S-Farnesyl-Thiopropionic Acd (FTPA) Triazoles as Potent Inhibitors of Isoprenylcysteine Carboxyl Methyltransferase

Supporting Information

Experimental Details

General: ^{1}H and ^{13}C spectra were obtained on a Bruker ARX-300 or DRX-500 MHz spectrometer (at 300/75 MHz or 500/125 MHz, respectively) with $CDCl_3$ or MeOD. Electrospray (ESI) mass spectra obtained on a FinniganMAT LCQ system and electron impact (EI) studies were carried out using a Hewlett-Packard Engine. Thin-layer chromatography was run on Baker-flex UV silica gel TLC plates and visualized with iodine or vanillin stains. Column chromatography stationary phase was Sorbent Technologies (65 – 200 mesh) silica gel. IR spectra obtained on a Perkin-Elmer SpectrumOne FT-IR instrument and reported as inverse centimeters (cm^{-1}). HPLC (A:Water w/ 0.05% TFA; B: MeOH; 60-100% B) determined purity for all final compounds to be greater than 95%.

Synthetic procedures

Typical procedure for the synthesis of azido-esters **3a-d**

The corresponding bromo ester (5 mmol,1 equiv) in DMF (5 mL) was added NaN_3 (5 equiv) and stirred at 80 °C for 15h. The reaction was quenched with 10% NH_4OH and extracted with ethyl acetate (3x 5 mL). The combined organic extracts with washed with brine (10 mL) and dried over Na_2SO_4 and concentrated in vacuo affording the product in 75-90% yield. The product was used without further purification.

Ethyl 2-azidoacetate (**3a**)
IR cm^{-1}: 2109, 1747
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 (q, J = 6.9 Hz, 2H), 3.86 (s, 2H), 1.30 (t, J = 6.9 Hz, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 168.26, 61.84, 50.31, 14.09
HRMS *m/z* (EI) $C_4H_7N_3O_2$ calcd. 129.0538 : found 129.0540

Ethyl 3-azidopropanoate (**3b**)
IR cm^{-1}: 2103, 1732
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.18 (q, J = 7.2 Hz, 2H), 3.56 (t, J = 6 Hz, 2H), 2.56 (t, J = 9, 2H), 1.29 (t, J = 6 Hz, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 170.82, 60.94, 46.76, 33.97, 14.10
HRMS *m/z* (EI) $C_5H_9N_3O_2$ calcd. (M+H) 144.0773 ; found (M+H) 144.0774

Ethyl 4-azidobutanoate (**3c**)
IR cm^{-1}: 2100, 1736
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (q, J = 7.2 Hz, 2 H), 3.35 (t, J = 6.9 Hz, 2 H), 2.40 (t, J = 6.3 Hz, 2 H), 1.91 (m, 2 H), 1.26 (t, J = 7.2 Hz, 3 H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.67, 60.54, 50.91, 31.13, 24.20, 14.16
HRMS *m/z* (EI) $C_6H_{11}N_3O_2$ calcd. (M+H) 158.0930 ; found (M+H) 158.0929

Ethyl 5-azidopentanoate (**3d**)
IR cm^{-1}: 2098, 1736
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (q, J = 7.2 Hz, 2 H), 3.29, (t, J = 6.6 Hz, 2 H), 2.33 (t, J = 7.2 Hz, 2H), 1.74-1.25 (m, 4 H), 1.25 (t, J = 6.3 Hz, 3 H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 173.16, 60.39, 51.03, 33.67, 28.25, 22.09, 14.21
HRMS *m/z* (EI) $C_7H_{13}N_3O_2$ calcd. (M+H) 172.1086 ; found (M+H) 172.1085

(4*E*,8*E*)-5,9,13-trimethyltetradeca-4,8,12-trien-1-yne (**4a**)

Synthesized according to the procedure of Chen and co-workers and matches previously reported spectra.[1]

(*E*)-6,10-dimethylundeca-5,9-dien-1-yne (**4b**)
A round bottom flask charged with TMS-propyne (0.896 mL, 6.0 mmol) in THF (10 mL) was cooled to -78°C whereby a solution of nBuLi (2.88 mL, 7.2 mmol) was added dropwise and the resulting reaction mixture was allowed to stir for 2 h at this temperature. Geranyl bromide (0.952 mL, 5.0 mmol) was then added neat and the solution was allowed to warm to room temperature slowly over 30 min. The reaction was quenched with 10% NH_4Cl and extracted with ether (3x 5 mL). The combined organic extract was washed with brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was taken up in THF (5 mL) and added a solution of TBAF (7.5 mL, 7.5 mmol) and allowed to stir for 30 min at room temperature. The reaction was again quenched and worked up in an identical manner as described above and the resulting oil was subject to silica gel chromatography (100% hexanes) affording a colorless oil (0.644 g, 73% over two steps).
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.23 - 5.14 (m, 1H), 5.09 (ddd, J = 6.9, 4.1, 1.3 Hz, 1H), 2.22 (dd, J = 9.7, 5.1 Hz, 4H), 2.14 - 2.03 (m, 2H), 2.03 - 1.96 (m, 2H), 1.94 (t, J = 2.4 Hz, 1H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H) Spectra data matches the published data in the literature.[2]

(5*E*,9*E*)-6,10,14-trimethylpentadeca-5,9,13-trien-1-yne (**4c**)
Synthesized in an analogous manner to that of (**4b**) affording a colorless oil (0.539 g, 85% over two steps). Spectral data matches the published data in the literature.[2]

2-(4-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1*H*-1,2,3-triazol-1-yl)acetic acid (**5a**)
A round bottom flask charged with **3a** (65 mg, 0.5 mmol) and **4a** (138 mg, 0.6 mmol) and taken up in a solution of tBuOH and water (4:1 4 mL). Sodium ascorbate (99 mg, 0.5 mmol) and cupric sulfate pentahydrate (62 mg, 0.5 mmol) were then added sequentially and the resulting reaction mixture was allowed to stir for 15 h at room temperature. The reaction was quenched by the addition of saturated aq NH_4Cl and was extracted with ethyl acetate (3x 5 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude triazole ester was then taken up in MeOH (2 mL) and added LiOH (41 mg, 1 mmol) and allowed to stir 12 h at room temperature. The solvent was removed in vacuo and 10% $NaHCO_3$ (2 mL) was added and was extracted with ethyl acetate (2x 2 mL). Careful titration of 10% HCl until pH 2 was followed by ethyl acetate extraction (3x 3 mL) and was followed by a brine wash (10 mL), drying over Na_2SO_4 and concentration in vacuo provided **7a** as a colorless oil (127 mg, 77% over two steps).
^{1}H NMR (300 MHz, MeOD) δ 7.69 (s, 1H), 5.38 (t, J = 7.2 Hz, 1H), 5.21 (s, 2H), 5.16 - 5.02 (m, 2H), 3.44 (d, J = 7.2 Hz, 2H), 2.07 (ddd, J = 21.2, 10.8, 4.5 Hz, 6H), 2.00 - 1.89 (m, 3H), 1.72 (s, 3H), 1.66 (s, 3H), 1.59 (s, 3H), 1.59 (s, 3H)
^{13}C NMR (75 MHz, MeOD) δ 169.89, 148.75, 138.57, 136.13, 132.09, 125.42, 125.27, 124.60, 121.64, 51.59, 40.84, 40.68, 27.77, 27.46, 25.91, 25.17, 17.76, 16.25, 16.10
HRMS *m/z* (ESI) $C_{19}H_{29}N_3O_2$ calcd. (M+H) 332.2338 ; found (M+H) 332.2340

3-(4-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1*H*-1,2,3-triazol-1-yl)propanoic acid (**5b**)
Light yellow oil, 49% yield over two steps
^{1}H NMR (300 MHz, MeOD) δ 7.72 (s, 1H), 5.16 (t, J = 7.1 Hz, 1H), 5.12 - 5.04 (m, 2H), 4.61 (t, J = 6.6 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H), 2.70 (t, J = 7.5 Hz, 2H), 2.34 (q, J = 7.3 Hz, 2H), 2.12 - 1.87 (m, 9H), 1.66 (s, 3H), 1.59 (s, 6H), 1.56 (s, 3H)
^{13}C NMR (75 MHz, MeOD) δ 173.75, 148.78, 137.25, 135.95, 132.05, 125.42, 125.33, 123.98, 123.73, 46.94, 43.88, 40.86, 40.75, 35.18, 28.84, 27.79, 27.57, 26.54, 25.94, 17.80, 16.14
HRMS *m/z* (ESI) $C_{20}H_{31}N_3O_2$ calcd. (M+H): 346.2494; found (M+H): 346.2495

4-(4-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1*H*-1,2,3-triazol-1-yl)butanoic acid (**5c**)

Light yellow oil, 37% yield over two steps
^{1}H NMR (300 MHz, MeOD) δ 7.67 (s, 1H), 5.36 (td, J = 7.1, 1.0 Hz, 1H), 5.18 - 5.01 (m, 2H), 4.96 (s, 1H), 4.41 (t, J = 7.0 Hz, 2H), 3.41 (d, J = 7.2 Hz, 2H), 2.32 (dd, J = 11.0, 3.9 Hz, 2H), 2.20 - 2.08 (m, 4H), 2.08 - 2.02 (m, 4H), 1.99 - 1.88 (m, 2H), 1.71 (s, 3H), 1.65 (s, 3H), 1.58 (s, 6H)
^{13}C NMR (75 MHz, MeOD) δ 175.94, 148.72, 138.40, 136.09, 132.08, 125.40, 125.24, 123.10, 121.77, 50.37, 40.85, 40.65, 31.37, 27.76, 27.42, 26.66, 25.93, 25.20, 17.79, 16.26, 16.13
HRMS *m/z* (ESI) $C_{21}H_{33}N_3O_2$ calcd. (M+H) 360.2651; found (M+H) 360.2654

5-(4-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1*H*-1,2,3-triazol-1-yl)pentanoic acid (**5d**)
Light yellow oil, 27% yield over two steps
^{1}H NMR (300 MHz, MeOD) δ 7.67 (s, 1H), 5.44 - 5.30 (m, 1H), 5.21 - 5.04 (m, 2H), 4.37 (t, J = 7.0 Hz, 2H), 3.41 (d, J = 7.1 Hz, 2H), 2.33 (t, J = 7.3 Hz, 2H), 2.19 - 1.85 (m, 12H), 1.71 (s, 3H), 1.65 (s, 3H), 1.59 (s, 6H)
^{13}C NMR (75 MHz, MeOD) δ 176.96, 148.63, 138.36, 136.08, 132.08, 125.40, 125.24, 123.00, 121.80, 50.91, 40.86, 40.65, 34.16, 30.69, 27.76, 27.41, 25.94, 25.21, 22.93, 17.81, 16.27, 16.15
HRMS *m/z* (ESI) $C_{22}H_{35}N_3O_2$ calcd. (M+H) 374.2808; found (M+H) 374.2806

3-(4-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trien-1-yl)-1*H*-1,2,3-triazol-1-yl)propanoic acid (**5e**)
Light yellow oil, 48% yield over two steps
^{1}H NMR (300 MHz, MeOD) δ 7.72 (s, 1H), 5.16 (t, J = 7.1 Hz, 1H), 5.12 - 5.03 (m, 2H), 4.61 (t, J = 6.6 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H), 2.70 (t, J = 7.5 Hz, 2H), 2.34 (q, J = 7.3 Hz, 2H), 2.14 - 1.88 (m, 8H), 1.66 (s, 3H), 1.59 (s, 6H), 1.56 (s, 3H)
^{13}C NMR (75 MHz, MeOD) δ 173.75, 148.78, 137.25, 135.95, 132.05, 125.42, 125.33, 123.98, 123.73, 46.94, 43.88, 40.86, 40.75, 35.18, 28.84, 27.79, 27.57, 26.54, 25.94, 17.80, 16.14
HRMS *m/z* (ESI) $C_{21}H_{33}N_3O_2$ calcd. (M+H): 360.2651; found (M+H): 360.2646

(*E*)-3-(4-(4,8-dimethylnona-3,7-dien-1-yl)-1*H*-1,2,3-triazol-1-yl)propanoic acid (**5f**)
Light yellow oil, 20% yield over two steps
^{1}H NMR (500 MHz, MeOD) δ 7.74 (s, 1H), 5.16 (t, J = 6.7 Hz, 1H), 5.11 - 5.02 (m, 1H), 4.60 (t, J = 6.1 Hz, 2H), 2.82 (s, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.33 (dd, J = 14.5, 7.2 Hz, 2H), 2.06 (dd, J = 14.5, 7.1 Hz, 2H), 2.02 - 1.91 (m, 2H), 1.66 (s, 3H), 1.59 (s, 3H), 1.56 (s, 3H)
^{13}C NMR (125 MHz, MeOD) δ176.75, 148.76, 137.41, 132.16, 125.33, 124.25, 123.59, 49.85, 47.89, 40.78, 28.90, 27.71, 26.59, 25.89, 17.76, 16.11
HRMS *m/z* (ESI) $C_{16}H_{25}N_3O_2$ calcd. (M+H) 292.2025 ; found (M+H) 292.2022

(*E*)-4-(4-(4,8-dimethylnona-3,7-dien-1-yl)-1*H*-1,2,3-triazol-1-yl)butanoic acid (**5g**)
Light yellow oil, 82% yield over two steps
^{1}H NMR (300 MHz, MeOD) δ 7.73 (s, 1H), 5.17 (dd, J = 7.1, 6.2 Hz, 1H), 5.11 - 5.01 (m, 1H), 4.40 (t, J = 6.7 Hz, 2H), 2.70 (t, J = 7.6 Hz, 2H), 2.35 (q, J = 7.3 Hz, 2H), 2.25 - 2.10 (m, 2H), 2.09 - 1.90 (m, 4H), 1.66 (s, 3H), 1.59 (s, 3H), 1.56 (s, 3H)
^{13}C NMR (75 MHz, MeOD) δ 174.84, 148.83, 137.39, 132.16, 125.32, 124.26, 123.32, 50.89, 40.79, 28.91, 28.01, 27.71, 26.58, 25.91, 17.77, 16.12

Experimental details for synthesis of FTP-triazole compounds

(*E*)-5-iodo-3-methylpent-2-en-1-ol (**7**)
A flame-dried round bottom flask charged with Cp_2ZrCl_2 (406 mg, 1.39 mmol) in DCM (10 mL) was cooled to 0°C where by a 2.0 M solution of Me_3Al in hexanes (5.55 mL, 11.1 mmol) was added under an atmosphere of argon and was allowed to stir 30 min at this temperature. A solution of 4-iodo-1-butyne (**6**) (1 g, 5.55 mmol) in DCM (3 mL) was then added dropwise over 5 min. The resulting solution was allowed to stir 12 h while slowly warming to room temperature. The reaction was quenched by slowly

pouring (caution exothermic!) into an ice cooled 10% HCl solution (20 mL). The aqueous layer was extracted with DCM (2x 10 mL), washed with brine (15 mL), dried over Na_2SO_4 and concentrated in vacuo and was subject to silica gel chromatography with 40% ethyl acetate in hexanes as eluent affording a colorless oil (0.753 g, 60%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.56 - 5.37 (m, 1H), 4.16 (d, J = 5.7 Hz, 2H), 3.24 (t, J = 7.5 Hz, 2H), 2.57 (t, J = 7.4 Hz, 2H), 1.68 (s, 3H), 1.30 (s, 1H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 136.76, 126.20, 58.78, 43.30, 15.66, 4.28

(*E*)-methyl 3-((5-iodo-3-methylpent-2-en-1-yl)thio)propanoate (**8**)
A round bottom flask charged with NCS (1.18 g, 8.82 mmol) in DCM (15 mL) was cooled to -40°C whereby dimethyl sulfide was added dropwise. The solution was placed in a 0°C bath and stirred for 5 min followed by cooling again to -40 °C whereby a solution of **7** (950 mg, 4.2 mmol) in DCM (2 mL) was added and allowed to stir for 15 min at 0 °C before warming to room temperature. TLC indicated complete chlorination after 3-4 h. The reaction was concentrated in vacuo and taken up in brine (10 mL) and extracted with ether (3x 5 mL). The combined organic extracts were dried over Na_2SO_4, concentrated in vacuo and used without further purification. In a second round bottom flask methyl mercaptopropionate (0.419 mL, 3.78 mmol) in DCM (5 mL) was added DIEA (1.32 mL, 7.56 mmol) while stirring at 0 °C. A solution of the above chloride in DCM (2 mL) was added and the reaction was allowed to stir for 15 min at this temperature before allowing to stir for 16 h at room temperature. The reaction was quenched with 10% citric acid (10 mL) and extracted with DCM (3x 5 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo and subject to purification with silica gel chromatography with 5-10% ethyl acetate in hexanes affording a colorless oil (682 mg, 55%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30 (td, J = 7.7, 1.2 Hz, 1H), 3.69 (s, 3H), 3.23 (t, J = 7.4 Hz, 2H), 3.17 (d, J = 7.7 Hz, 2H), 2.76 (dd, J = 11.3, 4.2 Hz, 2H), 2.58 (dd, J = 13.0, 7.0 Hz, 4H), 1.66 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.35, 137.08, 123.24, 51.78, 43.32, 34.58, 29.16, 26.03, 15.32, 4.12

(*E*)-methyl 3-((5-azido-3-methylpent-2-en-1-yl)thio)propanoate (**9**)

A round bottom flask charged with **8** (682 mg, 2.08 mmol) in DMF (5 mL) was added NaN_3 (540 mg, 8.32 mmol) and allowed to stir at 80 °C for 20 h. The reaction was cooled to room temperature and added 10% NH_4OH (5 mL), and extracted with ether (5x 5 mL). The combined organic extracts were washed with 10% NH_4OH (10 mL), brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was subject to silica gel chromatography with 10-15% ethyl acetate in hexanes as eluent affording a light yellow oil (395 mg, 78%).
IR (KBr disc, cm^{-1}): 2099, 1739
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (td, J = 7.7, 1.1 Hz, 1H), 3.68 (s, 3H), 3.34 (t, J = 7.0 Hz, 2H), 3.17 (d, J = 7.7 Hz, 2H), 2.74 (dd, J = 10.9, 4.1 Hz, 2H), 2.58 (dd, J = 11.3, 4.1 Hz, 2H), 2.31 (t, J = 7.0 Hz, 2H), 1.69 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.32, 134.93, 123.26, 51.74, 49.40, 38.50, 34.59, 29.23, 26.02, 15.89

General procedure for the synthesis of second generation FTP-triazoles (**10**)

A round bottom flask was added azido-ester (1 equiv) and alkyne (1.2 equiv) and taken up in a solution of tBuOH and water (4:1, 2 mL). Sodium ascorbate (0.5 equiv) and cupric sulfate pentahydrate (0.25 equiv) were added sequentially. The resulting solution was allowed to stir overnight at room temperature. The reaction was quenched by the addition of an aqueous 10% NH_4OH solution (2 mL) and was extracted with ethyl acetate (3x 5 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4, and concentrated in vacuo. Silica gel column chromatography (50 -80% ethyl acetate in hexanes) afforded the purified esters in 35-97% yield.

(*E*)-methyl 3-((3-methyl-5-(4-pentyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio) propanoate (**10a**)
Colorless oil, 77% yield
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (s, 1H), 5.19 (t, *J* = 7.7 Hz, 1H), 4.38 (t, *J* = 7.2 Hz, 2H), 3.66 (s, 3H), 3.09 (d, *J* = 7.7 Hz, 2H), 2.79 - 2.49 (m, 8H), 1.77 - 1.54 (m, 5H), 1.40 - 1.21 (m, 4H), 0.86 (t, *J* = 5.8 Hz, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.41, 148.45, 134.30, 123.92, 120.57, 51.87, 48.52, 40.21, 34.59, 31.47, 29.22, 26.14, 25.68, 22.47, 15.93, 14.08

(*E*)-methyl 3-((5-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio) propanoate (**10b**)
Colorless oil, 78% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (s, 1H), 5.21 (t, *J* = 7.8 Hz, 1H), 4.39 (t, *J* = 7.2 Hz, 2H), 3.68 (s, 3H), 3.10 (d, *J* = 7.8 Hz, 2H), 2.78 - 2.47 (m, 8H), 1.69 (s, 2H), 1.64 - 1.45 (m, 4H), 0.92 (s, 3H), 0.90 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.27, 148.47, 134.17, 123.79, 120.34, 51.75, 48.40, 40.11, 38.46, 34.48, 29.10, 27.57, 26.04, 23.53, 22.34, 15.82

(*E*)-methyl 3-((5-(4-decyl-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio) propanoate (**10c**)
White waxy-solid, 62% yield
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (s, 1H), 5.25 - 5.16 (m, 1H), 4.42 - 4.35 (m, 2H), 3.67 (d, *J* = 2.3 Hz, 3H), 3.10 (d, *J* = 7.8 Hz, 2H), 2.70 - 2.61 (m, 4H), 2.56 (ddd, *J* = 8.5, 7.9, 4.4 Hz, 4H), 1.69 (s, 3H), 1.66 - 1.57 (m, 2H), 1.35 - 1.16 (m, 14H), 0.85 (td, *J* = 6.8, 1.9 Hz, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.25, 148.33, 134.16, 123.78, 120.40, 51.72, 48.39, 40.08, 34.46, 31.81, 29.52, 29.49, 29.42, 29.31, 29.24, 29.18, 29.08, 26.01, 25.60, 22.59, 15.80, 14.04

Methyl 3-(((*E*)-5-(4-((*E*)-4,8-dimethylnona-3,7-dien-1-yl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio) propanoate (**10d**)
Light yellow oil, 73% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (s, 1H), 5.21 (t, *J* = 7.8 Hz, 1H), 5.14 (t, *J* = 7.0 Hz, 1H), 5.06 (t, *J* = 6.0 Hz, 1H), 4.39 (t, *J* = 7.2 Hz, 2H), 3.67 (d, *J* = 1.3 Hz, 3H), 3.10 (d, *J* = 7.7 Hz, 2H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.65 (dd, *J* = 11.7, 4.4 Hz, 2H), 2.57 (t, *J* = 6.3 Hz, 2H), 2.32 (q, *J* = 7.4 Hz, 4H), 2.09 - 1.86 (m, 4H), 1.69 (s, 3H), 1.65 (s, 3H), 1.57 (s, 3H), 1.55 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.28, 147.90, 136.13, 134.15, 131.33, 124.15, 123.77, 123.15, 120.54, 51.73, 48.42, 40.09, 39.59, 34.46, 29.08, 27.75, 26.59, 26.02, 25.83, 25.63, 17.62, 16.00, 15.81

(*E*)-methyl 3-((3-methyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio) propanoate (**10e**)
Colorless oil, 90% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.3, 3.2 Hz, 2H), 7.74 (s, 1H), 7.47 - 7.36 (m, 2H), 7.32 (dd, *J* = 6.8, 1.6 Hz, 1H), 5.25 (t, *J* = 7.7 Hz, 1H), 4.49 (t, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.69 - 2.56 (m, 4H), 2.54 - 2.45 (m, 2H), 1.73 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.24, 147.56, 133.92, 130.57, 128.72, 127.99, 125.58, 124.15, 119.57, 51.71, 48.57, 40.01, 34.38, 29.07, 25.99, 15.79
ESI MS *m/z* (M+H) 346

(*E*)-methyl 3-((3-methyl-5-(4-(thiophen-3-yl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio) propanoate (**10f**)
Off-white waxy-solid, 76% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 - 7.62 (m, 1H), 7.52 - 7.32 (m, 3H), 5.24 (t, *J* = 7.7 Hz, 1H), 4.48 (t, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.74 - 2.48 (m, 6H), 1.73 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.28, 143.77, 133.93, 131.83, 126.20, 125.75, 124.17, 120.89, 119.42, 51.74, 48.53, 40.02, 34.39, 29.08, 26.01, 15.80
ESI MS *m/z* (M+H) 352

(*E*)-methyl 3-((3-methyl-5-(4-(naphthalen-1-yl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl) thio)propanoate (**10g**)
Light beige oil, 75% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 - 8.31 (m, 1H), 7.96 - 7.84 (m, 2H), 7.79 (s, 1H), 7.71 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.58 - 7.47 (m, 3H), 5.31 (dd, *J* = 8.3, 7.2 Hz, 1H), 4.59 (t, *J* = 7.1 Hz, 2H), 3.65 (s, 3H), 3.14 (d, *J* = 7.7 Hz, 2H), 2.73 (t, *J* = 7.1 Hz, 2H), 2.65 (dd, *J* = 10.9, 3.9 Hz, 2H), 2.51 (dd, *J* = 11.2, 4.1 Hz, 2H), 1.78 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.27, 146.76, 134.01, 133.83, 131.10, 128.81, 128.40, 128.09, 127.18, 126.58, 125.94, 125.40, 125.31, 124.25, 122.48, 51.75, 48.68, 40.15, 34.43, 29.16, 26.08, 15.90
ESI MS *m/z* (M+H) 396

(*E*)-methyl 3-((5-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10h**)
Off-white waxy-solid, 97% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.7 Hz, 2H), 7.64 (s, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 5.23 (t, *J* = 7.7 Hz, 1H), 4.45 (t, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 3.65 (s, 3H), 3.09 (d, *J* = 7.7 Hz, 2H), 2.60 (dd, *J* = 13.2, 6.4 Hz, 4H), 2.50 (t, *J* = 4.5 Hz, 2H), 1.71 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.21, 159.39, 147.37, 133.94, 126.83, 124.02, 123.27, 118.76, 114.07, 77.42, 77.00, 76.58, 55.19, 51.66, 48.48, 39.97, 34.34, 29.01, 25.92, 15.7
ESI MS *m/z* (M+H) 376

(*E*)-methyl 3-((5-(4-(4-(tert-butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10i**)
Colorless oil, 88% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.71 (s, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 5.25 (t, *J* = 7.7 Hz, 1H), 4.49 (t, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.63 (dd, *J* = 14.6, 6.6 Hz, 4H), 2.50 (dd, *J* = 11.3, 4.3 Hz, 2H), 1.73 (s, 3H), 1.38 - 1.19 (m, 9H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.28, 151.09, 147.59, 133.99, 127.78, 125.65, 125.34, 124.14, 119.26, 51.72, 48.58, 40.05, 34.59, 34.38, 31.23, 29.10, 26.01, 15.82
ESI MS *m/z* (M+H) 402

(*E*)-methyl 3-((5-(4-benzyl-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10j**)
Colorless oil, 77% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.71 (s, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 5.25 (t, *J* = 7.7 Hz, 1H), 4.49 (t, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.63 (dd, *J* = 14.6, 6.6 Hz, 4H), 2.50 (dd, *J* = 11.3, 4.3 Hz, 2H), 1.73 (s, 3H), 1.38 - 1.19 (m, 9H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.28, 151.09, 147.59, 133.99, 127.78, 125.65, 125.34, 124.14, 119.26, 51.72, 48.58, 40.05, 34.59, 34.38, 31.23, 29.10, 26.01, 15.82
ESI MS *m/z* (M+H) 360

(*E*)-methyl 3-((3-methyl-5-(4-phenethyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio) propanoate (**10k**)
Off-white waxy-solid, 82% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 - 7.24 (m, 3H), 7.20 (dd, *J* = 9.2, 4.3 Hz, 2H), 7.09 (s, 1H), 5.19 (dd, *J* = 8.3, 7.2 Hz, 1H), 4.38 (t, *J* = 7.2 Hz, 2H), 3.68 (s, 3H), 3.11 (t, *J* = 7.5 Hz, 2H), 3.07 - 2.92 (m, 4H), 2.75 - 2.61 (m, 2H), 2.60 - 2.43 (m, 4H), 1.68 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.30, 147.16, 141.18, 134.13, 128.43, 128.33, 126.03, 123.82, 120.79, 51.78, 48.43, 40.10, 35.50, 34.51, 29.14, 27.42, 26.09, 15.83
ESI MS *m/z* (M+H) 374

(*E*)-methyl 3-((3-methyl-5-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoate (**10l**)

Light yellow oil, 80% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.27 (dd, *J* = 12.1, 3.9 Hz, 2H), 6.97 (d, *J* = 7.9 Hz, 3H), 5.19 (s, 3H), 4.44 (t, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.07 (d, *J* = 7.7 Hz, 2H), 2.69 - 2.47 (m, 6H), 1.69 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.25, 158.09, 144.09, 133.78, 129.43, 124.10, 122.54, 121.10, 114.65, 61.86, 51.72, 48.58, 39.96, 34.44, 29.02, 26.01, 15.75
ESI MS *m/z* (M+H) 376

(*E*)-methyl 3-((3-methyl-5-(4-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoate (**10m**)
Light yellow oil, 67% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, *J* = 4.4 Hz, 1H), 5.22 (t, *J* = 7.7 Hz, 1H), 4.60 (t, *J* = 3.4 Hz, 1H), 4.47 - 4.36 (m, 2H), 3.99 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.81 (ddd, *J* = 10.8, 7.3, 3.5 Hz, 1H), 3.71 - 3.68 (m, 3H), 3.49 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.11 (d, *J* = 7.7 Hz, 2H), 3.01 (t, *J* = 6.7 Hz, 2H), 2.70 - 2.51 (m, 6H), 1.78 - 1.64 (m, 5H), 1.55 (dd, *J* = 12.3, 4.1 Hz, 5H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 174.88, 145.23, 134.16, 123.84, 121.53, 99.02, 66.42, 62.53, 51.79, 48.51, 40.12, 34.51, 30.68, 29.13, 26.54, 26.07, 25.37, 19.72, 15.87

(*E*)-methyl 3-((5-(4-(2-([1,1'-biphenyl]-4-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10n**)
White waxy-solid (36 mg, 55%)
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.55 - 7.49 (m, 2H), 7.43 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.31 - 7.23 (m, 2H), 7.15 (s, 1H), 5.21 (dd, *J* = 8.3, 7.2 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 3.68 (d, *J* = 3.1 Hz, 2H), 3.19 - 2.99 (m, 4H), 2.65 (dd, *J* = 7.6, 2.0 Hz, 2H), 2.60 - 2.51 (m, 4H), 1.69 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.29, 147.21, 140.85, 140.24, 138.94, 134.08, 128.87, 128.70, 127.04, 126.90, 123.86, 120.97, 51.77, 48.53, 40.05, 35.09, 34.50, 29.14, 27.31, 26.11, 15.83
ESI MS *m/z* (M+H) 450

(*E*)-methyl 3-((5-(4-(2-([1,1'-biphenyl]-3-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10o**)
Colorless oil (44 mg, 68%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 - 7.55 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 4H), 7.38 - 7.31 (m, 2H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 5.18 (t, *J* = 7.7 Hz, 1H), 4.38 (t, *J* = 7.2 Hz, 2H), 3.68 (d, *J* = 0.5 Hz, 3H), 3.16 - 3.01 (m, 6H), 2.65 (t, *J* = 7.2 Hz, 2H), 2.60 - 2.50 (m, 4H), 1.67 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.31, 147.11, 141.69, 141.23, 134.14, 128.79, 128.71, 127.38, 127.23, 127.08, 124.92, 123.81, 120.86, 51.77, 48.45, 40.08, 35.62, 34.50, 29.12, 27.49, 26.08, 15.82
ESI MS *m/z* (M+H) 450

(*E*)-methyl 3-((5-(4-(2-([1,1'-biphenyl]-2-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10p**)
Colorless oil (20 mg, 36%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 11.1, 3.9 Hz, 2H), 7.37 - 7.32 (m, 2H), 7.32 - 7.27 (m, 3H), 7.22 (d, *J* = 7.4 Hz, 2H), 6.92 (s, 1H), 5.18 (t, *J* = 7.5 Hz, 1H), 4.42 - 4.24 (m, 2H), 3.69 (dt, *J* = 8.8, 4.0 Hz, 6H), 3.08 (d, *J* = 7.7 Hz, 2H), 2.96 (dd, *J* = 9.5, 6.4 Hz, 2H), 2.84 (dd, *J* = 9.4, 6.5 Hz, 2H), 2.73 - 2.61 (m, 2H), 2.61 - 2.47 (m, 2H), 1.68 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.31, 141.92, 141.63, 138.51, 134.11, 130.13, 129.28, 129.11, 128.14, 127.44, 126.88, 126.08, 123.80, 120.60, 51.79, 48.41, 40.07, 34.52, 32.81, 29.10, 26.94, 26.05, 15.85
ESI MS *m/z* (M+H) 450

(*E*)-methyl 3-((5-(4-(([1,1'-biphenyl]-4-yloxy)methyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10q**)

Colorless oil (47 mg, 75%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.57 - 7.49 (m, 4H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.34 - 7.24 (m, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 5.24 (s, 2H), 5.19 (dd, *J* = 7.7, 1.1 Hz, 1H), 4.45 (t, *J* = 7.1 Hz, 2H), 3.67 (d, *J* = 2.7 Hz, 3H), 3.08 (d, *J* = 7.7 Hz, 2H), 2.70 - 2.60 (m, 4H), 2.56 (dt, *J* = 6.9, 4.1 Hz, 2H), 1.70 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.24, 157.67, 143.98, 140.51, 134.14, 133.79, 128.64, 128.08, 126.62, 124.09, 122.60, 114.97, 62.02, 51.71, 48.60, 39.95, 34.43, 29.04, 26.02, 15.76
ESI MS *m/z* (M+H) 452

(*E*)-methyl 3-((5-(4-(2-([1,1':4',1''-terphenyl]-4-yl)ethyl)-1H-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10r**)
White solid (43 mg, 62%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 4H), 7.64 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.39 - 7.33 (m, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.15 (s, 1H), 5.21 (td, *J* = 7.7, 1.2 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 3.69 (s, 3H), 3.11 (d, *J* = 7.8 Hz, 2H), 3.07 (dd, *J* = 6.8, 4.0 Hz, 4H), 2.70 - 2.63 (m, 2H), 2.57 (dd, *J* = 11.0, 3.8 Hz, 4H), 1.70 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.28, 147.11, 140.62, 140.42, 139.88, 139.75, 138.38, 134.14, 128.93, 128.76, 127.43, 127.23, 126.95, 126.92, 123.82, 120.85, 51.76, 48.44, 40.09, 35.14, 34.49, 29.14, 27.37, 26.09, 15.83
ESI MS *m/z* (M+H) 526

(*E*)-methyl 3-((5-(4-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)ethyl)-1H-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10s**)
Light yellow oil (41 mg, 66%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (ddd, *J* = 8.6, 5.3, 2.0 Hz, 2H), 7.45 (dd, *J* = 8.2, 1.8 Hz, 2H), 7.26 - 7.22 (m, 2H), 7.15 (s, 1H), 7.10 (td, *J* = 8.7, 2.4 Hz, 2H), 5.19 (t, *J* = 7.7 Hz, 1H), 4.39 (td, *J* = 7.3, 1.8 Hz, 2H), 3.68 (s, 3H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.07 - 2.97 (m, 4H), 2.68 - 2.61 (m, 2H), 2.56 (dd, *J* = 11.0, 3.9 Hz, 4H), 1.68 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.25, 163.22, 161.26, 147.03, 140.29, 137.91, 136.93, 134.10, 128.87, 128.41, 128.35, 126.85, 123.78, 120.81, 115.58, 115.41, 51.72, 48.40, 40.05, 35.05, 34.45, 29.09, 27.31, 26.05, 15.78
ESI MS *m/z* (M+H) 468

(*E*)-methyl 3-((5-(4-(2-(3'-cyano-[1,1'-biphenyl]-4-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoate (**10t**)
Off-white waxy-solid (45 mg, 78%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 1.3 Hz, 1H), 7.81 - 7.77 (m, 1H), 7.60 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.52 (td, *J* = 7.8, 1.6 Hz, 1H), 7.48 (dd, *J* = 8.1, 1.8 Hz, 2H), 7.32 - 7.27 (m, 2H), 7.17 (s, 1H), 5.19 (t, *J* = 7.7 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 3.68 (d, *J* = 2.1 Hz, 3H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.05 (s, 4H), 2.65 (dd, *J* = 11.4, 4.2 Hz, 2H), 2.56 (dd, *J* = 10.9, 3.8 Hz, 4H), 1.69 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.27, 146.91, 142.09, 141.64, 136.56, 134.10, 131.23, 130.43, 129.54, 129.20, 126.97, 123.83, 120.81, 118.83, 112.83, 51.76, 48.44, 40.09, 35.10, 34.48, 29.13, 27.27, 26.08, 15.82
ESI MS *m/z* (M+H) 475

(*E*)-methyl 3-((3-methyl-5-(4-(4-(thiophen-2-yl)phenethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoate (**10u**)
White waxy-solid (49 mg, 74%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 3.6 Hz, 1H), 7.25 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.10 (s, 1H), 7.06 (ddd, *J* = 5.0, 3.6, 0.6 Hz, 1H), 5.20 (t, *J* = 7.7 Hz, 1H),

4.38 (t, *J* = 7.2 Hz, 2H), 3.69 (s, 3H), 3.10 (d, *J* = 7.8 Hz, 2H), 3.02 (dd, *J* = 12.6, 6.3 Hz, 4H), 2.65 (t, *J* = 7.1 Hz, 2H), 2.56 (dd, *J* = 13.2, 6.7 Hz, 4H), 1.68 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.32, 146.99, 144.28, 140.58, 134.16, 132.26, 128.98, 127.95, 125.89, 124.44, 123.82, 122.70, 120.88, 51.78, 48.45, 40.08, 35.13, 34.50, 29.14, 27.29, 26.10, 15.83
ESI MS *m/z* (M+H) 456

General procedure for the hydrolysis of FTP-triazoles (**11**)

A round bottom flask charged with FTP-triazole ester (1 equiv) in MeOH (2 mL) was added NaOH (2 equiv) and allowed to stir at room temperate overnight. The reaction solution was concentrated in vacuo and the crude product was taken up in a 2 N NaOH solution (2 mL).
This was carefully acidified to a pH of 2 with 10% HCl and extracted with chloroform (3x 5 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. Purification with silica gel (5-10% methanol in DCM) afforded the purified acids in 40-95% yield.

(*E*)-3-((3-methyl-5-(4-pentyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11a**)
Colorless oil, 64% yield
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (s, 1H), 5.19 (t, *J* = 7.6 Hz, 1H), 4.42 (t, *J* = 7.0 Hz, 2H), 3.10 (d, *J* = 7.7 Hz, 2H), 2.76 - 2.49 (m, 8H), 1.70 (s, 3H), 1.68 - 1.49 (m, 2H), 1.47 - 1.18 (m, 4H), 0.88 (q, *J* = 6.6 Hz, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 176.23, 148.31, 133.73, 124.41, 120.67, 48.46, 40.14, 35.16, 31.33, 29.17, 29.02, 26.07, 25.38, 22.36, 15.72, 13.98

(E)-3-((5-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11b**)
Colorless oil, 99% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (s, 1H), 5.19 (t, *J* = 7.7 Hz, 1H), 4.42 (t, *J* = 7.0 Hz, 2H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.81 - 2.47 (m, 10H), 1.70 - 1.66 (m, 2H), 1.63 - 1.41 (m, 4H), 0.92 (s, 3H), 0.90 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 175.86, 148.36, 133.75, 124.35, 120.67, 48.52, 40.11, 38.34, 34.92, 29.20, 27.55, 26.01, 23.29, 22.34, 15.74, 0.98

(*E*)-3-((3-methyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11e**)
Colorless oil, 56% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.2 Hz, 2H), 7.74 (s, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 7.0 Hz, 1H), 5.24 (t, *J* = 7.7 Hz, 1H), 4.51 (t, *J* = 7.0 Hz, 2H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.74 - 2.50 (m, 6H), 1.74 (s, 3H)
ESI MS *m/z* (M+H) 332

(*E*)-3-((3-methyl-5-(4-(thiophen-3-yl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11f**)
Off-white waxy-solid, 79% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.69 - 7.60 (m, 1H), 7.41 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.32 (dd, *J* = 5.0, 3.0 Hz, 1H), 5.11 (t, *J* = 6.9 Hz, 1H), 4.38 (t, *J* = 6.7 Hz, 2H), 2.96 (d, *J* = 7.0 Hz, 2H), 2.45 (m, 6H), 1.59 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 143.76, 133.54, 131.67, 126.43, 125.86, 124.19, 121.16, 119.88, 48.59, 39.91, 36.75, 28.92, 26.82, 15.78
ESI MS *m/z* (M+H) 338

(*E*)-3-((3-methyl-5-(4-(naphthalen-1-yl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11g**)
Light beige oil, 90% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 - 8.25 (m, 1H), 7.88 (dd, *J* = 8.9, 3.8 Hz, 2H), 7.78 (s, 1H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.56 - 7.45 (m, 3H), 5.28 (t, *J* = 7.6 Hz, 1H), 4.57 (t, *J* = 7.0 Hz, 2H), 3.13 (d, *J* = 7.7 Hz, 2H), 2.70 (t, *J* = 7.0 Hz, 2H), 2.66 - 2.57 (m, 2H), 2.52 (t, *J* = 6.8 Hz, 2H), 1.75 (s, 3H)

ESI MS *m/z* (M+H) 382

(*E*)-3-((5-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11h**)
Off-white waxy-solid, 90% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.8 Hz, 2H), 7.66 (s, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.23 (t, *J* = 7.7 Hz, 1H), 4.49 (t, *J* = 7.0 Hz, 2H), 3.83 (s, 3H), 3.11 (d, *J* = 7.7 Hz, 2H), 2.63 (dd, *J* = 10.9, 6.6 Hz, 4H), 2.57 - 2.50 (m, 2H), 1.73 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 176.33, 159.63, 147.50, 133.74, 127.22, 126.83, 122.92, 119.15, 118.70, 114.43, 114.09, 55.44, 48.57, 40.09, 39.91, 34.76, 29.21, 25.89
ESI MS *m/z* (M+H) 362

(*E*)-3-((5-(4-(4-(tert-butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio) propanoic acid (**11i**)
Colorless oil, 90% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 - 7.67 (m, 3H), 7.43 (d, *J* = 8.2 Hz, 2H), 5.22 (t, *J* = 7.0 Hz, 1H), 4.48 (t, *J* = 6.9 Hz, 2H), 3.09 (d, *J* = 7.6 Hz, 2H), 2.69 - 2.46 (m, 6H), 1.71 (s, 3H), 1.33 (s, 9H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 176.69, 151.32, 147.59, 133.72, 127.39, 125.92, 125.60, 125.25, 119.66, 48.65, 40.05, 34.99, 34.63, 31.48, 30.98, 29.10, 25.94
ESI MS *m/z* (M+H) 388

(*E*)-3-((5-(4-benzyl-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11j**)
Colorless oil, 53% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 - 7.67 (m, 3H), 7.43 (d, *J* = 8.2 Hz, 2H), 5.22 (t, *J* = 7.0 Hz, 1H), 4.48 (t, *J* = 6.9 Hz, 2H), 3.09 (d, *J* = 7.6 Hz, 2H), 2.69 - 2.46 (m, 6H), 1.71 (s, 3H), 1.33 (s, 9H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 176.69, 151.32, 147.59, 133.72, 127.39, 125.92, 125.60, 125.25, 119.66, 48.65, 40.05, 34.99, 34.63, 31.48, 30.98, 29.10, 25.94
ESI MS *m/z* (M+H) 346

(*E*)-3-((3-methyl-5-(4-phenethyl-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio) propanoic acid (**11k**)
Off-white waxy-solid, 95% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 - 7.23 (m, 3H), 7.19 (dd, *J* = 10.6, 4.7 Hz, 2H), 7.09 (s, 1H), 5.17 (t, *J* = 7.7 Hz, 1H), 4.38 (t, *J* = 7.0 Hz, 2H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.00 (dd, *J* = 11.6, 5.7 Hz, 4H), 2.59 (tdd, *J* = 17.4, 11.8, 5.4 Hz, 6H), 1.68 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 175.96, 147.02, 140.95, 133.78, 128.43, 128.34, 126.07, 124.22, 121.05, 48.48, 40.04, 35.35, 34.84, 29.15, 27.13, 25.96, 15.73
ESI MS *m/z* (M+H) 360

(*E*)-3-((3-methyl-5-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11l**)
Light yellow oil, 46% yield
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.28 (dd, *J* = 11.3, 4.5 Hz, 2H), 6.97 (d, *J* = 7.0 Hz, 3H), 5.21 (s, 3H), 4.46 (t, *J* = 7.0 Hz, 2H), 3.08 (d, *J* = 7.7 Hz, 2H), 2.61 (dd, *J* = 10.3, 5.1 Hz, 6H), 1.70 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 176.53, 158.08, 144.16, 133.69, 129.65, 129.39, 124.72, 124.02, 122.88, 121.39, 121.06, 114.55, 61.78, 48.66, 47.31, 39.97, 34.65, 29.09, 25.85

(*E*)-3-((3-methyl-5-(4-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11m**)
Light yellow oil, 76% yield
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 1H), 5.18 (t, *J* = 7.3 Hz, 1H), 4.62 (d, *J* = 4.6 Hz, 1H), 4.43 (t, *J* = 6.9 Hz, 2H), 3.97 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.89 - 3.79 (m, 1H), 3.67 (dt, *J* = 9.7, 6.8 Hz, 1H), 3.56 - 3.45 (m, 1H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.02 (t, *J* = 6.7 Hz, 2H), 2.69 - 2.50 (m, 6H), 1.80 (dd, *J* = 8.5, 3.4 Hz, 1H), 1.76 - 1.64 (m, 4H), 1.63 - 1.45 (m, 4H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.85, 145.17, 133.79, 124.44, 121.85, 99.08, 66.39, 62.60, 48.53, 40.07, 35.08, 30.64, 29.10, 26.34, 26.10, 25.30, 19.66, 15.73

(*E*)-3-((5-(4-(2-([1,1'-biphenyl]-4-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11n**)
White waxy-solid (19 mg, 90%)
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.29 - 7.20 (m, 2H), 7.13 (s, 1H), 5.17 (t, *J* = 7.3 Hz, 1H), 4.39 (t, *J* = 7.0 Hz, 2H), 3.15 - 2.94 (m, 6H), 2.69 - 2.40 (m, 6H), 1.68 (s, 3H)
^{13}C NMR (75 MHz, $CDCl_3$) δ 175.89, 142.65, 140.09, 138.97, 134.91, 133.74, 128.89, 128.73, 127.06, 126.91, 124.35, 121.37, 121.09, 48.48, 40.10, 34.89, 29.22, 27.13, 26.02, 15.73
ESI MS *m/z* (M+H) 436

(*E*)-3-((5-(4-(2-([1,1'-biphenyl]-3-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11o**)
Colorless oil (16 mg, 80%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 - 7.54 (m, 2H), 7.48 - 7.39 (m, 4H), 7.34 (dt, *J* = 7.7, 6.5 Hz, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.10 (s, 1H), 5.12 (dd, *J* = 8.2, 7.1 Hz, 1H), 4.37 (t, *J* = 7.0 Hz, 2H), 3.06 (d, *J* = 6.4 Hz, 6H), 2.63 (t, *J* = 6.7 Hz, 2H), 2.59 - 2.53 (m, 2H), 2.50 (t, *J* = 6.9 Hz, 2H), 1.65 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 164.04, 147.05, 141.49, 141.25, 141.05, 133.63, 128.83, 128.74, 127.40, 127.27, 127.09, 124.98, 124.42, 121.06, 109.30, 48.43, 40.11, 35.51, 35.12, 29.20, 27.27, 26.08, 15.68
ESI MS *m/z* (M+H) 436

(*E*)-3-((5-(4-(([1,1'-biphenyl]-4-yloxy)methyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11q**)
Colorless oil (24 mg, 96%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.58 - 7.49 (m, 4H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 5.25 (s, 2H), 5.19 (t, *J* = 7.3 Hz, 1H), 4.46 (t, *J* = 7.0 Hz, 2H), 3.09 (d, *J* = 7.7 Hz, 2H), 2.61 (dd, *J* = 9.3, 5.3 Hz, 6H), 1.70 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 176.51, 157.64, 144.05, 140.55, 133.69, 128.70, 128.16, 126.68, 124.35, 122.71, 115.03, 61.94, 48.68, 39.98, 34.60, 29.13, 25.86, 15.77
ESI MS *m/z* (M+H) 438

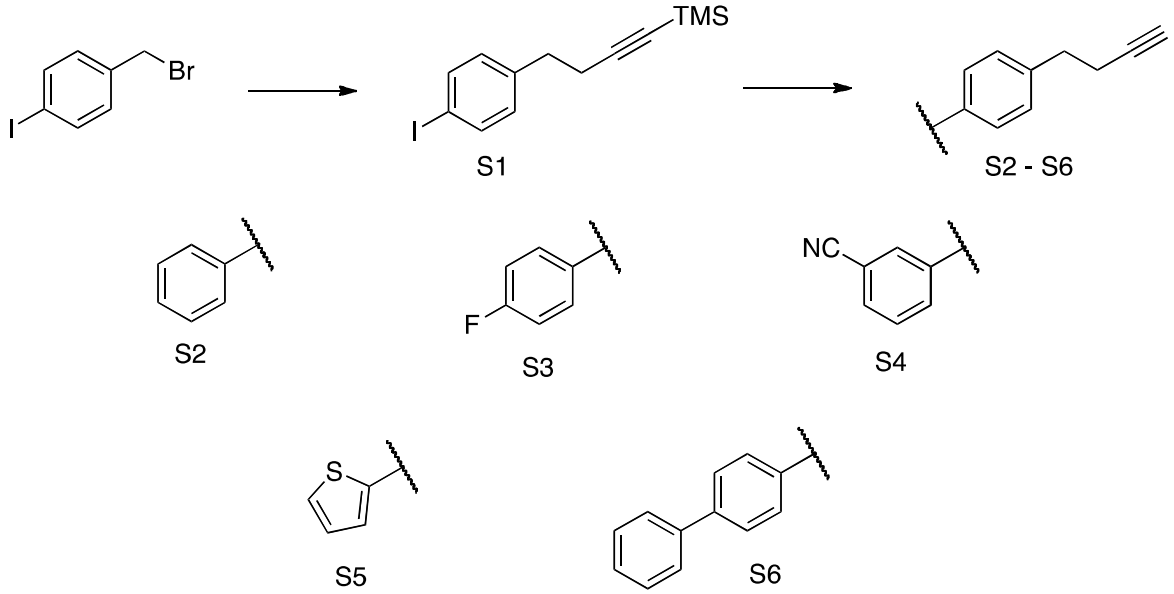
(*E*)-3-((5-(4-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11s**)
Light yellow oil (17 mg, 85%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 - 7.48 (m, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.15 (s, 1H), 7.10 (t, *J* = 8.7 Hz, 2H), 5.17 (td, *J* = 7.7, 1.1 Hz, 1H), 4.39 (t, *J* = 7.0 Hz, 2H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.08 - 3.04 (m, 2H), 3.04 - 2.99 (m, 2H), 2.68 - 2.62 (m, 2H), 2.61 - 2.57 (m, 2H), 2.54 (t, *J* = 7.0 Hz, 2H), 1.68 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 175.78, 163.27, 161.31, 146.98, 140.10, 137.99, 136.93, 133.76, 128.93, 128.44, 128.38, 126.91, 124.28, 121.08, 115.64, 115.47, 48.50, 40.06, 34.96, 34.84, 29.18, 27.09, 26.01, 15.72
ESI MS *m/z* (M+H) 453

(*E*)-3-((5-(4-(2-(3'-cyano-[1,1'-biphenyl]-4-yl)ethyl)-1*H*-1,2,3-triazol-1-yl)-3-methylpent-2-en-1-yl)thio)propanoic acid (**11t**)
Off-white waxy-solid (10 mg, 62%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.82 - 7.77 (m, 1H), 7.63 - 7.58 (m, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.50 - 7.44 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.17 (s, 1H), 5.15 (t, *J* = 7.8 Hz, 1H), 4.42 (t, *J* = 6.9

Hz, 2H), 3.10 (d, *J* = 7.7 Hz, 2H), 3.07 - 2.99 (m, 4H), 2.64 (d, *J* = 6.6 Hz, 2H), 2.60 - 2.51 (m, 4H), 1.70 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 174.97, 146.90, 141.42, 136.67, 133.59, 131.28, 130.49, 129.59, 129.26, 127.05, 121.05, 118.88, 112.87, 109.31, 48.44, 40.19, 35.02, 34.92, 29.30, 27.09, 26.13, 15.70
ESI MS *m/z* (M+H) 461

(*E*)-3-((3-methyl-5-(4-(4-(thiophen-2-yl)phenethyl)-1*H*-1,2,3-triazol-1-yl)pent-2-en-1-yl)thio)propanoic acid (**11u**)
White solid (15 mg, 50%)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.2 Hz, 2H), 7.28 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.25 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 2H), 7.10 (s, 1H), 7.07 (dd, *J* = 5.1, 3.6 Hz, 1H), 5.15 (td, *J* = 7.7, 1.2 Hz, 1H), 4.39 (t, *J* = 6.9 Hz, 2H), 3.09 (d, *J* = 7.7 Hz, 2H), 3.05 (dd, *J* = 8.2, 5.9 Hz, 2H), 3.00 (d, *J* = 7.3 Hz, 2H), 2.65 (dt, *J* = 8.6, 1.8 Hz, 2H), 2.61 - 2.56 (m, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 1.68 (s, 3H)
^{13}C NMR (125 MHz, $CDCl_3$) δ 175.56, 146.93, 144.25, 140.35, 133.68, 132.33, 129.01, 127.98, 125.91, 124.49, 122.74, 121.08, 48.42, 40.14, 35.03, 34.96, 29.28, 27.08, 26.09, 15.71
ESI MS *m/z* (M+H) 442

Synthesis of biphenyl alkynes S2 – S9



(4-(4-iodophenyl)but-1-yn-1-yl)trimethylsilane (**S1**)
A flame dried round bottom flask charged with TMS-propyne (3.76 mL, 25.2 mmol) in THF (20 mL) was cooled to -78 °C under and atmosphere of argon. Then n-BuLi (10.8 mL, 26.9 mmol) was added dropwise and the resulting solution was allowed to stir 30 min and then 30 min at 0 °C. A solution of 2.6 (5 g, 16.8 mmol) in THF (20 mL) was then added slowly via syringe and the reaction mixture was allowed to stir at room temperature 3 h. The reaction was quenched with water (10 mL), extracted with ether (3x 10 mL), washed with brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was subject to silica gel chromatography (0-10% ethyl acetate in hexanes) affording a yellow oil (5.06 g, 92%)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.3 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 2.48 (t, *J* = 7.4 Hz, 2H), 0.17 (s, 9H)
^{13}C NMR (75 MHz, $CDCl_3$): δ 140.05, 137.24, 130.60, 106.00, 91.48, 85.66, 34.42, 21.91, 0.04

General procedure for the Suzuki cross-coupling with **S1**

A round bottom flask charged with **S1** (164 mg, 0.5 mmol) in THF (3 mL) and water (2 mL) was added Na_2CO_3 (159 mg, 1.5 mmol), boronic acid (0.75 mmol) and $PdCl_2(PPh_3)_2$ (7 mg, 0.01 mmol) sequentially. The resulting solution was allowed to stir at 75 °C for 16 h. The separated and the aqueous layer was extracted with ether (3x 3 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was then taken up in THF (1 mL) and added a solution of TBAF (1 mL, 1 mmol) and allowed to stir for 30 min at room temperature. The reaction was quenched with 10% aqueous citric acid solution (5 mL) and worked up in the same manner. The crude product was subject to silica gel chromatography (typically 2% ethyl acetate in hexanes) affording the purified alkyne.

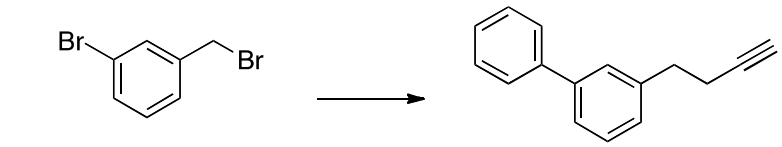
4-(but-3-yn-1-yl)-1,1'-biphenyl (**S2**)
Light yellow oil (150 mg, 87% over two steps)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 - 7.53 (m, 4H), 7.46 - 7.41 (m, 1H), 7.36 - 7.26 (m, 4H), 2.90 (t, *J* = 7.8 Hz, 2H), 2.53 (dt, *J* = 7.8, 3 Hz, 2H) 2.01 (t, *J* = 3 Hz, 1H)

4-(but-3-yn-1-yl)-4'-fluoro-1,1'-biphenyl (**S3**)
Light yellow oil (75 mg, 67% over two steps)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 - 7.44 (m, 4H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.12 (t, *J* = 8.7 Hz, 2H), 2.90 (t, *J* = 7.5 Hz, 2H), 2.53 (td, *J* = 7.5, 2.5 Hz, 2H), 2.01 (t, *J* = 2.6 Hz, 1H)
^{13}C NMR (75 MHz, $CDCl_3$): δ 139.50, 138.34, 128.90, 128.56, 128.46, 126.99, 115.71, 115.42, 83.69, 69.04, 34.38, 20.50

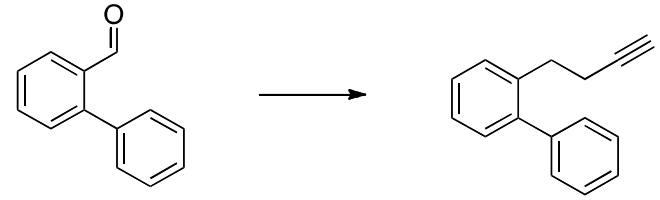
4'-(but-3-yn-1-yl)-[1,1'-biphenyl]-3-carbonitrile (**S4**)
^{1}H NMR (300 MHz, CDl_3): δ 7.85 (t, *J* = 1.5 Hz, 1H),7.83-7.76 (m, 1H), 7.62 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.57 - 7.47 (m, 3H), 7.35 (d, *J* = 8.2 Hz, 2H), 2.91 (t, *J* = 7.4 Hz, 2H), 2.53 (td, *J* = 7.4, 2.6 Hz, 2H), 2.01 (t, *J* = 2.6 Hz, 1H)
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.17, 140.78, 136.94, 131.31, 130.53, 129.56, 129.24, 127.06, 118.88, 112.90, 83.47, 69.20, 34.35, 20.42

2-(4-(but-3-yn-1-yl)phenyl)thiophene (**S5**)
1H NMR (300 MHz, $CDCl_3$): δ 7.62 - 7.51 (m, 2H), 7.33 - 7.21 (m, 4H), 7.08 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.87 (t, *J* = 7.5 Hz, 2H), 2.51 (td, *J* = 7.5, 2.6 Hz, 2H), 2.01 (t, *J* = 2.6 Hz, 1H)
^{13}C NMR (75 MHz, $CDCl_3$): δ 144.27, 139.72, 132.57, 128.93, 127.93, 125.95, 124.50, 122.79, 83.63, 69.06, 34.42, 20.45

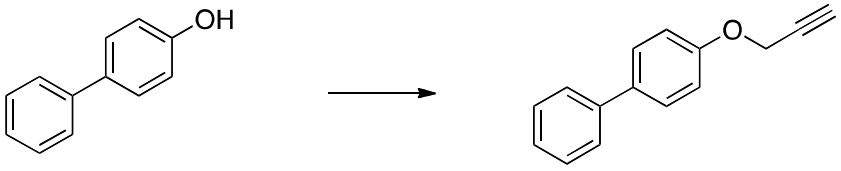
4-(but-3-yn-1-yl)-1,1':4',1"-terphenyl (**S6**)
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 - 7.64 (m, 7H), 7.63 - 7.57 (m, 1H), 7.47 (dd, *J* = 11.0, 4.6 Hz, 2H), 7.41 - 7.31 (m, 3H), 2.92 (t, *J* = 7.5 Hz, 2H), 2.55 (td, *J* = 7.6, 2.5 Hz, 2H), 2.03 (t, *J* = 2.6 Hz, 1H)



S7



S8



S9

3-(but-3-yn-1-yl)-1,1'-biphenyl (**S7**)
Procedure is identical to the alkylation and Suzuki cross-coupling (vida supra).
Light yellow oil (56% for two steps)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 - 7.58 (m, 2H), 7.47 - 7.45 (m, 3H), 7.42 - 7.33 (m, 3H), 7.22 (d, *J* = 7.5 Hz, 1H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.54 (dt, *J* = 7.5, 2.7 Hz, 2H), 2.01 (t, *J* = 2.7 Hz, 1H)

2-(but-3-yn-1-yl)-1,1'-biphenyl (**S8**)
A round bottom flask charged with 2-Biphenylcarboxaldehyde (Sigma) (484 mg, 3 mmol) in EtOH (6 mL) was added solid $NaBH_4$ (85 mg, 2.25 mmol) and the resulting reaction mixture was allowed to stir at room temperature for 30 min. The reaction was quenched with acetone (10 mL) and concentrated in vacuo. The crude product was passed through plug of silica affording the reduced alcohol (571 mg, 89%) and used without further purification. A second round bottom flask charged with NCS (746 mg, 5.59 mmol) in DCM (8 mL) was cooled to -40 °C and added dimethyl sulfide (0.410 mL, 5.59 mmol). The solution was allowed to stir at 0 °C for five minutes before again cooling to -40 °C at which time a solution of the alcohol in DCM (5 mL) was added and the solution was warmed to room temperature and stirring continued 2 h and was worked up in the usual way and taken up in THF (2 mL). A third round bottom charged with TMS-propyne (0.596 mL, 3.99 mmol) in THF (5 mL) was cooled to -78 °C and added nBuLi (1.7 mL, 4.26 mmol) and allowed to stir 1 h at -78 °C whereby a solution of the crude chloride was added and allowed to stir 4 h to room temperature. The reaction was quenched with 10% aqueous citric acid solution and extracted in the usual manner. The crude product was again taken up in THF (5 mL) and added TBAF (3 mL, 3.0 mmol) and stirred 30 min at room temperature. The reaction was concentrated in vacuo and subject to silica gel chromatography affording a colorless oil (271 mg, 45% over three steps).
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 - 7.18 (m, 9H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.31 (td, *J* = 7.7, 2.6 Hz, 2H), 1.92 (t, *J* = 2.6 Hz, 1H)
^{13}C NMR (75 Hz, $CDCl_3$): δ 141.91, 141.42, 137.67, 130.14, 129.22, 129.10, 128.15, 127.40, 126.95, 126.29, 83.85, 68.68, 31.97, 19.87

4-(prop-2-yn-1-yloxy)-1,1'-biphenyl (**S9**)
White solid, 94%
Prepared as previously reported by Bach et al.[3]
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 - 7.30 (m, 7H), 7.20 - 7.01 (m, 2H), 4.76 (d, *J* = 2.3 Hz, 2H), 2.57 (t, *J* = 2.3 Hz, 1H)
^{13}C NMR (CDCl3, 75 Hz): δ 157.18, 140.75, 134.79, 128.87, 12.30, 126.92, 115.28, 78.67, 75.76, 55.96

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