# A Highly Enantioenriched, Configurationally Stable α-Thioallyllithium Compound and the Stereochemical Course of its Electrophilic Alkylation

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**Supporting Information:**

Representative procedures for the synthesis are given:

(*R*)-*O*-(2-Cyclohexenyl) *N*-isopropylthiocarbamate (**7**): A solution of (*R*)-cyclohex-2-enol (245 mg, 2.50 mmol, 95% *ee*, determined by GC on a β-DEX 120 column [Supelco]) in dry THF (1.0 mL) was added dropwise to a stirred suspension of NaH (0.50 g, 3.0 mmol, 1.2 equiv) in dry THF (1.5 mL) via a syringe at 0 °C. The reaction mixture was stirred for 1h before a solution of isopropyl isothiocyanate (265 mg, 2.62 mmol, 1.05 equiv) in dry THF (1.0 mL) was added dropwise. After stirring for one additional hour, the reaction was quenched with saturated $NaHCO_3$ solution (2.5 mL). Ethyl acetate (5 mL) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate (2 times 10 mL each). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to afford a pale yellow vicous liquid that was subjected to column chromatography (silica gel, $Et_2O$/petrol ether gradient). (*R*)-**7** was isolated (462 mg, 2.32 mmol, 93%, $[\alpha]^D_{20}$ = +156 [*c* 1.13 in $CHCl_3$]) as a low melting white solid.

Resonance signals are doubled by *E*/*Z*-amide isomerization; the related signals consequently are given in groups, separated by a slash. $^1$H NMR (300 MHz, $CDCl_3$) δ 1.10/1.16 (d, *J* = 6.7 Hz, 6H), 1.51-2.11 (m, 6H), 3.93/4.32 (m, 1H), 5.71-5.79 (m, 2H), 5.86-5.94 (m, 1H), 6.04/6.74 (broad s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 18.8, 21.8/22.2, 24.8, 28.2, 45.2/46.8, 73.1/75.2, 125.2/125.7, 132.5/132.5, 188.3; FTIR (KBr) ν = 735, 927, 986, 1012, 1032, 1052, 1131, 1216, 1407, 1518, 1657, 2842, 2868, 2940, 2980, 3039, 3250 $cm^{-1}$; MS (EI) *m*/*z* 199 ($M^+$, 87), 120 (74), 97 (13), 81 (100), 58 (32).

(*S*)-*S*-(2-Cyclohexenyl) *N*-isopropylthiocarbamate (**8**): A flask, sealed with a rubber septum, was charged with (*R*)-**7** (156 mg, 0.78 mmol, 95% *ee*) under Ar and placed in an oil bath. The oil bath was heated to 105 °C and allowed to cool to room temperature after 3h. The obtained yellow solid was purified by column chromatography (silica gel, $Et_2O$/petrol ether gradient), yielding (*S*)-**8** (137 mg, 0.69 mmol, 88%) as white crystals, mp = 92 °C (pet ether). The *ee*

was determined to be 92% by GC on a β-DEX 120 column (Supelco). $[\alpha]^{D}_{20}$ = –194 (*c* 1.01 in $CHCl_3$).

$^1$H NMR (300 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.3 Hz, 6H), 1.55-1.72 (m, 2H), 1.73-1.84 (m, 1H), 1.93-2.04 (m, 3H), 3.99 (broad sept, *J* = 6.3 Hz, 1H), 4.09-4.15 (m, 1H), 5.24 (broad s, 1H), 5.61-5.67 (m, 1H), 5.72-5.78 (m, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 19.7, 22.7, 24.7, 30.2, 40.7, 43.5, 126.8, 130.3, 166.0; FTIR (KBr) ν = 637, 745, 815, 867, 1203, 1236, 1532, 1651, 2855, 2875, 2921, 2934, 2973, 3033, 3276 cm$^{-1}$; MS (EI) *m*/*z* 199 ($M^+$, 86), 120 (55), 114 (21), 86 (15), 81 (100), 53 (24); anal. calcd for $C_{10}H_{17}NOS$ (199.32): C, 60.26; H, 8.60; N, 7.03. Found: C, 60.40; H, 8.66; N, 7.07.

Lithiation of (*S*)-**8** and subsequent methylation: A solution of (*S*)-**8** (100 mg, 0.50 mmol, 92% *ee*) and TMEDA (151 mg, 1.30 mmol, 2.59 equiv) in dry THF (5.0 mL) under Ar in a flask, sealed with a rubber septum, was cooled to –78 °C. *s*-BuLi (1.02 mL, 1.25 mmol, 2.50 equiv, 1.23 N) was added dropwise over a period of 5 min. through a precooled needle. The yellow reaction mixture was stirred for additional 5 min. and MeI/THF (0.76 mL, 0.76 mmol, 1.5 equiv, 1.0 N) was added dropwise over a period of 3 min. through a precooled needle. The flask was sealed and after stirring for additional 12 h, HOAc/$Et_2O$ (1.25 mL, 1.25 mmol, 2.50 equiv, 1.00 N) was added. The reaction mixture was brought to approx. 0 °C and saturated $NaHCO_3$ solution (3 mL) and $Et_2O$ (10 mL) were added. The phases were separated and the aqueous phase was extracted with $Et_2O$ (2 times 5 mL each). The combined organic phases were washed with brine (3 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to afford a pale yellow oil which was subjected to column chromatography (silica gel, EtOAc/cyclohexane gradient). (*R*)-**10** (22 mg, 0.10 mmol, 21%) and 47 mg (*R*)-**11** (47 mg, 0.22 mmol, 44%) were isolated as white crystals.

The *ee* of (*R*)-**10** was determined to be 89% by GC on a α-DEX 120 column (Supelco), $[\alpha]^{D}_{20}$ = +159 (*c* 0.615 in $CHCl_3$). mp = 103 °C (cyclohexane). $^1$H NMR (400 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.4 Hz, 6H), 1.60-1.68 (m, 5H), 1.76-1.87 (m, 1H), 1.91-2.07 (m, 2H), 2.26-2.32 (m, 1H), 3.98 (broad sept, *J* = 6.4 Hz, 1H), 5.17 (broad s, 1H), 5.70-5.76 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 19.4, 22.8, 24.7, 29.0, 35.8, 43.1, 50.5, 128.6, 132.5; FTIR (KBr) ν = 630, 736, 815, 874, 1170, 1223, 1453, 1525, 1644, 2855, 2927, 2973, 3019, 3289 cm$^{-1}$; MS (EI) *m*/*z* 213 ($M^+$, 34), 191 (2), 155 (1), 120 (24), 95 (100), 79 (19), 55 (4); anal. calcd for $C_{11}H_{19}NOS$ (213.34): C, 61.93; H, 8.98; N, 6.57. Found: C, 62.09; H, 9.17; N, 6.46.

The *ee* of (*R*)-**11** was determined to be 68% by HPLC on a ZWE-805 column (Bayer),

1.00 (d, $J$ = 7.2 Hz, 3H), 1.14 (d, $J$ = 6.6 Hz, 6H), 1.57-1.84 (m, 4H), 2.19-2.40 (m, 3H), 4.00 (m, 1H), 5.24 (broad s, 1H), 6.07 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.5, 22.8, 29.9, 32.1, 32.3, 43.6, 127.7, 145.5; FTIR (KBr) ν = 611, 815, 867, 1131, 1223, 1453, 1532, 1657, 1848, 1868, 2927, 2960, 3026, 3302 $cm^{-1}$; MS (EI) $m/z$ 213 ($M^+$, 2), 170 (1), 128 (39), 95 (100), 79 (10), 55 (6); anal. calcd for $C_{11}H_{19}NOS$ (213.34): C, 61.93; H, 8.98; N, 6.57. Found: C, 62.09; H, 9.01; N, 6.42.