Experimental Data

Methyl 1,6-heptadiyne-4-carboxylate (1a):

The synthesis of 1a followed a literature reported method.1 4 (4.70 g, 22.6 mmol) and LiCl (2.95 g, 69.7 mmol) were dissolved a mixture of DMSO (40 mL) and water (1 mL). The reaction was refluxed for 1 h and subsequently cooled to room temperature. The mixture distributed between CHCl₃ and water and the aqueous layer was extracted repeatedly with CHCl₃. The combined organic phases were washed with brine, dried over MgSO₄, filtered through silica gel and concentrate to provide a crude product, which was purified by flash chromatography column using 20% ethyl acetate in hexane, to give 1a¹ (3.0 g, 90%) as pale yellow oil.

Ethyl 1,6-heptadiyne-4-carboxylate (1b):

A solution of 1d (0.70 g, 5 mmol) in EtOH (50 mL) was treated with H₂SO₄ (0.5 mL) and heated to reflux overnight. The solvent was carefully evaporated and the residue treated with aqueous NaHCO₃. The product was isolated by triple-extractions with CH₂Cl₂, dried over MgSO₄ and concentrated to give 1b² (0.75 g, 88 %). ¹H NMR (CDCl₃) δ= 4.20 (q, 2H, Et-CH₂), 2.76 (mc, CH), 2.66-2.61 (m, 4 H, CH₂), 2.02 (t, 2 H, C≡CH), 1.28 (t, 3 H, Et-CH₃).

tert.-Butyl 1,6-Heptadiyne-4-carboxylate (1c):

A solution of S1g (1.0 g, 6.5 mmol) and NEt$_3$ (1.0 g, 9.8 mmol) in CH$_2$Cl$_2$ (25 mL) was treated with tBuOH (0.70 g, 9.7 mmol). The reaction was left for 2 h at rt before it was washed with water. The organic phase was dried over MgSO$_4$ and the product purified by chromatography using 10% EtOAc in hexane, to give 1c (0.5 g, 40%) as yellow oil. $^1$H NMR (CDCl$_3$) $\delta$ = 2.79 (mc, CH), 2.66 (dd~mc, 4 H, CH$_2$), 2.15 (s, 9 H, CH$_3$), 2.05 (t~bs, 2 H, C≡CH). $^{13}$C NMR (CDCl$_3$) $\delta$ = 171.6, 80.7, 70.6, 70.3, 43.7, 28.0, 19.9.

1,6-Heptadiyne-4-carboxylic acid (1d):

Methyl ester 1a (3.0 g, 20 mmol) was dissolved in aqueous ethanol (24 mL, 75% v/v), before treatment with NaOH (2.4 g, 60 mmol), and the mixture was refluxed for 9 h. After removal of the solvent remaining starting material was extracted with CH$_2$Cl$_2$. The remaining material was acidified with diluted HCl and extracted with CH$_2$Cl$_2$. The organic phase was washed with brine, dried over MgSO$_4$ and concentrated. After chromatographic purification using hexane and ethyl acetate (4:1) the product crystallized upon evaporation of the solvent to give 1d$^3$ (1.7 g, 60%). $^1$H NMR (CDCl$_3$) $\delta$ = 10.29 (bs, OH), 2.83 (mc, CH), 2.68 (mc, 4 H, CH$_2$), 2.05 (t, 2 H, C≡CH). $^{13}$C NMR (CDCl$_3$) $\delta$ = 178.5, 80.2, 70.8, 42.9, 19.6.

Synthesis of 2-(2-propynyl)-4-pentynonitrile (1e):

Methyl cyanoacetate (4.0 g, 40 mmol) was added dropwise to a stirred suspension of KOtBu (7.6 g, 68 mmol) in THF (400 mL). After 10 min propargyl bromide (6.0 mL, 80 % in toluene, 54 mmol) was added dropwise. The reaction was left for 1 h and subsequently cooled to rt before a second batch of KOtBu (7.6 g, 68 mmol) followed by propargyl bromide (6.0 mL, 80 % in toluene,

---

54 mmol) was added. After stirring for several h the solvent was evaporated and the residue taken up in water and extracted 3 times with ether. The combined organic phase was washed with brine and dried over MgSO₄. Evaporation of the solvent furnished a black oil, which subjected to treatment with LiCl (3.0 g, 70 mmol) in refluxing DMSO (50 mL) containing water (1 mL) for 1 h. After cooling to rt the reaction mixture was pored into water and extracted repeatedly with CHCl₃. The combined organic phases was washed with brine and dried over MgSO₄. Chromatography with hexane and ethyl acetate (9:1) provided le (3.5 g, 74 %) as pale yellow liquid. $^1$H NMR (CDCl₃) $\delta$= 2.94 (mc, CH), 2.64 (dd~bd, 4 H, CH₂), 2.19 (t~bs, 2 H, C≡CH). $^{13}$C NMR (CDCl₃) $\delta$= 119.5, 78.2, 72.5, 30.3, 21.1.

1,6-Heptadiyne-4-carboxylic acid morpholide (1f):

Crude acid chloride S1f (0.60 g, 3.9 mmol) was dissolved in CH₂Cl₂ (50 mL) and treated with morpholine (0.40 g, 4.7 mmol) and triethylamine (5.4 ml, 39 mmol). The reaction was stirred overnight and then washed with aqueous NaHCO₃. The organic solution was dried over MgSO₄ and concentrated. The crude product was purified by chromatography using hexane and ethyl acetate (6:1) to give lc as a white solid (0.47 g, 60 %). $^1$H NMR (CDCl₃) $\delta$= 3.71-3.65 (m, 6 H), 3.63-3.59 (m, 2 H), 3.10 (mc, CH), 2.49 (dd, 4 H, CH₂), 2.01 (t, 2 H, C≡CH) H. $^{13}$C NMR (CDCl₃) $\delta$= 171.3, 81.2, 70.3, 67.0, 66.9, 46.5, 42.5, 39.3, 21.6.

3-(2-Propynyl)-hex-5-yn-2-one (3):

Crude S2 (4.3 g, 18 mmol) was treated with camphorsulfonic acid (250 mg) and the mixture was heated to 100 °C for 1 h, when the initial gas evolution had ceased. The cooled reaction mixture was taken up in CH₂Cl₂ and washed with NaHCO₃. After drying over MgSO₄ the solvent was carefully evaporated and the product was finally distilled in vacuum (~ 10 mbar, 80 °C) to leave 3 (680 mg, 27 %) as slightly yellow liquid. (Note: Insufficient cooling efficiency during distillation led to substantial loss of compounds inside the vacuum pump.) $^1$H NMR (CDCl₃) $\delta$= 2.81 (mc, CH), 2.52 (mc, 2 H, CH₂), 2.24 (s, 3 H, CH₃), 2.01 (t, 2 H, C≡CH). $^{13}$C NMR (CDCl₃) $\delta$= 207.7, 80.6, 70.7, 67.0, 49.7, 19.4.
Dimethyl 2,2-bis(2-propynyl)-malonate (4):
A procedure similar to a literature reported process\(^1\) was employed: Dimethyl malonate (6.0 ml, 52 mmol) was added dropwise to a stirred suspension of NaH (60% wt in mineral oil, 4.22 g, 106 mmol) in dry THF (100 mL) at 10°C. After 10 min propargyl bromide (80% w/w in toluene, 12.0 mL, 108 mmol) was added dropwise. The reaction was allowed to warm to room temperature and stirred overnight. The reaction mixture was distributed between water and ether, and the aqueous phase was extracted twice with ether. The combine organic phases were washed with brine, dried over MgSO\(_4\), filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 1A\(^{3,4}\) (9.44 g, 84%) as crystalline white solid.

2-(2-Propynyl)-pent-4-yn-1-ol (5):
LiAlH\(_4\) (0.27 g, 7.5 mmol) was added to stirred solution of 1d (1.1 g, 7.2 mmol) in anhydrous THF at 10 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Water (1.2 mL) was added carefully to destroy excess reagent, followed by 10% NaOH aq (1.2 mL) and more water (3.6 mL). Precipitating aluminates were filtered off and rinsed with CH\(_2\)Cl\(_2\). The aqueous phase was extracted with CH\(_2\)Cl\(_2\) and the combined organic phases were dried over MgSO\(_4\) and concentrate to leave 5\(^5\) (0.8 g, 91 %) as colorless oil.

\(\text{N} \text{C}_{12}\text{H}_{25}\)

\(\text{N},\text{N}-\text{Dipropargyl-dodecylamine} (6)\)
Dodecyl amine (2.0 g, 11 mmol) and K\(_2\)CO\(_3\) (3.1g, 23 mmol, 2.1eq.) were suspended in acetonitrile and propargyl bromide (2.5 ml, 23 mmol) was added drop-wise to the mixture. The reaction was stirred at room temperature for 24h, then filtered and the resulting solution was concentrated on a

rotary evaporator yielding a yellow oil. The crude oil was purified by flash chromatography on a silica gel using chloroform as eluent, providing 6 as clear oil (2.0 g, 71%). $^1$H NMR (CDCl$_3$) δ= 3.43 (t, 4 H), 2.51 (t, 2 H), 2.20 (q, 2 H), 1.46 (m, 2 H), 1.34-1.19 (m, 18 H), 0.88 (t, 3 H). $^{13}$C NMR (CDCl$_3$) δ= 78.9, 72.7, 53.1, 42.1, 31.9, 29.62, 29.59, 29.54, 29.47, 29.3, 27.4, 27.3, 22.6, 14.0.

1,6-Heptadiyne-4-carboxylic acid chloride (S1g):
A solution of 1d (2.0 g, 15 mmol) and (COCl)$_2$ (3.8 g, 30 mmol) in CHCl$_3$ (100 mL) was heated to reflux overnight. Excess reagent and solvent were evaporated and the remaining acid chloride S1g$^6$ (2.2 g, 98 %).

[Chemical structure of 1,6-Heptadiyne-4-carboxylic acid chloride]

tert.-Butyl 2,2-bis-(2-propynyl)-acetoacetate (S2):
A solution of tert.-butyl acetoacetate (3.0 g, 18 mmol) in dioxane (50 mL) was treated with KOtBu (2.0 g, 18 mmol) followed by propargyl bromide (2.5 mL, 80 % in toluene, 23 mmol). After 4 h stirring at rt the treatment with KOtBu (2.0 g, 18 mmol) and propargyl bromide (2.5 mL, 80 % in toluene, 23 mmol) was repeated and the reaction was stirred at rt overnight. Precipitated solid was removed by filtration and the solution was concentrated to be distributed between water and CH$_2$Cl$_2$. The organic layer was dried over MgSO$_4$ and concentrated to leave S2 (4.4 g, 78 %) as yellow liquid (contained ~ 0.7 eq. remaining dioxane, yield (%) is corrected based on $^1$H NMR integration). IR [KBr] 3291 (s, C≡CH), 2981 (s, CH), 2140 (w, C≡C), 1719 (s, C=O). $^1$H NMR (CDCl$_3$) δ= 2.87 & 2.80 (2 dd, 2 × 2 H, CH$_2$), 1.96 (t, 2 H, CH), 1.49 (s, 3 H, CH$_3$), 1.40 (s, 9 H, Bu-CH$_3$). $^{13}$C NMR (CDCl$_3$) δ= 201.1, 168.1, 78.8, 71.8, 70.1, 59.3, 28.0, 27.8, 21.7.

Selected Spectra

1c

![NMR Spectrum of 1c]

1e

![NMR Spectrum of 1e]

1f

![NMR Spectrum of 1f]
Base-induced cyclization of bispropargylated acetates – Supplementary Material

Tammar Hussein Ali, Thorsten Heidelberg and Rusnah Syahila Duali Hussen