonium intermediate formed from amines and aldehydes as well as the intramolecular hydride transfer in the step of transforming propargylic amines to final allenes.[3,10,11] Due to the easy availability of all the starting compounds as well as the catalyst and the potential of the functionalized allenes, this method will be of high interest to organic and medicinal chemists. Further studies in this area are being actively pursued in our laboratory.

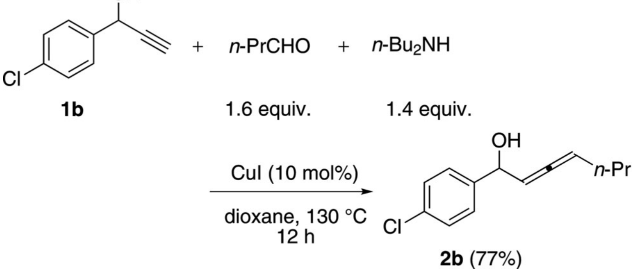
Experimental Section

General

Aldehydes were freshly distilled before use. CuI was purchased from Sinopharm Chemical Reagent Co., Ltd and used without further treatment. Dioxane was dried over sodium wire with benzophenone as indicator and distilled freshly before use. *n*-Pr_2NH, *n*-Bu_2NH, and *i*-Bu_2NH were dried over anhydrous barium oxide and distilled.[12] All the temperatures stated refer to the oil baths used.

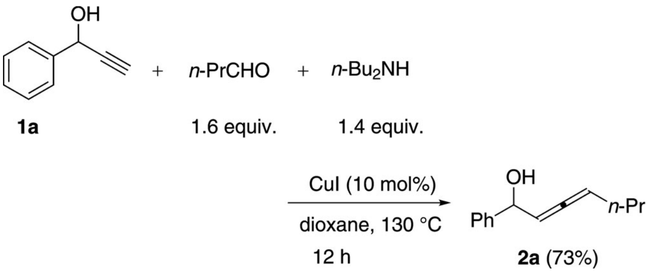
Typical Procedure: Synthesis of 1-(4-Chlorophenyl)-hepta-2,3-dien-1-ol (2b)

To an oven-dried reaction tube with a screw cap were added CuI (18.9 mg, 0.099 mmol), 1-(4-chlorophenyl)-2-propyn-1-ol **1b** (166.8 mg, 1.00 mmol), 3 mL of dioxane, *n*-butanal (142 μL, $d = 0.817\ \mathrm{g\,mL^{-1}}$, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d = 0.762\ \mathrm{g\,mL^{-1}}$, 181.4 mg, 1.40 mmol) under an argon atmosphere. The resulting mixture was sealed with the screw cap and stirred at 130 °C. When the reaction was complete as monitored by TLC upon cooling (during the reaction, the starting alkyne **1b** was consumed quickly and the corresponding propargylic amine was produced, which was then transformed to the allene product **2b** at a relatively slow rate), the reaction mixture was cooled to room temperature and filtered. Evaporation and column chromatography on silica gel afforded the corresponding allene **2b** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 15/1), liquid; yield: 172.0 mg (77%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.32$ (s, 4H, ArH), 5.41–5.30 (m, 2H, 2 × C=CH), 5.24–5.16 (m, 1H, OCH), 2.22 (bs, 1H, OH), 2.08–1.94 (m, 2H, CH_2), 1.52–1.33 (m, 2H, CH_2), 0.98–0.85 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.4, 202.2], [141.6, 141.5], [133.21, 133.17], 128.4, [127.5, 127.4], [95.8, 95.7], [95.2, 94.9], [71.7, 71.5], [30.7, 30.6], [22.21, 22.19], 13.6; MS (EI): $m/z = 224$ [M^+ (^{37}Cl), 0.26], 222 [M^+ (^{35}Cl), 0.72], 205 [M^+ (^{35}Cl)−OH, 0.51], 187 (M^+−Cl, 4.55), 141 (100); IR (neat): $\nu = 3362$, 2959, 2930, 2872, 1963, 1595, 1491, 1461, 1405, 1260, 1190, 1013 cm^{-1}; HR-MS (EI): $m/z = 222.0809$, calcd. for $C_{13}H_{15}{}^{35}ClO$ (M^+): 222.0811.

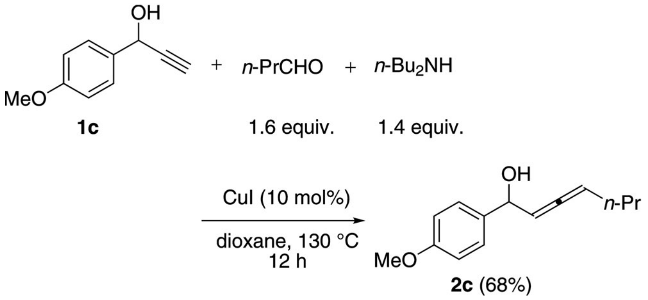


The following compounds (**2a**, **2c**–**2z**) were prepared according to this procedure.

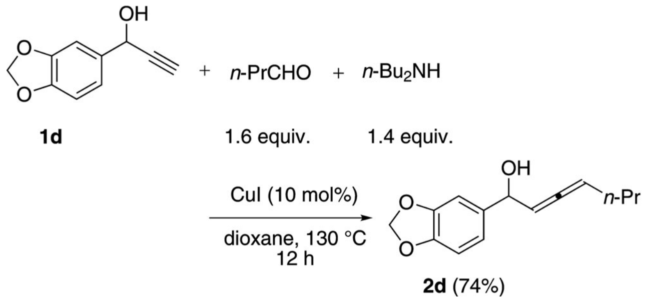
1-Phenylhepta-2,3-dien-1-ol (2a): The reaction of CuI (19.0 mg, 0.10 mmol), 1-phenyl-2-propyn-1-ol **1a** (133.7 mg, 1.01 mmol), 3 mL of dioxane, *n*-butanal (142 μL, $d = 0.817\ \mathrm{g\,mL^{-1}}$, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d = 0.762\ \mathrm{g\,mL^{-1}}$, 181.4 mg, 1.40 mmol) afforded the corresponding allene **2a**[13] as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 15/1), liquid; yield: 139.6 mg, (73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.21 (m, 5H, ArH), 5.47–5.28 (m, 2H, 2 × C=CH), 5.27–5.15 (m, 1H, OCH), 2.24 (bs, 1H, OH), 2.10–1.91 (m, 2H, CH_2), 1.52–1.33 (m, 2H, CH_2), 1.00–0.80 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.5, 202.2], [143.1, 143.0], 128.2, [127.4, 127.3], [126.0, 125.9], [95.83, 95.78], [94.4, 94.1], [72.3, 72.1], [30.63, 30.56], [22.14, 22.10], 13.5; MS (EI): $m/z = 188$ (M^+, 1.38), 107 (100); IR (neat): ν = 3362, 3063, 3030, 2959, 2930, 2872, 1963, 1603, 1493, 1453, 1335, 1258, 1193, 1010 cm^{-1}.



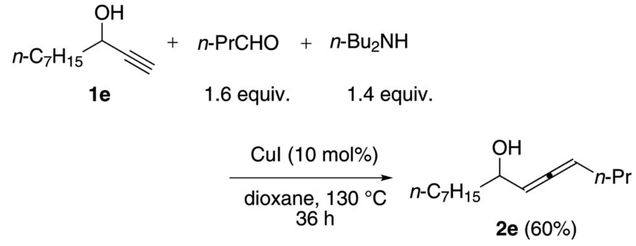
1-(4-Methoxyphenyl)hepta-2,3-dien-1-ol (2c): The reaction of CuI (19.0 mg, 0.10 mmol), 1-(4-methoxyphenyl)-2-propyn-1-ol **1c** (162.0 mg, 1.00 mmol), *n*-butanal (142 μL,



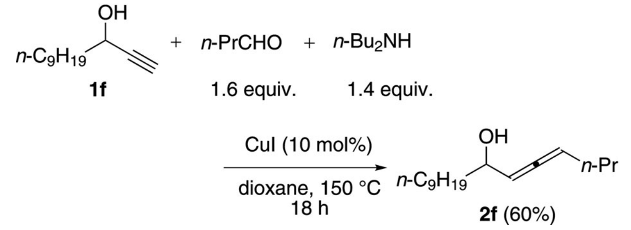
d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(n-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2c** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 15/1, then 10/1), liquid; yield: 148.6 mg (68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.7 Hz, 2H, ArH), 6.89 (d, J = 8.7 Hz, 2H, ArH), 5.47–5.29 (m, 2H, 2×C=CH), 5.24–5.12 (m, 1H, OCH), 3.80 (s, 3H, OCH_3), 2.19 (bs, 1H, OH), 2.10–1.94 (m, 2H, CH_2), 1.55–1.34 (m, 2H, CH_2), 1.00–0.84 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.3, 202.0], [159.03, 158.99], [135.4, 135.3], [127.4, 127.3], [113.71, 113.70], [96.1, 96.0], [94.8, 94.4], [71.9, 71.7], 55.2, [30.78, 30.70], [22.24, 22.20], [13.56, 13.55]; MS (EI): m/z = 218 (M$^+$, 1.29), 137 (100); IR (neat): ν = 3419, 2958, 2931, 2871, 2836, 1962, 1611, 1586, 1511, 1462, 1378, 1302, 1246, 1172, 1109, 1034 cm^{-1}; HR-MS (EI): m/z = 218.1305, calcd. for $C_{14}H_{18}O_2$ (M$^+$): 218.1307.



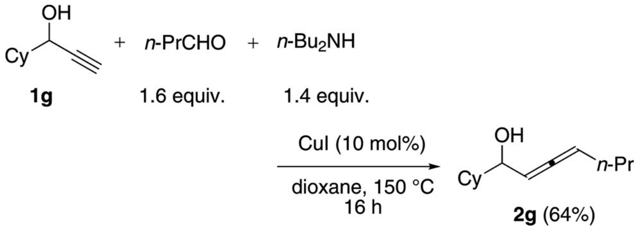
1-(3′,4′-Methylenedioxyphenyl)hepta-2,3-dien-1-ol (2d): The reaction of CuI (19.0 mg, 0.10 mmol), 1-(3′,4′-methylenedioxyphenyl)prop-2-yn-1-ol **1d** (176.6 mg, 1.00 mmol), n-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(n-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2d** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 15/1, then 10/1), liquid; yield: 172.8 mg (74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.89 (s, 1H, ArH), 6.85 (d, J = 8.1 Hz, 1H, ArH), 6.77 (d, J = 8.1 Hz, 1H, ArH), 5.94 (s, 2H, OCH_2O), 5.45–5.30 (m, 2H, 2×C=CH), 5.20–5.08 (m, 1H, OCH), 2.24 (bs, 1H, OH), 2.10–1.95 (m, 2H, CH_2 in Pr), 1.53–1.35 (m, 2H, CH_2 in Pr), 1.00–0.85 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.2, 202.0], 147.6, [147.0, 146.9], [137.3, 137.2], [119.5, 119.4], 108.0, [106.8, 106.7], 100.9, [96.04, 95.98], [95.0, 94.7], [72.1, 71.9], [30.8, 30.7], [22.3, 22.2], [13.57, 13.56]; MS (EI): m/z = 232 (M$^+$, 5.39), 65 (100); IR (neat): ν = 3383, 2959, 2930, 2777, 1962, 1609, 1503, 1487, 1441, 1377, 1243, 1123, 1093, 1038 cm^{-1}; HR-MS (EI): m/z = 232.1100, calcd. for $C_{14}H_{16}O_3$ (M$^+$): 232.1099.



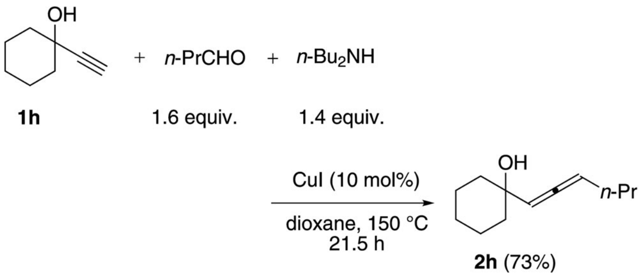
Tetradeca-4,5-dien-7-ol (2e): The reaction of CuI (19.1 mg, 0.10 mmol), 1-decyn-3-ol **1e** (153.4 mg, 0.99 mmol), n-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(n-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2e** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1), liquid: yield: 125.4 mg (60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.36–5.13 (m, 2H, 2×C=CH), 4.20–4.03 (m, 1H, OCH), 2.07–1.93 (m, 2H, CH_2), 1.67–1.17 (m, 15H, OH and 7×CH_2), 0.99–0.81 (m, 6H, 2×CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.3, 202.1], [95.7, 95.6], [94.0, 93.6], [70.3, 69.9], [37.52, 37.47], 31.8, 30.8, [29.5, 29.4], 29.2, [25.42, 25.37], 22.6, 22.3, 14.0, [13.59, 13.58]; MS (EI): m/z = 192 (M$^+$–H_2O, 1.21), 181 (M$^+$–C_2H_5, 6.80), 67 (100); IR (neat): ν = 3356, 2957, 2926, 2856, 1963, 1462, 1378, 1336, 1122, 1018 cm^{-1}; HR-MS (EI): m/z = 210.1986, calcd. for $C_{14}H_{26}O$ (M$^+$): 210.1984.



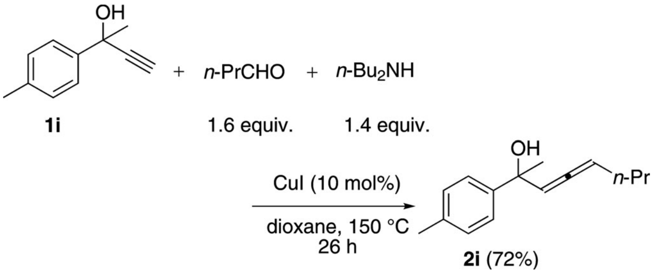
Hexadeca-4,5-dien-7-ol (2f): The reaction of CuI (19.1 mg, 0.10 mmol), 1-dodecyn-3-ol **1f** (182.6 mg, 1.00 mmol), n-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(n-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2f** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1), liquid; yield: 143.0 mg (60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.35–5.13 (m, 2H, 2×C=CH), 4.17–4.05 (m, 1H, OCH), 2.07–1.93 (m, 2H, CH_2), 1.72–1.62 (m, 1H, OH), 1.62–1.16 (m, 18H, 9×CH_2), 1.00–0.80 (m, 6H, 2×CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.3, 202.0], [95.7, 95.6], [94.1, 93.7], [70.3, 69.9], [37.54, 37.49], 31.9, 30.8, 29.6, 29.54, 29.50, 29.3, [25.43, 25.39], 22.7, 22.3, 14.1, 13.6; MS (EI): m/z = 209 (M$^+$–C_2H_5, 5.96), 194 (M$^+$–C_3H_8, 4.95), 67 (100); IR (neat): ν = 3346, 2957, 2924, 2854, 1963, 1463, 1378, 1258, 1123, 1010 cm^{-1}; HR-MS (EI): m/z = 238.2299, calcd. for $C_{16}H_{30}O$ (M$^+$): 238.2297.



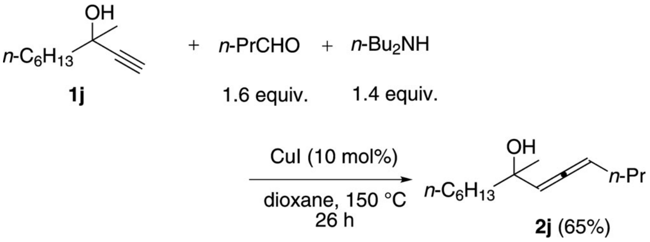
1-Cyclohexylhepta-2,3-dien-1-ol (2g): The reaction of CuI (19.0 mg, 0.10 mmol), 1-cyclohexyl-2-propyn-1-ol **1g** (137.8 mg, 1.00 mmol), *n*-butanal (142 μL, $d=0.817$ gmL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d=0.762$ gmL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2g** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1), liquid; yield: 123.7 mg (64%). ^{1}H NMR (300 MHz, CDCl$_3$): $\delta=5.34$–5.11 (m, 2H, 2×C=CH), 3.93–3.80 (m, 1H, OCH), 2.06–1.92 (m, 2H, CH$_2$), 1.92–1.58 (m, 6H, 3×CH$_2$), 1.52–1.32 (m, 3H, CH$_2$ and OH), 1.32–0.83 (m, 8H, 2×CH$_2$ and CH and CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): $\delta=$[202.7, 202.3], [94.1, 94.0], [93.9, 93.5], [74.6, 74.0], [44.1, 44.0], 30.9, 28.7, [28.4, 28.2], 26.5, [26.14, 26.11], [26.08, 26.03], 22.3, 13.6; MS (EI): $m/z=$ 194 (M$^+$, 0.35), 165 (M$^+$−C$_2$H$_5$, 1.06), 133 (M$^+$−C$_3$H$_7$−H$_2$O, 1.35), 41 (100); IR (neat): ν = 3384, 2924, 2852, 1962, 1450, 1378, 1261, 1175, 1141, 1083, 1010 cm^{-1}; HR-MS (EI): $m/z=$ 194.1670, calcd. for C$_{13}$H$_{22}$O (M$^+$): 194.1671.



1-(Hexa-1,2-dienyl)cyclohexanol (2h): The reaction of CuI (19.1 mg, 0.10 mmol), 1-ethynyl-cyclohexan-1-ol **1h** (124.2 mg, 1.00 mmol), *n*-butanal (142 μL, $d=0.817$ gmL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d=0.762$ gmL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2h** as a liquid (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1); yield: 131.1 mg (73%). ^{1}H NMR (300 MHz, CDCl$_3$): $\delta=5.37$–5.18 (m, 2H, 2×C=CH), 2.07–1.92 (m, 2H, CH$_2$), 1.73–1.26 (m, 13H, 6×CH$_2$ and OH), 0.93 (t, $J=7.4$ Hz, 3H, CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): $\delta=201.3$, 100.2, 94.6, 70.6, 38.3, 30.9, 25.5, 22.6, 22.5, 22.4, 13.7; MS (EI): $m/z=180$ (M$^+$, 1.28), 99 (100); IR (neat): ν = 3364, 2930, 2856, 1962, 1449, 1379, 1344, 1317, 1247, 1186, 1147, 1057, 1035 cm^{-1}; HR-MS (EI): $m/z=180.1514$, calcd. for C$_{12}$H$_{20}$O (M$^+$): 180.1514.

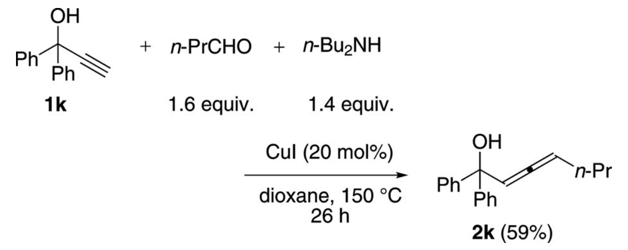


2-*p*-Tolylocta-3,4-dien-2-ol (2i): The reaction of CuI (19.0 mg, 0.10 mmol), 2-(*p*-tolyl)but-3-yn-2-ol **1i** (160.6 mg, 1.00 mmol), *n*-butanal (142 μL, $d=0.817$ gmL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d=0.762$ gmL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2i** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1), liquid; yield: 156.4 mg (72%). ^{1}H NMR (300 MHz, CDCl$_3$): $\delta=7.41$ (d, $J=8.1$ Hz, 2H, ArH), 7.17 (d, $J=7.8$ Hz, 2H, ArH), 5.58–5.48 (m, 1H, C=CH), 5.47–5.34 (m, 1H, C=CH), 2.36 (s, 3H, ArCH$_3$), 2.23–2.15 (m, 1H, OH), 2.13–1.98 (m, 2H, CH$_2$), 1.64 (s, 3H, CCH$_3$), 1.55–1.38 (m, 2H, CH$_2$), 1.02–0.88 (m, 3H, CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): $\delta=$[200.9, 200.8], [144.52, 144.46], 136.4, [128.75, 128.73], [124.9, 124.8], [101.01, 100.96], [95.6, 95.5], [73.1, 73.0], [30.92, 30.90], [30.4, 30.3], [22.4, 22.3], 21.0, 13.7; MS (EI): $m/z=216$ (M$^+$, 0.71), 201 (M$^+$−CH$_3$, 2.16), 135 (100); IR (neat): ν = 3390, 2960, 2929, 2872, 1963, 1512, 1456, 1410, 1369, 1335, 1284, 1208, 1183, 1088, 1061, 1020 cm^{-1}; HR-MS (EI): $m/z=216.1516$, calcd. for C$_{15}$H$_{20}$O (M$^+$): 216.1514.



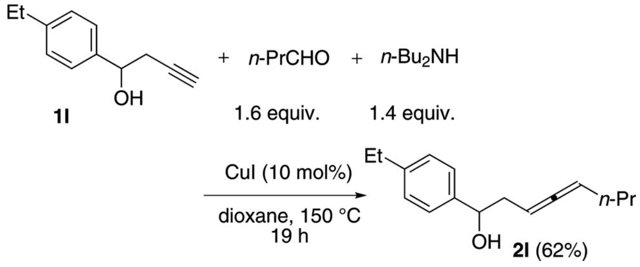
7-Methyltrideca-4,5-dien-7-ol (2j): The reaction of CuI (19.0 mg, 0.10 mmol), 3-methyl-l-nonyn-3-ol **1j** (153.7 mg, 1.00 mmol), *n*-butanal (142 μL, $d=0.817$ gmL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d=0.762$ gmL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2j** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1), liquid; yield: 136.1 mg (65%). ^{1}H NMR (300 MHz, CDCl$_3$): $\delta=5.37$–5.26 (m, 1H, C=CH), 5.26–5.18 (m, 1H, C=CH), 2.08–1.92 (m, 2H, CH$_2$), 1.70 (s, 1H, OH), 1.63–1.15 (m, 15H, 6×CH$_2$ and CH$_3$), 0.99–0.80 (m, 6H, 2×CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): $\delta=$[200.7, 200.6], [100.25, 100.23], [95.0, 94.9], [71.59, 71.56], [42.9, 42.8], 31.8, [31.03, 30.99], 29.7, [28.1, 28.0], 24.1, 22.6, [22.4, 22.3], 14.1, 13.7; MS (EI): $m/z=210$ (M$^+$, 0.50), 195 (M$^+$−CH$_3$, 1.22), 181 (M$^+$−C$_2$H$_5$, 1.02), 153 (M$^+$−C$_4$H$_9$, 3.26), 129 (100); IR (neat): ν = 3385, 2958, 2931, 2860, 1963, 1462, 1375, 1128, 1091, 1063 cm^{-1}; HR-MS (EI): $m/z=$ 210.1985, calcd. for C$_{14}$H$_{26}$O (M$^+$): 210.1984.

1,1-Diphenylhepta-2,3-dien-1-ol (2k): The reaction of CuI (38.0 mg, 0.10 mmol), 1,1-diphenyl-2-propyn-1-ol **1k** (208.0 mg, 1.00 mmol), *n*-butanal (142 μL, $d=0.817$ gmL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, $d=0.762$ gmL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane af-

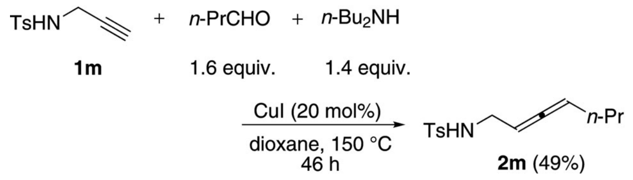


forded **2k** as a liquid (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1); yield: 155.8 mg (59%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.48–7.39 (m, 4H, ArH), 7.38–7.19 (m, 6H, ArH), 5.93–5.84 (m, 1H, C=CH), 5.44–5.32 (m, 1H, C=CH), 2.68 (s, 1H, OH), 2.06–1.91 (m, 2H, CH$_2$), 1.45–1.28 (m, 2H, CH$_2$), 0.87 (t, J=7.5 Hz, 3H, CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ=200.9, 146.24, 146.18, 127.80, 127.78, 126.9, 126.62, 126.55, 100.7, 96.6, 77.2, 66.7, 30.7, 22.1, 13.5; MS (EI): *m/z*=264 (M$^+$, 1.07), 77 (100); IR (neat): ν=3463, 3060, 3028, 2959, 2930, 2871, 1963, 1658, 1599, 1492, 1447, 1336, 1278, 1166, 1060, 1031, 1002 cm^{-1}; HR-MS (EI): *m/z*=264.1512, calcd. for C$_{19}$H$_{20}$O (M$^+$): 264.1514.

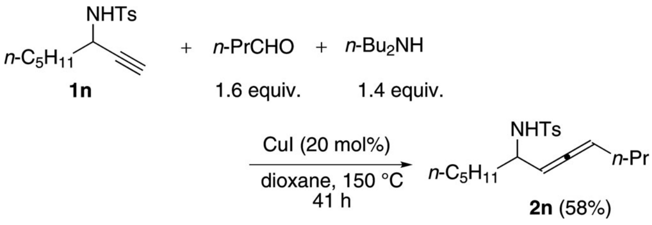
1-(4-Ethylphenyl)octa-3,4-dien-1-ol (2l): The reaction of CuI (18.9 mg, 0.10 mmol), 1-(4-ethylphenyl)but-3-yn-1-ol **1l** (174.1 mg, 1.00 mmol), *n*-butanal (142 μL, d=0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, d=0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2l** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate=20/1, then 10/1), liquid; yield: 143.0 mg (62%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.28 (d, J=7.8 Hz, 2H, ArH), 7.18 (d, J=7.8 Hz, 2H, ArH), 5.20–5.00 (m, 2H, 2×C=CH), 4.80–4.66 (m, 1H, OCH), 2.64 (q, J=7.6 Hz, 2H, CH$_2$ in Et), 2.50–2.38 (m, 2H, OCCH$_2$), 2.20–2.10 (m, 1H, OH), 2.02–1.85 (m, 2H, CH$_2$ in Pr), 1.49–1.30 (m, 2H, CH$_2$ in Pr), 1.23 (t, J=7.5 Hz, 3H, CH$_3$ in Et), 0.97–0.83 (m, 3H, CH$_3$ in Pr); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ=[205.2, 205.1], [143.5, 143.4], [141.01, 140.95], 127.8, [125.90, 125.87], [91.13, 91.07], 86.8, [73.6, 73.4], [39.2, 39.1], [30.84, 30.77], 28.5, [22.3, 22.2], 15.6, 13.6; MS (EI): *m/z*=230 (M$^+$, 1.04), 79 (100); IR (neat): ν=3389, 2964, 2932, 2899 2872, 2839, 1962, 1513, 1456, 1421, 1377, 1319, 1258, 1200, 1179, 1115, 1062, 1044, 1018 cm^{-1}; HR-MS (EI): *m/z*=230.1674, calcd. for C$_{16}$H$_{22}$O (M$^+$): 230.1671.



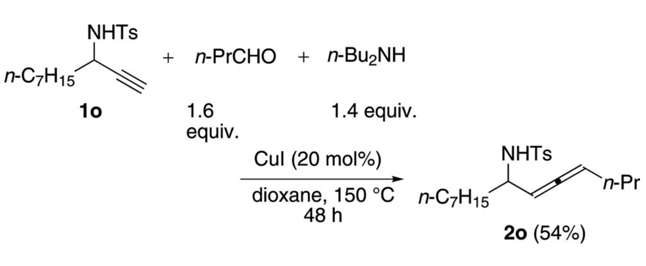
***N*-Tosyl(hepta-2,3-dienyl)amine (2m):** The reaction of CuI (38.7 mg, 0.20 mmol), *N*-tosylpropargylamine **1m** (209.3 mg, 1.00 mmol), *n*-butanal (116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (180.8 mg, 1.40 mmol) in 3 mL of dioxane afforded **2m** as a liquid (eluent: petroleum ether/DCM/ethyl acetate=40/40/1); yield: 131.1 mg (49%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.76 (d, J=8.1 Hz, 2H, ArH in Ts), 7.31 (d, J=7.8 Hz, 2H, ArH in Ts), 5.26–5.12 (m, 1H, C=CH), 5.10–4.97 (m, 1H, ArH), 4.70–4.51 (m, 1H, NH), 3.60–3.50 (m, 2H, NCH$_2$), 2.43 (s, 3H, CH$_3$ in Ts), 1.98–1.86 (m, 2H, CH$_2$ in Pr), 1.45–1.29 (m, 2H, CH$_2$ in Pr), 0.89 (t, J=7.3 Hz, 3H, CH$_3$ in Pr); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ=203.4, 143.4, 137.0, 129.7, 127.1, 94.5, 87.6, 41.9, 30.5, 22.1, 21.5, 13.6; MS (EI): *m/z*=265 (M$^+$, 1.41), 91 (100); IR (neat): ν=3280, 2959, 2871, 1965, 1599, 1495, 1423, 1325, 1158, 1094, 1069 cm^{-1}; HR-MS (EI): *m/z*=265.1135, calcd for C$_{14}$H$_{19}$NO$_2$S (M$^+$): 265.1137.



***N*-Tosyl(dodeca-4,5-dien-7-yl)amine (2n):** The reaction of CuI (37.6 mg, 0.20 mmol), *N*-tosyl(oct-1-yn-3-yl)amide **1n** (279.4 mg, 1.00 mmol), *n*-butanal (115.7 mg, 1.61 mmol), and di(*n*-butyl)amine (181.7 mg, 1.41 mmol) in 3 mL of dioxane afforded **2n** as a pair of diastereoisomers (eluent: petroleum ether/DCM/ethyl acetate=60/20/1, then 40/40/1), liquid: 195.9 mg (58%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.74 (d, J=8.7 Hz, 2H, ArH in Ts), 7.28 (d, J=7.8 Hz, 2H, ArH in Ts), 5.21–5.00 (m, 1H, C=CH), 4.99–4.86 (m, 1H, C=CH), 4.67–4.48 (m, 1H, NH), 3.84–3.67 (m, 1H, NCH), 2.42 (s, 3H, CH$_3$ in Ts), 1.96–1.76 (m, 2H, CH$_2$), 1.61–1.11 (m, 10H, 5×CH$_2$), 0.95–0.76 (m, 6H, 2×CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ=[202.3, 202.0], 143.0, [138.2, 138.1], [129.41, 129.39], 127.1, [95.0, 94.5], [93.0, 92.8], [52.7, 52.3], [36.2, 36.1], [31.4, 31.3], [30.63, 30.60], 24.9, 22.4, [22.3, 22.2], 21.4, 13.9, [13.59, 13.58]; MS (EI): *m/z*=335 (M$^+$, 0.94), 91 (100); IR (neat): ν=3276, 2957, 2930, 2860, 1965, 1599, 1496, 1426, 1328, 1159, 1094, 1041 cm^{-1}; HR-MS (EI): *m/z*=335.1920, calcd. for C$_{19}$H$_{29}$NO$_2$S (M$^+$): 335.1919.

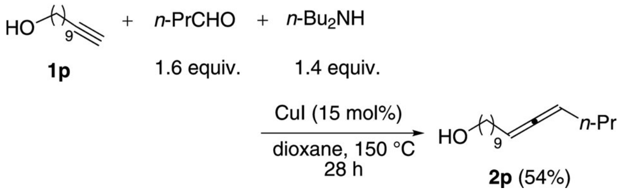


***N*-Tosyl(tetradeca-4,5-dien-7-yl)amine (2o):** The reaction of CuI (37.9 mg, 0.20 mmol), *N*-tosyl(dec-1-yn-3-yl)amide **1o** (306.5 mg, 1.00 mmol), *n*-butanal (116.0 mg, 1.61 mmol), and

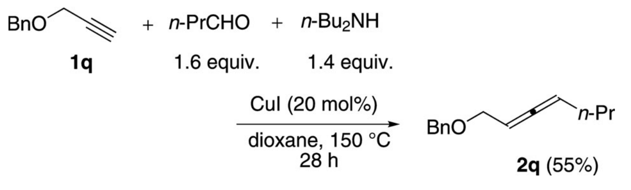


di(*n*-butyl)amine (179.5 mg, 1.39 mmol) in 3 mL of dioxane afforded **2o** as a pair of diastereoisomers (eluent: petroleum ether/DCM/ethyl acetate = 60/20/1, then 40/40/1), liquid; yield: 195.2 mg (54%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 5.22–5.00 (m, 1H, C=CH), 4.99–4.86 (m, 1H, C=CH), 4.71–4.45 (m, 1H, NH), 3.83–3.66 (m, 1H, NCH), 2.42 (s, 3H, CH_3 in Ts), 1.97–1.77 (m, 2H, CH_2), 1.61–1.11 (m, 14H, 7 × CH_2), 0.96–0.78 (m, 6H, 2 × CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.3, 202.0], [143.03, 143.01], [138.1, 138.0], [129.43, 129.40], 127.1, [95.0, 94.6], 94.5, [93.0, 92.8], [52.7, 52.3], [36.2, 36.1], 31.7, [30.64, 30.61], 29.09, 25.2, 22.6, [22.3, 22.2], 21.4, 14.0, 13.6; MS (EI): m/z = 363 (M^+, 1.11), 91 (100); IR (neat): ν = 3274, 2927, 2857, 1965, 1599, 1496, 1456, 1329, 1159, 1094 cm^{-1}; HR-MS (EI): m/z = 363.2230, calcd for $C_{21}H_{33}NO_2S$ (M^+): 363.2232.

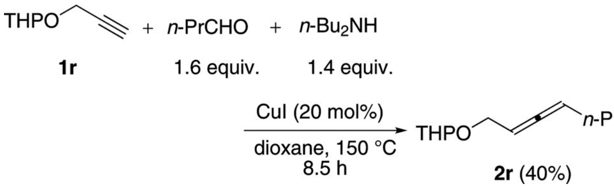
Pentadeca-10,11-dien-1-ol (2p): The reaction of CuI (28.5 mg, 0.15 mmol), 10-undecyn-1-ol **1p** (168.8 mg, 1.00 mmol), *n*-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2p** as a liquid (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1); yield: 120.7 mg (54%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.12–4.99 (m, 2H, 2 × C=CH), 3.62 (t, J = 6.6 Hz, 2H, OCH_2), 2.04–1.85 (m, 4H, 2 × CH_2), 1.70–1.20 (m, 17H, OH and 8 × CH_2), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 203.9, 90.8, 90.6, 62.9, 32.7, 31.1, 29.5, 29.38, 29.36, 29.2, 29.0, 28.9, 25.7, 22.4, 13.6; IR (neat): ν = 3331, 2926, 2854, 1962, 1462, 1057 cm^{-1}; MS (EI): m/z = 149 ($M^+ - H_2O - C_4H_9$, 0.93), 136 ($M^+ - H_2O - C_4H_9 - CH$, 1.68), 81 (100); HR-MS (EI): m/z = 224.2137, calcd for $C_{15}H_{28}O$ (M^+): 224.2140.



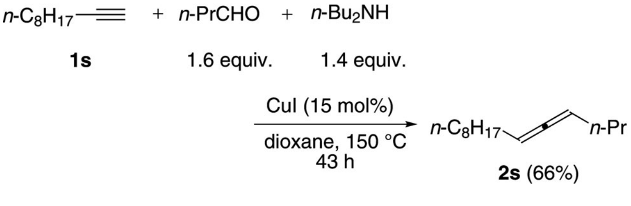
1-Benzyloxyhepta-2,3-diene (2q): The reaction of CuI (37.8 mg, 0.20 mmol), 1-benzyloxy-2-propyne **1q** (147.0 mg, 1.01 mmol), *n*-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2q** as a liquid (eluent: petroleum ether/ethyl acetate = 100/1); yield: 112.1 mg (55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.21 (m, 5H, ArH), 5.30–5.12 (m, 2H, 2 × C=CH), 4.53 (s, 2H, $PhCH_2$), 4.04 (dd, J = 6.5, 2.6 Hz, 2H, C=CCH_2O), 2.09–1.93 (m, 2H, CH_2 in Pr), 1.52–1.36 (m, 2H, CH_2 in Pr), 0.93 (t, J = 7.4 Hz, 3H, CH_3 in Pr); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 205.1, 138.2, 128.3, 127.8, 127.5, 91.6, 88.2, 71.5, 68.6, 30.6, 22.3, 13.5; MS (EI): m/z = 173 ($M^+ - C_2H_5$, 1.24), 172 ($M^+ - OCH_2$, 6.96), 143 ($M^+ - OCH_2 - C_2H_5$, 11.40), 91 (100); IR (neat): ν = 3031, 2959, 2931, 2870, 1963, 1454, 1352, 1204, 1093, 1074, 1028 cm^{-1}; HR-MS (EI): m/z = 202.1361, calcd. for $C_{14}H_{18}O$ (M^+): 202.1358.



1-(Tetrahydropyran-2-yl)oxyhepta-2,3-diene (2r): The reaction of CuI (37.8 mg, 0.20 mmol), 3-(tetrahydropyran-2-yl)oxy-1-propyne **1r** (141.9 mg, 1.01 mmol), *n*-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2r** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 30/1, then 20/1), liquid; yield: 79.7 mg (40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.31–5.09 (m, 2H, C=CH), 4.69 (t, J = 3.5 Hz, 1H, CH in THP), 4.28–4.13 (m, 1H, one proton from OCH_2C=C), 4.08–3.96 (m, 1H, one proton from OCH_2C=C), 3.95–3.81 (m, 1H, one proton from OCH_2 in THP), 3.59–3.43 (m, 1H, one proton from OCH_2 in THP), 2.06–1.92 (m, 2H, CH_2 in Pr), 1.91–1.32 (m, 8H, 3 × CH_2 in THP and CH_2 in Pr), 0.99–0.84 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [204.93, 204.91], [97.5, 97.4], [91.7, 91.6], [88.3, 88.2], 65.4, [62.14, 62.09], [30.60, 30.57], 30.5, 25.4, [22.3, 22.2], [19.45, 19.39], 13.5; MS (EI): m/z = 139 ($M^+ - CHOC_2H_4$, 1.78), 85 (100); IR (neat): ν = 2942, 2872, 1964, 1465, 1384, 1342, 1284, 1201, 1183, 1118, 1078, 1053, 1023 cm^{-1}; HR-MS (EI): m/z = 139.1125, calcd. for $C_9H_{15}O$ (M^+-$CHOC_2H_4$): 139.1123.

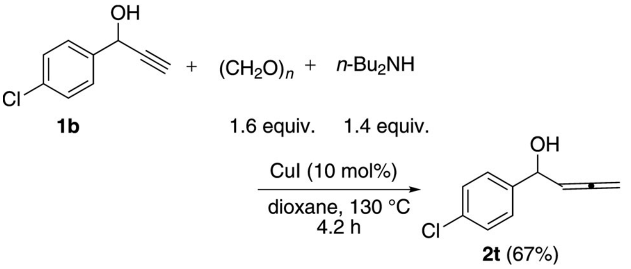


Tetradeca-4,5-diene (2s): The reaction of CuI (28.5 mg, 0.20 mmol), 1-decyne **1s** (180 μL, d = 0.766 g mL^{-1}, 137.9 mg, 1.00 mmol), *n*-butanal (142 μL, d = 0.817 g mL^{-1}, 116.0 mg, 1.61 mmol), and di(*n*-butyl)amine (238 μL, d = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2s**[14] as a liquid [eluent: petroleum ether (30–60 °C)]; yield: 128.2 mg (66%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.12–5.01 (m, 2H, 2 × C=CH), 2.04–1.88 (m, 4H, 2 × CH_2), 1.50–1.20 (m, 14H, 7 × CH_2), 0.98–0.82 (m, 6H, 2 × CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 204.0, 90.8, 90.6, 31.9, 31.2, 29.5, 29.4, 29.3, 29.1, 29.0, 22.7, 22.5, 14.1, 13.6; MS (EI): m/z = 194 (M^+, 0.65), 96 (100); IR (neat): ν = 2958, 2925, 2855, 1963, 1463, 1378,

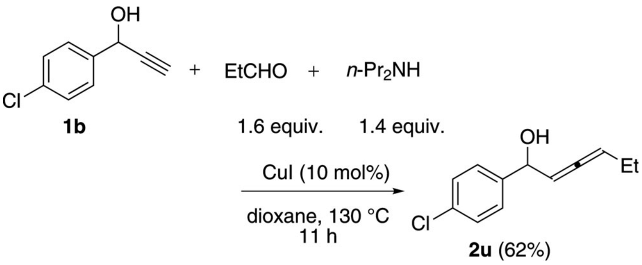


1337, 1288, 1069 cm^{-1}; HR-MS (EI): *m/z* = 194.2038, calcd. for $C_{14}H_{26}$ (M^+): 194.2035.

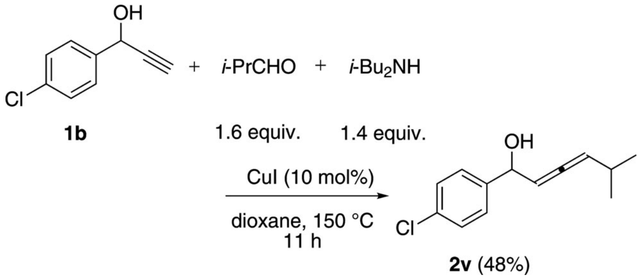
1-(4-Chlorophenyl)buta-2,3-dien-1-ol (2t): The reaction of CuI (19.0 mg, 0.10 mmol), 1-(4-chlorophenyl)-2-propyn-1-ol **1b** (166.3 mg, 1.00 mmol), paraformaldehyde (47.9 mg, 1.60 mmol), and di(*n*-butyl)amine (238 μL, *d* = 0.762 g mL^{-1}, 181.4 mg, 1.40 mmol) in 3 mL of dioxane afforded **2t**[15] as a liquid (eluent: petroleum ether/ethyl acetate = 10/1, then 5/1); yield: 119.9 mg (67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (s, 4H, ArH), 5.38 (q, *J* = 6.5 Hz, 1H, C=CH), 5.22 (dt, *J* = 6.3, 2.1 Hz, 1H, OCH), 4.92 (dd, *J* = 6.8, 2.3 Hz, 2H, C=CH_2), 2.54 (bs, 1H, OH); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 207.1, 141.2, 133.4, 128.5, 127.4, 94.9, 78.3, 71.3; MS (EI): *m/z* = 182 [M^+ (^{37}Cl), 1.05], 180 [M^+ (^{35}Cl), 3.17], 141 (100); IR (neat): ν = 3333, 2875, 1955, 1597, 1491, 1406, 1226, 1191, 1091, 1034, 1013 cm^{-1}.



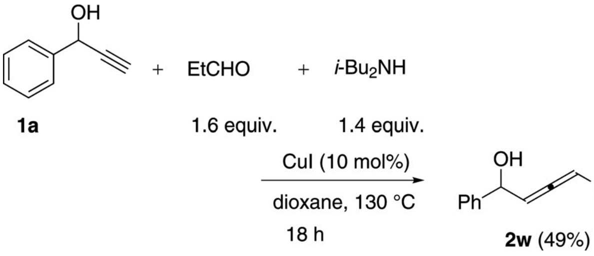
1-(4-Chlorophenyl)hexa-2,3-dien-1-ol (2u): The reaction of CuI (19.2 mg, 0.10 mmol), 1-(4-chlorophenyl)-2-propyn-1-ol **1b** (167.9 mg, 1.01 mmol), propanal (116 μL, *d* = 0.80 g mL^{-1}, 92.8 mg, 1.60 mmol), and di(*n*-propyl)amine (192 μL, *d* = 0.738 g mL^{-1}, 141.7 mg, 1.40 mmol) in 3 mL of dioxane afforded **2u** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 10/1), liquid; yield: 130.0 mg (62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (s, 4H, ArH), 5.50–5.32 (m, 2H, 2×C=CH), 5.23–5.14 (m, 1H, OCH), 2.29 (bs, 1H, OH), 2.12–1.96 (m, 2H, CH_2), 1.05–0.93 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.1, 201.8], [141.6, 141.5], [133.1, 133.0], 128.3, [127.4, 127.3], [96.9, 96.5], [96.4, 96.3], [71.7, 71.4], [21.64, 21.61], [13.2, 13.1]; MS (EI): *m/z* = 210 [M^+ (^{37}Cl), 0.49], 208 [M^+ (^{35}Cl), 1.41], 141 (100); IR (neat): ν = 3366, 2967, 2872, 1962, 1680, 1596, 1491, 1458, 1406, 1377, 1323, 1189, 1091, 1046, 1013 cm^{-1}; HR-MS (EI): *m/z* = 208.0655, calcd. for $C_{12}H_{13}{}^{35}ClO$ (M^+): 208.0655.



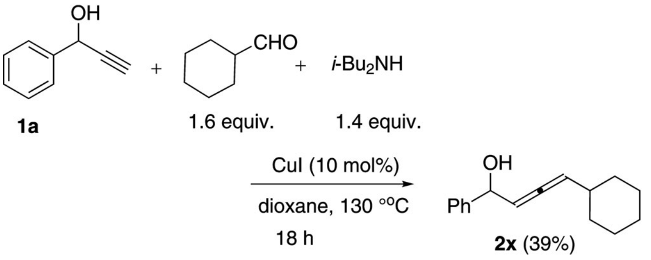
1-(4-Chlorophenyl)-5-methyl-hexa-2,3-dien-1-ol (2v): The reaction of CuI (19.2 mg, 0.10 mmol), 1-(4-chlorophenyl)-2-propyn-1-ol **1b** (166.1 mg, 1.00 mmol), isobutyral (146 μL, *d* = 0.794 g mL^{-1}, 115.9 mg, 1.61 mmol), and di(*i*-butyl)amine (244 μL, *d* = 0.74 g mL^{-1}, 180.6 mg, 1.40 mmol) in 3 mL of dioxane afforded **2v** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 10/1), liquid; yield: 105.7 mg (48%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (s, 4H, ArH), 5.48–5.33 (m, 2H, 2×C=CH), 5.23–5.14 (m, 1H, OCH), 2.40–2.21 (m, 2H, OH and CH in *i*-Pr), 1.05–0.93 (m, 6H, 2×CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [200.9, 200.5], [141.6, 141.5], [133.22, 133.17], 128.4, [127.5, 127.4], [103.1, 102.5], [97.2, 97.0], [71.8, 71.4], [27.91, 27.88], [22.38, 22.37], 22.3; MS (EI): *m/z* = 209 [M^+ (^{37}Cl)−CH_3, 0.17], 207 [M^+ (^{35}Cl)−CH_3, 0.50], 187 (M^+−Cl, 2.01), 141 (100); IR (neat): ν = 3357, 2962, 2868, 1961, 1596, 1491, 1465, 1405, 1382, 1365, 1297, 1221, 1191, 1127, 1091, 1044, 1013 cm^{-1}; HR-MS (EI): *m/z* = 222.0812, calcd. for $C_{13}H_{15}{}^{35}ClO$ (M^+): 222.0811.



1-Phenylhexa-2,3-dien-1-ol (2w): The reaction of CuI (19.0 mg, 0.10 mmol), 1-phenyl-2-propyn-1-ol **1a** (132.1 mg, 1.00 mmol), propanal (93.0 mg, 1.60 mmol), and di(*i*-butyl)amine (180.9 mg, 1.40 mmol) in 3 mL of dioxane afforded **2w** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 15/1), liquid; yield: 85.5 mg (49%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.22 (m, 5H, ArH), 5.49–5.35 (m, 2H, 2×C=CH), 5.26–5.14 (m, 1H, OCH), 2.51–2.16 (m, 1H, OH), 2.14–1.96 (m, 2H, CH_2), 1.08–0.90 (m, 3H, CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = [202.0, 201.7], [143.2, 143.0], [128.29, 128.28], [127.52, 127.47], [126.1, 126.0], [96.8, 96.7], 96.4, [72.3, 72.0], [21.73, 21.69], [13.3, 13.2]; MS (EI): *m/z* = 174 (M^+, 2.52), 107 (100); IR (neat): ν = 3343, 3063, 3030, 2966, 2932, 2872, 1961, 1603, 1493, 1453, 1377, 1325, 1193, 1133, 1006 cm^{-1}; HR-MS (EI): *m/z* = 174.1043, calcd. for $C_{12}H_{14}O$ (M^+): 174.1045.

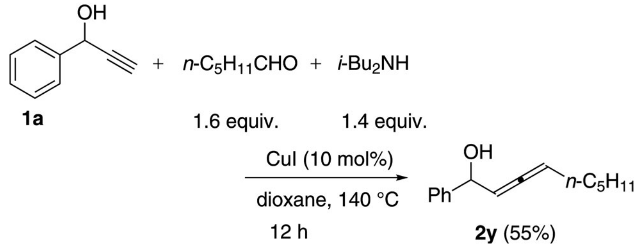


4-Cyclohexyl-1-phenylbuta-2,3-dien-1-ol (2x): The reaction of CuI (18.8 mg, 0.10 mmol), 1-phenyl-2-propyn-1-ol **1a** (132.1 mg, 1.00 mmol), cyclohexal (179.7 mg, 1.60 mmol), and di(*i*-butyl)amine (181.6 mg, 1.41 mmol) in 3 mL of dioxane afforded **2x**[11f] as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 15/1), liquid; yield: 88.2 mg

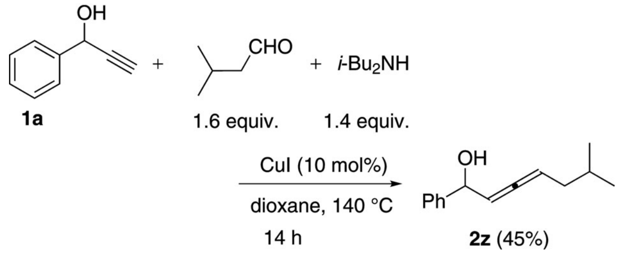


(39%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.44–7.22 (m, 5H, ArH), 5.51–5.40 (m, 1H, C=CH), 5.40–5.30 (m, 1H, C=CH), 5.26–5.16 (m, 1H, OCH), 2.35–2.13 (m, 1H, OH), 2.10–1.90 (m, 1H, CH in Cy), 1.83–1.56 (m, 5H, 2 × CH$_2$ and one proton of another CH$_2$), 1.39–0.96 (m, 5H, 2 × CH$_2$ and one proton of another CH$_2$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = [201.2, 200.9], [143.1, 143.0], [128.24, 128.22], [127.5, 127.4], [126.1, 126.0], [101.0, 100.6], [96.93, 96.86], [72.3, 72.1], [37.04, 37.01], 32.8, 26.0, 25.9; MS (EI): m/z = 228 (M$^+$, 1.25), 107 (100); IR (neat): ν = 3333, 3063, 3030, 2923, 2850, 1961, 1603, 1493, 1449, 1193, 1013 cm^{-1}.

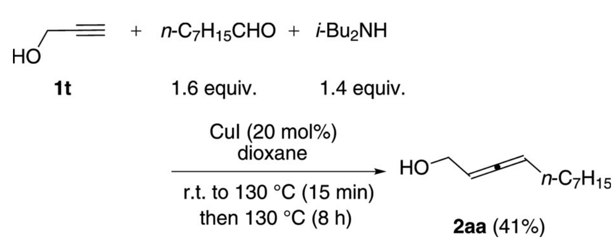
1-Phenylnona-2,3-dien-1-ol (2y): The reaction of CuI (19.4 mg, 0.10 mmol), 1-phenyl-2-propyn-1-ol **1a** (132.1 mg, 1.00 mmol), hexanal (159.7 mg, 1.60 mmol), and di(*i*-butyl)amine (181.2 mg, 1.40 mmol) in 3 mL of dioxane afforded **2y**[11f] as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 10/1), liquid; yield: 119.6 mg (55%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.45–7.21 (m, 5H, ArH), 5.47–5.29 (m, 2H, 2 × C=CH), 5.27–5.15 (m, 1H, OCH), 2.39–2.16 (m, 1H, OH), 2.12–1.94 (m, 2H, CH$_2$), 1.50–1.20 (m, 6H, 3 × CH$_2$), 0.97–0.80 (m, 3H, CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = [202.2, 202.0], [143.2, 143.0], 128.4, [127.6, 127.5], [126.1, 126.0], [96.1, 96.0], [95.3, 95.0], [72.4, 72.1], 31.2, [28.73, 28.68], 28.6, 22.4, 14.0; MS (EI): m/z = 216 (M$^+$, 1.18), 107 (100); IR (neat) ν = 3317, 3063, 3030, 2957, 2871, 1964, 1605, 1493, 1456, 1379, 1326, 1194, 1138, 1107, 1080, 1009 cm^{-1}; HR-MS (EI): m/z = 216.1512, calcd. for $C_{15}H_{20}O$ (M$^+$): 216.1514.



6-Methyl-1-phenylhepta-2,3-dien-1-ol (2z): The reaction of CuI (19.5 mg, 0.10 mmol), 1-phenyl-2-propyn-1-ol **1a** (131.4 mg, 1.00 mmol), 3-methylbutanal (138.2 mg, 1.61 mmol), and di(*i*-butyl)amine (181.6 mg, 1.41 mmol) in 3 mL of dioxane afforded **2y** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 15/1), liquid; yield: 89.7 mg (45%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.43–7.22 (m, 5H, ArH), 5.44–5.26 (m, 2H, 2 × C=CH), 5.26–5.16 (m, 1H, OCH), 2.55–2.11 (bs, 1H, OH), 2.04–1.84 (m, 2H, CH$_2$), 1.80–1.54 (m, 1H, CH in *i*Pr), 1.04–0.80 (m, 6H, 2 × CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = [202.9, 202.7], [143.14, 143.05], 128.3, [127.53, 127.47], [126.1, 125.9], [95.32, 95.27], [93.4, 93.1], [72.4, 72.2], [38.1, 38.0], [28.34, 28.31], 22.14, [22.09, 22.07]; MS (EI): m/z = 202 (M$^+$, 1.70), 107 (100); IR (neat): ν = 3331, 3063, 3030, 2955, 2869, 2840, 1963, 1603, 1493, 1454, 1384, 1367, 1336, 1261, 1193, 1170, 1106, 1080, 1008 cm^{-1}; HR-MS (EI): m/z = 202.1359, calcd. for $C_{14}H_{18}O$ (M$^+$): 202.1358.



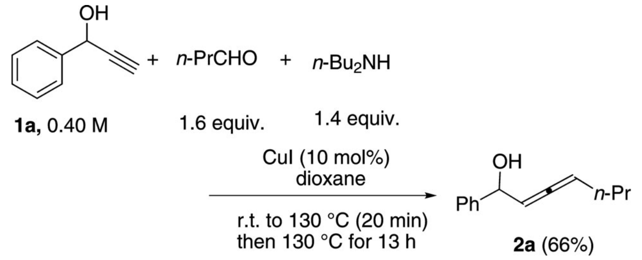
Typical Procedure for the Synthesis of Undeca-2,3-dien-1-ol (2aa)



To an oven-dried reaction tube with a screw cap were added CuI (38.3 mg, 0.20 mmol), prop-2-yn-1-ol **1t** (56.3 mg, 1.00 mmol), octanal (203.7 mg, 1.59 mmol), di(*i*-butyl)amine (179.9 mg, 1.39 mmol), and 3 mL of dioxane under an argon atmosphere. The resulting mixture sealed with the screw cap was then stirred in an oil bath at room temperature and heated to 130 °C gradually (in 15 min). When the reaction was complete after being stirred at 130 °C for 8 h as monitored by TLC upon cooling (during the reaction, prop-2-yn-1-ol was consumed quickly and the corresponding propargylic amine was produced, which was then transformed to the allene product at a relatively slow rate), the reaction mixture was cooled to room temperature and then filtered. Evaporation and column chromatography on silica gel afforded allene **2aa**[8k] as a liquid (eluent: petroleum ether/ethyl acetate = 20/1, then 10/1); yield: 70 mg (41%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.35–5.18 (m, 2H, 2 × C=CH), 4.08 (dd, J = 5.4, 3.0 Hz, 2H, OCH$_2$), 2.06–1.92 (m, 3H, OH and CH$_2$), 1.50–1.10 (m, 10H, 5 × CH$_2$), 0.92–0.79 (m, 3H, CH$_3$); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ = 203.0, 93.7, 91.6, 60.7, 31.8, 29.1, 29.04, 28.97, 28.6, 22.6, 14.0; MS (EI): m/z = 135 (M$^+$−H$_2$O−CH$_3$, 0.72), 121 (M$^+$−H$_2$O−C$_2$H$_5$, 3.24), 55 (100); IR (neat): ν = 3313, 2956, 2925, 2855, 1964, 1463, 1378, 1212, 1136, 1012 cm^{-1}; HR-MS (EI): m/z = 168.1515, calcd. for $C_{11}H_{20}O$ (M$^+$): 168.1514.

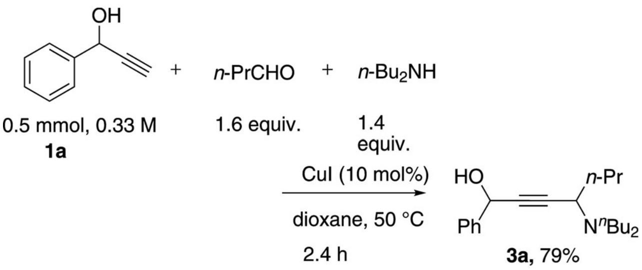
1 g-Scale Reaction

To an oven-dried reaction tube with a screw cap were added CuI (152.2 mg, 0.80 mmol), 1-phenyl-2-propyn-1-ol **1a**



(1.0547 g, 7.99 mmmol), 20 mL of dioxane, *n*-butanal (1.13 mL, $d=0.817\,\mathrm{g\,mL^{-1}}$, 923.2 mg, 116.0 mg, 12.8 mmol), and di(*n*-butyl)amine (1.90 mL, $0.762\,\mathrm{g\,mL^{-1}}$, 1.4478 g, 11.2 mmol) under an argon atmosphere. The resulting mixture sealed with the screw cap was then stirred in an oil bath at room temperature and heated to 130 °C gradually (in 20 min). When the reaction was complete after stirring at 130 °C for 13 h as monitored by TLC upon cooling (during the reaction, **1a** was consumed quickly and the corresponding propargylic amine was produced, which was then transformed to the allene product at a relatively slow rate). The reaction mixture was cooled to room temperature and then filtered. Evaporation and column chromatography on silica gel afforded allene **2a**[2] as a liquid (eluent: petroleum ether/DCM/ethyl acetate = 60/20/1); yield: 0.9854 g (66%).

Synthesis of 4-(*N*,*N*-Dibutylamino)-1-phenylhept-2-yn-1-ol (3a)



To an oven-dried reaction tube with a screw cap were added CuI (9.8 mg, 0.051 mmol), 1-phenyl-2-propyn-1-ol **1a** (65.8 mg, 0.50 mmol), 1.50 mL of dioxane, *n*-butanal (58.3 mg, 0.81 mmol), and di(*n*-butyl)amine (89.6 mg, 0.69 mmol) under an argon atmosphere. The resulting mixture was sealed with the screw cap and stirred at 50 °C. When the reaction was complete as monitored by TLC, the reaction mixture was cooled to room temperature. Evaporation and column chromatography on silica gel afforded the **3a** as a pair of diastereoisomers (eluent: petroleum ether/ethyl acetate = 10/1), liquid; yield: 125.0 mg (79%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.62$–7.51 (m, 2H, ArH), 7.43–7.27 (m, 3H, ArH), 5.53–5.45 (bs, 1H, OCH), 3.60–3.45 (m, 1H, NCH), 2.58–2.43 (m, 2H, CH_2), 2.40–2.27 (m, 2H, CH_2), 2.22–2.01 (bs, 1H, OH), 1.68–1.53 (m, 2H, CH_2), 1.53–1.16 (m, 10H, $5\times CH_2$), 1.00–0.80 (m, 9H, $3\times CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta=[141.24, 141.23]$, 128.4, 128.1, 126.6, [86.18, 86.16], 84.0, 64.5, 53.3, 51.3, [36.08, 36.07], 30.6, 20.6, 19.8, 14.0, 13.8; MS (EI): $m/z=315$ (M^+, 0.50), 272 (100); IR (neat): $\nu=3396$, 2957, 2932, 2871, 1493, 1455, 1378, 1306, 1174, 1124, 1076, 1004 cm^{-1}; HR-MS (EI): $m/z=315.2557$, calcd. for $C_{21}H_{33}NO$ (M^+): 315.2562.

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