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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...
Et$_2$O. The organic fractions were washed with water and brine, dried (MgSO$_4$), 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 CH$_2$Cl$_2$ (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. NH$_4$Cl solution and was extracted with Et$_2$O. The organic fractions were washed with water and brine, dried (MgSO$_4$), 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 BF$_3$·OEt$_2$ (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. NaHCO$_3$ solution, extracted with Et$_2$O, washed with water and brine, dried (MgSO$_4$), 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. NH$_4$Cl solution and was extracted with Et$_2$O. The organic fractions were washed with water and brine, dried (MgSO$_4$), concentrated under reduced pressure and purified by gradient flash column chromatography.

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

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

IR (neat) 2904, 1706, 1355 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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). $^{13}$C 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 C₁₃H₁₆OS₂Na: 275.0540].

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

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

IR (neat) 2929, 1694, 1252, 1093 cm⁻¹. ¹H 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). ¹³C 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 C₂₀H₃₂O₂S₂SiNa: 419.1511].

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

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

IR (neat) 2955, 2929, 1711, 1085 cm⁻¹. ¹H 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). ¹³C 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 C₁₇H₃₄O₂S₂SiNa: 385.1667].

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

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

[α]D²⁵ +21.7 (c 5.0, CHCl₃). IR (film) 2957, 2931, 2858, 1708, 1613, 1587, 1514 cm⁻¹. ¹H 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\(_3\)) \( \delta \) 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].

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

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

IR (neat) 2931, 1717, 1194, 1105 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 199.6, 135.6 (4 C), 134.0 (2 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].

\( [1,3\text{]Dithian-2-yl-acetic acid ethyl ester (2i)} \)

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

IR (neat) 2901, 1732, 1215, 1142 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 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].

\( 1\text{-}[2\text{-}[\text{2\text{''}}\text{-}(\text{tert-Butyldimethylsilanyloxy})\text{-ethyl}]\text{-}[1,3\text{dithian-2-yl}]\text{-3-[2\text{-}(\text{tetrahydro-pyran-2-ylloxymethyl})\text{-}[1,3\text{dithian-2-yl}]\text{-propan-2-one (21a)} \)

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

IR (neat) 2929, 1715, 1032 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 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), 24.8, 22.8, 19.4, 15.0, 14.0, 10.4.

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

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)\(^3\)

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)\(^3\)

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, \( J = 6.9 \) Hz).
$J = 6.8 \text{ Hz}$, 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, CDCl$_3$) $\delta$ 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 C$_{19}$H$_{36}$O$_2$S$_4$SiNa: 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, CHCl$_3$). IR (neat) 2932, 1723, 1077 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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, CDCl$_3$) $\delta$ 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 C$_{19}$H$_{32}$O$_3$S$_4$Na: 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, CHCl$_3$). IR (neat) 2898, 1717, 1421, 1088 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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, CDCl$_3$) $\delta$ 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 C$_{21}$H$_{30}$O$_2$S$_4$Na: 465.1031].
(2R)-1-Benzylxy-2-hydroxy-5-(trimethylsilyl)-pent-4-yne (25)

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, BF₃·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 NH₄Cl (200 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 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:Et₂O, 100:0 → 95:5 → 90:10 → 85:15) yielded 25 as a pale yellow oil.

[α]D²⁵
-16.4 (c 1.035, CHCl₃). IR (neat) 3429, 2959, 2176, 1249 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 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). ¹³C NMR (150 MHz, CDCl₃) δ 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 C₁₅H₂₂O₂SiNa: 285.1287].

(2R)-1-Benzylxy-2-hydroxy-pent-4-yne (26)

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:Et₂O, 100:0 → 80:20 → 70:30 → 60:40) afforded the title compound 26 (9.96 g, 86% over two steps) as a colorless oil.

[α]D²⁵
-12.1 (c 0.62, CHCl₃). IR (neat) 3417, 3293, 2862, 1454, 1074 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 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). ¹³C NMR (150 MHz, CDCl₃) δ 137.8, 128.5
(2 R)-1-Benzyloxy-2-triethylsilyloxy-pent-4-yne (27)\textsuperscript{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:Et\textsubscript{2}O, 100:0 → 90:10 → 80:20) afforded 27 as a colorless oil (27.12 g, 92\%).

\[
\begin{align*}
\alpha_{D}^{25} &\quad -0.60 (c 1.055, \text{CHCl}_3). \quad \text{IR (neat)} 2876, 1454, 1092 \text{ cm}^{-1}. \\
\delta_{\text{H}} &\quad 7.34-7.27 (5 \text{ H, m}), 4.56 (2 \text{ H, s}), 3.98 (1 \text{ H, m}), 3.51 (2 \text{ H, m}), 2.50 (1 \text{ H, ddd, } J = 16.6, 5.7, 2.6 \text{ Hz}), 2.38 (1 \text{ H, ddd, } J = 16.6, 5.7, 2.6 \text{ Hz}), 1.96 (1 \text{ H, t, } J = 2.5 \text{ Hz}), 0.96 (9 \text{ H, t, } J = 8.0 \text{ Hz}), 0.63 (6 \text{ H, q, } J = 8.0 \text{ Hz}). \\
\delta_{\text{C}} &\quad 138.3, 128.3 (2 \text{ C}), 127.6 (2 \text{ C}), 127.5, 81.2, 73.4, 73.4, 70.0, 69.8, 24.7, 6.8 (3 \text{ C}), 4.8 (3 \text{ C}). \\
\text{HRMS (+ESI)} &\quad \text{m/z 327.1764 [(M+Na)\textsuperscript{+}; calcd for C\textsubscript{18}H\textsubscript{28}O\textsubscript{2}SiNa: 327.1756].}
\end{align*}
\]

(2 R)-1-Benzyloxy-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 NH\textsubscript{4}Cl (100 mL). The layers were separated, and the aqueous phase was extracted with Et\textsubscript{2}O. The combined organic extracts were washed with water, and brine, dried (MgSO\textsubscript{4}), filtered and concentrated under reduced pressure. Gradient flash column chromatography (petroleum ether:Et\textsubscript{2}O, 100:0 → 95:05 → 90:10 → 80:20 → 0:100) afforded 28 (5.77 g, 57\%) as a clear yellow oil.

\[
\begin{align*}
\alpha_{D}^{25} &\quad +5.2 (c 1.19, \text{CHCl}_3). \quad \text{IR (neat) 2954, 2910, 2876, 2203, 1671, 1112 \text{ cm}^{-1}.} \\
\delta_{\text{H}} &\quad 9.15 (1 \text{ H, s}), 7.33 (4 \text{ H, m}), 7.32 (1 \text{ H, m}), 4.55 (2 \text{ H, s}), 4.04 (1 \text{ H, m}), 3.50 (1 \text{ H, dd, } J = 9.7, 2.6 \text{ Hz}).
\end{align*}
\]
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) Å^3

Z: 4

Density (calculated): 1.362 Mg/m^3

Absorption coefficient: 0.403 mm\(^{-1}\)

F(000): 560

Crystal size: 0.28 x 0.12 x 0.10 mm^3

Theta range for data collection: 4.19 to 25.00°.

Index ranges: -11 \( \leq h \leq 10 \), -10 \( \leq k \leq 11 \), -17 \( \leq l \leq 17 \)

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 F^2

Data / restraints / parameters: 2207 / 0 / 145

Goodness-of-fit on F^2: 1.049

Final R indices [I>2\sigma(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\(^{-3}\)
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<td>Temperature</td>
<td>180(2) K</td>
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<td>Space group</td>
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<td>Absorption correction</td>
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<td>Largest diff. peak and hole</td>
<td>0.499 and -0.360 e.Å⁻³</td>
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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) Å³
Z 4
Density (calculated) 1.440 Mg/m³
Absorption coefficient 0.471 mm⁻¹
F(000) 488
Crystal size 0.46 x 0.35 x 0.35 mm³
Theta range for data collection 3.94 to 27.48°.
Index ranges -12<=h<=12, -11<=k<=11, -16<=l<=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 F²
Data / restraints / parameters 2414 / 0 / 127
Goodness-of-fit on F² 1.101
Final R indices [I>2sigma(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


