Supporting Information

Dithiocarbamates strongly inhibit carbonic anhydrases and show antiglaucoma action in vivo[#]

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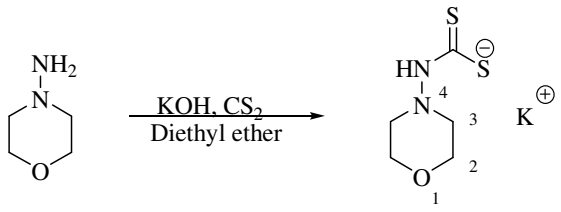
Detailed experimental and spectral data for the compounds reported in the paper are provided.

Synthesis of potassium morpholinocarbamodithioate **2a**

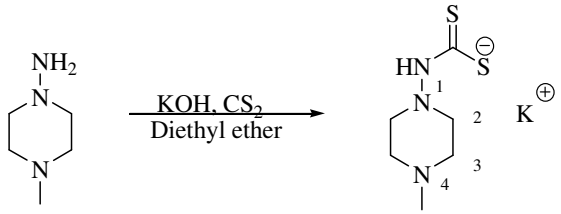


2 **2a**

Morpholin-4-amine **2** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t. and the precipitated formed collected by filtration, washed with diethyl ether and dried under *vacuo* to give the title compound as a pale yellow solid in 75 % yield.

Potassium morpholinocarbamodithioate **2a**: ν_{max} (KBr) cm^{-1}, 2960, 2890, 1648, 1598, 1520, 1430, 1190; δ_H (400 MHz, DMSO-*d*$_6$) 2.78 (4H, m, 2 x 3-H_2), 3.60 (4H, m, 2 x 2-H_2), 8.62 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-*d*$_6$) 55.0 (C-3), 66.9 (C-2), 213.4 (*C*=S); *m/z* (ESI), 177 $[M-Na]^-$.

Synthesis of potassium 4-methylpiperazin-1-ylcarbamodithioate **3a**

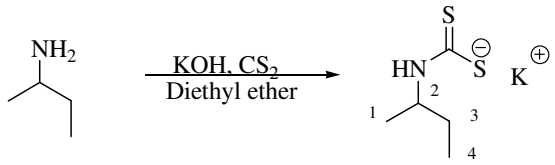


3 **3a**

4-Methylpiperazin-1-amine **3** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t. and the precipitated formed collected by filtration, washed with diethyl ether and dried under *vacuo* to give the title compound as a white solid in 66 % yield.

4-Methylpiperazin-1-ylcarbamodithioate **3a**: ν_{max} (KBr) cm^{-1}, 2954, 1630, 1597, 1520, 1424; δ_H (400 MHz, DMSO-*d*$_6$) 2.26 (3H, s, CH_3), 2.49 (4H, m, 2 x 3-H_2), 2.81 (4H, m, 2 x 2-H_2), 8.65 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-*d*$_6$) 46.4 (*C*H_3), 54.1, 55.2, 213.4 (*C*=S); *m/z* (ESI), 190 $[M-Na]^-$.

Synthesis of (±) potassium *sec*-butylcarbamodithioate **4a**

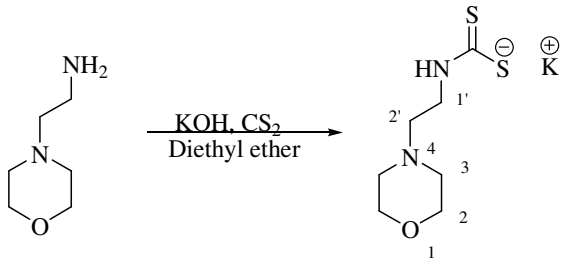


4 **4a**

(±) *sec*-Butylamine **4** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t.. The solvent was evaporated in *vacuo* to give a yellow residue that was dispersed in MeOH (15ml) filtered through Celite, the filtrated was concentrated in *vacuo* to afford the titled compound as a yellow semisolid in 65 % yield.

(±) Potassium *sec*-butylcarbamodithioate **4a**: ν_{max} (KBr) cm^{-1}, 2947, 2892, 1650, 1600, 1520, 1421, 1190; δ_H (400 MHz, DMSO-d_6) 0.86 (3H, t, *J* 6.7, 4-CH_3), 1.16 (3H, d, *J* 6.6, 1-CH_3), 1.20-1.60 (2H, m, 3-H_2), 4.30 (1H, m, 2-H), 7.68 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 11.5, 20.3, 29.4, 53.4, 214.7 (*C*=S); *m/z* (ESI), 148 $[M\text{-}Na]^-$.

Synthesis of potassium 2'-morpholinoethylcarbamodithioate **5a**

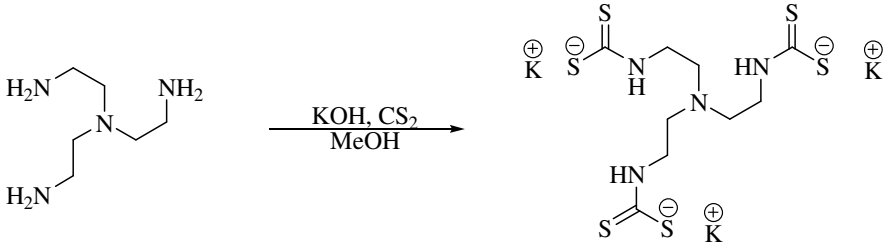


5 **5a**

2-Morpholinoethanamine **5** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t.. The solvent was evaporated in *vacuo* to give a pale yellow residue that was suspended in MeOH (15ml) filtered through Celite, the filtrated was concentrated in *vacuo* to afford a sticky solid that was triturated from DCM to afford the titled compound as a light brown solid in 58 % yield.

Potassium 2'-morpholinoethylcarbamodithioate **5a**: ν_{max} (KBr) cm^{-1}, 2970, 2888, 1650, 1600, 1520; δ_H (400 MHz, DMSO-d_6) 2.41 (6H, m, 2x 2-H_2, 2'-H_2), 3.52 (2H, m, 1'-H_2), 3.60 (4H, m, 3-H_2), 7.78 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 44.1, 54.2, 57.7, 67.1, 215.7 (*C*=S); *m/z* (ESI), 205 $[M\text{-}Na]^-$.

Synthesis of potassium 2,2',2''-nitrilotris(ethane-2,1-diyl)tricarbamodithioate **6a**

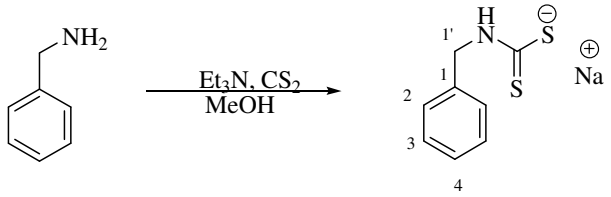


6 **6a**

N_1,N_1-bis(2-Aminoethyl)ethane-1,2-diamine **6** (0.5 g, 1.0 eq) was treated with powdered KOH (3.05 eq) in MeOH (50 ml) followed by addition of carbon disulfide (3.05 eq) at 0°C. The mixture was warmed to r.t. and stirred for 1.5h. The solution was filtered through Celite and the filtrate was concentrated in *vacuo* to give a solid that was triturated from DCM to afford the titled compound as a pale yellow solid in 59% yield.

Potassium 2,2',2''-nitrilotris(ethane-2,1-diyl)tricarbamodithioate **6a** ν_{max} (KBr) cm^{-1}, 2962, 2880, 1653, 1594, 1517, 1452; δ_H (400 MHz, DMSO-d_6) 2.60-2.90 (12H, m), 7.67 (1H,brs, exchange with D_2O, N-*H*), 7.92 (1H,brs, exchange with D_2O, N-*H*), 8.37 (1H,brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 45.24, 53.7, 215.5 (*C*=S); *m/z* (ESI), 371 $[M-Na]^-$.

Synthesis of sodium benzylcarbamodithioate **7a**

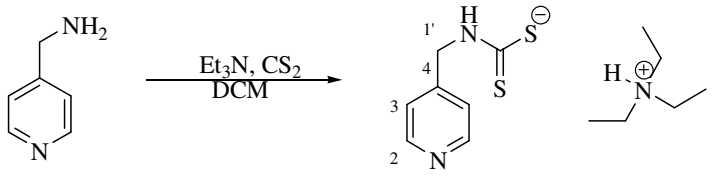


7 **7a**

Benzylamine **7** (0.5 g, 1.0 eq) was treated with NaOH (1.0 eq) in MeOH (20 ml) followed by addition of carbon disulfide (1.0 eq) at 0°C. The mixture was warmed to r.t. and stirred 7h. at r.t.. The solvent was removed in *vacuo* and the residue obtained was triturated from DCM, collected by filtration, dissolved in MeOH and filtered through Celite. The filtrate was concentrated under *vacuo* to give a solid that was triturated from diethyl ether to afford the titled compound as a pale yellow solid in 17 % yield.

Sodium benzylcarbamodithioate **7a:** ν_{max} (KBr) cm^{-1}, 2961, 2892, 1648, 1580, 1521, 1450; δ_H (400 MHz, DMSO-d_6) 4.75 (2H, d, *J* 6.6, 1'-H_2), 7.18-7.25 (5H, m, Ar-H), 8.42 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 50.5, 127.0, 128.3, 128.6, 141.5, 216.3 (*C*=S); *m/z* (ESI), 182 $[M-Na]^-$.

Synthesis of triethylammonium pyridin-4-ylmethylcarbamodithioate **8a**

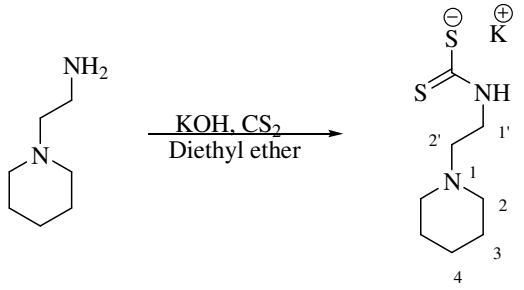


8 **8a**

Pyridin-4-ylmethanamine **8** (0.5 g, 1.0 eq) was treated with triethylamine (1.0 eq) in DCM (20 ml) followed by addition of carbon disulfide (1.0 eq) at 0°C. The mixture was warmed to r.t. and stirred 2h. at r.t.. The solvent was removed in *vacuo* and the residue dissolved in MeOH filtered through Celite, concentrated in *vacuo* to afford the titled compound as a light brown solid in 74 % yield.

Triethylammonium pyridin-4-ylmethylcarbamodithioate **8a:** ν_{max} (KBr) cm^{-1}, 2960, 2884, 1650, 1578, 1518, 1449; δ_H (400 MHz, DMSO-d_6) 1.22 (9H, t, *J* 7.4, 3x CH_2CH_3), 3.14 (6H, q, *J* 7.4, 3x CH_2CH_3), 4.74 (2H, d, *J* 6.4, 1'-H_2), 7.25 (2H, d, *J* 6.0, Ar-H), 8.46 (2H, d, *J* 6.0, Ar-H), 8.70 (1H, brs, exchange with D_2O, N-*H*), 9.18 (1H, brs, exchange with D_2O, $(CH_3CH_2)_3N^+$-*H*); δ_C (100 MHz, DMSO-d_6) 9.6, 46.6, 49.7, 123.3, 149.9, 150.5, 216.7 (*C*=S); *m/z* (ESI), 183 $[M-Na]^-$.

Synthesis of potassium 2'-(piperidin-1-yl)ethylcarbamodithioate **9a**

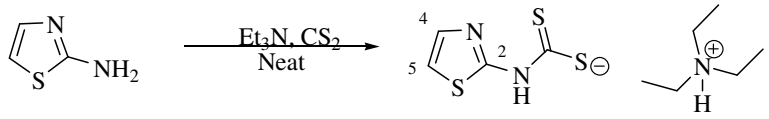


9 **9a**

2'-(Piperidin-1-yl)ethanamine **9** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t.. The solvent was evaporated in *vacuo* to give a pale yellow residue that was suspended in MeOH (15ml) filtered through Celite, the filtrated was concentrated in *vacuo* to afford a sticky solid that was triturated from DCM to afford the titled compound as a pale yellow solid in 65 % yield.

Potassium 2'-(piperidin-1-yl)ethylcarbamodithioate **9a**: ν_{max} (KBr) cm^{-1}, 2976, 2894, 1656, 1520; δ_H (400 MHz, DMSO-d_6) 1.42 (2H, m, 4-H_2), 1.53 (4H, m, 2x 3-H_2), 2.40 (6H, m, 2x 2-H_2, 2'-H_2), 3.48 (4H, m, 1'-H_2), 7.72 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 25.0, 26.4. 44.4, 54.9, 57.9, 215.7 (*C*=S); *m/z* (ESI), 203 $[M\text{-}Na]^-$.

Synthesis of triethylammonium thiazol-2-ylcarbamodithioate **10a**

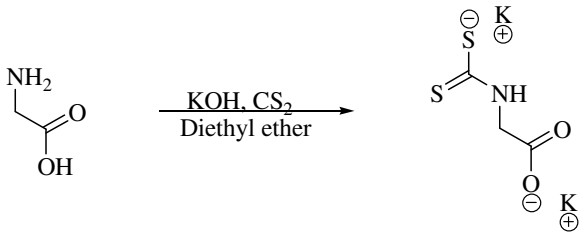


10 **10a**

2-Aminothiazole **10** (0.5 g, 1.0 eq) was treated with triethylamine (1.0 eq) followed by addition of carbon disulfide (1.0 eq) at 0°C. The mixture was warmed to r.t. and stirred O.N. at r.t. and 100°C for 1h. Then the mixture was cooled down to r.t., triturated with diethyl ether to afford the titled compound as a yellow solid in 11 % yield.

Triethylammonium thiazol-2-ylcarbamodithioate **10a:** ν_{max} (KBr) cm^{-1}, 2960, 2892, 1650, 1578, 1519, 1450; δ_H (400 MHz, DMSO-d_6) 1.21 (9H, t, *J* 7.2, 3x CH_2CH_3), 3.11 (6H, q, *J* 7.4, 3x CH_2CH_3), 6.87 (1H, d, *J* 3.2, Ar-H), 7.34 (1H, d, *J* 3.2, Ar-H), 9.25 (1H, brs, exchange with D_2O, $(CH_3CH_2)_3N^+$-*H*), 10.83 (1H, brs, exchange with D_2O, N-*H*); δ_C (100 MHz, DMSO-d_6) 9.6, 46.5, 111.7, 137.3, 162.6, 213.0 (*C*=S); *m/z* (ESI), 175 $[M\text{-}Na]^-$. These data are in agreement with reported literature data. [30]

Synthesis of potassium 2-(dithiocarboxylatoamino)acetate **11a**

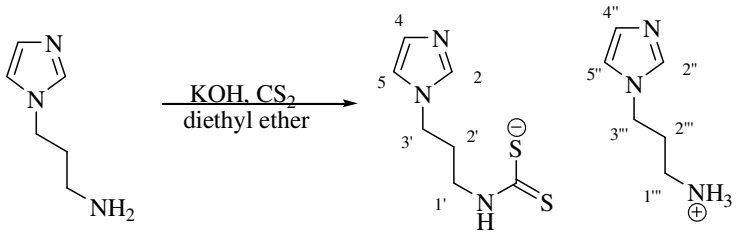


11 **11a**

Glycine **11** (0.5 g, 1.0 eq) was treated with powdered KOH (2.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (2.0 eq). The mixture was stirred at the same temperature for 6h, warmed to r.t.. The solid formed was collected by filtration and triturated from diethyl ether to afford the titled compound as a light-brown solid in 50% yield.

Potassium 2-(dithiocarboxylatoamino)acetate **11a**: ν_{max} (KBr) cm^{-1}, 2962, 2876, 1652, 1600, 1520, 1450; δ_H (400 MHz, DMSO-d_6) 3.52 (2H, d, *J* 5.2, CH_2), 7.80 (1H, brs, exchange with D_2O, N*H*); δ_C (100 MHz, DMSO-d_6) 53.4, 172.1, 213.0 (*C*=S); *m/z* (ESI), 149 $[M\text{-}Na]^-$.

Synthesis of 3‴-(1*H*-imidazol-1''-yl)propan-1'''-aminium 3'-(1*H*-imidazol-1'-yl)propylcarbamodithioate **12a**

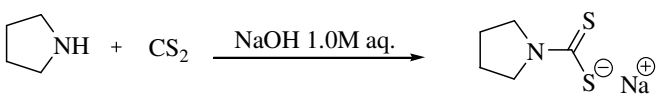


12 **12a**

3-(1*H*-Imidazol-1-yl)propan-1-amine **12** (0.5 g, 1.0 eq) was treated with powdered KOH (1.0 eq) at 0 °C in diethyl ether (20 ml) followed by addition of carbon disulfide (1.0 eq). The mixture was stirred at the same temperature for 4h, warmed to r.t.. The solid formed was collected by filtration and triturated from diethyl ether to afford the titled compound as a white solid in 17% yield.

3‴-(1*H*-Imidazol-1''-yl)propan-1'''-aminium 3'-(1*H*-imidazol-1'-yl)propylcarbamodithioate **12a**: ν_{max} (KBr) cm^{-1}, 2965, 2893, 1650, 1590, 1520, 1448; δ_H (400 MHz, DMSO-d_6) 1.99 (4H, m, 2'-H_2, 2'''-H_2), 2.76 (2H, t, J 7.6, 1'-H_2), 3.39 (2H, m, 1'''-H_2), 3.98 (2H, t, J 7.2, 3'/3'''-H_2), 4.10 (2H, t, J 7.2, 3'/3'''-H_2), 6.90 (1H, s, 5-H/5'-H), 6.95 (1H, s, 5-H/5'-H), 7.21 (2H, s, 4-H, 4'-H), 7.68 (2H, s, 2-H, 2'-H), 7.71 (3H, brs, exchange with D_2O, -NH_3), 8.29 (1H, brs, exchange with D_2O, -N*H*); δ_C (100 MHz, DMSO-d_6) 30.3, 31.7, 38.0, 45.1, 45.6, 45.9, 121.4, 124.5, 129.5, 130.0, 138.9, 139.0, 215.1 (*C*=S); *m/z* (ESI), 200 $[M\text{-}Na]^-$.

Synthesis of 1-pyrrolidinecarbodithioic acid sodium salt **15a**.

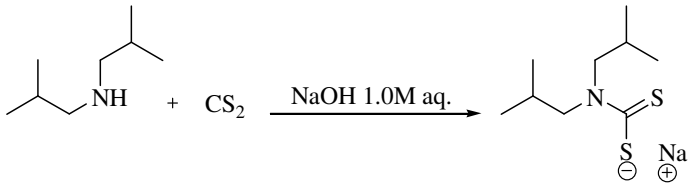


15 **15a**

Pyrrolidine **15** (1.0 g, 1.0 eq) was treated, according to the general procedure, with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a white solid in 56 % yield.

1-Pyrrolidinecarbodithioic acid sodium salt **15a**: m.p. > 300 °C (Lit[2] > 300 °C); ν_{max} (KBr) cm^{-1}, 2970, 2863, 1520, 1161; δ_H (400 MHz, D_2O) 2.01 (4H, m), 3.78 (4H, m); δ_C (100 MHz, D_2O) 26.1, 55.5, 203.1 (*C*=S); *m/z* (ESI), 146 [M-Na]$^-$. These data are in agreement with reported data.[30]

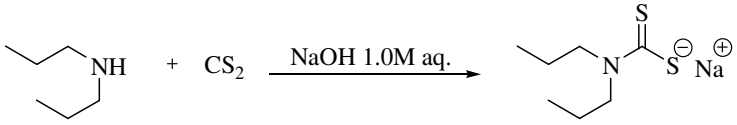
Synthesis of diisobutylcarbodithioic acid sodium salt **16a**.



16 **16a**

Diisobutylamine **16** (1.0 g, 1.0 eq) was treated according to the general procedure described above with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a white solid in 83 % yield.

Synthesis of dipropylcarbamodithioate sodium salt **17a**

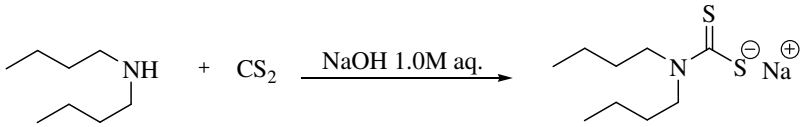


17 **17a**

Dipropylamine **17** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a white semisolid in 87 % yield.

Dipropylcarbamodithioate sodium salt **17a**: m.p.112- 114 °C ; ν_{max} (KBr) cm^{-1}, 2961, 2930, 2871, 1635, 1520, 1470, 1198; δ_H (400 MHz, DMSO-d_6) 0.82 (6H, t, *J* 7.6, 2 x CH_3), 1.65 (4H, m, 2 x CH_2), 3.90 (4H, m, 2 x CH_2); δ_C (100 MHz, DMSO-d_6) 12.3 (*C*H_3), 21.0, 55.2, 213.5 (*C*=S); *m/z* (ESI), 176 [M-Na]$^-$. Data are in agreement with reported data.[31]

Synthesis of dibutylcarbamodithioate sodium salt **18a**.

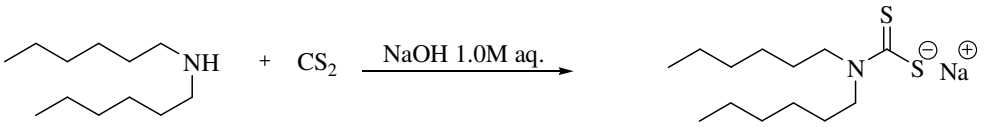


18 **18a**

Dibutylamine **18** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a white solid in 84 % yield.

Dibutylcarbamodithioate sodium salt **18a**: semisolid at r.t. ; ν_{max} (KBr) cm^{-1}, 2959, 2935, 2870, 1637, 1520, 1475, 1190; δ_H (400 MHz, DMSO-d_6) 0.91 (6H, t, *J* 8.0, 2 x CH_3), 1.26 (4H, m, 2 x CH_2), 1.62 (4H, m, 2 x CH_2), 3.95 (4H, m, 2 x CH_2); δ_C (100 MHz, DMSO-d_6) 14.9 (*C*H_3), 20.7, 30.0, 53.0, 213.5 (*C*=S); *m/z* (ESI), 204 [M-Na]$^-$. Data are in agreement with reported data.[30]

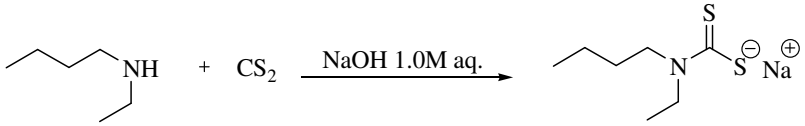
Synthesis of dihexylcarbamodithioate sodium salt **19a**.



19 **19a**

Dihexylamine **19** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a pale yellow semisolid in 64 % yield.
Dihexylcarbamodithioate sodium salt **19a**: semisolid at r.t.; ν_{max} (KBr) cm^{-1}, 2960, 2930, 2890, 1638, 1520, 1414, 1188; δ_H (400 MHz, DMSO-d_6) 0.91 (6H, t, *J* 6.8, 2 x CH_3), 1.29 (12H, m, 2 x CH_2), 1.63 (4H, m, 2 x CH_2), 3.93 (4H, m, 2 x CH_2); δ_C (100 MHz, DMSO-d_6) 14.9 (*C*H_3), 23.1, 27.2, 27.8, 32.1, 53.2, 213.6 (*C*=S); *m/z* (ESI), 260 $[M-Na]^-$.

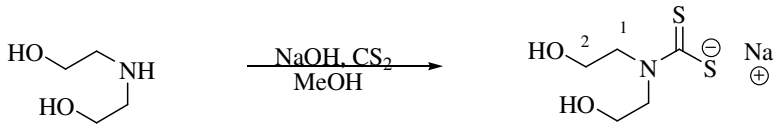
Synthesis of ethylbutylcarbamodithioate sodium salt **20a**.



20 **20a**

Ethylbutyamine **20** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (1.0 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a pale yellow semisolid in 98 % yield.
Ethylbutylcarbamodithioate sodium salt **20a**: m.p. 71-73 °C; ν_{max} (KBr) cm^{-1}, 2958, 2929, 2860, 1641, 1626, 1520, 1409, 1195; δ_H (400 MHz, DMSO-d_6) 0.92 (3H, t, *J* 8.0, CH_3), 1.12 (3H, t, *J* 8.0, CH_3), 1.27 (2H, m, CH_2), 1.61 (2H, m, CH_2), 3.95 (2H, m, CH_2), 4.03 (2H, q, *J* 8.0, CH_2); δ_C (100 MHz, DMSO-d_6) 13.4 (*C*H_3), 14.9 (*C*H_3), 20.8, 30.1, 47.6, 52.5, 213.3 (*C*=S); *m/z* (ESI), 176 $[M-Na]^-$.

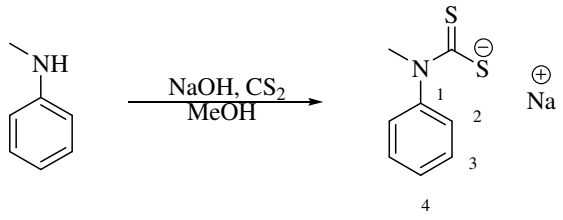
Synthesis of sodium bis(2-hydroxyethyl)carbamodithioate **21a**



21 **21a**

Diethanolamine **21** (0.5 g, 1.0 eq) was treated with powdered NaOH (1.0 eq) in MeOH (10 ml) followed by addition of carbon disulfide (1.0 eq) at 0°C. The mixture was warmed to r.t. and stirred for 4h. The solution was filtered through Celite and the filtrate was concentrated in vacuo to afford the titled compound as a light yellow solid in 81% yield.
Sodium bis(2-hydroxyethyl)carbamodithioate **21a**: ν_{max} (KBr) cm^{-1}, 2960, 2890, 1651, 1600, 1520, 1453; δ_H (400 MHz, DMSO-d_6) 3.67 (4H, q, *J* 6.8, 2x 2-H_2), 4.13 (4H, t, *J* 6.9, 2x 1-H_2), 4.90 (2H, t, *J* 6.8, exchange with D_2O, 2x O-*H*); δ_C (100 MHz, DMSO-d_6) 56.6, 60.3, 215.7 (*C*=S); *m/z* (ESI), 180 $[M-Na]^-$.

Synthesis of sodium methyl(phenyl)carbamodithioate **22a**

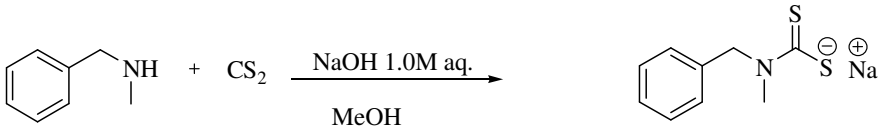


22 **22a**

N-methylbenzenamine **22** (0.5 g, 1.0 eq) was treated with powdered NaOH (1.0 eq) in MeOH (50 ml) followed by addition of carbon disulfide (1.0 eq) at 0°C. The mixture was warmed to r.t. and stirred for 5h at 40°C then cooled to r.t., filtered through Celite and the solvent removed in vacuo to give a solid that was triturated from diethyl ether to afford the titled compound as a pale yellow solid in 51 % yield.

Sodium methyl(phenyl)carbamodithioate **22a:** ν_{max} (KBr) cm^{-1}, 2958, 2890, 1630, 1582, 1520, 1450; δ_H (400 MHz, DMSO-d_6) 3.66 (3H, s, CH_3), 7.17 (3H, m, 2x 2-H, 4-H), 7.29 (2H, dd, *J* 8.3, 7.2, 2x 3-H); δ_C (100 MHz, DMSO-d_6) 46.7, 125.7, 128.3, 129.0, 151.6, 216.9 (*C*=S); *m/z* (ESI), 182 $[M\text{-}Na]^-$.

Synthesis of *N,N*-benzylmethylcarbamodithioate sodium salt **23a**.

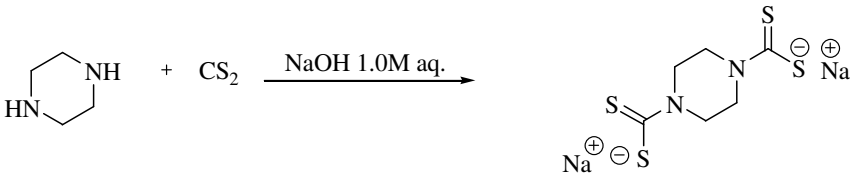


23 **23a**

N,N-Benzylmethylamine **23** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (1.2 eq) followed by addition of carbon disulfide (2.4 eq). The title compound was obtained as a white solid in 97% yield.

N,N-Benzylmethylcarbamodithioate sodium salt **23a**: m.p. 258-260 °C; ν_{max} (KBr) cm^{-1}, 2960, 2930, 1643, 1626, 1520, 1346, 1080; δ_H (400 MHz, DMSO-d_6) 3.32 (3H, s, CH_3), 5.50 (2H, s, CH_2), 7.26 (5H, m, Ar-*H*); δ_C (100 MHz, DMSO-d_6) 41.5 (*C*H_3), 58.4 (*C*H_2), 127.3, 128.2, 128.9, 140.0 (ipso), 216.1 (*C*=S); *m/z* (ESI), 196 $[M\text{-}Na]^-$.

Synthesis of piperazinecarbamodithioate disodium salt **25a**.

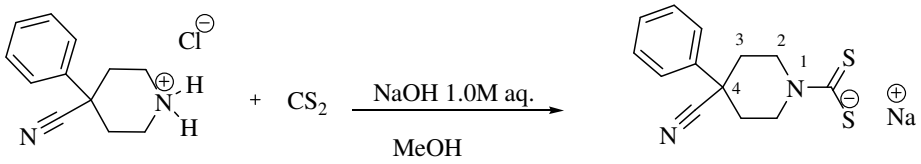


25 **25a**

Piperazine **25** (1.0 g, 1.0 eq) was treated according to the general procedure described above with 1.0 M aqueous solution of NaOH (2.2 eq) followed by addition of carbon disulfide (2.4 eq). The title compound was obtained as a white solid in 97% yield.

Piperazinecarbamodithioate disodium salt disodium salt **25a**: m.p. > 300 °C (Lit.[31] 110 °C); ν_{max} (KBr) cm^{-1}, 2939, 2917, 2890, 1520, 1618, 1419, 1154; δ_H (400 MHz, DMSO-d_6) 4.27 (8H, s, 4 x CH_2); δ_C (100 MHz, DMSO-d_6) 50.0, 214.7 (*C*=S); *m/z* (ESI), 258 $[M\text{-}Na]^-$, 160 $[M\text{-}CS_2Na]^-$. Data are in agreement with reported data.[31]

Synthesis of 4-cyano-4-phenylpiperidinecarbamodithiate sodium salt **26a**.

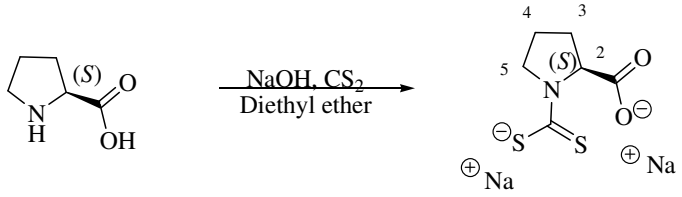


26 **26a**

4-Cyano-4-phenylpiperidine hydrochloride **26** (1.0 g, 1.0 eq) was treated according to the general procedure with 1.0 M aqueous solution of NaOH (2.2 eq) followed by addition of carbon disulfide (1.2 eq). The title compound was obtained as a white solid in 93 % yield.

4-Cyano-4-phenylpiperidinecarbamodithiate sodium salt **26a**: m.p. > 320 °C with dec; ν_{max} (KBr) cm^{-1}, 2961, 2891, 1648, 1598, 1520, 1414, 1186; δ_H (400 MHz, DMSO-d_6) 1.89 (2H, td, *J* 12.8, 3.6, 2 x 3H_{ax}), 2.14 (2H, d, *J* 12.8, 2 x 3H_{eq}), 3.15 (2H, t, *J* 12.8, 2 x 2H_{ax}), 6.15 (2H, d, *J* 12.8, 2 x 2H_{eq}); δ_C (100 MHz, DMSO-d_6) 36.6, 43.3, 51.1, 123.2, 126.5, 129.0, 130.0 (ipso), 141.0, 216.1 (*C*=S); *m/z* (ESI), 261 $[M\text{-}Na]^-$.

Synthesis of sodium (*S*)-1-dithiocarboxylatopyrrolidine-2-carboxylate **27a**



27 **27a**

L-Proline **27** (0.1 g, 1.0 eq) was treated with powdered NaOH (2.0 eq) at 0 °C in diethyl ether (5 ml) followed by addition of carbon disulfide (2.0 eq). The mixture was stirred at the same temperature for 3h, warmed to r.t.. The solid formed was collected by filtration and triturated from diethyl ether to afford the titled compound as a white solid in 52% yield.

Sodium (*S*)-1-dithiocarboxylatopyrrolidine-2-carboxylate **27a**: ν_{max} (KBr) cm^{-1}, 2962, 2892, 1650, 1598, 1519, 1445; δ_H (400 MHz, D_2O) 2.00 (3H, m), 2.30 (1H, m, 2-H), 3.81-4.00 (2H, m), 4.80 (1H, m); δ_C (100 MHz, D_2O) 24.9, 31.8, 49.5, 55.9, 69.7, 180.4 (C=O), 206.0 (*C*=S); *m/z* (ESI), 244 $[M\text{-}Na]^-$.