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FACILE ONE-POT SYNTHESIS OF FUNCTIONALIZED ACETYLENES FROM ARYL AND HETEROARYL ALDEHYDES USING LITHIUM TRIMETHYLSILYLDIAZOMETHANE

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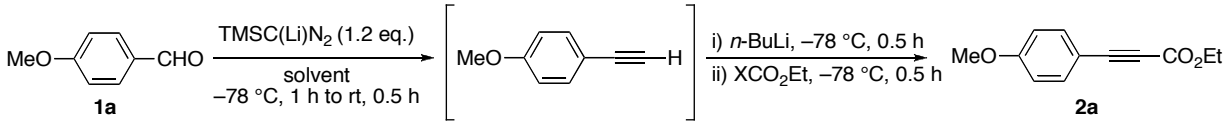
Abstract – The reaction of aryl and heteroaryl aldehydes with lithium trimethylsilyldiazomethane followed by treatment with *n*-BuLi and then electrophiles in one-pot efficiently afforded functionalized acetylenes.

Functionalized acetylenes are well-known to be useful building blocks in organic synthesis.[1] We have already reported that lithium trimethylsilyldiazomethane ($TMSC(Li)N_2$) smoothly reacted with aldehydes to give terminal acetylenes via alkylidene carbene intermediates.[2] We thought that if the resulting terminal acetylenes could be converted to functionalized ones in one-pot, the process would provide a simple and efficient method for the synthesis of functionalized acetylenes from aldehydes. Thus, we investigated a one-pot synthesis of functionalized acetylenes from aryl and heteroaryl aldehydes. In this paper, the results are described.

The reaction conditions were examined using 4-methoxybenzaldehyde **1a** as an aldehyde and ethyl chloroformate ($ClCO_2Et$) or ethyl cyanoformate ($NCCO_2Et$) as an electrophile (Table 1). After the reaction of **1a** with $TMSC(Li)N_2$ in THF,[3] treatment of the reaction mixture with *n*-BuLi (1.2 eq.) at

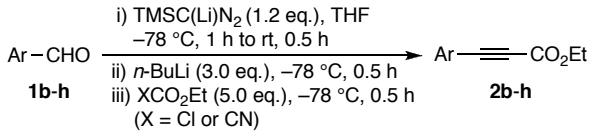
Table 1. Examination of reaction conditions

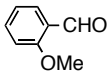
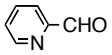
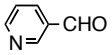
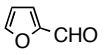
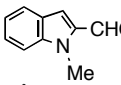
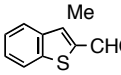


Entry	Solvent	Eq. of *n*-BuLi	XCO_2Et	Yield
1	THF	1.2 eq.	$ClCO_2Et$ (3.0 eq.)	11 %
2	THF	2.0 eq.	$ClCO_2Et$ (4.0 eq.)	32 %
3	THF	3.0 eq.	$ClCO_2Et$ (5.0 eq.)	74 %
4	THF	3.0 eq.	$NCCO_2Et$ (5.0 eq.)	79 %
5	Et_2O	3.0 eq.	$ClCO_2Et$ (3.0 eq.)	13 %

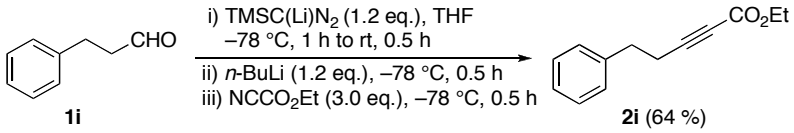
This paper is dedicated to Professor Dr. Ekkehard Winterfeldt on the occasion of his 75th birthday.

Table 2. Synthesis of ethyl aryl- and heteroarylpropiolates



Entry	Substrate	Yield
1[a]	(**1b**)	69 % (**2b**)
2[b]	 (**1c**)	72 % (**2c**)
3[b]	 (**1d**)	44 % (**2d**)
4[a]	 (**1e**)	52 % (**2e**)
5[b]	 (**1f**)	55 % (**2f**)
6[b]	 (**1g**)	71 % (**2g**)
7[a]	 (**1h**)	60 % (**2h**)

a, $NCCO_2Et$ was used as an electrophile. b, $ClCO_2Et$ was used as an electrophile.



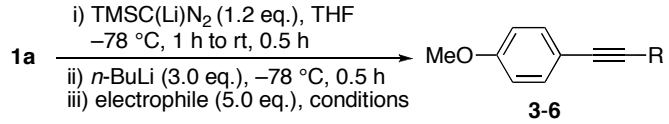
(**Eq. 1**)

–78 °C followed by with $ClCO_2Et$ (3.0 eq.) in one-pot afforded the desired arylpropiolate **2a**, but the yield was very low (entry 1). However, an increase in the amount of *n*-BuLi and $ClCO_2Et$ significantly improved the yield and the use of *n*-BuLi (3.0 eq.) and $ClCO_2Et$ (5.0 eq.) gave the best result affording **2a** (74 % yield) (entries 2 and 3). $NCCO_2Et$, in place of $ClCO_2Et$, could also be efficiently used (79 % yield) (entry 4). Et_2O as a solvent was found to be less effective in this reaction (entry 5).

Under the optimized reaction conditions as shown in entries 3 and 4 of Table 1, the one-pot synthesis of aryl- and heteroarylpropiolates was examined and the results were summarized in Table 2. Other aryl aldehdyes **1b** and **1c** afforded the desired arylpropiolates **2b** and **2c** in 69 % and 72 % yield, respectively (entries 1 and 2). Various heteroaryl aldehydes such as pyridyl, furyl, indolyl and benzo[*b*]thienyl ones **1d**-**h** also successfully underwent this one-pot reaction and the corresponding heteroarylpropiolates **2d**-**h** were obtained in good to moderate yields (entries 3–7). In addition, this reaction is applicable to aliphatic aldehydes. For instance, 3-phenylpropanal **1i** smoothly gave ethyl 5-phenylpent-2-ynoate **2i** in 64 % yield (Eq. 1).

Finally, the one-pot synthesis of functionalized acetylenes using other electrophiles was examined and the results were summarized in Table 3. By using *N*-methoxy-*N*-methylbenzamide, a Weinreb amide, the keto acetylene **3** was obtained in 73 % yield (entry 1). Aldehydes, like benzaldehyde and *n*-hexanal, also

Table 3. Synthesis of other functionalized acetylenes



Entry	Electrophile	Conditions	R	Yield
1	PhCON(Me)OMe	rt, 1 h	COPh	73 % (**3**)
2	PhCHO	–78 °C, 0.5 h	CH(OH)Ph	80 % (**4**)
3	$Me(CH_2)_4CHO$	–78 °C, 1 h	$CH(OH)C_5H_{11}$	59 % (**5**)
4	MeI	0 °C, 2 h	Me	75 % (**6**)

underwent the reaction to afford the corresponding hydroxy acetylenes **4** and **5** though the yield of **5** was somewhat low. The low yield of **5** might be considered to be due to the partial abstraction of the α-hydrogen of *n*-hexanal by the remaining acetylide. Furthermore, alkylation with iodomethane smoothly proceeded to give **6** in good yield (entry 4).

In conclusion, the present method using $TMSC(Li)N_2$ makes possible the easy conversion of aryl and heteroaryl aldehydes to functionalized acetylenes in a one-pot procedure and will provide an added flexibility in the synthesis of functionalized acetylenes.

EXPERIMENTAL

All melting points were measured on a Yanagimoto micro melting points apparatus and are uncorrected. IR spectra were recorded on a SHIMADZU FTIR-8400S spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-EX-270 spectrometer (^1H, 270 MHz; ^{13}C, 67.8 MHz). Mass spectra were recorded on a JEOL JMS-SX-102A spectrometer. The distillation was performed using a Kugelrohr distillation apparatus.

General procedure for ethyl aryl- or heteroarylpropiolates. Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of aryl or heteroaryl aldehyde **1** (0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.95 mL, 1.5 mmol) at -78 °C again, the mixture was further stirred at -78 °C for 0.5 h. An electrophile (2.5 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 0.5 h. After being quenched with sat. aqueous NH_4Cl at -78 °C, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-820 MH or BW-200) to give **2**.

Ethyl 3-(4-methoxyphenyl)prop-2-ynoate (2a). Prepared from 4-methoxybenzaldehyde **1a** (68.3 mg,

0.5 mmol) and $NCCO_2Et$. The residue was purified by column chromatography on silica gel (BW-200, 8 g, hexane : EtOAc = 20 : 1) to give **2a** (80.8 mg, 79 %). Light yellow oil, bp 120 °C / 1.5 mmHg (lit.,[4] 140 °C / 5 mmHg). IR (neat): 2204, 1701 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (t, *J* = 7.1 Hz, 3H), 3.83 (s, 3H), 4.29 (q, *J* = 7.1 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 7.54 (d, *J* = 8.9 Hz, 2H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 55.4, 62.0, 80.1, 86.9, 111.3, 114.2, 134.8, 154.2, 161.3. EI-MS *m/z*: 204 (M^+), 132 (bp).

Ethyl 3-(4-methylphenyl)prop-2-ynoate (2b). Prepared from 4-methylbenzaldehyde **1b** (59.3 mg, 0.5 mmol) and $NCCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 60 : 1 to 25 : 1) to give **2b** (64.5 mg, 69 %). Yellow oil, bp 108 °C / 1.0 mmHg (lit.,[4] 120 °C / 2 mmHg). IR (neat): 2208, 1707 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.36 (t, *J* = 7.2 Hz, 3H), 2.38 (s, 3H), 4.29 (q, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 21.7, 61.9, 80.3, 86.5, 116.4, 129.2, 132.8, 141.1, 154.0. EI-MS *m/z*: 188 (M^+), 116 (bp).

Ethyl 3-(2-methoxyphenyl)prop-2-ynoate (2c). Prepared from 2-methoxybenzaldehyde **1c** (65.9 mg, 0.5 mmol) and $ClCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 20 : 1) to give **2c** (70.9 mg, 72 %). Colorless oil, bp 95 °C / 1.2 mmHg. IR (neat): 2212, 1703 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.36 (t, *J* = 7.2 Hz, 3H), 3.90 (s, 3H), 4.30 (q, *J* = 7.2 Hz, 2H), 6.88-6.98 (m, 2H), 7.37-7.45 (m, 1H), 7.52 (dd, *J* = 1.6, 7.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 55.8, 62.0, 83.1, 84.5, 108.7, 110.7, 120.4, 132.2, 134.8, 154.1, 161.3. EI-MS *m/z*: 204 (M^+), 132 (bp). HR-MS calcd for $C_{12}H_{12}O_3$: 204.0787, found: 204.0795.

Ethyl 3-(pyridin-2-yl)prop-2-ynoate (2d). Prepared from pyridine-2-carbaldehyde **1d** (53.7 mg, 0.5 mmol) and $ClCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 8 g, hexane : EtOAc = 10 : 1 to 3 : 1) to give **2d** (38.6 mg, 44 %). Light brown crystals, mp 33-34 °C (hexane) and bp 115 °C / 1 mmHg (lit.,[5] 131 °C / 2.6 mmHg). IR (Nujol): 2216, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (t, *J* = 7.1 Hz, 3H), 4.31 (q, *J* = 7.1 Hz, 2H), 7.36 (ddd *J* = 1.2, 4.8, 7.7 Hz, 1H), 7.59 (td, *J* = 1.2, 7.7 Hz, 1H), 7.73 (dt, *J* = 1.8, 7.7 Hz, 1H), 8.66 (ddd, *J* = 1.2, 1.8, 4.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 62.4, 79.1, 83.7, 124.5, 128.4, 136.2, 140.4, 150.4, 153.3. EI-MS *m/z*: 175 (M^+), 130 (bp).

Ethyl 3-(pyridin-3-yl)prop-2-ynoate (2e). Prepared from pyridine-3-carbaldehyde **1e** (53.8 mg, 0.5 mmol) and $NCCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 10 : 1 to 3 : 1) to give **2e** (46.0 mg, 52 %). Yellow oil, bp 105 °C / 2 mmHg (lit.,[4] 140 °C / 3 mmHg). IR (neat): 2216, 1713 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.37 (t, *J* = 7.2 Hz, 3H), 4.32 (q, *J* = 7.2 Hz, 2H), 7.33 (dd, *J* = 4.9, 7.9 Hz, 1H), 7.88 (td, *J* = 1.7, 7.9 Hz, 1H), 8.66 (dd, *J* = 1.7, 4.9 Hz, 1H), 8.81 (d, *J* = 1.7 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 62.4, 82.3, 83.5, 116.9, 123.1, 139.7, 150.5, 153.2, 153.4. EI-MS *m/z*: 175 (M^+), 130 (bp).

Ethyl 3-(furan-2-yl)prop-2-ynoate (2f). Prepared from furan-2-carbaldehyde **1f** (48.6 mg, 0.5 mmol)

and $ClCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 8 g, hexane : EtOAc = 20 : 1) to give **2f** (45.6 mg, 55 %). Colorless crystals, mp 37-38 °C (hexane) (lit.,[6] 39.5-39.8 °C (hexane)) and bp 55 °C / 1.2 mmHg. IR (Nujol): 2210, 1703 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (t, *J* = 7.1 Hz, 3H), 4.30 (q, *J* = 7.1 Hz, 2H), 6.46 (dd, *J* = 1.7, 3.5 Hz, 1H), 6.93 (dd, *J* = 0.5, 3.5 Hz, 1H), 7.51 (dd, *J* = 0.5, 1.7 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 62.2, 76.4, 85.8, 111.5, 120.9, 134.5, 146.1, 153.5. EI-MS *m/z*: 164 (M^+), 92 (bp).

Ethyl 3-(1-methyl-1*H*-indol-2-yl)prop-2-ynoate (2g). Prepared from 1-methyl-1*H*-indole-2-carbaldehyde **1g** (79.9 mg, 0.5 mmol) and $ClCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 50 : 1) to give **2g** (80.6 mg, 71 %). Colorless crystals, mp 76 ºC (hexane). IR (Nujol): 2203, 2190, 1698 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38 (t, *J* = 7.1 Hz, 3H), 3.86 (s, 3H), 4.33 (q, *J* = 7.1 Hz, 2H), 7.05 (s, 1H), 7.11-7.18 (m, 1H), 7.28-7.38 (m, 2H), 7.62 (d, *J* = 8.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 31.0, 62.2, 78.7, 87.4, 109.7, 112.4, 118.3, 120.6, 121.7, 124.7, 126.6, 138.0, 153.8. EI-MS *m/z*: 227 (M^+), 155 (bp). HR-MS calcd for $C_{14}H_{13}O_2N$: 227.0946, found: 227.0943.

Ethyl 3-(benzo[*b*]thiophen-2-yl)prop-2-ynoate (2h). Prepared from benzo[*b*]thiophen-2-carbaldehyde **1h** (80.7 mg, 0.5 mmol) and $NCCO_2Et$. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 100 : 1) to give **2h** (68.2 mg, 60 %). Yellow solid, mp 48-49 °C. IR (Nujol): 2210, 1694 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38 (t, *J* = 7.1 Hz, 3H), 4.33 (q, *J* = 7.1 Hz, 2H), 7.36-7.49 (m, 2H), 7.73 (s, 1H), 7.77-7.84 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 62.3, 79.9, 85.7, 119.2, 122.1, 124.5, 125.0, 126.7, 133.5, 138.3, 141.3, 153.6. EI-MS *m/z*: 230 (M^+), 158 (bp). HR-MS calcd for $C_{13}H_{10}O_2S$: 230.0402, found: 230.0401.

Ethyl 5-phenylpent-2-ynoate (2i). Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of 3-phenylpropanal **1i** (68.3 mg, 0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) at -78 °C again, the mixture was further stirred at -78 °C for 0.5 h. $NCCO_2Et$ (0.15 mL, 1.5 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 0.5 h. After being quenched with sat. aqueous NH_4Cl at -78 °C, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-820 MH, 10 g, hexane : EtOAc = 100 : 1 to 20 : 1) to give **2i** (65.4 mg, 64 %). Colorless oil, bp 60 °C / 0.4 mmHg. IR (neat): 2235, 1711 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (t, *J* = 7.1 Hz, 3H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 7.16-7.34 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 20.9, 33.9, 61.8, 73.7, 88.2, 126.5, 128.2, 128.4, 139.5, 153.5. MS *m/z*: 202 (M^+), 91(bp). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.06; H, 7.23.

3-(4-Methoxyphenyl)-1-phenylprop-2-yn-1-one (3). Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of **1a** (68.4 mg, 0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.95 mL, 1.5 mmol) at -78 °C again, the mixture was further stirred at -78 °C for 0.5 h. *N*-Methoxy-*N*-methylbeznamide (0.38 mL, 2.5 mmol) was added dropwise at -78 °C and the mixture was stirred at rt for 1 h. After being quenched with sat. aqueous NH_4Cl at rt, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-200, 13 g, hexane : ethyl acetate = 30 : 1) to give **3** (86.3 mg, 73 %). Colorless crystals, mp 81-82 °C (hexane-EtOAc) (lit.,[7] 81 °C). IR (Nujol): 2188, 1626 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.86 (s, 3H), 6.94 (d, *J* = 8.7 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 2H), 8.21 (d, *J* = 7.2 Hz, 2H). ^{13}C-NMR ($CDCl_3$) δ: 55.5, 86.8, 94.3, 111.8, 114.3, 128.4, 129.4, 133.8, 135.0, 136.9, 161.5, 177.9. EI-MS *m/z*: 236 (M^+, bp).

3-(4-Methoxyphenyl)-1-phenylprop-2-yn-1-ol (4). Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of **1a** (68.4 mg, 0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.95 mL, 1.5 mmol) at -78 °C again, the mixture was further stirred at -78 °C for 0.5 h. Benzaldehyde (255 μL, 2.5 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 0.5 h. After being quenched with sat. aqueous NH_4Cl at -78 °C, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-200, 15 g, hexane : EtOAc = 20 : 1 to 5 : 1) to give **4** (96.1 mg, 80 %). Yellow oil, bp 140 °C / 2 mmHg. IR (neat): 3404, 2226 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.23 (d, *J* = 5.9 Hz, 1H → disappeared with D_2O), 3.81 (s, 3H), 5.68 (d, *J* = 5.9 Hz, 1H → s, 1H with D_2O), 6.84 (d, *J* = 8.9 Hz, 2H), 7.33-7.44 (m, 5H), 7.59-7.65 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ: 55.3, 65.2, 86.6, 87.3, 113.8, 114.3, 126.6, 128.3, 128.5, 133.1, 140.7, 159.6. EI-MS *m/z*: 238 (M^+, bp). HR-MS calcd for $C_{16}H_{14}O_2$: 238.0994, found: 238.0990.

3-(4-Methoxyphenyl)-oct-2-yn-3-ol (5). Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of **1a** (69.2 mg, 0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.95 mL, 1.5 mmol) at -78 °C again, the

mixture was further stirred at -78 °C for 0.5 h. *n*-Hexanal (0.3 mL, 2.5 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h. After being quenched with sat. aqueous NH_4Cl at -78 °C, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-200, 10 g, hexane : EtOAc = 30 : 1 to 10 : 1) to give **5** (69.1 mg, 59 %). Yellow oil, bp 110 °C / 2.5 mmHg. IR (neat): 3354, 2227 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (t, *J* = 6.8 Hz, 3H), 1.30-1.40 (m, 4H), 1.45-1.58 (m, 2H), 1.72-1.93 (m, 3H → m, 2H with D_2O), 3.81 (s, 3H), 4.58 (t, *J* = 6.6 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 7.36 (d, *J* = 8.7 Hz, 2H). ^{13}C-NMR ($CDCl_3$) δ: 14.1, 22.7, 25.0, 31.6, 38.0, 55.3, 63.1, 84.7, 88.8, 113.8, 114.6, 133.0, 159.4. EI-MS *m/z*: 232 (M^+), 161 (bp). HR-MS calcd for $C_{15}H_{20}O_2$: 232.1463, found: 232.1463.

1-Methoxy-4-(prop-1-ynyl)benzene (6). Under an argon atmosphere, *n*-BuLi (1.58 M in hexane, 0.38 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.6 M in hexane, 0.38 mL, 0.6 mmol) in THF (4.0 mL) at -78 °C and the mixture was stirred at -78 °C for 0.5 h. A solution of **1a** (67.7 mg, 0.5 mmol) in THF (1.0 mL) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h, then at rt for 0.5 h. After addition of *n*-BuLi (1.58 M in hexane, 0.95 mL, 1.5 mmol) at -78 °C again, the mixture was further stirred at -78 °C for 0.5 h. Iodomethane (0.16 mL, 2.5 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h. After being quenched with sat. aqueous NH_4Cl at -78 °C, the mixture was extracted with EtOAc (3 times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (BW-200, 10 g, hexane : EtOAc = 30 : 1) to give **6** (56.0, mg, 75 %). Colorless oil, bp 75 °C / 1.2 mmHg (lit.,[8] 115-117 °C / 9 mmHg). IR (neat): 2042 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.03 (s, 3H), 3.79 (s, 3H), 6.81 (d, *J* = 8.9 Hz, 2H), 7.32 (d, *J* = 8.9 Hz, 2H). ^{13}C-NMR ($CDCl_3$) δ: 4.4, 55.3, 79.4, 84.1, 113.7, 116.0, 132.7, 158.8. EI-MS *m/z*: 146 (M^+, bp).

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