A Convenient Procedure for the Synthesis of Novel Modified 3-Substituted 1*H*-Quinoxaline-2-thiones via Side-Chain Lithiation of 3-Alkyl-1*H*-quinoxaline-2-thiones

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Abstract: 3-Methyl-1*H*-quinoxaline-2-thione (**1**) has been doubly lithiated, at nitrogen and at the 3-methyl group, with *n*-butyllithium at –78 °C in THF. The resulting dilithium reagent obtained reacts with a variety of electrophiles (iodomethane, iodoethane, 1-bromobutane, D_2O, benzaldehyde, anisaldehyde, 2-hexanone, cyclohexanone, benzophenone, phenyl isothiocyanate) to give the corresponding modified 3-substituted 1*H*-quinoxaline-2-thiones **4**–**13** in high yields. Similarly, double lithiation of 3-ethyl- (**4**) and 3-propyl-1*H*-quinoxaline-2-thiones (**5**), followed by reaction with some electrophiles gave the corresponding modified 3-substituted derivatives **15**–**19** in high yields. Treatment of some of the products with trifluoroacetic acid in dichloromethane at room temperature led to formation of substituted 2,3-dihydrothieno[2,3-*b*]quinoxalines in good yields.

Key words: quinoxalines, lithiation, electrophilic additions, cyclizations, heterocycles , sulfur

Directed *ortho*-lithiation of aromatic compounds has proven to be an excellent synthetic tool for regioselective functionalization.[2] The use of directing groups to facilitate lithiation followed by reaction of the organolithium reagents obtained with various electrophiles has found wide application in a variety of synthetic transformations.[2,3] Recently, lithiation of various heterocycles has been achieved, and the lithiated reagents obtained in such lithiation reactions are very useful intermediates for the synthesis of more complex substituted heterocycles.[4] We have previously reported on the use of organolithiums in organic synthesis.[5] We have also shown that various 3*H*-quinazolin-4-one derivatives undergo double lithiation with lithium reagents at –78 °C.[6] The organolithium reagents obtained in such lithiation reactions reacted with various electrophiles to produce more complex substituted 3*H*-quinazolin-4-ones in good yields.[6] However, there are relatively few examples of the lithiation of quinoxaline derivatives.[7–12] Compounds possessing the quinoxaline ring system have important pharmacological activities.[13] We now report on the successful synthesis of more complex modified 3-substituted 1*H*-quinoxaline-2-thiones via side-chain lithiation of 3-alkyl-1*H*-quinoxaline-2-thiones.

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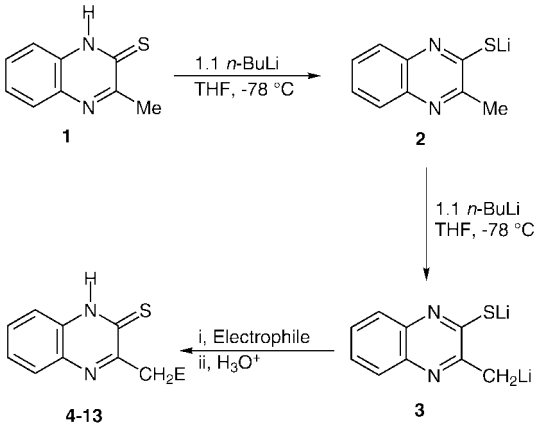
3-Methyl-1*H*-quinoxaline-2-thione (**1**) was prepared according to the literature procedure.[14] Double lithiation of **1** occurred smoothly with BuLi (2.2 equiv) at –78 °C in anhydrous THF. Two mole equivalents of BuLi were used, the first to remove the NH proton to give monolithium reagent **2** and the other to form the dilithium reagent **3**. Reactions of the dilithium reagent **3** with various electrophiles (iodomethane, iodoethane, 1-bromobutane, D_2O, benzaldehyde, anisaldehyde, 2-hexanone, cyclohexanone, benzophenone, phenyl isothiocyanate) gave the corresponding modified 3-substituted 1*H*-quinoxaline-2-thiones **4**–**13** (Scheme 1) in very good yields (Table 1).

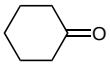
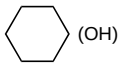


Scheme 1

As indicated in Table 1, the yields of isolated, purified products were extremely good. The reaction with iodomethane (1.2 equivalents) resulted in almost quantitative yields of alkylated products, but as a mixture of 2-ethyl-1*H*-quinoxaline-2-thione (**4**) and 3-ethyl-2-methylthio-1*H*-quinoxaline (**14**) in 89% and 4% yield, respectively.

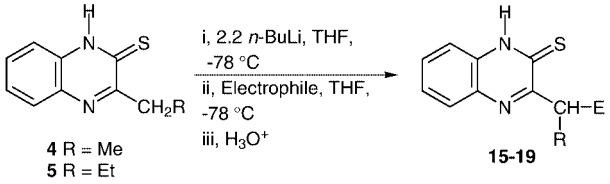
The spectral characteristics of compounds **4**–**14** were consistent with the assigned structures (see experimental section for details). The ^{1}H NMR spectra of compounds **8**–**10** show diastereotopism for the two hydrogens of the CH_2 group at position 3. The CH_2 signals resonate as two separated double doublets (J = 14 and 4.5 Hz for one double doublet, and 14 and 9 Hz for the other) in the case of compounds **8** and **9**, and two separated doublets (J = 14 Hz) in the case of compound **10**.

Table 1 Yields of Products **4**–**13** According to Scheme 1

Product	Electrophile	E	Yield (%)[a]
4	MeI	Me	89[b]
5	EtI	Et	90
6	BuBr	Bu	87
7	D_2O	D	92
8	PhCHO	PhCH(OH)	86
9	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	83
10	MeCOBu	MeC(OH)Bu	89
11			90
12	Ph_2CO	$Ph_2C(OH)$	91
13	PhNCS	PhNHCS	81

[a] Yield of isolated, purified products.
[b] Compound **14** was obtained in 4% yield.

Attention was next turned to the lithiation of 3-ethyl-1*H*-quinoxaline-2-thione (**4**) and 3-propyl-1*H*-quinoxaline-2-thione (**5**), which had been obtained by alkylation of the dilithium reagent **3** according to Scheme 1. If successful, this would suggest that the lithiation process was tolerant of a variety of primary alkyl groups at position 3. It was found that successful lithiation of **4** and **5** was achieved using BuLi (2.2 equivalents) in anhydrous THF at –78 °C under nitrogen for 2 hours. The dilithium reagents obtained reacted with several electrophiles (D_2O, cyclohexanone, benzophenone, benzaldehyde) (Scheme 2) to give the corresponding modified derivatives **15**–**19** in very good yields (Table 2).

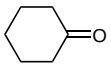
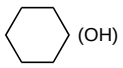


Scheme 2

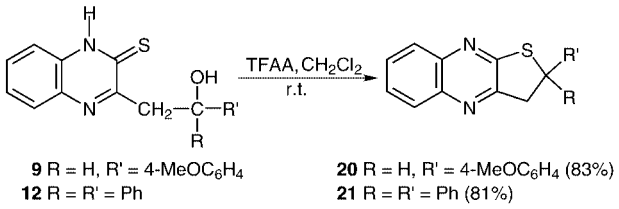
The NMR spectra of compound **18** show the expected presence of two racemic diastereoisomers in the ratio of 1:2.

Some of the products obtained from Scheme 1 can be used as starting materials for other transformations. As a demonstration of this, compounds **9** and **12** were converted to the corresponding 2,3-dihydrothieno[2,3-*b*]quioxalines **20** and **21** in 83% and 81% isolated yields, respectively, on treatment with trifluoroacetic acid (TFA) in dichloromethane (Scheme 3).

Table 2 Yields of Products **15**–**19** According to Scheme 2

Product	R	Electrophile	E	Yield (%)[a]
15	Me	D_2O	D	90
16	Me			88
17	Me	Ph_2CO	$Ph_2C(OH)$	91
18	Et	PhCHO	PhCH(OH)	89
19	Et	Ph_2CO	$Ph_2C(OH)$	92

[a] Yields of isolated, purified products.



Scheme 3

The ^1H NMR spectrum of compound **20** showed diastereotopism for the two hydrogens of the CH_2 group at position 3. The CH_2 signals resonate as two separated double doublets (J = 17 and 8 Hz).

In conclusion, this work describes a simple and convenient method for the side-chain substitution of 3-alkyl-1*H*-quinoxaline-2-thiones to produce more complex 3-substituted derivatives in very high yield. These derivatives might have pharmacological activities and could be difficult to prepare by other means.

Mps were determined on an electrothermal digital mp apparatus and are reported uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-400 Fourier Transform spectrometer operating at 400 MHz for ^1H and 100 MHz for ^{13}C measurement. Chemical shifts are reported in parts per million relative to tetramethylsilane. Low-resolution mass spectra were recorded on a VG 12-253 spectrometer, electron impact (E1) at 70 eV and chemical ionization (CI) by use of ammonia as ionizing gas. Accurate mass data were obtained on a VG ZAB-E instrument. BuLi was obtained from Aldrich Chemical Company and was estimated prior to use by the method of Watson and Eastham.[15] THF was distilled from sodium benzophenone ketyl. Other chemicals were obtained from Aldrich Chemical Company and used without further purification.

Modified 3-Substituted 1*H*-Quinoxaline-2-thiones 4–19; General Procedure

A solution of BuLi in hexane (1.8 mL, 2.5 M, 2.2 mmol) was added in a dropwise manner to a cold (–78 °C), stirred solution of 3-alkyl-1*H*-quinoxaline-2-thione (**1**, **4** or **5**) (2.0 mmol) in anhyd THF (30 mL) under N_2. The dilithium reagent of compound **1** was obtained as reddish brown precipitate while the dilithium reagents of compounds **4** and **5** were obtained as a deep red solution. The mixture was stirred at –78 °C for 2 h to complete the formation of the dilithium reagent. An electrophile (2.2 mmol), in anhyd THF (8 mL) if solid, otherwise neat, was added. The reaction mixture was stirred

for 2 h at –78 °C, then removed from the cooling bath and allowed to warm to r.t. The reaction mixture was diluted with EtOAc (20 mL) then quenched with sat. aq NH_4Cl (20 mL). The organic layer was separated, washed with H_2O (2 × 20 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The products obtained were recrystallized or subjected to column chromatography to give the appropriate pure products **4**–**19**.

3-Ethyl-1*H*-quinoxaline-2-thione (4)
Purified by column chromatography (silica gel; Et_2O–hexane, 2:1); mp 209–210 °C.

^{1}H NMR (DMSO-d_6): δ = 14.36 (s, exch., 1 H), 7.80 (d, *J* = 8 Hz, 1 H), 7.61–7.52 (m, 2 H), 7.42 (app. dt, *J* = 8, 1 Hz, 1 H), 3.08 (q, *J* = 7 Hz, 2 H), 1.24 (t, *J* = 7 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 175.1 (s), 164.9 (s), 135.2 (s), 131.6 (s), 130.5 (d), 128.6 (d), 126.0 (d), 116.0 (d), 29.6 (t), 11.5 (q).

EI-MS: *m*/*z* (%) = 191 (M^+ + 1, 12), 190 (M^+, 100), 189 (M^+ – 1, 68), 157 (32), 145 (15), 134 (18), 129 (47), 102 (42), 90 (19), 76 (23).

CI-MS: *m*/*z* (%) = 191 (MH^+, 91), 174 (5), 161 (19), 159 (100).

HRMS: *m*/*z* calcd for $C_{10}H_{11}N_2S$ (MH^+): 191.0637; found: 191.0637.

3-Propyl-1*H*-quinoxaline-2-thione (5)
Recrystallized from aq MeOH; mp 198–199 °C (lit.[16] 198 °C).

^{1}H NMR (DMSO-d_6): δ = 14.11 (s, exch., 1 H), 7.64 (d, *J* = 8 Hz, 1 H), 7.51 (d, *J* = 8 Hz, 1 H), 7.42 (app. t, *J* = 8 Hz, 1 H), 7.30 (app. t, *J* = 8 Hz, 1 H), 3.07 (q, *J* = 7 Hz, 2 H), 1.78 (sext, *J* = 7 Hz, 2 H), 0.96 (t, *J* = 7 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 175.4 (s), 164.2 (s), 135.4 (s), 131.6 (s), 129.7 (d), 128.3 (d), 125.3 (d), 115.8 (d), 38.3 (t), 20.3 (t), 14.1 (q).

EI-MS: *m*/*z* (%) = 204 (M^+, 100), 189 (31), 176 (60), 155 (23), 143 (27), 129 (38), 102 (51), 90 (42), 76 (40), 51 (49).

CI-MS: *m*/*z* (%) = 205 (MH^+, 79), 173 (100), 144 (20).

HRMS: *m*/*z* calcd for $C_{11}H_{13}N_2S$ (MH^+): 205.0794; found: 205.0791.

3-Pentyl-1*H*-quinoxaline-2-thione (6)
Recrystallized from MeOH; mp 167–169 °C.

^{1}H NMR (DMSO-d_6): δ = 14.41 (s, exch., 1 H), 7.79 (d, *J* = 8 Hz, 1 H), 7.59–7.52 (m, 2 H), 7.42 (app. dt, *J* = 8, 1 Hz, 1 H), 3.06 (t, *J* = 7.5 Hz, 2 H), 1.73 (pent, *J* = 7.5 Hz, 2 H), 1.38–1.27 (m, 4 H), 0.87 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 175.2 (s), 164.3 (s), 135.3 (s), 131.6 (s), 130.5 (d), 128.5 (d), 125.9 (d), 116.0 (d), 36.1 (t), 31.5 (t), 26.6 (t), 22.4 (t), 14.3 (q).

EI-MS: *m*/*z* (%) = 232 (M^+, 61), 203 (52), 199 (94), 189 (35), 176 (100), 155 (30), 143 (32), 129 (36), 102 (63), 90 (45), 76 (36), 41 (79).

CI-MS: *m*/*z* (%) = 233 (MH^+, 100), 201 (87), 144 (13).

HRMS: *m*/*z* calcd for $C_{13}H_{17}N_2S$ (MH^+): 233.1107; found: 233.1106.

3-Deuteriomethyl-1*H*-quinoxaline-2-thione (7)
Recrystallized from MeOH; mp 250–251 °C.

^{1}H NMR (DMSO-d_6): δ = 14.33 (s, exch., 1 H), 7.75 (dd, *J* = 8, 1 Hz, 1 H), 7.55–7.49 (m, 2 H), 7.41 (app. dt, *J* = 8, 1 Hz, 1 H), 2.58 (1:1:1 t, *J* = 2 Hz, 2 H).

^{13}C NMR (DMSO-d_6): δ = 175.2 (s), 161.7 (s), 135.1 (s), 131.7 (s), 130.5 (d), 128.3 (d), 126.0 (d), 115.8 (d), 24.8, 24.6, 24.4 (1:1:1 t).

EI-MS: *m*/*z* (%) = 177 (M^+, 100), 144 (89), 134 (20), 102 (35), 90 (47), 76 (77), 50 (86), 43 (82).

CI-MS: *m*/*z* (%) = 178 (MH^+, 100), 146 (62).

HRMS: *m*/*z* calcd for $C_9H_8N_2SD$ (MH^+): 178.0544; found: 178.0546.

3-(2-Hydroxy-2-phenylethyl)-1*H*-quinoxaline-2-thione (8)
Recrystallized from MeOH; mp 182–183 °C.

^{1}H NMR (DMSO-d_6): δ = 14.41 (s, exch., 1 H), 7.84 (d, *J* = 8 Hz, 1 H), 7.63–7.56 (m, 2 H), 7.46–7.43 (m, 3 H), 7.33 (t, *J* = 7.6 Hz, 2 H), 7.21 (app. dt, *J* = 8, 1 Hz, 1 H), 5.43 (m, 1 H), 5.28 (d, *J* = 4.5 Hz, exch., 1 H), 3.51 (dd, *J* = 14, 4.5 Hz, 1 H), 3.33 (dd, *J* = 14, 9 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 175.3 (s), 161.7 (s), 146.1 (s), 135.3 (s), 131.8 (s), 130.7 (d), 129.2 (d), 128.7 (d), 128.4 (d), 127.1 (d), 126.1 (d), 116.01 (d), 70.3 (d), 46.9 (t).

EI-MS: *m*/*z* (%) = 282 (M^+, 19), 249 (11), 176 (61), 143 (34), 105 (72), 77 (100), 51 (50).

HRMS: *m*/*z* calcd for $C_{16}H_{14}N_2OS$ (M^+): 282.0821; found: 282.0822.

3-[2-Hydroxy-2-(4-methoxyphenyl)ethyl]-1*H*-quinoxaline-2-thione (9)
Recrystallized from MeOH; mp 159–160 °C.

^{1}H NMR (DMSO-d_6): δ = 14.41 (s, exch., 1 H), 7.84 (dd, *J* = 8, 1 Hz, 1 H), 7.62–7.54 (m, 2 H), 7.45 (app. dt, *J* = 8, 1 Hz, 1 H), 7.35 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.37 (m, 1 H), 5.17 (d, *J* = 4.5 Hz, exch., 1 H), 3.72 (s, 3 H), 3.49 (dd, *J* = 14, 4.5 Hz, 1 H), 3.33 (dd, *J* = 14, 9 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 175.3 (s), 161.8 (s), 158.5 (s), 138.1 (s), 135.3 (s), 131.7 (s), 130.7 (d), 128.7 (d), 127.3 (d), 126.0 (d), 116.0 (d), 113.7 (d), 69.9 (d), 55.3 (q), 46.8 (t).

EI-MS: *m*/*z* (%) = 312 (M^+, 10), 294 (12), 176 (82), 143 (69), 135 (100), 102 (23), 77 (48).

CI-MS: *m*/*z* (%) = 313 (MH^+, 11), 295 (62), 177 (60), 154 (100), 145 (51), 137 (81).

HRMS: *m*/*z* calcd for $C_{17}H_{17}N_2O_2S$ (MH^+): 313.1005; found: 313.1006.

3-(2-Hydroxy-2-methylhexyl)-1*H*-quinoxaline-2-thione (10)
Recrystallized from MeOH; mp 102–103 °C.

^{1}H NMR (DMSO-d_6): δ = 14.44 (s, exch., 1 H), 7.81 (dd, *J* = 8, 1 Hz, 1 H), 7.62–7.54 (m, 2 H), 7.44 (app. dt, *J* = 8, 1 Hz, 1 H), 4.58 (s, exch., 1 H), 3.40, 3.35 (2 d, *J* = 14 Hz, 2 H), 1.51 (m, 2 H), 1.35 (m, 2 H), 1.25 (sext, *J* = 7 Hz, 2 H), 1.17 (s, 3 H), 0.85 (t, *J* = 7 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 176.2 (s), 162.5 (s), 134.8 (s), 131.5 (s), 130.9 (d), 128.6 (d), 126.2 (d), 116.0 (d), 72.9 (s), 45.0 (t), 42.0 (t), 27.4 (q), 25.12 (t), 23.2 (t), 14.4 (q).

EI-MS: *m*/*z* (%) = 276 (M^+, 10), 258 (9), 176 (100), 143 (61), 132 (22), 102 (23), 90 (18), 76 (17), 43 (75).

CI-MS: *m*/*z* (%) = 277 (MH^+, 52), 245 (100), 227 (15), 177 (63), 145 (65), 118 (33).

HRMS: *m*/*z* calcd for $C_{15}H_{21}N_2OS$ (MH^+): 277.1369; found: 277.1375.

3-[(1-Hydroxycyclohexyl)methyl]-1*H*-quinoxaline-2-thione (11)
Recrystallized from MeOH; mp 187–188 °C.

^{1}H NMR (DMSO-d_6): δ = 14.45 (s, exch., 1 H), 7.83 (d, *J* = 8 Hz, 1 H), 7.62–7.53 (m, 2 H), 7.44 (app. dt, *J* = 8, 1 Hz, 1 H), 4.52 (s, exch., 1 H), 3.37 (s, 2 H), 1.59–1.16 (m, 10 H).

^{13}C NMR (DMSO-d_6): δ = 176.3 (s), 162.4 (s), 134.8 (s), 131.6 (s), 130.9 (d), 128.6 (d), 126.1 (d), 116.0 (d), 72.0 (s), 46.1 (t), 37.6 (t), 25.8 (t), 22.0 (t).

EI-MS: *m*/*z* (%) = 274 (M^+, 11), 256 (18), 231 (8), 176 (100), 143 (42), 132 (22), 102 (25), 81 (30), 55 (68), 41 (77).

CI-MS: *m*/*z* (%) = 275 (MH^+, 48), 243 (92), 255 (19), 177 (22), 145 (82), 116 (100).

HRMS: *m*/*z* calcd for $C_{15}H_{19}N_2OS$ (MH^+): 275.1213; found: 275.1213.

3-(2-Hydroxy-2,2-diphenylethyl)-1*H*-quinoxaline-2-thione (12)
Recrystallized from MeOH; mp 185–186 °C.

^{1}H NMR (DMSO-d_6): δ = 14.58 (s, exch., 1 H), 7.72 (d, *J* = 8 Hz, 1 H), 7.57 (app. dt, *J* = 8, 1 Hz, 1 H), 7.52–7.48 (m, 5 H), 7.36 (app. dt, *J* = 8, 1 Hz, 1 H), 7.27 (t, *J* = 7.5 Hz, 4 H), 7.14 (t, *J* = 7.5 Hz, 2 H), 6.77 (s, exch., 1 H), 4.18 (s, 2 H).

^{13}C NMR (DMSO-d_6): δ = 175.5 (s), 162.4 (s), 147.9 (s), 133.8 (s), 131.5 (s), 131.3 (d), 128.4 (d), 128.3 (d), 126.8 (d), 126.3 (d), 125.9 (d), 116.1 (d), 78.5 (s), 43.9 (t).

EI-MS: *m*/*z* (%) = 358 (M^+, 22), 340 (87), 323 (76), 307 (51), 263 (100), 207 (79), 182 (33), 105 (90), 77 (78), 51 (35).

CI-MS: *m*/*z* (%) = 359 (MH^+, 5), 341 (12), 200 (54), 183 (70), 145 (100), 105 (35).

HRMS: *m*/*z* calcd for $C_{22}H_{19}N_2OS$ (MH^+): 359.1213; found: 359.1226.

3-(Phenylaminothiocarbonylmethyl)-1*H*-quinoxaline-2-thione (13)
Recrystallized from MeOH; mp >300 °C.

^{1}H NMR (DMSO-d_6): δ = 14.81 (s, exch., 1 H), 11.85 (s, exch., 1 H), 7.85 (d, *J* = 8 Hz, 1 H), 7.66–7.54 (m, 2 H), 7.47 (app. t, *J* = 8 Hz, 1 H), 7.40 (d, *J* = 7.5 Hz, 2 H), 7.37–7.11 (m, 3 H), 4.60 (s, 2 H).

^{13}C NMR (DMSO-d_6): δ = 187.2 (s), 180.8 (s), 160.5 (s), 144.8 (s), 139.7 (s), 128.3 (d), 126.7 (s), 126.6 (d), 126.0 (d), 124.1 (d), 123.5 (d), 116.1 (d), 115.6 (d), 53.5 (t).

EI-MS: *m*/*z* (%) = 311 (M^+, 18), 278 (5), 176 (91), 135 (53), 93 (100), 77 (89), 63 (49), 51 (47).

CI-MS: *m*/*z* (%) = 312 (MH^+, 26), 157 (32), 113 (100).

HRMS: *m*/*z* calcd for $C_{16}H_{14}N_3S_2$ (MH^+): 312.0624; found: 312.0623.

3-Ethyl-2-methylthio-1*H*-quinoxaline (14)
Purified by column chromatography (silica gel; Et_2O–hexane, 2:1); mp 76–77 °C.

^{1}H NMR ($CDCl_3$): δ = 7.89 (dd, *J* = 8, 1 Hz, 1 H), 7.73 (dd, *J* = 8, 1 Hz, 1 H), 7.56–7.48 (m, 2 H), 2.91 (q, *J* = 7 Hz, 2 H), 2.60 (s, 3 H), 0.86 (t, *J* = 7 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 156.6 (s), 156.5 (s), 141.7 (s), 139.7 (s), 129.2 (d), 129.0 (d), 128.1 (d), 127.8 (d), 28.5 (t), 13.2 (q), 11.9 (q).

EI-MS: *m*/*z* (%) = 204 (M^+, 80), 189 (51), 156 (19), 145 (29), 129 (71), 102 (100), 90 (43), 75 (73), 50 (69).

CI-MS: *m*/*z* (%) = 205 (MH^+, 100), 159 (21).

HRMS: *m*/*z* calcd for $C_{11}H_{13}N_2S$ (MH^+): 205.0794; found: 205.0794.

3-(1-Deuterioethyl)-1*H*-quinoxaline-2-thione (15)
Recrystallized from aq MeOH; mp 209–210 °C.

^{1}H NMR (DMSO-d_6): δ = 14.13 (s, exch., 1 H), 7.70 (d, *J* = 8 Hz, 1 H), 7.49 (dd, *J* = 8, 1 Hz, 1 H), 7.41 (app. dt, *J* = 8, 1 Hz, 1 H), 7.25 (app. dt, *J* = 8, 1 Hz, 1 H), 2.76 (q, *J* = 7.5 Hz, 1 H), 1.27 (d, *J* = 7.5 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 175.4 (s), 164.2 (s), 135.5 (s), 131.7 (s), 129.8 (d), 128.3 (d), 125.4 (d), 115.9 (d), 27.6, 27.3, 27.1 (1:1:1 d), 11.6 (q).

EI-MS: *m*/*z* (%) = 191 (M^+, 100), 158 (76), 129 (53), 102 (30), 76 (14).

CI-MS: *m*/*z* (%) = 192 (MH^+, 77), 160 (100).

HRMS: *m*/*z* calcd for $C_{10}H_{10}N_2SD$ (MH^+): 192.0700; found: 192.0703.

3-[1-(1-Hydroxycyclohexyl)ethyl]-1*H*-quinoxaline-2-thione (16)
Purified by column chromatography (silica gel; Et_2O–hexane, 2:1); mp 166–167 °C.

^{1}H NMR ($CDCl_3$) δ = 13.16 (s, exch., 1 H), 7.79 (dd, *J* = 8, 1 Hz, 1 H), 7.54–7.45 (m, 2 H), 7.40 (app. dt, *J* = 8, 1 Hz, 1 H), 5.00 (s, exch., 1 H), 4.40 (q, *J* = 7 Hz, 1 H), 1.62–1.38 (m, 10 H), 1.28 (d, *J* = 7 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 175.4 (s), 169.2 (s), 135.4 (s), 131.3 (d), 131.2 (s), 129.3 (d), 127.1 (d), 115.4 (d), 74.3 (s), 43.2 (d), 38.0 (t), 35.6 (t), 26.2 (t), 22.7 (t), 22.4 (t), 14.5 (q).

EI-MS: *m*/*z* (%) = 288 (M^+, 2), 270 (6), 239 (12), 190 (33), 158 (30), 129 (12), 98 (52), 84 (65), 55 (100), 42 (79).

CI-MS: *m*/*z* (%) = 289 (MH^+, 32), 257 (100), 191 (5), 159 (11), 116 (24).

HRMS: *m*/*z* calcd for $C_{16}H_{21}N_2OS$ (MH^+): 289.1369; found: 289.1371.

3-(2-Hydroxy-1-methyl-2,2-diphenylethyl)-1*H*-quinoxaline-2-thione (17)
Recrystallized from EtOAc; mp 190–192 °C.

^{1}H NMR (DMSO-d_6): δ = 14.62 (s, exch., 1 H), 7.81 (d, *J* = 8 Hz, 1 H), 7.56–7.49 (m, 5 H), 7.37 (d, *J* = 7.5 Hz, 4 H), 7.18 (app. t, *J* = 8 Hz, 1 H), 7.13 (t, *J* = 7.5 Hz, 2 H), 7.03 (app. t, *J* = 8 Hz, 1 H), 6.68 (s, exch., 1 H), 5.51 (q, *J* = 6.7 Hz, 1 H), 1.11 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (DMSO-d_6): δ = 174.6 (s), 168.2 (s), 149.2 (s), 146.5 (s), 133.8 (s), 131.4 (d), 128.5 (d), 128.4 (d), 126.7 (d), 126.6 (d), 125.4 (d), 116.2 (d), 80.6 (s), 42.4 (d), 14.9 (q).

EI-MS: *m*/*z* (%) = 372 (M^+, 1), 346 (22), 313 (100), 265 (51), 190 (45), 157 (33), 129 (24), 105 (80), 77 (61), 51 (22).

CI-MS: *m*/*z* (%) = 373 (MH^+, 6), 200 (71), 191 (100), 159 (32).

HRMS: *m*/*z* calcd for $C_{23}H_{21}N_2OS$ (MH^+): 373.1369; found: 373.1372.

3-[1-(Hydroxyphenylmethyl)propyl]-1*H*-quinoxaline-2-thione (18)
Purified by column chromatography (silica gel; Et_2O–hexane, 2:1); mp 127–129 °C; **18a**/**18b** 1:2 (^{1}H NMR).

EI-MS: *m*/*z* (%) = 310 (M^+, 11), 275 (6), 204 (38), 189 (18), 122 (12), 105 (93), 91 (17), 77 (100), 51 (25).

HRMS: *m*/*z* calcd for $C_{18}H_{18}N_2OS$ (M^+): 310.1134; found: 310.1129.

Compound 18a
^{1}H NMR ($CDCl_3$): δ = 12.95 (s, exch., 1 H), 7.79 (d, *J* = 8 Hz, 1 H), 7.49–7.25 (m, 8 H), 5.74 (m, 1 H), 5.31 (m, 1 H), 5.12 (d, *J* = 4 Hz, exch., 1 H), 192–1.60 (m, 2 H), 0.80 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 173.4 (s), 161.0 (s), 141.0 (s), 140.6 (s), 132.6 (s), 129.8 (d), 128.9 (d), 127.4 (d), 127.1 (d), 126.3 (d), 125.2 (d), 114.1 (d), 73.1 (d), 50.7 (d), 22.9 (t) 11.2 (q).

Compound 18b

^{1}H NMR ($CDCl_3$): δ = 12.95 (s, exch., 1 H), 7.92 (d, *J* = 8 Hz, 1 H), 7.49–7.25 (m, 8 H), 5.12 (d, *J* = 4 Hz, exch., 1 H), 4.72 (m, 1 H), 4.55 (m, 1 H), 192–1.60 (m, 2 H), 0.63 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 174.5 (s), 165.3 (s), 141.5 (s), 139.6 (s), 134.3 (s), 129.9 (d), 128.6 (d), 127.6 (d), 126.6 (d), 126.0 (d), 125.1 (d), 114.3 (d), 73.4 (d), 48.6 (d), 22.0 (t), 11.0 (q).

3-[1-(Hydroxydiphenylmethyl)propyl]-1*H*-quinoxaline-2-thione (19)

Purified by column chromatography (silica gel; Et_2O–hexane, 2:1); mp 115–116 °C.

^{1}H NMR ($CDCl_3$): δ = 13.81 (s, exch., 1 H), 7.70 (d, *J* = 8 Hz, 1 H), 7.64 (t, *J* = 7.5 Hz, 4 H), 7.44 (app. dt, *J* = 8, 1 Hz, 1 H), 7.30 (d, *J* = 7.5 Hz, 4 H), 7.16–6.98 (m, 3 H), 6.84 (app. t, *J* = 8 Hz, 1 H), 6.51 (s, exch., 1 H), 5.49 (2 d, *J* = 4 Hz, 1 H), 1.94–1.78 (m, 2 H), 0.77 (t, *J* = 8 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 176.5 (s), 168.6 (s), 149.0 (s), 146.6 (s), 135.1 (s), 131.5 (d), 128.7 (d), 128.4 (d), 127.1 (d), 126.8 (d), 125.8 (d), 115.4 (d), 81.8 (s), 49.2 (d), 26.0 (t), 12.8 (q).

EI-MS: *m*/*z* (%) = 386 (M^+, 4), 368 (39), 352 (100), 331 (61), 295 (59), 239 (67), 219 (54), 182 (32), 105 (52), 77 (81), 51 (56).

CI-MS: *m*/*z* (%): 387 (MH^+, 100), 369 (30), 355 (26), 242 (44), 200 (61).

HRMS: *m*/*z* calcd for $C_{24}H_{23}N_2OS$ (MH^+): 387.1526; found: 387.1524.

Substituted 2,3-Dihydrothieno[2,3-*b*]quinoxalines 20 and 21; General Procedure

To a stirred solution of **9** or **12** (0.15 mmol) in CH_2Cl_2 (10 mL), TFA (0.2 mL) was added. The mixture was stirred at r.t. for 1 h then sat. aq Na_2CO_3 (10 mL) was added and the mixture was then extracted with CH_2Cl_2 (10 mL). The organic layer was separated, washed with H_2O (2 × 10 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The solid obtained was recrystallized from EtOAc to give the pure products **20** and **21**.

2-(4-Methoxyphenyl)-2,3-dihydrothieno[2,3-*b*]quinoxaline (20)

Recrystallized from EtOAc; mp 138–140 °C.

^{1}H NMR (DMSO-d_6): δ = 7.95 (dd, *J* = 8, 1 Hz, 1 H), 7.85 (dd, *J* = 8, 1 Hz, 1 H), 7.73–7.64 (m, 2 H), 7.46 (d, *J* = 8.5 Hz, 2 H), 6.94 (d, *J* = 8.5 Hz, 2 H), 5.42 (t, *J* = 8 Hz, 1 H), 3.85 (dd, *J* = 17, 8 Hz, 1 H), 3.75 (s, 3 H), 3.66 (dd, *J* = 17, 8 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 161.5 (s), 159.4 (s), 158.4 (s), 141.4 (s), 139.4 (s), 132.5 (s), 129.8 (d), 129.0 (d), 128.8 (d), 128.6 (d), 127.6 (d), 114.6 (d), 55.5 (q), 48.0 (d), 42.0 (t).

EI-MS: *m*/*z* (%) = 294 (M^+, 100), 279 (26), 218 (31), 187 (46), 151 (26), 134 (40), 119 (29), 102 (35), 91 (62), 65 (39).

CI-MS: *m*/*z* (%) = 295 (MH^+, 100), 265 (31), 135 (22).

HRMS: *m*/*z* calcd for $C_{17}H_{15}N_2OS$ (MH^+): 295.0900; found: 295.0901.

2,3-Diphenyl-2,3-dihydrothieno[2,3-*b*]quinoxaline (21)

Recrystallized from EtOAc; mp 149–150 °C.

^{1}H NMR (DMSO-d_6): δ = 7.95 (dd, *J* = 8, 1 Hz, 1 H), 7.86 (dd, *J* = 8, 1 Hz, 1 H), 7.71–7.67 (m, 2 H), 7.52 (d, *J* = 7.8 Hz, 4 H), 7.35 (t, *J* = 7.8 Hz, 4 H), 7.26 (t, *J* = 7.8 Hz, 2 H), 4.35 (s, 2 H).

^{13}C NMR (DMSO-d_6): δ = 160.6 (s), 157.9 (s), 144.7 (s), 141.5 (s), 139.6 (s), 130.1 (d), 129.0 (d), 128.9 (d), 128.8 (d), 127.9 (d), 127.8 (d), 127.3 (d), 66.6 (s), 47.5 (t).

EI-MS: *m*/*z* (%) = 340 (M^+, 100), 305 (26), 263 (98), 191 (22), 178 (71), 165 (59), 152 (18), 102 (27), 77 (48), 51 (31).

CI-MS: *m*/*z* (%) = 341 (MH^+, 100), 308 (22), 230 (14), 181 (35), 131 (22), 78 (23), 60 (51).

HRMS: *m*/*z* calcd for $C_{22}H_{17}N_2S$ (MH^+): 341.1107; found: 341.1106.

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