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# Synthesis of thieno[2,3-*b*]quinoxalines and pyrrolo[1,2-*a*]-quinoxalines from 2-haloquinoxalines

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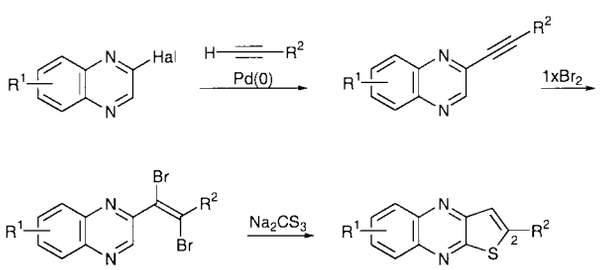
The palladium(0)-catalysed coupling of 2-haloquinoxalines with functionally substituted alkynes, addition of one mol equivalent of bromine to the 2-alkynylquinoxalines thus produced and then reaction of the resulting dibromides with disodium trithiocarbonate produced 2-hydroxymethyl- and 2-(diethoxymethyl)thieno[2,3-*b*]quinoxalines. Addition of bromine to some 6-substituted-2-(3,3-diethoxypropyn-1-yl)quinoxalines gave pyrrolo[1,2-*a*]quinoxalines. Treatment of a 3-(1,2-dibromoalkenyl)quinoline, a 3-(1,2-dibromoalkenyl)pyrazine, and a 5-(1,2-dibromoalkenyl)-pyrimidine with disodium trithiocarbonate failed to induce thiophene ring formation.

## Introduction

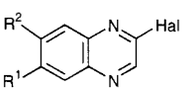
We have previously described[1] a route (Scheme 1) to thieno-[2,3-*b*]quinoxalines in which a 2-haloquinoxaline is cross-coupled with an alkyne, one mole of bromine is added across the triple bond and the resulting 1,2-dibromoalkene reacted with disodium trithiocarbonate[2] resulting in a cyclising ring closure to a thieno[2,3-*b*]quinoxaline with the loss of both bromine atoms. We have shown that the process works well for simple alkyl- and a range of aryl-alkynes, resulting in the corresponding 2-substituted heterocycles, and discussed the mechanism for the transformation.[1] In this paper we describe our further studies into the generality of the thiophene ring-closing process, the synthesis of thieno[2,3-*b*]quinoxalines with functionalised 2-alkyl side-chains, and the synthesis of pyrrolo[1,2-*a*]quinoxalines.




**Scheme 1**

## Results and discussion

Our route (Scheme 1) to thieno[2,3-*b*]quinoxalines begins with the construction of a 2-alkynylquinoxaline **2** by a cross-coupling reaction for which 2-chloro- or 2-iodoquinoxalines **1** can be used.[1] Coupling 2-iodoquinoxaline **1b** with propargyl alcohol (prop-2-ynyl alcohol) produced **2a** but attempted addition of bromine did not proceed smoothly and the complex mixture of products obtained was not further examined. Since it seemed likely that the alcohol function was responsible for the complexity of the product mixture, it was protected as a benzoate **2b** and then bromine addition proceeded smoothly giving **3a**. However attempted application of the (basic) ring-closing conditions again led to complex mixtures—clearly the choice of an ester for protection was not well advised.




| | $R^1$ | $R^2$ | Hal |
|---|---|---|---|
| **1** | | | |
| **a** | H | H | Cl |
| **b** | H | H | I |
| **c** | Cl | H | Cl |
| **d** | MeO | H | Cl |
| **e** | H | MeO | Cl |

2,6-Dichloroquinoxaline[3] **1c** was coupled with propargyl alcohol tetrahydropyranyl ether[4] giving **2c** and this was reacted with bromine. We were surprised to find that the two stereoisomeric products each contained three bromine atoms—two had added as usual to the triple bond but a third had been incorporated elsewhere. $^1$H-NMR analysis showed that the benzene ring still had three protons and thus the third bromine had to reside on the protecting group. Consideration of the possible mechanism whereby a bromine atom could have become incorporated into the tetrahydropyran ring (*via* a ring-opened enol ether), the presence of signals for only four protons at $\delta < 2.10$, and the observation that the tetrahydropyran C-2 proton was now a clear doublet (in one of the stereoisomers) lead us to suggest structure **3b** for these products. A search of the literature shows that this bromination of a tetrahydropyranyl ether is unprecedented. Reaction of the 1,2-dibromoalkenes **3b** with disodium trithiocarbonate brought about the desired ring-closure and formation of **4a**, aqueous acidic hydrolysis of which produced the alcohol **4b**.

At a higher oxidation level, we were unable to cross-couple methyl propiolate with 2-iodoquinoxaline and so resorted to using an ortho ester as surrogate. Coupling 3,3,3-triethoxypropyne[5] with 2-chloroquinoxaline gave **2d** and brief treatment with toluene-*p*-sulfonic acid monohydrate converted this into the ester **2e**. Addition of bromine to this was unexceptional, producing a mixture of double bond isomers **3c**, however on attempted thieno[2,3-*b*]quinoxaline formation, the reaction in methanol solution took an alternative course and 1,3-dithiole-3-thione **5**, as a mixture of methyl and ethyl esters, was formed efficiently. One can speculate that the Michael-type trithiocarbonate addition to this alkene, which is believed to be the initiating step in the thieno[2,3-*b*]quinoxaline synthesis,[1] is in this case governed by conjugation to the ester (rather than the ring imine) preventing the sequence which leads to the tricycle and allowing the alternative mode of reaction.[6]

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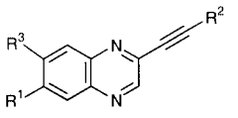
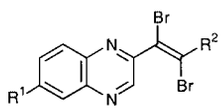
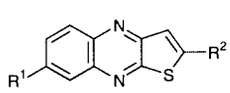


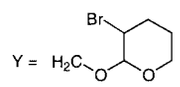
| 2 | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **a** | H | $CH_2OH$ | H |
| **b** | H | $CH_2OCOPh$ | H |
| **c** | Cl | $CH_2OTHP$ | H |
| **d** | H | $C(OEt)_3$ | H |
| **e** | H | $CO_2Et$ | H |
| **f** | H | $CH(OEt)_2$ | H |
| **g** | Cl | $CH(OEt)_2$ | H |
| **h** | MeO | $CH(OEt)_2$ | H |
| **i** | H | $CH(OEt)_2$ | MeO |

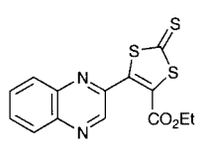


| 3 | $R^1$ | $R^2$ |
|---|---|---|
| **a** | H | $CH_2OCOPh$ |
| **b** | Cl | Y |
| **c** | H | $CO_2Et$ |
| **d** | H | $CH(OEt)_2$ |

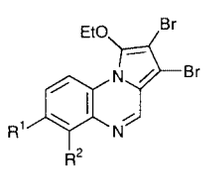


| 4 | $R^1$ | $R^2$ |
|---|---|---|
| **a** | Cl | Y |
| **b** | Cl | $CH_2OH$ |
| **c** | H | $CH(OEt)_2$ |

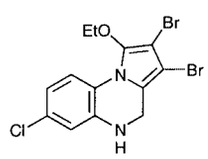




**5**



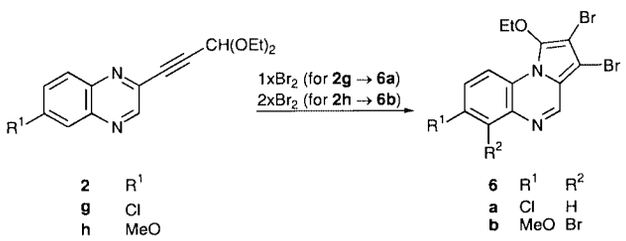
| 6 | $R^1$ | $R^2$ |
|---|---|---|
| **a** | Cl | H |
| **b** | MeO | Br |



**7**

Working at an intermediate oxidation level, 2-iodoquinoxaline was coupled with 3,3-diethoxypropyne giving **2f**, addition of bromine then gave **3d** and our standard ring-closing conditions produced the diethyl acetal **4c** of 2-formylthieno-[2,3-*b*]quinoxaline. However, when the 6-chloro-analogue **2g** was prepared by a comparable cross-coupling and subjected to bromine, a product $C_{13}H_9Br_2ClN_2O$ was formed in which it was evident that one ethoxy group had been lost while two bromine atoms had been incorporated. Additionally, the typical quinoxaline low field singlet signal was still present, though shifted somewhat to a higher field at $\delta$ 8.68. To this product we assigned structure **6a** and confirmed this assignment by a simple borohydride reduction when dihydro-derivative **7**, an *N*-arylpyrrole, was formed, lacking the quinoxaline singlet but having a $CH_2NH$ system (Scheme 2).

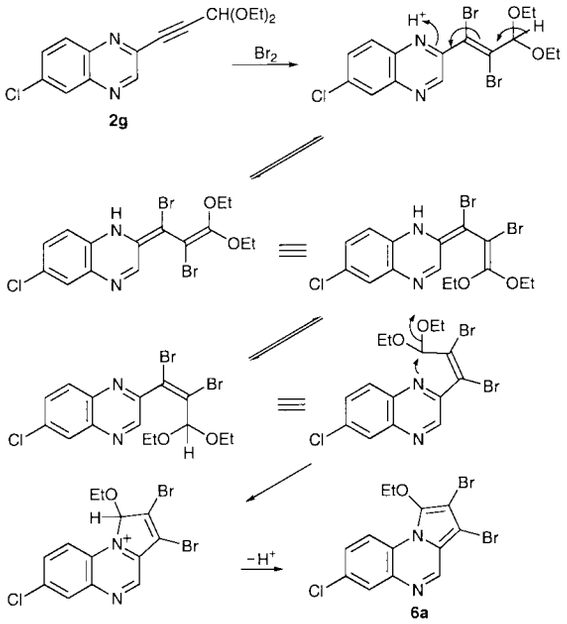
We speculate that this pyrrolo[1,2-*a*]quinoxaline **6a** is formed




| 2 | $R^1$ |
|---|---|
| **g** | Cl |
| **h** | MeO |

| 6 | $R^1$ | $R^2$ |
|---|---|---|
| **a** | Cl | H |
| **b** | MeO | Br |

**Scheme 2**



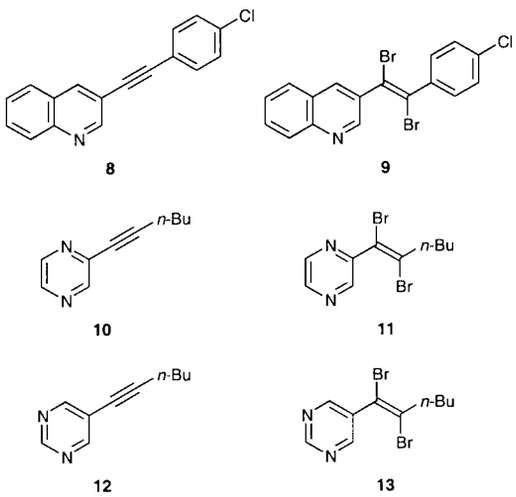

**Scheme 3**

as shown in Scheme 3, thus addition of bromine gives typically the *trans* product, which is in equilibrium *via* a tautomer with the *cis* isomer; ring-closure of the *cis* isomer then loss of ethanol provides the observed tricyclic product.

It seemed extraordinary that the presence of an apparently remote chlorine substituent should influence the course of the reaction between the alkynyl acetal **2g** and its unsubstituted prototype, **2f**. Accordingly we decided to prepare an alternatively 6-substituted quinoxalinylalkyne and examine its reaction with bromine. The interaction of 1,2-diaminobenzenes with glyoxylic acid esters is well known to give rise to quinoxalin-2(1*H*)-ones, and these in turn can be transformed into the corresponding 2-haloquinoxalines suitable for coupling; unsymmetrically substituted 1,2-diaminobenzenes give mixtures of quinoxalinone regioisomers. The use of glyoxylic acid, instead of the ester, with 4-substituted 1,2-diaminobenzenes was shown to produce a larger proportion of the 6-substituted-quinoxalin-2(1*H*)-one.[7] The reaction between 1,2-diamino-4-methoxybenzene and butyl glyoxylate gave a mixture of the quinoxalin-2(1*H*)-ones which were converted into the chlorides and these were separated by fractional crystallisation; the identities of these two halides have not been established.[8] We repeated the ring synthesis with this diamine, but using glyoxylic acid, and obtained a mixture of methoxyquinoxalin-2(1*H*)-ones, richer in one isomer than the other. The mixture was converted into the chlorides, from which pure samples of the major and the minor halides could be isolated by chromatography. On the basis of the earlier work,[7] we assign to the major halide structure **1d** while the less abundant halide is **1e**.

Each of these halides was separately coupled with 3,3-diethoxypropyne giving **2h** and **2i** respectively and these were then treated with bromine. In analogy with the reaction observed with the 6-chloro-alkyne **2g**, **2h** was transformed into a pyrrolo[1,2-*a*]quinoxaline; early experiments made it clear that a third bromine atom was being incorporated into the product so 2 mole equivalents were used and the product **6b** was isolated in high yield, the position of the benzene ring halogen following from the $^1$H-NMR spectrum of the product. The isomer **2i** on the other hand did not produce a pyrroloquinoxaline, but simply a mixture containing straightforward bromine adducts, one with the acetal intact and one with an aldehyde, which were not fully characterised. The role of the 6-substituent remains something of a mystery until further experiments can be carried out.

Returning to the mechanism by which the thieno[2,3-*b*]-quinoxalines are formed, we speculated that there may be two essential criteria for a successful sequence: (1) there must be a ring imine, in conjugation with the dibromoalkene, in order to encourage correctly oriented dithiocarbonate addition *and* (2) there must be another ring imine unit to encourage the intramolecular cyclising sulfur addition; both of these requirements are satisfied in the quinoxaline series. We sought confirmation of these ideas by preparing a quinoline analogue of the cyclisation substrates, thus 3-bromoquinoline was coupled to give **8** and bromine was added to produce **9**. On exposure of **9** to disodium trithiocarbonate no reaction occurred at room temperature and at reflux, only elimination to return the alkyne **8**.




We then considered whether the benzenoid ring is an essential component of the cyclising procedure and prepared pyrazinylalkyne **10**[9] and from it the dibromoalkene **11**. Exposure of this dihalide to the conditions which, in the quinoxaline series, lead to cyclisation resulted only in debromination and a return to the pyrazinylalkyne **10**; no thieno[2,3-*b*]pyrazine was formed. Similarly, the pyrimidinylalkyne **12**[10] was prepared and converted into dibromoalkene **13**. For this substrate, criterion (1) above is not met, though the double bond is activated in an inductive sense in the required direction by the electron-deficient heterocycle; criterion (2) is satisfied. However, once again exposure to disodium trithiocarbonate resulted only in debromination and a return to alkyne **12**.

We conclude that the formation of thieno[2,3-*b*]quinoxalines described previously[1] and in this paper requires *both* imine units *and* the fused benzene ring. The factor which allows success is the retention of an aromatic ring during the cyclising sequence in which the heterocyclic ring temporarily loses its aromatic status.

## 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 absorption data 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 ionization (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 for 10 min.

### 2-(3-Hydroxypropyn-1-yl)quinoxaline 2a

A mixture of 2-iodoquinoxaline (1.5 g, 5.8 mmol), propargyl alcohol (0.4 ml, 6.9 mmol), bis(triphenylphosphine)-palladium(II) chloride (100 mg, 0.14 mmol), copper(I) iodide (50 mg, 0.26 mmol), and triethylamine (12 ml) was heated at 60 °C and under nitrogen for 6 h. After evaporation of the triethylamine, the residue was diluted with 1 M hydrochloric acid and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with ethyl acetate to afford 2-(3-hydroxypropyn-1-yl)quinoxaline **2a** (700 mg, 66%) as a yellow solid, mp 140–141 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 2.17 (t, $J$ = 6.3 Hz, 1H), 4.67 (d, $J$ = 6.3 Hz, 2H), 7.84 (m, 2H), 8.14 (m, 2H), 8.97 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 51.2, 82.9, 92.0, 129.0, 129.1, 130.6, 130.7, 138.7, 141.1, 141.9, 146.8. MS (CI): 185 (M + 1, 100%), 169 (48). Calcd. for: $C_{11}H_8N_2O$: 184.0636. HRMS: found: $M^+$, 184.0635.

### 2-(3-Benzoyloxypropyn-1-yl)quinoxaline 2b

To a solution of 2-(3-hydroxypropyn-1-yl)quinoxaline **2a** (100 mg, 0.55 mmol) in dichloromethane (5 ml) and triethylamine (0.08 ml) at room temperature, benzoyl chloride (0.07 ml, 0.6 mmol) was added, under nitrogen. The mixture was stirred for 2 h. The reaction was quenched with aqueous saturated sodium hydrogencarbonate and extracted with dichloromethane. The combined organic extracts were dried and concentrated to give a brown oil which was purified by flash column chromatography over silica gel, eluting with dichloromethane to give 2-(3-benzoyloxypropyn-1-yl)quinoxaline **2b** (135 mg, 85%) as a brown solid, mp 94–97 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 5.32 (s, 2H), 7.53 (m, 2H), 7.65 (m, 1H), 7.85 (m, 2H), 8.14 (m, 4H), 8.93 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 52.6, 83.8, 87.3, 128.4, 129.1, 129.8 (2 × C), 130.7 (2 × C), 133.3, 138.3, 141.1, 141.9, 146.8, 165.6. MS (CI): 289 (M + 1, 100%), 169 (52). Calcd. for: $C_{18}H_{12}N_2O_2$: 288.0898. HRMS: found: $M^+$, 288.0893.

### (*E*)- and (*Z*)-2-(3-Benzoyloxy-1,2-dibromoprop-1-en-1-yl)-quinoxaline 3a

A solution of bromine (0.12 ml, 2.3 ml) in dichloromethane (10 ml) was added dropwise to a stirred solution of 2-(3-benzoyloxypropyn-1-yl)quinoxaline **2b** (600 mg, 2.08 mmol) dissolved in dichloromethane (25 ml). The resultant mixture was stirred for 2 h at room temperature. Addition of aqueous sodium metabisulfite and dichloromethane was followed by separation, drying, and evaporation of the organic phase under reduced pressure to give a brown oil. Purification of this by column chromatography over silica gel, eluting with dichloromethane–petroleum ether (8:2), gave the minor dibromoalkene **3a** (assumed to be $Z$) (300 mg, 32%) as a brown gum. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 5.23 (s, 2H), 7.45 (m, 2H), 7.60 (m, 1H), 7.87 (m, 2H), 8.04 (m, 2H), 8.15 (m, 2H), 9.20 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 65.4, 125.0, 128.3, 129.1, 129.2, 129.4, 129.5, 129.7, 130.9, 131.7, 133.3, 140.7, 141.4, 145.3, 150.3, 165.4. MS (CI): 447, 449, 451 (M + 1, 50, 100, 50%), 289 (90), 169 (75). Calcd. for: $C_{18}H_{12}{}^{79}Br_2N_2O_2$: 446.9344. HRMS:

found: $M^+$, 446.9349. Eluting with dichloromethane gave the major dibromoalkene **3a** (assumed to be *E*) (460 mg, 49%) as a white solid, mp 140–143 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 5.55 (s, 2H), 7.47 (m, 2H), 7.65 (m, 1H), 7.90 (m, 2H), 8.20 (m, 4H), 9.05 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 66.7, 125.0, 128.3, 128.9, 129.4, 129.5, 129.7, 130.0, 130.9, 131.7, 134.3, 140.7, 141.5, 145.2, 150.1, 165.4. MS (CI): 447, 449, 451 (M + 1, 50, 100, 50%), 289 (40). Calcd. for: $C_{18}H_{12}{}^{79}Br_2N_2O_2$: 446.9344. HRMS: found: $M^+$, 446.9344.

### 6-Chloro-2-[3-(tetrahydropyran-2-yloxy)propyn-1-yl]quinoxaline 2c

To a degassed solution of 2,6-dichloroquinoxaline (1.5 g, 7.5 mmol) and 3-(tetrahydropyran-2-yloxy)prop-1-yne[4] (1.1 g, 8.25 mmol) in acetonitrile (40 ml) and triethylamine (7.5 ml), palladium(II) acetate (130 mg, 0.57 mmol), copper(I) iodide (182 mg, 0.95 mmol), and triphenylphosphine (200 mg, 0.76 mmol) were added, under nitrogen. The mixture was heated at 60 °C for 4 h. After evaporation of the organic solvents, the residue was diluted with water and extracted with dichloromethane. The dichloromethane extract was purified by column chromatography over silica gel, eluting with petroleum ether–diethyl ether (8:2) to give 6-chloro-2-[3-(tetrahydropyran-2-yloxy)propyn-1-yl]quinoxaline **2c** (1.29 g, 56%) as a pale yellow coloured oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.60–1.95 (m, 6H), 3.64 (m, 1H), 3.94 (m, 1H), 4.61 (d, $J$ = 16.3 Hz, 1H), 4.66 (d, $J$ = 16.3 Hz, 1H), 4.97 (apparent triplet, $J$ = 3.4 Hz, 1H), 7.77 (dd, $J$ = 2.3 and 9.0 Hz, 1H), 8.05 (d, $J$ = 9.0 Hz, 1H), 8.13 (d, $J$ = 2.3 Hz, 1H), 8.90 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 18.8, 25.2, 30.1, 54.4, 61.9, 82.9, 90.6, 97.2, 128.1, 130.3, 131.6, 136.3, 138.9, 140.4, 141.1, 147.8. MS (EI): 305 ($M^+$, $^{37}$Cl, 30), 303 ($M^+$, $^{35}$Cl, 100). Calcd. for: $C_{16}H_{15}{}^{35}ClN_2O_2$: 303.0900. HRMS: found: $M^+$, 303.0907.

### (*E*)- and (*Z*)-6-Chloro-2-[1,2-dibromo-3-(3-bromotetrahydropyran-2-yloxy)prop-1-en-1-yl]quinoxaline 3b

A solution of bromine (0.13 ml, 2.43 mmol) in dichloromethane (5 ml) was added dropwise to a stirred solution of 6-chloro-2-[3-(tetrahydropyran-2-yloxy)propyn-1-yl]quinoxaline **2c** (700 mg, 2.3 mmol) dissolved in dichloromethane (15 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 of this by column chromatography over silica gel, eluting with dichloromethane, gave the major dibromoalkene **3b** (assumed to be *E*) as a brown oil (320 mg, 25%). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.60 (m, 1H), 2.10 (m, 2H), 2.50 (m, 1H), 3.76 (m, 1H), 4.13 (m, 2H), 4.94 (m, 3H), 7.80 (dd, $J$ = 2.2 and 8.8 Hz, 1H), 8.11 (d, $J$ = 8.8 Hz, 1H), 8.18 (d, $J$ = 2.2 Hz, 1H), 9.00 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 22.4, 29.2, 48.4, 62.4, 70.8, 100.2, 115.8, 123.2, 128.1, 130.7, 131.7, 137.0, 140.1, 141.8, 145.7, 152.0. MS (CI): 539, 541, 543, 545 (M + 1, 12, 29, 32, 20%), 385 (35), 383 (100), 381 (80), 303 (30). And the minor dibromoalkene **3b** (assumed to be *Z*) as a brown oil (220 mg, 17%). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.60 (m, 1H), 1.95 (m, 2H), 2.37 (m, 1H), 3.42 (m, 1H), 3.78 (m, 1H), 4.02 (m, 1H), 4.45 (d, $J$ = 17.5 Hz, 1H), 4.65 (d, $J$ = 17.5 Hz, 1H), 4.76 (d, $J$ = 3.0 Hz, 1H), 7.82 (dd, $J$ = 2.3 and 9.9 Hz, 1H), 8.07 (d, $J$ = 9.0 Hz, 1H), 8.17 (d, $J$ = 2.3 Hz, 1H), 9.09 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 22.3, 29.1, 48.1, 62.2, 68.7, 99.6, 114.9, 123.9, 128.1, 130.7, 132.0, 137.0, 139.4, 141.7, 146.1, 150.6. MS (CI): 539, 541, 543, 545 (M + 1, 8, 22, 29, 15%), 385 (30), 383 (100), 381 (70), 303 (50).

### 7-Chloro-2-(3-bromotetrahydropyran-2-yloxymethyl)thieno-[2,3-*b*]quinoxaline 4a

An aqueous solution of disodium trithiocarbonate[2] (33%, 1.5 ml) was added to a hot solution of (*E*)-6-chloro-2-[1,2-dibromo-3-(3-bromotetrahydropyran-2-yloxy)prop-2-en-1-yl]-quinoxaline (*E*)-**3b** (320 mg, 0.69 mmol) in methanol (20 ml) with stirring. The resulting solution was cooled to room temperature and stirred for a further 1 h. After evaporation of the methanol, water and dichloromethane were added. The organic layer was separated, dried, and evaporated under reduced pressure to give a red solid. Purification of this by column chromatography over silica gel, eluting with dichloromethane, gave thienoquinoxaline **4a** (85 mg, 30%) as a yellow solid, mp 106–108 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.52 (m, 1H), 1.90 (m, 2H), 2.40 (m, 1H), 3.57 (m, 1H), 3.95 (m, 2H), 4.76 (d, $J$ = 4.4 Hz, 1H), 4.91 (d, $J$ = 14.0 Hz, 1H), 5.06 (d, $J$ = 14.0 Hz, 1H), 7.39 (s, 1H), 7.65 (dd, $J$ = 2.3 and 9.1 Hz, 1H), 8.03 (d, $J$ = 9.1 Hz, 1H), 8.06 (d, $J$ = 2.3 Hz, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 23.0, 29.7, 48.3, 62.8, 65.3, 100.4, 119.7, 127.3, 130.3, 130.4, 135.0, 139.4, 140.1, 150.7, 151.6. MS (CI): 413, 415, 417 (M + 1, 75, 100, 35%), 335 (40), 235 (60). Calcd. for: $C_{16}H_{14}{}^{79}Br^{35}ClN_2O_2S$: 412.9727. HRMS: found: $(M + H)^+$, 412.9727.

### 7-Chloro-2-hydroxymethylthieno[2,3-*b*]quinoxaline 4b

A solution of 6-chloro-2-(3-bromotetrahydropyran-2-yloxymethyl)thieno[2,3-*b*]quinoxaline **4a** (20 mg, 0.05 mmol) in methanol (1 ml) was added to an aqueous solution of 4 M hydrochloric acid with stirring. The solution was heated for a further 24 h at 70 °C. The mixture was concentrated *in vacuo* and then basified with sodium carbonate and extracted with dichloromethane. The dichloromethane extract was purified by column chromatography over silica gel, eluting with dichloromethane, giving 6-chloro-2-hydroxymethylthieno[2,3-*b*]quinoxaline **4b** (6.5 mg, 52%) as a yellow solid. $^1$H-NMR (300 MHz, $d_6$-DMSO): $\delta$ 5.92 (s, 2H), 7.73 (s, 1H), 7.96 (dd, $J$ = 2.3 and 9.0 Hz, 1H), 8.28 (d, $J$ = 9.0 Hz, 1H), 8.31 (d, $J$ = 2.3 Hz, 1H). MS (CI): 251 (M + 1, $^{37}$Cl, 40%), 249 (M + 1, $^{35}$Cl, 100%), 235 (70).

### 2-(3,3,3-Triethoxypropyn-1-yl)quinoxaline 2d

To a degassed solution of 2-chloroquinoxaline (1 g, 6 mmol) and 3,3,3-triethoxypropyne[5] (1.13 g, 6.6 mmol) in acetonitrile (14 ml) and triethylamine (7 ml), palladium(II) acetate (40 mg, 0.18 mmol), copper(I) iodide (69 mg, 0.36 mmol), and triphenylphosphine (95 mg, 0.36 mmol) were added under nitrogen. The mixture was heated at 70 °C for 3 h. After evaporation, the residue was diluted with aqueous sodium carbonate and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with dichloromethane–ethyl acetate (1:1) to give 2-(3,3,3-triethoxypropyn-1-yl)quinoxaline **2d** (1.7 g, 97%) as an orange oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.34 (t, $J$ = 7.1 Hz, 9H), 3.87 (q, $J$ = 7.1 Hz, 6H), 7.82 (m, 2H), 8.18 (m, 2H), 8.95 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 14.83, 59.3, 81.9, 87.2, 109.0, 129.2, 129.3, 130.7, 130.8, 130.5, 141.8, 142.2, 147.1. MS (EI): 255 (M−EtO, 100%), 227 (50), 181 (40).

### Ethyl quinoxalin-2-ylpropiolate 2e

A mixture of the 2-(3,3,3-trimethoxypropyn-1-yl)quinoxaline **2d** (4.8 g, 16 mmol), toluene-*p*-sulfonic acid monohydrate (4.5 g, 24 mmol), and benzene was stirred at room temperature for 1 h. The organic layer was separated and the aqueous layer extracted with ether. The combined organic extracts were dried and evaporated *in vacuo* to give a residue which was purified by column chromatography over silica gel, eluting with petroleum ether–ethyl acetate (8:2), to give ethyl quinoxalin-2-ylpropiolate **2e** (2.8 g, 79%) as a yellow solid. IR (NaCl): 1717, 2341 cm$^{-1}$. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.43 (t, $J$ = 7.1 Hz, 3H), 4.39 (d, $J$ = 7.1 Hz, 2H), 7.88 (m, 2H), 8.1 (m, 2H), 9.04 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 13.9, 62.6, 81.9, 82.3, 129.3, 129.5, 131.0, 131.6, 136.6, 141.9, 142.1, 146.9, 152.7. MS (CI):

227 (M + 1, 100%). Calcd. for: $C_{13}H_{10}N_2O_2$: 226.0742. HRMS: found: $M^+$, 226.0740.

### Ethyl 2,3-dibromo-3-(quinoxalin-2-yl)prop-2-enoate 3c

A solution of bromine (0.18 ml, 3.6 mmol) in dichloromethane (10 ml) was added dropwise to a stirred solution of ethyl quinoxalin-2-ylpropiolate **2e** (1 g, 3.3 mmol) dissolved in dichloromethane (20 ml). The resultant mixture was stirred for 12 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 an orange oil. Purification of this by column chromatography over silica gel, eluting with petroleum ether–diethyl ether (8:1), gave the dibromoalkene **3c** as a mixture of stereoisomers (822 mg, 64%) in a ratio of *ca.* 2:3, as a yellow oil. IR (NaCl): 1732 $cm^{-1}$. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 0.98 (t, $J$ = 7.1 Hz, 1.8H), 1.47 (t, $J$ = 7.1 Hz, 1.2H), 4.10 (q, $J$ = 7.1 Hz, 1.2H), 4.48 (t, $J$ = 7.1 Hz, 0.8H), 7.88 (m, 2H), 8.18 (m, 2H), 9.07 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 13.5, 13.9, 62.7, 63.1, 116.1, 118.3, 119.1, 122.0, 128.4, 129.1, 129.2, 129.3, 129.6, 130.1, 130.8, 130.9, 131.0, 131.1, 131.3, 131.6, 141.6, 144.2, 144.2, 144.8, 163.2, 163.8. MS (CI): 385, 387, 389 ($M^+$, 40, 80, 40%), 227 (100). Calcd. for: $C_{13}H_{10}{}^{79}Br_2N_2O_2$: 383.911. HRMS: found: $(M + H)^+$, 383.9111.

### 4-Ethoxycarbonyl-5-(quinoxalin-2-yl)-1,3-dithiole-2-thione 5 and 4-methoxycarbonyl-5-(quinoxalin-2-yl)-1,3-dithiole-2-thione

An aqueous solution of disodium trithiocarbonate[2] (33%, 3.8 ml) was added to a hot solution of ethyl 2,3-dibromo-3-(quinoxalin-2-yl)prop-2-enoate (1.5 g, 3.8 mmol) in methanol (38 ml) with stirring. The resulting solution was cooled to room temperature and stirred for a further 1 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 give a black solid. Purification of this by column chromatography over silica gel, eluting with dichloromethane, gave a red solid, which was recrystallised from methanol to give a mixture of ethyl ester **5** and the corresponding methyl ester (800 mg, 63%) in a ratio of *ca.* 3:2, as a yellow solid. IR (NaCl): 1707, 1087 $cm^{-1}$. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.28 (t, $J$ = 7.1 Hz, 0.6 × 3H), 3.85 (s, 0.4 × 3H), 4.32 ($J$ = 7.1 Hz, 0.6 × 2H), 7.90 (m, 2H), 8.17 (m, 2H), 9.20 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 13.8 ($CH_3CH_2O$), 53.4 ($CH_3O$), 63.0 ($CH_3CH_2O$), 129.2, 129.5, 130.9, 131.5, 144.6. MS (CI): 335 (M + 1, 45%), 321 (M + 1, 100%).

### 2-(3,3-Diethoxypropyn-1-yl)quinoxaline 2f

To a degassed solution of 2-iodoquinoxaline (500 mg, 1.9 mmol) and 3,3-diethoxypropyne (0.33 ml, 2.3 mmol) in acetonitrile (4.6 ml) and triethylamine (2.3 ml), palladium(II) acetate (13 mg, 0.057 mmol), copper(I) iodide (21 mg, 0.114 mmol), and triphenylphosphine (30 mg, 0.114 mmol) were added under nitrogen. The mixture was heated at 80 °C for 1 h 30 min. After evaporation of organic solvents the residue was diluted with water and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with petroleum ether–diethyl ether (60:40) to give 2-(3,3-diethoxypropyn-1-yl)quinoxaline **2f** (398 mg, 82%) as a yellow oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.33 (t, $J$ = 7.1 Hz, 6H), 3.75 (m, 2H), 3.91 (m, 2H), 5.62 (s, 1H), 7.82 (m, 2H), 8.11 (m, 2H), 8.95 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 61.3, 100.2, 136.0, 82.2, 88.2, 91.5, 129.2, 129.3, 130.6, 130.7, 138.3, 141.1, 142.0, 147.0. MS (CI): 257 (M + 1, 25), 211 (100), 183 (65). Calcd. for: $C_{15}H_{16}N_2O_2$ + H, 257.1289. HRMS: found: $(M + H)^+$, 257.1293.

### 2-(1,2-Dibromo-3,3-diethoxypropen-1-yl)quinoxaline 3d

A solution of bromine (0.16 ml, 3.2 mmol) in dichloromethane (12 ml) was added dropwise to a stirred solution of 2-(3,3-diethoxypropyn-1-yl)quinoxaline **2f** (750 mg, 2.9 mmol) dissolved in dichloromethane (24 ml). The resultant mixture was stirred over 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 an orange oil. Purification of this by column chromatography with dichloromethane yielded 2-(1,2-dibromo-3,3-diethoxypropen-1-yl)quinoxaline **3d** (715 mg, 59%) as a pale yellow oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.37 (t, $J$ = 7.0 Hz, 6H), 3.77 (m, 2H), 3.90 (m, 2H), 5.67 (s, 1H), 7.82 (m, 2H), 8.19 (m, 2H), 9.00 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 63.3, 129.2, 129.5, 130.5, 130.9, 144.9. MS (CI): 415, 417, 419 (M + 1, 20, 30, 20%), 275 (100). Calcd. for: $C_{15}H_{16}{}^{79}Br_2N_2O_2$: 414.9657. HRMS: found: $M^+$, 414.9654.

### 2-(Diethoxymethyl)thieno[2,3-*b*]quinoxaline 4c

An aqueous solution of disodium trithiocarbonate[2] (33%, 1.6 ml) was added to a solution of the 2-(1,2-dibromo-3,3-diethoxypropen-1-yl)quinoxaline **3d** (415 mg, 1 mmol) in methanol (16 ml) with stirring. The resulting solution was stirred for a further 2 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 give a brown oil which was purified by column chromatography over silica gel, eluting with dichloromethane to obtain 2-(diethoxymethyl)thieno[2,3-*b*]quinoxaline **4c** (154 mg, 53%) as a yellow oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.23 (t, $J$ = 7.0 Hz, 6H), 3.63 (m, 4H), 5.80 (s, 1H), 7.47 (s, 1H), 7.47 (m, 2H), 8.10 (m, 2H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 61.7, 98.7, 120.0, 128.4 (2 × C), 129.1 (2 × C), 140.1, 140.9, 150.6, 153.1, 156.5. MS (CI): 289 (M + 1, 100). Calcd. for: $C_{15}H_{16}N_2O_2S$: 288.0932. HRMS: found: $M^+$, 288.0928.

### 6-Chloro-2-(3,3-diethoxypropyn-1-yl)quinoxaline 2g

To a degassed solution of 2,6-dichloroquinoxaline (500 mg, 2.5 mmol) and 3,3-diethoxypropyne (0.42 ml, 3 mmol) in acetonitrile (6.25 ml) and triethylamine (2.5 ml), palladium(II) acetate (50 mg, 0.22 mmol), copper(I) iodide (70 mg, 0.36 mmol), and triphenylphosphine (80 mg, 0.30 mmol) were added. The mixture was heated at 80 °C for 1 h 30 min. After evaporation of the solvent the residue was diluted with water and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with petroleum ether–diethyl ether (6:4) to yield 6-chloro-2-(3,3-diethoxypropyn-1-yl)quinoxaline **2g** (500 mg, 70%) as a white solid, mp 76–78 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.43 (t, $J$ = 7.0 Hz, 6H), 3.80 (m, 2H), 3.92 (m, 2H), 5.61 (s, 1H), 7.78 (dd, $J$ = 2.2 and 9.0 Hz, 1H), 8.06 (d, $J$ = 9.0 Hz, 1H), 8.14 (d, $J$ = 2.2 Hz, 1H), 8.98 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 61.4, 81.9, 88.9, 91.5, 128.1, 130.4, 131.8, 136.6, 138.4, 140.5, 141.3, 147.8. MS (CI): 293 (M + 1, $^{37}$Cl, 30), 291 (M + 1, $^{35}$Cl, 100), 216 (20). Calcd. for: $C_{15}H_{15}{}^{35}ClN_2O_2$: 290.0822. HRMS: found: $M^+$, 290.0822. Calcd. for: $C_{15}H_{15}ClN_2O_2$: C, 61.97; H, 5.20; N, 9.64; Cl, 12.19%. Anal.: found: C, 62.11; H, 4.99; N, 9.58; Cl, 12.28%.

### 2,3-Dibromo-7-chloro-1-ethoxypyrrolo[1,2-*a*]quinoxaline 6a

A solution of bromine (0.5 ml, 1.03 mmol) in dry dichloromethane (2.5 ml) was added dropwise to a stirred solution of 6-chloro-2-(3,3-diethoxypropyn-1-yl)quinoxaline **2g** (250 mg, 0.86 mmol) dissolved in dry dichloromethane (5 ml). The resultant mixture was stirred for 2 h at room temperature under nitrogen. Addition of aqueous sodium metabisulfite and dichloromethane followed by separation, drying, and evaporation of the organic phase, then purification by column chromatography over silica gel, eluting with dichloromethane, and then recrystallisation from ethanol gave the 2,3-dibromo-7-

chloro-1-ethoxypyrrolo[1,2-*a*]quinoxaline **6a** (200 mg, 58%) as yellow needles, mp (dec.) 120 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.60 (t, $J$ = 7.1 Hz, 3H), 4.52 (q, $J$ = 7.1 Hz, 2H), 7.52 (dd, $J$ = 2.3 and 9.0 Hz, 1H), 7.96 (d, $J$ = 2.3 Hz, 1H), 8.48 (d, $J$ = 9.0 Hz, 1H), 8.68 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.3, 71.6, 94.2, 97.2, 117.0, 117.2, 125.8, 127.5, 129.0, 131.0, 137.4, 141.9, 144.1. MS (CI): 403, 405, 407 (M + 1, 40, 100, 60%). Calcd. for: $C_{13}H_9{}^{79}Br_2{}^{35}ClN_2O$: 401.8771. HRMS: found: $M^+$, 401.8772. Calcd. for: $C_{13}H_9Br_2ClN_2O$: C, 38.60; H, 2.24; N, 6.93; Cl, 8.76; Br, 39.51%. Anal.: found: C, 38.67; H, 2.27; N, 6.85; Cl, 8.44; Br, 39.71%.

### 2,3-Dibromo-7-chloro-1-ethoxy-4,5-dihydropyrrolo[1,2-*a*]-quinoxaline 7

A solution of 2,3-dibromo-7-chloro-1-ethoxypyrrolo[1,2-*a*]-quinoxaline **6a** (55 mg, 0.13 mmol) and sodium borohydride (30 mg, 0.78 mmol) in tetrahydrofuran (3 ml) was stirred for 24 h at room temperature. The solvent was removed under reduced pressure and the residue was diluted with water and extracted with dichloromethane to obtain the 2,3-dibromo-7-chloro-1-ethoxy-4,5-dihydropyrrolo[1,2-*a*]quinoxaline **7** (45 mg, 85%) as yellow needles, mp (dec.) 140 °C (from methanol). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.31 (t, $J$ = 7.1 Hz, 3H), 3.92 (br s, 1H), 4.62 (q, $J$ = 7.1 Hz, 2H), 4.16 (s, 2H), 6.67 (d, $J$ = 2.3 Hz, 1H), 6.71 (dd, $J$ = 2.3 and 8.6 Hz, 1H), 7.73 (d, $J$ = 8.6 Hz, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.2, 39.9, 71.2, 86.3, 93.1, 115.4, 117.2, 118.5, 119.3, 123.5, 125.4, 130.3, 138.1. MS (CI): 405, 407, 409 (M + 1, 45, 100, 45%). Calcd. for: $C_{13}H_{11}{}^{79}Br_2ClN_2O$: 403.8927. HRMS: found: $M^+$, 403.8928. Calcd. for: $C_{13}H_{11}Br_2ClN_2O$: C, 38.41; H, 2.73; N, 6.89%. Anal.: found: C, 38.77; H, 2.41; N, 6.83%.

### 6- and 7-Methoxyquinoxalin-2(1*H*)-ones

A solution of glyoxylic acid (3 g, 33.6 mmol) in water (12 ml) was added dropwise to a stirred solution of 1,2-diamino-4-methoxybenzene (3.3 g, 24 mmol) in methanol (6 ml) and acetic acid (3 ml) at −15 °C. The reaction mixture was allowed to warm to room temperature, and stirred for 1 h. A voluminous precipitate was formed which was filtered and washed with water and methanol. The resulting solid was recrystallised from ethanol to afford a mixture of 6-methoxyquinoxalin-2(1*H*)-one and 7-methoxyquinoxalin-2(1*H*)-one (2.1 g, 50%) as a brown solid. MS (CI): 177 (M + 1, 100%).

### 2-Chloro-6-methoxyquinoxaline 1d and 2-chloro-7-methoxy-quinoxaline 1e

A solution of 6- and 7-methoxyquinoxalin-2(1*H*)-ones (500 mg, 2.8 mmol) in phosphoryl chloride (20 ml) was heated at reflux for 1 h. The reaction mixture was concentrated *in vacuo* and then poured onto ice and basified with sodium carbonate. The organic material was extracted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated to give a mixture of 2-chloro-6-methoxy- and 2-chloro-7-methoxyquinoxalines (300 mg, 55%) in a ratio of *ca.* 3:1 which were separated by chromatography, eluting with petroleum ether–ethyl acetate (95:5). 2-Chloro-6-methoxyquinoxaline: $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 3.90 (s, 3H), 7.31 (d, $J$ = 2.7 Hz, 1H), 7.37 (dd, $J$ = 2.7 and 9.2 Hz, 1H), 7.82 (d, $J$ = 9.2 Hz, 1H), 8.63 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 55.8, 106.7, 123.7, 124.2, 129.2, 130.4, 138.2, 142.7, 144.6. MS (CI): 197 (M + 1, $^{37}$Cl, 31%), 195 (M + 1, $^{35}$Cl, 100%). 2-Chloro-7-methoxyquinoxaline: $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 3.89 (s, 3H), 7.22 (d, $J$ = 2.7 Hz, 1H), 7.33 (m, 1H), 7.91 (d, $J$ = 9.2 Hz, 1H), 8.55 (s, 1H). MS (CI): 197 (M + 1, $^{37}$Cl, 31%), 195 (M + 1, $^{35}$Cl, 100%).

### 6-Methoxy-2-(3,3-diethoxypropyn-1-yl)quinoxaline 2h

To a degassed solution of 2-chloro-6-methoxyquinoxaline **1d** (200 mg, 1 mmol) and 3,3-diethoxypropyne (0.17 ml, 1.23 mmol) in acetonitrile (4 ml) and triethylamine (2 ml), palladium(II) acetate (12 mg, 0.05 mmol), copper(I) iodide (14 mg, 0.05 mmol), and triphenylphosphine (20 mg, 0.1 mmol) were added under nitrogen. The mixture was stirred under nitrogen at 70 °C for 2 h. After evaporation, the residue was diluted with aqueous sodium bicarbonate and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with diethyl ether–petroleum ether (1:1) to yield 6-methoxy-2-(3,3-diethoxypropyn-1-yl)quinoxaline **2h** (167 mg, 57%) as a white solid. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.25 (t, $J$ = 7.1 Hz, 6H), 3.75 (m, 2H), 3.90 (m, 2H), 4.02 (s, 3H), 5.60 (s, 1H), 7.37 (d, $J$ = 2.7 Hz, 1H), 7.45 (dd, $J$ = 2.7 and 9.2 Hz, 1H), 7.96 (d, $J$ = 9.2 Hz, 1H), 8.85 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 55.8, 61.2, 82.3, 87.3, 91.5, 106.5, 124.1, 130.2, 135.5, 138.2, 142.9, 147.1, 161.4. MS (CI): 287 (M + 1, 100%). Calcd. for: $C_{16}H_{18}N_2O_3$: 286.1317. HRMS: found: $M^+$, 286.1313.

### 7-Methoxy-2-(3,3-diethoxypropyn-1-yl)quinoxaline 2i

To a degassed solution of 2-chloro-7-methoxyquinoxaline **1e** (47 mg, 0.24 mmol) and 3,3-diethoxypropyne (0.04 ml, 0.28 mmol) in acetonitrile (1 ml) and triethylamine (0.5 ml), palladium(II) acetate (2.6 mg, 0.012 mmol), copper(I) iodide (4.5 mg, 0.024 mmol), and triphenylphosphine (6.3 mg, 0.024 mmol) were added under nitrogen. The mixture was stirred under nitrogen at room temperature overnight. After evaporation, the residue was diluted with aqueous solution of sodium bicarbonate and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with diethyl ether–petroleum ether (1:1) to yield 7-methoxy-2-(3,3-diethoxypropyn-1-yl)quinoxaline **2i** (46 mg, 67%) as a white solid. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.33 (t, $J$ = 7.1 Hz, 6H), 3.76 (m, 2H), 3.91 (m, 2H), 4.02 (s, 3H), 5.62 (s, 1H), 7.37 (d, $J$ = 2.7 Hz, 1H), 7.45 (dd, $J$ = 2.7 and 9.2 Hz, 1H), 7.98 (d, $J$ = 9.2 Hz, 1H), 8.80 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.0, 55.7, 61.3, 82.1, 87.9, 91.5, 106.2, 124.2, 130.0, 137.4, 138.1, 143.8, 144.5, 161.7. MS (CI): 287 (M + 1, 100%). Calcd. for: $C_{16}H_{18}N_2O_3$: $M^+$, 86.1317. HRMS: found: 286.1314.

### 2,3,6-Tribromo-1-ethoxy-7-methoxypyrrolo[1,2-*a*]quinoxaline 6b

A solution of bromine (0.036 ml, 0.7 mmol) in dry dichloromethane (0.5 ml) was added dropwise to a stirred solution of 6-methoxy-2-(3,3-diethoxypropyn-1-yl)quinoxaline **2h** (100 mg, 0.35 mmol) dissolved in dry dichloromethane (4 ml). The resultant mixture was stirred for 2 h at room temperature under nitrogen. Addition of aqueous sodium metabisulfite and dichloromethane followed by separation, drying, and evaporation of the organic phase under reduced pressure gave an orange solid. Purification of this by recrystallisation from ethanol gave the 2,3,6-tribromo-1-ethoxy-7-methoxypyrrolo-[1,2-*a*]quinoxaline **6b** (84 mg, 50%) as an orange solid, mp (dec.) 130 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.59 (t, $J$ = 7.1 Hz, 3H), 4.0 (s, 3H), 4.48 (q, $J$ = 7.1 Hz, 2H), 7.16 (d, $J$ = 9.3 Hz, 1H), 8.55 (d, $J$ = 9.3 Hz, 1H), 8.74 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 15.3, 56.8, 71.5, 94.0, 97.1, 102.3, 111.1, 115.3, 117.3, 122.0, 149.1, 144.2, 154.3. MS (CI): 477, 479, 481, 483 (M + 1, 30, 100, 98, 30%). Calcd. for: $C_{14}H_{11}{}^{79}Br_3N_2O_2$: 475.8372. HRMS: found: $M^+$, 475.8370.

### 3-(4-Chlorophenylethynyl)quinoline 8

To a degassed solution of 3-bromoquinoline (500 mg, 2.4 mmol) and 4-chlorophenylacetylene (327 mg, 2.4 mmol) in acetonitrile (10 ml) and triethylamine (5 ml), palladium(II) acetate (27 mg, 0.12 mmol), copper(I) iodide (46 mg, 0.24 mmol), and triphenylphosphine (60 mg, 0.24 mmol) were added

under nitrogen. The mixture was stirred under nitrogen at 80 °C for 24 h. After evaporation, the residue was diluted with aqueous sodium bicarbonate and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with dichloromethane. Recrystallisation from methanol gave 3-(4-chlorophenylethynyl)quinoline **8** (315 mg, 50%) as a white solid, mp 130–132 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 7.39 (d, $J$ = 8.7 Hz, 2H), 7.55 (d, $J$ = 8.7 Hz, 2H), 7.62 (m, 1H), 7.77 (m, 1H), 7.84 (m, 1H), 8.15 (d, $J$ = 8.5 Hz, 1H), 8.34 (s, 1H), 9.03 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 87.4, 91.3, 117.0, 121.0, 127.1, 127.2, 127.5, 128.7, 129.3, 130.1, 132.8, 134.8, 138.2, 146.8, 151.8. MS (CI): 266 (M + 1, $^{37}$Cl, 40%), 264 (M + 1, $^{35}$Cl, 100%). Calcd. for: $C_{17}H_{10}{}^{35}ClN$: 263.0501. HRMS: found: $M^+$, 263.0503. Calcd. for: $C_{17}H_{10}ClN$: C, 77.42; H, 3.82; N, 5.31%. Anal.: found: C, 76.91; H, 3.73; N, 5.14%.

### 3-[1,2-Dibromo-2-(4-chlorophenyl)ethenyl]quinoline 9

A solution of bromine (0.10 ml, 2 mmol) in dichloromethane (5 ml) was added dropwise to a stirred solution of 2-(4-chlorophenylethynyl)quinoline **8** (500 mg, 1.89 mmol) dissolved in dichloromethane (11 ml). The resultant mixture was stirred for 4 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 an orange solid. Purification of this by column chromatography over silica gel, eluting with dichloromethane, then recrystallisation from methanol, gave the 3-[1,2-dibromo-2-(4-chlorophenyl)ethenyl]quinoline **9** (536 mg, 68%) as white crystals, mp 135–138 °C. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 7.47 (d, $J$ = 8.7 Hz, 2H), 7.57 (d, $J$ = 8.7 Hz, 2H), 7.65 (m, 1H), 7.83 (m, 1H), 7.93 (d, $J$ = 8.2 Hz, 1H), 8.20 (d, $J$ = 8.5 Hz, 1H), 8.37 (s, 1H), 9.15 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 115.7, 119.5, 127.3, 128.1, 128.7, 130.4, 130.5, 135.1, 136.4, 138.5. MS (CI): 422, 424, 425, 428 (M + 1, 14, 32, 22, 45%), 266 (32), 264 (100). Calcd. for: $C_{17}H_{10}{}^{79}Br_2{}^{35}ClN$: 420.8869. HRMS: found: $M^+$, 420.8862. Calcd. for: $C_{17}H_{10}Br_2ClN$: C, 48.32; H, 2.14; N, 3.31; Cl, 8.39; Br, 37.82%. Anal.: found: C, 47.93; H, 2.33; N, 3.55; Cl, 8.12; Br, 37.17%.

### 2-(Hex-1-yn-1-yl)pyrazine 10

To a degassed solution of 2-chloropyrazine (1 g, 8.7 mmol) and hex-1-yne (1 ml, 10.4 mmol) in acetonitrile (16 ml) and triethylamine (8 ml), palladium(II) acetate (98 mg, 0.43 mmol), copper(I) iodide (166 mg, 0.87 mmol), and triphenylphosphine (288 mg, 0.87 mmol) were added under nitrogen. The mixture was stirred under nitrogen at 80 °C for 4 h. After evaporation, the residue was diluted with an aqueous solution of sodium bicarbonate and extracted with dichloromethane. The organic extract was purified by column chromatography over silica gel, eluting with dichloromethane–ethyl acetate (95:5) to yield 2-(hex-1-yn-1-yl)pyrazine **10** (990 mg, 71%) as an orange oil with spectroscopic properties identical with those reported previously.[9]

### 2-(1,2-Dibromohex-1-en-1-yl)pyrazine 11

A solution of bromine (0.28 ml, 6.16 mmol) in dichloromethane (12 ml) was added dropwise to a stirred solution of 2-(hex-1-yn-1-yl)pyrazine **10** (900 mg, 5.6 mmol) dissolved in dichloromethane (24 ml). The resultant mixture was stirred for 3 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 an oil. Purification of this by column chromatography over silica gel, eluting with dichloromethane–ethyl acetate (95:5) gave the 2-(1,2-dibromohex-1-en-1-yl)pyrazine **10** (1.4 g, 78%) as an oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.03 (t, $J$ = 6.4 Hz, 3H), 1.51 (m, 2H), 1.75 (m, 2H), 2.94 (t, $J$ = 6.8 Hz, 2H), 8.55 (br s, 1H), 8.66 (br s, 1H), 8.74 (br s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 13.8, 21.7, 29.3, 40.6, 143.6, 143.9, 145.5. MS (CI): 319, 321, 323 (M + 1, 46, 85, 43%), 161 (100%). Calcd. for: $C_{16}H_{12}{}^{79}BrN_2$ + H: 318.9446. HRMS: found: $(M + H)^+$: 318.9450.

### 5-(Hex-1-yn-1-yl)pyrimidine 12

A mixture of 5-bromopyrimidine (2 g, 12.5 mmol), hex-1-yne (1.4 ml, 25 mmol), bis(triphenylphosphine)palladium(II) chloride (263 mg, 0.37 mmol), copper(I) iodide (143 mg, 0.75 mmol) and triethylamine (20 ml) was heated at 80 °C overnight under nitrogen atmosphere. The residue was diluted with water and extracted with dichloromethane and the organic extract was washed with 1 M hydrochloric acid. Separation, drying and evaporation of the organic phase under reduced pressure gave an oil. Purification of this by column chromatography over silica gel eluting with dichloromethane–ethyl acetate (95:5), gave 5-(hex-1-yn-1-yl)pyrimidine **12** (1.85 g, 92%) as an orange oil with spectroscopic data identical to those reported previously.[10]

### 5-(1,2-Dibromohex-1-en-1-yl)pyrimidine 13

A solution of bromine (0.17 ml, 3.41 mmol) in dichloromethane (6 ml) was added dropwise to a stirred solution of 5-(hex-1-yn-1-yl)pyrimidine **12** (500 mg, 3.4 mmol) dissolved in dichloromethane (16 ml). The resultant mixture was stirred for 16 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 yellow oil. Purification of this by column chromatography over silica gel, eluting with dichloromethane–ethyl acetate (95:5), gave 5-(1,2-dibromohex-1-en-1-yl)-pyrimidine **13** (839 mg, 84%) as a colorless oil. $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ 1.04 (t, $J$ = 7.2 Hz, 3H), 1.50 (m, 2H), 2.17 (m, 2H), 2.92 (t, $J$ = 7.4 Hz, 2H), 8.79 (s, 2H), 9.18 (s, 1H). $^{13}$C-NMR (300 MHz, $CDCl_3$): $\delta$ 13.8, 21.7, 29.4, 40.8, 108.6, 127.9, 156.9, 157.7 (2 × C). MS (CI): 319, 321, 323 (M + 1, 15, 20, 13%), 161 (100). Calcd. for: $C_{10}H_{12}{}^{79}Br_2N_2$: 317.9368. HRMS: found: $M^+$: 317.9362.

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