Double Conjugate Addition of Dithiols to Propargylic Carbonyl Systems to Generate Protected 1,3-Dicarbonyl Compounds

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General Procedure A for the dithiol addition

NaOMe (1.3 eq.) was added in one portion to a stirred solution of propargylic carbonyl compound (1 eq.) and dithiol (1.1 eq.) in MeOH and CH₂Cl₂ (4:1, 0.05 M) at approximately -10 °C. The reaction mixture was stirred for 2-14 hours, allowing the temperature to rise to ambient temperature. On completion the reaction was quenched by addition of sat. NH₄Cl solution and extracted with Et₂O. The organic fractions were washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by flash column chromatography.

General Procedure B for the dithiol addition

NaOMe (1.3 eq.) was added in one portion to a stirred solution of propargylic carbonyl compound (1 eq.) and dithiol (1.1 eq.) in THF (0.1 M) at approximately -10 °C. The reaction mixture was stirred for 8-14 hours, allowing the temperature to rise to ambient temperature. On completion the reaction was quenched by addition of sat. NH₄Cl solution and extracted with Et₂O. The organic fractions were washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by flash column chromatography.

General Procedure C for the dithiol addition to bisynones.

To a solution of bisynone (1 eq.) and 1,3-propanedithiol (2.2 eq.) in MeOH and CH₂Cl₂ (4:1, 0.05 M) stirred at -10 °C for 30 min was added NaOMe (2.2 eq.). The mixture was allowed to warm to ambient temperature and was stirred until complete conversion (30 min to 20 h) of the starting material. The reaction mixture was quenched with sat. aqueous NH₄Cl. The aqueous phase was extracted with Et₂O. The combined organic extracts were washed with water and brine, dried (MgSO₄), filtered, concentrated under reduced pressure and purified by flash column chromatography.

General Procedure D for the tandem addition cyclisation

To a solution of propargylic carbonyl substrate (1 eq.) and dithiol (1.1 eq) in MeOH and CH₂Cl₂ (1:1, 0.05 M), stirred at -10 °C, was added NaOMe (1.1 eq.). The reaction mixture was allowed to warm to ambient temperature overnight, was quenched by addition of sat. NH₄Cl solution and was extracted with
Et₂O. The organic fractions were washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by gradient flash column chromatography.

**General Procedure E for the tandem addition cyclisation**

To a solution of bisynone (1 eq.) and 1,3-propanedithiol (2.2 eq) in MeOH and CH₂Cl₂ (1:1, 0.05 M), stirred at -10 °C, was added NaOMe (2.2 eq.). The reaction mixture was allowed to warm to ambient temperature overnight, was quenched by addition of sat. NH₄Cl solution and was extracted with Et₂O. The organic fractions were washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by gradient flash column chromatography.

**General procedure for the preparation of the ynoates**

The propiolate (1.5 eq.) was dissolved in THF (0.1 M) and the resulting solution cooled to -78 °C and n-BuLi (1.5 eq.) was added dropwise via syringe pump. The reaction mixture was stirred 30 min at -78 °C. Then BF₃·OEt₂ (1.5 eq.) was added dropwise via syringe pump. The red reaction was stirred at -78 °C for 45 min. The epoxide (1 eq.) was added dropwise and the reaction was stirred and the temperature was allowed to warm up to ambient temperature overnight. The reaction was quenched with sat. NaHCO₃ solution, extracted with Et₂O, washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by flash column chromatography.

**General Procedure F for the tandem addition cyclisation of ynoates**

To a solution of ynoates (1 eq.) and dithiol (1.1 eq) in THF (0.1 M), stirred at -10 °C, was added NaOMe (1.1 eq.). The reaction mixture was allowed to warm to ambient temperature overnight, was quenched by addition of sat. NH₄Cl solution and was extracted with Et₂O. The organic fractions were washed with water and brine, dried (MgSO₄), concentrated under reduced pressure and purified by gradient flash column chromatography.

**1-(2-Phenyl-[1,3]dithian-2-yl)-propan-2-one (2a)**

Compound 2a was prepared using procedure A in 82% yield.

IR (neat) 2904, 1706, 1355 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (2 H, d, J = 7.6 Hz), 7.40 (2 H, t, J = 7.5 Hz), 7.28 (1 H, m), 3.15 (2 H, s), 2.74 (4 H, m), 1.96 (2 H, m), 1.85 (3 H, s). ¹³C NMR
(100 MHz, CDCl3) δ 203.6, 140.7, 128.7 (2 C), 128.5 (2 C), 127.6, 57.0, 55.0, 31.9, 27.7 (2 C), 24.6.

HRMS (+ESI) m/z 275.0379 [(M+Na)+; calcd for C12H16OS2Na: 275.0540].

2-[(2-(tert-Butyldimethylsilanyloxy)-ethyl]-[1,3]dithian-2-yl]-1-phenyl-ethanone (2b)\(^1\)

Compound 2b was prepared using procedure A in 94% yield.

IR (neat) 2929, 1694, 1252, 1093 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl3) δ 7.96 (2 H, d, \(J = 7.9\) Hz), 7.54 (1 H, m), 7.44 (2 H, m), 3.89 (2 H, t, \(J = 6.4\) Hz), 3.64 (2 H, s), 2.89 (2 H, ddd, \(J = 11.4, 7.5, 4.0\) Hz), 2.79 (2 H, ddd, \(J = 11.4, 6.9, 4.0\) Hz), 2.54 (2 H, t, \(J = 6.4\) Hz), 1.98 (2 H, m), 0.82 (9 H, s), -0.03 (6 H, s). \(^13\)C NMR (100 MHz, CDCl3) δ 195.7, 137.9, 133.0, 128.5 (2 C), 128.2 (2 C), 60.2, 49.7, 46.1, 39.9, 26.4 (2 C), 25.9 (3 C), 24.9, 18.3, -5.4 (2 C). HRMS (+ESI) m/z 419.1511 [(M+Na)+; calcd for C\(_{20}\)H\(_{32}\)O\(_2\)S\(_2\)SiNa: 419.1511].

1-[(2-(tert-Butyldimethylsilanyloxy)-ethyl]-[1,3]dithian-2-yl]-pentan-2-one (2c)\(^1\)

Compound 2c was prepared using procedure A in 88% yield.

IR (neat) 2955, 2929, 1711, 1085 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl3) δ 3.86 (2 H, t, \(J = 6.8\) Hz), 3.05 (2 H, s), 2.84 (4 H, m), 2.48 (2 H, t, \(J = 7.3\) Hz), 2.40 (2 H, t, \(J = 6.8\) Hz), 1.97 (2 H, m), 1.60 (2 H, m), 0.92 (3 H, t, \(J = 7.4\) Hz), 0.89 (9 H, s), 0.07 (6 H, s). \(^13\)C NMR (100 MHz, CDCl3) δ 206.3, 59.9, 50.4, 48.9, 46.8, 40.4, 26.4 (2 C), 26.0 (3 C), 24.9, 18.3, 17.0, 13.6, -5.3 (2 C). HRMS (+ESI) m/z 385.1672 [(M+Na)+; calcd for C\(_{17}\)H\(_{34}\)O\(_2\)S\(_2\)SiNa: 385.1667].

\((2R,3R,4S)-1-(tert-Butyldiphenylsilanyloxy)-6-(2-butyl-[1,3]dithian-2-yl)-3-(4-methoxy-benzyloxy)-2,4-dimethyl-hexan-5-one (2f)\(^1\)

Compound 2f was prepared using procedure A in 80% yield.

\([\alpha]_D^{25} +21.7 (c 5.0, CHCl_3)\). IR (film) 2957, 2931, 2858, 1708, 1613, 1587, 1514 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl3) δ 7.66 (4 H, m), 7.41 (2 H, m), 7.36 (4 H, m), 7.05 (2 H, d, \(J = 8.7\) Hz), 6.77 (2 H, d, \(J = 8.7\) Hz), 4.38 (1 H, d, \(J = 10.4\) Hz), 4.28 (1 H, d, \(J = 10.4\) Hz), 3.86 (1 H, dd, \(J = 8.3, 2.5\) Hz), 3.79 (3 H, s), 3.76 (2 H, m), 3.33 (1 H, d, \(J = 10.4\) Hz), 3.01 (1 H, d, \(J = 10.4\) Hz), 2.93 (1 H, m), 2.78 (4 H, m), 2.09 (2 H, t, \(J = 7.2\) Hz), 1.94 (2 H, m), 1.85 (1 H, m), 1.50-1.30 (4 H, m), 1.12 (3 H, d, \(J = 7.0\) Hz),
1.08 (9 H, s, ), 1.04 (3 H, d, J = 7.1 Hz), 0.93 (3 H, t, J = 7.2 Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 208.8, 159.1, 135.7, 135.7, 133.6, 133.5, 130.6, 129.6, 129.4, 129.4, 127.7, 127.6, 113.7, 80.1, 73.5, 65.5, 55.3, 50.7, 50.3, 47.8, 39.5, 38.4, 27.0, 26.5, 26.3, 24.8, 22.8, 19.4, 15.0, 14.0, 10.4. HRMS (+ESI) m/z 715.3287 [(M+Na)$^+$; calcd for C$_{40}$H$_{56}$O$_4$S$_2$SiNa: 715.3298].

2-{2-[4'(tert-Butyldiphenylsilanyloxy)-butyl]-[1,3]dithian-2-yl}-acetaldehyde (2g)$^1$

Compound 2g was prepared using procedure A in 88% yield.

IR (neat) 2931, 1717, 1427, 1194, 1105 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 9.77 (1 H, t, J = 2.7 Hz), 7.67 (4 H, app. dd, J = 8.6, 1.4 Hz), 7.38 (6 H, m), 3.68 (2 H, t, J = 5.7 Hz), 2.87 (2 H, d, J = 2.7 Hz), 2.85 (4 H, m), 2.01 (2 H, m), 1.95 (2 H, m), 1.59 (4 H, m), 1.05 (9 H, s). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 199.6, 135.6 (4 C), 134.0 (2 C), 129.6 (2 C), 127.6 (4 C), 63.4, 50.2, 49.3, 40.2, 32.5, 26.9 (3 C), 26.2 (2 C), 24.7, 20.6, 19.2. HRMS (+ESI) m/z 495.1812 [(M+Na)$^+$; calcd for C$_{26}$H$_{36}$O$_2$S$_2$SiNa: 495.1824].

[1,3]Dithian-2-yl-acetic acid ethyl ester (2i)$^2$

Compound 2i was prepared using procedure B in 88% yield.

IR (neat) 2901, 1732, 1215, 1142 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 4.40 (1 H, t, J = 7.4 Hz), 4.18 (2 H, q, J = 7.1 Hz), 2.88 (4 H, m), 2.77 (2 H, d, J = 7.4 Hz), 2.10 (1 H, m), 1.90 (1 H, m), 1.27 (3 H, J = 7.1 Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 169.7, 61.0, 41.9, 40.6, 29.5 (2 C), 25.3, 14.1. HRMS (+EI) m/z 206.0436 [(M)$^+$; calcd for C$_8$H$_{14}$O$_2$S$_2$: 206.0435].

1-{2-[2-(tert-Butyldimethylsilanyloxy)-ethyl]-[1,3]dithian-2-yl}-3-[2-(tetrahydro-pyran-2-yloxymethyl)-[1,3]dithian-2-yl]-propan-2-one (21a)$^3$

Compound 21a was prepared using procedure C in 89% yield.

IR (neat) 2929, 1715, 1032 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 4.72 (1 H, t, J = 3.2 Hz), 4.17 (1 H, d, J = 10.5 Hz), 3.91 (1 H, m), 3.88 (1 H, d, J = 10.5 Hz), 3.86 (2 H, t, J = 7.0 Hz), 3.51 (1 H, m), 3.19 (2 H, s), 3.11 (2 H, d, J = 3.5 Hz), 2.97 (2 H, m), 2.86 (4 H, m), 2.76 (2 H, m), 2.36 (2 H, t, J = 7.0 Hz), 1.97 (4 H, m), 1.81 (1 H, m), 1.61 (5 H, m), 0.88 (9 H, s), 0.06 (6 H, s). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 202.1, 98.8, 70.3, 61.9, 59.7, 51.9, 50.9, 50.1, 48.8, 40.7, 30.3, 26.45, 26.43, 26.3, 26.1, 26.0 (3 C), 22.8, 19.4, 15.0, 14.0, 10.4.
25.4, 24.8, 24.7, 19.1, 18.3, -5.3 (2 C). HRMS (+ESI) \( m/z \) 589.1946 [(M+Na)+; calcd for C\(_{25}\)H\(_{46}\)O\(_4\)S\(_4\)SiNa: 589.1937].

1-{2-[2-(tert-Butyldimethylsilanyloxy)-ethyl]-[1,3]dithian-2-yl}-3-(2-phenyl-[1,3]dithian-2-yl)propan-2-one (21b)

Compound 21b was prepared using procedure C in 80% yield.

IR (neat) 2929, 1710, 1251, 1090 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.95 (2 H, d, \( J = 7.5 \) Hz), 7.40 (2 H, t, \( J = 7.5 \) Hz), 7.29 (1 H, t, \( J = 7.5 \) Hz), 3.74 (2 H, t, \( J = 7.1 \) Hz), 3.24 (2 H, s), 2.78 (2 H, s), 2.67 (8 H, m), 2.20 (2 H, t, \( J = 7.1 \) Hz), 1.95 (2 H, m), 1.87 (2 H, m), 0.87 (9 H, s), 0.03 (6 H, s). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 201.0, 140.8, 128.7 (2 C), 128.6 (2 C), 127.6, 59.5, 58.0, 55.2, 51.5, 48.6, 40.9, 27.7 (2 C), 26.4 (2 C), 26.0 (3 C), 24.7, 24.6, 18.3, -5.3 (2 C). HRMS (+ESI) \( m/z \) 551.1578 [(M+Na)+; calcd for C\(_{25}\)H\(_{40}\)O\(_2\)S\(_4\)SNa: 551.1588]..

1-{2-[4-(tert-Butyldiphenylsilanyloxy)-butyl]-[1,3]dithian-2-yl}-3-(2-butyl-[1,3]dithian-2-yl)propan-2-one (21c)

Compound 21c was prepared using procedure C in 90% yield.

IR (neat) 2930, 1717, 1427, 1107 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.66 (4 H, m), 7.40 (6 H, m), 3.68 (2 H, t, \( J = 5.5 \) Hz), 3.14 (4 H, m), 2.93-2.78 (8 H, m), 2.07 (4 H, m), 2.01 (2 H, m), 1.93 (2 H, m), 1.58 (4 H, m), 1.49 (2 H, m), 1.34 (2 H, qn, \( J = 7.3 \) Hz), 1.05 (9 H, s), 0.92 (3 H, t, \( J = 7.3 \) Hz). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 202.5, 135.6 (4 C), 134.1 (2 C), 129.5 (2 C), 127.6 (4 C), 63.7, 51.2, 51.0, 50.55, 50.48, 38.4, 38.3, 32.6, 26.9 (3 C), 26.5 (2 C), 26.4 (2 C), 26.3, 25.04, 25.00, 22.8, 19.2, 15.2, 14.0. HRMS (+ESI) \( m/z \) 683.2517 [(M+Na)+; calcd for C\(_{35}\)H\(_{52}\)O\(_2\)S\(_4\)SiNa: 683.2504].

1-{2-[2-(tert-Butyldimethylsilanyloxy)-ethyl]-[1,3]dithian-2-yl}-3-[1,3]dithian-2-yl-propan-2-one (21d)

Compound 21d was prepared using procedure C in 65% yield.

IR (neat) 2927, 1717, 1251, 1086 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 4.50 (1 H, t, \( J = 6.9 \) Hz), 3.86 (2 H, t, \( J = 6.8 \) Hz), 3.12 (2 H, s), 2.93 (2 H, m), 2.92 (2 H, d, \( J = 6.9 \) Hz), 2.84 (6 H, m), 2.36 (2 H, t,
$J = 6.8$ Hz, 2.08 (1 H, m), 1.88 (2 H, m), 1.85 (1 H, m), 0.89 (9 H, s), 0.06 (6 H, s). $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 201.7, 59.7 (2 C), 51.2, 49.7, 48.7, 41.2, 40.8, 30.2, 26.5, 26.0 25.3 (3 C), 24.8 (2 C), 18.3, -5.3 (2 C). HRMS (+ESI) $m/z$ 475.1265 [(M+Na)$^+$; calcd for C₁₉H₃₆O₂S₄SiNa: 475.1273].

(4R)-1-[2-(2',2'-Diethyl-[1,3]dioxolan-4'-yl-methyl)-[1,3]dithian-2-yl]-3-[1,3]dithian-2-yl-propan-2-one (21e)$^3$

Compound 21e was prepared using procedure C in 94% yield.

$[\alpha]_{D}^{25} +2.6$ (c 1.035, CHCl₃). IR (neat) 2932, 1723, 1077 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl₃) $\delta$ 4.49 (1 H, t, $J = 6.5$ Hz), 4.38 (1 H, m), 4.10 (1 H, dd, $J = 7.7$, 6.1 Hz), 3.48 (1 H, t, $J = 8.2$ Hz), 3.27 (1 H, d, $J = 16.5$ Hz), 3.13 (1 H, d, $J = 16.5$ Hz), 2.86 (10 H, m), 2.54 (1 H, dd, $J = 14.9$, 8.1 Hz), 2.29 (1 H, dd, $J = 14.9$, 2.7 Hz), 2.08 (1 H, m), 1.97 (2 H, app. q, $J = 6.0$ Hz), 1.85 (1 H, m), 1.59 (4 H, m), 0.88 (3 H, t, $J = 7.5$ Hz), 0.86 (3 H, t, $J = 7.5$ Hz). $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 201.4, 113.2, 73.0, 70.4, 51.0, 49.2, 48.6, 41.0, 40.9, 30.3, 30.2, 30.0 (2 C), 26.4 (2 C), 25.3, 24.8, 8.3, 7.9. HRMS (+ESI) $m/z$ 459.1132 [(M+Na)$^+$; calcd for C₁₉H₃₂O₃S₄Na: 459.1132]. Elemental analysis C, 52.40%; H, 7.38%.

(1'R)-1-[2-(2'-Benzyloxy-1'-methyl-ethyl)-[1,3]dithian-2-yl]-3-[1,3]dithian-2-yl-propan-2-one (21f)$^3$

Compound 21f was prepared using procedure C in 84% yield.

$[\alpha]_{D}^{25} +30.6$ (c 1.10, CHCl₃). IR (neat) 2988, 1717, 1421, 1088 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.33 (4 H, m), 7.27 (1 H, m), 4.52 (1 H, d, $J = 11.7$ Hz), 4.48 (1 H, t, $J = 7.0$ Hz), 4.47 (1 H, d, $J = 11.7$ Hz), 3.96 (1 H, dd, $J = 9.4$, 4.3 Hz), 3.48 (1 H, dd, $J = 9.4$, 7.3 Hz), 3.29 (1 H, d, $J = 15.6$ Hz), 3.15 (1 H, d, $J = 15.6$ Hz), 2.89 (2 H, m), 2.79 (8 H, m), 2.68 (1 H, m), 2.08 (1 H, m), 2.00 (1 H, m), 1.89 (1 H, m), 1.87 (1 H, m), 1.25 (3 H, d, $J = 6.9$ Hz). $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 202.2, 138.5, 128.3 (2 C), 127.6 (2 C), 127.4, 73.0, 72.2, 53.8, 49.6, 49.2, 41.3, 40.1, 30.2, 26.4 (2 C), 26.2, 25.3, 24.7, 13.5. HRMS (+ESI) $m/z$ 465.1026 [(M+Na)$^+$; calcd for C₂₁H₃₀O₂S₄Na: 465.1031].
(2R)-1-Benzyl-2-hydroxy-5-(trimethylsilyl)-pent-4-yne (25)\(^4\)

To a solution of trimethylsilylacetylene (8.97 g, 121.88 mmol) in THF (500 mL) at -78 °C was added \(n\)-BuLi (1.6 M in hexane) (57.13 mL, 91.41 mmol). After stirring at -78 °C for 30 min, BF\(_3\)-THF (12.79 g, 91.41 mmol) was added. After stirring at -78 °C for a further 30 min, (\(R\))-benzyl glycidol 24 (10.00 g, 60.94 mmol) in THF (50 mL) was added dropwise and the reaction mixture stirred at -78 °C for 18 h. The reaction was quenched with sat. aqueous NH\(_4\)Cl (200 mL). The layers were separated, and the aqueous phase was extracted with Et\(_2\)O. The combined organic extracts were washed with water, and brine, dried (MgSO\(_4\)), filtered and concentrated under reduced pressure to yield the crude product as a thick, black oil. The majority of the crude product was carried through without purification. Gradient flash column chromatography of a sample (petroleum ether:Et\(_2\)O, 100:0 → 95:5 → 90:10 → 85:15) yielded 25 as a pale yellow oil.

\[ [\alpha]_D^{25} -16.4 \ \text{(c 1.035, CHCl}_3) \]. IR (neat) 3429, 2959, 2176, 1249 cm\(^{-1}\). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta 7.34\) (5 H, m), 4.58 (2 H, s), 3.96 (1 H, m), 3.61 (1 H, dd, \(J = 9.5, 4.0\) Hz), 3.51 (1 H, dd, \(J = 9.5, 6.5\) Hz), 2.52 (1 H, dd, \(J = 16.9, 6.0\) Hz), 2.47 (1 H, dd, \(J = 16.9, 6.9\) Hz), 2.40 (1 H, d, \(J = 4.8\) Hz), 0.14 (9 H, s). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta 137.9, 128.4\) (2 C), 127.8 (2 C), 127.7, 102.5, 87.3, 73.4, 72.8, 68.8, 25.0, -0.01 (3 C). HRMS (+ESI) \(m/z\) 285.1275 [(M+Na)\(^+\); calcd for C\(_{15}\)H\(_{22}\)O\(_2\)SiNa: 285.1287].

(2R)-1-Benzyl-2-hydroxy-pent-4-yne (26)\(^5\)

To a solution of trimethylsilylalkyne 25 (15.67 g, 60.94 mmol) in MeOH (100 mL) at ambient temperature was added potassium carbonate (42.09 g, 304.50 mmol). After stirring at ambient temperature for 2 h, the reaction mixture was filtered through a pad of silica and concentrated under reduced pressure. Gradient flash column chromatography (petroleum ether:Et\(_2\)O, 100:0 → 80:20 → 70:30 → 60:40) afforded the title compound 26 (9.96 g, 86% over two steps) as a colorless oil.

\[ [\alpha]_D^{25} -12.1 \ \text{(c 0.62, CHCl}_3) \]. IR (neat) 3417, 3293, 2862, 1454, 1074 cm\(^{-1}\). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta 7.37-7.27\) (5 H, m), 4.58 (2 H, s), 3.99 (1 H, m), 3.62 (1 H, dd, \(J = 9.7, 4.0\) Hz), 3.52 (1 H, dd, \(J = 9.4, 6.6\) Hz), 2.46 (3 H, m), 2.03 (1 H, t, \(J = 2.7\) Hz). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta 137.8, 128.5\)
(2 C), 127.8 (2 C), 127.7, 80.2, 73.5, 72.8, 70.6, 68.8, 23.5. HRMS (+ESI) m/z 213.0884 [(M+Na)⁺; calcd for C₁₂H₁₄O₂Na: 213.0891].

(2R)-1-Benzzyloxy-2-triethylsilyloxy-pent-4-yne (27)⁶

To a solution of secondary alcohol 26 (18.47 g, 97.16 mmol) and imidazole (15.87 g, 233.18 mmol) in THF (500 mL) at ambient temperature was added TESCl (15.37 mL, 102.02 mmol). After stirring at ambient temperature for 16 h, the reaction mixture was filtered through a pad of silica and concentrated under reduced pressure. Gradient flash column chromatography (petroleum ether:Et₂O, 100:0 → 90:10 → 80:20) afforded 27 as a colorless oil (27.12 g, 92%).

\[\alpha\]D²⁵ -0.60 (c 1.055, CHCl₃). IR (neat) 2876, 1454, 1092 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 7.34-7.27 (5 H, m), 4.56 (2 H, s), 3.98 (1 H, m), 3.51 (2 H, m), 2.50 (1 H, ddd, J = 16.6, 5.7, 2.6 Hz), 2.38 (1 H, ddd, J = 16.6, 5.7, 2.6 Hz), 1.96 (1 H, t, J = 2.5 Hz), 0.96 (9 H, t, J = 8.0 Hz, 9 H), 0.63 (6 H, q, J = 8.0 Hz). ¹³C NMR (150 MHz, CDCl₃) δ 138.3, 128.3 (2 C), 127.6 (2 C), 127.5, 81.2, 73.4, 73.4, 70.0, 69.8, 24.7, 6.8 (3 C), 4.8 (3 C). HRMS (+ESI) m/z 327.1764 [(M+Na)⁺; calcd for C₁₈H₂₈O₂SiNa: 327.1756].

(2R)-1-Benzzyloxy-2-triethylsilyloxy-hex-4-ynal (28)

To a solution of alkyne 27 (9.26 g, 30.4 mmol) in THF (20 mL) at -78 °C was added n-BuLi (2.5 M, 13.38 mL, 33.44 mmol). The reaction mixture was stirred at -78 °C for 1 h. To the reaction mixture was added a solution of N-formyl morpholine (4.90 g, 42.56 mmol) in THF (80 mL). The reaction mixture was allowed to warm to ambient temperature over 16 h. The reaction mixture was quenched with sat. aqueous NH₄Cl (100 mL). The layers were separated, and the aqueous phase was extracted with Et₂O. The combined organic extracts were washed with water, and brine, dried (MgSO₄), filtered and concentrated under reduced pressure. Gradient flash column chromatography (petroleum ether:Et₂O, 100:0 → 95:05 → 90:10 → 80:20 → 0:100) afforded 28 (5.77 g, 57%) as a clear yellow oil.

\[\alpha\]D²⁵ +5.2 (c 1.19, CHCl₃). IR (neat) 2954, 2910, 2876, 2203, 1671, 1112 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 9.15 (1 H, s), 7.33 (4 H, m), 7.32 (1 H, m), 4.55 (2 H, s), 4.04 (1 H, m), 3.50 (1 H, dd, J = 9.7,
4.9 Hz), 3.45 (1 H, dd, $J = 9.7, 6.2$ Hz), 2.74 (1 H, dd, $J = 17.4, 5.3$ Hz), 2.61 (1 H, dd, $J = 17.4, 6.0$
Hz), 0.96 (9 H, t, $J = 8.0$ Hz), 0.62 (6 H, q, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.0, 137.9,
128.4 (2 C), 127.7, 127.6 (2 C), 96.2, 82.7, 73.4, 73.0, 69.2, 25.6, 6.7 (3 C), 4.8 (3 C). HRMS (+ESI)
m/z 355.1705 [(M+Na)$^+$; calcd for C$_{19}$H$_{28}$O$_3$SiNa: 355.1705].
Crystal data and structure refinement for compound 31c.

Empirical formula  
C12 H20 O2 S2

Formula weight  
260.40

Temperature  
180(2) K

Wavelength  
0.71073 Å

Crystal system  
Monoclinic

Space group  
P2(1)/c

Unit cell dimensions  
a = 9.4851(5) Å  \( \alpha = 90^\circ \).
b = 9.7208(5) Å  \( \beta = 107.390(3)^\circ \).
c = 14.4288(8) Å  \( \gamma = 90^\circ \).

Volume  
1269.57(12) Å³

Z  
4

Density (calculated)  
1.362 Mg/m³

Absorption coefficient  
0.403 mm⁻¹

F(000)  
560

Crystal size  
0.28 x 0.12 x 0.10 mm³

Theta range for data collection  
4.19 to 25.00°.

Index ranges  
-11 <= h <= 10, -10 <= k <= 11, -17 <= l <= 17

Reflections collected  
8207

Independent reflections  
2207 [R(int) = 0.0447]

Completeness to theta = 25.00°  
98.7 %

Absorption correction  
Semi-empirical from equivalents

Max. and min. transmission  
0.968 and 0.776

Refinement method  
Full-matrix least-squares on F²

Data / restraints / parameters  
2207 / 0 / 145

Goodness-of-fit on F²  
1.049

Final R indices [I>2sigma(I)]  
R1 = 0.0757, wR2 = 0.1889

R indices (all data)  
R1 = 0.0860, wR2 = 0.1964

Largest diff. peak and hole  
0.958 and -0.534 e.Å⁻³
Crystal data and structure refinement for compound 32c.

Empirical formula C11 H18 O2 S2
Formula weight 246.37
Temperature 180(2) K
Wavelength 0.71073 Å
Crystal system Orthorhombic
Space group Pbca
Unit cell dimensions
\[ a = 7.6871(3) \, \text{Å} \quad \alpha = 90°. \]
\[ b = 16.3111(6) \, \text{Å} \quad \beta = 90°. \]
\[ c = 18.5766(9) \, \text{Å} \quad \gamma = 90°. \]
Volume 2329.23(17) Å³
Z 8
Density (calculated) 1.405 Mg/m³
Absorption coefficient 0.435 mm⁻¹
F(000) 1056
Crystal size 0.35 x 0.12 x 0.12 mm³
Theta range for data collection 3.66 to 25.02°.
Index ranges -9 <= h <= 9, -15 <= k <= 19, -22 <= l <= 22
Reflections collected 12895
Independent reflections 2048 [R(int) = 0.0537]
Completeness to theta = 25.02° 99.7 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.956 and 0.846
Refinement method Full-matrix least-squares on F²
Data / restraints / parameters 2048 / 1 / 138
Goodness-of-fit on F² 1.054
Final R indices [I>2σ(I)] R1 = 0.0446, wR2 = 0.0988
R indices (all data) R1 = 0.0616, wR2 = 0.1069
Largest diff. peak and hole 0.499 and -0.360 e.Å⁻³
Crystal data and structure refinement for compound 39e.

Empirical formula  C10 H14 O2 S2
Formula weight  230.33
Temperature  180(2) K
Wavelength  0.71073 Å
Crystal system  Monoclinic
Space group  P2(1)/c
Unit cell dimensions
\[a = 9.7096(2) \text{ Å} \quad \alpha = 90°.\]
\[b = 9.0070(3) \text{ Å} \quad \beta = 110.406(2)°.\]
\[c = 12.9660(3) \text{ Å} \quad \gamma = 90°.\]
Volume  1062.77(5) Å\(^3\)
Z  4
Density (calculated)  1.440 Mg/m\(^3\)
Absorption coefficient  0.471 mm\(^{-1}\)
\[F(000) = 488\]
Crystal size  0.46 x 0.35 x 0.35 mm\(^3\)
Theta range for data collection  3.94 to 27.48°.
Index ranges  \(-12 \leq h \leq 12, -11 \leq k \leq 11, -16 \leq l \leq 16\)
Reflections collected  7321
Independent reflections  2414 [R(int) = 0.0198]
Completeness to theta = 27.48°  99.0 %
Absorption correction  Semi-empirical from equivalents
Max. and min. transmission  0.851 and 0.797
Refinement method  Full-matrix least-squares on F\(^2\)
Data / restraints / parameters  2414 / 0 / 127
Goodness-of-fit on F\(^2\)  1.101
Final R indices [I>2\sigma(I)]  \(R1 = 0.0380, wR2 = 0.1112\)
R indices (all data)  \(R1 = 0.0408, wR2 = 0.1142\)
Largest diff. peak and hole  0.963 and -0.366 e.Å\(^{-3}\)
Crystal data and structure refinement for compound 48.

Empirical formula: C19 H29 N O3 S3

Formula weight: 415.61

Temperature: 180(2) K

Wavelength: 0.71073 Å

Crystal system: Trigonal

Space group: P32

Unit cell dimensions:
\[ a = 10.556 \text{ Å} \quad \alpha = 90^\circ. \]
\[ b = 10.556 \text{ Å} \quad \beta = 90^\circ. \]
\[ c = 16.477 \text{ Å} \quad \gamma = 120^\circ. \]

Volume: 1590.0 Å³

Z: 3

Density (calculated): 1.302 Mg/m³

Absorption coefficient: 0.368 mm⁻¹

F(000): 666

Crystal size: 0.46 x 0.39 x 0.18 mm³

Theta range for data collection: 3.71 to 27.48°.

Index ranges: -13<=h<=12, -11<=k<=13, -21<=l<=21

Reflections collected: 6749

Independent reflections: 4006 [R(int) = 0.0232]

Completeness to theta = 27.48°: 99.7 %

Absorption correction: Semi-empirical from equivalents

Max. and min. transmission: 0.944 and 0.880

Refinement method: Full-matrix least-squares on F²

Data / restraints / parameters: 4006 / 1 / 239

Goodness-of-fit on F²: 1.174

Final R indices [I>2sigma(I)]: R1 = 0.0380, wR2 = 0.1063

R indices (all data): R1 = 0.0435, wR2 = 0.1130

Absolute structure parameter: 0.05(7)

Largest diff. peak and hole: 0.423 and -0.224 e.Å⁻³
References


