Enantioselective synthesis of (R) and (S)-α-alkylcysteines via phase-transfer catalytic alkylation

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General Methods

The $^1$H-NMRs were recorded at 300 MHz, 400 MHz, and 500 MHz. The $^{13}$C-NMRs were recorded at 75 MHz, 100 MHz, and 125 MHz. The chemical shifts were reported in ppm relative to CHCl$_3$ ($\delta$ 7.26) for $^1$H-NMR and relative to the central CDCl$_3$ ($\delta$ 77.23) resonance for $^{13}$C-NMR. Optical rotations were measured on a digital polarimeter. Melting points were not corrected. Flash column chromatography was carried out using silica gel (70~230 mesh). The enantiomeric excess (ee) of the products was determined by HPLC using 4.6 mm × 250 mm Chiralpak AD-H or OD-H columns. All solvents and commercially available chemicals were used without additional purification.

Experimental Section

2-Phenyl-2-thiazoline-4-carboxylic acid methyl ester (12)

To a methylene chloride solution (100 mL) of L-cysteine methyl ester hydrochloride (5.00 g, 29.13 mmol) and ethyl benzimidate hydrochloride (5.95 g, 32.04 mmol) was added triethylamine (6.08 mL, 43.69 mmol) and the reaction mixture was refluxed (6 h). After completion of the reaction, the reaction mixture was diluted with methylene chloride (500 mL), washed with saturated NaHCO$_3$ solution (70 mL) and brine (70 mL), dried over anhydrous MgSO$_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 30:1) to afford 12 (5.71 g, 89% yield) as a white solid (mp 67 °C).

$^1$H NMR (300 MHz, CD$_3$OD) 7.88~7.80(m, 2H), 7.59~7.39(m, 3H), 5.28 (t, $J = 17.9$ Hz, 1H), 3.66(d, $J = 9.2$ Hz, 1H), 3.65(d, $J = 8.8$ Hz, 1H) ppm; $^{13}$C-NMR (100 MHz, CD$_3$OD)
174.2, 173.4, 134.6, 133.8, 133.5, 130.3, 80.1, 53.9, 36.7 ppm; IR (KBr) 2950, 1742, 1599, 1490, 1441, 1233, 1047, 938, 768, 691 cm⁻¹; MS (ESI): 222 [M+H]⁺; HRMS (FAB) calcd for [C₁₁H₁₂NO₂S]⁺: 222.0589, found: 222.0588.

2-Phenyl-2-thiazoline-4-carboxylic acid tert-butyl ester (8a)

To a toluene solution (100 mL) of 2-phenyl-2-thiazoline-4-carboxylic acid methyl ester (12, 54 g, 20.51 mmol) was added trimethylaluminum (2 M solution in toluene, 10.3 mL, 20.51 mmol) and the reaction mixture was stirred at –78 °C (0.5 h). Dry t-BuOH (15.20 mL, 205.12 mmol) was added and stirred at room temperature (0.5 h). After reflux for 4 days, the reaction mixture was quenched with 1N-HCl at 0 °C, then filtered through Celite pad, diluted with ethyl acetate (200 mL), washed with brine (2 x 50 mL), dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 30:1) to afford 8a (5.71 g, 90% yield) as a yellow oil.

¹H-NMR (300 MHz, CDCl₃) δ 7.87~7.83(m, 2H), 7.48~7.35(m, 3H), 7.30~7.18(m, 5H), 5.15(t, J = 9.0 Hz, 1H), 3.59(d, J = 8.8 Hz, 2H), 1.49(s, 9H) ppm; ¹³C-NMR (100 MHz, CDCl₃) 170.5, 169.9, 132.7, 131.5, 128.6, 128.4, 82.1, 79.2, 35.7, 28.1 ppm; IR (KBr) 2977, 1734, 1601, 1448, 1368, 1254, 1155, 938, 767, 690 cm⁻¹; MS (ESI): 264 [M+H]⁺; HRMS (FAB) calcd for [C₁₄H₁₈NO₂S]⁺: 264.1058, found: 264.1056.

Representative procedure for enantioselective phase-transfer catalytic alkylation of 2-phenyl-2-thiazoline-4-carboxylic acid tert-butyl ester (8a) (Benzylation)
To a toluene (1.0 mL) solution of 2-phenyl-2-thiazoline-4-carboxylic acid tert-butyl ester (8a, 50.0 mg, 0.2 mmol) were added the chiral catalyst 1 (1.8 mg, 0.002 mmol), KOH (56.1 mg, 1.0 mmol) and benzyl bromide (0.1 mL, 1.0 mmol) at 0 °C and the reaction mixture was stirred (40 min). After completion of the reaction, the reaction mixture was diluted with ethyl acetate (20 mL), washed with brine (2 x 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 50:1) to afford 9a-e (63.7 mg, 90% yield) as a pale yellow oil. Because the two enantiomers of 9a-e were not fully separated by chiral HPLC, the enantioselectivity was determined by the chiral HPLC analysis of the corresponding methyl ester, prepared from the hydrolysis of 9a-e followed by methylation using excess of diazomethane. The enantioselectivity was determined as >99% ee [chiral HPLC analysis (Chiralcel AD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, = 254 nm, retention time, S (minor) 12.3 min, R (major) 15.5 min, >99% ee]. Absolute configuration was determined by comparison of the optical rotation of α-benzylcysteine prepared from the acidic hydrolysis of 9a-e with the reported value.

1H-NMR (300 MHz, CDCl₃) δ 7.87~7.83(m, 2H), 7.36~7.48(m, 3H), 7.30~7.10(m, 5H), 3.76~3.72(d, J = 11.6 Hz, 1H), 3.39~3.35(d, J = 11.6 Hz, 1H), 3.30~3.29(d, J = 2.9 Hz, 1H), 1.43(s, 9H) ppm; 13C-NMR (125 MHz, CDCl₃) 170.9, 168.0, 135.2, 133.0, 131.1, 130.3, 128.3, 128.2, 127.8, 126.6, 89.0, 81.8, 42.9, 39.1, 27.7 ppm; IR (KBr) 2977, 1725, 1601, 1450, 1368, 1251, 1154, 944, 846, 767, 694 cm⁻¹; MS (ESI): 354 [M+H]⁺; HRMS (FAB): calcd for [C₂₁H₂₄NO₂S]⁺ 354.1528, found 354.1537.
Acidic hydrolysis of 9a-e for (R)-α-benzylcysteine.

4-Benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester (9a-e) (354 mg, 1.00 mmol) was added to 6N-HCl (4 mL) and the reaction mixture was refluxed (20 h). The reaction solvent was removed by vacuum evaporation and the residue was purified through DOWEX 50WX8-100 column eluting with 15% NH₄OH to give (R)-α-benzylcysteine (207 mg, 98% yield) as a white solid. \([\alpha]_{20}^D = +7.07\) (c 1.00, H₂O) [lit.\([\alpha]_{20}^D = +7.07\) (c 1.07, H₂O)]. Physical and spectral properties were consistent with the literature values.

Representative Procedure for 4-benzyl-2-biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester.

The solution (3 mL) of 4-benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester (9a, 300 mg, 0.85 mmol) in methylene chloride and trifluoroacetic acid (1:1) was added and stirred at room temperature (6 h). After completion of the reaction, the organic solvent was removed by vacuum evaporation. To the solution (3 mL) of the residue in toluene:MeOH (4:1) was added (trimethylsilyldiazomethane (2.0 M solution, 2.55 mmol) at 0°C. After stirring (15 min), the reaction mixture was quenched with few drops of acetic acid, evaporated, and purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford the methyl ester product (259 mg, 98%) as a yellow oil.

\(^1\)H-NMR (300 MHz, CDCl₃) \(\delta\) 7.90~7.87(m, 2H), 7.53~7.41(m, 3H), 7.32~7.26(m, 5H), 3.87~3.83(d, \(J = 11.7\) Hz, 1H), 3.81(s, 3H), 3.48~3.44(d, \(J = 11.7\) Hz, 1H), 3.35(s, 2H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl₃) \(\delta\) 172.8, 135.4, 132.6, 131.8, 130.3, 128.6, 128.5, 128.3, 127.07, 88.7, 52.9, 43.1, 38.6 ppm; IR (KBr) 2924, 2852, 1736, 1601, 1494, 1447, 1231,
1084, 945, 817, 768, 695 cm⁻¹; MS (FAB): 312 [M+H]⁺; HRMS (FAB): calcd for
[C₁₈H₁₈NO₂S]⁺ 312.1058, found 312.1057.

2-[(Biphenyl-2-carbonyl)-amino]-3-tritylsulfanyl-propionic acid methyl ester (15)
To a DMF solution (10 mL) of Cys(Tr)-OMe (14, 576.2 mg, 1.7073 mmol) were added 2-
biphenyl carboxylic acid (13, 372.3 mg, 1.88 mmol), HBTU (712.2 mg, 1.88 mmol), and
diisopropylethylamine (0.63 mL, 3.59 mmol). The reaction mixture was stirred at room
temperature (3 h). After completion of the reaction, the organic solvent was removed by
vacuum evaporation and the residue was diluted with ethyl acetate (300 mL), washed with
brine (5 x 50 mL), dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The
residue was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to
afford 15 (887.5 mg, 98% yield) as an white solid (mp 64 °C).

1H-NMR (300 MHz, CDCl₃) δ 7.66~7.63 (m, 1H), 7.50~7.15 (m, 23H), 4.46~4.40 (m, 1H),
3.60 (s, 3H), 2.54~2.37 (m, 2H) ppm; 13C-NMR (100 MHz, CDCl₃) δ 170.3, 168.6, 144.1,
139.9, 139.7, 134.5, 130.3, 130.2, 129.3, 128.64, 128.58, 128.4, 127.8, 127.5, 127.3, 126.7,
66.7, 52.3, 51.5, 33.3 ppm; IR (KBr) 3399, 3058, 1744, 1658, 1509, 1442, 1214, 747, 700
cm⁻¹; MS (FAB): 558 [M+H]⁺; HRMS (FAB): calcd for [C₃₆H₃₂NO₃S]⁺ 558.2103, found
558.2109.

2-Biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester (16)
To a methylene chloride solution (100 mL) of triphenylphosphine oxide (1.36 g, 49.03
mmol) was added trifluoromethanesulfonic anhydride (6.9 g, 24.52 mmol) dropwise at 0 °C.
Then the methylene chloride solution (50 mL) of 2-[(biphenyl-2-carbonyl)-amino]-3-tritylsulfanyl-propionic acid methyl ester (15, 9.11 g, 16.34 mmol) was added at 0 °C. After completion of the reaction, the reaction mixture was quenched with saturated aq. NaHCO₃ solution at 0 °C and diluted with methylene chloride (300 mL), washed with brine (50 mL x 2), dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford 16 (4.8 g, 99% yield) as a pale yellow oil.

1H-NMR (300 MHz, CDCl₃) δ 7.67~7.64(m, 1H) 7.49~7.44(m, 1H), 7.39~7.31(m, 6H), 7.29~7.26(m, 1H), 5.13~5.07(t, J = 9.0 Hz, 1H), 3.75(s, 3H), 3.61~3.43(m, 2H) ppm; 13C-NMR (125 MHz, CDCl₃) δ 171.6, 170.6, 141.0, 139.9, 132.1, 130.1, 130.0, 129.0, 128.9, 127.7, 127.1, 126.8, 77.7, 52.3, 36.2 ppm; IR (KBr) 3059, 2950, 1741, 1616, 1475, 1437, 1338, 1222, 1045, 934, 748, 701 cm⁻¹; MS (FAB): 298 [M+H]+; HRMS (FAB): calcd for [C₁₇H₁₆NO₂S]+ 298.0902, found 298.0905.

2-Biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester (8b)

The synthetic procedure was same as that of 8a. The residue was purified by column chromatography (silica gel, hexanes : EtOAc = 30:1) to afford 8b (5.71 g, 90% yield) as a white solid (mp 81°C).

1H-NMR (300 MHz, CDCl₃) δ 7.69~7.66(m, 1H), 7.49~7.44(m, 1H), 7.39~7.33(m, 8H), 5.04~4.98(t, J = 8.6 Hz, 1H), 3.39~3.52(m, 2H), 1.48(s, 9H) ppm; 13C-NMR (125 MHz, CDCl₃) δ 171.0, 169.2, 140.8, 139.8, 132.4, 129.9, 129.7, 128.9, 128.9, 128.8, 127.6, 127.1, 126.8, 81.4, 78.6, 36.5, 27.6 ppm; IR (KBr) 2978, 2928, 1735, 1614, 1475, 1368, 1229, 1155, 1037, 935, 845, 749, 701
Representative procedure for enantioselective phase-transfer catalytic alkylation of 8b (Benzylation).

To a methylene chloride solution (1.0 mL) of 2-biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester (8b, 50. mg, 0.15 mmol) were added chiral catalyst 2 (9 mg, 0.015 mmol), CsOH (124 mg, 0.74 mmol) and benzyl bromide (88 µL, 0.74 mmol) at 0 °C and the reaction mixture was stirred (45 min). After completion of the reaction, the reaction mixture was diluted with ethyl acetate (20 mL), washed with brine (2 x 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes:EtOAc = 50:1) to afford 9b (63.1 mg, 99.7% yield) as a pale yellow oil. The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; R (minor) 10.2 min, S (major) 12.7 min.

H-NMR (300 MHz, CDCl₃) δ 7.62~7.59(m, 1H), 7.48~7.20(m, 13H), 3.64~3.60(d, J = 11.5 Hz, 1H), 3.23~3.19(d, J = 11.4 Hz, 1H), 3.34~3.14(dd, J = 48.3 Hz, 2H), 1.15(s, 9H) ppm; C-NMR (100 MH, CDCl₃) δ 170.9, 169.8, 140.8, 139.8, 135.7, 132.8, 130.5, 129.9, 129.0, 127.8, 127.6, 127.1, 126.9, 126.5, 88.2, 81.7, 77.2, 42.3, 40.3, 27.6 ppm; IR (KBr) 2976, 2926, 1730, 1601, 1453, 1368, 1254, 1155, 940, 846, 747, 701 cm⁻¹; MS (FAB): 430 [M+H]⁺; HRMS (FAB): calcd for [C₂₇H₂₈NO₅S]⁺ 430.1841, found 430.1842.
Acidic hydrolysis of 9b for (S)-α- benzylcysteine.

4-Benzyl-2-(2-biphenyl)-4,5-dihydro-oxazole-4-carboxylic acid tert-butyl ester (9b) (452 mg, 1.21 mmol) was added to 6N-HCl (4 mL) and the reaction mixture was refluxed (24 h). After completion of the reaction, the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (5 mL x 2). The combined ethyl acetate was concentrated to give pure 2-biphenylcarboxylic acid (13, 196 mg, 97% yield). The aqueous layer was concentrated and purified through DOWEX 50WX8-100 column eluting with 15% NH₄OH to give (S)-α-benzylcysteine (218 mg, 97% yield) as a white solid.

Characterization of enantioselective phase-transfer catalytic alkylation products.

Entry a in Table 1; [9a-a, R = hexyl]

1H-NMR (300 MHz, CDCl₃) δ 7.83~7.81(m, 2H), 7.47~7.34(m, 3H), 3.81~3.77(d, J = 11.4 Hz, 1H), 3.29~3.26(d, J = 11.3 Hz, 1H), 2.00~1.94(m, 2H), 1.47(s, 9H), 1.24~0.43(m, 8H), 0.83~0.87(m, 3H) ppm; 13C-NMR (100 MHz, CDCl₃) δ 171.9, 167.5, 133.3, 131.3, 128.6, 128.4, 89.2, 81.7, 40.0, 38.3, 31.6, 29.5, 28.0, 24.5, 22.6, 14.1 ppm; IR (KBr) 2927, 2857, 1725, 1604, 1454, 1368, 1254, 1150, 940, 848, 767 cm⁻¹; MS (FAB): 348 [M+H]+; HRMS (FAB): calcd for [C₂₀H₃₀NO₂S]⁺ 348.1997, found 348.1989.

Entry b in Table 1; [9a-β, R = allyl]

1H-NMR (300 MHz, CDCl₃) δ 7.86~7.82(m, 2H), 7.46~7.33(m, 3H), 5.89~5.75(m, 1H), 5.19~5.11(m, 2H), 3.79~3.75(d, J = 11.3 Hz, 1H), 3.34~3.30(d, J = 11.6 Hz, 1H), 2.66~2.79(m, 2H), 1.47(s, 9H) ppm; 13C-NMR (100 MHz, CD₃Cl₃) δ 171.1, 168.1,133.0,
132.6, 131.3, 128.5, 128.3, 119.1, 88.3, 81.9, 42.0, 38.9, 27.9 ppm; IR (KBr) 2977, 1727, 1602, 1448, 1368, 1250, 1151, 943, 846, 767, 690, 614 cm⁻¹; MS (FAB): 304 [M+H]⁺; HRMS (FAB): calcd for [C₁₇H₂₂NO₂S]⁺ 304.1371, found 304.1372.

**Entry c in Table 1; [9a-c, R = 2-methyl-allyl]**

¹H-NMR (300 MHz, CDCl₃) δ 7.84~7.83(m, 2H), 7.48~7.35(m, 3H), 4.90~4.82(m, 2H), 3.82~3.78(d, J = 11.4 Hz, 1H), 3.42~3.38(d, J = 11.3 Hz, 1H), 2.80~2.70(dd, J = 18.5 Hz, 2H), 1.80(s, 3H), 1.47(s, 9H) ppm; ¹³C-NMR (100 MHz, CDCl₃) δ 171.3, 167.6, 141.5, 133.2, 131.3, 128.5, 128.3, 115.1, 88.5, 81.9, 45.3, 39.6, 27.9, 23.9 ppm; IR (KBr) 2977, 1725, 1602, 1449, 1368, 1252, 1156, 943, 846, 767, 690 cm⁻¹; MS (FAB): 318 [M+H]⁺; HRMS (FAB): calcd for [C₁₈H₂₄NO₂S]⁺ 318.1528, found 318.1528.

**Entry d in Table 1; [9a-d, R = propargyl]**

¹H-NMR (300 MHz, CDCl₃) δ 7.86~7.82(m, 2H), 7.48~7.35(m, 3H), 3.96~3.92(d, J = 11.6 Hz, 1H), 3.58~3.54(d, J = 11.7 Hz, 1H), 2.99~2.98(dd, J = 16.6 Hz, 1H), 2.79~2.73(dd, J = 16.56 Hz, 1H), 2.03~2.01(t, J = 2.6 Hz, 1H), 1.50(s, 9H) ppm; ¹³C-NMR (100 MHz, CD₃Cl₃) δ 169.6, 169.5, 132.7, 131.5, 128.5, 128.3, 87.6, 82.4, 79.2, 71.1, 38.4, 27.8, 27.0 ppm; IR (KBr) 3298, 2977, 1731, 1599, 1369, 1320, 1245, 1156, 947, 844, 767, 618 cm⁻¹; MS (FAB): 302 [M+H]⁺; HRMS (FAB): calcd for [C₁₇H₂₀NO₂]⁺ 302.1215 found 302.1212.

**Entry f in Table 1; [9a-f, R = 4-cyanobenzyl]**
$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.83~7.81(d, $J = 7.2$ Hz, 2H), 7.75~7.50(d, $J = 8.0$ Hz, 2H), 7.47~7.36(m, 5H), 3.77~3.74(d, $J = 11.6$ Hz, 1H), 3.37~3.25(dd, $J = 37.8$ Hz, 2H), 3.33~3.30(d, $J = 11.6$ Hz, 1H), 1.39(s, 9H) ppm; $^{13}$C-NMR (100 MHz, CD$_3$Cl$_3$) $\delta$ 170.5, 168.8, 141.7, 132.6, 131.4, 131.4, 131.1, 128.3, 118.7, 110.4, 88.2, 82.2, 77.2, 43.1, 40.0, 27.7 ppm; IR (KBr) 2978, 2227, 1727, 1604, 1447, 1368, 1254, 1153, 944, 847, 768, 617 cm$^{-1}$; MS (FAB): 379 [M+H]$^+$; HRMS (FAB): calcd for [C$_{22}$H$_{23}$N$_2$O$_2$S]$^+$ 379.1480 found 379.1483.

**Entry g in Table 1; [9a-g, R = 4-fluorobenzyl]**

$^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.88~7.83(m, 2H), 7.49~7.36(m, 3H), 7.28~7.23(m, 2H), 6.97~6.89(m, 2H), 3.76~3.72(d, $J = 11.5$ Hz, 1H), 3.35~3.32(d, $J = 11.5$ Hz, 1H), 3.32~3.21(dd, $J = 18.5$ Hz, 2H), 1.42(s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 171.1, 168.5, 133.1, 132.0, 131.9, 131.4, 128.5, 128.4, 114.9, 114.7, 89.0, 82.2, 42.4, 39.6, 27.9 ppm; IR (KBr) 2927, 1726, 1604, 1510, 1368, 1227, 1155, 944, 845, 768, 689 cm$^{-1}$; MS (FAB): 372 [M+H]$^+$; HRMS (FAB): calcd for [C$_{21}$H$_{23}$FNO$_2$S]$^+$ 372.1434 found 372.1445.

**Entry h in Table 1; [9a-h, R = 4-methylbenzyl]**

$^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.89~7.83(m, 2H), 7.48~7.36(m, 3H), 7.16~7.14(dd, $J = 7.9$ Hz, 2H), 7.06~7.03(dd, $J = 7.9$ Hz, 2H), 3.74~3.70(d, $J = 11.5$ Hz, 1H), 3.37~3.34(d, $J = 11.6$ Hz, 1H), 3.31~3.20(dd, $J = 17.9$ Hz, 2H), 2.28(s, 3H), 1.44(s, 9H) ppm; $^{13}$C-NMR (100 MHz, CD$_3$Cl$_3$) $\delta$ 171.1, 168.1, 136.2, 133.1, 132.8, 131.2, 130.3, 128.7, 128.4, 128.27, 89.2, 81.9, 42.5, 39.0, 27.8, 21.0 ppm; IR (KBr) 2925, 1726, 1601, 1448, 1368, 1252, 1154,
944, 845, 690, 618 cm\(^{-1}\); MS (FAB): 368 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{22}H_{26}NO_2S\)]\(^+\) 368.1684 found 368.1679.

Entry i in Table 1; [9\(a\)-i, R = 2-naphthylmethyl]

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.88~7.85(m, 2H), 7.79~7.70(m, 4H), 7.50~7.37(m, 6H), 3.79~3.75(d, \(J = 11.5\) Hz, 1H), 3.48(s, 2H), 3.45~3.41(d, \(J = 11.6\) Hz, 1H), 1.44(s, 9H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.1, 168.4, 133.7, 133.2, 133.1, 132.3, 131.3, 129.1, 128.7, 128.5, 128.3, 127.5, 127.5, 127.5, 125.8, 125.5, 89.3, 82.1, 43.1, 39.3, 27.9 ppm; IR (KBr) 2976, 1726, 1602, 1367, 1251, 1153, 944, 848, 761, 689, 615 cm\(^{-1}\); MS (FAB): 404 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{25}H_{26}NO_2S\)]\(^+\) 404.1684 found 404.1681.

Characterization of alkylated methyl ester used for the determination of enantioselectivity.

4-Hexyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.85~7.83(m, 2H), 7.46~7.36(m, 3H), 3.89~3.86(d, \(J = 11.6\) Hz, 1H), 3.78(s, 3H), 3.33~3.31(d, \(J = 11.2\) Hz, 1H), 2.01~1.97(m, 2H), 1.45~1.25(m, 8H), 0.86~0.83(t, \(J = 6.6\) Hz, 3H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.6, 168.1, 132.9, 131.4, 128.5, 128.4, 88.7, 52.7, 39.6, 38.3, 31.5, 29.3, 24.3, 22.5, 14.0 ppm; IR (KBr) 2926, 2856, 1735, 1603, 1448, 1254, 1034, 941, 768, 690 cm\(^{-1}\); MS (FAB): 306 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{17}H_{24}NO_2S\)]\(^+\) 306.1528 found 306.1519.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H,
hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 7.3 min, R (major) 8.7 min.

4-Allyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$^1$H-NMR (300 MHz, CDCl$_3$) δ 7.86~7.82(m, 2H), 7.49~7.36(m, 3H), 5.85~5.71(m, 1H), 5.21~5.13(m, 2H), 3.88~3.84(d, $J = 11.6$ Hz, 1H), 3.79(s, 3H), 3.40~3.36(d, $J = 11.5$ Hz, 1H), 2.76~2.73(m, 2H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 172.7, 168.9, 132.7, 132.0, 131.5, 128.4, 128.3, 119.5, 88.0, 52.7, 42.0, 38.5 ppm; IR (KBr) 2951, 1737, 1601, 1491, 1442, 1316, 1232, 1146, 998, 943, 818, 768, 690 cm$^{-1}$; MS (FAB): 262 [M+H]$^+$; HRMS (FAB): calcd for [C$_{14}$H$_{16}$NO$_2$S]$^+$ 262.0902 found 262.0906.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 9.5 min, R (major) 13.2 min.

4-(2-Methyl-allyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$^1$H-NMR (300 MHz, CDCl$_3$) δ 7.86~7.83(m, 2H), 7.48~7.35(m, 3H), 4.91~4.80(m, 2H), 3.91~3.87(d, $J = 11.6$ Hz, 1H), 3.78(s, 3H), 3.49~3.45(d, $J = 11.5$ Hz, 1H), 2.81~2.71(dd, $J = 19.0$ Hz, 2H), 1.77(s, 3H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 172.90, 168.22, 140.87, 132.76, 131.37, 128.37, 128.29, 115.49, 88.15, 52.57, 45.36, 38.88, 23.52 ppm; IR (KBr) 2950, 1735, 1645, 1601, 1492, 1444, 1232, 1073, 944, 900, 768, 690 cm$^{-1}$; MS (FAB): 276 [M+H]$^+$; HRMS (FAB): calcd for [C$_{15}$H$_{18}$NO$_2$S]$^+$ 276.1058 found 276.1053.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H,
hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 8.3 min, R (major) 11.4 min.

**2-Phenyl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester**

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.85~7.81(m, 2H), 7.49~7.35(m, 3H), 4.07~4.03(d, \(J = 11.7\) Hz, 1H), 3.83(s, 3H), 3.63~3.59(d, \(J = 11.7\) Hz, 1H), 3.03~2.96(dd, \(J = 16.7\) Hz, 1H), 2.82~2.76(dd, \(J = 16.7\) Hz, 1H), 2.05~2.03(t, \(J = 2.7\) Hz, 1H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.2, 170.2, 132.3, 131.6, 128.4, 128.3, 87.1, 78.6, 71.4, 53.0, 38.3, 27.0 ppm; IR (KBr) 3293, 2952, 1740, 1599, 1442, 1317, 1232, 1067, 948, 768, 689 cm\(^{-1}\); MS (FAB): 260 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{14}\)H\(_{14}\)NO\(_2\)S]\(^+\)260.0745 found 260.0747.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, hexanes:2-propanol = 95:5), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 9.6 min, R (major) 19.5 min.

**4-(4-Cyano-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester**

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.83~7.80(m, 2H), 7.55~7.52(d, \(J = 8.2\) Hz, 2H), 7.50~7.38(m, 3H), 7.36~7.33(d, \(J = 8.3\) Hz, 2H), 3.84~3.80(d, \(J = 11.7\) Hz, 1H), 3.75(s, 3H), 3.44~3.26(dd, \(J = 39.5\) Hz, 2H), 3.39~3.35(d, \(J = 11.7\) Hz, 1H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.5, 169.2, 141.3, 132.4, 131.8, 131.1, 128.5, 128.4, 118.7, 110.8, 88.1, 52.9, 43.3, 39.6 ppm; IR (KBr) 2925, 2852, 2227, 1736, 1603, 1505, 1442, 1235, 1057, 944, 852, 768, 691 cm\(^{-1}\); MS (FAB): 337 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{19}\)H\(_{17}\)N\(_2\)O\(_2\)S]\(^+\)337.1011 found 337.1007.
The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 42.8 min, R (major) 45.2 min.

4-(4-Fluoro-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$^1$H-NMR (400 MHz, CDCl$_3$) δ 7.88~7.86(m, 2H), 7.53~7.50(m, 1H), 7.46~7.42(m, 2H), 7.23~7.20(m, 2H), 7.00~6.95(m, 2H), 3.86~3.83(d, $J$ = 11.6 Hz, 1H), 3.80(s, 3H), 3.44~3.41(d, $J$ = 11.6 Hz, 1H), 3.36~3.27(dd, $J$ = 22.8 Hz, 2H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 172.9, 169.3, 132.7, 131.8, 131.7, 131.6, 131.2, 128.5, 115.2, 115.0, 88.8, 52.8, 42.5, 38.9 ppm; IR (KBr) 2925, 2853, 1737, 1603, 1510, 1443, 1226, 1102, 945, 841, 768, 690 cm$^{-1}$; MS (FAB): 330 [M+H]$^+$; HRMS (FAB): calcd for [C$_{18}$H$_{17}$FNO$_2$S]$^+$ 330.0964 found 330.0955.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; S (minor) 14.1 min, R (major) 15.4 min.

4-(4-Methyl-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$^1$H-NMR (400 MHz, CDCl$_3$) δ 7.89~7.87(m, 2H), 7.53~7.42(m, 3H), 7.14~7.09(m, 4H), 3.85~3.82(d, $J$ = 12.0 Hz, 1H), 3.81(s, 3H), 3.47~3.45(d, $J$ = 11.6 Hz, 1H), 3.35~3.26(dd, $J$ = 21.2 Hz, 2H), 2.33(s, 3H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 172.8, 168.8, 136.5, 132.8, 132.3, 131.4, 130.0, 128.9, 128.4, 128.3, 89.0, 52.6, 42.6, 38.4, 21.0 ppm; IR (KBr) 2924, 2853, 1737, 1600, 1514, 1444, 1230, 1114, 1057, 944, 824, 768, 690 690 cm$^{-1}$; MS
(FAB): 326 [M+H]^+; HRMS (FAB): calcd for [C_{19}H_{20}NO_2S]^+ 326.1215 found 326.1223.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, \( \lambda = 254 \) nm, retention time; \( S \) (minor) 13.9 min, \( R \) (major) 17.6 min.

4-Naphthalen-2-ylmethyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.86~7.83(m, 2H), 7.80~7.71(m, 3H), 7.66(s, 1H), 7.50~7.33(m, 6H), 3.85~3.81(d, \( J = 11.6 \) Hz, 1H), 3.77(s, 3H), 3.51~3.47(d, \( J = 11.5 \) Hz, 1H), 3.48(s, 2H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) 172.8, 169.1, 133.1, 133.0, 132.7, 132.3, 131.4, 129.0, 128.4, 128.3, 128.2, 127.6, 127.5, 127.4, 125.8, 125.5, 88.9, 52.6, 43.1, 38.6 ppm; IR (KBr) 3056, 2925, 1736, 1600, 1442, 1231, 1061, 945, 858, 821, 767, 690 cm\(^{-1}\); MS (FAB): 362 [M+H]^+; HRMS (FAB): calcd for [C\(_{22}\)H\(_{20}\)NO\(_2\)S]\(^+\) 362.1215 found 362.1220.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, \( \lambda = 254 \) nm, retention time; \( S \) (minor) 19.2 min, \( R \) (major) 26.6 min.

**Characterization of Alkylation Products.**

**Entry a in Table 2; [9b-a, \( R = \) allyl]**

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.66~7.58(m, 1H), 7.47~7.33(m, 8H), 5.76~5.62(m, 1H), 5.16~5.10(m, 2H), 3.67~3.63(d, \( J = 11.3 \) Hz, 1H), 3.19~3.16(d, \( J = 11.3 \) Hz, 1H),
2.70–2.57 (m, 2H), 1.48 (s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 171.0, 169.9, 140.9, 140.2, 133.0, 132.6, 130.2, 130.0, 129.2, 129.1, 127.9, 127.4, 127.1, 119.1, 87.7, 82.0, 41.5, 40.3, 27.9 ppm; IR (KBr) 2926, 2854, 1730, 1600, 1453, 1368, 1252, 1160, 992, 937, 847, 754, 701 cm$^{-1}$; MS (FAB): 380 [M+H]$^+$; HRMS (FAB): calcd for [C$_{23}$H$_{26}$NO$_2$S]$^+$ 380.1684 found 380.1686.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; $R$ (minor) 9.5 min, $S$ (major) 11.2 min.

**Entry b in Table 2; [9b-b, $R$ = 2-methallyl]**

$^1$H-NMR (300 MHz, CDCl$_3$) δ 7.64–7.61 (m, 1H), 7.46–7.34 (m, 8H), 4.90–4.79 (m, 2H), 3.72–3.68 (d, $J$ = 11.6 Hz, 1H), 3.27–3.23 (d, $J$ = 11.3 Hz, 1H), 2.75–2.63 (dd, $J$ = 21.8 Hz, 2H), 1.77 (s, 3H), 1.49 (s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 170.9, 169.1, 141.0, 140.8, 140.0, 133.0, 130.0, 129.8, 129.1, 128.9, 128.5, 128.3, 127.7, 127.3, 127.0, 114.9, 87.5, 81.7, 44.4, 40.7, 27.7, 23.6 ppm; IR (KBr) 2977, 1724, 1616, 1451, 1368, 1244, 1156, 939, 847, 753, 700 cm$^{-1}$; MS (FAB): 394 [M+H]$^+$; HRMS (FAB): calcd for [C$_{24}$H$_{28}$NO$_2$S]$^+$ 394.1841, found 394.1838.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; $R$ (minor) 8.5 min, $S$ (major) 11.0 min.

**Entry c in Table 2; [9b-c, $R$ = propargyl]**
$^1$H-NMR (300 MHz, CDCl$_3$) δ 7.66~7.58 (m, 1H), 7.47~7.33 (m, 8H), 3.83~3.79 (d, $J = 11.6$ Hz, 1H), 3.41~3.37 (d, $J = 11.6$ Hz, 1H), 2.82~2.76 (dd, $J = 16.5$ Hz, 1H), 2.68~2.62 (dd, $J = 16.5$ Hz, 1H), 2.03~2.01 (t, $J = 2.7$ Hz, 1H), 1.49 (s, 9H) ppm; $^{13}$C-NMR (75 MHz, CD$_3$Cl$_3$) δ 171.5, 169.5, 141.0, 140.1, 132.6, 130.2, 130.2, 129.3, 129.2, 128.0, 127.5, 127.2, 86.9, 82.5, 79.2, 71.1, 30.9, 27.9, 26.4 ppm; IR (KBr) 3294, 2926, 1732, 1602, 1475, 1368, 1240, 1157, 1067, 942, 845, 754, 701 cm$^{-1}$; MS (FAB): 378 [M+H]$^+$; HRMS (FAB): calcd for [C$_{23}$H$_{24}$NO$_2$S]$^+$ 378.1528, found 378.1527.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; $R$ (minor) 11.2 min, $S$ (major) 13.3 min.

**Entry e in Table 2; [9b-e, R = 4-cyanobenzyl]**

$^1$H-NMR (300 MHz, CDCl$_3$) δ 7.66~7.57 (m, 1H), 7.52~7.17 (m, 12H), 3.67~3.63 (d, $J = 11.5$ Hz, 1H), 3.32~3.08 (dd, $J = 60.2$ Hz, 2H), 3.20~3.16 (d, $J = 11.6$ Hz, 1H), 1.38 (s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 170.6, 141.9, 141.1, 140.2, 132.7, 131.6, 131.4, 130.4, 130.2, 129.2, 129.1, 127.9, 127.5, 127.2, 118.9, 110.5, 88.0, 82.5, 43.0, 41.9, 30.8, 27.8 ppm; IR (KBr) 2926, 2227, 1729, 1608, 1474, 1368, 1256, 1152, 940, 846, 753, 701 cm$^{-1}$; MS (FAB): 455 [M+H]$^+$; HRMS (FAB): calcd for [C$_{28}$H$_{27}$N$_2$O$_2$S]$^+$ 455.1793, found 455.1792.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; $R$ (minor) 21.9 min, $S$ (major) 26.6 min.
Entry f in Table 2; [9b-f, R = 4-fluorobenzyl]

$^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.63–7.56 (m, 1H), 7.51–7.28 (m, 8H), 7.18–7.14 (m, 2H), 6.98–6.92 (m, 2H), 3.66–3.62 (d, $J = 11.3$ Hz, 1H), 3.31–3.08 (dd, $J = 56.2$ Hz, 2H), 1.44 (s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 171.1, 170.2, 141.1, 140.1, 133.0, 132.2, 132.1, 131.8, 131.8, 130.3, 130.1, 129.2, 129.2, 127.9, 127.5, 127.1, 114.9, 114.7, 88.4, 82.2, 41.9, 40.9, 27.9 ppm; IR (KBr) 2926, 1729, 1604, 1510, 1368, 1226, 1157, 939, 845, 754, 701 cm$^{-1}$; MS (FAB): 448 [M+H]$^+$; HRMS (FAB): calcd for [C$_{27}$H$_{27}$FNO$_2$S]$^+$ 448.1747, found 448.1744.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, $\lambda = 254$ nm, retention time; $R$ (minor) 12.3 min, $S$ (major) 18.2 min.

Entry g in Table 2; [9b-g, R = 4-methylbenzyl]

$^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.62–7.56 (m, 1H), 7.48–7.22 (m, 9H), 7.13–7.06 (m, 3H), 3.62–3.58 (d, $J = 12.0$ Hz, 1H), 3.32–3.10 (dd, $J = 50.0$ Hz, 2H), 3.22–3.18 (d, $J = 11.3$ Hz), 2.32 (s, 3H), 1.46 (s, 9H) ppm; $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 171.2, 170.0, 141.0, 140.0, 136.2, 133.1, 132.8, 130.5, 130.1, 130.0, 129.2, 129.2, 128.8, 127.8, 127.4, 127.1, 88.5, 82.0, 41.9, 40.3, 27.9, 21.0 ppm; IR (KBr) 2925, 1727, 1611, 1514, 1453, 1368, 1253, 1154, 940, 846, 752, 700 cm$^{-1}$; MS (FAB): 444 [M+H]$^+$; HRMS (FAB): calcd for [C$_{28}$H$_{30}$NO$_2$S]$^+$ 444.1997, found 444.1995.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 99.5:0.5), flow rate = 1.0 mL/min, 23 °C, $\lambda = 254$ nm, retention time; $R$ (minor) 12.3 min, $S$ (major) 18.2 min.
hexanes:2-propanol = 99:1), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; \( R \) (minor) 9.0 min, \( S \) (major) 11.3 min.

**Entry h in Table 2; [9b-\( h \), \( R \) = 2-naphthylmethyl]**

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.84–7.71(m, 4H), 7.64–7.62(m, 1H), 7.47–7.32(m, 6H), 7.28–7.26(m, 2H), 7.21–7.16(m, 1H), 7.07–7.02(m, 2H), 3.70–3.66(d, \( J = 11.4 \) Hz, 1H), 3.59–3.31(dd, \( J = 70.7 \) Hz, 2H), 3.31–3.27(d, \( J = 11.5 \) Hz, 1H), 1.48(s, 9H) ppm; \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) 171.3, 170.4, 141.1, 140.0, 133.6, 133.2, 133.0, 132.4, 130.2, 130.9, 129.4, 129.2, 129.5, 129.1, 127.8, 127.6, 127.6, 127.5, 127.4, 127.2, 125.9, 125.6, 88.6, 82.2, 42.5, 40.4, 27.9 ppm; IR (KBr) 2924, 1726, 1539, 1473, 1368, 1257, 1151, 941, 751, 700 cm\(^{-1}\); MS (FAB): 480 [M+H]\(^+\); HRMS (FAB): calcd for [C\(_{31}\)H\(_{30}\)NO\(_2\)S]\(^+\) 480.1997, found 480.1988.

The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel AD-H, hexanes:2-propanol = 97:3), flow rate = 1.0 mL/min, 23 °C, λ = 254 nm, retention time; \( R \) (minor) 7.8 min, \( S \) (major) 10.0 min.
2-Phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

300MHz, CD$_2$OD

12

2-Phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

100MHz, CD$_2$OD

12
2-Phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

2-Phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃
4-Hexyl-2-phenyl-4,5-dihydro-thiazol-4-carboxylic acid tert-butyl ester

300MHz, CDCl<sub>3</sub>

4-Hexyl-2-phenyl-4,5-dihydro-thiazol-4-carboxylic acid tert-butyl ester

100MHz, CDCl<sub>3</sub>
4-Allyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9a-b

4-Allyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃

9a-b
4-(2-Methyl-allyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9a-c

100MHz, CDCl₃

9a-c
2-Phenyl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9a-d

2-Phenyl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃

9a-d
4-Benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl3

9a-e

4-Benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

125MHz, CDCl3

9a-e
4-(4-Cyano-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

400MHz, CDCl₃

9a-f

4-(4-Cyano-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃

9a-f
4-(4-Fluoro-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9a-g

4-(4-Fluoro-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃

ppm 160 150 140 130 120 110 60 50 40 20

S-29
4-(4-Methyl-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

4-(4-Methyl-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃
4-Naphthalen-1-ylmethyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9a-i

4-Naphthalen-1-ylmethyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃

9a-i
4-Hexyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

- 400MHz, CDCl₃

4-Hexyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

- 100MHz, CDCl₃
4-Allyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

300MHz, CDCl₃

4-Allyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

100MHz, CDCl₃
4-(2-Methyl-allyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

300MHz, CDCl₃

4-(2-Methyl-allyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

100MHz, CDCl₃
4-(2-Methyl-allyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

300MHz, CDCl₃

2-Phenyl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

9a'-d

300MHz, CDCl₃

2-Phenyl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

100MHz, CDCl₃

S-35
4-Benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

1H-NMR (300 MHz, CDCl₃)

9a'-e

4-Benzyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

13C-NMR (125 MHz, CDCl₃)
4-(4-Cyano-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester
300MHz, CDCl₃

4-(4-Cyano-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester
100MHz, CDCl₃
4-(4-Fluoro-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

400MHz, CDCl₃

9a'-g

4-(4-Fluoro-benzyl)-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

100MHz, CDCl₃

S-38
4-(4-Methyl-benzyl)-2-phenyl-
4,5-dihydro-thiazole-4-
carboxylic acid methyl ester

400MHz , CDCl3

9a'-h

4-(4-Methyl-benzyl)-2-phenyl-
4,5-dihydro-thiazole-4-
carboxylic acid methyl ester

100MHz , CDCl3

9a'-h
4-Naphthalen-1-ylmethyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$300\text{MHz, CDCl}_3$

9a'•i

4-Naphthalen-1-ylmethyl-2-phenyl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

$100\text{MHz, CDCl}_3$

9a'•i
4-Biphenyl-2-yl-4-oxo-2-
tritylsulfanylmethyl-
butyric acid methyl ester

300MHz, CDCl₃

15

4-Biphenyl-2-yl-4-oxo-2-
tritylsulfanylmethyl-
butyric acid methyl ester

100MHz, CDCl₃

15
2-Biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

300MHz, CDCl₃

16

2-Biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid methyl ester

125MHz, CDCl₃

16

ppm  120  140  160  180  20  40  60  80  100  120
2-Biphenyl-2-yl-4,5-dihydro-thiazol-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

8b

2-Biphenyl-2-yl-4,5-dihydro-thiazol-4-carboxylic acid tert-butyl ester

125MHz, CDCl₃

8b
4-Allyl-2-biphenyl-2-yl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

$^{300\text{MHz}, \text{CDCl}_3}$

$^{100\text{MHz}, \text{CDCl}_3}$
2-Biphenyl-2-yl-4-(2-methyl-allyl)-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

$\delta$ 300MHz , CDCl$_3$

9b-b

2-Biphenyl-2-yl-4-(2-methyl-allyl)-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

$\delta$ 100MHz , CDCl$_3$

9b-b
9b-c

2-Biphenyl-2-yl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

9b-c

2-Biphenyl-2-yl-4-prop-2-ynyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

75MHz, CDCl₃
9b-d
4-Benzyl-2-biphenyl-2-yl-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester
300MHz, CDCl₃

9b-d
4-Benzyl-2-biphenyl-2-yl-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester
100MHz, CDCl₃
9b-e
2-Biphenyl-2-yl-4-(4-cyano-benzyl)-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester

300MHz, CDCl₃

9b-e
2-Biphenyl-2-yl-4-(4-cyano-benzyl)-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester

100MHz, CDCl₃
2-Biphenyl-2-yl-4-(4-fluoro-benzyl)-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl₃

2-Biphenyl-2-yl-4-(4-fluoro-benzyl)-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl₃
2-Biphenyl-2-yl-4-(4-methyl-benzyl)-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester
300MHz, CDCl3

2-Biphenyl-2-yl-4-(4-methyl-benzyl)-
4,5-dihydro-thiazole-4-
carboxylic acid tert-butyl ester
100MHz, CDCl3
2-Biphenyl-2-yl-4-naphthalen-1-ylmethyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

300MHz, CDCl3

9b-h

2-Biphenyl-2-yl-4-naphthalen-1-ylmethyl-4,5-dihydro-thiazole-4-carboxylic acid tert-butyl ester

100MHz, CDCl3

9b-h
\( \text{\(\text{H}_2\text{N}\_\text{CO}_2\text{H}\)} \)

\( \text{\(\text{SH}\)} \)

\( (R)-\text{o-Benzylcysteine} \)

500MHz, D\(_2\)O

\( \text{\(\text{H}_2\text{N}\_\text{CO}_2\text{H}\)} \)

\( \text{\(\text{SH}\)} \)

\( (R)-\text{o-Benzylcysteine} \)

125MHz, D\(_2\)O