Supporting Information

An easy access to thiazolines and thiazines via tandem S-alkylation-cyclodeamination of thioamides/haloamines

Uma Pathak,* Shubhankar Bhattacharyya, Vishwanath Dhruwansh, Lokesh Kumar Pandey, Rekha Tank and M. V. S. Suryanarayana

Synthetic Chemistry Division, Defence R & D Establishment, Jhansi Road, Gwalior-474002 (M. P.) India.

Contents

1. General details P2
2. Experimental procedure P3
3. Spectroscopic characterization data P4-P5
4. Selected copies of $^1$H, $^{13}$C NMR and Mass spectra P6-P11
1. General details

Reagents were obtained from commercial supplier, and used without further purification. Thioamide for Entry No. 4–12, 14 were prepared by thionation of corresponding amide by reported method. Melting point were measured by scientific-MP-DS melting point apparatus. Column chromatographic purification of products was performed on silica gel (60-120 mesh). $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AVANCE II 400 MHz. Chemical shifts were expressed in parts per millions (δ) downfield from the internal standard tetramethylsilane and were reported as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Mass spectra was obtained in Agilent 5975C GC-MS and Elemental analysis was performed on Elementar vario MICRO cube CHNS analyser.

2. Experimental procedure

(1) General experimental procedure- 250 µl of water was added to 2/3-haloalkylamine salt (5.5 mmol) and mixed thoroughly. To this thioamide (5 mmol) was added and the reaction mixture was heated at 60-70 °C till the reaction is complete. Contents were cooled and neutralized with cold 5% sodium carbonate solution. Yellow oil gets separated which was extracted with ethyl acetate. Solvent removal under vacuum yielded the pure thiazoline/thiazine. If required the compound can be further purified by column chromatography.

(2) Procedure for the preparation of 2-substituted thiazolines and thiazines from electronically deficient thioamides. Water (10-20µl per mmol) was added to an equimolar mixture of thioamide and 2/3-haloalkylamine salt, and mixed thoroughly. Contents were then heated on an oil bath at 90-100°C with constant stirring till the reaction is complete. On completion of the reaction product isolation and purification is done similar to the general experimental procedure.
3. Spectroscopic characterization data

2-Phenyl-5, 6-dihydro-4H-[1, 3]-thiazine (2): Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.75 (m, 2H), 7.42-7.34 (m, 3H), 3.91 (t, 2H, $J_1$=5.6 Hz, $J_2$=5.2 Hz), 3.15 (t, 3H, $J_1$=6.0 Hz), 1.93-1.89 (m, 2H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 158.00, 139.48, 130.19, 128.19, 126.17, 47.93, 26.45, 19.05; EIMS: m/z 177 [M$^+$], 130, 121, 104, 74; Anal. Calcd for C$_{10}$H$_{11}$NS. C, 67.75; H, 6.25; N, 7.90; S, 18.09. Found C, 67.87; H, 6.31; N, 7.94; S, 17.86.

2-(4-Tolyl)-4, 5-dihydro-[1, 3]-thiazole (4): Yellow solid (m.p: 41-42°C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.69 (d, 2H, $J_1$=8.0 Hz), 7.17 (d, 2H, $J_1$=8.0 Hz), 4.41 (t, 2H, $J_1$=8.4 Hz), 3.36 (t, 2H, $J_1$=8.4 Hz), 2.35 (s, 3H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 168.81, 141.66, 130.43, 129.23, 128.37, 64.95, 33.56, 21.53; EIMS: m/z 177 [M$^+$], 118, 60; Anal. Calcd for C$_{10}$H$_{11}$NS. C, 67.75; H, 6.25; N, 7.90; S, 18.09. Found C, 67.86; H, 6.37; N, 7.72; S, 18.03.

2-(4-Methoxy-phenyl)-4, 5-dihydro- [1, 3]-thiazole (5): Pale yellow solid (m.p.: 43-44 °C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78 (dd, 2H, $J_1$=6.8 Hz, $J_2$=2.0 Hz), 6.91 (dd, 2H, $J_1$=6.8 Hz, $J_2$=2.0 Hz), 4.42 (t, 2H, $J_1$=8.4 Hz), 3.84 (s, 3H), 3.39 (t, 2H, $J_1$=8.0, $J_2$=8.4); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 167.99, 161.94, 130.05, 125.77, 113.74, 64.78, 55.30, 33.55; EIMS: m/z 193 [M$^+$], 147, 133, 103, 60; Anal. Calcd for C$_{10}$H$_{11}$NOS. C, 62.15; H, 5.74; N, 7.25; S, 16.59. Found  C, 62.23; H, 5.80; N, 7.15; S, 16.54.

2-(4-Bromo-phenyl)-4, 5-dihydro-[1, 3]-thiazole (6): Colourless solid (m.p.: 90-92 °C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.71-7.68 (m, 2H), 7.56-7.52 (m, 2H), 4.45 (t, 2H, $J_1$=8.4 Hz), 3.43 (t, 2H, $J_1$=8.4 Hz); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 167.67, 131.85, 129.98, 125.83, 123.27, 65.37, 34.30; EIMS: m/z 243 [M$^+$+2], 241 [M$^+$], 102, 75, 60; Anal. Calcd for C$_9$H$_8$BrNS. C, 44.64; H, 3.33; N, 5.78; S, 13.24. Found C, 44.71; H, 3.41; N, 5.63; S, 13.23.

2-(4-Hydroxy-phenyl)-4, 5-dihydro-[1, 3]-thiazole (7): Light yellow solid (m.p.: 198-199 °C); $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.94 (s, 1H, OH), 7.64-7.58 (m, 2H), 6.85-6.80 (m, 2H), 4.30 (t, 2H, $J_1$=8.0 Hz), 3.36 (t, 2H, $J_1$=8.4 Hz); $^{13}$C NMR (100.6 MHz, DMSO-d$_6$) $\delta$ 165.42, 160.16, 129.84, 124.06, 115.21, 64.54, 33.06.; EIMS: m/z 179 [M$^+$], 119, 91, 60.; Anal. Cal. for C$_9$H$_9$NOS. C, 60.31; H, 5.06; N, 7.81; S, 17.89. Found C, 60.43; H, 4.96; N, 7.75; S, 17.91.

2-(3-Nitro-phenyl)-4, 5-dihydro-[1, 3]-thiazole (8): Yellow solid (m.p.: 135-137 °C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (dd, 2H, $J_1$=7.2 Hz, $J_2$=1.6 Hz), 7.60 (t, 1H, $J_1$=8.0 Hz), 4.51 (t, 2H, $J_1$=8.4 Hz), 3.50 (t, 2H, $J_1$=8.4 Hz); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 166.36, 148.24, 134.84, 134.03, 129.59, 125.55, 123.27, 65.37, 34.30; EIMS: m/z 208 [M$^+$], 178, 118, 60; Anal. Calcd for C$_9$H$_8$N$_2$O$_2$S, C, 51.91; H, 3.87; N, 13.45; S, 15.40. Found C, 51.98; H, 3.98; N, 13.58; S, 15.07.

2-(4-Nitro-phenyl)-4, 5-dihydro-[1, 3]-thiazole (9): Yellow solid (m.p.: 150-152 °C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (dd, 2H, $J_1$=7.2 Hz, $J_2$=1.6 Hz), 8.00-7.98 (m, 2H), 4.51 (t, 2H, $J_1$=8.4 Hz), 3.50 (t, 2H, $J_1$=8.4 Hz); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 166.61, 149.22, 138.72, 129.27, 123.71, 65.54, 34.28; EIMS: m/z 208 [M$^+$],
178, 118, 60; Anal. Calcd for C₈H₆N₂O₂S. C, 51.91; H, 3.87; N, 13.45; S, 15.40. Found C, 51.96; H, 3.97; N, 13.35; S, 15.34.

2-(2, 6-Dichloro-phenyl)-4, 5-dihydro-[1, 3]-thiazole (10): Yellow solid (m.p.: 71-72 °C); ¹H NMR (400 MHz, CDCl₃): δ 7.27-7.16 (m, 3H), 4.42 (d, 2H, J=8 Hz), 3.48 (d, 2H, J=8 Hz); ¹³C NMR (100.6 MHz, CDCl₃) δ 163.65, 133.49, 132.40, 130.56, 127.80, 64.86, 34.97; EIMS: 231 [M⁺], 185, 171, 150, 136, 123, 109, 100, 75, 60.; Anal. calc. for C₉H₇Cl₂NS. C, 46.57; H, 3.04; N, 6.03; S, 13.81. Found C, 46.68; H, 2.91; N, 5.93; S, 13.91.

2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11): Yellow oil; ¹H NMR (400 MHz, CDCl₃): δ 7.45-7.41 (m, 2H), 7.07-7.05 (m, 1H), 4.40 (t, 2H, J=8.4 Hz), 3.44 (t, 2H, J=8.0 Hz); ¹³C NMR (100.6 MHz, CDCl₃) δ 161.61, 137.04, 130.75, 129.66, 127.54, 64.70, 34.44; EIMS: m/z 169 [M⁺], 123, 108, 60; Anal. Calcd for C₇H₇NS₂. C, 49.67; H, 4.17; N, 8.27; S, 37.89. Found C, 49.81; H, 4.67; N, 8.34; S, 37.16

2-Thiophen-3-yl-5,6-dihydro-4H-[1, 3]-thiazine (12): Yellow oil; ¹H NMR (400 MHz, CDCl₃): δ 7.44 (d, 1H, J=3.6 Hz), 7.35 (d, 1H, J=5.2 Hz), 7.02-7.00 (m, 1H), 3.86 (t, 2H, J=5.6 Hz), 3.14 (t, 2H, J=6.0 Hz), 1.95-1.89 (m, 2H); ¹³C NMR (100.6 MHz, CDCl₃) δ: 152.01, 144.30, 128.00, 127.12, 126.12, 47.69, 26.36, 19.61; EIMS: m/z 183 [M⁺], 136, 127, 110, 74; Anal. Calcd for C₈H₉NS₂. C, 52.42; H, 4.95; N, 7.64; S, 34.99. Found C, 52.54; H, 5.07; N, 7.77; S, 34.61

3-(4, 5-Dihydrothiazol-2-yl)-pyridine (13): Yellow solid (m.p.: 111-113 °C); ¹H NMR (400 MHz, CDCl₃): δ 9.04 (s, 1H), 8.68 (d, 1H, J=4.4 Hz), 8.13 (dt, 1H, J₁=8.0 Hz, J₂=1.6 Hz), 7.38 (dd, 1H, J₁=8.0 Hz, J₂=4.8 Hz), 4.48 (t, 2H, J=8.4 Hz), 3.46 (t, 2H, J=8.4 Hz); ¹³C NMR (100.6 MHz, CDCl₃) δ 165.67, 151.30, 148.87, 135.96, 129.24, 123.57, 65.11, 33.91; EIMS: m/z 164 [M⁺], 118, 105, 60; Anal. Calcd for C₈H₈N₂S. C, 58.51; H, 4.91; N, 17.06; S, 19.53. Found C, 58.59; H, 4.95; N, 17.09; S, 19.36.

2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14): Yellow oil; ¹H NMR (400 MHz, CDCl₃): δ 3.64 (t, 2H, J=4.0 Hz), 3.00 (t, 2H, J=8.0 Hz), 1.88-1.80 (m, 2H), 1.79-1.76 (m, 4H), 1.47-1.33 (m, 2H), 1.31-1.21 (m, 4H); ¹³C NMR (100.6 MHz, CDCl₃) δ 165.74, 50.49, 47.23, 31.20, 26.33, 26.23, 25.92, 19.45; EIMS: 183 [M⁺], 155, 142, 128, 115, 100, 83, 74, 55.; Anal. Calcd for C₁₀H₁₇NS. C, 65.52; H, 9.35; N, 7.64; S, 17.49. Found C, 65.63; H, 9.26; N, 7.55; S, 17.54.

2-amino-4, 5-dihydro-[1, 3]-thiazole (15): Yellow solid (m.p.: 80-82 °C); ¹H NMR (400 MHz, DMSO-d₆) δ 6.22 (s, br, 2H, NH₂), 3.77 (t, 2H, J=7.6 Hz), 3.21 (t, 2H, J=7.6 Hz); ¹³C NMR (100.6 MHz, DMSO-d₆) δ 159.84, 60.07, 35.04. EIMS: 102 [M⁺], 74, 60. Anal. Calcd for C₃H₆N₂S. C, 35.27; H, 5.92; N, 27.42; S, 31.39. Found C, 35.35; H, 5.80; N, 27.51; S, 31.32.
4. Selected copies of $^1$H NMR and $^{13}$C NMR

(i) $^1$H NMR spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)

(ii) $^{13}$C NMR spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)

(iii) Mass spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)

(iv) $^1$H NMR spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)

(v) $^{13}$C NMR spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)

(vi) Mass spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)

(vii) $^1$H NMR spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)

(viii) $^{13}$C NMR spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)

(ix) Mass spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)
$^1$H NMR spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)

$^{13}$C NMR spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)
Mass spectra of 2-Thiophen-3-yl-4, 5-dihydro-[1, 3]-thiazole (11)

$^1$H NMR spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)
$^{13}$C NMR spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)

Mass spectra of 2-Thiophen-3-yl-5, 6-dihydro-4H-[1, 3]-thiazine (12)
$^1$H NMR spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)

$^{13}$C NMR spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)
Mass spectra of 2-Cyclohexyl-5, 6-dihydro-4H-[1, 3]-thiazine (14)