Synthesis of thieno[2,3-*b*]quinoxalines from 2-haloquinoxalines

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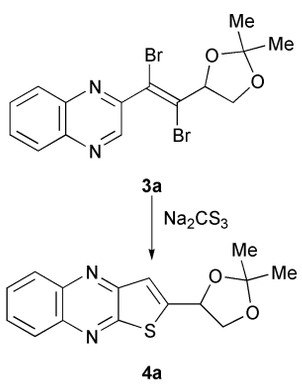
The palladium(0)-catalysed coupling of 2-haloquinoxalines with alkynes, addition of one mol equivalent of bromine to the 2-alkynylquinoxalines thus produced and then reaction of the resulting dibromides with dipotassium trithiocarbonate produces thieno[2,3-*b*]quinoxalines.

Introduction

In the course of our synthetic work connected with the cofactor of the oxomolybdoenzymes[1] we have developed methods for the synthesis of unsymmetrically substituted 1,3-dithiole-2-thiones. As part of that development work we exposed dibromide **3a** to disodium trithiocarbonate[2] anticipating[3] formation of a 4-quinoxalinyl-1,3-dithiole but found that it was converted instead (Scheme 1) in high yield into thieno[2,3-*b*]quinoxaline



Scheme 1

4a.[4] We have now had the opportunity to investigate this ring closing process in a broader context and find that it is a general and efficient process for the construction of tricycles **4** (Scheme 2 and Table 1).

Previously described ring syntheses of tricyclic thieno-[2,3-*b*]quinoxalines have all utilised 2,3-disubstituted quinoxalines as starting materials, and in most instances have been illustrated only with a limited number of examples. Thus, 2-chloro-3-formylquinoxaline reacts with ethyl thioglycolate to give 2-ethoxycarbonylthieno[2,3-*b*]quinoxaline,[5] 2-chloro-3-cyanoquinoxaline with the same reactant produces the 3-amino-2-ester,[6] 3-cyanoquinoxaline-2(1*H*)-thione reacts with 2-bromoketones to give 3-amino-2-acyl- derivatives,[7] 3-alkenylquinoxalin-2(1*H*)-ones and 3-acylmethylquinoxalin-2(1*H*)-ones react with phosphorus pentasulfide giving 2-alkylthieno[2,3-*b*]quinoxalines,[8] certain 3-thioacylmethylquinoxalin-2(1*H*)-ones ring-close in acid and produce 2-arylthieno[2,3-*b*]quinoxalines,[9] and finally, 2-chloro-3-alkynylquinoxalines react with disodium sulfide generating 2-substituted thieno[2,3-*b*]quinoxalines.[10] It was reported that thieno[2,3-*b*]quinoxaline itself was formed in 5% yield on exposure of 3-phenylamino-2-nitrothiophene to iron(II) oxalate.[11]

Results and discussion

Our route (Scheme 2) begins with the construction of a 2-alkynylquinoxaline **2** by a cross coupling reaction. As quinoxaline coupling partner we have utilised 2-chloroquinoxaline **1a**, prepared from quinoxalin-2(1*H*)-one using phosphoryl chloride,[12] 2-iodoquinoxaline **1b** easily prepared from the chloro compound using hydrogen iodide in hot butanone,[13] and 2,6-dichloroquinoxaline[14] **1c** which reacted selectively in the desired sense. The second step involves addition of bromine to the triple bond in **2**, in most instances producing just one stereoisomer, assumed to be the *E*-isomer **3** shown, in some cases accompanied by the *Z*-isomer. In no instance were these separated and yields suggest that both isomers take part in the final stage of the synthesis which involves reaction of the dibromides **3** with disodium trithiocarbonate to give the tricyclic products **4**. In products **4** the typically low field quinoxaline 2-proton of the precursors was no longer present, replaced by a singlet signal for the thiophene ring proton (H-3): this appeared in the range δ 7.17–7.30 for 2-alkylthieno[2,3-*b*]quinoxalines and in the range δ 7.60–7.98 for 2-arylthieno[2,3-*b*]quinoxalines.

We began our investigation into the scope of the thieno-[2,3-*b*]quinoxaline ring forming process, its precedent being the formation of **4a** from **3a**, by examining the synthesis of other 2-alkylthieno[2,3-*b*]quinoxalines. Using bis(triphenylphosphine)palladium(II) chloride, copper(I) iodide and triethylamine, alkynes **2b** and **2c** were readily prepared from 2-iodoquinoxaline **1b** and hex-1-yne and 3,3-dimethylbut-1-yne, respectively. We found that the combination palladium(II) acetate, copper(I) iodide and triphenylphosphine is superior for the coupling of 2-chloroquinoxalines and using these conditions **2d** was prepared from 2,6-dichloroquinoxaline **1c** and hex-1-yne. Addition of bromine to the hindered **2c** was the only instance in all of our studies in which reaction in refluxing dichloromethane was required, other additions taking place smoothly at room temperature. Finally, aqueous ethanolic disodium trithiocarbonate[2] converted the dibromides **3b**, **3c**, and **3d** into the cyclised products **4b**, **4c**, and **4d** respectively.

We suggest that for all the ring closures described in this paper the mechanistic sequence set out in Scheme 3 operates. Thus, addition of the trithiocarbonate anion at that position on the side-chain which is conjugated with the ring imine unit generates **5**. Next, we envisage an intramolecular cyclising addition of sulfur to the quinoxaline 3-position, with loss of carbon disulfide and subsequent, or synchronous expulsion of bromide as suggested by the arrows on **5**. Finally, rearomatisation as shown by the arrows on **6** by loss of hydrogen bromide leads to the observed products **4**.

In the hope that the route could be modified to allow synthesis of 2-unsubstituted thieno[2,3-*b*]quinoxalines, 2-chloroquinoxaline **1a** and 2,6-dichloroquinoxaline **1c** were coupled with trimethylsilylacetylene giving **2e** and **2f** and each of these desilylated with potassium carbonate in methanol forming **2g** and **2h**. Working in the 6-chloro-series, bromine addition to **2f**

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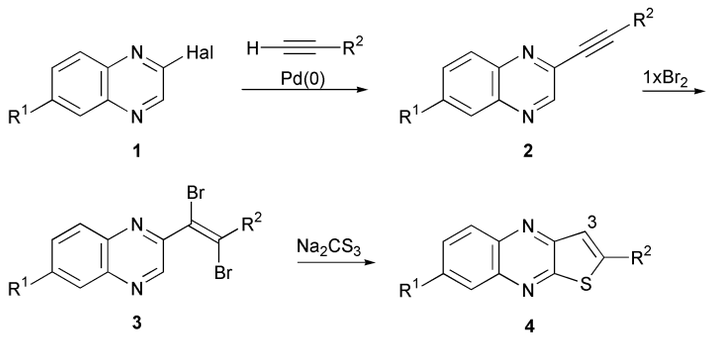
Table 1

Compound	Yield (%)	Mp/°C	Molecular formula	Found (M^+; $[M + H]^+$ (^{35}Cl, ^{79}Br); C, H, Br, Cl, N, S%)	Calculated (M^+; $[M + H]^+$ (^{35}Cl, ^{79}Br); C, H, Br, Cl, N, S%)
2b	97	Oil	$C_{14}H_{14}N_2$	M^+, 210.1158	210.1157
2c	97	Oil	$C_{14}H_{14}N_2$	M^+, 210.1164	210.1157
2d	54	42–43	$C_{14}H_{13}ClN_2$	M^+, 244.0776	244.0767
2e	54	Oil	$C_{13}H_{14}N_2Si$	M^+, 226.0925	226.0926
2f	67	107–109	$C_{13}H_{13}ClN_2S$	M^+, 260.0532	260.0536
2g	88	95–98	$C_{10}H_6N_2$	M^+, 154.0533	154.0531
2h	73	157–160	$C_{10}H_5ClN_2$	M^+, 188.0142 C, 63.32; H, 2.59; N, 14.51, Cl, 18.87	188.014 C, 63.68; H, 2.67; N, 14.85; Cl, 18.80
2i	84	Oil	$C_{16}H_{10}N_2$	M^+, 230.0839	230.0843
2j	90	118–120	$C_{16}H_9ClN_2$	M^+, 264.045 C, 71.74; H, 3.44; N, 10.49; Cl, 13.99	264.0451 C, 72.60; H, 3.43; N, 10.56; Cl, 13.39
2k	86	96–97	$C_{17}H_{12}N_2O$	M^+, 260.0965	260.0949
2l	90	125–127	$C_{16}H_9ClN_2$	M^+, 264.0459 C, 72.12; H, 2.95; N, 10.15; Cl, 13.39	264.0452 C, 72.60; H, 4.33; N, 10.58; Cl, 13.39
2m	57	185–188	$C_{16}H_9N_3O_2$	$[M + H]^+$, 276.0773 C, 69.31; H, 3.34; N, 15.14	276.0773 C, 69.81; H, 3.30; N, 15.27
2n	47	196–198	$C_{16}H_9N_3O_2$	$[M + H]^+$, 276.0770 C, 69.81; H, 3.30; N, 15.27	276.0773 C, 69.37; H, 3.24; N, 15.10
2o	49	146–149	$C_{16}H_9IN_2$	M^+, 355.9818 C, 54.30; H, 2.61; N, 7.71; I, 35.17	355.9812 C, 53.96; H, 2.56; N, 7.86; I, 35.63
2p	30	152–154	$C_{16}H_8F_3N_3$	C, 63.20; H, 2.79; N, 13.92; F, 19.00	C, 64.22; H, 2.69; N, 14.04; F, 19.05
3b	64	Oil	$C_{14}H_{14}Br_2N_2$	M^+, 367.9524	367.9524
3c	71	Oil	$C_{14}H_{14}Br_2N_2$	M^+, 367.9533	367.9524
3d	98	Oil	$C_{14}H_{13}Br_2ClN_2$	$[M + H]^+$, 402.9215	402.9214
3e	83	Oil	$C_{13}H_{13}Br_2ClN_2Si$	$[M + H]^+$, 418.8984	418.8982
3f	63	139–143	$C_{10}H_5Br_2ClN_2$	$[M + H]^+$, 346.8585	346.8587
3g	79	98–102	$C_{16}H_{10}Br_2N_2$	M^+, 387.9220 C, 49.33; H, 2.37; N, 7.38; Br, 41.27	387.9211 C, 49.26; H, 2.58; N, 7.18; Br, 40.96
3h	87	159–162	$C_{16}H_9Br_2ClN_2$	$[M + H]^+$, 422.8899 C, 45.29; H, 2.28; N, 6.52	422.8900 C, 45.26; H, 2.14; N, 6.60
3i	90	138–141	$C_{17}H_{12}Br_2N_2O$	M^+, 417.9311 C, 48.38; H, 3.00; N, 6.62; Br, 37.93	417.9317 C, 48.60; H, 2.88; N, 6.66; Br, 38.04
3j	89	128–130	$C_{16}H_9Br_2ClN_2$	$[M + H]^+$, 422.8907 C, 45.16; H, 2.25; N, 6.69; Br, 38.26; Cl, 8.24	422.8900 C, 45.26; H, 2.13; N, 6.60; Br, 37.65; Cl, 8.35
3k	56	146–148	$C_{16}H_9Br_2N_3O_2$	$(M + H)^+$, 433.9143 C, 44.24; H, 1.93; N, 9.50; Br, 36.48	433.9141 C, 44.17; H, 2.08; N, 9.66; Br, 36.73
3l	70	141–143	$C_{16}H_9Br_2N_3O_2$	$[M + H]^+$, 433.9137 44.00; H, 2.03; N, 9.52	433.9141 C, 44.17; H, 2.09; N, 9.66
3m	65	162–165	$C_{16}H_9Br_2IN_2$	$[M + H]^+$, 514.8253	514.8258
3n	79	107–109	$C_{16}H_8Br_2F_3N_3$	M^+, 456.9042 C, 44.04; H, 1.71; N, 9.22	456.9038 C, 41.86; H, 1.76; N, 9.15
4b	58	52–55	$C_{14}H_{14}N_2S$	M^+, 242.0879 C, 69.53; H, 5.81; N, 11.32; S, 13.18	242.0877 C, 69.39; H, 5.82; N, 11.55; S, 13.22
4c	62	60–62	$C_{14}H_{14}N_2S$	M^+, 242.0874	242.0878
4d	71	69–71	$C_{14}H_{13}ClN_2S$	M^+, 276.0491 C, 60.78; H, 4.85; N, 10.03; S, 11.13	276.0487 C, 60.75; H, 4.73; N, 10.12; S, 11.58
4e	53	186–188 (lit.[8b] 185)	$C_{16}H_{10}N_2S$	M^+, 262.0570 C, 72.99; H, 3.97; N, 10.48; S, 11.99	262.0564 C, 73.25; H, 3.84; N, 10.67; S, 12.22
4f	58	210–212	$C_{16}H_9ClN_2$	C, 64.74; H, 3.05; N, 9.44; S, 10.80	C, 64.90; H, 2.90; N, 9.07; S, 10.48
4g	79	208–210 (lit.[8b] 207)	$C_{17}H_{12}N_2OS$	M^+, 292.0662 C, 69.13; H, 4.08; N, 9.51; S, 11.10	292.0670 C, 69.83; H, 4.13; N, 9.50; S, 10.96
4h	80	235 dec.	$C_{16}H_9ClN_2S$	M^+, 296.0180 C, 65.02; H, 2.83; N, 9.42; Cl, 12.14; S, 11.10	296.0175 C, 64.75; H, 3.05; N, 9.44; Cl, 11.95; S, 10.80
4i	13	>300	$C_{16}H_9N_3O_2S$	M^+, 307.0412	307.0415
4j	34	205–207	$C_{16}H_9N_3S$	M^+, 277.0670	277.0673
4k	59	287–291	$C_{16}H_9N_3S$	M^+, 307.0409 C, 61.53; H, 3.29; N, 13.23	307.0415 C, 62.53; H, 2.95; N, 13.67
4l	59	254–257 (lit.[9] 255–256)	$C_{16}H_9IN_2S$	M^+, 387.9539	387.9533
4m	43	287–291	$C_{16}H_8F_3N_3S$	M^+, 332.0467	332.0469

was shown to be unexceptional giving **3e**, desilylation of this affording **3f**. Unfortunately, the cyclising thiophene ring-forming process failed with both of the dibromo substrates **3e** and **3f**.

Next we examined the formation of 2-arylthieno[2,3-*b*]-quinoxalines. Using the coupling conditions appropriate for 2-iodo- and 2-chloroquinoxalines (discussed above), 2-alkynyl-quinoxalines **2i**–**2n** were prepared using the corresponding arylalkynes.[15] 2-Ethynylquinoxaline **2g** (see above) was utilised for the synthesis of 4-iodophenyl derivative **2o** by coupling to 1,4-diiodobenzene, and for the synthesis of **2p** by cross coupling with 2-iodo-5-trifluoromethylpyridine, prepared from the commercial 2-chloro-5-trifluoromethylpyridine by reaction with sodium iodide in refluxing aqueous hydriodic acid.

Addition of bromine to alkynes **2i**–**2p** then produced 1,2-dibromoalkenes **3g**–**3n** respectively. Dibromides **3g**–**3j**, **3l**–**3n** reacted smoothly and efficiently with disodium trithio-carbonate to give the 2-arylthieno[2,3-*b*]quinoxalines **4e**–**4h**,



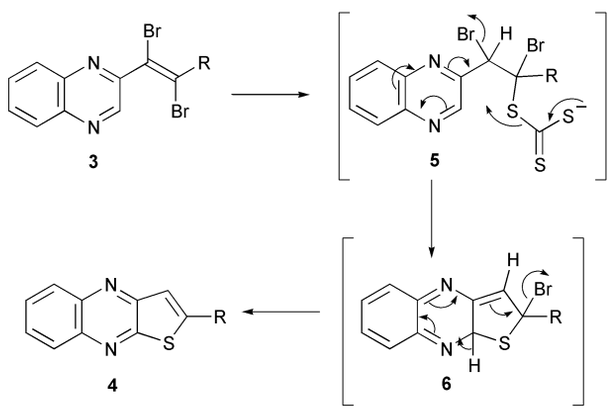
1	R^1	Hal
a	H	Cl
b	H	I
c	Cl	Cl

2	R^1	R^2
b	H	*n*-Bu
c	H	*t*-Bu
d	Cl	*n*-Bu
e	H	$SiMe_3$
f	Cl	$SiMe_3$
g	H	H
h	Cl	H
i	H	Ph
j	Cl	Ph
k	H	4-MeO-C_6H_4
l	H	4-Cl-C_6H_4
m	H	4-O_2N-C_6H_4
n	H	3-O_2N-C_6H_4
o	H	4-I-C_6H_4
p	H	5-CF_3-C_5H_3N

3	R^1	R^2
b	H	*n*-Bu
c	H	*t*-Bu
d	Cl	*n*-Bu
e	Cl	$SiMe_3$
f	Cl	H
g	H	Ph
h	Cl	Ph
i	H	4-MeO-C_6H_4
j	H	4-Cl-C_6H_4
k	H	4-O_2N-C_6H_4
l	H	3-O_2N-C_6H_4
m	H	4-I-C_6H_4
n	H	5-CF_3-C_5H_3N

4	R^1	R^2
b	H	*n*-Bu
c	H	*t*-Bu
d	Cl	*n*-Bu
e	H	Ph
f	Cl	Ph
g	H	4-MeO-C_6H_4
h	H	4-Cl-C_6H_4
i	H	4-O_2N-C_6H_4
j	H	4-H_2N-C_6H_4
k	H	3-O_2N-C_6H_4
l	H	4-I-C_6H_4
m	H	5-CF_3-C_5H_3N

Scheme 2



Scheme 3

and **4k**–**4m** respectively. In the case of the 4-nitrophenyl substrate **3k**, partial reduction of the nitro group occurred during the ring closure process and a separable mixture of 4-nitrophenyl- and 4-aminophenylthieno[2,3-*b*]quinoxalines **4i** and **4j** was obtained.

Future work will seek to enlarge on the process described in this paper, looking for example to the possibility of producing 2-side-chain functionalised thieno[2,3-*b*]quinoxalines, and to the possible use of quinoline, isoquinoline, pyrazine, pyrimidine, or pyridazine substrates instead of quinoxalines.

Experimental

General

Thin layer chromatography was carried out on Merck silica gel F_{254} 0.255 mm plates, and spots were visualised, where appropriate, by ultraviolet fluorescence at 254 or 297 nm. Flash column chromatography was performed using Merck Kiesel gel 60 (230–400 mesh). Tetrahydrofuran was dried by distillation from potassium–benzophenone; dichloromethane was dried by distillation from calcium hydride. All other chemicals were purified using standard procedures as required. Organic solutions were dried over anhydrous magnesium sulfate. IR spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer and are given in cm^{-1}. ^{1}H-NMR spectra were recorded on a Varian AC 300E NMR spectrometer operating at 300 MHz. All chemical shifts are reported in parts per million downfield from tetramethylsilane. Peak multiplicities are denoted by s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet) and m (multiplet) or by a combination of these *e.g.* dd (double doublet), with coupling constants (J) given in Hz. ^{13}C-NMR spectra were recorded on a Bruker AC 300 spectrometer operating at 75 MHz. Mass spectra were recorded on a Fisons VG Trio 2000 for electron impact (EI) and chemical ionisation (CI) modes. Accurate mass measurements were made on a Kratos Concept. Melting points were recorded on a Reichert heated stage microscope and are uncorrected. Petroleum ether refers to the fraction bp 40–60 °C. Solutions were degassed by bubbling nitrogen through them for 10 min.

Typical coupling using 2-iodoquinoxaline to give 2

2-(Phenylethynyl)quinoxaline 2i. A mixture of 2-iodoquinoxaline (512 mg, 2 mmol), phenylacetylene (0.26 ml, 2.4 mmol), bis(triphenylphosphine)palladium(II) chloride (36 mg), copper(I) iodide (16 mg), and triethylamine (4 ml) was heated at 60 °C under nitrogen for 24 h. After evaporation of the triethylamine, the residue was diluted with 1 M hydrochloric acid and extracted with dichloromethane. The dried dichloromethane extract was evaporated and the residue purified by column chromatography, eluting with dichloromethane–petroleum ether (1 : 1) giving 2-(phenylethynyl)quinoxaline **2i** (385 mg, 84%) as a yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.42 (3H, m), 7.75 (2H, m), 7.82 (2H, m), 8.08 (2H, m), 9.05 (s, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 86.9, 93.6, 121.3, 128.5, 129.1, 129.2, 129.7, 130.3, 130.6, 132.3, 139.5, 140.8, 142.1, 147.2; MS (EI): *m/z* 230 (M^+, 88%), 127 (80), 76 (100).

Typical coupling using 2-chloroquinoxalines to give 2

6-Chloro-2-(hex-1-yn-1-yl)quinoxaline 2d. To a degassed solution of 2,6-dichloroquinoxaline (1.5 g, 7.5 mmol) and hex-1-yne (0.57 ml, 9.75 mmol) in acetonitrile (40 ml) and triethylamine (7.5 ml), palladium(II) acetate (130 mg), copper(I) iodide (182 mg), and triphenylphosphine (200 mg) were added under nitrogen. The mixture was heated at 60 °C for 6 h. After evaporation of the solvent, the residue was diluted with water and extracted with dichloromethane. The dried organic extract was evaporated and the residue purified by column chromatography, eluting with petroleum ether–diethyl ether (9:1) to give 6-chloro-2-(hex-1-yn-1-yl)quinoxaline **2d** (944 mg, 54%) as a brown solid, mp 42–43 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.02 (3H, t, J = 6.9 Hz), 1.55 (2H, m), 1.71 (2H, m), 2.58 (2H, t, J = 7.0 Hz), 7.73 (1H, dd, J = 8.9 and 2.3 Hz), 7.90 (1H, d, J = 8.9 Hz), 8.08 (1H, d, J = 2.3 Hz), 8.85 (1H, s); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 13.5, 19.2, 22.0, 30.0, 78.6, 96.9, 128.0, 130.1, 131.4, 135.7, 140.0, 140.5, 140.8, 148.1; MS (CI): *m*/*z* 247 ($[M + H]^+$, ^{37}Cl, 30%), 245 ($[M + H]^+$, ^{35}Cl, 100%), 76 (100).

Typical couplings with 2-ethynylquinoxaline to give 2

(a) 2-(4-Iodophenylethynyl)quinoxaline 2o. To a degassed solution of 2-ethynylquinoxaline (492 mg, 3.2 mmol) and 1,4-diiodobenzene (5.3 g, 16 mmol) in acetonitrile (30 ml) and triethylamine (15 ml), palladium(II) acetate (36 mg, 0.16 mmol), copper(I) iodide (61 mg, 0.32 mmol), and triphenylphosphine (84 mg, 0.32 mmol), were added under nitrogen. The mixture was stirred under nitrogen at room temperature for 3 h. After evaporation, the residue was diluted with aqueous sodium bicarbonate and extracted with dichloromethane. The dried organic extract was evaporated and the residue purified by column chromatography, eluting with dichloromethane to yield 2-(4-iodophenylethynyl)quinoxaline **2o** (557 mg, 49%) as a crystalline yellow solid, mp 146–149 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.31 (2H, d, J = 8.3 Hz), 7.67 (2H, d, J = 8.3 Hz), 7.72 (2H, m), 8.01 (2H, m), 8.88 (1H, s); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 88.1, 92.4, 96.1, 120.8, 129.1, 129.2, 130.4, 130.6, 133.5, 137.7, 139.9, 140.9, 142.1, 147.0; MS (CI): *m*/*z* 357 ($[M + H]^+$, 100%). Further elution with dichloromethane–ethyl acetate (7:3) gave 1,4-bis(quinoxalin-2-ylethynyl)benzene (129 mg, 14%), mp 262–263 °C.

(b) 2-(5-Trifluoromethylpyridin-2-ylethynyl)quinoxaline 2p. To a degassed solution of 2-ethynylquinoxaline **2g** (500 mg, 3.24 mmol), and 2-iodo-5-trifluoromethylpyridine (1.7 g, 6.48 mmol) in acetonitrile (13 ml) and triethylamine (6.5 ml), palladium(II) acetate (36 mg, 0.16 mmol), copper(I) iodide (62 mg, 0.32 mmol), and triphenylphosphine (85 mg, 0.32 mmol), were added under nitrogen. The mixture was stirred under nitrogen at room temperature for 3 h. After evaporation, the residue was diluted with aqueous sodium bicarbonate and extracted with dichloromethane. The dried organic extract was evaporated and the residue purified by column chromatography, eluting with dichloromethane–ethyl acetate (95:5) to yield 2-(5-trifluoromethylpyridin-2-ylethynyl)quinoxaline **2p** (450 mg, 30%), as a yellow solid, mp 152–154 °C (from methanol); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (3H, m), 7.94 (1H, dd, J = 1.7 and 7.7 Hz), 8.06 (2H, m), 8.88 (1H, s), 9.01 (1H, s); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 87.8, 90.1, 127.5, 129.3, 129.4 (2), 130.9, 131.7 (2), 133.5, 138.0, 141.3, 142.1, 145.2, 147.1 (2).

Typical addition of bromine to give 3

2-(1,2-Dibromo-2-phenylethenyl)quinoxaline 3g. A solution of bromine (0.36 ml, 7.15 mmol) in dichloromethane (10 ml) was added dropwise to a stirred solution of 2-(phenylethynyl)-quinoxaline **2i** (1.5 g, 6.5 mmol) dissolved in dichloromethane (20 ml). The resultant mixture was stirred for 2 h at room temperature. Addition of aqueous sodium metabisulfite and dichloromethane followed by separation, drying, and evaporation of the organic phase under reduced pressure gave a brown oil. Purification by column chromatography eluting with petroleum ether–ethyl acetate (93:7) gave the pure dibromoalkene **3g** (1.99 g, 79%) as a yellow solid, mp 98–102 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.50 (3H, m), 7.64 (2H, m), 7.90 (2H, m), 8.22 (2H, m), 9.02 (1H, s); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 113.6, 122.5, 128.4, 128.9, 129.2, 129.5, 130.6, 130.9, 139.2, 141.5, 141.6, 145.2, 152.8; MS (CI): *m*/*z* 389, 391, 393 ($[M + H]^+$, 6, 12, 6%), 231 (100).

Typical ring closure to form thieno[2,3-*b*]quinoxalines 4

2-Phenylthieno[2,3-*b*]quinoxaline 4e. An aqueous solution of disodium trithiocarbonate[2] (33%, 3 ml) was added to a hot solution of 2-(1,2-dibromo-2-phenylethenyl)quinoxaline **3g** (200 mg, 0.51 mmol) in methanol (8 ml) with stirring. The resulting solution was cooled to room temperature and stirred for a further 3 h. After evaporation of methanol, the residue was diluted with water and extracted with dichloromethane. The organic extract was dried and evaporated under reduced pressure to leave a brown oil. Purification by column chromatography over silica gel eluting with petroleum ether–diethyl ether (2:1) gave a red solid, which was further purified by treating with charcoal in dichloromethane to give the pure thienoquinoxaline **4e** (71 mg, 53%) as a yellow solid, mp 186–188 °C (lit.[8b] mp 185 °C).

Typical desilylation

2-Ethynylquinoxaline 2g. To a suspension of 2-(trimethylsilylethynyl)quinoxaline **2e** (3 g, 13.2 mmol) in dry methanol (34 ml) at room temperature was added potassium carbonate (188 mg, 1.32 mmol) under nitrogen and the mixture stirred for 1 h. The methanol was evaporated under reduced pressure and the residue dissolved in dichloromethane, the solution washed with water, dried, and evaporated under reduced pressure, to give a brown solid. Purification by column chromatography over silica gel eluting with dichloromethane gave 2-ethynylquinoxaline **2g** (1.8 g, 88%) as a white solid, mp 95–98 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.30 (1H, s), 7.72 (2H, m), 8.05 (2H, m), 8.82 (1H, s); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 80.9, 81.2, 129.1, 129.2, 130.6, 130.7, 138.3, 141.2, 141.9, 147.0; MS (CI): *m*/*z* 155 ($[M + H]^+$, 100%).

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References

1 For reviews, see P. E. Baugh, D. Collison, C. D. Garner and J. A. Joule, *Comprehensive Biological Catalysis*, 1998, **Vol. III**, 377; C. D. Garner, P. Baugh, D. Collison, E. S. Davies, A. Dinsmore, J. A. Joule, E. Pidcock and C. Wilson, *Pure Appl. Chem.*, 1997, **69**, 2205; D. Collison, C. D. Garner and J. A. Joule, *Chem. Soc. Rev.*, 1996, 25; for more recent work, see E. S. Davies, G. M. Aston, R. L. Beddoes, D. Collison, A. Dinsmore, A. Docrat, J. A. Joule, C. R. Wilson and C. D. Garner, *J. Chem. Soc.*, *Dalton Trans.*, 1998, 3647; A. Dinsmore, C. D. Garner and J. A. Joule, *Tetrahedron*, 1998, **54**, 3291; A. Dinsmore, C. D. Garner and J. A. Joule, *Tetrahedron*, 1998, **54**, 9559; B. Bradshaw, A. Dinsmore, C. D. Garner and J. A. Joule, *Chem. Commun.*, 1998, 417.
2 D. J. Martin and C. C. Greco, *J. Org. Chem.*, 1968, **33**, 1275.

3 *cf.* F. Runge, Z. El-Heweki, J. J. Renner and E. Taeger, *J. Prakt. Chem.*, 1960, **11**, 284.
4 L. Larsen, D. J. Rowe, C. D. Garner and J. A. Joule, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2317.
5 E. Lippmann and W. Shilov, *Collect. Czech. Chem. Commun.*, 1984, **49**, 1304; W. Shilov and E. Lippmann, *Z. Chem.*, 1986, **26**, 101.
6 S. A. Mahgoub, *Phosphorus Sulfur*, 1991, **61**, 151.
7 M. Z. A. Badr, S. A. Mahgoub, O. S. Moustafa and A. A. Gries, *Phosphorus Sulfur*, 1993, **79**, 77; O. S. Moustafa, *Phosphorus Sulfur*, 1997, **131**, 49.
8 (*a*) Y. A. Ibrahim, *Chem. Ind.* (*London*), 1978, 585; Y. A. Ibrahim, *Chem. Ind.* (*London*), 1980, 536; (*b*) Y. A. Ibrahim, M. A. Badaway and S. El-Bahaie, *J. Heterocycl. Chem.*, 1982, **19**, 699.
9 E. Terpetschinig, W. Ott, G. Kollenz, K. Peters, E.-M. Peters and H. G. von Schnering, *Montsh. Chem.*, 1988, **119**, 367; T. N. Yamborisov, N. N. Kasimova, O. A. Yamborisova, I. A. Zhikina, Y. S. Andreichikov, G. N. Novoselova and A. V. Milyutin, *Pharm. Chem. J.* (*Engl. Transl.*), 1996, **30**, 101.
10 D. E. Ames, J. C. Mitchel and C. Takundwa, *J. Chem. Res.* (*M*), 1985, 1683.
11 R. G. R. Bacon and S. D. Hamilton, *J. Chem. Soc.*, 1974, 1970.
12 H. Gowenlock, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1945, 622.
13 P. J. Lont and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, 1972, **91**, 850.
14 We thank the Nissan Chemical Company for a generous supply of 2,6-dichloroquinoxaline.
15 4-Methoxyphenylethyne and 4-chlorophenylethyne were prepared *via* coupling of trimethylsilylacetylene with 4-methoxy- and 4-chloroiodobenzene respectively followed by desilylation (R. Liu and T. T. Tidwell, *J. Chem. Soc., Perkin Trans. 2*, 1996, 2757; G. T. Crisp and B. L. Flynn, *J. Org. Chem.*, 1993, **58**, 6614; E.-i. Negishi and T. Takahashi, *J. Am. Chem. Soc.*, 1986, **108**, 3402). 4-Nitro- and 3-nitrophenylethyne were prepared by condensation of the arylaldehyde with malonic acid, addition of bromine, and sequential eliminations of carbon dioxide and bromide and then hydrogen bromide (D. F. Delar, *Org. Synth.*, 1963, **Coll. Vol. IV**, 731; C. P. Krimmel, L. E. Thielen, E. A. Brown and W. J. Heidtke, *Org. Synth.*, 1962, **Coll. Vol. IV**, 961; E. R. Trumbull, R. T. Finn, K. M. Ibne-Rase and C. K. Saunders, *J. Org. Chem.*, 1962, **27**, 2343 (we found sodium hydrogen carbonate to be preferable to sodium hydroxide for the decarboxylative debromination); A. D. Allen and C. D. Cook, *Can. J. Chem.*, 1963, **41**, 1085). We thank Miss Mélanie Liutkus, a student from the University of Montpellier, France, for preparing the nitroarylethynes during a work experience period in Manchester.